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Effects of preoperative and postoperative albumin levels on postoperative arrhythmias after open heart surgeries with cardiopulmonary bypass

Kevser Tural [1], Ali Alper Kahraman [2]

[1] Kafkas University, School of Medicine, Department of Cardiovascular Surgery, Kars, 36100, Turkey
[2] Kafkas University, Health Research and Application Center, Perfusionist, Kars, 36100, Turkey

ORCID ID of the author(s)
KT: 0000-0003-4490-037X
AAK: 0000-0003-2924-2655

Corresponding Author
Kevser Tural
Kafkas University, Faculty of Medicine, Department of Cardiovascular Surgery, Kars, Turkey
E-mail: ktrl2011@hotmail.com

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All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Ischemia-reperfusion injury is associated with transient contractility disorders and lethal arrhythmias. The main reason for this is the increase in the oxidants and the decrease in the antioxidants. This study aimed to investigate the relationship between albumin, known to have antioxidant properties, and arrhythmias seen in the early postoperative period in patients undergoing open heart surgery.

Methods: Adult patients undergoing open heart surgery with cardiopulmonary bypass within 5 years were included in this single-center, retrospective cohort study. The relationship of arrhythmias within the first 24 hours after the operation with the albumin levels obtained within 6 hours before the operation and within 4 hours after the operation was investigated. The difference between preoperative and postoperative albumin levels was evaluated using the Wilcoxon test and the relationship between albumin levels and arrhythmias, using the Mann-Whitney U test. The relationship between the results was evaluated by Pearson's correlation analysis, and the interaction of the results with correlations was evaluated by regression analysis.

Results: A total of 56 patients were included in the study. The average age of the patients was 63.07 years (11.24) (range, 42-89). The mean preoperative and postoperative albumin levels were 4.04 (0.51) g/dL, and 3.21 (0.45) g/dL, respectively. The mean postoperative albumin level was significantly lower than the preoperative mean albumin level ($P<0.001$). In the analyses performed to find the relationship between albumin levels and postoperative arrhythmias, the effects of postoperative albumin levels on postoperative arrhythmias were significant ($P=0.016$). In the regression analysis, there was an interaction between postoperative albumin levels and preoperative albumin levels ($P<0.001$), postoperative arrhythmia status ($P=0.005$), postoperative sinus tachycardia status ($P=0.002$), and postoperative lactate levels ($P=0.005$).

Conclusion: The present study suggests that high albumin levels may have a protective effect against postoperative arrhythmias. For all that, prospective studies may be planned with more patients and by examining the biochemical mechanism more comprehensively.

Keywords: Cardiopulmonary bypass, Ischemia-reperfusion injury, Arrhythmia, Sinus tachycardia, Albumin

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Introduction

Heart diseases are still among the major causes of mortality worldwide [1, 2]. Cardiopulmonary bypass (CPB) is a system that provides blood circulation and oxygen needs of the body by undertaking the function of the heart and lungs during cardiac surgery [3]. CPB provides a stationary and bloodless surgical area, which is considered as the optimum condition in cardiac surgical treatment. During CPB, the selected cardiac arrest method creates a stationary surgical environment and a transient ischemic condition occurs. Hemodilution is also required for CPB [4].

Cardiac arrhythmias are associated with various conditions, such as heart failure and myocardial ischemia. Arrhythmias due to myocardial ischemia and ischemia-reperfusion (I-R) damage are among the most important causes of death of the myocardium. In addition, arrhythmias due to ischemia and I-R damage occur with oxidative and inflammatory responses leading to impaired myocardial electrical stability [5, 6]. Although reperfusion is necessary for the survival of ischemic tissue, it causes cell damage [7, 8]. The main reason for this damage is the increase in the number of oxidants [9]. When this increase in oxidants exceeds the antioxidant defense capacity, oxidative stress increases with a detrimental effect on the functional and structural integrity of the tissue and organ [10].

Serum albumin (SA) is seen as the most important antioxidant in the blood. It has a prognostic value in many cardiovascular diseases. Serum albumin contains abundant thiol groups that make up >80% of total thiols in plasma-clearing reactive oxygen and nitrogen species. Some substances such as nitric oxide and bilirubin are carried by SA and provide additional protection against oxidative stress [11]. SA creates its antioxidant effects largely by maintaining colloid osmotic pressure and hemostasis [12]. In addition, human serum albumin has N-terminal regions that detoxify oxidant agents. In the case of ischemia-reperfusion, N terminal areas of SA are damaged by oxidant agents [13, 14], antioxidant systems are damaged after reperfusion [15], and reduction in the amount of SA [4] occurs due to hemodilution during CPB. In this study, our aim was to investigate the relationship between preoperative and postoperative albumin levels, and postoperative arrhythmias in patients undergoing open heart surgery.

