

# Outcomes of Dual Adult Kidney Transplants in the United States: An Analysis of the OPTN/UNOS Database

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**Background.** The organ shortage has resulted in increased use of kidneys from expanded criteria donors (ECD). For ECD kidneys unsuitable for single use, dual kidney transplants (DKT) may be possible. There are limited data comparing outcomes of DKT to single kidney ECD transplants, making it unclear where DKT fits in the current allocation scheme. Our purpose was to compare outcomes of DKT and ECD transplants in the United States.

**Methods.** From 2000 to 2005, a total of 625 DKT, 7686 single kidney ECD, and 6,044 SCD transplants from donors aged  $\geq 50$  years were identified from the Organ Procurement and Transplantation Network/United Network for Organ Sharing data. Allograft survival was the primary outcome.

**Results.** DKT comprised 4% of kidney transplants from donors aged  $\geq 50$  years. Compared to the ECD donor group, the DKT donor group was older (mean age  $64.6 \pm 7.7$  years vs.  $59.9 \pm 6.2$  years) and consisted of more African Americans (13.1% vs. 9.9%), and more diabetic donors (16.3% vs. 10.4%;  $P < 0.001$ ). Mean cold ischemic time was longer in DKT ( $22.2 \pm 9.7$  hr), but rates of delayed graft function were lower (29.3%) compared to ECD transplants (33.6%,  $P = 0.03$ ). Three-year overall graft survival was 79.8% for DKT and 78.3% for ECD transplants.

**Conclusion.** DKT were infrequent and had outcomes comparable to ECD transplants, despite the use of organs from higher risk donors. With a more upfront approach to DKT by offering this option to patients at the time of wait-listing as part of an ECD algorithm, we may be able to further optimize outcomes of DKT and minimize discard of potential organs.

**Keywords:** Transplant, Dual kidney, Older donor, Outcomes.

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The organ shortage is a preeminent issue in the current era of transplantation. The increasing disparity between supply and demand of organs has spawned the increased use of organs from older and more marginal donors, mostly in the form of expanded criteria donor (ECD) kidneys (1). Dual kidney transplantation (DKT) is an alternative approach to expand the existing deceased donor pool. Based on the premise of transplanting a larger initial nephron mass, this strategy has produced favorable outcomes in single center reports (2–6). In an analysis of all DKT transplants in the United States reported to the United Network for Organ Sharing (UNOS) between 1997 and 2002, allograft survival at 3 years posttransplant was inferior to those of single kidney transplants from all donors (7). When this analysis was restricted to donors more than 50 years of age, there was no significant difference in allograft survival between recipients of DKT and single kidney transplants. Remuzzi et al. (8) subsequently reported excellent outcomes in recipients of DKT, utilizing an allocation system incorporating pre-transplant donor biopsies to guide the use of older donor organs.

In the existing allocation algorithm in the United States, where transplant candidates are given the option of enlisting for standard criteria donors (SCD) and/or ECD, the role of DKT remains less clearly defined. Additionally, while DKT have been compared to single kidney transplants as a whole, to our knowledge there is limited data that has directly compared the outcomes of DKT to SCD and ECD transplants.

Therefore, we proposed to compare transplant outcomes between DKT, ECD, and SCD transplants.

## METHODS

### Study Design

We studied all kidney-only transplants from deceased donors (age  $\geq 50$  years) from January 1, 2000 to December 31, 2005, based on data from the Organ Procurement and Transplantation Network (OPTN)/UNOS database as of September 11, 2006. The analysis was restricted to transplants from donors aged 50 or older as this is the cutoff for designation as ECD and minimized donor age as a factor in the outcomes of SCD and DKT. Transplants from pediatric en-bloc kidneys were excluded from the analysis.

We first compared donor and recipient characteristics between DKT, ECD transplants, and SCD transplants. We then compared allograft survival, the incidence of delayed graft function (DGF), primary nonfunction, and acute rejection between DKT, ECD transplants and SCD transplants. Next, we used multivariate modeling to assess the adjusted risk of DKT on allograft loss.

