

# Relationship between the albumin level and the anesthesia method and the effect on clinical course in patients with major burns

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## ABSTRACT

**BACKGROUND:** Due to a massive increase in capillary permeability during the state of shock caused by burns, albumin and intravascular fluid rapidly move to the extravascular areas. Therefore, hypoalbuminemia is seen as an early and prolonged finding in major burns. Hypoalbuminemia leads to various problems. The aim of this study was to investigate the effect of the preoperative albumin level on perioperative morbidity and mortality in patients with major burns.

**METHODS:** Demographic data, preoperative albumin levels, surgical records, and clinical follow-up records of a total of 61 patients who underwent surgery for major burns in our hospital for the last 2 years were examined. Intraoperative complications were recorded, such as hypotension, bradycardia, low saturation, metabolic acidosis, reduced urine output, and hyperglycemia. Postoperative complications were recorded as intubation and the use of mechanical ventilator, sepsis, ARDS, acute renal failure, tracheotomy, hemorrhage, arrest, pneumonia, urinary tract infection, tissue infection, congestive heart failure, and pleural effusion.

**RESULTS:** In patients with albumin levels measured as <2 gr/dL and >2 gr/dL, intraoperative complications were determined at the rates of 31.4% and 20.8%, respectively, postoperative complications at 60.0% and 51.5%, respectively, and mortality rates at 40% and 25.8%, respectively (p=0.148, p=0.251, p=0.85, respectively). The cut-off point for the preoperative albumin level affecting postoperative morbidity was determined as ≥2.3 gr/dL (Area Under Curve=0.587; p<0.001; 95% Confidence Interval, 0.476–0.699; Cut-Off Albumin, ≥2.3).

**CONCLUSION:** There is as yet no consensus on the time and dosage of the delivery of albumin in patients with major burns. Although there are studies in the literature that have shown increased morbidity and mortality rates in individuals given albumin in the intensive care, there are also reports supporting the finding that it makes a positive contribution. No useful guidelines have been obtained on the subject of hypoalbuminemia in patients with major burns. The results of this study showed that the albumin level above or below 2 gr/dL did not create any change in perioperative morbidity and mortality; however, the preoperative level above 2.3 gr/dL was the cut-off value for morbidity.

**Keywords:** Albumin; burn; mortality.

## INTRODUCTION

Albumin is an intravascular protein, 70,000 Dalton in weight,

formed from 585 amino acids, and it plays a significant role in the maintenance of capillary oncotic pressure.<sup>[1]</sup> Burns shock causes a massive increase in the capillary permeability. Thus,

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albumin from plasma is rapidly released into the interstitial fluid and extracellular areas. Consequently, hypoalbuminemia emerges as an early finding and can continue in a long term.<sup>[2,3]</sup> In addition, the albumin production is reduced, and edema forms in the interstitial tissue.<sup>[4]</sup> Thus, complications such as pulmonary edema develop, which can possibly lead to mortality, wound and soft tissue edema, and intra-abdominal edema.

In addition to the key role in the balance of the oncotic pressure, endogenous substances and drugs are transported via binding to albumin. It is also thought that it plays an antioxidant function. Due to this clinical potential, albumin replacement is applied as a volume expander in the burns shock resuscitation and to correct hypoalbuminemia in the chronic period.<sup>[3]</sup>

Albumin replacement applied in the preoperative period is a controversial subject. Furthermore, a minimum albumin value desired has not been determined in patients with major burns who are to undergo surgery. As the replacement does not correct the underlying cause and does not provide permanence, there are opinions that the treatment is not effective.<sup>[5]</sup> The aim of the current study was to determine the effect of preoperative albumin levels on perioperative morbidity and mortality in patients with major burns.

## MATERIALS AND METHODS

Approval for the study was granted by the Local Ethics Committee. A retrospective screening of 136 operations in 61 patients who underwent surgery for burns covering over 30% of the body surface area in our burns treatment unit for the last 2 years was conducted. Patients included in the study were those operated under general anesthesia.

A record was made of the patient demographic data, the percentage of the body surface area affected by burns, the American Society of Anesthesiology (ASA) scores, and the preoperative blood albumin and hemoglobin levels. Intraoperative pulmonary edema, hypo/hypertension, bradycardia, a decrease in peripheral oxygen saturation, the development of acidosis/alkalosis in the blood, and the development of hypo/hyperglycemia or the development of renal failure were accepted as perioperative morbidity. In the postoperative pe-

riod, morbidity included sepsis, a need for mechanical ventilation, acute renal failure, a need for tracheostomy, pneumonia, urinary tract infection, congestive heart failure, and pleural effusion. Perioperative mortality of patients was recorded.

