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Simultaneous Liver-Kidney versus Liver Transplantation Alone in Patients with End-Stage Liver Disease and Kidney Dysfunction Not on Dialysis

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Abstract

Background—Since implementation of the Model for End-Stage Liver Disease (MELD), the number of simultaneous liver-kidney transplantations (SLKT) has increased in the US. However, predictors and survival benefit of SLKT compared to liver transplantation alone (LTA) are not well defined.

Methods—Organ Procurement and Transplantation Network data of patients with End-Stage Liver Disease (ESLD) with estimated GFR (eGFR) < 60 ml/minute/1.73m² who had not been on dialysis while on the waiting list and underwent liver transplantation between 2002 and 2008 were analyzed. To identify predictors of undergoing SLKT vs. LTA, multiple logistic regression analysis was performed. Cox proportional hazards regression analysis was used to assess the association between SLKT and post liver transplant patient and graft survival.

Results—The study cohort comprised 5443 patients; 262 (5%) underwent SLKT and 5181 (95%) underwent LTA. Adjusting for potential confounders, patients who underwent SLKT were 34% less likely to die after liver transplantation than those who underwent LTA (hazard ratio [HR]=0.66, P=0.012) and 33% less likely to have liver graft failure than those who underwent LTA (HR=0.67, P=0.010). Among those who underwent SLKT, 1-, 3- and 5-year kidney graft

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survival probabilities were 88%, 80% and 77%, respectively. Black race and diabetes were associated with a higher likelihood of SLKT vs. LTA; female sex, a higher eGFR and higher MELD score reduced the likelihood of SLKT.

Conclusions—Among those with ESLD and kidney dysfunction not on dialysis, post-liver transplant patient and liver graft survivals of patients who underwent SLKT were superior to those of patients who underwent LTA. Whether this reflects differences in the two groups that could not be adjusted in survival models or a specific effect of kidney dysfunction cannot be established.

Keywords

Simultaneous liver-kidney transplantation; liver transplantation; end-stage liver disease; glomerular filtration rate; CKD-EPI equation

INTRODUCTION

In the United States, the shortage of donor organs for transplant requires that kidneys be allocated to patients with the greatest need. In 2009, 16,829 patients underwent kidney transplantation (1). Nonetheless, based on Organ Procurement and Transplantation Network (OPTN) data as of August 5, 2011, 89,285 patients remained on the United Network for Organ Sharing (UNOS) kidney waiting list (1).

Since the Model for End-Stage Liver Disease (MELD) was adopted to prioritize patients for liver transplantation in 2002 (2-4), simultaneous liver-kidney transplantation (SLKT) has become more frequent (5-8). The MELD score is calculated from the serum creatinine, total bilirubin and international normalized ratio (INR) (2-4). Emphasis placed on serum creatinine in calculating MELD scores might result in unexpected consequences regarding liver or liver-kidney allocation. First, transplant candidates with well-compensated cirrhosis but with advanced kidney dysfunction may receive a higher priority for liver transplantation (5, 9). Second, a transplant candidate with ESLD may undergo SLKT rather than LTA in the presence of a reversible kidney dysfunction. This removes a potential donor kidney from the pool available to patients with end-stage renal disease. On the other hand, renal failure is associated with worse outcomes in liver transplant recipients (10). Thus, SLKT is a justifiable approach to improving survival in these patients.

In an effort to prevent unnecessary kidney transplantation in patients with ESLD on the liver transplant waiting list, in 2009, the International Liver Transplantation Society convened an expert panel to develop consensus criteria to indicate which liver transplant waiting list patients should be candidates for SLKT (11). According to these criteria, among those not on dialysis, patients with ESLD and chronic kidney disease (CKD) with a glomerular filtration rate (GFR) < 30 ml/minute/1.73m² and proteinuria > 3 g/day, not on dialysis should be listed for SLKT (11).

