

Factors affecting perioperative serum albumin variation and short-term complications in pediatric patients undergoing major gastroenterology surgery

Qingshuang Liu

Chongqing Medical University Affiliated Children's Hospital

Kai Gao

Chongqing Medical University Affiliated Children's Hospital

Xiaomin Sun

Chongqing Medical University Affiliated Children's Hospital

chunbao guo (✉ guochunbao@foxmail.com)

Chongqing Medical University <https://orcid.org/0000-0002-9132-3096>

Research article

Keywords: Δ ALB, Roux-en-Y hepaticojejunostomy; Postoperative recovery; Perioperative complications

Posted Date: June 4th, 2020

DOI: <https://doi.org/10.21203/rs.2.24434/v3>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Albumin is considered a negative acute-phase protein because its concentration decreases during injury and sepsis. The decrease in serum albumin may be important for perioperative morbidity, even in patients with normal preoperative levels in the pediatric population. Here, we intend to determine the perioperative factors associated with the reduction in serum albumin within 2 postoperative days compared with the preoperative level (Δ ALB) and its influence on perioperative outcome in a pediatric general surgical cohort.

Methods: This single-center retrospective review included 939 patients who underwent Roux-en-Y hepaticojejunostomy between August 2010 and August 2019. Based on the mean value of Δ ALB (14.6%), patients were separated into two groups, a high Δ ALB group ($\geq 14.6\%$) and a low Δ ALB group ($< 14.6\%$). Multivariable logistic regression analyses were performed to determine the independent risk factors for a reduction in serum albumin. Propensity score matching was performed to adjust for any potential selection bias for the two groups. In 366 matched patients, the influences of operating time on perioperative outcomes, including postoperative recovery, complications measurement, and length of hospital stay between the two groups were analyzed.

Results: Among the 996 patients reviewed, 939 patient records were enrolled in the final analysis. Controlling for other factors, multivariable analysis showed that a high CRP on POD 3 or 4 (odds ratio [OR] =2.36 [95% CI, 1.51-3.86]; $p=0.007$), the presence of Charcot's triad (OR=1.73 [95% CI, 1.05-2.83]; $p=0.031$), and a longer operating time (OR=1.18 [95% CI, 1.00-1.53]; $p=0.014$) were factors that predicted a high Δ ALB level. A high Δ ALB level was associated with postoperative gastrointestinal functional recovery, reflected by the first defecation ($p=0.013$) and first bowel movement ($p=0.019$) and the high occurrence of postoperative complications (16.1% vs 10.9%, OR, 1.57; 95% CI, 1.02-2.41, $P=0.0026$). The mean length of postoperative stay of patients in the high Δ ALB group was longer than that of patients in the Δ ALB $< 14.0\%$ group, although no statistically significant difference was observed ($p=0.057$).

Conclusions: We showed that a change in albumin level was associated with postoperative outcome. The risk factors for Δ ALB could be addressed in the perioperative period to permit patients to obtain a safe recovery and discharge after a major abdominal operation.

Background

As an acute-phase protein, albumin (ALB) usually negatively responds to surgical stress, injury or sepsis [1, 2]. A decrease in plasma albumin concentration is considered one of the features of systemic inflammation due to the loss of albumin to the tissue spaces [3, 4] and postoperative infectious complications [4]. The transcapillary leakage of albumin can be elevated by more than 300 % in systemic inflammatory pathogenesis [11, 12]. Preoperative hypoalbuminemia has also been confirmed as an indicator for poor nutritional status, mortality and postoperative complications such as surgical site infections (SSIs) after spine surgery [5], GI surgery [6], and acute kidney injury [7]. Because albumin has

quick kinetics after surgery, the response of albumin to surgical stress can even occur earlier than that of CRP, making it an intense focus of perioperative management [8, 9].

A sharp decrease of 33% in serum ALB within 2 days has been observed after major abdominal surgery[2, 10]. There are many factors that may potentially impact the reduction in ALB level (Δ ALB), including the pathology being treated and the actual procedure undertaken [13]. Few studies have examined the factors that could be used to predict postoperative hypoalbuminemia in pediatric patients after major gastroenterology surgery. A clear evaluation of these factors could lead to the development of optimized perioperative care protocols.

This study aimed to investigate the risk factors for the reduction in ALB by retrospectively reviewing data on pediatric patients that had undergone major gastroenterological surgery. We further sought to clarify the association between Δ ALB and postoperative recovery and outcomes.

