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Living donor kidney paired donation transplantation: experience as a founding member center of the National Kidney Registry

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Abstract: Kidney paired donation (KPD) is a safe and effective means of transplantation for transplant candidates with willing but incompatible donors. We report our single-center experience with KPD through participation in the National Kidney Registry. Patient demographics, transplant rates, and clinical outcomes including delayed graft function (DGF), rejection, and survival were analyzed. We also review strategies employed by our center to maximize living donor transplantation through KPD. We entered 44 incompatible donor/recipient pairs into KPD from 9/2007 to 1/2011, enabling 50 transplants. Incompatibility was attributable to blood type (54.4%) and donor-specific sensitization (43.2%). Thirty-six candidates (81.8%) were transplanted after 157 d (median), enabling pre-emptive transplantation in eight patients. Fourteen candidates on the deceased donor waiting list also received transplants. More than 50% of kidneys were received from other transplant centers. DGF occurred in 6%; one-yr rejection rate was 9.1%. One-yr patient and graft survival was 98.0% and 94.8%. KPD involving participation of multiple transplant centers can provide opportunities for transplantation, with potential to expand the donor pool, minimize waiting times, and enable pre-emptive transplantation. Our experience demonstrates promising short-term outcomes; however, longer follow-up is needed to assess the impact of KPD on the shortage of organs available for transplantation.

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Approximately one-third of kidney transplant candidates who present with a potential living donor (s) will be incompatible owing to blood type or crossmatch incompatibility (1). Historically, these donors would be ruled out, or more aggressive transplant centers might employ desensitization strategies to attempt to overcome the incompatibility. Although success has been achieved utilizing desensitization techniques, they do require additional immune therapy with associated risks, do not guarantee that transplantation is feasible, and may carry increased risk of rejection (2, 3).

Kidney paired donation (KPD) has emerged as an effective tool to facilitate the transplantation of incompatible donor/recipient pairs, whether this is the result of blood type or crossmatch incompatibility (4–10). The ability to "swap" living donors began with individual transplant centers performing two or three paired donor exchanges (11). Since then, KPD has grown substantially, with many transplant centers participating in nationwide registries of incompatible donor/recipient pairs. Various KPD models exist, as described by Wallis et al. (12). A key element to maximizing KPD appears to be altruistic (also known as nondirected or Good Samaritan) donors, who wish to donate but have no intended recipient. Entry of such donors into KPD registries facilitates chains of transplants, leaving an "extra" donor, called a bridge donor, who is free to donate at a later time. This gives rise to the possibility of creating nonsimultaneous extended altruistic donor (NEAD)

chains or, in other scenarios, donation to a candidate on the deceased donor waiting list (13, 14), thus creating a hybrid of NEAD chains and domino-paired donation (12).

Several major KPD registries exist in the United States and have facilitated the majority of KPD transplants performed to date. One of these, the National Kidney Registry (NKR), was established in 2007; details about the NKR approach to KPD have been published (15). By pooling incompatible donor/recipient pairs, increased numbers of transplants can be generated by utilizing sophisticated mathematical modeling software to match suitable donor/recipient pairs. Our center took part in the first series of NKR transplants performed in February 2008. As of April 2011, the NKR had facilitated more than 250 kidney transplants nationwide. The NKR uses altruistic donors to begin chains of transplants that continue via bridge donors and, in theory, can become a NEAD chain. However, practical experience has shown that at times, it may be beneficial for a bridge donor to donate to the deceased donor waiting list (15). The time required for a suitable recipient to enter the registry and be matched with the bridge donor may result in the donor reneging because of alteration in work status with resultant economic inability to donate, resulting in the loss of the bridge donor and associated transplant(s). Bridge donors with blood type "O" may be preferentially kept within the registry owing to their ability to generate a future transplant chain (15). Various ethical issues related to KPD have been raised (16, 17); however, detailed review of these issues is beyond the scope of this report.

Herein, we outline our single-center experience utilizing KPD to maximize opportunities for kidney transplantation for our patients. We also explore the strategies that have been fundamental to the success of KPD at our center.

Patients and methods

Study population

Retrospective review was performed for all donor and recipient pairs from the New York-Presbyterian Hospital/Weill Cornell Kidney Transplant Program that were entered into the NKR database from 9/2007 to 1/2011. The Weill Cornell Medical College Institutional Review Board approved this review (protocol # 1105011723).

Donor and recipient pairs were categorized based on reason for entry into the NKR, and demographic data, waiting time on the United Network for Organ Sharing (UNOS) list, and immunologic status (calculated panel reactive antibody [CPRA] levels) were collected. For all candidates, the antigen targets of recipient antibodies with mean fluorescence intensity >5000 using single antigen bead assay (Luminex platform) were listed as unacceptable antigens in the NKR database and used to calculate the CPRA (18). All recipients had a negative donor T-cell complement–dependent cytotoxicity crossmatch at the time of transplant. Outcomes of KPD participation were analyzed, including transplant rate, need for additional immune therapy based on crossmatch results and/or the presence of donor-specific antibody (DSA), and time from NKR entry to transplant or last follow-up for candidates not yet transplanted.

