

Original Research Article

Effect of albumin administration on post-operation mortality, duration on ventilator, and hospital stay on patients in cardiac intensive care: An observational study

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Abstract

Purpose: To justify the use of albumin infusion in patients in post-surgery cardiac intensive care unit.

Methods: All patients who were hemodynamically stable before the operation and admitted into the surgical intensive care unit following coronary artery bypass, cardiopulmonary bypass, or aortic surgery, had no excessive postoperative bleeding and not on diuretic treatment, were included in the analysis. A total of 1998 patients were divided into two cohorts, viz, the first group was placed on albumin infusion ($n = 999$) while the second group received normal saline infusion ($n = 999$). Data were obtained from DICOM files of patients and records of pharmacy. Wilcoxon test or two-tailed paired t-test followed by Tukey post-hoc tests were performed for statistical analysis at 95 % of confidence level.

Results: Albumin and normal saline administration did not decrease the duration of mechanical ventilation, incidence of mechanical ventilation, need for blood transfusion, and length of hospital stay ($p > 0.05$). Albumin infusion decreased the need for fresh frozen plasma transfusion from 85 to 67, reduced mortality ($p = 0.0005$, $q = 3.959$), lowered serum lactate level ($p < 0.0001$, $q = 43.853$), but increased cardiac index ($p < 0.0001$, $q = 12.192$) as well as financial burden ($p < 0.0001$, $q = 95.158$) for the patients, compared to normal saline group.

Conclusion: In view of the foregoing, it is recommended that the use of restriction of albumin resuscitation in surgical intensive care unit should be restricted in this subset of patients evaluated in this study.

Keywords: Artificial respiration, Cardiac surgical procedures, Intensive care unit, Mortality, Infusion, Serum albumin

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INTRODUCTION

Generally, low serum albumin levels commonly occur in patients following cardiac surgery [1] and are associated with poorer outcomes [2]. In such conditions, plasma volume expansion is

often necessary [3]. However, there is no clear guideline regarding intravenous infusion for resuscitation [4] but albumin solution is the first choice of the surgeon as plasma expander before or after cardiac surgery in critically ill patients [5]. However, albumin solutions have a

high cost [6], chances of anaphylactoid reactions, and transmission of allergens, anticoagulants, and microorganisms [7]. In short, use of albumin solutions in critical conditions as resuscitation is controversial [6]. However, several published studies also have such type of controversies in their conclusions as patients with severe sepsis, albumin replacement has not been shown to improve the survival rate [8] another study stated that in patients with severe sepsis, administration of albumin does not alter organ function and have decreased mortality [9]. Both studies are available on high impact factor journals and the results contradict each other. Therefore, there is need for accurate observational study to justify the use of albumin solutions as resuscitation.

The primary aim of the analysis was to evaluate the effectiveness of albumin administration for resuscitation on mortality, freshly frozen plasma transfusions, lactate level, and cardiac index in post-operative patients within the cardiac intensive care unit. The secondary endpoint of the study was to compare incidences and time of mechanical ventilation, requirements of blood transfusion, length of hospital stay, and cost of albumin and normal saline administration in resuscitation in two cohorts.

METHODS

Ethics statement

The study was registered in a research registry (www.researchregistry.com), UID No. research

registry3953, dated 15 January 2016. The protocol (20160101025JC/OS/19/16, dated 1 January 2016) was approved by First Hospital of Jilin University review board. The study reporting was adhered to the law of China, STROBE (the strengthening the reporting of observational studies in epidemiology) guidelines, STROCCS (the strengthening the reporting of cohort studies in surgery) guidelines, and 2013 Declarations of Helsinki [10]. A written informed consent was obtained from all the enrolled patients or their relatives (legally authorized person) by signing a pre-designed patient consent form regarding the interventions, pathology, and publication of work-up in all formats of publication house (hard and/or electronic) irrespective to time and language.

