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ORIGINAL ARTICLE

Intraoperative risk factors of acute kidney injury after liver transplantation

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Abstract

Acute kidney injury (AKI) is one of the most common complications of liver transplantation (LT). We examined the impact of intraoperative management on risk for AKI following LT. In this retrospective observational study, we linked data from the electronic health record with standardized transplant outcomes. Our primary outcome was stage 2 or 3 AKI as defined by Kidney Disease Improving Global Outcomes guidelines within the first 7 days of LT. We used logistic regression models to test the hypothesis that the addition of intraoperative variables, including inotropic/vasopressor administration, transfusion requirements, and hemodynamic markers improves our ability to predict AKI following LT. We also examined the impact of postoperative AKI on mortality. Of the 598 adult primary LT recipients included in our study, 43% (n = 255) were diagnosed with AKI within the first 7 postoperative days. Several preoperative and intraoperative variables including (1) electrolyte/acid-base balance disorder (International Classification of Diseases, Ninth Revision codes 253.6 or 276.x and International Classification of Diseases, Tenth Revision codes E22.2 or E87.x, where x is any digit; adjusted odds ratio [aOR], 1.917, 95% confidence interval [CI], 1.280–2.869; p = 0.002); (2) preoperative

Abbreviations: aHR, adjusted hazard ratio; AKI, acute kidney injury; aOR, adjusted odds ratio; BMI, body mass index; BUN, blood urea nitrogen; CDC, Center for Disease Control and Prevention; CI, confidence interval; CMV, cytomegalovirus; c-statistic, concordance statistic; DBD, donation after brain death; DCD, donation after circulatory death; EBV, Epstein-Barr virus; eGFR, estimated glomerular filtration rate; FFP, fresh frozen plasma; ICD-9, International Classification of Diseases, Ninth Revision; ICD-10, International Classification of Diseases, Tenth Revision; INR, international normalized ratio; KDIGO, Kidney Disease Improving Global Outcomes; LT, liver transplantation; MAP, mean arterial pressure; MDRD-4, Modification of Diet in Renal Disease, 4 variable; MELD, Model for End-Stage Liver Disease; MPOG, Multicenter Perioperative Outcomes Group; OTIS, Organ Transplant Information System; pRBC, packed red blood cells; RRT, renal replacement therapy; SD, standard deviation.

SEE EDITORIAL ON PAGE 1131

anemia (aOR, 2.612; 95% CI, 1.405–4.854; $p = 0.002$); (3) low serum albumin (aOR, 0.576; 95% CI, 0.410–0.808; $p = 0.001$), increased potassium value during reperfusion (aOR, 1.513; 95% CI, 1.103–2.077; $p = 0.01$), and lactate during reperfusion (aOR, 1.081; 95% CI, 1.003–1.166; $p = 0.04$) were associated with posttransplant AKI. New dialysis requirement within the first 7 days postoperatively predicted the posttransplant mortality. Our study identified significant association between several potentially modifiable variables with posttransplant AKI. The addition of intraoperative data did not improve overall model discrimination.

INTRODUCTION

Acute kidney injury (AKI) is one of the most common complications following liver transplantation (LT), with more than half of all LT recipients demonstrating at least acute renal failure.[1,2] Posttransplant AKI is associated with longer stays in the intensive care unit,[3] increased graft rejection,[4] higher hospital costs,[3] and higher mortality[5,6] independent of pretransplant renal function.[7]

Previous studies have shown that donor factors and recipient preoperative factors increase the risk of AKI[8,9] and chronic kidney disease[10,11] following LT. A variety of preoperative and postoperative factors (eg, exposure to calcineurin inhibitors) have been linked to post-LT AKI.[7] The long-term impact of intraoperative events, such as acidosis, low hematocrit values, or duration of each transplant stage, and anesthesia factors, such as norepinephrine and blood transfusion (including red blood cells, plasma, and cryoprecipitate) on posttransplant AKI is not well studied.

Real-time data capture within electronic medical records allows the opportunity to link intraoperative data[12] with postoperative outcomes, thus refining our understanding of the impact of the perioperative period. Given the time-sensitive nature of the development of AKI, the identification of perioperative predictors of posttransplant renal dysfunction could allow the development of renal protection strategies directed at high-risk patients, and the identification of intraoperative predictors may enable modification of intraoperative care to reduce the risk of renal injury in at risk patients.

The objective of this study is to identify modifiable risk factors associated with AKI following LT. Our hypothesis was that the addition of intraoperative variables, including inotropic/vasopressor administration, transfusion requirements, and hemodynamic markers, improves our ability to predict AKI following LT. In addition, intraoperative variables specifically curated at key stages of the transplant, such as reperfusion, might further improve our ability to predict AKI and provide insight into the mechanism of renal injury.

PATIENTS AND METHODS

Study design

For this retrospective observational study performed at our academic quaternary care center, we obtained institutional review board (HUM00153452) approval. This article was prepared in accordance with the standards set forth by the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[13] Study methods including data collection, outcomes, and statistical analyses were established prospectively and presented at an institutional peer review committee on October 10, 2018, prior to data access.[14] No organs from executed prisoners were used.

Data collection

Our primary data sources were collected via combined queries of (1) the local University of Michigan Multicenter Perioperative Outcomes Group (MPOG) data set and (2) Michigan Medicine's Organ Transplant Information System (OTIS). The local MPOG data set collects information from the electronic perioperative anesthesia database (Centricity, General Electric Healthcare, Waukesha, WI) and electronic health record (Epic, Verona, WI). OTIS is an internal clinical database that tracks patients from waitlist enrollment through death and contains demographic, clinical, and donor variables. In addition, OTIS contains the information reported to the Scientific Registry of Transplant Recipients and tracks standardized outcomes, including (1) AKI, (2) postoperative dialysis, (3) mortality, (4) graft failure, and (5) retransplantation.

Inclusion and exclusion criteria

All primary, adult liver recipients who received transplants at Michigan Medicine between 2008 and 2018 were included in our study. Patients were excluded if they had preoperative stage 5 end-stage renal

disease, as defined by the Modification of Diet in Renal Disease–4 variable (MDRD-4) equation or were on dialysis prior to transplant. If a patient had more than 1 documented LT during the time period, only their first transplant was included in analysis. Patients entered the cohort at the time of their surgery and continued for as long as followed in the OTIS database.

Primary outcome

Our primary outcome was stage 2 or 3 AKI as defined by Kidney Disease Improving Global Outcomes (KDIGO) guidelines, using the maximum measured serum creatinine within the first 7 days following transplantation compared with preoperative serum creatinine closest to the time of transplant. These guidelines specify stage 2 as 2.0 to 2.9 times baseline and stage 3 as 3.0 times baseline or ≥4.0 mg/dL or the initiation of renal replacement therapy (RRT).[15] RRT receipt within the 7 days was considered stage 3 regardless of the creatinine change. We did not consider urine output rate in our classification, as this information was not uniformly available within our database. Only considering KDIGO stage 2 or 3 AKI allowed us to model the most severe and drastic changes in kidney function.

