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The Landscape of International Living Kidney Donation in the United States

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Study concept and design: Al Ammary, Thomas, Henderson. Acquisition of data: Al Ammary, Thomas, Massie, Segev, Henderson. Analysis and interpretation of data: Al Ammary, Thomas, Muzaale, Lentine, Massie, Segev, Henderson. Drafting of the manuscript: Al Ammary, Thomas, Koons, Shaffer, Segev, Henderson. Critical revision of the manuscript for important intellectual content: Al Ammary, Thomas, Massie, Koons, Muzaale, Shaffer, Crews, Garonzik-Wang, Fang, Lentine, Qadi, Brennan, Segev, Henderson. Statistical analysis: Al Ammary, Thomas, Massie, Segev. Obtained funding: Massie, Shaffer, Lentine, Segev, Henderson. Administrative, technical, and material support: Henderson, Massie. Study supervision: Segev, Henderson.

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DISCLOSURE

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Supporting Information

Additional material may be found online in the Supporting Information section for this article.

Abstract

In the United States, kidney donation from international (non-citizen/non-resident) living kidney donors (LKDs) is permitted; however, given heterogeneity of healthcare systems, concerns remain regarding international LKD practice and recipient outcomes. We studied a US cohort of 102,315 LKD transplants from 2000–2016, including 2,088 international LKDs, as reported to the Organ Procurement and Transplantation Network. International LKDs were more tightly clustered among a small number of centers than domestic LKDs (Gini coefficient 0.76 vs. 0.58, p<0.001). Compared with domestic LKDs, international LKDs were more often young, male, Hispanic or Asian, and biologically-related to their recipient (p<0.001). Policy-compliant donor follow-up was substantially lower for international LKDs at 6, 12, and 24 months post-nephrectomy (2015 cohort: 45%, 33%, 36% vs. 76%, 71%, 70% for domestic LKDs, p<0.001). Among international LKDs, Hispanic (aOR=$_{0.23}0.36_{0.56}$, p<0.001) and biologically-related (aOR=$_{0.39}0.59_{0.89}$, p<0.01) donors were more compliant in donor follow-up than white and unrelated donors. Recipients of international living donor kidney transplant (LDKT) had similar graft failure (aHR=$_{0.78}0.89_{1.02}$, p=0.1), but lower mortality (aHR=$_{0.53}0.62_{0.72}$, p<0.001) compared with recipients of domestic LDKT after adjusting for recipient, transplant, and donor factors. International LKDs may provide an alternative opportunity for living donation. However, efforts to improve international LKD follow-up and engagement are warranted.

INTRODUCTION

Over 700,000 individuals in the United States (US) are burdened with end-stage renal disease (ESRD) (1). Living donor kidney transplantation (LDKT) is the optimal therapy for most ESRD patients, as it is associated with improved outcomes and quality of life compared to receiving long-term dialysis or deceased donor KT (1, 2). Yet, the total number of living donor kidney transplant (LDKT) performed annually in the US has declined since 2004 (2). During this period, racial/ethnic disparities in access to LDKT has worsened (3). In the context of growing demand for LDKT and a persistent shortage of donor organs (1, 2), travel for transplantation has emerged. Travel for transplantation is defined as the movement of organs, donors, recipients, or transplant professionals across jurisdictional borders for transplantation purposes (4). In the US, the Organ Procurement and Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS) policy permits organ registration and transplantation of non-US Citizens/non-US residents (5), and the Ad Hoc International Relations Committee of OPTN/UNOS releases an annual public report of such transplant center activities (6–8).

End-stage renal disease (ESRD) patients in the US may have family members or friends who are not US citizens or residents but are willing to serve as a living kidney donor (LKD) in the US. However, very little is known about non-US citizens/non-US residents who undergo donor nephrectomy in the US, hereafter referred to as international LKDs. While transplant centers in the US are required to report LKD follow-up at 6,12, and 24 months post-donation, there are logistical and financial challenges that serve as barriers to LKDs follow-up in the US (9), and donor geographic distance from the transplant center is associated with non-timely or incomplete 6-month follow-up compliance (10). Follow-up of international LKDs potentially involves additional challenges, including cost of communication, time

zone differences, and language barriers. Furthermore, international LKDs may expose recipients to risk of transmissible infections based on the international LKDs geographic endemic infections exposure (11–13). Given the heterogeneity of healthcare systems, concerns remain regarding international LKD practice and recipient outcomes.

To address this knowledge gap, we conducted a national registry study to present the landscape of international living kidney donation in the US. We describe characteristics of international LKDs, compare international LKDs follow-up rates to domestic LKDs, and quantify their counterpart recipient outcomes.

METHODS

National Registry Data Source

This cohort study used data from the Scientific Registry of Transplant Recipients (SRTR) external release made available in March 2018. The SRTR data system includes data on all donors, waitlist candidates, and transplant recipients in the US, submitted by members of OPTN, and has been previously described (14, 15). The Health Resources and Services Administration under the US Department of Health and Human Services provides federal government oversight to the activities of the OPTN and SRTR contractors. Additionally, we obtained summary data on the country of origin for international donors from the OPTN.

Socioeconomic Status Index Data Source

Permanent home ZIP codes were linked to the socioeconomic status (SES) index, which was originally derived in the Medicare population by the Agency for Healthcare Research and Quality (AHRQ) and has been used in studies of transplantation (16–19). The SES Index used data from the 2010 census to estimate ZIP code level SES based on multiple factors including unemployment, poverty, property values, median household income, education, and household crowding (16, 18). ZIP codes can have a SES index score between 0–100, and a higher score indicates higher SES.

Study Population

Using SRTR, we studied 102,315 LKDs who underwent donor nephrectomy between January 1, 2000 and December 31, 2016, and their counterpart recipients. Differences in donor, recipient, and transplant characteristics by international LKD status were assessed using the χ^2 (categorical variables) and Mann-Whitney rank-sum (continuous variables) tests.