Inclusion criteria

All patients who had been admitted into the surgical intensive care unit (SICU) in the First Hospital of Jilin University from 16 January 2016 to 1 March 2017 following coronary artery bypass, cardiopulmonary bypass, or aortic surgery procedures were included in the study cohort. Other inclusion criteria were patients who are aged 18 years and above, had normal preoperative serum creatinine and were hemodynamically stable before surgery [11]. The demographic characteristics of the enrolled patients are reported in Table 1. There were no significant differences between the demographic characteristics of patients between groups at the time of analysis ($p > 0.01$).

Table 1: Demographic characteristics of the enrolled patients at the time of analysis

Patient characteristics		Intravenous infusion		P-value
		Albumin, N (%)	Normal saline N (%)	
Sample size		999	999	
Gender	Male	390(39)	421(42)	0.172
	Female	609(61)	578(58)	
Age (years)	<40	88(9)	98(10)	0.85
	40–60	782(78)	766(77)	
	>60	129(13)	135(13)	
Time of resuscitation*	Before surgeries	323(33)	288(29)	0.098
	After surgeries	676(67)	711(71)	
Numbers of organ(s) abnormalities	0	649(65)	647(65)	0.515
	1	247(25)	231(23)	
	2	103(10)	121(12)	
	20–24.9	247(25)	255(26)	
Serum albumin (g/L)	25–29.9	644(64)	626(62)	0.939
	>30	108(11)	118(12)	
	80–89	798(80)	783(78)	
Central venous oxygen saturation (%)	90–95	146(15)	151(15)	0.787
	>95	55(5)	65(7)	
	20–24.9	252(25)	261(26)	
Body mass index	25–29.9	624(63)	607(61)	0.971
	>30	123(12)	131(13)	

Data were represented as a number (Percentage). Albumin or normal saline. The Chi-square Independence test was performed for statistical analysis. A $p < 0.01$ was considered as significant

Exclusion criteria

The patients who had refused to sign an informed consent form and planned any organ transplant with cardiac surgical procedure were excluded from the enrollment. The patients who were admitted into SICU but had not undergone cardiac surgeries were excluded from the study. Patients who were placed on any other kind of crystalloid solutions and/or synthetic colloids resuscitation (other than albumin and normal saline) were also excluded from the analysis. The patients who were first placed on albumin and subsequently given crystalloid solutions and/or synthetic colloids were also excluded from the final analysis. The patients who had discharged against medical advice (DAMA) were also excluded from the analysis. Patients who had excessive postoperative bleeding and on diuretics treatments were excluded from the study.

A total of 1998 patients were included in the two cohorts: First, group of patients were those placed on albumin administration for resuscitation ($n = 999$) and the second, were those placed on normal saline ($n = 999$). STARD (standards for reporting of diagnostic accuracy) flowchart of the analysis is presented in Fig. 1.

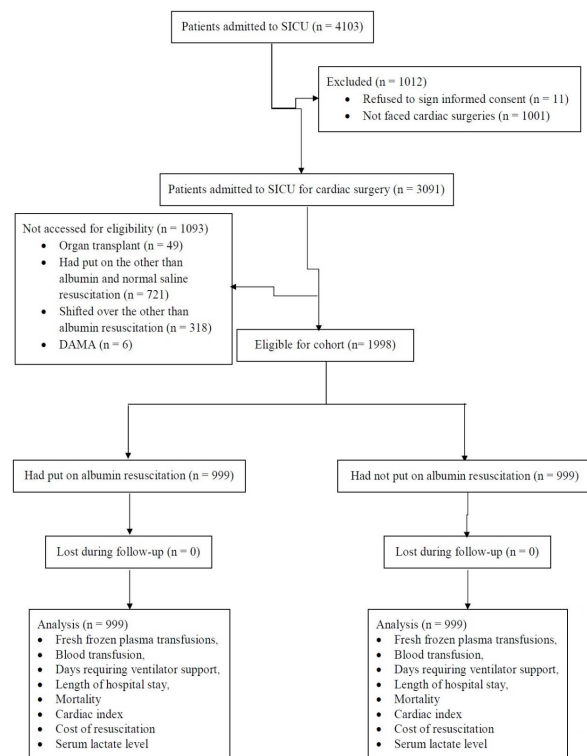


Figure 1: STARD flowchart. Intention-to-treat analysis method. DAMA: Discharged against medical advice, SICU: Surgical intensive care unit

Data collection

Data regarding the demographic characteristics, number of freshly frozen plasma transfusions, patients requiring blood transfusion, days requiring ventilator support, length of hospital stay, and mortality were obtained from Digital Imaging and Communications in Medicine (DICOM) files of patients preserved in hospital. Albumin utilization and costs were obtained from records of pharmacy.