Transplant outcomes were collected and analyzed, including transplant characteristics, human leukocyte antigen (HLA) matching, incidence of delayed graft function (DGF, need for dialysis within one wk of transplant), acute rejection rates, function of the transplanted kidney, and patient and graft survival.

Transplant candidates on the UNOS waiting list without potential living donors who received a transplant from a bridge donor (thus ending the chain) were also reviewed. Initially, these recipients were chosen using established UNOS criteria for allocation based on the current point system for distribution of organs. In 2010, a new program introduced by the NKR, the Children and High PRA (CHiP) program, prioritized providing chain-ending bridge donor kidneys to children or highly sensitized patients (CPRA score >50%) on the UNOS waiting list for a deceased donor transplant. Since that time, bridge donors are first allocated to the CHiP program, and if no suitable recipient is identified, then UNOS criteria are used as described above.

Participation in KPD does have financial implications for transplant centers that choose to participate. The NKR's financial model has evolved as KPD has grown and has become more successful in facilitating transplants. As a member center, our transplant program participated without incurring fees until August 2010. Since that time, the primary fees paid by our transplant center on an ongoing basis (which are paid by our transplant center and not charged to the patient's insurance) include an annual membership fee of $2500, a $3000 fee for each transplant facilitated, and the cost of shipping the donor kidney from an outside transplant center, when applicable. It is our understanding that transplant centers becoming NKR member centers after August 2010 also incur a one-time start-up and training fee.

Immunosuppression

Our standard immunosuppression regimen includes rabbit anti-thymocyte globulin (rATG) induction with tacrolimus (FK) and mycophenolate maintenance, and early steroid withdrawal; patients with sensitization and/or those on steroids prior to transplant remain on maintenance steroids. Patients who were highly sensitized and/or had a positive T- and/or B-cell flow crossmatch received additional peri-transplant therapy consisting of rituximab +/−intravenous immune globulin (IVIG), with the exact regimen tailored to each case. Biopsy-proven acute cellular rejection was treated with a methylprednisolone pulse and/or rATG. Biopsy-proven acute antibody-mediated rejection (AMR) was treated with plasmapheresis, IVIG, +/−rituximab or bortezomib. All patients received *Pneumocystis jiroveci* prophylaxis for one yr and cytomegalovirus prophylaxis with valganciclovir for six months.

Statistical analyses

Statistical analyses were performed using MedCalc for Windows, version 11.6.0 (MedCalc Software, Mariakerke, Belgium). Data are reported as median and range in the tables unless otherwise specified. Descriptive statistics were calculated using Fisher's exact test or chi-square test. Continuous variables were compared using the *t* test. Survival curves were generated using the Kaplan–Meier method.

Results

Characteristics of kidney transplant candidates with willing but incompatible living donors

Between 9/2007 and 1/2011, 44 incompatible donor/recipient pairs were entered into the NKR by our center. Candidates were 5–83 yr old and were ethnically diverse, and genders were roughly equally represented (Table 1). More than 25% had received a prior transplant(s), 41% entered NKR owing to donor-specific sensitization, while 57% were blood group incompatible [ABOi]. One pair entered owing to a wide age discrepancy (83-yr-old candidate with 43-yr-old donor). Candidates with donor-specific sensitization were more likely to have received a prior transplant(s) (47.4% vs. 12.0% of all other candidates; $p = 0.02$) and had a higher CPRA (median 87% vs. 0% in all other candidates; $p < 0.0001$). More than 80% of candidates were on the UNOS waiting list at the time of NKR entry and had been waiting 155 d (median). As of 3/31/2011, 86% of the candidates had been transplanted (n = 36) or were scheduled for transplant (n = 2).

Table 1. Characteristics of kidney transplant candidates with willing but incompatible living donors that were entered into the National Kidney Registry (n = 44)

