A Tale of Two Kidneys: Differences in Graft Survival for Kidneys Allocated to Simultaneous Liver Kidney Transplant Compared with Contralateral Kidney from the Same Donor

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BACKGROUND: Renal graft lifespan in simultaneous liver kidney transplant (SLK) is generally thought to be shorter than in kidney transplant (KT) alone, raising questions about the utility of SLK. This study aims to estimate what the outcomes would be for a kidney allocated to SLK if it were allocated to KT instead.

METHODS: Using United Network for Organ Sharing data, recipients of SLK from 2003 to 2012 were paired with the recipient who received the partner kidney from the same donor in a kidney or kidney pancreas transplant for analysis. The primary outcomes were long-term patient and renal graft survival. This was investigated using modified multivariable Cox regression, which allowed for changes in the hazard ratio (HR) associated with SLK over time (non-proportional hazards), accounted for the paired nature of the study, and adjusted for differences in recipient characteristics.

RESULTS: There were 3,721 recipients in each group. Ninety-day mortality was 8.0% for SLK vs 1.9% for KT recipients (p < 0.001). Median unadjusted renal graft survival was 11 years for the SLK group vs 10.5 years for KT (p < 0.001). The baseline adjusted HRs for death and renal graft loss associated with SLK were 3.03 and 2.05. These HRs became equal to 1 at 6.5 years for death and 5 years for renal graft loss. The HRs for death and renal graft loss associated with SLK at 10 years were 0.55 and 0.50.

CONCLUSIONS: Although kidneys allocated to SLK vs KT demonstrate worse short-term survival, this risk appears to be reversed when follow-up is extended long-term. (J Am Coll Surg 2019;229: 7−17. © 2019 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

The benefit of simultaneous liver kidney (SLK) transplant in patients with combined hepatic and renal failure over liver transplant alone has been well established,[1-4] particularly for patients with a prolonged dialysis course before transplantation.[5] Because the introduction of the Model for End-Stage Liver Disease (MELD) system for liver allocation, there has been a substantial increase in the number of SLKs performed annually.[3,6,7] The lifesaving benefit of SLK does not come without significant tradeoff, however.

For example, a large single-center study recently demonstrated a 20% rate of short-term renal graft loss after SLK,[8] essentially wasting a scarce resource that might otherwise have been allocated to a recipient on the renal transplant list for whom it would have also been lifesaving. Several national registry-based studies have questioned the utility of allocating a kidney to SLK, citing potentially inferior renal outcomes in this setting compared with kidney transplant alone.[5,9,10] On the other hand, a pre-MELD

era national registry study actually demonstrated improved renal allograft survival in SLK vs kidney transplant alone.[10]

Some of these studies either focused only on short- and intermediate-term outcomes[10] or were undertaken relatively early in the MELD era.[5] The MELD system has now been in place for long enough to allow evaluation of long-term survival outcomes. Here we present an evaluation of long-term renal allograft survival in simultaneous liver kidney transplantation using national-level United Network for Organ Sharing (UNOS) data. Specifically, we sought to determine what the lifespan of a renal allograft allocated to SLK might have been if it were instead allocated to kidney or kidney pancreas transplant. The use of a paired kidney study design allows us to answer this question because the recipient of the contralateral kidney from the SLK donor presumably had the highest priority on the kidney match run, and would have otherwise received the kidney allocated to SLK if the liver had instead been offered as a single-organ transplant.

METHODS

Retrospective analysis of the December 2017 UNOS Standard Transplant Analysis and Research file was performed. This file contains a record of all organ transplants performed in the US and reported to UNOS from October 1, 1987 through September 2017. The study population consisted of recipients of simultaneous liver kidney (SLK group) transplants between 2003 and 2012 and a paired cohort of either kidney transplant alone or simultaneous kidney pancreas transplant (referred to as the KT group hereafter) recipients who received the contralateral kidney from same donor as the SLK recipient. As such, donor characteristics between the SLK and KT groups are identical. The study starting year was chosen to coincide with in the initiation of the MELD system for liver allocation, and the ending year was chosen to allow for at least 5 years of follow-up in all recipients.

Continuous variables for the SLK and KT groups were summarized by mean and SD and compared using paired t-tests. Categorical variables were summarized by count and percentage and compared using McNemar's test for 2×2 tables and either chi-square or Fisher's exact test otherwise. Patient and kidney graft survival were estimated using the Kaplan-Meier method, and univariable survival differences between groups were compared using the log-rank test. Kidney graft survival in the Kaplan-Meier analysis was measured from transplantation until return to dialysis, transplantation nephrectomy, patient death, or last follow-up. Death with a functioning graft was counted as a graft failure. An additional kidney graft survival analysis was performed treating death with a functioning graft as a competing risk according to the method of Fine and Gray.[11]

The hazard ratio for death or renal graft loss (not censored for patient death) associated with SLK vs KT was estimated using a marginal Cox proportional hazards model according to the method of Lee and colleagues[12] to account for the paired nature of the data. Because the hazard associated with SLK was found to violate the proportional hazards assumption (ie it changed over time), SLK was treated as a time-varying hazard by including an interaction between SLK and follow-up time.[13] Multivariable analysis adjusting for recipient age, sex, race, BMI, diabetes status, pretransplantation dialysis status, pretransplantation medical condition (home, hospitalized, or in ICU), and share type (local, regional, national) was performed subsequently. The adjusting factors were selected empirically. Cold ischemia time (CIT) was not included in the main multivariable analysis due to a high proportion of patients for whom this value was missing in the data, which would introduce the potential for significant bias. Sensitivity analysis for the effect of CIT on the results of the main analysis was performed using multiple imputations, as outlined here. Donor factors were not included in the model, as they were, by definition, identical in the SLK and KT groups. All statistical analysis was performed using SAS, version 9.4 (SAS Institute).

