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Favorable Living Donor Kidney Transplantation Outcomes within a National Kidney Exchange Program

A Propensity Score–Matching Analysis

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Key Points

- KEP recipients have comparable long-term graft survival to direct living donor kidney transplantation recipients, which underscores the need to prioritize KEP over other's therapies.
- Our outcomes can be achieved regardless of whether the donor travels or the graft is transported, offering flexibility in program implementation.

Abstract

Background KEPs (kidney exchange programs) facilitate living donor kidney transplantations (LDKTs) for patients with incompatible donors, who are typically at higher risk than non-KEP patients because of higher sensitization and longer dialysis vintage. We conducted a comparative analysis of graft outcomes and risk factors for both KEP and non-KEP living donor kidney transplants.

Methods All LDKTs performed in The Netherlands between 2004 and 2021 were included. The primary outcome measures were 1-, 5-, and 10-year death-censored graft survival. The secondary outcome measures were delayed graft function, graft function, rejection rates, and patient survival. We used a propensity score–matching model to account for differences at baseline.

Results Of 7536 LDKTs, 694 (9%) were transplanted through the KEP. Ten-year graft survival was similar for KEP (0.916; 95% confidence interval, 0.894 to 0.939) and non-KEP (0.919; 0.912 to 0.926, $P = 0.82$). We found significant differences in 5-year rejection (12% versus 7%) and 5-year patient survival (KEP: 84%, non-KEP: 90%), which was nonsignificant after propensity score matching. Significant risk factors of lower graft survival included high donor age, retransplantations, extended dialysis vintage, higher panel reactive antibodies, and nephrotic syndrome as the cause of ESKD.

Conclusions Transplantation through KEP offers a viable alternative for patients lacking compatible donors, avoiding specific and invasive pre- and post-transplant treatments. KEP's similar survival rate to non-KEPs suggests prioritizing KEP LDKTs over deceased donor kidney transplantation, desensitization, and dialysis. However, clinicians should consider the identified risk factors when planning and managing pre- and post-transplant care to enhance patient outcomes. Thus, we advocate for the broad adoption of KEP and establishment in regions lacking such programs, alongside initiation and expansion of international collaborations.

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Introduction

Living donor kidney transplantation (LDKT) results in better graft survival and less economic costs^{1,2} as compared with deceased donor kidney transplantation (DDKT). The shorter cold ischemia time (CIT) and selection of living donors for their good health, younger age, and fewer comorbidities contribute to its superiority.^{3–7} In addition, preemptive kidney transplantation is more feasible in LDKT, providing higher quality donor organs.^{8,9} Avoiding complications linked to intensive care stays and brain or circulatory death in deceased donors further enhances graft outcomes.¹⁰

By the end of 2019, over 58,000 patients in the European Union were waiting for organ transplants,^{11,12} with significant variation in transplantation rates between countries.^{13,14} In recent years, the number of transplantations has risen across Europe, partly because of increasing LDKT rates.^{10,11,13,15–17} However, direct LDKT is not always possible because of HLA or ABO blood group (ABO) incompatibility. Incompatible pairs can pursue immunological barrier-crossing transplantation (*e.g.*, ABO-incompatible or desensitized HLA-incompatible transplantation) or participate in a kidney exchange program (KEP), if available.^{18,19} KEP offers benefits, such as reduced immunosuppressive therapy, lower rejection risk, and higher graft survival, along with lower costs compared with incompatible transplants.^{20,21} Nevertheless, not all countries with LDKT programs facilitate KEP.^{22–26} In countries with KEPs, recipients often face additional waiting time after medical approval, depending on matching rates and program logistics. These matching rates vary significantly—*e.g.*, approximately 30% per run in the United Kingdom, 46% in the United States, and approximately 30% annually in The Netherlands—on the basis of HLA and blood type compatibility.^{27–29} KEP matching algorithms pair incompatible recipients with compatible donors and may also optimize matches for better HLA compatibility, improved age alignment, or altruistic reasons. Established in 2004, the Dutch national KEP served as a model, with other programs following worldwide,^{30,31} and since then, more KEPs were initiated.^{32–37} Our prior research in the United Kingdom showed comparable graft survival for KEP and non-KEP recipients, despite higher sensitization rates, increased retransplantation, and longer dialysis vintage in KEP participants.¹⁵ Donor–recipient exchanges in KEP can occur by three scenarios: (1) the recipient travels to the donor's center, (2) the kidney is transported to the recipient's center (similar to deceased donor allocation), or (3) the donor travels to the recipient's center, where both donor nephrectomy and transplantation occur, inherently reducing CIT.³⁸ Countries such as The Netherlands, Canada, Slovakia, and Switzerland adopt the third scenario, whereas the United States and the United Kingdom primarily ship donor kidneys.^{19,33} Although studies have addressed CIT in LDKT, its effect on outcomes in programs where both surgeries occur in the same center remains unclear.³⁹

This study compares transplant outcomes between KEP participants and non-KEP LDKT recipients. We hypothesize that KEP graft outcomes are comparable with non-KEP LDKT. A detailed risk factor analysis identifies key donor and recipient characteristics contributing to graft failure and delayed graft function (DGF) in both groups.

