Original Article

Evaluation of age-sex relationship on BUN and Cr variables; report of four-year mortality of hospitalized patients due to acute myocardial infarction

Shokouh Taghipour Zahir [1], Seyed Hani Mosavi Bioki [1], Maryam Rahimi Tesiye [2], Parvin Fonooni Torshiz [3,], Negin Salehi [4], Amir mohammad Babaiemahani [5]*

[1] Faculty of Medicine Pathology Ward, Shahid Sadoughi Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[2] Faculty of Life Science and Biotechnology, Shahid Beheshti University, Tehran, Iran

[3] Faculty of Nursing and Midwifery, Shahid Sadoughi University, Yazd, Iran

[4] School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[5] Biotechnology Research Center, International Campus, Shahid Sadoughi University of Medical Science, Yazd, Iran

* Corresponding Author:
Address: Mashhad, Hesabi St, Sina Complex, Mashhad, Iran. **Postal code:** 9187155451; **Tel:** +98 9154427686; **Email:** Parvin.Fonooni.97@gmail.com

Abstract

Objectives: Blood urea nitrogen (BUN) and serum creatinine (Cr) levels are the risk factors associated with prognosis in patients with the acute coronary syndrome. This study aimed to investigate whether BUN and Cr have a predictive value in patients diagnosed with acute myocardial infarction **(AMI)** and their mortality.

Methods: This descriptive-analytical study was performed retrospectively by referring to the archives of Shahid Sadoughi Hospital in Yazd, Iran. The participants were 131 patients with acute myocardial infarction whose files were accessible from 2014 until 2018. Parameters such as age, sex, type of stroke, Cr and BUN levels at the time of admission, and outcome were examined. A questionnaire was used to collect data. Data analysis was performed using SPSS software version 21, and graphs were drawn with Sigma Plot software version 12.5.

Results: Data analysis showed no significant difference between Cr and BUN levels between men and women ($P = 0 > 05$). The levels of both of these factors elevated with age in the patients (BUN: $P \leq 0.01$), (Cr: $P \leq 0.05$). In addition, both Cr ($P \leq 0.05$) and BUN ($P \leq 0.001$) had higher levels in the deceased patients than in the discharged ones.

Conclusions: The results revealed that in addition to elevated Cr and BUN, which are indicators of renal function, age is a significant risk factor in predicting mortality in **AMI** patients.

Keywords: Acute myocardial infarction, **AMI,** Blood urea nitrogen, Creatinine, Mortality

Introduction

Acute myocardial infarction (AMI) is a subset of a spectrum of the acute coronary syndrome (ACS) and is a leading cause of hospital admission and mortality in the world (1, 2)

The high percentage of deaths worldwide is due to previous vascular disorders. In addition, ischemic heart disease and myocardial infarction are the most important causes of the disease, respectively, and are

often assessed based on adjusted disability for life (3). According to official statistics from the Ministry of Health in 2011, 38% of deaths in Iran were to heart attacks. Subsequent studies in 2014 showed that the short-term survival rates of one month and one year after myocardial infarction were 85% and 80%, respectively (4). After myocardial infarction, the survival rate in patients is one of the significant indicators in disease control and evaluation of treatment methods (5).

Blood urea nitrogen (BUN) and serum creatinine (Cr) are both molecules containing nitrogen that is produced in the body, and because of their small size, they can be easily filtered from renal glomeruli (6). Studies indicate that the levels of Cr and BUN are closely related to predicting the mortality prognosis of hospitalized patients with AMI (6-8). This close bilateral relationship between heart and kidney is clinically known as cardiorenal syndrome (CRS) (9). Previous research has revealed that by decreasing cardiac contractility and subsequent renal hypo-perfusion, nephrons decrease glomerular filtration rate (GFR) and increase water and salt reabsorption, thereby reducing urea excretion and elevated BUN (5). Therefore, it seems that BUN levels can be a separate risk factor or even predictor of mortality in patients with myocardial infarction (7). Also, previous findings suggest that BUN and Cr, instead of BUN or Cr alone, are related to the outcomes of patients with acute heart failure and subsequent AMI (6, 10, 11).It is clear that these indicators are affected by various factors, but there is insufficient information about the impact of these indicators on the prognosis of mortality in patients with AMI at a young age and of different sexes. This study aimed to evaluate BUN and Cr in patients with AMI to shed some light on the effect of age and sex as effective predictors of mortality in this population.