Exposure: Non-US Citizen/Non-US Resident (International) Living Kidney Donation

The SRTR collects citizenship status on living donors and transplant recipients from the OPTN/UNOS LKD and transplant candidate registration forms. Prior to March 2012, citizenship was categorized as US citizen, resident alien, and non-resident alien. However, after March 2012, citizenship was classified as US citizen, non-US citizen/US resident, and non-US citizen/non-US resident (traveling to the US for reasons other than transplant or traveling to the US for transplant). For the purpose of this study, from 2000 to February 2012, we defined international LKDs as non-resident aliens; from March 2012 to December

2016, we defined international LKDs as non-US citizens/non-US residents (traveling to the US for reason other than transplant or traveling to the US for transplant). Domestic LKDs were defined as US citizens or US residents.

Trends in International Living Kidney Donation

We assessed temporal trends in LDKT with international donors using the Cuzick global, a non-parametric test of trends (20, 21). In a post-hoc analysis of temporal trends, we used the Bonferroni multiple comparisons correction with a two-sided α of 0.009 (22). The multiple comparisons that we defined prior to testing were 4 groups (2000–2004, 2005–2008, 2009–2012, and 2013–2016) and 2 groups (2000–2004 and 2005–2016) for a total of 6 comparisons. This resulted in a Bonferroni correction of 0.009.

Center-Level Distribution of International Living Kidney Donation

We estimated the Gini coefficient to assess the degree of center-level distribution of international LKDs. For comparison, we also estimated the Gini coefficient for domestic LKDs. The Gini coefficient (range 0–1) is a measure of inequality/equality. A Gini coefficient close to 1 would indicate that a few centers account for almost all the international LKDs, whereas a Gini coefficient close to 0 would indicate that the use of international LKDs was equal among all centers (23–25). The Lorenz curve is a graphical representation of inequality (26–28). When plotted, we generate Lorenz curves which are compared to the “line of equality” which is the 45° line. The closer a Lorenz curve is to the line of equality, the closer that population is to equal distribution.

Donor Follow-up

The OPTN/UNOS began collecting data about living donor follow-up in 1999. However, since February 2013, the OPTN has enforced US transplant centers to report living donor follow-up data at 6, 12, and 24 months post donor nephrectomy, including required clinical and laboratory data elements and completion thresholds to define compliance(29). We report policy-compliant 6, 12, and 24 months follow-up for LKDs who donated after the implementation of this policy (February 1, 2013). Donors were followed through May 31, 2018. To meet the requirements of the OPTN policy, follow-up data must be complete and submitted in a timely manner (60 days before or after the expected collection date) and has been described elsewhere (30).

We explored potential risk factors for incomplete living donor follow-up after the implementation of the OPTN living donor follow-up policy using univariable and multivariable logistic regression. We assessed the following risk factors: male, race/ethnicity, age (by 10 years), obesity (BMI>30), eGFR prior to transplant, biological relationship to paired recipient, and non-US citizen/non-US resident (international) paired recipient.

Recipient Outcomes

Recipient outcomes were death-censored graft failure (DCGF) and mortality. DCGF was defined as the earliest of resumption of maintenance dialysis, relisting for kidney transplant, or re-transplantation. DCGF was assessed by transplant center report to the OPTN supplemented by Centers for Medicare and Medicaid Services (CMS) Form 2728. Recipient

mortality was assessed by transplant center report to the OPTN supplemented by Social Security Death Master File. Recipients were followed until the earliest of: center-reported last date of follow-up, time of event (DCGF or mortality), or administrative censorship on December 31, 2017 (whichever came earliest). For analysis of recipient outcomes, we excluded international (non-US citizen/non-US resident) recipients (N=1,036 including 488 with international donors), including only recipients who were US citizens or US residents (N=101,279). Our decisions to censor at center-reported last date of follow-up and the exclusion of international recipients were made to accurately estimate long-term outcomes of the recipients and avoid information bias.

Differences in recipient survival were assessed using the log-rank test. We used a two-sided α of 0.05 to indicate a statistically significant difference. We used Cox proportional hazards regression to assess the independent association between international living kidney donation and recipient DCGF and mortality. We adjusted for recipient characteristics (sex, Black race, Hispanic ethnicity, age at the time of transplant, body mass index (BMI), diabetes status, HCV, HBV, HIV, history of previous transplant, panel reactive antibody (PRA)>80, college education, public insurance, and SES index); transplant characteristics (year of transplant, 0 HLA mismatches, ABO incompatibility); and donor characteristics (sex, Black race, Hispanic ethnicity, age at the time of donation, BMI, and estimated glomerular filtration rate (eGFR) based on the CKD-EPI equation (31), biological relationship between donor and recipient). We built four Cox regression models: model 1 was unadjusted; model 2 adjusted for recipient characteristics only; model 3 adjusted for recipient and transplant characteristics; model 4 adjusted for recipient, transplant, and donor characteristics. All models were stratified by transplant center to account for center-level differences, assuming equal coefficients across strata but a baseline hazard unique to each stratum. Furthermore, we examined effect modification of recipient outcomes by donor/recipient relationship among the recipients of international LKDs.

Sensitivity analyses

We examined potential effect modification of the association between international donor status and post-transplant outcomes by pediatric recipient (<18-year-old), recipient sex, and recipient US citizenship (vs. resident status).

Statistical analysis

We report aOR and aHR with 95% confidence interval [CI] as per the method of Louis and Zeger (32). All analyses were performed using Stata 15/MP for Linux (College Station, Texas).

RESULTS

Study Population

There were 102,315 LKDs who underwent donor nephrectomy between January 2000 and December 2016, of whom 2,088 (2%) were international LKDs. International LKDs had the following relationships with their recipient: 39% were siblings, 12% were parents, 7% were children, 16% were another biological relationship, 4% were a spouse or life partner, and

22% were another non-biological relationship. Compared to domestic LKDs (US citizen (N=96,790 [94.6%]) or US resident LKDs (N=3,437 [3.4%]), international LKDs were more likely to be Hispanic or Asian, younger, biologically related, and have higher eGFR at baseline (p<0.001) (Table 1). Of the 102,315 LDKT recipients, 5.5% (N=5586) were pediatric. Compared to recipients of domestic LDKT, recipients of international LDKT were more likely to be Hispanic or Asian, younger, have lower BMI, and have hypertension (p<0.001) (Table 2). Further, recipients of international LDKT were less likely to have diabetes, be college educated, and have a history of previous transplantation (p<0.001).

