

# Can the blood urea nitrogen to serum albumin ratio be used as a mortality predictor in patients with pneumonia after cardiac surgery?

Ahmet Kağan As<sup>1</sup>, Arda Aybars Pala<sup>1</sup>, Orhan Güvenç<sup>2</sup>, Şenol Yavuz<sup>1</sup>

<sup>1</sup>Department of Cardiovascular Surgery, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey

<sup>2</sup>Department of Cardiovascular Surgery, Uludağ University Medical Faculty, Bursa, Turkey

## ABSTRACT

**Objectives:** Serious complications are seen after cardiac surgery operations. Postoperative pneumonia is one of the most important of these complications. Some biomarkers have been examined in the prediction of mortality in special groups such as hospital-acquired pneumonia or aspiration pneumonia. In addition to parameters such as blood-urea nitrogen and albumin, the blood urea nitrogen to albumin ratio obtained by the ratio of these two parameters is also used as a mortality predictor. In this study, it was aimed to investigate the effect of the blood urea nitrogen to albumin ratio at the time of diagnosis of pneumonia on mortality in patients who developed pneumonia in the early period after cardiac surgery.

**Methods:** In this study, 138 patients who developed pneumonia in the early period after cardiac surgery were examined. Complete blood count and biochemical test results were analyzed for all patients, and differences between groups were investigated. The patients who developed in-hospital pneumonia and were discharged as survivors were classified as Group 1, and non-survivor patients were determined as Group 2.

**Results:** Patients who did not develop in-hospital mortality were included in Group 1 (n = 105, mean age = 63.7 ± 9.2 years), and those with non-survivor were included in Group 2 (n = 33, mean age = 66.9 ± 9.6 years). At the time of diagnosis neutrophil-lymphocyte ratio, C-reactive protein, blood-urea nitrogen and blood urea nitrogen to albumin ratio values were significantly higher in Group 2 ( $p < 0.001$ ,  $p < 0.001$ ,  $p = 0.004$  and  $p < 0.001$ ; respectively) ROC curve analysis was performed to evaluate blood urea nitrogen to albumin ratio in predicting mortality. The cut-off value of blood urea nitrogen to albumin ratio was 4.1 (Area under the curve [AUC]: 0.740, 95% CI: 0.690-0.820,  $p < 0.001$ , with sensitivity of 72.5% and specificity of 68.6%).

**Conclusions:** In pneumonia developing after cardiac surgery, we found that the peripheral blood blood urea nitrogen to albumin ratio at the time of the first symptom in the patient has a high predictive power for the development of mortality in this particular patient group.

**Keywords:** Cardiac surgery, postoperative pneumonia, mortality, prediction

Cardiac surgery is a procedure that is applied with high success rates in the treatment of cardiovascular diseases, and various serious complications after these operations still maintain their importance [1]. Postoperative pneumonia is one of the most important complications [2]. Due to this complication, the length

Received: December 2, 2021; Accepted: December 29, 2021; Published Online: January 13, 2022



e-ISSN: 2149-3189

**How to cite this article:** As AK, Pala AA, Güvenç O, Yavuz Ş. Can the blood urea nitrogen to serum albumin ratio be used as a mortality predictor in patients with pneumonia after cardiac surgery? Eur Res J 2022;8(2):155-161. DOI: 10.18621/eurj.1030236

**Address for correspondence:** Ahmet Kağan As, MD., University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Department of Cardiovascular Surgery, Mimar Sinan Mah., Emniyet Cad., Yıldırım, 16290, Bursa, Turkey. E-mail: ahmetkagan\_as@hotmail.com, Tel: +90 224 295 50 00, Fax: +90 224 275 67 67

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of hospital stay is prolonged, and the risk of morbidity and mortality increases. Previous studies reported that the rate of development of postoperative pneumonia has been shown to be between 5% and 21%, and mortality rates in these cases range from 6.2% to 28% [2-5].

