Favorable living donor kidney transplantation outcomes within a national kidney exchange program

Laar, S.C. van de; Weerd, A.E. de; Bemelman, F.J.; Idu, M.M.; Vries, A.P.J. de; Alwayn, I.P.J.; ... ; Minnee, R.C.

OPEN

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

A Propensity Score–Matching Analysis

Stijn C. van de Laar[1,2] *Annelies E. de Weerd*[3] *Frederike J. Bemelman*[4] *Mirza M. Idu*[5] *Aiko P.J. de Vries*[6,7] *Ian P.J. Alwayn*,[7,8] *Stefan P. Berger*[9] *Robert A. Pol*,[10] *Arjan D. van Zuilen*[11] *Raechel J. Toorop*,[12] *Luuk B. Hilbrands*[13] *Paul P.C. Poyck*[14] *Maarten H.L. Christiaans*[15] *Jorinde H.H. van Laanen*,[16] *Jacqueline van de Wetering*,[3] *Hendrikus J.A.N. Kimenai*[1] *Marlies E.J. Reinders*[3] *Robert J. Porte*,[1] *Frank J.M.F. Dor*,[1,2,17] *and Robert C. Minnee*[1]

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.

CJASN 20: 440–450, 2025. doi: https://doi.org/10.2215/CJN.0000000611

Due to the number of contributing authors, the affiliations are listed at the end of this article.

Correspondence: Dr. Robert C. Minnee, email: r.minnee@erasmusmc.nl

Received: June 13, 2024 **Accepted:** January 10, 2025
Published Online Ahead of Print: January 29, 2025

See related editorial, "Favorable Outcomes of Kidney Exchange Program Live Donor Transplants: A Path to Increasing Transplant Rates," on pages 317–319.

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 DCGL. 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).

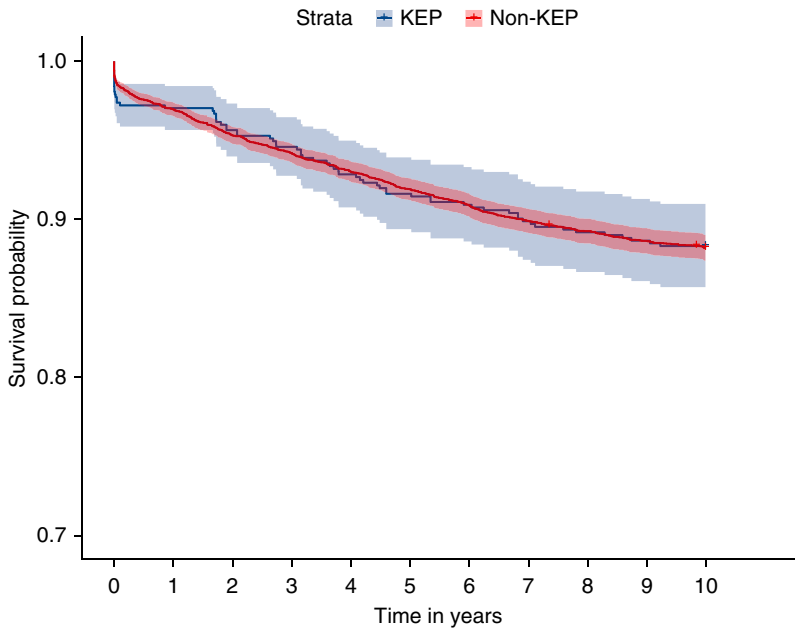

Figure 1. Kaplan–Meier survival estimates for 1-, 5-, and 10-year DCGS. DCGS, death-censored graft survival. Figure 1 can be viewed in color online at www.cjasn.org.

