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ORIGINAL ARTICLE

Early acute kidney injury after liver transplantation in patients with normal preoperative renal function

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KEYWORDS
Liver transplantation;
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Risk factors;
KDIGO;
Clinical outcomes

Summary
Aim: Acute kidney injury (AKI) commonly occurs in patients after liver transplantation (LT). However, few studies have focused on AKI and its correlation with clinical outcomes under the Kidney Disease Improving Global Outcomes (KDIGO) criteria. This study aimed to identity the incidence, risk factors, and impacts of early AKI on outcomes in LT recipients with normal preoperative renal function, according to the KDIGO criteria.
Methods: Clinical and laboratory data of 227 patients with normal preoperative renal function who underwent LT from January 2011 to January 2015 were retrospectively analyzed.
Results: During the first week after LT, 106 patients (46.7%) developed AKI based on the KDIGO criteria. A multivariate analysis revealed that BMI of > 25, prolonged inferior vena cava clamping, prolonged cold ischemia time, and post-operative RBC requirements > 10 units were independent risk factors for AKI after LT. The area under the receiver operating characteristic curve for the predictive ability of AKI under these risk factors was 0.748. The occurrence of AKI was associated with longer mechanical ventilation time and post-operative ICU stay, increased post-operative 30-day mortality and decreased long-term patient survival.
Conclusions: Even in patients with normal preoperative renal function, AKI was a frequent complication in LT recipients and had both negative short- or long-term effects on patient outcomes, also the severity of AKI had a dose-response relationship with worse outcomes. Patients with BMI > 25, prolonged inferior vena cava clamping, prolonged cold ischemia time, or post-operative RBC requirement > 10 units should be pay particular attention, which may assist in achieving better clinical outcomes.

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Introduction

Liver transplantation (LT) remains an effective treatment for end-stage liver disease (ESLD). However, acute kidney injury (AKI) is a common life-threatening complication after LT and has a wide range of incidence based on different diagnostic criteria [1—4]. The etiology of AKI after LT is multifactorial and includes ischemic renal tubular necrosis, the use of nephrotoxic drugs, and the effects of severe liver disease on the kidneys, such as hepatitis-associated glomerulonephritis, alcoholic liver disease, and related IgA kidney disease [5,6]. The Kidney Disease Improving Global Outcomes (KDIGO) criteria is considered to combine the merits of the Risk, Injury, Failure, Loss, and End-stage kidney disease (RIFLE) and acute Kidney Injury Network (AKIN) criteria [7,8], showing that even slight changes in renal function are associated with adverse outcomes [9]. The KDIGO criteria is reportedly more suitable than the RIFLE criteria for acute myocardial infarction patients [10], and superior to both the RIFLE and AKIN criteria in early cardiorenal syndrome type 1 patients, irrespective of the identified or predicted short-term prognosis [11]. AKI is associated with an increased mortality rate after LT however, few studies have used the KDIGO criteria [12]. Otherwise, a good deal of previous studies has showed that patients with preoperative renal impairment were at significant risk for developing AKI after LT [1,2,4], but it is less clear among patients with normal pre-operative renal function. We aimed to identify the incidence and risk factors for AKI in adult LT patients with normal pre-operative renal function and clarify the short- and long-term effects of early AKI on patient outcomes.

Patients and methods

After obtaining approval from the Committee of Ethics from Sichuan University (protocol number 2016100), we retrospectively reviewed medical records of 277 consecutive adult patients (age, > 18 years) with ESLD who underwent LT from January 2011 to January 2015 at the West China Hospital, Sichuan University, China. Twenty-six patients were pediatric LT recipients, 3 patients received second LT, 4 patients who died or were automatically discharged within 48 h after surgery and 17 cases were fulminant hepatic failure patients. All fulminant hepatic failure patients had preoperative renal dysfunction, 12 of which received preoperative RRT for high SCr, anuria or serious fluid and electrolyte disorders such as hyperkalemia. These patients were all excluded. Finally, 227 patients with preoperative SCr within normal limits (SCr $\leq$ 1.3 mg/dL for men and 1.0 mg/dL) for women were included. Pre-, intra-, and post-operative clinical and laboratory data were used to identify the incidence and risk factors for AKI. Post-operative data were mainly used to analyze patient outcomes. The study flow chart of the selection and exclusion criteria of patients is shown in Fig. 1.