Materials and Methods

To investigate the relationship between BUN / Cr levels and mortality rate, a retrospective descriptive-analytical study was performed on adult AMI patients (25 years and older) by referring to the archives of Shahid Sadoughi Hospital in Yazd.

Sample collection: The study population consisted of the 349 hospital archived files of AMI patients from September 2014 to September 2018. The hospital reports were studied and evaluated based on a checklist that included the patient's age, sex, type of myocardial infarction, and the amount of BUN and Cr (mg/dL) at the time of emergency hospitalization and the outcome of hospitalization (death or discharge). A related questionnaire was used to collect the data. Of all the 349 participants, 106 patients were excluded due to the lack of BUN or Cr files, and 11 cases were transferred to another hospital. Moreover, there were 2 files of fugitive-uncertain and unknown cases, 18 voluntary discharges, and 2 prosecutorial files. Out of the remaining 210, 79 cases with no emergency files or a test interval of more than 6 hours from the admission time were excluded from the study. Finally, 131 patients were selected. This study was approved by the Ethics Committee of the University and approved with the protocol number IR.SSU.MEDICINE.REC.1397.083.The mentioned parameters were extracted from the files of 131 patients and were analyzed using SPSS software version 21. Appropriate statistical methods such as descriptive statistical methods (frequency indices and relative percentage), and appropriate statistical tests (chi-square test, independent t-test, and paired sample t-test) were used. Statistical significance was defined as a *p-value* of ≤ 0.05. Graphs were drawn with Sigma Plot software version 12.5.

Results

In the current study, the mean age of the patients was $68/32 \pm 16.1$ years old (60/3% males vs. 39/7% females). The mean Cr of the patients was 1.92 (mg/dL) with a standard deviation of 1.59. The average BUN proved to be 65.73 (mg/dL), and the standard deviation appeared to be 74.86. In addition, 64 (48.9 %) patients died.

Determination of BUN and Cr in patients based on sex

As shown in Figure 1, the mean serum Cr in male and female patients was 1.8 and 2.1 (mg/dL), respectively. However, there was no significant difference between the two sexes (P>0.05). The mean of BUN was 58.08 in men and 77.35 (mg/dL) in women, and the difference was not statistically significant (P <0.05) (Figure 1).
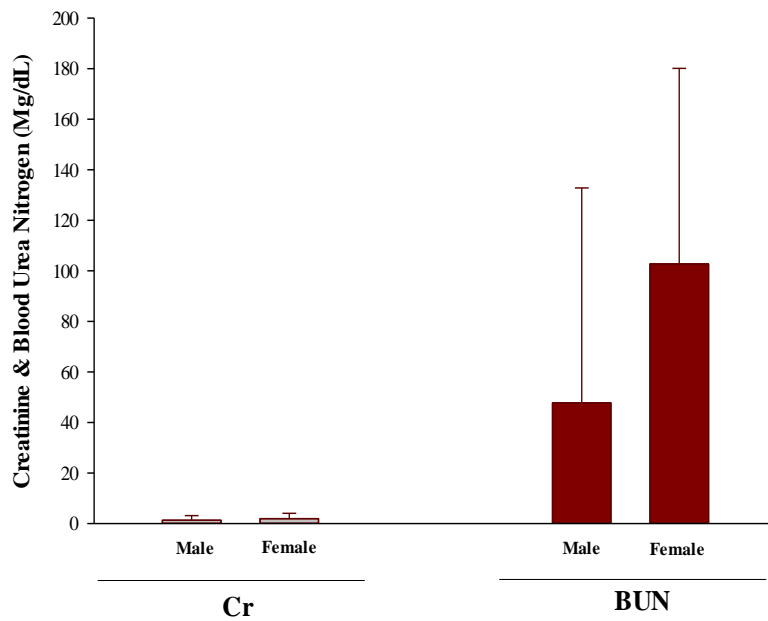
Figure 1. Differences in serum Cr and BUN levels between the sexes