Trends in International Living Kidney Donation

International LKDs represented 1–3% of the annual number of LKDs 2000–2016 (Figure 1). There was no global trend over this time period (Cuzick p=0.4). In a post-hoc analysis, there was a statistically significant increasing trend in donation from international LKDs from 2005 to 2016 (p=0.005) using the Bonferroni multiple comparisons correction with a two-sided α of 0.009.

Center-Level Distribution of International Living Kidney Donation

Over the study period, there were 277 centers that performed at least one LDKT. Of these, 193 (70%) performed at least one transplant with an international LKD. The Gini coefficient of center-level clustering was higher for international LKDs (0.76) than for domestic LKDs (0.58), indicating that as compared to the domestic LKD population, international LKDs are more tightly clustered among fewer transplant centers (Figure 2). We compared the Lorenz curves for domestic and international LKDs to the “line of equality.” There was more inequality in the use of international LKDs (fewer centers doing more international LDKT) since it was farther from the line of equality than the curve for domestic LKDs. For example, 5 centers account for 21.5% of all international LKDs whereas 11 centers account for 21.2% of all domestic LKDs.

Living Donor Follow-up

While donor follow-up increased after the implementation of the OPTN living donor follow-up policy on February 1, 2013, there were differences in follow-up between domestic and international LKDs. For the 2013 cohort, policy-compliant donor follow-up at 6, 12, and 24 months was 37.1%, 36.2%, and 37.2% respectively for international LKDs vs. 63.7%, 59.3%, and 55.7% respectively for domestic LKDs (P<0.001). For the 2014 cohort, policy-compliant donor follow-up was reported for 43.2%, 38.5%, and 31.1% international LKDs vs. 72.4%, 67.9%, and 60.9% domestic LKDs (P<0.001). Finally, for the 2015 cohort, policy-compliant donor follow-up occurred for 45.3%, 32.9%, and 36.0% international LKDs vs. 76.3%, 71.0%, and 70.0% domestic LKDs (P<0.001) (Figure 3).

After adjustment for potential risk factors of incomplete or non-timely (noncompliant) 6-month donor follow-up among international LKDs who donated from 2013–2016, Hispanic (adjusted odds ratio [aOR]=$_{0.23}0.36_{0.56}$, p<0.001) and biologically related (aOR=$_{0.39}0.59_{0.89}$, p<0.01) donors were more compliant in donor follow-up than white and unrelated donors (Table 3).

Graft Survival

Recipients of domestic LDKT contributed 839,823 years at risk and were followed for a median (interquartile range [IQR]) 8.1 (4.5–12.2) years. Recipients of international LDKT contributed 14,872 years at risk and were followed for a median (IQR) 9.3 (4.5–14.3) years. Among recipients of international LDKT, graft survival was 97.9% (95%CI: 97.1%−98.5%) at 1 year, 92.4% (95%CI: 90.9%−93.7%) at 5 years, 85.0% (95%CI: 82.7%−86.9%) at 10 years, and 77.6% (95%CI: 74.7%−80.3%) at 15 years post-LDKT. Among recipients of domestic LDKT, graft survival was 97.6% (95%CI: 97.5%−97.7%) at 1 year, 90.9% (95%CI: 90.7%−91.0%) at 5 years, 82.1% (95%CI: 81.8%−82.4%) at 10 years, and 74.9% (95% CI: 74.5%−75.3%) at 15 years post-LDKT (Figure 4A). In unadjusted Cox models, recipients of international LDKT had 13% lower risk of DCGF (p=0.03). This association remained statistically significant after adjustment for recipient characteristics only and recipient and transplant characteristics only; however, after further adjustment for donor characteristics, there was no evidence of association between international LKDs and recipient DCGF (adjusted hazard ratio [aHR]=$_{0.78}0.89_{1.02,}$ p=0.1) (Table 4) (Supplementary Appendix, Table S1). Among recipients of international LDKT, there was no evidence of effect modification by donor/recipient biological relationship (interaction p=0.8).

Patient Survival

In the US, among recipients of international LDKT, patient survival was 99.0% (95%CI: 98.4%−99.4%) at 1 year, 96.0% (95%CI: 94.8%−96.9%) at 5 years, 89.9% (95%CI: 87.9% −91.5%) at 10 years, and 81.6% (95%CI: 78.6%−84.1%) at 15 years post-LDKT. Among recipients of domestic LDKT, patient survival was 98.3% (95%CI: 98.2%−98.4%) at 1 year, 91.8% (95%CI: 91.6%−92.0%) at 5 years, 78.9% (95%CI: 78.6%−79.2%) at 10 years, and 65.6% (95%CI: 65.1%−66.0%) at 15 years post-LDKT (Figure 4B). In unadjusted Cox models, recipients of international LDKT had 49% lower risk of mortality (p<0.001). This association remained statistically significant after adjustment for recipient, transplant, and donor characteristics in the full model with a 38% lower risk of mortality (aHR=$_{0.53}0.62_{0.72,}$ p<0.001) (Table 4), (Supplementary Appendix, Table S2). Among recipients of international LDKT, the association between international LKD and recipient mortality differed by donor/recipient biological relationship (interaction p<0.01). Compared to recipients of international LDKT that did not have a biological relationship with their donor, recipients of international LDKT with a biological relationship to their donor had 37% lower mortality risk (aHR = $_{0.46}0.63_{0.86}$, p<0.01). Among non-biologically related donor/recipient pairs, there was no association between receipt of an international LDKT and mortality (aHR = $_{0.66}0.84_{1.08}$, p=0.2).

Sensitivity Analyses

Across all four analytical models, there was no evidence of effect modification of the association between international LDKT and graft survival by pediatric recipient (interaction p>0.9), recipient sex (interaction p=0.9), or recipient US citizenship (interaction p=0.6). Similarly, across all four analytic models, there was no evidence of effect modification of the association between international LKD and recipient survival by pediatric recipient

(interaction p=0.8), recipient sex (interaction p=0.4), or recipient US citizenship (interaction p=0.7).

