The Association Between Myoglobin, Troponin I, Hfabp and Nt-Probnp Levels with Acute Myocardial Infarction in Patients with Acute Coronary Syndrome

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Abstract

Introduction: Myocardial infarction is one of the five major manifestations of coronary heart disease. Myoglobin heart markers, Isoenzyme Creatine Kinase-MB (CK-MB), cardiac Troponin I (cTnI) or Troponin T (cTnT), Heart type fatty acid-binding protein (HFABP) and NT-proBNPare currently used in assisting the diagnosis of acute myocardial infarction. The study aimed to analyze the association of cardiac marker examination results of myoglobin, cTnI, HFABP and NT-proBNP with AMIoccurrence on examination I and examination II.

Method: This study enrolled33 patients in Installation of Emergency Carewith suspected acute coronary syndrome, from March to August 2013. Serum samples were taken including cTnT, myoglobin, cTnI, HFABP and NT-proBNP. Then, it was further analyzed.

Results: There was an association between myoglobin, cTnI, HFABP, and NT-proBNP with AMI events. Myoglobin and HFABP wereearly markers for the diagnosis of AMI, the mean levels of both markers was higher at the first examination (≤1 hour admitted patients) when compared with 6 hours later after being tested. Essentially, the diagnostic value of both did not differ, only HFABP was more specific than myoglobin. Troponin I showed to be the best choice in the diagnosis of AMI because of the high sensitivity and specificity.

Conclusion: An association between myoglobin, cTnI, HFABP, and NT-proBNP with AMI events was found. Myoglobin, cTnI, HFABP can be used in diagnosing AMI patients, whereas NT-proBNP is not recommended for the diagnosis of AMI due to its low specificity.

***Keywords**: AMI, ACS, myoglobin, cTnI, HFABP, NT-proBNP*

Introduction

Cardiovascular disease is a global public health problem, contributing to 30% of global deaths and 10% of global diseases.[1]

Acute myocardial infarction is part of the spectrum of acute coronary syndrome. Acute coronary syndromes include Unstable angina (UA), Non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI) .[1,2]

World Health Organization (WHO) also shows that deaths from ischemic heart disease ranked at 12.2% in 2004 and 14.2% in 2008.[3] Indonesia's health profile in 2009 expended by the Ministry of Health of Indonesia shows that in 2008 vascular system disease was highest among 11.06% of all causes of death in the hospital.[4]

Early diagnosis of myocardial infarction is still a problem because not all patients who later prove to be suffering from AMI come with clear diagnostic criteria, especially in the early hours. Cardiac serial examination

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is now universally accepted as an important determinant in the diagnosis of acute myocardial infarction. Appropriate and rapid method of examination for early diagnosis of myocardial infarction is essential.[5-9]

Myoglobin heart markers, Isoenzyme Creatine Kinase-MB (CK-MB), cardiac Troponin I (cTnI) or Troponin T (cTnT), Heart type fatty acid-binding protein (HFABP) and NT-proBNP are currently used in assisting the diagnosis of acute myocardial infarction.[8]

Heart type fatty acid-binding protein (HFABP) is a low-BM-dissolved protein, which is widely present in the myocardial cell cytoplasm. HFABP is a rapid biological marker in the circulation after myocardial injury.[10-11] B-type natriuretic peptide is a hormone that is structurally included in the group of natriuretic peptide hormones associated with renal and cardiovascular function. Increased levels of natriuretic peptide, especially NT-proBNP, are also found in post-myocardial infarction, which may be caused by localized infarct strains and are associated with activation of the neurohormonal system.[12-13] This study aimed to analyze the association of cardiac marker examination results of myoglobin, cTnI, HFABP, NT-proBNP with the incidence of AMI in patients suspected of acute coronary syndrome who came to emergency unit of Dr. SoetomoGeneral Hospital on examination I (<1 hour on admission) and examination II (6 hours after admission), and compare the sensitivity and specificity of the heart marker.

