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Therapeutic Donor Kidney Transplant Outcomes: Comparing Early US Experiences Using Optimal Matching

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Background. Therapeutic donors (TDs) are individuals who undergo organ removal for medical treatment with no replacement organ, and the organ is then transplanted into another person. Transplant centers in the United States have started using TDs for kidney transplantation (KT). TD-KT recipient outcomes may be inferior to those of non-TD-living-donor (non-TD-LD)-KT or deceased-donor (DD)-KT because of the conditions that led to nephrectomy; however, these outcomes have not been sufficiently evaluated. **Methods.** This was a retrospective cohort study using Organ Procurement and Transplantation Network data. Via optimal matching methods, we created 1:4 fivesomes with highly similar characteristics for TD-KT and non-TD-LD-KT recipients and then separately for TD-KT and DD-KT recipients. We compared a 6-mo estimated glomerular filtration rate (eGFR) between groups (primary endpoint) and a composite of death, graft loss, or eGFR <30 mL/min/1.73 m^2 at 6 mo (secondary). **Results.** We identified 36 TD-KT recipients with 6-mo eGFR. There was also 1 death and 2 graft losses within 6 mo. Mean ± SD 6-mo eGFR was not significantly different between TD-KT, non-TD-LD-KT, and DD-KT recipients (59.9 ± 20.7, 63.3 ± 17.9, and 59.9 ± 23.0 mL/min/1.73 m^2, respectively; $P > 0.05$). However, the 6-mo composite outcome occurred more frequently with TD-KT than with non-TD-LD-KT and DD-KT (18%, 2% [$P < 0.001$], and 8% [$P = 0.053$], respectively). **Conclusions.** Early graft function was no different between well-matched groups, but TD-KT demonstrated a higher risk of otherwise poor 6-mo outcomes compared with non-TD-LD-KT and DD-KT. Our results support selective utilization of TD kidneys; however, additional studies are needed with more detailed TD kidney information to understand how to best utilize these kidneys.

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A nondomino therapeutic donor (TD) is defined by the Organ Procurement and Transplantation Network (OPTN) as an individual who undergoes organ removal as a component of medical treatment without receiving a replacement organ, and the organ is then transplanted into another person rather than it being autotransplanted or discarded.[1] Some transplant centers in the United States have recently started using TDs for kidney transplantation (KT).[2] Given the severe organ shortage, TD-KT is a promising option to further utilize transplantable kidneys and expand the donor pool. However, outcomes of TD-KT have not been sufficiently evaluated.

To date, the published literature on TD-KT has been sparse. Available reports have been single-center experiences of transplanting small numbers of kidneys from patients who had undergone nephrectomy for medical conditions refractory

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to other therapies, including ureteral abnormalities, loin pain hematuria syndrome, and nutcracker syndrome.[2-4] The reported posttransplant recipient outcomes of these TD-KTs have been described as generally acceptable; however, they have not been systematically compared with more typical KT from living or deceased donors (DDs). TD-KT recipients may have inferior graft function compared with usual KT recipients due to the underlying disease processes and/or prenephrectomy interventions in the TD that may have damaged the kidney, such as ureteral obstruction, vascular interventions, nephrostomy, and long-term use of analgesics.[3,5,6] Given these potential differences, it is important to understand TD-KT outcomes in relation to non-TD-KT to help guide shared decision-making with potential recipients, promote effective utilization of these kidneys, and assess the potential effect on performance measures for centers that utilize TDs as living donors.

In this retrospective cohort study of US national transplant registry data, we aimed to evaluate short-term outcomes for TD-KT recipients compared with those with highly similar characteristics who received kidneys from non-TD living donors (non-TD-LDs) as well as DDs. We hypothesized that short-term graft function for TD-KT recipients is worse than that of well-matched non-TD-LD-KT but better than that of well-matched DD-KT.

MATERIALS AND METHODS

Data Source and Study Population

This study utilized deidentified registry data from the OPTN. The OPTN data system includes information on all donors, waitlisted candidates, and transplant recipients in the United States submitted by the members of the OPTN. The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight of the activities of the OPTN contractor. This study was approved by the University of Utah Institutional Review Board (approval number, IRB_00159502). Informed consent was waived given the use of the publicly available deidentified dataset.

The baseline cohort included recipients who underwent KT from January 1, 2015, to September 30, 2022, based on OPTN data as of September 30, 2022 (Figure 1). We excluded recipients <18 y of age, those receiving kidneys from LDs with no data about the relation between donor and recipient, and those with no estimated glomerular filtration rate (eGFR) at 6-mo posttransplant.

Exposure Variables

The exposure group was defined as TD-KT recipients, and we generated separate control groups of non-TD-LD-KT and DD-KT recipients. We identified TD-KT recipients using the OPTN variable for "living donor relationship to recipient," which has included an option for "nondomino TD" since 2016 (LIV_DON_TY = 14 or 15).

