Impact of Deceased Donor Diabetes Mellitus on Kidney Transplant Outcomes: A Propensity Score-Matched Study

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Background. There is a paucity of population-level data on the long-term outcomes of kidney transplants from deceased donors with a history of diabetes mellitus (DM).

Methods. We examined the association of donor DM with graft and patient survival in 66,654 deceased donor kidney transplant recipients (KTR) from January 1, 1994, to December 31, 2003, in the United States. KTR receiving kidneys from DM versus non-DM donors were compared in the total study population and in a 1:1 propensity score-matched cohort.

Results. A total of 2302 KTR received kidneys from DM donors over the study period. Older and female recipients, increased donor age, longer cold ischemia time, and transplants after 2000 were associated with a greater odds of receiving a DM donor. After propensity score matching, Cox proportional hazards models revealed hazard ratios of 1.11 (95% CI: 1.02–1.22), 1.17 (95% CI: 1.04–1.33), and 1.06 (95% CI: 0.94–1.18) for graft failure, death-censored graft failure, and patient mortality, respectively. No significant effect measure modification was seen across various patient subgroups. Longer duration of donor DM was generally associated with an increased risk of adverse outcomes. The results were robust to several sensitivity analyses.

Conclusions. The long-term graft survival of KTR with DM donors is significantly inferior to non-DM donors, but the absolute difference is small. DM donors do not adversely impact patient survival. This suggests that DM donors may be effectively used to expand the donor pool, but evidence-based guidelines on the appropriate selection of these donors are needed.

Keywords: Deceased donor, Diabetes mellitus, Kidney transplant outcomes, Propensity score.

(*Transplantation* 2009;88: 251–260)

In view of the increasing gap between the supply and demand of deceased donor kidneys for transplantation, donor acceptability criteria have been revisited, and as a result, expanded criteria donor (ECD) kidneys have been used as a means to increase the potential donor pool over the last several years. ECD kidneys are associated with more than or equal to 70% increase in the risk of graft failure versus standard criteria donor kidneys and are defined as donors age more than or equal to 60 years or age 50 to 59 years in the presence of at least two of three risk factors (i.e., hypertension [HTN], serum creatinine >1.5 mg/dL, or donor death due to cerebrovascular accident) (*1*). Despite their inferior outcomes, recipients of ECD kidneys experience improved survival when compared with their wait-listed counterparts on dialysis (*2*, *3*).

Diabetes mellitus (DM) in a potential deceased kidney donor has been generally regarded as a relative contraindication to kidney donation. In support of this claim, Sung et al. (*4*) used data from the Scientific Registry of Transplant Recipients to show that the adjusted odds ratio for discarding

This work was supported by the Phase 1 Clinician-Scientist Award of the Canadian Institutes of Health Research (S.J.K.).

The authors declare no conflict of interest.

The interpretation and reporting of these data is the responsibility of the author and in no way should be seen as an official policy or interpretation of the U.S. government, the NIDDK, or the National Institutes of Health.

S.J. Kim had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: M. Ahmad, S.J. Kim, E.H. Cole. Acquisition of data: S.J. Kim. Data analysis and interpretation: M. Ahmad, E.H. Cole, C.J. Cardella, D.C. Cattran, J. Schiff, K.J. Tinckam, S.J. Kim. Drafting of the manuscript: M. Ahmad, S.J. Kim. Critical revision of the manuscript for important intellectual content: M. Ahmad, E.H. Cole, C.J. Cardella, D.C. Cattran, J. Schiff, K.J. Tinckam, S.J. Kim. Statistical analysis: S.J. Kim. Study supervision: S.J. Kim, E.H. Cole.

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Received 5 March 2009. Revision requested 23 March 2009.

Accepted 16 April 2009.

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ISSN 0041-1337/09/8802-251

DOI: 10.1097/TP.0b013e3181ac68a9

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kidneys from deceased donors with a history of DM was 1.89 ($P<0.0001$) when compared with non-DM kidney donors. The higher discard rate of these kidney donors likely reflects the impression that the damage incurred by DM reduces the kidney's ability to withstand procurement injury and decreases the likelihood of favorable long-term allograft outcomes (*5*). Interestingly, the original ECD analysis by Port et al. (*1*) revealed that DM in the donor did not independently predict graft failure. However, this study did not specifically perform a comparative analysis of DM versus non-DM donors and their associated outcomes.

The extent to which DM donors are being used and their associated outcomes compared with appropriate concurrent controls are largely unknown. DM (both diagnosed and undiagnosed) affects approximately 9.3% of the U.S. adult population and, thus, represents a substantial number of potential deceased kidney donors (*6*). Successful clinical utilization of even some of these kidneys is likely to be of considerable benefit to end-stage renal disease (ESRD) patients awaiting kidney transplantation. Therefore, the aim of this study is to evaluate the long-term outcomes (i.e., graft failure, death-censored graft failure, and patient mortality) of kidney transplants from deceased donors with a history of DM versus no DM using standard multivariable statistical methods and 1:1 propensity score matching to optimally adjust for measured confounders. The potential impact of concomitant recipient DM and the duration of donor DM are also explored.

PATIENTS AND METHODS

Data for this study were obtained from the United States Renal Data System (USRDS). The study population comprised of adult (age ≥18 years) recipients of a solitary, first, deceased donor kidney transplant in the United States from January 1, 1994, to December 31, 2003, with follow-up until December 31, 2004.

