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Authors
Kamgar, Mandana
Huang, Edmund
Kamgar, Mohammad
et al.

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Zero-Mismatch Deceased-Donor Kidney Versus Simultaneous Pancreas-Kidney Transplantation

Mandana Kamgar,[1] Edmund Huang,[1] Mohammad Kamgar,[2] Naowanit Nata,[1] Napat Leeaphorn,[1] Kamyar Kalantar-Zadeh,[3] and Suphamai Bunnapradist[1,4]

Background. Patients with type 1 diabetes mellitus (T1DM) and end-stage renal disease may receive a simultaneous pancreas-kidney (SPK), living-donor kidney (LDK), or deceased-donor kidney (DDK) with possible pancreas after kidney transplantation. SPK is associated with superior patient and kidney graft survival compared with DDK, whereas SPK and LDK have comparable outcomes. It is unclear whether SPK and LDK offer a survival benefit over zero-mismatch (0MM) DDK. In this study, we compared the outcomes of T1DM recipients using data from the Organ Procurement and Transplant Network/United Network for Organ Sharing.

Methods. Adult (≥18 years) first-time transplant recipients with T1DM waitlisted for SPK and transplanted from 1995 to 2010 were included in this study. Patient and death-censored kidney graft survival were compared between 0MMDDK (n=228), mismatched (MM) DDK (n=964), 0MMSPK (n=215), MMSPK (n=11951), 2 haplotype identical (2hap) LDK (n=205), and non-2hapLDK (n=1719) recipients. Multivariate analysis was performed using stepwise Cox proportional hazards models.

Results. At 7 years, patient and death-censored graft survival of 0MMDDK recipients (85% and 81%, respectively) were not statistically different from that of 0MMSPK (81% and 85%; log-rank *P* value vs. 0MMDDK, 0.17 and 0.48, respectively) and 2hapLDK recipients (89% and 86%; log-rank *P* value vs. 0MMDDK, 0.34 and 0.18, respectively). Among all groups, MMDDK showed the worst patient survival (71%; log-rank *P* value vs. 0MMDDK, 0.001)

Conclusion. Patient and kidney graft survival of 0MMDDK recipients were comparable to both SPK and LDK recipients. These findings suggest that T1DM patients awaiting SPK may consider accepting a 0MMDDK if an offer is available.

Keywords: Deceased-donor kidney transplantation, Simultaneous pancreas-kidney transplantation, Kidney survival, Patient survival, HLA matching.

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Kidney transplantation is the renal replacement therapy of choice for patients with type 1 diabetes mellitus (T1DM) approaching end-stage renal disease. This preference is in part because of the beneficial effect of transplantation on patient survival when compared with dialysis (*1–3*). Available solid organ transplantation options for these patients include simultaneous pancreas-kidney (SPK), living-donor kidney (LDK), or deceased-donor kidney (DDK) with possible pancreas after kidney (PAK) transplantation (*4, 5*).

There is lower kidney and patient survival with DDK compared with LDK and SPK (*6–11*). Potential reasons for lower survival include differences in organ quality, waiting time, or recipient characteristics (*7, 12, 13*). It is known that zero-mismatched (0MM) DDK transplants are associated with better kidney survival compared with mismatched (MM) DDK transplants (*14, 15*). Furthermore, current United Network for Organ Sharing (UNOS) policies prioritize allocation of 0MM kidneys, which often results in shorter waiting time for their recipients. It is not known

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[1] Division of Nephrology, Department of Medicine, David Geffen School of Medicine, University of California at Los Angeles, CA.
[2] Long Beach Memorial Medical Center, Long Beach, CA.
[3] Division of Nephrology and Hypertension, University of California Irvine Medical Center, Orange, CA.
[4] Address correspondence to: Suphamai Bunnapradist, M.D., Kidney Transplant Research Program at UCLA, 1033 Gayley Ave., Suite 208, Los Angeles, CA 90024.
E-mail: bunnapradist@mednet.ucla.edu
Data reported here have been taken from the Organ Procurement Transplant Network/United Network for Organ Sharing database as of March 2011.

