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Renal Outcomes After Simultaneous Liver-Kidney Transplantation: Results from the US Multicenter Simultaneous Liver-Kidney Transplantation Consortium

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Abstract

Simultaneous liver-kidney transplantation (SLKT) is increasingly common in the United States. However, little is known about the renal-related outcomes following SLKT, which are essential to maximize the health of these allografts. We examined the factors impacting renal function following SLKT. This is an observational multicenter cohort study from the US Multicenter SLKT Consortium consisting of recipients of SLKT aged ≥18 years of transplantations performed between February 2002 and June 2017 at 6 large US centers in 6 different United Network for

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Pratima Sharma participated in the research design, performance of research, data collection and interpretation, and manuscript writing and editing. Zhiyu Sui participated in the research design, performance of research, data collection and interpretation, and manuscript writing. Min Zhang participated in the performance of research, data collection and interpretation, and manuscript editing. John C. Magee participated in the data interpretation and manuscript editing. Pranab Barman, Aaron Schluger, and Kara Walter participated in the data collection and interpretation and manuscript editing. Yuval Patel, Giuseppe Cullaro, Jennifer Jo, Jasmine Sinha, and Lisa VanWagner participated in the research design, data collection and interpretation, and manuscript editing. Scott W. Biggins and Jennifer C. Lai participated in the research design, data interpretation, and manuscript editing. Randi Wong participated in the data collection. Elizabeth C. Verna participated in the research design, performance of research, data collection and interpretation, and manuscript editing.

Additional supporting information may be found in the online version of this article.

Organ Sharing regions. The primary outcome was incident post-SLKT stage 4–5 chronic kidney disease (CKD) defined as <30 mL/minute/1.73 m^2 or listing for kidney transplant. The median age of the recipients (n = 570) was 58 years (interquartile range, 51–64 years), and 37% were women, 76% were White, 33% had hepatitis C virus infection, 20% had nonalcoholic steatohepatitis (NASH), and 23% had alcohol-related liver disease; 68% developed ≥ stage 3 CKD at the end of follow-up. The 1-year, 3-year, and 5-year incidence rates of post-SLKT stage 4–5 CKD were 10%, 12%, and 16%, respectively. Pre-SLKT diabetes mellitus (hazard ratio [HR], 1.45; 95% CI, 1.00–2.15), NASH (HR, 1.58; 95% CI, 1.01–2.45), and delayed kidney graft function (HR, 1.72; 95% CI, 1.10–2.71) were the recipient factors independently associated with high risk, whereas the use of tacrolimus (HR, 0.44; 95% CI, 0.22–0.89) reduced the risk. Women (β = −6.22 ± 2.16 mL/minute/1.73 m^2; P = 0.004), NASH (β = −7.27 ± 3.27 mL/minute/1.73 m^2; P = 0.027), and delayed kidney graft function (β = −7.25 ± 2.26 mL/minute/1.73 m^2; P = 0.007) were independently associated with low estimated glomerular filtration rate at last follow-up. Stage 4–5 CKD is common after SLKT. There remains an unmet need for personalized renal protective strategies, specifically stratified by sex, diabetes mellitus, and liver disease, to preserve renal function among SLKT recipients.

Simultaneous liver-kidney transplantation (SLKT) is an important option for liver transplantation (LT) candidates with stage 4 chronic kidney disease (CKD) and end-stage renal disease (ESRD), sustained acute kidney injury (AKI) deemed unlikely to recover after LT, and select inherited metabolic disorders such as primary hyperoxaluria.[1–4] The revised Organ Procurement and Transplantation Network (OPTN) SLKT policy implemented in 2017 included medical eligibility criteria that were lacking in the previous allocation guidance. In addition, a “safety-net” option was created to prioritize kidney transplantation for those LT-only recipients who were unlikely to recover their renal function within 60 to 365 days after LT.[3,4]

The Model for End-Stage Liver disease (MELD)–based policy, adopted in February 2002 for liver allocation, improved the access of deceased donor liver allografts to the sickest while maintaining optimal short-term and long-term posttransplant survival.[5–7] Since then, there have been several evidence-based modifications to the policy,[8–11] including the revised criteria for SLKT.[1–4,12] Increased SLKT use is one of the important unintended consequences of the MELD-based allocation policy[2,3,13] because each SLKT performed draws a renal allograft away from a kidney transplantation–only recipient. Although SLKT use has increased by 200% in the MELD era, data on CKD after SLKT is lacking, and the risk factors that impact the long-term estimated glomerular filtration rate (eGFR) after SLKT are not well studied.

