

Brief Communication

Center-Level Utilization of Kidney Paired Donation

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With many multicenter consortia and a United Network for Organ Sharing program, participation in kidney paired donation (KPD) has become mainstream in the United States and should be feasible for any center that performs live donor kidney transplantation (LDKT). Lack of participation in KPD may significantly disadvantage patients with incompatible donors. To explore utilization of this modality, we analyzed adjusted center-specific KPD rates based on casemix of adult LDKT-eligible patients at 207 centers between 2006 and 2011 using SRTR data. From 2006 to 2008, KPD transplants became more evenly distributed across centers, but from 2008 to 2011 the distribution remained unchanged (Gini coefficient = 0.91 for 2006, 0.76 for 2008 and 0.77 for 2011), showing an unfortunate stall in dissemination. At the 10% of centers with the highest KPD rates, 9.9–38.5% of LDKTs occurred through KPD during 2009–2011; if all centers adopted KPD at rates observed in the very high-KPD centers, the number of KPD transplants per year would increase by a factor of 3.2 (from 494 to 1593). Broader implementation of KPD across a wide number of centers is crucial to properly serve transplant candidates with healthy but incompatible live donors.

Key words: Kidney exchanges

Abbreviations: KPD, kidney paired donation; LDKT, live donor kidney transplantation; SRTR, Scientific Registry of Transplant Recipients; UNOS, United Network for Organ Sharing.

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Introduction

Kidney paired donation (KPD) is a rapidly emerging transplant modality that potentially facilitates live donor kid-

ney transplantation (LDKT) for transplant candidates who identify a willing but incompatible donor (1–6). Few KPD transplants were performed in the United States before 2003, but since then the number of KPD transplants rose steadily to over 300 per year in 2009 (5). Several multicenter registries of incompatible pairs offer transplant centers the ability to participate in KPD, and a program through the United Network for Organ Sharing (UNOS) has also been recently introduced (5). A single-center report from Methodist Specialty and Transplant Hospital in San Antonio, Texas illustrated the feasibility and impact of building a KPD program in the modern era, describing how that center performed 134 KPD transplants within 3 years of starting its KPD program, with KPD accounting for 35% of all transplants in the third year (7). Similarly, Northwestern Memorial Hospital in Chicago, Illinois performed 74 KPD transplants in the first 22 months of its KPD program (8).

However, adoption of KPD has historically been restricted to a small number of centers (9). As the likelihood of finding a match among a pool of transplant candidates and their incompatible donors grows with the number of incompatible pairs in that pool, it is expected that broader participation in KPD will not only result in more transplants because more patients/centers participate, but also because a higher proportion of participants—particularly those who are highly sensitized—will match in any program, whether single-center or multicenter (5).

We hypothesized that use of KPD (including variants such as *n*-way paired donation, dominos, and chains) (4,10–12) remains concentrated among a small number of high-utilizer centers. To test our hypotheses, we conducted a retrospective study of national patterns of KPD use. Our goals were: (1) to describe the use of KPD over time, (2) to describe center-level differences in use of KPD, accounting for differences in casemix and (3) to estimate the number of additional live donor transplants that would occur each year if all centers utilized KPD at rates currently observed among the centers with the highest KPD use.

Methods

Study population

This study used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donor, wait-listed candidates, and transplant recipients in the US, submitted by the members of the Organ Procurement and Transplantation Network (OPTN), and has been described elsewhere. The Health Resources and Services Administration

(HRSA), U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors.

Using data from the SRTR, we defined a population of “LDKT-eligible patients” to include any adult patient who registered for the deceased donor waitlist between January 1, 2006 and December 31, 2011, or who underwent LDKT during that time without registering. Adult patients at pediatric transplant centers (centers at which more than 50% of LDKT-eligible patients were under 18) were excluded from the study. A KPD transplant was defined as any LDKT for which the donor type (as reported on the OPTN Living Donor Registration Form) was coded as “Non-Biological, Unrelated: Paired Donation” (which includes paired donations, dominos, and chains) or “Non-Biological, Living/Deceased Donation” (what has previously been referred to as “list exchange”). Center demographics were based on LDKT-eligible patients who registered in the final 3 years of the study.