Method

This study was an observational analytic study using a cross-sectional study design. The study was implemented in Emergency Department Dr. Soetomo Teaching Hospital, Surabaya Indonesia. The samples were 50 patients who came to emergency unit Dr. SoetomoTeaching Hospital within 1 month of suspected ACS, suspected acute myocardial infarction fulfilled the sample criteria.

The inclusion criteria in the study included patients with chest pain complaints with suspected ACS, willing to participate in the research and signed informed consent and had a complete medical record. On the other hand, the exclusion criteria included patients with serum creatinine >2mg/dL, sepsis patients, cirrhosis hepatis and acute stroke. The flow of the study began when emergency unit patients were diagnosed with acute syndrome syndrome, and matched with inclusion criteria. If it was appropriate, it was continued for the next stage of anamensis, physical examination, ECG, cTnT examination, myoglobin, cTnI, HFABP and NT-proBNP. Examination I (<1 hour of patient admission) and examination II (6 hours after admission) were conducted. The subjects were distinguished into AMI patients and non AMI patients. Afterwards, the data collection and data processing were conducted using statistical analysis.

All data was obtained and inserted into the computer, then then processed statistically. The results were presented in tables or graphs. The diagnostic test criteria included sensitivity, specificity; negative and positive predictive value calculated using 2x2 tables based on 95% CI. An association analysis between the levels of myoglobin, troponin I, HFABP and NT-proBNP with AMI events was analyzed by Chi-square test.

Results

The sample characteristics showed in table 1.

Table. 1 Characteristics of Research Sample and Characteristics of AMI Patients

Characteristics of samples	N (%)
Gender	
Male	15 (45.45%)
Female	18 (54.55%)
Age	
20 – 29 years old	1 (3%)
30 – 39 years old	1 (3%)
40 – 49 years old	5 (15.2%)
50 – 59 years old	18 (54.5%)

Cont... **Table. 1 Characteristics of Research Sample and Characteristics of AMI Patients**

60 – 69 years old	3 (9.1%)
70 – 79 years old	5 (15.2%)
AMI	
STEMI	16 (84.2%)
NSTEMI	3 (15.8%)
Non AMI	14 (42.4%)
Characteritics of AMI patients	N(%)
Gender	
Male	12 (63.2%)
Female	7 (36.8%)
Age	
20 – 29 years old	1 (5.3%)
30 – 39 years old	1 (5.3%)
40 – 49 years old	4 (21%)
50 – 59 years old	9 (47.4%)
60 – 69 years old	2 (10.5%)
70 – 79 years old	2 (10.5%)
History	
Diabetes Mellitus	
Yes	12 (63.2%)
No	7 (36.8%)
Hypertension	
Yes	13 (68.4%)
No	6 (31.6%)
Smoking	
Yes	11 (57.9%)
No	8 (42.1%)
Dyslipidemia	
Total cholesterol	
> 200 mg/dL	8 (42.1%)
< 200 mg/dL	11 (57.9%)
Triglycerides	
> 150 mg/dL	12 (63.2%)
< 150 mg/dL	7 (36.8%)
HDL Cholesterol	
> 40 mg/dL	2 (10.5%)
< 40 mg/dL	17 (89.5%)
LDL Cholesterol	
> 100 mg/dL	13 (68.4%)
< 100 mg/dL	6 (31.6%)

The results of cTnT examination showed that there were 3 patients who were at the beginning of the negative examination and on the 6th positive check. The mean cTnI, HFABP and NT-proBNP levels were higher in the 6 hours of patient admission. The mean myoglobin levels was higher at examination I (<1 hour of admission) (Table 2). HFABP levels in AMI (STEMI and NSTEMI) patients were higher than in non-IMA patients, with higher HFABP levels of STEMI patients than in NSTEMI patients.