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TABLE 1. Baseline characteristics

	2hapLDK (n=205)	Non-2hapLDK (n=1719)	0MMDDK (n=228)	MMDDK (n=964)	0MMSPK (n=215)	MMSPK (n=11951)
Recipient variables						
Age, median (25th, 75th)	39 (34, 45)	40 (34, 46)	40 (34, 47)	42 (36, 48)[a]	41 (34, 47)	39 (34, 45)
Male, %	53.2	57.1	55.7	58.6	53.0	60.7[a]
Race, %						
White	82.4[a]	82.4[a]	92.1	75.2[a]	92.1	77.8[a]
Black	6.4	8.5[a]	3.5	15.6[a]	4.2	13.2[a]
Hispanic	8.3	7.8	4.4	7.3	3.2	7.3
Other	2.9[a]	1.3	0.0	1.9[a]	0.5	1.7[a]
Peak PRA, %						
Missing	21.5[a]	22.5[a]	7.4	8.9	45.1[a]	39.8[a]
≤10%	67.3	67.0	68.9	67.3	39.1[a]	52.5[a]
>10%	11.2[a]	10.5[a]	23.7	23.8	15.8[a]	7.7[a]
Creatinine level at time of transplantation, mean (SD), mg/dL	5.9 (2.6)[a]	6.4 (2.8)	6.7 (2.9)	7.4 (2.9)[a]	6.5 (2.8)	6.7 (3.0)[a]
GFR, median (25th, 75th), mL/min	10.8 (7.9, 15.6)[a]	10.4 (7.3, 14.7)[a]	8.9 (6.3, 12.9)	7.8 (5.6, 10.6)[a]	9.0 (6.7, 12.9)	8.9 (6.3, 13.0)
Preemptive, %	28.3[a]	28.2[a]	13.2	9.0	23.7[a]	18.5[a]
Dialysis time, median (25th, 75th)[b]	313 (168, 503)[a]	360 (206, 665)[a]	671 (305, 1099)	1100 (627, 1648)[a]	474 (260, 868)[a]	572 (322, 937)
BMI						
<25	56.6[a]	54.1[a]	46.9	47.6	63.1[a]	59.3[a]
25–29.9	32.5	32.6	37.5	33.3	24.3[a]	31.0[a]
≥30	10.8	13.3	15.6	19.1	12.6	9.7[a]
Median kidney waiting time, days (25th, 75th)[c]	125 (60, 256)[a]	153 (70, 308)[a]	276 (101, 540)	398 (152, 805)[a]	196 (87, 413)	237 (93, 462)
Donor variables						
Age, median (25th, 75th)	39 (32, 45)[a]	41 (33, 49)[a]	35 (20, 48)	36 (21, 48)	26 (20, 37)[a]	23 (18, 34)[a]
Male, %	43.9[a]	40.3[a]	53.5	63.7[a]	63.3[a]	67.5[a]
Race, %						
White	83.4[a]	82.7[a]	91.2	74.5[a]	92.6	70.5[a]
Black	6.8[a]	7.3[a]	0.9	10.3[a]	1.9[a]	14.7[a]
Hispanic	7.3	8.3	5.7	12.4[a]	5.6	12.1[a]
Other	2.5	1.7	2.2	2.8	0.0[a]	2.7[a]
Hypertension, %	0.0[a]	1.2[a]	13.2	19.8[a]	6.1[a]	5.8[a]
BMI						
<25	35.3[a]	36.4[a]	50.9	47.2	61.0	64.3[a]
25-29.9	43.8	42.6	36.0	28.2[a]	28.8	26.9[a]
≥30	20.9	21.0	13.1	24.6[a]	10.2	8.8[a]
ECD, %	—	—	9.7	10.5	0.5[a]	0.5[a]
Transplant variables						
Transplant yr						
1995–1999	19.5[a]	15.2[a]	29.8	21.6[a]	42.3[a]	31.7
2000–2004	41.5	38.7	38.6	36.2	41.9	30.1[a]
2005–2010	39.0	46.1[a]	31.6	42.2[a]	15.8[a]	38.2[a]
CMV serostatus, %						
Missing	31.7	24.8	28.5	23.1	31.2	28.3
D^+/R^-	11.2[a]	17.9	23.2	21.9	20.0	22.4
D^+/R^+	18.5	18.6	17.6	25.3[a]	18.1	20.4
D^-/R^+	13.2	14.1	12.7	12.9	11.2	12.7
D^-/R^-	25.4	24.6[a]	18.0	16.8	19.5	16.2
Cold ischemic time, mean (SD), hr	2.52 (6.2)[a]	2.12 (5.0)[a]	20.7 (7.1)	17.7 (8.5)[a]	15.9 (6.6)[a]	12.8 (6.0)[a]
Antibody induction, %						
None	44.9[a]	34.9	34.2	29.9	32.5	22.5[a]
Antithymocyte globulin	18.1	26.5	25.4	27.2	18.6	29.8