To address baseline differences between KEP and non-KEP cohorts, propensity score matching is used to adjust for confounders. This will ensure a robust comparison and provides insights to inform clinical decision making and transplantation policies.

Methods

This study included all consecutive ABO-compatible LDKTs (KEP and non-KEP) performed in The Netherlands between January 2004 and December 2021. Anonymized data from all seven Dutch transplant centers, collected by the Dutch Transplant Foundation, included donor and recipient demographics, warm and CITs, and HLA mismatches. The primary outcomes were 1-, 5-, and 10-year death-censored graft survival (DCGS) or graft loss, focusing on graft performance independent of unrelated patient mortality. Secondary outcomes included DGF, defined as at least one dialysis session during the first postoperative week; primary nonfunction, defined as the permanent lack of graft function from transplantation; eGFRs at 1, 5, and 10 years, rejection rates; and patient survival at the same intervals. Rejection was defined as any treated episode. This study complied with the principles of the Declaration of Helsinki, received approval from the National Kidney Transplantation Committee and the Dutch Transplant Society, and adhered to the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.

In the Dutch National Living Donor Kidney Exchange Program, the donor travels to the recipient's hospital where both donor nephrectomy and transplantation are performed. Chains initiated by unspecified altruistic donors default to benefiting deceased donor waiting list patients as end-of-chain recipients. The program is also referred to as kidney paired donation or crossover transplantation.

Statistical Methods

Baseline characteristics and outcomes were analyzed using chi-square tests with Yates' continuity correction for categorical variables or Fisher's exact test when cell counts were low. Continuous variables were analyzed using one-way ANOVA or Kruskal–Wallis test for non-normally distributed variables. Median CIT differences among donor types were evaluated using *post hoc* multiple comparisons with Tukey's honestly significant difference test at a 95% family-wise confidence level. Associations between DGF, primary nonfunction, and transplantation type were assessed using Pearson's chi-square test with Yates' continuity correction. Survival curves were generated using the Kaplan–Meier method, with differences tested using log-rank test.⁴⁰ We used multivariate Cox proportional hazards regression models to estimate the association between recipients' survival time and various predictors, including both recipient and donor characteristics, to determine graft survival probability.⁴¹ We analyzed donor and recipient sex, age, donor body mass index, panel reactive antibody (PRA) percentage, serum creatinine, CIT, warm ischemia time, preemptive transplantation status, HLA mismatch, and dialysis vintage. Univariate Cox regression identified significant predictors, followed by a backward selection process where variables with $P > 0.05$ were excluded. Significant variables were

included in a multivariate model to assess their effect on graft loss. Transplant year was added to account for variations in medical practices, surgical advancements, and postoperative care, adjusting for time-related confounding effects. Variance inflation factors ensured no collinearity from this temporal variable, preserving model integrity. Model diagnostics, including Schoenfeld residuals, confirmed the proportional hazards assumption. DGF, although not before transplant, was analyzed separately to assess its adjusted effect on graft survival. Reporting adhered to the Strengthening the Reporting of Observational Studies in Epidemiology cohort checklist.⁴²

Propensity Score Matching

To address baseline differences between the groups in death-censored graft and patient survival, propensity score matching was implemented. Propensity scores, calculated using a logistic regression model with KEP participation as the dependent variable, included age, sex, primary kidney disease, body mass index, ischemia times, prior KRT, HLA compatibility, dialysis vintage, and preemptive transplantation status. These variables were chosen on the basis of significant baseline differences between KEP and non-KEP LDKTs. Nearest neighbor matching without replacement was performed with a 0.2 SD caliper of the logit of the propensity score. Matched data were analyzed using conditional logistic regression to account for paired dependencies. A sensitivity analysis was conducted to test result robustness against unmeasured confounding.

Results

A total of 7536 LDKTs were performed between January 1, 2004, and December 15, 2021, in The Netherlands. A total of 913 recipients (12%) died with a functioning graft during the study period. Recipients were stratified on the basis of the type of kidney transplant and crossover/domino transplantation (related, unrelated, or initiated by an altruistic donor) by the KEP or non-KEP LDKT, which resulted in 694 (9%) versus 6842 (91%) recipients, respectively. The median follow-up time was 98 months (interquartile range, 55–147 months).