Secondary outcome

The secondary outcome was survival, censored at the length of follow-up in our database.

Covariates

In the MPOG database, data are stored, validated, and extracted for quality improvement and research purposes.[16,17] From the combined data set, we curated 107 covariates that were grouped as (1) demographic, (2) procedural, (3) etiology of liver failure, (4) donor/graft-specific factors, (5) preoperative laboratory studies, and (6) intraoperative data (Table S1). Intraoperative measures included vasopressor/inotropic support, mean arterial pressure (MAP), resuscitation with blood products and fluids, and laboratory studies. Intraoperative variables were also classified according to the following stages of transplantation to enable additional phase-specific modeling: (1) dissection, (2) anhepatic phase, and (3) reperfusion phase. Laboratory and vital sign values were quantified as a time-weighted average over the entire window, assuming the most recent result as current, until a new value is documented. Medication and transfusion values were calculated as total administration during the phase of interest. Recipient comorbidities were curated from a combination of diagnostic codes, standardized entry in the history and physical evaluation perfomed preoperatively by the anesthesia provider, and free-text search for relevant terminology. Diagnostic codes were grouped according to a previously validated approach.[18] Examples include (1) preoperative anemia (defined as iron deficiency or folate and B12 deficiencies)[19] and (2) preoperative electrolyte/acid-base balance disorders (defined as syndrome of inappropriate antidiuretic hormone secretion or various electrolyte and acid/base disorders).[20] (Electrolyte/acid-base balance disorders are based on the Elixhauser Comorbidity Index, which is positive if the patient has International Classification of Diseases, Ninth Revision [ICD-9]/ International Classification of Diseases, Tenth Revision [ICD-10] diagnosis codes for syndrome of inappropriate antidiuretic hormone secretion [ICD-9 253.6x and ICD-10 E22.2x] or various electrolyte and acid/base disorders [ICD-9 276 and 276.x and ICD-10 E86.x, E87.x, E88.x], where x is any digit.) In addition, we calculated time-weighted averages of physiologic measures taken throughout the LT process. Finally, we adjusted for preoperative (baseline) estimated glomerular filtration rate (eGFR) calculated using the MDRD-4.[21]

Statistical analysis

Exploratory data analysis techniques, such as histograms, QQ-Plots, box-plots, scatterplots and basic descriptive (means, medians, interquartile ranges) were used to assess the distribution of dependent measures. This allowed us to identify the distribution of outcomes which in turn facilitated appropriate modeling strategies. In addition, these techniques also were used to explore the most informative transformations of the covariates, confounders, and relevant predictors considered in the analysis. Extreme values were identified and their removal from the analysis was determined. Missing patterns and rates were assessed. Descriptive statistics were compiled on LT patients developing and not developing postoperative AKI.

Patients who had not received pretransplant dialysis were analyzed for development of AKI and subsequent mortality. Mortality was determined from the LT database. First, patients who developed AKI were compared with patients without AKI using Fisher's exact and chi-square tests for categorical variables and an independent *t* test for continuous variables. Heavily skewed variables, such as transfusion quantities and norepinephrine doses, were log transformed for inclusion in the regressions. Missing data were imputed via the method of multiple imputation using fully conditional specification and predictive mean matching. To determine the independent associations with AKI, we used logistic regressions with forward selection using the likelihood ratio.

Mortality was analyzed using Cox proportional hazards models. First, the proportionality assumption was confirmed with Schoenfeld residuals. Then all variables

were entered using forward selection. For both the logistic regression and Cox proportional hazards models, the multiple imputation models were combined with Rubin's rules. Variables with $p < 0.05$ and 95% confidence intervals (CIs) that excluded 1 were deemed statistically significant. No adjustment was made for multiple models. Discriminations of the logistic regression models were assessed with the concordance statistic (c-statistic), which was calculated separately for each model, and the pooled results and standard errors were calculated after logistic transform using the method of DeBray. Pooled results were then back transformed for presentation.[22]

Power

Power analysis and sample size determination were done for 2 correlated proportions with a range between 10% and 20% dropout. Parameters used for this analysis were determined based on previous knowledge. We assumed the incidence of AKI to be 40% and that mild hypotension was associated with an increased adjusted odds ratio (aOR) of AKI of 1.34 (95% CI, 1.16–1.56). In addition, we assumed a 2-sided test with $\alpha = 0.05$ and an intracluster correlation of 0.5. Results from this analysis indicated that a sample ranging between 185 and 600 would provide 85% power to test our research questions. Power analysis was performed with PASS 2021 software (NCSS Statistical Software, Kaysville, UT, USA). In addition, simulation studies show that for different intraclass correlations structures a sample size ranging between 150 to 500 will provide power ranging between 80% and 90% to test the significance of parameters.[23] Although the study was powered to detect the significance of individual parameters, the study may be underpowered to find a difference in discrimination between the preoperative (models 1 and 2) and preoperative and intraoperative (models 3 and 4) models.

Models

Preoperative recipient-specific model (Model 1)

We first created a model that assessed association between our primary outcome, AKI, and a variety of patient-specific variables that would be known preoperatively (model 1). Variables included in each model can be found in Table S1.

Preoperative and donor-specific model (Model 2)

The next model incorporated donor-specific variables, including donor age, donor sex, donor cause of death, and graft ischemic time.

Phase-specific model: Reperfusion (Model 3)

To test our hypothesis that variables specific to each phase of transplantation may have a previously undetected association that could further improve AKI prediction, we created a model using intraoperative data censored to the period following reperfusion. Additional variables in this model included transfusions and norepinephrine administration given during reperfusion and laboratory values, including lactate, potassium, and ionized calcium measured during reperfusion.

Model with data at case completion (Model 4)

Model 4 was composed of full data known at case completion, including case duration, total transfusion requirements, and cumulative dosage of norepinephrine.

Mortality (Models 5 and 6)

Model 5 comprised data known by the end of the operation plus AKI and receipt or not of dialysis. We also performed a nonpredetermined analysis to assess the relationship between the subset of patients with stage 3 AKI needing dialysis within 7 days following transplantation and mortality (model 6). All statistical analyses were performed in SPSS 27.0 (IBM, Armonk, NY).

