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Copeptin levels as a predictor of acute kidney injury (AKI) in ST-segment elevation myocardial infarction (STEMI)

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ABSTRACT

Background: Acute myocardial infarction is a cardiac emergency with a high mortality rate. The ST-segment elevation myocardial infarction (STEMI) patients have complete coronary artery occlusion, so they usually present with severe symptoms and a higher risk of early mortality. The prevalence of type 1 cardiorenal syndrome (CRS), namely acute kidney injury (AKI) in acute heart failure, is 24%-45%. Copeptin is the C-terminus of pro-vasopressin's peptide, the arginine vasopressin's precursor. This study aimed to prove whether copeptin is a predictor of AKI in the STEMI patient population after adjusting for confounding variables.

Methods: This prospective cohort study was conducted between March and December 2020. Eighty-four subjects with STEMI who came to the emergency department at Dr. Moewardi Hospital and met the inclusion and exclusion criteria were enrolled. The data were analyzed to calculate relative risk and 95%CI for each variable, followed by multivariate analysis with logistic regression. Data were analyzed using SPSS version 23 for Windows.

Results: The prevalence of AKI in this study was 67%. The copeptin level at the cut-off of 273.6 pg/ml has an AUC of 0.774 (95%CI=0.676-0.873, p=0.000). Copeptin level, acute heart failure, and risk of renal ischemia associated with AKI in STEMI. Copeptin >273.6 pg/ml showed a statistically significant association with AKI in STEMI (adjusted RR 5.298; 95%CI=1.771-15.847; p=0.003).

Conclusion: Copeptin levels higher than 273.6 pg/ml is known to be an independent predictor of AKI in STEMI.

Keywords: copeptin; risk factors; type 1 cardiorenal syndrome.
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INTRODUCTION

Acute myocardial infarction (AMI), both ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI), is a cardiac emergency that has a high rate of morbidity and mortality. The STEMI patients have complete coronary artery occlusion, so they usually present with severe chest pain, a wider potential area of injury, and a higher risk of early mortality.[1,2]

Kidney disease in heart disease is a serious health problem, thus increasing morbidity, mortality, and cost of health care. Complex physiological, biochemical, and hormonal interactions exist between the heart and the kidney. Problems with these interactions are collectively called cardiorenal syndrome (CRS). The prevalence of type 1 CRS, acute kidney injury (AKI) in acute heart failure (AHF), is 24%-45%. The occurrence of AKI results in prolonged hospital stays and increased risk of death during hospitalization and a worsening long-term prognosis.[3-10] Other risk factors for AKI in STEMI include age, diabetes mellitus, previous history of chronic kidney disease, dehydration, and anemia.[3-5]

Acute kidney injury is defined as an increase in serum creatinine ≥ 0.3 mg/dL within 48 hours, an increase in serum creatinine ≥ 1.5 times baseline within 7 days, or urine output < 0.5 ml/kg/hour for 6 hours.[6] As a marker of kidney function, creatinine has several drawbacks, such as being influenced by non-renal factors. Measurement of urine volume to detect decreased urine production (oliguria) as one of the diagnostic criteria for AKI is also not an objective indicator. It is difficult to perform in patients who are not catheterized.[7,8]

Research on markers for cardiorenal syndrome continues to this day. One such marker is copeptin (C-terminal pro-Arginine Vasopressin/CTproAVP), the precursor of arginine vasopressin (AVP), a hypothalamic antidiuretic hormone. Its release is triggered by decreased cardiac output, increased osmolality, and physiological stress. The advantages of copeptin compared to AVP are that it lasts 7-14 days at room temperature, has high platelet affinity (>90%), has a large molecular size, has easy storage, and has a short examination time (1-5.5 hours).[9-13]

Many studies have been conducted to find predictors of type 1 CRS using various clinical and laboratory parameters. Still, research on copeptin levels as a predictor

of AKI in STEMI patients has never been done. This study wanted to prove whether Copeptin is a predictor of AKI in the STEMI after adjusting for confounding variables, including age >60 years, female sex, history of diabetes mellitus (DM) or hypertension, anemia (hemoglobin (Hb) level < 10.5 g/dL), the incidence of acute heart failure (AHF) during treatment and risk of renal ischemia.

