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ORIGINAL ARTICLE

Observational Study

Cumulative positive fluid balance is a risk factor for acute kidney injury and requirement for renal replacement therapy after liver transplantation

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Abstract

AIM

To analyze whether fluid overload is an independent risk factor of adverse outcomes after liver transplantation (LT).

METHODS

One hundred and twenty-one patients submitted to LT were retrospectively evaluated. Data regarding perioperative and postoperative variables previously associated with adverse outcomes after LT were reviewed. Cumulative fluid balance (FB) in the first 12 h and 4 d after surgery were compared with major adverse outcomes after LT.

RESULTS

Most of the patients were submitted to a liberal approach of fluid administration with a mean cumulative FB over 5 L and 10 L, respectively, in the first 12 h and 4 d after LT. Cumulative FB in 4 d was independently associated with occurrence of both AKI and requirement for renal replacement therapy (RRT) (OR = 2.3; 95%CI: 1.37-3.86, P = 0.02 and OR = 2.89; 95%CI: 1.52-5.49, P = 0.001 respectively). Other variables on multivariate analysis associated with AKI and RRT were, respectively, male sex and Acute Physiology and Chronic Health Disease Classification System (APACHE II) levels and sepsis or septic shock. Mortality was shown to be independently related to AST and APACHE II levels (OR = 2.35; 95%CI: 1.1-5.05, P = 0.02 and 2.63; 95%CI: 1.0-6.87, P = 0.04 respectively), probably reflecting the degree of graft dysfunction and severity of early postoperative course of LT. No effect of FB on mortality after LT was disclosed.

CONCLUSION

Cumulative positive FB over 4 d after LT is independently associated with the development of AKI and the requirement of RRT. Survival was not independently related to FB, but to surrogate markers of graft dysfunction and severity of postoperative course of LT.

Key words: Liver transplantation; Fluid balance; Acute kidney injury

Core tip: Whether fluid overload is an independent mediator of adverse outcomes on early postoperative liver transplantation (LT). The influence of fluid accumulation on morbidity and mortality after LT has not been well evaluated up to now. This study aims to analyze whether fluid management influences the early postoperative outcome after LT. Cumulative positive fluid balance (FB) over 4 d after LT influence the development of acute kidney injury and it is a risk factor for the requirement for renal replacement therapy. Survival is not independently related to FB but to surrogate markers of graft dysfunction.

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INTRODUCTION

It is well recognized that fluid overload in critically-ill patients may lead to anasarca, pulmonary edema, abdominal compartment syndrome (ACS) and also multiple organ dysfunction due to its deleterious effect in tissue perfusion[1-3]. In this regard, positive fluid balance (FB) has been shown to be associated with adverse outcomes in patients admitted to the intensive care unit (ICU) with sepsis and septic shock[4-6], acute respiratory distress syndrome (ARDS)[7,8], acute kidney injury (AKI)[9-15] and cancer[16]. Conversely, positive FB was also linked to increased morbidity and mortality after abdominal surgery[17-19], including esophagectomy[20], open aortic aneurysm repair[21] and rectal cancer surgery[22]. In most of these reports cumulative FB in the first 4 d were reliable indicators of worse outcomes in clinical[4] and surgical[21] ICU patients. On the contrary, restrictive fluid administration policies have led to a reduction in overall morbidity, including AKI, and increased survival in surgical[23-26] and medical[9,27,28] patients in the ICU. Few data is available in the literature concerning the impact of positive FB in the postoperative course of liver transplantation (LT)[29-32]. Some authors have described an increased frequency of postoperative pulmonary morbidity[29-32] and ileus[31] that could be prevented with restrictive administration of fluids[30,31]. No association between FB and AKI or survival after LT was disclosed in those aforementioned studies[29-32].

The aims of the present study were analyze whether cumulative positive FB is associated with the occurrence of AKI, requirement for renal replacement therapy (RRT) and 28-d mortality after LT.

