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Original Article

Asessment of blood urea nitrogen to creatinine ratio as a predictor of mortality in ST-elevation myocardial infarction patients undergoing thrombolytic therapy: a cross-sectional study

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Abstract

Objectives: Given the increasing number of ST-elevation myocardial infarction (STEMI) and the related healthcare expenses and medical outcomes, as well as the frequent occurrence of kidney problems in this patient population, the current research aims to explore the effect of blood urea nitrogen to creatinine (BUN/Cr) ratio on the in-hospital mortality (IHM) of STEMI patients undergoing thrombolytic therapy.

Methods: This study is a cross-sectional analytical study conducted in 2021 at Shahid Madani Hospital, affiliated with Tabriz University of Medical Science, which investigated the relationship between the BUN/Cr ratio and IHM in patients with STEMI who received thrombolytic treatment between 2017 and 2019. Patients with other causes of ST elevation, those undergoing dialysis, or those with incomplete medical records were excluded. Data were collected from patient medical records. The primary outcome was in-hospital mortality, with secondary outcomes including the occurrence of heart failure and the need for blood transfusion—chi-square tests for categorical and t-tests for continuous variables. A p-value of less than 0.05 was considered statistically significant.

Results: A total of 398 patients were diagnosed with STEMI and treated with thrombolytic 330 (82.9%) patients were men. High BUN and Cr had a significant correlation with high mortality rates (P < 0.01). However, BUN/Cr didn't have a substantial relationship with IHM and one-year mortality (P-value = 0.46). The most common in-hospital complication was heart failure (HF), and a higher need for blood transfusion was significantly related to high rates of BUN/Cr (P < 0.01).

Conclusions: While high BUN and Cr levels were significantly associated with increased mortality rates, the BUN/Cr ratio was not significantly related to IHM. These results suggest that although elevated BUN and creatinine indicate poor prognosis, the BUN/Cr ratio may not be a standalone predictor of in-hospital mortality. Further research is needed to validate these findings and identify other factors affecting patient outcomes.

Keywords: ST Elevation Myocardial Infarction, BUN/Cr Ratio, Thrombolytic Therapy, In -hospital mortality

Introduction

schemic heart disease (IHD) is the predominant cardiovascular condition globally and is the primary contributor to mortality on a worldwide scale. IHD poses a significant health challenge in both developing and developed nations. (1). STEMI is a clinical condition characterized by symptoms of myocardial ischemia. This condition is identified by an elevation in the ST segment on the electrocardiogram (ECG) and an elevation in biomarkers associated with cardiac necrosis (2). Atherosclerosis within the coronary arteries stands as the primary culprit behind acute ST-elevation myocardial infarction (STEMI). Various pathophysiological elements, such as inflammation, can trigger the formation of atherosclerotic conditions (3). The inflammatory mechanisms that ensue after the development of atherosclerosis are pivotal in the destabilization of atherosclerotic plaques. Moreover, these mechanisms can induce thrombus formation upon interaction with erosions surface of atherosclerotic on the plaques. consequently leading to myocardial infarctions (MI) (4). The severity of coronary disease and the short and long-term prognosis are associated with the rise in serum inflammatory markers (5). The estimated in-hospital mortality (IHM) for STEMI ranges from 4 to 12%. The management of STEMI focuses on prompt diagnosis and timely restoration of blood flow. Therefore, the hospital system should aim to minimize delays in treating STEMI patients (6). Restoring blood flow in a blocked artery within 12 hours of symptom onset reduces morbidity and mortality rates. This can be achieved through primary percutaneous coronary intervention (PCI) or thrombolytic medication. Thrombolytic therapy should only be considered if PCI cannot be performed within 2 hours of admission. Failure to promptly open the blocked artery can lead to significant myocardial damage and an increased risk of mortality for the patient (7, 8) A risk assessment is essential in determining the appropriate treatment method for patients, leading to the correct procedure (9, 10). Various risk assessment models have been utilized in these patients, incorporating different prognostic factors like age, gender, angina, CVD risk factors, heart failure symptoms, systolic blood pressure, heart rate, ST segment changes, cardiac enzymes, and serum creatinine (10, 11). Creatinine serves as an indicator of renal dysfunction and is associated with increased cardiovascular mortality (12). Additionally, glomerular filtration rate (GFR) is associated with the prognosis of patients with

