Utilization and Outcomes of Kidney Paired Donation in the United States

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Background. Kidney paired donation (KPD) offers the best transplant option for patients with incompatible live kidney donors. Although studies suggest substantial expansion of the donor pool if fully used, few patients in the United States have undergone KPD.
Methods. We analyzed the 209 KPD and 89 list paired donation (LPD) transplants reported to United Network for Organ Sharing to better understand access to these modalities, clinical outcomes, and areas of potential expansion.
Results. Although many centers offer KPD/LPD, most centers have performed no more than a handful of transplants. As expected, outcomes with KPD/LPD were equivalent to direct donation matched controls. In analyzing current practice, we identified two limitations to KPD in its current use. First, KPD is likely limited now by benefiting mostly patients who are easy to identify and match (such as A donors with B recipients or B donors with A recipients). Second, although some expansion of local KPD availability has reduced travel requirements for patients in those areas, significant room for growth remains.
Conclusions. Our results suggest that full utilization of KPD would encourage registration of and improve matching for patients who are more difficult to identify and match (such as highly sensitized recipients). Furthermore, expansion of KPD would likely reduce travel requirements and thereby improve access to this treatment modality.

Keywords: Live donation, Kidney transplantation, Donor exchange, Paired kidney exchange.

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To date, 209 patients in the United States have undergone transplantation through kidney paired donation (KPD), a modality which allows pairs of recipients and their willing but incompatible live donors to find reciprocal matches and undergo transplantation by exchanging donors (Fig. 1A, upper panel) (*1–7*). Additionally, 89 patients have been transplanted through list paired donation (LPD), or live donor list exchange, a modality through which an incompatible pair's recipient is given priority on the deceased donor waiting list in exchange for a donation that the pair's donor makes to the list (Fig. 1A, lower panel) (*1*, *8–11*). Both modalities expand the donor pool and offer an opportunity for transplantation to a recipient who has a willing donor who is either human leukocyte antigen (positive crossmatch) or ABO incompatible.

However, evidence suggests that paired donation is grossly underutilized in the U.S. Simulations estimate that approximately 1000 patients per year could benefit from KPD if a national program were implemented in the United States (*9*, *12–14*). These simulations are corroborated by clinical experience from other countries with established KPD programs. For example, 26 patients were transplanted in the Netherlands in 2004, the first year that a national KPD program was established in that country. Scaling up by a factor of 23 (comparing 9357 deceased donor transplants performed in the United States with 402 performed in the Netherlands), this might suggest that approximately 600 patients could have been transplanted (while only 34 were) in that year through KPD in the United States (*1*).

The goal of this study was to evaluate trends and current practice patterns of KPD and LPD to (1) assess access to these modalities, (2) compare clinical outcomes with direct transplantation, and (3) identify areas of potential expansion and improvement.

METHODS

Study Design

We analyzed 209 live donor KPD recipients and 89 live donor LPD recipients between January 1, 2000 and August 27, 2007 as reported to United Network for Organ Sharing

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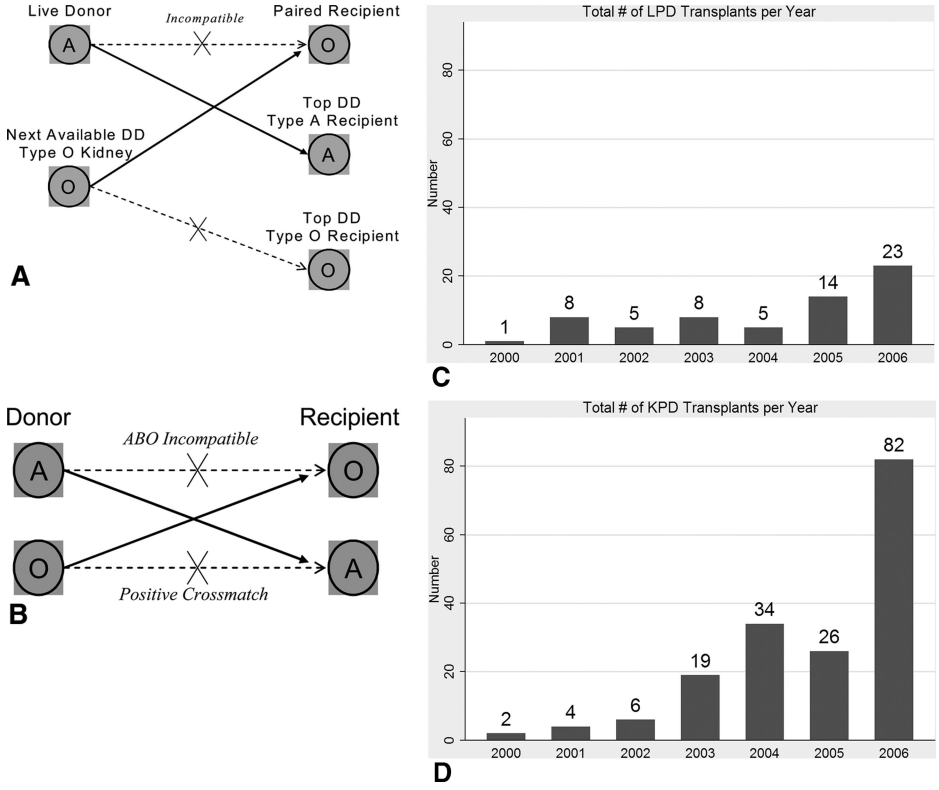