Various inflammatory markers obtained from routine blood parameters have been the subject of research in cardiovascular surgery. These markers have been used both in the diagnostic sense and in predicting the prognosis of developing complications [6, 7]. Albumin, as a negative acute phase reactant, is an important inflammatory marker and plays an important role in maintaining osmotic pressure and in interstitial transport of vital molecules [8]. Increased blood urea nitrogen (BUN) levels in blood is also an important indicator of dehydration and has poor prognostic importance in pneumonia patients [9]. In the light of this information, blood urea nitrogen to albumin (B/A) ratio seems to be an important marker. In two recent studies, B/A ratio has been shown as an independent predictor of mortality in patients with hospital-acquired pneumonia and aspiration pneumonia [10, 11].

In this current study, we aimed to investigate the effect of the B/A ratio at the time of diagnosis of pneumonia on mortality in cases who developed early pneumonia after cardiac surgery.

## METHODS

This study was approved with the protocol dated 09.06.2021 and numbered 2011-KAEK-25 2021/06-16 of the Bursa Yüksek İhtisas Training and Research Hospital Clinical Research Ethics Committee. In this study, which was planned as a single center, patients between the ages of 20-90 who underwent open heart surgery at Bursa Yüksek İhtisas Training and Research Hospital between January 01, 2014 and January 01, 2020 were included in the study. The patients who had undergone redo cardiac operation, emergency cases, those with a known history of lung disease, those with chronic renal failure, and those with a history of pneumonia were excluded from the study. A total of 138 patients were evaluated for the study.

Laboratory values, demographic characteristics and blood values on the day they were diagnosed with pneumonia were recorded for all patients at the time

of admission to the hospital. The patients who developed in-hospital pneumonia and were discharged as survivor were classified as Group 1, and non-survivor patients were classified as Group 2.

## Variables

Variables were recorded as of the first admission of the patients to the hospital. Demographic data, identity information, age, gender, smoking were determined and recorded. Their medical histories were analyzed in detail. Presence of hypertension, diabetes, chronic obstructive pulmonary disease, congestive heart failure and coronary artery disease were recorded. By following the clinical outcome; Discharge or death information, duration of intensive care stay and total hospital stay were noted. Laboratory data including complete blood count values (white blood cell [WBC], hemoglobin [Hb], neutrophil, lymphocyte, platelet [PLT]), neutrophil-lymphocyte ratio (NLR), C-reactive protein (CRP), biochemical studies (BUN, Albumin, B/A ratio) was recorded. In addition, inflammatory blood markers were recorded on the basis of the day of diagnosis of pneumonia, and the B/A ratio was recalculated.

## Postoperative Pneumonia Diagnosis

In patients with clinically suspected pneumonia, newly detected infiltration on chest X-ray or an increase in the current infiltration degree were taken into account. In addition, pneumonia was diagnosed with the presence of at least two of the following criteria [12]: 1) Fever ( $> 38.5^{\circ}\text{C}$ ) or hypothermia ( $< 36.0^{\circ}\text{C}$ ); 2) Presence of purulent tracheo-bronchial secretion or an increase in the amount of existing secretion; and 3) Leukocytosis ( $12,000/\mu\text{L}$ ) or leukopenia ( $4,000/\mu\text{L}$ ).

## Statistical Analysis

Data were analyzed by SPSS 21.0 (IBM Statistical Package for the Social Sciences Statistic Inc. version 21.0, Chicago, IL, USA) program. "Kolmogorov-Smirnov test and Shapiro-Wilk test" were used for normality distribution analysis. While "Student's t test was used for the data presenting normal distribution, Mann-Whitney U test was used for data that did not conform to normal distribution. These data were shown as mean  $\pm$  standart deviation or as median (minimum-maximum) respectively. Categorical variables were shown as frequency and percentage, and

“Chi Square test” was used for analysis. Multivariate binary logistic regression analysis was utilized to analyze mortality predictors. A *p* value’s being less than 0.05 was accepted statistically significant. In predicting in-hospital mortality, receiver operating characteristics (ROC) curve analysis was performed for B/A ratio and area under the curve (AUC) was calculated.

