Propensity Score-Based Survival Benefit of Simultaneous Liver-Kidney Transplant Over Liver Transplant Alone for Recipients With Pretransplant Renal Dysfunction

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The survival benefit of simultaneous liver-kidney transplantation (SLKT) over liver transplantation alone (LTA) is unclear from the current literature. Additionally, the role of donor kidney quality, measured by the kidney donor risk index (KDRI), in survival benefit of SLKT is not studied. We compared survival benefit after SLKT and LTA among recipients with similar pre-transplant renal dysfunction using novel methodology, specifically with respect to survival probability and area under the survival curve by dialysis status and KDRI. Data were obtained from the Scientific Registry of Transplant Recipients. The study cohort included patients with pre-liver transplantation (LT) renal dysfunction who were wait-listed and received either a SLKT (n = 1326) or a LTA (n = 4283) between March 1, 2002 and December 31, 2009. Inverse Probability of Treatment Weighting–SLKT and LTA survival curves, along with the 5-year area under the survival curve, were computed by dialysis status at transplant. The difference in the area under the curve represents the average additional survival time gained via SLKT over LTA. For patients not on dialysis, SLKT resulted in a significant 3.7-month gain in 5-year mean posttransplant survival time. The decrease in mortality rate differs significantly by KDRI, and an estimated 76% of SLKT recipients received a kidney with KDRI sufficiently low for mortality. The mortality decrease for SLKT was concentrated in the first year after transplant. The difference between SLKT and LTA 5-year mean posttransplant survival time was 1.4 months and was non-significant for patients on dialysis. In conclusion, the propensity score-adjusted survival among SLKT and LTA recipients was similar for those who were on dialysis at LT. Although statistically significant, the survival advantage of SLKT over LTA was of marginal clinical significance among patients not on dialysis and occurred only if the donor kidney was of sufficient quality. These results should be considered in the ongoing debate regarding the allocation of kidneys to extra-renal transplant candidates. Liver Transpl 22:71-79, 2016. © 2015 AASLD.

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Abbreviations: AKI, acute kidney injury; BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; Cr, creatinine; DRI, donor risk index; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; GFR, glomerular filtration rate; HCV, hepatitis C virus; HR, hazard ratio; HRS, hepatorenal syndrome; ICU, intensive care unit; INR, international normalized ratio; IPTW, Inverse Probability of Treatment Weighting; KDRI, kidney donor risk index; LT, liver transplantation; LTA, liver transplantation alone; MELD, Model for End-Stage Liver Disease; MDRD, Modified Diet in Renal Disease; OPTN, Organ Procurement and Transplantation Network; OR, odds ratio; RIFLE, Risk, Injury, Failure, Loss, and End-Stage Kidney Disease; SLKT, simultaneous liver-kidney transplantation; SRTR, Scientific Registry of Transplant Recipients.

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Model for End-Stage Liver Disease (MELD)-based allocation, adopted in 2002, has been successful in achieving the goals put forth by the Institute of Medicine in 1999 of decreasing wait-list mortality among liver transplantation (LT) candidates by promoting the efficient use of scarce donor organs.\textsuperscript{1,2} Compared to the pre-MELD era, the MELD era has witnessed a substantial increase in the proportion of candidates with pre-LT renal dysfunction and in the rates of simultaneous liver-kidney transplantation (SLKT).\textsuperscript{3-5} Candidates who meet the specific criteria for SLKT can be listed for kidney transplant at or subsequent to the time of initial listing for LT. Such patients are allocated both organs from the same deceased donor on the basis of their MELD score.