MATERIALS AND METHODS

One-hundred twenty one patients submitted to LT at the Portuguese Hospital of Salvador, Bahia, Brazil who underwent surgery in a period of 5 years were retrospectively evaluated. All medical and surgical charts as well as electronic files were reviewed by a single observer in order to collect data regarding perioperative and postoperative variables, previously associated with adverse outcomes after LT, including demographics; etiology of liver disease; indication for LT; severity of liver disease assessed by MELD and Child-Pugh scores; perioperative parameters such as cold ischemia time, duration of surgery, need for inotropic support, FB and use of vasoactive drugs; Acute Physiology and Chronic Health Disease Classification System (APACHE II) score, peak lactate, AST and ALT levels; occurrence of postoperative complications, including early allograft dysfunction (EAD) and primary graft non-function (PGNF), biliary strictures or leaks, hepatic artery thrombosis or stenosis, AKI and requirement for RRT, acute rejection, sepsis and septic shock; cumulative FB in the first 12 h and 4 d; length of stay (LOS) in the ICU and in the hospital; mortality and causes of death in the first 28 d. The patients were evaluated in a single admission, when they entered the hospital to be transplanted

Child-Pugh, MELD and APACHE II scores were calculated as previously described[33-35]. Early allograft dysfunction was defined according to the definition of Olthoff *et al*[36] and PGNF was defining as EAD

Table 1 Baseline characteristics before liver transplantation (*n* = 121)

Male sex	106 (88%)
Age (yr)	50 ± 13
Etiology of chronic liver disease	
Hepatitis C	39 (32%)
Hepatitis C and alcoholic liver disease	12 (10%)
Alcoholic liver disease	36 (30%)
Cryptogenic and/or non-alcoholic steatohepatitis	10 (8%)
Hepatitis B	4 (3%)
Cholestatic liver disease	6 (5%)
Autoimmune hepatitis	4 (3%)
Others	10 (8%)
Indication for liver transplantation	
Decompensated cirrhosis	93 (77%)
Hepatocellular carcinoma	28 (23%)
Severity of liver disease at admission	
Child-Pugh score	9 ± 2
MELD score	18 ± 6

Data are expressed as mean ± SD. MELD: Model for end-stage liver disease.

Table 2 Intraoperative and postoperative features of the patients submitted to liver transplantation (*n* = 121)

Cold ischemia time (min)	520 ± 170
Duration of surgery (min)	333 ± 104
Use of blood products	77 (63%)
Number of packed red blood cell units	1.9 ± 3.1
Use of vasoactive drugs (norepinephrine)	38 (31%)
Peak of arterial lactate in the first 24 h (mmol/L)	2.3 ± 2.0
APACHE II score 24 h after admission	15 ± 4
Peak of AST levels (U/L)	3058 ± 4820
Peak of ALT levels (U/L)	1357 ± 1542
Postoperative complications	
Early allograft dysfunction	26 (22%)
Primary graft non-function	7 (6%)
Biliary strictures and/or leaks	5 (4%)
Arterial thrombosis or stenosis	5 (4%)
Acute rejection	32 (26%)
Sepsis or septic shock	38 (31%)
AKI	87 (72%)
AKI type 1	0
AKI type 2	44 (36%)
AKI type 3	43 (36%)
RRT	26 (22%)
Fluid balance (mL)	
Intraoperative	3829 ± 1904
Cumulative FB in the first 12 h	5473 ± 2417
Cumulative FB in the first 4 d	10956 ± 5117
Length of stay in ICU (d)	12 ± 11
Length of stay in the hospital (d)	19 ± 12
Mortality	11 (9%)

Data are expressed as mean ± SD. APACHE II: Acute Physiology and Chronic Health Disease Classification System; AKI: Acute kidney injury; RRT: Renal replacement therapy; FB: Fluid balance; ICU: Intensive care unit.