Candidate demographics					
Age (yr)				47 (5–83)	
Gender (male)				23 (52.3%)	
Ethnicity					
African American				11 (25.0%)	
Asian				3 (6.8%)	
Caucasian				20 (45.4%)	
Hispanic				9 (20.5%)	
All Other				1 (2.3%)	
Cause of end-stage renal disease					
Diabetes mellitus				5 (11.4%)	
Focal segmental glomerulosclerosis				5 (11.4%)	
Glomerulonephritis				7 (15.9%)	
Hypertension				2 (4.5%)	
Polycystic kidney disease				7 (15.9%)	
Systemic lupus erythematosus				3 (6.8%)	
Other				12 (27.3%)	
Unknown				3 (6.8%)	
Donor/recipient blood types	Donor	A	B	AB	O
Recipient	A	3	3	1	6
	B	5	2	0	1
	AB	0	0	0	1
	O	11	3	2	6
Prior transplant (yes)				12 (27.3%)	
Relationship to intended donor					
Living related				17 (38.6%)	
Living unrelated				27 (61.4%)	
Spouse				14/27 (51.9%)	
Other				13/27 (48.1%)	
Reason for entry into National Kidney Registry					
Blood type incompatible with intended donor				25 (56.8%)	
Donor-specific sensitization				18 (40.9%)	
Wide age discrepancy with intended donor				1 (2.3%)	
CPRA range, n (%)					
0–50%				24 (54.6%)	
51–80%				10 (22.7%)	
81–100%				10 (22.7%)	
CPRA (%), median (range)					
Candidates entering NKR owing to sensitization (n=19)				87 (0–100)	
All other candidates (n=25)				0 (0–76)	
Candidates on UNOS waiting list at time of entry into NKR				36 (81.8%)	
Length of time on UNOS waiting list at time of entry into NKR (n = 36) (d)				155 (9–662)	
Candidate status					
Transplanted				36 (81.8%)	
Transplant scheduled				2 (4.5%)	
Match found but financial issue				1 (2.3%)	
Match not yet found				5 (11.4%)	

All data presented as n (%) or median (range), unless otherwise specified.
NKR, National Kidney Registry; UNOS, United Network for Organ Sharing; CPRA, calculated panel reactive antibody.

Characteristics of kidney transplant candidates who received a transplant through a chain facilitated by NKR

Between 2/2008 and 3/2011, 36 of 44 candidates (81.8%) received a kidney transplant. Recipients were 5–83 yr old, 61% men, and ethnically diverse (Table 2). Recipient-level data regarding reason for KPD participation, intended and actual donors, and position within transplant chains are shown in Table 3. Nineteen percent were repeat transplant recipients, and one-third had a CPRA > 50%. One-third had entered the NKR owing to donor-specific sensitization, while 64% were ABOi. The recipients had been entered into the NKR a median of five months prior to transplant, and 29 (80.6%) were transplanted within six months of NKR entry, enabling 22% to receive a pre-emptive transplant (30.4% of candidates with ABOi donor vs. 8.3% of sensitized candidates; p = 0.2). Patients participating in KPD owing to ABOi were more likely to be transplanted than sensitized patients (95.8% vs. 63.2%; p = 0.01). Median time from NKR entry to transplant was 157 d in both the ABOi and sensitized groups (range 22–450 d for ABOi vs. 76–525 d for sensitization) (p = 0.2). Candidates with donor-specific sensitization who had not yet been transplanted had been entered into the NKR for a median of 226 d (range 130–471). Sensitized candidates who were transplanted had a median CPRA of 75% compared to 100% in those not yet transplanted (p = 0.03), and three of 10 patients (30%) with a CPRA > 80% were transplanted.

Almost 60% received a kidney procured at another transplant center, leading to median cold ischemia times (CIT) of five and 12 h for ground and air-shipped kidneys, respectively. Two recipients developed DGF (one had been ground-shipped); however, both cases were attributed to factors unrelated to the procurement/CIT (acute AMR and urine leak). Median hourly urine output in the first eight h after transplant (585 mL/h for internally procured vs. 694 mL/h for shipped; p = NS) and median time to serum creatinine less than 2 mg/dL (1.1 d for internally procured vs. 2.5 d for shipped; p = NS) were not significantly different. One recipient's creatinine never fell below 2.3 mg/dL (internal procurement with prolonged warm ischemia time).

A flow crossmatch was performed in 28 recipients; five were positive (17.9%) (B-cell positive [n = 2] and T- and B-cell positive [n = 3]). Approximately 35% of recipients required maintenance steroids and/or additional peri-transplant therapy because of presence of DSA and/or based on cross-

Table 2. Characteristics and outcomes of kidney transplant candidates with willing but incompatible donors who received a transplant through a National Kidney Registry–facilitated transplant chain (n = 36)