To evaluate these criteria, we investigated whether those who meet these criteria and receive SLKT have a survival advantage over those who meet these criteria and receive LTA. In addition, since we found that many patients who had $eGFR \geq 30$ and < 60 ml/minute/1.73m² also received SLKT, we explored whether SLKT conferred a survival advantage in that group. Finally, we determined clinical and demographic variables associated with receiving SLKT vs. LTA.

METHODS

Study Population

The analysis was based on Organ Procurement and Transplantation Network data as of November 27, 2009. Patients with ESLD and $eGFR < 60$ ml/minute/1.73m² (at last follow-up on the waiting list), who had never been on dialysis while on the liver transplant waiting list and underwent liver transplantation between February 27, 2002 and September 27, 2008 were included in the analysis. Transplant recipients younger than 18 years, exceptional (e.g., hepatocellular carcinoma who received a priority MELD score) and status 1 cases (e.g., acute liver failure), those with a diagnosis other than ESLD, and those receiving living-donor LT or simultaneous multiorgan transplantation other than SLKT were excluded. Patients who were on dialysis anytime on the liver transplant waiting list were excluded. Dialysis status was ascertained from UNOS liver transplant waiting list history data that was updated periodically for each transplant candidate from the time of initial registration until removal from the waiting list.

Variables

Patients' demographic, clinical and laboratory variables at the last follow-up on the liver transplant waiting list and donor variables were used in the analysis. For serum creatinine and $eGFR$, values at both registration and last follow-up were used. $eGFR$ was calculated using the CKD Epidemiology Collaboration (CKD-EPI) equation (12) and categorized according to National Kidney Foundation Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines for CKD (13, 14). The World Health Organization classification was used to categorize body mass index (BMI) (15).

Statistical Analysis

Statistical analyses were performed using SAS software, Version 9.2 (Cary, NC) (16). The statistical significance of differences between patients who underwent SLKT and LTA with respect to categorical variables was assessed using the Chi-square test. For quantitative variables, the Wilcoxon Rank-Sum test was used to assess differences between patients who underwent SLKT and LTA. Multiple stepwise logistic regression analysis was used to determine pretransplant predictors of undergoing SLKT vs. LTA (entry and stay cutoff levels were set at 0.05). Goodness-of-fit of the multivariable logistic model was assessed and confirmed by Hosmer and Lemeshow Goodness-of-Fit test (17) ($P=0.137$).

Patient survival time was defined as the time from a patient's first transplant to death irrespective of whether they had additional transplants. Liver graft survival was defined as the time from first liver transplant until the first liver graft failure/death. Kidney graft survival was defined as the time from first liver transplant until the first kidney graft failure/death in patients who underwent SLKT. Patients alive at the end of follow-up or whose grafts had not failed by the end of follow-up were considered right-censored in the analysis. For univariate analysis, the Kaplan-Meier method was used to estimate the survival function (18). Survival functions in those who underwent SLKT and LTA were compared by the log-rank test (19, 20). For multivariate analysis, Cox proportional hazards regression analysis (21) was used to assess the association between the recipient/donor variables and post liver transplant patient, liver and kidney graft survival, controlling for potential confounders. Variables that had a P value < 0.10 in univariate Cox models were included in the multivariable Cox models. Non-proportional hazards were assessed by introducing interactions terms between follow-up time and predictor. Those with P values < 0.05 were included to allow for non-proportional hazards.

RESULTS

Characteristics of Patients at Last Follow-up on the Liver Transplant Waiting List

After excluding patients who did not fulfill inclusion criteria, we included 5443 patients. Among these 5443 patients, 262 (5%) underwent SLKT and 5181 (95%) underwent LTA (Table 1). Among 262 patients who underwent SLKT, there were 199 (76%) patients with $\text{eGFR} < 30 \text{ ml/minute/1.73m}^2$, 42 (16%) with $\text{eGFR} \geq 30$ and $< 40 \text{ ml/minute/1.73m}^2$, 15 (6%) with $\text{eGFR} \geq 40$ and $< 50 \text{ ml/minute/1.73m}^2$ and 6 (2%) with $\text{eGFR} \geq 50$ and $< 60 \text{ ml/minute/1.73m}^2$.