## RESULTS

A total of 138 patients were included in the study. Patients who did not develop in-hospital mortality were included in Group 1 (n = 105, mean age = 63.7 ± 9.2 years), and those with non-survivor were included in Group 2 (n = 33, mean age = 66.9 ± 9.6 years). There were no statistically significant differ-

ences between the two groups in terms of age, gender, body mass index, smoking, hypertension and chronic obstructive pulmonary disease rates (*p* > 0.05). Also preoperative blood parameters of the patients were similar between two groups. Demographic characteristics and preoperative blood parameters of all patients are presented in Table 1.

Operative and postoperative features and blood parameters of the patients at the time of diagnosis were shown in Table 2. The two groups were similar in terms of perfusion times, need of positive inotropic support and use of blood products. There were no statistically significant differences between the two groups in terms of (at the time of diagnosis) WBC, creatinine, neutrophil counts, lymphocyte counts and albumin values (*p* > 0.05). At the time of diagnosis NLR, CRP, BUN and B/A ratio values were signifi-

**Table 1. Preoperative features and preoperative laboratory variables of the patients**

Variables	Group 1 (Survivor) (n = 105)	Group 2 (Non-Survivor) (n = 33)	<i>p</i> value
Age (years)	63.7 ± 9.2	66.9 ± 9.6	0.179
Male gender, n (%)	73 (69.5%)	25 (75.8%)	0.491
BMI (kg/m <sup>2</sup> )	26.4 (22.4-38)	27.2 (21.6-39)	0.293
Hypertension, n (%)	61 (58.1%)	21 (63.6%)	0.572
Diabetesmellitus, n (%)	30 (28.6%)	14 (42.4%)	0.136
COPD, n (%)	25 (23.8%)	11 (33.3%)	0.277
Smoking, n (%)	23 (21.9%)	8 (24.2%)	0.779
Hiperlipidemia, n (%)	54 (51.4%)	15 (45.5%)	0.549
Ejection fraction (%)	54.2 ± 9.7	50.2 ± 9.6	0.209
White blood cell (10 <sup>3</sup> /μL)	9.2 (4.9-12.4)	8.9 (5.1-13.7)	0.259
Hemoglobin (mg/dl)	12.8 (10-15.7)	12.2 (10.4-16)	0.314
Platelet (10 <sup>3</sup> /μL)	254.2 (129-460.4)	258.5 (128-450)	0.204
Neutrophil (10 <sup>3</sup> /μL)	4.2 (1.8-5.7)	4.4 (2.5-6.9)	0.251
Lymphocyte (10 <sup>3</sup> /μL)	2 (0.8- 4.1)	1.8 (0.9- 4.5)	0.102
NLR	2.3 (1.4-13.4)	2.4 (1.3-11.9)	0.096
Creatinine (mg/dL)	1.1 ± 0.8	1.3 ± 0.7	0.495
BUN, (mg/dL)	12 (9-18)	13 (10-20)	0.229
Albumin, (g/dL)	4.2 (3.9 5.5)	4.3 (3.8-5.4)	0.375
CRP (mg/L)	6.9 (0.5-12)	6.2 (0.6-15)	0.194
B/A ratio (mg/g)	1.96 (0.4-4.1)	2.08 (0.5-4.9)	0.174

BMI = Body mass index, COPD = Chronic obstructive pulmonary disease, BUN = Blood urea nitrogen, NLR = Neutrophil to lymphocyte ratio, CRP = C-reactive protein, B/A ratio = Blood urea nitrogen to albumin ratio

cantly higher in Group 2 ( $p < 0.001$ ,  $p < 0.001$ ,  $p = 0.004$  and  $p < 0.001$ ; respectively).