Center-level utilization of KPD

To explore utilization of KPD across transplant centers, we examined scatter plots of the number of KPD transplants at each center as a function of non-KPD LDKTs at that center, and also as a function of LDKT-eligible patients at that center. We further evaluated center-level utilization of KPD using the Lorenz curve, a graphical representation of heterogeneity (13,14). The Lorenz curve displays the cumulative proportion of a value (e.g. number of KPD transplants performed at each center), in order from the smallest value (center with the fewest KPD transplants) to the largest value (center with the most KPD transplants) (14); in this context, it can show how concentrated a practice is among certain centers. We produced Lorenz curves comparing (1) the raw number of KPD transplants to the number of non-KPD LDKTs at each center; (2) KPD to non-KPD transplants, normalized by the mean yearly number of adult transplant LDKT-eligible patients at each center and (3) the number of KPD transplants at each center each year. For each Lorenz curve, we computed the Gini coefficient, a dimensionless value between 0 and 1 with a higher number representing, in this context, a higher concentration of KPD transplants at a smaller number of centers.

High-KPD centers

For each center, we calculated the KPD rate as the number of KPD transplants during that time period divided by the number of new LDKT-eligible patients. The 20% of centers with the highest KPD rate were designated “high-KPD centers.” Likewise, the 10% of centers that performed the highest rates of KPD were designated “very high-KPD centers.” As preliminary analysis showed that 2006–2008 was a time of rapid increase in the uptake of KPD, the determination of “high-KPD centers” and subsequent analyses were based on data from the final 3 years of the study (January 2009–December 2011), a time period which we deemed most relevant for predicting future KPD capacity.

Expected number of KPD transplants

We constructed a negative binomial regression model of the number of KPD transplants at each center between January 2009 and December 2011. The negative binomial model fits a nonnegative count distribution where variance exceeds the mean (in our sample, variance = 203.0 and mean = 7.2). We used this model to predict an expected number of KPD transplants at each center based on center waitlist size (represented by the number of LDKT-eligible patients over the same period), casemix (represented by center level frequency distributions of the following characteristics: race, education, age, insurance, dialysis and PRA) and proportion of patients on the waitlist who obtained a non-KPD LDKT. This model yielded, for each transplant center, an expected number of KPD LDKT based on that center’s waitlist size, casemix and rate of non-KPD LDKT.

Estimating the national potential utilization of KPD

We then refit the model using only high-KPD centers, constraining the coefficients for the casemix variables to equal the values fit for the original model. This produced an expected count of KPD transplants based on the 42 high-KPD centers, but adjusted for casemix using data from all 207 centers, resulting in more stable estimates. The number of total KPD transplants that would have been performed if each center that performed fewer KPD transplants than the high-KPD centers had instead performed the expected number of transplants for a high-KPD center was estimated in the following manner:

$$\sum_{\text{all centers}} \max(KPD_{\text{observed}}, KPD_{\text{expected}}).$$

We repeated the process again using only the very high-KPD centers.

Statistical analysis

Even if the distribution of KPD were completely random and patients at each center had equal access to KPD, over a given period of time some centers would by chance have higher rates of KPD than others. Therefore, some centers would be defined as “high-KPD” per the above definition, and a subset of those would be defined as “very high-KPD.” In this case a model based on rates of KPD at high-KPD centers would overestimate the capacity for KPD at the remaining centers. Although actual access to KPD is not the same at all centers, a model based on high-KPD centers or very high-KPD centers runs the risk of overestimating KPD potential, because centers attain high-KPD status partly through improved access (e.g. successful listing of incompatible donors in a registry) and partly by random chance (e.g. donor/recipient pairs happen to find a match in the registry).

To correct for this bias, we performed a Monte Carlo simulation (in which outcomes are repeatedly simulated by drawing from a random distribution) (15) with 100 repetitions. For each repetition, a proportion of LDKT-eligible patients were randomly assigned a simulated KPD outcome. Then the high-KPD and very high-KPD regression models were rebuilt on these simulated KPD counts. The number of additional transplants predicted in these models thus quantified the bias introduced by the process, because (by design of the simulation) KPD counts were independent and identically distributed. The mean bias observed in the Monte Carlo simulation was subtracted from estimates of the number of additional transplants from the high-KPD and very high-KPD models (as described above) to give corrected estimates of the number of additional transplants that would have been performed. Interquartile ranges are reported as per the Louis and Zeger method of reporting confidence intervals (16). All analyses were performed using Stata 12.0/MP for Linux (College Station, TX, USA).

