CMJ Original Research September 2018, Volume: 40, Number: 3
Cumhuriyet Medical Journal 265-275
http://dx.doi.org/10.7197/223.vi.418591

The association between admission blood urea nitrogen levels with in-hospital and long-term mortality in ST-segment elevation myocardial infarction

ST-segment elevasyonlu miyokard infarktüsünde başvuru kan üre azotu ile hastane içi ve uzun dönem mortalite arasındaki ilişki

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Received/Accepted: April 25, 2018 / September 28, 2018
Conflict of interest: There is not a conflict of interest.

SUMMARY

Objective: The aim of this study was to investigate the association of blood urine nitrogen (BUN) levels with all-cause mortality in ST-segment elevation myocardial infarction (STEMI).

Method: This study included 3778 patients with STEMI treated with primary percutaneous coronary intervention. An admission BUN of 17.5 mg/dL was identified through a ROC analysis as an optimal cutoff value to predict the in-hospital mortality with 68% sensitivity and 66% specificity (AUC: 0.75; 95% CI:0.72-0.88; $p < 0.001$).

Results: The patients were followed up for a mean period of 33±0.14 months. Patients with higher BUN levels had 5.3-times higher in-hospital (OR: 6.0, 95% CI: 4.4-8.3) and 5-times higher long-term (HR: 5.3, 95% CI: 4.2-6.8) mortality rates than patients with lower BUN levels.

Conclusions: This study demonstrated that elevated BUN level was independently associated with increased in-hospital and long-term mortality. BUN test is a simple, inexpensive, and easily bedside applicable method. Hence, it can be used to detect high-risk patients in the setting of STEMI.

Keywords: Blood urine nitrogen; ST-segment elevation myocardial infarction; primary percutaneous coronary intervention; mortality

ÖZET

Amaç: Çalışmanın amacı kan üre azotu (KÜA) seviyesi ile ST-elevasyonlu miyokard infarktüsündeki (STEMİ) tüm nedenli mortalite arasındaki ilişkiyi araştırmaktı.

Yöntem: Bu çalışma primer perkütan koroner girişim yapılan 3378 STEMİ hastalarını içermekteydi. Hastane içi mortalitede başvuru KÜA seviyesi eşik değeri ROC analizinde 17.5 mg/dL olarak ve sensivite %68, spesifite %66 olarak saptanmıştır (AUC: 0.75; 95% CI:0.72-0.88; $p < 0.001$).

Bulgular: Hastalar ortalama olarak 33±0.14 ay izlenmiştir. Yüksek KÜA seviyesine sahip hastalarda düşük KÜA seviyesine sahip hastalara göre hastane içi mortalite 5.3 kat (OR: 6.0, 95% CI: 4.4-8.3), uzun dönem mortalite 5 kat (HR: 5.3, 95% CI: 4.2-6.8) yüksek olarak saptanmıştır.

Sonuç: Bu çalışmada yüksek KÜA seviyesi bağımsız olarak hastane içi ve uzun dönem mortalite ile ilişkili olarak bulunmuştur. KÜA testi basit, ucuz ve kolaylıkla uygulanabilen bir yöntemdir. Bu yüzden, STEMİ geçiren yüksek riskli hastaları saptamada kullanılabilir.

Anahtar sözcükler: Kan üre azotu, ST-elevasyonlu miyokard infarktüsü, primer perkütan koroner girişim

INTRODUCTION

Risk stratification of patients with acute coronary syndrome (ACS), which is the leading cause of death worldwide[1], is so important in order to initiate appropriate medical treatment. There are several parameters used for prediction of mortality in ACS[2-7]. An increase in serum creatinine (sCr) levels has been found as a predictor of adverse events and mortality in ACS[7-11]. Despite the fact that blood urea nitrogen (BUN) is another commonly used parameter to evaluate kidney function in routine clinical practice, the impact of increased BUN levels on mortality in ACS has not been well established yet. The aim of this study was to investigate the association of BUN levels with all-cause mortality and major cardiac events (MACE) in ST-segment elevation myocardial infarction (STEMI) patients treated with primary percutaneous coronary intervention (pPCI).