Most large observational studies have used data from the OPTN to examine post-SLKT survival and not renal function because such data are lacking in the OPTN data.[3,14–16] Therefore, we formed a multicenter consortium called the US Multicenter SLKT Consortium study to improve our understanding of post-SLKT CKD and related outcomes using patient-level granular data, which makes this study unique and novel. In this study, we examined the long-term renal outcomes after SLKT including the incidence of stage 4–5 CKD after SLKT and predictors of estimated GFR at last follow-up.

Patients and Methods

PATIENTS AND DATA COLLECTION

The US Multicenter SLKT Consortium (Fig. 1) includes candidate, donor, and recipient data on all adult recipients (≥18 years) of SLKT performed at 6 large US centers (Columbia University Irving Medical Center; Duke University; Northwestern University; University of California, San Francisco; Michigan Medicine, University of Michigan; University of Washington) in 6 different United Network for Organ Sharing regions between February 2002 and June 2017. The study was approved by each participating center's institutional review board, and the data use agreements were established. Deidentified coded data were uploaded in the Research Electronic Data Capture at the University of Michigan, the data coordinating center for this consortium.

The data collection sheets included the recipients' demographic information, listing, transplant, donor, and posttransplant characteristics as well as donor characteristics (see Supporting Information collection sheets S.1).

IMMUNOSUPPRESSION

The immunosuppression protocols among all 6 centers were similar. All of the centers use tacrolimus-based immunosuppression with mycophenolic acid and corticosteroids. Northwestern University revised their immunosuppression protocol in April 2015 and included induction with basiliximab on days 0 and 2 in addition to corticosteroids and a maintenance phase with tacrolimus, mycophenolic acid, and a corticosteroid taper to 5 mg indefinitely. In all other centers, immunosuppression protocols for SKLT were similar to the kidney transplantation immunosuppression protocol. Induction with thymoglobulin, basiliximab, and dacluzimab was based on the presence of panel reactive antibodies and sensitization. The therapeutic tacrolimus trough levels in all of the centers were similar and based on days after SLKT. The levels were maintained between 8 and 12 ng/mL in the first 90 days among all the centers.

ANALYTIC APPROACH

The continuous variables were expressed as median (interquartile range [IQR]), and the categorical variables were expressed as percentages. The eGFR was collected at 1 year, 2 years, 3 years, and 5 years after SLKT and at the end of follow-up. The Model for End-Stage Liver Disease–sodium (MELD-Na) score was calculated using the OPTN calculator. The renal risk index (RRI) score was calculated using the RRI calculator (https://rri.med.umich.edu). The RRI score combines 14 recipient factors at the time of transplant to summarize the post-LT ESRD risk into a single number. The RRI expresses the relative risk of incident ESRD for a given LT recipient compared with the reference LT recipient with an RRI of 1; values exceeding 1 have higher-than-expected ESRD risk than the reference LT recipient and vice versa. All of the components of the Kidney Donor Profile Index (KDPI) were not available on all the patients. Therefore, we used the kidney donor age as a covariate for donor quality in the models.

The primary outcome was post-SLKT stage 4–5 CKD defined as eGFR ≤ 30 mL/minute per 1.73 m^2 at last follow-up or listed for kidney transplantation. The secondary outcomes were (1) eGFR at the last follow-up and (2) post-SLKT mortality.

Incidence and Risk Factors of New-Onset Stage 4–5 CKD—We used the Kaplan-Meier analysis to examine the cumulative incidence of post-SLKT stage 4–5 and post-SLKT survival. We used Cox regression to assess the risk factors of stage 4–5 CKD after SLKT. The covariates with $P < 0.15$ were used in the multivariable model to examine the independent association between donor and recipient factors and stage 4–5 CKD. We forced the center in the final adjusted model to examine the unmeasured center effect.

eGFR at Last Follow-Up and eGFR Slope—Using linear regression, we modeled eGFR at the last follow-up. For this model, we adjusted for covariates a priori: age, sex, etiology of liver disease, year of SLKT, pretransplant hypertension, diabetes mellitus, MELD-Na, body mass index (BMI), pretransplant renal dysfunction type, renal replacement therapy (RRT), time of follow-up, kidney delayed graft function (DGF), immunosuppression, induction therapy, donor age, cold ischemia time (CIT), warm ischemia time (WIT), and RRI.