Materials and methods

In this retrospective cohort study, we analyzed 56 patients who underwent open heart surgery in our center between January 2015 and December 2020. The data were obtained from file scans and electronic records. All patients with normal sinus rhythm were included in the study in the preoperative period. In the preoperative period, patients with arrhythmia, those who underwent cardiopulmonary resuscitation, received ventilator, inotropic, or intra-aortic balloon pump support to ensure normal hemodynamics were excluded in the study. In addition, patients with malignancy, liver disease, collagen tissue disease, steroid use, psychosis, and a history of inflammatory disease including infection or sepsis were not included in the study. The STROBE checklist was used in the study design and drafting of the manuscript [16]. This study was approved by the ethics committee of Kafkas University, School of Medicine Ethics Committee (Date: 06.05.2020, No: 80576354-050-99/133), and conducted in accordance with the principles of the Declaration of Helsinki.

Arrhythmias occurring within the first 24 hours in the postoperative period were evaluated. Human albumin was not used in CPB circuits. Cold blood cardioplegia was used as the cardiac arrest method during CPB. In the study, serum albumin levels obtained from the antecubital vein within 6 hours before the operation and within 4 hours after the operation were evaluated. Albumin levels were analyzed by Cobas® 6000 c501-e601, Roche®, Switzerland, and lactate levels, by Radiometer ABL 90 Series, Radiometer, Denmark. Hemoglobin levels were assessed with Horiba ABX-120, Horiba, Japan. The definitions of arrhythmia are based on those detailed in the Lambeth Conventions [5], and electrocardiography results were determined by examining the patient files.

Statistical analysis

The statistical significance levels of the results were determined with SPSS® Statistic Version 20 (IBM®, USA). Continuous variables are expressed as mean (standard deviation) (min-max) and categorical variables, as numbers and percentages. The difference between preoperative and postoperative albumin levels was evaluated using the Wilcoxon test and the relationship between albumin levels and arrhythmias, using the Mann-Whitney U test. The relationship between the results was evaluated by Pearson's correlation analysis, and the interaction of the results with correlations was evaluated by regression analysis. Any p value less than 0.05 was considered statistically significant.

Results

The mean age of the patients included in the study was 63.07 years (11.24) (range, 42-89) and 42 were male and 14 were female. Demographic, preoperative, and intraoperative data of the patients are given in Table 1.

Table 1: Demographic and operation data of patients

Parameter	Value
	n=56
Gender n (%)	
Male	42 (75)
Female	14 (25)
Age (mean (SD) (min-max))	63.07 (11.24) (42-89)
Hypertension n (%)	19 (33.92)
Chronic renal failure n (%)	2(3.57)
Diabetes mellitus n (%)	10(17.85)
Chronic obstructive lung disease n (%)	5(8.92)
Cerebrovascular disease n (%)	1(1.78)
CABG n (%)	51 (91.07)
AVR n (%)	2 (3.57)
CABG+ AVR n (%)	1(1.78)
MVR n (%)	1 (1.78)
ASD repair n (%)	1 (1.78)
Ejection Fractions (EF) n (%)	
%30-40	8 (14.28)
%41-50	27 (48.21)
>%51	21 (37.5)
EuroSCORE (mean (SD) (min-max))	2.04 (2.02) (0.65-10.69)
CPB Time (mean (SD) (min-max)) (minute)	112.28 (32.09) (44-193)
Cross-Clamp Time (mean (SD) (min-max)) (minute)	62.07 (23.69) (18-126)

CABG: coronary artery bypass graft, AVR: aortic valve replacement, MVR: mitral valve replacement, ASD: atrial septal defect, SD: standard deviation

A comparison of the means of albumin, lactate, and hemoglobin levels in the preoperative and postoperative period showed that albumin and hemoglobin levels decreased significantly while lactate levels significantly increased (P<0.001, P<0.001, P=0.004, respectively) (Table 2). The means of the preoperative and postoperative albumin, lactate, and hemoglobin levels of the patients are given in Table 2. Postoperative arrhythmia rates are presented in Table 3.