MATERIAL AND METHODS

Study participants

This retrospective study included 3844 consecutive patients with STEMI undergoing pPCI from January 2008 to December 2011 at the tertiary research hospital of a high volume center (1194 pPCI and 2032 elective PCI were performed by 25 interventional cardiologists in 2010). The only exclusion criterion was current renal replacement therapy. A total of 26 patients were excluded because of having at least one of the exclusion criteria. An additional 12 patients were excluded from the study due to the fact that BUN measurements were not performed at admission. An additional 28 patients were excluded from the study due to loss to follow-up. All follow-up data were obtained from hospital medical records or by interviewing (directly or by telephone) patients, their families, or their personal physicians. The study was terminated after a follow-up period of 36 months. The study was approved by the Institutional Ethics Committee.

Analysis of patient data

A clinical history of risk factors, such as age, gender, hypertension, diabetes mellitus, hyperlipidemia, renal insufficiency was determined from the hospital's medical database. Echocardiographic and coronary angiographic findings were also obtained from the same database. An echocardiogram was performed in 93 % patients at first 48 hours in the coronary care unit and left ventricular ejection fraction (LVEF) was calculated by using Simpson method[12]. Non-ionic low osmolality contrast media was used in all patients (616 mosmol/kg). The occurrences of in-hospital and long-term events were evaluated by a trained study coordinator. Following coronary angiography or pPCI, the patients were admitted to coronary care unit for follow-up monitorization. The estimated glomerular filtration rate (eGFR) was calculated by using Cockcroft-Gault equation[13]. The drugs were administered during and after the hospitalization according to the European Society of Cardiology Guidelines[14]. Acute kidney injury is defined as an increase in serum creatinine level of ≥0.5 mg/dL or a relative 25 % increase from baseline creatinine value, assessed at 48 hours after the angiography [15]. Blood values obtained from venous blood samples at hospital admission were recorded from the medical reports. White blood cell, hemoglobin level, and platelet counts were measured as a part of the automated complete blood count using a Coulter LH 780 Hematology Analyzer (Beckman Coulter Ireland, Inc, Galway, Ireland). Biochemical measurements were performed using Siemens Healthcare Diagnostic Products kits and calibrators (Marburg, Germany). Creatine kinase isoenzyme–MB (CK-MB) levels were measured using an immune-inhibition method (Architect C 8000; Abbott Inc).

Angiographic analysis

All patients underwent pPCI within 60 minutes of admission. All pPCI procedures were performed

using the standard femoral approach with a 6-Fr guiding catheter. Medication before the pPCI included 600 mg of clopidogrel and 300 mg of chewable aspirin. Direct stenting was performed whenever possible; in the remaining cases, balloon predilatation was performed. The drug-eluting stent was used whenever possible. To achieve maximal dilation, an intracoronary injection of nitroglycerin (100 μg) was administered in each coronary angiogram. All patients were treated with maintenance doses of clopidogrel (75 mg once daily for 12 months) and aspirin (100 mg indefinitely).

Endpoints

The primary endpoints were the incidence of in-hospital and long-term all-cause mortality. The secondary endpoint was MACE, which includes all-cause death, non-fatal acute coronary syndrome (ACS), and target lesion revascularization (TLR). Evaluation of MACE was obtained from hospital's medical database or by follow-up interviews (directly or by telephone).

Definition of short-term and long-term events

TLR was defined as vascularization of the stented segment or within 5-mm margins proximal or distal to the stent by either repeat PCI or coronary artery bypass grafting. Non-fatal ACS was described as a 2-fold increase in serum CK-MB enzyme levels and/or ST segment re-elevations. Stent thrombosis and in-hospital ventricular arrhythmias were also analyzed. Stent thrombosis was defined as an abrupt onset of cardiac symptoms along with an elevation in levels of biomarkers or electrocardiographic evidence of myocardial injury after stent deployment in the first 24 h. This was accompanied by angiographic evidence of a flow-limiting thrombus near a previously placed coronary stent.

