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ORIGINAL ARTICLE

The type, duration, and severity of pretransplant kidney injury predict prolonged kidney dysfunction after liver transplantation

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Abstract

Chronic kidney disease (CKD) is a major complication of liver transplantation (LT) associated with substantial morbidity and mortality. Knowing the drivers of post-LT kidney dysfunction—with a granular focus on the type, duration, and severity of pre-LT kidney disease—can highlight intervention opportunities and inform dual-organ allocation policies. We retrospectively analyzed predictors of safety net kidney after liver transplant (KALT) eligibility and kidney replacement therapy (KRT) for $>$ 14 days after LT. Among 557 recipients of adult deceased-donor LT, 49% had normal kidney function, 25% had acute kidney injury (AKI), and 25% had CKD $\pm$ AKI at the time of LT. A total of 36 (6.5%) qualified for KALT and 63 (11%) required KRT $>$ 14 days. In univariable analysis, factors associated with KALT eligibility and KRT $>$ 14 days, respectively, included stage 3 AKI (OR 7.87; OR 7.06), CKD $\pm$ AKI (OR 4.58; OR 4.22), CKD III-V duration (OR 1.10 per week; OR 1.06 per week), and increasing CKD stage (stage III: OR 3.90, IV: OR 5.24, V: OR 16.8; stage III: OR 2.23, IV: OR 3.62, V: OR 19.4). AKI stage I-II and AKI duration in the absence of CKD were not associated with the outcomes. Pre-LT KRT had a robust impact on KALT eligibility (OR 4.00 per week) and prolonged post-LT KRT (OR 5.22 per week), with 19.8% of patients who received any pre-LT KRT ultimately qualifying for KALT. Eligibility for KALT was similar between those who received 0 days and $\leq$ 14 days of KRT after LT (2.1% vs. 2.9%, $p = 0.53$). In conclusion, the type, duration, and severity of pre-LT kidney dysfunction have unique impacts on post-LT kidney-related morbidity, and future research must use these novel classifications to study mitigation strategies.

Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; DCD, donation after cardiac death; eGFR, estimated glomerular filtration rate; HD, hemodialysis; HRS, hepatorenal syndrome; KALT, kidney after liver transplant; KRT, kidney replacement therapy; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; sCr, serum creatinine; SLK, simultaneous liver-kidney.

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INTRODUCTION

Kidney disease is a major complication of liver transplantation (LT) associated with substantial morbidity, mortality, and health care cost.[1–3] Incidence of kidney disease after LT is increasing—a consequence of an aging population, the rising prevalence of metabolic dysfunction–associated steatotic liver disease with its associated comorbidities (eg, diabetes), and as an unintended result of a Model for End-Stage Liver Disease (MELD)-based allocation system.[4–6] Thus, there have been significant increases in the downstream complications of post-LT kidney disease—specifically, end-stage renal disease, kidney after liver transplant (KALT), cardiovascular disease, and mortality.[1]

Identifying which recipients will develop acute kidney injury (AKI) and/or chronic kidney disease (CKD) after LT is difficult, as post-LT kidney disease represents the additive sequelae of multiple factors that come into play sequentially: (1) recipient factors, such as age and pretransplant kidney dysfunction, (2) donor factors, particularly donation after cardiac death (DCD), (3) intraoperative factors, such as the severity of hepatic ischemia-reperfusion injury, and finally, (4) postoperative factors, including use of calcineurin inhibitors.[2,7–9] Understanding which patients are most at risk for kidney dysfunction post-LT is essential, as there may be opportunities along this continuum of care to prevent adverse outcomes, including the need for prolonged post-LT kidney replacement therapy (KRT) or KALT. Potential examples of interventions include (1) treatment of pre-LT hepatorenal syndrome-acute kidney injury with terlipressin, (2) strategic donor-recipient matching, (3) utilization of normothermic machine perfusion to attenuate ischemia-reperfusion injury, and/or (4) conversion to everolimus-based immunosuppression after LT.[10–12] Detailed knowledge about specific drivers will highlight the key opportunities for impactful interventions while also informing which LT candidates should be considered for dual-organ transplantation.

Many prior studies have examined the risk of AKI and CKD after LT and the role that pre-transplant kidney dysfunction plays in posttransplant outcomes.[2,3,6,13–17] However, few studies have analyzed the severity of these outcomes, such as the duration of KRT required after LT.[13,15,18] Moreover, prior studies fail to accurately account for the type of kidney dysfunction before LT (ie, AKI, CKD ± AKI), duration (ie, days with an estimated glomerular filtration rate [eGFR] < 60 mL/min/1.73m^2, days with an AKI episode), and severity (ie, CKD stage and AKI stage). The data granularity needed for these analyses is often unavailable in large registries.

