

## BRIEF COMMUNICATION

# Risk aversion in the use of complex kidneys in paired exchange programs: Opportunities for even more transplants?

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This retrospective review of the largest United States kidney exchange reports characteristics, utilization, and recipient outcomes of kidneys with simple compared to complex anatomy and extrapolates reluctance to accept these kidneys. Of 3105 transplants performed, only 12.8% were right kidneys and 23.1% had multiple renal arteries. 59.3% of centers used fewer right kidneys than expected and 12.1% transplanted zero right kidneys or kidneys with more than 1 artery. Five centers transplanted a third of these kidneys (35.8% of right kidneys and 36.7% of kidneys with multiple renal arteries). 22.5% and 25.5% of centers currently will not entertain a match offer for a left or right kidney with more than one artery, respectively. There were no significant differences in all-cause graft failure or death-censored graft loss for kidneys with multiple arteries, and a very small increased risk of graft failure for right kidneys versus left of limited clinical relevance for most recipients. Kidneys with complex anatomy can be used with excellent outcomes at many centers. Variation in use (lack of demand) for these kidneys reduces the number of transplants, so systems to facilitate use could increase demand. We cannot know how many donors are turned away because perceived demand is limited.

## KEYWORDS

kidney paired exchange, multiple renal artery kidneys, right donor nephrectomy

## 1 | INTRODUCTION

Living donor right kidneys and kidneys with multiple renal arteries (MRAKs) present some degree of complexity for donor and recipient surgeons seeking the best outcome for their patient. While there was initial concern that right kidneys<sup>1-4</sup> and MRAKs<sup>5,6</sup> from living

donors may have inferior outcomes compared to left kidneys with conventional anatomy, multiple studies have found equivalent and excellent short and long-term outcomes between right and left kidneys<sup>7-15</sup> and single renal artery kidneys compared with MRAKs.<sup>16-20</sup> Despite this evidence, concern still exists from experts at kidney programs about enrolling right kidney and/or MRAK living donors

**Abbreviations:** CHiP, children and highly sensitized patients; KPD, kidney paired donation; MRAKs, multiple renal artery kidneys; NKR, National Kidney Registry; PRA, panel reactive antibody; SD, standard deviation.

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into paired exchange programs. While limited demand for these kidneys may reduce the size and diversity of the donor pool, both to the detriment of potential donors and recipients, differential demand based on kidney anatomy has never been investigated.

The National Kidney Registry (NKR) is a large kidney exchange program where potential donors and recipients are paired based on risk-benefit decisions made at transplant centers. Organ offers for biologically compatible donors can be declined at the time of the offer. Additionally, the NKR has a robust system to filter donors due to age, size, or anatomy, etc., prior to match offers. Much of the filtering of potential donors occurs in this pre-offer stage, but specific reasons for each pre-offer decline were not recorded with granularity over most of the study period. Starting in early 2020 participating centers have entered anatomy preferences to filter potential donor offers as a component of this pre-offer system. Our exploratory study utilized data from the NKR over an 8-year period to examine transplant outcomes for kidneys with complex anatomy compared with kidneys with conventional anatomy and assess center level risk tolerance variation in utilization of these kidneys within paired exchange programs based on clinical activity. The conclusions drawn from this data was then corroborated with the current pre-offer anatomy preferences submitted by participating centers.

## 2 | METHODS

### 2.1 | Study design

This retrospective study of 3105 adult recipients of a kidney transplanted between January 2012 and August 2019 was IRB approved (IRB Number: 18-26804) and used data from the NKR, a nonprofit, 501(c) organization that facilitates kidney paired donations for members of its clinical network. The research activities of this study are consistent with the Declarations of Helsinki and Istanbul.

#### 2.1.1 | Data source

The NKR is composed of over 90 transplant center members and acts as a clearing house to facilitate Kidney Paired Donation (KPD) that has facilitated over 5,000 transplants. Data was collected prospectively and includes donor- and recipient-related characteristics such as demographics, blood group, anatomy (e.g., left/right kidney and single or multiple arteries), and transplant center. Recipient panel reactive antibody (PRA) and whether the recipient was listed as a CHiP (Children and Highly Sensitized Patients) recipient, often the recipients of end-chain living donor offers, were also evaluated.