The Jaffe colorimetric method (ADVIA 1650, Bayer, Germany) was used to measure the SCr concentration. The reference value for adults is 0.6 to 1.3 mg/dL for men and 0.6 to 1.0 mg/dL for women. Pre-operative renal dysfunction included elevated preoperative serum creatine, with SCr > 1.3 mg/dL for men and > 1.0 mg/dL for women, and pre-operative renal replacement treatment.

Owing to high prevalence of HBV in China and its poor long-term clinical outcome [13], HBV-related hepatic cirrhosis and HBV-associated hepatocellular carcinoma were major indications for the 227 LT patients, the other indications were miscellaneous ESLD, including primary or secondary cholestatic cirrhosis, HCV-related hepatic cirrhosis, autoimmune hepatitis, cholangio cellular carcinoma, and Wilson's disease. We also included patient demographics, history of hypertension, diabetes mellitus, encephalopathy, ascites, variceal bleeding, portal venous thrombosis, Model for End-stage Liver Disease (MELD) Score, and Child—Pugh Scores. Pre-operative laboratory data included RBC, platelet counts, hemoglobin, total bilirubin, serum albumin, glucose, serum creatinine (Scr), serum sodium, and serum potassium levels, and coagulation parameters (INR, APTT, and FIB).

Intra-operative data included type of liver allograft [donation after circulatory death (DCD) or living donor], graft-recipient weight ratio, operation selection (piggy-back or classic), warm ischemia time, cold ischemia time, duration of inferior vena cava (IVC) clamping, anhepatic phase, operation time, blood loss volume, blood products, and fluid transfusion. Only two LTs were performed with a veno-venous bypass. Post-operative data included daily Scr level in the first week after LT, post-operative blood product requirements in the first week after LT, duration of mechanical ventilation, duration of post-operative ICU stay and hospitalization, and post-operative 30-day mortality. All patients were accepted follow up for at least 1 year, long-term survival data were also collected.

The KDIGO criteria used to define early AKI (first week after LT) were a 50% increase from the baseline (pre-operative value) Scr level or a 26.4-mmol/L increase from baseline within 48 h. Immunosuppression after LT was provided as the standard protocol and calcineurin inhibitors (tacrolimus), mycophenolate mofetil, and corticosteroids were all initiated within 24 h after LT. Dosage adjustments of tacrolimus was guided by the daily blood concentration and replaced with sirolimus if renal impairment continued. Mycophenolate mofetil and corticosteroids were tapered and discontinued. None of patients received an induction therapy for delaying use of calcineurin inhibitors.

All analyses were performed using the statistical package for the social sciences version 21.0 (SPSS Inc., Chicago, IL). Continuous variables were tested for normality of distribution and if not normally distributed were presented as median and interquartile ranges and analyzed using the Mann—Whitney U test. Normally distributed continuous variables were presented as mean $\pm$ SD and analyzed using the Student's *t*-test. Categorical variables were described as frequency and analyzed using the Pearson Chi^2 test or Fisher's exact test. All variables were investigated using a univariate analysis, and only those variables found to be statistically significant were included in the multivariate analysis. In the multivariate analysis, a backward stepwise elimination algorithm was used to retain risk factors in the final model when $P = 0.05$. A collinearity diagnostics was used to estimate the risk of collinearity of multivariate analysis. The Kaplan—Meier method was used to estimate patient survival, long-term patient survival between AKI and non-AKI