Determination of BUN and serum Cr in patients based on age

Figure 2 is illustrates the data obtained from the difference between BUN and serum Cr by age. Based on the data analysis, the level of these two parameters increases significantly with age (Cr = $P \leq 0.05$ & BUN = $P \leq 0.01$) (Figure 2).

Determination of BUN and Cr in patients based on mortality

The results showed that in those who died, the mean of serum Cr was 2.47 (mg/dL), and in patients with partial recovery who were discharged it was 1.47 (mg/dL), and the difference was significant ($P \leq 0.01$). Regarding BUN, similar results were obtained, with the rate of BUN in the deceased people being 85.97 (mg/dL) but in the recovered being 47.89 (mg/dL). This difference was statistically significant ($P \leq 0.001$) (Figure 3).
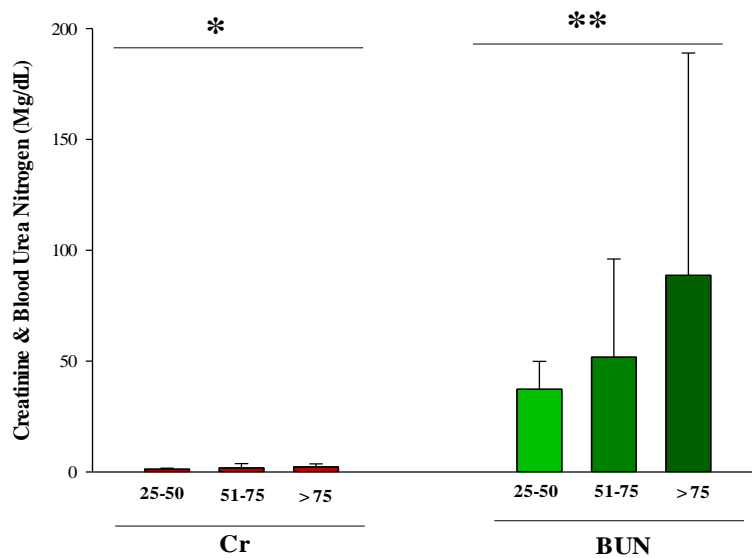

Figure 2. Differences in serum Cr and BUN levels in different age groups
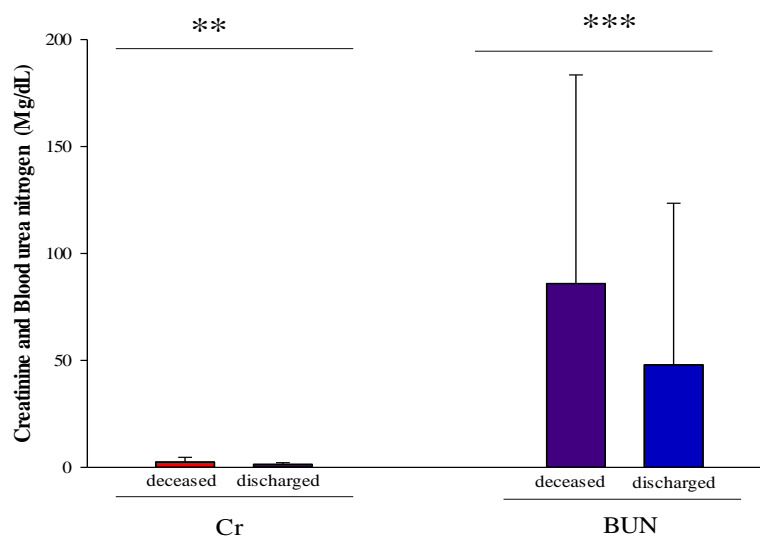Mark ** indicates $P \leq 0.01$, and * = $P \leq 0.05$