Outcome Variables

The primary endpoint was 6-mo posttransplant recipient eGFR calculated using the serum creatinine-based 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[7] Secondary outcomes were 12-mo eGFR, length of hospital stay (LOS), and delayed graft function (DGF, defined as any dialysis in the first-week posttransplant). We also evaluated a composite of death, graft loss, or eGFR <30 mL/min/1.73 m^2 at 6- and 12-mo posttransplant.

Covariates

We extracted the following donor/kidney variables from the OPTN database for matching: age, sex, race, body mass index (BMI), diabetes, and serum creatinine at donation. Donor eGFR was also calculated using the 2021 CKD-EPI equation. Because this study included both LDs and DDs, we

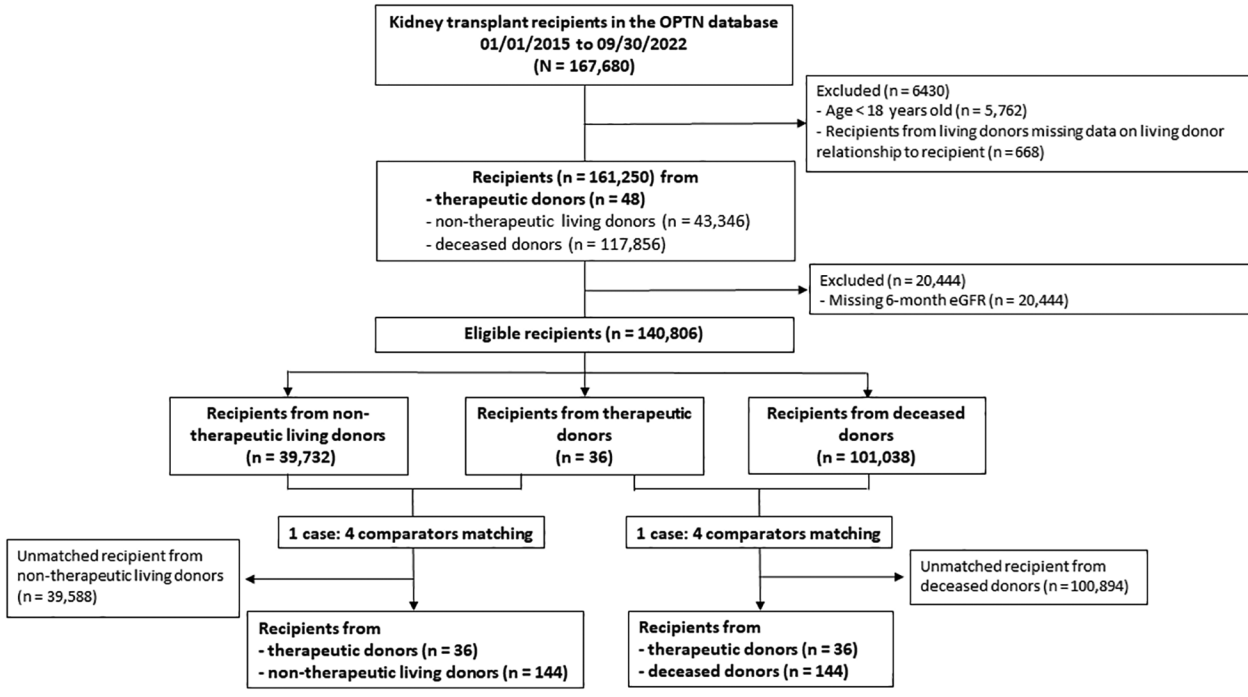

FIGURE 1. Study flow chart. eGFR, estimated glomerular filtration rate; OPTN, Organ Procurement and Transplantation Network.

did not use the Kidney Donor Profile Index as a covariate. The following recipient variables were also collected: age, sex, race, BMI, diabetes, previous solid organ transplantation, dialysis duration, cause of end-stage kidney disease (ESKD), human leukocyte antigen (HLA) mismatch, calculated panel-reactive antibody (cPRA), cold ischemia time (CIT), and use of lymphocyte-depleting antibody for induction immunosuppression (antithymocyte globulin or alemtuzumab).

Matching Process

We used optimal matching methods to develop 1:4 matching (fivesome, 1 case matched to 4 controls) with highly similar background characteristics for TD-KT and non-TD-LD-KT recipients and then separately for TD-KT and DD-KT recipients (Figure 1). The matching process included recipient factors (age, sex, race, BMI, history of diabetes, prior transplant, dialysis vintage, cause of ESKD, and cPRA), donor factors (age, sex, race, BMI, history of diabetes, and eGFR at donation), and transplant factors (HLA mismatch, CIT, and lymphocyte-depleting induction). Matching was performed via an iterative process. A propensity score model was first built using all the variables in the matching algorithm. We then built a Mahalanobis distance matrix for important continuous variables (recipient age, BMI, and cPRA; donor age, BMI, and eGFR at donation; and CIT). Finally, bipartite cardinality matching was performed to identify the optimal fivesomes. We matched exactly on recipient sex, race, history of diabetes, and prior transplant; donor sex, race, and history of diabetes; and lymphocyte-depleting induction. We used mean constraint to balance continuous variables and fine balance to match categorical variables, including dialysis vintage, cause of ESKD, and HLA mismatch. Balance was assessed using absolute standardized differences (cutoff < 0.1) and visual inspection of the distribution plots.[8,9] Study outcomes were examined only after the balance had been assessed by study investigators (J.Y., I.E.H., and M.Z.M.) and the match had been finalized. Optimal matching was performed using R statistical software (R Foundation for Statistical Computing version 4.2.2; packages "designmatch").

