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Blood urea nitrogen as a predictor of mortality in myocardial infarction

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ABSTRACT

INTRODUCTION

Blood urea nitrogen and creatinine levels are routine laboratory tests for evaluating renal function. Renal dysfunction has been related to worse prognosis of cardiovascular diseases. The purpose of this study was to determine the relationship between admission blood urea nitrogen and creatinine levels with in-hospital mortality in acute myocardial infarction patients.

METHODS

A cross-sectional study was performed using secondary data of 80 acute myocardial infarction patients hospitalized in Intensive Cardiac Care Unit of dr. Wahidin Sudirohusodo Hospital, Makassar, from June 2010 to July 2011. Admission blood urea nitrogen and creatinine levels were analyzed with Mann Whitney and Chi-Square tests.

RESULTS

Mortality risk in the patients with blood urea nitrogen levels >50 mg/dL was 3.58 higher compared with those with blood urea nitrogen levels ≤50 mg/dL [OR=3.58; 95% confidence interval (CI) =1.27-10.11, p=0.013]. Mean admission creatinine levels in surviving and non- surviving patients were 0.99 ± 0.30 mg/dL and 1.70 ± 1.99 mg/dL, respectively (p=0.043). Mortality risk in patients with creatinine levels >1.1 mg/dL was 3.0-fold higher compared to patients with creatinine levels ≤1.1 mg/dL [OR=3.00; 95% confidence interval (CI) =1.13-7.92, p=0.024]. Multiple logistic regression showed blood urea nitrogen to be a better predictor of mortality than creatinine (OR= 3.583, p=0.016 vs OR 1.844, p=0.317).

CONCLUSIONS

Patients with high levels of blood urea nitrogen and creatinine had higher mortality risks than patients with normal levels. Blood urea nitrogen was a better predictor of mortality than creatinine.

Key words: Blood urea nitrogen, creatinine, myocardial infarction, mortality

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Kadar ureum darah sebagai prediktor mortalitas infark miokard

ABSTRAK

PENDAHULUAN

Ureum dan kreatinin merupakan tes laboratorium rutin yang sering digunakan untuk menilai fungsi ginjal. Disfungsi ginjal telah lama dihubungkan dengan prognosis buruk penyakit kardiovaskuler. Tujuan penelitian ini adalah untuk menentukan adanya hubungan antara kadar ureum dan kreatinin saat masuk rumah sakit dengan mortalitas selama perawatan di rumah sakit.pada pasien infark miokard akut.

METODE

Penelitian ini merupakan studi potong silang dengan menggunakan data sekunder dari rekam medik sebanyak 80 pasien infark miokard akut yang dirawat di Unit Perawatan Jantung Intensif Rumah Sakit dr. Wahidin Sudirohusodo Makassar selama bulan Juli 2010 hingga Juni 2011. Kadar ureum dan kreatinin yang diteliti adalah kadar saat pasien masuk rumah sakit. Uji statistik dilakukan dengan Uji Mann Whitney dan Chi-Square.

HASIL

Risiko terjadinya mortalitas pasien infark miokard dengan kadar ureum >50 mg/dL adalah 3,58 kali lebih besar dibandingkan kadar ureuM ≤50 mg/dL (OR=3,58; interval kepercayaan = 1,27 - 10,11, p=0,013). Rerata kadar kreatinin pada penderita infark miokard akut yang survive *dan yang meninggal masing-masing adalah 0,99 ± 0,30 mg/dl dan 1,70 ± 1,99 mg/dL (p=0,043). Risiko mortalitas pasien infark miokard dengan kreatinin >1,1 mg/dL 3,0 kali lebih besar dibandingkan ≤1,1 mg/dL (OR=3,00; 95% interval kepercayaan = 1,13 - 7,92, p=0,024). Analisis regresi logistik ganda kadar ureum merupakan prediktor mortalitas yang lebih baik dibandingkan kreatinin (OR= 3,583, p=0,016 vs OR 1,844, p=0,317).*

KESIMPULAN

Pasien infark miokard akut dengan kadar ureum dan kreatinin dalam darah yang tinggi memiliki risiko mortalitas lebih besar dibandingkan pasien dengan kadar normal. Kadar ureum dalam darah merupakan prediktor mortalitas yang lebih baik dibandingkan kreatinin.

