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Outcomes of Liver Transplantation in Patients on Renal Replacement Therapy: Considerations for Simultaneous Liver Kidney Transplantation Versus Safety Net

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Background. As the liver transplant (LT) waiting list continues to outpace organ availability, many patients require renal replacement therapy (RRT) before LT. It is unclear which patients will benefit from simultaneous liver kidney (SLK) transplant as opposed to awaiting a Safety Net kidney transplant (KT) post-LT. **Methods.** In this study, a retrospective analysis of the United Network for Organ Sharing dataset was performed to identify risk factors associated with poor outcome for patients on RRT before LT who were listed for SLK and received either SLK vs LT alone (LTA). **Results.** Between January 2003 and December 2016, 8971 adult LT recipients were on RRT at the time of LT. 5359 were listed for and received LTA (Group 1). Of 3612 patients listed for SLK, 3414 (38.1%) received SLK (Group 2) and 198 (2.2%) received LTA (Group 3). Overall, Group 3 had lower graft and patient survival post-LT when compared with Groups 1 and 2 ($P < 0.001$). Serum creatinine at 1 year post-LT and cumulative incidence for KT at 3 years post-LT were higher for Group 3 ($P < 0.001$). On multivariate analysis, pre-LT diabetes ($P = 0.002$), Model of End-Stage Liver Disease score ($P = 0.01$), and donor kidney donor profile index ($P = 0.025$) were significant in Group 2. Recipient age >60 ($P < 0.001$) and RRT pre-LT (>90 days; $P = 0.001$) were associated with lower patient survival in Group 3. **Conclusions.** Among LT recipients on RRT before LT who were listed for SLK, RRT >90 days, and age >60 were associated with poor outcome following LTA. This suggests that programs should carefully weigh the decision to proceed with LTA vs waiting for SLK in this patient population. Future access to Safety Net KT will be an important consideration for these patients moving forward.

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Since the adoption of the Model of End-Stage Liver Disease (MELD)-based allocation system in February 2002 and the subsequent implementation of Share 35 in June 2013, the total number and proportion of simultaneous liver and kidney (SLK) transplants in the United States has increased by >200%, accounting for 8.6% of the total number of adult liver transplants (LT) in 2018.[1,2] The reasons

for this increase are multifactorial. First, allocation using the MELD score prioritizes patients with renal dysfunction, as the score incorporates both serum creatinine (Scr) and utilization of pretransplant renal replacement therapy (RRT). Second, superior outcomes have been observed following SLK in recipients with advanced pretransplant renal dysfunction.[3] Finally, there has been a steady increase in the incidence of

nonalcoholic fatty liver disease, resulting in more patients on the LT waiting list with this diagnosis.[4] When compared with other types of chronic liver disease, nonalcoholic fatty liver disease is directly associated with metabolic disorders, further contributing to chronic kidney disease (CKD) in this patient population.[5-7]

Before the establishment of new eligibility criteria for SLK listing by the Organ Procurement and Transplantation Network in August 2017 (**Table S1, SDC**, http://links.lww.com/TXD/A222),[8] significant regional variability in listing practices for SLK was observed among US transplant centers.[8-10] The severity and duration of pretransplant renal disease have long been known to be associated with increased risk of persistent posttransplant renal dysfunction, ranging from acute kidney injury (AKI) to end-stage renal disease.[11,12] Multiple studies have evaluated the outcomes of SLK versus LT alone (LTA) in patients with renal dysfunction, and these have consistently demonstrated superior graft and patient survival for SLK in recipients with longstanding CKD or on long-term hemodialysis (HD; >3 mo), high MELD scores, and those with hepatorenal syndrome.[13-17] While these studies have shown superior results for SLK in these recipient groups, predicting renal recovery following LTA still represents a significant dilemma. Several groups have attempted to devise models or identify biomarkers to predict renal dysfunction post-LT, while others have attempted to distinguish risk factors associated with futility of SLK.[18-23] The recent establishment of the "safety net" criteria attempted to address this challenge by providing a period of time to allow for renal function recovery following LTA, prioritizing kidney transplant (KT) in recipients with persistent renal dysfunction (glomerular filtration rate ≤ 20 mL/min) or continued dialysis in the period between 2 and 12 months following LTA (**Table S1, SDC**, http://links.lww.com/TXD/A222).[24,25]

The impact of the implementation of the updated Organ Procurement and Transplantation Network SLK listing guidelines and the creation of a "safety net" for LTA recipients with persistent renal dysfunction following LT on the overall number and proportion of SLK remains undetermined. Hmoud et al[26] compared the outcomes between SLK and LTA in patients listed for SLK and observed that approximately 12% of patients listed for SLK underwent LTA. In this study, SLK recipients had increased graft and patient survival, as well as improved posttransplant renal function when compared with LTA, even when controlling for factors such as early post-LT cardiopulmonary events as well as other events leading to early death. This study highlights the importance of identifying risk factors for post-LTA patients awaiting a safety net kidney, as it can be anticipated that there will be an increasing number of patients for whom it will be necessary to weigh SLK against the LTA/safety net KT option.

Given the wealth of evidence supporting that patients with chronic liver disease on HD benefit from SLK and the change in policy, which is expected to result in improved access to KT for patients who fail to recover renal function, it is important to identify which patients must not wait for the safety net and instead should undergo SLK. It will require several years to analyze outcomes in the post safety net era to determine which patients benefit most from SLK. The purpose of this study was to analyze demographic, recipient, and donor characteristics in LT recipients on RRT in the post-MELD era to identify risk factors for poor outcome, to determine which patients on RRT at the time of LT will benefit from SLK as opposed to receiving LTA and awaiting a safety net KT.

MATERIALS AND METHODS

The study was approved by the Health Science Campus Institutional Review Board of the University of Southern California.

