Original Article

Effect of positive cumulative fluid balance on postoperative complications after living donor liver transplantation: A retrospective analysis

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ABSTRACT

Background and Aims: Fluid administration during liver transplant (LT) surgery is controversial. Although adverse outcomes following positive intraoperative fluid balance have been reported, studies presenting the influence of cumulative postoperative fluid balance (CFB) on complications following LT are sparse. Patients with chronic liver disease tend to receive more fluid during and after surgery due to their unique physiological disease state. The aim of this study was to evaluate the influence of 48-hour CFB on the development of acute kidney injury (AKI) and pulmonary complications on day 4 after live donor LT. **Methods:** This retrospective study included 230 patients undergoing live donor LT. The effect of CFB on day 2 on AKI and pulmonary complications was analysed. Chi-square test, Fisher's exact test, samples t-test, Mann-Whitney U-test were used. **Results:** Bivariate analysis showed a lower graft vs recipient weight ratio (GRWR), sepsis ($P < 0.001$) and a higher 48-hour CFB after surgery significantly increased the development of AKI. For pulmonary complications, higher Model for End- stage Liver Disease-Na (MELD-Na) score, higher peak arterial lactate, higher 48-hour CFB ($P = 0.016$) and sepsis ($P = 0.003$) were found to be statistically significant. Upon multivariate analysis, CFB at 48 hours was significantly higher in patients suffering from pulmonary complications, and GRWR and sepsis were significant for AKI. For every one litre increase in CFB on day 2, the odds of pulmonary complications increased by 37%. **Conclusion:** A more positive CFB on day 2 increased the development of pulmonary complications and lower GRWR and sepsis increased the development of AKI.

Key words: Acute kidney injury, cold ischaemia, live donor, liver transplantation, postoperative period, risk factors, saline solutions

INTRODUCTION

Respiratory and renal insufficiencies are common after liver transplantation (LT) and lead to increased postoperative morbidity and mortality. Positive fluid balance may be an important causative factor for these complications.[1] However, definitive evidence in this regard is lacking in the field of LT.

The practice of liberal fluid administration has evolved into a restrictive approach over the last few years in postsurgical patients due to the evolution of dynamic techniques for measuring fluid requirement like stroke volume variation, pulse pressure variation, transoesophageal echocardiography apart from the standard parameters such as blood pressure, central venous pressure, heart rate and urine output. However, there are many challenges to a restrictive fluid approach

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in LT due to the physiology of chronic liver disease, especially low systemic vascular resistance, presence of collaterals, coagulation defects, portal hypertension and the presence of leaky capillaries that hinder the practice of restrictive approach.[2] In addition, patients with end-stage liver disease (ESLD) have a fragile renal system, so it is important to avoid hypovolemic stress on the kidneys during LT.[2]

A positive fluid balance increases the postoperative mortality and morbidity in many postsurgical procedures.[3] It increases interstitial oedema in the renal parenchyma and leads to increased venous pressure. Kidneys being an encapsulated organ, increased venous pressure can jeopardise the renal blood supply making them susceptible to injury.[4] The literature is controversial on this subject with one study showing that increased cumulative fluid balance on day 4 can lead to AKI with a need for renal replacement therapy.[1] A few others showed an increased risk of AKI with the restrictive fluid approach,[5] and yet, others showed a beneficial effect of early goal-directed fluid resuscitation on the overall prognosis of postsurgical patients.[6] There are no definitive guidelines on the subject. The aim of the present study was to find the influence of 48-hour cumulative fluid balance on the development of AKI and pulmonary complications on day 4 after live donor LT.

METHODS

After approval by the Institutional Ethics Committee of the Institute of Liver and Biliary Sciences (ILBS) on 18.2.2019 (Ref No. F.25/5/107/ILBS/AC/2016/11252/293-303), this retrospective analysis was performed.