We therefore investigated the impact of pre-LT kidney dysfunction type, duration, and severity on early kidney-related outcomes at a high-acuity transplant center, specifically qualification for safety net KALT as the primary outcome and the need for KRT beyond 14 days after LT as a secondary outcome. We hypothesized that the 14-day threshold confers a high risk of eligibility for KALT or long-term CKD, as most patients are able to recover from mild to moderate reperfusion injury by this time. In addition, the 14-day threshold often reflects an inflection point where patients will either be discharged on or off KRT, highlighting a substantial burden from both a health care utilization and patient symptom burden perspective.

METHODS

Study population

We conducted a single-center retrospective cohort study using institutional data of adults (age $>$ 18 y) who received an LT at the University of California, San Francisco Medical Center between January 1, 2016 and January 1, 2021. Patients who received living-donor or multi-organ transplants were excluded. All research was conducted in accordance with the Declarations of Helsinki and Istanbul. Retrospective review of trial period data was approved by our Institutional Review Board (IRB 20-31396).

Data collection

Demographic and laboratory data were compiled from 3 sources: (1) the EPIC-based (Verona, WI) electronic health record used at our center, (2) the patient-linked electronic health record embedded within our electronic health record, and (3) a center-based transplant database.

Exposure variables

We determined sociodemographic, clinical, and donor characteristics, as well as laboratory variables at the time of LT, with the exception of kidney dysfunction, which was defined by the severity, type, and duration continuously preceding LT. Waiting time was time from listing to LT.

Kidney function was assessed by analyzing all serum creatinine (sCr) and KRT data starting at the time of transplant and moving backward toward transplant evaluation and beyond, if available. In accordance with the International Club of Ascites, the AKI stage at LT was assessed by comparing sCr at LT to baseline sCr, defined as the most recent sCr value that is $\geq$ 7 days before the episode of AKI.[19] Stage 1, 2, and 3 AKI corresponded to sCr $\geq 1.5 \times$ baseline, $\geq 2 \times$ baseline, and $\geq 3 \times$ baseline or $<$ 72 days of KRT before transplant, respectively. AKI duration was the time from AKI initiation to LT. EGFR was calculated using the race-free creatinine-based 2021 CKD-EPI equation.[20]

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Patients having eGFR $\leq$ 60 mL/min/1.73 m^2 for $\geq$ 90 days or having $\geq$ 72 days of KRT before transplant were categorized as having CKD. CKD stage was determined at the time of LT according to KDIGO guidelines.[21] CKD duration was the number of continuous days of eGFR $\leq$ 60 mL/min/1.73 m^2 before LT. Patients satisfying CKD criteria alone or both CKD and AKI criteria were labeled "CKD $\pm$ AKI" and analyzed together. Patients meeting neither set of criteria were categorized as having normal pretransplant kidney function. Eligibility for simultaneous liver-kidney (SLK) transplantation was determined according to the United Network for Organ Sharing policy.[22]

Outcome variables

Our primary outcome was qualification for safety net KALT. According to the United Network for Organ Sharing policy, patients qualify if they are on KRT or have an eGFR $\leq$ 20 mL/min/1.73 m^2 between 2 and 12 months after LT.[22] Duration of KRT after transplant was the secondary outcome in this study. In particular, we examined patients who required $>$ 14 days of KRT after LT.

Statistical analysis

Categorical variables were compared using χ^2 or Fisher exact tests. Continuous variables, reported using median and IQR, were compared using nonparametric Wilcoxon rank sum or Kruskal-Wallis tests. Univariable and multivariable logistic regression models were used to determine factors associated with qualification for safety net KALT and $>$ 14 days of KRT after LT. We completed multivariable logistic regression using backward selection. We calculated hypothesis-driven interactions between variables after controlling for each set of multivariable model factors identified. Results are expressed as OR with 95% CI. Statistical analyses were performed using R 4.2.1 (Vienna, Austria).[23] Statistical significance was defined by a 2-sided *p*-value less than 0.05.