(Continued on next page)

TABLE 1. *(Continued)*

	2hapLDK (n=205)	Non-2hapLDK (n=1719)	0MMDDK (n=228)	MMDDK (n=964)	0MMSPK (n=215)	MMSPK (n=11951)
IL-2RA	30.2	31.8[a]	26.0	26.7	24.7	23.6
Alemtuzumab/other/missing	6.8[a]	6.8[a]	15.4	16.2	24.2[a]	24.1[a]
Maintenance immunosuppression, %[d]						
Tacrolimus/cyclosporine	91.7	91.7	88.6	89.7	92.1	92.9[a]
Mycophenolic acid	77.1	76.6	73.7	72.4	74.4	74.6
Everolimus/rapamycin	2.9	7.1	4.8	6.7	6.0	6.6
Corticosteroids	68.8[a]	66.4[a]	78.1	76.4	82.8	78.4
UNOS region						
1	5.8	6.5	6.1	7.3	2.3[a]	1.0[a]
2	22.0	20.0	22.8	20.9	13.5[a]	11.9[a]
3	4.9	4.1	5.7	8.8	7.4	14.3[a]
4	4.9	4.1[a]	7.0	5.9	3.7	6.0
5	12.7[a]	11.0[a]	6.6	9.5	7.0	14.2[a]
6	2.4	1.7	1.8	3.2	6.1[a]	3.7
7	16.6	22.6	17.1	11.8[a]	30.2[a]	17.4
8	4.9	5.1	6.1	6.1	5.6	6.9
9	5.8	8.4	7.5	9.34	2.8[a]	2.9[a]
10	11.7	10.5[a]	14.9	11.3	12.6	11.2
11	8.3	6.0	4.4	5.8	8.8	10.5[a]

[a] $P<0.05$, vs. 0MMDDK group
[b] Before transplantation.
[c] Of those listed for kidney transplantation (498 missing values).
[d] As of discharge from the initial transplant hospitalization.
+, cytomegalovirus seropositive; −, cytomegalovirus seronegative; 0MMDDK, kidney transplant from zero HLA mismatched deceased donors; 0MMSPK, kidney-pancreas transplant from zero HLA mismatched deceased donors; 2hapLDK, kidney transplant from living donors sharing 2 haplotypes with recipients; BMI, body mass index; D, donor; ECD, expanded criteria donor; GFR, glomerular filtration rate; HLA, human leukocyte antigen; IL-2RA, interleukin-2 receptor antagonists; MMDDK, kidney transplant from deceased donors with any degree of HLA mismatch with recipients; MMSPK, kidney-pancreas transplant from deceased donors with any degree of HLA mismatch with recipients; Non-2hapLDK, kidney transplant from non-HLA identical living donors; PRA, panel reactive antibody; R, recipient; UNOS, United Network for Organ Sharing.

how patient and allograft survival between 0MMDDK, LDK, and SPK compare and how this should influence a candidate who is awaiting SPK but is offered a 0MMDDK. In answering this question, we used data from the Organ Procurement and Transplantation Network (OPTN)/UNOS and compared kidney graft and patient survival among those receiving 0MMDDK with those receiving SPK and LDK transplantation.

RESULTS

Patients

Among all adult T1DM first-time transplant recipients (who underwent transplantation from 1995–2010) and waitlisted for pancreas/kidney-pancreas (before or by the time of transplant) for which data on human leukocyte antigen (HLA) matching was available, there were 12,166 SPK recipients, 1192 DDK recipients, and 1924 LDK recipients. Of these, 2% (n=215) of SPK and 19% (n=228) of DDK recipients received 0MM organs. For the LDK recipients, the number of transplants with donors and recipients sharing 2 HLA haplotypes (2hap) was 205 (11% of all LDK transplants). After 7 years of follow-up, 49.8% of 2hapLDK, 44.9% of non-HLA identical (non-2hap) LDK, 43.9% of 0MMDDK, and 19.9% of MMDDK patients received a PAK transplant. The median time from kidney transplant to the PAK was 330 days (25th, 149; 75th, 562) for the 2hapLDK (*P* value vs. 0MMDDK, 0.36), 278 days (25th, 144; 75th, 542) for the non-2hapLDK (*P* value vs. 0MMDDK, 0.04), 354 days (25th, 149; 75th, 705) for the 0MMDDK, and 387 days (25th, 149; 75th, 705) for the MMDDK (*P* value vs. 0MMDDK, 0.56) recipients.