Statistical analysis

The Chi-square independent test was performed for the demographic characteristics of patients and constant data of requirements of life support parameters between the groups. Wilcoxon test following Turkey *post hoc* test (considering critical value (q) > 3.314 as significant) were performed to compare before and after resuscitation conditions [5]. Two-tailed paired *t*-test [12] following Turkey *post hoc* test (q > 3.314 as significant) were performed for the cost of resuscitation, cardiac index, and lactate level between groups. InStat (GraphPad, San Diego, IL, USA) was used for statistical analysis purposes. The demographical characteristics were considered significant at 99 % of confidence level and requirements of life support parameters were considered significant at 95 % of confidence level.

RESULTS

Albumin and normal saline administration for resuscitation both failed to decrease the length of time on mechanical ventilation, incidences of mechanical ventilation, the requirement for blood transfusion, and length of hospital stay (Table 2).

Albumin resuscitation decreased mortality ($p = 0.0005$, $q = 3.959$) however normal saline did not decrease mortality ($p = 0.0039$, $q = 3.021$). The overall survival in both groups was the same ($p = 0.928$, Figure 2).

Albumin resuscitation decreased the number of fresh frozen plasma transfusions from 85 to 67. However, the data was not statistically significant ($p < 0.0001$, $q = 2.786$). Similarly, normal saline resuscitation decreased the number of fresh frozen plasma transfusions from 91 to 87 and the data also was not statistically significant ($p = 0.25$, Figure 3).

Table 2: Effect of fluid resuscitation on hemodynamic and blood gas parameters

Variable		Intravenous infusion		P-value
		Albumin 999	Normal saline 999	
	Total	91(9)	97(10)	0.702
On mechanical Ventilation	Before resuscitation	47(5)	49(5)	0.917
	After resuscitation	44(4)	48(5)	0.749
	P- value	0.25	>0.9999	N/A
Total time of mechanical ventilation (days)	0	16(2)	12(1)	0.096
	1–10	548(55)	503(50)	
	10–19	347(34)	399(40)	
	20–30	88(9)	85(9)	
Need for blood transfusion	Before resuscitation	97(10)	93(9)	0.837
	After resuscitation	87(9)	89(9)	
	P-value	0.0039	0.25	N/A
Total hospital stays (days)	q-value	1.34	N/A	N/A
	<50	145(14)	153(15)	0.114
	51–99	247(25)	271(27)	
	100–149	455(46)	447(45)	
	>150	152(15)	128(13)	
Before resuscitation	1.88±0.04	1.87±0.04	* 0.908	
Serum lactate level (mmol/L)	After resuscitation	1.84±0.03	1.84±0.03	* 0.742
	P-value	<0.0001	<0.0001	N/A
	q-value	43.853	43.636	N/A

Nominal data were presented as a number (percentage) and continuous data were represented as mean \pm SD. Wilcoxon test following Turkey post hoc test was used for statistical analysis between before and after resuscitation conditions, a $p < 0.05$ and $q > 3.314$ were considered as significant. The Chi-square independence test was used for statistical analysis between groups, a $p < 0.05$ was considered as significant. Two-tailed paired t-test was used for statistical analysis, a $p < 0.05$ was considered as significant. N/A: Not applicable. For statistical analysis requirement of life-support was considered as 1 and no requirement of that was considered as 0