RESULTS

Population characteristics

Among 802 LTs performed during the study period, 44 pediatric, 133 living donor, and 76 multi-organ transplants were excluded, leaving 557 adults, deceased-donor liver-only transplant recipients in the study (Table 1). Median (IQR) recipient age at transplant was 41 (29–55) years, 376 (68%) were male, and MELD-Sodium was 23 (10–35). Viral hepatitis, including HBV and HBC, was the most common primary

TABLE 1 Population characteristics

Characteristic	n = 557
Donor factors, n (%)	
Age (y)	41 (29–55)
Male	342 (61)
Donation after cardiac death	77 (14)
Recipient factors, n (%)	
Age (y)	60 (54–65)
Male	376 (68)
Race, n (%)	
White	398 (71)
Black	22 (3.9)
Other	137 (25)
Etiology of liver disease, n (%)	
Viral	185 (33)
Alcohol	111 (20)
MASLD	108 (19)
Other	153 (27)
HCC	205 (37)
Waiting time (mo)	11 (2–18)
Laboratory values at transplant	
Serum creatinine (mg/dL)	1.0 (0.8–1.3)
INR	1.7 (1.2–2.5)
Albumin (g/dL)	3.1 (2.7–3.6)
Total bilirubin (mg/dL)	4 (1–14)
Sodium (mEq/L)	136 (133–139)
MELD-Na	23 (10–35)
Hemoglobin A1c (%)	5.7 (5.2–6.4)
Kidney function at transplant, n (%)	
Category	
Normal	274 (49)
AKI	141 (25)
CKD $\pm$ AKI	142 (25)
AKI stage, n (%)	
1	143 (26)
2	21 (3.8)
3	112 (20)
AKI duration, if present (d)	7 (2–20)
CKD stage, n (%)	
III	96 (17)
IV	38 (6.8)
V	8 (1.4)
CKD III-V duration (d)	109 (97–139)
Receiving KRT	111 (20)
KRT duration, if present (d)	4.0 (2.0–6.5)
Qualified for SLK transplant	46 (8.3)
Kidney function after transplant, n (%)	
Discharged on KRT	66 (12)
eGFR at 1 y (mL/min/1.73m^2)	67 (54–87)
Qualified for safety net KALT	36 (6.5)

Note: Continuous variables were reported with median (IQR) and categorical variables were reported with frequency (%).
Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; KALT, kidney after liver transplant; MASLD, metabolic dysfunction–associated steatotic liver disease; MELD-Na, Model for End-Stage Liver Disease-Sodium; KRT, kidney replacement therapy; SLK, simultaneous liver-kidney.

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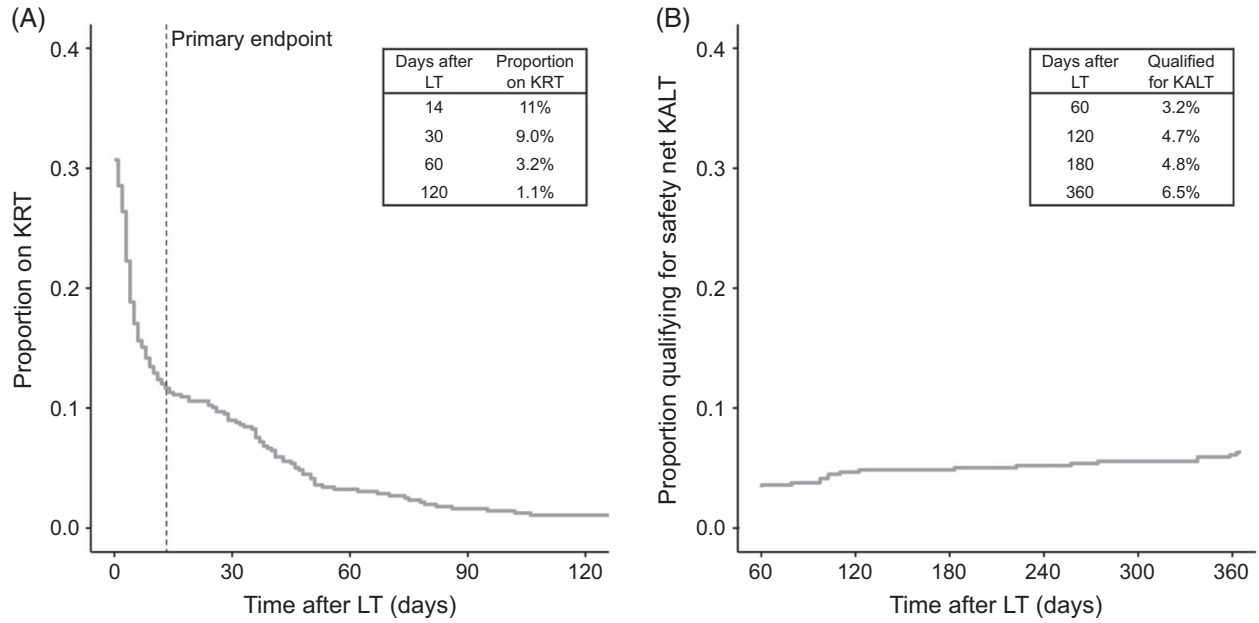

FIGURE 1 (A) Duration of KRT after LT (n = 557). (B) Time to qualification for safety net KALT (n = 557). Abbreviations: KALT, kidney after liver transplant; KRT, kidney replacement therapy; LT, liver transplant.

indication for LT (185; 33%), followed by alcohol-associated liver disease (111; 20%) and metabolic dysfunction–associated steatotic liver disease (108; 19%). HCC was present in 205 (37%) recipients. Median donor age was 41 (29–55) years, and 77 (14%) of allografts were DCD. None of the patients had a prior LT or kidney transplant. Death within 1 year occurred in 9 (1.6%) recipients.