FIGURE 1. (A) Schematic of kidney paired donation (KPD) and list paired donation (LPD). DD=Deceased Donor. (B) Utilization of KPD and LPD transplants, by year.

(UNOS) and available for summary statistics through the UNOS website (*15*). Of these patients, the details of 186 KPD recipients and 70 LPD recipients transplanted between January 1, 2000 and April 27, 2007 were available for analysis in the UNOS STAR (Standard Transplant Analysis and Research) files (*15*). For a reference group, we analyzed 45,486 direct live donor recipients transplanted during the study period and available for analysis in the STAR files. Differences in demographics between KPD, LPD, and direct transplant recipients were analyzed by chi-squared tests of independence (categorical variables) and unpaired two-sided *t* tests (continuous variables). For each comparison, separate *P* values are reported for the comparison between (a) KPD and direct recipients and (b) LPD and direct recipients. Some characteristics were compared based on volume of KPD transplants performed at a given center, with a cutoff of more than or equal to five transplants considered high volume.

Blood Type Distributions

Blood types of the live donors and their matched recipients were available directly from the STAR files. For LPD, the original incompatible intended recipients for each live donor could not be identified, because these patients received deceased donor kidneys at an unknown interval of time after their live donor's operation, and no link between the transplants is tracked through UNOS. For KPD, the original incompatible recipients were determined by identifying the reciprocally matched pair that participated in the KPD. Because various possible exchange arrangements exist in matches of larger than two patients, this analysis was restricted to two-way KPD.

Donor and Recipient Travel

Differences in donor, recipient, and transplant center location were evaluated across transplant categories as follows: (1) the proportion of recipients whose home state was different from their transplant center (i.e., the recipient traveled out of state to receive a transplant); (2) the proportion of donors whose home state was different from the matched recipient's transplant center (i.e., the donor traveled out of state to donate); and (3) the proportion of transplants where both the recipients home state and donor home state were different from that of the transplant center (i.e., both the donor and the recipient traveled out of state for the transplant); and (4) the proportion of recipients whose home state was different from the donor's home state (i.e., the recipient and matched donor came from different states). An identical analysis was performed assessing inter-regional travel, using the 11 regions of the United States as defined by UNOS. Because patients living in the Washington, DC metropolitan area often have addresses in Maryland or Virginia, we considered DC to be a wildcard for both states.

The proportion of transplants requiring travel for the recipient, the donor, and both donor and recipient, across states and regions, was compared between low and high volume KPD centers. To see if travel was related to availability of a KPD program in the state or the region, similar travel statistics were calculated for recipients and donors who had KPD programs available in their home state and region on the day that the transplant occurred. To see if travel requirements have changed over time, travel statistics as above were calculated by year of transplant. All *P* values were derived using

two-sided chi-squared tests of independence, with two-way comparisons reported for comparisons of travel by center volume, and test of trend reported for comparisons of travel over time.