The baseline donor and recipient characteristics are presented in [Table 1](#) and [Supplemental Table 1](#). The KEP group contained more male donors, older donors, less male recipients, older recipients, longer dialysis vintage, more often retransplantations, higher HLA mismatch, and more often highly sensitized recipients. We used propensity score matching to account for baseline differences between both groups. In our propensity score-matching model, 547 recipients included in the KEP group were matched with 1573 recipients in the non-KEP group (1:3 ratio) because in this fashion, the standard mean difference was kept below 0.2 in all variables ([Supplemental Table 3](#)). The pre- and postmatching baseline characteristics of these recipients on the variables used for matching are presented in [Supplemental Tables 2](#) and [3](#). These adjustments allowed us to mitigate the effect of confounding variables, ensuring a more robust comparison of long-term outcomes between the KEP and non-KEP groups, despite their distinct baseline characteristics.

Graft Survival

We compared the difference in 10-year DCGS between KEP LDKT and non-KEP LDKT ([Figure 1](#)). A total of 538 recipients (8%) experienced death-censored graft loss (DCGL). For 1-, 5-, and 10-year DCGS, there was no significant difference between both groups, with a survival probability of 0.97 (95% confidence interval [CI], 0.95 to 0.98) for KEP versus 0.96 (95% CI, 0.96% to 0.97%; $P = 0.51$) for non-KEP in 1 year, 0.91 (95% CI, 0.89 to 0.93) for KEP versus 0.91 (0.91 to 0.92) for non-KEP in 5 years ($P = 0.82$), and finally 0.88 (95% CI, 0.85 to 0.91) for KEP and 0.88 (95% CI, 0.87 to 0.89; $P < 0.01$) for non-KEP in 10 years. These findings were consistent in the propensity score-matched cohort with a P value of 0.49 at 5 years ([Supplemental Figure 1](#)). Most graft failures were caused by rejection while on immunosuppressive drugs (8% of all recipients), and thrombosis or infarction occurred in around 1% of the recipients. [Table 2](#) identified several risk factors of 5-year DCGL using a multivariate Cox proportional hazards regression model analysis, such as older donor (older than 60 years), male recipients, a third transplantation, dialysis vintage, higher PRAs, and nephrotic syndrome as the cause of ESKD. The separate risk factors for KEP and non-KEP are slightly different ([Table 3](#)).

CIT

CIT was, as expected in this form of KEP, comparable in KEP and non-KEP with a mean of 150 minutes (SD, 37 minutes) in KEP and 151 minutes (SD, 60 minutes) in non-KEP ($P = 0.55$). In the multivariate regression analysis ([Table 2](#)), we found that every additional hour of CIT was not significantly associated with higher DCGL (hazard ratio (HR), 1.07; 95% CI, 0.99 to 1.15; $P = 0.08$). However, in the KEP group, every additional hour of CIT was significantly associated with higher DCGL ([Table 3](#)), with an HR of 2.5 (95% CI, 1.25 to 5.15; $P = 0.01$).

DGF

DGF occurred in 66 transplants (12%) in KEP and 264 transplants (5%) in non-KEP, which resulted in a significantly higher incidence of DGF in KEP ($P < 0.01$). The DGF was higher than what we expected clinically. In the most recent 10 years, the DGF was higher with 7% in KEP and 4% in non-KEP ($P = 0.07$). In the propensity score-matched cohort, we found that 6% and 13% of the recipients experienced DGF in the non-KEP and KEP group, respectively ($P < 0.001$). Risk factors of DGF were older donor age, donor obesity, dialysis vintage, and recipients transplanted through KEP ([Supplemental Table 4](#)). Recipients who experienced DGF had a HR of 3.25 (95% CI, 1.97 to 5.37; $P < 0.001$) compared with direct graft function for 5-year death-censored graft failure.

Kidney Function

There was no significant difference in kidney function between KEP and non-KEP; at 1 year, eGFR was 46.6 (95% CI, 45.3 to 47.9) in KEP versus 46.6 (95% CI, 46.2 to 47.9; $P = 0.96$) ml/min in non-KEP. At 5 years, the eGFR was 45.6 (95% CI, 44.2 to 46.9) in KEP versus 45.5 (95% CI, 45.1 to 46.0; $P = 0.99$) ml/min in non-KEP.