Comparison of model discrimination

Model discrimination was quantified using the area under the receiver operator characteristic curve (c-statistic). Comparison between the discrimination of preoperative models (models 1 and 2) and preoperative and intraoperative models (models 3 and 4) was done using the Hanley and McNeil method to calculate the z score for each of the values. We then combined the z scores with Rubin's rules and calculated the 2-tailed p value.[24]

RESULTS

Cohort characteristics and univariate associations

Of the 598 adult primary LT recipients included in our study, 43% (n = 255) were diagnosed with AKI within the first 7 postoperative days, and 149 (25%) had KDIGO stage 2 and 106 (18%) stage 4. Of the patients, 66.1% (n = 395) were men, and the median age at the time of transplant was 54 years (standard deviation [SD], 11 years). A total of 80.6% of the patients (n = 482) identified as White, and 7.5% (n = 45) identified as Black. Median body mass index (BMI)

was 29.2 kg/m^2 (SD, 6.1 kg/m^2). Patients had a median baseline eGFR of 78.7 mL/min/1.73 m^2 (SD, 41) and Model for End-Stage Liver Disease (MELD) of 19 (SD, 8). In addition, 11% (n = 63) had preoperative anemia, 61% (n = 365) had a preoperative electrolyte/acid-base balance disorder, and 35% (n = 208) had preexisting cardiac arrhythmia.

Patients subsequently developing AKI were more likely to have a higher BMI (30.3 kg/m^2 [SD, 6.6 kg/m^2] compared with 28.4 kg/m^2 [SD, 5.5 kg/m^2]; $p < 0.001$), preexisting anemia (14.9% vs. 7.3%; $p = 0.003$), cardiac arrhythmia (41.2% vs. 30.0%; $p = 0.006$), and fluid/electrolyte disorder (70.2% vs. 54.2%; $p < 0.001$). Somewhat surprisingly, patients developing AKI following LT also had a higher baseline eGFR (87.3 mL/min/1.73 m^2 [SD, 42.9 mL/min/1.73 m^2] compared with 72.4 mL/min/1.73 m^2 [SD, 37.7 mL/min/1.73 m^2]; $p < 0.001$) and lower MELD scores (18 [SD, 7] compared with 20 [SD, 9]; $p < 0.001$). Intraoperatively, patients developing AKI required larger volume transfusion with red cells (10.7 units [SD, 17.1 units] vs. 8.2 units [SD, 14.5 units]; $p < 0.001$) and plasma (13.7 units [SD, 17.6 units] vs. 11.0 units [SD, 13.6 units]; $p < 0.001$). Characteristics for our full cohort, as well as the univariate descriptive differences between the AKI and non-AKI cohorts are presented in Tables 1–3.

We found that 3.8% (n = 23) patients died within 30 days of transplant, 9.0% (n = 54) died within 1 year, and 13.0% (n = 78) died within 3 years. Additional details can be found in Table 4.

Model composed of recipient-specific, preoperative variables (Model 1)

In an adjusted multivariate logistic model, several preoperative variables, including (1) BMI (aOR, 1.077; 95% CI, 1.044–1.112; $p < 0.001$), (2) electrolyte/acid-base balance disorder (aOR, 2.040; 95% CI, 1.374–3.030; $p < 0.001$), (3) preoperative anemia (aOR, 2.985; 95% CI, 1.623–5.489; $p < 0.001$), and (4) cardiac arrhythmia (aOR, 1.818; 95% CI, 1.240–2.666; $p = 0.002$) were associated with post-LT AKI. (Cardiac arrhythmias are based on the Elixhauser Comorbidity Index, which is positive if the patient has ICD-9/ICD-10 diagnosis codes for mechanical complication of pacemaker/defibrillator [ICD-9 996.01, 996.04; ICD-10 T82.1x], atrioventricular block and various dysrhythmias [ICD-9 426.0x, 426.7x, 426.9x, 426.1, 426.0, 426.2, 426.3, 427.x except 427.5; ICD-10: I441.x, I442.x, I443.x, I45.6x, I45.9x, I47, I48, I49, I47.x, I48.x, I49.x], tachycardia, bradycardia unspecified [ICD-9 785.0x; ICD-10: R00.0x, R00.1x, R00.8x]; or defibrillator, pacemaker, cardiac device [ICD-9 V45.0x, V53.3x; ICD-10: Z45.0x, Z95.0x], where x is any digit.)

In addition, the preoperative laboratory data, including (1) lower serum albumin (aOR, 0.611; 95% CI, 0.431–0.865; $p = 0.01$), (2) lower blood urea nitrogen (BUN; aOR, 0.963; 95% CI, 0.944–0.982; $p < 0.001$), (3) lower international normalized ratio (INR; aOR, 0.606; 95% CI, 0.420–0.875; $p = 0.01$), and (4) higher eGFR (aOR, 1.007; 95% CI, 1.001–1.013; $p = 0.03$), were also associated with AKI. Full results of the multivariate logistic regression are provided in Table 5. Model 1 had good discrimination (c-statistic, 0.741 ± 0.026). (The following is the interpretation of the c-statistic: 0.5 or less for a poor model, more than 0.7 for a good model, more than 0.8 for a strong model, and 1.0 for a perfect model.)

Model composed of preoperative recipient and donor variables (Model 2)

We incorporated additional donor-specific factors, including (1) donor age, (2) donor sex, (3) Center for Disease Control and Prevention (CDC) high-risk donor, (4) donation after circulatory death (DCD)/donation after brain death (DBD), (5) graft ischemia times (warm, cold, total), (6) donor cytomegalovirus (CMV)/Epstein-Barr virus (EBV) status, and (7) donor cause of death into the original model. Notably, none of these additional variables were selected for inclusion with Model 2 (Table 5), and the discrimination remained unchanged (c-statistic, 0.741 ± 0.026). A calibration plot for model 2 showing the proportion of patients with AKI for each quintile of risk is shown in Figure S1A.

Phase-specific modeling—Reperfusion phase (Model 3)

Next we created a model that examined the contribution from individual phases of LT. Based on univariate analysis (Table 4), we selected reperfusion phase as the phase of transplantation that provided the most informative, phase-specific data. Model 3 includes laboratory studies, MAP, and norepinephrine administration from the reperfusion phase. Notably, reperfusion potassium (aOR, 1.513; 95% CI, 1.103–2.077; $p = 0.01$) and reperfusion lactate (aOR, 1.081; 95% CI, 1.003–1.166; $p = 0.04$) were the only reperfusion phase-specific variables included in model 3. In addition, lower age (aOR, 0.979; 95% CI, 0.962–0.995; $p = 0.01$) and unexpected preoperative weight loss (aOR, 1.596; 95% CI, 1.006–2.532; $p = 0.05$) now became significant. Model discrimination increased to 0.759 ± 0.032. A calibration plot for model 3 showing the proportion of patients with AKI for each quintile of risk is shown in Figure S1B.

