

# Can Biomarkers be used for Prognosis Prediction in Patients with Acute Mesenteric Ischemia?

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## ABSTRACT

**Introduction:** Acute mesenteric ischemia (AMI) is a severe clinical condition that leads to intestinal ischemia and necrosis due to acute blockage of the mesenteric arteries. The mortality rate of AMI is still high, and early diagnosis and treatment are lifesaving. This study provides an overview of the biochemical parameters used to determine the prognosis of AMI patients.

**Methods:** This was an observational and single-center study. Demographic data, vital signs, comorbidities, laboratory tests, operative status, length of hospital stay, and outcome information of patients diagnosed with AMI were recorded.

**Results:** Twenty-eight (41.2%) female and 40 (58.8%) male patients were included in the study. Of the patients diagnosed with AMI, 45 (66.2%) underwent surgery. Twenty-six patients (38.2%) had a fatal outcome. The area under the curve (AUC) values for blood urea nitrogen (BUN)/albumin [0.850 (0.743-0.925)] and lactate/albumin [0.753 (0.633-0.849)] were statistically significant ( $p < 0.001$ ) for the outcome. The AUC analysis for C-reactive protein/albumin [0.654 (0.529-0.765)] indicated a significant relationship for surgical settings ( $p < 0.05$ ). In the intensive care unit setting, all ratios were statistically significant.

**Conclusion:** This study shows that the BUN/albumin ratio is a robust prognostic indicator of patients with AMI and guides clinicians' decision-making. However, further studies are required to confirm these data.

**Keywords:** Acute mesenteric ischemia, early prediction, BUN, albumin

## Introduction

Acute mesenteric ischemia (AMI) is a pathological disease characterized by intestinal ischemia and necrosis due to sudden occlusion of the mesenteric arteries. The mortality rate associated with acute myocardial infarction remains considerable, underscoring the critical need for timely identification and intervention to preserve lives (1). Several biochemical indicators are employed to assess the clinical prognosis of patients with acute myocardial infarction. Numerous blood tests, including blood urea nitrogen (BUN), have demonstrated associations with illness severity and prognosis. Measurement of BUN provides valuable insights into the functioning of the liver and kidneys. In addition, it is a useful tool in assessing the prognosis of patients with acute myocardial infarction (2,3).

Albumin is a biomarker that is closely linked to the severity of illnesses and can provide valuable insights into the prognosis of many medical conditions. Patients diagnosed with acute myocardial infarction who exhibit low albumin levels are more prone to have a worse prognosis.

This trend is also observed in other pathological conditions (4,5). Lactate is a noteworthy indicator of cellular hypoxia and exhibits elevated levels in individuals with impaired tissue perfusion. Elevated lactate levels in patients with acute myocardial infarction have been correlated with a worse prognosis, as indicated by previous studies (6,7). C-reactive protein (CRP) serves as a biomarker for inflammation. Elevated levels of CRP are correlated with the severity of illness and prognosis in individuals with acute myocardial infarction (8). Historically, biochemical ratios, including BUN/albumin, lactate/albumin, and CRP/albumin ratios, have been used to assess the prognosis of patients with acute myocardial infarction. The predictive values of these ratios are greater than those of individual biochemical tests, as reported in previous studies (5).

This study comprehensively examines the biochemical measures employed for prognostic evaluation in patients with acute myocardial infarction. Therefore, it is possible to enhance comprehension regarding the timely identification and suitable management of patients with acute myocardial infarction.



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## Methods

### Study Design

This observational, single-center study was conducted in the emergency department of a tertiary care hospital. Ethical approval was obtained from the İzmir Katip Çelebi University Local Committee before the study (approval number: 0095, date: 24.02.2022). Demographic data, vital signs, comorbidities, laboratory tests, operative status, length of hospital stay, and outcome information of patients who presented to the emergency department and were diagnosed with AMI between March 2017 and May 2022 were recorded in a data form. BUN/albumin, lactate/albumin, and CRP/albumin ratios were calculated using the obtained data. All data were used for statistical analysis.