Statistical Analysis

Baseline characteristics were summarized as mean and SD or median and interquartile range (IQR) for continuous variables and numbers and percentages (%) for categorical variables, as appropriate. Differences in baseline characteristics between the TD-KT group and the non-TD-LD-KT and DD-KT groups before and after matching were evaluated by standardized mean differences. We used the generalized Wilcoxon–Mann–Whitney rank-sum test (van Elteren test) to compare LOS, 6- and 12-mo eGFR between groups. We used chi-square tests to compare DGF frequency. *P* values were two-sided and considered statistically significant when <0.05 for all analyses. All analyses except matching were conducted using STATA version 17 (STATA Corporation, College Station, TX).

Secondary Analysis

For the primary analysis of graft function at 6 mo, we excluded recipients with no 6-mo eGFR. Thus, those who died or lost their graft within 6 mo were initially excluded. We therefore conducted a secondary analysis for the composite outcome (death, graft loss, or eGFR <30 mL/min/1.73 m^2 at 6 mo) without excluding recipients missing 6-mo eGFR. We separately created a cohort of recipients who had 6-mo eGFR data and those who died or lost their graft within 6 mo by excluding recipients who were alive with a functioning graft but had not reached 6-mo follow-up or had no reported 6-mo eGFR (**Figure S1, SDC**, http://links.lww.com/TXD/A586). We then generated matched fivesome groups using the aforementioned matching methods and compared the frequency of the composite outcome by the chi-square test.

Missing Data

Data were missing in small fractions of the prematched recipients for the following: donor age (n = 1, <0.01%), BMI (n = 1,482, 1.05%), diabetes (n = 985, 0.70%), and eGFR at donation (n = 56, 0.04%); recipient BMI (n = 78, 0.06%), diabetes (n = 32, 0.02%), dialysis duration (n = 1, <0.01%), and cPRA (n = 27, 0.02%); HLA mismatch (n = 820, 0.58%); and CIT (n = 1211, 0.86%). Missing data were imputed with the mean value for continuous variables or with the most frequent category for categorical ones.

RESULTS

Cohort Description

The study flow diagram is shown in Figure 1. We identified 48 TD-KT recipients within the 161 250 KT recipients that met inclusion criteria (see **Table S1** [**SDC,** http://links.lww.com/TXD/A586] for basic TD and recipient information). These TD-KTs were performed at 35 (14%) of 250 transplant centers in the United States: 4 transplants at 1 center, 3 transplants at 3 centers, 2 transplants at 4 centers, and 1 transplant at 27 centers. After excluding recipients with no 6-mo eGFR, there were 140,806 eligible recipients, including 36 TD-KT, 39,732 non-TD-LD-KT, and 101,038 DD-KT recipients. Among the 12 TD-KT recipients with no 6-mo eGFR, 1 lost their graft because of primary nonfunction, 1 to graft thrombosis on day 21, and 1 recipient died from bacterial sepsis on day 3. The other 9 recipients were reported as alive with a functioning graft, but follow-up was shorter than 6 mo (n = 8) or 6-mo serum creatinine was simply missing (n = 1).

Tables 1 and 2 show pre- and postmatch baseline characteristics of TD-KT versus non-TD-LD-KT and versus DD-KT, respectively. Before matching, mean ± SD age for TDs was similar to non-TD-LDs but higher than that for DDs (43 ± 13, 44 ± 13, and 39 ± 15 y, respectively). The proportion of female donors was much higher for TDs (81%) than for non-TD-LDs (64%) and DDs (38%). None of the TDs were Black, compared with 9% of non-TD-LDs and 14% of DDs. TDs and non-TD-LDs had higher eGFR at donation than DDs (100 ± 18, 99 ± 16, and 89 ± 41 mL/min/1.73 m^2, respectively).

Mean TD-KT recipient age was 52 ± 14 y, and 44% were female, similar to non-TD-LD-KT and DD-KT recipients. There were lower proportions of Black recipients of TD-KT and non-TD-LD-KT compared with DD-KT recipients (11%, 12%, and 33%, respectively). The frequency of preemptive TD-KT (22%) was lower than that of non-TD-LD-KT (37%) but higher than that of DD-KT (14%). TD-KT recipients had lower cPRA than the others (5.4 ± 15.2, 11.2 ± 24.2, and 24.8 ± 37.2, respectively). As expected, CIT in TD-KT and non-TD-LD-KT was similar but much shorter than DD-KT (2.7 ± 3.3, 2.5 ± 4.1, and 18.1 ± 8.5 h, respectively).