SLKT listing criteria are straightforward for LT candidates with end-stage renal disease (ESRD) and stage 4 chronic kidney disease (CKD).\textsuperscript{5-7} However, recommended SLKT listing criteria are not very clear for candidates with acute kidney injury (AKI) deemed irreversible.\textsuperscript{5-7} In 2006, SLKT was not recommended for candidates with AKI who were not on renal replacement therapy.\textsuperscript{5} Since then, these listing criteria have changed many times. The duration of AKI (with dialysis) recommended for SLKT listing has decreased from 8 to 4 weeks.\textsuperscript{5-7} More recently, a consensus report from 2012 recommends candidates with persistent AKI for \textsuperscript{$\geq$}4 weeks with either stage 3 AKI based on modified Risk, Injury, Failure, Loss, and End-Stage Kidney Disease (RIFLE) criteria or estimated glomerular filtration rate (eGFR) $\leq$ 35 mL/minute (Modified Diet in Renal Disease [MDRD]–6 equation) or glomerular filtration rate (GFR) $\leq$ 25 mL/minute (iothalamate clearance) to be considered for SLKT listing,\textsuperscript{5} even though the evidence behind these recommendations are lacking. One survey study showed that 60% of transplant physicians do not use RIFLE criteria in their practice.\textsuperscript{4}

There is a wide variation in the SLKT rates across all 11 Organ Procurement and Transplantation Network (OPTN) regions.\textsuperscript{4} Some centers have pursued SLKT to maximize the outcomes of their patients who have pretransplant renal dysfunction.\textsuperscript{4,8} The data regarding favorable outcomes for SLKT recipients over liver transplantation alone (LTA) among patients with pre-LT renal dysfunction are conflicting in the current literature with some studies showing advantage and some showing no survival advantage of SLKT over LTA.\textsuperscript{8-13} Furthermore, there remained a wide variation in the definition of AKI in these studies.\textsuperscript{9,10,13} Although many studies attempted to restrict their sample patients with some degree of renal dysfunction, few studies attempted to distinguish between patients receiving pretransplant dialysis (versus not). Moreover, to the best of our knowledge, no previous study has examined the survival benefit of SLKT in contrast to LTA with similar pretransplant renal dysfunction with respect to kidney donor quality, as measured by the kidney donor risk index (KDRI),\textsuperscript{14} which is a strong predictor of kidney graft failure and, hence, patient survival.

We aimed to determine the survival benefit of SLKT over LTA by dialysis status before transplant for recipients with pretransplant renal dysfunction. The secondary aim was to determine whether the survival benefit of SLKT relative to LTA depends on kidney donor, as reflected by the KDRI.

**PATIENTS AND METHODS**

**Study Population**

The study was based on data obtained from the Scientific Registry of Transplant Recipients (SRTR). The SRTR maintains a database of all candidates for and recipients of solid organ transplants in the United States. Candidates on waiting lists for organ transplantation and those who receive organ transplants are tracked on a periodic basis with the use of data collection forms completed by organ transplant programs and submitted to the OPTN at the time of placement on the wait list (transplant candidate registration form); status updates for MELD scores and other clinical measures while the candidate is wait-listed, at the time of LT (transplant recipient registration form), and during follow-up are required at 6 months after transplant, 1 year after transplant, and yearly thereafter (transplant follow-up form).\textsuperscript{15} These data, in addition to data from the OPTN regarding candidates on the waiting list and the allocation of organs, are included in the SRTR database.\textsuperscript{16} These publically available data can be acquired through a data use agreement from the SRTR. This study was approved by the University of Michigan institutional review board.

The selection of the study population is displayed in Fig. 1. The first screen was that both wait listing and LT had to occur at age $\geq$ 18 years and between March 1, 2002 and December 31, 2009. Status 1, living donor, retransplant, and multiorgan transplant recipients other than SLKT were excluded. The next screen was evidence of pretransplant renal dysfunction, defined as either receipt of dialysis or having creatinine (Cr) $\geq$ 2.0 mg/dL at the time of LT. Next, we excluded LTA patients who underwent transplantation at a center that performed no SLK transplants during the study period. The final exclusion was applied to ensure overlap in the propensity score distributions, with the propensity score (described in the analytic approach) reflecting the probability of receiving an SLKT (versus LTA) given the patient’s characteristics. Note that the cutoff value for serum Cr was based on Davis et al.\textsuperscript{6} and Eason et al.\textsuperscript{7} recommendations of Cr $\geq$ 2.0 mg/dL and/or dialysis $\geq$ 8 weeks as listing criteria for SLKT for candidates with AKI/hepatorenal syndrome (HRS). These criteria were appropriate for our sample selection because our study cohort was representative of that era.