Results

Study population

Of 34 843 adult LDKTs performed between January 2006 and December 2011, 2089 (6.0%) were KPD transplants. KPD steadily increased from 93 transplants (1.5% of all LDKTs) in 2006 to 553 transplants (9.2% of all LDKTs) in 2010 (Figure 1). In 2011, the number of KPD transplants decreased to 537, whereas the proportion of all LDKTs which were KPD transplants increased to 9.9%. Non-KPD LDKTs decreased from 5994 in 2006 to 4982 in 2011; total LDKTs decreased slightly from 6087 in 2006 to 5429 in 2011.

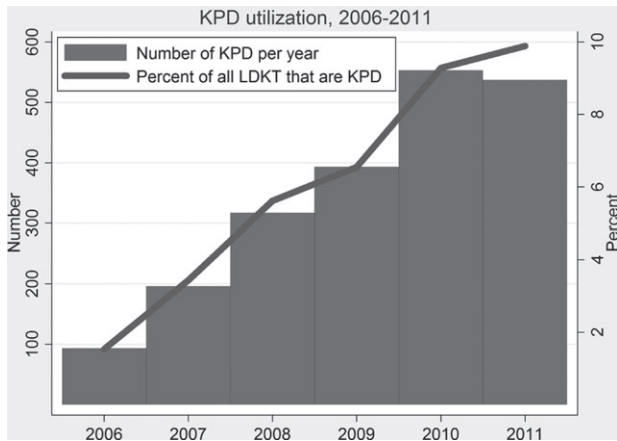


Figure 1: KPD in the United States over time, 2006–2011. Each bar represents 1 year; the red line represents the percent of all LDKTs performed that year that were accomplished through KPD. KPD utilization increased from 93 in 2006 to 553 in 2010, then decreased slightly to 537 in 2011.

Center-level utilization of KPD

Across 207 transplant centers, median (IQR) number of KPD transplants performed between January 2009 and December 2011 was 3 (1–8); 161 centers (77%) performed at least one KPD transplant. The largest number of KPD transplants performed at a single center was 137. Number of KPD transplants per center was moderately correlated both with the number of non-KPD LDKTs ($r = 0.58$) and the number of patients on the waitlist ($r = 0.44$); however, some centers had many more KPD transplants than other centers of comparable size (Figure 2).

KPD transplants were tightly clustered among a few centers, with 50% of all KPD transplants performed by the top 22 centers (Gini coefficient = 0.67 for KPD vs. 0.51 for non-KPD, Figure 3A). This clustering was more pronounced when normalizing the number of transplants by the number of LDKT-eligible patients, with a Gini coefficient of 0.59 for KPD transplants and 0.27 for non-KPD LDKTs (Figure 3B). From 2006 to 2008, the clustering of KPD among a small number of centers decreased as KPD was spread over a larger number of centers over time (Gini coefficient = 0.91 in 2006 and 0.76 in 2008, Figure 3C). However, from 2008 to 2011, the trend halted and the clustering of KPD among the top centers stayed relatively constant (Gini coefficient = 0.76 in 2008 and 0.77 in 2011).

High-KPD centers

The 41 high-KPD centers (the top 20% of centers by KPD utilization) performed at least 2.00 KPD transplants per 100 LDKT-eligible patients (combined waitlist registrants and live donor recipients) between 2009 and 2011 (range 2.00–8.82, mean = 4.01). The 21 very high-KPD centers (the top 10% of centers by KPD utilization) performed at least 3.66 KPD transplants per 100 LDKT-eligible patients