TABLE 1.

Baseline characteristics of therapeutic and nontherapeutic living-donor transplant recipients

	Prematch			Postmatch		
	Nontherapeutic living donor	Therapeutic donor	Std. diff.	Nontherapeutic living donor	Therapeutic donor	Std. diff.
Baseline characteristic	**(n = 39 732)**	**(n = 36)**		**(n = 144)**	**(n = 36)**	
Donor variable						
Age (y)	43.9 (12.5)	43.3 (13.3)	–0.049	43.4 (12.6)	43.3 (13.3)	–0.009
Sex			–0.376			0.000
Female	25 396 (64%)	29 (81%)		116 (81%)	29 (81%)	
Male	14 336 (36%)	7 (19%)		28 (19%)	7 (19%)	
Black race	3444 (9%)	0 (0%)	–0.436	0 (0%)	0 (0%)	—
BMI (kg/m^2)	26.9 (4.0)	26.2 (4.8)	–0.160	26.2 (3.8)	26.2 (4.8)	0.002
History of diabetes	12 (0%)	0 (0%)	–0.025	0 (0%)	0 (0%)	—
eGFR at donation (mL/min/1.73 m^2)	99.1 (15.9)	100.7 (17.6)	0.094	100.7 (17.5)	100.7 (17.6)	–0.001
Recipient variable						
Age (y)	50.1 (14.4)	52.1 (14.1)	0.135	52.0 (13.0)	52.1 (14.1)	0.004
Sex			–0.147			0.000
Female	14 772 (37%)	16 (44%)		64 (44%)	16 (44%)	
Male	24 960 (63%)	20 (56%)		80 (56%)	20 (56%)	
Black race	4925 (12%)	4 (11%)	–0.040	16 (11%)	4 (11%)	0.000
BMI (kg/m^2)	27.9 (5.4)	28.4 (4.4)	0.105	28.4 (5.4)	28.4 (4.4)	–0.005
History of diabetes	11 565 (29%)	13 (36%)	0.149	52 (36%)	13 (36%)	0.000
Previous organ transplantation	4275 (11%)	5 (14%)	0.095	20 (14%)	5 (14%)	0.000
Dialysis duration category			0.465			0.000
Preemptive	14 695 (37%)	8 (22%)		32 (22%)	8 (22%)	
≤1 y	9632 (24%)	8 (22%)		32 (22%)	8 (22%)	
1–3 y	10 474 (26%)	8 (22%)		32 (22%)	8 (22%)	
3–5 y	3304 (8%)	9 (25%)		36 (25%)	9 (25%)	
>5 y	1627 (4%)	3 (8%)		12 (8%)	3 (8%)	
Cause of end-stage kidney disease			–0.215			0.000
Glomerular disease	10 170 (26%)	12 (33%)		48 (33%)	12 (33%)	
Diabetes	9037 (23%)	10 (28%)		40 (28%)	10 (28%)	
Hypertension	6003 (15%)	3 (8%)		12 (8%)	3 (8%)	
Other	14 522 (37%)	11 (31%)		44 (31%)	11 (31%)	
Calculated PRA (%)	11.2 (24.2)	5.4 (15.2)	–0.283	5.5 (14.3)	5.4 (15.2)	
HLA mismatch level			0.589			0.000
0	2168 (5%)	0 (0%)		0 (0%)	0 (0%)	
1	1957 (5%)	0 (0%)		0 (0%)	0 (0%)	
2	4921 (12%)	1 (3%)		4 (3%)	1 (3%)	
3	9130 (23%)	5 (14%)		20 (14%)	5 (14%)	
4	7298 (18%)	13 (36%)		52 (36%)	13 (36%)	
5	9204 (23%)	11 (31%)		44 (31%)	11 (31%)	
6	5054 (13%)	6 (17%)		24 (17%)	6 (17%)	
Cold ischemia time (h)	2.5 (4.1)	2.7 (3.3)	0.050	2.7 (3.4)	2.7 (3.3)	0.003
Lymphocyte-depleting induction (%)	26 497 (67%)	24 (67%)	0.000	96 (67%)	24 (67%)	0.000

Values are expressed as mean (SD) or number (%).
BMI, body mass index; HLA, human leukocyte antigen; PRA, panel-reactive antibody; Std. diff., standardized mean difference.

Lymphocyte-depleting induction was used in 67% of TD-KT and non-TD-LD-KT and 75% of DD-KT. After matching, all adjusted baseline characteristics were well-balanced and had small standardized mean differences and similar distribution plots (**Tables 1 and 2; Figures S2 and S3, SDC,** http://links.lww.com/TXD/A586).

