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Original Article

Superiority of Admission Blood Urea Nitrogen over Serum Creatinine in Predicting In-Hospital Outcome of Patients with Acute Coronary Syndrome

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Key Words : *Acute coronary syndrome, BUN, Serum creatinine.*

Abstract:

Background: *Serum creatinine and blood urea nitrogen (BUN) are the common markers of renal function and also one of the known predictors of adverse outcomes of acute coronary syndrome (ACS). The aim of this study is to assess the impact of elevated BUN on in-hospital outcome of ACS patients and superiority of BUN over creatinine for the assessment of in-hospital outcome in our setting.*

Methods: *This prospective observational study with purposive sampling of a total of 184 patients was conducted from October, 2009 to September, 2010. Based on normal cut off values (BUN and serum creatinine was <20 mg/dl and <1.4 mg/dl respectively) all the patients were divided into four groups; group I- both BUN and serum creatinine are normal, group-II- normal BUN and high serum creatinine, group-III- high BUN and normal serum creatinine, group-IV- - both BUN and serum creatinine are high. In-hospital data like hemodynamic conditions, heart failure, arrhythmias, conduction abnormalities, death etc. were noted. Assessment of in-hospital outcome of ACS patients and comparison to elevated serum creatinine and elevated BUN was done.*

Results: *ACS patients with only raised BUN level had more occurrence of cardiogenic shock (p=0.008), left ventricular failure (p=0.020), ventricular Tachycardia (p=0.022), ventricular fibrillation (P=0.037) and complete AV block (p=0.022) than those with only raised serum creatinine. In hospital mortality and hospital stay was also increased in ACS patients with elevated BUN than elevated serum creatinine (p value is 0.022 and 0.007 respectively).*

Conclusion: *Incidence of in-hospital death, cardiogenic shock, left ventricular failure, arrhythmia and duration of hospital stay were significantly (p<0.05) higher in patients who had raised BUN than raised serum creatinine. It is observed that elevated BUN is a better predictor of in-hospital outcome of ACS patients than elevated creatinine.*

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Introduction:

The coronary heart disease is the leading cause of morbidity and mortality in western society and is a worldwide health epidemic. It is emerging as a major health problem in developing countries like Bangladesh.[1] By 2020 it is estimated that it will be the major cause of death in all region of the world.[2] National data on incidence and mortality of coronary heart disease are few in Bangladesh. The prevalence of coronary heart disease in Bangladesh

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was estimated as 3.3/1000 in 1976 and 17.2/1000 in 1986 indicating 5 folds increase of the disease in 10 years.[3] ACS is the leading cause of death in the developed countries & second leading cause of death in developing countries.[4] ACS is becoming a significant burden on healthcare services in Bangladesh too.[5] Advantages of determining specific markers in predicting ACS outcome e.g. ECG, Troponin-I, Troponin-T, CK- MB, serum creatinine, echocardiography, myocardial viability scan, are well established but cost effectiveness of their assessment are still being discussed.[6]

Numerous risk score models have been developed to assay ACS outcome but only few of them have been used in practice.[7-9] All the risk scores are multivariate. Univariate risk scores may be easier & more cost effective.

An increase of serum creatinine level, which is traditionally used as a marker of renal function, is one of the known predictors of adverse outcomes of ACS.[10] An increase in creatinine concentration of 1.0 mg/dl raises the risk of death among patients with ACS by 15-35%.[10] Another marker of renal function blood urea nitrogen (BUN) has been analysed much less frequently as a predictor of adverse outcome of ACS.[11] Increases in BUN and creatinine are highly prevalent in patients with ACS, with one in three patients having an increased level of either BUN or creatinine.[4] An increased level of only creatinine or only BUN was seen in 20% and 40% of patients of ACS respectively & more than 40% have increased levels of both BUN and creatinine.[12] Significance of determining BUN levels is higher than that of creatinine alone for assessing ACS outcome,[13] mainly death risk in patients with myocardial infarction (MI).[14] The calculation of the risk in patient with ACS based on the BUN level are said to be more accurate.[12] The advantage of BUN increases with age.[11,12,15] The risk of death in patients with raised BUN levels is not explained only by renal function-either initially impaired or reduced as a result of hypo-perfusion but has some other explanation. This may be due to increase age, large body mass, increase catabolic rate, haemolysis, pre-renal & renal causes.