We then restricted our analysis to all DKT from deceased donors  $\geq 50$  years during the study period. We, first, identified all DKT which met the UNOS guidelines for use of

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dual kidneys. We, then, repeated the above analyses comparing the outcomes of ECD and SCD transplants to only those DKT which met the UNOS guidelines for use of dual kidneys. Next, we identified all DKT in which donor kidneys underwent pulsatile perfusion (PP) prior to transplantation. Rates of DGF, acute rejection, and allograft failure were compared between the PP and cold storage (CS) groups.

### Definitions

ECD was defined as all deceased donors  $\geq 60$  years of age or donors who were 50–59 years of age and had two of the following: donor history of hypertension; donor death due to cerebrovascular accident/stroke; or terminal serum creatinine value greater than 1.5 mg/dl. SCD was defined as all deceased donors other than ECD.

Overall allograft survival was determined from the date of transplantation until death, return to dialysis or the end of the study period. Death-censored allograft survival was censored for death with a functioning graft. DGF was defined as the need for dialysis within the first week post transplantation. Primary nonfunction was identified from the cause of graft failure reported to UNOS and did not include thrombosis.

### Statistical Analysis

Donor and recipient characteristics were described using means  $\pm$  standard deviation or frequencies. Comparisons between groups were made using Kruskal-Wallis or chi-square tests, as appropriate. Graft survival rates were estimated by the Kaplan-Meier product limit method and the test for equality of survival curves was performed using the log-rank test. A Cox regression model, adjusting for all recipient and transplant factors significantly associated with allograft survival on univariate analysis ( $P < 0.05$ ), was used to estimate the adjusted relative risk of DKT on allograft loss.

## RESULTS

### Baseline Characteristics of DKT and ECD Transplants (Table 1)

A total of 14,355 kidney-only transplants were performed from deceased donors  $\geq 50$  years of age during the study period. Single kidney transplants from ECD were the most common ( $n=7686$ ), followed by single kidney transplants from SCD ( $n=6044$ ). Six hundred and twenty-five DKT were performed. Eighty-eight percent of donors for DKT met ECD criteria. The 12% of DKT donors who did not meet ECD criteria did not have additional high-risk characteristics beyond those captured by the ECD classification (donor age, donor hypertension, donor cerebrovascular accident).

Compared to the single kidney ECD donor group, the DKT group was older and comprised of more females, African Americans, donors with a history of diabetes, and donors with a serum creatinine  $> 1.5$  mg/dl. In contrast, there were more donors who died as a result of a cerebrovascular accident in the ECD group. The mean calculated creatinine clearance (based on the terminal serum creatinine measurement) was  $70.2 \pm 28.4$  ml/min for donors for DKT, compared to  $88.8 \pm 38.3$  ml/min for ECD and  $103.1 \pm 43.8$  ml/min for SCD.

Recipients of DKT were older and consisted of more African Americans and more diabetic patients compared to recipients of both ECD and SCD transplants. Mean cold ischemic time (CIT) was longest in DKT ( $22.2 \pm 9.7$  hr), followed by ECD transplants ( $19.5 \pm 8.8$  hr) and SCD transplants ( $18.7 \pm 8.1$  hr;  $P < 0.001$ ).

### Transplant Outcomes of DKT vs. ECD Transplants

Early outcomes from DKT, ECD and SCD transplants are outlined in Table 2. Despite longer mean CIT in the DKT group, the incidence of DGF among recipients of DKT (29.3%) was statistically less than in recipients of ECD transplants (33.6%,  $P=0.03$ ) and was similar to recipients of SCD transplants (28.3%,  $P=0.62$ ).

The incidence of primary nonfunction (1.8%), and of acute rejection at discharge (5%) and at 1 year post transplant (12.1%) in the DKT group was lower than in the ECD group ( $P < 0.001$ , 0.019, and 0.028 respectively). Overall and death-censored allograft survival of DKT and ECD transplants were not significantly different up to 4 years posttransplant (Fig. 1). Recipients of SCD transplants had superior overall and death-censored allograft survival compared to DKT (Fig. 1).