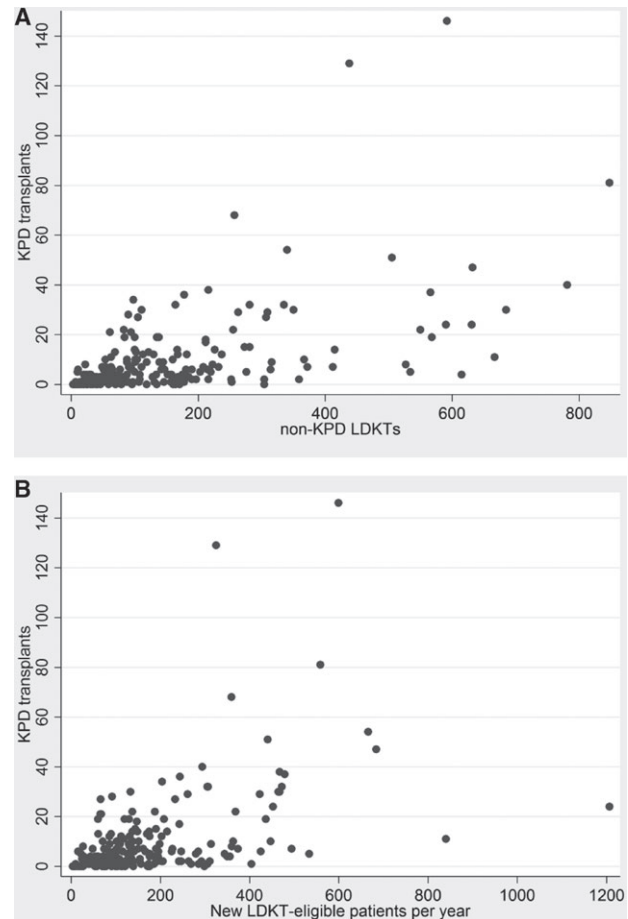


Figure 2: Scatter plots of KPD transplants by transplant center between January 2006 and December 2011, as a function of (A) non-KPD LDKTs and (B) mean adult LDKT-eligible patients per year. Dots that appear in the upper portion of the graph represent centers that performed a disproportionately high number of KPD transplants.

(range 3.66–8.82, mean = 5.52). As compared to other centers, the high-KPD centers and very high-KPD centers tended to have fewer African-American patients and more patients with private insurance (Table 1).

Estimating the national potential utilization of KPD

On average, there were 494 KPD transplants per year between January 2009 and December 2011. If all centers had performed at least as many KPD transplants as expected from the national average rate (adjusted for casemix), 711 KPD transplants per year would have been expected. If all centers had performed at least as many KPD as expected from the high-KPD centers, 1217 per year would have been expected. And if all centers had performed at least as many KPD as expected from the very high-KPD centers, 1593 KPD transplants per year would have been expected, or an additional 1099 KPD transplants per year above the current rate.