All patients of age ≥18 years who underwent living donor LT at the ILBS for chronic liver disease and acute on chronic liver disease from January 2015 to July 2018 were included in the study. All medical and surgical charts were reviewed by a single observer. Paediatric patients (<18 years), patients with acute liver failure, patients on dialysis or mechanical ventilation pre-operatively, deceased donor LT and patients with incomplete records were excluded.

The demographics, diagnosis, graft-to-recipient weight ratio (GRWR), Model for end-stage liver disease-Na scoring (MELD-Na) and hepatorenal and hepatopulmonary syndromes were noted. The intra-operative data collected were duration of surgery, warm ischaemia and cold ischaemia times (in minutes), amount of crystalloids (plasmaLyte was used at our centre) and colloids (albumin was the only colloid used), urine output, blood loss and use of inotropes (norepinephrine and vasopressin). In general, fluid administration was guided by stroke volume variation (more than 10%) or a decrease in cardiac output by 20% on FloTrac (Edward Lifesciences, Irvine, USA) or MAP ≤55 mm Hg; however, the volume of plasmaLyte or albumin administered was at the discretion of the anaesthetist conducting the case.

The intraoperative fluid balance was calculated by subtracting the urine output and blood loss from the total amount of crystalloid, colloid, and blood products transfused. Blood loss was calculated by the amount of blood in drains and the weight of sponges and gauzes measured on a weighing scale minus the wash (amount of normal saline to wash the surgical site and wet the gauzes and sponges) used. The day-wise postoperative fluid balance was calculated by subtracting the sum total of urine output and drain output from the total fluid intake orally or intravenously and the blood products administered on the respective day in ICU. The above-mentioned intraoperative and postoperative fluid balances on day 1 and day 2 were added to find the cumulative fluid balance at 48 hours. Postoperative acute kidney injury (AKI, grades 1, 2 and 3) was defined according to the kidney disease improving global outcome (KDIGO) criteria.[7] Regarding pulmonary complications, pleural effusion was diagnosed on the basis of blunting of angle on chest X-ray, pulmonary oedema by fine crepitations on auscultation of the chest and/or clinical detection of pink frothy sputum, consolidation by lung ultrasound by coalesced B lines or diffuse B lines, transfusion-associated lung injury as a diagnosis of exclusion and adult respiratory distress syndrome (ARDS) according to the Berlin Criteria,[8] and sepsis was defined according to the surviving sepsis guidelines.[9] The duration of mechanical ventilation, length of ICU stay and hospital stay and mortality (up to 30 days) were also noted.

The primary objective of the study was to find whether an increased 48-hour cumulative fluid balance leads to increased postoperative AKI and pulmonary complications on day 4 of live donor LT. The secondary objective of the study was to find if increased cumulative fluid balance on day 2 led to increased development of sepsis, and increased the length of mechanical ventilation, length of ICU and hospital stay and mortality.

Descriptive statistics were presented in the form of mean and standard deviation for all continuous variables, and in the form of frequencies (percentages) for all categorical variables. Bivariate association between categorical variables was assessed using the Chi-square test or Fisher's exact test, whichever were applicable. To test the difference in mean values between two groups, either independent samples t-test or Mann-Whitney U-test, whichever were suitable was used. Logistic regression analyses were performed to identify independent factors associated with various postoperative complications. Receiver operating curve (ROC) analysis was performed to identify the best cut-off point for better risk stratification. The data were initially entered into Microsoft Excel and then imported to Statistical Package for the Social Sciences (SPSS). All statistical analyses were performed using SPSS for Windows version 23 (Armonk, IBM Corp.).

RESULTS

A total of 230 live donor LT recipients with a mean age of 47 ± 9.7 years were studied. The demographics, perioperative characteristics and postoperative complications are listed in Table 1. The cold ischaemia time ranged from 41 to 198 minutes with a mean of 94.9 ± 25.5 minutes. The average duration of surgery was 13.7 ± 2.2 hours [Table 1].