Table 2. The mean of preoperative and postoperative albumin, hemoglobin, and lactate levels of patients

	Preoperative Mean (SD) (min-max)	Postoperative Mean (SD) (min-max)	Z	*P*-value
Albumin (g/dL)	4.04 (0.51) (2.79-5.26)	3.21 (0.45) (2.02-4.24)	-6.249	<0.001
Hemoglobin (gr/dL)	13.81 (2.07) (8.34-18.80)	10.30 (1.43) (7.10-13.50)	-6.469	<0.001
Lactate (u/Lt.)	2.15 (2.68) (0.40-19.0)	3.55 (3.83) (0.60-21.0)	-2.904	0.004

Table 3: Postoperative arrhythmia results

Postoperative Electrocardiographic Rhythm Status	n (%)
Normal Sinus Rhythm (NSR)	26 (46.42)
Total Arrhythmia	30 (53.57)
Sinus Tachycardia (ST)	27 (48.21)
Atrial Fibrillation (AF)	2 (3.57)
Ventricular Fibrillation (VF)	1 (1.78)

In the comparisons made to evaluate whether there is a relationship between preoperative and postoperative albumin, lactate, and hemoglobin levels and postoperative arrhythmias, a significant association was found between postoperative albumin levels and postoperative arrhythmias (*P*=0.016) (Table 4). In the comparisons made to evaluate whether there is a relationship between preoperative and postoperative albumin, lactate and hemoglobin levels and postoperative sinus tachycardia formation, a significant association was found between preoperative and postoperative albumin levels and postoperative sinus tachycardia development (*P*=0.032 and *P*=0.010, respectively) (Table 5).

Table 4: The relationship of preoperative and postoperative albumin lactate and hemoglobin levels with postoperative arrhythmia formation

	Preoperative Albumin(g/dL) Mean (SD) (min-max)	Postoperative Albumin(g/dL) Mean (SD) (min-max)	*P*-value (Wilcoxon)
Postoperative Arrhythmia + (n=30)	3.93 (0.57) (2.79-4.77)	3.07 (0.49) (2.02-3.90)	<0.001
P-value	0.230	0.016	
	Preoperative Hemoglobin(gr/dL) Mean (SD) (min-max)	Postoperative Hemoglobin(gr/dL) Mean (SD) (min-max)	*P*-value (Wilcoxon)
Postoperative Arrhythmia + (n=30)	13.76 (2.32) (9.20-18.80)	10.09 (1.41) (7.80-13.40)	<0.001
P-value	0.895	0.200	
	Preoperative Lactate(u/Lt.) Mean (SD) (min-max)	Postoperative Lactate(u/Lt.) Mean (SD) (min-max)	*P*-value (Wilcoxon)
Postoperative Arrhythmia + (n=30)	2.62 (3.50) (0.40-19.00)	4.60 (4.92) (0.70-21.00)	0.050
P-value	0.411	0.143	

Table 5: Relationship between preoperative and postoperative albumin lactate and hemoglobin levels and postoperative sinus tachycardia

	Preoperative Albumin(g/dL) Mean (SD) (min-max)	Postoperative Albumin(g/dL) Mean (SD) (min-max)	*P*-value (Wilcoxon)
Postoperative sinus Tachycardia + (n=27)	3.87 (0.56) (2.79-4.77)	3.04 (0.49) (2.02-3.90)	<0.001
P-value	0.032	0.010	
	Preoperative Hemoglobin(gr/dL) Mean (SD) (min-max)	Postoperative Hemoglobin(gr/dL) Mean (SD) (min-max)	*P*-value (Wilcoxon)
Postoperative sinus Tachycardia + (n=27)	13.61 (2.40) (9.20-18.80)	10.06 (1.46) (7.80-13.40)	<0.001
P-value	0.501	0.184	
	Preoperative Lactate(u/Lt.) Mean (SD) (min-max)	Postoperative Lactate(u/Lt.) Mean (SD) (min-max)	*P*-value (Wilcoxon)
Postoperative sinus Tachycardia + (n=27)	2.77 (3.66) (0.40-19.00)	4.04 (3.95) (0.70-17.00)	0.118
P-value	0.275	0.317	

An inverse correlation was found between preoperative albumin levels and postoperative sinus tachycardia status (*P*=0.011), and between postoperative albumin levels and postoperative arrhythmia status (*P*=0.011), postoperative sinus tachycardia status (*P*=0.004), postoperative lactate levels (*P*=0.009), and cross clamp time (*P*=0.035). An inverse correlation was found between postoperative lactate levels and postoperative arrhythmia status (*P*=0.028). Regression analysis revealed an interaction between postoperative albumin levels and preoperative albumin levels (*P*<0.001), postoperative arrhythmia status (*P*=0.005), postoperative sinus tachycardia status (*P*=0.002), postoperative lactate levels (*P*=0.005), and cross clamp time (*P*=0.018).