Survival Analysis

Death-censored graft survival and patient survival after KPD, LPD, and direct live donor transplantation were analyzed by Kaplan-Meier estimates and compared by log-rank test. First, crude survival was compared between all KPD, LPD and direct transplant recipients. To account for differences in the patient populations, KPD and LPD survival were compared with sets of matched controls drawn from direct live donor recipients. Each KPD and LPD recipient was matched to three direct transplant recipients on the following potential confounders: recipient age, ethnicity, panel reactive antibody (PRA), previous transplant, dialysis at the time of transplant, and diabetes; donor age and ethnicity. With these matching criteria, we were able to find controls for 173 of 186 KPD patients and 69 of the 70 LPD patients. This methodology allowed us to accurately account for differences in donor and recipient characteristics in a sample size small enough to result in unreliable multivariate Cox proportional hazards models.

Statistical Analysis

Unless otherwise specified, all tests were two-sided with statistical significance set at $\alpha=0.05$. All analyses were performed using STATA 10 (StataCorp, College Station, TX).

RESULTS

Utilization of Paired Donation

Utilization of KPD and LPD increased significantly during the study period (Fig. 1B). To date, KPD transplants have been performed in 27 states (Table 1) and 55 transplant centers (Table 2), whereas LPD transplants have been performed in 19 states and 34 transplant centers. Still, most of these transplants were performed by only a handful of transplant centers, with nine centers performing more than 50% of KPD transplants and eight centers performing more than 50% of LPD transplants. Kidney paired donation and LPD programs might interfere with each other if both are offered at the same transplant center, because recipients with incompatible donors may be eligible for both modalities, but choosing one precludes choosing the other. Interestingly, only 29% of KPD transplants were performed at centers which also performed LPD, and 47% of LPD transplants were performed at centers which also performed KPD.

To validate reporting accuracy, we compared the UNOS data recorded for patients transplanted in our center with our own records. In addition to KPD, our center uses procedures where non-directed donors start chains of domino paired donation (DPD) (*16*). We also perform rescue DPD, where a patient who fails desensitization to his intended donor receives a non-directed donor kidney up front (to avoid severe antibody rebound), and later that recipient's intended donor makes a non-directed donation to a DPD. During the study period, the Johns Hopkins single-center experience included 2-way KPD (12 transplants or 24 recipients), 3-way KPD (9 recipients), 2-way DPD (2 recipients), 3-way DPD (3 recipients), 5-way DPD (5 recipients), rescue DPD (1 recipient), and KPD with other transplant centers (1 recipient). Of 45 recipients transplanted a Johns Hopkins during the study period, 44 were captured through our study design. The recipient of the non-directed donor in a DPD was coded as donor type "Anonymous Donation" rather than "Paired Exchange" and as such was missed by our study design.

TABLE 1. Number of KPD and LPD transplants performed, by state

State	KPDs	LPDs
Alabama	6	0
Arizona	4	0
California	14	14
Connecticut	0	4
District of Columbia	1	3
Florida	2	2
Georgia	3	0
Hawaii	9	0
Illinois	6	0
Indiana	3	0
Iowa	2	1
Kentucky	3	2
Louisiana	0	1
Maine	0	5
Maryland	44	0
Massachusetts	13	12
Michigan	0	1
Minnesota	1	1
Missouri	0	3
Nebraska	2	0
New Hampshire	4	0
New Jersey	2	0
New York	19	0
Ohio	17	0
Pennsylvania	15	7
Rhode Island	6	3
South Dakota	0	1
Tennessee	3	4
Texas	2	3
Utah	7	0
Virginia	15	19
Washington	2	3
Wisconsin	4	0

KPD, kidney paired donation; LPD, list paired donation.

Demographics

Characteristics of donors and recipients participating in KPD, LPD, and direct live donation are shown in Table 3. For each KPD procedure performed, data were likely available from all participants because all participants received live donor kidneys; the characteristics reported are for the matched pairs (i.e., the donor from one incompatible pair whose kidney was actually transplanted into the recipient of a

TABLE 2. Number of KPD and LPD transplants performed, by center

Center	KPDs
MDJH	44
NYCP	15
HISF	9
OHCO, VAFH	8
UTLD	7
ALUA, CASF, PAUP, RIRH	6
MAMG, PAHH	5
AZGS, CASM, ILNM, NHDH, VAMC, WIUW	4
INIM, MABI	3
CAPM, GAEM, IAIM, ILUI, KYUK, MANM, MAPB, NEUN, NJSB, NYMS, NYNY, OHOU, OHTC, OHUH, PATJ, TNVU, TXJS, VANG, WASM	2
CALA, CAUC, DCWH, FLJM, FLUF, GAEH, KYJH, MACH, MNMC, OHAC, OHCC, OHUC, PACP, PAHE, TNMH, VAUV	1
	LPDs
CAPM	8
VAMC	7
CASF, VAHD	6
MAPB, MEMC, PAUP	5
CTYN, TNVU	4
MABI, RIRH, VANG	3
DCWH, FLJM, KYUK, MAMG, MOLH, TXAS, VAUV, WASH	2
DCCH, IAIV, LATU, MANM, MAUM, MIUM, MNAN, MORH, PAAE, PALH, SDSV, TXRM, VAFH, WAVM	1

KPD, kidney paired donation; LPD, list paired donation.

different incompatible pair). For each LPD procedure performed, data were only available from the participant who received a live donor kidney.