Kata kunci: *Ureum, kreatinin, infark miokard, mortalitas*

INTRODUCTION

Acute myocardial infarction is caused by the interruption of blood supply to cardiac muscle, resulting in gross necrosis of the myocardium. The diagnosis of acute myocardial infarction according to World Health Organization criteria should be established on the basis of at least two of these criteria, including a history of chest pain, evolving changes on the electrocardiogram and/or elevations of serial cardiac markers.[1] Urea is the major nitrogen-containing metabolic product of protein catabolism in humans, and more than 90% of this compound is excreted through the kidney. Creatinine is an endogenous substance produced by muscle from creatine and creatine phosphate, with a rate of production proportionate to the muscle mass. Creatinine is filtered freely by the glomerulus, is not

reabsorbed by the renal tubulus, and is secreted by the renal tubules only in small amounts. Urea and creatinine are both used for evaluation of kidney function.[2] The levels of blood urea and creatinine may increase in some conditions, including decreased cardiac output from cardiac failure.[3] Carter et al.[4] found that low spot urine creatinine is associated with cardiovascular disease risk. Some studies have suggested that patients with renal failure have poorer outcomes in the setting of unstable angina and myocardial infarction.[5] Cakar et al.[6] observed the effect of admission creatinine levels on one-year mortality of myocardial infarction patients and found that the mortality rate in the group with elevated creatinine levels was higher than that in the group with normal levels. Kirtane et al.[7] also found that blood urea nitrogen (BUN) could be used as an independent marker of mortality among patients with acute coronary syndromes in six months of follow up. Sorensen et al.[8] observed that decreased creatinine clearance was related to an increased mortality rate among myocardial infarction patients in six years of follow up. Worsening of renal function (defined as an increase in creatinine level of > 0.3 mg/dL) during the first 2 weeks after myocardial infarction also showed an increased risk of cardiovascular death.[9] Smith et al.[10] found that in older myocardial infarction patients, adjusted mortality increased by 3% per 5U increase in blood urea nitrogen. Limited information is available about the effect of acute kidney injury during hospitalization on clinical outcomes after myocardial infarction (MI).[11,12]

The objective of the present study was to evaluate the effect of admission BUN and creatinine levels on in-hospital mortality among myocardial infarction patients. In this study, we also analyzed whether BUN or creatinine levels could be used as better markers of mortality risk in acute myocardial infarction patients during hospitalization, which had not been mentioned in previous studies.

METHODS

Research design

A cross-sectional study was conducted using secondary data of 80 acute myocardial infarction patients hospitalized in the Intensive Cardiac Care Unit of dr. Wahidin Sudirohusodo Hospital, Makassar, from June 2010 to July 2011.

Research subjects

During the abovementioned period, 146 myocardial infarction patients were hospitalized, but only 80 patients had their admission BUN and creatinine levels recorded. Admission BUN and creatinine levels in surviving and non-surviving patients were then analyzed.

The diagnosis of acute myocardial infarction was established by a cardiologist using World Health Organization criteria. Acute myocardial infarction patients who had no admission BUN and creatinine levels in their medical records were excluded from analysis. Patients who survived hospitalization and were allowed by the clinician to have outpatient care were defined as surviving and those who died during hospitalization were defined as non-surviving.

Laboratory analysis

Blood urea nitrogen, creatinine, total cholesterol, low density lipoprotein, high density lipoprotein and triglycerides were determined with an ABX Pentra 400.

Statistical analysis

Kolmogorov-Smirnov normality tests showed that BUN and creatinine levels were not normally distributed, so that the data were analyzed with the Mann Whitney test. We also used a BUN level of >50 mg/dl as the cut-off for high BUN levels and >1.1 mg/dl for high creatinine levels; values below the cut-off were defined as normal. Mortality risks between high

Table 1. Characteristics distribution of the subjects (n=80)

Variable	n (%)	Mean ± SD
Gender		
Male	57 (71.3)	
Female	23 (28.7)	
Survival		
Survival	52 (65.0)	
No survival	28 (35.0)	
Age (years)		58.05 ± 11.44
Lenght of hospitalization (days)		6.62 ± 4.52
Blood urea nitrogen (mg/dL)		41.36 ± 31.84
Creatinine (mg/dL)		1.25 ± 1.23
Total cholesterol (mg/dL)		211.49 ± 46.83
HDL (mg/dL)		36.81 ± 9.27
LDL (mg/dL)		143.21 ± 39.57
Triglycerides (mg/dL)		137.81 ± 73.36

HDL = high density lipoprotein; LDL = low density lipoprotein

and normal BUN and creatinine levels were then analyzed using the respective cut-offs. All p values were two-sided, and a p value of < 0.05 was considered to indicate statistical significance. Multiple logistic regression analysis of BUN and creatinine levels was then performed to determine which of the two was the better predictor of mortality. All data were analyzed using SPSS version 21.

Ethical clearance

This study was performed after obtaining permission from the Educational and Training Unit *(Diklat)* of Wahidin Sudirohusodo Hospital to access the medical records.

RESULTS

During the study, we found 80 subjects with admission BUN and creatinine levels recorded in the medical records. There were 57 male patients (71.3%) and 23 female patients (28.7%). Fifty two patients (65.0%) survived and 28 (35.0%) patients did not survive hospitalization. The characteristics of the subjects are shown in Table 1. There were significant differences in BUN and creatinine levels between surviving and non-surviving groups (Table 2).