A history of DM in the deceased donor of a kidney transplant recipients (KTR) was the main exposure variable of interest. Donor DM status and duration of DM were retrieved from the variable "dhdiab" in the USRDS Standard Analysis Files. This information was originally collected and recorded on the United Network for Organ Sharing deceased donor registration form based on the donor's medical records or the next of kin at the time of the organ donation request. Recipients of living donor kidneys, retransplants, multiorgan transplants (including kidney-pancreas), and pediatric patients (i.e., age <18 years at the time of transplantation) were excluded from the analysis. DM status in the deceased donor, duration of DM, and the interaction of donor and recipient DM status were analyzed in multivariable statistical models.

The outcomes of interest in this study included graft failure, death-censored graft failure, and patient mortality. Graft failure was defined as a return to maintenance dialysis, preemptive retransplant, or death. Death-censored graft failure was similarly defined, except event times were censored when patients died with a functioning graft. Patient mortality included all causes of death after transplantation. Survival analyses were performed from the time of transplantation to a maximum follow-up of 10 years. In addition, conditional survival analyses were performed whereby patients experiencing a failure event in the first year after transplantation were excluded from the analysis.

A multivariable logistic regression model was fitted to estimate the relative odds of receiving a DM (vs. non-DM) donor kidney as a function of recipient factors (including age, sex, race, cause of ESRD, peak panel reactive antibodies, and time on dialysis before transplant), donor factors (including age, sex, race, cause of death, history of HTN, and terminal serum creatinine), and transplant factors (including cold ischemia time, human leukocyte antigen mismatches, and year of transplant) in the total study population. These covariates are used in registry-based outcomes analyses of KTR. The logistic model was also used to generate a propensity score for each individual in the dataset. The propensity score is the probability of receiving a DM (vs. non-DM) donor given the covariates in the model (*7*). Matching, stratification, and adjustment on the propensity score is an alternate, and potentially more effective, way to comprehensively account for imbalances in measured baseline characteristics because of nonrandom allocation of the exposure of interest (*8–10*). The Hosmer-Lemeshow goodness-of-fit test showed that the propensity score model adequately explained the data ($P=0.50$), and the area under the receiver operating characteristic curve indicated reasonable model discrimination (c-statistic=0.7655). The propensity scores were subsequently used by the Stata command "psmatch2" to optimally match each DM donor KTR with a non-DM donor KTR having a similar probability of receiving a DM donor (*11*). A caliper width of 0.015 was used and nonexposed KTR were sampled without replacement. The effectiveness of bias reduction after matching was assessed by absolute standardized differences expressed as a percentage of the pooled standard deviation (*12*, *13*). A value closer to zero for a given baseline characteristic indicates greater balance in the distribution of that characteristic across exposure groups.

The Kaplan-Meier product limit method was used to examine all time-to-event outcomes across the exposure groups of interest. The log-rank statistic was used to test the null hypothesis of no difference between the survival curves. Cox proportional hazards models were fitted to ascertain the relative hazard of graft failure, death-censored graft failure, and patient mortality in DM versus non-DM donor KTR while adjusting for potential confounders. These models were fitted to both the total study population and the propensity score-matched cohort. For the latter, robust standard errors were used to account for the individual-level matching of exposed and unexposed KTR. The assumption of proportionality was evaluated using scaled Schoenfeld residuals and log(−log[survival]) versus log(survival time) curves. No significant departures from proportionality were detected.

Prespecified subgroup analyses were performed in patient subpopulations, considered to be at increased risk for graft failure and patient mortality. Moreover, the impact of DM duration in deceased kidney donors on the main study outcomes was also evaluated. Finally, a number of sensitivity analyses were performed including (1) adjustments for comorbidity based on the Center for Medicare and Medicaid Services (CMS) ESRD 2728 form and (2) an assessment of study outcomes conditional on 6-month posttransplant survival and 1-year posttransplant survival. Analyses were performed using Stata/MP, version 10 for Windows (StataCorp, College Station, TX). A two-sided P value less than 0.05 was considered

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significant. The research ethics board of the Toronto General Hospital, University Health Network, approved the study.

RESULTS

A total of 108,669 kidney transplants, performed from January 1, 1994, to December 31, 2003, were evaluated for inclusion into the study cohort. The following exclusions were made: (1) 40,958 living donor transplants and (2) 1057 KTR with less than 3% missingness on specific recipient (i.e., sex and race) and donor (i.e., sex, cause of death, serum creatinine, and HTN) variables. Of the remaining 66,654 KTR, 2302 (3.5%) received a DM donor and 64,352 (96.5%) received a non-DM donor. After 1:1 propensity score matching, 2302 patients were selected from the pool of 64,352 non-DM deceased donor KTR as controls for the 2302 DM deceased donor KTR (total sample size for the propensity score-matched cohort=4604).

Table 1 shows the baseline recipient, donor, and transplant characteristics for both the total and propensity score-matched study cohorts. The distribution of recipient age, donor age, donor cause of death, donor HTN, donor serum creatinine, and transplant era showed substantial differences across DM donor groups in the total study population. After propensity score matching, differences across the groups diminished considerably. This was reflected by reductions in the absolute standardized difference across almost all baseline variables when comparing the matched with the total study cohort (Table 1). Of note, the mean (±SD) donor Cockcroft-Gault creatinine clearance in DM versus non-DM donors were 97.8 (±48.4) versus 92.7 (±52.9) mL/min ($P=0.0006$). These differences were adjusted for in Cox regression models (see below).