Both KPD and LPD donors were slightly older than direct donors and more likely to be white. When comparing KPD and LPD recipients with the reference group of direct live donation recipients, we highlight the fact that KPD recipients are drawn from a pool of patients who come forward with live donors, whereas the recipient of the live donor kidney in an LPD is drawn from the deceased donor waiting list. Donors for KPD and LPD were more likely to be white (not statistically significant for LPD). Kidney paired donation recipients were more likely to be white (even compared with the direct live donation pool which is already enriched for white recipients). List paired donation recipients were more likely to be African American, which is not surprising given that these patients are drawn from the deceased donor waiting list and not from a pool of patients who come forward with a live donor. Kidney paired donation patients were more likely to be college educated, more likely to have undergone a prior transplant, and more likely to be moderately or highly sensitized. Kidney paired donation patients waited longer and LPD patients waited the longest for the transplant, with few LPD recipients transplanted before initiation of dialysis. Centers with high KPD volumes (five or more transplants through KPD) had more recipients with prior transplants (25.2% vs. 17.3%) and high PRA (15% vs. 10% with PRA ≥80%).

Blood Type Distributions

Donor and recipient blood types are shown in Table 4. Compared with direct live donor transplants, fewer type O recipients were transplanted through paired donation (45.6% for direct donation vs. 22.6% for KPD and 27.1% for LPD). The low match rate for O recipients in KPD reflects the fact that O recipients must find O donors for reciprocal matches, but incompatible pairs only contain O donors when there is a positive crossmatch. Conversely, more type B recipients were transplanted through paired donation (12.7% for direct donation vs. 31.2% for KPD and 22.9% for LPD).

More than 50% of two-way incompatible pairs who were transplanted through KPD in the United States were comprised of type A donors with type B recipients or type B donors with type A recipients (Table 4B). This is not surprising because these pairs are easy to identify and "easy-to-match" in small KPD programs. However, predictions from simulations (*9*) and experience in the Netherlands (*17*) suggest that a larger scale program, such as a national KPD program, would have benefited many more "difficult-to-match" pairs such as those who are ABO incompatible with O recipients or those who are ABO compatible with O donors but sensitized, crossmatch positive recipients. For example, Table 4B shows that only 36% were positive crossmatch pairs, whereas in the Netherlands where a national program exists, 55% were positive crossmatch, and U.S. simulations suggest that approximately 67% should be positive crossmatch.

Of live donors allocated to LPD, 41.4% were blood type A and 20% were type B (Table 4D). This is consistent with reports that most incompatible pairs participating in LPD consist of type O recipients with non-O donors, and as such a deceased donor kidney from the O list is exchanged for a live donor kidney given to the A or B list (*8*). This controversial exodus of blood type O kidneys from the deceased donor pool has raised ethical concerns regarding widespread use of LPD (*10*, *11*, *18*).

Donor and Recipient Travel

List paired donation recipients traveled at similar rates to direct donor recipients, and LPD donors traveled much less (Table 5A). Conversely, both KPD recipients and donors were much more likely to travel, with 37.6% of KPD recipients and 42.4% of KPD donors traveling out of state, compared with 16.2% and 28.8% for direct donation. Travel in KPD was strongly associated with center volume, with 2-fold higher travel rates in high-volume KPD centers (Table 5B). Travel was also strongly associated with availability of a KPD program in the donor or recipient's home state, with out-of-state travel rates falling to 20.5% for recipients and 25.4% for donors when an in-state KPD program was available (Table 5C). Despite the fact that both donor and recipient travel decreased significantly as KPD programs became available in different states, the total proportion of KPD transplants requiring recipient and donor travel has not decreased over time (Table 5D).