Recipient demographics					
Age (yr)					47 (5–83)
Gender (male)					22 (61.1%)
Ethnicity					
African American					9 (25.0%)
Asian					3 (8.3%)
Caucasian					17 (47.2%)
Hispanic					6 (16.7%)
All other					1 (2.8%)
Cause of end-stage renal disease					
Diabetes mellitus					5 (13.9%)
Focal segmental glomerulosclerosis					4 (11.1%)
Glomerulonephritis					5 (13.9%)
Hypertension					2 (5.6%)
Polycystic kidney disease					6 (16.7%)
Systemic lupus erythematosus					2 (5.6%)
Other					9 (25.0%)
Unknown					3 (8.3%)
Donor/recipient blood types	Donor	A	B	AB	O
Recipient	A	2	3	1	5
	B	5	2	0	0
	AB	0	0	0	1
	O	10	3	1	3
Prior transplant (yes)					7 (19.4%)
Relationship to intended donor					
Living related					14 (38.9%)
Living unrelated					22 (61.1%)
Spouse					13/22 (59%)
Other					9/22 (41%)
Reason for entry into NKR					
Blood type incompatible with intended donor					23 (63.9%)
Donor-specific sensitization					12 (33.3%)
Wide age discrepancy with intended donor					1 (2.8%)
CPRA range, n (%)					
0–50%					24 (66.7%)
51–80%					9 (25.0%)
81–100%					3 (8.3%)
CPRA (%), median (range)					
Candidates entering NKR owing to sensitization (n=12)					75 (0–99)
All other candidates (n=24)					0 (0–64)
Candidates on UNOS waiting list at time of entry into NKR					32 (88.9%)
Length of time on UNOS waiting list at time of entry into NKR (d)					144 (9–630)
Transplant information					
Time from NKR entry to transplant (d)					157 (22–525)
Recipients transplanted pre-emptively					8 (22.2%)
HLA mismatches					4 (2–6)
Presence of donor-specific antibody					
None					25 (69.4%)
Class I					7 (19.4%)
Class II					2 (5.6%)
Classes I and II					2 (5.6%)
Source of donor kidney					
In-house					15 (41.7%)
Ground-shipped					8 (22.2%)
Air-shipped					13 (36.1%)

Table 2 Continued

Recipient demographics	
Cold ischemia time (h)	
In-house	N/A
Ground-shipped	5 (3–6)
Air-shipped	12 (8–14)
Delayed graft function (n)	
In-house	1
Ground-shipped	1
Air-shipped	0
Immunosuppression – all received rATG/FK/MPA with	
Steroid sparing maintenance	23 (63.9%)
Steroid maintenance	8 (22.2%)
Steroid maintenance/rituximab 1g (POD −7)/ IVIG 500mg/kg (POD −1, +2, +4)	2 (5.6%)
Steroid maintenance/rituximab 1g (POD +1)	2 (5.6%)
Steroid maintenance/rituximab 1g (POD +1)/ IVIG 500mg/kg (POD +2, +4)	1 (2.7%)
Serum creatinine (mg/dL)	
1 wk	1.4 (0.7–6.2)
1 month	1.3 (0.8–3.5)
6 months	1.3 (0.7–2.5)
12 months	1.2 (0.7–3.0)
24 months	1.1 (0.6–3.2)
36 months	1.0 (0.8–1.0)
Follow-up time (months)	16 (1–39)

All data presented as n (%) or median (range), unless otherwise specified.
N/A, not applicable; NKR, National Kidney Registry; UNOS, United Network for Organ Sharing; HLA, human leukocyte antigen; rATG, rabbit anti-thymocyte globulin; FK: tacrolimus; MPA, mycophenolic acid; CPRA, calculated panel reactive antibody; IVIG, intravenous immune globulin.

match results. Three developed rejection (one Banff 2a, one Banff 2b, and one AMR); all had received additional peri-transplant therapy, with CPRAs of 64%, 98%, and 99% and DSAs of moderate class II, strong class II, and moderate class I, respectively. One graft was lost (Banff 2b), owing to non-adherence with immunosuppression. Transplant function (serum creatinine; Table 2) has been excellent through a median follow-up time of 16 months. Early in the experience, two bridge donors did back out of donating after their intended recipient had been transplanted owing to changes in circumstances while waiting to be matched with a suitable recipient. In the first case, the intended donor was the husband of a recipient who was blood type A and despite multiple crossmatches in the period of one yr after his wife's transplant was not matched to any recipient. After a year, owing to changes in the economy, the husband withdrew from participating because he would have lost his job by donating, thus leaving his family (including his transplanted wife) with no health insurance. In the second case, after attempting to contact the donor several months after the candidate received their transplant, the transplant center was unable to reach the potential donor, nor was the transplant recipient, despite numerous attempts.

Characteristics of kidney transplant recipients from the deceased donor waiting list who received a transplant from a bridge donor facilitated by NKR

Fourteen transplant candidates with no available living donors who were on the deceased donor waiting list (median waiting time 500 d) received a chain-ending kidney transplant from a bridge donor. Sixty-four percent were chosen from the deceased donor waiting list based on blood type, waiting time, sensitization, and other factors (Tables 3 and 4). No specific selection criteria for these recipients exist, although this will likely be developed in the future. The remaining 36% had been entered into the CHiP program after its introduction in 2010. Recipients were 15–65 yr old, 50% men, and ethnically diverse (Table 3). Thirty-six percent were repeat transplant recipients and were highly sensitized; a flow crossmatch was performed in 10 recipients, and none were positive. Recipients were selected to receive a bridge donor kidney a median of one month prior to the transplant date.