Table 3 shows the results of a Cox multivariate regression analysis to estimate the adjusted risk of DKT on allograft loss. This model shows the relative risk of graft loss compared to the reference group of SCD transplants, adjusted for recipient and transplant factors found to be significantly associated with allograft survival in univariate analysis. As donors were stratified by risk (SCD, ECD) additional donor factors were not incorporated into the multivariate model. According to the model, recipients of DKT (hazard ratio [HR] 1.25; 95% confidence interval [CI]: 1.07–1.46) and ECD transplants (HR 1.29; 95% CI: 1.20–1.38) both had a higher relative risk of graft loss compared to SCD transplant recipients. Similar results were found when death with a functioning graft was excluded as a cause of graft loss (data not shown).

### Selection of Donors: Adherence to UNOS Guidelines and the Use of Pretransplant Donor Biopsies

Current UNOS guidelines suggest consideration of DKT if any two of the following criteria exist: donor age greater than 60 years; estimated donor creatinine clearance less than 65 ml/min, rising serum creatinine (greater than 2.5 mg/dl) at time of retrieval; history of medical disease in donor (defined as either longstanding hypertension or diabetes mellitus; adverse donor kidney histology (defined as moderate to severe glomerulosclerosis (greater than 15% and less than 50%). In our analysis of all DKT performed, 75% of donors met these criteria. Additionally, pre transplant donor biopsies were performed in the majority (84%) of DKT, compared with 75.4% of ECD transplants and 46.6% of SCD transplants ( $P=0.001$ ). Among the 526 biopsied in the DKT group, 35.9% had 0–5% glomerulosclerosis (GS), while 31.6% had 5–15% GS, and 32.5% had  $> 15\%$  GS on pretransplant donor biopsy.

Donors who underwent biopsy were older and were more likely to have a history of hypertension, and to have died as a

**TABLE 1.** Baseline characteristics from deceased donors  $\geq 50$  years of age by donor type

	DKT	ECD	SCD	P value
N	625	7,686	6,044	
Donors				
Mean age (years)	64.6 $\pm$ 7.7	59.9 $\pm$ 6.2	54.0 $\pm$ 2.8	<0.001
Age (%)				
50–59 years	29.6	45.5	100	
60–69 years	39.0	48.1	–	
$\geq 70$ years	31.4	6.4	–	
Female (%)	57.1	52.4	50.5	0.002
African American (%)	13.1	9.9	6.9	<0.001
Death due to cerebrovascular accident (%)	76.6	84.9	53.2	<0.001
Mean serum creatinine (mg/dl)	1.3 $\pm$ 1.9	1.1 $\pm$ 1.0	1.0 $\pm$ 0.6	<0.001
Serum creatinine >1.5 mg/dl (%)	16	14.9	3.7	<0.001
Mean creatinine clearance (ml/min)	70.2 $\pm$ 28.4	88.8 $\pm$ 38.3	103.1 $\pm$ 43.8	<0.001
Creatinine clearance <65 ml/min (%)	48.9	27.7	14.3	<0.001
History of diabetes mellitus (%)	16.3	10.4	5.9	<0.001
History of hypertension (%)	61.4	67.6	12.5	<0.001
Recipients				
Mean age (years)	58.2 $\pm$ 10.8	56.1 $\pm$ 12.0	50.6 $\pm$ 12.8	<0.001
Age (%)				
<50 years	19.5	26.0	42.9	
50–59 years	31.7	29.8	31.0	
60–69 years	36.0	32.8	21.1	
$\geq 70$ years	12.8	11.4	5.1	
Female (%)	38.4	37.9	39.5	0.19
African American (%)	37.8	30.2	28.6	<0.001
Regraft (%)	2.7	8.3	12.5	<0.001
Diabetes mellitus (%)	21.1	19.9	15.9	<0.001
Pretransplant dialysis exposure (%)				
<36 months	62.7	53.6	53.1	0.002
36–48 months	15.3	18.3	17.5	0.31
>48 months	22.0	28.1	29.4	0.008
Peak panel reactive antibody (%)				
0–10	80.3	78.2	73.7	<0.001
10–50	13.0	12.9	13.1	
>50	6.7	8.9	13.2	
Pretransplant donor biopsy (%)	84.2	75.4	46.6	<0.001
Pulsatile perfusion (%)	30.7	24.6	15.7	<0.001
Cold ischemic time				
Mean hours	22.2 $\pm$ 9.7	19.5 $\pm$ 8.8	18.7 $\pm$ 8.1	<0.001
$\leq 24$ hours (%)	66.3	75.2	77.7	
25–36 hours (%)	24.9	20.9	19.8	
>36 hours (%)	8.9	3.9	2.5	
HLA-A, -B, -DR mismatches (%)				<0.001
0	2.7	8.4	15.3	
1–2	7.4	7.6	9.5	
3–4	41.3	39.1	39.0	
5–6	48.6	45.0	36.3	