RESULTS

There were 176,380 recipients of SLK, kidney transplant alone, or simultaneous kidney pancreas transplant during the time period of the study. Of this initial cohort, there were 3,749 SLK donors, of whom 3,721 donated the contralateral kidney as either a solitary kidney or simultaneous kidney pancreas transplant. The final study cohort consisted of 3,721 recipients in the SLK group and 3,721 recipients in the KT group. Of the KT group, 2,687 underwent solitary kidney transplantation and 1,034 underwent simultaneous kidney pancreas transplantation.

The donors were mostly men (62.6%) with a mean age of 32.7 years. The majority (53.6%) of donors had

Kidney Donor Profile Index (KDPI) <35%, and only 4.4% had KDPI >85%. The mean KDPI was 35.7%. Caucasians were the most frequently represented race (65%), followed by Hispanics (15.9%) and African Americans (15.6%). Donor characteristics are found in Table 1.

The recipients in the SLK group were significantly older (52.6 vs 46.6 years; p < 0.001) than their KT counterparts, with a significantly lower proportion of recipients aged younger than 18 years (3.2% vs 4.4%). Caucasians were also overrepresented in the SLK group compared with the KT group (63.5% vs 54.2%), while

Table 1. Characteristics of the 3,721 Deceased Donors Between 2002 and 2012 from the United Network for Organ Sharing Data Set Included in the Study

Variable	Data
Age, y, mean (SD)	32.7 (14.4)
Sex, n (%)	
Male	2,331 (62.6)
Female	1,390 (37.4)
Race, n (%)	
Caucasian	2,417 (65.0)
African American	579 (15.6)
Hispanic	591 (15.9)
Asian	90 (2.4)
Other	44 (1.2)
BMI, kg/m^2, mean (SD)	25.8 (5.3)
Terminal creatinine, mg/dL, mean (SD)	1.06 (0.76)
Diabetes, n (%)	
Yes	135 (3.6)
No	3,577 (96.1)
Unknown	9 (0.2)
Hypertension, n (%)	
Yes	645 (17.3)
No	3,061 (82.3)
Unknown	15 (0.4)
Hepatitis C virus antibody positive, n (%)	45 (1.2)
Cause of death, n (%)	
Anoxia	603 (16.2)
CVA	1,139 (30.6)
Trauma	1,872 (50.3)
CNS tumor	28 (0.8)
Other	79 (2.1)
KDPI, n (%)	35.7 (26.0)
KDPI category, n (%)	
<20%	1,311 (35.2)
20% to 34.9%	683 (18.4)
35% to 85%	1,562 (42.0)
>85%	165 (4.4)

KDPI, kidney donor profile index.

African Americans were underrepresented (15.2% vs 25.2%). The SLK group was less likely to be diabetic or on dialysis at the time of transplantation than their KT counterparts, but they were significantly more likely to be hospitalized at the time of transplantation (Table 2). The mean laboratory MELD score for the SLK recipients was 28.8 (SD 9.2). As expected, length of stay was longer in the SLK group (22.2 vs 8.6 days; p < 0.001), and 90-day mortality was significantly higher (8.0% vs 1.9%; p < 0.001). The comparisons between the SLK and KT groups are summarized in Table 2.

In the univariable analysis, patient survival was higher at 1, 3, 5, and 10 years in the KT vs SLK group. Median survival was significantly higher in the KT vs SLK group (12.6 vs 11.5 years; p < 0.001; Fig. 1). Renal graft survival was higher at 1, 3, and 5 years in the KT group, and it was slightly higher at 10 years in the SLK group, which also had a higher median survival (11.0 vs 10.5 years; p < 0.001; Fig. 2). When renal graft failure was analyzed with patient death treated as a competing risk, the cumulative incidence of renal graft failure was higher in the SLK group at 1 year (4.5% vs 3.8%), but was significantly lower at 3, 5, and 10 years compared with the KT group (6.0%, 7.2%, 11.1% vs 7.8%, 12.0%, 21.0%; p < 0.001; Fig. 3).

Univariable Cox regression analysis demonstrated significantly higher baseline hazard for patient death (hazard ratio [HR] 3.24; 95% CI 2.82 to 3.71; p < 0.001) and non-death-censored renal graft failure (HR 1.98; 95% CI 1.76 to 2.23; p < 0.001) associated with the SLK vs the KT groups. The interaction between SLK and follow-up time, however, demonstrated a decreasing HR for both patient death and renal graft loss associated with SLK as follow-up time increased (interaction HR for patient survival 0.99; 95% CI 0.98 to 0.99; p < 0.001; interaction HR for renal graft survival 0.99; 95% CI 0.99 to 0.99; p < 0.001). Combining the HRs for the SLK main effect and the interaction term allowed estimation of the HR associated with SLK at various points during patient follow-up. The HRs for patient death associated with SLK at 1, 3, 5, and 10 years were 2.73, 1.94, 1.39, and 0.60 (Fig. 4A). The HRs for non-death-censored renal graft survival associated with SLK at 12, 36, 60, and 120 months were 1.72, 1.30, 0.98, and 0.49 (Fig. 5A).

Adjusted for the recipient factors mentioned in the Methods section, SLK continued to demonstrate an increased baseline hazard for patient death (HR 3.03; 95% CI 2.60 to 3.54; p < 0.001), which declined over time (interaction HR 0.99; 95% CI 0.98 to 0.99; p < 0.001). The adjusted HRs for patient death at 1, 3, 5, and 10 years were 2.56, 1.82, 1.29, and 0.55 (Fig. 4B).