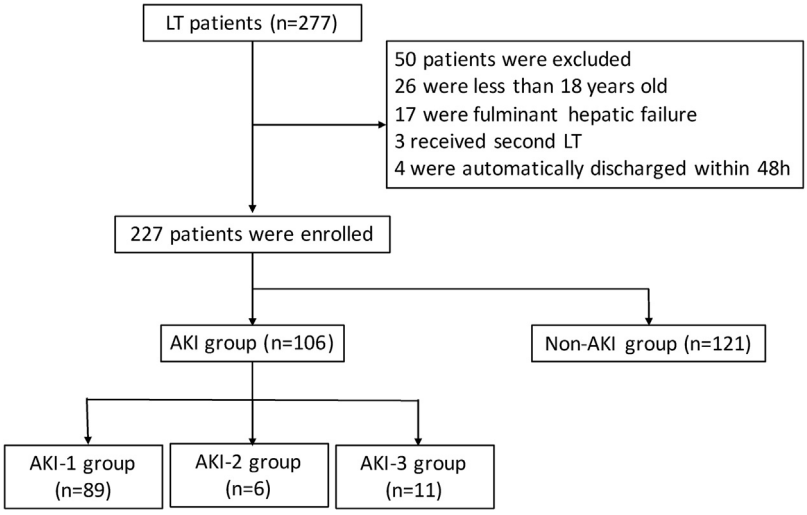

Figure 1 Screening and enrolment of patients.

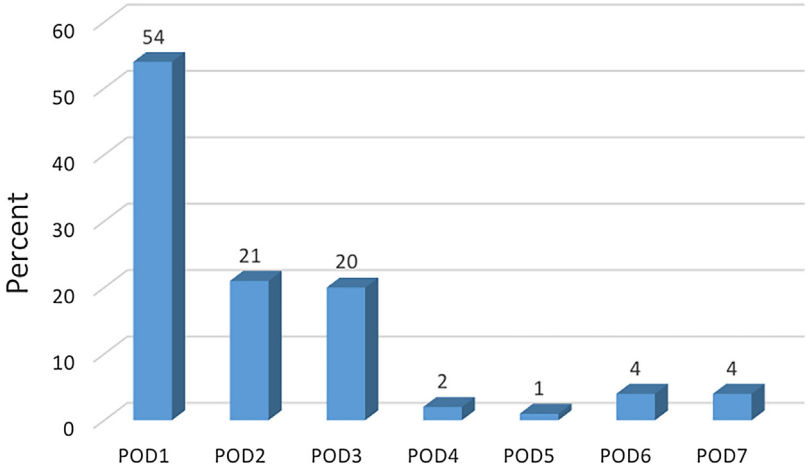

Figure 2 SCr peak time of patients with acute kidney injury (AKI).

group were compared with the log-rank test, $P \leq 0.05$ was considered statistically significant.

Results

Incidence of early AKI after LT

Among 227 patients, 106 (46.7%) developed early AKI within 7 days after LT based on the KDIGO criteria, the incidence of AKI stage 1 was 39.2% (89 of 227 patients), stage 2 was 2.6% (6 of 227 patients) and stage 3 was 4.8% (11 of 227 patients). In our study, stage 1 was defined as mild AKI, while stage 2 and 3 were combined as severe AKI. Of those 106 patients, 10.4% (11 of 106) needed renal replacement therapy (RRT) during the first week. It was worthy of note that Scr of all patients with AKI increased within 48 hours after LT, 93 patients appeared on first post-operative day, and 13 patients appeared on second day. Meanwhile, it was also noted that 95 patients with AKI reached a peak of Scr within 3 days after LT (Fig. 2).

Risk factors for early AKI after LT

Pre-, intra-, post-operative and donor graft data and the univariate results are shown in Tables 1—3. Results revealed that only a BMI > 25, prolonged IVC clamping, prolonged cold ischemia time, and a post-operative RBC requirement > 10 units were significantly associated with the development of early AKI after LT (Table 4). The area under the receiver operating characteristic curve for the predictive ability of AKI under these risk factors was 0.748, and the specificity of the predictive test was 0.6, the sensitivity was 0.786, also with the positive likelihood ratio of 1.96, and the negative likelihood ration of 0.36, ($P < 0.001$, Fig. 3).