Study on predictive role of BUN & serum creatinine on ACS patients has not yet been conducted in Bangladeshi patients. The aim of this study is to assess the impact of elevated BUN on in-hospital outcome of ACS patients and superiority of BUN over creatinine for the assessment of in-hospital outcome in our setting.

Methods:

It was a prospective observational study. The study was conducted in the Department of Cardiology, Dhaka Medical College & Hospital, Dhaka (DMCH) from October, 2009 to September, 2010.Purposive sampling was done and a total of 184 patients were taken for the study. All the patients with ACS admitted in the Department of Cardiology, DMCH, who did not have cardiomyopathy, congenital heart disease, valvular heart disease, serious co-morbid conditions, previous history of PCI or CABG and who were not immediately referred to other hospital for any reason were included in the study. Initial evaluation of the study population by age, sex, occupation, clinical history and examination were performed. Risk factors of ischemic heart disease like hypertension, smoking, dyslipidemia, diabetes mellitus, and obesity were noted. Base-line laboratory investigations-ECG, S. Troponin-I, Blood was collected for BUN & serum creatinine from all patients with ACS taking part in this study. Echocardiography, RBS/FBS, fasting lipid profile, were done and recorded. Different types of in-hospital data like hemodynamic conditions, heart failure, arrhythmias, conduction abnormalities, death etc. were noted during hospital stay. All the information was properly noted in the preformed data sheet. The normal cut off value for BUN and serum creatinine was <20 mg/dl and <1.4 mg/dl respectively and based on these cut off values all the patients were divided into four groups; Group I- both BUN and serum creatinine are normal, Group-II- normal BUN and high serum creatinine, Group-III- high BUN and normal serum creatinine, Group-IV- - both BUN and serum creatinine are high.

Data was analyzed by using SPSS version 12. Usual statistical tools like t-test, Chi square test and ANOVA were used to test the significance of difference between BUN & serum creatinine value. The distributions of continuous variables were described using mean and discrete variables were presented as frequencies and percentages. Group differences in base line characteristics were assessed with X2 test. The results were considered

as statistically signiûcant at p<0.05. The impact of the independent variable on the probability of the primary outcome (in-hospital death) was determined by X2 test.

Results:

The study subjects were divided into four groups depending on the values of their BUN and serum creatinine, group I- both BUN and serum creatinine are normal, group-II- normal BUN and high serum creatinine, group-III- high BUN and normal serum creatinine, group-IV- both BUN and serum creatinine are high. Assessment of demographic characteristics, risk factors and in-hospital outcome of patients were done. Comparison of in-hospital outcome related to elevated serum creatinine and elevated BUN was also done.

The study included 184 ACS patients and they were divided into seven age class and four groups as shown above. In group I, the mean age was 50.9±12 years ranging from 25 to 80 years. In group II, the mean age was 54.3±14.6 years ranging from 32 to 90 years. In group III, the mean age was 56.5±15.3 years ranging from 25 to 92 years. In group IV, the mean age was 60.0±18.0 years ranging from 40 to 100 years. Maximum number of ACS patients was found in the age class of 41-50 years in all groups. The mean age difference among study groups was statistically significant (p<0.05).

A total of 184 ACS patients were included in this study, out of which 122 patients were male and 62 patients were female. Among male patients 61 (67.0%) in group I, 11(50.0%) in group II, 24(70.6%) in group III and 26(70.3%) in group IV. Among female 30(33.0%) in group I, 11(50.0%) in group II, 10(29.4%) in group III and 11(29.7%) in group IV. The sex difference was not statistically significant (p>0.05) among groups. Male female ratio was 2.0:1 in the whole study subjects.

Regarding traditional risks smoking and dyslipidemia were almost similar among the study groups (p> 0.05), but HTN and DM were statistically significant (p<0.05) among the study groups.

Regarding types of ACS patient's maximum 89(48.4%) was UA followed by 56(30.4%) was STEMI and 39(21.2%) was NSTEMI. However, STEMI patients were observed 17 in group I, 4 in group II, 20 in group III and 15 in group IV. NSTEMI patients were found 13 in group I, 6 in group II, 8 in group III and 12 in group IV. UA patients were found 61 in group I, 12 in group II, 6 in group III and 10 in group IV.