Statistical analysis

In a first step, an admission BUN of 17.5 mg/dL was identified through a ROC analysis as an optimal cutoff value to predict the in-hospital mortality. Two groups were formed accordingly: one with 2328 patients (BUN<17.5) and the other with 1450 patients (BUN≥17.5). In a second step, baseline characteristics were compared between two groups. Kolmogorov-Smirnov test was used for testing of normality. All continuous variables showed skewed distributions and expressed as median and, 25th and 75th percentiles; and compared using the Kruskal-Wallis test. Categorical variables were expressed as number and percentages, and Pearson's chi-square or Fisher's exact tests were used to evaluate the differences. In a third step, to analyze the prediction for in-hospital mortality, data from the admission parameters were employed as independent variables. The univariate relationship between baseline characteristics and in-hospital mortality were assessed by univariate hierarchical logistic regression analysis. Multivariate analysis by stepwise logistic regression models (backward elimination) tested variables that were significant at $p<0.1$ in the univariate analysis. In a fourth step, after a mean follow-up period of 33±0.14 months, the median survival times (MST) of two groups were compared using the Kaplan-Meier survival method. Overall survival was calculated from the day of diagnosis to the day of death or last follow-up. Differences between the groups were analyzed by the log-rank test. A forward Cox proportional regression model was used for multivariable analysis. The univariate relationship between baseline characteristics and long-term mortality were assessed by univariate Cox regression analysis. Multivariate analysis by stepwise Cox regression models (backward elimination) tested variables that were significant at $p<0.1$ in the univariate analysis. A two-tailed p-value of <0.05 was considered as statistically significant, and 95% CIs were presented for all odds ratios and hazard ratios. Analyses were performed using Statistical Package for Social Sciences software, version 16.0 (SPSS; IBM, Armonk, New York, USA).

RESULTS

A total of 3778 patients (mean age 58.3± 11.8 years; men 81%) with STEMI were included. The patients' baseline characteristics, categorized by admission BUN, are listed in Table 1. There was a significant difference in terms of age ($p<0.001$) and gender ($p<0.001$) among the subgroups of BUN. The history of patients was similar in terms of hyperlipidemia ($p=0.632$), current smoking status ($p=0.280$) and previous PCI ($p=0.375$). Whereas, the history of patients was significantly different in terms of hypertension ($p<0.001$), diabetes mellitus ($p<0.001$), previous MI ($p=0.009$), previous CABG ($p=0.003$), and chronic kidney disease ($p<0.001$). At admission, the groups were similar in terms of systolic blood pressure ($p=0.069$), diastolic blood pressure ($p=0.921$), heart rate ($p=0.254$), Killip class ($p=0.243$), LVEF ($p=0.076$), and anterior myocardial infarction incidence ($p=0.161$). Patients' chest-pain-period and door-to-balloon-

time were similar (p=0.383 and p=0.103 respectively).

The patients' laboratory parameters are summarized in Table 1. In laboratory parameters, the patients showed significant differences by the respect of admission creatinine (p<0.001) and eGFR (p<0.001). Whereas; the groups were similar with respect to CK-MB (p=0.060), peak CK-MB (p=0.083), white blood cell count (p=0.214), hematocrit (p=0.159) and platelet count (p=0.195). The patients' coronary angiographic parameters are summarized in Table 1. The patients with higher BUN levels had significantly higher 3-vessels disease (p<0.001). The type of PCI and stent were similar between the groups. Generally, TIMI flow grades between the groups were similar before the intervention. However, patients with higher BUN levels had significantly lower TIMI III flow grade ratios after intervention compared to patients with lower BUN levels.