Table 1. Baseline donor and recipient characteristics stratified by type of transplantation

Variable	KEP	Non-KEP
No. (%)	694	6842
Transplant year (SD)	2014.00 (4.41)	2012.97 (4.72)
Donor sex=male (%)	336 (48.4)	2995 (43.8)
Donor age (SD)	54.36 (12.00)	52.91 (11.92)
Recipient sex=male (%)	373 (53.7)	4186 (61.2)
Recipient age (SD)	52.86 (13.21)	49.55 (14.29)
Donor BMI (SD)	25.91 (3.60)	25.96 (3.63)
Years on dialysis, yr		
Preemptive	249 (35.9)	3847 (56.3)
0–1	111 (16.0)	1064 (15.6)
1–3	223 (32.2)	1411 (20.7)
>3	110 (15.9)	508 (7.4)
Graft number (SD)	1.32 (0.62)	1.14 (0.43)
HLA mismatch (SD)	3.81 (1.31)	3.29 (1.60)
Mismatch HLA DR (%)		
0	58 (8.36)	576 (8.42)
1	217 (31.27)	1587 (23.19)
2	136 (19.60)	805 (11.77)
PRAs (SD)	7.69 (18.28)	2.39 (9.65)
Hypertension	7 (16.7)	103 (9.5)
Serum creatinine		
Donor in mmol/L (SD)	132.78 (72.85)	133.30 (54.82)
CIT in min (SD)	149.84 (36.61)	151.33 (59.91)
WIT in min (SD)	25.47 (10.67)	27.49 (12.78)
Cause of ESKD		
Diabetes mellitus type 2 (%)	45 (6.5)	259 (3.8)
Diabetes mellitus type 1 (%)	23 (3.3)	135 (2.0)
Hypertension (%)	64 (9.2)	519 (7.6)
Polycystic (%)	78 (11.2)	944 (13.8)
Nephrotic syndrome (%)	43 (6.2)	354 (5.2)
Nephritic syndrome (%)	51 (7.3)	733 (10.7)
Pyelonephritis (%)	30 (4.3)	311 (4.5)
Chronic renal failure (other, %)	66 (9.5)	747 (10.9)

For categorical variables, the number of recipients in either group are shown, and for continuous variables, mean and SD are shown. KEP recipients are more likely to have a male donor, have higher donor serum creatinine levels, be relatively older and have older donors, be less often male, be less often transplanted preemptively and longer on dialysis, have more HLA mismatches, and be more often highly sensitized, with a higher percentage of panel reactive antibodies, compared with non-KEP recipients. BMI, body mass index; CIT, cold ischemia time; DM, diabetes mellitus; DR, DR isotype; KEP, kidney exchange program; PRA, panel reactive antibody; WIT, warm ischemia time.

At 10 years after transplantation, the eGFR was 44.5 (95% CI, 43.0 to 46.0) in KEP versus 44.7 (95% CI, 44.3 to 45.2; $P = 0.90$) in non-KEP. Likewise, we did not find a significant difference in the propensity score-matched cohort ($P = 0.10$).

Rejection

The incidence of rejection was significantly different between KEP and non-KEP at 1 year (6% versus 4%, respectively, $P = 0.03$), 5 years (12% versus 7%, respectively, $P < 0.001$) and 10 years (14% versus 8%, respectively, $P < 0.001$). Recipients who experienced rejection had a HR of 2.51 (95% CI, 1.92 to 3.29; $P < 0.001$) for 5-year DCGI. Recipients who experienced rejection had a higher PRA level before transplant (mean: 7% without rejection and 10% with rejection in KEP, $P < 0.001$; 2% without rejection and 5% with rejection in non-KEP, $P < 0.001$) and a comparable HLA mismatch (mean: 3.83 with nonrejection and 3.76 with rejection in KEP, $P = 0.94$; 3.28 without rejection and 3.53 with rejection in non-KEP, $P = 0.04$). In the propensity score-matched cohort, we found no significant difference

anymore with 12% and 13% in the non-KEP and KEP groups, respectively ($P = 0.60$).

Patient Survival

The results for patient survival up to 10-year follow-up are shown in [Figure 2](#). We found a significant difference in patient survival between KEP and non-KEP: At 1 year, the patient survival were 97% (95% CI, 96% to 99%) versus 99% (95% CI, 99% to 99%; $P < 0.001$). The 5-year patient survival rates were 89% (95% CI, 88% to 92%) in KEP and 94% (95% CI, 94% to 95%; $P < 0.001$) in non-KEP, and the 10-year patient survival rates were 84% (95% CI, 81% to 87%) in KEP and 90% (95% CI, 89% to 90%; $P < 0.001$) in non-KEP.

Comparing the KEP group with the non-KEP group in the propensity score-matched cohort showed that there is no longer a significant difference for 1-, 5-, and 10-year patient survival, with 96% (95% CI, 94% to 98%) versus 99% (95% CI, 98% to 100%), 91% (95% CI, 88% to 94%) versus 95% (95% CI, 93% to 96%), and 86% (95% CI, 82% to 90%) versus 90% (95% CI, 86% to 90%) survival probability, respectively ([Supplemental Figure 2](#)).

