The Correlation between Myelucleopidase Levels and the Event of the Acute Coronary Syndrome

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Abstract

Background: Acute coronary syndrome (ACS) is a collection of symptoms due to cardiac blood flow disorders consisting of acute myocardial infarction (AMI) with increased ST segment (STEMI), AMI without increased ST segment (NSTEMI) and unstable angina pectoris (UA). Myeloperoxidase (MPO) is an enzyme that plays a role in the destabilization and rupture of plaque that rises earlier within 2 hours after AMI attack so it can be used as an early marker of ACS without depending on evidence of myocardial necrosis. So, the purpose of this study is to determine the relationship between MPO levels and ACS events.

Methods: This study is using quantitative method. Research sample was 40 patients serum with the main complaint of chest pain that fulfilled the inclusion criteria who came to the emergency unit of Dr.Soetomo General Hospital Surabaya. The blood samples were examined for MPO with MPO kit from Quanticine (R & D system) using ELISA method. The diagnostic value obtained from the calculation with the 2x2 table.

Results: Patients with chest pain were 27 persons (67.5%), while non-ACS patients were 13 persons (32.5%). There were significant differences in MPO levels between the STA (STEMI, NSTEMI, UA) groups of 986.48 ng/ml and non-ACS 381.08 ng/ml ($p = 0.002$). Diagnostic sensitivity was 88.88%, diagnostic specificity 69.23%, negative predictive value 75% and positive predictive value 85.71%. The correlation coefficient between MPO and ACS content is $r = 0.45$ with $p = 0.003$.

Conclusion: There was a correlation between MPO levels and the incidence of ACS. The higher the MPO level the higher the incidence of ACS.

Keywords: *sindroma coroner, infark miokard akut, unstable angina, nekrosis miokard.*

Introduction

Cardiovascular disease is the first cause of death in the world and in Europe. Acute Coronary Syndrome (ACS) is one of the manifestations of coronary artery disease that is still a major health problem in the world. The American Heart Association (AHA) Statistics Data, in 2005 the number of patients undergoing medical treatment in the United States due to ACS is nearly one point five million people with one point one million people (80%) indicate instances of unstable angina (UA) or infarction myocardial infarction without ST-segment elevation (NSTEMI), whereas 20% of cases recorded suffer from myocardial infarction with increasing ST segment (STEMI)[1].

The results from the Jakarta cardiovascular study in 2008 recorded a prevalence of overall myocardial infarction reaching five-point twenty-five percent. This figure is far above the prevalence of myocardial infarction in 2000, i.e., only one point two percent. This supports the Ministry of Health's survey results showing that the prevalence of Coronary Heart Disease (CHD) in Indonesia is increasing from every year[2].

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The American College Cardiology (ACC) in its 2009 consensus states that the diagnosis of ACS if it meets at least two of the three characteristics is the presence of typical clinical symptoms, increased or decreased cardiac markers (Creatinine Kinase – Myocardial Band (CKMB), troponin T or I serum) and typical Electrocardiogram (ECG) patterns[3,4]. Acute coronary syndrome (ACS) consists of acute myocardial infarction (AMI) with increased ST-segment (STEMI), IMA without increasing ST-segment (NSTEMI) and unstable angina pectoris (UA). Clinical presentation is different but has a pathophysiological similarity. If there is NSTEMI increase in cardiac marker but without an increase in ST-segment, if there is an increase STEMI in ST-segment accompanied by elevated cardiac markers and is called UA when no increase in ST segment or elevated cardiac marker [5,6].

The long-lasting troponin-inducing pattern may make troponin a good marker in detecting myocardial necrosis, but the limitation of its sensitivity makes it difficult to diagnose ACS at an early stage so that there is a need for a marker that can increase rapidly after the onset of clinical symptoms can speed up diagnosis and appropriate therapy in patients with an alleged ACS[7].

Oxidative stress and inflammation play an important role in the pathogenesis of destabilization of the coronary arteries which refers to the onset of ACS. Macrophage and neutrophil infiltration play a role in the transformation of stable coronary artery plaques into unstable lesions. Recently, there is an increasing interest from researchers to MPO which is a proinflammatory enzyme that plays a role in the occurrence of plaque rupture. This MPO can be measured by using peripheral blood[8].

The relationship between MPO levels and the incidence of ACS has not been widely studied, especially in Indonesia, the commercial kit of MPO is not yet widely available in the market so based on some of the above descriptions it is necessary to conduct research in RSUD dr. Soetomo Surabaya which aims to determine the relationship between MPO levels and the incidence of ACS so that handling and prevention can be done earlier to prevent fatal complications.