We collected the number of declines made after a match offer was generated, although declines that occurred prior to a match offer could not be collected. The most direct surrogate of pre-offer decision making over the study period, the current anatomy preferences submitted by participating centers, was obtained from the NKR.

### 2.2 | Study endpoint definitions

For each center, we determined the number of complex kidneys (e.g., right and multiple artery) transplanted. Under the assumption that transplant centers should have similar levels of risk aversion for using MRAK kidneys, the expected number of MRAK transplants per center was calculated by multiplying the number of kidney transplants performed at the center by the proportion of MRAK transplants performed overall. Similarly, under the assumption that transplant centers should have the same risk aversion for using donor right kidneys, the expected number of right kidneys transplanted per center was calculated by multiplying the number of kidney transplants performed at the center by the proportion of donor right kidneys utilized overall.

The primary endpoint was time to all-cause graft failure, defined as recipient death or graft loss for any reason (i.e., re-transplantation or need for permanent dialysis post-transplant), whichever occurred first. Graft survival was calculated from the transplant date until date of all-cause graft failure. Recipients alive with a functioning graft were right censored at date of last known follow-up.

The secondary endpoint was time to death-censored graft failure, defined as re-transplantation or need for permanent dialysis post-transplant. Patients alive or who died with a functioning graft were censored at date of last known follow-up.

### 2.3 | Statistical analysis

Continuous variables are presented as mean and standard deviation (SD) or median and inter-quartile range (25th and 75th percentile) and compared by the standard two-sample *t*-test or Wilcoxon Rank Sum test. Categorical variables are presented as counts and percentages and compared using chi-square test. Summaries are provided overall and by kidney laterality (left vs. right).

Graft survival was estimated using the product-limit (Kaplan-Meier) method and compared by the log-rank test. The competing risk method was used to estimate the cumulative incidence function for graft loss with death as a competing event and compared between groups using Gray's test. Multivariable Cox hazard model was used to evaluate the association of donor kidney laterality and renal anatomy (single versus multiple arteries) with risk of all-cause graft failure and death-censored graft loss. Proportional hazards assumption was evaluated using numerical and graphical techniques. Hazard ratio and 95% confidence interval are provided as measures of strength of association and precision, respectively.

Analyses were conducted using the SAS Statistical Software, version 9.4 (SAS Institute). A *p*-value < .05 was considered statistically significant.

## 3 | RESULTS

The characteristics for 3105 donor-recipient pairs are listed in [Table 1](#), representing transplants done at 91 transplant centers, with

a mean of 34 transplants per center (range = 1–244 transplants per center). Three hundred ninety-nine (12.8%) were right kidneys, and 714 (23.1%) had multiple renal arteries (of which 611 were left kidneys, and 103 right kidneys), with a median follow up of 34.8 months.

Left kidney donors tended to be younger than right kidney donors (44.4 vs. 45.6 years old, respectively,  $p = .066$ ). Left kidneys were transplanted into patients with higher median cPRA (16.0% vs. 0%, respectively,  $p < .001$ ). When a right kidney had multiple renal arteries, it was more commonly used in a recipient with a lower cPRA compared to a left kidney with multiple arteries ( $p = .005$ ).

Graft survival for single versus MRAKs stratified on donor left versus donor right kidneys are provided in [Figure 1A,B](#), and single artery kidneys are compared ([Figure 1C](#)), and left MRAKs are compared to right MRAKs ([Figure 1D](#)). For left kidneys, the 1-, 3-, and 5-year graft survival was 98.0%, 94.8% and 90.2% with single artery, respectively, versus 97.5%, 93.9% and 89.1% with multiple renal arteries (log rank test:  $p = .3108$ ). For right kidneys, the 1-, 3-, and 5-year graft survival was 96.9%, 91.8% and 89.4%, respectively, with single artery versus 95.0%, 95.0%, and 80.5% with multiple renal arteries (log rank test:  $p = .3189$ ). Additionally, graft loss (unadjusted) rates were low, and not statistically different between single versus MRAK for left and right kidneys (Gray's test:  $p = .8586$  and  $p = .6085$ , respectively) ([Figure 2A,B](#)), or for left kidneys with a single artery versus rights with a single artery ( $p = .27440$ ) ([Figure 2C](#)), or left MRAKs versus right MRAKs ( $p = .8892$ ) ([Figure 1D](#)).