Country of Origin

Data on country of origin for international LKDs were available for 0% of LKDs 2000–2010, 1% (1/92) of LKDS in 2011, 3% (4/126) of LKDs in 2012, 5% (6/113) of LKDs in 2013, 6% (9/148) of LKDs in 2014, 88% (141/161) of LKDs in 2015, and 100% (133/133) of LKDs in 2016. We used data from 2015–2016 to assess the most frequent countries of origins among international LKDs (Figure 5). The most frequent countries of origin were Mexico (N=55), Kuwait (N=22), Canada (N=16), India (N=16), Qatar (N=15), the Dominican Republic (N=14), the Philippines (N=11), and the United Arab Emirates (N=10). There were 63 other countries represented with 29 countries with a single donor each and 19 countries with 2 donors each.

DISCUSSION

In this study of international living kidney donation in the US from 2000–2016, the annual number of international LKDs has nearly doubled in the last decade. However, a few centers did most of the international LDKT. The majority of international LKDs were Hispanic (40%) or Asian (21%), which is a noteworthy observation in the context of increasing disparity in access to LDKT in these recipient subgroups (3). Donor follow-up for international LKDs was low when compared with domestic donors. But among international donors, Hispanic ethnicity and donor/recipient biological relationship were associated with relatively better donor follow-up. Recipients of international LDKT had similar risk of graft failure, but lower mortality at 15 years compared with recipients of domestic LDKT.

Previous studies reported barriers to donor follow-up including donor inconvenience, out-of-date contact information, and lack of reimbursement for follow-up services (9, 30). Our study extends this list to include international LKD status. For international LKDs, barriers are more challenging given greater distance and US visa requirement issues. Our study findings are consistent with a prior study of international liver transplant recipients that demonstrated reduced rates of follow-up (33). Our study raises a critical concern for post-donation health monitoring of international LKDs given that the majority of them lose follow-up as early as 6 months post-donation. Out study highlights the importance that transplant centers adopt best practice in the international donor selection process to ensure proper donor follow up. International LKDs are not excluded from the OPTN/UNOS follow-up requirement (34); a transplant center is responsible for reporting follow-up data to the OPTN on 80% of their living donors (10, 29). The reliability of follow-up for international living donors should be considered in donor selection and our study calls for process improvement efforts focused specifically on the short- and long-term follow-up are needed to assure that international LKDs receive optimal care, regardless of place of residence. It is worth noting that under this OPTN/UNOS policy, international LKDs are eligible for deceased donor kidney transplant in the US, in the unfortunate case that they develop post-donation ESRD (35). This is important information to be disclosed in the informed consent of international LKDs prior to donation (35–37).

Unlike studies of candidates who traveled outside the US and received LDKT (transplant tourism) with inferior outcomes, in our study US citizens or US residents who received a kidney transplant from international LDKs in the US had favorable outcomes (38, 39). We cannot extend these inferences to international recipients with international donors because we did not assess their outcomes which may differ from those reported in our study. However, our study results may reassure the transplant community that international LKDs may provide an acceptable living donation opportunity to ESRD patients in the US without compromising kidney transplant recipient long-term outcomes. Nonetheless, it is important that transplant centers identify and adopt best strategies in the international donor selection process to ensure against commercialism, especially among unrelated foreign donors.

A key strength of our study is that it includes the largest international LKD cohort to date, allowing us to make inferences specific to a small, but growing subgroup of donors. However, our study must be interpreted in the context of its limitations. Although the SRTR data source was enhanced with the 2010 US census data to account for zip-code level SES differences between recipients, household-level income was not captured; as such, it is plausible that residual confounding by SES may have persisted in our analysis. Second, we are limited to the reported citizenship status in the SRTR database, and we cannot verify it by other data sources; however, the donor citizenship status was completely reported, and it is assumed that transplant centers verified donor citizenship status. Also, we were not able to differentiate between undocumented and documented international LKDs, but regardless of international LKDs legal status, our study highlights a critical message about the deficiencies in the follow-up of international LKDs, which applies to all international LKDs irrespective of their background. Moreover, because our study design accounted for well-established recipient, transplant, and donor characteristics, recipients' results are unlikely to be confounded by these factors, but we cannot rule out the contribution to our inferences of genetic, lifestyle, or other clinical factors not reported to the registry.

In conclusion, International LKDs may provide an alternative opportunity for living donation in the US. However, the follow-up for international LKDs is significantly less than optimal. Our study calls for efforts to improve international LKD follow-up and engagement. We recommend that transplant centers ensure adequate verifications of proper follow-up for international donors to improve long-term follow-up.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

aHR	adjusted hazard ratio
aOR	adjusted odd ratio
AHRQ	Agency for Healthcare Research and Quality
BMI	body mass index
CI	confidence interval
DCGF	death-censored graft failure
ESRD	end-stage renal disease
IQR	interquartile range
LDKT	living donor Kidney transplant
LKD	living kidney donor
OPTN	Organ Procurement and Transplantation Network
PRA	panel reactive antibody
SES	Socioeconomic Status
SRTR	Scientific Registry of Transplant Recipients
UNOS	United Network for Organ Sharing
US	United States