TABLE 3. Baseline characteristics of donor and recipients in direct, KPD, and LPD transplants

	Direct (n=45, 486)	KPD (n=186)	LPD (n=70)	KPD vs. direct	LPD vs. direct
(A) Donor characteristics					
Age	40.0	43.4	43.4	<0.001	0.01
Female gender	58.5	65.1	55.7	0.1	0.6
Ethnicity (%)					
Caucasian	69.8	83.9	78.6	<0.001	0.1
African American	13.3	8.6	11.4		
Hispanic	12.4	4.3	2.9		
Asian	3.1	2.2	5.7		
Other	1.5	1.1	1.4		
BMI (%)					
18.5–24.99	35.8	39.2	45.7	0.6	0.5
25–29.99	40.8	35.4	34.3		
30–34.99	18.5	22.8	20.0		
35–39.99	3.9	2.5	0.0		
40–60	0.9	0.0	0.0		
Hypertension	1.6	1.5	4.4	0.9	0.1
(B) Recipient characteristics					
Age	43.6	46.2	44.8	0.028	0.6
Female gender	40.7	45.7	42.9	0.2	0.7
Ethnicity (%)					
Caucasian	68.0	73.1	52.9	0.002	0.003
African American	14.5	12.4	28.6		
Hispanic	12.3	4.8	8.6		
Asian	3.4	6.5	7.1		
Other	1.7	3.2	2.9		
Diabetes	26.3	24.4	22.4	0.6	0.5
College education	50.7	63.3	41.8	0.002	0.2
Insurance (%)					
Private	62.0	59.7	58.6	0.3	0.5
Medicare	28.8	33.9	34.3		
Medicaid	5.9	4.3	2.9		
Other	3.3	2.2	4.3		
Previous transplant (%)	9.8	22.0	7.1	<0.001	0.5
Days on waitlist	312.3	423.6	770.1	<0.001	<0.001
Preemptive transplant	71.3	69.0	91.4	0.5	<0.001
Peak PRA (%)					
0–19	87.0	67.5	83.9	<0.001	0.8
20–49	5.9	10.0	8.1		
50–79	3.7	10.0	4.8		
80–100	3.4	12.5	3.2		

KPD, kidney paired donation; LPD, list paired donation; PRA, panel reactive antibody.

Outcomes

There were no statistically significant differences in patient and death-censored graft survival rates when comparing KPD and direct recipients and LPD and direct recipients, in both the unmatched and matched analyses (Fig. 2).

DISCUSSION

Although paired donation is increasing in the United States, we have not nearly reached the estimated potential of this modality. By definition, KPD affords transplants for patients with live donors, and LPD affords transplants for both patients with live donors and patients without live donors who are waiting on the deceased donor waiting list. Kidney paired donation recipients were more likely to be white, college educated, sensitized, and repeat transplants. Because live donor kidneys in LPD are allocated to the recipients at the top of the deceased donor waiting list, LPD recipients had the longest waiting times and were likely to be African American. Patient and graft survival from both paired donation modalities were equivalent to matched direct live donor transplants.

TABLE 4. Donor and recipient blood types

No.	dO	dA	dB	dAB	Total	%	dO	dA	dB	dAB	Total
(A) Direct transplants											
rO	20446	226	61	9	20742	rO	45.0	0.5	0.1	0.0	45.6
rA	6237	10969	38	12	17256	rA	13.7	24.1	0.1	0.0	37.9
rB	2806	42	2920	21	5789	rB	6.2	0.1	6.4	0.0	12.7
rAB	360	602	408	329	1699	rAB	0.8	1.3	0.9	0.7	3.7
Total	29849	11839	3427	371	45486	Total	65.6	26.0	7.5	0.8	100.0
(B) Incompatible pairs who participated and matched in KPD (intended donor)											
rO	9	9	4	0	22	rO	6.6	6.6	2.9	0.0	16.2
rA	16	9	36	1	62	rA	11.8	6.6	26.5	0.7	45.6
rB	7	37	4	0	48	rB	5.1	27.2	2.9	0.0	35.3
rAB	2	2	0	0	4	rAB	1.5	1.5	0.0	0.0	2.9
Total	34	57	44	1	136	Total	25.0	41.9	32.4	0.7	100.0
(C) Resulting compatible KPD matches that underwent transplantation (matched donor)											
rO	38	3	0	1	42	rO	20.4	1.6	0.0	0.5	22.6
rA	17	64	0	0	81	rA	9.1	34.4	0.0	0.0	43.5
rB	6	1	51	0	58	rB	3.2	0.5	27.4	0.0	31.2
rAB	1	1	2	1	5	rAB	0.5	0.5	1.1	0.5	2.7
Total	62	69	53	2	186	Total	33.3	37.1	28.5	1.1	100.0
(D) Live donor component of LPD matches that underwent transplantation											
rO	19	0	0	0	19	rO	27.1	0.0	0.0	0.0	27.1
rA	3	27	0	0	30	rA	4.3	38.6	0.0	0.0	42.9
rB	2	0	14	0	16	rB	2.9	0.0	20.0	0.0	22.9
rAB	0	2	0	3	5	rAB	0.0	2.9	0.0	4.3	7.1
Total	24	29	14	3	70	Total	34.3	41.4	20.0	4.3	100.0