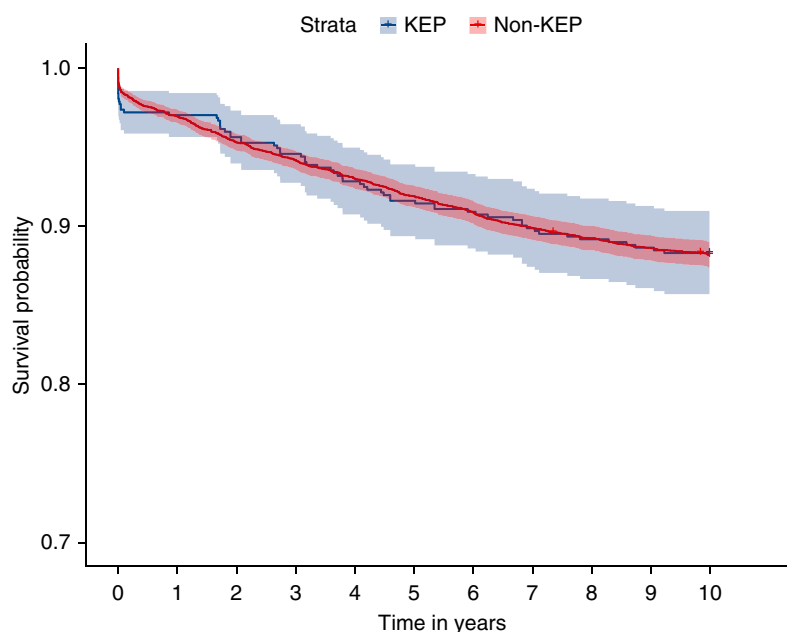


Figure 1. Kaplan–Meier survival estimates for 1-, 5-, and 10-year DCGS. DCGS, death-censored graft survival. Figure 1 can be viewed in color online at www.cjasn.org.

Discussion

This study provides insights from the longest follow-up data available for a KEP cohort. Recipients in KEP are typically at higher risk compared with direct LDKT recipients. These findings reinforce KEP as a crucial option for patients facing barriers such as high sensitization or lack of compatible donors. Despite higher risk profiles,

comparable outcomes highlight the efficacy of KEP in managing complex cases. However, KEP poses unique logistical and clinical challenges, such as higher DGF rates, which require tailored strategies to optimize post-transplant success.

Moreover, the KEP outcomes are superior to those observed in DDKT,⁴³ transplantation after desensitization,²⁰

Table 2. Hazard ratio of different patient/transplant variables on 5-year death-censored graft loss (for all living donor kidney transplantations)

Risk Factors	Reference	LDKT	
		HR (95% CI)	P Value
KEP	Non-KEP	1.23 (0.83 to 1.83)	0.28
Donor age <40	Donor aged 40–60	0.93 (0.66 to 1.32)	0.69
Donor age >60	Donor aged 40–60	1.39 (1.05 to 1.83)	0.01 ^a
Recipient age <40	Recipient aged 40–60	1.21 (0.92 to 1.60)	0.16
Recipient age >60	Recipient aged 40–60	1.74 (0.85 to 1.62)	0.33
Recipient sex=male	Female	0.75 (0.59 to 0.97)	0.03 ^a
Second KTx	First KTx	0.84 (0.57 to 1.25)	0.39
≥3rd KTx	First KTx	2.23 (1.65 to 4.27)	<0.001 ^b
Dialysis 0–1 yr	Preemptive transplant	1.29 (0.91 to 1.84)	0.15
Dialysis >1 yr	Preemptive transplant	1.33 (1.02 to 1.74)	0.03 ^a
PRA 1–30	PRA 0	2.20 (1.69 to 2.85)	<0.001 ^b
PRA >31	PRA 0	1.82 (1.00 to 3.30)	0.03 ^a
Donor serum creatinine <75	Donor serum creatinine >90	1.45 (0.85 to 2.46)	0.17
Donor serum creatinine 75–90	Donor serum creatinine >90	0.39 (0.20 to 0.72)	<0.01 ^c
Nephrotic syndrome	—	1.67 (1.09 to 2.56)	0.02 ^a
CIT	Continuous (in hours)	1.04 (0.97 to 1.12)	0.27
WIT	Continuous	1.00 (0.99 to 1.01)	0.30

CI, confidence interval; CIT, cold ischemia time; CRF, calculated reaction fraction; HR, hazard ratio; KTx, kidney transplantation; LDKT, living donor kidney transplantation; PRA, panel reactive antibody; WIT, warm ischemia time.

^a*P* < 0.05.

^b*P* < 0.001.

^c*P* < 0.01.