DKT, dual kidney transplants; ECD, expanded criteria donor transplants; SCD, standard criteria donor transplants.

result of a cerebrovascular accident. Meanwhile, donor race, mean serum creatinine level, and the proportion of donors with a history of diabetes did not significantly differ in those who did and did not undergo biopsy. Recipients of DKT where pre trans-

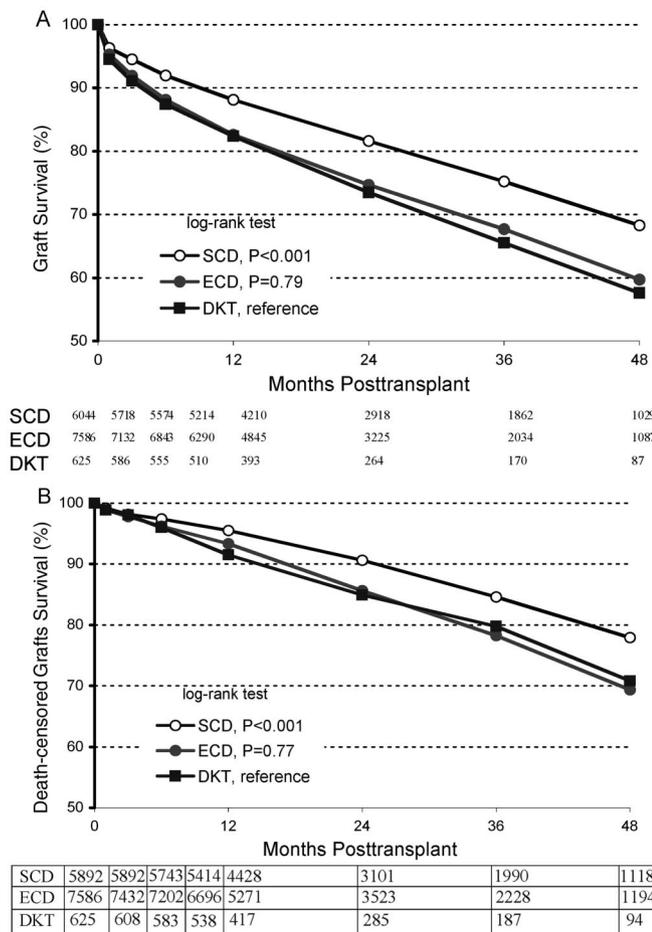
plant donor biopsies were performed did not differ significantly from recipients of DKT where no donor biopsy was done.

When we repeated the primary analysis comparing allograft survival between ECD, SCD, and only those DKT who

**TABLE 2. Early transplant outcomes by transplant type**

	DKT	ECD	SCD	P value
N	625	7,685	6,044	
Delayed graft function (%)	29.3	33.6	28.3	<0.001
Acute rejection (%)				
At discharge	5.0	7.3	6.4	0.02
At 1 year	12.1	17.6	16.9	0.03
25% decline in serum creatinine in first week (%)	50.1	42.8	48.2	<0.001
Primary nonfunction (%)	1.8	3	1.5	<0.001

DKT, dual kidney transplants; ECD, expanded criteria donor transplants; SCD, standard criteria donor transplants.