MATERIAL AND METHODS

This prospective cohort study was conducted on newly diagnosed STEMI patients who were brought to the emergency department of Dr. Moewardi hospital in Surakarta during March - December 2020. The diagnosis criteria for STEMI were chief complaints of angina pectoris accompanied by an electrocardiogram showing ST-segment elevation and an increase in cardiac troponin I (cTnI) at T0 100 ng/L or T2h 10 ng/L and creatinine kinase-myocardial band (CKMB)-mass of 4.3 ng/L).

The research subjects were taken consecutively based on inclusion and exclusion criteria. Inclusion criteria included ages 30-80 with normal kidney and liver function tests, normal hydration status, and no visible signs of bleeding and infection. We excluded patients receiving radiocontrast or undergoing cardiac surgery for coronary revascularization, a subject who died before the AKI assessment was carried out, discharged from the hospital at their request and incomplete data. The number of research subjects was 84 patients.

Acute kidney injury was defined based on Acute Kidney Injury Network (AKIN) criteria.[6] Gender, age, and history of diabetes mellitus or hypertension were obtained from the medical records. The diagnosis and severity of acute heart failure were established using the Killip score. The risk of renal ischemia is defined as the presence of one or more of the following signs; (1) Hypotension is a condition in which the systolic blood pressure is less than 90 mmHg, or the mean arterial pressure (MAP) is less than 80 mmHg or the decrease in MAP is more than 40 mmHg. The mean arterial pressure is calculated from the formula: MAP = DP + 1/3(SP – DP), where DP is the diastolic pressure and SP is systolic pressure; (2) Hypoxemia is a state of decreased oxygen supply to a level that is insufficient to maintain cellular function. Hypoxemia is characterized by arterial oxygen saturation (SaO2) <92%; (3) Acidosis is the occurrence of acidemia (pH <7.35) or metabolic acidosis or decreased bicarbonate ($HCO3^-$ <22 mmol/L). MAP, SaO2 and pH data were the lowest at a maximum of 48 hours before the onset of AKI.

Anemia was defined as a Hb level <10.5 mg/dL. The EDTA tubes were used to collect blood samples for hemoglobin measurement. The hemoglobin measurement method is cyanide-free, using an automated hematology analyzer Advia 2120. The non-fasting blood samples for all laboratory parameters and copeptin assay were collected in plain tubes, then centrifuged for 10-15 minutes at the speed of 6000 rotations per minute (rpm) to obtain the serum and immediately stored at -80°C until the time of analysis. Copeptin level was measured by sandwich enzyme-linked immunoassay (ELISA) using Rayto RT – 2100C (microplate reader) with reagents from Human CPP (Copeptin) ELISA kit (E-EL-H0851) Elabscience. All the laboratory parameters were carried out in an accredited laboratory. Internal quality control of all laboratory parameters and the Copeptin assay was performed before the study.

The characteristics of the study variables were distinguished between the AKI and no AKI groups. Gender, history of hypertension and diabetes, the incidence of acute heart failure (AHF), risk of renal ischemia, and levels of copeptin were reported as the number of subjects (%). A comparison test was performed using the Chi-square test. The variables of age and serum Copeptin levels were tested for normality using the Shapiro-Wilk test. Bivariate analysis was conducted to find out the relationship between AKI and other variables (including copeptin level) using a 2x2 table to get the relative risk (RR) and 95% confidence of intervals (95%CI). Multivariate analysis was carried out by analyzing the influence of other variables on the relationship between AKI and copeptin level. The analysis was processed using SPSS version 23.0 for Windows. The p-value was considered significant if <0.05.

RESULTS

The research subjects comprised 59 males (70.2%) and 25 females (29.8%), with a mean age of 59.8±11.1 years. The number of subjects with and without AKI during treatment was 35 subjects (42%) and 49 subjects (58%), respectively. Clinical characteristics such as age, gender, history of hypertension, diabetes, smoking, clinical outcome (deceased or survived), heart rate, and respiratory rate were not significantly different in the group without AKI and with AKI (p-value = 0.825; 0.493; 0.339; 0.488; 0.329; 0.432; 0.371; 0.790 and 0.914, respectively). Clinical characteristics that were significantly different between the two groups were the Killip class (p=0.031), AHF incidence (p=0.003), systolic pressure (p=0.000), diastolic pressure (p=0.000), and MAP (p=0.000). The laboratory characteristics that were significantly different between the two groups were baseline BUN levels (p=0.000), baseline creatinine levels (p=0.000), baseline eGFR (p=0.014), pH (p=0.001), HCO3- (p=0.002) and Copeptin levels (p=0.001). The length of stay was longer in the AKI group than in the group without AKI.