The median waiting time on the liver transplant waiting list did not differ between patients who underwent SLKT and LTA (58 vs. 55 days, $P=0.186$). Median total bilirubin and INR at last follow-up on the waiting list were significantly lower in patients who underwent SLKT compared to those who underwent LTA (total bilirubin, 2.7 vs. 4.7 mg/dl, $P<0.0001$; INR, 1.6 vs. 1.7, $P=0.0003$). Patients who underwent SLKT had significantly higher median serum creatinine and lower eGFR at both registration and last follow-up on the waiting list than patients who underwent LTA (serum creatinine at registration, 2.3 vs. 1.4 mg/dl, $P<0.0001$; serum creatinine at last follow-up, 2.7 vs. 1.7 mg/dl, $P<0.0001$; eGFR at registration, 29.2 vs. 53.1 ml/minute/1.73m², $P<0.0001$; eGFR at last follow-up on the waiting list, 23.9 vs. 39.8 ml/minute/1.73m², $P<0.0001$). The proportion of patients with diabetes was significantly greater for SLKT compared to LTA (41% vs. 25%, $P<0.0001$). Patients who underwent SLKT had significantly lower median cold (6.5 vs. 7.0 hours, $P=0.004$) and warm ischemia time (36 vs. 40 minutes, $P=0.001$) than those who underwent LTA. The median serum creatinine was significantly lower in women than men at both registration (1.2 vs. 1.5 mg/dl, $P<0.0001$) and last follow-up on the waiting list (1.6 vs. 1.9 mg/dl, $p<0.0001$). Nonetheless, women had significantly reduced eGFR compared to men at both listing (49.4 vs. 53.5 ml/minute/1.73m², $P<0.0001$) and last follow-up on the waiting list (36.7 vs. 40.1 ml/minute/1.73m², $P<0.0001$).

Pre-Liver Transplant Predictors of Undergoing SLKT instead of LTA

Based on multivariable logistic model that was controlled for region, sex, diabetes, eGFR and MELD (Table 2), black patients were 2.91 times more likely to undergo SLKT than LTA compared to non-black patients (Odds Ratio [OR]=2.91, $P<0.0001$). In the same model, patients with diabetes were 1.76 times more likely to undergo SLKT (OR=1.76, $P<0.0001$). For every 1 unit increase in MELD score, the odds of undergoing SLKT decreased by 8% (OR=0.92, $P<0.0001$). Women were 50% less likely to have SLKT vs. LTA when controlling for eGFR and other variables in the model (OR=0.50, $P<0.0001$). For every 1 ml/minute/1.73m² increase in eGFR, the odds of undergoing SLKT decreased by 10% (OR=0.90, $P<0.0001$). When we controlled for serum creatinine in the model in place of eGFR, the association between gender and SLKT disappeared (OR=1.08, $P=0.614$). We also obtained similar results for hazard ratios when we replaced MELD score with total bilirubin and INR in the multivariable logistic model; women were 44% less likely to undergo SLKT vs. LTA (OR=0.56, $P<0.0001$). When we controlled for serum creatinine in the model in place of eGFR, the association between gender and SLKT disappeared (OR=1.098, $P=0.523$).

Post-Liver Transplant Patient Survival

In univariate analysis, post-liver transplant patient survival was greater in those who underwent SLKT (1-year, 3-year and 5-year survival probabilities were 89%, 82%, 78%, respectively) compared to those who underwent LTA (1-year, 3-year and 5-year survival probabilities were 85%, 78%, 72% respectively). This difference approached statistical significance ($P=0.076$).