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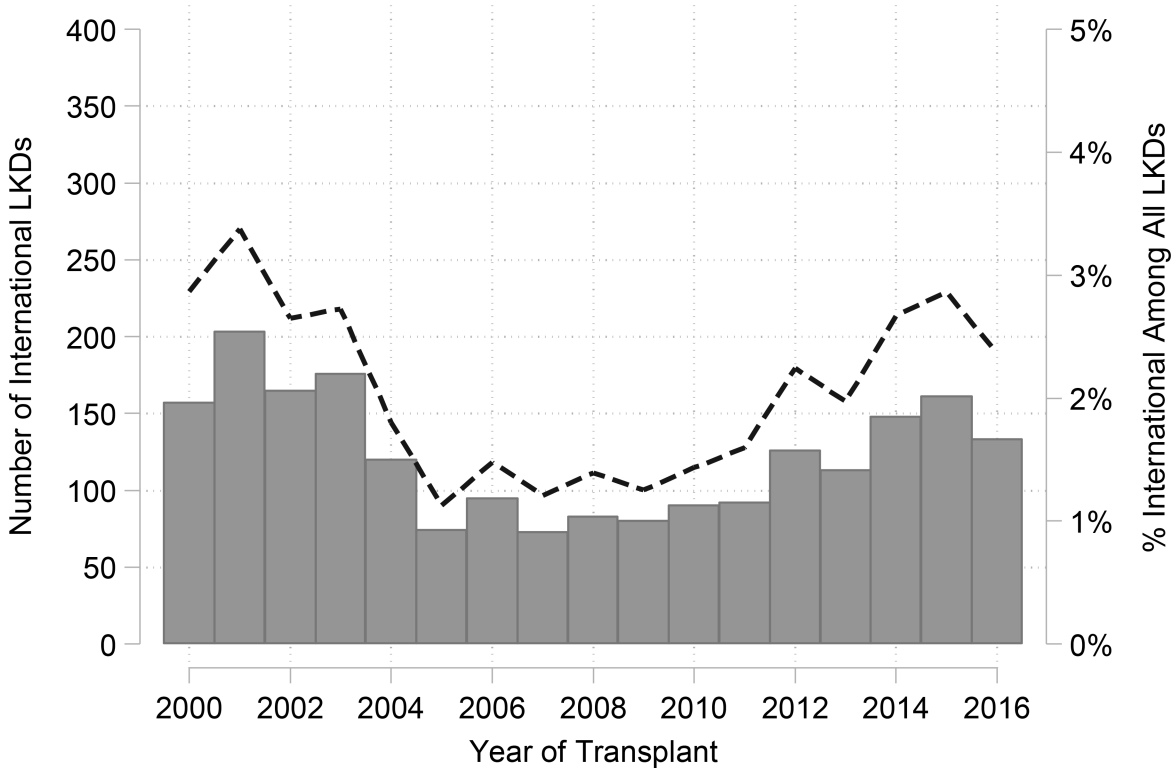

Figure 1. The trend of Non-US Citizen/Non-US Resident (International) Living Kidney Donation in the United States 2000–2016.

International living kidney donors (LKDs) were captured by the OPTN as non-resident aliens (prior to March 2012), non-US citizens/non-US residents traveling to the US for reasons other than transplant, and non-US citizens/non-US residents traveling to the US for transplant. The global, non-parametric Cuzick test for trend that did not suggest evidence of a global trend over this time period (p=0.4). In a post-hoc analysis, there was evidence of an increasing trend in international living kidney donation 2005–2016 after adjusting for multiple comparisons (Cuzick p=0.005; Bonferroni α=0.009).

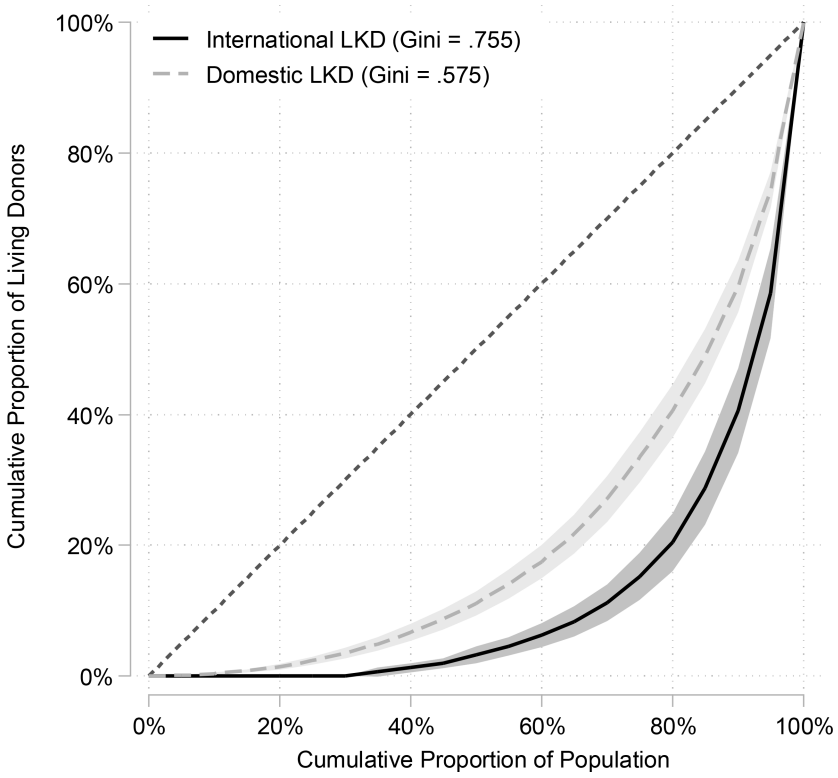

Figure 2. Center-level Distribution in the Use of International Donors.

We estimated the Gini coefficient for international (LKDs) vs. domestic LKDs. The Gini coefficient (range 0–1) is a measure of inequality/equality. A Gini coefficient near 1 would indicate that a few centers account of all international LKDs whereas a Gini coefficient near 0 would indicate that all center accept LKDs equally. The Gini for international LKDs was 0.76 indicating tighter clustering among a small number of centers compared to the general donor population (Gini=0.58). When plotted as the Lorenz curve, we compare the curves for domestic and international LKDs to the “line of equality” which is the dotted line. The closer they are to the line, the closer that population is to equal distribution; thus, there is more inequality in the use of international LKDs (few centers doing more international living donor kidney transplant) since it is farther from the line of equality than the curve for domestic LKDs.