Patients were followed up from the date of LT to the earliest of posttransplant death, loss to follow-up, or end of observation period (December 31, 2009). The primary outcome was posttransplant mortality.
Analytic Approach

Preliminary SLKT Versus LTA Contrasts Through Cox Regression

Preliminary analysis was carried out using Cox regression. Specifically, separate covariate-adjusted SLKT/LTA hazard ratios (HRs) were estimated for time since transplant windows 0 to 1 year, 1 to 2 years, and >2 years after transplant. Adjustment covariates included age, sex, race, diagnosis, serum bilirubin, serum Cr, international normalized ratio (INR), serum albumin, hepatic encephalopathy, ascites, blood type, body mass index (BMI), time from wait listing to transplant, calendar year of transplant, estimated slope of Cr trajectory from wait list to transplant, and percentage of time on dialysis from wait list to transplant, liver donor risk index (DRI), and center. The Cr slope was only computed when the patient was not receiving dialysis.

Allowing the SLKT/LTA HRs to depend on time since transplant alleviates the assumption of proportionality regarding the SLKT and LTA hazards. Limitations of such an approach include potential difficulties in interpreting the SLKT effect, and the fact that proportionality is still assumed for all adjustment covariates. In particular, difficulty in interpreting a set of time-dependent HRs (that change direction over time) motivates the examination of survival curves, which we now describe.

Contrasts between survival curves (eg, estimated by the Kaplan-Meier method) are typically of interest when treatment is randomized. The need for covariate adjustment characteristic of observational studies typically produces a shift in focus to HR estimated through Cox regression. Despite the well-established utility of Cox regression, the shift in focus from the survival curve to the HR is itself undesirable, because differences in survival probability are more easily interpreted and have greater clinical relevance than ratios of death rates. The focus of our current analysis is on differences between SLKT and LTA specifically with respect to survival probability (and area under the survival curve). For such comparisons to be meaningful, it is necessary to factor out imbalances between the SLKT and LTA adjustment covariate distributions. We accomplish this by inverse weighting based on the propensity score.

Development of Propensity Score

For each patient, the propensity score is a monotone function of the probability of receiving a SLKT (as opposed to a LTA) given the patient’s covariate pattern. Imbalances between the SLKT and LTA recipients were factored out using the well-established Inverse Probability of Treatment Weighting (IPTW). Applying IPTW to our set-up, each SLKT patient is divided by the probability of receiving SLKT (versus LTA); ie, the probability of SLKT, given the patient’s particular covariate pattern. Analogously, each LTA patient is divided by the probability of receiving a LTA. The treatment probabilities are based on a logistic regression model with response variable defined as a 0 to 1 indicator for SLKT. Essentially, IPTW creates 2 weighted populations with the same covariate distributions. Used in this context, IPTW serves a purpose similar to the weighting commonly used in survey sampling. An advantage of IPTW is that it avoids
choices regarding caliper size or cut points essential to matching methods.

The weights used in the IPTW were based on a logistic regression model with a 0 and 1 outcome coded as 1 for SLKT patients and 0 for LTA patients. Covariate selection for these models consisted of several steps. First, a model with the following covariates was fitted: age, sex, race, diagnosis, serum bilirubin, serum Cr, INR, serum albumin, hepatic encephalopathy, ascites, blood type, BMI, time from wait listing to transplant, calendar year of transplant, estimated slope of Cr trajectory from wait list to transplant, and percentage of time on dialysis from the wait list to transplant, liver DRI, and center.