Correlates of receiving a DM donor among patients in the total study population are shown in Table 2. Older recipient age, older donor age, presence of donor HTN, moderate elevations in donor serum creatinine, cold ischemia time more than 12 hr, and transplants since 2000 were positively associated with receiving a DM donor. There was also a trend toward slightly greater use of DM donors in female recipients. On the other hand, DM or other causes of ESRD, female donor sex, and donor death due to cerebrovascular accident/stroke, head trauma, or central nervous system tumor were negatively associated with DM in the donor.

Figure 1 shows Kaplan-Meier survival curves for each of the three main outcomes (i.e., graft survival, death-censored graft survival, and patient survival) in both the total and propensity score-matched study populations. The 10-year survival estimates for non-DM versus DM donors in the total study population were 42.9% versus 30.9% (Fig. 1A), respectively. Estimates for death-censored graft survival and patient survival were 63.7% versus 54.6% (Fig. 1C) and 59.8% versus 50.8% (Fig. 1E), respectively. The log-rank test was significant for all of these outcomes ($P<0.0001$). Differences in the survival curves for non-DM versus DM donors diminished considerably after propensity score matching. Ten-year estimates of graft survival, death-censored graft survival, and patient survival in the matched cohort were 34.4% versus 30.9% (Fig. 1B), 57.1% versus 54.6% (Fig. 1D), and 52.1% versus 50.8% (Fig. 1F), respectively. The log-rank tests for graft and death-censored graft survival were statistically significant ($P=0.02$ and 0.01), whereas patient survival was not significant ($P=0.34$).

The results of the Cox proportional hazards models are presented in Table 3. Unadjusted analyses in the total study cohort, comparing DM with non-DM donors, revealed significant hazard ratios (HR) of 1.40 to 1.41 for all study outcomes. After adjustment for the recipient, donor, and transplant characteristics outlined in Table 1, the HR were substantially diminished but remained significantly elevated. HR estimates from the propensity score-matched cohort were 1.11 (95% CI: 1.01–1.21) for graft failure, 1.17 (95% CI: 1.03–1.32) for death-censored graft failure, and 1.06 (95% CI: 0.95–1.18) for patient mortality. The graft survival figures were similar to the fully adjusted model from the total study population, but the relative hazard for patient mortality was considerably diminished and no longer statistically significant. Adjustment for donor Cockcroft-Gault creatinine clearance did not appreciably change the results.

Table 4 displays the results of subgroup analyses. The relation between DM status of the donor and the three main study outcomes generally showed no significant heterogeneity across the subgroups. Of note, the donor DM-outcome HR were similar across recipient DM groups. There was a suggestion that standard criteria donor transplants were relatively more susceptible to the detrimental effects of donor DM when compared with ECD transplants. However, this effect measure modification was only significant for death-censored graft failure and modest in overall magnitude.

Table 5 displays the impact of donor DM duration on the risk of graft failure, death-censored graft failure, and patient mortality. Using non-DM donors as the reference group, donors with a history of DM for more than 5 years had a significantly increased risk of graft failure by 22%. A similar threshold or dose-response relation was not observed for death-censored graft failure. Although the risk of death-censored graft failure was significantly elevated by 33% for donors with DM of 6 to 10 years duration, donors with DM for more than 10 years were not associated with a significantly increased risk. Patient mortality was significantly increased by 27% in KTR receiving a donor with more than 10 years of DM.

The main results were robust to the following sensitivity analyses: (1) adjustments for co-morbidities captured at dialysis initiation; (2) conditional survival beyond 6-months posttransplant; and (3) conditional survival beyond 1-year posttransplant.

DISCUSSION

This study revealed that transplanting kidneys from deceased donors with a history of DM have implications for long-term graft outcome. The relative hazards for graft failure, death-censored graft failure, and patient mortality over a 10-year follow-up period were modestly elevated at 11%, 17%, and 6%, respectively. Patient mortality was not statistically significant. Despite the increased risk of adverse graft outcomes for KTR of DM donors, the absolute difference in adjusted graft survival (3.3%) and death-censored graft survival (2.5%) at 10 years was relatively small. This implies that the number of patients who need to be transplanted before one additional graft failure event is 30. Similarly, 40 kidney transplants may be performed for every additional death-

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TABLE 1. Characteristics of the total and propensity score-matched population