Logistic regression analysis was performed to evaluate the predictive value of certain parameters in terms of in-hospital mortality (Table 3). In univariate

analysis, age > 70 years (OR [odds ratio]: 1.125, 95% CI [confidence interval]: 1.080-1.548,  $p = 0.014$ ), ejection fraction < 35% (OR: 1.956, 95% CI: 1.318-2.865,  $P = 0.002$ ), need for inotropic support (OR: 0.875, 95% CI: 0.582-0.961,  $p = 0.036$ ), Time of di-

**Table 2. Operative and postoperative features of the patients**

Variables	Group 1 (n = 105)	Group 2 (n = 33)	P value
Total perfusion time (min)	86 (65-210)	88 (68-196)	0.148
Cross-clamp time (min)	55 (22-145)	52 (25-150)	0.362
Combined surgery, n (%)	23 (21.9%)	8 (24.2%)	0.779
Packed blood products (units)	6 (4-12)	7 (4-14)	0.194
Inotropic support, n (%)	30 (28.6%)	16 (48.5%)	<b>0.034</b>
<b>At the time of diagnosis</b>			
White blood cell (103/ $\mu$ L)	12.9 (13.2- 21.8)	13.1 (11.3- 25.6)	0.107
Neutrophil (103/ $\mu$ L)	4.2 (2.8- 8.4)	4.4 (2.6-9.7)	0.075
Lymphocyte (103/ $\mu$ L)	1.5 (0.9- 2.1)	1.2 (1- 2.5)	0.152
NLR	3.2 (2.1- 15.4)	4.9 (2.4- 22.6)	<b>&lt; 0.001</b>
Creatinine (mg/dL)	1.2 (0.9- 1.6)	1.1 (0.7- 2)	0.192
BUN (mg/dL)	12 (8.5- 28.6)	15.6 (8- 46.8)	<b>0.004</b>
Albumin (g/dL)	3.6 (2.6- 4.4)	3.5 (2.4- 4.2)	0.076
B/A ratio (mg/g)	3.36 (0.38-10.08)	4.89 (1.18-18.9)	<b>&lt; 0.001</b>
CRP (mg/L)	154 (85- 350)	238 (120-450)	<b>&lt; 0.001</b>

NLR = Neutrophil to lymphocyte ratio, BUN = Blood urea nitrogen, B/A ratio = Blood urea nitrogen to albumin ratio, CRP = C-reactive protein

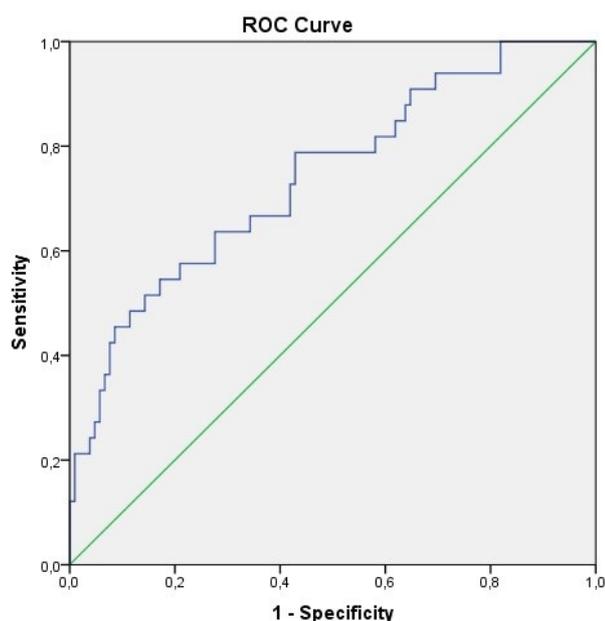
**Table 3. Logistic regression analysis to identify factors affecting postoperative pneumonia mortality**