More than 60% received a kidney procured at another center, leading to a median CIT of four and nine h for ground and air-shipped kidneys, respectively. One recipient developed DGF (ground-shipped); however, the DGF was attributed to severe early focal segmental glomerulosclerosis (FSGS) recurrence. Median hourly urine output in the first eight h after transplant (672 mL/h for internally procured vs. 788 mL/h for shipped; p = NS) and median time to serum creatinine less than 2 mg/dL (1.4 d for internally procured vs. 2.2 d for shipped; p = NS) were not significantly different. One recipient's creatinine never fell below 2.3 mg/dL (owing to recurrent FSGS). Fifty percent of recipients required maintenance steroids and/or additional peri-transplant therapy owing to the presence of DSA.

One patient died of respiratory failure 1.5 months post-transplant after experiencing severe early FSGS recurrence, having lost the graft on post-operative day 30. Two patients developed rejection (one Banff 2a/AMR, one AMR); one graft was lost (Banff 2a/AMR) owing to non-adherence. In the remaining patients, transplant function (Table 3) has been excellent through a median follow-up time of seven months.

All transplant recipients

Patient and graft survival and acute rejection for all 50 patients receiving a kidney transplant are

Table 3. Patient-level data for all patients receiving a kidney transplant through kidney paired donation

Recipient	Intended donor	Incompatibility	Actual donor	Chain	Cluster	Position	Shipping method	Cold ischemia time (h)	DGF	Average urine output (mL/h) (1st 8 h)	Time to Cr < 2.0 (d)
R1	Parent	ABO	R3	1	1	1	–	–	No	152	0.3
R2	Spouse	XCM	NDD	1	1	2	–	–	No	694	1.3
R3	Spouse	XCM	R2	1	1	3	–	–	No	296	1.0
R4	Sibling	ABO	R1 (bridge)	1	2	1	–	–	No	585	1.2
R5	Spouse	ABO	R4	1	2	2	–	–	No	1738	0.2
R6	Spouse	ABO	Import	2	3	2	Air	11	No	350	2.4
R7	Spouse	ABO	Import	3	1	2	Ground	5	No	1331	1.7
R8	Friend	ABO	R7	3	1	3	–	–	No	781	Never
R9	Friend	XCM	Import	5	5	1	Air	12	No	514	2.5
R10	Parent	ABO	Import	5	6	7	Air	12	No	343	1.5
R11	Spouse	ABO	NDD	9	1	1	–	–	No	466	0.5
R12	Other relative	XCM	R11	9	1	2	–	–	No	81	3.4
R13	Spouse	ABO	Import	10	1	2	Ground	4	No	182	6.0
R14	Sibling	XCM	Import	10	2	4	Ground	3	No	568	0.3
R15	Sibling	XCM	Import	10	3	2	Air	5	Yes	20	27.0
R16	Spouse	ABO	R15 (bridge)	10	4	1	–	–	No	969	6.0
R17	Friend	ABO	R16	10	4	2	–	–	Yes	113	7.0
R18	Child	ABO	NDD	16	1	1	–	–	No	694	0.7
R19	Friend	ABO	Import	16	2	3	Air	13	No	397	4.7
R20	Child	XCM	NDD	18	1	1	–	–	No	355	0.4
R21	Other relative	ABO	Import	19	3	3	Ground	6	No	1675	0.6
R22	Other relative	XCM	R21	19	3	4	–	–	No	972	1.2
R23	Sibling	XCM	Import	19	3	6	Ground	5	No	1088	1.9
R24	Spouse	ABO	Import	19	3	8	Ground	4	No	738	25.0
R25	Friend	Age	Import	20	2	1	Air	13	No	800	6.0
R26	Spouse	ABO	NDD	47	1	1	–	–	No	448	21.0
R27	Spouse	XCM	Import	53	1	3	Air	14	No	719	26.0
R28	In-law	ABO	Import	66	2	1	Ground	5	No	654	2.2
R29	Spouse	ABO	Import	69	3	2	Air	13	No	1238	3.3
R30	Spouse	ABO	Import	76	1	2	Air	8	No	694	3.4
R31	In-law	ABO	Import (NDD)	88	1	1	Air	9	No	625	8.0
R32	Other relative	ABO	Import	95	2	3	Air	11	No	1144	0.8
R33	Friend	XCM	R32 (bridge)	95	3	1	–	–	No	1272	0.5
R34	In-law	ABO	Import	95	3	3	Air	12	No	263	9.0
R35	Sibling	ABO	Import	98	1	2	Air	10	No	838	0.8
R36	Friend	ABO	Import (NDD)	105	1	1	Air	13	No	919	1.5