Inclusion/Exclusion Criteria

Data for adult primary LT recipients performed from January 1, 2003, to December 31, 2016, were obtained from the United Network for Organ Sharing (UNOS). Included in the study group were all adult (age ≥18 y) recipients of deceased donor LTs who had been on RRT at the time of the transplant. Patients listed for an organ transplant other than liver or kidney, and patients who received live donor allografts, were excluded from the study. Recipient data included demographics, region, history of diabetes mellitus (DM), number of days on dialysis, calculated MELD score, patient and graft survival, time and cause of death, relisting, retransplant, and posttransplant creatinine. Donor data included demographics, history of DM, hypertension and smoking, kidney donor profile index (KDPI), and terminal Scr. Among the patients eligible for the study, three groups were identified: Group 1 included LTA recipients with no prior history of kidney listing; Group 2 consisted of recipients listed for SLK who underwent SLK; and Group 3 were those patients listed for SLK who underwent LTA (outlined in Figure 1).

STATISTICAL METHODS

One and 3-year patient and graft survival were calculated using the Kaplan–Meier method. Patient survival was defined as time from initial LT to death or last follow-up date. Graft survival was defined as time from organ transplant to graft failure or patient death. Patients with follow-up >3 years were censored at 3 years. To examine whether differences in 1-year survival were due to early deaths from immediate operative or perioperative events, variables were also examined excluding recipients who survived <2 days following initial LT.

A competing risk analysis was used to calculate the cumulative incidence of liver relisting and KT after the initial LT. For the cumulative incidence of liver relisting, the outcome of interest was the liver relisting and the competing event was death. For the cumulative incidence of KT, the outcome of interest was the KT following the initial liver or SLK transplant and the competing event was death. Gray's test was used to compare the cumulative incidence functions among the 3 groups.

For the 2 groups that were listed for SLK (Groups 2 and 3), the association between factors and patient survival was analyzed using Cox proportional hazards. Variables analyzed were age, gender, ethnicity, region, diabetes, days on dialysis, MELD, and donor data including history of DM, hypertension, smoking, age, KDPI, and creatinine. Variables with a $P \leq 0.1$ in the univariate model were included in a multivariate model. The SAS 9.4 (SAS Institute Inc., Cary, NC) software was used for statistical analysis, while both SAS and R (R Foundation for Statistical Computing, Vienna, Austria) were used for graphing.
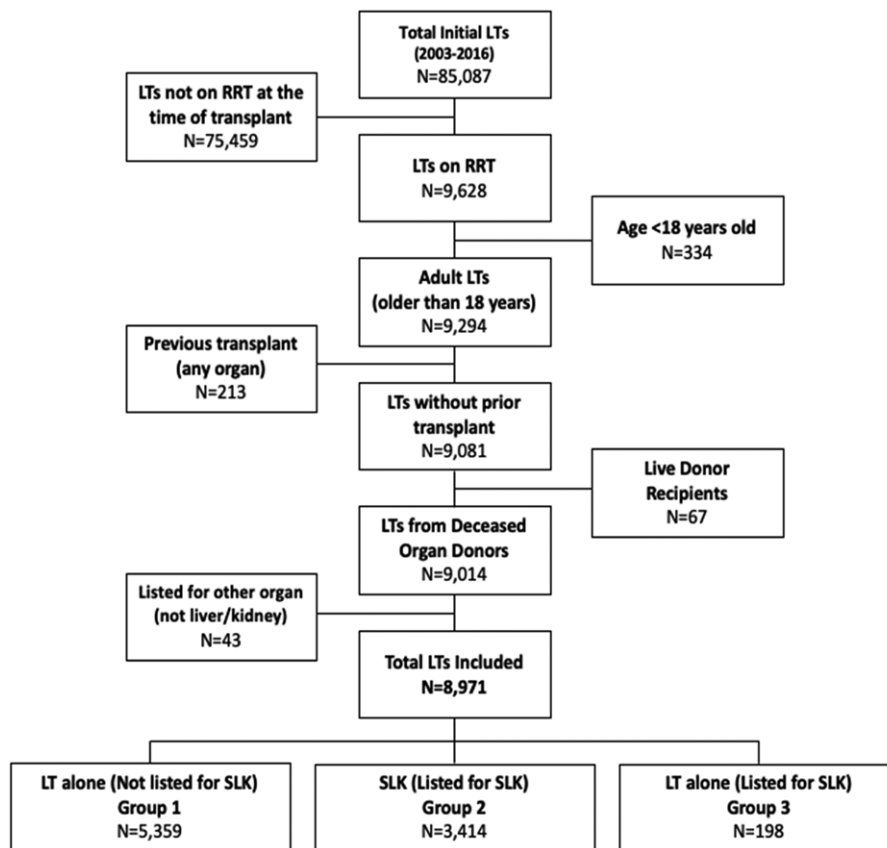
FIGURE 1. Schematic outline of inclusion and exclusion criteria utilized in this study. LT, liver transplant; RRT, renal replacement therapy; SLK, simultaneous liver kidney.

RESULTS

Among the 8971 eligible patients identified, Group 1 included 5359 (59.7%) LTA recipients with no prior kidney listing, to serve as a reference group for all LT performed. Group 2 included 3414 patients (38.1%) listed for SLK who received SLK, while Group 3 included 198 patients (2.2%) listed for SLK who underwent LTA (Figure 1).