The various fluids administered intraoperatively were as follows: crystalloid 65.6%, albumin 7.7%, packed red blood cells (PRBC) 17.1%, FFP 6.8%, cryoprecipitate 1.1% and platelet 1.6%.

The bivariate analysis revealed that the GRWR was significantly lower ($P = 0.006$) and the cumulative fluid balance on day 2 ($P = 0.016$) and incidence of sepsis ($P < 0.001$) were significantly higher in patients who developed AKI [Table 2]. Upon multivariate analysis, lower GRWR and sepsis were independent predictors of AKI [Table 3].

Upon bivariate analysis, younger age ($P = 0.002$), male sex ($P = 0.010$), higher MELD-Na ($P = 0.002$), higher GRWR ($P = 0.028$), higher peak arterial lactate ($P = 0.031$), a higher cumulative fluid balance on day 2 ($P = 0.005$) and sepsis ($P = 0.003$) were found statistically significant for patients who developed pulmonary complications [Table 4]. But upon multivariate analysis, only age, male sex, GRWR, MELD Na, sepsis and cumulative fluid balance on day 2 were found to be independent predictors of pulmonary complications [Table 3]. It was seen that for every one litre increase in cumulative fluid balance on day 2, the odds of pulmonary complications increased by 37% and a 95% CI for it suggested that this increase could be as low as 8% and as high as 74%.

Upon comparison between the patients who had sepsis and those who did not, it was seen that there was a statistically significant difference in the percentage of patients with the right lobe as a graft ($P = 0.001$), lower BMI ($P = 0.008$), higher number of packed red blood cells given ($P = 0.033$), higher peak arterial lactate ($P < 0.001$),

Table 1: Baseline, intraoperative and postoperative characteristics of patients (*n*=230)

Preoperative factors	Values
Age (Years)	47.1±9.7
Sex - Male/Female	198/32
BMI (kg/m^2)	24.8±4.5
Indication for liver transplant (LT)	
Decompensated chronic liver disease	198 (85.7%)
Hepatocellular carcinoma	14 (6.1%)
Acute on chronic liver failure	19 (8.2%)
Severity of disease- MELD Na score	23.3±5.9
Hepatopulmonary syndrome	14 (6%)
Hepatorenal syndrome	9 (4%)
Intraoperative factors	
Duration of surgery (hours)	13.7±2.2
Cold ischaemia time (CIT) in minutes	94.9±25.5
Graft to recipient weight ratio (GRWR)	0.9±0.2
Lobe - left/right	48/182
Packed red blood cells (PRBC)	8.4±5.5
Total number of blood products	14.9±12.4
Norepinephrine (% patients)	230 (99.5%)
Vasopressin (% patients)	190 (82.2%)
Peak arterial lactate (mmol/L)	5.7±2.0
Blood loss (in litres)	3.2±2.1
Postoperative cumulative fluid balance at Day 2 (ml)	13075.4±4768.9
Postoperative complications	
Pleural effusion	69 (29.9%)
Consolidation/Pneumonia	33 (14.3%)
Acute respiratory distress syndrome	5 (29.2%)
Pulmonary oedema	5 (2.2%)
Transfusion-related acute lung injury	2 (0.9%)
Reintubation	34 (14.7%)
Acute kidney injury Stage 1	39 (16.9%)
Acute kidney injury Stage 2	32 (13.9%)
Acute kidney injury Stage 3	24 (10.4%)
Sepsis	63 (27.3%)
Mortality within first 30 days	14 (6.1%)
Length of mechanical ventilation (days)	1.99±5.70
Length of ICU stay	10 (4-64)
Length of hospital	21 (5-300)

Values presented as mean±SD or as median (minimum-maximum) or as both. BMI: Body mass index, MELD: Model for End-stage Liver Disease, ICU: Intensive care unit, Total blood products = PRBC + Cryoprecipitate + Fresh Frozen Plasma + Single donor platelet

Table 2: Comparison of baseline, intraoperative and postoperative characteristics of patients by development of postoperative AKI