Methods

Population selection

The Ethics Committee of Chongqing Medical University gave expedited approval to this protocol. This retrospective study included 996 consecutive patients who underwent elective Roux-en-Y hepaticojejunostomy between August 2010 and August 2019 at the Department of General Surgery of the Affiliated Chongqing Children's Hospital, Chongqing Medical University. Exclusion criteria included patients with ALB infusion performed preoperatively or within postoperative day (POD 1) or with incomplete laboratory data.

Data collection and definitions

Electronic medical records generated upon admission or referral and including clinician and nurse notes, laboratory tests, imaging exams, surgical records and histopathology results were individually reviewed by two well-trained clinical investigators who collected the relevant data. Data extraction included (1) preoperative data, including demographic data and clinical details, such as preoperative neutrophils, lymphocytes, hemoglobin, preoperative CRP and ALB, and pre-existing comorbidities; (2) intraoperative variables, including surgical procedures (surgical approach, type of resection), American Society of Anesthesiology (ASA) classification, operation time, duration of operation, estimated blood loss (EBL), intraoperative blood transfusion, and intraoperative hemoglobin levels; and (3) postoperative outcomes, including CRP on POD 3 or 4, ALB on POD 1, prompt postoperative biochemical profiles (hemoglobin, blood glucose, creatinine, serum electrolytes, albumin, retinol binding protein, WBC, CRP, etc.), gastrointestinal function recovery features and postoperative complications. The following laboratory data were determined preoperatively and on PODs 3 and 7: serum albumin, CRP, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (γ -GTP), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), serum creatinine (Scr), blood urea nitrogen (BUN), hemoglobin (Hb), and white blood cell (WBC) count. Gastrointestinal symptoms were recorded for

the first 5 postoperative days, including the first postoperative flatus or defecation, gastric retention, nausea or vomiting, time to normal diet, abdominal bloating and/or cramps. All postoperative complications were recorded and ranked according to the Clavien-Dindo classification system [14], such as postoperative hemorrhage, anastomotic fistula, anastomotic stenosis and wound infection, intra-abdominal abscesses, pneumonia, bacteremia, renal failure and respiratory failure.

The relative change in serum albumin (Δ ALB) was calculated as follows: (preoperative albumin level – nadir albumin level within POD 2)/albumin level before surgery \times 100% [17]. We evaluated Δ ALB as normally distributed data and decided to use the mean value of the (14.6%) to dichotomize the groups. For the purpose of analysis, the patients were dichotomized into a low ($<14.6\%$) and a high ($\geq 14.6\%$) Δ ALB group based on the cutoff value (14.6%).

According to criteria reported in previous studies, all patient data were reviewed for postoperative surgical and nonsurgical outcomes, including complication rates, complication types, mortality rates, ventilator rates, ICU-stay rates, and total lengths of hospital stay (the number of days from the day of operation until the day of discharge). The primary outcome based on Δ ALB was prompt postoperative gastrointestinal function recovery. The secondary outcomes were postoperative complications and immunologic and inflammatory variables. Gastrointestinal symptoms were assessed and recorded daily for the first 5 postoperative days, including first bowel movement (gas and feces) after operation, abdominal bloating, abdominal cramps, diarrhea (defined as more than three bowel movements per day), and vomiting. Wound complications consisted of wound dehiscence, erythema, swelling, and pus.

Propensity scores and matching

To minimize selection biases in the baseline characteristics between the two groups, propensity score matching was accomplished using a multivariable logistic regression model using SPSS 20.0 (IBM, Armonk, NY) or R 3.1.2 (The R Foundation for Statistical Computing). A 1:1 propensity score matching with a caliper distance of 0.2 without replacement was accomplished using nearest-neighbor analysis, which included the demographic and clinical variables. The selected variables entered into the propensity model were based on theoretical and empirical considerations according to the scientific literature and biological plausibility, including demographic data, laboratory values, treatment protocols, surgical features, etc. We further measured the interaction among all pretest covariables. The assumption of linearity of the PS model was checked using the generalized additive model, subsequently matching 366 patients with high Δ ALB $\geq 14.6\%$ and 366 patients with Δ ALB $<14.6\%$. The perioperative outcomes between the two groups were compared after propensity score matching.