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

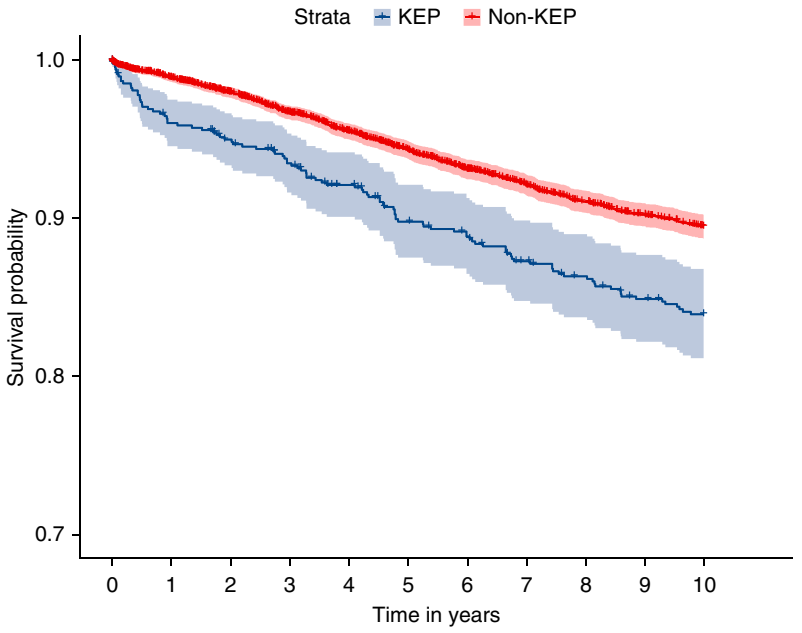

Figure 2. Kaplan–Meier survival estimates for 1-, 5-, and 10-year patient survival comparing LDKT by kidney exchange programs (KEPs) with non-KEP. LDKT, living donor kidney transplantation. Figure 2 can be viewed in color online at www.cjasn.org.

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).
[a]Indicates 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 American[45] and UK[15] 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 rates[47] 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 Program[82]) 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.

Funding

None.

Acknowledgments

The authors acknowledge gratefully the Dutch Transplant Foundation and Cynthia Konijn for their support and providing the data of our study.

Author Contributions

Conceptualization: Annelies E. de Weerd, Frank J.M.F. Dor, Robert C. Minnee, Stijn C. van de Laar.
Data curation: Stijn C. van de Laar.
Formal analysis: Frank J.M.F. Dor, Stijn C. van de Laar.
Investigation: Annelies E. de Weerd, Frank J.M.F. Dor, Robert C. Minnee, Robert J. Porte, Stijn C. van de Laar.
Methodology: Maarten H.L. Christiaans, Annelies E. de Weerd, Frank J.M.F. Dor, Robert C. Minnee, Robert J. Porte, Stijn C. van de Laar.
Project administration: Robert C. Minnee.
Software: Stijn C. van de Laar.
Supervision: Frank J.M.F. Dor, Robert C. Minnee, Robert J. Porte, Stijn C. van de Laar.
Validation: Maarten H.L. Christiaans, Annelies E. de Weerd, Stijn C. van de Laar.
Visualization: Stijn C. van de Laar.
Writing – original draft: Frank J.M.F. Dor, Robert C. Minnee, Stijn C. van de Laar.
Writing – review & editing: Ian P.J. Alwayn, Frederike J. Bemelman, Stefan P. Berger, Maarten H.L. Christiaans, Annelies E. de Weerd, Frank J.M.F. Dor, Luuk B. Hilbrands, Mirza M. Idu, Diederik H.J.A.N. Kimenai, Robert C. Minnee, Robert A. Pol, Robert J. Porte, Paul P.C. Poyck, Marlies E.J. Reinders, Raechel J. Toorop, Aiko P.J. de Vries, Stijn C. van de Laar, Jacqueline van de Wetering, Jorinde H.H. van Laanen, Arjan D. van Zuilen.

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.