Results of the multivariable Cox hazards model for all cause graft failure and death-censored graft loss are provided in [Table 2](#). There was no significant difference in the rates of all-cause graft failure and death-censored graft loss for donor left versus donor right kidney transplants (adjusted HR = 1.240,  $p = .253$  and Adjusted HR = 1.236,  $p = 0.400$ , respectively) ([Table 2](#)). To further evaluate this, we estimated the adjusted death censored graft survival up to 5 years after transplant for MRAK versus kidneys with a single artery. Rates were adjusted at the average level of each covariate in the Cox multivariable model. The 5-year adjusted graft survival for MRAK is 93.1% (95% CI: 90.8%, 95.4%) compared to 95.4% (95% CI: 94.3%, 96.6%). The HR of 1.54 translates to a graft survival difference of only 2.3% (adjusted death-censored graft survival curves are displayed in supplemental [Figure 1](#)).

The observed-to-expected number of MRAK and right kidneys utilized per center is provided in [Figure 3](#). Of the 91 centers, 56 (61.5%) performed less than expected MRAK transplants, assuming a 23.1% MRAK transplant rate. A small group of 5 centers transplanted 143 (35.8%) of the right kidneys and 262 (36.7%) of the MRAKs over the study period. Of the 714 kidneys with multiple renal arteries, 55 had >2 arteries (42 left kidney and 13 right kidney). The number of kidneys with >2 renal arteries was too small to perform a meaningful survival analysis, but it was notable that only 3 centers (3.3%) transplanted 29 (52.7%) of all kidneys with >2 renal arteries. Of the 5 centers with highest volume of utilization of kidneys with complex anatomy over the study period only 2 used more right kidneys than expected and none used more MRAKs than expected. Some centers who did no MRAK transplants had a 98%

probability of performing one or more MRAK transplants, assuming a 23.1% MRAK transplant rate. Of the 91 NKR centers, 59.3% used fewer right kidneys than expected over the study period, assuming a 12.8% donor right kidney utilization rate. ([Figure 3](#)). Of the 91 centers, 11 centers transplanted neither a right kidney nor MRAK. Of the remaining 80 centers, 10 centers did not transplant a right MRAK over the study period.

Actual match offers for right kidneys were declined significantly more commonly than left kidneys ([Table 1](#)). Much of the filtering process in KPD occurs prior to an organ offer. Unfortunately, specific reasons for pre-offer declines were not recorded with granularity over the study period, so the current anatomy preferences were used as a surrogate of anatomy risk aversion over the study period. Currently, 22 NKR participating centers (22.5%) will not entertain a match offer for a left kidney with more than one artery, and 25 centers (25.5%) will not entertain a match offer for right kidney with more than one artery. Nine centers (9.2%) will not entertain a match offer for any right kidney. Only 18 centers (18.8%) agree to entertain an offer for a left kidney with any number of arteries, and 16 (16.3%) for a right kidney with any number of arteries.

## 4 | DISCUSSION

KPD depends on complex joint decision making about donor kidney laterality and arterial anatomy across transplant centers when accepting a donor offer, with well-intentioned transplant providers working towards the optimal outcome for their patient. This exploratory study of transplantation of over 3000 kidneys with varying anatomic complexity revealed no differences in outcomes for kidneys with multiple arteries and a very small increased risk of graft failure for right kidneys. Much of the filtering of potential donors occurs prior to an organ offer for a biologically compatible donor, and the anatomy preferences are a significant component of that pre-offer selection system. At the individual patient level, the risk of remaining on dialysis and waiting for a left kidney must be weighed against a very low increased risk of graft loss. For centers participating in exchange programs, the ubiquitous risk aversion by some centers and resulting lack of demand for kidneys with complex anatomy may have significant upstream effects on lowering the number of donors with complex anatomy enrolled and utilized in exchanges.