Statistical analysis

Statistical analyses were performed using SPSS version 19.0 (SPSS Inc., Chicago, IL, United States). Categorical data are expressed as counts with percentages and were analyzed using Fisher's exact test or Pearson's χ^2 test when appropriate. Continuous data are expressed as the means \pm (standard deviations) for normally distributed data and medians (interquartile ranges) for nonnormally distributed data, which

were tested with Student's t-test or Mann-Whitney U test and the Wilcoxon rank-sum test, respectively. To verify independent predictors for postoperative complications, multivariate analysis was performed using multivariate logistic regression analysis after univariate analysis to identify predictors with a significance level of $P < 0.30$ (Table 3). The results of the multivariate logistic regression analysis were expressed using the P value, odds ratio (OR), and 95% confidence interval (CI). In all cases, $P < 0.05$ was considered significant.

Results

Patient population characteristics

Among the initial 996 pediatric patients in our department who underwent hepaticojejunostomy resection, 41 did not fulfill the inclusion criteria and were initially excluded, and sixteen patients were excluded because their notes were unobtainable for data extraction. Finally, a total of 939 patient records were enrolled in the final analysis (Table 1).

Table 1. Univariate analyses of perioperative factors associated with Δ ALB

	Total Population		
	Δ ALB \geq 14.6%(471)	Δ ALB<14.6%(468)	p Values
Age (yrs) , mean \pm SD	2.13 \pm 1.02	2.16 \pm 1.07	0.21
Female: Male	183(37.5)	191(39.9)	0.31
Weight (kg) , mean \pm SD	11.38 \pm 2.96	11.52 \pm 3.68	0.22
BMI, median (range)	24(20-30)	25 (21-31)	0.13
Laboratory findings			
hypertransaminasemia, n (%)	325(69.0)	334(71.4)	0.47
hyperbilirubinemia, n (%)	186(39.5)	173(37.0)	0.39
Preoperative ALB(g/L), mean \pm SD	39.28 \pm 4.72	41.41 \pm 5.39	0.016
Preoperative CRP(g/L), mean \pm SD	11.24 \pm 3.26	12.56 \pm 4.17	0.15
Preoperative WBC(10 ⁹ /L), mean \pm SD	7.9 \pm 2.8	8.2 \pm 3.1	0.52
Ultrasound presentation			
Mean CBD(cm), mean \pm SD	1.53 \pm 0.58	2.34 \pm 0.97	0.042
Charcot's triad, n (%)	142(30.1)	109(23.3)	0.011
Nadir ALB within POD 2(g/L), mean \pm SD	34.94 \pm 8.92	30.22 \pm 7.83	0.0012
CRP on POD 3 or 4(mg/L), mean \pm SD	41.45 \pm 13.65	29.8 \pm 7.69	<0.001
Postoperative WBC(10 ⁹ /L), mean \pm SD	15.8 \pm 4.9	14.9 \pm 4.8	0.350

Mode of surgical approach, n(%)			
Laparoscopic	168(35.7)	139(29.7)	
Open	303(64.3)	329(70.3)	0.03
Operation time, median (range), min	175 (132-418)	143 (115-367)	0.0024
Nadir of hemoglobin(g/L)	9.18±1.32	9.64±1.68	0.28
Operative blood loss (mL), mean ± SD	36.78±16.84	33.86±15.88	0.26
Intraoperative fluid utilization(mL/kg*h) , mean ± SD	16.74±6.88	14.26±6.72	0.017
Intraoperative transfusion, n (%)	131 (27.8)	115(24.6)	0.15
ASA classification			
ASA1-2	338(72.6)	319(67.7)	0.13
ASA3-4	133(27.4)	149(22.3)	

Abbreviations:ALB, albumin; Δ ALB, reduction of ALB level; ASA, American Society of Anesthesiology; CBD, Common bile duct; CRP, C-reactive protein; POD, postoperative day; SD, standard deviation; WBC, white blood cell.

Factors associated with Δ ALB

Based on the cutoff value of Δ ALB, we dichotomized the patients into two groups, the Δ ALB \geq 14.6% and Δ ALB <14.6% groups. The baseline features of the two groups are summarized in Table 1. There were no significant differences in the demographic features of the patients, ASA classification, or preoperative CRP between the two groups (Table 1). Furthermore, the nadir of hemoglobin and operative blood loss were similar between the two groups ($P > 0.05$). A larger choledochal cyst size ($p=0.042$), worse comorbidity (Charcot's triad) ($p=0.011$), lower preoperative ALB ($p=0.016$), CRP on POD 3 or 4 ($p<0.001$), and a longer surgery duration ($p=0.0024$) were associated with a greater Δ ALB ($P < 0.05$) in the univariable analysis. Multivariable analysis revealed three independent risk factors. As shown in

Table 2, CRP on POD 3 or 4 (OR =2.36 [95% CI, 1.51-3.86]; p =0.007), the presence of Charcot's triad (OR = 1.73 [95% CI, 1.05-2.83]; p = 0.031), and a longer operating time (OR=1.18 [95% CI, 1.00 -1.53]; p=0.014) were independent risk factors associated with Δ ALB.