At LT, 274 (49%) recipients had normal kidney function, 141 (25%) had AKI without underlying CKD, and 142 (25%) had CKD ± AKI. Among those with AKI (n = 276), 143 (52%), 21 (7.6%), and 112 (41%) had Stage 1, 2, and 3, respectively. Among those with CKD (n = 142), 106 (75%), 38 (27%), and 8 (5.6%) had Stage III, IV, and V, respectively. Pretransplant AKI duration was 7.0 (2.0–20) days, and CKD III-V duration was 109 (97–139) days. At LT, 111 (20%) of our study cohort were receiving KRT for a median (IQR) of 4.0 (2.0–6.5) days. A total of 46 (8.3%) patients qualified for SLK transplantation at the time of liver-only transplant, all of whom had AKI on CKD. Only 9 of these subsequently qualified for safety net KALT, 8 (89%) of which had Stage 3 AKI requiring KRT before LT for 2.0 (1.0–3.5) days. The remaining 37 who qualified for SLK but not KALT included 23 (62%) with Stage 3 AKI with KRT for 3.0 (1.0–4.0) days.

Trajectory of kidney dysfunction after LT

Among the 171 (31%) recipients who required KRT after LT, only 63 (11%), 50 (9.0%), and 18 (3.2%) required KRT for > 14, > 30, and > 60 days, respectively (Figure 1A). Hospital discharge while still on KRT occurred for 66 (12%) patients. Ultimately, 36 (6.5%) patients qualified for safety net KALT during the first year after LT (Figure 1B). Eligibility for KALT was similar between those who received 0 days and ≤ 14 days of KRT after LT (2.1% vs. 2.9%; $p = 0.53$) (Figure 2). However, patients who required KRT for 15–30 days and > 30 days after LT had

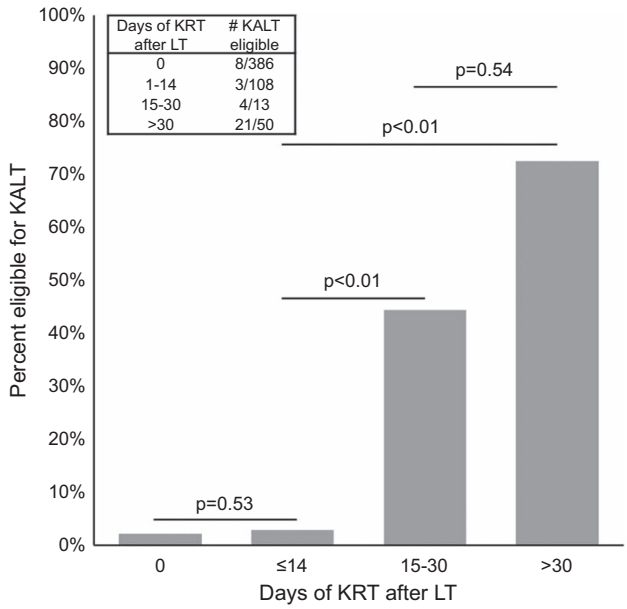

FIGURE 2 Percent of patients eligible for KALT stratified by the post-LT KRT duration. Abbreviations: KALT, kidney after liver transplant; KRT, kidney replacement therapy; LT, liver transplant.

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higher rates of KALT eligibility (44% and 72%, respectively).

Risk factors for safety net KALT eligibility

Characteristics of the 36 (6.5%) patients eligible for KALT are shown in Supplementary Table S1, http://links.lww.com/LVT/A603. The majority (25 [69%]) required KRT for > 14 days after LT. In univariable analysis, factors associated with KALT eligibility were: donor age (OR 0.79 per 10 y, CI: 0.63–0.99), recipient sCr at LT (OR 1.80 per 1 mg/dL, CI 1.35–2.38), increasing AKI stage (stage 1 [OR 2.53, CI: 1.20–5.62], stage 3 [OR 7.87, CI: 3.5-19.5]), CKD ± AKI (OR 4.58, CI 2.13–10.5), CKD stage III-V duration (OR 1.10 per week, CI 1.05–1.16), KRT (OR 7.63, CI: 3.80–15.8), and KRT duration before LT (OR 4.00 per week, CI: 2.37–6.81) (Table 2). Notably, DCD transplantation (OR 1.27, CI: 0.46-2.96) was not associated with safety net KALT qualification. Time-weighted average tacrolimus troughs in the first year after transplant were inversely associated with eligibility (OR 0.83, CI: 0.69–1.00).