Using linear regression, we modeled the slope of eGFR decline from the first available eGFR following SLKT or at the 1-year follow-up to estimate the eGFR decline per year. We tested the eGFR decline by sex, race, etiology of liver disease, and kidney DGF. This model was adjusted for age, sex, etiology of liver disease, year of SLKT, pretransplant hypertension, diabetes mellitus, MELD-Na, BMI, pretransplant renal dysfunction type, RRT, time of follow-up, kidney DGF, immunosuppression, induction therapy, donor age, CIT, WIT, and RRI.

Subset Analysis Limited to those Who Had Data on KDPI—We performed a subset analysis limiting to the patients who had information on KDPI. We fitted the Cox regression model to examine the effect of KDPI on kidney DGF, new-onset stage 4–5 CKD, and patient survival. This model was stratified by center and adjusted for age, sex, nonalcoholic steatohepatitis (NASH), RRT at SKLT, MELD score, donor age, and CIT.

All analyses were performed in SAS 9.4 (SAS Institute, Cary, NC).

Results

CLINICAL CHARACTERISTICS

Table 1 shows the clinical characteristics of the cohort. The median age of the cohort (n = 570) was 58 years, 63% were men, and 76% were White. The etiology of liver disease was hepatitis C virus infection in 33%, NASH or cryptogenic cirrhosis in 20%, alcohol-related liver disease in 23%, and 24% had other etiologies. The median MELD-Na at SLKT score was 28 (IQR, 23–34). Only 39% were on hemodialysis or RRT at the time of SLKT. The traditional risk factors of CKD, hypertension, and diabetes mellitus were seen in 45%, 54%, and 42% of the SLKT candidates, respectively. The median BMI was 27 kg/m^2, and 25%

had a BMI ≥32 kg/m^2 at the time of SLKT (Table 1). The median RRI score was 7.57 and three-fourths of the cohort had an RRI score in the 10th decile (highest risk group; Table 1).

Donor characteristics are outlined in Table 1. The median donor age was 36 years (IQR, 23–48), 93% were donations after brain death, and cerebrovascular disease or head injury were the most common causes of death (68%) followed by anoxia or asphyxiation (20%). Donor biopsy data were not available across the center. KDPI information was available in 184 SLKT recipients. The features of the KDPI subset are described in the "Subset Analysis" section.

Almost all of the SLKT recipients were on tacrolimus (95%), 82% were on triple immunosuppression (calcineurin inhibitors, mycophenolate, and corticosteroids), and only 3% were on calcineurin inhibitor monotherapy. Of the patients, one-fourth (24%) received induction therapy after SLKT: 74% received basiliximab, 18% received thymoglobulin, and 7% received dacluzimab as induction therapy. Within the first 6 months after SLKT, there were 80 rejection episodes among 71 SLKT recipients; 36 were kidney rejection episodes and 44 were liver rejection episodes. Of note, 12 patients had both liver and kidney rejection episodes within the first 6 months after SLKT.

A total of 133 (23%) patients developed kidney DGF requiring RRT during transplant hospitalization. The median time spent on RRT was 13 days (IQR, 4–40). Post-SLKT stage 4–5 CKD was higher in patients with DGF versus those without (32% versus 17%; $P < 0.001$).

INCIDENCE OF STAGE 4–5 CKD

A total of 120 (21%) SLKT recipients developed stage 4–5 CKD at the end of the follow-up period. The median follow-up time was 63 months. The crude incidence rate was 3.8 per 100 patient-years. The cumulative incidence of posttransplant stage 4–5 CKD at 1 year, 3 years, 5 years, and 10 years was 10%, 12%, 16%, and 25%, respectively (Fig. 2).

In the univariate analysis, NASH ($P = 0.004$), pre-SLKT diabetes mellitus ($P = 0.01$), use of tacrolimus compared with cyclosporine ($P = 0.015$), kidney DGF ($P < 0.001$), donor age ($P < 0.001$), CIT ($P = 0.002$), and WIT ($P = 0.044$) were significant. In an adjusted model that included these factors and age at SLKT, alcohol-related liver disease ($P < 0.15$), and center, we found that pre-SLKT diabetes mellitus, NASH, and kidney DGF were independently associated with high risk, whereas the use of tacrolimus compared with cyclosporine was independently associated with the reduced risk of post-SLKT stage 4–5 CKD (Table 2). Donor age, CIT, and WIT were independent donor risk factors associated with a high risk of stage 4–5 CKD, and transplant center did not affect the risk of post-SLKT stage 4–5 CKD (Table 2).