Table 2. Multivariate analysis of perioperative factors associated with Δ ALB.

	OR	95%CI	p
BMI>26	1.26	(0.97-1.89)	0.16
Preoperative ALB<32g/L	1.68	(0.91-2.35)	0.27
Preoperative CRP>12g/L	1.12	(0.94-1.73)	0.18
CRP on POD 3 or 4 (>135mg/L)	2.36	(1.51-3.86)	0.007
Charcot's triad	1.73	(1.05-2.83)	0.031
Operation time(>165m)	1.18	(1.01-1.53)	0.014
Open surgical approach	2.31	(0.89-4.76)	0.31
Intraoperative fluid utilization>17mL/kg*h	1.07	(0.96-1.78)	0.22
Intraoperative transfusion	1.38	(0.98-2.16)	0.092
ASA classification(ASA1-2)	1.74	(0.96-3.24)	0.39

Influences of Δ ALB on postoperative outcomes

To explore the association between Δ ALB and perioperative outcome, we performed PS matching between the Δ ALB \geq 14.6% and Δ ALB <14.6% groups to adjust for potential confounding factors and exclude the effects of correlations between factors. Under PS matching, 366 patients in the Δ ALB \geq 14.6% group were matched to 366 patients in the Δ ALB <14.6% group. The absolute standardized mean differences reduced the values, indicating that the continuous and categorical variables were very similar and comparable between the two groups (Table 3).

Table 3. The inclusion variables in the PS-matching analysis

	Total Population		
	Δ ALB \geq 14.6%(366)	Δ ALB<14.6%(366)	p Values
Age (yrs)	2.14 \pm 1.01	2.15 \pm 1.03	0.45
Female: Male	135(36.9)	136(37.2)	0.50
Weight (kg)	11.44 \pm 2.76	11.46 \pm 3.11	0.34
BMI, median (range)	25(21-28)	25 (21-29)	0.28
Laboratory findings			
hypertransaminasemia, n (%)	252(68.9)	251(68.6)	0.50
hyperbilirubinemia, n (%)	146(39.9)	143(39.1)	0.44
Preoperative ALB(g/L), mean \pm SD	39.83 \pm 4.26	40.63 \pm 4.96	0.18
Preoperative CRP(g/L), mean \pm SD	11.87 \pm 3.16	12.04 \pm 3.88	0.35
Preoperative WBC(10 ⁹ /L), mean \pm SD	8.01 \pm 2.62	8.14 \pm 2.69	0.39
Ultrasound presentation			
Mean CBD(cm), mean \pm SD	1.75 \pm 0.53	2.07 \pm 0.86	0.18
Nadir ALB within POD 2 (g/L), mean \pm SD	33.13 \pm 8.56	32.34 \pm 7.69	0.23
Postoperative WBC(10 ⁹ /L), mean \pm SD	15.56 \pm 4.64	15.12 \pm 4.63	0.46
Mode of surgical approach, n(%)			
Laparoscopic	131(35.8)	126(34.4)	

Open	235(64.2)	240(65.6)	0.38
Nadir of hemoglobin(g/L)	9.35±1.25	9.48±1.52	0.33
Operative blood loss (mL)	35.16±14.69	34.47±13.53	0.29
Intraoperative fluid utilization(mL/kg*h) , mean ± SD	15.59±6.54	14.93±6.18	0.27
Intraoperative transfusion, n (%)	102 (27.9)	98(26.8)	0.40
ASA classification			
ASA1-2	262(71.6)	257(70.2)	0.37
ASA3-4	104(28.4)	109(29.8)	

Overall, there were no differences in vasopressor support, diuresis usage and the number of intraoperative hypotensive events, hypokalemic episodes, metabolic acidosis (defined by low bicarbonate) or other laboratory and hemodynamic parameters throughout the perioperative period between the $\Delta\text{ALB} \geq 14.6\%$ and $\Delta\text{ALB} < 14.6\%$ groups (Table 4).