In multivariable analysis, recipient age (OR 1.61 per 10 y, CI 1.05–2.63), sCr at LT (OR 1.43 per 1 mg/dL, CI: 1.01–2.00), CKD III-V duration (OR 1.07 per week, CI: 1.01–1.13), and KRT duration (OR 4.19 per week, CI: 2.42–7.39) were associated with safety net KALT eligibility.

To better understand the drivers of KALT eligibility, we conducted a subgroup analysis among those with normal kidney function or AKI alone (no CKD). Compared to patients with normal renal function, only stage 3 AKI (OR 4.12, CI: 1.04–14.3), but not stage 1 (OR 1.77, CI: 0.46–6.02), nor stage 2 (insufficient sample size), nor AKI duration (OR 0.91 per week, CI: 0.60–1.13) was associated with KALT eligibility. In a subgroup including only those with normal renal function, recipient age (OR 8.09 per 10 years, CI: 1.72–57.2) and sCr at LT (OR 10.3 per 1 mg/dL, CI: 1.02–104) but not DCD (OR 1.82, CI: 0.26–8.75) were associated with KALT eligibility. Wait time was associated with KALT eligibility in recipients with AKI (OR 1.01 per mo, CI: 1.00–1.03), but not recipients with normal kidney function or CKD.

Furthermore, we explored the association of dichotomous duration thresholds of pre-LT KRT with the outcome. In patients with AKI, a cutoff of 15 days of pre-LT KRT was most strongly associated with KALT eligibility (OR 20.5, CI: 3.80–154). Next, we explored several hypothesis-driven interactions and found no significant interactions between DCD status, KRT duration, recipient age, and CKD duration (Supplemental Table S3, http://links.lww.com/LVT/A603). Finally, a receiver operating characteristic curve analysis of the predictive capacity of KRT duration alone for qualification for KALT showed that the AUC was 0.67 (Figure 3).

Risk factors for KRT > 14 days after LT

Characteristics of the 63 (11%) patients who required > 14 days of KRT after LT are shown in Supplementary Table S2, http://links.lww.com/LVT/A603. Univariable logistic regression showed that the factors associated with KRT > 14 days after LT were largely the same as those associated with safety net KALT eligibility (Table 3). However, DCD transplantation was associated with KRT > 14 days (OR 2.18, CI: 1.12–4.04). Multivariable analysis showed that DCD (OR 3.65, CI: 1.76–7.34), recipient age (OR 1.64 per 10 y, CI 1.16–2.39), sCr at LT (OR 1.65 per 1 mg/dL, CI: 1.24–2.20), and pre-LT KRT duration (OR 6.54 per week, CI 3.74–12.2) were independently associated with KRT > 14 days after LT. The associations were generally stronger in the KRT > 14 days analysis compared to the KALT eligibility analysis, except for recipient age.

To better understand the drivers of prolonged KRT after LT, we again performed a subgroup analysis of patients with normal kidney function or AKI alone (no CKD). Relative to patients with normal kidney function, pre-LT AKI stage 3 (OR 7.88, CI: 2.49–30.2) was associated with KRT > 14 days but not stage 1 (OR 0.70, CI: 0.20–1.96) or stage 2 (insufficient sample size). Duration of AKI was not associated with KRT > 14 days (OR 0.89 per week, CI: 0.65–1.07). In a subgroup including only those with normal renal function, recipient age (OR 2.45 per 10 years, CI: 1.17–6.24) and DCD (OR 3.48, CI: 1.21–9.59) were the only significant factors and had larger associations than the primary analysis. Wait time was associated with prolonged KRT in recipients with AKI (OR 1.01 per month, CI: 1.00–1.03) but not recipients with normal kidney function or CKD.

We again explored the association of dichotomous duration thresholds of pre-LT KRT with the outcome. Similar to prior studies, in patients with AKI, a cutoff of 15 days of pre-LT KRT was most strongly associated with KRT > 14 days after LT (OR 10.9, CI: 2.05–8.01). Last, we performed the same hypothesis-driven interactions as above and again found no significant interactions (Supplemental Table S3, http://links.lww.com/LVT/A603).