Figure 3. Differences between serum Cr and BUN in deceased and discharged individuals
Mark ** Indicates P ≤ 0.01, and *** = P ≤ 0.001

Discussion

The concept of the cardiovascular syndrome (CRS) was introduced about 10 years ago, and classified into five categories (13, 12). CRS type 1 is characterized by a rapid deterioration of cardiac function, subsequently leading to acute kidney injury (14). It is well established that BUN, Cr, and BUN/Cr ratios are among the currently recognized indicators of kidney function (15). The aim of tht present study was to evaluate the BUN/Cr ratio in patients with AMI at the beginning of hospitalization and its relationship with mortality. Data analysis showed that BUN/Cr levels were not significantly different between men and women. However, BUN/Cr levels increased considerably with age. In addition, the rate of both parameters was significantly higher in people who died than in those who had a relative recovery. These results suggest that the BUN/Cr measurements can be an important prognostic factor in the likelihood of developing AMI. Also, considering that the level of these two parameters was higher in people who died from AMI, it seems that its measurement can be effective in selecting the appropriate treatment methods, thus providing more care.

There is a close two-way relationship between renal function and patients suffering from AMI, and previous studies have shown serum BUN and Cr levels as parameters indicating renal function (16, 17). There is also growing evidence that high levels of BUN and Cr are associated with mortality in patients with AMI (15). BUN as a kidney marker

that indicates GFR is influenced by other factors such as renal hypoperfusion, low cardiac output, and neurohumoral activation, all of which are seen in AMI patients (18, 19). Moreover, the serum Cr level of AMI patients is an independent factor showing heart failure (20). In this regard, it was demonstrated that there is an association between Cr, as a marker of renal function, and AMI mortality (21).

The concentration of these agents is influenced by several factors, some of which are extra-renal such as sex, age, muscle mass, race, and nutrition. In addition, in patients with heart failure, intensive diuretic therapy causes evaluation of Cr due to hypovolemia; such an increase is not simply due to kidney problems (22, 23). Similarly, BUN is also affected by many factors such as an increment in urea excretion load, urea reabsorption in renal tubules, and a reduction in GFR (22). Based on the reports of patients with heart failure, the BUN/Cr is an independent prognostic factor of mortality (24, 25). Consistent with this, Massari et al., 2020 also suggested that examining this ratio when admitting patients would provide independent prognostic information in patients with heart failure (26). Matsue et al.'s (2017) retrospective study conducted on 1,956 patients with heart failure indicated that the BUN/Cr ratio remained a significant predictor of all-cause mortality (27). The result is in line with the findings of Horiuchi et al. 2018 (8). Although, it seems that the importance of BUN assessment in predicting AMI mortality is higher than Cr alone (21).

AMI and kidney disorders are consistent with increasing BUN. Notably, AMI and kidney disorders, systemic hemodynamic alterations, and acute neurohumoral can enhance reabsorbing of water, urea, and sodium from the renal tubules. As a result, the BUN level increases, which is not just a sign of a change in kidney function but is a normal response (8). Overall, the findings of this study, consistent with the previous research, showed that BUN and Cr could be valuable diagnostic parameters in predicting mortality in patients with AMI. However, the present study had some limitations. First, the study was an observational study, and a multi-factor analysis was performed. However, other confounding factors might still exist. Second, only BUN / Cr testprovided the data at the admission time. And the sample size used in this study was small. A larger sample size will provide mor generalizable results. Moreover, other factors might also have influenced the measured variables.

Conclusion
Reducing the length of hospital stay and reducing mortality are among the most challenging issues in patients with myocardial infarction. Therefore, identifying modifiable risk factors in mortality and length of hospital stay can play a valuable role in improving the prognosis of these patients. In this study, elevated serum Cr and BUN levels as indicators of renal impairment were associated with increased mortality. Therefore, early detection of kidney disorders and the use of effective treatments, in addition to reducing kidney damage, are effective inreducing mortality due to AMI.

Conflicts of Interest
The authors state that there is no conflict of interest.

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