leading to death or retransplantation. The definition of AKI was based on The Kidney Disease Improving Global Outcomes (KDIGO) criteria published 2012[37]. Patients were evaluated by a nephrologist when dialysis was indicated. Fluid balance was defined as the difference between oral intake and/or intravenous fluid administration and urine output. Other potential causes for fluid losses including nasogastric aspirates, vomiting or diarrhea were not recorded. All patients received either normal saline or Ringer's lactate solution. Cumulative FB was calculated arbitrarily 12 h and 4 d after LT in order to evaluate the impact of fluid administration early in the postoperative period and thereafter after the initial phases of volume resuscitation. Cumulative FB in those chosen periods after admission to the ICU were also previously associated with adverse outcomes in other reports[4,26,30].

Cumulative FB in the first 12 h and 4 d after surgery were compared with three major adverse outcomes after LT, including the occurrence of AKI, requirement for RRT and 28-d mortality, as well as the other aforementioned variables previously known to influence morbidity and mortality after LT.

All patients granted informed consent at hospital admission. The study was approved by the Ethics Committee in Research of the Portuguese Hospital of Salvador, Bahia.

Statistical analysis

Descriptive analysis was performed. Continuous variables were expressed as mean ± SD and categorical variables as proportions. Univariate analysis of perioperative and postoperative parameters was tested using χ^2 test or the Fisher exact probability test when appropriate. Continuous variables were compared using the Mann-Whitney test[38]. Multivariate analysis using stepwise logistic regression was performed to evaluate the specific effect of each predictor[39]. Variables included in the multivariate model were those that achieved significance level of $P < 0.20$ in the univariate analysis. *P* value equal or less than 0.05 were considered significant. 95% confidence intervals were reported, when appropriate. The analysis of the residues was included in the steps of the logistic regression. All statistical analysis was performed using SPSS version 17.0 for Windows (SPSS Inc, Chicago, IL, United States).

RESULTS

Baseline clinical and laboratory data of those 121 patients included in the study are depicted in Table 1. Briefly most of the patients were males with a mean age of 50 ± 13 years and had decompensated cirrhosis (77%) due to hepatitis C and or alcoholic liver disease (72%) with mean Child-Pugh and MELD, respectively, of 9 ± 2 and 18 ± 6 (Table 1). The perioperative and postoperative information concerning the clinical course of those subjects are summarized in Table 2. Median cold ischemia time and duration of surgery were 520 ± 170 and 333 ± 104 min respectively. High peak AST and ALT levels were observed (Table 2) and the frequencies of EAD and PGNF encountered were 22% and 6%, respectively. Cumulative FB observed in the first 12 h and 4 d were, respectively, 5573 ±

Table 3 Comparison of baseline, intra-operative and postoperative features of patients submitted to liver transplantation according to the presence of acute kidney injury

	No AKI (*n* = 34)	AKI (*n* = 87)	*P* value
Age (yr)	51 ± 13	50 ± 12	0.643
Male sex	24 (71%)	82 (94%)	0.0001
Child-Pugh score at admission	8 ± 2	10 ± 2	0.840
MELD score at admission	17 ± 6	18 ± 6	0.868
APACHE II score 24 h after admission	14 ± 3	15 ± 4	0.142
Cold ischemia time (min)	537 ± 187	513 ± 164	0.267
Duration of surgery (min)	324 ± 131	336 ± 92	0.439
Use of blood products	59%	66%	0.490
Number of packed red blood cell units	1.0 ± 1.7	2.2 ± 3.4	0.010
Use of vasoactive drugs	6 (18%)	32 (37%)	0.032
Peak of arterial lactate in the first 24 h (mmol/L)	2.2 ± 1.4	2.4 ± 2.2	0.208
Peak AST levels (U/L)	1789 ± 1524	3535 ± 5511	0.022
Postoperative complications			
Early allograft dysfunction	3 (4%)	24 (28%)	0.019
Biliary strictures and/or leaks	1 (3%)	4 (5%)	0.567
Arterial thrombosis or stenosis	2 (6%)	3 (3%)	0.433
Acute rejection	10 (29%)	22 (25%)	0.402
Sepsis or septic shock	8 (24%)	30 (34%)	0.305
Cumulative FB in the first 12 h	4780 ± 1673	5743 ± 2610	0.050
Cumulative FB in the first 4 d	8690 ± 3463	11841 ± 5395	0.050
Length of stay in ICU (d)	8 ± 8	13 ± 11	0.087
Length of stay in the hospital (d)	15 ± 7	20 ± 12	0.001
Mortality	1 (3%)	10 (12%)	0.128