Table 2. Comparison of Recipient Characteristics Between Simultaneous Liver Kidney Transplant and Kidney Alone/Kidney Pancreas Group Matched by Donor the United Network for Organ Sharing Data Set Between 2002 and 2013

Variable	Kidney/KP (n = 3,721)	SLK (n = 3,721)	p Value
Age, y, mean (SD)	46.6 (14.6)	52.6 (12.6)	<0.001*
Age category, n (%)			<0.001*
Younger than 18 y	164 (4.4)	120 (3.2)	
18 to 30 y	317 (8.5)	132 (3.5)	
31 to 40 y	740 (19.9)	189 (5.1)	
41 to 50 y	945 (25.4)	754 (20.3)	
51 to 60 y	887 (23.8)	1,562 (42.0)	
Older than 60 y	668 (18.0)	964 (25.9)	
Male sex, n (%)	2,211 (59.4)	2,417 (65.0)	<0.001*
Race, n (%)			<0.001*
Caucasian	2,018 (54.2)	2,364 (63.5)	
African American	938 (25.2)	566 (15.2)	
Hispanic	530 (14.2)	597 (16.0)	
Asian	151 (4.1)	138 (3.7)	
Other	84 (2.3)	56 (1.5)	
BMI, kg/m^2, mean (SD)	26.8 (5.4)	26.7 (5.8)	0.51
Diabetes, n (%)	1,857 (49.9)	1,354 (36.4)	<0.001*
Pretransplantation dialysis, n (%)			<0.001*
Yes	2,912 (78.3)	2,182 (58.6)	
No	790 (21.2)	1,402 (37.7)	
Unknown	19 (0.5)	136 (3.7)	
Medical condition, n (%)			<0.001*
ICU	7 (0.2)	600 (16.1)	
Hospitalized, not in ICU	35 (0.9)	836 (22.5)	
Home	3,679 (98.9)	2,284 (61.4)	
Wait time, d, mean (SD)	734.5 (733.3)	133.6 (298.1)	<0.001*
Share type, n (%)			<0.001*
Local	2,722 (73.2)	3,248 (87.3)	
Regional	334 (9.0)	430 (11.6)	
National	665 (17.9)	43 (1.2)	
Distance from donor hospital to transplantation center, miles, mean (SD)	243.4 (450.1)	94.7 (179.3)	<0.001*
Cold ischemia time, h, mean (SD)[†]	16.1 (8.5)	11.8 (7.2)	<0.001*
Delayed graft function[‡], n (%)	631 (18.9)	667 (17.9)	<0.001*
Length of stay, d, mean (SD)	8.6 (8.4)	22.2 (30.6)	<0.001*
90-day mortality, n (%)	69 (1.9)	296 (8.0)	<0.001*

Percentages in this table are reflective of a total of 3,334 patients in the kidney/KP group and 3,720 in the SLK group.
*Statistically significant.
[†]The value for cold ischemia time was missing for 16.4% of patients, the means reflect 3,124 patients in the kidney/KP group and 3097 in the SLK group.
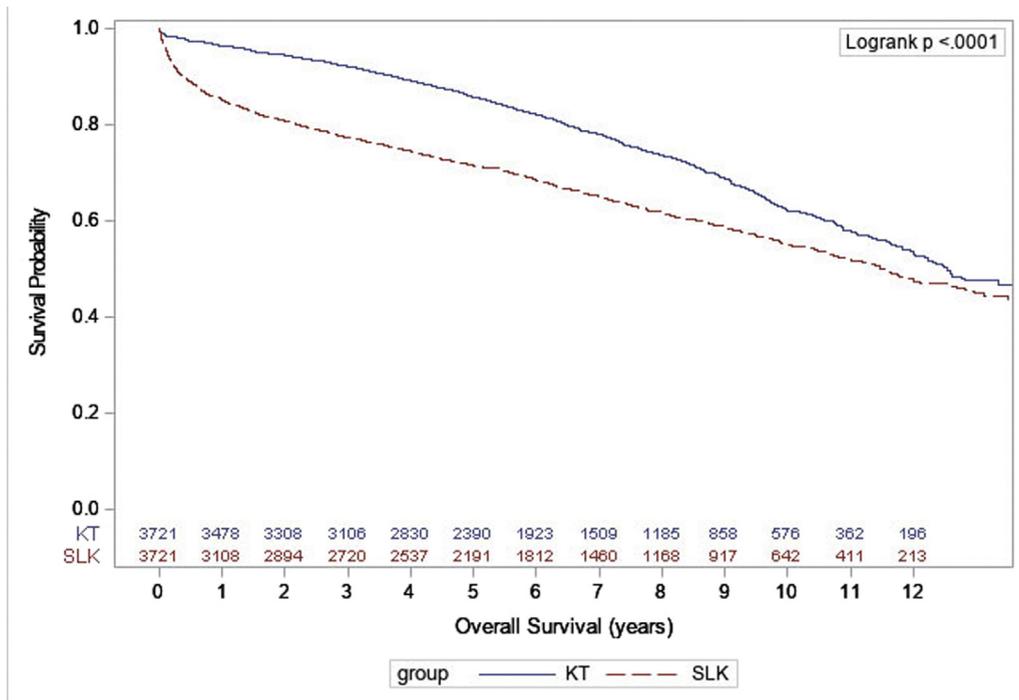[‡]Data on delayed graft function were missing for 5.2% of patients overall.
KP, kidney pancreas; SLK, simultaneous liver kidney.