Patient Demographics

In the first part of the analysis, demographic and clinical variables between the 3 groups were compared and are summarized in Table 1. Significant recipient differences among the 3 groups were found when age, gender, ethnicity, DM, days on dialysis, and lab MELD score were analyzed. The organ donors across all groups had significant differences pertaining to age, DM, hypertension, smoking history, KDPI, and terminal creatinine. Very few of the donors in Group 2 or Group 3 were procured as donation after circulatory death. In comparison to patients receiving LTA (Group 1 and 3), SLK recipients (Group 2) had lower lab MELD scores ($P < 0.001$), were more likely to be male ($P < 0.001$), had younger donors ($P < 0.001$), lower donor KDPI ($P < 0.001$) and lower donor terminal creatinine ($P < 0.001$). Patients who received SLK (Group 2) had longer duration of pretransplant dialysis ($P < 0.001$), received organs from donors who were younger ($P = 0.002$), less often diabetic ($P = 0.024$) and hypertensive ($P = 0.003$), had less smoking history ($P = 0.004$), and had lower KDPI and terminal creatinine ($P < 0.001$) when compared with patients who were listed for SLK but received LTA (Group 3). Regional differences were also observed, which a noticeable lower relative

proportion of patients receiving SLK (Group 2) compared with patients in both Groups 1 and 3 in the region with the largest overall number of LTs, region 5 (20% versus 34% and 31%, respectively; $P < 0.001$).

Patient and Graft Survival

Next, patient and graft survival between the 3 cohorts were compared using Kaplan–Meier analyses. Group 3 had lower patient survival of 63% at 1 year, compared with 82.8% and 87% for Groups 1 and 2, respectively (Figure 2A; $P < 0.001$). Group 3 also had lower liver graft survival of 60.1% at 1 year compared with 80.6% and 86% for Groups 1 and 2, respectively (Figure 2B; $P < 0.001$). When patients who expired within the first 48 hours following LT were excluded from the analysis, 1- and 3-year patient and liver allograft survival remained significantly lower for patients in Group 3 (Table 2). At 1 year post-LT, the cumulative rate of relisting for LT was lower for Group 2 at 2.7%, compared with 6.6% for Group 3 and 5.2% for Group 1 ($P < 0.001$; Figure 3). At 3 years post-LT, the cumulative incidence of relisting for LT for Group 3 was 7.1%, compared with 6.0% and 3.5% for Groups 1 and 2.

Renal Function

Post-LT renal function and rates of KT were examined. Not surprisingly, the cumulative incidence of KT after the initial LT was higher for Group 3 than for Groups 1 and 2 ($P < 0.001$; Figure 4). At 1-year post-LT, the cumulative incidence for KT for Group 3 was 4.1%, compared with 0.6% and 0.3% for Groups 1 and 2. The cumulative incidence for KT at 3 years for Group 3 was 7.4%, compared with 1.7% and 1% for Groups

TABLE 1.

Demographic and clinical variables of Group 1 (LTA without kidney listing), Group 2 (SLK), and Group 3 (LTA)

Variable	Group 1 — Liver transplant alone, not listed for kidney (n = 5359) (%)	Group 2 — Simultaneous liver kidney transplant (n = 3414) (%)	Group 3 — Liver transplant alone, listed for kidney (n = 198) (%)	P
Recipient age, y				<0.001
≤50	1866 (35)	913 (27)	62 (31)	0.31[a]
51–60	2205 (41)	1430 (42)	74 (37)	
>60	1288 (24)	1071 (31)	62 (31)	
Sex				<0.001
Male	3125 (58)	2228 (65)	111 (56)	0.008[a]
Ethnicity				<0.001
White	3643 (68)	2082 (61)	120 (61)	0.67[a]
Black	411 (8)	500 (15)	28 (14)	
Hispanic	1040 (19)	638 (19)	42 (21)	
Other	265 (5)	194 (6)	8 (4)	
Region				<0.001
1	176 (3)	134 (4)	7 (4)	0.011[a]
2	498 (9)	344 (10)	20 (10)	
3	584 (11)	481 (14)	27 (14)	
4	501 (9)	378 (11)	8 (4)	
5	1814 (34)	674 (20)	61 (31)	
6	169 (3)	64 (2)	3 (2)	
7	556 (10)	517 (15)	34 (17)	
8	242 (5)	190 (6)	8 (4)	
9	272 (5)	135 (4)	8 (4)	
10	305 (6)	281 (8)	12 (6)	
11	242 (5)	216 (6)	10 (5)	
Diabetes (recipient)	1243 (24)	1392 (41)	69 (35)	<0.001
				0.09[a]
Days on dialysis[b], d				<0.001[a]
1–30		755 (26)	62 (42)	
31–90		601 (21)	35 (24)	
>90		1568 (54)	49 (34)	
MELD				<0.001
≤35	1463 (27)	2355 (69)	100 (51)	<0.001[a]
36–40	1640 (31)	555 (16)	43 (22)	
>40	2256 (42)	504 (15)	55 (28)	
DCD	162 (3)	142 (4)	11 (6)	0.005
				0.34[a]
Donor age, y				<0.001
≤50	3889 (73)	2785 (82)	143 (72)	0.002[a]
51–60	979 (18)	480 (14)	38 (19)	
>60	491 (9)	149 (4)	17 (9)	
Diabetes (donor)	500 (9)	157 (5)	16 (8)	<0.001
				0.024[a]
Hypertension (donor)	1605 (30)	734 (22)	60 (31)	<0.001
				0.003[a]
Donor history of smoking	1115 (21)	725 (22)	59 (30)	<0.009
				0.004[a]
KDPI				<0.001
0–50	3013 (57)	2281 (67)	99 (50)	<0.001[a]
>50–85	1536 (29)	903 (27)	71 (36)	
>85	782 (15)	219 (6)	27 (14)	
Donor creatinine (mg/dL)				<0.001
≤2	4496 (84)	3275 (96)	178 (90)	<0.001[a]