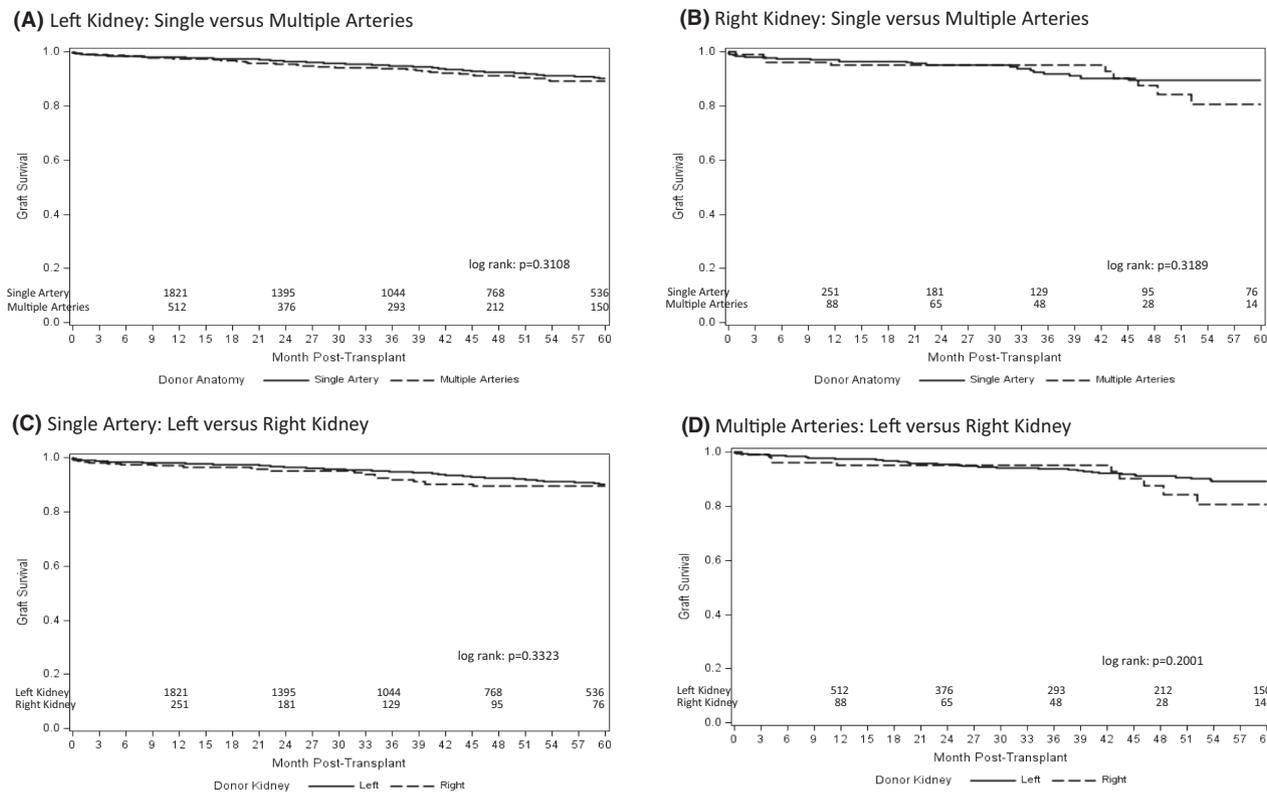
There has been widespread reluctance to accept kidneys with complex anatomy due to potential surgical complications and unfamiliarity with the donor surgeon. Generally donor laterality is not considered a major factor in difficulty of the donor operation, and donor outcomes have not been determined by laterality.<sup>8,18,19</sup> Therefore, it is presumed that donor laterality is used in decision making only for the infrequent donor for whom a right nephrectomy optimizes long-term donor renal function, such as patients with a size discrepancy between the kidneys, unilateral kidney stones, anomalous venous drainage, unilateral renal artery calcification/fibromuscular dysplasia, females that may become pregnant after donation, or the presence of unilateral renal cysts.