The incidence of AKI during treatment will significantly extend the length of stay, both in the ICVCU (4.67±1.27 vs. 5.83±2.41, p=0.035) and the overall length of stay in the hospital (6.78±1.76 vs. 8.34±4.0, p=0.017). Based on the stage, AKI stage 3 had the longest median length of stay in the hospital, which was 14 (5-16) days, compared to AKI stages 1 and 2, which were 7 (2-10) days and 7 (92-22) days with p = 0.028. The subject characteristics are shown in Table 1.

Based on the ROC curve and the area under the ROC (AUC), the accuracy of copeptin as a predictor of AKI in STEMI was 0.774 with 95% CI 0.676-0.873, p = 0.000. The copeptin level of 273.6 pg/mL was chosen as the cut-off with the most optimal sensitivity and specificity performance. Forty-four subjects (52.4%) were below the cut-off value, and 40 subjects (47.5%) had copeptin levels at or above the cut-off value. Bivariate analysis

to assess the relationship between each independent variable and the incidence of AKI in STEMI (table 2) showed that the significant parameters in the bivariate analysis were the incidence of AKI, renal ischemia and levels of copeptin with an RR of 2.105 (95% CI 1.320-3.359, p=0.003), RR 3.026 (95% CI 1.670-5.483, p =0.000) and RR 3.178 (95% CI 11.700-5.940, p=0.000), respectively.

Table 1. Subject characteristics based on the incidence of AKI.

Characteristics	AKI (n=35)	Without AKI (n=49)	p
Clinical characteristics:			
Age (years)	61.0±10.7	58.9±11.3	0.392
Gender^			
Woman	9 (36.0)	16 (64.0)	0.493
Man	26 (44.1)	33 (55.9)	
History of hypertension^			
Yes	20 (37.7)	33 (62.3)	0.339
Not	15 (48.4)	16 (51.6)	
DM history^			
Yes	14 (46.7)	16 (53.3)	0.488
Not	21 (38.9)	33 (61.1)	
Smoking history^			
Yes	12 (35.3)	22 (64.7)	0.329
Not	23 (46.0)	27 (54.0)	
Length of stay (days):			
ICVCU	5.83±2.41	4.67±1.26	0.005*
Hospital	8.34±4.0	6.78±1.76	0.017*
Clinical outcome:			
Deceased	5 (55.6)	4 (44.4)	0.371
Survived	30 (40.0)	45 (60.0)	
AHF incident^			
Yes	16 (66.7)	8 (33.3)	0.003*
Not	19 (31.7)	41 (68.3)	
Killip Class:			
1	8 (34.8)	15 (65.2)	0.031*
2	11 (29.7)	26 (70.3	
3	11 (64.7)	6 (35.3)	
4	5 (71.4)	2 (28.6)	
Heart rate (x/min)#	90 (76-104)	88 (80-105)	0.790
Respiratory rate (x/min)#	24 916-32)	24 (16-32)	0914
Systolic (mm/Hg)#	92 (70-148)	112 (75-164)	0.000*
Diastolic (mm/Hg)	66.3±11.9	78.8±14.1	0.000*
Mean arterial pressure (mmHg)#	62 (47-99)	75 (50-110)	0.000*
Laboratory characteristics:			
Hb (g/dl)#	12.8 (7.9-17.2)	13.3 (6.7-16.2)	0.184
Glucose (mg/dl)#	158 (77-386)	123 (70-317)	0.068
Total cholesterol (mg/dl)	164.3±51.8	170.8±41.6	0.530
LDL cholesterol (mg/dl)	107.9±41.2	118.6±39.9	0.237
HDL Cholesterol (mg/dl)	33.1±11.8	37.0±7.7	0.068
Triglycerides (mg/dl)	151.8±92.6	133.4±48.4	0.240
Sodium (mmol/l)#	136 (128-144)	136 (126-146)	0.409
BUN (mg/dl)	51.2±26	30.6±13.7	0.000*
Baseline creatinine (mg/dl)	1.03±0.18	0.87±0.26	0.008*
Baseline eGFR (ml/min, CG)	65.6±16.4	87.8±22.1	0.014*
pH	7.41±0.08	7.47±0.07	0.001*
pCO2 (mmHg)#	34.1 (18-50)	32.5 (16.9-46)	0.924
HCO3- (mmol/l)#	22.8 (7-49)	25.1 (7.6-33.7)	0.002*
SaO2 (%)#	96.8 (39-100)	98.2 (90.8-100)	0.055
Copeptin (pg/ml)	415.3±294.5	239.8±148.8	0.001*