Factors	No AKI (*n*=135)	Had AKI (*n*=95)	*P*
Age (Years)	46.4±9.9	48.1±9.4	0.18
Sex - Female/male	17/118	15/80	0.49
Duration of surgery (hours)	13.8±2.3	13.4±2.1	0.16
BMI	24.8±4.1	24.8±5.0	0.90
MELD Na	23.7±5.9	22.8±5.9	0.24
GRWR	1.0±0.2	0.9±0.2	0.006**
Lobe- left/right	25/110	23/72	0.30
HRS	3 (2.2%)	6 (6.3%)	0.11
Cold ischemia time (minutes)	95.6±25.9	93.9±25.1	0.62
PRBC	8.1±5.1	8.9±6.0	0.24
Total number of blood products	14.3±11.2	15.7±13.9	0.39
Norepinephrine	9.9±3.9	10.5±5.7	0.35
Vasopressin	1.7±1.2	2.0±1.5	0.11
Peak arterial lactate	5.7±2.0	5.8±2.0	0.77
Blood loss	3.1±1.3	3.2±2.8	0.76
CFB Day 2	12442.6±4169.4	13974.7±5406.5	0.016*
Sepsis	23 (17.0%)	40 (42.1%)	<0.001**

*P<0.05, **P<0.01 BMI - Body mass index, MELD: Model for End-stage Liver Disease, GRWR - Graft vs recipient weight ratio, PRBC- Packed red blood cell, HRS- Hepatorenal syndrome, CFB day 2- Postoperative cumulative fluid balance on day 2, AKI-Acute kidney injury

Table 3: Multivariate analysis of the predictors of AKI, respiratory complication, length of mechanical ventilation, ICU stay and hospital stay

Complication	Odds ratio/Beta	95% CI
AKI	Odds Ratio	
Graft to recipient weight ratio	0.140*	[0.029,0.682]
Sepsis	3.565**	[1.898,6.696]
Respiratory Complications	Odds Ratio	
Age (years.)	0.954**	[0.924,0.986]
Male sex	3.607**	[1.536,8.468]
MELD Na score	1.062*	[1.009,1.118]
Graft vs recipient weight ratio	8.017*	[1.573,40.850]
Cumulative fluid balance-Day 2	1.367*	[1.076,1.736]
Sepsis	1.965*	[1.010,3.821]
Sepsis	Odds Ratio	
Right Lobe	0.332**	[0.153,0.717]
Peak arterial lactate	1.208*	[1.014,1.439]
AKI stage	3.880**	[1.931,7.799]
Lung complications	2.088*	[1.064,4.097]
Length of Mechanical Ventilation	Beta	
Peak arterial lactate	0.561*	[0.132,0.990]
Length of ICU Stay	Beta	
Age (years)	-0.199**	[-0.328,-0.070]
Right lobe	-4.124**	[-7.157,-1.090]
Peak arterial lactate	1.093**	[0.421,1.765]
Length of Hospital Stay	Beta	
BMI	-0.829*	[-1.547,-0.111]
Graft to recipient weight ratio	-19.51*	[-35.930,-3.090]

*P<0.05, **P<0.01, BMI - Body mass index, MELD - Model for End-stage Liver Disease, AKI-Acute kidney injury. ICU-Intensive care unit

with higher requirements of intraoperative noradrenaline and vasopressin ($P < 0.05$), higher incidence of AKI ($P < 0.001$) and pulmonary complications ($P = 0.003$) and higher cumulative fluid balance on day 2. ($P = 0.028$) [Table 5]. The selection of right lobe graft, higher intraoperative peak arterial lactate and higher incidence of AKI and pulmonary complications remained as the independent predictors of sepsis amongst the factors analysed by multivariate analysis [Table 3].