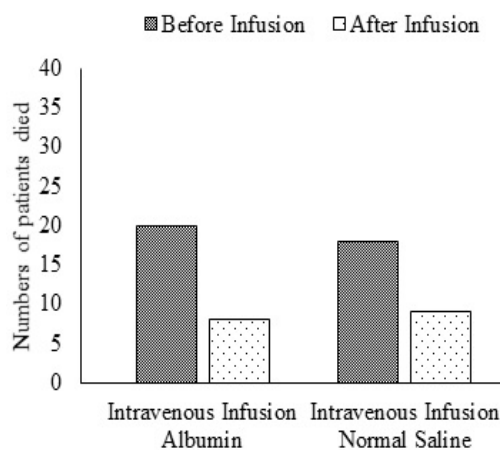


Figure 2: Effect of fluid resuscitation on mortality. The p and q values between before and after resuscitation for albumin and normal saline were 0.0005 and 3.959 and 0.0039 and 3.021 respectively. There was no significant difference in the rate of mortality between albumin and normal saline resuscitation ($p = 0.928$). Wilcoxon test following Turkey post hoc test was used for statistical analysis between before and after resuscitation conditions, a $p < 0.05$ and $q > 3.314$ were considered as significant. Chi-square independence test was used for statistical analysis between groups, a $p < 0.05$ was considered as significant. For statistical analysis mortality was considered as 1 and survival was considered as 0

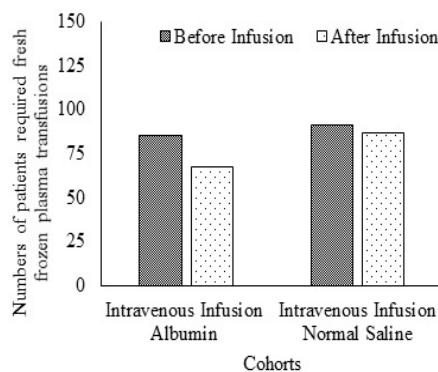


Figure 3: Effect of fluid resuscitation on numbers of fresh frozen plasma transfusions. The p and q values between before and after resuscitation for albumin and normal saline were < 0.0001 and 2.786 and 0.25 respectively. There was no significant difference for numbers of fresh frozen plasma transfusions between albumin and normal saline resuscitation ($p = 0.447$). Wilcoxon test following Turkey post hoc test was used for statistical analysis between before and after resuscitation conditions, $p < 0.05$ and $q > 3.314$ were considered as significant. Chi-square independence test was used for statistical analysis between groups, $p < 0.05$ was considered as significant. For statistical analysis requirement of fresh frozen plasma, transfusion was considered as 1 and no requirement of that was considered as 0

The data derived regarding cost from the pharmacy indicated that the consultant had no clear idea regarding albumin resuscitation. Albumin resuscitation was shown to increase the financial burden to the patients compared to normal saline (341.25 ± 165.03 \$ vs. 53.72 ± 11.75 \$, $p < 0.0001$, $q = 95.158$).

Before resuscitation, there was no significant difference in cardiac index between groups ($p = 0.39$). Albumin resuscitation increased the cardiac index of patients after resuscitation of the same patients ($p < 0.0001$, $q = 12.192$). However, normal saline did not improve the cardiac index of patients after resuscitation of the same patients ($p = 0.0001$, $q = 1.781$). In comparison with normal saline, albumin administration successfully improved the cardiac index of patients after resuscitation ($p < 0.0001$, $q = 11.0$, Figure 4).

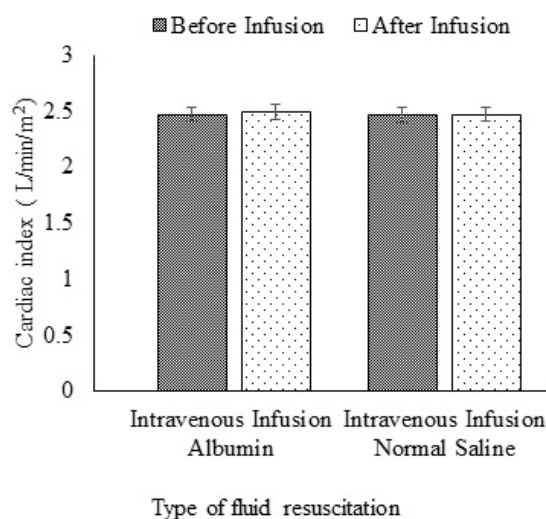


Figure 4: Effect of fluid resuscitation on the cardiac index. The p and q values between before and after resuscitation for albumin and normal saline were < 0.0001 and 12.192 and 0.0001 and 1.781 respectively. Data were represented as mean \pm SD all of them, $n = 999$. Wilcoxon test following Turkey post hoc test was used for statistical analysis between before and after resuscitation conditions. Two-tailed paired t -test following Turkey post hoc test was used for statistical analysis. $P < 0.05$ and $q > 3.314$ were considered significant. Cardiac index was found as the ratio of cardiac output to body surface area