FACTORS AFFECTING eGFR AT LAST FOLLOW-UP

The median eGFR at last follow-up was 54 mL/minute per 1.73 m^2 (IQR, 33–65) with 68% having CKD stage 3 or higher (eGFR ≤ 60 mL/minute per 1.73 m^2). The median time of last follow-up was 64 months (IQR, 28.2–110.7). Of those who had stage 3 CKD (eGFR 30–59 mL/minute per 1.73 m^2) at the last follow-up, 43% had stage 3A (eGFR

45–59 mL/minute) and 56% had stage 3B CKD (eGFR 30–44 mL/minute). There were no significant differences between the baseline recipients and donor characteristics between these 2 groups. The mean decline in the slope of eGFR after SLKT was −0.76 mL/minute per 1.73 m^2 per year. eGFR slope did not differ by sex, etiology, race, or presence of kidney DGF.

Female sex (β = −6.35 ± 2.11 mL/minute per 1.73 m^2; $P = 0.003$), NASH (β = −7.58 ± 3.20 mL/minute per 1.73 m^2; $P = 0.018$), kidney DGF (β = −7.74 ± 2.60 mL/minute per 1.73 m^2; $P = 0.003$), and donor age per year (β = −0.36 ± 0.07 mL/minute per 1.73 m^2; $P < 0.0001$) were independently associated with low eGFR at last follow-up, whereas each calendar year increase in SLKT procedure performed was associated with high eGFR (β = 1.46 ± 0.03 mL/minute per 1.73 m^2; $P < 0.001$).

POST-SLKT MORTALITY

Figure 3 shows the unadjusted patient survival after SLKT. Posttransplant mortality was significantly higher in patients with post-SLKT stage 4–5 CKD compared with those without (55% versus 25%; $P < 0.001$). Although post-SLKT stage 4–5 CKD was higher in the kidney DGF group, patient mortality was similar (36% versus 32%; $P = 0.3$) in both groups.

Subset Analysis—We performed the subset analysis on SLKT recipients with data on KDPI (n = 184). The median age of this group was 59 years (IQR, 51–64); 63% were men; 64% White, 13% were Black, and 23% were other races; 34% had hepatitis C virus infection; 22% had alcohol-related liver disease; 20% had NASH; 24% had other etiologies of liver disease; 49% were hypertensive; 45% had diabetes mellitus; and 57% were on RRT at SLKT. The median MELD score at SLKT was 25 (IQR, 21–32). The median donor age was 34 years (IQR, 23–47), and the median KDPI was 32% (IQR, 16%−55%).

In this subset, 80 had kidney DGF, 33 developed stage 4–5 CKD and 32 died. The median follow-up time was 49.2 (IQR, 29.3–74.6) months. In an adjusted model, KDPI was neither associated with stage 4–5 CKD nor with post-SLKT mortality.

Discussion

In this largest (to date) study of long-term renal outcomes following SLKT, we have shown that recurrent CKD impacts most patients after SLKT. Two-thirds had at least stage 3 CKD and one-fifth had advanced CKD (stage 4–5) after a median follow-up of 5 years. There are several recipient and donor factors that affect the risk of incident stage 4–5 CKD after SLKT; female sex, NASH, kidney DGF, and advanced donor age were all associated with significant reduction in eGFR over time. Although kidney DGF was 1 of the independent predictors of posttransplant stage 4–5 CKD, it did not affect overall survival. Donor age, CIT, and WIT were also associated with incident stage 4–5 CKD. Posttransplant stage 4–5 CKD, similar to other studies,[17,18] was associated with increased mortality among SLKT recipients.