Recipient	Reason for selection	CPRA/ABO/ wait	Actual donor	Chain	Cluster	Position	Shipping method	Cold ischemia time (h)	DGF	Average urine output (mL/h) (1st 8 h)	Time to Cr < 2.0 (d)
WL1	Waiting time/ last access	0%/B/375	R17	10	4	3	–	–	No	154	3.9
WL2	Waiting time	0%/B/544	R19	16	2	4	–	–	No	838	0.8
WL3	Waiting time/ sensitization	59%/A/1164	Import	19	3	10	Ground	5	No	481	14.0
WL4	Waiting time	0%/A/457	Import	58	1	4	Ground	3	No	1288	0.8
WL5	CHiP/ sensitization	79%/A/837	Import	61	4	5	Air	9	No	223	20.0
WL6	Waiting time/ sensitization	36%/A/669	Import	68	1	4	Ground	2	No	500	2.5
WL7	Waiting time	0%/AB/234	R29	69	3	3	–	–	No	672	0.7

Table 3. Patient-level data for all patients receiving a kidney transplant through kidney paired donation

Recipient	Reason for selection	CPRA/ ABO/wait	Actual donor	Chain	Cluster	Position	Shipping method	Cold ischemia time (h)	DGF	Average urine output (mL/h) (1st 8 h)	Time to Cr < 2.0 (d)
WL8	CHiP/ sensitization	98%/AB/3159		Import (NDD)	70	1	1	Ground 7	No	950	1.6
WL9	Waiting time/ sensitization	57%/AB/631		R30	76	1	3	– –	No	1356	2.3
WL10	CHiP/ sensitization	100%/A/588		Import (NDD)	77	1	1	Air 8	No	1350	3.2
WL11	Waiting time	0%/A/1312		Import	80	1	3	Air 14	No	1081	1.8
WL12	CHiP/ pediatric	0%/A/70		Import	92	1	5	Ground 4	Yes	481	Never
WL13	CHiP/ pediatric	0%/B/188		Import	95	3	11	Ground 3	No	788	1.6
WL14	Waiting time	0%/AB/436		R35	98	1	3	– –	No	437	1.4

Recipient, R#, kidney paired donation participant who entered with an incompatible donor; Recipient, WL#, Patient on deceased donor waiting list who received a bridge donor kidney; CHiP, Children and High PRA program; Incompatibility: ABO, blood type incompatible; XCM, crossmatch incompatible; CPRA/ABO/wait, calculated panel reactive antibody/blood type/waiting time (d) of candidate; Actual donor, R#, original intended donor of the indicated recipient; Actual donor, NDD, non-directed donor that originated at our transplant center; Actual donor, R# (bridge), donor was a bridge donor that perpetuated a chain into another cluster; Actual donor, Import, kidney paired donation donor that originated at another transplant center; Actual donor, Import (NDD), non-directed donor that originated at another transplant center; DGF, delayed graft function.

presented in Fig. 1. Actuarial patient survival at one-yr post-transplant was 98.0% [SE: 2.0], while graft survival was 94.8% [SE: 3.7]. Actuarial acute rejection rate at one yr was 9.1% [SE: 4.5].

Discussion

At our transplant center, KPD utilizing a national registry enabled 50 living donor kidney transplants for candidates who might otherwise have spent years on the UNOS waiting list. KPD provides opportunity for living donor transplantation that did not exist until recently. Although our series is early and the majority of transplant recipients have short-term follow-up, patient and graft survival, acute rejection rates, and transplant function are excellent. The most recent national data available report one-yr patient and graft survivals of 98.5% and 96.3%, respectively, in all living donor recipients (related and unrelated) (19). The outcomes in our patients (98.0% and 94.8%, respectively) are comparable, particularly considering that all patients received living unrelated transplants and many were at high immunologic risk.

Benefits of KPD range from the ability to remove patients from the UNOS waiting list, thus avoiding the associated morbidity and mortality (20), to the superior outcomes afforded by living donor transplantation while minimizing the immune therapy required for incompatible transplants. Living donor transplants have superior graft half-life compared to deceased donor organs (21), provide a higher-quality organ, and have low rates of DGF, even when transported for KPD, despite CITs that may exceed 12 h (4). In our series, cases of DGF were attributable to factors unrelated to procurement and CIT. Higher-quality living donor allografts may provide better transplant function, which in turn may offer better quality of life (22, 23).

Nationally, only 20.3% of highly sensitized candidates received a transplant by two yr on the waiting list, and this was even lower in our donation service area (Region 9) (16.7%) (24). Although participation in KPD did not completely eliminate the need for additional immunosuppressive therapy for some patients, it did eliminate peri-transplant plasmapheresis, and the amount of immunosuppression received was lower than regimens traditionally utilized by our center for desensitization (data not shown). Sensitized candidates may be more difficult to match within KPD registries, and desensitization regimens will continue to play an important role in enabling transplantation. However, these regimens may be less intensive than traditionally utilized. All rejection episodes occurred in patients who had received additional immunosuppression owing to their sensitization status, except for those attributed to non-adherence. However, all adherent patients had successful reversal of rejection and have sustained good transplant function. Despite best efforts to provide patients with living donor opportunities through KPD, human behavior remains difficult to predict, and non-adherence may not be avoidable despite these best efforts.