[a]P value comparing SLK transplanted patients and patients waitlisted for kidney receiving liver alone (Groups 2 and 3).
[b]Days on dialysis not available for patients receiving LTA and not listed for KT.
DCD, donation after circulatory death; KDPI, kidney donor profile index; KT, kidney transplant; LTA, liver transplant alone; MELD, Model of End-Stage Liver Disease; SLK, simultaneous liver kidney.
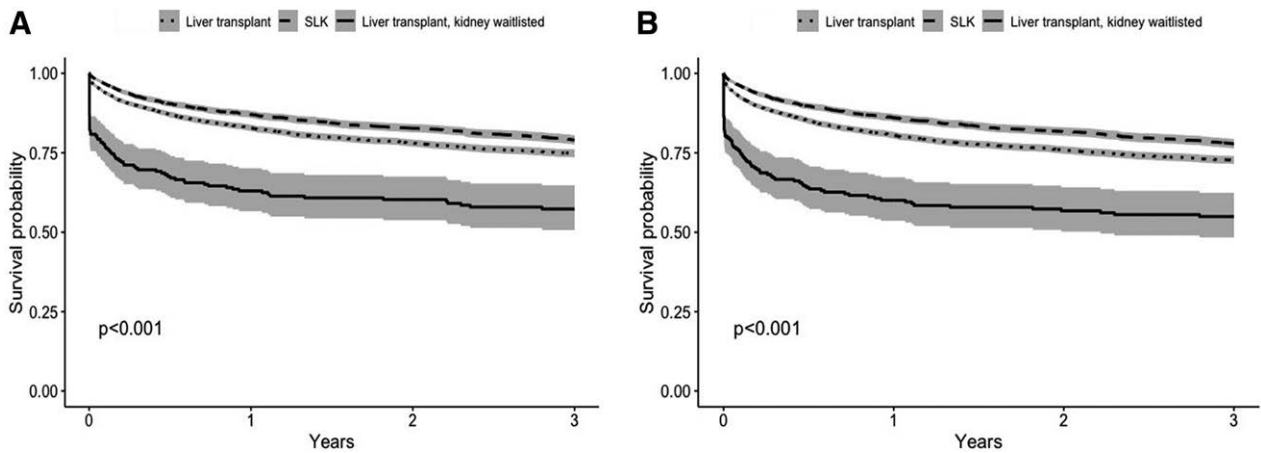
FIGURE 2. Liver transplant alone (LTA) for patients listed for simultaneous liver kidney (SLK) resulted in reduced patient and graft survival post-liver transplant when compared with LTA (no kidney listing) or SLK. A, Illustrates patient survival with 95% confidence interval (CI) for Group 1 (LTA, dots), Group 2 (SLK, dash), and Group 3 (LTA while listed for SLK, solid line). Patient survival for Group 1 was 82.8% (81.8%–83.9%), Group 2 was 87% (85.9%–88.2%), and Group 3 was 63% (56.3%–69.8%). B, Illustrates liver allograft survival for the same groups with 95% CI. For liver graft survival at 1 y, Group 1 was 80.6% (79.5%–81.6%), Group 2 was 86% (84.9%–87.2%), and Group 3 was 60.1% (53%.2–66.9%) ($P < 0.001$ for A and B by Kaplan–Meier analysis).

TABLE 2.

Patient survival and graft survival by group, excluding patients with <2 days post-LT survival

Survival post-LT (y)	Group 1 Liver transplant alone, not listed for kidney (n = 5251)	Group 2 Simultaneous liver kidney transplant (n = 3395)	Group 3 Liver transplant alone, listed for kidney (n = 162)	P
Patient survival (%) ± SE, y				<0.001
1	85 ± 0.5	88 ± 0.6	77 ± 3.3	
3	76 ± 0.6	80 ± 0.7	70 ± 3.7	
Liver graft survival (%) ± SE, y				<0.001
1	82 ± 0.5	87 ± 0.6	73 ± 3.5	
3	74 ± 0.6	78 ± 0.8	67 ± 3.8	

There was a significant difference in both patient and graft survival at 1- and 3-y post-LT between the groups.
LT, liver transplant; SE, standard error.

1 and 2. Kidney graft survival at 1 year was 84.1% for Group 2, which is comparable to what has been reported for KT alone in the Scientific Registry of Transplant Recipients annual report.[27] The mean Scr at 3, 6, and 12 months was higher for Group 3 than for Groups 1 and 2 ($P < 0.001$; Table 3).

Prognostic Factors

In order to understand what factors are associated with reduced patient and graft survival in Group 3, a series of univariate and multivariate analyses were conducted. The number of days on dialysis before LT significantly impacted patient and graft survival in Group 3, while not impacting Group 2. As shown in Table 4, 1–year patient survival for Group 3 decreased from 73% to 69% to 46% for 30 days, 31–90 days, and >90 days of dialysis before transplant, respectively ($P = 0.004$). Liver graft survival decreased from 71% to 66% to 43% for the same time periods ($P = 0.002$). The test for interaction showed a significant difference in the effect of days on dialysis between Group 2 and Group 3 ($P < 0.001$).

For Group 2, recipient factors which impacted patient survival on univariate analysis included age ($P = 0.035$), DM ($P < 0.001$), and MELD score ($P = 0.038$) (Table 5). Donor factors including age ($P < 0.001$), hypertension ($P = 0.003$), smoking history ($P = 0.033$), and KDPI ($P < 0.001$) also impacted patient survival for Group 2 on univariate analysis.

The only factors which significantly impacted survival in this group on multivariate analysis were recipient history of diabetes ($P = 0.002$), MELD score ($P = 0.01$), and donor KDPI ($P = 0.025$) (Table 5). For Group 3, the only factors which impacted patient survival on univariate and multivariate analysis were age (>60 y) and number of days on pre-LT dialysis (>90 days) (multivariate $P < 0.001$ and $P = 0.001$, respectively) (Table 6).