Table-I

Age distribution of the study populations (N=184).

Age group (years)	Group-I (n=91)		Group-II (n=22)		Group-III (n=34)		Group-IV (n=37)		p value
	n	%	n	%	N	%	n	%	
<30	4	4.4	0	0.0	1	2.9	0	0.0	0.009[s]
31-40	14	15.4	3	13.6	4	11.8	1	2.7	
41-50	39	42.9	10	45.5	10	29.4	15	40.5	
51-60	15	16.5	2	9.1	7	20.6	7	18.9	
61-70	15	16.5	4	18.2	7	20.6	9	24.3	
71-80	4	4.4	2	9.1	3	8.8	1	2.7	
>81	0	0.0	1	4.5	2	5.9	4	10.8	
Mean ±SD	50.9	±12.0	54.3	±14.6	56.5	±15.3	60.0	±18.0	
Range (min, max)	(25	-80)	(32	-90)	(25	-92)	(40	-100)	

S=Significant (p > 0.05) with ANOVA test

Table-II

Sex distribution of the study population (N=184).

Sex	Group-I (n=91)		Group-II (n=22)		Group-III (n=34)		Group-IV (n=37)		p value
	n	%	n	%	N	%	n	%	
Male	61	67.0	11	50.0	24	70.6	26	70.3	0.364[ns]
Female	30	33.0	11	50.0	10	29.4	11	29.7	

NS=Not Significant (p>0.05) in Chi square test

Table-III

Risk factors of IHD among the study population (N=184)

Traditional risk factors	Group-I (n=91)		Group-II (n=22)		Group-III (n=34)		Group-IV (n=37)		p value
	n	%	n	%	N	%	n	%	
Smoking	47	51.6	12	54.5	26	76.5	25	67.6	0.054^{ns}
Hypertension	26	28.6	9	40.9	23	67.6	16	43.2	0.001^{s}
Diabetes mellitus	19	20.9	8	36.4	16	47.1	20	54.1	0.001^{s}
Dyslipidemia	15	16.5	8	36.4	10	29.4	13	35.1	0.059^{ns}

NS=Not Significant (p>0.05) in Chi square test

Table-IV

Distribution of ACS patients (N=184)

ACS patients	Group-I (n=91)	Group-II (n=22)	Group-III (n=34)	Group-IV (n=37)	Total	Percentage
STEMI	17	4	20	15	56	30.4
NSTEMI	13	6	8	12	39	21.2
UA	61	12	6	10	89	48.4

NS=Not Significant (p>0.05) in Chi square test

Regarding the in-hospital outcome assessment of the ACS patients, a total 23(12.5%) died. Out of 23 deaths; 4 died out of 91(4.4%) in group I, 1 died out of 22(4.5%) in group II, 10 died out of 34(29.4%) in group III and 8 died of 37(21.6%) in group IV. The death was statistically significant among groups (p<0.05).

Cardiogenic shock was found in 31(16.8%) of ACS admission. Out of which 7 out of 91(7.7%) in group I, none in group II, 9 out of 34(26.5%) in group III and 15 out of 37(40.5%) in group IV patients, which was statistically significant (p<0.05) among the study groups.

A total of 66(35.9%) patients had left ventricular failure. Occurrence of left ventricular failure was 19 out of 91(20.9%) found in group I, 6 out of 22(27.3%) group II, 20 out of 34(58.8%) in group III and 21 out of 37(56.8%) in group IV patients. Which was also statistically significant (p<0.05) among study groups.

Regarding the arrhythmia, VT was found in 25(13.6%), VF 13(7.1%) and AF 31(16.8%). VT was observed in 8 out of 91(8.8%) in group I, none in group II, 7 out of 34(20.6%) in group III and 10 out of 37(27.0%) in group IV. VF was found 2 out of 91(2.2%) in group I, none in group II, 6 out of 34(17.6%) in group III and 6 out of 37(16.2%) in group IV. AF was found 12 out of 91(3.2%) in group I, 2 out of 22(9.1%) in group II, 7 out of 34(20.6%) in group III and 10 out of 37(27.0%) in group IV. Incidence of VT & VF found statistically significant (p<0.05) but AF was not statistically significant (p>0.05) among groups in Chi square test.