### Patients and the Setting

The study included 104 patients aged 18 years who presented to the emergency department with an AMI diagnosis. Thirty-six patients whose laboratory test results or outcome information could not be accessed were excluded from the study. Information about 68 patients was retrieved from the hospital's electronic records. Patients under 18 years of age, those with end-stage renal failure, those previously diagnosed with AMI, and those with end-stage malignancy were excluded from the study.

### Outcomes

The primary outcome of this study was to determine the predictive power of the BUN/Alb ratio on mortality and morbidity in AMI, and the secondary outcome was to investigate the superiority of the BUN/Alb ratio over the lactate/albumin and CRP/Alb ratios.

### Data Collection

Data of the included patients were collected from the hospital information system, and their vital parameters, demographic data, and laboratory test results were recorded on patient forms created

for statistical analysis. Information regarding admission to the service and intensive care unit (ICU) for AMI treatment, including mortality and discharge, was noted. The effects of the calculated BUN/albumin, lactate/albumin, and CRP/albumin ratios on hospital discharge and outcome were compared.

### Statistical Analysis

The data were analyzed using IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA). The descriptive statistics comprised the mean ( $\bar{x}$ ), standard deviation, median, and interquartile range. The "Levene" test was used to evaluate variance homogeneity, a prerequisite for parametric testing. The normality assumption was tested using the Shapiro-Wilk test. If the data had a normal distribution, the "Independent two-sample t-test" was used to compare the groups. If data did not fit a normal distribution, the "Mann-Whitney U test" was used. Two or more diagnostic or laboratory tests were compared using the "receiver operating characteristic (ROC) curve" analytic method. Because the data did not meet the usual distribution standards, Spearman's rho coefficient was used to examine the relationship between the two quantitative variables. The chi-square test analyzed categorical data. P-values below 0.05 were considered significant.

## Results

Twenty-eight (41.2%) female and 40 (58.8%) male patients were included in the study. Of the patients diagnosed with AMI, 45 (66.2%) underwent surgery, whereas 23 patients did not undergo surgery because of the lack of surgical indication. Twenty-six patients (38.2%) had fatal outcomes. Forty-two patients were discharged after the completion of their treatments. The average length of hospital stay for the patients was  $7.98 \pm 9.41$  days. Mean laboratory values were calculated on the basis of the obtained data. The mean BUN value was  $29.82 \pm 19.84$  mg/dL, creatinine value was  $1.57 \pm 1.33$  mg/dL, CRP value was  $94.15 \pm 260.22$  mg/L, albumin value was  $31.92 \pm 8.58$  g/dL, and lactate value was  $3.42 \pm 3.61$  U/L. The calculated BUN/albumin, lactate/albumin, and

**Table 1. Laboratory values of the patients**

Variables	Detailed statistics	
BUN (mmol/L)	$\bar{x} \pm$ SD Median (min.-max.)	29.82±19.84 23 (7-87)
Creatinine (mg/dL)	$\bar{x} \pm$ SD Median (min.-max.)	1.57±1.33 1.21 (0.49-8.64)
CRP (g/dL)	$\bar{x} \pm$ SD Median (min.-max.)	94.15±260.22 20.08 (0.10-1528.0)
Albumin (g/dL)	$\bar{x} \pm$ SD Median (min.-max.)	31.92±8.58 33 (10-48)
Lactate (mmol/L)	$\bar{x} \pm$ SD Median (min.-max.)	3.42±3.61 2.20 (0.60-23.0)
BUN/albumin	$\bar{x} \pm$ SD Median (min.-max.)	1.04±0.80 0.83 (0.19-4.35)
Lactate/albumin	$\bar{x} \pm$ SD Median (min.-max.)	0.12±0.17 0.07 (0.02-1.10)
CRP/albumin	$\bar{x} \pm$ SD Median (min.-max.)	1.91±3.29 0.53 (0-15)

$\bar{x}$ : Mean, SD: Standard deviation, BUN: Blood urea nitrogen, CRP: C-reactive protein, min.: Minimum, max.: Maximum

CRP/albumin ratios were  $1.04 \pm 0.80$ ,  $0.12 \pm 0.17$ , and  $1.91 \pm 3.29$ , respectively (Table 1).