DISCUSSION

Improvements in survival after LT have escalated the importance of limiting late complications. Prolonged kidney dysfunction early after LT has long been known

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TABLE 2 Univariable and multivariable logistic regression analysis of patients who qualify for safety net KALT (n = 36)

	Qualification for safety net KALT			
	Univariable		Multivariable	
Characteristic	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
Donor factors				
Age (10 y)	0.79 (0.63–0.99)	0.04	—	—
Male	1.46 (0.72–3.16)	0.31	—	—
Donation after cardiac death	1.27 (0.46–2.96)	0.61	—	—
Recipient factors				
Age (10 y)	1.39 (0.96–2.13)	0.11	1.61 (1.05–2.63)	0.04
Male	0.65 (0.33–1.32)	0.23	—	—
Black race	1.47 (0.23–5.34)	0.61	—	—
Etiology of liver disease				
Viral	REF (REF)	REF	—	—
MASLD	1.77 (0.63–4.95)	0.27	—	—
Alcohol	2.43 (0.95–6.48)	0.06	—	—
Other	1.38 (0.52–3.77)	0.52	—	—
HCC	1.24 (0.62–2.46)	0.53	—	—
Waiting time (1 mo)	1.00 (0.98–1.01)	0.78	—	—
Laboratory values at transplant				
Serum creatinine (mg/dL)	1.80 (1.35-2.38)	< 0.01	1.43 (1.01–2.00)	0.04
INR	1.07 (0.76–1.44	0.66	—	—
Albumin (g/dL)	1.39 (0.85–2.23)	0.18	—	—
Total bilirubin (mg/dL)	1.02 (0.99–1.04)	0.16	—	—
Sodium (mEq/L)	1.05 (0.98–1.13)	0.19	—	—
Hemoglobin A1c (%)	0.59 (0.36–0.90)	0.02	—	—
Kidney function at transplant				
Category				
Normal	REF (REF)	REF	—	—
AKI	1.35 (0.45–3.72)	0.57	—	—
CKD ± AKI	4.58 (2.13–10.5)	< 0.01	—	—
AKI stage				
0	REF (REF)	REF	—	—
1	2.53 (1.20–5.62)	0.02	—	—
2	—	—	—	—
3	7.87 (3.5–19.5)	< 0.01	—	—
AKI duration (wk)	1.07 (0.97–1.15)	0.13	—	—
CKD stage				
I-II	REF (REF)	REF	—	—
III	3.90 (1.76–8.63)	< 0.01	—	—
IV	5.24 (1.76–14.0)	< 0.01	—	—
V	16.8 (3.19–75.6)	< 0.01	—	—
CKD III-V duration (wk)	1.10 (1.05–1.16)	< 0.01	1.07 (1.01–1.13)	0.02
Receiving KRT	7.63 (3.80–15.8)	< 0.01	—	—
Pre-LT KRT duration (wk)	4.00 (2.37–6.81)	< 0.01	4.19 (2.42–7.39)	< 0.01

Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; INR, international normalized ratio; MASLD, metabolic dysfunction–associated steatotic liver disease; KALT, kidney after liver transplant; KRT, kidney replacement therapy; REF, reference group.

to predispose recipients to long-term CKD, which incurs morbidity and mortality and worsens quality of life.[1] Thus, a detailed understanding of the peri-transplant factors that contribute to CKD is critical for implementing mitigation strategies. Previous studies have treated pre-LT renal dysfunction monolithically,

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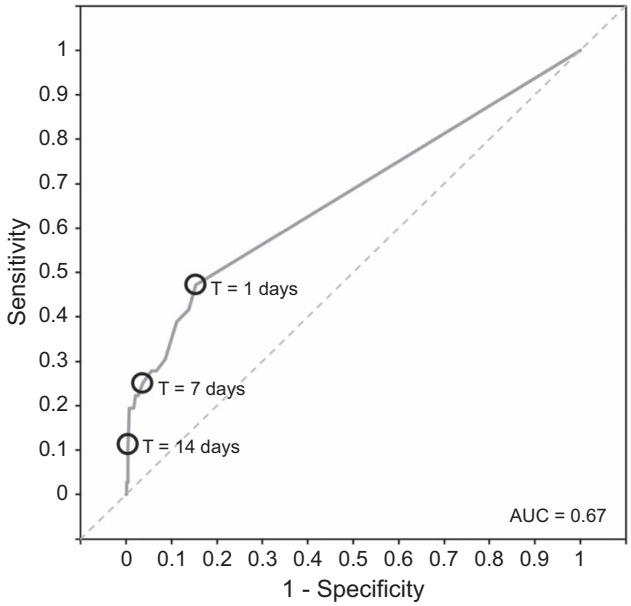