acute MI (13). Blood urea nitrogen (BUN) is another marker used to evaluate renal dysfunction, with high BUN levels in HF patients indicating a poor prognosis. Research by Richter et al. indicates that admission BUN is an independent predictor of long-term cardiovascular mortality in acute MI patients, offering predictive value beyond GFR (14). According to a separate investigation conducted by Wang et al., it has been asserted that an admission BUN level exceeding 8.95 millimoles per liter is significantly linked to an elevated risk of short-term mortality and major adverse cardiac events (MACE) in patients experiencing cardiogenic shock (CS) myocardial following an acute infarction (MI).Furthermore, the prognostic significance of BUN surpasses that of other renal markers (15). Despite BUN serving as an indicator of neurohormonal activity and glomerular filtration rate (GFR), as well as a robust predictor of mortality in individuals with congestive heart failure (HF), the precise correlation between BUN/Cr and clinical outcomes in patients with acute MI remains incompletely understood (16, 17). In light of this context, the present study was designed and executed to assess the impact of serum BUN/Cr on in-hospital mortality (IHM) and one-year mortality among patients diagnosed with ST-segment elevation myocardial infarction (STEMI) who underwent thrombolytic therapy.

Materials and Methods

Study Design and Setting

This is a retrospective analytical study aiming to investigate the effect of BUN/Cr on IHM and on patients diagnosed with STEMI who underwent thrombolytic therapy.

Study Population

The study population included patients diagnosed with STEMI who received thrombolytic therapy between 2017 and 2019. The exclusion criteria were: 1. ST elevations not caused by STEMI (e.g., myocarditis, Prinzmetal's angina, pericarditis)

2. Patients undergoing dialysis

3. Incomplete medical records.

Data collection and study conduct

The patient's medical reports were used to collect data. The documented variables were demographic characteristics such as age and gender, as well as risk factors like diabetes mellitus (DM), hypertension (HTN), smoking, and renal failure. Additionally, the medical history of coronary artery bypass grafting (CABG) and myocardial infarction (MI), vital signs (systolic and diastolic blood pressure), laboratory tests (BUN, creatinine, hemoglobin, hematocrit (HCT), white blood cell (WBC), platelet count, blood glucose, and peak troponin level), echocardiography findings (ejection fraction), and in-hospital mortality (IHM) were recorded. Furthermore, in-hospital complications such as transfusions, pulmonary edema, cardiogenic shock (CS), stroke, vascular complications, bleeding, and heart failure (HF) were assessed based on the available records included in the study checklist. Quantitative data were presented as mean and standard deviation for normally distributed variables and median and interquartile range for skewed variables.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 23. Descriptive statistics were used to summarize the data. Continuous variables were reported as mean \pm standard deviation (SD) or median with interquartile range (IQR) as appropriate. Categorical variables were presented as frequencies and percentages. The normality of the data was checked using the Kolmogorov-Smirnov test. For inferential statistics, chi-square tests were used for categorical variables, and t-tests were used for continuous variables. A p-value of less than 0.05 was considered statistically significant.

Results

Table 1 shows the demographic characteristics, laboratory findings, and risk factors of the 398 patients diagnosed with STEM who received thrombolytic therapy. The mean age of the patients was 61.0, and the standard deviation of 11.4 years. Most patients were male, accounting for 82.9% of the study population. Among the risk factors, smoking was the most prevalent, observed in 33.7% of the patients, followed by hypertension in 28.1% and diabetes mellitus in 18.1%. Hyperlipidemia was noted in 5.8% of the patients. Laboratory findings showed a mean blood BUN level of 19.3 mg/dL with a standard deviation of 8.9 mg/dL and a Cr level of 1.2 mg/dL with a standard deviation of 0.5 mg/dL. The IHM rate was 7.3%, with 29 patients passing away during their hospital stay. Additionally, the one-year mortality rate was 4.3%, with 17 patients dying within one year post-discharge. The most common in-hospital complication was HF, occurring in 71.9% of the patients. The need for blood transfusion was observed in 10.6% of the patients, while cardiogenic shock was noted in 4.8% of the cases.