KPD, kidney paired donation; LPD, list paired donation.

Two potential advantages of expanding KPD have been identified by our results. First, we found that more than half of the incompatible pairs involved in two-way KPD were comprised of type A donors with type B recipients or type B donors with type A recipients. This suggests that, in current practice, KPD programs benefit mostly pairs that are easy to identify and easy-to-match, although prior data suggest that expansion of KPD to a national level should benefit many more difficult-to-match pairs.

Second, expansion of KPD has clear implications on the need for donors and recipients to travel for this modality. Out-of-state travel was substantial with KPD (37.6% of recipients and 42.4% of donors), and was strongly associated with center volume (more patients traveling to high-volume centers). The cohort using high-KPD-volume centers were more likely to be college educated (71.1% vs. 53.7%, $P=0.028$), which might mean they were more likely to bypass normal channels and actively seek out KPD even when a center wasn't available in their home state or region. Alternatively, patients transplanted in high-KPD-volume centers were also more likely to be repeat transplants and to be highly sensitized, so patients using these centers might have required travel to find a center that was willing to transplant them. Travel was also strongly associated with availability of a KPD program in the state. However, despite decreased travel in states where KPD was available, the total proportion of KPD transplants requiring travel did not decrease over time. This suggests that the demand for KPD continues to outpace the expansion of KPD availability, and thus travel remains a major issue.

Several limitations merit discussion. Because we are analyzing reports of live donor transplants, our study design inherently limits our conclusions to those who were successfully transplanted. In other words, we have no information about those who participated in a paired donation program but failed to find a match. For LPD, we are further limited to analyzing only the live donation component of the matching and not the deceased donor kidney that is allocated to the intended recipient of the live donor. For KPD, only the resulting compatible KPD matches that underwent transplantation (i.e., recipients and their matched donors) are reported to UNOS, although it was possible to reconstruct the incompatible pairings for two-way matches. Because UNOS data are self-reported by transplant centers, we are also limited by reporting error, especially with regards to the "type of transplant" variable, and any systematic errors would cause a selection bias in our study. However, we believe that any errors in the reporting of this variable would likely be random. Finally, the nature of the coding system for "type of transplant" variable might not capture the initial non-directed donor element of DPD chains. In other words, "type of transplant" can be coded as either "Anonymous Donation" or "Paired Exchange" but not both as would be applicable to DPD.

Furthermore, matching algorithms have been shown to play a critical role in the success rate for KPD, especially with

TABLE 5. Proportion of donors and recipients traveling for the transplant

(A) All live donor transplants, stratified by type of transplant

Percent traveling	Direct	KPD	LPD	KPD vs. direct	LPD vs. direct
Interstate travel for recipient	16.2	37.6	11.4	<0.001	0.3
Interstate travel for donor	28.8	42.4	13.0	<0.001	0.004
Interstate travel for both donor and recipient	14.1	27.2	8.7	<0.001	0.2
Interstate match for donor and recipient	20.3	44.0	10.1	<0.001	0.037
Inter-regional travel for recipient	8.3	25.8	2.9	<0.001	0.1
Inter-regional travel for donor	19.2	30.4	5.8	<0.001	0.005
Inter-regional travel for both donor and recipient	6.8	16.3	1.5	<0.001	0.1
Inter-regional match for donor and recipient	15.2	31.0	7.4	<0.001	0.1