The point at which the adjusted HR for patient death associated with SLK crossed 1 was at 78 months (6.5 years). Adjusted analysis for renal graft failure revealed similar findings, an increased baseline HR for graft loss (HR 2.05; 95% CI 1.80 to 2.34; p < 0.001), which decreased over time (interaction HR 0.99; 95% CI 0.99 to 0.99; p < 0.001). The adjusted HRs for renal graft loss at 1, 3, 5, and 10 years were 1.78, 1.35, 1.02, and 0.50 (Fig. 5B). The point at which the adjusted HR for renal graft loss associated with SLK crossed 1 was at 61 months (5 years).

The following variables had missing values: recipient BMI (1.2% missing), recipient diabetes status (0.01% missing), pretransplantation dialysis status
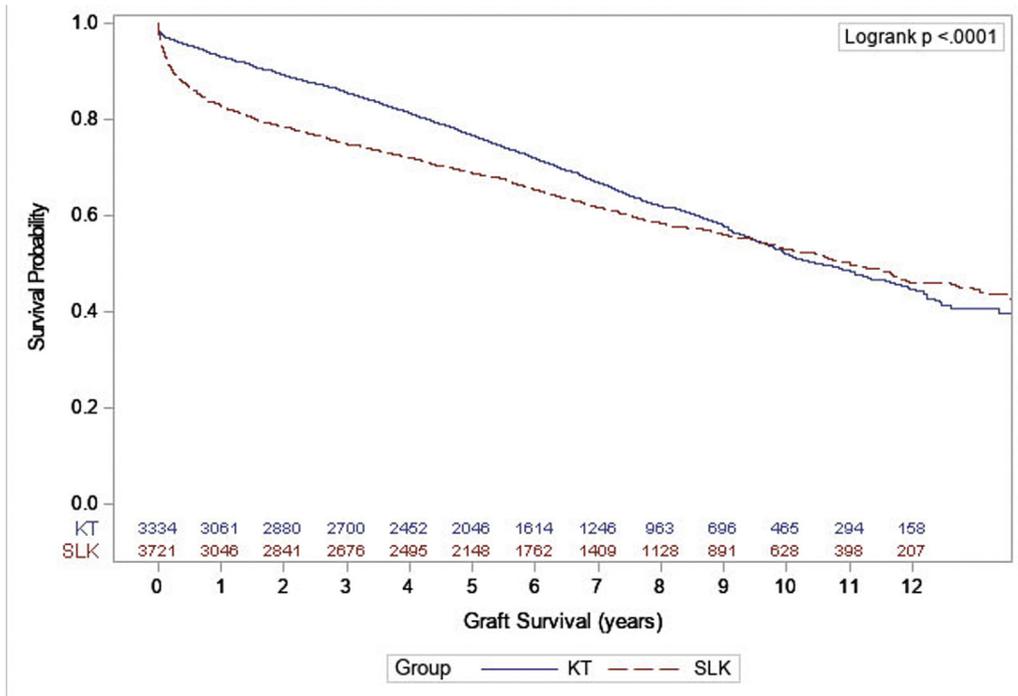
Figure 1. Kaplan-Meier estimates of overall patient survival for simultaneous liver kidney (SLK) transplant and kidney transplant alone or kidney pancreas transplant (KT). The number of patients at risk for each group is displayed at the bottom of the graph. The chart at the bottom of the figure contains point estimates for survival.

	1-Year	3-Year	5-Year	10-Year	Median (years)	p-value
SLK	85.2%	77.3%	71.5%	55.0%	11.5	**<0.001**
Kidney/Kidney-Pancreas	96.4%	92.1%	85.7%	62.1%	12.6	

(0.01% missing), delayed renal graft function (5.2% missing), donor BMI (0.05% missing), donor terminal creatinine (0.08% missing), KDPI (0.51% missing), renal CIT (16.4% missing), and renal graft status at time of last follow-up (5.2% missing). Variables with <5% of values missing were ignored as this level is considered inconsequential.[14] Sensitivity analysis was performed for renal graft status and CIT. Missing renal graft status was only found in the KT group and, on additional investigation, all patients with missing renal graft status were found to be deceased at time of last follow-up, with graft survival equal to patient survival. Accordingly, additional proportional hazards models were run including these patients as graft failures. This analysis demonstrated that the findings of the main analysis were conservative with respect to the HR for renal graft failure associated with SLK. Missing values for CIT were distributed equally between the SLK and KT groups (16.8% vs 16.0% missing, respectively; p = 0.40). Values for missing CIT were imputed using 5 imputations, followed by multivariable Cox regression analysis of patient and renal graft survival using

the imputed values. The results of analysis without CIT were found to be similar to or conservative compared with the multiple imputation analysis. A final sensitivity analysis was performed in which kidney pancreas recipients were excluded from the KT group. The results of this analysis confirmed that inclusion of kidney pancreas recipients resulted in a conservative estimate of the increase in long-term kidney graft survival in the SLK vs KT groups.