Impact of AKI on patient outcomes

Table 5 shows that compared with non-AKI group, the AKI group had significantly longer mechanical ventilation (31 vs. 17 h, $P = 0.001$) and post-operative ICU stay (10.4 vs. 9.1 days, $P = 0.018$). Post-operative nosocomial infection was also more common ($P = 0.001$) and hospital mortality rate

Table 1 Descriptions of preoperative variables and univariate results.

Pre-operative variables	Total ($n = 227$)	AKI ($n = 106$)	Non-AKI ($n = 121$)	*P*-value
Female, *n* (%)	43 (18.9)	16 (15.1)	27 (22.3)	0.166
Age, mean (SD), year	46.2 (9.7)	46.8 (9.8)	45.6 (9.5)	0.344
BMI > 25, *n* (%)	53 (23.3)	36 (34)	17 (14)	< 0.001
Etiology, *n* (%)				
HBV-related hepatic cirrhosis	66 (29.1)	34 (32.1)	32 (26.4)	0.351
HBV-associated hepatocellular carcinoma	149 (65.6)	66 (66.2)	83 (68.6)	0.316
Miscellaneous ESLD	12 (5.3)	6 (5.7)	6 (5)	0.814
Hypertension, *n* (%)	8 (3.6)	5 (4.8)	3 (2.5)	0.478
Diabetes mellitus, *n* (%)	19 (8.4)	11 (10.5)	8 (6.7)	0.305
Encephalopathy, *n* (%)	10 (4.4)	6 (5.7)	4 (3.3)	0.521
Ascites, *n* (%)	49 (21.6)	23 (21.7)	26 (21.5)	0.969
Variceal bleeding, *n* (%)	21 (9.3)	11 (10.4)	10 (8.3)	0.584
MELD Score, median (IR)	11 (9—17)	12 (9—17.3)	11 (8.5—17)	0.289
Child—Pugh Score, median (IR)	9 (7—11)	9 (7—11)	8 (7—11)	0.105
Hemoglobin, mean (SD), g/L	116.94 (29.1)	114.64 (28.8)	118.96 (29.3)	0.265
Platelet, median (IR), 10^9/L	73 (40—110)	71 (38.75—109.3)	75 (40—112.5)	0.88
WBC, median (IR), 10^9/L	4.51 (3.1—6.2)	4.32 (2.9—6.0)	4.77 (3.2—6.6)	0.338
Total bilirubin, median (IR), μmol/L	26.7 (15.2—73.7)	30.75 (18.4—75.6)	24.6 (13.9—73.6)	0.287
BUN, median (IR), mmol/L	4.92 (4.0—6.3)	4.99 (4.0—6.4)	4.81 (3.9—6.1)	0.417
Serum creatinine, median (IR), μmol/L	71 (61.5—83.2)	72 (72.68—83.4)	71 (60—83.5)	0.259

AKI: acute kidney injury; ESLD: end-stage liver disease; MELD: Model for End-stage Liver Disease.

Table 2 Descriptions of donor graft characteristics.

Variables	Total ($n = 227$)	AKI ($n = 106$)	Non-AKI ($n = 121$)	*P*-value
Graft characteristics				
Donor age, mean (SD), year	35.05 (11.6)	35.01 (11.4)	35.08 (11.9)	0.965
Graft—recipient weight ratio, mean (SD)	1.6% (0.6%)	1.58% (0.6%)	1.61% (0.7%)	0.786
Organ status				
DCD *n* (%)	156 (68.7)	79 (74.5)	77 (63.6)	0.077
Cold ischemia time, median (IR), h	6.3 (4.4—97)	6.9 (5—10)	5.8 (4.2—8.6)	0.011

AKI: acute kidney injury; DCD: donation after circulatory death.

Table 3 Descriptions of intra-operative and post-operative variables and univariate results.