**TABLE 1** Summary of donor and recipient characteristics stratified by donor laterality. Similarly, for the 714 kidneys with multiple arteries, these characteristics varied

		Left	Right		Overall
		N = 2706	N = 399 (12.8%)	p-value	N = 3105
Mean (SD) recipient age at transplant (year)	Mean (SD)	49.0 (14.4)	49.3 (14.7)	.754	49.0 (14.5)
Recipient sex	Male	1425 (52.7%)	227 (56.9%)	.114	1453 (46.8%)
	Female	1281 (47.3%)	172 (43.1%)		1652 (53.2%)
Recipient race	White	1647 (60.9%)	232 (58.1%)	.202	1879 (60.5%)
	Black	464 (17.1%)	83 (20.8%)		547 (17.6%)
	Other	595 (22.0%)	84 (21.1%)		679 (21.9%)
Recipient is waitlist CHIP?	No	2092 (77.3%)	276 (69.2%)	<.001	2368 (76.3%)
	Yes	614 (22.7%)	123 (30.8%)		737 (23.7%)
Recipient blood group	A	990 (36.6%)	152 (38.1%)	.424	1142 (36.8%)
	B	468 (17.3%)	79 (19.8%)		547 (17.6%)
	AB	199 (7.3%)	25 (6.3%)		224 (7.2%)
	O	1049 (38.8%)	143 (35.8%)		1192 (38.4%)
Calculated PRA	Median (25th–75th)	16.1 (0–81.4)	0 (0–71.8)	<.001	11.4 (0–80.8)
Donor age (years)	Mean (SD)	44.4 (12.4)	45.6 (12.3)	.066	44.6 (12.4)
Donor sex	Male	1013 (37.4%)	150 (37.6%)	.913	1163 (37.5%)
	Female	1693 (62.6%)	249 (62.4%)		1942 (62.5%)
Donor race	White	2056 (76.0%)	319 (80.0%)	.192	2375 (76.5%)
	Black	231 (8.5%)	26 (6.5%)		257 (8.3%)
	Other	419 (15.5%)	54 (13.5%)		473 (15.2%)
Donor blood group	A	1086 (40.1%)	160 (40.1%)	.739	1246 (40.1%)
	B	439 (16.2%)	73 (18.3%)		512 (16.5%)
	AB	138 (5.1%)	20 (5.0%)		158 (5.1%)
	O	1043 (38.5%)	146 (36.6%)		1189 (38.3%)
Multiple renal artery kidney (MRAK)	No	2082 (77.3%)	295 (74.1%)	.159	2377 (76.9%)
	Yes	611 (22.7%)	103 (25.9%)		714 (23.1%)
	Missing	13	1		14
	>2 arteries	42 (1.6%)	13 (3.3%)		55 (1.8%)
Number of donor declines	Median (25th–75th)	0 (0–1)	1 (0–2)	<.001	0 (0–1)
	Missing	491	71		562
Follow-up for graft failure <sup>1</sup> (months)	Median (25th–75th)	38.5 (20.6–63.6)	35.4 (19.2–61.8)		38.4 (20.5–63.6)

Our data about the outcomes of complex anatomy kidneys from a diverse group of transplant centers with long term follow up suggests there may be a slight increase in the risk of graft loss in the recipient when a right kidney from a living donor is transplanted, but a very low absolute risk. Despite this, almost 60% of centers in the NKR are not utilizing right kidneys at the expected rate, disadvantaging pairs entering with a right-sided donor. We can also potentially infer programs with this mindset are denying suitable donors if anatomy demands a right donor nephrectomy. There are a few centers utilizing a large number of right kidneys, whose patients therefore carry the burden of this potential small increased absolute risk of graft loss.