For outcome, the area under the curve (AUC) value for BUN/albumin [0.850 (0.743-0.925)] was statistically significant ( $p < 0.05$ ). A diagnostic value for BUN/Alb was considered to be above 0.7. The AUC analysis for BUN/albumin indicated a statistically significant diagnostic marker for the outcome. In addition, a value above 0.7 was an essential indicator in patient selection. The AUC value for lactate/albumin [0.753 (0.633-0.849)] was statistically significant ( $p < 0.001$ ). The diagnostic value for lactate/albumin was above 0.09. The AUC analysis confirmed that lactate/albumin is a statistically significant diagnostic marker for the outcome. Furthermore, a value above 0.09 was an essential indicator of patient selection. The ROC (AUC) analysis for CRP/albumin did not show statistical significance ( $p = 0.342$ ) (Table 2).

In the ICU setting, the AUC value for BUN/albumin [0.832 (0.722-0.912)] was statistically significant ( $p < 0.05$ ). The diagnostic value for BUN/Alb was considered to be above 1.04. The AUC analysis confirmed that BUN/albumin is a statistically significant diagnostic marker for the outcome. Additionally, a value above 1.04 was an essential indicator of patient selection. The AUC value for lactate/albumin [0.663 (0.539-0.774)] was statistically significant ( $p < 0.05$ ). The diagnostic value for lactate/albumin was above 0.09. The AUC analysis confirmed that lactate/albumin is a statistically significant diagnostic marker for the outcome. Furthermore, a value above 0.09 was an essential indicator of patient selection. The AUC value for CRP/albumin [0.657 (0.532-0.768)] was statistically significant ( $p < 0.05$ ). The diagnostic value for CRP/albumin was above 0.14. The AUC analysis confirmed that CRP/albumin is a statistically significant diagnostic marker for the outcome. Additionally, a value above 0.14 was a significant indicator of patient selection.

The AUC value for BUN/albumin in the surgical setting was insignificant ( $p = 0.690$ ). The AUC value for lactate/albumin was not statistically significant ( $p = 0.311$ ). The AUC analysis for CRP/albumin [0.654 (0.529-0.765)] indicated that the AUC was statistically significant ( $p < 0.05$ ). The diagnostic value for CRP/albumin was above 0.17. The AUC analysis confirmed that CRP/albumin was a statistically significant diagnostic marker for the outcome. Furthermore, a value above 0.17 was an important indicator of patient selection.

Patients admitted to the ICU with a high BUN/albumin ratio showed a 7.5 times higher risk than those receiving outpatient treatment (1,434-39,246). We observed a 4.56 (1,773-12,048) times higher BUN/albumin ratio in patients with fatal outcomes than in discharged patients ( $p = 0.002$ ). Among comorbidities, the mortality risk in patients with congestive heart failure was 5.23 (1,050-12,048) times higher than that in discharged patients ( $p = 0.043$ ). However, determining the lactate/albumin and CRP/albumin ratios was not statistically significant for distinguishing mortality ( $p > 0.05$ ).

While 65.5% of patients with a BUN/albumin ratio  $\leq 0.7$  were in the ward follow-up ( $p < 0.001$ ), this ratio was  $> 0.7$  in 85% of patients in the ICU ( $p < 0.001$ ). Among the surviving patients, 29 (69.0%) had a BUN/albumin value  $\leq 0.7$ , which was statistically higher than that in patients with a BUN/albumin value  $> 0.7$ . All patients with fatal outcomes ( $n = 26$ ) had a BUN/albumin value  $> 0.7$ .