## Statistical Analysis

Descriptive statistics were calculated, and results were stated as mean±standard deviation (SD), number (n), and percentage (%) values. Non-parametric data were compared using the chi-square test. When determining the preoperative albumin level affecting postoperative morbidity, the ROC analysis was used. The Mann–Whitney U univariate analysis was applied in the determination of the effect on intraoperative morbidity of preoperative albumin, hemoglobin, ASA, and total body surface area percentage of burns. A value of  $p < 0.05$  was accepted as statistically significant.

## RESULTS

Throughout the study period, 136 operations were performed on 61 patients who were admitted for treatment in our clinic with burns covering over 30% of the total body surface area. There were 115 (84.6%) operations performed on male patients and 21 (15.4%) on female patients. The mean age of patients was  $36.5 \pm 17.1$  years, and the mean percentage of body surface area with burns was  $51 \pm 13.5\%$  (30%–95%). The height, weight, and preoperative albumin levels of the patients are shown in Table 1.

In the risk grouping of the patients according to the American Society of Anesthesiology (ASA) scores, a median value of 3 was determined. The ASA risk scores and the effect on intraoperative morbidity are shown in Table 2 ( $p = 0.001$ ).

The effects of preoperative albumin, ASA, total burned body surface area, and preoperative hemoglobin on intraoperative morbidity were determined with  $p$ -values of 0.135, 0.001, 0.714, and 0.002, respectively. According to these results, the ASA values and preoperative hemoglobin levels were found to be statistically significant, whereas the effect of the preoperative albumin level was not significant. The intraoperative and postoperative complication rates and the mortality rates of the patients are shown according to the albumin level  $< 2$  gr/dL and  $> 2$  gr/dL in Table 3.

**Table 1.** Height, weight, and preoperative mean albumin and hemoglobin values

	Mean±SD	Minimum-Maximum	Median
Height (cm)	167.5±6.0	155–180	170
Weight (kg)	76.4±9.8	55–94	80
Preoperative albumin (g/dL)	2.42±0.58	1.18–4.22	2.4
Preoperative hemoglobin (g/dL)	10.9±3.3	6.5–23	10.1

SD: Standard deviation.

**Table 2.** American Society of Anesthesiology (ASA) scores and the effect on intraoperative morbidity of patients

ASA	n	%	Intraoperative morbidity		Total	p
			Absent (%)	Present (%)		
1	4	2.9	4 (100.0)	0 (0)	4	0.001
2	47	34.6	45 (95.7)	2 (4.3)	47	
3	58	42.6	39 (67.2)	19 (32.8)	58	
4	22	16.2	13 (59.1)	9 (40.9)	22	
5	5	3.7	3 (60.0)	2 (40.0)	5	

**Table 3.** Intraoperative and postoperative complication rates and patient mortality rates according to the albumin level <2 gr/dL and >2 gr/dL

	Albumin <2 g/dL		Albumin ≥2 g/dL		p
	n	%	n	%	
Intraoperative complications					
Absent	24	68.6	80	79.2	0.148
Present	11	31.4	21	20.8	
Postoperative complications					
Absent	14	40	49	48.5	0.251
Present	21	60	52	51.5	
Mortality					
Absent	21	60	75	74.2	0.85
Present	14	40	26	25.8	

As a result of the evaluation made with the ROC analysis, the albumin cut-off value was found to be  $\geq 2.3$  gr/dL for the preoperative albumin level affecting postoperative morbidity (Area Under Curve=0.587,  $p < 0.001$ , 95% Confidence Interval: 0.476–0.699, Cut-Off Albumin  $\geq 2.3$ ).

The morbidities in the intraoperative and postoperative periods of the 136 operations are shown in Table 4. Although more than one morbidity was observed in some patients, the most common intraoperative complication was hypotension ( $n=18$ , 56%) followed by low  $SPO_2$  ( $n=7$ , 22%).