Table. 2 The mean levels of examination results and diagnostic value

Level of examination results (n=33)	Mean	Sensitivity (%)	Specificity (%)	Positive prediction value(%)	Negative prediction value (%)	Positive likelihood ratio	Negative likelihood ratio
Myoglobin							
Myoglobin I (≤ 1 hour)	146.4079±146	78.9% (0.57-0.91)	92.9%(0.69 – 1.0)	93.8%(0.72-9.9)	76.5%(0.53-0.91)	11.052(1.95-9.23)	0.23(0.08-0.59)
Myoglobin II (6 hours)	139.8897±123	78.9% (0.57-0.91)	92.9%(0.69 – 1.0)	93.8%(0.72-9.9)	76.5%(0.53-0.91)	11.052(1.95-9.23)	0.23(0.08-0.59)
cTnI							
cTnI I (≤ 1 hour)	3.9921±6.27	94.7%(0.75-0.99)	100%(0.78-1.0)	100%(0.7-0.99)	93.3%(0.7-0.91)	9.22(0.0-9.23)	0.05(0.01-0.37)
cTnI II (6 hours)	4.9242±6.96	100%(0.83-1)	100%(0.78-1.0)	100%(0.83-1)	76.5%(0.78-1)	9.2(0.0-9.23)	0.0(0.0-0.0)
HFABP							
HFABP I (≤ 1 hour)	32.6334±43.19	78.9%(0.57-0.91)	100%(0.78-1.0)	100%(0.8-1.0)	77.8%(0.55-0.91)	9.2(1.95-9.23)	0.21(0.08-0.56)
HFABP II (6 hours)	33.3712±42.78	73.7%(0.51-0.88)	100%(0.78-1.0)	100%(0.8-1.0)	73.7%(0.51-0.88)	9.2(1.95-9.23)	0.26(0.11-0.63)
NT-proBNP							
NT-proBNP I (≤ 1 hour)	1656.5039±3537	78.9%(0.57-0.91)	50%(0.27-73)	68.2%(0.47-84)	63.6%(0.35-0.85)	1.58(0.84-2.96)	0.42(0.15-1.15)
NT-proBNP II (6 hours)	2301.4624±3639	89.5%90.89-0.97)	50%(0.27-73)	70.8% (0.51-0.85)	77.8% (0.45-0.94)	1.79(0.92-3.40)	0.21(0.06-0.8)

The suitability of myoglobin, cTnI, HFABP, NT-proBNP towards cTnT results showed in Table 3.

Table 3 Suitability of myoglobin, cTnI, HFABP, NT-proBNP towards cTnT results

Examination results I (≤ 1 jam)	**cTnT**		**P**
	Positive	**Negative**	
Myoglobin			0.009
Positive	11	5	
Negative	4	13	
cTnI			0.001
Positive	15	3	
Negative	0	15	
HFABP			0.003
Positive	11	4	
Negative	4	14	
NT-proBNP			0.026
Positive	13	9	
Negative	2	9	
Result of Examination I (6 jam)			
Myoglobin			0.001
Positive	15	1	
Negative	3	14	
cTnI			0.001
Positive	18	1	
Negative	0	14	
HFABP			0.001
Positive	14	0	
Negative	4	15	
NT-proBNP			0.022
Positive	16	8	
Negative	2	7	

The results of conformity of myoglobin, cTnI, HFABP, NT-proBNP results towards the golden standard in AMI patients showed in Table 4.

Table.4 Conformity of myoglobin, cTnI, HFABP, NT-proBNP results towards the golden standard in AMI patients

Examination result I (≤ 1 hour)	**Golden standard**		**P**
	Positive	**Negative**	
Myoglobin			0.009
Positive	15	1	
Negative	4	13	
cTnI			<0.005
Positive	18	0	
Negative	1	14	
HFABP			<0.005
Positive	15	0	
Negative	4	14	
NT-proBNP			<0.008
Positive	15	7	
Negative	4	7	
Examination result I (6 hours)			
Myoglobin			<0.005
Positive	15	1	
Negative	4	13	
cTnI			<0.005
Positive	19	0	
Negative	0	14	
HFABP			<0.005
Positive	14	0	
Negative	5	14	
NT-proBNP			0.01
Positive	17	7	
Negative	2	7	

Analysis of associations of myoglobin, cTnI, HFABP and NT-proBNP with AMI incidence

Based on Fisher's exact test, in examination I, (<1 hour of MRS patient) the value of p was 0.005 which meant less than $\alpha = 0.05$. It can be concluded that there was significant association between myoglobin and AMI event. Fisher's exact test result on examination 6 hours after patient admission showed that $p = 0.005$ which meant less than $\alpha = 0.05$. Thus, it can be concluded that there was significant association between myoglobin and AMI event. Fisher's exact test result, on examination I

(<1 hour of patient MRS), the p value was 0.000 which meant less than α = 0,05. Thus, it can be concluded that there was a significant association between cTnI with AMI event. Fisher's exact test result on examination 6 hours after patient admission showed that p = 0,000 which meant less than α = 0.05. Therefore, it can be concluded that there was significant association between cTnI and AMI event.