Table 3. Hazard ratio of different patient/transplant variables on 5-year death-censored graft loss (for KEP and non-KEP)

Risk Factors	Reference	Non-KEP		KEP	
		HR (95% CI)	P Value	HR (95% CI)	P Value
Donor age <40	Donor aged 40–60	0.91 (0.64 to 1.30)	0.63	1.20 (0.34 to 4.28)	0.78
Donor age >60	Donor aged 40–60	1.18 (0.89 to 1.57)	0.24	2.93 (1.32 to 6.51)	0.01 ^a
Recipient age <40	Recipient aged 40–60	1.26 (0.96 to 1.65)	0.10	1.08 (0.47 to 2.49)	0.86
Recipient age >60	Recipient aged 40–60	1.09 (0.78 to 1.50)	0.61	0.85 (0.31 to 2.32)	0.75
Recipient sex=male	Female	0.73 (0.57 to 0.93)	0.01 ^a	NS	NS
Second KTx	First KTx	0.70 (0.45 to 1.09)	0.11	2.99 (1.23 to 7.23)	0.02 ^a
≥3rd KTx	First KTx	2.09 (1.22 to 3.56)	<0.01 ^b	4.67 (1.38 to 15.75)	0.01 ^a
Dialysis 0–1 yr	Preemptive transplant	1.39 (0.97 to 1.97)	0.07	0.51 (0.10 to 2.50)	0.40
Dialysis >1 yr	Preemptive transplant	1.71 (1.28 to 2.30)	<0.001 ^c	4.59 (1.67 to 12.50)	<0.01 ^c
PRA 1–30	PRA 0	2.25 (1.72 to 2.95)	<0.001 ^c	2.64 (1.20 to 5.81)	0.02
PRA ≥31	PRA 0	2.63 (1.41 to 4.91)	<0.01 ^b	2.57 (1.16 to 4.76)	<0.001 ^c
Donor serum creatinine <75	Donor serum creatinine >90	0.96 (0.52 to 1.72)	0.88	0.93 (0.52 to 1.70)	0.07
Donor serum creatinine 75–90	Donor serum creatinine >90	0.37 (0.19 to 0.70)	<0.01 ^b	0.36 (0.19 to 0.69)	<0.01 ^b
Nephrotic syndrome	—	1.53 (1.01 to 2.32)	0.04 ^a	1.17 (1.01 to 2.33)	0.04 ^a
CIT	Continuous	1.06 (0.99 to 1.12)	0.07	2.50 (1.25 to 5.15)	0.01 ^a
WIT	Continuous	1.00 (0.99 to 1.01)	0.36	NS	NS

CI, confidence interval; CIT, cold ischemia time (in hours); CRF, calculated reaction fraction; HR, hazard ratio; KTx, kidney transplantation; PRA, panel reactive antibody; WIT, warm ischemia time (in minutes).

^a $P < 0.05$.

^b $P < 0.01$.

^c $P < 0.001$.

and dialysis.⁴⁴ We propose a sequential approach for managing patients with ESKD, prioritizing transplantation options by outcomes and resource availability. Clinicians should first identify a compatible living donor for direct LDKT, which offers superior immediate and long-term outcomes. If incompatible, patients should join a KEP to broaden the donor pool while maintaining excellent graft survival rates. Desensitization transplantation should be pursued if KEP is not feasible, followed by DDKT if all other options fail. Maintenance dialysis remains the last

resort. In addition, incorporating directly compatible donor–recipient pairs into KEP could expand donor pools, especially when the donor has suboptimal HLA, age, or size matches. This strategy could increase transplant rates and improve outcomes.

Notably, KEP recipients exhibited lower patient survival, which was no longer significant after propensity score matching. The baseline disparities—longer dialysis vintage, higher sensitization, more retransplants, and comorbidities—underscore the need for thorough