From this list, covariates having \( P < 0.10 \) were then retained. For this first step, center was adjusted through a set of indicator covariates, with the center having the greatest number of transplants chosen as the reference. From this model, the center-specific odds ratios (ORs) were ordered, and the center with the median OR was chosen as the new reference. The model was then refitted in order to identify centers with \( P \geq 0.10 \), which were then combined with the reference. We then fitted the final model, through which the propensity scores (and, hence, probabilities of SLKT and LTA) were estimated. Note that the above-described algorithm was carried out separately for on-dialysis and not-on-dialysis patients. In each case, the logistic model was found to be quite accurate in terms of discrimination, as evidenced by an index of concordance (area under the receiver operating characteristic curve) of \( C = 0.83 \) (patients not on dialysis) and \( C = 0.84 \) (on dialysis). For model validation, we randomly split each of the on-dialysis and not-on-dialysis samples into 10 mutually exclusive groups. For each of 10 iterations, we then used 9 groups to fit the model (training sample) and computed the C index using the “tenth” group. The C index was then computed as a weighted average across the 10 iterates.

Comparing SLKT and LTA Survival Curves

For the main part of the analysis, inverse-weighted survival curves were computed nonparametrically for the SLKT and LTA subgroups, by dialysis status. The IPTW weighting was intended to produce SLKT and LTA groups (by dialysis status at transplant) with the same adjustment covariate distribution. The area under each of the SLKT and LTA survival curves was also computed. Differences between the curves were estimated, along with 95% confidence intervals (CIs). The total area between the average SLKT and LTA survival curves was estimated, along with 95% CIs. Standard errors and CIs were computed based on the bootstrap.

KDRI and Posttransplant Mortality: Cox Regression

Cox regression was used to examine the effect of KDRI on post-LT mortality among SLKT recipients.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Dialysis, n (%)</th>
<th>Cr ≥ 2.0 mg/dL, n (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLKT</td>
<td>892 (67%)</td>
<td>434 (33%)</td>
<td>1326</td>
</tr>
<tr>
<td>LTA</td>
<td>1288 (30%)</td>
<td>2995 (70%)</td>
<td>4283</td>
</tr>
<tr>
<td>Total</td>
<td>2180 (39%)</td>
<td>3429 (61%)</td>
<td>5609</td>
</tr>
</tbody>
</table>

The model was adjusted for aforementioned covariates and a SLKT × KDRI interaction term and was fitted to only patients not on dialysis.

All statistical analyses were conducted using SAS, version 9.3 (SAS Institute, Cary, NC).

RESULTS

Selection of Study Population and Posttransplant Deaths

A schematic diagram of the study population selection is presented in Fig. 1. A total of 1884 and 31,882 candidates were wait-listed and underwent SLKT and LTA, respectively, at age \( \geq 18 \) years between March 1, 2002 and December 31, 2009; these numbers include only primary transplants and nonstatus 1 patients. After excluding patients who did not meet our definition of pretransplant renal dysfunction (who were neither on dialysis nor had serum Cr \( \geq 2.0 \) mg/dL), a total of 1768 SLKT and 4996 (ie, 1499 + 3497) LTA patients remained. We then excluded patients transplanted at centers that did not perform any SLKT during the study observation period, which reduced the sample size to 1768 SLKT and 4939 LTA patients.

To enforce overlap in the SLKT and LTA propensity score distributions, we excluded extremely high- or low-probability transplant recipients (ie, patients with propensity scores present in only the SLKT or only the LTA group). Such propensity score–based exclusions reduced the final sample size to 1326 SLKT and 4283 LTA patients (Fig. 1, last 2 columns). Therefore, the final study population consisted of 70% of the 1884 original SLKT recipients and only 13% of the original 31,882 LTA recipients. Naturally, our objective in selecting the study population was not to get a representative sample of LTA patients but to exclude subgroups of LTA patients unlikely to be comparable to the SLKT recipients. Sixty-seven percent of SLKT and 30% of LTA recipients were on dialysis at LT (Table 1). The median MELD score of SLKT recipients (MELD score = 28.9) was lower than LTA recipients (MELD score = 32.4).