Notes:^Categorical data are expressed by numbers (percentages); the difference test uses the Chi-square test; #data that are not normally distributed are expressed by the median (min-max), the difference test uses the Mann-Whitney-U test; *p-value is statisctially significant if <0.05.

Abbreviations: AKI, acute kidney injury; DM, diabetes mellitus; ICVCU, intensive cardiovascular care unit; AHF, acute heart failure; /min, per minute; mmHg, millimeters of mercury; g/dl, gram per deciliter; mg/dl, milligram per deciliter; mmol/l, millimoles per liter; CG Cockcroft-Gault; pg/ml, picogram per milliliter.

The multivariate analysis was carried out to obtain a predictive model. Only one model was obtained: AHF, risk of renal ischemia, and copeptin levels (table 3). The incidence of acute heart failure during treatment, the presence of risk factors for renal ischemia (such as hypotension, hypoxemia, or acidosis), and copeptin levels >273.6 pg/mL had adjusted RR 3,551 (CI 95% 1.075-11.736, p=0.038), 5.809 (CI95% 1.951-17.296, p=0.002) and 5.298 (CI 95% 1.771-15.847, p=0.003), respectively, indicating that the three variables are predictors of the incidence of AKI after STEMI. After adjusting for the incidence of acute heart failure and the risk of renal ischemia, copeptin was an independent predictor of AKI after STEMI.

From the multivariate analysis, the logistic regression equation of this model is y = -2.416 + (1,267 x AHF) + (1,759 x renal ischemia) + (1,667 x copeptin levels). The quality of the prediction model from the calibration aspect is good, with the p-value on the Hosmer and Lemeshow test being 0.218. This model also has good accuracy with AUC 0.844 (CI 95% 0.751-0.937, p=0.000), as seen in Figure 1.

DISCUSSION

In this study, the incidence of CRS1 was 42%. This incidence rate is higher than the incidence data obtained from several studies, that is 11%, 17.5%, 19.2%, 22.5%, 26.9%, 29.9% and 31%, but lower than the reported incidence by Fuhrman DY et al. and Hu W et al. (52.6% each) and also Hoste EA et al. (57.3%).[14-23]

The mortality of all STEMI subjects during hospitalization was 10.7%. The mortality of CRS1 was 14.3%. Overall mortality was influenced by the incidence of AHF (RR=1.176, 95% CI=1.058-1.308, p=0.045) and renal ischemia (RR=1.181, 95% CI=1.020-27.01, p=0.031). The mortality rate of CRS1 varies in several studies, which were 5.7%, 7.8%, 8% and 13.8%. In this study, the incidence of AKI did not affect mortality during

Table 2. Bivariate analysis between independent variables with the incidence of AKI after STEMI.

Variable		AKI (n=35)	No AKI (n=49)	RR (CI 95%)	p
Gender	Woman (n=25)	9 (36.0)	16 (64.0)	0.817 (0.450-1.483)	0.493
	Man (n=59)	26 (44.1)	33 (55.9)		
Age	≥60 years (n=42)	18 (42.9)	24 (57.1)	1.059 (0.638-1.757)	0.825
	<60 years (n=42)	17 (40.5)	25 (59.5)		
History of DM/ hypertension	Yes (n=60)	25 (41.7)	35 (58.3)	1.000 (0.571-1.751)	1.000
	No (n=24)	10 (41.7)	14 (58.3)		
AHF incident	Yes (n=24)	16 (66.7)	8 (33.3)	2.105 (1.320-3.359)	0.003*
	No (n=60)	19 (31.7)	41 (68.3)		
Anemia	Hb <10.5 g/dl (n=9)	5 (55.6)	4 (44.4)	1.389 (0.727-2.652)	0.480^
	Hb ≥10.5 g/dl) (n=75)	30 (40.0)	45 (60.0)		
Renal ischemia	Yes (n=37)	25 (67.6)	12 (32.4)	3.176 (1.754-5.749)	0.000*
	No (n=47)	10 (21.3)	37 (78.7)		
Copeptin	≥ 273.6 pg/mL (n=40)	26 (65.0)	14 (35.0)	3.178 (1.700-5.940)	0.000*
	< 273.6 pg/mL (n=44)	9 (20.5)	35 (79.5)		