Based on Fisher's exact test, on examination I (<1 hour of patient admission) the value of p was 0.002 which meant less than α = 0,05. Thus, it can be concluded that there was a significant association between HFABP and AMI event. Fisher's exact test result on examination 6 hours after patient admission showed that p = 0.002 which meant less than α = 0.05. Therefore, it can be concluded that there was a significant association between HFABP and AMI event. Result of Fisher's exact test test, on examination I (<1 hour of patient admission) the p value was 0.026 which meant less than α = 0.05. Thus, it can be concluded that there was significant association between NT-proBNP and AMI event. Fisher's exact test result on examination 6 hours after patient admission showed that p = 0.017 which meant less than α = 0.05. Therefore, it can be concluded that there was significant association between NT-proBNP and AMI event.

Discussion

An individual is very susceptible to coronary atherosclerosis along with the aging process. The incidence of AMI increased fivefold at the age of 40 to 60 years old. It is associated with increasing age (especially in the menopausal phase), where there is a decrease in endogenous estrogen levels.[14] Most AMI patients suffer from dyslipidemia. The study of multiple risk factor intervention trials in 356,222 subjects showed that cholesterol levels rise in proportion to the increase of AMI attacks. Increased LDL and HDL decline are important risk factors for AMI. Any decrease of 4 mg% of HDL will increase AMI risk by about 10%.[15] The National Academy of Clinical Biochemistry (NACB) recommends serial examination and the use of 2 cardiac markers of myocardial necrosis: early and slow-emerging cardiac markers.[16]

Myoglobin examination showed if the highest results in the STEMI group, it corresponds to several literatures that stated that the increase in myoglobin in the blood occurs 1-4 hours after damage of the heart muscle tissue or skeletal muscle, reaches peak within 6-7 hours after myocardial infarction, and returns to normal within 24 hours. Because myoglobin is an early heart marker, it is necessary to check with other cardiac markers.[17-18]

Based on the results of research on the highest average cTnI examination in the STEMI group on the second examination, it is consistent with the literature which states that troponin I begins to increase 3 to 5 hours after myocardial injury, peaking at 14 to 18 hours and keep increasing for 5 to 7 days .[19-20] Increased concentrations of BNP and NT-proBNP during the arrival in hospital under conditions of acute coronary syndrome are associated with poor prognosis, including increased mortality, congestive heart failure, and recurrent ischemic events.[21]

Suitability of myoglobin, cTnI, HFAB, NT-proBNP results against gold standard in AMI patients.[17] Troponin I is an ideal AMI biochemical marker because of its sensitivity and specificity. These biochemical markers are not affected by skeletal muscle disease, skeletal muscle trauma, renal disease or surgery.[20] A multifaceted mobile technology-supported primary health care intervention was associated with greater use of preventive CVD medication and lower BP levels among high-risk individuals in a rural Indonesian population.[22] Conclusions High cardiovascular risk is common among Indonesian adults aged 40 years, and rates of preventive treatment are low.[23]

Conclusion

It can be concluded that there was an association between myoglobin, cTnI, HFABP and NT-proBNP with the incidence of AMI. The emergence of biomarkers does not occur at the same time, therefore serial cardiovascular examination and use of 2 cardiac markers in diagnosing AMI are required, considering the presence of early marker and a marker that appears more slowly, and in view of the different sensitivity and specificity of each cardiac marker.

Ethical Clearance: This research is approved by Ethical Clearance from Universitas Airlangga dan Dr Soetomo Teaching Hospital

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