Intra-operative variables	Total ($n = 227$)	AKI ($n = 106$)	Non-AKI ($n = 121$)	*P*-value
Piggyback, *n* (%)	130 (57.3)	59 (55.7)	71 (58.7)	0.647
Warm ischemia time, median (IR), min	18 (10—30)	19 (11—30)	17 (10—30)	0.432
Cold ischemia time, median (IR), h	6.3 (4.4—97)	6.9 (5—10)	5.8 (4.2—8.6)	0.011
Duration of clamping IVC (IR), min	85 (68—105)	95 (71.8—111.3)	80 (63.5—95)	< 0.001
Anhepatic phase, median (IR), min	86 (67—106)	95 (75—115)	8 0(65—100)	< 0.001
Operation time, median (IR), h	8.8 (7.8—10.3)	9.1 (7.9—10.8)	8.5 (7.5—9.9)	0.061
Blood loss, median (IR), mL	1150 (800—2000)	1200 (1000—2500)	1000 (700—2000)	0.034
RBC transfusion, median (IR), unit	5.5 (0—10.3)	6.5 (1.3—11.5)	5 (0—9.9)	0.303
FFP transfusion, median (IR), mL	600 (0—1150)	750 (0—1200)	550 (0—1025)	0.108
Cryoprecipitate, median (IR), unit	0 (0—0)	0 (0—7.25)	0 (0—0)	0.176
Fluid transfusion, median (IR), mL	6500 (5000—8000)	7000 (5250—8050)	6300 (5000—8000)	0.122
Post-operative variables				
RBC transfusion, median (IR), unit	0 (0—5)	1.75 (0—7.25)	0 (0—2)	< 0.001
RBC transfusion, *n* (%)				
≤ 5 units	174	72	102	0.077
5—10 units	24	14	10	0.193
> 10 units	29	20	9	0.029
FFP transfusion, median (IR), mL	0 (0—0)	0 (0—637.5)	0 (0—0)	0.007

AKI: acute kidney injury.

Table 4 Multivariate logistic regression analysis to evaluate risk factors for AKI.

Variables	Odds ratio	95% CI	*P*-value
BMI > 25	3.403	1.688—6.86	0.001
Duration of clamping IVC	1.015	1.005—1.024	0.003
Cold ischemia time	1.068	1.001—1.139	0.047
Post-operative RBC			
≤ 5 units	1.701	0.757—3.819	0.198
5—10 units	2.314	0.89—6.016	0.085
> 10 units	4.884	1.963—12.15	0.001

AKI: acute kidney injury; IVC: inferior vena cava.

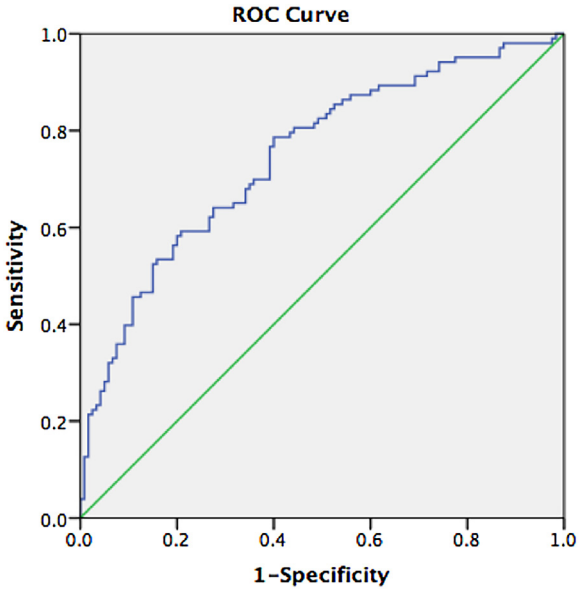

Figure 3 Area under the receiver operating characteristic curves for the predictive ability of acute kidney injury (AKI) under these risk factors.

was significantly higher in the AKI group (9.43% vs. 2.5%, $P = 0.024$). Furthermore, increasing severity of AKI was associated with both longer mechanical ventilation and higher incidence of post-operative infection (Table 6). Although the overall hospital stay was longer and the incidence of acute rejection and reoperation was higher in the AKI group, the results were not significantly different from the non-AKI group.