The true incidence of stage 4–5 CKD after primary kidney transplantation is not known. In 2018, 12% of kidney allograft listing occurred in patients with primary kidney transplantation.[19] In a previous large cohort study of 43,514 LT recipients that excluded SLKT, the 5-year cumulative incidence of post-LT ESRD for those who had RRI ≥5.22 (10th decile) was 18%.[20] We believe that the 5-year cumulative incidence in their study would be even higher if they included stage 4 CKD in addition to ESRD. RRI score stratifies LT recipients at the varying risk of posttransplant ESRD. The risk of posttransplant ESRD and mortality increases with the increase in RRI score. Our study found the 5-year cumulative incidence of stage 4–5 CKD following SLKT to be 16%. The median RRI of SLKT patients in our data was 7.57, which falls into the 10th decile (highest risk group).

In our study, eGFR at the last follow-up was significantly lower in women compared with men. Studies comparing post–kidney transplantation graft outcomes between men and women demonstrated conflicting results with many showing either no difference or survival advantage in favor of women attributed to the smaller body size and therefore lower metabolic demand on the transplanted organ.[21–26] The pattern of sex differences in eGFR we observed may likely be attributed to the interplay of several factors, including the high incidence of autoimmune diseases in women, the effect of sex hormones on immune activation, and sex differences in adherence to immunosuppressive medications in women.[27] We, similar to others, had previously reported the sex-based differences in the relative risk of incident stage 4–5 CKD after LT alone.[28,29]

There is an emerging association between NASH and CKD because of the traditional risk factors such as hypertension, diabetes mellitus, and obesity, which are common to both. The important implication of this association may lead to an increase in SLKT listing among candidates with NASH cirrhosis. Our study showed a higher risk of stage 4–5 CKD and lower eGFR among NASH SLKT recipients compared with all other etiologies of liver diseases. NASH is also a risk factor for stage 4–5 CKD after LT.[28] Because NASH is the leading indication for LT in females,[30] we examined the impact of this relationship on eGFR. This interaction was not significant.

On average, the rate of kidney DGF is about 30.8% in US deceased donor kidney transplant recipients, and donor factors significantly affect the likelihood of DGF.[19,31–33] In our study, 23% of SLKT recipients developed DGF, which is somewhat lower than kidney transplant recipients. However, we cannot draw this inference without directly comparing kidney transplantation–only recipients with SLKT recipients. Although kidney donor age has been associated with increased incidence of DGF, the median donor age in our cohort was lower than the donor age reported for kidney transplantation–only recipients.[34] This could be the plausible explanation for lower DGF in SLKT recipients than kidney transplant recipients.

Our study showed modest rate of rejection in the kidney grafts. This may be attributed to the protective effect of liver allograft against antibody-mediated kidney rejection as shown by previous studies.[35–37] Some studies suggest the role of preformed cytotoxic and neutralizing antibodies through the release of soluble class I antigens in reducing kidney allograft rejection in patients with SLKT.[38,39] A previous study demonstrated a 26% higher

risk of stage 4–5 CKD with cyclosporine compared with tacrolimus among nonrenal organ transplantation.[17] Our study validated these results in SLKT recipients.

CKD progression adversely impacts patient and graft survival and adds to health care costs.[17,18,20,40,41] We hypothesize that CKD progression is accelerated in LT and SLKT recipients given the prevalent traditional risk factors such as diabetes mellitus, hypertension, obesity, and calcineurin inhibitors. Therefore, recognizing the phenotypes that are at the highest risk of CKD progression is an important first step to focus on intervention(s) that may reduce the CKD progression. Hence, there is an unmet need to develop personalized risk-based immunosuppression regimens to further prevent the renal insult because 1 size does not fit all.

A majority of SLKT patients remain on triple immunosuppression including prednisone that can worsen preexisting diabetes mellitus and may cause new-onset diabetes mellitus in these patients. Metabolic disorder, hypertension, diabetes mellitus, and obesity are also prevalent among SLKT recipients. Although we cannot modify many of the risk factors associated with stage 4–5 CKD and low eGFR, attempts should be made to minimize any additional insult to the allograft kidneys to prevent further reduction in eGFR. Immunosuppression (for example, discontinuation of prednisone in those with stable renal function), risk factor modification with life style modification and weight management, stricter control of diabetes and hypertension, especially in high-risk group identified in our study (females, NASH and kidney DGF). Implementation of these measures may attenuate CKD progression and improve renal as well as overall health outcomes among SLKT recipients.