Table 4. Outcome characteristics in the matched population depended on the mean value of ΔALB

	Δ ALB>14.6% (366)	Δ ALB<14.6% (366)	p Values	Odds ratio (95% CI)
Hypotensive events, n(%)	42(10.47)	38(11.88)	0.36	
Norepinephrine usage, n(%)	45(13.95)	40(12.17)	0.32	
Furosemidum, n(%)	36(9.88)	34(11.30)	0.50	
Metabolic acidosis, n(%)	18(3.20)	13(4.93)	0.23	
hypokalemic episodes, n(%)	24	25	0.50	
Serum albumin				
First defecation (days)	3.13±1.32	2.88±1.27	0.12	
First flatus	3.56± 0.88	3.07 ± 0.90	0.013	
First bowel movement(days), Mean ± SD	2.75± 0.82	2.14 ± 0.78	0.019	
Stool within 72 hours, n (%)	123(32.75)	147(40.12)	0.039	1.33(0.98-1.79)
Abdominal distension, n (%)	36(13.5)	28(19.8)	0.18	
Diarrhea, n (%)	23 (6.8)	21(10.9)	0.50	
Vomiting, n (%)	35(13.0)	31(16.1)	0.38	
No. of patients with mild complications, n(%)	45(11.7)	29(9.0)	0.033	1.63(1.00-2.66)
No. of patients with major complications, n(%)	28(7.7)	21	0.19	
Total number of complications, n(%)	59(16.1)	40(10.9)	0.026	1.57(1.02-2.41)
Length of stay (d), mean ± SD	8.19±3.16	7.69±2.67	0.057	

In the propensity matched cohort, patients with $\Delta\text{ALB} < 14.6\%$ had reduced time to first flatus ($p=0.013$) and first bowel movement ($p=0.019$) (Table 4). In the $\Delta\text{ALB} < 14.6\%$ group, 40.2% (147/366) of patients spontaneously passed stool within 72 hours, whereas only 33.6% (123/366) of patients with high ΔALB passed stool within the same period (OR, 1.33; 95% CI, 0.98-1.79, $p=0.039$). The incidences of diarrhea ($p=0.50$), vomiting ($p=0.38$) and abdominal distention ($p=0.18$) within 5 PODs in patients with $\Delta\text{ALB} < 14.6\%$ were similar to those in patients with $\Delta\text{ALB} \geq 14.6\%$.

According to the Clavien-Dindo classification, 74 patients (20.2%) had mild complications (Grade I or II), and 49 (13.4%) had major complications (Grade III or greater). As shown in Table 4, patients with $\Delta\text{ALB} \geq 14.6\%$ were found to have more total complications than those with $\Delta\text{ALB} < 14.0\%$ (16.1% vs 10.9%, OR, 1.57; 95% CI, 1.02-2.41, $P=0.0026$), including anastomotic leakage, infectious complications of pneumonia, incision dehiscence, intraperitoneal abscess, sepsis, and surgical site infections. In addition, the mean length of postoperative stay was 8.19 ± 3.16 days in the $\Delta\text{ALB} \geq 14.0\%$ group, which was longer than that of the $\Delta\text{ALB} < 14.0\%$ group (7.69 ± 2.67 days), although no statistically significant difference was observed ($p=0.057$).

Discussion

We conducted the present analysis to focus on serum albumin as an acute phase protein for a pediatric surgical cohort that underwent the same surgical procedure. This study revealed that several factors were associated with high ΔALB , such as operative duration, disease comorbidities, and mean CBD. Furthermore, patients with a greater relative decrease in serum albumin were associated with postoperative gastrointestinal function recovery, postoperative complications, and prolonged postoperative hospital stay.

The factors leading to hypoalbuminemia are often complicated and associated with operative case type, ALB loss, redistribution, catabolism, or their combination [15, 16, 17, 18]. Numerous studies have focused on preoperative and postoperative hypoalbuminemia as risk factors for postoperative complications [5, 19], while few have specifically stressed the perioperative factors related to ΔALB , which may be clinically significant for postoperative care. In the present study, several clinical factors related to the decrease in postoperative albumin were presented, including longer operating time, severe comorbidities, such as Charcot's triad, and high CRP. All these factors might be associated with an inflammatory response caused by surgical stress. During surgery, manipulation of the intestine has been proven to initiate gastrointestinal edema [20, 21]. Postoperative edema might be attributed to the low colloid osmotic pressure and fluid accumulation, themselves resulting from a low postoperative ΔALB [11]. Norberg Å [2] reported that the stress response led to a reduction in postoperative albumin levels, which was consistent with the findings in our study.