Data are expressed as mean ± SD. AKI: Acute kidney injury; MELD: Model for end-stage liver disease; APACHE II: Acute Physiology and Chronic Health Disease Classification System; FB: Fluid balance; ICU: Intensive care unit.

2417 and 10956 ± 5117 mL. AKI occurred in 87 (72%) patients, all with either type 2 (*n* = 44) or type 3 (*n* = 43) AKI. Twenty six patients required RRT 4 ± 2 d after surgery. The LOS in the ICU and in the hospital was, respectively, 12 ± 11 d and 19 ± 12 d. Eleven (9%) patients died due to PGNF (*n* = 7), septic shock (*n* = 2) and intraabdominal bleeding (*n* = 1) 10 9 d after surgery (Table 2).

The occurrence of AKI was associated with male sex (94% *vs* 71% of the patients without AKI, *P* = 0.0001), number of packed red blood cells transfused (2.2 ± 3.4 *vs* 1.0 ± 1.7 of subjects without AKI, *P* = 0.01), use of norepinephrine (37% *vs* 18% of patients without AKI, *P* = 0.032), peak AST levels (3535 ± 5511 *vs* 1789 ± 1524 of patients without AKI, *P* = 0.022), occurrence of EAD (28% *vs* 4% of patients without AKI) and cumulative FB in the first 12 h (5743 ± 2610 mL *vs* 4780 ± 1673 mL of patients without AKI, *P* = 0.05) and 4 d (11841 ± 5395 mL *vs* 8690 ± 3469 mL of patients without AKI, *P* = 0.05) (Table 3), but the difference remained significant in the multivariate analysis only for male sex and cumulative FB over 4 d.

In the univariate analysis, RRT was related to male sex (100% *vs* 84% in patients without RRT, *P* = 0.0001), APACHE II levels (18% ± 6% *vs* 14% ± 4% in patients without RRT, *P* = 0.03), use of blood products (81% *vs* 59% in patients without RRT, *P* = 0.03), use of norepinephrine (50% *vs* 26% in patients without RRT, *P* = 0.02), peak levels of arterial lactate in the first 24 h (3.3 ± 3.5 mmol/l *vs* 2.1 ± 1.3 mmol/L in patients without RRT, *P* = 0.0001), peak of AST level (6599 ± 9060 U/L *vs* 2144 ± 2157 U/L, in patients without RRT, p 0.0001), occurrence of EAD (50% *vs* 15% in patients without RRT, *P* = 0.0001), septic shock (58% *vs* 24% in patients without RRT, *P* = 0.0001), cumulative FB in the first 12 h (7146 ± 2538 mL *vs* 5014 ± 2181 mL in patients without RRT, *P* = 0.005) and cumulative FB over 4 d (14924 ± 7345 mL *vs* 9868 ± 3677 mL in patients without RRT, *P* = 0.0001) (Table 4). As expected, mortality (35% *vs* 2% in patients without RRT, *P* = 0.0001), LOS in the ICU (20 ± 14 *vs* 9 ± 9 in patients without RRT, *P* = 0.002) and in the hospital (24 ± 14 *vs* 17 ± 10 in patients without RRT, *P* = 0.007) were significantly increased in those patients requiring RRT (Table 4). However, only APACHE II levels, occurrence of sepsis or septic shock and cumulative FB in the first 4 d remained significant variables related to RRT in the multivariate analysis.