However, after controlling for potential confounders in the multivariable model, patients who underwent SLKT were 34% less likely to die after liver transplantation than those who underwent LTA (hazard ratio [HR]=0.66, $P=0.012$) (Table 3). In the same model, independent predictors of post-liver transplant mortality included black race compared to other races, HCV-associated cirrhosis, diabetes, life support, age, donor age, reduced eGFR and INR (Table 3). For every 1 ml/minute/1.73m² increase in eGFR, the risk of death decreased by 1%. For every 1 unit increase in INR, the risk of death increased by 11%. In univariate models, significant non-proportional hazards were detected for hepatitis C, being on life support at transplantation, INR, eGFR and total bilirubin at last follow-up on the waiting list. Interaction terms between time and these variables to account for these non-proportional hazards were included in the final model (those with a P value < 0.05 are shown in Table 3).

To assess whether the survival benefit of SLKT depended on the severity of kidney dysfunction, we fit the same multivariable models in subgroups of those with eGFR < 30 ml/minute/1.73m² and those with eGFR ≥ 30 ml/minute/1.73m² and < 60 ml/minute/1.73m². The survival benefit among those with eGFR < 30 ml/minute/1.73m² (HR=0.73, $P=0.070$) was not as strong as among those with eGFR ≥ 30 ml/minute/1.73m² and < 60 ml/minute/1.73m² (HR=0.41, $P=0.047$). However, the observed difference in the HRs between the two eGFR groups was not statistically significant ($P=0.196$).

Post-Liver Transplant Liver Graft Survival

Patients who underwent SLKT had significantly greater liver graft survival (1-year, 3-year and 5-year survival probabilities were 87%, 80%, 77%, respectively) compared to those who underwent LTA (1-year, 3-year and 5-year survival probabilities were 83%, 75%, 69%; respectively) ($P=0.037$).

After controlling for potential confounders in the multivariable model, patients who underwent SLKT were 33% less likely to have liver graft failure than those who underwent LTA (HR=0.67, $P=0.010$) (Table 4). In the same model, independent predictors of liver graft failure included black race, HCV-associated cirrhosis, diabetes, life support, age, donor age, non-heart beating donor, cold ischemia time, reduced eGFR and INR (Table 4). For every 1 ml/minute/1.73m² increase in eGFR, the risk of liver graft failure decreased by 1%. For every 1 unit increase in INR, the risk of liver graft failure increased by 9%. In univariate models, significant non-proportional hazards were detected for hepatitis C, being on life support at transplantation, INR, eGFR and total bilirubin at last follow-up. Interaction terms between time and these variables were included in the final model to account for these non-proportional hazards (those with a P value < 0.05 are shown in Table 4).

Post-Liver Transplant Kidney Graft Survival

In univariate analysis, among patients who underwent SLKT, 1-year, 3-year and 5-year kidney graft survival probabilities were 88%, 80% and 77%, respectively. In the multivariable model, independent predictors of kidney graft failure included INR at last follow-up (HR=1.35, $P=0.035$) and donor age ≥ 50 compared with donor age < 23 years (HR=9.15, $P=0.018$). For every 1 unit increase in INR, the risk of kidney graft failure increased by 35%. In univariate models, significant non-proportional hazards were detected for donor age and hepatitis C and included in the model. For every 1 year post-liver transplant, the impact of donor age ≥ 50 years diminished by 79% ($P=0.019$).

DISCUSSION

In the US, emphasis placed on serum creatinine in calculating MELD scores for liver allocation has resulted in a large increase in SLKT for patients with ESLD and advanced kidney dysfunction (5-8). Consequently, the increase in SLKT among patients with ESLD reduces potential donor kidneys available to patients with end-stage renal disease waiting for kidney transplantation. This effect may be justified if there is clear benefit from SLKT compared to LTA.

In our univariate analysis, although post-liver transplant survival probability was greater for those with ESLD and kidney dysfunction not on dialysis who underwent SLKT than for those who underwent LTA, the difference was not statistically significant. However, liver graft survival was significantly higher among those who underwent SLKT compared to those who underwent LTA. Also, controlling for recipient and donor characteristics, our results revealed that among patients with ESLD and kidney dysfunction not on dialysis, both post-liver transplant patient and liver graft survivals were superior to those who underwent LTA. Among patients who underwent SLKT, kidney graft survival was almost identical to liver graft survival.