Recipient Outcomes

There were no significant differences in LOS, DGF, and eGFR at 6 and 12 mo between TD-KT and non-TD-LD-KT recipients (Table 3). Median (IQR) LOS was 4 (3–5) d in both groups (P = 0.66). DGF was reported in 3% and 5%, respectively (P = 0.59). Mean ± SD eGFR values at 6 and 12 mo posttransplant were also similar between the TD-KT and non-TD-LD-KT groups (59.9 ± 20.7 versus 63.3 ± 17.9 mL/min/1.73 m^2 at 6 mo, P = 0.35; 60.6 ± 18.2 versus 65.7 ± 19.6 mL/min/1.73 m^2 at 12 mo, P = 0.77). Compared with TD-KT recipients, DD-KT recipients had significantly longer median LOS (4 [3–5] versus 5 [4–8] d, P < 0.001) and a higher DGF rate (3% versus 20%, P = 0.012). However, posttransplant eGFR values were similar between the TD-KT and DD-KT groups (59.9 ± 20.7 versus 59.9 ± 23.0 mL/min/1.73 m^2 at 6 mo, P = 0.48; 60.6 ± 18.2 versus 62.5 ± 22.4 mL/min/1.73 m^2 at 12 mo, P = 0.96).

TABLE 2.

Baseline characteristics of therapeutic and deceased-donor transplant recipients

	Prematch			Postmatch		
	Deceased donor	Therapeutic donor	Std. diff.	Deceased donor	Therapeutic donor	Std. diff.
Baseline characteristic	**(n = 101 038)**	**(n = 36)**		**(n = 144)**	**(n = 36)**	
Donor variable						
Age (y)	38.5 (15.1)	43.1 (13.4)	0.327	43.1 (13.2)	43.1 (13.4)	0.001
Sex			−0.963			0.000
Female	38 090 (38%)	29 (81%)		116 (81%)	29 (81%)	
Male	62 948 (62%)	7 (19%)		28 (19%)	7 (19%)	
Black race	13 638 (13%)	0 (0%)	−0.559	0 (0%)	0 (0%)	—
BMI (kg/m^2)	27.9 (6.5)	26.2 (4.9)	−0.299	26.3 (6.0)	26.2 (4.9)	−0.006
History of diabetes	7354 (7%)	0 (0%)	−0.396	0 (0%)	0 (0%)	—
eGFR at donation (mL/min/1.73 m^2)	89.4 (40.6)	100.2 (17.8)	0.343	100.2 (31.0)	100.2 (17.8)	−0.001
Recipient variable						
Age (y)	52.9 (13.3)	52.1 (14.1)	−0.065	52.1 (13.8)	52.1 (14.1)	−0.004
Sex			−0.090			0.000
Female	40 367 (40%)	16 (44%)		64 (44%)	16 (44%)	
Male	60 671 (60%)	20 (56%)		80 (56%)	20 (56%)	
Black race	33 703 (33%)	4 (11%)	−0.553	16 (11%)	4 (11%)	0.000
BMI (kg/m^2)	28.3 (5.4)	28.4 (4.4)	0.012	28.4 (5.4)	28.4 (4.4)	0.001
History of diabetes	36 913 (37%)	13 (36%)	−0.009	52 (36%)	13 (36%)	0.000
Previous organ transplantation	13 903 (14%)	5 (14%)	0.004	20 (14%)	5 (14%)	0.000
Dialysis duration category			−0.597			0.000
Preemptive	13 802 (14%)	8 (22%)		32 (22%)	8 (22%)	
≤1 y	9589 (9%)	8 (22%)		32 (22%)	8 (22%)	
1–3 y	20 308 (20%)	8 (22%)		32 (22%)	8 (22%)	
3–5 y	21 220 (21%)	9 (25%)		36 (25%)	9 (25%)	
>5 y	36 119 (36%)	3 (8%)		12 (8%)	3 (8%)	
Cause of end-stage kidney disease			−0.272			0.000
Glomerular disease	18 086 (18%)	12 (33%)		48 (33%)	12 (33%)	
Diabetes	28 121 (28%)	10 (28%)		40 (28%)	10 (28%)	
Hypertension	22 743 (23%)	3 (8%)		12 (8%)	3 (8%)	
Other	32 088 (32%)	11 (31%)		44 (31%)	11 (31%)	
Calculated PRA (%)	24.8 (37.2)	5.4 (15.2)	−0.682	5.3 (17.7)	5.4 (15.2)	0.006
HLA mismatch level			0.233			0.000
0	4755 (5%)	0 (0%)		0 (0%)	0 (0%)	
1	1370 (1%)	0 (0%)		0 (0%)	0 (0%)	
2	4992 (5%)	1 (3%)		4 (3%)	1 (3%)	
3	14 401 (14%)	5 (14%)		20 (14%)	5 (14%)	
4	27 760 (27%)	13 (36%)		52 (36%)	13 (36%)	
5	32 687 (32%)	11 (31%)		44 (31%)	11 (31%)	
6	15 073 (15%)	6 (17%)		24 (17%)	6 (17%)	
Cold ischemia time (h)	18.1 (8.5)	2.7 (3.3)	−2.380	2.8 (2.1)	2.7 (3.3)	−0.020
Lymphocyte-depleting induction (%)	75 714 (75%)	24 (67%)	−0.181	96 (67%)	24 (67%)	0.000

Values are expressed as mean (SD) or number (%).
BMI, body mass index; HLA, human leukocyte antigen; PRA, panel-reactive antibody; Std. diff., standardized mean difference.