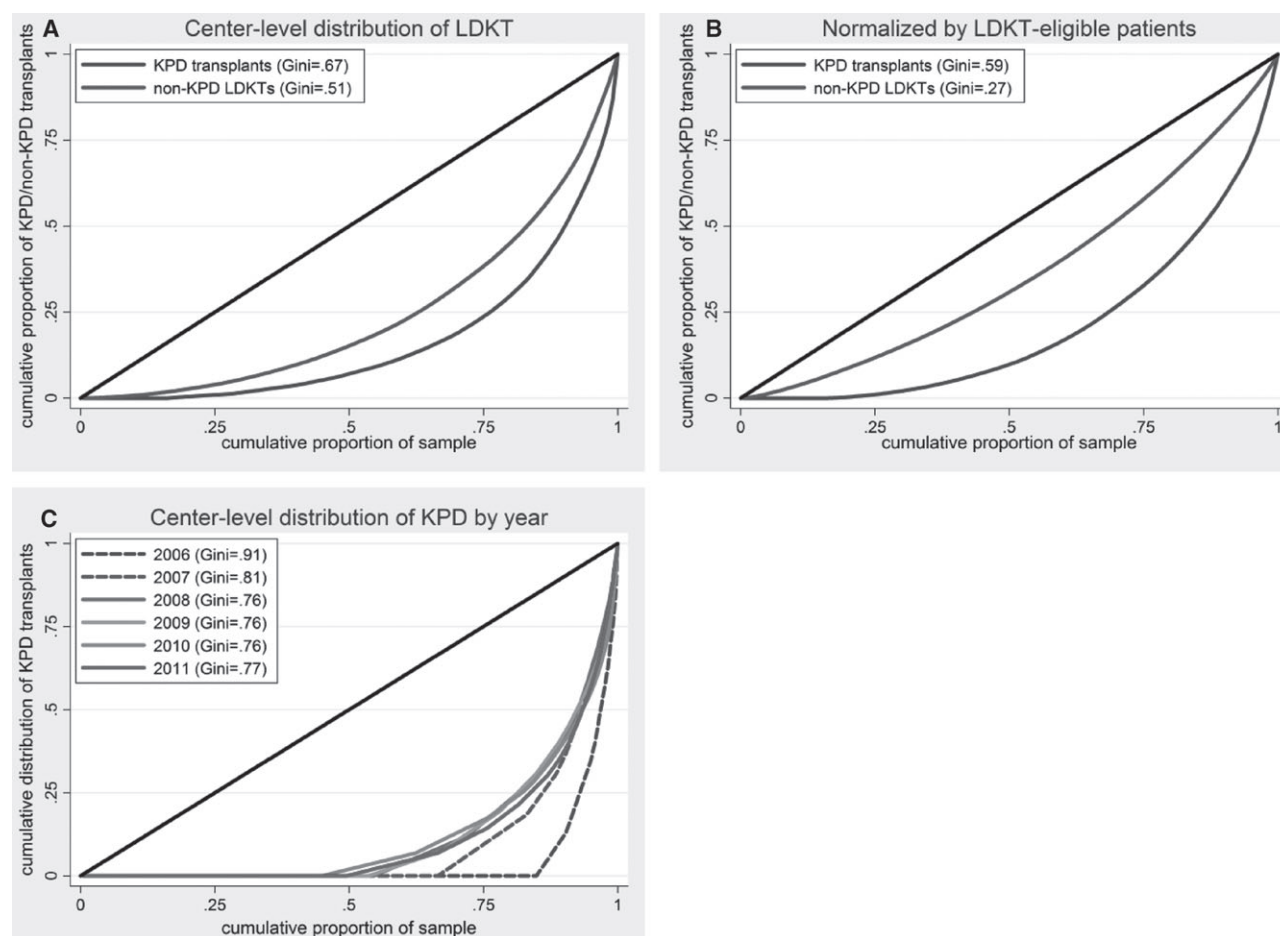


Figure 3: Center-level clustering of KPD transplants. Lorenz curves are shown. The diagonal reference line represents no clustering, i.e. the same number at each center; distance between the curve and the reference line represents the degree of clustering. Panel (A) compares center-level distributions of KPD and non-KPD LDKTs; KPD transplants are more tightly concentrated among a smaller number of centers. Panel (B) makes the same comparison, normalized by number of LDKT-eligible patients at a center. Panel (C) compares center-level distribution of KPD transplants from year to year. From 2006 to 2008, the curve moves upward, indicating that KPD utilization was distributing more evenly across an increasing number of centers; after 2008, the curve stays the same, indicating that no change in the distribution of KPD utilization.

Discussion

In this national study of KPD utilization and dissemination in the United States, we have shown that, despite early growth in the number of KPD transplants, utilization of KPD remains more tightly clustered among a small number of centers than LDKT in general. From 2005 to 2008, KPD disseminated among a wider number of centers, but since 2008, dissemination has remained stagnant. Although most centers performed fewer than 1 KPD transplant per 100 LDKT-eligible patients, some centers performed KPD at much higher rates (as high as 8.8 KPD transplants per 100 LDKT-eligible patients). If all transplant centers performed KPD at rates observed in the very high-performing centers, there would be an estimated additional 1099 live donor transplants per year facilitated through KPD.

KPD provides a unique opportunity for safe, effective transplantation for patients with ABO or HLA incompatible donors. By finding compatible donors through KPD, outcomes of incompatible transplants are equivalent to those of compatible ones (17); without KPD, desensitization protocols are required, and outcomes from these protocols, while better than waiting for a compatible deceased donor or remaining on dialysis, are associated with a lower overall survival (18,19). Candidates with a compatible donor may also benefit from KPD by obtaining a kidney from a younger donor (20,21). Furthermore, KPD does not require the establishment of complex systems required for desensitization and rapid antibody characterization. In fact, with many networks available in the United States, any center that performs LDKT can register incompatible pairs for KPD. When participating in a network, pairs from small centers have the same probability of matching as pairs from larger

Table 1: Patient demographics of transplant centers, 2009–2011, stratified by utilization of KPD

Characteristic	Median (IQR) value		
	Very high-KPD centers	High-KPD centers	Other centers
KPD transplants	8.5 17 28.5	6 13 19	0 2 4
Other LD transplants	32.5 47.5 123	31 54 84	22 49 99
% Age ≥ 60y	26.9 32.5 37.9	27.4 31.8 37.5	26.6 31.5 36.0
% African-American	8.2 17.4 33.7	9.0 17.5 34.0	14.8 28.7 46.1
% Not high school graduate	2.4 3.5 5.3	2.8 3.8 6.5	3.2 4.9 9.0
% College graduate	19.1 25.7 28.6	17.3 21.7 27.4	14.6 18.6 23.8
% Medicaid	2.3 5.1 8.8	3.2 4.5 7.9	2.6 5.3 9.7
% Private insurance	37.3 46.9 53.5	42.4 49.2 53.9	30.0 40.6 49.6

Very high-KPD centers represent the top 10% of centers by KPD per 100 LDKT-eligible patients; high-KPD centers represent the top 20% by KPD per 100 LDKT-eligible patients (including very high-KPD centers). High-KPD and very high-KPD centers tended to have a smaller proportion of LDKT-eligible patients who were African American, and a larger proportion of LDKT-eligible patients who were college graduates or on private insurance.