Baseline Characteristics

Baseline characteristics of the six cohort groups are described in Table 1. The MMDDK recipients were older than all other groups. Between both DDK and SPK recipients, 0MM groups were composed of proportionally more whites than the HLA-MM groups. A higher proportion of 0MMDDK recipients were classified as overweight (body mass index [BMI], 25–29.9 kg/m^2) compared with both SPK groups. A similar proportion of 0MMDDK and 0MMSPK recipients were obese (BMI ≥30 kg/m^2); in contrast, fewer MMSPK recipients were obese compared with 0MMDDK. The proportion of preemptive transplants was lowest among the two DDK groups.

Donor age was higher for both DDK groups compared with the SPK groups. There were proportionally more white donors and less blacks in the 0MMDDK and SPK groups compared with their MM counterparts. Among all groups, the proportion of donor hypertension was highest for DDK recipients.

Patient Survival

Figure 1A shows unadjusted Kaplan-Meier curves for patient survival. During the 7-year follow-up period, survival of 0MMDDK recipients (84%) was not different from that of the 2hapLDK (89%; log-rank *P*=0.34), non-2hapLDK (83%; log-rank *P*=0.61), 0MMSPK (81%; log-rank *P*=0.17), and MMSPK groups (82%; log-rank *P*=0.38). Patient survival for MMDDK recipients, on the other hand, was significantly lower when compared with the 0MMDDK group (71%; log-rank *P*=0.001).

Cox proportional hazard models were fitted to adjust for risk factors associated with patient survival (Table 2). On univariate analysis, there was no increased risk of death between any of the LDK and SPK groups compared with 0MMDDK. MMDDK was associated with a 94% increased risk of death compared with 0MMDDK (95% confidence