Secondary Analysis for the Composite Outcome

The secondary analysis cohort included 39 TD-KT recipients (**Figure S1, SDC,** http://links.lww.com/TXD/A586). We created matched fivesome groups in the same manner as the primary analysis (**Tables S2 and S3; Figures S4 and S5, SDC,** http://links.lww.com/TXD/A586). The 6-mo composite outcome occurred more frequently in the TD-KT recipients compared with the non-TD-LD-KT and DD-KT recipients (18%, 2% [$P < 0.001$], and 8% [$P = 0.053$], respectively; Table 3). The 12-mo composite outcome was similar to the 6-mo outcome (13%, 4% [$P < 0.001$], and 10% [$P = 0.38$] in TD-KT, non-TD-LD-KT, and DD-KT recipients, respectively).

DISCUSSION

In this study, we evaluated short-term outcomes of TD-KT recipients compared with well-matched non-TD-LD-KT and DD-KT recipients. DGF frequency and LOS for TD-KT recipients were not different compared with non-TD-LD-KT recipients, and both outcomes were lower in TD-KT recipients than in DD-KT recipients. Posttransplant recipient eGFR at 6 and 12 mo was not significantly different between groups. However, the composite outcome of death, graft loss, or low eGFR occurred more frequently in TD-KT recipients.

Overall, short-term outcomes for TD-KT recipients were acceptable in this cohort and were comparable with those

TABLE 3.

Recipient outcomes

Outcome	Therapeutic donor	Nontherapeutic living donor	P[a]	Deceased donor	P[b]
Length of hospital stay (d), median (IQR)	4 (3–5)	4 (3–5)	0.66	5 (4–8)	<0.001
Delayed graft function, n (%)	1 (3%)	7 (5%)	0.59	29 (20%)	0.012
6-mo eGFR (mL/min/1.73 m^2), mean (SD)	59.9 (20.7)	63.3 (17.9)	0.35	59.9 (23.0)	0.48
12-mo eGFR (mL/min/1.73 m^2), mean (SD)[c]	60.6 (18.2)	65.7 (19.6)	0.77	62.5 (22.4)	0.96
6-mo composite outcome, n (%)[d]	7 (18%)	3 (2%)	<0.001	12 (8%)	0.053
Death	1	0		2	
Graft loss	2	0		3	
eGFR < 30 mL/min/1.73 m^2	4	3		8	
12-mo composite outcome, n (%)[e]	4 (13.3%)	5 (3.6%)	<0.001	14 (9.6%)	0.38
Death	1	0		3	
Graft loss	2	0		6	
eGFR < 30 mL/min/1.73 m^2	1	5		7	

Between-group differences in the length of hospital stay and eGFR were analyzed using the generalized Wilcoxon–Mann–Whitney rank-sum test (van Elteren test). The chi-square test was used for delayed graft function and the composite outcome.

[a]*P* values for therapeutic donor versus nontherapeutic living-donor groups.

[b]*P* value for therapeutic donor versus deceased-donor groups.

[c]For the 12-mo eGFR analysis, 27, 95, and 99 recipients were included in the therapeutic donor, nontherapeutic living-donor, and deceased-donor groups, respectively.

[d]For the 6-mo composite outcome analysis, 39, 156, and 156 recipients were included in the therapeutic donor, nontherapeutic living-donor, and deceased-donor groups, respectively. One recipient in the deceased-donor group died after graft loss.

[e]For the 12-mo composite outcome analysis, 30, 141, and 146 recipients were included in the therapeutic donor, nontherapeutic living-donor, and deceased-donor groups, respectively. Two recipients in the deceased-donor group died after graft loss.

eGFR, estimated glomerular filtration rate; IQR, interquartile range.

of non-TD-LD-KT and DD-KT recipients. This is reassuring given that TD kidneys could have some degree of damage because of the underlying conditions and prior treatments leading up to the therapeutic nephrectomy. Our findings suggest that the current utilization of TD kidneys is safe and effective; however, these early experiences may be the result of a very careful selection of TD kidneys and recipients for transplantation. As indicated by their excellent eGFR at donation, which was similar to that of non-TD-LDs, TDs in this study may be quite different from most other patients undergoing therapeutic nephrectomy that do not currently result in transplantation. Although we could not analyze potential underlying kidney damage or disease because the OPTN dataset does not include such data (apart from serum creatinine at donation), careful evaluation and selection of potential TDs are likely tremendously important for successful TD-KT.