For patients not on dialysis, there were 83 and 795 posttransplant deaths among SLKT and LTA patients, respectively. Among patients receiving dialysis, there were 230 SLKT and 382 LTA deaths.
Preliminary SLKT Versus LTA Contrasts Through Cox Regression

For patients not on dialysis (Fig. 2A), SLKT is associated with a significant 49% mortality reduction during the first posttransplant year (HR = 0.51; P < 0.001). The SLKT/LTA HR is not significant after 1 year and shows an uprising trend that increases above 1 (note that HR = 1 corresponds to equality between SLKT and LTA) implying that the mortality rate is eventually higher for SLKT after 2 years of follow-up, albeit not significantly so (HR = 1.48; P = 0.09).

A somewhat similar pattern is observed for dialysis patients (Fig. 2B). The trend over follow-up time in the HR for SLKT/LTA was similar as that for not-on-dialysis patients (ie, the HR increase with increasing follow-up time). For dialysis patients, the mortality rate decrease in follow-up year 1 is less pronounced and not significant (HR = 0.80; P = 0.08), and the rise in the HR is more pronounced.

Results depicted in Fig. 2A,B are useful for descriptive purposes only and could not be used to determine the effect of SLKT on survival, individually or in aggregate. For example, the HR for 0 to 1 years only applies until 1 year after transplant. Conversely, the >2 year HR only applies after a patient has already survived 2 years after LT. There are no established methods in the survival analysis literature for formally combining 0 to 1, 1 to 2, and >2 year HRs, which is particularly important here because the HR changes direction as post-LT follow-up time increases.

Propensity Score: Probability of SLKT

Table 2 enlisted the adjustment covariates (P < 0.1) used in the final propensity score models for patients who were not on dialysis (Table 2, top) and on dialysis (Table 2, bottom). Centers were included in the propensity score but not shown in these tables because of the space considerations.
Checking Balance Between the Weighted SLKT and LTA Samples

The IPTW weighting was intended to produce SLKT and LTA groups (by dialysis status) with the same adjustment covariate distribution. To check this, we estimated a prognostic score for each patient using the covariates identified in the Cox regression (predictors of posttransplant mortality). Transplant type was handled through stratification in this model, akin to nonparametric adjustment. On the basis of this model, a HR can be computed for each patient based on their adjustment covariate pattern. The prognostic score is then the Log (ie, ln) of the patient-specific HR. Without inverse weighting (IPTW), the mean prognostic score was significantly different for dialysis patients ($P < 0.001$) and for patients not on dialysis ($P < 0.01$). However, differences between SLKT and LTA mean prognostic scores were not significantly different for either patients on dialysis ($P = 0.46$) or not on dialysis ($P = 0.4$). This is evidence that the inverse weighting eliminated potential bias due to imbalances between the SLKT and LTA mortality risk factor distributions. Having verified comparability between the inverse-weighted SLKT and LTA populations, we now compare their respective inverse-weighted survival curves.

Comparison of LKT Over LTA Survival Curves

For each of SLKT and LTA, inverse-weighted survival curves were computed. This produced survival curves for the hypothetical SLKT and LTA cohorts of the same size and with the same adjustment covariate distribution.

As shown in Fig. 3A, among patients not on dialysis, the SLKT survival curve lies above the LTA curve quite consistently during the first 5 years after transplant. Figure 3B displays the difference in inverse-weighted survival curves (SLKT–LTA), along with pointwise 95% CIs. The area between the survival curves is 3.7 months, indicating that on average, SLKT is associated with a 3.7-month expected gain in survival time during 0 to 5 years after transplant. Figure 3B displays the difference in inverse-weighted survival curves (SLKT–LTA), along with pointwise 95% CIs. In Fig. 3B, when the difference between average SLKT and LTA posttransplant survival was evaluated at significant time points, it was mild (ranged between 0% and 10%) and generally nonsignificant (pointwise CIs including the null value, 0). However, the SLKT curve clearly dominated the LTA curve. In an effort to gain a more comprehensive assessment, we evaluated the total difference between SLKT and LTA survival curves over 0- to 5-year intervals; this amounts to totaling the area between the 0 line and SLKT–LTA difference (from Fig. 3B) or equivalently the area between the SLKT and LTA survival curves (Fig. 3A). As tabulated in Fig. 3B, this difference of 0.31 years (≈3.7 months) was significant.