The BUN/albumin ratio was  $\leq 1.04$  in 90.9% of outpatients ( $p < 0.001$ ). This ratio was  $\leq 1.04$  in 86.2% of patients in the ward follow-up ( $p < 0.001$ ). On the other hand, the BUN/albumin ratio was  $> 1.04$  in 67.9% of ICU patients ( $p < 0.001$ ).

In the comparison of endpoint analysis, the number of patients with a BUN/albumin value  $\leq 1.04$  with a fatal outcome was 35 (83.3%), which was statistically higher than that of the patient group with a BUN/albumin ratio  $> 1.04$ . The results supported the ROC analysis (Figure 1, Table 3).

## Discussion

In this study, 68 patients with AMI were evaluated. Of the patients, 58.8% were male, 41.2% were female, and the mean hospitalization duration was  $7.98 \pm 9.41$  days. Similarly, Kougiyas et al. (9) reported that male patients were at higher risk, and the mean hospitalization period was 9.1 days. The treatment and outcomes of patients with AMI may show different outcomes in different studies. In our study, 66.2% of the patients underwent surgery.

In contrast, several studies noted different rates of operated patients. For instance, Reintam Blaser et al. (10) reported that only 31.8% of the patients underwent surgery; however, Yıldırım et al. (11) showed that 77.8% of the patients underwent surgery. It is known that patients

**Table 2. ROC analysis for the outcome**

ROC analysis for the outcome		Area under the curve	Standard mistake	p	Area under the curve 95% confidence bounds		Sensitivity	Specificity	Limits
					Lower bound	Upper bound			
ROC analysis for the outcome	BUN/Alb	0.850	0.047	<0.001	0.743	0.925	69.05	100.0	>0.7
	Lactate/Alb	0.753	0.064	<0.001	0.633	0.849	69.23	80.95	>0.09
	CRP/Alb	0.570	0.073	0.342	0.444	0.690	76.92	45.24	-
ROC analysis for intensive care	BUN/Alb	0.832	0.050	<0.001	0.722	0.912	67.86	87.50	>1.04
	Lactate/Alb	0.663	0.069	0.019	0.539	0.774	57.14	75.0	>0.09
	CRP/Alb	0.657	0.067	0.020	0.532	0.768	85.71	42.50	>0.14
ROC analysis for surgery	BUN/Alb	0.629	0.070	0.690	0.503	0.743	85.0	46.43	-
	Lactate/Alb	0.571	0.070	0.311	0.445	0.690	37.50	78.57	-
	CRP/Alb	0.654	0.067	0.023	0.529	0.765	77.50	50.0	>0.17

ROC: Receiver operating characteristic, BUN: Blood urea nitrogen, CRP: C-reactive protein

diagnosed in the emergency department with AMI have a high mortality risk. In this study, 38.2% of the patients showed mortality. This rate was similar to that reported by Yıldırım et al. (11) in 2017. They showed that 31.2% of patients with AMI had a fatal outcome. Delayed diagnosis may be the main reason for higher mortality rates.

ROC analyses revealed that BUN/albumin, lactate/albumin, and CRP/albumin ratios are important prognostic indicators in patients with AMI. The AUC value for all three ratios (BUN/albumin especially) was statistically significant. These results are consistent with those of other studies in the literature. For instance, the BUN/albumin ratio is an important indicator in determining the mortality risks of patients with acute kidney injury during the ICU period (12-14). Similarly, the lactate/albumin ratio has been detected as a prognostic indicator of mortality in patients with severe sepsis (15). The CRP/albumin ratio has also