Study characteristics	All KTR with non-DM donors (N=64,352)	Propensity score-matched cohort: KTR with DM donors (N=2302)	Propensity score-matched cohort: KTR with non-DM donors[a] (N=2302)	Absolute standardized difference before matching	Absolute standardized difference after matching
Recipient age (yr)					
18–34.9	10,758 (16.7)	257 (11.2)	224 (9.7)	16.1	4.7
35–49.9	23,158 (36.0)	673 (29.2)	683 (29.7)	14.4	1.0
50–64.9	23,884 (37.1)	1016 (44.1)	1050 (45.6)	14.3	3.0
≥65	6552 (10.2)	356 (15.5)	345 (15.0)	15.8	1.3
Recipient sex					
Male	39,036 (60.7)	1377 (59.8)	1401 (60.9)	1.7	2.0
Female	25,316 (39.3)	925 (40.2)	901 (39.1)	1.7	2.0
Recipient race					
White	41,787 (64.9)	1416 (61.5)	1426 (61.9)	2.0	1.1
Black	18,523 (28.8)	731 (31.7)	714 (31.0)	4.9	0.8
Asian	3120 (4.9)	119 (5.2)	127 (5.5)	8.0	1.1
Other	922 (1.4)	36 (1.6)	35 (1.5)	1.3	1.0
Cause of ESRD					
Glomerulonephritis	15,317 (23.8)	568 (24.7)	580 (25.2)	2.0	1.1
Diabetes mellitus	18,855 (29.3)	624 (27.1)	631 (27.4)	4.9	0.8
Hypertension	13,544 (21.1)	562 (24.4)	551 (23.9)	8.0	1.1
Other	13,851 (21.5)	442 (19.2)	429 (18.6)	5.8	1.4
Unknown/missing	2785 (4.3)	106 (4.6)	111 (4.8)	1.3	1.0
Peak PRA (%)					
<10	49,148 (74.8)	1725 (74.9)	1740 (75.6)	0.3	1.5
≥10	15,653 (22.8)	503 (21.9)	491 (21.3)	2.2	1.3
Unknown/missing	1551 (2.4)	74 (3.2)	71 (3.1)	4.9	0.7
Time on dialysis					
Preemptive	3549 (5.5)	108 (4.7)	88 (3.8)	3.7	4.3
0–5 mo	3257 (5.1)	88 (3.8)	94 (4.1)	6.0	1.3
6–11 mo	5947 (9.2)	171 (7.4)	152 (6.6)	6.6	3.2
12–23 mo	14,442 (22.4)	463 (20.1)	452 (19.6)	5.7	1.2
24–35 mo	12,251 (19.0)	475 (20.6)	489 (21.2)	4.0	1.5
36–47 mo	9060 (14.1)	346 (15.0)	348 (15.1)	2.7	0.2
≥48 mo	15,846 (24.6)	651 (28.3)	679 (29.5)	8.3	2.7
ECD transplant					
Yes	14,760 (22.9)	949 (41.2)	911 (39.6)	39.9	3.4
No	49,592 (77.1)	1353 (58.8)	1391 (60.4)	39.9	3.4
Donor age (yr)					
0–9	3280 (5.1)	29 (1.3)	21 (0.9)	22.0	3.5
10–39	29,398 (45.7)	458 (19.9)	442 (19.2)	57.1	1.7
40–59	19,824 (30.8)	1203 (52.3)	1233 (53.6)	44.6	2.6
≥60	4769 (7.4)	377 (16.4)	371 (16.1)	28.0	0.7
Unknown/missing	7081 (11.0)	235 (10.2)	235 (10.2)	2.6	0.0
Donor sex					
Male	38,369 (59.6)	1273 (55.3)	1262 (54.8)	8.7	1.0
Female	25,983 (40.4)	1029 (44.7)	1040 (45.2)	8.7	1.0
Donor race					
White	54,113 (84.1)	1904 (82.7)	1919 (83.4)	3.7	1.7
Black	7045 (11.0)	256 (11.1)	241 (10.5)	0.5	2.1
Asian	975 (1.5)	42 (1.8)	45 (1.9)	2.4	0.9
Other	472 (0.7)	18 (0.8)	16 (0.7)	0.6	1.0
Unknown/missing	1747 (2.7)	82 (3.6)	81 (3.5)	4.9	0.2

(*Continued*)

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TABLE 1. Continued

Study characteristics	All KTR with non-DM donors (N=64,352)	Propensity score-matched cohort: KTR with DM donors (N=2302)	Propensity score-matched cohort: KTR with non-DM donors[a] (N=2302)	Absolute standardized difference before matching	Absolute standardized difference after matching
Cause of death					
Anoxia	6241 (9.7)	360 (15.7)	364 (15.8)	17.9	0.5
CVA/stroke	24,593 (38.2)	1320 (57.3)	1326 (57.6)	39.0	0.6
Head trauma	31,597 (49.1)	522 (22.7)	516 (22.4)	57.3	0.7
CNS tumor	625 (1.0)	24 (1.0)	28 (1.2)	0.7	1.6
Other	1296 (2.0)	76 (3.3)	68 (2.9)	8.0	2.0
Donor hypertension					
Yes	11,328 (17.6)	1058 (46.0)	1079 (46.9)	82.1	1.8
No	53,024 (82.4)	1244 (54.0)	1223 (53.1)	82.1	1.8
Donor serum creatinine (mg/dL)					
<1.0	32,562 (50.6)	960 (41.7)	982 (42.7)	17.9	1.9
1.0–1.4	22,416 (34.8)	918 (39.9)	907 (39.4)	10.4	1.0
1.5–1.9	5888 (9.2)	274 (11.9)	265 (11.5)	9.0	1.2
≥2.0	3486 (5.4)	150 (6.5)	148 (6.4)	4.6	0.3
Cold ischemia time (hr)					
0–11.9	9421 (14.6)	254 (11.0)	245 (10.6)	10.8	1.3
12–23.9	30,988 (48.1)	1115 (48.4)	1110 (48.2)	0.6	0.5
24–35.9	15,370 (23.9)	588 (25.5)	576 (25.0)	3.8	1.2
≥36	2550 (4.0)	103 (4.5)	124 (5.4)	2.5	4.2
Unknown/missing	6023 (9.4)	242 (10.5)	247 (10.7)	3.9	0.8
HLA mismatches					
0	7833 (12.2)	255 (11.1)	223 (9.7)	3.4	4.5
1	2209 (3.4)	65 (2.8)	68 (2.9)	3.5	0.8
2	6053 (9.4)	201 (8.7)	208 (9.0)	2.3	1.1
3	12,675 (19.7)	415 (18.0)	422 (18.3)	4.3	0.8
4	15,190 (23.6)	576 (25.0)	599 (26.0)	3.3	2.3
5	12,680 (19.7)	475 (20.6)	463 (20.1)	2.3	1.3
6	6354 (9.9)	247 (10.7)	245 (10.6)	2.8	0.3
Unknown/missing	1358 (2.1)	68 (3.0)	74 (3.2)	5.4	1.5
Transplant era					
1994–1996	17,171 (26.7)	437 (19.0)	431 (18.7)	18.4	0.7
1997–1999	18,917 (29.4)	628 (27.3)	617 (26.8)	4.7	1.1
2000–2003	28,264 (43.9)	1237 (53.7)	1254 (54.5)	19.7	1.4