References

1. Baid-Agrawal S, Frei UA. Living donor renal transplantation: recent developments and perspectives. *Nat Clin Pract Nephrol.* 2007;3(1):31–41. doi:10.1038/ncpneph0383

2. Held PJ, McCormick F, Ojo A, Roberts JP. A cost-benefit analysis of government compensation of kidney donors. *Am J Transplant.* 2016;16(3):877–885. doi:10.1111/ajt.13490
3. Lumsdaine JA, Wray A, Power MJ, et al. Higher quality of life in living donor kidney transplantation: prospective cohort study. *Transpl Int.* 2005;18(8):975–980. doi:10.1111/j.1432-2277.2005.00175.x
4. Tonelli M, Wiebe N, Knoll G, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant.* 2011;11(10):2093–2109. doi:10.1111/j.1600-6143.2011.03686.x
5. Hariharan S, Johnson CP, Bresnahan BA, Taranto SE, McIntosh MJ, Stablein D. Improved graft survival after renal transplantation in the United States, 1988 to 1996. *New Engl J Med.* 2000;342(9):605–612. doi:10.1056/NEJM200003023420901
6. Øien CM, Reisaeter AV, Leivestad T, Dekker FW, Line PD, Os I. Living donor kidney transplantation: the effects of donor age and gender on short- and long-term outcomes. *Transplantation.* 2007;83(5):600–606. doi:10.1097/01.tp.0000255583.34329.dd
7. Øien CM, Reisaeter AV, Leivestad T, Pfeffer P, Fauchald P, Os I. Gender imbalance among donors in living kidney transplantation: the Norwegian experience. *Nephrol Dial Transplant.* 2005;20(4):783–789. doi:10.1093/ndt/gfh696
8. van Dellen D, Burnapp L, Citterio F, et al. Pre-emptive live donor kidney transplantation-moving barriers to opportunities: an ethical, legal and psychological aspects of organ transplantation view. *World J Transplant.* 2021;11(4):88–98. doi:10.5500/wjt.v11.i4.88
9. Kim I, Maggiore U, Knight SR, Rana Magar R, Pengel LHM, Dor FJMF. Pre-emptive living donor kidney transplantation: a public health justification to change the default. *Front Public Health.* 2023;11:1124453. doi:10.3389/fpubh.2023.1124453
10. *Toolbox Living Kidney Donation.* European Union; 2016.
11. Vanholder R, Domínguez-Gil B, Busic M, et al. Organ donation and transplantation: a multi-stakeholder call to action. *Nat Rev Nephrol.* 2021;17(8):554–568. doi:10.1038/s41581-021-00425-3
12. Dominguez-Gil B. *International Figures on Donation and Transplantation 2019.* European Parliament; 2020.
13. Boenink R, Kramer A, Tuinhout RE, et al. Trends in kidney transplantation rate across Europe: study from the ERA Registry. *Nephrol Dial Transplant.* 2023;38(6):1528–1539. doi:10.1093/ndt/gfac333
14. Boenink R, Kramer A, Masoud S, et al. International comparison and time trends of first kidney transplant recipient characteristics across Europe: an ERA Registry study. *Nephrol Dial Transplant.* 2024;39(4):648–658. doi:10.1093/ndt/gfad189
15. van de Laar SC, Robb ML, Hogg R, Burnapp L, Papalois VE, Dor FJMF. The impact of cold ischaemia time on outcomes of living donor kidney transplantation in the UK living kidney sharing scheme. *Ann Surg.* 2021;274(5):859–865. doi:10.1097/SLA.0000000000005123
16. Hariharan S, Israni AK, Danovitch G. Long-term survival after kidney transplantation. *N Engl J Med.* 2021;385(8):729–743. doi:10.1056/NEJMra2014530
17. Abd ElHafeez S, Noordzij M, Kramer A, et al. The association of living donor source with patient and graft survival among kidney transplant recipients in the ERA-EDTA Registry - a retrospective study. *Transpl Int.* 2021;34(1):76–86. doi:10.1111/tri.13759
18. Jackson KR, Motter JD, Kernodle A, et al. How do highly sensitized patients get kidney transplants in the United States? Trends over the last decade. *Am J Transplant.* 2020;20(8):2101–2112. doi:10.1111/ajt.15825
19. Kher V, Jha PK. Paired kidney exchange transplantation – pushing the boundaries. *Transpl Int.* 2020;33(9):975–984. doi:10.1111/tri.13693
20. de Weerd AE, Betjes MGH. ABO-incompatible kidney transplant outcomes: a meta-analysis. *Clin J Am Soc Nephrol.* 2018;13(8):1234–1243. doi:10.2215/CJN.00540118
21. Axelrod D, Lentine KL, Schnitzler MA, et al. The incremental cost of incompatible living donor kidney transplantation: a national cohort analysis. *Am J Transplant.* 2017;17(12):3123–3130. doi:10.1111/ajt.14392