Overall, 49 patients developed at least one kind of infections within hospitalization following LT, including 46 bacterial infections, 2 fungus infections and 1 EBV infection. Among the bacterial infections, pulmonary infections cases were 34, abdominal infections were 7 cases, bloodstream infections were 3 cases, urinary infection was 1 case and incision infection was 1 case. 13 patients were combined with more than one kind of infections. Among of these, pulmonary infections were the most common (69.4%), including 7 cases in non-AKI group and 27 cases in AKI group, which was consist with longer mechanical ventilation time in AKI patients. Gram-negative bacteria mainly accounted for it. The most frequent pathogens in pulmonary infections were *Acinetobacter baumanii*, *Pseudomonas aeruginosa* and *Klebsiella pneumonia*.

To examine the possible impact of AKI risk factors on post-operative complications, a Spearman's rank-order cor-

Table 5 Comparisons of post-operative rehabilitation between the AKI and non-AKI groups.

Variables	Total ($n = 227$)	AKI ($n = 106$)	Non-AKI ($n = 121$)	*P*-value
Ventilation time, median (IR), h	19 (11—42.5)	31 (12.3—79)	17 (10—35)	0.001
ICU stay, median (IR), h	234 (179—303.5)	250.5 (187.5—363.5)	220 (173—292)	0.018
Hospitalization duration, (IR), d	25 (19—36)	24 (19.8—38.3)	25 (18—34.5)	0.231
Post-operative nosocomial infection, *n* (%)	49 (21.6)	35 (33)	14 (11.57)	0.001
Reoperation, *n* (%)	25 (11)	12 (11.2)	13 (10.7)	0.834
Acute rejection, *n* (%)	19 (8.4)	10 (9.4)	9 (7.4)	0.588

AKI: acute kidney injury.

Table 6 Comparisons of mechanical ventilation and post-operative infection of different AKI classes.

Variables	Non-AKI($n = 121$)	Mild AKI($n = 89$)	Severe AKI($n = 17$)	*P*-value
Ventilation time, median (IR), h	17 (10—35)	27 (12—57)	130 (46—186.5)	< 0.001
Post-operative nosocomial infection, *n* (%)	14 (11.6)	26 (29.2)	9 (52.9)	< 0.001

AKI: acute kidney injury.

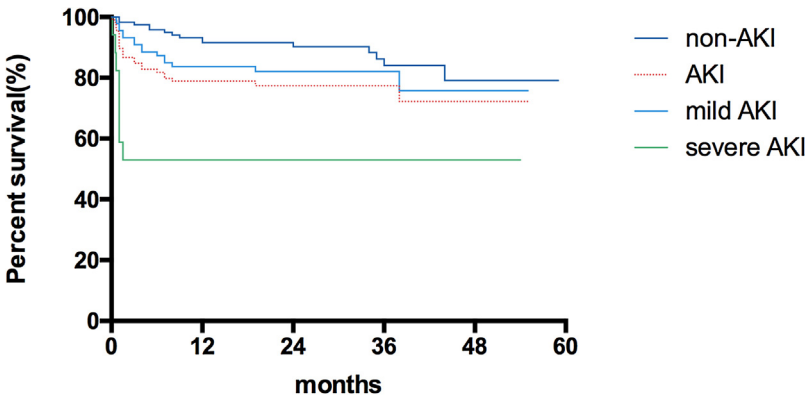

Figure 4 Kaplan—Meier survival curves of patients with and without acute kidney injury (AKI). Log-rank comparisons: non-AKI vs. AKI: $P = 0.024$; non-AKI vs. mild AKI: $P = 0.177$; non-AKI vs. severe AKI: $P < 0.001$; mild AKI vs. severe AKI: $P = 0.002$; non-AKI group: patients without AKI; AKI group: all patients with AKI; mild AKI group: patients of AKI stage 1; severe AKI group: patients of AKI stage 2 and stage 3.

relation was run to examine the relationship between RBC transfusion and post-operative infection, which revealed a positive correlation between the two (Spearman's $r = 0.306$, $P < 0.001$). Similarly, increasing requirements for RBC correlated well with more frequent use of RRT (Spearman's $r = 0.377$, $P < 0.001$), which further corroborated the impact of blood transfusion on AKI and clinical outcomes.