Changes in plasma volume and altered distributions between the intravascular and extravascular space also play a significant role in plasma albumin concentration. The reasons for this association may pertain to hemodilution, which might contribute to the decreased albumin level after surgery. In our previous study [22], postoperative complications were shown to be related to conventional intraoperative and postoperative fluid usage, which might also affect the albumin level after surgery. Excessive fluid could also promote capillary permeability and leakage of serum albumin into the extravascular space [23]. Capillary leakage is especially common in some malnourished patients with surgical trauma, followed by an increased transcapillary escape rate of $\geq 100\%$ [24], which was not observed in the current study. Serum albumin on POD 3 has been observed to be correlated with preoperative CRP level [13, 25]. In the current study, we indeed found that a high Δ ALB was associated with CRP on POD 3 or 4.

Prompt postoperative recovery serves as the main focus of all surgical specialties for postoperative rehabilitation [26]. As indicated in the current study, although uneventful recovery was present for most patients following choledochal cyst resection, unfavorable postoperative gastroenterological recovery was associated with a high Δ ALB. Previous biological investigations have demonstrated that edema has detrimental effects on intestinal function by directly affecting muscle function and force transmission [27, 28]. Serum ALB is a predictor of both systemic inflammation and nutritional status, which should account for postoperative intestinal edema after a major operation or severe trauma. Furthermore, tissue oxygenation could decrease with fluid accumulation, which is also unfavorable for postoperative recovery and complications. In this study, we detected an increased total number of complications, including anastomotic leakage, in patients with high Δ ALB. A possible explanation at the tissue level may be that the low ALB level reduced collagen deposition for the tissue connections and, therefore, resulted in poor structural integrity. The effect of Δ ALB on the local inflammatory response and edema recovery is also important and might also explain postoperative recovery and complications [29, 30]. It remains to be determined whether ALB supplementation reduces postoperative intestinal edema and cellular swelling to and promote intestinal function recovery in patients undergoing major upper gastrointestinal surgery in the pediatric population [31, 32].

There were several limitations in the current study. First, it was a retrospective observational analysis, where unmeasured differences and known selection and treatment biases may have contributed to confounding effects, which could not be entirely excluded. Second, this was a single-center study, and the general surgery procedures were performed in our hospital over a long period of time; therefore, there may have been many practice changes within both the surgical and ICU divisions, leading to different care practices between study patients, which may not reflect the outcomes from current treatment algorithms. Another point of emphasis was that although we did not find differences in baseline characteristics after PS matching, the patients with high Δ ALB might have been more surgically challenged than those with low Δ ALB. To limit the influence of confounding variables on the actual effects of Δ ALB, large, multicenter prospective studies must be performed to verify the conclusions of the current study.

Conclusions

In the current study, we characterized some risk factors that may predispose patients to high Δ ALB, which could negatively impact postoperative recovery after a major abdominal operation in a pediatric population. The surgeons should be aware of Δ ALB in the early postoperative period to optimize preoperative planning and maximize surgical efficiency.

Abbreviations

ALB: albumin;

ALP: alkaline phosphatase;

ALT: alanine aminotransferase;

Δ ALB: reduction in ALB level;

ASA: American Society of Anesthesiology;

AST: aspartate aminotransferase;

BUN: blood urea nitrogen;

CBD: Common bile duct;

CI: confidence interval;

CRP: C-reactive protein;

γ -GTP: gamma-glutamyl transpeptidase;

Hb: hemoglobin

LDH: lactate dehydrogenase;

OR: odds ratio;

POD: postoperative day;

Scr: serum creatinine;

SD: standard deviation;

WBC: white blood cell

Declarations

* Ethics approval and consent to participate

Expedited approval by The Ethics Committee of Chongqing Medical University

* Consent for publication

Not applicable

* Availability of data and material

The dataset analyzed during the current study is available from the corresponding author on reasonable request.

* Competing interests

No potential conflicts of interest relevant to this article are reported.

* Funding

This study was supported by grants from the National Natural Science Foundation of China (Nos: 30973440 and 30770950) for the design of the study, the Key Project of the Chongqing Natural Science Foundation (CSTC, 2008BA0021, cstc2012jjA0155) for collection, analysis, and interpretation of data and the Chongqing Health Planning Commission of Research Fund (No: 2016MSXM044) for writing the manuscript.