In respect to mortality in 28 d (Table 5), univariate analysis revealed an association with the number of packed red blood cell units transfused (3.6 ± 6 units *vs* 1.7 ± 2.6 units in survivors, *P* = 0.0001), peak of arterial lactate in the first 24 h (4.9 ± 4.2 mmol/L *vs* 2.1 ± 1.4 mmol/L in survivors, *P* = 0.0001), peak AST levels (11289 ± 13591 U/L *vs* 2372 ± 2280 U/L in survivors, *P* = 0.0001), EAD (72% *vs* 17% in survivors, *P* = 0.0001), acute rejection (0% *vs* 29% in survivors, *P* = 0.03), cumulative FB in 4 d (19073 ± 9416 mL *vs* 10144 ± 3656 mL in survivors, *P* = 0.00001), RRT (82% *vs* 15% in survivors, *P* = 0.001) (Table 5), but only APACHE II and AST levels remained significant in the multivariate analysis (Table 6).

Table 4 Comparison of baseline, intra-operative and postoperative features of patients submitted to liver transplantation according to requirement of renal replacement therapy

	No RRT (n = 95)	RRT (n = 26)	P value
Age (yr)	49 ± 12	53 ± 12	0.960
Male sex	80 (84%)	26 (100%)	0.0001
Child-Pugh score at admission	9 ± 2	10 ± 2	0.800
MELD score at admission	18 ± 6	19 ± 7	0.420
APACHE II 24 h after admission	14 ± 4	18 ± 6	0.030
Cold ischemia time (min)	506 ± 166	587 ± 175	0.470
Duration of surgery (min)	322 ± 103	372 ± 102	0.500
Use of blood products	59%	81%	0.030
Number of packed red blood cell units	1.6 ± 2.7	2.7 ± 4.2	0.080
Use of vasoactive drugs	25 (26%)	13 (50%)	0.020
Peak of arterial lactate in the first 24 h (mmol/L)	2.1 ± 1.3	3.3 ± 3.5	0.0001
Peak AST levels (U/L)	2144 ± 2157	6599 ± 9060	0.0001
Postoperative complications			
Early allograft dysfunction	14 (15%)	13 (50%)	0.0001
Biliary strictures and/or leaks	3 (3%)	2 (8%)	0.292
Arterial thrombosis or stenosis	5 (5%)	0 (0)	0.290
Acute rejection	27 (28%)	5 (19%)	0.249
Sepsis or septic shock	23 (24%)	15 (58%)	0.0001
Cumulative FB in the first 12 h	5014 ± 2181	7146 ± 2538	0.005
Cumulative FB in the first 4 d	9868 ± 3677	14924 ± 7345	0.0001
Length of stay in ICU (d)	9 ± 9	20 ± 14	0.002
Length of stay in the hospital (d)	17 ± 10	24 ± 14	0.007
Mortality	2 (2%)	9 (35%)	0.0001

Data are expressed as mean ± SD. RRT: Renal replacement therapy; MELD: Model for end-stage liver disease; APACHE II: Acute Physiology and Chronic Health Disease Classification System; FB: Fluid balance; ICU: Intensive care unit.

Table 5 Comparison of baseline, intra-operative and postoperative features of patients submitted to liver transplantation according to mortality in 28 d