Discussion

In our study, a significant relationship was found between decreased postoperative albumin levels and postoperative sinus tachycardia/arrhythmias status, and between preoperative albumin levels and postoperative sinus tachycardia status. Postoperative decreased albumin levels were significantly related with postoperative increased lactate levels and cross-clamping time.

In addition to its positive effects for open heart surgery, CPB also has negative effects, cardiac arrest being the leading one. Cardiac arrest has a direct relationship with I-R damage in myocardium [17]. Another negative effect of CPB is the decrease in albumin levels as in other biochemical parameters due to the hemodilution required during CPB [4]. In our study, postoperative albumin levels decreased significantly with the increase of cross-clamping time and postoperative lactate levels.

A study examining the I-R damage reported the effects of antioxidant systems on myocardial protection and their importance in inhibiting harmful cardiac changes during the damage caused by I-R in myocardium [18]. In another study, oxidative stress increase due to the increase in oxidants and the decrease in antioxidants after ischemia was shown as the main cause of I-R-related damage [15]. Albumin is known as an important antioxidant [11] and low albumin levels have been linked to increased oxidative stress [19]. It was reported that low albumin levels may be an independent predictor of heart failure and poor prognosis in patients with ischemic heart disease [20]. van Beeket al. [4] reported that albumin levels had effects on the contraction of the heart, and low albumin levels in the postoperative period were associated with an increase in myocardial damage. It was reported that low albumin levels caused the formation of myocardial edema, thereby contributing to worsening of heart diseases, and was associated with an increased incidence of atrial fibrillation [11]. On the other hand, albumin has N-terminal regions detoxifying oxidant substances, but the structure of albumin changed in the case of ischemia and thus the oxidant agent binding capacity of albumin reduced [13]. In addition, albumin provides a cardioprotective effect in the postoperative period due to its nitric oxide-sparing effect, which can potentially reduce nitric oxide-induced vasodilation [21].

Di Filippo et al. [5] investigated whether increasing the number of antioxidants has positive effects on arrhythmias and reported that the increase in the number of antioxidant systems significantly reduced the incidence of ventricular tachycardia and ventricular fibrillation and increased the survival rate. It was also reported that low serum albumin levels were associated with atrial fibrillation (AF) formation [22]. He et al. [23] suggested that hypoalbuminemia is an independent risk factor of paroxysmal AF. On the other hand, although serum albumin level was inversely related with AF incidence in a linear pattern in the study of Liao et al. [19], no causal role of serum albumin in AF etiology was found by two-sample Mendelian randomization.

In the light of these studies, we tried to determine the effects of preoperative and postoperative albumin levels and changes in the postoperative albumin levels on postoperative arrhythmias. The significant postoperative decrease in albumin levels, as well as the decreases in the antioxidant amounts due to I-R injury, may be explained by hemodilution [4] [15]. There was also an inverse correlation between postoperative albumin levels and postoperative lactate levels. This outcome was significant in the regression analysis.

When the albumin levels and postoperative arrhythmias were examined by correlation and regression tests, the level of preoperative albumin was not associated with postoperative arrhythmias, and there was no significant difference in the comparisons between the binary groups. However, there was an inverse relationship between preoperative albumin levels and postoperative sinus tachycardia. As the preoperative albumin levels decreased, postoperative sinus tachycardia increased. On the other hand, as the difference between preoperative and postoperative albumin levels increased, the frequency of sinus tachycardia increased.

When the relationship between postoperative arrhythmias and sinus tachycardia with postoperative albumin levels was examined, an inverse correlation was observed. In addition, this outcome was significant in regression analysis and comparisons between the binary groups. These analyses suggest that low albumin levels may cause arrhythmias in patients underwent CPB, in agreement with other studies.

Among the limitations of our study are the low number of subjects. Another limitation was that the basic mechanism of damage could not be understood since more extensive tests could not be performed due to its retrospective nature. Despite these limitations, the results of our study support the idea that low albumin levels may lead to the development of postoperative arrhythmias in patients who underwent CPB.

Conclusion

In the light of these results, it can be concluded that disturbance between oxidant and antioxidant mechanisms affects myocardial functions. Furthermore, high albumin levels may have a protective effect against postoperative sinus tachycardia/arrhythmias. To explain these effects more clearly, prospective studies can be planned by increasing the number of subjects and examining the mechanism of the relationship between arrhythmias and albumin levels extensively.

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