In our study, more than half of the patients were not on dialysis or RRT at the time of SLKT. This is likely related to the changing practices and SLKT guidance during the 15-year study period.[1,2,42] The first policy was put forth in 2009 by the OPTN based on the recommendations from the first SLKT consensus conference.[1] The SLKT guidance changed substantially between 2002 and 2012, especially for sustained AKI deemed irreversible with respect to dialysis or renal dysfunction duration before transplant. Recently, the OPTN implemented an SLKT policy that has the following 2 important components: medical eligibility criteria and the option of a “safety net.”[4] This change in SLKT allocation has streamlined the SLKT usage to some extent. The earliest signs of this policy change resulted in a slight reduction in SLKT rates in 2018.

Our study has limitations that include the retrospective design, heterogeneity, and variability in practices during the long study period across the 6 centers, resulting in potential bias as a result of unmeasured characteristics and patient selection. To overcome some of these limitations, we adjusted for the year of SLKT and forced the center in the final model for incident stage 4–5 CKD. Although the KDPI data were not available on all of the patients, we performed the subset analysis to examine its effect on long-term renal function and survival. However, the KDPI data did not affect long-term renal function or survival. Finally, one may argue that the lack of a comparison arm makes it difficult to put these results in perspective. The valid comparison group would be either a lung-kidney group or heart-kidney group. There are no studies to date that examined the renal outcomes after

simultaneous lung-kidney or heart-kidney transplant.[43,44] Despite these shortcomings, this is the first and the largest study to examine the renal outcomes after SLKT.

In conclusion, incident stage 4–5 CKD impacts SLKT recipients. Several recipient and donor factors affect the renal function after SKLT. Further prospective studies are warranted to identify the role of personalized immunosuppression based on sex and etiology of liver disease in preserving renal function among SLKT recipients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

AKI	acute kidney injury
BMI	body mass index
CKD	chronic kidney disease
CIT	cold ischemia time
DCD	donation after circulatory death
DGF	delayed graft function
ESRD	end-stage renal disease
eGFR	estimated glomerular filtration rate
HR	hazard ratio
IQR	interquartile range
KDPI	Kidney Donor Profile Index
LT	liver transplantation
MELD	Model for End-Stage Liver Disease
MELD-Na	Model for End-Stage Liver Disease–sodium
NASH	nonalcoholic steatohepatitis
OPTN	Organ Procurement and Transplantation Network

PI	principal investigator
RRI	renal risk index
RRT	renal replacement therapy
SLKT	simultaneous liver-kidney transplantation
WIT	warm ischemia time

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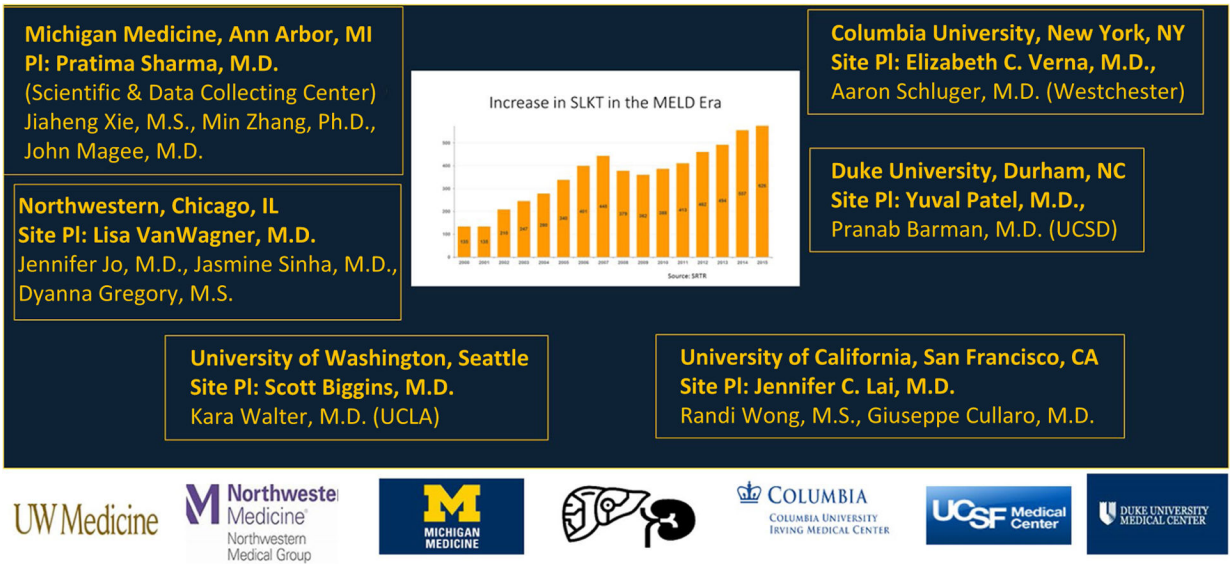

FIG. 1.
The US Multicenter SLKT Consortium.