Table 1. Baseline characteristics of patients stratified by admission blood urea nitrogen level

	Blood Urea Nitrogen Level (mg/dL)		
	<17.5 mg/dL (n= 2328)	≥17.5 mg/dL (n= 1450)	P Value
Age	55.0 (48.0-62.0)	63 (55.0-71.0)	<0.001
Male gender	1951 (83.8)	1118 (78.7)	<0.001
Body mass index	134 (120-156)	133 (118-156)	0.193
History			
Hypertension	205 (21.5)	456 (32.1)	<0.001
Diabetes mellitus	455 (19.7)	354 (25.1)	<0.001
Hyperlipidemia	535 (23)	336 (23.7)	0.632
Current smoking status	650 (27.9)	420 (29.6)	0.280
Previous MI	482 (20.7)	347 (24.4)	0.009
Previous PCI	451 (19.4)	292 (20.6)	0.375
Previous CABG	95 (4.1)	89 (6.3)	0.003
Chronic kidney disease	58 (2.5)	173 (12.2)	<0.001
At admission			
Systolic blood pressure (mm Hg)	134 (120-156)	133 (118-156)	0.069
Diastolic blood pressure (mm Hg)	70 (64-79)	70 (64-81)	0.921
Heart rate (beats per minute)	78 (70-85)	78 (69-88)	0.254
Killip classification	2.0 (1.0-2.5)	2 (1.0-2.5)	0.243
Left ventricular ejection fraction (%)	50 (45-60)	50 (45-55)	0.076
Anterior myocardial infarction	944 (40.5)	609 (42.9)	0.161
Chest pain period (hours)	6.0 (2.0-12.0)	6.0 (2.0-12.0)	0.383
Pain-to-balloon time (hours)	6.2 (2.4-12.2)	6.2 (2.3-12.1)	0.347
Door-to-balloon time (minutes)	28 (22-31)	26 (18-30)	0.103
Admission laboratory variables			
Admission CK-MB (ng/mL)	48 (23-118)	50 (25-123)	0.060
Peak creatine kinase-MB (ng/mL)	101 (40-197)	103 (45-214)	0.083
Creatinine (mg/dL)	0.8 (0.7-0.9)	1.0 (0.8-1.2)	<0.001
eGFR (ml/min/1.73 m^2)	121 (112-146)	89 (81-126)	<0.001
White blood cell count, cells/µL	11.0 (9.0-13.6)	11.2 (8.9-14.0)	0.214
Hematocrit, %	41.0 (38.0-44.0)	40.0 (36.0-43.0)	0.159
Platelet count, cells/µL	235 (200-280)	232 (192-277)	0.061
Blood urea nitrogen (mg/dL)	13 (7-16)	23 (19-27)	<0.001
Vessel disease (stenosis > 50%)			
1 vessel	1401 (60.2)	739 (52.0)	<0.001
2 vessels	541 (23.2)	368 (25.9)	0.064
3 vessels	386 (16.6)	312 (22.0)	<0.001
PCI type			
Only PTCA	337 (14.5)	222 (15.6)	0.334
Only Stent	342 (14.7)	180 (12.7)	0.084
PTCA and Stent	1346 (57.8)	809 (57.0)	0.634
Stent type			
Drug eluting stent	1442 (61.9)	842 (59.3)	0.115
Bare metal stent	246 (10.6)	147 (10.4)	0.869
TIMI flow grade before intervention			
TIMI 0	1522 (65.4)	915 (64.4)	0.572
TIMI I	230 (9.9)	143 (10.1)	0.850
TIMI II	206 (8.8)	138 (9.7)	0.371
TIMI III	574 (24.7)	402 (28.3)	0.013
TIMI flow grade after intervention			
TIMI 0	132 (5.7)	106 (7.5)	0.029
TIMI I	153 (6.6)	170 (12.0)	<0.001
TIMI II	229 (9.8)	141 (9.9)	0.926
TIMI III	1821 (78.2)	1008 (71.0)	<0.001

Discharge medication			
B-blocker	2044 (87.8)	1248 (87.9)	0.217
Statin	821 (87.5)	820 (87.5)	0.937
Diuretics	204 (8.8)	138 (9.7)	0.324
ACEIs or ARBs	2189 (94)	1325 (93.3)	0.377

Continuous variables are presented as median and 25-75 percentiles; nominal variables presented as frequency (%). Mann-Whitney-U test was used for continuous variables. Pearson-Chi-Square test was used for nominal variables.