**FIGURE 1. (A) Unadjusted graft survival of DKT, SCD, and ECD transplants. (B) Death-censored graft survival of DKT, SCD, and ECD transplants.**

met UNOS criteria, we found the same outcomes as reported above, with DKT and ECD demonstrating similar allograft survival up to 4 years post transplantation.

**The Use of Pulsatile Perfusion in DKT**

Kidneys used in DKT were more likely to undergo PP (30.7% of DKT underwent PP, compared to 24.6% of ECD kidneys and 15.7% of SCD kidneys,  $P<0.001$ ). Table 4 out-

lines early post transplant outcomes in DKT performed with and without with and without PP. The use of PP was associated with no significant difference in rates of DGF, acute rejection, and primary nonfunction in DKT. Furthermore, there was no significant difference in overall allograft survival among recipients of DKT utilizing kidneys with and without PP (Fig. 2).

**DISCUSSION**

Faced with an immense demand for organs the transplant community needs to continue to develop strategies to maximize the yield of the existing donor pool. In the past decade, efforts to increase the use of organs from deceased donors with expanded criteria characteristics have resulted in an increase in the number of transplants (9). This has, in part, been due to the acceptance of older deceased donors. During our study period, the percentage of deceased donors >60 years of age increased from 8.5% (n=669) in 2000 to 9.2% (n=872) in 2005. However, it is notable that 37% of kidneys recovered from donors aged 61–65 years and 54% of kidneys from donors more than 65 years were discarded in the United States between 2000 and 2003 (10), suggesting that while we may be harvesting more organs from older donors, we may not be utilizing them to their maximum capacity.

In our analysis of UNOS data from 2000 to 2005, we found that DKT are infrequent, suggesting that they may be performed by only a select number of transplant centers. However, during the study period, the percentage of DKT performed in the United States increased from 1.0% to 1.5%, which may reflect a growing interest in this strategy. Moreover, we found that despite having higher risk donor characteristics, recipients of DKT had lower rates of DGF and had similar allograft survival (overall and death-censored) up to 4 years posttransplant compared to recipients of single ECD transplants. Previous studies have reported comparable allograft survival between carefully selected DKT and single kidney transplants (2–7, 11–14). Moore et al. (15) recently reported results from a single center case control study comparing outcomes of 16 DKT, with ECD and SCD transplants and reported similar 2-year patient and allograft survival between DKT, SCD, and ECD transplants. However, they noted higher rates of DGF and complication rates in the SCD group than reported norms. Additionally, low-risk younger recipients were selected to minimize surgical risks. In our analysis, there was a greater incidence of high risk characteristics among recipients of DKT compared to both ECD and SCD transplants. Despite this, DKT were associated with outcomes comparable to single kidney ECD transplants.

The increased risk of DGF due to longer cold ischemic times in DKT is believed to be offset by an increase in the transplanted nephron mass. Our findings support this belief by demonstrating a reduced incidence of DGF in DKT compared to single kidney ECD transplants despite a longer mean CIT in DKT. It follows that if we could achieve shorter CIT we may, in fact, improve the rates of DGF further in this group. Of note, organs used in DKT were more likely to undergo PP, which has been shown to be associated with reduced rates of DGF in ECD transplants (16, 17). We found no significant decrease in rates of DGF or allograft survival with the use of PP in DKT. However, it is important to recall that the use of