Our findings differ from results of previous analyses of UNOS data. Schmitt *et al.* (22) analyzed UNOS data from 2002-2006, considering patients with ESLD on the waiting list and not on dialysis. They found no significant difference in post-LT survival between those who underwent SLKT and those who underwent LTA (22). This difference may be explained by different study populations. The analysis of Schmitt *et al.* (22) was based on patients with greater kidney dysfunction (serum creatinine > 2.5 mg/dl) and did not exclude patients who might have been on dialysis part of the time on the waiting list. In contrast, we included patients with eGFR < 60 ml/minute/1.73m² using the CKD-EPI equation and excluded those on dialysis at any time during their waiting list experience. Our subgroup analysis revealed that SLKT might be more protective on post-liver transplant survival among patients with eGFR ≥ 30 ml/minute/1.73m² and < 60 ml/minute/1.73m² (HR=0.41, P=0.047) compared to those with eGFR < 30 ml/minute/1.73m² (HR=0.73, P=0.070). These findings may explain why Schmitt *et al.* (22) did not find significant survival benefit of SLKT vs. LTA among those with serum creatinine > 2.5 mg/dl on the waiting list, but not on dialysis.

Gonwa *et al.* (23) analyzed post-liver transplant outcomes of patients who underwent SLKT and LTA in the pre-MELD and MELD eras extending from 1999 until 2004. Combining both pre-MELD and MELD eras, they found that among patients with serum creatinine ≥ 2.0 mg/dl who were not on dialysis on the liver transplant waiting list, those who underwent SLKT had similar survival rates to those who underwent LTA (23). However, they did not adjust for differences between patients who underwent SLKT and LTA among those with serum creatinine ≥ 2.0 mg/dl who were not on dialysis on the liver transplant waiting list; and those who received an SLKT were likely to have had greater kidney dysfunction (23). Also, their analysis included a wider range of patients than our study including children and patients with different etiologies (i.e. acute liver failure, hepatocellular carcinoma, cirrhosis, metabolic and other liver diseases) (23). Our population is restricted to ESLD and eGFR < 60 ml/minute/1.73m², not on dialysis who underwent liver transplantation only in the MELD era (7 years of MELD experience vs. 34 months of MELD experience in Gonwa *et al.*) (23).

In our study cohort, patients who had SLKT appeared to have less severe liver disease and more advanced kidney dysfunction than patients who underwent LTA; with significantly lower median total bilirubin and INR at transplantation. This could be due to the emphasis

placed on serum creatinine in calculating MELD scores (5, 9). Transplant candidates with well-compensated cirrhosis but with advanced kidney dysfunction may have received a higher priority for liver transplantation (5, 9). These results are similar to those in Schmitt *et al.* (22). One can conclude that these factors may account for greater post-liver transplant survival probability in patients who underwent SLKT than those who underwent LTA. However, even after we controlled for these factors in the Cox model, post-liver transplant survival remained significantly greater for those who underwent SLKT.

Our results suggest that patients progressed to more advanced kidney dysfunction while on the liver transplant waiting list. Of patients with stage 1 and 2 kidney disease at listing; 10% who underwent SLKT and 39% who underwent LTA had progressed to stage 3 to 5 kidney disease before transplantation (Table 1).

Our results also revealed gender disparity for undergoing SLKT vs. LTA. After controlling for MELD, eGFR and potential confounders, women were significantly less likely than men to have SLKT (Table 2). However, when controlling for serum creatinine level, the gender disparity almost disappeared. This suggests that decisions regarding whether to perform a SLKT are based on serum creatinine rather than GFR. This finding is consistent with our previous report that among patients with kidney dysfunction not on dialysis women had a higher mortality on the liver transplant waiting list (24). This was due, in part, to underestimation of kidney disease when using serum creatinine rather than GFR in calculating the MELD score (24). Women had significantly lower median serum creatinine concentrations than men, both at listing and last follow-up on the waiting list, even though they had lower median eGFR. Women have lower muscle mass on average than men and, therefore, have lower creatinine generation (24-30). Hence, listing women for SLKT vs. LTA based on serum creatinine rather than GFR may result in gender bias (24, 31).