Table 4. Characteristics and outcomes of kidney transplant candidates on the UNOS deceased donor waiting list who received a transplant from a bridge donor facilitated by the National Kidney Registry (n = 14)

Recipient demographics	
Age (yr)	46 (15–65)
Gender (male)	7 (50%)
Ethnicity	
African American	4 (28.6%)
Asian	3 (21.4%)
Caucasian	3 (21.4%)
Hispanic	2 (14.3%)
All other	2 (14.3%)
Cause of end-stage renal disease	
Diabetes mellitus	4 (28.6%)
Focal segmental glomerulosclerosis	3 (21.4%)
IGA nephropathy	2 (14.3%)
Other/unknown	5 (35.7%)
Prior transplant (yes)	5 (35.7%)
Reason for consideration for NKR bridge donor kidney	
Child (CHIP program)	2 (14.3%)
Highly sensitized (CHIP program)	3 (21.4%)
Waiting time (+/−sensitization)	8 (57.2%)
Using last dialysis access site	1 (7.1%)
Calculated panel reactive antibody (%)	
Candidates with sensitization (n=5)	79 (57–100)
All other candidates (n=9)	0 (0–36)
Candidates on UNOS waiting list at time of entry into NKR	14 (100%)
Length of time on UNOS waiting list at time of match within NKR (d)	500 (48–3078)
Transplant information	
Time from NKR selection to transplant (d)	31 (8–159)
Recipients transplanted pre-emptively	2 (14.3%)
HLA mismatches	5 (0–6)
Presence of donor-specific antibody	
None	9 (64.3%)
Class I	2 (14.3%)
Class II	1 (7.1%)
Classes I and II	2 (14.3%)
Source of donor kidney	
In-house	5 (35.7%)
Ground-shipped	6 (42.9%)
Air-shipped	3 (21.4%)
Cold ischemia time	
In-house	N/A
Ground-shipped	4 (2–7)
Air-shipped	9 (8–14)
Delayed graft function (n)	
In-house	0
Ground-shipped	1
Air-shipped	0
Immunosuppression – all received rATG/FK/MPA with	
Steroid sparing maintenance	7 (50.0%)
Steroid maintenance	6 (42.9%)
Steroid maintenance/rituximab 1g (POD −7)/IVIG 500mg/kg (POD −1, +2, +4)	1 (7.1%)
Serum creatinine (mg/dL)	
1 wk	1.5 (0.6–8.1)
1 month	1.3 (0.7–2.0)
6 months	1.2 (0.8–1.6)
12 months	1.1 (0.9–1.8)
Follow-up time (months)	7 (2–22)

All data presented as n (%) or median (range), unless otherwise specified. N/A, not applicable; CHIP, children and high PRA; NKR, National Kidney Registry; UNOS, United Network for Organ Sharing; HLA, human leukocyte antigen; rATG, rabbit anti-thymocyte globulin; FK, tacrolimus; MPA, mycophenolic acid; IVIG, intravenous immune globulin.

Participation in KPD through the NKR has enabled us to find a suitable donor for more than 85% of the candidates who entered with an incompatible intended donor, a success rate superior to that experienced within the NKR to date (15), and more than 80% of the transplants occurred <6 months following entry into the NKR. As one of the first centers participating with the NKR, lessons learned over the past three yr have likely contributed to this success. Many factors have to converge, as these transplants are logistically challenging and centers wishing to participate will have to give thought to the infrastructure and resources needed for meaningful participation.

Flexibility in scheduling of both donor and recipient surgery is essential, requiring 24/7 operating room availability. Surgeries may need to be re-scheduled or rearranged on short notice, essential in ensuring continuity of the transplant chains. Last-minute issues, such as cancellation of flights, require availability of resources to find an alternate solution such as to charter a flight. Active participation and support from hospital administration and finance are essential, as complex insurance and financial issues may arise that require problem-solving at a higher level than the transplant program. Resolution of issues is facilitated when hospital administrators have clear understanding of the benefits of transplantation over dialysis and the positive financial impact of a successful living donor transplant to the hospital system. Financially, we have found participation with the NKR to be beneficial to our system despite the required fees.

Dedicated resources are a key to the success of KPD. A physician champion is essential in bringing together key players from both the transplant program and administration. A transplant coordinator with intimate knowledge of the KPD process is needed to manage the complex logistics, including entry of donors and recipients into the registry, receiving match offers, and managing logistics among transplant centers involved in a particular chain. The coordinator also maintains medical records for donor organs procured at outside centers needed for the recipient medical record, tracks the organ(s) en route via global positioning system (GPS), fields issues arising on the day of the surgery, and arranges contact between donors and recipients who wish to meet after their surgeries. Other aspects of success include performing altruistic donor surgeries, which may enable a candidate on that center's UNOS waiting list to receive a bridge donor kidney.