DISCUSSION

In this long-term analysis of UNOS data during the MELD era, we found that the median lifespan of kidneys transplanted as part of an SLK transplant actually exceeds that of kidneys transplanted alone or with a pancreas by approximately 6 months. There is inferior patient and renal graft survival in the early time periods, which appears to be driven largely by excess early mortality in the SLK group. This is evidenced by baseline and early interval HRs >1 for death and renal graft loss associated

Non-Death Censored Graft Survival						
	1-Year	3-Year	5-Year	10-Year	Median (years)	p-value
SLK	83.0%	74.9%	68.8%	53.1%	11.0	<0.001
Kidney/Kidney-Pancreas	93.1%	85.5%	76.6%	52.0%	10.5	

Figure 2. Kaplan-Meier estimates of non-death-censored renal allograft survival for simultaneous liver kidney (SLK) transplant and kidney transplant alone or kidney pancreas transplant (KT). The number of patients at risk for each group is displayed at the bottom of the graph. The chart at the bottom of the figure contains point estimates for survival.

with SLK. The hazard associated with SLK had a decreasing slope over time, however, such that the SLK was "protective" after 6.5 years for patient survival and after 5 years for renal graft survival. This finding is somewhat counterintuitive, and is different from much of the more recent literature on this subject. Cheng and colleagues[9] recently reviewed Scientific Registry of Transplant Recipients data from 1995 through 2014 using a paired kidney design similar to the current study. In their analysis, they found the mean kidney allograft lifespan for KT to be 0.99 years longer than in SLK[9] in the MELD era. There are several notable differences between their study and the current one that could account for these differences. Cheng and colleagues' study excluded pediatric patients, SLK recipients on dialysis for >90 days before transplantation, and SLK transplantations performed for metabolic disorders of familial amyloidosis. These exclusions were made to focus only on the more controversial cases of SLK, making the goal and population of their study different than ours. In addition, follow-up in Cheng

and colleagues' study was censored at 10 years post-transplantation, which would fall short of the median survival times observed in our study and miss the point at which the survival curves for the SLK and KT groups cross.

Another recent study with similar design to ours comes from Choudhury and colleagues,[10] in which a paired kidney design was used to study a cohort of SLK vs KT alone performed between 2002 and 2012 in the UNOS database. They found a significantly smaller 5-year kidney graft survival rate in the SLK vs KT groups (64% vs 75%), with an HR for kidney graft failure of 1.9 associated with SLK.[10] These 5-year differences in kidney graft survival rates are actually not very different from those we report (68.8% vs 76.6%) at 5 years. As noted earlier, the focus on shorter-term survival misses the point at which the SLK and KT survival curves cross. The study by Choudhury and colleagues also chose to analyze mean survival times, which will be biased downward, particularly for SLK, due to the skewed distribution of survival
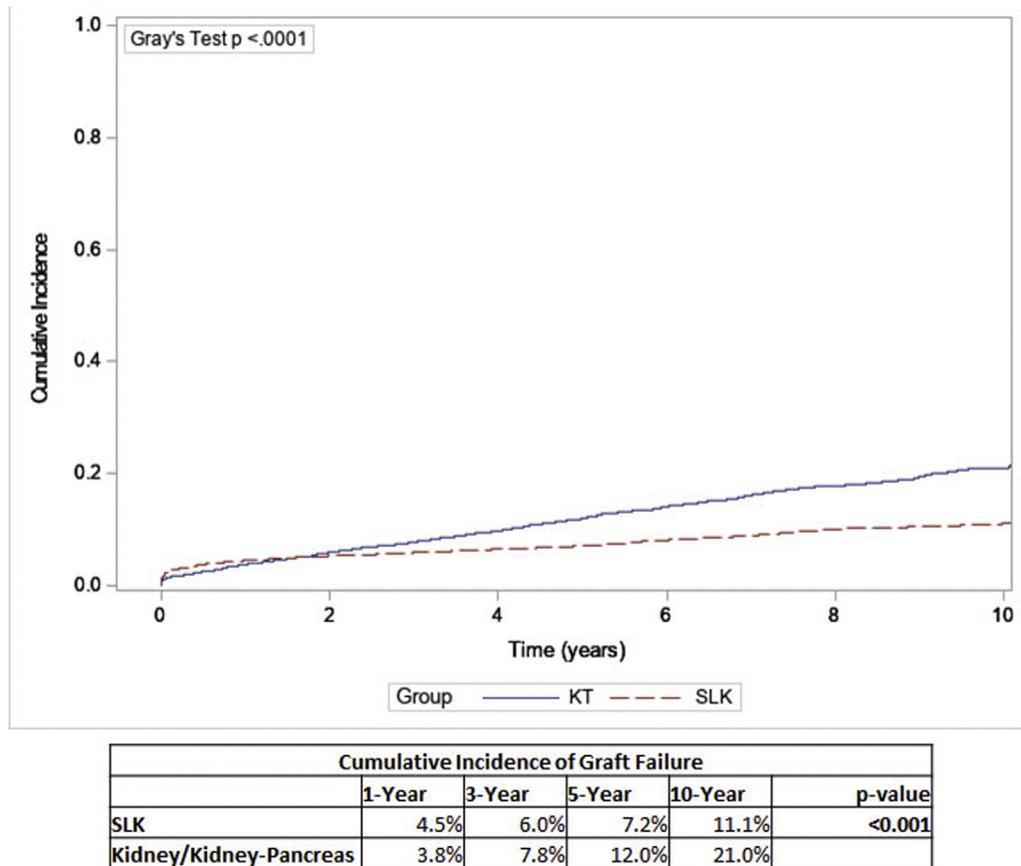
Cumulative Incidence of Graft Failure					
	1-Year	3-Year	5-Year	10-Year	p-value
SLK	4.5%	6.0%	7.2%	11.1%	<0.001
Kidney/Kidney-Pancreas	3.8%	7.8%	12.0%	21.0%	

Figure 3. Cumulative incidence of renal allograft failure (patient death is treated as a competing risk) for simultaneous liver kidney (SLK) transplant and kidney transplant alone or kidney pancreas transplant (KT).

times caused by the excess early deaths in that group. Finally, Choudhury and colleagues excluded pediatric recipients as well as kidney pancreas recipients, making their population somewhat different than the one in the current study.