	Survivors (n = 110)	Non survivors (n = 11)	P value
Age (yr)	50 ± 12	52 ± 13	0.780
Male sex	95 (86%)	11 (100%)	0.218
Child-Pugh score at admission	9 ± 2	10 ± 3	0.360
MELD score at admission	18 ± 6	19 ± 9	0.060
APACHE II 24 h after admission	14 ± 3	21 ± 6	0.060
Cold ischemia time (min)	512 ± 167	628 ± 177	0.080
Duration of surgery (min)	324 ± 98	417 ± 130	0.060
Use of blood products	64%	64%	0.620
Number of packed red blood cell units	1.7 ± 2.6	3.6 ± 6	0.000
Use of vasoactive drugs	32(29%)	6 (55%)	0.090
Peak of arterial lactate in the first 24 h (mmol/L)	2.1 ± 1.4	4.9 ± 4.2	0.0001
Peak AST levels (U/L)	2372 ± 2280	11289 ± 13591	0.0001
Postoperative complications			
Early allograft dysfunction	19 (17%)	8 (72%)	0.0001
Biliary strictures and/or leaks	5 (5%)	0	0.620
Arterial thrombosis or stenosis	5 (5%)	0	0.620
Acute rejection	32 (29%)	0	0.030
Sepsis or septic shock	34 (31%)	4 (36%)	0.740
Cumulative FB in the first 12 h	5205 ± 2233	8140 ± 2677	0.600
Cumulative FB in the first 4 d	10144 ± 3656	19073 ± 9416	0.00001
Length of stay in ICU (d)	12 ± 10	14 ± 11	0.360
Length of stay in the hospital (d)	18 ± 11	13 ± 10	0.070
AKI	77 (70%)	10 (90%)	0.140
RRT	17 (15%)	9 (82%)	0.0001

Data are expressed as mean ± SD. LT: Liver transplantation; MELD: Model for end-stage liver disease; APACHE II: Acute Physiology and Chronic Health Disease Classification System; FB: Fluid balance; ICU: Intensive care unit; AKI: Acute kidney injury; RRT: Renal replacement therapy.

DISCUSSION

Despite the development of several strategies to assess fluid responsiveness[40], fluid administration in the ICU remains largely empirical in daily practice. It is usually guided by bedside simple hemodynamic and laboratory parameters and urine output measurement. Early-goal directed therapy using large volume of

Table 6 Multivariate analysis of predictors of acute kidney injury, renal replacement therapy and mortality of patients submitted to liver transplantation

	Odds ratio	95%CI	*P* value
AKI			
Male sex	9.29	1.48-58.24	0.017
Cumulative FB in the first 4 d	2.3	1.37-3.86	0.020
RRT			
APACHE II 24 h after admission	2.5	1.36-4.62	0.003
Sepsis or septic shock	14.7	0.99-2.18	0.050
Cumulative FB in the first 4 d	2.89	1.52-5.49	0.001
Mortality			
AST levels (U/L)	2.35	1.1-5.05	0.020
APACHE II 24 h after admission	2.63	1.0-6.87	0.040

AKI: Acute kidney injury; RRT: Renal replacement therapy; APACHE II: Acute Physiology and Chronic Health Disease Classification System; FB: Fluid balance.

fluids to restore tissue perfusion in sepsis and septic shock has been shown to improve survival[41] and it is still considered today as the cornerstone of resuscitation in septic shock and sepsis-induced tissue hypoperfusion[42]. It may lead however, on the other hand, to post-resuscitation fluid overload with its detrimental effect in tissue perfusion leading to organ dysfunction and failure[1-3]. In surgical patients, fluid overload, usually assessed by cumulative FB, has been associated with impaired wound healing, ACS, postoperative pulmonary morbidity, as well as AKI with a detrimental influence not only on morbidity[1-3,10,11], but also on patient survival[13]. On the contrary, a restrictive approach on fluid administration has been shown to improve morbidity after major surgery, including LT[17,29-32], and mortality[17]. Concerning the influence of FB on the outcome of LT, other authors have shown detrimental effects of a cumulative positive FB concerning postoperative pulmonary complications and ileus[29-32]. Jiang *et al*[29], have demonstrated that a negative FB in the first 3 d after LT was linked to a decrease the frequency of early pulmonary complications. Lin *et al*[32] furthermore have described an increased incidence of postoperative pulmonary morbidity in patients submitted to LT who received a large amount of fluids and blood transfusions intraoperatively. Not surprisingly, protection from postoperative pulmonary morbidity was related to a negative FB in the first three days after LT. Later on, the same group of investigators demonstrated that employment of more than 100 mL/kg of blood transfusion intraoperatively and a FB equal or less than -14 mL/kg per day in the first three days after LT were inversely associated with postoperative pulmonary complications, when assessed by extubation time. Beneficial effects were also observed in frequency of postoperative ileus and ICU LOS. Reydellet *et al*[31] performed a before and after study comparing two resuscitation protocols after LT. The patients submitted to a liberal approach of fluid administration had significantly increased cumulative FB at 24 and 48 h when compared to their counterparts submitted to a more restricted fluid approach per protocol. Those patients submitted to a more restricted fluid approach had fewer days on mechanical ventilation and on postoperative ileus. None of the authors have investigated the influence of FB in the development of AKI after LT.