In this study, long-held beliefs that right kidneys and MRAKs might have significantly inferior results appears to have led to cautious selection of only single vessel, left kidneys by some. Literature on use of MRAKs in single centers varies, with one meta-analysis finding increased risk of graft loss at 1-year<sup>5</sup> and long term graft function,<sup>6</sup> while other studies finding no outcome differences.<sup>6,16–20</sup> In the data presented here, similar to the utilization of right kidneys, 61.4% of centers used fewer MRAKs than expected, and 21 centers did not use any right MRAKs during the study period. There may be a break point for centers considering multiple renal arteries between a kidney with 2 arteries compared to >2, but the number of kidneys with >2 arteries in the data set was too small to allow for statistical



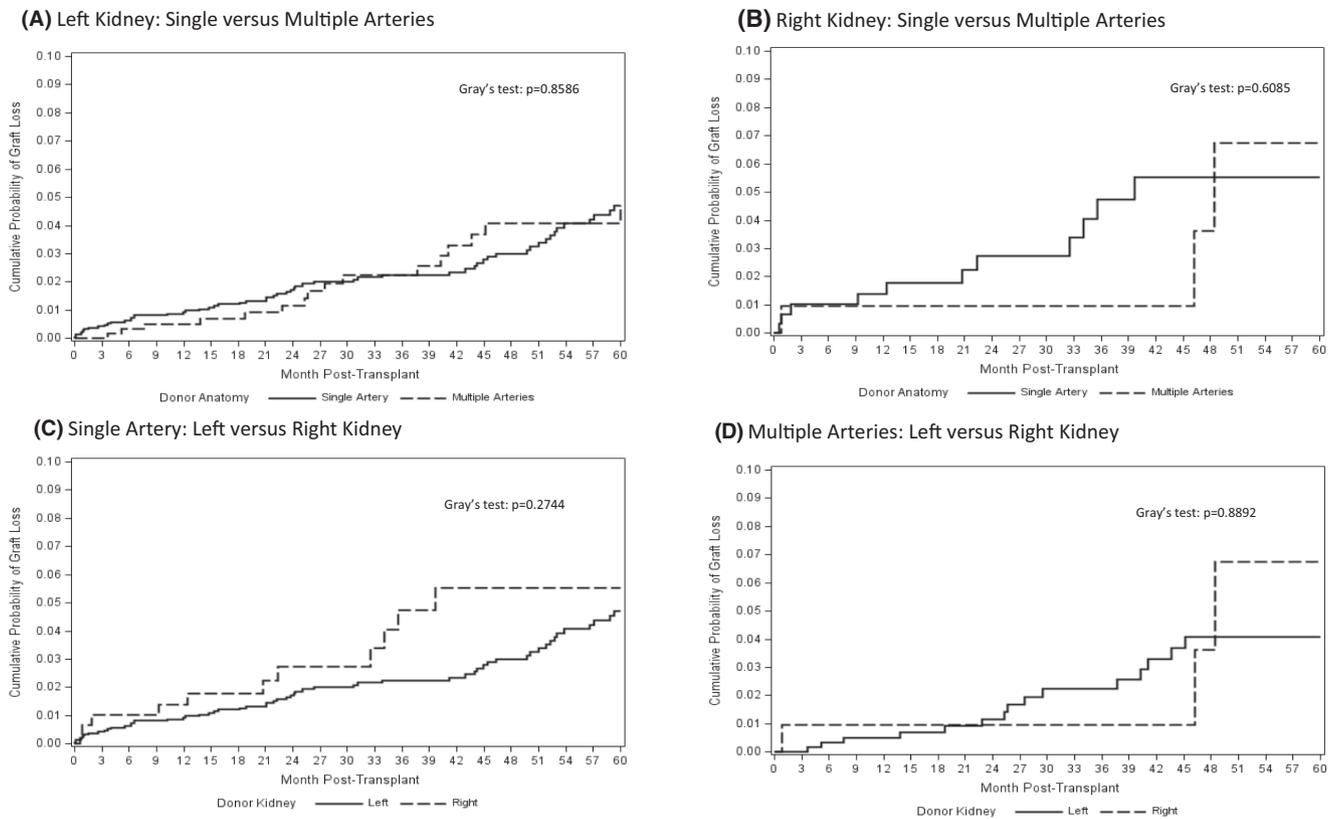
**FIGURE 1** Unadjusted Kaplan-Meier graft survival for (A) left and (B) right kidneys, and (C) left kidneys with a single artery compared to right kidneys with a single artery, and (D) left MRAKs compared to right MRAKs