(B) KPD transplants, stratified by center volume

Percent traveling	Low volume center	High volume center	*P*
Interstate travel for recipient	21.3	48.6	<0.001
Interstate travel for donor	26.7	53.2	<0.001
Interstate travel for both donor and recipient	12.0	37.6	<0.001
Interstate match for donor and recipient	29.3	54.1	<0.001
Inter-regional travel for recipient	9.3	36.9	<0.001
Inter-regional travel for donor	12.0	43.1	<0.001
Inter-regional travel for both donor and recipient	1.3	26.6	<0.001
Inter-regional match for donor and recipient	21.3	37.6	0.019

(C) KPD transplants, stratified by availability of KPD

Percent traveling	KPD program in home state or region[a]
Interstate travel for recipient	20.5
Interstate travel for donor	25.4
Interstate travel for both donor and recipient	16.9
Inter-regional travel for recipient	22.0
Inter-regional travel for donor	26.0
Inter-regional travel for donor and recipient	14.5

(D) KPD transplants, stratified by year

Percent of total KPD	2000	2001	2002	2003	2004	2005	2006	*P*
Interstate travel for recipient	0.0	25.0	50.0	68.4	41.2	30.8	34.1	0.1
Interstate travel for donor	50.0	50.0	50.0	68.4	39.4	26.9	45.7	0.2
Interstate travel for both donor and recipient	0.0	25.0	33.3	52.6	30.3	15.4	25.9	0.2
Interstate match for donor and recipient	50.0	50.0	33.3	63.2	39.4	42.3	46.9	0.8
Inter-regional travel for recipient	0.0	50.0	16.7	36.8	38.2	23.1	23.2	0.4
Inter-regional travel for donor	50.0	75.0	16.7	31.6	36.4	26.9	32.1	0.6
Inter-regional travel for both donor and recipient	0.0	50.0	0.0	21.1	24.2	11.5	16.0	0.4
Inter-regional match for donor and recipient	50.0	25.0	33.3	36.8	27.3	34.6	33.3	1

[a] Refers to the home state of the traveler (recipient, donor, or both recipient and donor).
KPD, kidney paired donation; LPD, list paired donation.

regards to highly sensitized patients. Only one collaborative (the New England Organ Bank) (*8*, *19*) and one single center program (Johns Hopkins Hospital) (*3*,*14*) have published their results and matching algorithms. Both reported matching algorithms based on principles of graph optimization, integer programming, and the Edmonds algorithm. The Johns Hopkins program also combines KPD and desensitization, with a matching process to accommodate this extension of KPD (*20*, *21*). For patients who are both difficult-to-match and difficult-to-desensitize, the requirement for a blood type compatible, negative crossmatch organ can be relaxed and the goal of the KPD is then to find a more immunologically favorable barrier which can be crossed with a less intensive desensitization regimen and lower risk. As an example, a pa-