Notes: ^ Fisher's exact test; *p is significant if <0.25
Abbreviations: AKI, acute kidney injury; RR, relative risk; CI, confidence interval; DM, diabetes mellitus; AHF, acute heart failure; Hb, hemoglobin; g/dl, gram per deciliter; pg/ml, picogram per milliliter.

Table 3. Multivariate logistic regression analysis between independent variables with the incidence of AKI after STEMI.

Variable	Adjusted RR (CI 95%)	p	AUC (CI 95%)
AHF	3.551 (1.075-11.736)	0.038*	
Renal ischemia	5.809 (1.951-17.296)	0.002*	0.844 (0.751-0.937)
Copeptin ≥273.6 pg/mL	5.298 (1.771-15.847)	0.003*	

Notes: *p is significant if <0.05
Abbreviations: RR, relative risk; CI, confidence interval; AUC, area under the curve; AHF, acute heart failure; pg/ml, picogram per milliliter.

hospitalization. The incidence and mortality of CRS1 vary depending on variations in AKI criteria used, location research, and research subjects.[17,19,20,24]

Female gender was not a risk factor for AKI at STEMI [RR 0.714 (CI 95% 0.272-1.874), p=0.493). Kanic V et al. stated that female gender was an independent predictor of AKI [(OR 1.28 95% CI 1.01-1.63, p=0.048)].[24] Women are thought to have fewer glomeruli than men. A lower number of nephrons results in a lower functional reserve of the kidney, a lower glomerular filtration rate, and a higher susceptibility to hyperfiltration. Several studies have found the female sex to be an independent predictor of AKI at IMA,[25,26] but some other researchers did not find it.[27-29] In this study, the female gender was not a risk factor for AKI at STEMI. This is probably because the number of male subjects was much higher (70.2%) than female subjects (29.8%) and that males tended to have a higher Killip-grade higher risk of renal ischemia and copeptin levels. However, this difference was not significant between the two sex groups.

In this study, age >60 years and a history of DM and/or hypertension were not risk factors for AKI in STEMI, although the mean age in the AKI group was higher than in the non-AKI group (61.0±10.7 years vs. 58.9±11.3 years, p= 0.392). 74.3% of subjects with AKI were aged <60 years. The distribution of all risk factor variables studied between the age groups <60 years and >60 years was not significantly different, except for anemia (2.4% vs. 19.0%, p=0.014). Anemia was not a risk factor for AKI. Decreased Hb levels in men were a predictor of AKI in acute coronary syndrome (OR 0.684; 95% CI 0.53–0.88; p = 0.03). Anemia (Hb <10 g/dL) has an odds ratio of 1.65, 95% CI 1.104-2.466; p = 0.015) for the risk of AKI compared to non-anemia.[8,30] Anemia was not proven to be a predictor of AKI at STEMI, possibly because the number of subjects with anemia in this study was too small (9 subjects, 10.7%).

The incidence of AHF in this study is a predictor of AKI in STEMI. Heart failure was the strongest predictor of AKI in STEMI patients undergoing percutaneous intervention (adjusted RR 3.35; 1.64–6.83, p=0.001). Wang C et al. reported that heart failure with Killip class >3 was a strong predictor of AKI post-STEMI (Killip class 3 (OR 5.22, 95% CI 3.07–8.87, p=0.000).[31] The underlying mechanism was hemodynamic abnormalities (hypoperfusion with decreased renal preload, increased central venous pressure with increased renal afterload), sympathetic hyperactivity, activation of the renin-angiotensin-aldosterone system, the release of adenosine, and oxidative stress.[32]