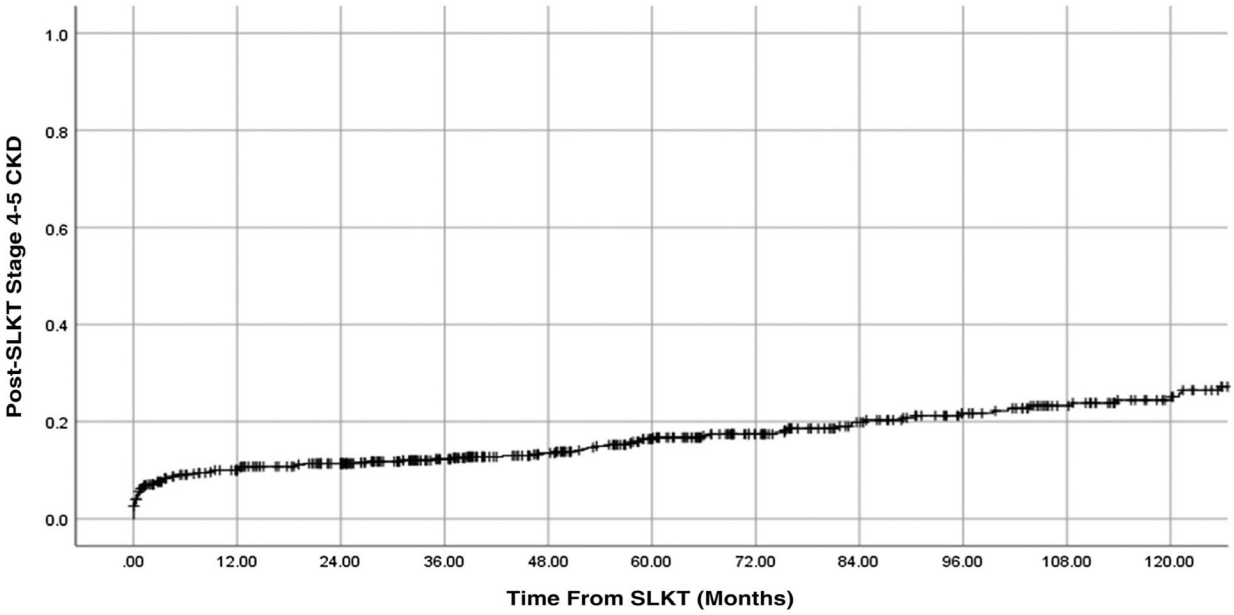

FIG. 2.
Cumulative incidence of stage 4–5 CKD after SLKT.