Numbers shown are median, with IQR range shown as left and right subscripts.

centers, so center size should also not be a barrier; this is echoed in our findings that the number of non-KPD LDKTs was not associated with the KPD transplant rate.

However, there are still potential barriers to participation in KPD, highlighted by the wide range of KPD transplant rates throughout the country (22). First, centers must educate their transplant candidates about the possibility of KPD if they have incompatible donors. Second, there is administrative burden to registering with one of the existing KPD networks, or start a single-center KPD program; furthermore, some of the existing KPD networks charge a registration fee (23). Third, centers must have a system by which information about incompatible donors is collected and registered with a KPD network. And finally, centers must have processes in place for exporting and importing kidneys when KPD is performed across transplant centers.

Perhaps one of the most challenging barriers to KPD in the United States at this time is financial (6,24,25). As the donor is not compatible with the intended recipient, and as such the kidney will not be transplanted directly into the intended recipient, reimbursement for donor evaluation is challenging, because the identity of the ultimate recipient is unknown at the time of evaluation (25). In addition, there is no standardized mechanism to pay for donor travel or shipment of live donor kidneys (24). A standardized national framework for KPD administration has been proposed, based on a Standard Acquisition Charge Model (25); however, feasibility of such a model would likely require a single national KPD system, as has been suggested by the private payers (26).

Several limitations of our study merit consideration. First, we used center-level rates of non-KPD LDKT as a proxy for patients' potential access to KPD transplantation. As noted, exploratory data analysis showed no relationship between patient demographic variables and the ratio of KPD to non-KPD transplantation at a center. Nevertheless,

there may be differences in unmeasured patient demographics that would subtly affect rates of KPD transplantation differently from rates of non-KPD LDKT, even if all centers pursued KPD transplantation equally. Describing the yield from increased KPD as "additional" LDKTs assumes that KPD recipients would not otherwise have received LDKT. In fact, some participants in KPD may have exchanged a kidney from a compatible older donor for a younger donor kidney; others may have eventually located a compatible live donor without KPD, or undergone desensitization (18). However, we believe that most KPD recipients would otherwise not have received LDKT, and that inferences about dissemination of this modality would not be significantly biased by these issues. Our study used rates of KPD in very high-performing centers over the past 3 years to estimate attainable rates of KPD nationwide. However, overall rates of KPD did increase from 2008 to 2010, perhaps driven partly by innovations such as shipping of donor kidneys and the combination of KPD and desensitization. Moreover, because the chance of a match per user increases with the size of the registry, our results may actually underestimate the attainable rate of KPD in the United States.

Finally, we only evaluated actual KPD transplants rather than efforts made by centers to implement KPD. It is possible that there is currently more KPD potential than reflected in our study, but that there is a lag before these steps taken to implement KPD will have led to matched pairs and a noticeable increase in KPD at that center. In other words, the low rates of KPD at most centers observed in our study may increase in the near future due to actions already taken by transplant programs. However, the relative lack of change in KPD dissemination and rates between 2008 and 2010 suggests that there remains quite a bit of room for improvement among low-performing centers. Over 75% of centers have performed at least one KPD transplant over the past 3 years, suggesting that most of the limitation is not a willingness to participate in KPD, but rather barriers to execution.

Wider adoption of KPD in the transplant community has the potential to lead to more than 1000 additional live donor kidney transplants every year. Decreasing rates of LDKT nationwide increase the urgency of fully realizing the gains of KPD. This would benefit not only the recipients of those live donor kidneys, but all waitlist registrants who would benefit from reduced rate of growth in the kidney donor waitlist. Dozens of successful centers show that high rates of KPD are possible, both at large and small transplant centers; in fact, center volume does not correlate with utilization of KPD at a center, and enough KPD programs and networks currently exist that every transplant center in the United States should be able to transplant patients through this important modality. The potential benefits to patient survival and quality of life from KPD are great, but will only be fully realized when all transplant centers aim to make KPD available to their patients at the highest possible level of utilization.

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Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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