* Authors' contributions

QL, KG and XS designed the study and analyzed the data. KG, XS and CG evaluated the manuscript. CG and KG performed the statistical measurements and analyzed the data. CG analyzed the data and wrote the paper. All authors have read and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

* Acknowledgments

We thank Prof. Bailin Chen for providing technical assistance and for insightful discussions during the preparation of the manuscript and Dr Xiaoyong Zhang at the Wistar Institute for help with the linguistic revision of the manuscript.

* Authors' information (optional)

Correspondence to Xiaomin Sun or [Chunbao Guo](#).

References

1. Wierdak M, Pisarska M, Kuśnierz-Cabala B, Witowski J, Dworak J, Major P, Małczak P, Ceranowicz P, Budzyński A, Pędziwiatr M. Changes in plasma albumin levels in early detection of infectious

- complications after laparoscopic colorectal cancer surgery with ERAS protocol. *Surg Endosc.* 2018 Jul;32(7):3225-3233.
- 2.Norberg Å, Rooyackers O, Segersvärd R, Wernerman J. Albumin Kinetics in Patients Undergoing Major Abdominal Surgery. *PLoS One.* 2015 Aug 27;10(8):e0136371.
- 3.Norberg Å, Rooyackers O, Segersvärd R, Wernerman J. Leakage of albumin in major abdominal surgery. *Crit Care.* 2016 Apr 26;20(1):113.
- 4.Migita K, Matsumoto S, Wakatsuki K, Kunishige T, Nakade H, Miyao S, Sho M. Postoperative Serum C-Reactive Protein Level Predicts Long-term Outcomes in Stage I Gastric Cancer. *J Surg Res.* 2019 Oct;242:323-331.
- 5.Adogwa O, Martin JR, Huang K, Verla T, Fatemi P, Thompson P, Cheng J, Kuchibhatla M, Lad SP, Bagley CA, Gottfried ON. Preoperative serum albumin level as a predictor of postoperative complication after spine fusion. *Spine (Phila Pa 1976).* 2014 Aug 15;39(18):1513-9.
- 6.Rudasill SE, Morales RR, Sanaiha Y, Sareh S, Antonios JW, Khoury H, Mardock AL, Benharash P. Predicting morbidity and mortality in laparoscopic cholecystectomy: Preoperative serum albumin still matters. *Am J Surg.* 2019 Dec 6. pii: S0002-9610(19)31556-9.
- 7.Cabezuelo JB, Ramírez P, Ríos A, Acosta F, Torres D, Sansano T, Pons JA, Bru M, Montoya M, Bueno FS, Robles R, Parrilla P. Risk factors of acute renal failure after liver transplantation. *Kidney Int.* 2006 Mar;69(6):1073-80.
- 8.Amouzandeh M, Nowak G, Januszkiewicz A, Wernerman J, Rooyackers O, Norberg Å. Albumin mass balance and kinetics in liver transplantation. *Crit Care.* 2018 Jun 7;22(1):152.
- 9.Komáromi A, Estenberg U, Hammarqvist F, Rooyackers O, Wernerman J, Norberg Å. Simultaneous assessment of the synthesis rate and transcapillary escape rate of albumin in inflammation and surgery. *Crit Care.* 2016 Nov 15;20(1):370.
- 10.Dumitrescu G, Komaromi A, Rooyackers O, Klaude M, Hebert C, Wernerman J, Norberg Å. Repeated quantitative measurements of De Novo synthesis of albumin and fibrinogen. *PLoS One.* 2017 Mar 28;12(3):e0174611.
- 11.Fleck A, Raines G, Hawker F, Trotter J, Wallace PI, Ledingham IM, Calman KC. Increased vascular permeability: a major cause of hypoalbuminaemia in disease and injury. *Lancet.* 1985;1:781–4.
- 12.Nicholson JP, Wolmarans MR, Park GR. The role of albumin in critical illness. *Br J Anaesth.* 2000;85:599–610.
- 13.Sonoda A, Ohnishi S, Nakao S, Iwashita Y, Hashimoto N, Ishida K, Kondo Y, Ishitsuka Y, Irie T. Factors affecting serum albumin in the perioperative period of colorectal surgery: a retrospective study. *BMC Res*

Notes. 2015 Nov 3;8:638.

14.Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004 Aug; 240(2):205-13

15.Norberg Å, Rooyackers O, Segersvärd R, Wernerman J. Albumin kinetics in patients undergoing major abdominal surgery. *PLoS One*. 2015;10:e0136371.