DISCUSSION

In the present study, when comparing outcomes among patients listed for SLK who received either SLK versus LTA, the data demonstrate that proceeding with LTA in this population results in decreased graft and patient survival, particularly among patients >60 years of age and with >90 days of HD. Ultimately, only a small proportion of these patients (7.4%) undergo KT within 3 years post-LT. Thus, individual programs should carefully consider when to proceed with LTA in patients listed for SLK.

Before the implementation of the UNOS listing guidelines for SLK transplant candidates, individual centers were given latitude to select which patients could receive SLK versus LTA, which led to significant variability between centers due to the lack of standardized criteria. As a result, the ability to
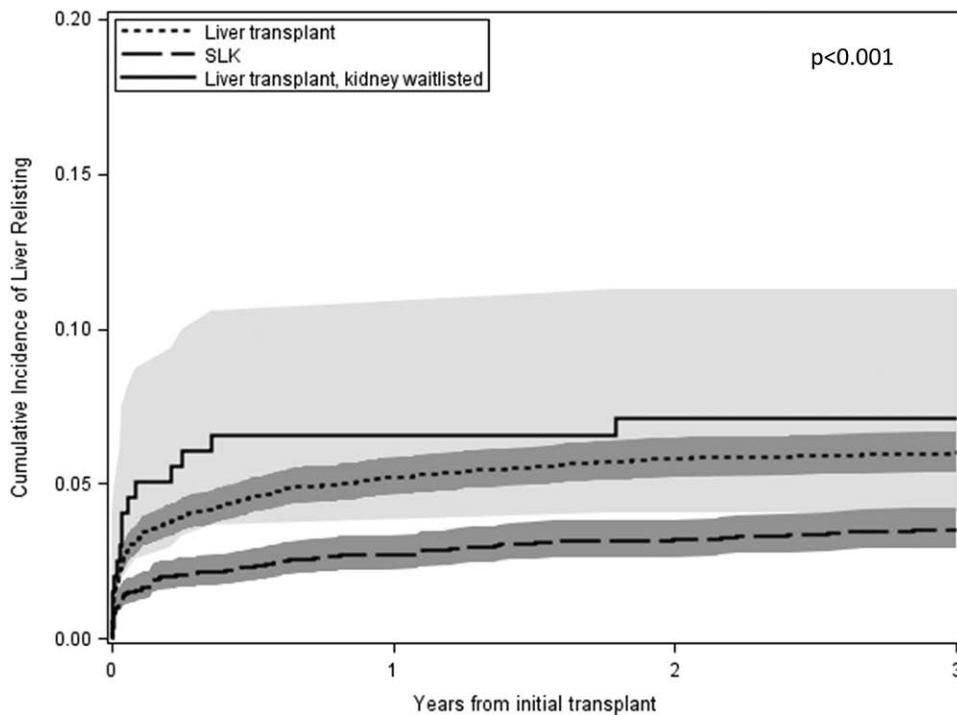
FIGURE 3. Cumulative incidence of post-liver transplant (LT) liver relisting (with 95% confidence interval) by group demonstrates higher rates of relisting for Group 3 (liver transplant alone [LTA]) vs Group 1 (LTA, no kidney listing) and Group 2 (simultaneous liver kidney [SLK]). The rate of relisting at 1 y post-LT was 5.2% (4.6%–5.8%) for Group 1 (dots), 2.7% (2.2%–3.3%) for Group 2 (dashes), and 6.6% (3.7%–10.6%) for Group 3 (solid line) ($P<0.001$).
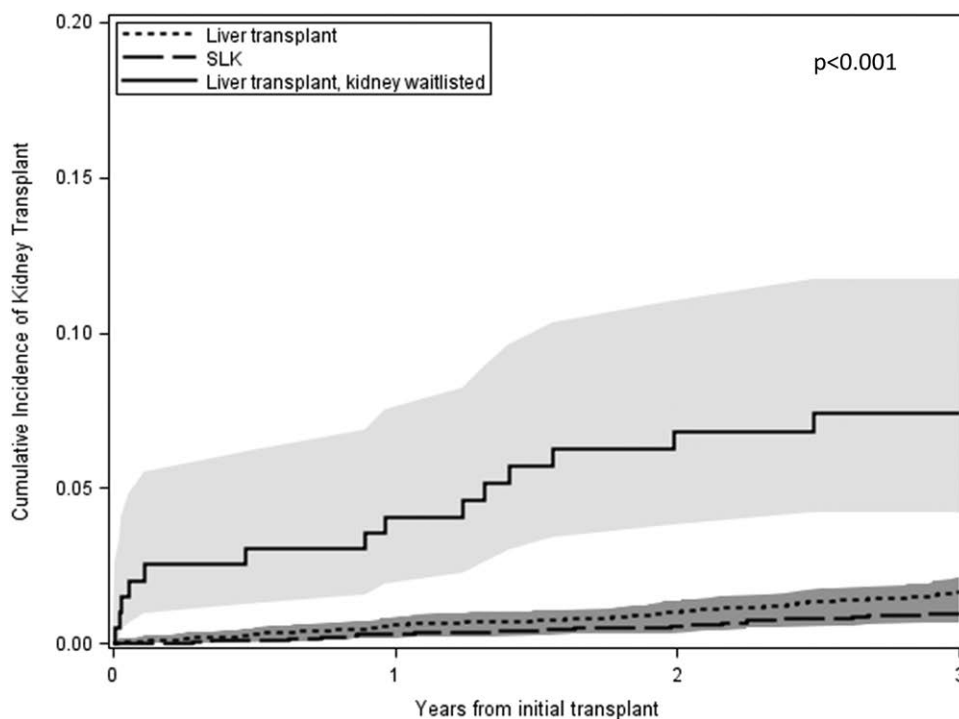
FIGURE 4. Cumulative incidence of post-liver transplant kidney transplant (KT) (with 95% confidence interval) by group demonstrated that Group 3 (liver transplant alone [LTA]) had high rates of KT compared with Group 1 (LTA, no kidney listing) and Group 2 (simultaneous liver kidney [SLK]). At 1 y, the cumulative incidence of post-LT KT was 0.6% (0.4%–0.8%) in Group 1 (dots), 0.3% (0.2%–0.5%) in Group 2 (dashes), and 4.1% (1.9%–7.5%) in Group 3 (solid line).