[a] This group is a subset of all KTR with non-DM donors who were propensity score matched to KTR with DM donors.

KTR, kidney transplant recipients; DM, diabetes mellitus; ESRD, end-stage renal disease; PRA, panel reactive antibody; ECD, expanded criteria donor; HLA, human leukocyte antigen; CVA, cerebrovascular accident; CNS, central nervous system.

censored graft failure event. Importantly, recipient DM status did not significantly modify the relation between donor DM and each of the three main study outcomes. Furthermore, donor DM duration of more than 5 and 10 years were associated with a significantly increased risk of graft failure and patient mortality, respectively.

Most previous studies examining DM donors have been anecdotal, uncontrolled, with small sample sizes, short-term follow-up, and subject to strong selection biases (*14–22*). The two largest comparative studies of DM versus non-DM donors include a single-center study and an earlier analysis of U.S. registry data (*5*, *23*). Becker et al. (*5*) reviewed their experience using DM donors at the University of Wisconsin Kidney Transplant Program from 1983 to 2000. Of 2013 total deceased donor kidney transplants, 42 were DM donors. In univariable analyses, DM donors were associated with a slightly higher mean discharge serum creatinine and a significantly increased frequency of posttransplant proteinuria. However, there was no difference in intermediate (i.e., acute rejection) or long-term (i.e., graft and patient survival) outcomes. Unfortunately, the study by Becker et al. included a relatively small number of DM donor transplants and the analysis did not adjust for potential confounders. In addition, the generalizability of the findings may be limited because there are likely center-based differences in donor manage-

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TABLE 2. Logistic regression model relating baseline factors and receipt of a diabetic donor in the total study population (N=66,654)

Study variable	Odds ratio	95% Confidence interval	*P*
Recipient age (yr)			
18–4.9	1.00	Reference	—
35–9.9	1.10	0.95–1.28	0.20
50–4.9	1.35	1.17–1.56	<0.0001
≥5	1.47	1.24–1.75	<0.0001
Recipient sex			
Male	1.00	Reference	—
Female	1.09	1.00–1.19	0.06
Recipient race			
White	1.00	Reference	—
Black	1.03	0.93–1.14	0.56
Asian	0.97	0.79–1.18	0.74
Other	1.09	0.77–1.54	0.64
Cause of ESRD			
Glomerulonephritis	1.00	Reference	—
Diabetes mellitus	0.84	0.74–0.95	0.005
Hypertension	1.00	0.88–1.13	0.95
Other	0.83	0.73–0.95	0.007
Unknown/missing	0.99	0.79–1.23	0.90
Peak PRA (%)			
<10	1.00	Reference	—
≥10	0.95	0.86–1.06	0.38
Unknown/missing	1.20	0.93–1.55	0.16
Time on dialysis			
Preemptive	1.00	Reference	—
0–5 mo	0.91	0.68–1.23	0.55
6–11 mo	0.95	0.74–1.22	0.68
12–23 mo	0.98	0.78–1.22	0.85
24–35 mo	1.12	0.90–1.40	0.31
36–47 mo	1.03	0.81–1.29	0.82
≥48 mo	1.03	0.83–1.28	0.80
Donor age (yr)			
0–9	1.00	Reference	—
10–39	1.86	1.27–2.72	0.001
40–59	3.92	2.68–5.74	<0.0001
≥60	4.26	2.87–6.32	<0.0001
Unknown/missing	2.46	1.65–3.66	<0.0001
Donor sex			
Male	1.00	Reference	—
Female	0.88	0.80–0.97	0.008
Donor race			
White	1.00	Reference	—
Black	0.97	0.85–1.12	0.72
Asian	1.01	0.73–1.40	0.93
Other	0.96	0.59–1.57	0.89
Unknown/missing	1.65	1.31–2.09	<0.0001
Cause of death			
Anoxia	1.00	Reference	—
CVA/stroke	0.48	0.42–0.55	<0.0001
Head trauma	0.38	0.33–0.43	<0.0001
CNS tumor	0.63	0.41–0.97	0.03
Other	0.91	0.70–1.18	0.48
Donor hypertension			
No	1.00	Reference	—
Yes	3.60	3.27–3.97	<0.0001
Donor serum creatinine (mg/dL)			
<1.0	1.00	Reference	—
1.0–1.4	1.21	1.10–1.34	<0.0001
1.5–1.9	1.17	1.01–1.35	0.04
≥2.0	1.15	0.95–1.38	0.14
Cold ischemia time (hr)			
0–11.9	1.00	Reference	—
12–23.9	1.27	1.10–1.46	0.001
24–35.9	1.31	1.12–1.53	0.001
≥36	1.27	1.00–1.62	0.05
Unknown/missing	1.24	1.03–1.49	0.02
HLA mismatches			
0	1.00	Reference	—
1	0.85	0.64–1.13	0.27
2	0.95	0.78–1.15	0.58
3	0.93	0.79–1.09	0.36
4	1.04	0.89–1.22	0.63
5	0.99	0.84–1.16	0.89
6	0.97	0.80–1.17	0.74
Unknown/missing	1.19	0.89–1.60	0.25
Transplant era			
1994–1996	1.00	Reference	—
1997–1999	1.12	0.99–1.27	0.08
2000–2003	1.53	1.35–1.72	<0.0001