Because our transplant center's mission is to maximize opportunities for transplantation for all patients, KPD has become an important option

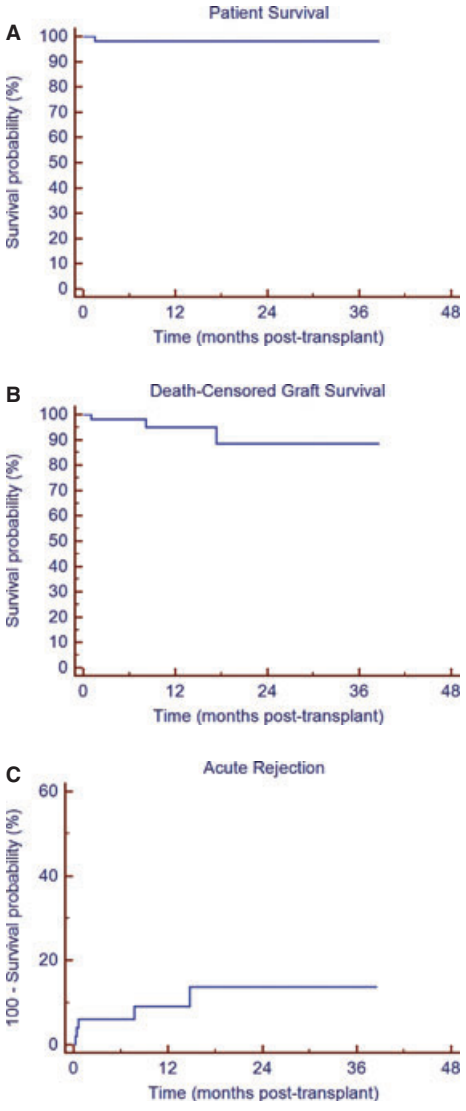

Fig. 1. The graphs depict the patient (Panel A) and death-censored graft survival (Panel B), and acute rejection (Panel C) for all 50 patients who received a kidney transplant through kidney paired donation. The *y*-axis is the number of months post-transplant.

for our patients. Broadening the scope to include both incompatible and compatible donor/recipient pairs is an area of growth being targeted. Transplant candidates, prospective donors, and healthcare professionals must be educated about the enormous potential that can be realized. Education may focus on the established practice of KPD, data supporting the safety and effectiveness of KPD, and the number of people that could be helped if compatible donors and recipients are willing and open-minded to the possibility of participating (for example, if "O" donors with "A," "B," or "AB" intended recipients would enter KPD to enable a candidate with type "O" blood to be transplanted). The donor's intended recipient may also benefit by finding a better HLA match or age match, particularly as the donor/recipient pool size expands (1). If an intended donor is willing and able (medically, psychologically, and psychosocially fit), traditional compatibility issues may not need to play such a prominent role in living donor transplantation. The living donor team must be vigilant in ensuring that coercion does not exist, and continue to provide an alternative reason for donors who do not want to donate and may no longer have incompatibility as a "way out." Interestingly, a survey of 174 ABOi or crossmatch-incompatible intended donors found 64% willing to participate in KPD as opposed to only 38% willing to participate in list donation where their intended recipient would move to the top of the deceased donor waiting list (25). This may be a positive sign for incompatible and compatible KPD as it may show awareness of the benefits of living over deceased donor kidney transplantation.

Participation in KPD should not alter risk to the living donor and may even improve the donor's perception of the benefit owing to the ability to impact multiple patients awaiting transplant and/or impact someone who is difficult to match owing to sensitization. Shipping of the donor kidney does not increase risk of DGF (4, 26), and with today's GPS technology, loss of organs has not been an issue to date.

In conclusion, KPD offers an innovative and exciting option for transplant candidates and their intended living donors. With the plateau of deceased donor organ availability and little opportunity to maximize the donor pool further, living donation remains the best driver in growth of kidney transplantation. The transplant community must remain vigilant in continuing to provide care that is in the best interest of the potential living donors while attempting to utilize these precious gifts in a way that benefits as many candidates as possible. With the expansion of KPD to include compatible pairs, KPD has the potential ability to offer a meaningful solution to the organ shortage.

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Author contributions

David B. Leeser participated in research design, drafting the article, and critical revision of the manuscript. Meredith J. Aull participated in research design, data collection, data analysis, drafting the article, and critical revision of the manuscript. Cheguevara Afaneh participated in research design, data collection, data analysis, and drafting the article. Darshana Dadhania participated in research design and critical revision of the manuscript. Marian Charlton participated in research design and data collection. Jennifer K. Walker participated in research design and critical revision of the manuscript. Choli Hartono, David Serur, and Joseph J. Del Pizzo participated in research design. Sandip Kapur participated in research design, critical revision of the manuscript, and approval of article.

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