definitively predict when and if renal function will return post-LTA, the potential impact of poor renal function on post=LT outcomes, and the lack of a mechanism to undergo KT in an expedited fashion post-LT, have all contributed to a rise in the frequency of SLK. Over time, two concerns arose, leading to a reevaluation of this strategy. Firstly, there was the concern that post-LT patients on the KT waiting list would have to wait a prolonged amount of time and secondly, with time, it was

TABLE 3.

Mean Scr at 3, 6, and 12 mo by group

Time post-LT (mo)	Group 1 Liver transplant alone, not listed for kidney		Group 2 Simultaneous liver kidney transplant		Group 3 Liver transplant alone, listed for kidney		P
	n	Mean Scr (mg/dL) ± SE	n	Mean Scr (mg/dL) ± SE	n	Mean Scr (mg/dL) ± SE	
3 mo	262	1.6 ± 0.07	185	1.5 ± 0.08	7	3.4 ± 0.42	<0.001
6 mo	3515	1.7 ± 0.02	2355	1.4 ± 0.02	105	2.7 ± 0.11	<0.001
12 mo	2966	1.7 ± 0.02	2046	1.4 ± 0.03	91	2.5 ± 0.12	<0.001

There was a significant difference in mean Scr at 3, 6, and 12 mo post-LT between the groups.
LT, liver transplant; Scr, serum creatinine; SE, standard error.

TABLE 4.

Patient and liver graft survival by days on dialysis for Group 2 and Group 3

Days on dialysis	Group 2 Simultaneous liver kidney transplant			Group 3 Liver transplant alone, listed for kidney		
	n	1-y survival (%) ± SE	P	n	1-y survival (%) ± SE	P
Patient survival, d						
1–30	755	87 ± 1.2	0.10	62	73 ± 5.7	0.004
31–90	601	84 ± 1.5		35	69 ± 7.8	
>90	1568	88 ± 0.8		48	46 ± 7.2	
Liver graft survival, d						
1–30	755	86 ± 1.3	0.21	62	71 ± 5.8	0.002
31–90	601	83 ± 1.5		35	66 ± 8.1	
>90	1568	87 ± 0.9		49	43 ± 7.1	

Bold values indicate statistical significance ($p<0.05$).
There was a significant difference in both patient and graft survival when days on dialysis pre-LT was compared between Group 2 and Group 3.
LT, liver transplant; SE, standard error.

evident that many patients in all 3 groups recovered function in their native kidneys. Recent studies have shown that nearly half (48.3%) of kidney allografts for SLK had KDPI <35%, suggesting that many high-quality kidneys were being diverted to SLK recipients.[28,29] In the present study, our analysis of donor criteria was consistent with these findings (Tables 5 and 6), where SLK recipients were noted to have younger donors with lower terminal creatinine and lower KDPI.

In mid-2017, UNOS updated the policy for eligibility for SLK and established the "safety net" policy allowing prioritization of kidney graft allocation to LTA recipients with renal dysfunction in their first year following LT, in an attempt to improve outcomes while preventing unnecessary SLK listings.[30] Some would argue, however, that the eligibility criteria for patients with AKI are still too liberal since a significant number of these LTA recipients recover their native renal function.[31] A preliminary analysis of LT data following the safety net policy change showed an overall decrease in SLK transplants, a smaller number of deceased donor kidney allografts going to LT recipients, and more LT recipients utilizing the safety net to get a subsequent KT.[32] Following the implementation of the new criteria, the year 2018 was the first in nearly a decade where the number of SLK did not exceed the amount performed during the previous year (677 SLK performed in 2018 from 739 performed in 2017).[2]

In patients listed for SLK, a multifactorial combination of recipient and donor characteristics influences the decision of waiting for an appropriate dual organ donor or proceeding with LTA, while allowing a period of time to assess for

renal recovery.[24,33] Our results demonstrated that kidney-listed patients with high MELD scores were more likely to undergo LTA as opposed to SLK (Table 1). In these patients with advanced liver disease and high 90-day mortality, poor prognosis paired with apparent clinical deterioration may make the option of a more expeditious LTA necessary. This may also explain our findings that patients in region 5 were more likely to undergo LTA instead of SLK, as region 5 has one of the highest acuities and mean MELD scores at the time of transplant in the United States.[34] However, since many high MELD patients would obtain the greatest benefit from SLK, the implications of performing LTA in these higher-risk patients must be carefully weighed when deciding whether LTA or SLK should be performed and will likely be driven by patient, center, and/or region specific concerns.

Improved survival following SLK is not a unique finding and the data reported here confirms what is well known. The primary purpose of this analysis was to facilitate decision-making related to proceeding without a kidney in dual-listed patients. Our data demonstrated that the SLK group had younger donors with lower KDPIs, less diabetes and hypertension, and lower creatinine. Conversely, donors for Group 3 were older with higher KDPI and more comorbidities, and as such likely contributed to the decision to forego KT. The transplant team must weigh the benefit of moving ahead with a transplant earlier in a sick patient versus awaiting a suitable donor for a combined organ transplant. To inform this decision, we have identified certain risk factors which contribute to poor outcome following LTA, specifically, prolonged

TABLE 5.