analysis. Given the small but identifiable increase in risk of graft failure with complex anatomy it may be optimal to wait for a lower risk kidney in certain circumstances, based on expected waiting time, anatomic complexity, and center experience. During informed consent discussions with patients, it is also important to point out KPD exchanges provide a back stop to correct these infrequent technical failures.

The main shortcoming of the data presented here is the retrospective nature of the study, requiring some extrapolation of center risk aversion from center activity. This study found that match offer declines were more common for right kidneys compared to left, and infers from available data that kidneys with complex anatomy were filtered prior to a match offer significantly more frequently than left kidneys with a single artery. The current anatomy preferences suggest this data likely underestimates center risk aversion because NKR centers must preselect donor characteristics like right kidneys and kidneys with multiple renal arteries that they are willing to accept prior to organ offers even being made. Since our observed-to-expected utilization ratio was calculated based on the frequency of these complex kidneys being transplanted per center, it likely underestimates the availability of these kidneys in the population of potential donors. Unfortunately, we do not have data about center pre-offer declines to define the actual demand for kidneys during the study period, but we extrapolate risk aversion using the clinical activity over the study period augmented by analysis of the current anatomy preferences.

Even when looking more closely at the 5 centers transplanting the highest number of kidneys with complex anatomy none used more MRAKs than expected and only 2 used more right kidneys than expected, so even this group can improve. Another limitation of this study is that we also were not able to correlate center risk-taking behavior with waiting time. Future prospective studies should examine anatomy preference patterns and outcomes for right and MRAK kidneys. Also, it would be interesting to compare KPD practices to non-KPD living donor kidney transplant practices at participating centers.

The study presented here, encompassing a large number of donor-recipient pairs from 91 transplant centers, with long-term follow up suggests a national reluctance to transplant kidneys with complex anatomy. When used, these kidneys with complex anatomy are more frequently transplanted in CHIP patients and patients with a lower cPRA. It is unknown how many potential right kidney donors are never entered into paired exchange programs due to perceived risks, lowering the number of kidneys possible for matching. Potential ways to systematically encourage the use of right kidneys and MRAKs in large kidney exchanges could be to reduce waiting time for recipients of these kidneys. Center level utilization of these kidneys could be encouraged by adding center liquidity contribution points or additional kidneys for chain ending transplants to recipients at high utilizing centers. Donors with complex anatomy are undervalued, but should still be entered into the exchange pool, as that kidney could be



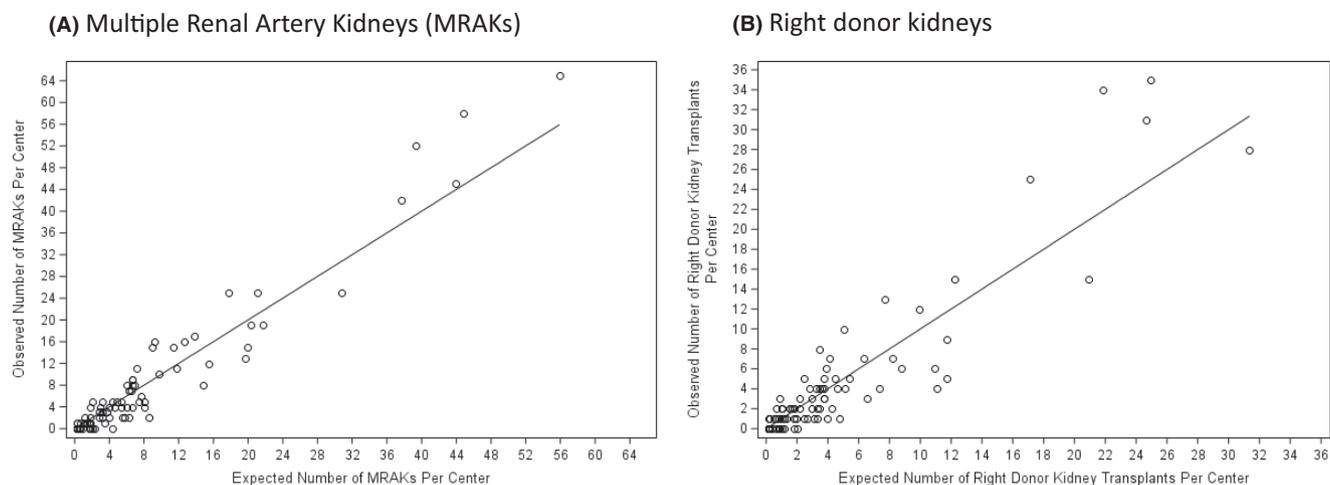
**FIGURE 2** Unadjusted cumulative incidence function for graft loss with death as a competing event for MRAKs compared to single artery (A) left and (B) right kidneys, and (C) left and right single artery kidneys, and (D) left and right MRAKs, including the relatively small number of right MRAK transplants