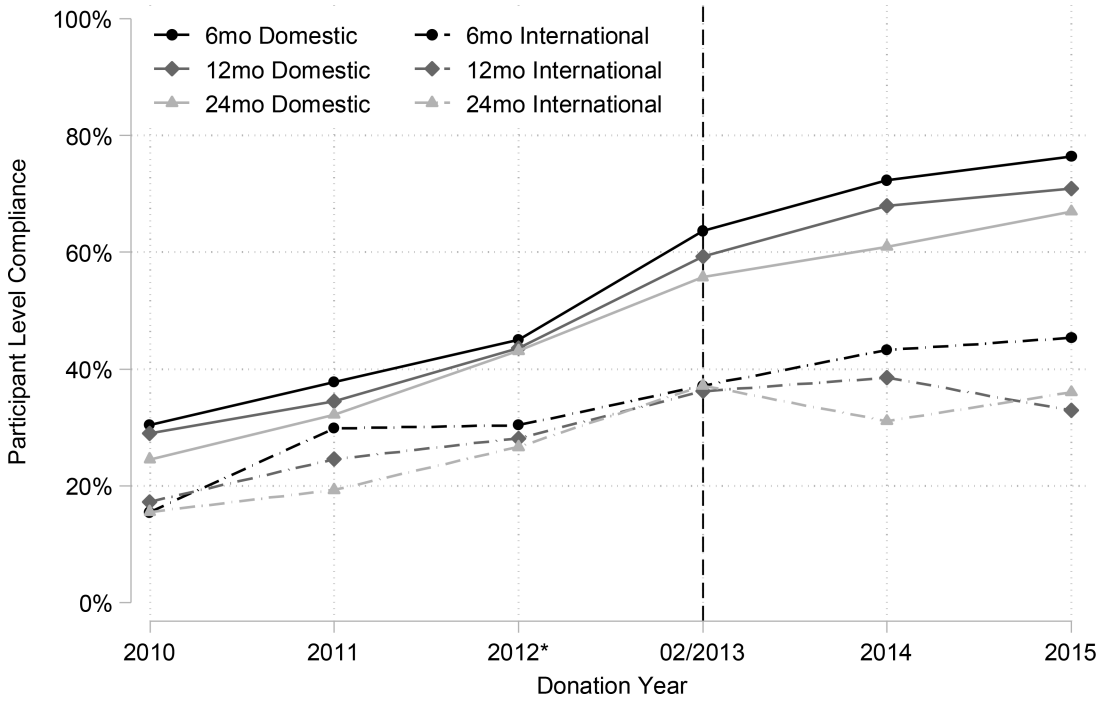

Figure 3: Living Donor Follow-up by International Donor Status 2010–2015.

In February 2013, the OPTN/UNOS mandated living donor follow-up at 6, 12, and 24 months post-donation for all living kidney donors. In this figure, we present the rates of complete and timely (policy-compliant) follow-up visits at the donor level starting in 2010 prior to the implementation of the policy. Living donor follow-up among international donors was low prior to the policy implementation. For donor in the 2015 cohort, international donor follow-up rates were nearly half the follow-up rates for domestic donors.

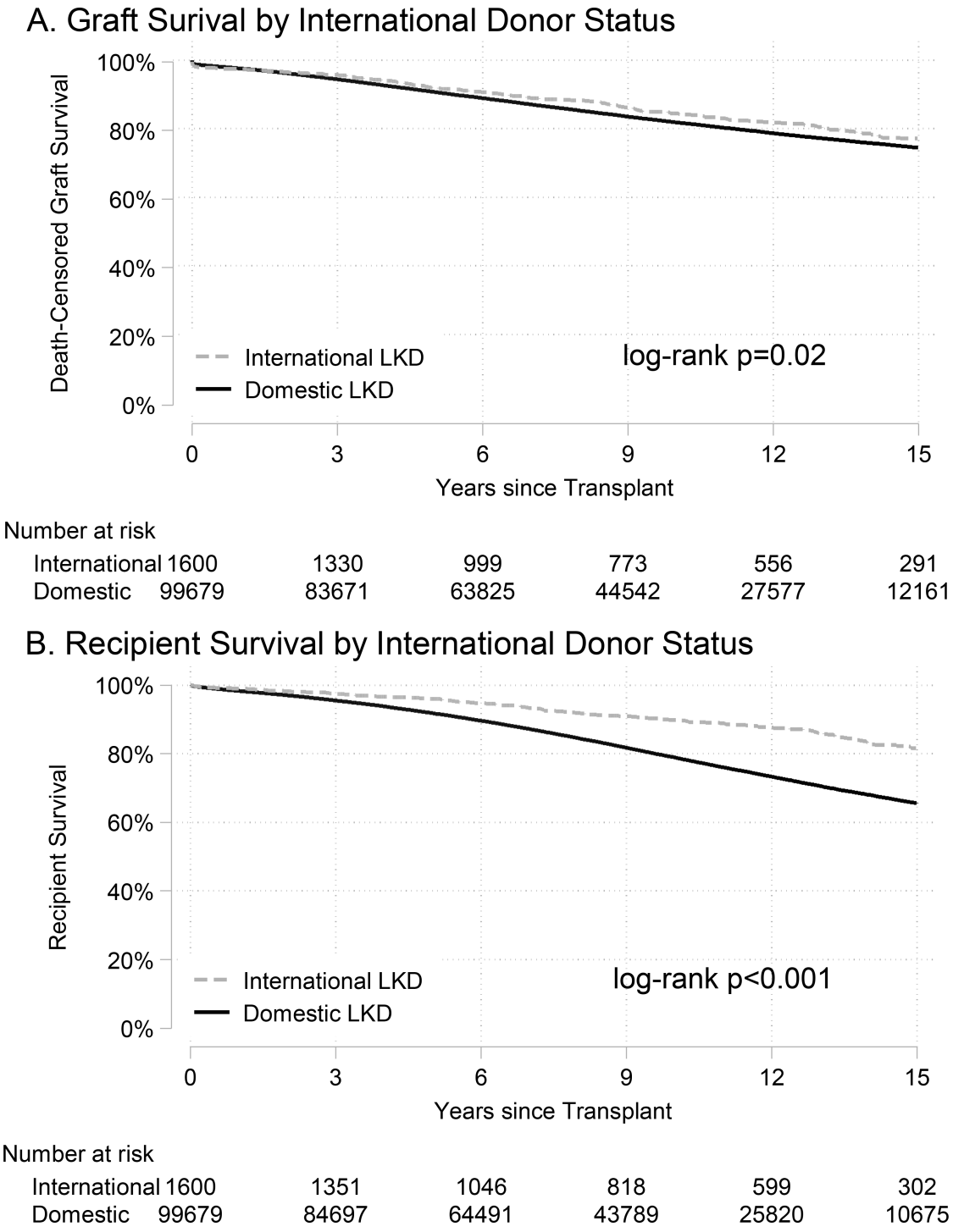

Figure 4. Living Donor Kidney Transplant Graft and Recipient Survival in the United States between 2000–2016 by International Donor Status. All survival analyses were limited to recipients who were US citizens or US residents (N=101,279).