Table 2 presents the in-hospital and long-term clinical outcomes of the study population. During hospitalization, patients with higher BUN levels showed significantly higher cardiogenic shock, acute respiratory failure, ventricular arrhythmia, MACE, and mortality rate compared to patients with lower BUN levels. An admission BUN of 17.5 mg/dL was identified through a ROC analysis as an optimal cutoff value to predict the in-hospital mortality with 68% sensitivity and 66% specificity (AUC: 0.75; 95% CI:0.72-0.88; $p < 0.001$) (Figure 1). Table 3 lists univariate and multivariate hierarchical logistic regression analyses for in-hospital mortality. The univariate predictors of in-hospital mortality were age, male gender, hypertension, diabetes mellitus, previous CABG, chronic kidney disease, systolic blood pressure, glucose, creatinine, admission CK-MB, white blood cell count, hematocrit, heart rate, left ventricular ejection fraction, heart rate and the BUN value higher than 17.5 mg/dl. By multivariate hierarchical logistic regression analysis, the 5 independent factors that increased the risk of in-hospital mortality were Age [Odds ratio (OR), 1.02; Confidence interval (CI), 1.01 – 1.04], systolic blood pressure (OR, 0.99; CI, 0.98– 0.99), glucose (OR, 1.03; CI, 1.01 – 1.05), creatinine (OR, 1.86; CI, 1.48 – 2.39), left ventricular ejection fraction (OR, 0.94; CI, 0.89 – 0.99) and the BUN value higher than 17.5 mg/dL (OR, 3.42; CI, 2.86 – 4.08).

Table 2. In-hospital and long-term outcomes of patients stratified by admission blood urea nitrogen level.

	Blood Urea Nitrogen Level (mg/dL)		
	<17.5 mg/dL (n= 2328)	≥17.5 mg/dL (n= 1450)	P Value
In-hospital course			
Cardiogenic shock	74 (3.2)	91 (6.4)	<0.001
Acute respiratory failure	87 (3.7)	85 (6.0)	0.001
Acute kidney injury	280 (12.0)	165 (11.6)	0.708
Ventricular arrhythmia	125 (5.5)	100 (7.0)	0.055
Major adverse cardiac events	143 (6.1)	212 (14.9)	<0.001
Mortality	53 (2.3)	176 (12.4)	<0.001
Out-hospital course			
Follow-up time (month)	36 (36-36)	36 (36-36)	<0.001
Major adverse cardiac events	281 (12.1)	326 (23.0)	<0.001
All cause mortality	86 (3.7)	263 (18.5)	<0.001

Values in parentheses are percentages. Pearson Chi-Square test used for analyses. Continuous variables are presented as median and 25-75 percentiles; nominal variables presented as frequency (%). Mann-Whitney-U test used for continuous variables and Pearson-Chi-Square test used for nominal variables.