DISCUSSION

The study examined the use of albumin administration for resuscitation in post-operative cardiac patients admitted into the SICU. Hypovolemia after cardiac surgery stimulates an inflammatory response, bleeding, actual volume loss, capillary leak, a high degree of vascular permeability, and vasodilation [5]. There are choices of expensive colloid solutions (albumin

or hetastarch) and cost-effective crystalloid fluids (isotonic sodium chloride solution or Ringer lactate) for resuscitation purposes [13]. Crystalloid fluids cause increase in pulmonary edema [14]. Moreover, current guidelines recommended albumin rather than normal saline for resuscitation purposes [15,16]. In respect to the choice of resuscitation method adopted in the study, the work has justified the use of albumin.

Unlike normal saline, albumin resuscitation had beneficial effects on short-term physiologic markers, mortality, cardiac index, and numbers of fresh frozen plasma transfusions. These were because albumin has physiological effects as antioxidant, transportation, and binding of hormones and drugs within the blood, regulation of colloid osmotic pressure, buffer capabilities and nitric oxide modulation [17], and improving lung function [9], which are necessary for critically ill patients. However, albumin resuscitation had no beneficial effects on incidences and time of mechanical ventilation, requirements of blood transfusion, and hospital stay. Moreover, poor outcomes are associated with high morbidity [5]. These data had supported the finding of the previous studies [5,12,18]. However, paradox results were observed with the other studies [2,9]. In considering effective results of outcomes from the study, it is difficult to conclude that there were sustained clinical benefit of albumin resuscitation in patients in the cardiac intensive care but it however increased the unwanted financial burden on the patient.

In the study, all the enrolled patients in both groups had no overall potential benefits to reduce morbidity. Fluid resuscitation is considered the first line therapy for critically ill patients because it increases intravascular volume and perfusion [19,20] but fluid resuscitation is beneficial only if the patient is on ascending limb of the Frank-Starling curve [21]. Moreover, large fluid resuscitation may also lead to clinical edema [22,23] and this is harmful [24]. In regards to the results from the observational study, the guideline for fluid resuscitation for the single aim of correcting hypovolemia in critically ill patients requires revision to include adequate monitoring and appropriate fluid selection.

Normal saline and albumin resuscitation both succeeded in maintaining serum lactate levels. Lactate is mainly maintained by fluid resuscitation in critically ill patients [25]. However, albumin administration was not superior to normal saline for maintenance of serum lactate level. In respect to biochemical parameters of patients, normal saline and

albumin administration both had the same effects in fluid resuscitation.

Limitations of the study

The first limitation was that the study was observational and thus lacked randomization of patients into the two groups. The study did not use the dose oscillation analysis of albumin administration. The observation period at the end of the study was too short. Long-term effects of resuscitation were not evaluated. The study did not report cause of death. The study did not consider the effects of resuscitation on hemoglobin, platelets, and the other blood cells.

CONCLUSION

The findings of this study show that normal saline administration for resuscitation is safe and feasible in patients under cardiac intensive care, it is surprising why albumin administration for resuscitation is prevalent in clinical practice. The study therefore recommends the restriction of albumin administration for resuscitation and the need for individualized fluid resuscitation therapies in surgical intensive care units.

DECLARATIONS

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Zhen Zhang and Xinlun Dai contributed equally to this study,

more specifically to the conceptualization of the study and acquisition of data. Ji Qi had contributed to design of the study, analysis, and interpretation of data. Yu Ao had contributed to the conceptualization and funding for the study. Chunfeng Yang had contributed to design of the study and project administrator. Yumei Li had contributed to the analysis of data, drafted, critically revised the manuscript, and given final approval. All authors have agreed to be accountable for all aspects of work ensuring integrity and accuracy. All authors had read and approved the manuscript sent for publication.

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