Among the three risk factors for renal ischemia, hypotension was the main contributor to renal ischemia as a risk factor for AKI (RR 10.104, 95% CI 3.334-30.622, p=0.000). Eren Z et al. stated a decrease in systolic pressure (OR 0.96; 95% CI 0.92–0.99; p=0.022) and a decrease in diastolic pressure (OR 0.914; 95% CI 0.85–0.97, p=0.009) were risk factors for AKI in acute decompensated heart failure.[33] Hypotension was also reported as a risk factor for AKI with OR 1.03, 95% CI 1.02-1.04 (p < 0.0001) per 1 mmHg decrease in minimum MAP 80 mmHg. For MAP less than 70, 60, 50 mmHg, the risk of AKI increased to 2% (OR 1.02, 95% CI 1.00-

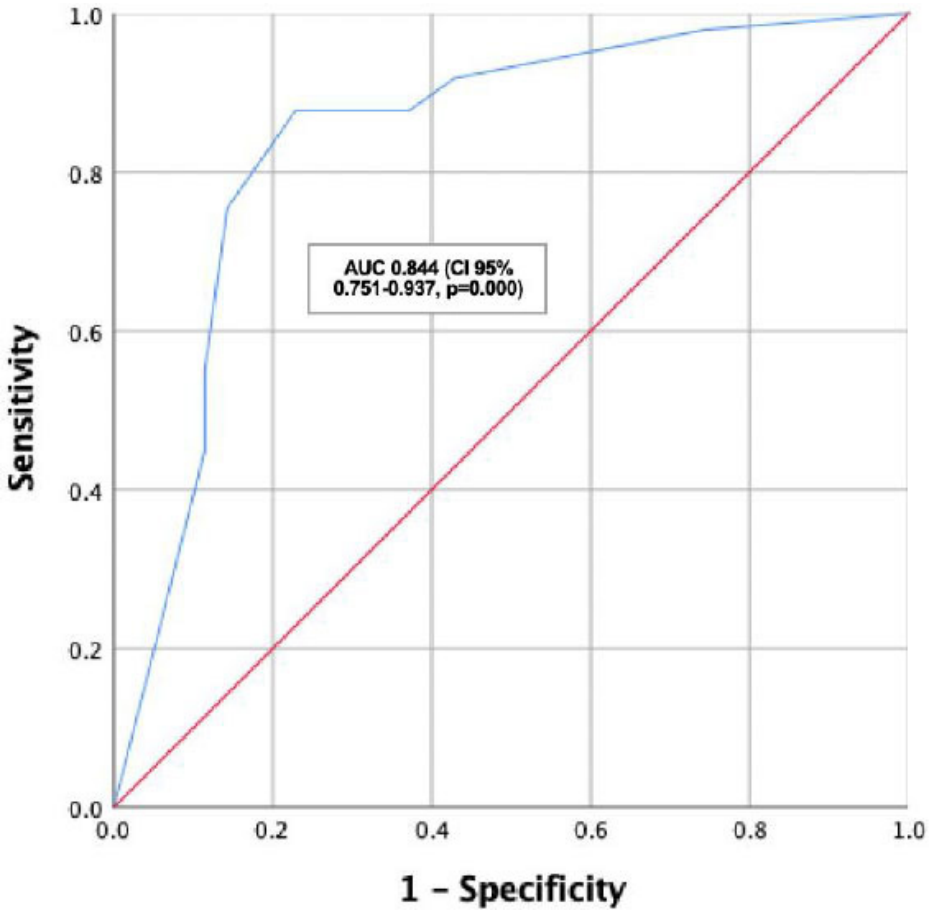

Figure 1. The ROC curve represents the accuracy of the predictive model.

1.03, p=0.0034), 5% (OR 1.05, 95% CI 1.02-1.08, p=0.0028), and 22% (OR 1.22, 95% CI 1.04-1.43, p=0.0122).[34] Badin J et al. reported that the best threshold of mean MAP at 12-24 hours for predicting AKI at 72 hours was 72-82 mmHg. Acute circulatory failure is the leading cause of renal failure in ICU patients, caused by low cardiac output and/or MAP, resulting in reduced renal blood flow. MAP is important for protecting kidney function because below a certain MAP threshold, when the autoregulatory ability of the kidney is exceeded, blood flow to the kidney decreases and lead to AKI.[35] Hu W et al. reported that acidosis, metabolic acidosis, and decreased $HCO3^-$ at admission were associated with the development of AKI. Acidosis (pH <7.35) had HR 1.810, 95% CI 1.298-2,524, p <0.001), $HCO3^-$ <22 mmol/L had HR 2.051, 95% CI 1.498-2.809, p<0.001), metabolic acidosis had HR 1,160, IK95 % 1.001-1.344, p=0.049).[22]