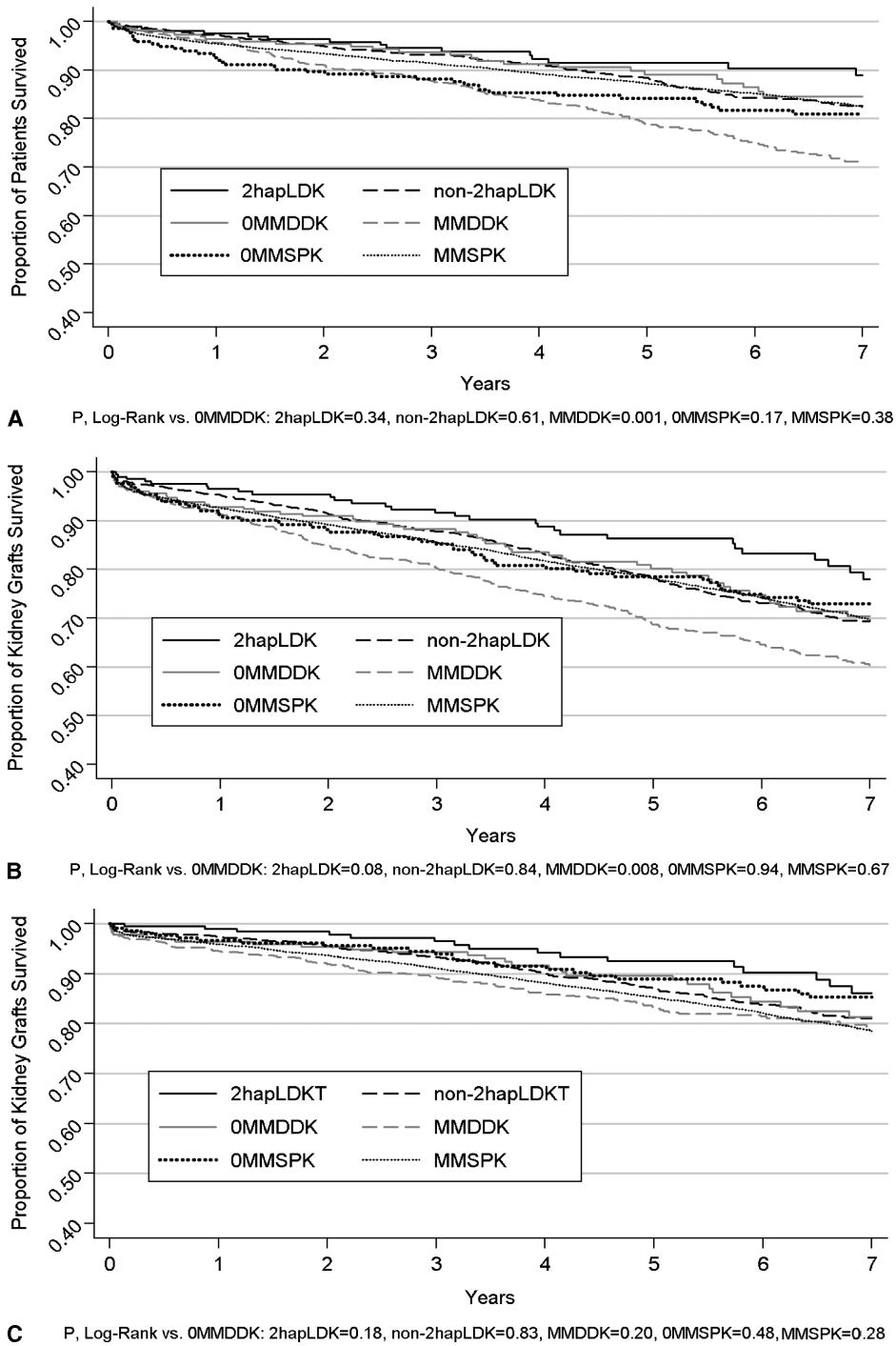

FIGURE 1. Kaplan-Meier survival curves. A, Patient survival; B, Overall kidney survival; C, Death-censored kidney survival.

interval [CI], 1.27–2.95). On multivariate analysis, we performed three levels of adjustment. In the +recipient model, we adjusted for recipient factors only. In this model, there was no increased risk of death between either LDK or SPK group compared with 0MMDDK. MMDDK was associated with more risk of death compared with 0MMDDK (hazard ratio, 1.82; 95% CI, 1.20–2.77). When donor factors were added to the +recipient model (+donor model), there was no effect on our observations from the unadjusted and +recipient models. Finally, after adding transplant characteristics, which consisted of the covariates of induction and maintenance immunosuppression, cytomegalovirus serostatus, transplant year, and transplant region (+transplant model), there was no association between the transplant types of 0MMDDK, 0MMSPK, MMSPK, 2hapLDK, non-2hapLDK, and death. MMDDK continued to have a 73% increased risk of death compared with 0MMDDK (95% CI, 1.14–2.64).

Kidney Allograft Survival

Overall unadjusted kidney graft survival is shown in Figure 1B. There was no difference in kidney graft survival between the 0MMDDK and any of the other SPK or LDK groups. The MMDDK group showed significantly lower kidney survival than that of the 0MMDDK group (60% vs. 70%, respectively; log-rank P=0.007). On comparison of death-censored kidney survival (Fig. 1C), there was no difference between the MMDDK and the 0MMDDK groups (79% vs. 81%, P=0.2), suggesting that the difference in overall unadjusted kidney survival between the 0MMDDK and MMDDK group was mostly because of death with allograft function.

Results of Cox proportional hazards models fitted to adjust for risk factors associated with kidney graft loss are presented in Table 2. On univariate analysis, there was no increased risk of kidney graft loss between any of the LDK and SPK groups compared with 0MMDDK. MMDDK on the other hand was associated with a 50% increased risk of graft failure compared with 0MMDDK (95% CI, 1.11–2.02). On multivariate analysis, neither of the three +recipient, +donor, and +transplant models demonstrated a significant association between the transplant types of 0MMDDK, 0MMSPK, MMSPK, 2hapLDK, non-2hapLDK, and overall kidney failure. In contrast, MMDDK transplantation, even after full adjustment for all donor, recipient, and transplant factors, was associated with a 37% increase in risk of kidney failure compared with 0MMDDK (95% CI, 1.01–1.85). However, after censoring patients because of death with functioning graft from the Cox models, this figure was reduced to 24% and was no longer statistically significant (95% CI, 0.82–1.87). In other words, there was no association between transplant type and the risk of