Our results showed that black race and diabetes were independent predictors of undergoing SLKT instead of LTA. These results were anticipated due to the high incidence of renal disease among African-Americans (32). Moreover, in the U.S., diabetes is the most common cause of renal failure (32, 33).

Strengths of our study were that we used GFR estimated by the CKD-EPI equation rather than serum creatinine to determine the severity of kidney dysfunction. Although estimation of GFR by Modification of Diet in Renal Disease (MDRD) is recommended in International Liver Transplantation Society guidelines for SLKT (11), the CKD-EPI equation was shown to be more accurate than the MDRD equation for all levels of kidney function, especially for the characterization of mild-moderate renal impairment (12, 34).

We used the UNOS liver transplant waiting list dataset that contains longitudinal updated information regarding the dialysis status of each transplant candidate throughout their stay on the list. By using the UNOS longitudinal dataset, we were able to exclude patients who received dialysis at any time on the waiting list.

Our analysis, based on retrospective data, has limitations. Although among those with ESLD and kidney dysfunction not on dialysis post-liver transplant patient and liver graft survivals of patients who underwent SLKT were superior to those of patients who underwent LTA, we were unable to adjust our survival models for the etiology of kidney disease. Whether higher post-liver transplant patient and liver graft survivals reflect differences in the two groups that could not be adjusted in the survival models or a specific effect of kidney dysfunction cannot be established.

In addition, we were unable to verify the accuracy of eGFR by measured GFR. No study has yet assessed the accuracy of the CKD-EPI equation in estimating true GFR in patients with

cirrhosis. However, several studies conducted in cirrhotics document the poor accuracy and precision of both the MDRD and Cockcroft-Gault equations in estimating true GFR (31, 35, 36). One study conducted in cirrhotics reported overestimation of true GFR when Cr-based estimating equations were used in this population (36).

As serum creatinine was measured in different laboratories, we were not able to confirm if a standardized assay was used. Moreover, information regarding potential factors that might affect post-liver transplant outcome (e.g. treatment for hepatitis C, type of immunosuppression, infection, biliary complications) as well as the cause of death was limited. In addition, as there were no standardized criteria for considering SLKT, multiple factors may have played a role in listing candidates for SLKT rather than LTA. By including transplant center-specific practices, these unmeasured differences between patients who underwent SLKT and LTA have almost certainly confounded our results. Based on these limitations, there is a need for multicenter prospective trial to assess the outcome of SLKT vs. LTA in patients with ESLD and kidney dysfunction not on dialysis.

In conclusion, based on the results of our retrospective analysis, among patients with ESLD and kidney dysfunction not on dialysis, those who underwent SLKT appear to have significant patient and liver graft survival advantage compared to those who underwent LTA. In addition, it should be recognized that for each new patient undergoing SLKT, one less kidney is available for patients on the kidney transplant waiting list. While black race and diabetes favored undergoing SLKT vs. LTA, female sex, higher eGFR and higher MELD score at last follow-up on the liver transplant waiting list reduced the likelihood of SLKT.

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Table 1

Baseline Characteristics of Patients with ESLD and Kidney Dysfunction not on Dialysis while on Waiting List and who Underwent Liver Transplantation between February 27, 2002 and September 27, 2008*