Despite reassuring graft function at 6 and 12 mo, our finding that TD-KT recipients had a significantly higher rate of the composite outcome compared with non-TD-LD-KT requires careful consideration. Eighteen percent of TD-KT recipients experienced the unfavorable 6-mo outcome, including 2 graft losses (1 primary nonfunction and 1 graft thrombosis). These findings may be at least partly influenced by the relatively small sample size currently available in the database and the small number of transplant centers that have only recently started gaining experience with these transplants, or potentially problematic prenephrectomy kidney conditions. Additional information, such as kidney histology or the underlying condition that led to nephrectomy, is not available in the OPTN database. Nutcracker syndrome, for example, is a rare condition that typically manifests with hematuria, flank pain, pelvic varicosities, or chronic pelvic congestion because of left renal vein entrapment.[10] When symptoms are refractory to conservative treatment, some patients undergo renal vein stenting or transposition, which sometimes leads to renal vein stenosis or occlusion.[11,12] Some patients also undergo prolonged treatment with analgesics for pain control. Because therapeutic nephrectomy is usually performed as a last resort after multiple procedures for underlying diseases,[2-4] subclinical structural and functional damage to the renal parenchyma or vasculature may exist in some TD kidney allografts even with apparently normal eGFR.

Moreover, the risk of TD-KT may differ according to the indication for nephrectomy. Apart from our study, current literature on TD-KT is limited to 3 published case series/reports consisting of 12 TDs with loin pain hematuria syndrome, ureteral abnormalities/injuries, nutcracker syndrome, or unilateral renal mass, with all cases reporting excellent graft function.[2-4] Beyond these limited reports, however, prior studies of kidney autotransplantation may help elucidate risks because the indications for kidney autotransplantation and possible TD-KT often overlap. In kidney autotransplantation, the affected kidney is removed, repaired/prepared on the back table in the operating room, and then reimplanted into the same patient, usually in the pelvis.[13] When autotransplantation is contraindicated because of anatomy or other surgical concerns, or the patient refuses autotransplantation because of its associated risks and opts for nephrectomy alone, TD-KT may be an option over simply discarding an otherwise transplantable kidney.[4] Indications for kidney autotransplantation include renovascular disease, ureteral stricture and trauma, excisable malignancy in the kidney and/or urinary tract, and loin pain hematuria syndrome.[14-20] The kidney failure rate with autotransplantation is approximately 10%.[19-21] However, success rates differ between underlying diseases, with loin pain hematuria syndrome having the highest autotransplant graft success rate of 92%–100%, presumably because of the lack of structural abnormalities.[13,22] Mortality is generally low; however, postoperative complications are frequent (40%–50%), including hemorrhage, urinary tract infection, ureteral stricture, and graft thrombosis.[19,20] As such, additional studies that include detailed background information on the indications for nephrectomy are needed to further evaluate the potential risks associated with TD-KT. To facilitate this crucial research, the OPTN Living-Donor Registration Form should be revised

to require additional data entry on nephrectomy indication whenever "TD" is selected for donor type.

It is important to acknowledge that US transplant centers' LD transplant performance measures currently do not differentiate between TDs and healthy LDs. Outcomes for recipients of kidneys from TDs are included in the center's LD performance measures. Our findings indicate that the short-term composite outcome (death, graft loss, 6-mo eGFR) for these recipients may be worse than recipients of kidneys from healthy LDs. Such outcomes might discourage centers from using TDs because the practice could possibly result in undesirable LD transplant performance data for these centers. Transplant regulatory bodies should give serious consideration for evaluating TD-KT outcomes as a separate category or allow exemptions for these transplants to encourage the use of these transplantable organs rather than discarding them.

Despite potential fears of punitive regulatory review, there is a fervent culture within the transplant community to save and improve more lives by expanding the organ donor pool and maximally utilizing transplantable organs. To this end, and given our overall findings from the early national TD-KT experience, we believe careful expansion of the donor pool with selected utilization of these kidneys is warranted. For centers interested in these types of transplants, multidisciplinary collaboration with the providers who have been caring for the patient considering therapeutic nephrectomy is beneficial.[13,19,22] Such patients have typically undergone extensive evaluations for their conditions, sometimes including direct GFR measurement and split kidney function testing. When available, these data can help facilitate patient counseling about nephrectomy alone versus autotransplantation as well as appropriate recipient selection if TD-KT is ultimately pursued.

To our knowledge, this is the first comparative study of TD-KT using national data. We evaluated short-term outcomes of TD-KT recipients compared with those of usual LD and DD-KT recipients with otherwise highly similar characteristics using advanced matching methods to address potential confounding factors.

This study has important limitations. Because this is a retrospective study using the OPTN registry, all possible confounders could not be addressed. Also, the available sample size was small, and none of the TDs were Black. Thus, generalizability for all patient populations may be limited. Posttransplant recipient eGFR was defined using the serum creatinine values reported on the 6- and 12-mo OPTN follow-up forms. The accuracy of these values has been demonstrated in a prior report,[23] although accuracy in the era of the COVID-19 pandemic has not yet been described. Finally, we could not analyze the underlying diseases and potential prenephrectomy damage of TD kidneys.