Using 50 mg/dL as the cut-off value for BUN, we found significant mortality risks among patients with high as compared with normal

Table 2. Differences in blood urea nitrogen and creatinine levels between surviving and non-surviving groups

Variable	Surviving (n=52)	Non-Surviving (n=28)	p
Age (years)	58.61 ± 11.26	57.00 ± 11.91	0.550*
Blood Urea Nitrogen (mg/dl)	33.38 ± 16.43	56.18 ± 45.88	0.031**
Creatinine (mg/dl)	0.99 ± 0.30	1.70 ± 1.99	0.043**

* Student T Test; **Mann Whitney Test

Table 3. Mortality risks of patients using blood urea nitrogen and creatinine group

Variable	Mortality		p	OR (CI 95%)
	Yes	No		
Blood urea nitrogen (mg/dL)				
> 50	12	9	0.013	3.58 (1.27-10.11)
≤ 50	16	43		
Creatinine (mg/dL)				3.00 (1.36-7.92)
> 1.1	14	13	0.024	
≤ 1.1	14	39		

levels of BUN. Logistic regression tests showed that patients with BUN levels of >50 mg/dL had mortality risks 3.58 times higher than those with BUN levels of ≤50 mg/dL. Similarly, using 1.1 mg/dL as the cut-off value for creatinine, we found significant mortality risks among patients with high as compared with those with normal creatinine levels. Patients with creatinine levels of >1.1 mg/dL had mortality risks 3.00 times than those with levels of ≤1.1 mg/dL (Table 3). Multiple logistic regression analysis showed that BUN had more influence on mortality than creatinine (OR= 3.583, p=0.016 vs OR 1.844, p=0.317) (Table 4).

DISCUSSION

In this study we found significant difference of BUN levels between survive and non survive groups. Patients with BUN levels >50 mg/dL had mortality risks 3.58 times compared with BUN levels ≤50 mg/dL. Kirtane et al.[7] found that myocardial infarction patients with BUN levels ≥25 mg/dL had mortality risks 3.2 times and patients with BUN 20-25 mg/dL had 1.9 times of mortality risks compared with patiens with BUN ≤20 mg/dL in six months. Aronson et al.[13] found that elevated admission BUN (≥25 mg/dL) was an independent predictor of mortality in median follow up of 27 months in myocardial infarction patients and an increase in BUN 50% above admission value was associated with increased risk of mortality (hazard ratio 1.7; 95% CI 1.3 to 2.2). Another study found that serum blood urea was significantly higher in MI patients.[14] Furthermore, Ostfield et al.[15] found that admission serum BUN was associated with an increased burden of coronary artery disease on cardiac catheterization.

We also found that creatinine levels of non-surviving patients were higher than in surviving patients. Patients with high creatinine levels (>1.1 mg/dL) had a threefold higher mortality risk than patients with normal levels (≤1.1 mg/dL). This was concordant with the study of Gibson et al.,[16] who found that 30 days mortality increased stepwise among patients with normal (creatinine ≤1.2 mg/dL), mildly impaired (creatinine >1.2 to 2 mg/dL) and severely impaired (creatinine >2mg/dL) renal function. Patients with mild, moderate, and severe impairment had respectively 1.38, 2.06 and 3.81 times higher mortality risks compared with normal ones. Jose et al.[9] found that in patients with systolic dysfunction after myocardial infarction, worsening renal function (an increase of creatinine >0.3 mg/dL measured from baseline after 2 weeks) showed an increased risk for

Table 4. Multiple logistic regression analysis of blood urea nitrogen and creatinine on mortality of acute myocardial infarction patients

Covariate	B	OR	p
Blood urea nitrogen	1.276	3.583	0.016
Creatinine	0.898	1.844	0.317

cardiovascular death (hazard ratio 1.62; 95% CI 1.14 to 2.30) during 42 months follow up. Cakar et al.[6] observed that the mortality rate in acute myocardial infarction patients with elevated creatinine (defined as creatinine levels >1.3 mg/dL) was higher than in the normal creatinine group (25.9% vs 6.8%) after 1 year follow up. In our study, multiple logistic regression analysis also showed that blood urea nitrogen had more influence on mortality than creatinine.

Renal insufficiency has been related to adverse cardiovascular outcomes in patients with cardiovascular disease. Sachdeva et al.[17] found that patients with renal dysfunction had a significantly increased risk (almost 4 times) of developing adverse outcomes after acute myocardial infarction.

A limitation of this study was the unavailability of blood urea nitrogen and creatinine levels before the onset of myocardial infarction, preventing the exclusion of patients with nonsymptomatic renal dysfunction, which may have introduced bias into the statistical analysis. As a follow-up to this study, a cohort study should be performed about the effect of blood urea nitrogen and creatinine levels on short and long term mortality risks among patients with acute myocardial infarction. Further studies about evaluation of blood urea nitrogen creatinine changes during hospitalization and their effect on mortality are also necessary. Admission blood urea nitrogen and creatinine levels could be used as predictors of mortality in acute myocardial infarction patients during hospitalization.

CONCLUSIONS

Blood urea nitrogen and creatinine levels in non-surviving patients with acute myocardial infarction were higher than in surviving patients. Patients with high levels of blood urea nitrogen and creatinine had higher mortality risks than patients with normal levels. Blood urea nitrogen was a better predictor of mortality than creatinine.

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