Variables	n/Mean	%)	SD
Age (years)	61.0	11.4	
Sex (male)	330	82.9	
MR	Yes	283	71.1
	No	66	16.6
Blood group	A+	136	34.2
	B+	74	18.6
	AB+	27	6.8
	O+	88	22.1
	O-	7	1.8
	A-	16	4.0
	B-	6	1.5
	AB-	2	0.5
CTNI	Positive	271	68.1
	Negative	56	14.1
Family history	Yes	53	13.3
	No	103	25.9
Final status	IHM	29	7.3
	One year	17	4.3
Hospital	mortality Transfusion	42	10.6
complications	Heart failure	42 286	71.9
complications			4.8
	Cardiogenic	19	4.8

Table1. Demographic profile, laboratory findings, and risk factors of STEMI patients

Variables	n/Mean	%)	SD
	shock		
Number of involved	1	152	38.2
vessels	2	89	21.4
	3	64	16.1
Risk factor	CKD	6	1.5
	DM	72	18.1
	HTN	112	28.1
	HLP	23	5.8
	Smoke	134	33.7
LVEDP	47.2	5.3	
Chol	173.5	41.8	
Troponin	17.0	11.1	
TG	128.6	63.1	
HDL	40.0	11.1	
LDL	106.4	35.1	
SBP	124.6	60.7	
DBP	76.3	14.0	
GFR	68.2	21.3	
PR	78.5	14.1	
Bun	19.3	8.9	
CR	1.2	0.5	
Hb	14.8	2.2	
PLT	228.2	66.9	
WBC	12.2	4.8	
Ck_MB	77.0	58.9	

MR: Mitral Regurgitation; CTNI: Cardiac Troponin; IHM: In-hospital Mortality; CKD: Chronic Kidney Disease; DM: Diabetes Mellitus; HTN: Hypertension; HLP: Hyperlipidemia; LVEDP: Left ventricular end-diastolic pressure; Chol: Cholesterol; TG: Triglycerides; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; GFR: Glomerular Fraction Rate; PR: Peripheral Rate; BUN: Blood urea nitrogen; CR: Creatinine; Hb: Hemoglobin; PLT: Platelets; WBC: White blood cells; CK-MB: creatine kinase-myocardial band.

Figure 1 shows the Receiver Operating Characteristic (ROC) curve for the BUN/Cr ratio. ROC curve evaluates the diagnostic performance of the BUN/Cr ratio in predicting IHM among patients diagnosed with STEMI undergoing thrombolytic therapy. The curve plots the true positive rate (sensitivity) against the false positive rate (1-specificity) at different

threshold values. The area under the curve (AUC) closer to 1.0 indicates better diagnostic accuracy. In the present study, although the BUN/Cr ratio provided some insights into renal function, it did not show a significant relationship with IHM (P-value=0.46), indicating limited predictive value for mortality outcomes in this patient population.

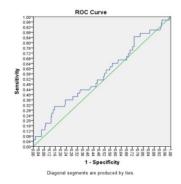


Figure 1: The ROC curve for BUN/Cr

Table 2 illustrates the distribution of BUN/Cr ratios among STEMI patients who received thrombolytic therapy. The BUN/Cr ratio was categorized into two groups: less than 12.5 and greater than 12.5. From among the total patient population, 96 patients (24.1%) had a BUN/Cr

ratio of less than 12.5. Conversely, most patients, 238 (59.8%), had a BUN/Cr ratio higher than the cut-off value. This distribution indicates that a significant proportion of STEMI patients had higher BUN/Cr ratios, reflecting potential kidney function abnormalities prevalent in this group.

Table2. BUN/Cr range in STEMI patients

Variable		n	%
Bun/Cr	<12.5	96	24.1
	>12.5	238	59.8

Table 3 displays the significant relationship between the BUN/Cr ratio and various risk factors in patients with STEMI. BUN/Cr didn't have a significant relationship with IHM and one-year mortality (Pvalue=0.46), indicating no significant difference between the groups. For patients with a BUN/Cr ratio less than 12.5, one-year mortality was 3.1%, and 7.4% for those with a ratio greater than 12.5, suggesting that the BUN/Cr ratio does not significantly correlate with most of the risk factors analyzed, including in-hospital and one-year mortality, gender distribution, single vessel disease, and positive CTNI. However, there is a trend towards older age in patients with higher BUN/Cr ratios.