22. Segev DL, Gentry SE, Warren DS, Reeb B, Montgomery RA. Kidney paired donation and optimizing the use of live donor organs. *JAMA.* 2005;293(15):1883–1890. doi:10.1001/jama.293.15.1883
23. Blumberg JM, Gritsch HA, Reed EF, et al. Kidney paired donation in the presence of donor-specific antibodies. *Kidney Int.* 2013;84(5):1009–1016. doi:10.1038/ki.2013.206
24. Gentry SE, Segev DL, Simmerling M, Montgomery RA. Expanding kidney paired donation through participation by compatible pairs. *Am J Transplant.* 2007;7(10):2361–2370. doi:10.1111/j.1600-6143.2007.01935.x
25. Massie AB, Gentry SE, Montgomery RA, Bingaman AA, Segev DL. Center-level utilization of kidney paired donation. *Am J Transplant.* 2013;13(5):1317–1322. doi:10.1111/ajt.12189
26. Hart A, Smith JM, Skeans MA, et al. OPTN/SRTR 2015 annual data report: kidney. *Am J Transplant.* 2017;17(suppl 1):21–116. doi:10.1111/ajt.14124
27. NHSBT. *Annual Report on Living Donor Kidney Transplantation.* NHS Blood and Transplant; 2021.
28. Holscher CM, Jackson K, Chow EKH, et al. Kidney exchange match rates in a large multicenter clearinghouse. *Am J Transplant.* 2018;18(6):1510–1517. doi:10.1111/ajt.14689
29. Wang W, Leichtman AB, Rees MA, et al. Kidney paired donation chains initiated by deceased donors. *Kidney Int Rep.* 2022;7(6):1278–1288. doi:10.1016/j.ekir.2022.03.023
30. de Klerk M, Kal-van Gestel JA, Haase-Kromwijk BJ, Claas FH, Weimar W.; Living Donor Kidney Exchange Program. Eight years of outcomes of the Dutch living donor kidney exchange program. *Clin Transpl.* 2011;1:287–290. PMID: 22755421
31. de Klerk M, Keizer KM, Claas FH, Witvliet M, Haase-Kromwijk BJ, Weimar W. The Dutch national living donor kidney exchange program. *Am J Transplant.* 2005;5(9):2302–2305. doi:10.1111/j.1600-6143.2005.01024.x
32. Johnson RJ, Allen JE, Fuggle SV, Bradley JA, Rudge C.; Kidney Advisory Group, UK Transplant NHSBT. Early experience of paired living kidney donation in the United Kingdom. *Transplantation.* 2008;86(12):1672–1677. doi:10.1097/TP.0b013e3181901a3d
33. Biró P, Haase-Kromwijk B, Andersson T, et al.; ENCKEP COST Action. Building kidney exchange programmes in europe-an overview of exchange practice and activities. *Transplantation.* 2019;103(7):1514–1522. doi:10.1097/TP.0000000000002432
34. Akkina SK, Muster H, Steffens E, Kim SJ, Kasiske BL, Israni AK. Donor exchange programs in kidney transplantation: rationale and operational details from the north central donor exchange cooperative. *Am J Kidney Dis.* 2011;57(1):152–158. doi:10.1053/j.ajkd.2010.06.012
35. Flechner SM, Thomas AG, Ronin M, et al. The first 9 years of kidney paired donation through the national kidney registry: characteristics of donors and recipients compared with national live donor transplant registries. *Am J Transplant.* 2018;18(11):2730–2738. doi:10.1111/ajt.14744
36. Cole EH, Nickerson P, Campbell P, et al. The Canadian kidney paired donation program: a national program to increase living donor transplantation. *Transplantation.* 2015;99(5):985–990. doi:10.1097/TP.0000000000000455
37. Cantwell L, Woodroffe C, Holdsworth R, Ferrari P. Four years of experience with the Australian kidney paired donation programme. *Nephrology (Carlton).* 2015;20(3):124–131. doi:10.1111/nep.12369
38. Segev DL, Veale JL, Berger JC, et al. Transporting live donor kidneys for kidney paired donation: initial national results. *Am J Transplant.* 2011;11(2):356–360. doi:10.1111/j.1600-6143.2010.03386.x
39. van de Laar SC, Lafranca JA, Minnee RC, Papalois V, Dor F. The impact of cold ischaemia time on outcomes of living donor kidney transplantation: a systematic review and meta-analysis. *J Clin Med.* 2022;11(6):1620. doi:10.3390/jcm11061620
40. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc.* 1958;53(282):457–481. doi:10.1080/01621459.1958.10501452
41. Cox DR. Regression models and life-tables. *J R Stat Soc Ser B.* 1972;34(2):187–202. doi:10.1111/j.2517-6161.1972.tb00899.x
42. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP.; STROBE Initiative. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)