In the present study, most of the patients were submitted to a liberal approach of fluid administration with a mean cumulative FB over 5 and 10 L in the first 12 h and 4 d after LT. Several preoperative and postoperative variables were associated either with development of AKI and/or requirement for RRT, but only cumulative FB in 4 d were independently associated with occurrence of both AKI and requirement for RRT. Other variables on multivariate analysis associated with AKI and RRT were, respectively, male and APACHE II levels and sepsis or septic shock. Mortality was shown to be independently related to AST and APACHE II levels, probably reflecting the degree of graft dysfunction and severity of early postoperative course of LT. No effect of FB on mortality after LT was disclosed in the present study.

Although there is an increasing interest in the use of biomarkers to help identify AKI at an earlier stage, they were not used in the study. Patients with cirrhosis frequently have predisposing factors for the development of kidney diseases, such as advanced age, diabetes, and hypertension. In addition, specific liver diseases may be associated with kidney disease, such as HBV/HCV-associated glomerulonephritis or alcohol-related IgA nephropathy. In this study, the definition of AKI was based on The Kidney Disease Improving Global Outcomes criteria. This definition has been validated and it considers increases in serum creatinine from baseline known or presumed to have occurred within the prior 7 d. Early recognition of AKI in cirrhosis or in post-transplant is important in order to avoid factors that may contribute to further deterioration of renal function and to initiate appropriate management.

One of the major limitations of the present study is its retrospective design as well as the number of patients included in our cohort. We tried to control confounding variables through multivariate analysis. The authors also have to acknowledge that it is difficult to determine in such a study design whether cumulative FB may be a cause or consequence of disease severity or of AKI development, as postoperative resuscitation protocols were not standardized. However, our results do corroborate the detrimental effects of cumulative FB on the occurrence of AKI and requirement of RRT after LT, as demonstrated in several other clinical scenarios in the ICU[10-13,27,43].

In summary, cumulative positive fluid balance over 4 d after LT influence the development of AKI and is a risk factor for requirement of RRT. No effect on patient survival was independently related to FB, but to surrogate markers of graft dysfunction and severity of postoperative course of LT.

ARTICLE HIGHLIGHTS

Research background

Liver transplantation (LT) has become an option in treating a wide variety of liver diseases. Patients undergoing LT are at high risk of perioperative complications and death. Recently, there has been considerable interest in perioperative fluid therapy following major surgeries. Important question is whether fluid overload is an independent risk factor for adverse outcomes after LT. Previous reports indicate that restrictive strategy of fluids in surgical patients is beneficial. The influence of fluid accumulation on morbidity and mortality after LT has not been well evaluated up to now.

Research objectives

The aim of the study was to analyze whether cumulative positive fluid balance (FB) is associated with the occurrence of adverse outcomes after LT.

Research methods

Patients were retrospectively evaluated. In the present study, most of the patients were submitted to a liberal approach of fluid administration. Accumulated fluid balance (acFB), assessed within the first 12 hours and the 4 days following surgery, was compared with major adverse outcomes after LT.

Research results

Cumulative positive FB over 4 d after LT influences the development of acute kidney injury and it is a risk factor for the requirement for dialysis. No effect on patient survival was independently related to fluid balance.

Research conclusions

Our results show that fluid overload is a marker of severity of illness.

Research perspectives

We hope that these results may contribute to the management of liver grafted patients.

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