Upon simple linear regression analysis, a higher peak arterial lactate and vasopressin requirement were found to significantly increase the length of mechanical ventilation, ICU and hospital stay. The length of mechanical ventilation was prolonged in patients with a higher preoperative MELD-Na, increased requirement of norepinephrine, increased number of PRBCs, total number of products transfused and increased cumulative fluid balance on day 2. The duration of ICU stay was significantly increased with increased age and increased cumulative fluid balance on day 2, whereas higher BMI and a lower GRWR significantly increased the duration of hospital stay [Table 6].

Upon multivariate analysis, peak arterial lactate was the only independent predictor of longer duration of mechanical ventilation. Age and the selection of right lobe graft were seen to predict longer duration of ICU stay, and increased BMI and lower GRWR were seen for increased duration of hospital stay [Table 3].

DISCUSSION

The major findings of the present study include that for every litre of cumulative fluid balance on day 2, the odds of pulmonary complications increased by 37%. Although a positive cumulative fluid balance was significantly higher in patients who developed AKI and sepsis or had a longer duration of mechanical ventilation and ICU stay, it was not significant on multivariate analysis. Although many studies on deceased donor LT have reported similar results, the data are sparse for live donor LT.[10-12] Furthermore, no study has evaluated cumulative fluid balance at 48 hours. Patients after LT generally resume oral feeds after 48 hours. Therefore, determining a cumulative fluid requirement becomes important till then and has to be primarily determined by dynamic and static measures such as stroke volume variation, blood pressure and heart rate. Once the patient starts taking food orally, the fluid intake becomes on-demand and is regulated mostly by the patients themselves.

Table 4: Comparison of baseline, intraoperative and postoperative characteristics of patients by their postoperative pulmonary complications

Factors	Pulmonary complication absent (*n*=141)	Pulmonary complication present (*n*=89)	*P*
Age (Years)	48.7±9.0	44.6±10.3	0.002**
Sex - female/male	13/128	19/70	0.010*
Duration of surgery (hours)	13.7±1.9	13.6±2.7	0.68
BMI	25.1±4.6	24.4±4.3	0.30
MELD Na	22.3±5.8	24.8±5.9	0.002**
GRWR	0.9±0.2	1.0±0.2	0.028*
Lobe- left/right	26/115	22/67	0.25
HPS	6 (4.3%)	8 (9.0%)	0.14
Cold ischaemia time (minutes)	94.5±26.8	95.6±23.4	0.76
PRBC	8.0±5.6	9.1±5.2	0.17
Total number of blood products	14.0±12.0	16.3±12.9	0.16
Norepinephrine	9.9±4.3	10.4±5.3	0.44
Vasopressin	1.8±1.4	1.9±1.4	0.43
Peak arterial lactate	5.5±1.7	6.1±2.3	0.031*
Blood loss	3.1±2.3	3.3±1.5	0.60
CFB Day 2	12373±4511.0	14187.6±4976.7	0.005**
Sepsis	29 (20.6%)	34 (38.2%)	0.003**

*P<0.05, **P<0.01, BMI- Body mass index, MELD: Model for End-stage Liver Disease, GRWR- Graft vs recipient weight ratio, HPS - Hepatopulmonary syndrome, PRBC- Packed red blood cell, Total blood products = PRBC + Cryoprecipitate + Fresh Frozen Plasma + Single donor platelet, CFB day 2- Postoperative cumulative fluid balance on day 2

Table 5: Comparison of baseline, intraoperative and postoperative characteristics of patients by development of postoperative sepsis