statement: guidelines for reporting observational studies. *BMJ.* 2007;335(7624):806–808. doi:10.1136/bmj.39335.541782.AD
43. de Kok MJ, Schaapherder AF, Mensink JW, et al. A nationwide evaluation of deceased donor kidney transplantation indicates detrimental consequences of early graft loss. *Kidney Int.* 2020; 97(6):1243–1252. doi:10.1016/j.kint.2020.01.043
44. *Renine Registry Annual Report 2022*; 2022.
45. Leeser DB, Thomas AG, Shaffer AA, et al. Patient and kidney allograft survival with national kidney paired donation. *Clin J Am Soc Nephrol.* 2020;15(2):228–237. doi:10.2215/CJN.06660619
46. Wang JH, Skeans MA, Israni AK. Current status of kidney transplant outcomes: dying to survive. *Adv Chronic Kidney Dis.* 2016;23(5):281–286. doi:10.1053/j.ackd.2016.07.001
47. Wu WK, Famure O, Li Y, Kim SJ. Delayed graft function and the risk of acute rejection in the modern era of kidney transplantation. *Kidney Int.* 2015;88(4):851–858. doi:10.1038/ki.2015.190
48. Redfield RR, Scalea JR, Zens TJ, et al. Predictors and outcomes of delayed graft function after living-donor kidney transplantation. *Transpl Int.* 2016;29(1):81–87. doi:10.1111/tri.12696
49. Palmisano A, Gandolfini I, Delsante M, et al. Acute kidney injury (AKI) before and after kidney transplantation: causes, medical approach, and implications for the long-term outcomes. *J Clin Med.* 2021;10(7):1484. doi:10.3390/jcm10071484
50. Cherukuri A, Mehta R, Sood P, Hariharan S. Early allograft inflammation and scarring associate with graft dysfunction and poor outcomes in renal transplant recipients with delayed graft function: a prospective single center cohort study. *Transpl Int.* 2018;31(12):1369–1379. doi:10.1111/tri.13318
51. Moser MAJ, Ginther N, Luo Y, et al. Early experience with hypothermic machine perfusion of living donor kidneys - a retrospective study. *Transpl Int.* 2017;30(7):706–712. doi:10.1111/tri.12964
52. Moers C, Smits JM, Maathuis MH, et al. Machine perfusion or cold storage in deceased-donor kidney transplantation. *N Engl J Med.* 2009;360(1):7–19. doi:10.1056/NEJMoa0802289
53. Summers DM, Ahmad N, Randle LV, et al. Cold pulsatile machine perfusion versus static cold storage for kidneys donated after circulatory death: a multicenter randomized controlled trial. *Transplantation.* 2020;104(5):1019–1025. doi:10.1097/TP.0000000000002907
54. Mogulla MR, Bhattacharjya S, Clayton PA. Risk factors for and outcomes of delayed graft function in live donor kidney transplantation – a retrospective study. *Transpl Int.* 2019;32(11): 1151–1160. doi:10.1111/tri.13472
55. Mannon RB. Delayed graft function: the AKI of kidney transplantation. *Nephron.* 2018;140(2):94–98. doi:10.1159/000491558
56. Davis CL, Delmonico FL. Living-donor kidney transplantation: a review of the current practices for the live donor. *J Am Soc Nephrol.* 2005;16(7):2098–2110. doi:10.1681/ASN.2004100824
57. Issa N, Stephany B, Fatica R, et al. Donor factors influencing graft outcomes in live donor kidney transplantation. *Transplantation.* 2007;83(5):593–599. doi:10.1097/01.tp.0000256284.78721.ba
58. Kaboré R, Haller MC, Harambat J, Heinze G, Leffondré K. Risk prediction models for graft failure in kidney transplantation: a systematic review. *Nephrol Dial Transplant.* 2017;32(suppl 2): ii68–ii76. doi:10.1093/ndt/gfw405
59. Foroutan F, Friesen EL, Clark KE, et al. Risk factors for 1-year graft loss after kidney transplantation systematic review and meta-analysis. *Clin J Am Soc Nephrol.* 2019;14(11):1642–1650. doi:10.2215/CJN.05560519
60. Oweira H, Ramouz A, Ghamarnejad O, et al. Risk factors of rejection in renal transplant recipients: a narrative review. *J Clin Med.* 2022;11(5):1392. doi:10.3390/jcm11051392
61. Lebranchu Y, Baan C, Biancone L, et al. Pretransplant identification of acute rejection risk following kidney transplantation. *Transpl Int.* 2014;27(2):129–138. doi:10.1111/tri.12205
62. Lan JH, Kadatz M, Chang DT, Gill J, Gebel HM, Gill JS. Pretransplant calculated panel reactive antibody in the absence of donor-specific antibody and kidney allograft survival. *Clin J Am Soc Nephrol.* 2021;16(2):275–283. doi:10.2215/CJN.13640820