Full data, case completion model (Model 4)

Model 4 included the full available data at case completion. This included data from all 3 phases of

TABLE 1 Characteristics of LT patients developing stage 2 or 3 AKI: recipient and donor factors

		All data (n = 598)		No KDIGO Stage 2 or 3 (n = 343)		KDIGO Stage 2 or 3 (n = 255)		*p* value
Variable	**Level**	**Mean, n**	**SD, Percentage**	**Mean, n**	**SD, Percentage**	**Mean, n**	**SD, Percentage**	**Chi-square test, *t* test**
Age, years		54	11.0	54	11	52	11	0.06
BMI, kg/m^2		29.2	6.1	28.4	5.5	30.3	6.6	<0.001
Sex	Female	203	33.9	117	34.1	86	33.7	0.92
	Male	395	66.1	226	65.9	169	66.3	
Race	White/Caucasian (3)	482	80.6	278	81.0	204	80.0	0.65
	Black (reference)	45	7.5	25	7.3	20	7.8	
	Other (Not White/ Caucasian or Black) (1)	19	3.2	13	3.8	6	2.4	
	Unknown (2)	52	8.7	27	7.9	25	9.8	
Liver failure etiology	Hepatitis B virus	18	3.0	9	2.6	9	3.5	0.52
	Hepatitis C virus	183	30.6	99	28.9	84	32.9	0.29
	Hepatocellular carcinoma	170	28.4	96	28.0	74	29.0	0.78
	Nonalcoholic steatohepatitis	84	14.0	43	12.5	41	16.1	0.22
	Cryptogenic cirrhosis	52	8.7	29	8.5	23	9.0	0.81
	Primary sclerosing cholangitis	62	10.4	36	10.5	26	10.2	0.91
	Alpha-1-antitrypsin deficiency	19	3.2	12	3.5	7	2.7	0.60
	Fulminant liver failure	25	4.2	19	5.5	6	2.4	0.05
	Alcohol-related cirrhosis	127	21.2	74	21.6	53	20.8	0.82
	Biliary Etiology	33	5.5	22	6.4	11	4.3	0.27
	Autoimmune hepatitis	24	4.0	16	4.7	8	3.1	0.35
Donor factors	Age, years	40	16.0	40	16	40	15	0.67
Donor sex	Female	226	37.8	132	38.5	94	36.9	0.53
	Male	367	61.4	207	60.3	160	62.7	
	CDC high-risk donor	91	15.2	47	13.7	44	17.3	0.23
	DBD	536	89.6	315	91.8	221	86.7	0.11
	DCD	40	6.7	19	5.5	21	8.2	
Graft ischemic times	Warm ischemia, minutes	31	9.0	31	9	32	9	0.24
	Cold ischemia, minutes	364	170.0	371	180	355	156	0.26
	Total ischemia, minutes	391	153.0	394	149	387	157	0.60

TABLE 1 (Continued)

		All data (n = 598)		No KDIGO Stage 2 or 3 (n = 343)		KDIGO Stage 2 or 3 (n = 255)		*p* value
Variable	**Level**	**Mean, n**	**SD, Percentage**	**Mean, n**	**SD, Percentage**	**Mean, n**	**SD, Percentage**	**Chi-square test, *t* test**
Donor CMV status	Positive	345	57.7	195	56.9	150	58.8	0.35
	Negative	249	41.6	147	42.9	102	40.0	
	Unknown	4	0.7	1	0.3	3	1.2	
Donor EBV status	Positive	401	67.1	228	66.5	173	67.8	0.54
	Negative	33	5.5	22	6.4	11	4.3	
	Unknown	164	27.4	93	27.1	71	27.8	
Donor cause of death	Anoxia	124	20.7	71	20.7	53	20.8	0.20
	Asphyxiation	19	3.2	12	3.5	7	2.7	
	Blunt injury	2	0.3	1	0.3	1	0.4	
	Cardiovascular	23	3.8	15	4.4	8	3.1	
	Cerebrovascular	174	29.1	108	31.5	66	25.9	
	Central nervous system tumor	1	0.2	1	0.3	0	0.0	
	Drowning	3	0.5	0	0.0	3	1.2	
	Drug intoxication	25	4.2	12	3.5	13	5.1	
	Electrical	1	0.2	0	0.0	1	0.4	
	Gunshot/stab	47	7.9	29	8.5	18	7.1	
	Intracranial hemorrhage/ stroke	34	5.7	16	4.7	18	7.1	
	Motor vehicle accident	30	5.0	16	4.7	14	5.5	
	Other (Not White/ Caucasian or Black)	9	1.5	5	1.5	4	1.6	
	Seizure	1	0.2	0	0.0	1	0.4	
Donor cause of death (categorical)	Trauma	164	27.4	97	28.3	67	26.3	0.80
	Anoxia/asphyxiation	143	23.9	83	24.2	60	23.5	0.94
	Stroke	208	34.8	124	36.2	84	32.9	0.63
	Drug intoxication	25	4.2	12	3.5	13	5.1	0.29
	Cardiovascular	23	3.8	15	4.4	8	3.1	0.49
	Anemia (iron deficiency)	63	10.5	25	7.3	38	14.9	0.00
	Cardiac arrhythmia	208	34.8	103	30.0	105	41.2	0.01

(Continues)

TABLE 1 (Continued)

		All data (n = 598)		No KDIGO Stage 2 or 3 (n = 343)		KDIGO Stage 2 or 3 (n = 255)		*p* value
Variable	**Level**	**Mean, n**	**SD, Percentage**	**Mean, n**	**SD, Percentage**	**Mean, n**	**SD, Percentage**	**Chi-square test, *t* test**
	Valvular diseases of the heart	46	7.7	24	7.0	22	8.6	0.48
	Chronic obstructive pulmonary disease	93	15.6	58	16.9	35	13.7	0.27
	Fluid and electrolyte disorders	365	61.0	186	54.2	179	70.2	<0.001
Diabetes mellitus (recipient)	None	379	63.4	215	62.7	164	64.3	0.96
	Uncomplicated	175	29.3	101	29.4	74	29.0	
	Complicated	29	4.8	17	5.0	12	4.7	
	Missing/unknown	15	2.5	10	2.9	5	2.0	
Hypertension (recipient)	None	304	50.8	179	52.2	125	49.0	0.63
	Uncomplicated	195	32.6	109	31.8	86	33.7	
	Complicated	84	14.0	45	13.1	39	15.3	
	Missing/unknown	15	2.5	10	2.9	5	2.0	
	Hypothyroidism	87	14.5	50	14.6	37	14.5	
	Neurologic disorders	73	12.2	38	11.1	35	13.7	0.35
	Peripheral vascular disorders	37	6.2	16	4.7	21	8.2	0.08
	Pulmonary circulation disorders	39	6.5	18	5.2	21	8.2	0.15
	Unexpected or unanticipated weight loss	132	22.1	63	18.4	69	27.1	0.01
Other comorbidities	Cerebrovascular disease	6	1.0	3	0.9	3	1.2	0.71
	Ischemic heart disease	19	3.2	13	3.8	6	2.4	0.32
	Snoring	184	30.8	97	28.3	87	34.1	0.10
Recipient CMV status	Positive	332	55.5	200	58.3	132	51.8	0.12
	Negative	259	43.3	137	39.9	122	47.8	
	Equivocal	5	0.8	4	1.2	1	0.4	
Recipient EBV status	Positive	556	93.0	317	92.4	239	93.7	0.15
	Negative	26	4.3	15	4.4	11	4.3	