ESRD, end-stage renal disease; PRA, panel reactive antibody; HLA, human leukocyte antigen; CVA, cerebrovascular accident; CNS, central nervous system.

ment and selection strategies that can impact both the likelihood of using DM donors and their associated outcomes.

In an analysis of the USRDS, Ojo et al. (*23*) studied 25,039 deceased donor, KTR from July 1, 1994, to June 30, 1997, to determine the impact of donor HTN or DM on graft and patient survival. In total, 4035 patients received transplants from donors with a history of HTN or DM (n=3472 with HTN alone, n=322 with DM only, and n=241 with both). Each affected (i.e., donor HTN or DM or both) KTR was matched 1:1 with an unaffected KTR of the same donor age (in 5-year age groups), donor and recipient race, and year of transplantation. Three-year graft survival was 75% in unaffected KTR versus 72% in KTR with DM donors ($P=0.012$). The comparable figures for 3-year patient survival were 88% versus 84% ($P=0.03$). Although an adjusted HR for affected versus unaffected KTR was presented (HR=1.09, $P=0.07$), the HR for DM donor status was not reported. When compared with Ojo et al., our study had a longer follow-up period, examined four-times the number of DM donor KTR, excluded retransplants, and used a propensity score matching algorithm that optimally matched DM and non-DM donor KTR using all baseline characteristics.

It has been shown that DM-related histologic changes may resolve over time when the kidneys from diabetic donors are transplanted into non-DM recipients (*24*, *25*). Moreover, the achievement of long-standing euglycemia after pancreas transplantation in nonuremic patients with type 1 DM may reverse the functional and structural changes associated with diabetic nephropathy (*26*). These studies indirectly question the policy of discarding potential kidney donors with DM, particularly for recipients without DM at the time of transplantation. Although experimental data suggest that diabetic kidneys sustain greater injury after an ischemic insult (*27*–*32*), there was no significant effect measure modification in

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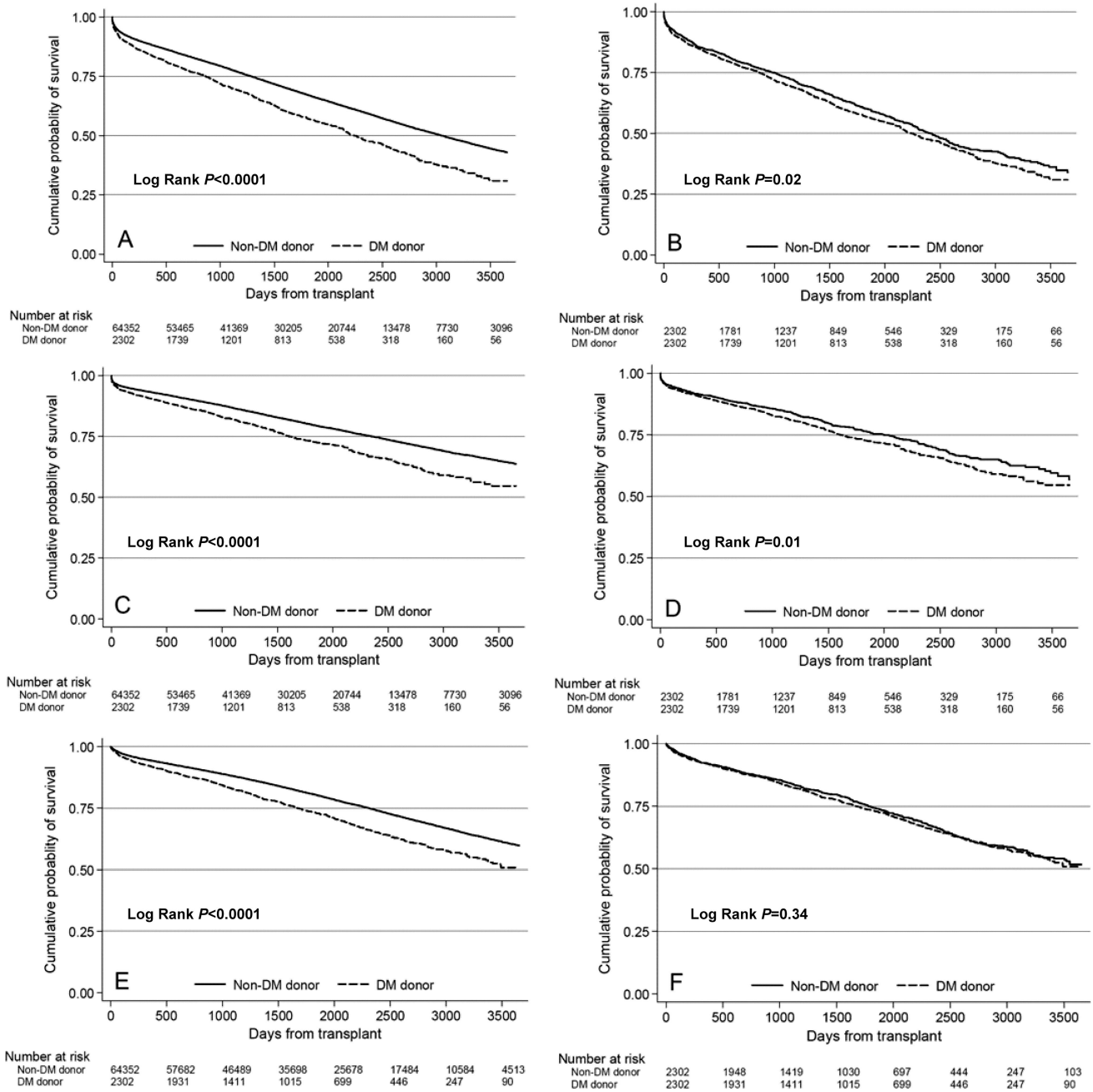