TABLE 2. Cox analysis of risk factors for patient death and kidney graft loss

	Unadjusted	P	+Recipient Factors[a]	P	+Donor Factors[b]	P	+Transplant Factors[c]	P
Patient death								
0MMDDK	Reference	—	Reference	—	Reference	—	Reference	—
MMDDK	1.94 (1.27–2.95)	**0.002**	1.82 (1.20–2.77)	**0.005**	1.75 (1.15–2.66)	**0.01**	1.73 (1.14–2.64)	**0.01**
0MMSPK	1.39 (0.84–2.32)	0.20	1.41 (0.85–2.34)	0.19	1.50 (0.90–2.51)	0.12	1.59 (0.95–2.65)	0.07
MMSPK	1.19 (0.80–1.77)	0.88	1.22 (0.82–1.81)	0.33	1.27 (0.85–1.90)	0.23	1.35 (0.90–2.02)	0.14
2hapLDK	0.73 (0.39–1.38)	0.34	0.79 (0.42–1.48)	0.46	0.76 (0.40–1.43)	0.39	0.85 (0.45–1.61)	0.62
Non-2hapLDK	1.10 (0.73–1.67)	0.65	1.17 (0.77–1.77)	0.47	1.12 (0.73–1.71)	0.60	1.28 (0.83–1.96)	0.27
Overall kidney loss								
0MMDDK	Reference	—	Reference	—	Reference	—	Reference	—
MMDDK	1.50 (1.11–2.02)	**0.01**	1.45 (1.07–1.96)	**0.02**	1.38 (1.02–1.86)	**0.04**	1.37 (1.01–1.85)	**0.04**
0MMSPK	0.97 (0.66–1.43)	0.89	0.98 (0.66–1.44)	0.90	1.06 (0.71–1.56)	0.78	1.11 (0.75–1.64)	0.60
MMSPK	1.06 (0.80–1.41)	0.66	1.05 (0.79–1.39)	0.72	1.12 (0.84–1.49)	0.42	1.17 (0.88–1.56)	0.27
2hapLDK	0.66 (0.42–1.04)	0.07	0.69 (0.43–1.08)	0.11	0.65 (0.41–1.04)	0.07	0.70 (0.44–1.12)	0.13
Non-2hapLDK	1.01 (0.76–1.37)	0.90	1.04 (0.78–1.41)	0.77	0.98 (0.73–1.33)	0.92	1.06 (0.78–1.44)	0.70
Death-censored kidney loss								
0MMDDK	Reference	—	Reference	—	Reference	—	Reference	—
MMDDK	1.32 (0.88–1.99)	0.17	1.32 (0.87–1.98)	0.18	1.25 (0.83–1.89)	0.28	1.24 (0.82–1.87)	0.30
0MMSPK	0.83 (0.48–1.42)	0.49	0.82 (0.48–1.41)	0.47	0.89 (0.52–1.53)	0.67	0.93 (0.54–1.60)	0.80
MMSPK	1.23 (0.84–1.78)	0.28	1.17 (0.80–1.70)	0.42	1.27 (0.87–1.85)	0.22	1.32 (090–1.93)	0.15
2hapLDK	0.66 (0.35–1.20)	0.17	0.66 (0.36–1.22)	0.17	0.62 (0.34–1.16)	0.14	0.66 (0.35–1.23)	0.19
Non-2hapLDK	1.03 (0.70–1.54)	0.87	1.02 (0.70–1.53)	0.89	0.95 (0.63–1.43)	0.81	1.00 (0.67–1.52)	0.98

Bold values indicate P<0.05.

[a] Adjusted for recipient age, race/ethnicity, gender, BMI, preemptive, and PRA.

[b] Adjusted for all of the above plus donor age, race/ethnicity, gender, BMI, and hypertension.

[c] Adjusted for all of the above plus induction therapy, immunosuppression therapy, CMV serostatus, transplant year, and transplant region.

0MMDDK, kidney transplant from zero HLA mismatched deceased donors; 0MMSPK, kidney-pancreas transplant from zero HLA mismatched deceased donors; 2hapLDK, kidney transplant from living donors sharing 2 haplotypes with recipients; BMI, body mass index; CMV, cytomegalovirus; MMDDK, kidney transplant from deceased donors with any degree of HLA mismatch with recipients; MMSPK, kidney-pancreas transplant from deceased donors with any degree of HLA mismatch with recipients; Non-2hapLDK, kidney transplant from non-HLA identical living donors; PRA, panel reactive antibody.

death-censored kidney graft loss in any of the Cox proportional hazards regression models.

DISCUSSION

Beginning January 29, 2009, OPTN/UNOS eliminated mandatory sharing of nonlocal 0MMDDK for candidates with calculated panel reactive antibody of 20% or less. Subsequent to this, there has been a decrease in the number of 0MMDDK transplants occurring in the United States (*16*). Although 0MMDDK transplants now occur less frequently, some patients may still receive 0MM organ offers. Results of our study show that, among T1DM patients with end-stage renal disease who were listed for SPK and received a kidney transplant (either kidney alone or SPK) through 1995 to 2010, recipients of a 0MMDDK showed comparable kidney allograft and patient survival with SPK and LDK recipients. In contrast, recipients of an MMDDK showed significantly lower patient survival at 7 years after transplantation compared with all other transplant types. In our study, T1DM candidates who were awaiting a SPK did not compromise kidney allograft or patient survival by receiving a 0MMDDK as opposed to SPK.