Variables	p value	Univariate analysis		p value	Multivariate analysis	
		Exp (B) Odds Ratio	95% C.I. Lower Upper		Exp (B) Odds Ratio	95% C.I. Lower Upper
Age >70 years	<b>0.014</b>	1.125	1.080- 1. 548	0.276	1.345	0.844- 1.694
Ejection fraction < 35%	<b>0.002</b>	1.956	1.318- 2.865	0.019	1.127	1.045- 1.539
COPD	0.304	0.696	0.538- 1.183	--	--	--
Inotropic support	<b>0.036</b>	0.875	0.582- 0.961	0.332	0.976	0.882- 1.145
Preop NLR	0.098	0.763	0.594- 1.110	--	--	--
Preop B/A ratio	0.175	0.976	0.775- 1.194	--	--	--
Td NLR	<b>&lt; 0.001</b>	1.554	1.196- 2.872	0.094	0.887	0.697- 1.148
Td B/A ratio	<b>&lt; 0.001</b>	1.668	1.441- 2.152	<b>&lt; 0.001</b>	1.224	1.090- 1.792
Td CRP	<b>&lt; 0.001</b>	3.336	2.178- 4.894	<b>&lt; 0.001</b>	2.628	1.945- 4.136

COPD = Chronic obstructive pulmonary disease, NLR = Neutrophil to lymphocyte ratio, B/A ratio = Blood urea nitrogen to albumin ratio, CRP = C-reactive protein, Td = Time of diagnosis

agnosis (Td) NLR (OR: 1.554, 95% CI: 1.196-2.872,  $p < 0.001$ ), Td B/A ratio (OR: 1.668, 95% CI: 1.441-2.152,  $p < 0.001$ ) and Td CRP (OR: 3.336, 95% CI: 2.178-4.894,  $p < 0.001$ ) values were found to be significantly correlated with the development of in-hospital mortality. As a result of multivariate analysis, ejection fraction  $< 35\%$  (OR: 1.127 CI 95%: 1.045-1.539,  $p = 0.019$ ), Td B/A ratio (OR: 1.224, CI 95%: 1.090-1.79452,  $p < 0.001$ ) and Td CRP (OR: 2.628, CI 95%: 1.945-4.136,  $p < 0.001$ ) values were determined as independent predictors for predicting in-hospital mortality.

ROC curve analysis was performed to evaluate B/A ratio in predicting mortality. The cut-off value of B/A ratio was 4.1 (Area under the curve [AUC]: 0.740, 95% CI: 0.690-0.820,  $p < 0.001$ , with sensitivity of 72.5% and specificity of 68.6%) (Fig. 1).



**Fig. 1.** The area under the curve (AUC), confidence interval (CI), and cut-off values in receiver-operating characteristic (ROC) curve analysis for B/A ratio to predict mortality (cut off:4.1, AUC: 0.740, 95%CI: 0.690- 0.820,  $p < 0.001$ , with 72.5% sensitivity and 68.6% specificity).

## DISCUSSION

Postoperative pneumonia is one of the most important complications after open heart surgery. In addition to prolonging hospitalizations, this may result in mortality rates up to 50%. In this current study, it was shown for the first time in the literature that the B/A ratio is an independent predictor of mortality in

cases of pneumonia occurring in the early period after cardiac surgery. In addition to this marker, CRP value and ejection fraction below 35% at the time of diagnosis of pneumonia were also determined as independent predictors of mortality.

Serum albumin plays a key role in maintaining physiological homeostasis. It undertakes important tasks such as balancing osmotic pressure and transporting some components in the blood. The presence of low albumin levels in some chronic diseases such as heart failure, COPD and diabetes, as well as in malignancies with a predominant course of catabolism, has been associated with increased mortality and morbidity [13]. In a study by Yayla *et al.* [14], albumin levels were found to be significantly lower in patients who developed saphenous vein occlusion after CABG operations. In other studies, significant correlations were found between atrial fibrillation developing after cardiac surgery and low albumin [15, 16]. In our study, we found that albumin levels at the time of pneumonia diagnosis were low in patients who developed mortality, although it was not statistically significant ( $p = 0.076$ ).