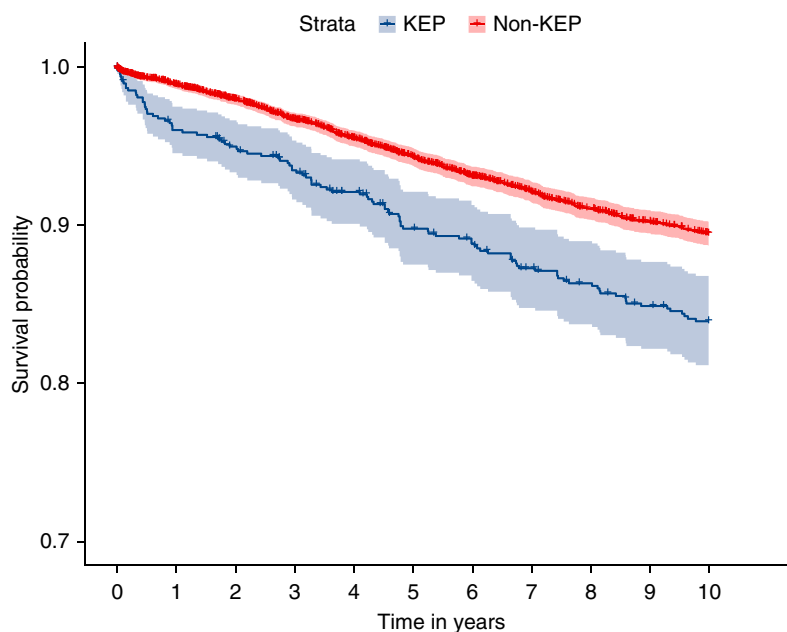


Figure 2. Kaplan–Meier survival estimates for 1-, 5-, and 10-year patient survival comparing LDKT by kidney exchange programs (KEPs) with non-KEP. LDKT, living donor kidney transplantation. Figure 2 can be viewed in color online at www.cjasn.org.

Table 4. Comparison between living donor kidney transplantation outcomes in The Netherlands and the United Kingdom (on the basis of data presented in ref. 15)

Outcome	KEP		Non-KEP	
	The Netherlands	United Kingdom	The Netherlands	United Kingdom
DGF	7.20%	5.73%	4.15% ^a	2.91% ^a
Graft survival				
1-year	97%	96%	97%	98%
5-year	92%	92%	92%	93%
Graft function				
1-year eGFR	46.6	55.25	46.6	57.90
5-year eGFR	45.5	53.09	45.6	55.62
Incidence of rejection	11.76%	14.61%	7.09% ^a	12.20% ^a

DGF, delayed graft function; KEP, kidney exchange program (only analyzed within countries).
^aIndicates a significant difference with $P < 0.05$ between non-KEP and KEP.

adjustments in survival analyses. Our matched analysis revealed a significant association between KEP participation and higher DGF rates ($P < 0.001$), likely influenced by procedural and recipient characteristics rather than baseline disparities alone.

In an additional analysis, we found that recipients with DGF were more often nonpreemptively transplanted and had longer dialysis vintage, higher PRA, and nephrotic syndrome as the cause of ESKD. These findings indicate that both procedural and clinical factors inherent to KEP contribute to DGF. Despite this, long-term outcomes, such as kidney function and rejection rates, remain unaffected once baseline differences are adjusted for. This underscores the importance of tailored patient counseling and decision making in KEP settings.

The strengths of this study include a robust dataset spanning multiple transplant centers and comprehensive adjustments for confounders through multivariable modeling. Future research should identify modifiable factors contributing to DGF risk in KEP recipients and explore interventions to mitigate these risks, further improving outcomes.

Our study's findings are consistent with those of recent American⁴⁵ and UK¹⁵ research but surpass previous follow-ups with a median duration exceeding 8 years. KEP demonstrated superior long-term outcomes compared with other countries, including the United States (85%) and Europe (87%).⁴⁶ However, DGF rates in our cohort (7% and 4%) were higher than expected, although CITs were comparable between KEP and non-KEP and rarely exceeded 4 hours.

Although the incidence of DGF is lower compared with DDKT, DGF after LDKT is associated with higher rejection rates⁴⁷ and inferior graft survival.^{15,48,49} In this study, recipients with DGF had a HR of 3.25 for graft failure compared with those with immediate graft function. This aligns with the hypothesis that DGF increases graft inflammation and fibrosis, accelerating dysfunction and leading to premature failure.^{16,50} The role of hypothermic machine perfusion (HMP) likely decreases this risk of DGF,⁴⁹ but evidence of using HMP in LDKT is limited to one non-randomized controlled trial,⁵¹ whereas DDKT has extensive evidence supporting HMP.^{52,53} Whether

LDKT recipients, especially in KEP, at higher risk of DGF,^{54,55} graft failure,^{56–59} or rejection^{60,61} benefit from HMP or other preventive treatments remains unclear. We identified significant risk factors of graft failure, including high donor age, retransplantations, long dialysis vintage, elevated PRA, nephrotic syndrome as the cause of ESKD, and high donor serum creatinine levels. These findings align with prior research^{62–64} and highlight the importance of close monitoring and tailored interventions to improve long-term outcomes. Initially, we categorized dialysis vintage into groups (1–3 and >3 years). Combining these categories because of the small sample size and survivor bias revealed a HR of 1.33 (95% CI, 1.02 to 1.74; $P = 0.03$), indicating higher risk with longer dialysis duration. Similarly, PRA levels were initially stratified into four categories (0%, 1%–30%, 31%–79%, >80%). Because of small sample sizes and wide CIs in the >80% group, the 31%–79% and >80% groups were combined, revealing a HR of 1.82 (95% CI, 1.00 to 3.30; $P = 0.03$) for graft loss. This adjustment aligns with prior findings and ensures robust comparisons. The risk index highlights high-risk recipients, supporting personalized interventions to enhance both short- and long-term transplant success. These patients may benefit from HMP or improved KEP donor-recipient matching.