Multiple studies have reported that DDK transplantation is associated with inferior outcomes compared with SPK. Although some have postulated that better late-term patient survival associated with SPK compared with kidney transplant alone is caused by improved glycemic control (*17*), other studies have indicated that the difference in survival is related more to confounding factors and not the transplant type itself. In an analysis of 6016 type 1 diabetic transplant recipients, SPK recipients showed lower unadjusted kidney allograft loss and death compared with DDK (*7*). However, after multivariate adjustment for recipient and donor characteristics, there was no difference in kidney allograft and patient survival between SPK and DDK transplantation. Wiseman et al. (*13*) attempted to control for differences in donor characteristics between SPK and DDK transplant recipients by comparing outcomes between SPK recipients, DDK alone recipients from donors who also donated a pancreas, and DDK alone recipients from non-pancreas donors. Although the number of DDK alone recipients from pancreas donors was small, there were no differences in kidney allograft and patient survival at 5 years between SPK recipients and DDK alone recipients from a pancreas donor (graft survival, SPK and DDK were 76.2% and 81.9%, respectively, P=0.15; patient survival, SPK and DDK were 89.4% and 87.6%, respectively, P=0.99). In contrast, survival among DDK alone recipients from nonpancreas donors was inferior to the previous two groups.

If a pancreas transplant candidate is simultaneously offered a SPK or DDK, it would be justifiable should the patient opt for SPK, given the glycemic benefits of pancreas transplantation. However, rarely does a candidate receive simultaneous organ offers, and it may be a complicated decision if a pancreas candidate is offered a 0MMDDK before a SPK offer. In this instance, it is important to ascertain whether or not DDK transplantation would compromise patient or allograft longevity compared with SPK. Although survival differences between DDK and SPK may be because of confounding donor factors such as differences in donor quality, these characteristics may be considered to be inherent to the transplant type. For example, in our study, a greater proportion of 0MMDDK donors experienced a history of hypertension and was of older age than SPK donors. These factors have been shown to negatively impact posttransplantation survival in previous studies (*7, 12, 18, 19*).

To account for differences in donor factors, we performed several levels of multivariate adjustment. In an unadjusted model, there was no difference in patient and kidney allograft survival between 0MMDDK, 0MMSPK, and MMSPK. Given that donor characteristics are inherently different between DDK and SPK donors, we performed a + recipient model to adjust for differences in recipient factors alone. In this model, we found no difference in the risk of patient death or kidney allograft loss between 0MMDDK, 0MMSPK, and MMSPK. Finally, we performed a fully adjusted multivariate model that adjusted for recipient, donor, and transplant characteristics (+transplant model in Table 2) to evaluate whether transplant type was independently associated with outcome. This model also did not show any independent association between transplant type and kidney allograft or patient survival when comparing 0MMDDK, 0MMSPK, and MMSPK. Therefore, our study suggests that type 1 diabetic recipients awaiting SPK did not compromise kidney allograft or patient survival by receiving a 0MMDDK as opposed to SPK.

Our study does not account for a number of factors that may influence whether or not a candidate should accept a 0MMDDK offer versus wait for an SPK. Our observations primarily reflect those associated with transplantation of a standard criteria donor, which was the case in approximately 90% of 0MMDDK recipients. Given the low number of expanded criteria donor transplants among the 0MMDDK group, it is not known whether our observations can be generalized to 0MMDDK transplants from expanded criteria donors. Therefore transplant professionals should carefully consider issues of donor quality when presenting a 0MMDDK offer to a type 1 diabetic SPK candidate. Second, regional waiting times and the likelihood of pancreas transplantation should be considered when deciding between 0MMDDK or waiting for an SPK. Given that only 44% of 0MMDDK recipients in our study went on to receive a PAK transplant, it is possible that untoward complications after kidney transplantation including postoperative complications, acute rejection episodes, and compromised kidney function could jeopardize a patient's future candidacy for pancreas transplant. Furthermore, it has been previously described by our group and others that pancreas graft survival among PAK recipients is approximately 20% lower than that of SPK recipients (*8, 20, 21*). Last, other factors, such as the patient's interests and how a patient's quality of life may be affected by the inclusion or omission of a pancreas transplant should be considered.