International living kidney donors (LKDs) were captured by the OPTN as non-resident aliens (prior to March 2012), non-US citizen/non-US resident traveling to the US for reasons other than transplant, and non-US citizen/non-US resident traveling to the US for transplant.

Panel A shows unadjusted recipient death-censored graft survival (log-rank p=0.02). Panel B shows unadjusted recipient survival (log-rank p<0.001).

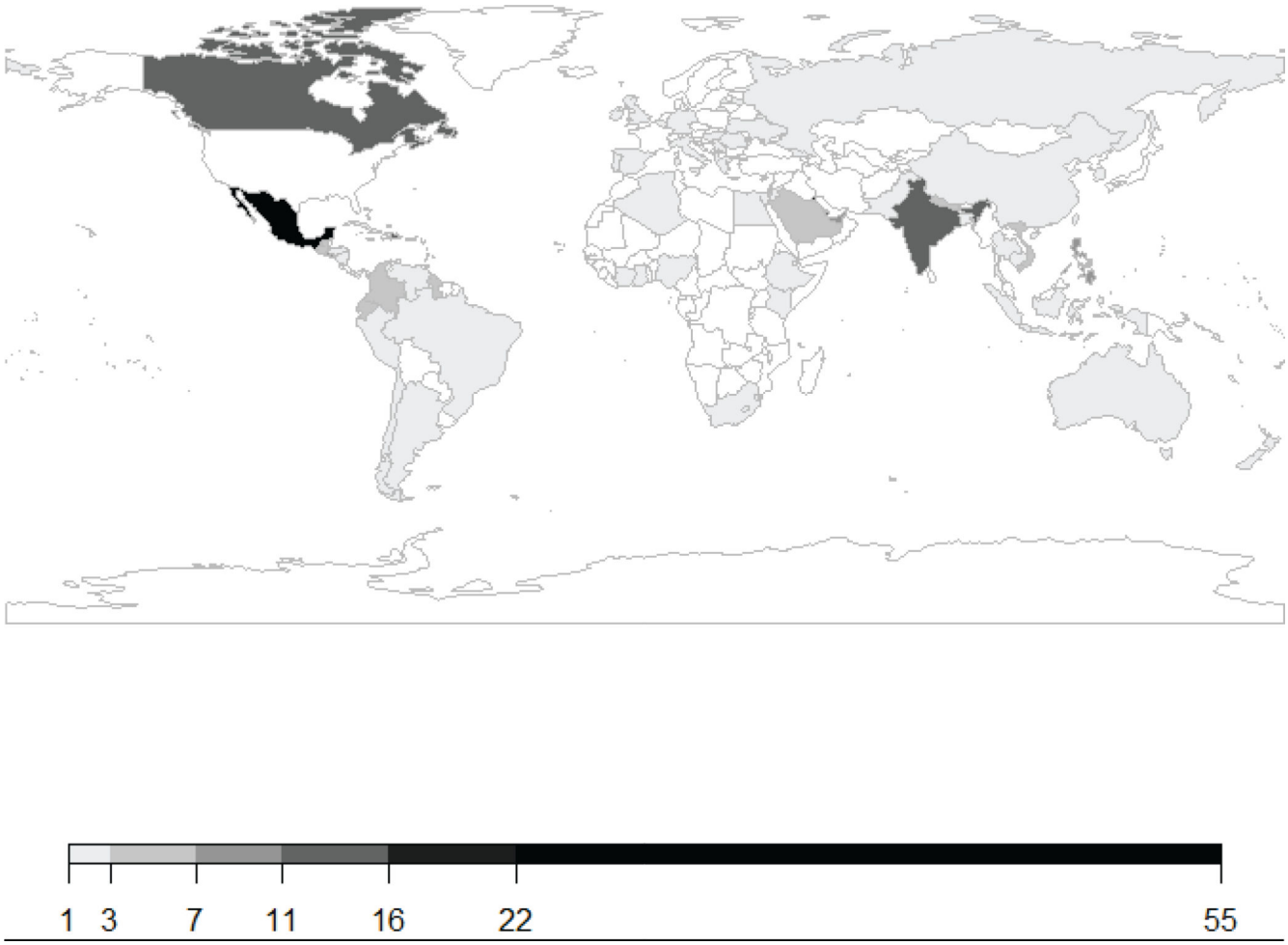

Figure 5. Country of Origin for International Living Kidney Donors 2015–2016.

During 2015–2016, international living kidney donors (LKDs) were captured by the OPTN as non-US citizen/non-US resident traveling to the US for reasons other than transplant, and non-US citizen/non-US resident traveling to the US for transplant. The most common countries of origin were Mexico (N=55), Kuwait (N=22), Canada (N=16), India (N=16), Qatar (N=15), the Dominican Republic (N=14), the Philippines (N=11), and the United Arab Emirates (N=10).

Table 1.

Baseline Donor Characteristics: Living Kidney Donors in the United States between 2000–2016 by International Donor Status.

International living kidney donors (LKDs) were captured by the OPTN as non-US citizen/non-US resident (traveling to the US for reasons other than transplant or traveling to the US for transplant), or non-resident aliens (prior to March 2012).