**TABLE 3.** Multivariate Cox proportional hazards analysis for allograft survival

	Unadjusted		Adjusted	
	HR (95% CI)	P value	HR (95% CI)	P value
DKT	1.17 (1.01–1.36)	0.03	1.25 (1.07–1.46)	0.006
ECD	1.34 (1.26–1.43)	<0.001	1.29 (1.20–1.38)	<0.001
SCD	1.00		1.00	
Recipient age				
≤60	1.00		1.00	<0.001
>60	1.36 (1.27–1.45)	<0.001	1.36 (1.25–1.43)	
Recipient race				
Non-African American	1.00		1.00	
African American	1.34 (1.25–1.43)	<0.001	1.33 (1.25–1.43)	<0.001
HLA mismatch				
0 mismatches	0.67 (0.60–0.75)	<0.001	0.73 (0.65–0.82)	<0.001
>0 mismatches	1.00			
Dialysis duration				
<48 months	1.00		1.00	
>48 mo	1.31 (1.19–1.43)	<0.001	1.24 (1.13–1.36)	<0.001
Cause of end-stage renal disease				
Diabetes mellitus	1.17 (1.08–1.27)	<0.001	1.18 (1.09–1.29)	<0.001
Other	1.00		1.00	
Biopsy pretransplant				
Yes	1.24 (1.16–1.33)	<0.001	1.11 (1.03–1.19)	0.008
No	1.00		1.00	
Panel reactive antibodies				
<50%	1.00		1.00	
>50%	1.31 (1.19–1.44)	<0.001	1.33 (1.20–1.48)	<0.001
Prior transplant				
No	1.00		1.00	
Yes	1.20 (1.09–1.32)	<0.001	1.34 (1.20–1.49)	<0.001
Storage				
Cold storage	1.00		1.00	
Pulsatile perfusion	1.07 (0.99–1.16)	0.08	0.97 (0.90–1.06)	0.51
Cold ischemic time				
≤24 hours	1.00		1.00	
25–36 hours	1.14 (1.07–1.22)	<0.001	1.09 (1.01–1.19)	<0.001
>36 hours	1.34 (1.13–1.60)	0.001	1.26 (1.06–1.50)	0.003

DKT, dual kidney transplants; ECD, expanded criteria donor transplants; SCD, standard criteria donor transplants.

PP allows monitoring of parameters that factor into the decision whether to use the kidney and its implications cannot be adequately assessed in a retrospective manner.

### Which Kidneys Should Be Used for DKT?

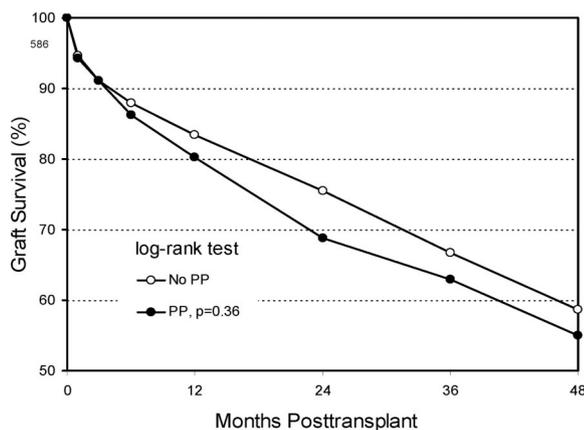
A major limitation to DKT is effectively determining which kidneys should be used for single versus dual use. Remuzzi et al. reported the results of a biopsy scoring system to guide allocation of single versus dual organs with remarkable success. Current UNOS guidelines recommend consideration of DKT if any two of the following criteria exist: donor age greater than 60 years; estimated donor creatinine clearance less than 65 ml/min, rising serum creatinine (greater than 2.5 mg/dl) at time of retrieval; history of medical disease in donor (defined as either longstanding hypertension or diabetes mellitus; adverse donor kidney histology (defined as

moderate to severe glomerulosclerosis (greater than 15% and less than 50%). When we repeated our analysis restricting the DKT group to only those meeting these UNOS criteria for DKT (75% of DKT), our results did not significantly differ. Therefore these criteria are likely reasonable guidelines at this stage as they are associated with outcomes which are at least as good as ECD transplants utilizing organs from higher risk donors. It is, however, disconcerting that 25% of DKT were performed with organs that did not meet these high risk UNOS criteria and that 12% of organs used for DKT were from SCDs. This may reflect inconsistencies in clinical practice that resulted in the use of organs that possibly could have been used for single kidney transplants. Additionally, there is likely room for improving outcomes with DKT by optimizing donor and recipient selection. We propose that prospective studies are needed to determine criteria that would optimize