Method

This research was used observational analytic with the cross-sectional design. The study was conducted for 6 months starting from May to October 2013. The location of the research was in the emergency room of Dr.Soetomo General Hospital for the selection and sampling of blood and Department or Installation of Clinical Pathology Faculty of Medicine, Universitas Airlangga R & D section for serum separation and MPO examination.

The samples used were patients with chest pain complaints less than six hours with an alleged ACS that meets the criteria of sample acceptance. Inclusion criteria include patients with chest pain with less than 6 hours of onset suspected ACS, aged ≥ 30 years. Laboratory procedures in the form of inspection of MPO content of enzyme-linked immunosorbent assay (ELISA) method from Quanticine

MPO examination sample is serum. The patient's blood is taken and inserted into a yellow vacutainer containing serum separator without anticoagulation. The blood is then allowed to freeze for one to two hours at room temperature (18-250C). The blood is then separated from the serum to avoid hemolysis by centrifugation 3000 rpm for 15 minutes in the vacutainer tube. The obtained serum is then transferred into the aliquot tube and stored at -200C.

Results

All data were statistically tested using descriptive and inferential statistical analysis. Descriptive statistics for the distribution and frequency of sample characteristics is needed. Inferential statistics using Pearson correlation test to determine the relationship between MPO levels with the incidence of ACS and Kruskal Wallis test for the analysis of MPO levels between groups that all use the computer program SPSS 17.0 (SPSS, Inc. Chicago IL) Diagnostic value of MPO concentration as an ACS marker in Dr. Soetomo General Hospital Surabaya obtained from the calculation formula using 2x2 table to calculate the sensitivity, specificity, positive predictive value and negative predictive value.

Patients suspected of heart disease were 60 people, while those who meet the criteria of acceptance of the sample amounted to 40 people. The mean age of the sample was 57 years with an age range of between 36 and 79 years. Most of the subjects were male sex by 65%, where most of ACS patients had male sex 74.07% while for female patients only 25.93%.

Non-ACS patients of male and female were almost comparable, 46.15% and 53.85%. ACS patients were

on average 56 years of age with a 50-59 year age range of 52.5%, while non-ACS patients were on average 59 years old. Male subjects had an age range of 39 to 79 years, while female subjects had an age range of 47 to 78 years. There was an age difference between ACS and non-ACS patients but the difference was not significant (p = 0.333). Patients with chest pain suffering from ACS in this study were 27 people (67.5%) while for non-ACS chest pain patients only 13 people (32.5%). The highest number of ACS patients were STEMI, NSTEMI, and UA, which was 62.96%, 25.92% and 11.11%

Distribution of ACS Risk Factors

The highest risk factors for ACS in this study were dyslipidemia (indicated by elevated triglyceride levels of 19 patients), hypertension in 18 patients, diabetes mellitus in 15 patients and smoking of 12 patients. Non-ACS patients with dyslipidemia were also the highest (12 patients) of all non-ACS patients followed by hypertension, diabetes mellitus, and smoking. ACS and non-ACS patients of the female sex all had HDL cholesterol levels <50 mg/dl. HDL cholesterol levels <40 mg / dl in male patients found a difference between ACS and non-ACS patients 85% and 50%. The results of statistical analysis showed that the RR value of the four risk factors for ACS was not significant.

Fat profile data in this study showed a significant difference in mean total cholesterol and HDL cholesterol levels among ACS patients with non-ACS (p = 0.019 and p = 0.001). Levels of triglycerides and LDL cholesterol were found to differ between ACS and non-ACS patients but the difference was not significant (p = 0.871 and p = 0.613) The number of leukocytes between the two groups in this study was significantly different with the error rate of 5% obtained significance value of 0.001 (p = 0.001).

The Inspection Results Standard Content of MPO Solution

The absorbance data of the standard solution content of MPO with dilution of hundred times obtained by ELISA method after the reading then the absorbance value obtained is plotted in the form of points and drawn a straight line so that obtained linear line forming a standard curve.