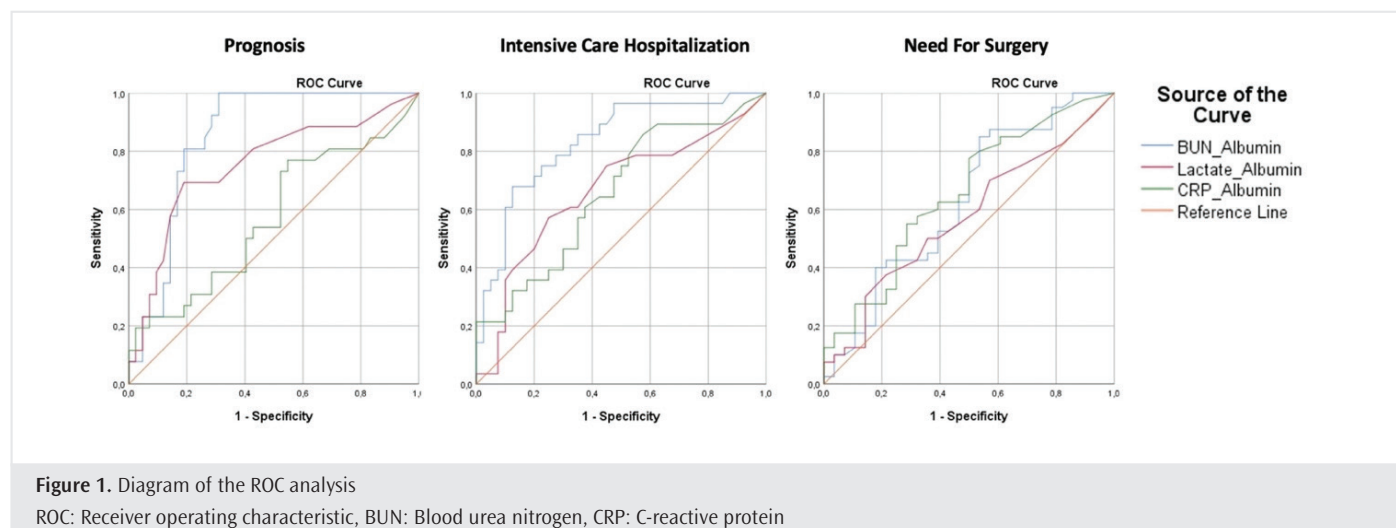
been reported to be used as a prognostic tool in inflammation-related diseases (16). Although all ratios have a significant relationship, our results showed that the BUN/albumin ratio was the best predictor tool for determining mortality risk. Decreased effective circulating volume secondary to the body's defense mechanism caused by stress and indirectly high BUN level and/or meeting the energy need from protein (albumin) due to stress may be one of the reasons that increase this rate.

Numerous studies documented in the existing literature have demonstrated the potential use of the CRP/albumin ratio as a predictive tool for postoperative problems. Xu et al. (13) demonstrated that the CRP/albumin ratio serves as a reliable biomarker in the prediction of postoperative problems following colorectal cancer surgery. In a similar vein, Kougias et al. (9) found that the CRP/albumin ratio demonstrated a notable level of sensitivity and specificity when used as a predictive

**Table 3. Reference value table for the BUN/albumin ratio**

Prognosis boundary of the BUN/Alb ratio	Groups		$\chi^2$ value	p-value
	$\leq 0.7$ n, (%)	$> 0.7$ n, (%)		
Outpatient	6 (54.5) <sup>a</sup>	5 (45.5) <sup>a</sup>	16,046	<0.001
Ward	19 (65.5) <sup>a</sup>	10 (34.5) <sup>b</sup>		
Intensive care	4 (14.3) <sup>a</sup>	24 (85.7) <sup>b</sup>		
<b>Outcome</b>				
Survivor	29 (69.0) <sup>a</sup>	13 (31.0) <sup>b</sup>	31,302	<0.001
Ex	0 (0.0) <sup>a</sup>	26 (100.0) <sup>b</sup>		
to the limit value of BUN/albumin ratio (ICU and others)	Groups		$\chi^2$ value	p-value
	$\leq 1,04$ n, (%)	$> 1,04$ n, (%)		
Outpatient	10 (90.9) <sup>a</sup>	1 (9.1) <sup>b</sup>	22,178	<0.001
Ward	25 (86.2) <sup>a</sup>	4 (13.8) <sup>b</sup>		
Intensive care	9 (32.1) <sup>a</sup>	19 (67.9) <sup>b</sup>		
<b>Outcome</b>				
Survivor	9 (34.6)	17 (65.4)	16,690	<0.001
Ex	35 (83.3)	7 (16.7)		