Dehydration may occur in patients who need hospitalization, especially in infectious diseases where inflammation is at the forefront. The resulting increase in urea reabsorption from the kidneys results in increased BUN levels. This value is an important parameter indicating the state of dehydration in individuals and has been associated with poor clinical outcomes in patients with heart failure and pneumonia [9, 17]. In a study by Akgül *et al.* [16], a significant relationship was found between the development of postoperative atrial fibrillation, which is closely related to inflammation, and high BUN values after CABG operations. In our patients, BUN values at the time of diagnosis of pneumonia were significantly higher in the mortality group ( $p = 0.004$ ).

In line with all this literature information, the B/A ratio emerges as a valuable prognostic marker. There are various studies on various medical problems and B/A ratio in the literature. In a study conducted by Bae *et al.* [18] on patients with ischemic stroke, the B/A ratio was shown as a poor prognostic marker. In a study conducted by Dundar *et al.* [19], the B/A ratio at the time of admission was shown as an independent predictor of mortality in patients over the age of 65 who applied to the emergency department. In addition,

the authors emphasized in this study that the B/A ratio is a stronger predictor than albumin, BUN, creatinine, and glomerular filtration ratio alone [19]. In another study by Fang and XU [20], B/A ratio was found to be a strong predictor of mortality in critically ill patients in intensive care units who developed pulmonary embolism.

Recently, the relationship between B/A ratio and mortality in various pneumonia cases has been the subject of research. In the article published by Feng *et al.* [10] in 2019, the effect of B/A ratio on mortality in hospital-acquired pneumonia cases was investigated. In the study, which included 1158 cases, 150 patients (13%) died within 30 days. At the end of their study, the authors determined the high B/A ratio as an important value in predicting 30-day mortality [10]. In a study by Ryu *et al.* [11], at the beginning of 2021, the relationship between B/A ratio and mortality in aspiration pneumonia cases was investigated. In the study, which included 443 patients, mortality was observed in 90 (20.3%) patients in the first 28 days. As a result of the multivariate analysis, a B/A ratio above 7 was shown as a strong and independent predictor of mortality (OR 3.40, 95% CI 1.87-6.21,  $p < 0.001$ ). In another recent study by Ata *et al.* [21], B/A ratio was found to be an independent predictor for mortality in intensive care patients with COVID-19 pneumonia.

In our study, the other independent predictors of mortality in patients who developed pneumonia, apart from the B/A ratio, were preoperative ejection fraction below 35% and high CRP at the time of diagnosis. Comprehensive studies and meta-analyses have similar results with our study. Having a low ejection fraction in pneumonia that develops after cardiac surgery plays an important role in both the development of postoperative pneumonia and mortality after pneumonia [2, 12, 22-24]. Similarly, there are studies showing that increased CRP levels are also important in the development of postoperative pneumonia and associated mortality [25-27].

### Limitations

The most important limitations of our study are that it is single-centered, retrospective, and the number of patients is low. More comprehensive publications with larger numbers of patients are needed to support existing data.

### CONCLUSION

In our study, we examined a patient group that developed pneumonia after open heart surgery, which has not been evaluated in the literature before. In pneumonia developing after cardiac surgery, we found that the peripheral blood B/A ratio at the time of the first symptom in the patient has a high predictive power for the development of mortality in this particular patient group. This predictive ability will enable us to predict the risk of pneumonia-related mortality in patients undergoing cardiac surgery and to prevent adverse outcomes by taking necessary precautions in these patients.

### Authors' Contribution

Study Conception: AKA, AAP; Study Design: AKA, AAP; Supervision: AKA, AAP, ŞY; Funding: AKA, AAP, OG; Materials: AKA, AAP, OG; Data Collection and/or Processing: AKA, AAP, OG; Statistical Analysis and/or Data Interpretation: AKA, AAP, OG, ŞY; Literature Review: AKA, AAP, OG, ŞY; Manuscript Preparation: AKA, AAP, OG, ŞY and Critical Review: AKA, AAP, OG, ŞY.

### Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

### Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

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