	SLKT N=262		LTA N=5181		P Value
	N	%	N	%	
Sex					0.0798
Male	180	69	3283	63	
Female	82	31	1898	37	
Race or Ethnicity					0.0001
White	182	69	4028	78	
Black	39	15	351	7	
Hispanic	31	12	627	12	
Asian	6	2	117	2	
Other	4	2	58	1	
Etiology of Cirrhosis					0.9124
Hepatitis C	109	42	2107	41	
Hepatitis B	9	3	159	3	
Alcohol	56	21	1072	21	
Cryptogenic	31	12	682	13	
Nonalcoholic Fatty Liver Disease	23	9	364	7	
Primary Sclerosing Cholangitis	9	3	185	4	
Primary Biliary Cirrhosis	10	4	255	5	
Autoimmune Hepatitis	6	2	181	3	
Other	9	3	176	3	
GFR_{CKD-EPI} at Registration (ml/min/1.73m²)					<0.0001
≥ 90 (Stage 1)	9	3	654	13	
≥ 60 and < 90 (Stage 2)	17	6	1362	26	
≥ 30 and < 60 (Stage 3)	98	37	2414	47	
≥ 15 and < 30 (Stage 4)	113	43	623	12	
< 15 (Stage 5)	25	10	128	2	

	SLKT N=262	LTA N=5181	P Value
	N	%	%
GFR_{CKD-EPI} at Last Follow-up on the Waiting List (ml/min/1.73m²)			<0.0001
≥ 90 (Stage 1)	0	0	0
≥ 60 and < 90 (Stage 2)	0	0	0
≥ 30 and < 60 (Stage 3)	63	24	71
≥ 15 and < 30 (Stage 4)	148	56	23
< 15 (Stage 5)	51	19	5
Life Support at Transplantation			0.5063
Yes	8	3	4
No	254	97	96
UNOS Region			<0.0001
1	27	10	3
2	24	9	12
3	55	21	16
4	19	7	10
5	27	10	13
6	4	2	3
7	37	14	10
8	17	6	7
9	5	2	7
10	31	12	9
11	16	6	11
ABO Blood Type			0.3774
A	96	37	39
B	40	15	12
AB	17	6	5
O	109	42	44
Diabetes			<0.0001
Yes	108	41	25
No	154	59	75

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	SLKT		LTA		P Value
	N=262		N=5181		
	N	%	N	%	
GFR _{CKD-EPI} at Registration (ml/min/1.73m ²)	29.2	21.1	53.1	34.5	<0.0001
GFR _{CKD-EPI} at Last Follow-up on the Waiting List (ml/min/1.73m ²)	23.9	12.4	39.8	21.8	<0.0001
Cold Ischemia Time (hr)	6.5	3.2	7.0	3.7	0.0039
Warm Ischemia Time (min)	36	22	40	19	0.0006

* Quantitative variables are expressed as median (interquartile range [IQR]). The statistical significance of differences between patients who underwent SLKT and LTA with respect to categorical variables was assessed using the Chi-square test. For quantitative variables, the Wilcoxon Rank-Sum test was used to assess differences between patients who underwent SLKT and LTA.

Table 2
Pretransplant Predictors of Undergoing SLKT vs. LTA in Patients with ESLD and Kidney Dysfunction not on Dialysis while on the Liver Transplant Waiting List and who Underwent Liver Transplantation¹

		Odds Ratio	95% CI	P Value
Black Race	No	1.00		
	Yes	2.91	1.96 4.30	<0.0001
Diabetes	No	1.00		
	Yes	1.76	1.34 2.32	<0.0001
Sex	Male	1.00		
	Female	0.50	0.37 0.67	<0.0001
GFR _{CKD-EPI} at Last Follow-up on the Waiting List (ml/min/1.73m ²)				
		0.90	0.89 0.91	<0.0001
MELD Score at Last Follow-Up on the Waiting List				
		0.92	0.91 0.94	<0.0001

¹ Controlled for region.