The patients were followed up for a mean period of 33 ± 0.1 months. At the out-hospital course, patients with higher BUN levels showed significantly higher MACE and all-cause mortality rate compared to patients with lower BUN levels. The 3-year Kaplan-Meier curve for overall survival in patients with lower and higher BUN levels were 96.3% and 81.5%, respectively (Figure 1). Table 4 lists univariate and multivariate Cox regression analyses for 3-year long-term mortality. The univariate predictors of long-term mortality were age, male gender, hypertension, diabetes mellitus, previous CABG, chronic kidney disease, systolic blood pressure,

glucose, creatinine, admission CK-MB, white blood cell count, hematocrit, heart rate, left ventricular ejection fraction and the BUN value higher than 17.5 mg/dL. By multivariate Cox logistic regression analysis, the 5 independent factors that increased the risk of long-term mortality were age [Hazard ratio (HR), 1.02; Confidence interval (CI), 1.01 – 1.04], systolic blood pressure (HR, 0.99; CI, 0.98–0.99), glucose (HR, 1.02; CI, 1.01 – 1.05), creatinine (HR, 1.79; CI, 1.42 – 2.26) and the BUN value higher than 17.5 mg/dL (HR, 3.91; CI, 3.04 – 4.68).

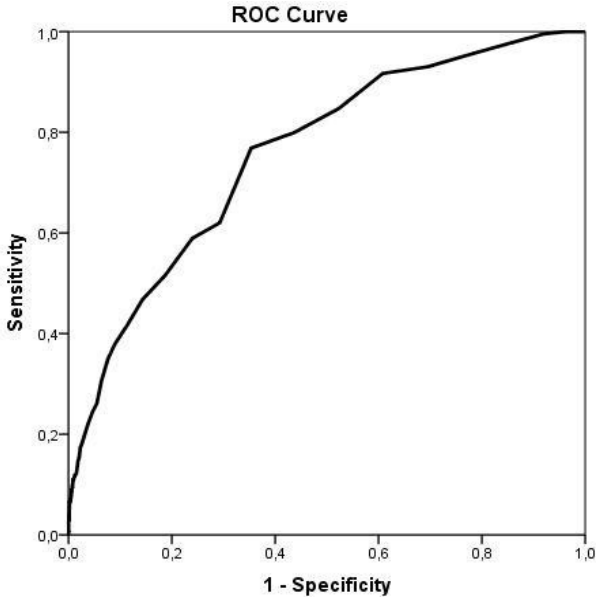

Figure 1. ROC analysis showed that the best cut-off value of the BUN to predict the in-hospital mortality was 17.5 mg/dL with 68% sensitivity and 66% specificity (AUC: 0.75; 95% CI:0.72-0.88; $p < 0.001$).

As a summary; patients with higher BUN levels had 5.3-times higher in-hospital mortality rates (OR: 6.0, 95% CI: 4.4-8.3) than patients with lower BUN levels. This significant relationship was persisted even after adjustment for all confounders. Patients with higher BUN levels had 5- times higher long-term mortality rates (HR: 5.3, 95% CI: 4.2-6.8) than patients with lower BUN levels. This significant relationship was also persisted even after adjustment for all confounders.

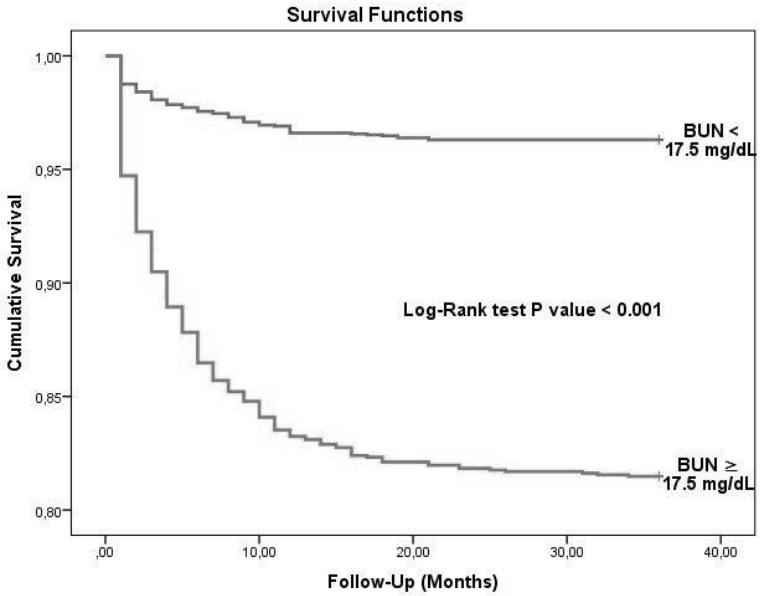

Figure 2. Kaplan-Meier curve for overall survival in patients with ST-segment elevation myocardial infarction (STEMI) (n = 3778) stratified by BUN level.