TABLE 1 (Continued)

Variable	Level	All data (n = 598)		No KDIGO Stage 2 or 3 (n = 343)		KDIGO Stage 2 or 3 (n = 255)		p value
		Mean, n	SD, Percentage	Mean, n	SD, Percentage	Mean, n	SD, Percentage	Chi-square test, t test
	Equivocal	2	0.3	0	0.0	1	0.4	
Outcomes	30-day mortality	23	3.8	14	4.1	9	3.5	0.73
	90-day mortality	31	5.2	16	4.7	15	5.9	0.51
	1-year mortality	54	9.0	30	8.7	24	9.4	0.78
	3-year mortality	78	13.0	35	10.2	43	16.9	0.02

transplantation as well as cumulative case totals (eg, norepinephrine dose during dissection, norepinephrine dose during anhepatic phase, norepinephrine dose during reperfusion, and total norepinephrine administered intraoperatively). For laboratory studies, time-weighted averages (using preoperative values from case initiation until the first intraoperative value was obtained) were calculated for each phase of transplantation and again for the total case duration. Notably, the addition of full case data did not alter the model selected or improve discrimination when compared with the model comprised entirely of preoperative and reperfusion phase data (Table 5).

Comparison of model discrimination

There was no difference in discrimination between the 2 preoperative models (model 1, recipient-specific; and model 2, recipient and donor characteristics; c-statistic, 0.741 ± 0.026). Furthermore, there was no statistically significant difference in discrimination between the 2 preoperative and intraoperative models (model 3, reperfusion phase; and model 4, full data, case completion; c-statistic, 0.759 ± 0.032). The addition of intraoperative details also did not significantly improve model discrimination (comparing the c-statistic of models 2 and 3 using the method of Hanley and McNeil[24]; $p = 0.10$).

Association with mortality

Next, we determined the independent associations between factors and mortality using Cox proportional hazards models. The first mortality model (model 5) included our primary outcome (KDIGO stage 2 or 3 AKI) as a covariate in addition to other factors specified previously. In this model, we found patients with hepatocellular carcinoma (adjusted hazard ratio [aHR], 1.611; 95% CI, 1.075–2.414; $p = 0.02$), longer warm ischemia time in minutes (aHR, 1.025; 95% CI, 1.006–1.045; $p = 0.01$), logarithm of total fresh frozen plasma (FFP) administered (aHR, 3.412; 95% CI, 1.959–5.942; $p < 0.001$), lower reperfusion ionized calcium (aHR, 0.835; 95% CI, 0.707–0.987; $p = 0.04$), and more acidic reperfusion pH (per 0.10 point change; aHR, 0.469; 95% CI, 0.367–0.601; $p < 0.001$) had a greater hazard for mortality. Notably, posttransplant AKI was not associated with mortality (Table 6).

In model 6, receipt of dialysis was a strong independent predictor of mortality (aOR, 3.324; 95% CI, 1.603–6.894; $p = 0.001$; Table 6). A Kaplan-Meier curve showing survival in the population requiring dialysis compared with not requiring dialysis is shown in Figure 1.

TABLE 2 Characteristics of LT patients developing Stage 2 or 3 AKI: Baseline laboratory values

		All data (n = 598)		No KDIGO Stage 2 or 3 (n = 343)		KDIGO Stage 2 or 3 (n = 255)		*p* value
Variable	**Level**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	***t* test**
Baseline	Serum creatinine (mg/dL)	1.2	0.7	1.3	0.7	1.0	0.6	<0.001
	eGFR, mL/minute/1.37 m^2	78.7	40.6	72.4	37.7	87.3	42.9	<0.001
	Bilirubin (mg/dL)	8.1	9.1	8.6	9.5	7.3	8.3	0.09
	BUN (mg/dL)	22.0	15.0	24.7	17.6	18.4	11.1	<0.001
	White blood cell count (K/uL)	6.1	3.3	6.2	3.5	5.9	3.0	0.33
	Hematocrit (%)	31.4	6.2	31.3	6.3	31.6	6.1	0.64
	Platelets (%)	97.8	71.2	102	75	92	65	0.07
	Sodium	136	5.0	136	5	135	5	0.10
	Albumin (g/dL)	3	0.6	3.1	0.6	2.9	0.6	<0.001
	Fibrinogen (mg/dL)	222	131	224	130	220	132	0.73
	INR	1.6	0	1.7	0.7	1.6	0.5	0.05
	MELD score	19	8	20	9	18	7	0.01
	MELD (laboratory)	19	8	20	9	18	7	0.01
	MELD (with exception points added)	23	6	24	6	22	6	<0.001
	MAP (prior to reperfusion), mm Hg	73	11	72	11	73	11	0.44

DISCUSSION

Using robust, validated observational databases, we report an overall AKI incidence of 43% within the first 7 days following LT. We identify several demographics and comorbidities including BMI, preexisting electrolyte/acid-base balance disorder, anemia, and cardiac arrhythmias that are associated with the primary outcome. In addition, preoperative studies including serum albumin, BUN, and INR informed the risk of AKI.

Our study builds on prior studies to integrate data from the electronic health record and intraoperative record with standard, reportable transplantation outcomes. We leveraged this capability to study associations through the intraoperative course. Our results show that increased potassium and lactate following graft reperfusion improve the prediction of patients susceptible to postoperative AKI. Furthermore, the addition of full case data does not improve model discrimination.

Concordance with previous studies

Our observed incidence of 43% is consistent with previous studies when accounting for differences in defining AKI (≥KDIGO stage 1 vs. ≥stage 2) and more stringent exclusion of patients with baseline renal dysfunction.[25–27] Although it is known that men are more at risk for end-stage liver disease, there is not an agreed consensus of the impact sex has on developing AKI requiring RRT.[28,29] We found a consistent relationship between larger BMI and AKI, which agrees with previous studies.[25,30,31] We found no relationship between female sex and AKI, which agrees with some studies[32,33] but contrasts with another study placing female patients at increased risk.[25] The influence of preoperative risk factors such as anemia and electrolyte/acid-base balance disorders have been found in previous studies.[7,9,34]

Our finding that preoperative hypoalbuminemia is associated with postoperative AKI agrees with previous findings in the LT population[35] as well as other surgical populations.[36–39] Other preoperative variables, including hyponatremia[40] and etiology of liver failure,[25] have been shown to influence postoperative AKI; however, these were not found to be significant in our study. This could be secondary to differences in patient population or, potentially, results from a redundancy in preoperative variables, leading to the selection of some variables and nonselection of others by our methodology. Specifically, our methodology selected preoperative diagnosis of electrolyte/acid-base balance disorders as a significant risk factor, which also includes the ICD-10 code for hyponatremia (E87.1), suggesting that it is electrolyte disorders in general not just 1 type (hyponatremia) that is associated with AKI.