Figure 3. (A) Inverse-weighted posttransplant survival: not-on-dialysis. (B) Difference in inverse-weighted posttransplant survival probability (SLKT minus LTA): not-on-dialysis and 95% CI.

Similar patterns were observed for patients on dialysis in Fig. 4A,B. However, the trend toward increased survival for SLKT was not nearly as pronounced for those SLKT recipients who were on dialysis at transplant than LTA recipients who were not on dialysis at transplant. As shown in Fig. 4B, the average number of life years gained by SLKT compared to LTA is an estimated 0.12 years (≈1.4 months), which was not significant ($P = 0.3$).

Posttransplant Among SLKT by KDRI

The distribution of KDRI among SLKT patients not on dialysis was shown in Fig. 5. On the basis of this model, the SLKT/LTA HR was found to increase significantly ($P = 0.01$) with increasing KDRI, indicating that the survival advantage of SLKT (relative to LTA) diminished significantly as KDRI increased. The adjusted posttransplant mortality rate among SLKT recipients with KDRI $\leq 1.1$ (accounted for 76% of SLKT) was significantly lower than that for LTA recipients. However, the adjusted post-LT mortality rates for SLKT with KDRI > 1.1 (24% of SLKT) were not different than LTA recipients.

DISCUSSION

The results of our study showed no difference in the posttransplant survival among SLKT and LTA
recipients who were on dialysis at LT and a marginal 3.7-month increase in 5-year mean posttransplant survival for SLKT recipients over LTA among patients with pretransplant renal dysfunction who were not on dialysis. The survival advantage in the not-on-dialysis group was mainly concentrated in the first year of SLKT. Furthermore, the decrease in mortality associated with SLKT was further restricted to recipients who received a donor kidney of sufficiently low KDRI.

In the dialysis group, it is possible that patients who received SLKT had either ESRD or AKI that was deemed irreversible, whereas patients who received LTA most likely had AKI (HRS) and were likely to have renal recovery after LTA. Assuming that the appropriate treatments (SLKT versus LTA) were assigned to appropriate candidates with pretransplant renal dysfunction on dialysis, their posttransplant survival should be similar. From this perspective, our finding of no difference in mean 5-year posttransplant survival for SLKT versus LTA could be interpreted as demonstrating the accuracy of the transplant community with respect to differentiating between irreversible and reversible kidney disease among dialysis patients.

In their study, they also demonstrated 15% higher risk of graft failure associated with SLKT compared to LTA among those who were on recent pretransplant dialysis, although it was not a statistically significant difference.8

Our definition of pretransplant renal dysfunction was based on the Cr cutoff used by Eason et al.7 and Davis et al.6 and mirrored the prevalent practice patterns representative of 2002 to 2009. Serum Cr is generally a poor measure of renal function, and the eGFR by MDRD equation underestimate the GFR, especially when the measured GFR is <40 mL/minute.24 Moreover, liver allocation is prioritized by MELD score, and serum Cr is one of the overweighted components of MELD.25 Therefore, we used serum Cr measurements despite its inherent weakness to define pretransplant renal dysfunction. One study that evaluated the survival advantage of SLKT defined pretransplant renal dysfunction as eGFR of <60 mL/minute, which is a very generous definition because greater than 50% of transplant recipients have eGFR <60 mL/minute.13 Moreover, the cutoff for the listing for SLKT is <30 mL/minute.