FIGURE 3 Receiver operating characteristic curve analysis of the predictive capacity of the duration of KRT for KALT eligibility. Specific thresholds of KRT duration are labeled. Abbreviations: KALT, kidney after liver transplant; KRT, kidney replacement therapy.

without differentiation as to type (AKI, CKD, or CKD + AKI), duration, or severity. Similarly, post-LT renal dysfunction has been considered as a binary end point without consideration of severity. These deficiencies in the literature motivated the current study, which takes advantage of the large volume of high MELD transplants performed at our center and the availability of highly granular pre-LT and post-LT data. Our end points of KALT eligibility and long KRT duration are intuitively logical surrogates for severe post-LT renal dysfunction.

In our cohort, the proportion of recipients requiring KRT decayed exponentially during the first 14 days post-LT: nearly two-thirds recovered sufficient renal function to stop KRT within 2 weeks. The rate of recovery flattened during the next 2 weeks (only 13 [8%] recipients recovered) but accelerated during days 31–60 (32 [19%] recipients recovered); 18 (11%) patients remained on KRT beyond 60 days. This shape of this recovery curve drives 2 observations: (1) 14 days of KRT may be a reasonable threshold for "severe" post-LT renal dysfunction and (2) 60 days is an appropriate time point to adjudicate safety net KALT eligibility. The former observation is supported by our finding that KRT $<$ 14 days compared to no KRT after LT was not associated with an increased risk of KALT eligibility. In total, ~6% of the patients in our cohort ultimately qualified for KALT, half based on KRT and half based on low eGFR. About 8% of our cohort qualified for SLK transplantation at the time of LT, but all of these patients had short-term acute on chronic kidney injury likely attributed to reversible pathophysiology.

Consistent with previous studies, we found that adverse kidney outcomes after LT strongly correlated with kidney dysfunction before transplant. Historically, pre-LT kidney dysfunction was typically assessed solely by MELD score without consideration of type, duration, or severity.[1–3] Our more granular analyses showed that low-stage pre-LT AKI and AKI duration (without CKD) were not associated with either KALT qualification or prolonged KRT, while severe AKI and CKD $\pm$ AKI were major determinants of unfavorable post-LT renal outcomes. Pre-LT KRT duration had an especially robust impact on post-LT kidney outcomes. Approximately 20% of patients who received $\geq$ 1 day of KRT before LT qualified for KALT qualification. Consistent with prior studies, 2 weeks was the duration of KRT before LT with the strongest association with both prolonged KRT after LT and KALT qualification.[24] However, pre-LT KRT on its own was only a modest predictor of KALT eligibility, given that the area under the receiver operator characteristic curve was 0.67. To guide SLK allocation policies, future research in larger cohorts must further examine the predictive capacity of combining this variable with others for KALT eligibility.

Donor selection and recipient matching clearly play a key role in kidney outcomes after LT. Older recipients, as expected, tended to have worse kidney outcomes, but, interestingly, recipient age did not exhibit a significant interaction with other negative post-LT renal function predictors. Livers from DCD donors were also associated with increased post-LT KRT utilization, as previously reported, although we did not identify an association with KALT eligibility.[8,25] However, while the DCD effect appeared transient, prolonged post-LT KRT undoubtedly exerts a negative impact on the recipient quality of life, hinders full postoperative recovery, and may be associated with long-term CKD.

The potent association that pre-LT kidney dysfunction had on post-LT outcomes suggests that improving pre-LT kidney function, perhaps with terlipressin as appropriate, might be a priority.[26] Waiting time, interestingly, only had a minimal association with our outcomes and only in patients with AKI. Second, knowing that DCD donor livers increase the risk of prolonged post-LT KRT, favoring younger recipients and/or ensuring perfusional rather than static preservation could mitigate the risk.[11,27] And third, in the postoperative period, the final available lever to optimize renal recovery and avoid long-term dysfunction is the administration of kidney-sparing immunosuppression.[28] Consideration of everolimus-based immunosuppression regimens must be made in selected patients most at risk of kidney dysfunction.