63. Massie AB, Leanza J, Fahmy LM, et al. A risk index for living donor kidney transplantation. *Am J Transplant.* 2016;16(7): 2077–2084. doi:10.1111/ajt.13709
64. Rana Magar R, Knight SR, Maggiore U, Lafranca JA, Dor F, Pengel LHM. What are the benefits of preemptive versus nonpreemptive kidney transplantation? A systematic review and meta-analysis. *Transpl Rev (Orlando).* 2023;37(4):100798. doi:10.1016/j.trre.2023.100798
65. Simpkins CE, Montgomery RA, Hawxby AM, et al. Cold ischemia time and allograft outcomes in live donor renal transplantation: is live donor organ transport feasible? *Am J Transplant.* 2007;7(1): 99–107. doi:10.1111/j.1600-6143.2006.01597.x
66. Gill J, Rose C, Joffres Y, Kadatz M, Gill J. Cold ischemia time up to 16 hours has little impact on living donor kidney transplant outcomes in the era of kidney paired donation. *Kidney Int.* 2017;92(2):490–496. doi:10.1016/j.kint.2017.01.032
67. Nath J, Hodson J, Canbilen SW, et al. Effect of cold ischaemia time on outcome after living donor renal transplantation. *Br J Surg.* 2016;103(9):1230–1236. doi:10.1002/bjs.10165
68. Nassiri N, Kwan L, Bolagani A, et al. The ''oldest and coldest'' shipped living donor kidneys transplanted through kidney paired donation. *Am J Transplant.* 2020;20(1):137–144. doi:10.1111/ajt.15527
69. Krishnan AR, Wong G, Chapman JR, et al. Prolonged ischemic time, delayed graft function, and graft and patient outcomes in live donor kidney transplant recipients. *Am J Transplant.* 2016; 16(9):2714–2723. doi:10.1111/ajt.13817
70. Ponticelli CE. The impact of cold ischemia time on renal transplant outcome. *Kidney Int.* 2015;87(2):272–275. doi:10.1038/ki.2014.359
71. Rosner MH. Acute kidney injury in the elderly. *Clin Geriatr Med.* 2013;29(3):565–578. doi:10.1016/j.cger.2013.05.001
72. Salvadori M, Rosso G, Bertoni E. Update on ischemia-reperfusion injury in kidney transplantation: pathogenesis and treatment. *World J Transplant.* 2015;5(2):52–67. doi:10.5500/wjt.v5.i2.52
73. Treat E, Chow EKH, Peipert JD, et al. Shipping living donor kidneys and transplant recipient outcomes. *Am J Transplant.* 2018;18(3):632–641. doi:10.1111/ajt.14597
74. Böhmig GA, Fronek J, Slavcev A, Fischer GF, Berlakovich G, Viklicky O. Czech-Austrian kidney paired donation: first European cross-border living donor kidney exchange. *Transpl Int.* 2017;30(6):638–639. doi:10.1111/tri.12945
75. Kute VB, Patel HV, Shah PR, et al. Past, present and future of kidney paired donation transplantation in India. *World J Transplant.* 2017;7(2):134–143. doi:10.5500/wjt.v7.i2.134
76. Minerva F, Savulescu J, Singer P. The ethics of the global kidney exchange programme. *Lancet.* 2019;394(10210):1775–1778. doi:10.1016/S0140-6736(19)32474-2
77. Danovitch GM. The global kidney exchange programme. *Lancet.* 2020;395(10235):1485. doi:10.1016/S0140-6736(20)30615-2
78. Ambagtsheer F, Haase-Kromwijk B, Dor FJMF, et al. Global Kidney Exchange: opportunity or exploitation? An ELPAT/ESOT appraisal. *Transpl Int.* 2020;33(9):989–998. doi:10.1111/tri.13630
79. Roth AE, Marino IR, Ekwenna O, et al. Global kidney exchange should expand wisely. *Transpl Int.* 2020;33(9):985–988. doi:10.1111/tri.13656
80. Pullen LC. Global kidney exchange: overcoming the barrier of poverty. *Am J Transplant.* 2017;17(10):2499–2500. doi:10.1111/ajt.14469
81. Delmonico FL, Ascher NL. Opposition to irresponsible global kidney exchange. *Am J Transplant.* 2017;17(10):2745–2746. doi:10.1111/ajt.14473
82. Duus Weinreich I, Andersson T, Birna Andrésdóttir M, et al. Scandiatransplant exchange program (STEP): development and results from an international kidney exchange program. *Transplant Direct.* 2023;9(11):e1549. doi:10.1097/TXD.0000000000001549
83. Fewell Z, Davey Smith G, Sterne JA. The impact of residual and unmeasured confounding in epidemiologic studies: a simulation study. *Am J Epidemiol.* 2007;166(6):646–655. doi:10.1093/aje/kwm165