One possible explanation for the increase in long-term kidney graft survival observed with SLK could be immunologic protection conferred on the kidney by the liver graft.[15] In a pre-MELD era study, Fong and colleagues[16] found that 1-year rejection-free survival was highest in SLK vs kidney or kidney pancreas transplant (70% vs 61% vs 57%), and that renal graft loss due to chronic rejection was significantly lower among SLK recipients compared with kidney or kidney pancreas recipients (2% vs 8% vs 6%, respectively). Additional evidence for the potential role of immunologic protection comes from reports of successful SLK without hyperacute rejection of the kidney in the face of preformed cytotoxic antibodies.[17,18] Proposed mechanisms for immunologic protection include secretion of soluble HLA antigens that neutralize circulating donor-specific antibodies,[19]

absorption of antibodies by the reticuloendothelial system of the liver,[20] and interactions between passenger donor lymphocytes within the graft and the host immune system.[21] This protection is not completely robust,[22,23] however, so likely does not provide the complete story behind prolonged renal allograft survival in SLK vs KT.

Another possible explanation for the increased long-term kidney allograft survival in the SLK group in this study can be found in the comparison of baseline recipient characteristics in the SLK and KT groups. Although SLK patients were older and more acutely ill, KT patients were significantly more likely to be diabetic and on dialysis before transplantation. Unfortunately, the Expected Post Transplant Survival score is not recorded in UNOS data before 2014 so is unavailable for the patients in this study. Given that diabetes and pretransplantation dialysis account for much of the Expected Post Transplant Survival score,[24] it is reasonable to speculate that the Expected Post Transplant Survival score would be significantly higher in the KT cohort. In addition, our center and others will allow a greater burden of chronic
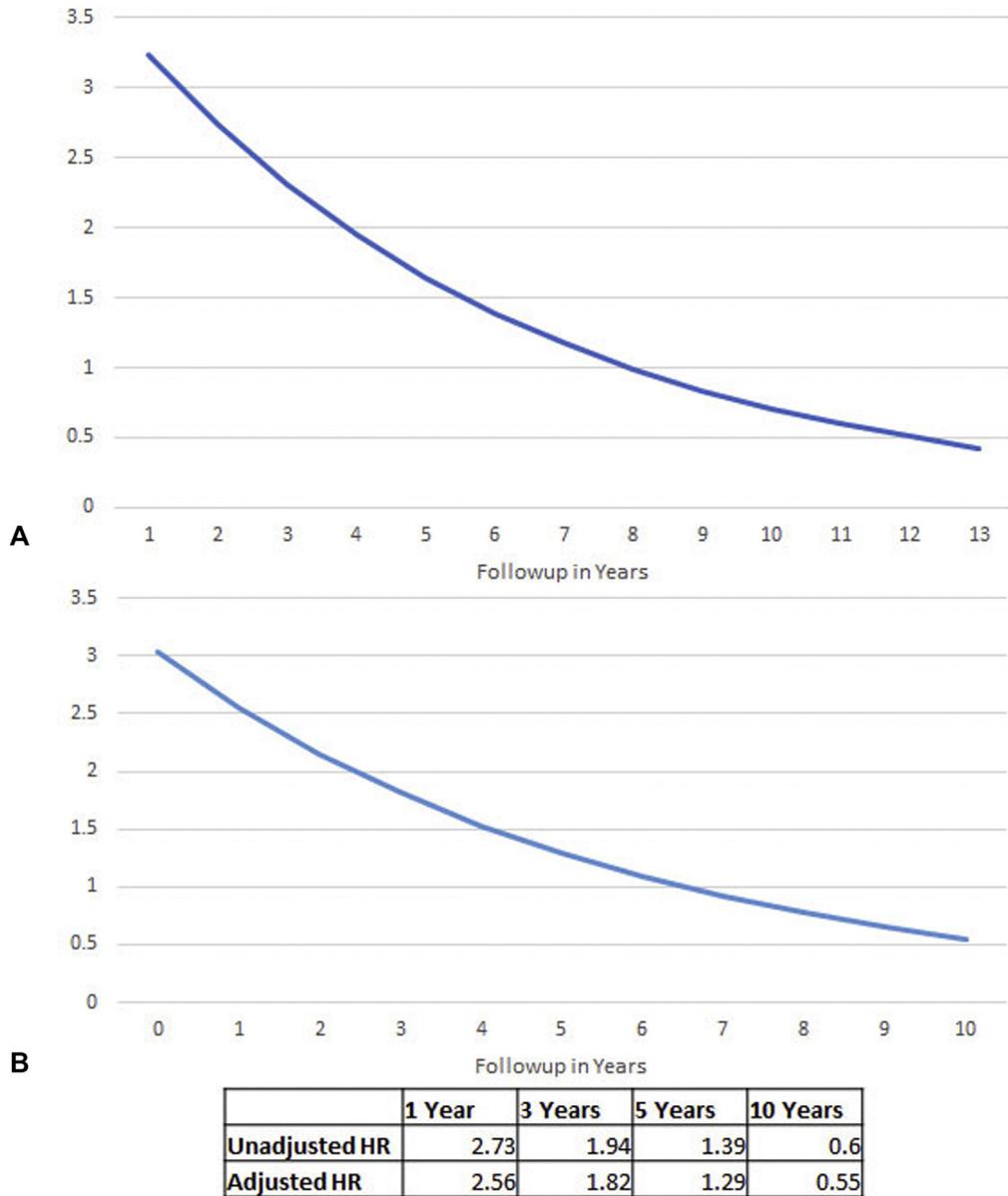
	1 Year	3 Years	5 Years	10 Years
Unadjusted HR	2.73	1.94	1.39	0.6
Adjusted HR	2.56	1.82	1.29	0.55