Three-y patient survival and univariable and multivariable analyses of simultaneous liver kidney transplant patients (Group 2)

Variable	n	3-y patient survival (%) ± SE	Univariable hazard ratio (95% CI)	Univariable *P*	Multivariable hazard ratio (95% CI)	Multivariable *P*
Recipient age, y				**0.035**		0.14
≤50	913	82 ± 1.4	1.00		1.00	
51–60	1430	77 ± 1.2	1.29 (1.06-1.57)		1.23 (0.99-1.53)	
>60	1071	79 ± 1.4	1.17 (0.94-1.44)		1.09 (0.86-1.39)	
Sex				0.16		
Male	2228	78 ± 0.9	1.00			
Female	1186	81 ± 1.2	0.89 (0.75-1.05)			
Ethnicity				0.44		
White	2082	79 ± 0.9	1.00			
Black	500	76 ± 2.0	1.13 (0.91-1.40)			
Hispanic	638	81 ± 1.7	0.91 (0.74-1.12)			
Other	194	78 ± 3.1	1.05 (0.75-1.45)			
Region				0.31		
1	134	79 ± 3.6	1.15 (0.75-1.76)			
2	344	74 ± 2.6	1.43 (1.08-1.90)			
3	481	78 ± 2.1	1.14 (0.86-1.50)			
4	378	76 ± 2.4	1.30 (0.98-1.73)			
5	674	81 ± 1.6	1.00			
6	64	86 ± 4.5	0.81 (0.41-1.59)			
7	517	79 ± 1.9	1.13 (0.87-1.48)			
8	190	83 ± 2.8	0.88 (0.59-1.32)			
9	135	78 ± 3.7	1.25 (0.83-1.90)			
10	281	81 ± 2.5	1.04 (0.75-1.46)			
11	216	81 ± 2.8	1.02 (0.71-1.48)			
Diabetes				**<0.001**		**0.002**
No	1980	82 ± 0.9	1.00		1.00	
Yes	1392	75 ± 1.3	1.34 (1.15-1.57)		1.31 (1.10-1.56)	
Days on dialysis, d				0.10		0.31
1–30	755	79 ± 1.6	1.00		1.00	
31–90	601	77 ± 1.8	1.11 (0.88-1.41)		1.20 (0.94-1.54)	
≥90	1568	80 ± 1.1	0.89 (0.73-1.09)		1.06 (0.84-1.34)	
MELD				**0.038**		**0.010**
≤35	2355	80 ± 0.9	1.00		1.00	
36–40	555	77 ± 2.0	1.16 (0.94-1.43)		1.17 (0.91-1.50)	
>40	504	76 ± 2.0	1.30 (1.05-1.60)		1.47 (1.15-1.89)	
Donor age, y				**<0.001**		0.19
≤50	2785	80 ± 0.9	1.00		1.00	
51–60	480	77 ± 2.0	1.45 (1.19-1.78)		1.12 (0.85-1.48)	
>60	149	62 ± 4.2	2.32 (1.75-3.09)		1.48 (0.97-2.27)	
Donor diabetes				0.10		0.30
No	4832	79 ± 0.8	1.00		1.00	
Yes	500	74 ± 3.7	1.34 (0.96-1.86)		1.21 (0.84-1.73)	
Donor hypertension				**0.003**		0.29
No	2659	80 ± 0.8	1.00		1.00	
Yes	734	76 ± 1.7	1.31 (1.10-1.56)		0.88 (0.69-1.12)	
Donor history of smoking				**0.033**		0.38
No	4167	80 ± 0.8	1.00		1.00	
Yes	1115	76 ± 1.7	1.22 (1.02-1.45)		1.10 (0.89-1.34)	
KDPI				**<0.001**		**0.025**
0–50	2281	82 ± 0.9	1.00		1.00	
>50–85	903	75 ± 1.5	1.50 (1.26-1.78)		1.40 (1.09-1.79)	
>85	219	68 ± 3.3	2.05 (1.58-2.65)		1.59 (1.01-2.51)	
Donor creatinine (mg/dL)				0.68		
≤2	3275	79 ± 0.8	1.00			
>2	137	79 ± 3.7	1.02 (0.69-1.51)			

CI, confidence interval; KDPI, kidney donor profile index; MELD, Model of End-Stage Liver Disease; SE, standard error.

Three-y patient survival and univariable and multivariable analyses of liver transplant alone while listed for SLK (Group 3)