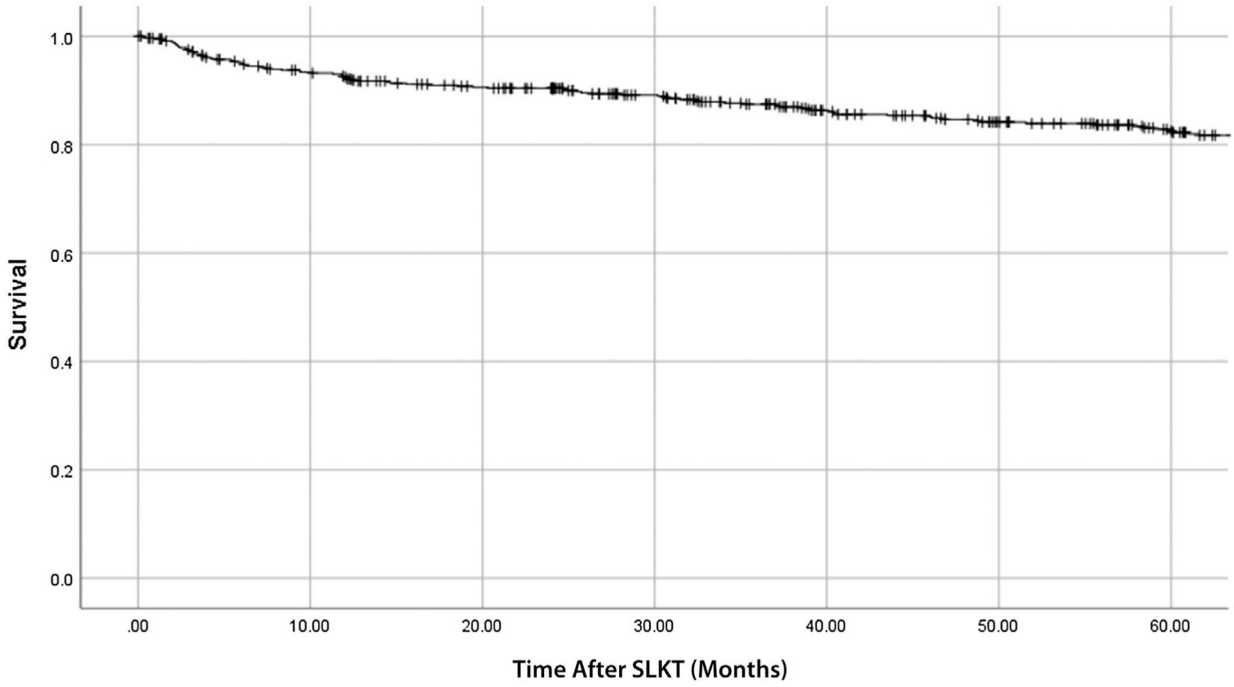

FIG. 3.
Patient survival after SLKT.

TABLE 1.

Baseline Characteristics at SLKT

Variables at LT (n = 570)	Median (IQR) or n (%)
Recipient characteristics	
Age at LT, years	58 (51–64)
Columbia	47 (8.3)
Duke University	43 (7.5)
Northwestern University	281 (49.3)
University of California, San Francisco	100 (17.5)
University of Michigan	51 (9.0)
University of Washington	48 (8.4)
Male	361 (63)
Female	209 (37)
White	432 (75.8)
Black	71 (12.5)
Other races	67 (11.7)
Hepatitis C virus infection	189 (33)
Alcohol-related cirrhosis	131 (23)
NASH/cryptogenic cirrhosis	112 (20)
Other etiologies	138 (24)
AKI	149 (26)
CKD	257 (45)
Other	164 (29)
Pre-LT dialysis or RRT	220 (39)
Hypertension	306 (54)
Diabetes mellitus	237 (42)
BMI, kg/m^2	27 (24–32)
RRI score	7.57 (5.2–12.2)
MELD-NA score	28 (23–34)
Donor and transplant characteristics	
Donor age, years	36 (23–48)
DCD	24 (4.2)
Donor, male	318 (55.7)
Donor cause of death, cerebrovascular deaths	382 (67)
KDPI score, n = 184	32 (15–66)
CIT, minutes	360 (300–465)
WIT, minutes	37.5 (25–60)
Tacrolimus	541 (95)
Cyclosporine	29 (5)
Induction, yes	138 (24)
Kidney DGF	133 (23.3)
Length of stay, transplant admission, days	19 (9–33)

Variables at LT (n = 570)	Median (IQR) or n (%)
eGFR at last follow-up	54 ml/minute per 1.73 m^2 (33–65)
Time to last follow-up	63.6 months (28.2–110.6)

TABLE 2.

Independent Predictors of Stage 4–5 CKD

Covariates	HR (95% CI)	*P* Value
Recipient factors		
NASH, reference: no NASH	1.58 (1.01–2.45)	0.044
Pre-SLKT diabetes mellitus	1.45 (1.00–2.15)	0.049
Tacrolimus, reference: cyclosporine	0.44 (0.22–0.89)	0.023
Kidney DGF, reference: none	1.72 (1.10–2.71)	0.018
Donor factors		
Donor age, per year	1.02 (1.01–1.03)	0.001
CIT, per 10 minutes	1.01 (1.00–1.03)	0.019
WIT, per 10 minutes	1.05 (1.00–1.10)	0.05
Center		
1	0.53 (0.24–1.18)	0.12
2	0.51 (0.19–1.32)	0.17
3	0.83 (0.45–1.53)	0.56
4	1.09 (0.56–2.12)	0.79
5	0.72 (0.31–1.66)	0.44
6, reference	1.00	