Figure 4. Time-varying hazard ratios for patient death associated with simultaneous liver kidney (SLK) vs kidney/kidney pancreas transplantation (A) before and (B) after adjustment for baseline differences in recipient factors. The y-axis represents the specific hazard ratio associated with SLK at the time point indicated on the x-axis. The hazard ratio crosses 1 at 6.9 years in unadjusted analysis and at 6.5 years in the adjusted analysis.

comorbidities and patient frailty in a patient being listed for kidney transplant alone, or even kidney pancreas transplant, then would be considered acceptable in an SLK patient. There is no measure of patient frailty included in the UNOS database that would allow us to objectively evaluate this conjecture; however, we suspect that the KT patients in this study would have a greater burden of chronic comorbidities that can limit long-term post-transplantation survival. It is our opinion that this difference in comorbidity burden is the largest driver

of the differing survival rates in the SLK and KT groups. Finally, there is also the possibility that return of native kidney function in the SLK patients prevents return to dialysis (which defines renal graft failure) when the kidney graft has declined to a point that would otherwise necessitate dialysis in a patient without contribution from the native kidneys, as would be the case in the KT group.[9]

Much of the controversy about SLK has arisen from concerns that the previous liver allocation system allowed overuse of SLK, resulting in potential waste of years of
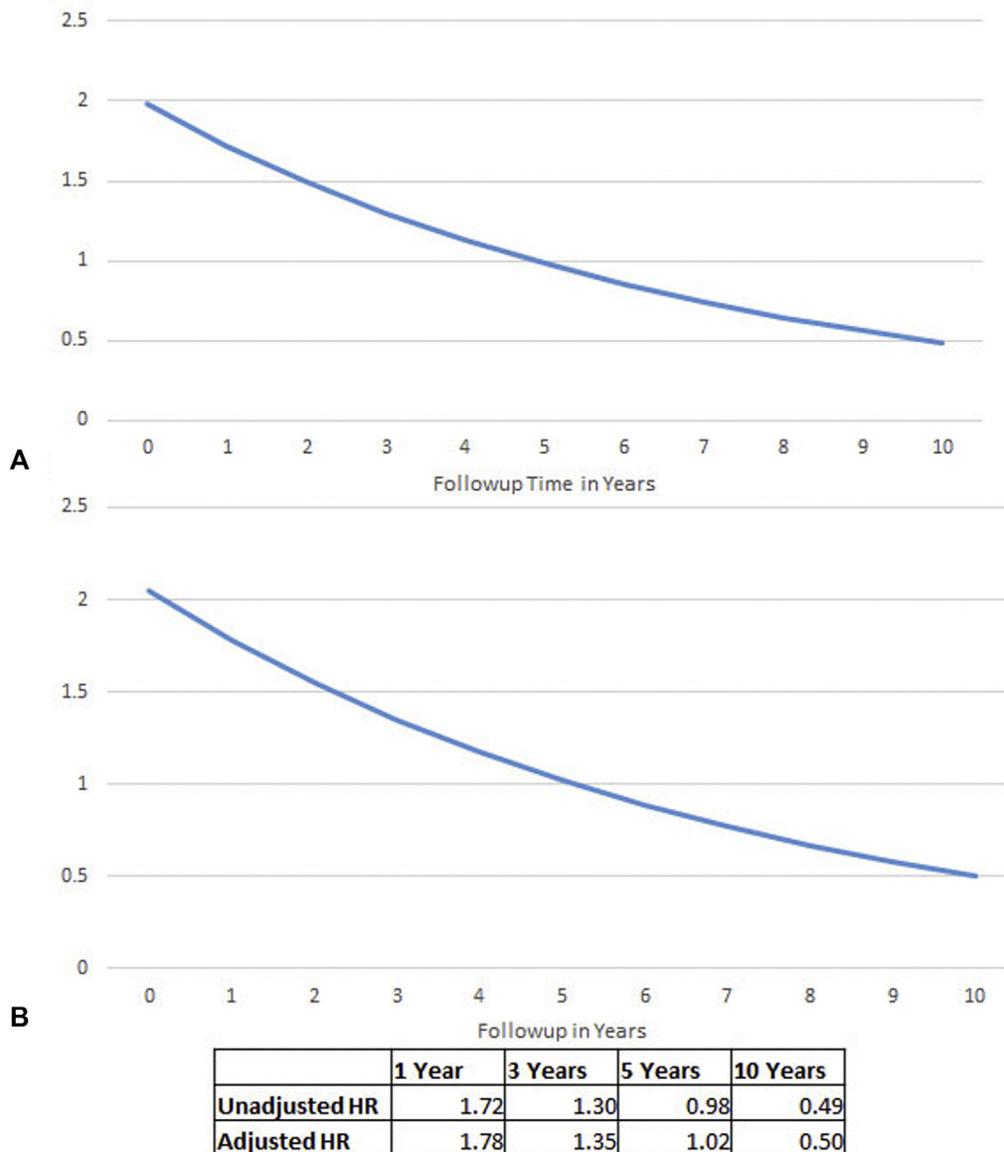
	1 Year	3 Years	5 Years	10 Years
Unadjusted HR	1.72	1.30	0.98	0.49
Adjusted HR	1.78	1.35	1.02	0.50

Figure 5. Time varying hazard ratios for non-death-censored renal graft failure associated with simultaneous liver kidney (SLK) vs kidney/kidney pancreas transplantation (A) before and (B) after adjustment for baseline differences in recipient factors. The y-axis represents the specific hazard ratio associated with SLK at the time point indicated on the x-axis. The hazard ratio crosses 1 at 4.8 years in unadjusted analysis and at 5 years in the adjusted analysis.