FIGURE 1. Kaplan-Meier curves for graft survival (A, B), death-censored graft survival (C, D), and patient survival (E, F) stratified by donor diabetes mellitus status for the total (*left column*) and propensity score-matched (*right column*) cohorts.

the relation between donor DM status and outcome across cold ischemia time groups in this study (Table 4). Moreover, there was no difference in the adjusted relative odds of delayed graft function by donor DM status (data not shown). Based on these population-level data, it would appear that the findings from rat models of ischemic kidney injury do not directly translate to human kidney transplantation.

Some limitations of this study deserve mention. First, large population-based registries comprehensively capture patients along with exposure, confounder, and outcome data. However, the quality of data capture may be suboptimal, and the observational study designs needed to make inferences from these data may lead to selection bias and residual confounding. In an attempt to address these latter two problems, we used propensity score matching to create a study cohort of DM and non-DM donor KTR who were well balanced for all measured baseline characteristics. Matching has been shown to be the most effective way to use propensity scores for confounder adjustment (*33*, *34*). It also provides a systematic approach to exclude exposed or unexposed individuals who do not have a counterpart in the dataset sharing a similar pattern of baseline characteristics other than the exposure of interest (*35*). This provides a means to more closely estimate the true relation between exposure and outcome. Although a

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TABLE 3. Cox proportional hazards models for the relation between donor diabetes mellitus status and the primary study outcomes

Statistical models	Hazard ratio (95% CI)		
	Graft failure	Death-censored graft failure	Patient mortality
Unadjusted	1.41 (1.32–1.50)	1.40 (1.28–1.52)	1.41 (1.30–1.53)
Adjusted for recipient characteristics[a]	1.34 (1.26–1.43)	1.42 (1.30–1.55)	1.28 (1.18–1.38)
Adjusted for recipient and donor characteristics[b]	1.12 (1.05–1.19)	1.12 (1.03–1.22)	1.13 (1.04–1.22)
Adjusted for recipient, donor, and transplant characteristics[c]	1.13 (1.06–1.21)	1.14 (1.04–1.24)	1.14 (1.05–1.24)
Propensity score-matched cohort	1.11 (1.01–1.21)	1.17 (1.03–1.32)	1.06 (0.95–1.18)

Donors without diabetes mellitus is the reference group.
[a] Recipient characteristics: age, sex, race, cause of ESRD, peak PRA, and time on dialysis.
[b] Donor characteristics: age, sex, race, cause of death, history of hypertension, and terminal serum creatinine.
[c] Transplant characteristics: cold ischemia time, HLA mismatches, and transplant era.
ESRD, end-stage renal disease; PRA, panel reactive antibody; HLA, human leukocyte antigen.