Donor Characteristic	Domestic LKD	International LKD
N (%)	100,227 (98%)	2,088 (2.0%)
% Female	60.5	49.3
% Black	12.2	9.6
% Hispanic/Latino	12.7	39.5
% Asian	3.1	20.9
% White/others	72	30
% College Educated	76.5	51.2
Median (IQR) Age	41.0 (32.0–50.0)	37.0 (30.0–46.0)
Median (IQR) BMI	26.6 (23.7–29.7)	25.4 (22.7–28.4)
Median (IQR) eGFR	98.2 (84.6–110.3)	106.4 (92.9–117.3)
% Biologically Related	58.6	74.2

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; IQR, interquartile range

Table 2.

Baseline Recipients Characteristics: Living Donor Kidney Transplant Recipients in the United States between 2000–2016 by International Donor Status.

International living kidney donors (LKDs) were captured by the OPTN as non-US citizen/non-US resident (traveling to the US for reasons other than transplant or traveling to the US for transplant), or non-resident aliens (prior to March 2012).

Recipient Characteristic	**Domestic LKD**	**International LKD**
N (%)	**100,227 (98%)**	**2,088 (2.0%)**
% Female	39.4	35.6
% Black	14	10.5
% Hispanic	13.3	37.6
% Asian	3.8	20.5
% White/others	68.9	31.4
Median (IQR) Age	47.7 (34.8–58.0)	42.6 (31.9–53.3)
Median (IQR) BMI	26.6 (23.1–30.8)	24.6 (21.8–28.1)
Median (IQR) SES index	61.7 (56.0–67.4)	62.8 (57.0–68.5)
% College Educated	55.9	52.6
% Diabetes	21.7	12.3
% Hypertension	14.5	20.6
% Glomerulonephritis	30.3	34.9
% Preemptive Transplant	32.3	23.00
% Previous Transplant	12	7.3
% Private insurance	58.5	50.1
% HIV antibody positive	0.3	0.4
% HCV antibody positive	2.5	2.7
% HBV status positive	5.8	13.8
% PRA>80	4.4	3.9
Transplant Characteristic		
% ABO Incompatible	1.3	1.1
% Zero HLA mismatch	8.3	11.3
Median (IQR) Cold Ischemia Time	1.0 (1.0–2.0)	1.0 (0.9–2.0)

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; IQR, interquartile range; PRA, panel reactive antibody; SES, Socioeconomic Status

Table 3.

Risk Factors for Incomplete or Non-Timely (Non-Compliant) 6-Month Living Donor Follow-up Among International Donors between 2013–2016.

We used logistic regression to assess potential risk factors for incomplete or non-timely (non-compliant) 6-month living donor follow-up. We restricted these analyses to international donors who donated after the implementation of the 2013 living donor follow-up policy which required all donors to have complete/timely follow-up forms at 6, 12, and 24 months post-donation. We present univariable odd ratios (ORs) and multivariable adjusted odds ratios from the model including all potential risk factors. An OR above 1 would indicate a donor characteristic associated with non-compliant 6-month follow-up.

Donor Characteristic	Univariable OR	p value	Adjusted OR	p-value
Male	$_{0.74}1.05_{1.50}$	0.7	$_{0.59}0.88_{1.30}$	0.5
Race (Reference: White)				
Asian	$_{0.54}0.94_{1.64}$	0.8	$_{0.59}1.07_{1.95}$	0.8
Black	$_{0.26}0.53_{1.06}$	0.07	$_{0.31}0.65_{1.36}$	0.3
Hispanic	$_{0.23}0.36_{0.56}$	<0.001	$_{0.23}0.37_{0.58}$	<0.001
Other	$_{0.02}0.29_{4.75}$	0.4	$_{0.02}0.33_{6.01}$	0.5
Age (by 10 years)	$_{0.85}1.00_{1.17}$	>0.9	$_{0.69}0.86_{1.07}$	0.2
BMI>30	$_{0.49}0.77_{1.23}$	0.3	$_{0.46}0.75_{1.23}$	0.3
Donor eGFR	$_{0.98}0.99_{1.00}$	0.1	$_{0.98}0.99_{1.00}$	0.08
Biologically Related	$_{0.39}0.59_{0.89}$	0.01	$_{0.35}0.55_{0.85}$	<0.01
International Recipient	$_{0.96}1.45_{2.19}$	0.08	$_{0.87}1.37_{2.16}$	0.2

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; OR, odds ratio

Table 4.

Death-Censored Graft Failure and Mortality among Living Kidney Donor Transplant Recipients in the United States between 2000–2016.

The association between receipt of an international donor kidney and survival were assessed using 4 Cox regression models. Model 1 is unadjusted. Model 2 adjusts for recipient characteristics. Model 3 adjusts for recipient and transplant characteristics. Model 4 adjusts for recipient, transplant, and donor characteristics. Across all models, there was a statistically significant association between international donor status and graft and recipient survival. In general, recipients of international donor kidneys had better graft and patient survival.

	Model 1 (HR, p)[a]	Model 2 (aHR, p)[b]	Model 3 (aHR, p)[c]	Model 4 (aHR, p)[d]
Graft Failure[*]	$_{0.76}0.87_{0.99}$, p=0.03	$_{0.75}0.86_{0.98}$, p=0.02	$_{0.75}0.85_{0.97}$, p=0.02	$_{0.78}0.89_{1.02}$, p=0.1
Mortality[*]	$_{0.44}0.51_{0.60}$, p<0.001	$_{0.53}0.61_{0.71}$, p<0.001	$_{0.52}0.60_{0.70}$, p<0.001	$_{0.53}0.62_{0.72}$, p<0.001

Abbreviations: aHR, adjusted hazard ratio

[*] All models were stratified by transplant center to account for center-level differences.

[a] Model 1 was unadjusted.

[b] Model 2 was adjusted for recipient age, pediatric status (age<18), sex, African-American race, Hispanic ethnicity, BMI, diabetes status, history of previous transplant, PRA>80, HCV, HBV, HIV, college education, public insurance, and SES index.

[c] Model 3 was adjusted for the recipient characteristics in model 2 plus 0 HLA mismatch, ABO-incompatible, and transplant year.

[d] Model 4 was adjusted for by the recipient and transplant characteristics in model 3 plus donor age, sex, African-American race, Hispanic ethnicity, BMI, and biological relation to the donor.