Conduction abnormality e.g.: 2°HB & 3°HB were found 17(9.2%) and 28(15.2%) of total admission respectively. 2°HB was found 6 out of 91(6.6%) in group I, 1 out of 22(4.5%) in group II, 4 out of 34(11.8%) in group III and 6 out of 37(16.2%) in group IV and 3°HB was 7 out of 91(7.7%) in group I, 1 out of 22(4.5%) in group II, 10 out of 34(29.4%) in group III and 10 out of 37(27.0%) in group IV. Significant (p<0.05) difference was observed in 3°HB and but 2°HB was not statistically significant (p>0.05) among groups.

Above table shows the distribution of the study population according to duration of hospital stay. In group I, the mean hospital stay was observed 4.9±1.6 days ranging from 1 to 8 days. In group II, the mean hospital stay was 5.5±3.2 days ranging from 1 to 10 days. In group III, the mean hospital stay was 6.5±4.2 days ranging from 1 to 16 days. In group IV, the mean hospital stay was 12.1±2.9 days ranging from 6 to 21 days. The mean hospital stay difference was statistically significant (p<0.05) among the groups in ANOVA test.

Above table shows the comparison of outcome related to s. creatinine elevated group and BUN elevated group. In-hospital death was found 1out 22(4.5%) in s. creatinine elevated group and 10 out of 34(29.4%) in BUN elevated group. Cardiogenic shock was found no cardiogenic shock in s. creatinine elevated group and 9 out of 34(26.5%) in BUN elevated group. LVF was found 6 out of 22(27.3%) in s. creatinine elevated group and 20 out of 34(58.8%) in BUN elevated group. Significant ($p<0.05$) difference was found regarding In-hospital death, Cardiogenic shock and left ventricular failure between two groups.

Regarding the arrhythmia, no VT was observed in s. creatinine elevated group and 7 out of 34(20.6%) in BUN elevated group. VF was observed none in s. creatinine elevated group and 6 out of 34(17.6%) in BUN elevated group. AF was found 2 out of 22(9.1%) in s. creatinine elevated group and 7 out of 34(20.6%) in BUN elevated group. Significant ($p<0.05$) difference was found between two groups in VT and VF but not in AF ($p>0.05$).

Conduction abnormality e.g.: 2°HB was found 1 out of 22(4.5%) and 4 out of 34(11.4%) in s. creatinine elevated group and in BUN elevated group respectively. 3°HB were found 1 out of 22(4.5%) and 10 out of 34(29.4%) in s. creatinine elevated group and in BUN elevated group respectively. Significant ($p<0.05$) difference was found between two groups for 3°HB but not for 2°HB ($p>0.05$).

Mean hospital stay was 5.5±3.2 days in only elevated s. creatinine and 6.5±4.2 days in only elevated BUN. Most of the patients stayed d"5 days in both groups which was 10(45.5%) in only elevated s. creatinine and 19(55.9%) in only elevated BUN. Other results are depicted in the above table. Mean duration of hospital stay was statistically significant ($p<0.05$) between two groups.

Table-V

ACS outcome assessment of the study population (N=184).

ACS outcome assessment	Group-I (n=91)		Group-II (n=22)		Group-III (n=34)		Group-IV (n=37)		p value
	n	%	n	%	N	%	n	%	
In-hospital death	4	4.4	1	4.5	10	29.4	8	21.6	0.007[s]
Cardiogenic shock	7	7.7	0	0.0	9	26.5	15	40.5	0.001[s]
Left ventricular failure	19	20.9	6	27.3	20	58.8	21	56.8	0.001[s]
Arrhythmia									
VT	8	8.8	0	0.0	7	20.6	10	27.0	0.029[s]
VF	2	2.2	0	0.0	6	17.6	6	16.2	0.025[s]
AF	12	13.2	2	9.1	7	20.6	10	27.0	0.179[ns]
No arrhythmia	69	75.8	22	100.0	12	35.3	11	29.7	0.001[s]
Conduction abnormality									
2° HB	6	6.6	1	4.5	4	11.8	6	16.2	0.290[ns]
3° HB	7	7.7	1	4.5	10	29.4	10	27.0	0.007[s]
No HB	78	85.7	21	95.5	18	52.9	21	56.8	0.001[s]