Table3. The relationship between BUN/Cr and risk factors in patients diagnosed with ST-segment elevation myocardial
infarction undergoing thrombolytic therapy

	Bun/Cr			
Variable	<12.5	>12.5	P-value	
Final status	IHM	7(10.8)	17(9.7)	0.46
	One year	2(3.1)	13(7.4)	
	mortality			
Gender	Male	81(84.4)	193(81.8)	0.34
	Female	14(14.6)	42(17.8)	
Vessels	1	41(57.7)	88(48.9)	0.56
involved	2	16(22.5)	53(29.5)	
	3	14(19.7)	39(21.7)	
CTNI	Positive	67(81.7)	163(83.6)	0.70
	Negative	15(18.3)	32(16.4)	
MR	Yes	75(88.2)	159(77.6)	0.36
	No	10(11.8)	46(22.4)	
Age	58.3(12.6)	61.9(10.8)	0.07	
LVEDP	46.7(5.2)	47.6(5.3)	0.96	
Chol	176.2(41.7)	170.6(40.1)	0.75	
Troponin	17.6(11.3)	17.3(10.9)	0.59	
TG	136.4(64.1)	126.7(66.2)	0.71	
HDL	39.7(11.8)	40.3(10.8)	0.16	
LDL	112.3(33.5)	101.5(35.1)	0.38	
SBP	119.2(21.2)	127.8(76.5)	0.53	
DBP	74.6(13.0)	77.1(14.7)	0.42	
GFR	62.8(22.4)	69.6(20.7)	0.53	
PR	79.3(14.0)	78.8(14.5)	0.21	
Hb	14.9(2.0)	14.8(2.2)	0.53	
Plt	240.7(80.3)	222.9(62.4)	< 0.01*	
WBC	11.7(4.3)	12.4(4.7)	0.69	
CK-MB	79.5(71.2)	77.1(56.5)	0.09	

IHM: In-hospital Mortality; CTNI: Cardiac Troponin; MR: Mitral Regurgitation; LVEDP: Left ventricular end-diastolic pressure; Chol: Cholesterol; TG: Triglycerides; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; GFR: Glomerular Fraction Rate; PR: Peripheral Rate; Hb: Hemoglobin; PLT: Platelets; WBC: White blood cells; CK-MB: creatine kinase-myocardial band.

However, the other risk factors and laboratory findings did not elucidate this correlation. Table 4 shows the relationship between BUN/Cr and hospital complications in patients with Ant-STEMI. The most in-hospital complication was HF, occurring in 115

(66.6%) patients, followed by CS in 59 (34.6%) and blood transfusion in 47 (19.1%) patients. There was a significant relationship between a higher need for blood transfusion and high rates of BUN/Cr (P-value<0.01).

	Bun/Cr				
Variable	<12.5	>1	P-value		
Transfusion	Yes	4(4.4)	37(14.7)	< 0.01*	
	No	87(95.6)	214(85.3)		
Heart failure	Yes	36(32.4)	79(34.2)	0.972	
	No	75(67.6)	152(65.8)		
Cardiogenic shock	Yes	16(17.4)	43(17.2)	0.967	
	No	76(82.6)	207(82.8)		

Table4. The relationship between Bun/Cr and hospital complications in STEMI patients

Finally, Table 5 demonstrates the relationship between mortality and risk factors in patients diagnosed with STEMI. During hospitalization, 29 patients succumbed, with 17 (58.6%) being men. Additionally, 17 patients passed away during the oneyear follow-up, among whom 14 (82.4%) were men. This association proved statistically significant (P <0.01). Age and the extent of vessel involvement also exhibited a significant relationship with higher mortality rates (P <0.01). Furthermore, increased BUN, Cr, and decreased GFR rates were associated with higher mortality rates (P <0.01). Furthermore, elevated WBC counts and diminished hemoglobin levels were linked to increased mortality (P <0.01).