$\chi^2$ : Chi-square test, %: Percentage of rows, BUN: Blood urea nitrogen, ICU: Intensive care unit



measure for post-gastrectomy problems. Furthermore, several studies have demonstrated that the CRP/albumin ratio can serve as an effective tool for assessing inflammatory conditions. Zhang et al. (12) conducted a study that found that the CRP/albumin ratio was useful in predicting the outcomes of individuals afflicted with coronavirus disease-19. The findings of our study indicate that a CRP/albumin ratio of  $\geq 0.17$  may serve as a reliable predictor of postoperative problems. The observation that CRP exhibits positive acute phase reactivity, whereas albumin demonstrates negative acute phase reactivity, suggests that AMI, a significant stressor affecting several physiological systems, have the potential to enhance this phenomenon.

Another critical issue is anticipating the need for ICU in patients with AMI. Our results indicated that the BUN/albumin ratio was the best predictor of determining this requirement. In addition, lactate/albumin and CRP/albumin values were also effective parameters for predicting patients. These findings were consistent with those of other studies. Caluwaerts et al. (17) demonstrated that patients exhibiting an elevated BUN/albumin ratio have a heightened need for ICU services.

Furthermore, these patients experience elevated rates of death. In a similar vein, it was shown that a greater lactate/albumin ratio exhibited a positive correlation with a heightened need for ICU admission and an elevated risk of mortality (18). Moreover, this association was noted in patients with an elevated CRP/albumin ratio (19,20). This study examined the BUN/albumin ratio as a prognostic indicator in critical care unit hospitalizations, revealing its significant predictive capacity. In comparison with the other ratios discussed, it was determined that the BUN/albumin number is the most practical measure.

In a study by Efgan et al. (21), they found that the BUN/albumin ratio is as effective as the BISAP scores in determining high-risk acute pancreatitis. It also has powerful predictive power in pancreatitis, an inflammatory process like AMI.

### Study Limitations

The most important limitations of this study are that it was retrospective and included only patients diagnosed with acute mesenteric artery ischaemia and not all patients presenting to the emergency department. The study was conducted using patient records. The onset and duration of symptoms and the time until diagnosis and treatment are important determinants of morbidity and mortality in patients with AMI; however, because, this study was designed as a retrospective study, appropriate data could not be accessed due to archiving deficiencies. another limitation is that the study could not be detailed in terms of imaging (affected vessel, affected bowel section, etc.).

### Conclusion

This study shows that the BUN/albumin ratio is a robust prognostic indicator of patients with AMI and guides clinicians' decision-making. However, further studies are required to confirm these data.

**Ethics Committee Approval:** Ethics committee approval was obtained for the study from the İzmir Katip Çelebi University Non-Interventional

Clinical Research Ethics Committee to which the hospital is affiliated (approval number: 0095, date: 24.02.2022).

**Informed consent:** Retrospective study.

**Peer review:** Externally and internally peer-reviewed.

**Authorship Contributions:** Concept - O.S.Ç., E.S.B., M.G.E., D.Ç.; Design - O.S.Ç., U.P.; Data Collection or Processing - M.G.E., D.Ç.; Analysis or Interpretation - E.S.B., U.P.; Literature Search - O.S.Ç.; Writing - D.Ç.

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