**Table 4.** Intraoperative morbidities and postoperative morbidities in patients

Intraoperative morbidity	n	%	Postoperative morbidity	n	%
None	104	76.5	None	63	46.3
Hypotension	10	31	Anemia and blood transfusion	23	32
Hypotension+bradycardia	5	16	Intubation and mechanical ventilator	20	27
Low $SPO_2$	4	13	Sepsis	18	25
Hypertension	4	13	Urinary tract infection	14	19
Hypotension+low $SPO_2$	2	6	Tissue infection	11	15
Metabolic acidosis	2	6	Impaired renal function	12	16
Low $SPO_2$ +oliguria	1	3	Arrest	7	10
Hypotension+Hyperglycaemia	1	3	ARDS	6	8
Hyperglycaemia (dextrose+insulin treatment)	1	3	Tracheostomy	2	3
Metabolic acidosis+hypotension+bradycardia	1	3			

ARDS: Acute respiratory distress syndrome.

More than one postoperative morbidity was observed in some patients, and the most common morbidities were found to be anemia with blood transfusion (n=23, 32%) and intubation with the start of mechanical ventilator treatment (n=20, 27%).

In this group of patients who were admitted for treatment of extensive major burns and could be operated on, the mortality rate was 44.2% (27/61).

## DISCUSSION

Although serum albumin levels are affected by acute factors, such as surgical stress and trauma, they have been found to be predictive of unwanted postoperative outcomes, as a marker of malnutrition and disease, just as much as the potential protective effects through significant biological mechanisms.<sup>[6]</sup> While hypoalbuminemia in the preoperative period has been associated with an increase in postoperative morbidity and mortality following general and thoracic surgery, it has not been found as a useful preoperative risk marker in orthopedic operations.<sup>[7]</sup> However, in cases of hip fractures, an albumin level <35 g/L has been found to be related to an increase in postoperative complications and mortality, and routine measurement is therefore recommended because of this prognostic importance.<sup>[8]</sup> In radical cystectomy operations in urological surgery, a relationship has been reported between preoperative albumin <3.5 gr/dL and high ASA scores and postoperative morbidity and mortality.<sup>[9]</sup> Although there are various opinions about the preoperative evaluation of burns and the management of the perioperative process, albumin replacement in acute fluid resuscitation decreases the formation of edema and the fluid requirement, but no consensus has yet been reached about the time of albumin application, and variations are seen according to the approaches of different burns centers.<sup>[3]</sup>

On the subject of albumin replacement, the use of saline and albumin for hypovolemia treatment within the first 28 days in the intensive care was not shown to make any difference to mortality in a study of 7000 patients.<sup>[10]</sup> In another report where replacement was evaluated, 15 mL/kg 5% albumin was used to help prevent hypotension by providing intravascular volume, but this was found to have no place in routine use because of the high costs.<sup>[11]</sup> In another study, it was reported that the colloid oncotic pressure was increased by 2 mmHg with the use of a mixture of 25% albumin and Ringer's lactate.<sup>[12]</sup> Maintaining high levels of colloid oncotic pressure reduces tissue edema by maintaining normal levels of capillary permeability. However, in the current study, these effects were not found to be related to postoperative complications.

In a study of patients with burns who were applied albumin treatment, the mortality risk was determined to be higher than that of a control group.<sup>[13]</sup> According to one group of authors, the administration of albumin to intensive care patients increases mortality; therefore, it should not be applied.<sup>[14]</sup>

In a previous study of children with burns covering a surface greater than 20%, for 6 weeks after the burn occurred, in one group, 25% albumin was used to keep the serum albumin level at 25–35 g/L, and in the other group, 25% albumin was administered directly to those patients with values <15 g/L. It was reported that there was no difference between these two groups of high (31–32 g/L) and low (21–24 g/L) albumin levels obtained with respect to fluid intake, urine output, subjective edema scores, requirement for mechanical ventilation, diarrhea, positivity in blood culture, the length of hospital stay, and mortality. According to these results, there was no benefit in holding the serum albumin within the recommended normal limits, and there were high costs. In our study, the ROC cut-off value was found to be 23 g/L. In our opinion, the results were not different in the studies due to the level of the albumin studied. Regarding our cut-off level, the threshold should be lower to see the difference.<sup>[15]</sup> However, in several studies, it has been reported to be an important marker of hypoalbuminemia in the evaluation of disease severity and nutritional status in intensive care patients. Thus, no useful guidelines have been obtained from literature on the subject of hypoalbuminemia in patients with burns, and chronic albumin replacement has not been shown to improve hypoalbuminemia.<sup>[3,16]</sup> In another study, the albumin levels obtained at 72 hours after admittance were seen to affect the length of hospital stay in patients with burns.<sup>[17]</sup> In the clinical evaluations of another study, the measurement of serum albumin levels slightly increased the accuracy of mortality predictions.<sup>[18]</sup>