 Table5. The relationship between mortality and risk factors in patients diagnosed with ST-segment elevation myocardial infarction undergoing thrombolytic therapy

Variables	Normal	IHM	O	ne year mortality	Р-
					value
Gender	Male	205(86.5)	17(58.6)	14(82.4)	< 0.01*
	Female	31(13.5)	12(41.4)	3(17.6)	
Vessels	1	100(52.6)	3(23.1)	2(22.2)	< 0.01*
involved	2	57(30.0)	4(30.8)	2(22.2)	
	3	33(17.4)	6(46.2)	6(55.6)	
CTNI	Positive	167(85.6)	17(81.0)	10(71.4)	0.33
	Negative	28(14.4)	4(19.0)	4(28.6)	
MR	Yes	169(79.3)	20(83.3)	14(93.3)	0.39
	No	44(20.7)	4(16.7)	1(6.7)	
Age	60.4(11.1)	68.6(9.8	3)	69.9(11.4)	< 0.01*
Cr	1.1(0.3)	1.9(0.7))	1.1(0.3)	< 0.01*
Bun	17.9(6.2)	32.9(16.	5)	20.9(9.3)	< 0.01*
LVEDP	47.3(5.0)	46.6(7.2	2)	51.1(4.5)	0.03*
Chol	172.5(41.7)	177.0(51	.0)	183.1(35.4)	0.64
Troponin	16.6(10.8)	18.5(12.)	2)	15.4(9.2)	0.75
TG	130.2((62.9)	125.8(45.	.4)	104.7(39.3)	0.34
HDL	39.6(11.1)	40.7(13.	6)	42.6(9.0)	0.63
LDL	107.1(37.0)	96.1(31.4	4)	119.4(38.1)	0.33
SBP	126.5(76.3)	117.0(26	.8)	124.4(14.8)	0.79
DBP	75.8(13.1)	74.2(20.9	9)	80.5(10.5)	0.32
GFR	71.8(19.2)	38.6(19.1	10	66.5(18.3)	< 0.01*

Variables	Normal	IHM	One year mortality	P-
				value
PR	77.9(13.5)	86.8(17.2)	81.6(11.7)	< 0.01*
Hb	14.9(2.2)	14.2(2.1)	14.1(1.5)	< 0.01*
WBC	11.7(4.3)	16.3(5.7)	12.1(2.6)	< 0.01*
PLT	225.6(69.6)	249.8(73.3)	221.9(53.5)	0.23
CK-MB	79.1(60.9)	76.2(64.7)	67.7(28.7)	0.93

IHM: In-hospital Mortality; CTNI: Cardiac Troponin; MR: Mitral Regurgitation; CR: Creatinine; BUN: Blood urea nitrogen; LVEDP: Left ventricular end-diastolic pressure; Chol: Cholesterol; TG: Triglycerides; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; GFR: Glomerular Fraction Rate; PR: Peripheral Rate; Hb: Hemoglobin; PLT: Platelets; WBC: White blood cells; CK-MB: creatine kinase-myocardial band.

Discussion

The present study is a retrospective cross-sectional study aimed at determining the effect of BUN/Cr on IHM and one-year mortality of patients diagnosed with ST-segment elevation myocardial infarction and undergoing thrombolytic treatment in 2021. The findings of the research conducted by Hartopo et al. Indicated a correlation between elevated levels of BUN and cr, as well as their ratio, and cardiac side effects.Through multivariate analysis, it was determined that only high BUN levels independently predicted adverse cardiac events (18). Similarly, Smith et al.'s study demonstrated that a higher renal clearance reduced mortality in patients following an acute myocardial infarction (AMI). They concluded that renal function plays a significant and independent role in the risk of mortality after AMI (19). Furthermore, Huang et al.'s study revealed that acute heart failure accompanied by an increase in BUN/Cr levels is associated with a higher risk of mortality in patients with AMI. The BUN/Cr ratio was found to have predictive value for prognosis in patients with acute heart failure (20).

Additionally, Adam et al.'s study investigated the effectiveness of serum BUN, creatinine, and electrolytes in diagnosing and assessing mortality risk in patients with acute coronary syndrome (ACS). Their findings indicated that along with cardiac enzymes, potassium (K) in conjunction with BUN and Cr can be valuable in diagnosing ACS. BUN and Cr are essential for evaluating mortality risk in patients with acute coronary syndromes (21). Several studies have examined the effect of MI on kidney function and concluded that kidney failure develops gradually over time. Bataille et al.'s study found a correlation between low kidney function and increased mortality rates in MI patients, as well as a higher risk of one-year mortality. Their findings indicate that reduced renal function contributes to 37