Acute kidney injury (AKI) and chronic kidney disease (CKD) can cause metabolic acidosis. Still, on the other hand, metabolic acidosis is not only a consequence but also a contributor to kidney dysfunction. The mechanism may be that metabolic acidosis can reduce blood flow to the kidneys and increase the release of inflammatory mediators. Nuclear factor kappa B (NF-KB) is pro-inflammatory and increases the expression of heme-oxygenase-1 in response to oxidative stress.[36-38] The cut-off of copeptin as a predictor of AKI at STEMI was 273.6 pg/ml with an AUC of 0.774, and sensitivity and specificity were 74.3% and 71.4%, respectively. Sheng XS et al. reported the cut-off of copeptin as a predictor of cardiorenal syndrome in model mice was 56.59 pg/ml with an AUC of 0.908, and the diagnostic sensitivity and specificity were 87.5% and 80.0%, respectively.[39]

The copeptin levels >273.6 pg/ml were predictors of the incidence of AKI. Ponte B et al. reported that plasma copeptin levels increased before eGFR decreased. An increase in AVP also has an albuminuric effect. Whether copeptin has any adverse effects on kidney function is not known. Vasopressin and Copeptin levels were significantly higher in the critically ill patient group (sepsis and SIRS after cardiac surgery) than in the healthy control group. An increase in plasma osmolality above 280 mOsm/kg is the main stimulus for AVP release, while non-osmotic stimuli include decreased blood volume and hypotension, as well as nausea, vomiting, pain, various drugs, and insulin-induced hypoglycemia.[40,41]

The strength of this study is that we build a predictive model consisting of 3 risk factors, including AHF, risk of renal ischemia and copeptin level. The predictive model logistic regression equation obtained is y=-2.416+(1.267xAHF)+(1.759xrenal ischemia)+(1.667xcopeptin levels). If an AMI-EST patient does not have AHF, does not have risk factors for renal ischemia and has a copeptin level <273.6 pg/ml, the probability of AKI is 11%. If a patient only has 1 (one) risk factor, namely renal failure or ischemia or copeptin levels > 273.6 pg/ml, then the probability of experiencing AKI is 24%, 34%, and 32%, respectively. If a STEMI patient has two risk factors, then the probability of AKI will increase to 63% -73%. If a STEMI patient has all three risk factors, then the probability of AKI occurring during treatment will increase to 91%. Without copeptin testing, the presence of AKI and risk factors for renal ischemia accurately predicted AKI of 79.1% (95% CI 69.1%-89.0%, p=0.017). The addition of copeptin to the model increased the prediction accuracy of AKI to 84.4% (95% CI 75.1%-93.7%, p=0.000).

The limitation of this study is diagnostic criteria for AKI are only determined based on creatinine level, not taking into account urine output. For patients referred from other hospitals, creatinine examination is carried out using various methods and machines. Researchers cannot control for other variables that influence the incidence of AKI in critically ill patients, including fluid overload, administration of vasopressors, mechanical ventilation, SIRS and sepsis, inflammation, various comorbidities and nephrotoxic drugs. This study is a single-center study, so the strength of the results still needs to be validated using other multi-center studies.

Therefore, further research controlling for factors that contribute to AKI, with a larger number of subjects or multi-center study, may be required to validate the result of this study.

CONCLUSION

The level of copeptin over 273.6 pg/ml is an independent predictor of acute kidney injury in ST-elevation myocardial infarction.

CONFLICT OF INTEREST

The authors declare no competing interest regarding the research and the manuscript.

ETHICAL CONSIDERATION

This study was approved by the Medical Research Ethics Committee number 045/7.325/2020, issued by the research ethics committee of Dr. Moewardi Hospital.

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AUTHOR CONTRIBUTION

All authors contributed to the study from the conceptual framework, data gathering, and analysis until the study's results were interpreted upon publication.

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