For all patients, the 30-day mortality was 5.7% (13 of 227). In the non-AKI group, it was 2.5% (3 of 121) and 9.4% (10 of 106) in the AKI group which was significantly higher than non-AKI group. Furthermore, compared to severe AKI group (35.3%), both non-AKI group and mild AKI group had lower 30-day mortality (4.5%), $P < 0.001$. However, there was no significance between non-AKI group and mild AKI group.

In Kaplan-Meier curves, the 1-year survival rates of non-AKI, mild AKI and severe AKI were 97.5%, 90.8.4%, 52.9%, respectively. Compared with non-AKI group, the patient survival of AKI group was significantly lower ($P = 0.024$), as well as severe AKI ($P < 0.001$), whereas there was no significant difference between non-AKI and mild AKI. Among AKI group, severe AKI patients did worse than mild AKI patients ($P = 0.002$, Fig. 4).

Discussion

Emerging evidence shows that LT patients experience a high incidence of AKI after LT, leading to a poor prognosis. In our study, the AKI time limit set was the first 7 days after LT for we aimed to discuss early AKI and its perioperative causes and strategies. Based on the KDIGO criteria, we found that patients with normal preoperative renal function were at significant risk for developing AKI after LT, evidently indicating AKI was a frequent and early complication after LT, worthy sufficient attention as early as possible. Furthermore, AKI was associated with prolonged mechanical ventilation and ICU stays, increased 30-day mortality and 1-year mortality, and patient outcomes worsened with the severity of AKI, similar to a previous study [14], providing further evidence that AKI is a potentially devastating complication for LT patients and has significant adverse impacts both on short- and long-term clinical outcomes.

We noted, differing from others [15], there was no association between AKI and the MELD Scores in our study. Unlike others, we excluded patients who underwent pre-operative RRT and who had fulminant hepatic failure, as we aimed to explore AKI after LT in patients with normal pre-operative renal function. Patients with fulminant hepatic failure were often accompanied with serious hepatorenal syndromes that requiring pre-operative RRT, also with high MELD Scores. After excluding patients with high MELD Scores, the importance of its association with AKI was not apparent as the MELD Score was not a risk factor in our study. On the other hand, high incidence of AKI might be associated with high prevalence of HBV, for HBV infection patients may be susceptible to renal impairment such as membranous nephropathy and polyarthritis nodosa [16], which was consistent with HBV-related hepatic cirrhosis and hepatocellular carcinoma as major indications for LT in this study.

With advance of living standards and change of life style in China, incidence of overweight and obesity are improving year after year, which has become important public health problems. The BMI cut-off values once to define overweight and obesity [17], might not apply to current Chinese population. Furthermore, a growing number of studies have demonstrated that the standards of overweight and obesity has been increased [18]. Therefore, we adopted the standards from WHO defining BMI > 25 as overweight in our study. It was noteworthy that BMI of > 25 was a strong independent risk factor for AKI after LT, consistent with the study by Iglesias [3,19]. Although there is link between high BMI and the development of chronic kidney disease [20], the association with AKI is less clear. Patients with high BMI have an increased potential risk of serious metabolic syndromes, including hypertension, dyslipidemia, cardiovascular and cerebrovascular diseases [21]. Obesity-induced changes, such as hyperfiltration syndrome, glomerular hypertrophy, and mesangial hyperplasia, can potentially affect kidney function, even if there were no apparent changes under normal conditions before LT. However, after a long-term surgical strike, AKI maybe the result of combined function changes. Furthermore, obese LT recipients may have higher rates of post-operative infection [22,23]. In the present study, patients with BMI of > 25 in the AKI group (14 of 36)

suffered a significantly higher incidence of post-operative infection compared with those in the non-AKI group (2 of 19) ($P = 0.017$). It was evident that obesity was closely linked with AKI after LT, although further studies are required to elucidate the pathophysiological process.