Variable	n	3-y patient survival (%) ± SE	Univariable hazard ratio (95% CI)	Univariable *P*	Multivariable hazard ratio (95% CI)	Multivariable *P*
Recipient age, y				**0.003**		<0.001
≤50	62	65 ± 6.2	1.00		1.00	
51–60	74	65 ± 5.7	1.00 (0.56-1.78)		0.77 (0.40-1.49)	
>60	62	40 ± 6.3	2.17 (1.27-3.71)		2.47 (1.34-4.56)	
Gender				0.58		
Male	111	59 ± 4.7	1.00			
Female	87	56 ± 5.4	1.13 (0.73-1.74)			
Ethnicity				0.16		
White	120	59 ± 4.6	1.00			
Black	28	42 ± 9.5	1.60 (0.91-2.81)			
Hispanic	42	66 ± 7.5	0.79 (0.44-1.43)			
Other	8	38 ± 17.1	1.84 (0.73-4.62)			
Region				0.69		
1	7	57 ± 18.7	1.25 (0.38-4.16)			
2	20	73 ± 10.7	0.61 (0.23-1.61)			
3	27	50 ± 10.0	1.29 (0.65-2.55)			
4	8	25 ± 15.3	2.55 (1.04-6.27)			
5	61	62 ± 6.3	1.00			
6	3	33 ± 27.2	2.13 (0.50-9.05)			
7	34	56 ± 8.6	1.24 (0.65-2.37)			
8	8	63 ± 17.1	1.10 (0.33-3.66)			
9	8	50 ± 17.7	1.27 (0.44-3.66)			
10	12	67 ± 13.6	0.88 (0.30-2.54)			
11	10	50 ± 15.8	1.46 (0.55-3.83)			
Diabetes				0.73		
No	127	58 ± 4.4	1.00			
Yes	69	55 ± 6.1	1.08 (0.69-1.70)			
Days on dialysis, d				**0.009**		**0.001**
1–30	62	66 ± 6.1	1.00		1.00	
31–90	35	69 ± 7.8	0.99 (0.48-2.06)		1.07 (0.51-2.23)	
>90	49	40 ± 7.1	2.24 (1.27-3.93)		2.63 (1.48-4.65)	
MELD				0.12		
≤35	100	50 ± 5.1	1.00			
36–40	43	72 ± 6.8	0.54 (0.29-1.01)			
>40	55	58 ± 6.7	0.84 (0.51-1.38)			
Donor age, y				0.85		
≤50	143	57 ± 4.2	1.00			
51–60	38	55 ± 8.2	0.97 (0.57-1.67)			
>60	17	65 ± 11.6	0.79 (0.34-1.82)			
Donor diabetes				0.90		
No	180	57 ± 3.8	1.00			
Yes	16	56 ± 12.4	1.05 (0.48-2.28)			
Donor hypertension				0.75		
No	136	59 ± 4.3	1.00			
Yes	60	55 ± 6.5	1.08 (0.68-1.71)			
Donor history of smoking				0.88		
No	136	58 ± 4.3	1.00			
Yes	59	55 ± 6.5	1.04 (0.65-1.65)			
KDPI				0.96		
0–50	99	59 ± 5.1	1.00			
>50–85	71	56 ± 5.9	1.06 (0.66-1.70)			
>85	27	56 ± 9.6	1.07 (0.56-2.05)			
Donor creatinine (mg/dL)				0.28		
≤2	178	56 ± 3.8	1.00			
>2	20	70 ± 10.3	0.65 (0.28-1.49)			

Bold values indicate statistical significance (*p*<0.05).
CI, confidence interval; KDPI, kidney donor profile index; MELD, Model of End-Stage Liver Disease; SE, standard error; SLK, simultaneous liver kidney.

pretransplant RRT duration >90 days and recipient age >60 years. This finding is expected, given the decreased likelihood of renal recovery after LT in recipients with chronic RRT compared with those with a more acute nature of renal dysfunction. Our findings demonstrated that duration of RRT had a significant effect in patient survival and liver graft survival for Group 3; however, it did not impact Group 2. It is important to note that duration of dialysis and glomerular filtration rate are only captured as UNOS variables for patients listed for KT, and as such there was insufficient data regarding renal dysfunction in Group 1, which may include some patients who were not listed for SLK, underwent LTA, and eventually were listed for KT.

The reasons for proceeding with LTA in Group 3 were not available in this dataset. In an effort to better understand this group, the time and causes of death were reviewed. Of the 198 patients in this group, 36 patients died within 2 days of transplant. The majority of these patients died from cardiopulmonary arrest, while few died secondary to uncontrolled hemorrhage or pulmonary embolism. Assuming that these patients were either too unstable for the renal transplant or died before the renal transplant could be performed, the 1-year patient and liver allograft survival after excluding recipients surviving <2 days still remained statistically lower for Group 3. Unfortunately, the lack of granular data related to cause of death in the UNOS dataset prevents detailed determination of the role of persistent renal failure in deaths for patients in Group 3, where cardiac arrest, multiple organ system failure, and infection were the most common reported etiologies.

Predicting de novo renal dysfunction following LT and renal recovery in patients with pre-LT AKI or CKD is an area of ongoing research. By anticipating recovery of renal function after LTA, SLK could be reserved for those with a decreased chance of recovery, allowing high-quality kidney allografts to be used in kidney alone recipients. Renal biopsies can be useful to help determine reversibility of some types of renal failure; however, complications associated with these biopsies may prevent their widespread usage; thus, blood markers would be favorable.[35] While this is an exciting area of ongoing research, recent studies have failed to demonstrate an association between serum and urine biomarkers with renal function recovery, highlighting the importance of further multicenter studies to derive novel biomarkers, as they have a promising role as an adjunct in the determination of whether to proceed with SLK or LTA.[36-38]

There are several limitations to the present study. Firstly, while utilization of a large database allows for a substantial sample size, certain factors are not available for analysis. These include, for example, important recipient characteristics such as etiology of renal dysfunction, the adequacy, frequency, and patient compliance with HD, as well as duration of pretransplant renal dysfunction without RRT. Also, the total number of patients in Group 3 is low, although the distribution of patients over the study period illustrates a similar increase over time as SLK patients in Group 2 (**Figure S1, SDC,** http://links.lww.com/TXD/A222). Before the implementation of the safety net KT mechanism, the small number of LTA patients who underwent KT within 1 year of LT did not allow for an accurate comparison between this group and SLK recipients. It can be anticipated that this number will go up as more centers proceed with LTA under the umbrella of the safety net policy. Given the lower survival for LTA in patients who have

been deemed to require a kidney, as the numbers increase, it is more important to utilize predictive clinical prognostic factors in the decision-making process.

In conclusion, the lack of accurate predictors of renal function recovery among patients on RRT who are awaiting LT still poses a significant challenge in the decision to perform SLK versus LTA. The updated policy for SLK listing criteria was an important step in addressing the increasing number of SLK transplants being performed, allowing the prioritization for KT in patients with renal dysfunction during the first year following LTA. However, for patients on prolonged pretransplant dialysis (>90 days) and those older than 60 years, the decision to forego SLK for LTA must be carefully considered as they may have significantly poorer outcomes with LTA. Further studies are needed to evaluate the outcomes between these groups as soon as long-term follow-up data from safety net recipients become available.

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