Although most previous studies, like ours, have shown improved overall survival associated with SLKT compared to LTA especially in those with pretransplant renal dysfunction,8,9,11,13 the survival advantage varied based on dialysis status.9,10 Fong et al.9 showed that survival advantage of SLKT was independent of pretransplant dialysis status, whereas Schmitt et al.10 showed no survival advantage of SLKT (versus LTA) among those who were not on dialysis before transplant despite using the similar definition of pretransplant renal dysfunction (serum Cr ≥2.5 mg/dL). In contrast to both these studies, our study of 5962 patients, which used a serum Cr ≥2.0 mg/dL as renal dysfunction to be consistent with the consensus recommendation and practice pattern(s) of the cohort, showed a significant survival advantage to those SLKT recipients who were not on dialysis.
dialysis before transplant. Because the survival advantage was mainly concentrated in the first year of transplant, improved renal function following SLKT may be responsible for lower mortality during perioperative and immediate postoperative period in this subgroup.

The KDRI provides a continuous risk score accounting for all donor and transplant factors independently associated with all-cause kidney allograft failure. GDRI values exceeding 1.0 have higher expected risk than the median donor, and vice versa. Our study showed that three-fourths of the SLKT recipients received a high-quality kidney allograft. These findings were in line with the data from Reese et al. who showed that higher-quality renal allografts were going to multiorgan transplant recipients including SLKT. The better organ quality for both kidney and liver in addition to relatively better liver function at LT (median MELD score 29 which is mainly driven by renal function) may attribute to survival benefit among SLKT recipients who were not on dialysis at transplant. These observations raise another ethical question that better-quality organs (liver as well as kidney) are directed toward the SLKT recipients, therefore driving these organs (liver) away for LTA and (kidneys) away from the kidney transplant recipients as shown by Reese et al.

Current listing practices for SLKT are not evidence-based. The duration of dialysis and renal dysfunction among those with AKI has been reduced from 8 to 6 weeks to more recently 4 weeks for listing for SLKT in the 2012 consensus conference. This change in listing practices may further increase SLKT rates and affect the pool of deceased donor kidney candidates by draining the deceased donor kidney allograft from kidney-alone candidates.

It is clear that there exists a selection bias because of variability in clinical judgment, listing, and transplanting practices for SLKT because of a lack of use of criteria for SLKT listing by individual centers. Our comparison between SLKT and LTA survival was the most comprehensive to date, with distinguishing features that included the following:

1. Explicit restriction of the study population to promote comparability between the SLKT and LTA groups.
2. Use of propensity scoring through IPTW, instead of standard adjustment through Cox model covariates.
3. Additional restriction of the study sample based on the propensity score, such that the sample selection had an empirical component.
4. Expression of the main study finding as differences in area under the survival curve (5-year mean survival time), instead of HRs.
5. Examination of the interaction between SLKT and renal allograft quality via the KDRI.
6. Addition of center to the propensity score to account for center-level variation in the utilization of SLKT.

Limitations of this study include its observational study design, which could result in selection bias and unmeasured confounding. Registry data lack granularity and do not include urine analysis data. Because it is difficult to ascertain CKD/ESRD and AKI based on serum Cr and dialysis information in the SRTR database, there may be dissimilarity in the 2 groups; ie, residual to our having adjusted for the duration of dialysis as well as the slope of Cr (between listing and transplant) in order to ascertain the duration of renal dysfunction. Our use of propensity scores is a particular strength of the current study. Adjustment covariates are typically accounted for through inclusion in a Cox model. We found that a Cox model fitted to our study population had an index of concordance of C = 0.62, much lower than the logistic regression models which were the basis of our propensity scoring (patients not on dialysis, C = 0.83; on dialysis, C = 0.84). The best way to examine the survival advantage of SLKT in those with AKI could be through a randomized clinical trial of SLKT versus LTA, which could be unethical for this group of patients.

In conclusion, the clinical importance of the marginal additional 5-year post-LT mean survival time associated with SLKT among those who are not on dialysis should be considered in the ongoing debate regarding the allocation of kidneys to extra-renal transplant candidates.

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