kidney graft function had allocation been to a patient on the kidney transplant list.[5,9,10] We agree that the former system of liver kidney allocation was too subjective and frequently might have resulted in transplantation of kidneys into patients who either would have recovered native renal function after liver transplantation or were so acutely ill that renal transplantation was futile.[8] The newly implemented SLK allocation system now provides objective criteria of either chronic kidney disease or prolonged

acute kidney injury that must be met to qualify for SLK.[25] We applaud this new policy, which should be a major step toward reducing the number of kidneys unnecessarily allocated to recipients with significant potential for native renal recovery. The findings of our current study, however, point to a problem in the kidney allocation system as well. One of the stated goals of the current kidney allocation system implemented in 2014 was to "make better use of available kidneys."[9] Our data demonstrate that the

previous kidney allocation system failed in this goal by allocating typically high-quality kidneys in a manner that resulted in lower overall kidney graft survival than seen in the SLK cohort, despite much higher short-term acuity and patient death rates in the SLK group. For example, the mean KDPI in this study was 35%. Under the new kidney allocation system, these kidneys would have been prioritized for pediatric recipients[24]; however, in the period studied, only 4.4% of kidneys in the KT group went to pediatric recipients. The principle of longevity matching introduced with the new kidney allocation system is expected to significantly increase the average lifespan of kidney grafts to a degree that will greatly overshadow what would be accomplished by modifications to SLK.[26]

There are a number of limitations to this study. As noted earlier, the differing recipient characteristics produced by the separate KT and SLK allocation systems likely account for the majority of the survival differences. As a national registry study, there is a lack of granularity to the data that would be beneficial to better elucidate such important differences, such as patient frailty. Missing data are also a problem for some variables of interest. Panel reactive antibody would also be a beneficial data point to include to better understand whether an immunologic component is at play, however, as noted in other similar studies, the level of missing data for this variable precludes reliable analysis.[9,27] We used multiple imputation in our sensitivity analysis to attempt to account for the effects of differing CIT, although this does not substitute for analysis of a complete data set. Even without the ability to fully adjust for differences in recipient characteristics, the main finding of increased long-term renal graft survival after SLK vs KT is not changed, only our ability to explain the reasons behind it. Although we accounted for the paired nature of the study in the Cox regression models, as well as with the use of paired *t*-tests and McNemar's test for 2 × 2 tables, our analysis of categorical variables that were unordered or had more than 2 categories did not account for the paired study design. The comparison of Kaplan-Meier estimates of patient and graft survival similarly did not account for the paired design of the study. This limitation can have an effect on the estimates of variance in the data, which could affect conclusions of statistical significance in the descriptive and unadjusted survival analyses.

Another potential drawback is our inclusion of kidney pancreas transplants in the comparator (KT) group. Although this makes for a more heterogeneous group, we believe the inclusion of simultaneous pancreas recipients is justified by the excellent outcomes achieved with kidney pancreas transplantation[28] and the fact that

exclusion of pancreas recipients would have also excluded a significant number of SLK recipients who would no longer have a kidney matched pair, limiting our ability to accurately describe long-term renal graft survival after SLK. Sensitivity analysis comparing SLKs with a comparator KT group excluding kidney pancreas transplants confirmed that the inclusion of kidney pancreas recipients in the primary analysis is actually slightly conservative in its estimation of the long-term increased renal graft survival in SLK recipients. We speculate that because pancreas donors tend to be highly selected, removing the kidney pancreas recipients has the effect of removing the highest-quality donors, which will subsequently enrich the SLK cohort with more robust recipients who are expected to be able to tolerate a lower-quality donor. Finally, as mentioned earlier, the policies governing both liver and kidney allocation have been substantially overhauled since the time period covered by this study. We expect that these changes will significantly alter the median renal allograft lifespan going forward and will have to await enough years of follow-up to repeat this analysis under the current regulatory regime to see what effect these policy changes have had.

CONCLUSIONS

Tension between the ethical principles of equity, which would seek to provide access to kidney transplant for all patients who stand to benefit, and utility, which seeks to maximize transplant allograft survival, ensures that there will always be some degree of controversy surround SLK, or any multi-organ transplant for that matter. This study demonstrates that the practice of SLK is not as wasteful of donor kidney lifespan as previously believed, at the same time illustrating drawbacks of the earlier kidney allocation system in terms of potential renal allograft lifespan. The revision of the kidney allocation system in 2014 is likely to significantly alter the kidney portion of this equation through longevity matching. Under the new system, the highest-quality kidneys (which account for 35% of the donors in this study) will be exclusively allocated to recipients with the longest expected survival. This change should result in improved overall patient and kidney graft survival times. The more recent revision of liver allocation policy hopefully will put a curb on the number of unnecessary SLKs performed when native renal recovery remains likely. The remaining step now is to more precisely define which candidates are most appropriate for SLK. The survival curves presented in this study demonstrate that early patient death remains a major driver of premature graft loss in SLK. As such, efforts going forward will be needed to better define

which candidates have risk factors portending poor overall survival if we are to achieve a fair balance between equity and utility in simultaneous liver kidney transplantation.

Author Contributions

Study conception and design: Cannon
Acquisition of data: Cannon
Analysis and interpretation of data: Cannon, Davis, Jones
Drafting of manuscript: Cannon, Davis, Jones
Critical revision: Cannon, Davis, Jones

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Discussion

DR JASON WELLEN (St Louis, MO): Dr Cannon and colleagues have presented a retrospective analysis of United Network for Organ Sharing (UNOS) data comparing the outcomes of kidney transplantation, after a simultaneous liver kidney transplantation (SLK), compared with a matched cohort of kidney transplants. They used UNOS data between 2003 and 2012 in order to