Although MELD score has been previously shown to predict AKI after LT,[9,32,33] other studies have failed to replicate this association.[25,41] Our study did not find any association between MELD score and AKI. An additional surprising finding was that patients with a higher baseline eGFR have a higher susceptibility for post-transplant AKI. This conflicts with prior studies showing higher serum creatinine (lower eGFR) to be associated

TABLE 3 Characteristics of LT patients developing Stage 2 or 3 AKI: Intraoperative details (by phase of transplantation)

		All data (n = 598)		No KDIGO Stage 2 or 3 (n = 343)		KDIGO Stage 2 or 3 (n = 255)		*p* value
Variable	**Level**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	***t* test**
Intraoperative data	Transfusion pRBC, units	2	3	2	3	2	3	1.00
Dissection phase	Transfusion FFP, units	3	4	3	4	3	5	0.80
	Transfusion cryoprecipitate (5-packs)	0	2	0	2	0	1	0.86
	Hematocrit (%)	28.9	5.7	28.9	5.9	28.8	5.4	0.84
	Glucose (mg/dL)	119	34	119	30	120	39	0.80
	Lactate (mmol/L)	2.1	1.2	2.1	1.2	2.1	1.2	0.85
	pH	7.4	0.1	7.4	0.1	7.4	0.1	0.61
	Ionized calcium (mmol/L)	1.16	0.80	1.22	1.03	1.06	0.12	0.04
	Sodium (mmol/L)	136	5	136	5	136	5	0.27
	Potassium (mmol/L)	3.9	0.5	3.9	0.5	3.9	0.5	0.83
	Norepinephrine, μg	141	386	135	394	148	376	0.70
Anhepatic	Transfusion pRBC, units	2	5	2	5	2	4	0.93
	Transfusion FFP, units	3	4	2	5	3	4	0.75
	Transfusion cryoprecipitate (5-packs)	0	1	0	1	0	0	0.49
	Hematocrit	26.4	5.0	26.4	5.5	26.3	4.7	0.69
	Glucose	145	46	146	45	144	47	0.50
	Lactate	4.1	1.9	4.1	1.9	4.2	1.9	0.54
	pH	7.35	0.10	7.35	0.12	7.36	0.06	0.45
	Ionized calcium	1.08	0.19	1.08	0.19	1.09	0.20	0.55
	Sodium	137	6	137	5	136	7	0.17
	Potassium	4.0	0.6	4.0	0.7	3.9	0.6	0.21
	Norepinephrine, μg	104	241	99	241	110	241	0.57
Immediate reperfusion	Norepinephrine, μg	6	14	6	14	6	14	0.74
	MAP, mm Hg	55	14	55	14	56	14	0.45
Reperfusion	Transfusion pRBC, units	5	10	4	9	6	12	0.02
	Transfusion FFP, units	6	10	5	8	7	12	0.01
	Transfusion cryoprecipitate (5-packs)	2	5	2	4	3	5	0.05
	Hematocrit	23.4	4.9	23.8	5.7	23.0	3.6	0.05
	Glucose	204	54	201	54	208	53	0.13
	Lactate	5.1	2.5	4.9	2.4	5.4	2.5	0.01
	pH	7.34	0.06	7.34	0.07	7.34	0.06	0.91
	Ionized calcium	1.88	2.41	1.87	2.27	1.89	2.59	0.94
	Sodium	138	5	138	5	138	5	0.95
	Potassium	3.8	0.6	3.8	0.6	3.9	0.6	0.02
	Norepinephrine, μg	623	1227	514	1157	770	1303	0.01
Total intraoperative results	Transfusion pRBC, units	9	16	8	14	10	17	<0.001
	Transfusion FFP, units	12	16	11	14	14	18	<0.001
	Hematocrit	26.5	4.3	26.6	4.5	26.3	4.0	0.33
	Glucose	156	38	154	37	158	40	0.13
	Lactate	3.5	1.7	3.4	1.7	3.6	1.7	0.04

(Continues)

TABLE 3 (Continued)

Variable	Level	All data (n = 598)		No KDIGO Stage 2 or 3 (n = 343)		KDIGO Stage 2 or 3 (n = 255)		*p* value
		Mean	SD	Mean	SD	Mean	SD	*t* test
	pH	7.36	0.06	7.36	0.06	7.36	0.07	0.90
	Ionized calcium	1.79	2.43	1.80	2.31	1.78	2.60	0.95
	Sodium	137	5	137	5	137	5	0.92
	Potassium	3.9	0.5	3.9	0.5	3.9	0.5	0.41

TABLE 4 Patient outcomes after LT (n = 598)

Stage	n	Percentage	Stage	Total	Percentage
(A) Outcome: KDIGO					
0	227	38.0	0 or 1	343	57.4
1	116	19.4			
2	149	24.9	2 or 3	255	42.6
3	106	17.7			

			AKI (Stage 2 or 3)				
	Total	Percentage	Yes (n = 255)	Percentage	No (n = 343)	Percentage	*p* value (chi-square test)
(B) Outcome: mortality							
30 days	23	3.8	9	3.5	14	4.1	0.12
90 days	31	5.2	15	5.9	16	4.7	0.44
1 year	54	9.0	24	9.4	30	8.7	0.08
3 years	78	13.0	43	16.9	35	10.2	0.02

with posttransplant AKI.[2,42–44] This interesting result could result from (1) covariates that were unable to be quantified in our data (such as graft mismatch), (2) inefficiencies associated with eGFR equation accuracy in patients with cirrhosis, (3) unaccounted operative factors such as procedural or technical complexity (eg, with vascular clamping for anastomosis), or (3) physiologic etiology (BUN is also lower in the AKI, perhaps secondary to dilutional effect from ascites).[45] Finally, Black patients were not more likely to develop AKI following LT, which builds on an earlier study showing no difference in early hemodialysis based on race, but lower discontinuation of dialysis in Black transplant patients.[46]

A variety of donor factors have been shown to be associated with posttransplant AKI, including donation after cardiac death,[47] ischemia time,[48,49] high-risk grafts,[32] and older donor age.[32] Our study failed to show any association between donor-specific variables and posttransplant AKI. This may be the result of improved institutional effort in matching high-risk donors with recipients at lower risk for complications such as AKI and lower risk donors with higher risk recipients.