AFFILIATIONS

[1]Division of HPB and Transplant Surgery, Department of Surgery, Erasmus MC Transplant Institute, Erasmus University Medical Center, Rotterdam, The Netherlands
[2]Imperial College Renal and Transplant Centre, Hammersmith Hospital, Imperial College Healthcare NHS Trust, London, United Kingdom
[3]Department of Internal Medicine, Erasmus Medical Center Transplant Institute, University Medical Center Rotterdam, Rotterdam, The Netherlands
[4]Department of Internal Medicine, Infectious Diseases, Amsterdam Infection and Immunity Institute (AI&II), Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands
[5]Department of Surgery, Academic Medical Center Amsterdam, Amsterdam, The Netherlands
[6]Division of Nephrology, Department of Internal Medicine, Leiden University Medical Center, Leiden, The Netherlands
[7]Transplant Center, Leiden University Medical Center, Leiden, The Netherlands
[8]Department of Surgery, Leiden University Medical Center, Leiden, The Netherlands
[9]Division of Nephrology, Department of Internal Medicine, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands
[10]Division of Transplant Surgery, Department of Surgery, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands
[11]Department of Nephrology, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands
[12]Department of Surgery, Utrecht University Medical Centre, Utrecht, The Netherlands
[13]Department of Nephrology, Radboud University Medical Center, Nijmegen, The Netherlands
[14]Department of Vascular and Transplant Surgery, Radboudumc, Nijmegen, The Netherlands
[15]Division of Nephrology, Department of Internal Medicine, Maastricht University Medical Center+, Maastricht, The Netherlands
[16]Department of Vascular Surgery, Maastricht University Medical Center, Maastricht, The Netherlands
[17]Department of Surgery and Cancer, Imperial College London, London, United Kingdom