In this study, we applied the same methodology used in our latest study about the UK's KEP (UK Living Kidney Sharing Scheme)¹⁵ to compare KEP performance across countries. In the United Kingdom, kidneys are transported to the recipient center, whereas in The Netherlands, donors travel for nephrectomy and transplantation. Five-year DCGS rates were comparable between the UK and The Netherlands (93% and 92% versus 92% and 92%, respectively), outperforming rates in the United States (85%) and Europe (87%) overall.⁴⁶ Remarkably, DGF rates were higher in The Netherlands for both KEP and non-KEP (Table 4). We observed significant differences in eGFR in the United Kingdom between KEP and non-KEP at 1 and 5 years, although rejection rates were similar (Table 4). These findings suggest that transporting kidneys does not adversely affect transplant outcomes, despite longer CIT because of shipping.

A recent meta-analysis has shown that CIT extending beyond 4 hours seem to minimally affect graft survival.³⁹

However, longer CIT is associated with higher DGF and graft loss in LDKT.^{65–69} In our cohort, extended CIT was attributed to procedural factors, including complex recipient cases, prolonged anesthesia, or arterial reconstruction. Vulnerability to ischemia-reperfusion injury, such as in retransplantations or older donor age, may also play a role.^{70–72} A recent study from the United States, by Treat *et al.*,⁷³ found higher mortality with shipped grafts compared with in-center exchanges but no significant differences in death-censored graft failure. These findings align with ours: Additional CIT did not significantly increase graft loss but was associated with higher mortality.

These data are relevant for countries in their design of new KEP programs and for expansion of transnational KEPs in LDKT.^{74,75} Challenges of the latter are multifactorial,^{33,76–81} with ethical, legislative, medical, and financial barriers. International collaboration on DDKT (*i.e.*, Eurotransplant and Scandiatransplant) and LDKT (Scandiatransplant Exchange Program⁸²) show that these international cooperations are feasible and beneficial for all stakeholders. Expanding KEPs internationally could improve access and equity for transplant candidates while maintaining positive outcomes, even with longer CIT. Our findings support the viability of transnational programs and highlight the potential for transformative crossborder kidney exchange initiatives.

Limitations

Our study has several limitations. Its observational design, while capturing real-world data across diverse patient populations, does not establish causality between treatment approaches and outcomes. Despite using propensity score matching to mitigate confounding, residual confounding from unmeasured or inadequately measured variables remains possible, including factors such as hospital volume or health care professional experience with LDKT.⁸³ The use of registry data also limits the granularity of key clinical variables, such as perioperative management strategies, which may influence outcomes. In addition, differences in logistics, including organ transport protocols and surgical techniques, were not fully analyzed and could affect results. Future studies should address these factors to enhance understanding of their influence on transplant success.

KEPs provide an effective solution for patients with ESKD with incompatible living donors, those needing a better HLA match, or recipients of end-of-chain offers from the DDKT waiting list. Our findings demonstrate that KEP recipients achieve comparable long-term DCGS with direct LDKT recipients, highlighting the importance of prioritizing KEP over DDKT, desensitization, or dialysis when feasible. These outcomes are achievable whether the donor or graft travels, offering flexibility in program implementation.

Given these results, we strongly advocate for the global adoption and expansion of KEPs. Establishing and scaling such programs improves access to transplantation for hard-to-match patients, optimizes donor organ utilization, and enhances the efficiency of national transplant systems.

Disclosures

Disclosure forms, as provided by each author, are available with the online version of the article at <http://links.lww.com/CJN/C163>.

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Data Sharing Statement

All data are included in the manuscript and/or supporting information.

Supplemental Material

This article contains the following supplemental material online at <http://links.lww.com/CJN/C151>.

Supplemental Table 1. Baseline donor and recipient characteristics divided per 3-year period.

Supplemental Table 2. Baseline characteristics of selected variables before propensity score matching.

Supplemental Table 3. Baseline characteristics after propensity score matching.

Supplemental Table 4. Odds ratio of different patient/transplant variables on DGF (for all LDKTs).

Supplemental Figure 1. DCGS after LDKT in The Netherlands (2004–2018) with a propensity score-matched cohort.

Supplemental Figure 2. Patient survival after LDKT in The Netherlands (2004–2018) with a propensity score-matched cohort.

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