DISCUSSION

The mechanisms of acute kidney injury in the setting of cardiac systolic and/or diastolic dysfunction have not been well established due to the lack of studies. The reduction of cardiac output is not the only reason to explain the reduction in GFR. Ljungman *et al.* [16] found that GFR was not reduced until the cardiac index dropped to <1.6 L/min. There are several studies suggesting that fluid overload which results in renal venous congestion may be the main mechanism of renal dysfunction in cardiac dysfunction. Nohria *et al.* [17], which was supported by another study [18], demonstrated that only the higher CVP correlated with the lower GFR among all hemodynamic parameters.

In prerenal azotemia, urea increases disproportionately to sCr on account of enhanced proximal tubular reabsorption that follows the enhanced transport of water and sodium [19]. In distal nephron, urea reabsorption depends on antidiuretic hormone [20], which is potentiated by angiotensin II [21]. Hence, in addition to reflecting kidney function, BUN levels can reflect a state of hypoperfusion. We hypothesized that BUN might be a good indicator for renal hypoperfusion as a result of cardiac systolic and/or diastolic dysfunction in the setting of coronary ischemia. Despite the fact that multiple etiologies other than renal hypoperfusion, such as gastrointestinal (GI) bleeding, may explain BUN elevations at baseline; GI bleeding was rare in our study population (n=8). Hence, hemodynamic factors were most likely to contribute to elevated BUN levels in our study population. Another reason for choosing BUN instead of sCr was that it remains constant throughout the aging process. Elderly patients may tend to have sCr levels within normal range despite the fact that their renal function is severely compromised; due to decreased muscle mass[22, 23]. In our study, the ROC analysis established that the area under the curve for BUN (AUC: 0.75; 95% CI 0.72 to 0.88; p<0.001) was higher than that of creatinine (AUC: 0.69; 95% CI 0.65 to 0.74; p<0.001).

The impact of elevated BUN on mortality in the setting of acute decompensated heart failure (ADHF) has been shown in some large-scale studies. Aronson *et al.* [24] studied 541 patients with a previous diagnosis of heart failure admitted for clinical decompensation. They found that elevated BUN level was a predictor of mortality in patients admitted for ADHF. In a large-scale study also showed that high admission level of BUN was the best single predictor of mortality in patients with ADHF [25]. Thus, the association of BUN levels with mortality in ADHF has been established in a large-scale study.

Some studies have already shown an association between BUN levels and mortality in patients with ACS. Kirtane *et al.* [26] studied 9420 patients with ACS, and they found a correlation between increased BUN level and mortality. Their study population consisted of both STEMI (30%) and non-STEMI (70%) patients. Another prospective study included both STEMI and non-STEMI patients showed that increased BUN level was associated with in-hospital mortality [27]. However, our study population consisted of only patients with STEMI treated with pPCI. This difference limits the direct comparison of two studies. Aronson *et al.* [28] studied 1507 patients with STEMI treated with thrombolytic therapy or pPCI, and they showed the relationship between elevated BUN levels and long-term mortality. In spite of the fact that the study population was not homogeneous in terms of treatment, they included only STEMI patients and our study supports their findings indicating that elevated BUN level predicts long-term of mortality. Our study showed that an increase in BUN levels was independently associated with a high risk of in-hospital and long-term all-cause mortality, and MACE (Table 3). Patients with higher BUN levels on admission had 5.3-times higher in-hospital and 5-times higher long-term mortality rates, which had higher sensitivity and specificity over sCr levels.