Factors	No sepsis (*n*=167)	Had sepsis (*n*=63)	*P*
Age (Years)	47.7±9.6	45.6±10.0	0.16
Sex- Female/male	23/144	9/54	0.92
Duration of surgery (hours)	13.8±2.0	13.4±2.8	0.36
BMI	25.3±4.4	23.5±4.6	0.008**
MELD Na score	23.1±5.9	23.9±6.2	0.36
GRWR	0.9±0.2	0.9±0.2	0.59
Lobe- left/right	26/141	22/41	0.001**
HRS	6 (3.6%)	3 (4.8%)	0.68
HPS	10 (6.0%)	4 (6.3%)	0.92
Cold ischaemia time (minutes)	96.2±25.1	91.6±26.5	0.22
PRBC	8.0±5.5	9.7±5.2	0.033*
Total number of blood products	14.0±12.3	17.2±12.5	0.085
Norepinephrine	9.6±4.3	11.6±5.5	0.003**
Vasopressin	1.7±1.3	2.2±1.5	0.008**
Peak arterial lactate	5.4±1.8	6.4±2.2	<0.001**
Blood loss	3.2±2.3	3.2±1.2	0.91
CFB Day 2	12653.1±4493.8	14195.0±5308.2	0.028*
AKI	55 (32.9%)	40 (63.5%)	<0.001*
Pulmonary complication	55 (32.9%)	34 (54.0%)	0.003**

*P<0.05, **P<0.01. BMI - Body mass index, MELD: Model for end-stage liver disease, GRWR - Graft vs recipient weight ratio, PRBC - packed red blood cell, HRS - Hepatorenal syndrome, HPS - Hepatopulmonary syndrome, Total blood products=PRBC + Cryoprecipitate + Fresh Frozen Plasma + Single donor platelet, CFB - Postoperative cumulative fluid balance, AKI-Acute kidney injury

AKI is the most common complication following LT. The present study did not show any influence of CFB on AKI, which is similar to other reports that studied the CFB at 24 and 72 hrs.[11,13] However, Codes *et al.* reported an increased incidence of early AKI (as high as 72%) with a positive day-4 CFB of 11841 ± 5395 ml after surgery.[1]

The aetiology of AKI in LT is multifactorial and includes high level of toxic free radicals during ischaemia reperfusion injury, renal ischemia caused by hypotension due to sudden blood loss during surgery or clamping of inferior vena cava, use of nephrotoxic medications (tacrolimus) etc.[5,11,14]

Various other risk factors are associated with the development of AKI such as advanced age, diabetes mellitus and high MELD;[1,11,15-18] however, in the present study, only GRWR and presence of sepsis

Table 6: Bivariate association, as assessed based on simple linear regression, of baseline, intraoperative and postoperative characteristics of present study participants with the length of- mechanical ventilation, ICU stay and hospital stay

Characteristic	Length of Mechanical Ventilation		ICU stay		Hospital stay	
	Beta	95% CI	Beta	95% CI	Beta	95% CI
Age (Years)	-0.0197	-0.097, 0.058	-0.216**	-0.343-0.089	-0.0427	-0.341,0.255
Sex - Male	0	0.000,0.00	0	0.000,0.00	0	0.000,0.000
Female	0.67	-1.502, 2.843	1.131	-2.518, 4.780	3.389	-4.970,11.747
Duration of Surgery (hours)	0.112	-0.227, 0.451	-0.459	-1.025, 0.106	-0.869	-2.170,0.432
BMI	-0.0546	-0.222,0.113	-0.0822	-0.364, 0.200	-0.646*	-1.287,-0.005
MELD Na	0.178**	0.053,0.303	0.0677	-0.145, 0.281	-0.395	-0.881,0.091
Graft to recipient weight ratio	-0.886	-4.813, 3.042	-4.537	-10.993, 1.918	-15.49*	-30.441,-0.538
Left Lobe	0	0.000,0.000	0	0.000,0.000	0	0.000,0.000
Right Lobe	0.429	-1.421,2.280	-4.113**	-7.177,-1.050	-4.121	-11.229,2.987
Cold ischaemia time (in minutes)	0.00726	-0.022, 0.037	0.0156	-0.034, 0.065	-0.0248	-0.139,0.089
PRBC	0.155*	0.019,0.292	0.158	-0.072, 0.388	0.33	-0.198,0.859
Total number of blood products	0.0989**	0.039,0.158	0.0896	-0.012, 0.191	0.19	-0.044,0.423
Norepinephrine	0.271**	0.114,0.427	0.156	-0.113, 0.424	0.690*	0.080,1.301
Vasopressin	0.762**	0.223,1.301	0.997*	0.086,1.908	2.497*	0.413,4.581
Peak arterial lactate	0.781**	0.414,1.149	1.415**	0.802,2.028	1.879*	0.432,3.326
Blood loss	0.15	-0.217,0.517	-0.0512	-0.668, 0.566	0.329	-1.085,1.743
CFB Day2	0.213*	0.057,0.369	0.308*	0.045,0.570	0.460	-0.145,1.066