**TABLE 4.** Early transplant outcomes of DKT with and without pulsatile perfusion (PP)

	DKT with PP	DKT without PP	P value
N	192	433	—
Delayed graft function (%)	28.1	29.8	0.67
Acute rejection (%)			
At discharge	3.1	5.8	0.16
At 1 year	13.6	11.4	0.55
25% decline in serum creatinine in first week (%)	50	50.1	0.98
Primary nonfunction (%)	1.0	2.1	0.36

DKT, dual kidney transplants; ECD, expanded criteria donor transplants; SCD, standard criteria donor transplants.

**FIGURE 2.** Overall allograft survival in DKT with and without pulsatile perfusion (PP).

outcomes of DKT while ensuring that DKT should be restricted to organs that would otherwise be discarded.

The current ECD algorithm allows us to streamline allocation of marginal organs to transplant candidates. However, no such approach exists for DKT, as current guidelines for DKT do not involve upfront involvement of the waitlisted transplant candidate. It is conceivable that many of the kidneys used for DKT would otherwise have been discarded based on their high-risk characteristics, making DKT a potentially useful strategy for using kidneys that may otherwise be discarded. We propose an approach where DKT should be considered a form of ECD transplants and should be incorporated into ECD algorithms, creating a “DKT list” of patients willing to accept DKT using organs considered higher risk for single ECD transplants. A streamlined approach such as this may, in fact, result in superior early outcomes with DKT with shorter CIT contributing to lower rates of DGF.

If successful, the impact of such a strategy would clearly be enhanced by widespread adoption of DKT. Our analysis of the UNOS data, however, indicates that we are clearly far from this point. With outcomes that seem to be at least as good as ECD transplants, why are DKT so uncommon? It is possible that there may be reluctance on the part of transplant

centers due to concerns about the increased risk of surgical complications, the prolonged warm and cold ischemic time and associated risk of DGF, and the uncertainty in determining which organs are suitable for single versus dual use. Longer time under anesthesia, and twice the number of dissections and vascular anastomoses, may contribute to a higher surgical risk with DKT (18). It is important to note, however, that since the first reported DKT in 1996 (19), there have been various surgical techniques, including unilateral placement of both kidneys (20), which successfully minimize the length of surgery and may ameliorate some of these concerns. Additionally, as reported above, in contrast to concerns regarding DGF, we found lower rates of DGF with DKT compared to single ECD transplants. Finally, while future prospective studies need to be performed in the US to determine the optimal characteristics to guide the definition and allocation of single versus dual kidneys, we feel that the existing guidelines proposed by UNOS for the use of dual kidneys are reasonable at this stage as acceptable outcomes have been achieved with DKT that appear to have been performed following these guidelines.

In interpreting these results, readers must consider the limitations inherent to observational studies using registry data. Although this is a large retrospective study, the numbers of DKT may not have been sufficient to detect certain significant risk factors on multivariate analysis. Also, our secondary analysis looking at the impact of PP must be interpreted with the understanding that these strategies are utilized to determine which organs are transplanted and our analysis only looked at the outcomes among transplanted kidneys. Therefore, definitive conclusions regarding their utility cannot be drawn until further studies evaluate them in a prospective manner.

## CONCLUSION

In summary, adult dual kidney transplants remain infrequent in the United States while the numbers of discarded organs continues to grow. Despite using kidneys from donors with higher risk characteristics, DKT achieved similar outcomes to ECD transplants. These results support the practice of DKT as a means of using kidneys that may otherwise be discarded. With further studies to better define selection of organs for DKT, and a more upfront approach to DKT by offering this option to patients at the time of wait-listing as part of an ECD algorithm, we may be able to further optimize outcomes of DKT and minimize discard of potential organs.

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