**TABLE 2** Results of the multivariable Cox hazards model

	Comparison	All-cause graft failure				Death-censored graft loss			
		Hazard ratio	Lower	Upper	p-value	Hazard ratio	Lower	Upper	p-value
Renal arteries	MRAK versus single	1.250	0.923	1.693	.150	1.540	1.045	2.270	.029
Donor kidney	Right versus left	1.240	0.857	1.793	.253	1.236	0.755	2.026	.400
Recipient age	Per year increase	1.009	0.999	1.019	.090	0.977	0.965	0.989	.000
Recipient sex	Male versus female	1.083	0.822	1.427	.571	0.990	0.689	1.422	.956
Recipient race:	Black versus White	0.749	0.517	1.085	.126	0.991	0.632	1.553	.967
	Other versus White	0.493	0.328	0.741	.001	0.478	0.277	0.825	.008
Donor age	Per year increase	1.009	0.997	1.021	.158	1.015	0.999	1.032	.063
Is waitlist chip?	Yes versus no	1.847	1.240	2.749	.003	1.483	0.867	2.535	.150
Donor blood type	AB versus A	1.471	0.860	2.515	.159	1.999	1.019	3.922	.044
	B versus A	0.899	0.592	1.365	.616	0.987	0.576	1.690	.962
	O versus A	1.201	0.861	1.677	.281	1.036	0.665	1.615	.874
Calculated PRA	Per percent increase	1.003	0.999	1.006	.160	1.004	0.999	1.009	.109

blood group O, or initiate a high PRA transplant in the exchange. Importantly, that donor center could be matched with a kidney with straightforward anatomy in return. Potential kidney donors with complex anatomy should not be discouraged from participating in paired exchange programs, as there will always be centers

willing to utilize these kidneys. Donor centers should avoid the urge to include perceived demand into their decision making, as they can be assured that practically all donors they want to enter in the exchange will be considered acceptable by some recipient centers.



**FIGURE 3** Scatter plot of the observed-to-expected number of (A) multiple renal artery transplants and (B) right donor kidneys

In summary, surgical and selection caution about complex kidneys must also be weighed against the risks that pairs are taking, particularly blood group O and high PRA patients, when they stay on dialysis longer waiting for a left, single artery kidney. Complex living donor kidneys can be used with excellent results at many centers and are still more likely to have better long-term outcomes than deceased donor kidneys. Decision-making should be driven by efforts to increase the volume of living donor kidney transplants.

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#### DISCLOSURE

The authors of this manuscript have conflicts of interest to disclose as described by the *American Journal of Transplantation*. Authors MC, JLV, ADW, SMF and DBL serve as unpaid members of the Medical Board of the National Kidney Registry, with MC as the Surgical Director and ADW as the Research Director. MR is a full-time employee of the National Kidney Registry. Other authors have no conflicts.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the NKR. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from D.B.L. with the permission of the NKR.

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## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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