This study has definite limitations, the most important of which is the single-center, retrospective design with the possibilities of bias, uncontrolled confounders, and nongeneralizability. Differences in immunosuppression protocols across centers, in particular, including target tacrolimus troughs and use of everolimus, may limit

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TABLE 3 Univariable and multivariable logistic regression analysis of patients receiving KRT > 14 days after liver transplant (n = 63)

	KRT > 14 d after transplant			
	Univariable		Multivariable	
Characteristic	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
Donor factors				
Age (10 y)	0.75 (0.62–0.89)	< 0.01	—	—
Male	1.40 (0.81–2.50)	0.24	—	—
Donation after cardiac death	2.18 (1.12–4.04)	0.02	3.65 (1.76-7.34)	< 0.01
Recipient factors				
Age (10 y)	1.30 (0.98–1.78)	0.08	1.64 (1.16-2.39)	< 0.01
Male	0.70 (0.41–1.21)	0.20	—	—
Black race	0.36 (0.02–1.78)	0.33	—	—
Etiology of liver disease				
Viral	REF (REF)	REF	—	—
MASLD	1.63 (0.80–3.30)	0.17	—	—
Alcohol	0.68 (0.27–1.56)	0.38	—	—
Other	1.23 (0.63–2.45)	0.53	—	—
HCC	0.91 (0.52–1.56)	0.74	—	—
Waiting time (1 mo)	1.00 (0.98–1.01)	0.71	—	—
Laboratory values at transplant				
Serum creatinine (mg/dL)	1.77 (1.38–2.29)	< 0.01	1.65 (1.24–2.20)	< 0.01
INR	1.13 (0.88–1.43)	0.32	—	—
Albumin (g/dL)	1.26 (0.86–1.84)	0.23	—	—
Total bilirubin (mg/dL)	1.02 (1.00–1.04)	0.08	—	—
Sodium (mEq/L)	1.06 (1.00–1.04)	0.07	—	—
Hemoglobin A1c (%)	0.76 (0.54–1.01)	0.10	—	—
Kidney function at transplant				
Category				
Normal	REF (REF)	REF	—	—
AKI	1.80 (0.86-3.73)	0.11	—	—
CKD ± AKI	4.22 (2.27-8.10)	< 0.01	—	—
AKI stage				
0	REF (REF)	REF	—	—
1	1.96 (1.10–3.55)	0.02	—	—
2	2.39 (0.57–2.13)	0.16	—	—
3	7.06 (3.8–13.6)	< 0.01	—	—
AKI duration (wk)	1.07 (1.00–1.14)	0.04	—	—
CKD stage				
I-II	REF (REF)	REF	—	—
III	2.23 (1.16–4.14)	0.01	—	—
IV	3.62 (1.51–8.07)	< 0.01	—	—
V	19.4 (4.56–98.2)	< 0.01	—	—
CKD III-V duration (wk)	1.06 (1.02–1.11)	< 0.01	—	—
Receiving KRT	10.4 (5.91–18.6)	< 0.01	—	—
Pre-LT KRT duration (wk)	5.22 (3.15–9.01)	< 0.01	6.54 (3.74–12.2)	< 0.01

Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; INR, international normalized ratio; MASLD, metabolic dysfunction–associated steatotic liver disease; KRT, kidney replacement therapy; REF, reference group.

external validity.[29] Nevertheless, to support this hypothesis-generating effort, we maximized the advantages offered by our center: large adult LT center, high volume of high MELD candidates, aggressive liver utilization practices, and quality data, both complete and granular. Second, classifying candidates into distinct

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categories of kidney function at LT may insufficiently capture complexity. In reality, kidney function spreads over a continuum and is frequently dynamic such that a patient with normal creatinine at LT may have had recent AKI episodes that would increase vulnerability to post-LT dysfunction.[26] Some patients may also present for transplant evaluation with pre-existing kidney dysfunction of unknown duration, which is not captured. Third, our study does not investigate intraoperative or early postoperative contributors to kidney outcomes, such as blood loss/transfusions, vasopressors, or early allograft dysfunction.[30,31] However, these factors are not known before LT, nor are they readily modifiable. Similarly, obesity and diabetes are key risk factors for post-LT CKD but were unable to be reliably collected in our cohort. Finally, our study focuses on early post-LT outcomes reflecting severe post-LT renal dysfunction. Less severe degrees of renal dysfunction in the mid-term to long-term timeframe certainly deserve detailed exploration in light of the known negative impact on the quality and quantity of life.

In conclusion, we found that the type, duration, and severity of pre-LT kidney dysfunction have unique impacts on safety net KALT eligibility and KRT utilization after LT. Future research should explore whether identifying recipients at high risk for post-LT kidney–related morbidity can drive effective mitigation strategies that attenuate this risk, thereby improving post-LT renal outcomes.

CONFLICTS OF INTEREST

Sandy Feng consults for Quell Therapeutics Ltd, received grants from Eurofins Transplant Genomics, Inc. and Randox Laboratories, advises and received grants from eGenesis, and owns stock in Johnson & Johnson. Giuseppe Cullaro consults for Ocelot Bio and Retro. The remaining authors have no conflicts to report.

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