Our study was limited by its retrospective design. There are inherent differences in recipient and donor baseline characteristics between those who are offered and receive a 0MMDDK rather than SPK. Nevertheless, one of the strengths of our study is that we attempted to minimize selection bias by including only candidates who were waitlisted for a pancreas transplant. Despite no appreciable

difference in effect size of transplant type (excluding MMDDK) on patient and kidney allograft survival after multivariate adjustment for recipient and donor characteristics, there may be unmeasured differences that were not accounted for because of this study's retrospective design. Our study has mainly addressed differences in survival up to 7 years, although it is possible that survival differences may become apparent in subsequent years. Our group, along with others, has previously shown that early patient survival with SPK is lower compared with LDK but exceeds that of LDK after a period of anywhere from 5 to 10 years (*11, 22, 23*). It is unclear whether a similar phenomenon exists for SPK compared with 0MMDDK. Last, further insight as to how acute rejection impacted the findings in our study was limited because of uncertainty in the definition of rejection in kidney-pancreas recipients in the OPTN/UNOS database. Episodes of acute rejection were recorded on separate kidney and pancreas recipient follow-up forms before 2003 and then on a single kidney-pancreas recipient follow-up form after January 2003. It was unclear whether a kidney rejection in a kidney-pancreas recipient was defined as a rejection occurring in one or both organs and whether this would be an appropriate comparison to rejections occurring in a recipient of a single organ.

In conclusion, our study has shown that there were no differences in patient and kidney allograft survival among 0MMDDK recipients compared with SPK. These results suggest that it may be reasonable for a candidate awaiting SPK to consider accepting a 0MMDDK if offered.

MATERIALS AND METHODS

Sources of Data and Study Population

The OPTN/UNOS database (as of March 31, 2011) was used to select adults (≥18 years) with T1DM with at least one follow-up report, who received LDK, DDK, or SPK transplantation between January 1995 and December 2010. Patients with a history of any prior organ transplantation were excluded. In addition, to include only those who were potential candidates for kidney-pancreas transplantation, only those recipients who were placed on the pancreas/kidney waitlist before or by the time of kidney transplant were included in the kidney transplant subgroups. To further categorize the SPK and DDK recipients into 0MM and MM subgroups, the "HLAMIS" variable, a calculated UNOS variable which assesses the level of mismatch between donor and recipient was used. Recipients with missing HLAMIS values were excluded (n=157). LDK recipients were subdivided into 2hap and non-2hap groups. 2hapLDK was defined as the donor being a 0MM full sibling, excluding identical twins of the recipient. Other LDK recipients were considered non-2hap. The final study population included 15,282 recipients (2hapLDK, 205; non-2hapLDK, 1719; 0MMDDK, 228; MMDDK, 964; 0MMSPK, 215; MMSPK, 11,951).

Statistical Analysis

Donor, recipient, and transplant characteristics were described using mean (SD), medians with interquartile ranges, or frequencies, where appropriate. To compare categorical and continuous variables, the chi-square and Kruskal-Wallis tests were used, respectively. Patients were followed up to a maximum of 7 years, and the outcomes of kidney allograft and patient survival were analyzed using the Kaplan-Meier product limit method with significance tested using the log-rank test. For patient survival analyses, patients were censored for death or at 7 years of follow-up. For kidney graft survival analyses, patients were censored for patient death, kidney failure (defined as a return to dialysis or retransplantation), or at the end of 7 years.

Hazard ratios and 95% CIs of death, kidney graft loss, and death-censored kidney graft failure were calculated using stepwise Cox proportional hazards.

For mortality and graft failure analysis, the following four models of multivariate analysis were used: (1) an unadjusted model only comparing transplant types, (2) a recipient-adjusted model (+recipient) that included transplant type and recipient variables (gender, race, age, percentage of peak panel reactive antibodies, BMI, and history of dialysis before transplantation), (3) a recipient and donor-adjusted model (+donor) including all of the previously mentioned plus donor variables (age, gender, race, BMI, and hypertension), and (4) a fully adjusted model (+transplant) including all of the factors in +donor model plus transplant factors (UNOS region, donor/recipient cytomegalovirus seropairing, transplant year, and induction/maintenance immunosuppression therapy). All P values were two-tailed, and P values of <0.05 were considered significant. STATA version 9.2 (StataCorp, College Station, TX) was used for all statistical analyses.

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