The Results of MPO Levels

There was a significant difference of MPO levels between groups of ACS patients (STEMI, NSTEMI, UA) and non-ACS using Kruskal Wallis test with 5% error rate obtained significance value p = 0.002 (Table 1). In contrast, there was no significant difference between patients STEMI, NSTEMI and UA with 5% error rate obtained significance value of 0.698 (p = 0.698). The mean values of MPO levels between groups were between ACS and non-ACS patients of 986.48 ng/ml and 381.08 ng/ml

Calculation results based on table 2x2 with cut off of MPO350 ng/ml obtained the diagnostic sensitivity of 88.88%, diagnostic specificity 69.23%, negative predictive value 75% and positive predictive value 85.71%

Table 1. Risk Ratio (RR) risk factor for ACS and Number of ACS events based on ACS based on cut off of MPO

Risk factor	Positive ACS	Negative ACS	RR	p
Smoking	12	4	1.20	0.22
Diabetes mellitus	15	4	1.38	0.08
Hypertension	18	6	1.33	0.12
Dyslipidemia	26	12	1.36	0.36
MPO Level				
MPO positive	24	4		
MPO negatifve	3	9		

The Relationship between MPO Levels and ACS Levels

The result of data analysis by using correlation test of Pearson was got correlation that equal to 45% which included in medium correlation with error rate 5% got significance equal to 0.003 (p = 0.003).

Table 2. The Relation of MPO and ACS

		ACS Group	**MPO Level**
ACS Group	Pearson Correlaation Significance of 2 Subjects	1	0.452 0.003
	N	40	40
MPO Level	Pearson Correlation	0.452	1
	Significance of 2 Subjects	0.003	
	N	40	40

Discussion

Based on the results of this study was in accordance with previous research which states that the highest number of ACS sufferers in male aged 37 to 66 years. The study also obtained that the age of female to suffer from ACS was nearly 10 years older than men[9]. This was because of pre-menopausal women being protected by estrogen hormones that are thought to play a role in maintaining the integrity of vascular endothelium, increasing insulin sensitivity and contributing to maintaining an ideal fat profile through decreased LDL and increased HDL[10].

STEMI patients have typical clinical symptoms so that in this study the number of events was ranked highest. Researchers previously stated in STEMI there is a total thrombus clogged coronary arteries, so clinical symptoms look more striking compared with NSTEMI and UA that only clog the coronary artery in part so that the resulting clinical symptoms are also not too severe than STEMI[6]. This was what drives patients to get to the hospital so that hospital events tend to be higher for STEMI than NSTEMI and UA.

High blood glucose levels in ACS patients are associated with high levels of free fatty acids, insulin resistance and impaired glucose use by cardiac muscle, thus increasing potential oxygen consumption in exacerbating the incidence of ischemia and cardiac infarction, leading to organ failure and death[14]. This study shows that elevated cholesterol levels are directly proportional to an increase in the incidence of ACS. Any decrease of 4 mg% of HDL cholesterol, will increase the risk of AMI by 10%[13].

The results of leukocyte count analysis showed significant differences in the previous study which stated that there was a significant increase in leukocyte levels of ACS and non-ACS patients. Patients with elevated levels of leukocytes have a higher risk of death and recurrent AMI (16). Previous studies have suggested that ACS patients with negative troponin levels of 25% have positive MPO levels. MPO was also said to be more sensitive because of its increased levels in STEMI and NSTEMI patients with negative troponin levels in the first hour compared with UA patients. This supports the theory that MPO increases within two hours and reaches peak levels within 9-12 hours after symptoms in AMI patients.

Other researchers also stated the same thing that the MPO rises earlier between the hour of zero to the third hour in patients with chest pain compared with the new troponin increased between the fourth hour to the sixth hour after complaints of chest pain[11,15]. MPO along with several other enzymes such as lipoxygenase will initiate lipid oxidation of the su bendothelial vessel wall. MPO and products of lipid oxidation are commonly found

in atherosclerotic lesions along with macrophages. Endothelial dysfunction in smokers is due to the presence of thiocyanate which is a substrate for increased MPO in smokers' plasma, forming a carbonylated LDL that is easily captured by receptors on the surface of foam cells[16].

Conclusion

There was a relationship with the strength between the increase in MPO levels with the incidence of ACS. The MMO of this study had a diagnostic sensitivity score of 88.88%, diagnostic specificity of 69.23%, negative predictive value of 75% and a positive predictive value of 85.71% so that MPO could not be used as a single heart marker in diagnosing ACS and non ACS patients due to its low specificity.

Ethical Clearance: This study protocol was approved by ethical clearance Dr. Soetomo Surabaya, Indonesia teaching hospital research.

Conflict of Interest: This study protocol was approved by ethical clearance Dr. Soetomo Surabaya, Indonesia teaching hospital research.

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