NS=Not Significant ($p>0.05$) in Chi square test

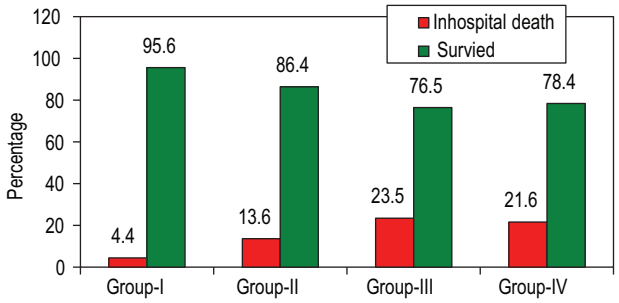

Fig.-1: *Bar diagram showing the in-hospital death of the study patients.*

Table-VI

Hospital stay distribution of the study population (n=184)

Hospital stays (days)	Group-I (n=91)		Group-II (n=22)		Group-III (n=34)		Group-IV (n=37)		p value
	n	%	n	%	N	%	n	%	
≤5	61	67.0	10	45.5	19	55.9	0	0.0	
6-10	30	33.0	12	54.5	7	20.6	11	29.7	
11-15	0	0.0	0	0.00	7	20.6	23	62.2	
>15	0	0.0	0	0.00	1	2.9	3	8.1	
Mean ±SD	4.9	±1.6	5.5	±3.2	6.5	±4.2	12.1	±2.9	0.001[s]
Range (min, max)	(1	-8)	(1	-10)	(1	-16)	(6	-21)	

S=Significant ($p < 0.05$) with ANOVA test

Table-VII

Comparison of outcome related to elevated s. creatinine and elevated BUN.

ACS outcome	Increased Creatinine only (n=22)		Increased BUN only (n=34)		p value
	n	%	n	%	
In-hospital death	1	4.5	10	29.4	0.022[S]
Cardiogenic shock	0	0.0	9	26.5	0.008[S]
Left ventricular failure	6	27.3	20	58.8	0.020[S]
Arrhythmia					
VT	0	0.0	7	20.6	0.022[S]
VF	0	0.0	6	17.6	0.037[S]
AF	2	9.1	7	20.6	0.252[NS]
Conduction abnormality					
2° HB	1	4.5	4	11.8	0.354[NS]
3° HB	1	4.5	10	29.4	0.022[S]
Hospital stays (days)					
d”5	10	45.5	19	55.9	
6-10	12	54.5	7	20.6	
11-15	0	0.00	7	20.6	
>15	0	0.00	1	2.9	
Mean ±SD	5.5	±3.2	6.5	±4.2	[a]0.007[s]
Range (min, max)	(1	-10)	(1	-16)	

S=Significant, NS= Not Significant, p value reached form Chi square test, p value reached form ANOVA test

Discussion:

This prospective observational study was carried out to compare the role of admission blood urea nitrogen (BUN) & serum creatinine level in predicting in-hospital outcome in ACS patient and to assess the superiority of BUN over serum creatinine in outcome prediction.

A total of 184 patients of ACS, age ranging from 25 to 100 years admitted in the CCU, Department of Cardiology, Dhaka Medical College Hospital, Dhaka, during Oct-2009 to Sept-2010 was taken as study population. Population was grouped as- with normal BUN & creatinine (<20 mg/dl &<1.4 mg/dl respectively) was considered as group I, BUN normal and creatinine high (<20 mg/dl & creatinine ≥1.4 mg/dl respectively) considered as group II, BUN high and creatinine normal (≥20 mg/dl & creatinine <1.4 mg/dl respectively) considered as group III and both BUN & creatinine high (≥20 mg/dl & creatinine ≥1.4 mg/dl respectively) considered as group IV. The present study findings were discussed and compared with previously published relevant studies.

In this current study the mean age was significantly higher in patients who has got higher BUN and creatinine level. The mean age of the

current study is nearly consistent with the other studies.[16-19] Slipak et al. found the mean age was 75±9 years in patients with creatinine <1.5 mg/dl, 78±9 years with creatinine 1.5-2.4 mg/dl and 71±9 years with creatinine 2.5-3.9 mg/dl.[20] In MI patients Smith et al. observed the mean age was 78±8 years.[14] The difference in age may be due to increased life expectancy, geographical and racial influences, subjective awareness of health and health care delivery system. In Indian subcontinent, ACS occurs 10 years earlier than that of Western population.