16.Ruot B, Papet I, Bechereau F, Denis P, Buffiere C, Gimonet J, Glomot F, Elyousfi M, Breuille D, Obléd C. Increased albumin plasma efflux contributes to hypoalbuminemia only during early phase of sepsis in rats. *Am J Physiol Regul Integr Comp Physiol*. 2003 Mar;284(3):R707-13.

17.Giovannini I, Chiarla C, Giuliani F, Vellone M, Ardito F, Nuzzo G. The relationship between albumin, other plasma proteins and variables, and age in the acute phase response after liver resection in man. *Amino Acids*. 2006 Nov;31(4):463-9.

18.Labgaa I, Joliat GR, Kefleyesus A, Mantziari S, Schäfer M, Demartines N, Hübner M. Is postoperative decrease of serum albumin an early predictor of complications after major abdominal surgery? A prospective cohort study in a European centre. *BMJ Open*. 2017 Apr 8;7(4):e013966.

19.Labgaa I, Joliat GR, Demartines N, Hübner M. Serum albumin is an early predictor of complications after liver surgery. *Dig Liver Dis*. 2016 May;48(5):559-561.

20.Boelens PG, Heesakkers FF, Luyer MD, et al. Reduction of postoperative ileus by early enteral nutrition in patients undergoing major rectal surgery: prospective, randomized, controlled trial. *Ann Surg*. 2014;259:649-655.

21.Ozacmak HS, Ozacmak VH, Barut F, et al. Pretreatment with mineralocorticoid receptor blocker reduces intestinal injury induced by ischemia and reperfusion: involvement of inhibition of inflammatory response, oxidative stress, nuclear factor κ B, and inducible nitric oxide synthase. *J Surg Res*. 2014;191:350-361.

22.Tan X, Liu J, Guo C. Crystalloid Administration Is Associated with the Recovery of Pediatric Elective Roux-en-Y Hepaticojejunostomy. *Eur J Pediatr Surg*. 2019 Jan 21. doi: 10.1055/s-0038-1677544. [Epub ahead of print]

23.Nicholson JP, Wolmarans MR, Park GR. The role of albumin in critical illness. *Br J Anaesth*. 2000;85:599–610.

24.Lee WL, Slutsky AS. Sepsis and endothelial permeability. *N Engl J Med* 2010; 363: 689-691

25.Bona D, Micheletto G, Bonitta G, Panizzo V, Cavalli M, Rausa E, Cirri S, Aiolfi A. Does C-reactive Protein Have a Predictive Role in the Early Diagnosis of Postoperative Complications After Bariatric Surgery? Systematic Review and Bayesian Meta-analysis. *Obes Surg*. 2019 Nov;29(11):3448-3456.

- 26.Hao F, Guo H, Zhong J, Geng Q, Yang Y, Chen B, Guo C. Effects of Prostaglandin E1 on Patients Undergoing Major Gastrointestinal Surgery. *Ann Surg.* 2018 Apr;267(4):759-765.
- 27.Kinsky MP, Milner SM, Button B, et al. Resuscitation of severe thermal injury with hypertonic saline dextran: effects on peripheral and visceral edema in sheep. *J Trauma.* 2000;49:844-53.
- 28.Luiz Zanoni F, Costa Cruz JW, et al. Hypertonic saline solution reduces mesenteric microcirculatory dysfunctions and bacterial translocation in a rat model of strangulated small bowel obstruction. *Shock.* 2013;40:35-44.
- 29.Rasslan R, Utiyama EM, Marques GM, et al. Inflammatory activity modulation by hypertonic saline and pentoxifylline in a rat model of strangulated closed loop small bowel obstruction. *Int J Surg.* 2014;12:594-600.
- 30.Vincent JL, De Backer D, Wiedermann CJ. Fluid management in sepsis: The potential beneficial effects of albumin. *J Crit Care.* 2016 Oct;35:161-7
- 31.Vincent JL, Sakr Y, Reinhart K, Sprung CL, Gerlach H, Ranieri VM; 'Sepsis Occurrence in Acutely Ill Patients' Investigators. Is albumin administration in the acutely ill associated with increased mortality? Results of the SOAP study. *Crit Care.* 2005;9(6):R745-54.
- 32.Margarson MP, Soni N. Serum albumin: touchstone or totem? *Anaesthesia.* 1998;53:789–803.