BMI - Body mass index, MELD: Model for End-stage Liver Disease, PRBC - packed red blood cell, Total blood products = PRBC + Cryoprecipitate + Fresh Frozen Plasma + Single donor platelet, HRS - Hepatorenal syndrome, HPS - Hepatopulmonary syndrome, CFB - Cumulative fluid balance. *P<0.05, **P<0.01

were found to be significant. Whether sepsis was the cause or effect of AKI is difficult to interpret due to the retrospective design of the study. To the best of our knowledge, no study on LT surgery has investigated the relation of sepsis with AKI or pulmonary complications following live donor LT. Patients with cirrhosis are predisposed to the development of AKI due to the existence of excessive splanchnic vasodilation and hyperaemia which causes prerenal failure in these patients. These changes may take up to two years to resolve post LT.[19] In the postoperative period, if this vasodilation is superimposed by sepsis, it may further lead to the development of AKI.

The incidence of postoperative pulmonary complications ranges from 40 to 80% in various studies.[10,20-22] In our study, the pulmonary complications rate was 38.7%. Pulmonary complications after LT may be due to preoperative lung pathology due to cirrhosis (hepatic hydrothorax, hepatopulmonary syndrome, portopulmonary syndrome), increased susceptibility of infection due to immunosuppressive drugs and high incidence of blood transfusion during LT.

We observed a statistically significant increase in the incidence of postoperative pulmonary complications with an increase in positive CFB on day 2. Although we could not find any study evaluating the influence of positive postoperative CFB on pulmonary complications, a few studies in diseased donor LT report the beneficial effects of negative fluid balance (on one of the days in the first 3 days) on pulmonary complications.[12,20] A few other studies have demonstrated that increased intraoperative fluid balance adversely affects lung functions in LT recipients. Jipa *et al.* found that an intraoperative fluid balance of more than 7600 ml is associated with the development of postoperative pulmonary complications versus 5085 ml in patients without pulmonary complications.[20]

Sahmeddini *et al.*, in 2014, demonstrated increased pulmonary complications in the non-restricted group (received 10 ml/kg/hr) vs the restricted group who received 5 ml/kg/hr intraoperatively.[2]

Measures to prevent positive CFB should include reliance on dynamic indices for fluid administration such as stroke volume variation, pulse pressure variation, transoesophageal echocardiography for administering fluids. Similarly, inotropes should be administered only when the indices indicate a lack of fluid responsiveness. Another approach can be to administer more colloids than crystalloids for resuscitation. Blood products must be replaced instead of crystalloids when acutely bleeding with haemodynamic instability in correlation with the dynamic measure of coagulation such as thromboelastography. However, these approaches

are not proven and further studies are needed in this field.

One of the major limitations of the present study is its retrospective design. No standardised protocol was followed for fluid administration and some may have preferred fluid to vasopressors and vice versa. In addition, due to the retrospective nature of the analysis, some of the confounding factors such as intraoperative haemodynamic instability and postoperative drugs like tacrolimus which have a direct impact on the development of AKI could not be taken into account. Thus, randomised controlled trials may be needed in this field to overcome these limitations.

CONCLUSION

We conclude that increased positive 48-hour CFB after LT increases the development of pulmonary complications but has no effect on the development of AKI. A lower GRWR and sepsis increased the development of AKI.

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Conflicts of interest

There are no conflicts of interest.

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