The study observed male preponderance all the groups. However, no significant difference was observed regarding the proportion of male and female patients in different groups. Similar observation was obtained by other studies also.[4,9,11,12,16-20]

Current study observed that smoking and dyslipidemia were almost similar among the study groups. Similar observations regarding the smoking and dyslipidemia were also made by Saygitov et al., Radovanovic et al., Khan et al., Sarker et al., and Kang et al.[4,12,16-18] On the other hand, HTN and diabetes mellitus were significantly higher in patients who had increased BUN, creatinine or both.

In this current study it was observed that a total 23 died out of 184 which were 12.5% of ACS admission. The death was statistically significant high in group III and IV in comparison to Group II. Kang et al. showed in-hospital death was 4.0% and distribution was 0.7% in group I, 0.8% in group II, 3.9% in group III and 29.8% in group IV.[4] The percentage of in-hospital death was nearly similar in other studies also.[17, 18, 21-23] Slight difference may be due small sample size, admission criteria and lack of subjective awareness of immediate entry to hospitalization in our country. In this study it was observed that Cardiogenic shock was found in 31 (16.8%) of ACS admission. This was high especially in patients who have got high BUN ± serum creatinine (26.5% & 40.5% respectively) in comparison to with normal BUN ± increased creatinine. Calvin et al., Radovanovic et al. and Sarker et al. showed cardiogentic shock in 6.6, 6.7% and 7.7% respectively, which support the present study findings.[17, 18, 21]

The present study showed A total of 66 (35.9%) patients had left ventricular failure. Incidence of left ventricular failure was also high in patients with high BUN (58.8% in group II and 56.8% in group IV vs. 20.9% in Group I & 27.3% in Group II). Other studies also revealed similar results.[9,11,14,16,17]

Regarding the arrhythmia, VT was found in 25(13.6%), VF 13(7.1%) and AF 31(16.8%). Incidences of all the arrhythmia were higher in patients who has got high BUN ± serum creatinine in comparison to with normal BUN ± increased creatinine. Khan et al. found AF in 10.3%. The finding is similar to my present study. VT & VF was 7.6% which also favored the present study.[16] Graham et al. found VF 2.6%. This finding was not similar to the present study.[23] This dissimilarity may be due to advanced management facilities & early reporting to hospital that are lacking in our country. Conduction abnormalities were also higher in patients who had got high BUN ± serum creatinine in comparison to with normal BUN ± increased creatinine Khan et al showed 3^{o}HB was 3.2%. This difference may be due to cause mentioned above.[16] In this current study it was observed that the mean hospital stay was observed 4.9±1.6 days ranging from 1 to 8 days in group I. 5.5±3.2 days ranging from 1 to 10 days in group II, 6.5±4.2 days ranging from 1 to 16 days the in group III and 12.1±2.9 days ranging from 6 to 21 days in group IV. The mean hospital stay was significantly ($p<0.05$) increased in patients who had increased BUN, creatinine or both. Similarly, Sarker et al showed the mean duration of hospital stay was 7.6±2.2 days in patients with ACS, which is comparable with the current study.[17]

Regarding the superiority assessment of BUN over creatinine, observed In-hospital death was found 1 out 22 (4.5%) in s. creatinine elevated group and 10 out of 34(29.4%) in BUN elevated group. Cardiogenic shock was not found in S. creatinine elevated group and 9 out of 34(26.5%) in BUN elevated group. LVF was found 6 out of 22(27.3%) in s. creatinine elevated group and 20 out of 34(58.8%) in BUN elevated group. In-hospital death, cardiogenic shock and LVF were significantly higher in BUN elevated group than s. creatinine group.

Conclusion :

This prospective observational study was carried out to find out role of admission blood urea nitrogen & serum creatinine in predicting in-hospital outcome in ACS patient. This study revealed that incidence of in-hospital death, cardiogenic shock, LVF, arrhythmia, duration of hospital stay was significantly higher in patients who had increased BUN ± creatinine. So, BUN should be used for prediction of in-hospital outcome of patients with acute coronary syndrome.

Conflict of Interest - None.

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