higher mortality rates in MI patients (22). Přeček et al. also concluded that biomarkers of renal function are linked to the prognosis of ACS patients. This revealed systematic review а close pathophysiological relationship between the heart and the kidneys (23). However, the findings of our study differed from other studies. While there was a significant association between elevated levels of BUN and Cr and increased mortality rates in STEMI patients, there was no significant correlation between the serum BUN/Cr ratio and IHM or one-year mortality in patients diagnosed with STEMI who received thrombolytic treatment. This inconsistency may be attributed to variations in the individual characteristics of the participants and the methodology employed in these studies compared to our own. Another possible explanation could be the smaller sample size in our study compared to previous ones. Additionally, the limited number of fatalities in our study may also contribute to these discrepancies. Finally, missing data in our study could be another potential reason for the differences observed. Previous research has demonstrated that individuals suffering from renal failure face a heightened susceptibility to bleeding as a result of thrombocytopenia and platelet dysfunction. In 1987, Gafter U et al. examined the platelet count in patients with end-stage renal failure and those with chronic renal failure (CRF) before undergoing hemodialysis. Their investigation revealed a decrease in platelet count and the presence of mild thrombocytopenia among CRF patients (24). Similarly, Dorgalaleh et al. examined 132 patients with renal impairment and 179 healthy individuals, finding a higher incidence of thrombocytopenia in those with chronic renal failure (25). Furthermore, Mohamed et al. conducted a comparable study which also highlighted the elevated risk of bleeding due to thrombocytopenia and platelet

dysfunction in patients with renal failure (26). Notably, this study observed a significant decrease in platelet counts among STEMI patients with higher serum BUN levels.

Limitations and Suggestions

Our study had several limitations. Firstly, data were generated from a single-center hospital, which may limit the generalizability of the findings to other populations or healthcare settings. Secondly, due to the observational design of this study, it is impossible to prove causality. The findings of our research are hypothesis-generating. Thirdly, there is the limited sample size. Fourth is the lack of long-term follow-up in the study. Finally, the study did not assess the impact of other potential confounding factors, such as time to reperfusion, door-to-needle time, or utilizing other medications, which could influence the outcomes.

Suggestions for Future Research

Conduct a multicenter, prospective study to validate the findings and improve the generalizability of the results. Investigate the impact of other factors, such as time to reperfusion, door-to-needle time, and medication use, on the relationship between BUN/Cr and clinical outcomes. Assess the impact of interventions targeting renal function on the outcomes of STEMI patients undergoing thrombolytic therapy.

Conclusion

In conclusion, our research indicates that the rise in BUN/Cr ratio is not significantly correlated with IHM and one-year mortality among STEMI patients. Moreover, there is no notable connection with the incidence of in-hospital complications such as HF and CS. Nevertheless, a significant association was observed between BUN/Cr ratio and blood transfusion in our patient cohort. It is imperative to conduct future prospective multicenter studies to establish a more robust level of evidence on this matter.

Current Knowledge

Renal function has been recognized as a significant prognostic factor in patients with cardiovascular diseases. Elevated blood urea nitrogen (BUN) and

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1.Go AS, Mozaffarian D, Roger VL, et al. Executive summary: heart disease and stroke statistics-2014 update: a report from the American Heart Association. creatinine (Cr) levels, indicators of renal dysfunction, are associated with adverse outcomes in patients with heart failure and myocardial infarction. The BUN/Cr ratio is a useful marker for assessing renal function and has been studied as a predictor of mortality and morbidity in various clinical scenarios.

What is New Here?

Unlike previous studies that identified high BUN and creatinine levels as significant predictors of mortality in cardiovascular patients, our findings reveal that the BUN/Cr ratio itself does not significantly correlate with IHM or one-year mortality in this specific patient population. This suggests that while renal function markers are critical, the combined BUN/Cr ratio may not provide additional prognostic value beyond individual BUN and creatinine levels. This study highlights the need for further research to identify more precise biomarkers or combinations thereof to improve mortality risk prediction in STEMI patients.

Acknowledgments

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Ethical approval

The study process was reviewed and approved by the Ethics Committee of Tabriz University of Medical Sciences, according to the Declaration of Helsinki (Ethics Code: IR.TBZMED.REC.1399.970).

Consent for publication

Not applicable

Availability of data and materials

The dataset analyzed in the current study is available from the corresponding author upon a reasonable request.

Conflicts of Interest

None

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