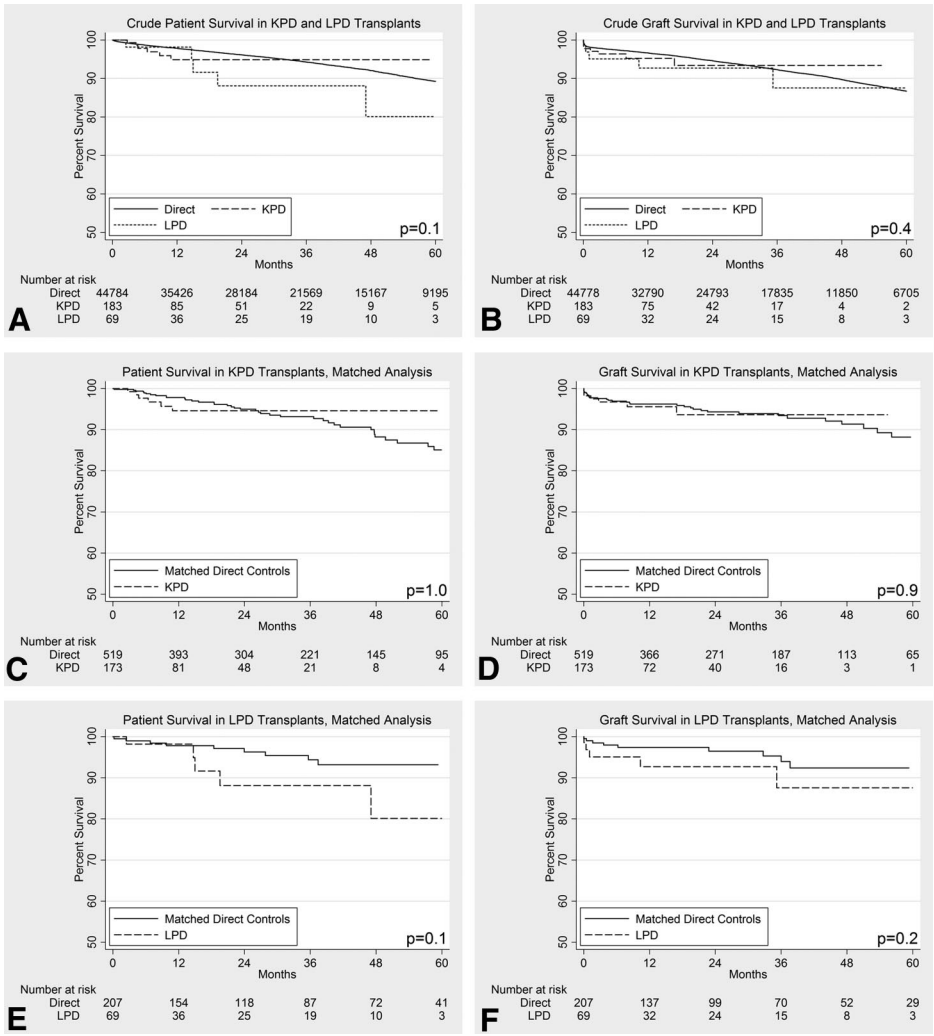

FIGURE 2. (A) Crude death-censored graft survival (upper panel) and patient survival (lower panel), comparing KPD, LPD, and direct transplants. (B) Death-censored graft survival (upper panel) and patient survival (lower panel) in KPD vs. direct matched controls. (C) Death-censored graft survival (upper panel) and patient survival (lower panel) in LPD vs. direct matched controls.

tient may have a positive cytotoxic crossmatch at a titer of more than 1024 with their intended donor, but in a KPD pool the patient could be matched with a donor for whom they have a low titer crossmatch; in this way the KPD enables desensitization. The Hopkins group has performed 20 transplants of these KPDs that have also included desensitization.

There are currently two options available to patients with incompatible live donors: desensitization and paired donation. We do not see these as competing modalities, given that even a large, national, optimized KPD program is predicted to match fewer than 50% of its participants. Stated simply, pairs who are most likely to benefit from KPD are those who are easy-to-match or difficult-to-desensitize, whereas pairs that are difficult-to-match or easy-to-desensitize will benefit more from desensitization. Although it is interesting to compare outcomes between KPD and desensitization, these comparisons are limited by variance in recipient and donor factors and sample sizes not large enough for appropriate matched-control or regression analyses. In this study, graft survival (not censored for death) from KPD transplants was 92.4% at 1-year and 90.7% at 3-years; from LPD transplants, graft survival was 91.0% at 1-year and 85.9% at 3-years. After ABO incompatible transplants, Takahashi et al. (*22*) have reported graft survival of 84% at 1-year and 80% at 3-years, and Tyden and coworkers have reported graft survival of 93% at 1-year and 87% at 3-years (*23*). Graft survival from 60 ABOi transplants at Johns Hopkins has been 98.3% at 1-year and 92.9% at 3-years (unpublished data).

A U.S. national KPD program has been designed by a committee with representation from most of the programs with an interest in participating, and has been proposed by UNOS (*24*). We strongly support this effort. Given that all transplant candidates are already registered through UNOS for possible deceased donor transplantation, adding incompatible donor information for the purposes of KPD seems a natural extension of UNOS's existing functionality. Furthermore, UNOS has already established committees to oversee ethics, finance, histocompatibility, living donors, minority affairs, and patient affairs, and this infrastructure would be paramount to the creation and legitimacy of an ethical, equitable, and efficient national program.

Paired donation offers the best transplant option for many patients with incompatible live donors and could substantially expand the donor pool if fully used in the United States. Prior evidence has suggested that a national KPD program will increase the number of patients that benefit from KPD. This study has shown that KPD is likely limited now by benefiting mostly patients who are easy to identify and easy-

to-match, whereas expansion to a national system would encourage registration of and improve match opportunities for patients who are more difficult to identify and difficult to match. Furthermore, some expansion of local KPD availability has already reduced travel requirements for patients in those areas, but room for growth remains and a national program would likely reduce travel requirements further.

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