In conclusion, we report the first retrospective comparative cohort study of early national TD-KT cases. Recipient graft function within the first year posttransplant was essentially no different compared with highly similar non-TD-LD-KT and DD-KT recipients. Our results support the selective utilization of TD kidneys; however, we found that TD-KT may carry a higher risk of poor early outcomes. Therefore, additional studies with more detailed TD kidney information are needed to broaden our understanding of how to best utilize these kidneys.

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REFERENCES

1. Organ Procurement and Transplantation Network (OPTN) Policies. Available at https://optn.transplant.hrsa.gov/policies-bylaws/policies/. Accessed February 1, 2023.
2. Dale L-A, Silva MV, Sandoval PR, et al. Therapeutic living donor nephrectomy. *Clin Transplant*. 2019;33:e13715.
3. Freise J, Nunez M, Chi T, et al. Therapeutic living donor nephrectomy for proximal ureteral pathology: a longitudinal case series. *Urology*. 2022;166:277–282.
4. Fonseca Bauza MV, Toledo AH, Rodriguez PS. Using the resected kidney for transplantation after nephrectomy for nutcracker syndrome. *Am Surg*. 2022;31348221117043:000313482211170.
5. Ananthan K, Onida S, Davies AH. Nutcracker syndrome: an update on current diagnostic criteria and management guidelines. *Eur J Vasc Endovasc Surg*. 2017;53:886–894.
6. Zubair AS, Salameh H, Erickson SB, et al. Loin pain hematuria syndrome. *Clin Kidney J*. 2016;9:128–134.
7. Inker LA, Eneanya ND, Coresh J, et al; Chronic Kidney Disease Epidemiology Collaboration. New creatinine- and cystatin C-based equations to estimate GFR without race. *N Engl J Med*. 2021;385:1737–1749.
8. Rosenbaum PR, Rubin DB. Constructing a control group using multivariate matched sampling methods that incorporate the propensity score. *Am Stat*. 1985;39:33–38.
9. Silber JH, Rosenbaum PR, Trudeau ME, et al. Multivariate matching and bias reduction in the surgical outcomes study. *Med Care*. 2001;39:1048–1064.
10. Kolber MK, Cui Z, Chen CK, et al. Nutcracker syndrome: diagnosis and therapy. *Cardiovasc Diagn Ther*. 2021;11:1140–1149.
11. Avgerinos ED, Saadeddin Z, Humar R, et al. Outcomes of left renal vein stenting in patients with nutcracker syndrome. *J Vasc Surg Venous Lymphat Disord*. 2019;7:853–859.
12. Erben Y, Gloviczki P, Kalra M, et al. Treatment of nutcracker syndrome with open and endovascular interventions. *J Vasc Surg Venous Lymphat Disord*. 2015;3:389–396.
13. Han DS, Johnson JP, Schulster ML, et al. Indications for and results of renal autotransplantation. *Curr Opin Nephrol Hypertens*. 2023;32:183–192.
14. Babazade R, Devarajan J, Bonavia AS, et al. Anesthetic management and 30-day outcomes after renal autotransplantation. *Ochsner J*. 2020;20:267–271.
15. Ruiz M, Hevia V, Fabuel JJ, et al. Kidney autotransplantation: long-term outcomes and complications experience in a tertiary hospital and literature review. *Int Urol Nephrol*. 2017;49:1929–1935.
16. Ramouz A, Hafezi M, Ali-Hasan-Al-Saegh S, et al. Renal artery repair with kidney autotransplantation for renal artery aneurysms. *Eur J Vasc Endovasc Surg*. 2022;63:732–742.
17. Bath NM, Al-Qaoud T, Williams DH, et al. Renal autotransplantation results in pain resolution after left renal vein transposition. *J Vasc Surg Venous Lymphat Disord*. 2019;7:739–741.
18. Mejia A, Barrera Gutierrez JC, Vivian E, et al. Robotic assisted kidney auto-transplantation as a safe alternative for treatment of nutcracker syndrome and loin pain haematuria syndrome: a case series report. *Int J Med Robot*. 2023;19:e2508.
19. Vrakas G, Sullivan M. Current review of renal autotransplantation in the UK. *Curr Urol Rep*. 2020;21:33.
20. Moghadamyeghaneh Z, Hanna MH, Fazlalizadeh R, et al. A nationwide analysis of kidney autotransplantation. *Am Surg*. 2017;83:162–169.
21. Tran G, Ramaswamy K, Chi T, et al. Laparoscopic nephrectomy with autotransplantation: safety, efficacy and long-term durability. *J Urol*. 2015;194:738–743.
22. Campsen J, Pan G, Quencer K, et al. Renal auto-transplantation for loin pain hematuria syndrome using a multidisciplinary team model: intermediate-term results. *Cureus*. 2020;12:e12379.
23. Potluri VS, Parikh CR, Hall IE, et al. Validating early post-transplant outcomes reported for recipients of deceased donor kidney transplants. *Clin J Am Soc Nephrol*. 2016;11:324–331.