Prolonged IVC clamping was another strong predisposing factor related to AKI after LT because during the anhepatic phase, there is a progressive decrease in cardiac output and increase in the IVC pressure as blocking IVC. This results in a sudden decrease in renal perfusion and a decline in the glomerular filtration rate [24], leading to renal function impairment. Meanwhile, serious intra-operative acidosis indicates poor perfusion of the whole body, and the kidneys would be the first organs to be affected [1]. Moreover, an unstable hemodynamic situation during IVC blocking can be overcorrected by administering excessive fluids and overusing vasoactive agents. As duration of IVC clamping increases, the abovementioned problems interact with each other, further complicating the intra-operative situation and may contribute to a worsening of the clinical situation. Donor age and cold ischemic time are considered to be vitally important for assessing the graft quality [25,26]. However, a prolonged cold ischemic time exacerbates graft ischemic injury and worsens the liver graft quality, thereby negatively influencing the outcome for LT recipients [26]. This poses a problem in that some strategies are required to optimize graft allocation. In contrast, some novel preservation techniques, such as hypothermic and subnormothermic machine perfusion, may minimize graft ischemic injury [27,28].

The development of AKI was related to massive blood transfusion within the first week after LT. In addition, the current study also corroborated that blood transfusion might result in higher incidence of post-operative infection and more requirements of RRT. It is evident that massive blood product transfusion has a number of well-recognized adverse effects. First, as storage time increases, 2, 3-diphosphoglycerate, adenosine triphosphate, and reactive nitric oxide in the RBCs decrease, impairing oxygen delivery and vascular regulation [29,30]. Conversely, an iron overload can induce oxidative stress by catalyzing oxygen free radicals, leading to acute renal tubule epithelium injury [31]. Furthermore, various blood product components are considered to produce a large amount of inflammatory mediators and induce systemic inflammatory response syndrome [32,33]. Cumulatively, the interactions of these factors may exacerbate tissue perfusion, thereby harming the kidneys. On the other hand, systemic inflammatory response syndrome and immunosuppression caused by blood transfusion, might be associated with increased risk of infection complications, which was also consistent with previous study [34,35].

What can be done to prevent occurrence of AKI? Intra-operative management of renal function may be a key to peri-operative renal protection. Vasopressors should be applied with caution, for risk of decreasing renal perfusion [36]. Other measures include avoiding unnecessary radio contrasts, nephrotoxic drugs and possible post-operative infection. In addition, individualized immunosuppression also plays a vital role [37]. Moreover, emerging biomarkers, such as neutrophil gelatinase-associated lipocalin, kidney injury molecule-1, and cystatin C may facilitate earlier detection of renal deterioration and permits an earlier intervention [38—41].

The limitations of our study include its retrospective, uncontrolled design and some important data were missing. First, intra- and post-operative urine output was incomplete, although the urine output is easily impacted by clinical factors such as diuretics and intravascular volume, and it is inappropriate for acute non-oliguricacute kidney injury [42]. Furthermore, the small sample size and not very long follow-up period may undermine the validity of our results. Thus, there is clearly a requirement for a prospective large scale trial to further understand LT-associated AKI in the future, including its pathophysiology, prevention sand treatments.

Conclusions

Even in patients with normal preoperative renal function, the high incidence of AKI during the first week after LT was evidenced based on the KDIGO criteria, demonstrating the significant adverse impacts of AKI on short- and long-term clinical outcomes, and the severity of AKI has a dose-response relationship with worse outcomes. Moreover, BMI of > 25, prolonged IVC clamping, prolonged cold ischemia time, and post-operative RBC requirements > 10 units were risk factors for AKI after LT. Adequate perioperative management of renal function should be the focus for preventing AKI. Prospective and large sample studies are warranted to further understand the pathophysiology of LT recipients at risk of renal dysfunction.

Author contributions

L.T., J.Y., Y.Y. and T.Z. contributed to the study design. L.T., Y.Y., G.M., J.Y. performed the data acquisition. L.T., Y.Y., G.M. and W.Z. did the statistical analysis. L.T., G.M., H.L. and T.Z. did the article writing.

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Disclosure of interest

The authors declare that they have no competing interest.

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