Our study builds on prior work incorporating intraoperative variables into the prediction model. Prior studies have characterized the effect of major classes of intraoperative variables, including blood transfusion,[25,49] hemodynamic variables (most notably, intraoperative hypotension),[25,50–52] vasopressor/inotropic support,[25,51,52] surgical technique,[25] laboratory values,[12,25,52] and hypovolemia.[26,30] Our study failed to show an association between intraoperative MAP or intraoperative transfusion (packed red blood cells [pRBC], FFP, or cryoprecipitate) with the primary outcome. We did, however, find an association between higher lactate and potassium levels, but not norepinephrine doses and AKI. Further study is needed to determine if potassium and lactate levels may act as intermediate variables, mediating the effects of blood transfusions and blood pressure. Further study is also needed to determine if factors such as hypotension, which seems to fluctuate earlier, may be an earlier marker than potassium and lactate, which would be lagging indicators. The kidney excretes potassium and metabolizes lactate. Rises in potassium and lactate may be an early marker of renal dysfunction and ischemia. This might allow for an early intervention that reverses renal ischemia and prevents dysfunction from progressing to AKI. Further study is needed to better understand the possible protective association of INR with AKI. One potential explanation is that correction of INR leads to resuscitation with a high volume of FFP, which may lead to a better volume reserve that protects

TABLE 5 Multivariate logistic regression results in Models 1 to 4

		aOR	95% CI	*p* value
Model 1				
Patient demographics	BMI	1.077	1.044–1.112	<0.001
Comorbidities	Fluid or electrolyte disorders	2.040	1.374–3.030	<0.001
	Iron-deficiency anemia	2.985	1.623–5.489	<0.001
	Cardiac arrhythmia	1.818	1.240–2.666	0.00
Preoperative laboratory values	Albumin	0.611	0.431–0.865	0.01
	Sodium	0.965	0.928–1.003	0.07
	BUN	0.963	0.944–0.982	<0.001
	INR	0.606	0.420–0.875	0.01
	eGFR, MDRD-4	1.007	1.001–1.013	0.03
Model 2				
Patient demographics	BMI	1.077	1.044–1.112	<0.001
Comorbidities	Fluid or electrolyte disorders	2.040	1.374–3.030	<0.001
	Iron-deficiency anemia	2.985	1.623–5.489	<0.001
	Cardiac arrhythmia	1.818	1.240–2.666	0.00
Preoperative laboratory values	Albumin	0.611	0.431–0.865	0.01
	Sodium	0.965	0.928–1.003	0.07
	BUN	0.963	0.944–0.982	<0.001
	INR	0.606	0.420–0.875	0.01
	eGFR, MDRD-4	1.007	1.001–1.013	0.03
Model 3				
Patient demographics	Age	0.979	0.962–0.995	0.01
	BMI	1.079	1.044–1.114	<0.001
Comorbidities	Fluid or electrolyte disorders	1.917	1.280–2.869	0.00
	Iron-deficiency anemia	2.612	1.405–4.854	0.00
	Cardiac arrhythmia	1.629	1.101–2.410	0.02
	Unexpected weight loss	1.596	1.006–2.532	0.05
Preoperative laboratory values	Albumin	0.576	0.410–0.808	0.00
	BUN	0.952	0.935–0.969	<0.001
	INR	0.469	0.321–0.685	<0.001
	eGFR, MDRD-4	1.007	1.001–1.013	0.03
Reperfusion variables	Reperfusion potassium	1.513	1.103–2.077	0.01
	Reperfusion lactate	1.081	1.003–1.166	0.04
Model 4				
Patient demographics	Age	0.979	0.962–0.995	0.01
	BMI	1.079	1.044–1.114	<0.001
Comorbidities	Fluid or electrolyte disorders	1.917	1.280–2.869	0.00
	Iron-deficiency anemia	2.612	1.405–4.854	0.00
	Cardiac arrhythmia	1.629	1.101–2.410	0.15
	Unexpected weight loss	1.596	1.006–2.532	0.05
Preoperative laboratory values	Albumin	0.576	0.410–0.808	0.00
	BUN	0.952	0.935–0.969	<0.001
	INR	0.469	0.321–0.685	<0.001

(Continues)

TABLE 5 (Continued)

		aOR	95% CI	*p* value
	eGFR, MDRD-4	1.007	1.001–1.013	0.03
Reperfusion variables	Reperfusion potassium, mmol/L	1.513	1.103–2.077	0.01
	Reperfusion lactate, mmol/L	1.081	1.003–1.166	0.04

Note: Model 1, preoperative variables: AKI after LT (c-statistic = 0.741 ± 0.026); model 2, preoperative variables plus donor factors (c-statistic = 0.741 ± 0.026); model 3, preoperative variables, donor factors, and intraoperative variables: reperfusion (c-statistic = 0.759 ± 0.032); model 4, complete end of case data (c-statistic = 0.759 ± 0.032).

TABLE 6 Cox proportional hazards ratio models associated with mortality in Models 5 and 6

		aHR	95% CI	*p* value
Model 5				
Patient demographics	Black/African American	Reference		
Race	White	1.010	0.498–2.045	0.98
	Unknown	3.058	1.314–7.117	0.01
	Other	3.388	1.159–9.902	0.03
Comorbidities	Pulmonary/circulation disorders	1.731	0.863–3.472	0.12
	Hepatocellular carcinoma	1.611	1.075–2.414	0.02
Preoperative laboratory values	Platelets	1.005	1.003–1.007	<0.001
	eGFR, MDRD-4	1.008	1.003–1.013	0.00
Donor factors	CMV positive	1.431	0.964–2.124	0.08
	EBV positive	0.702	0.352–1.399	0.29
	Warm ischemia time, minutes	1.025	1.006–1.045	0.01
Intraoperative details	log(cryoprecipitate total)	2.345	0.865–6.359	0.09
	log(FFP total)	3.412	1.959–5.942	<0.001
	Reperfusion ionized calcium	0.835	0.707–0.987	0.04
	Reperfusion pH (scale 10)	0.469	0.367–0.601	<0.001
Outcomes	KDIGO stage 2 or 3	1.202	0.818–1.767	0.35
Model 6				
Patient demographics	Black/African American	Reference		
Race	White	0.926	0.455–1.884	0.83
	Unknown	2.962	1.286–6.822	0.01
	Other	3.138	1.066–9.232	0.04
Comorbidities	Pulmonary/circulation disorders	1.453	0.714–2.957	0.30
	Hepatocellular carcinoma	1.72	1.138–2.599	0.01
Preoperative laboratory values	Platelets	1.005	1.003–1.007	<0.001
	eGFR, MDRD-4	1.009	1.004–1.014	<0.001
Donor factors	CMV positive	1.523	1.021–2.271	0.04
	EBV positive	0.758	0.399–1.44	0.38
	Warm ischemia time, minutes	1.025	1.005–1.045	0.02
Intraoperative details	log(cryoprecipitate total)	2.115	0.742–6.024	0.16
	log(FFP total)	3.152	1.801–5.517	<0.001
	Reperfusion ionized calcium	0.830	0.696–0.991	0.04
	Reperfusion pH (scale 10)	0.499	0.385–0.647	<0.001
Outcomes	Dialysis by day 7	3.324	1.603–6.894	0.001

Note: In model 5, the primary outcome KDIGO 2 or 3 is included. In model 6, RRT is included.