TABLE 4. Prespecified subgroup analyses for the relation between donor diabetes mellitus status and the primary study outcomes in the propensity score-matched cohort

Patient subgroup	HR (95% CI)					
	Graft failure	*P* value for interaction	Death-censored graft failure	*P* value for interaction	Patient mortality	*P* value for interaction
Recipient age (yr)						
18–34.9	0.99 (0.74–1.31)	0.614	1.01 (0.75–1.38)	0.167	0.86 (0.53–1.40)	0.383
35–49.9	1.08 (0.91–1.29)		1.16 (0.93–1.45)		0.96 (0.76–1.22)	
50–64.9	1.13 (0.99–1.29)		1.09 (0.90–1.32)		1.13 (0.97–1.33)	
≥65	1.24 (1.00–1.55)		1.69 (1.16–2.45)		1.22 (0.96–1.54)	
DM causing ESRD						
Yes	1.16 (0.99–1.35)	0.480	1.32 (1.03–1.69)	0.249	1.07 (0.90–1.28)	0.753
No	1.08 (0.97–1.21)		1.12 (0.97–1.29)		1.03 (0.90–1.19)	
Time on dialysis						
Preemptive	1.10 (0.61–1.97)	0.517	0.85 (0.40–1.81)	0.100	0.98 (0.47–2.04)	0.826
0–5 mo	1.37 (0.85–2.23)		1.70 (0.89–3.24)		1.24 (0.66–2.32)	
6–11 mo	0.97 (0.69–1.36)		0.84 (0.53–1.31)		1.04 (0.67–1.61)	
12–23 mo	1.32 (1.09–1.61)		1.48 (1.14–1.92)		1.17 (0.92–1.50)	
24–35 mo	1.10 (0.90–1.33)		1.10 (0.84–1.43)		1.07 (0.84–1.36)	
36–47 mo	1.01 (0.80–1.28)		0.89 (0.65–1.24)		1.18 (0.89–1.57)	
±48 mo	1.07 (0.90–1.27)		1.28 (1.02–1.61)		0.93 (0.76–1.15)	
ECD transplant						
Yes	0.99 (0.85–1.14)	0.060	0.99 (0.81–1.20)	0.043	0.98 (0.82–1.17)	0.342
No	1.18 (1.05–1.32)		1.28 (1.09–1.50)		1.10 (0.95–1.27)	
Cold ischemia time (hr)						
0–11.9	1.11 (0.82–1.50)	0.567	1.31 (0.85–2.03)	0.535	0.90 (0.63–1.29)	0.660
12–23.9	1.05 (0.93–1.20)		1.11 (0.92–1.33)		1.01 (0.86–1.18)	
24–35.9	1.13 (0.95–1.34)		1.11 (0.89–1.39)		1.18 (0.95–1.46)	
±36	1.04 (0.71–1.51)		1.19 (0.76–1.87)		0.95 (0.59–1.54)	
Unknown/missing	1.41 (1.03–1.95)		1.61 (1.07–2.42)		1.14 (0.76–1.71)	
Transplant era						
1994–1996	1.18 (0.99–1.40)	0.323	1.18 (0.94–1.48)	0.588	1.15 (0.93–1.41)	0.268
1997–1999	1.01 (0.86–1.18)		1.07 (0.87–1.33)		0.93 (0.77–1.13)	
2000–2003	1.16 (1.00–1.34)		1.25 (1.02–1.54)		1.12 (0.93–1.34)	

Donors with diabetes mellitus is the reference group.
HR (95% CI), hazard ratio (95% confidence interval); DM, diabetes mellitus; ESRD, end-stage renal disease; ECD, expanded criteria donor.

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TABLE 5. Impact of the duration of donor diabetes mellitus on outcome

Duration of donor DM (yr)	Number of patients	HR (95% CI)		
		Graft failure	Death-censored graft failure	Patient mortality
No DM	64,352	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
0–5	1214	1.08 (0.97–1.21)	1.15 (0.99–1.34)	1.05 (0.92–1.20)
6–10	336	1.22 (1.03–1.45)	1.33 (1.06–1.66)	1.06 (0.85–1.33)
>10	407	1.22 (1.05–1.42)	1.15 (0.93–1.44)	1.27 (1.05–1.53)
Unknown	345	0.96 (0.80–1.15)	1.09 (0.86–1.38)	0.83 (0.66–1.05)

HR (95% CI), hazard ratio (95% confidence interval); DM, diabetes mellitus.

randomized controlled trial of DM versus non-DM donors would provide the most definitive evidence, it would not be logistically feasible, and, thus, a well-designed observational study is the next best approach to address this important question.

Second, no data on proteinuria or a detailed histologic assessment of all deceased donor kidneys were available for analysis. Decision-making regarding the acceptability of a given DM donor likely involves these factors, but their impact could not be evaluated here. Third, data on the duration of donor DM were derived from medical records or next of kin and, thus, may be subject to considerable measurement error. However, the finding that a longer duration of DM in the donor negatively affects graft and patient outcomes is in keeping with a priori knowledge on the effects of long-term hyperglycemia on the structure and function of native kidneys (*36*). Finally, observations with missing data on important covariates were excluded from the analysis. However, for covariates with more than or equal to 3% of values missing, a missing value indicator was used to retain these observations. A supplementary analysis of only those observations with complete covariate data revealed similar results to the primary analysis (data not shown).

In summary, the long-term graft survival of KTR with DM donors is significantly inferior to non-DM donors, but the absolute difference is small. DM donors do not adversely impact patient survival. Donors with a reported duration of DM less than 5 years have no adverse impact on graft survival. These findings suggest that some DM donors may be effectively used for kidney transplantation. However, these donors are likely not being used to their full potential as a means to expand the donor pool. Further research is needed to clearly define the role of other donor factors not captured in the registry (e.g., proteinuria, detailed graft histology) in predicting transplant outcomes and to support the development of evidence-based guidelines for the appropriate selection of potential kidney donors with a history of DM.

ACKNOWLEDGMENTS

These data have been supplied by the U.S. Renal Data System.

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