Table 3. Univariate predictors and multivariate hierarchical logistic regression analysis for in-hospital mortality. All clinically relevant parameters were included in the model.

Univariate Analysis	P value	Multivariate Model	P value	OR (95% CI)
Age	<0.001	Age	<0.001	1.02 (1.01 – 1.04)
Male gender	0.001			
Hypertension	0.051			
Diabetes Mellitus	0.001			
Previous CABG	0.016			
Chronic kidney disease	<0.001			
Systolic blood pressure	<0.001	Systolic blood pressure	0.006	0.99 (0.98 – 0.99)
Glucose	<0.001	Glucose	<0.001	1.03 (1.01 – 1.05)
Creatinine	<0.001	Creatinine	<0.001	1.86 (1.48 – 2.39)
Admission CK-MB	<0.001			
White blood cell count	0.003			
Hematocrit	0.006			
Heart rate	0.059			
LVEF	<0.001	LVEF	0.004	0.94 (0.89 – 0.99)
BUN ≥17.5 mg/dL	<0.0010	BUN ≥17.5 mg/dL	<0.001	3.42 (2.86 – 4.08)

Only parameters that reached statistical significance at univariate analysis were given in the rightmost column. OR, Odds ratio; CI, confidence interval; CABG; Coronary artery bypass graft surgery; CK-MB, creatine kinase-myocardial band; LVEF, left ventricular ejection fraction; BUN, blood urea nitrogen.

Table 4. Univariate predictors and multivariate Cox proportional analysis of 3-year mortality. All clinically relevant parameters were included in the model.

Univariate Analysis	P value	Multivariate Model	P value	HR (95% CI)
Age	<0.001	Age	<0.001	1.02 (1.01 – 1.04)
Male gender	<0.001			
Hypertension	<0.001			
Diabetes Mellitus	0.002			
Previous CABG	0.005			
Chronic kidney disease	<0.001			
Systolic blood pressure	<0.001	Systolic blood pressure	0.006	0.99 (0.98 – 0.99)
Glucose	<0.001	Glucose	<0.001	1.02 (1.01 – 1.05)
Creatinine	<0.001	Creatinine	<0.001	1.79 (1.42 – 2.26)
Admission CK-MB	<0.001			
White blood cell count	0.001			
Hematocrit	0.021			
Heart rate	0.078			
LVEF	<0.001			
BUN ≥17.5 mg/dL	<0.001	BUN ≥17.5 mg/dL	<0.001	3.91 (3.04 – 4.68)

Only parameters that reached statistical significance at univariate analysis were given in the leftmost column. OR, Odds ratio; CI, confidence interval; CABG; Coronary artery bypass graft surgery; CK-MB, creatine kinase-myocardial band; LVEF, left ventricular ejection fraction; BUN, blood urea nitrogen.

Limitations

There are some limitations of our study. A total of 66 patients were excluded from the study due to inaccurate recording of the laboratory results and historical data. Thus, neither in-hospital nor long-term mortality was assessed for those patients. Our population was limited to patients with STEMI undergoing pPCI. Hence our results should not be generalized to all patients with ACS. There were significant differences in terms of gender and age between two groups. It might affect the findings of the study. The study was carried out in a single tertiary referral heart center. On account of the fact that high-risk patients are referred for pPCI to our heart center, it may have affected our results. So, there was a possibility of selection bias although great attention was paid to include all consecutive STEMI patients managed with pPCI to avoid selection bias. Another limitation of the study originates from the nature of retrospective design. We were not able to reach all baseline characteristics and follow-up parameters, which can affect the eGFR of the patients such as body mass index, medications, and the daily urine output.

CONCLUSION

In conclusion, this study demonstrated that elevated BUN level was independently associated with increased in-hospital and long-term mortality, and MACE. BUN test is a simple, inexpensive, and easily bedside applicable method. Hence, it can be used to detect high-risk patients in the setting of STEMI.

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