In animal studies, while the use of albumin and other colloids in acute fluid resuscitation has been shown not to halt the edema of burns injuries, it reduces the need for resuscitation fluid by protecting the intravascular volume and does not cause an increase in extravascular fluid accumulation in the lungs as it lessens the increase in edema of soft tissues that are not burned.<sup>[3]</sup> It has been reported that if clinical studies support these findings, there could be a relationship between an increase in edema associated with extravasation in the lungs and albumin resuscitation in the first week after burns injury.<sup>[3]</sup> As a result of resuscitation with 5% albumin, cardiac output has been reported to reach pre-injury values in 6 hours.<sup>[19]</sup> Aktaş et al.<sup>[20]</sup> showed that the preoperative albumin levels were associated with wound infection in patients undergoing colorectal surgery.

In conclusion, the results of our study showed that ASA and hemoglobin levels were the markers of perioperative morbidity and mortality, and although albumin levels >2 g/dL or <2 g/dL were not observed to create any difference, the cut-off value was found to be 2.3 g/dL. Previous publications have shown variations in whether albumin replacement increases or decreases morbidity and mortality in patients with major burns. Therefore, there is a need for further studies to be able to establish a consensus on the subject of time and dose of the application of albumin in patients with major burns.

Conflict of interest: None declared.

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## ORIJİNAL ÇALIŞMA - ÖZET

## Majör yanıklı hastaların albümin düzeyinin anestezi yönetimi ile ilişkisi ve klinik gidişte etkinliği

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**AMAÇ:** Yanık şokunda, kapiller permabilitedeki masif artış sebebiyle albümin ve intravasküler sıvı hızlica ekstravasküler alana yer değiştirir. Bu nedenle hypoalbuminemi majör yanıklarda erken ve uzamış bir bulgu olarak karşımıza çıkar. Hypoalbuminemi çeşitli sorunlara yol açmaktadır. Bu çalışmada, majör yanıklı hastaların ameliyat öncesi dönem albümin düzeylerinin ameliyattaki morbidite ve mortaliteye etkisi araştırıldı.

**GEREÇ VE YÖNTEM:** Hastanemizde 2011–2013 yılları arasında majör yanık nedeniyle ameliyat olmuş 61 hastanın demografik verileri, ameliyat öncesi albümin düzeyleri, ameliyat kayıtları ve servis takipleri incelendi. Ameliyat sırasında komplikasyonlar; hipotansiyon, bradikardi, satürasyon düşüklüğü, metabolik asidoz, idrar çıkımında azalma, hiperglisemi olarak kaydedildi. Ameliyat sonrası komplikasyonlar; entübasyon ve mekanik ventilatöre bağlanma, sepsis, ARDS, akut böbrek yetersizliği, trakeotomi, kanama, arrest, pnömoni, idrar yolu enfeksiyonu, doku enfeksiyon, konjektif kalp yetersizliği, pleval efüzyon olarak kaydedildi.

**BULGULAR:** Albümin düzeyi 2 gr/dL değerinin altında ve üstünde olan hastalar arasında ameliyat esnasında komplikasyonlar sırasıyla 31.4 ve 20.8; ameliyat sonrası komplikasyonlar %60.0 ve %51.5; mortalite oranları %40 ve %25.8 olarak bulunmuştur (p=0.148; p=0.251; p=0.85). Ameliyat sonrası morbiditeyi etkileyen ameliyat öncesi albümin düzeyi için, albümin (g/dL) değerinde  $\geq 2.3$ 'ün kesim noktası olduğu bulunmuştur (AUC=0.587, p<0.001, %95 GA: 0.476–0.699, cut-off albumin  $\geq 2.3$ ).

**TARTIŞMA:** Majör yanıklı hastalarda, albümin uygulaması, zamanı ve dozu konusunda görüş birliği oluşturulamamıştır. Yoğun bakım literatüründe albümin verilenlerde mortalite ve morbiditenin arttığını gösteren yayınlar olmakla beraber, olumlu katkısı olduğunu destekleyen yayınlar vardır. Majör yanıklı hastalarda hypoalbuminemi konusunda yardımcı bir rehber elde edilememiştir. Bu çalışmada, albümin düzeyinin 2 gr/dL seviyesinin altında veya üstünde olması perioperatif morbidite ve mortalitede bir değişikliğe sebep olmamıştır.

**Anahtar sözcükler:** Albümin; mortalite; yanık.

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