Table 3
Multivariate Analysis of Risk Factors for Mortality after Liver Transplantation in Patients with ESLD and Kidney Dysfunction not on Dialysis while on the Liver Transplant Waiting List and who Underwent Liver Transplantation¹

	Hazard Ratio	95% CI	P Value
LTA	1.00		
SLKT	0.66	0.48 0.91	0.012
Black Race	1.00		
	No		
	Yes	1.32 1.07 1.62	0.009
Hepatitis C-associated Cirrhosis ²	1.00		
	No		
	Yes	1.40 1.20 1.64	<0.0001
Diabetes	1.00		
	No		
	Yes	1.27 1.11 1.45	0.0004
Life Support at Transplantation ³	1.00		
	No		
	Yes	2.29 1.70 3.08	<0.0001
Age (yr)	1.00		
	< 50		
	≥ 50 and < 55	0.89 1.27	0.514
	≥ 55 and < 61	1.29 1.08 1.54	0.005
	≥ 61	1.49 1.25 1.78	<0.0001
Donor Age (yr)	1.00		
	< 26		
	≥ 26 and < 43	1.24 1.03 1.50	0.024
	≥ 43 and < 55	1.55 1.29 1.86	<0.0001
	≥ 55	1.83 1.53 2.19	<0.0001
Donor Sex	1.00		
	Male		
	Female	0.99 0.88 1.12	0.846
Type of Transplanted Liver	1.00		
	Split		
	Whole	1.68 0.75 3.77	0.206
GFR _{CKD-EPI} at Last Follow-up on the Waiting List (ml/min/1.73m ²)	0.99	0.98 1.00	0.0002
INR at Last Follow-up on the Waiting List ⁴	1.11	1.06 1.15	<0.0001
Total Bilirubin at Last Follow-up on the Waiting List (mg/dl)	1.00	1.00 1.01	0.274

¹ Controlled for region.

² For every 1 year post-liver transplant, the impact of hepatitis C on mortality increased by 12% ($P=0.020$).

³ For every 1 year post-liver transplant, the impact of being on life support at transplantation on mortality diminished by 22% ($P=0.038$).

⁴ For every 1 year post-liver transplant, the impact of INR at last follow-up on the waiting list on mortality diminished by 5% ($P=0.028$).

Table 4
Multivariate Analysis of Risk Factors for Liver Graft Failure in Patients with ESLD and Kidney Dysfunction not on Dialysis while on the Liver Transplant Waiting List and underwent Liver Transplantation¹

	Hazard Ratio	95% CI	P Value
LTA	1.00		
SLKT	0.67	0.49 0.91	0.010
Black Race	1.00		
	No		
	Yes	1.32 1.09 1.60	0.005
Hepatitis C-associated Cirrhosis ²	1.00		
	No		
	Yes	1.33 1.15 1.54	0.0001
Diabetes	1.00		
	No		
	Yes	1.20 1.06 1.37	0.005
Life Support at Transplantation	1.00		
	No		
	Yes	2.17 1.63 2.88	<0.0001
Age (y)	1.00		
	< 50		
	≥ 50 and <55	0.99 0.84 1.17	0.910
	≥ 55 and <61	1.19 1.01 1.40	0.040
	≥ 61	1.31 1.11 1.54	0.002
Donor Age (y)	1.00		
	< 26		
	≥ 26 and <43	1.24 1.04 1.48	0.016
	≥ 43 and <55	1.55 1.31 1.85	<0.0001
	≥ 55	1.91 1.61 2.26	<0.0001
Donor Sex	1.00		
	Male		
	Female	1.04 0.93 1.16	0.521
Non-Heart Beating Donor	1.00		
	No		
	Yes	1.43 1.10 1.86	0.008
Cold Ischemia Time (h)	1.02	1.00 1.04	0.018
INR at Last Follow-up on the Waiting List ³	1.09	1.05 1.14	<0.0001
GFR _{KD-EPI} at Last Follow-up on the Waiting List (ml/min/1.73m ²)	0.99	0.99 1.00	0.007
Total Bilirubin at Last Follow-up on the Waiting List	1.00	1.00 1.01	0.332

	Hazard Ratio	95% CI	P Value
(mg/dl)			

¹ Controlled for region.

² For every 1 year post-liver transplant, the impact of hepatitis C on mortality increased by 13% (P=0.009).

³ For every 1 year post-liver transplant, the impact of INR at last follow-up on the waiting list on mortality diminished by 5% (P=0.041).