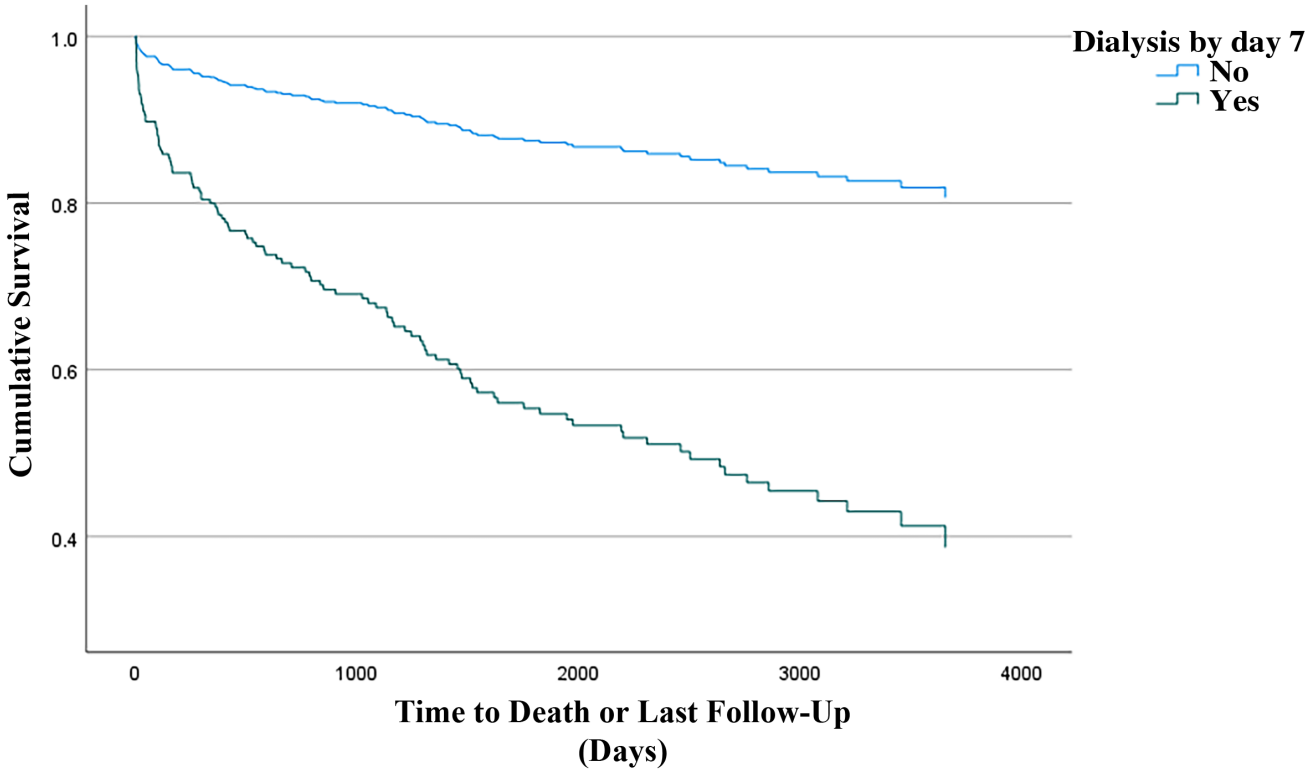

FIGURE 1 Kaplan-Meier curve estimate of mortality as a function of time for patients requiring dialysis within 7 days after transplantation

against the decreased organ perfusion associated with large hemorrhages.

Posttransplant AKI was not an independent risk for mortality. This contrasts with prior studies showing a strong association.[27,48] This could be because the study was powered to detect the secondary outcome of mortality, which occurred with much lower frequency than the primary outcome. However, as we found that receipt of dialysis within 7 days after transplant was associated with late mortality, it may be that AKI with recovery of renal function has little effect on mortality, whereas AKI that persists is associated with mortality. This is similar to a study in cardiac surgery patients where AKI, defined by KDIGO, was not associated with late mortality when discharge renal function was included in the model[53] or, as the subanalysis in patients requiring dialysis within 7 days suggests, that the effect may be driven by a smaller subset of all posttransplant patients with AKI.

Strengths and weaknesses

The limitations of our study include the retrospective design from a single center that limits the causality. In addition, this cross-sectional study only allows us to look at associations at isolated time points, limiting how much we can truly infer from the results. However, given the extreme strength of associations, stage-specific prediction models based on these findings would elucidate specific intraoperative changes needed to prevent AKIs. This risk-prediction model could be trained with multicenter data, allowing it to be widely applicable and implemented into current anesthesia management best practices. Although we had accurate and complete urine output during the intraoperative period, we did not have urine output consistently documented for 7 postoperative days. Therefore, our primary outcome did not include urine output in the diagnostic criteria despite inclusion in the KDIGO definition. Another limitation is that surgical technique (classical bicaval anastomosis vs. piggyback) was not collected as part of our standardized reporting metrics. Future studies will control for this covariate through the language processing of operative reports. A final limitation is that our objective was to stratify the risk for postoperative AKI at the time of transplantation completion. Model discrimination might be improved by incorporating postoperative data, specifically administration of nephrotoxic immunosuppressants,[54] subsequent development of sepsis,[41] and early allograft dysfunction[55]; however, this was beyond the scope of our objective.

Conclusions

In this retrospective observational study performed at an academic quaternary care center, we found a 43% incidence of AKI within the first

7 days following LT and receipt of dialysis within 7 days of LT was associated with increased mortality. Our study demonstrated that most AKI discrimination (0.741 ± 0.026 compared with 0.759 ± 0.032 for full model) can be obtained with preoperative factors. The addition of intraoperative data did not improve overall model discrimination, although the study may have been underpowered to detect this change. Even if adequately powered, the overall improvement in discrimination by adding intraoperative data is minimal. This may suggest that by the time the intraoperative data are collected, renal injury has already mostly occurred. These high-risk patients would be ideal for prospective studies to prevent AKI. In addition, intraoperative intermediate outcomes of potassium and lactate levels, potentially indicative of early renal ischemia or dysfunction, contribute a small component of overall AKI risk. Future studies on intraoperative and postoperative management may assess whether early intervention can mitigate this risk.

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CONFLICT OF INTEREST

Nothing to report.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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