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THE DIFFERENCES IN TROPONIN I AND CK-MB VALUES IN ACUTE MYOCARDIAL INFARCTION PATIENTS WITH ST ELEVATION AND WITHOUT ST ELEVATION

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ABSTRACT

Background: Acute myocardial infarction includes STEMI and NSTEMI. In STEMI and NSTEMI, an increase in cardiac biomarkers especially troponin I and CK-MB are affected by the ischemic process. The increase in troponin I values is due to proteolytic degradation of the troponin-tropomyosin protein complex. The increase in CK-MB values is due to disruption of the sarcolemma membrane. In STEMI thrombus blocks the entire artery lumen while in NSTEMI thrombus does not block the entire artery lumen. This can lead to different ischemic processes. **Aim:** To prove the differences in troponin I and CK-MB values in acute myocardial infarction patients with ST-elevation and without ST-elevation. **Methods:** An observational analytic study using a cross-sectional design was conducted between April and September 2020. The total sample of the study was 48 samples, consists of 25 samples with STEMI and 23 samples with NSTEMI. The normality test was analyzed using Shapiro-Wilk test. The difference test was analyzed using Mann-Whitney test. **Results:** Mean troponin I values of STEMI and NSTEMI patients were 30.40 ± 20.79 ng/mL; 1.38 ± 1.76 ng/mL, respectively. Mean CK-MB values in STEMI and NSTEMI patients were 386.12 ± 319.70 U/L; 42.39 ± 27.54 U/L, respectively. There were statistically significant differences in troponin I and CK-MB values (p respectively 0.00; 0.00) in STEMI patients compared to NSTEMI patients. **Conclusion:** There are differences in troponin I and CK-MB values between STEMI and NSTEMI patients. The troponin I and CK-MB values in STEMI patients are higher than in NSTEMI patients.

Keywords: Troponin I, CK-MB, Acute Myocardial Infarction, STEMI, NSTEMI

INTRODUCTION

Coronary heart disease (CHD) is the number one cause of death in industrialized countries and a huge public health problem. The prevalence of heart disease in people of all ages in Indonesia based on the criteria of having been diagnosed by a doctor according to the Indonesian Ministry of Health in 2018 was 1.5 percent. The prevalence of coronary heart disease increases with the increasing age of respondents.[1] The American Heart Association (AHA) estimates that more than 6 million Americans suffer from coronary heart disease and more than 1 million people are estimated to have attacks of myocardial infarction each year with a prevalence of 19.5% and the mortality rate is around 30%.[2]

Acute Coronary Syndrome (ACS) is part of the clinical manifestations of CHD. The acute pathophysiology of ACS is preceded by coronary artery atheroma plaque rupture associated with plaque composition and thinning of the fibrous cap. This process causes platelet aggregation and activation of the coagulation pathway resulting in the formation of a thrombus that clogs coronary artery lumen. The clog makes oxygen supply decreases and induces myocardial ischemia. The supply of oxygen to the blood flow that stops continuously for about 20 minutes causes necrosis of myocardium cells.[3] Acute myocardial infarction (AMI) is a condition where myocardial necrosis or death of heart muscle cells results in an imbalance between the supply and demand for cardiac muscle oxygen.[4]

AMI includes ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI).[5] STEMI occurs when the thrombus volume is sufficient to block the entire artery lumen persistently while NSTEMI occurs when the thrombus volume is insufficient to block the entire artery lumen. In STEMI, there is an ECG abnormality in the form of ST-elevation while NSTEMI does not find this image. There are elevated levels of specific cardiac biomarkers especially troponin and CK-MB in STEMI and NSTEMI.[6] The diagnosis of ACS is confirmed by identification of ischemia, continuous assessment of symptoms and ECG changes, and examination of biomarkers as the gold standard for myocardial

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infarction. Based on the World Health Organization (WHO), the diagnosis of AMI is based on obtaining 2 or more than 3 criteria, namely: based on anamnesis or history of chest pain, electrocardiographic changes, and an increase in biochemical markers of heart muscle necrosis.[3,7]

Several biomarkers play an important role in diagnosis, risk stratification, management guidance, and clinical decision-making for patients with symptomatic signs of myocardial infarction.[8] The use of troponin biomarkers supporting the CK-MB test is a relatively recent change in diagnosing AMI. Measurement of troponin as a cardiac biomarker is an important objective aspect in diagnosing AMI.[9] The TnI (Troponin I) biomarker has high sensitivity and specificity in supporting the diagnosis of AMI and has become a new gold standard by the European Society of Cardiology (ESC). Troponin is a cardiac protein found in the heart muscle and functions as a regulator of muscle contraction specific to the heart muscle. In the heart muscle, there is troponin I which will be released into the circulation if there is necrosis of heart muscle cells so that troponin I can be used to diagnose AMI.[4,10] CK-MB is one of the Creatine Kinase (CK) isoenzymes that is released into the circulation during ischemia, injury, or inflammation of heart muscle and it used to diagnose AMI. Troponin I levels increase 3 to 5 hours after myocardial injury and remain elevated approximately 4-5 times longer than CK-MB. TnI examination has not been used routinely and troponin examination is not yet available in all health facilities in Indonesia.[4,11] In previous studies, the results showed that the velocity of increase in cTnI (cardiac Troponin I) in STEMI patients was higher than NSTEMI patients due to pathophysiological differences between STEMI and NSTEMI. It allows differences in values of cardiac biomarkers. This study was conducted to determine the differences in troponin I and CK-MB values in acute myocardial infarction with ST-elevation and without ST-elevation.[12]

METHOD

This research is an analytic observational study with cross-sectional design. The study was conducted on 48 patients with acute myocardial infarction based on doctor's diagnosis who were treated at the Dr. Kariadi General Hospital, Semarang, Central Java, and the Diponegoro National Hospital, Semarang, Central Java between April to September 2020. The study subjects were determined by consecutive sampling which met the inclusion and exclusion criteria. The inclusion criteria were acute myocardial infarction patients both STEMI and NSTEMI. The exclusion criteria were patients with sepsis, patients with congestive heart failure, patients with myocarditis, patients with arrhythmias, and patients with chronic kidney disease. This study has obtained informed consent from research subjects.

The independent variable in this study was acute myocardial infarction (STEMI and NSTEMI). The dependent variables in this study were the values of troponin I and CK-MB. The materials and tools used for blood sampling in this study were blood samples from patients with acute myocardial infarction, alcohol swab, 3cc syringe, heparin tube, tube without anticoagulant, and a tourniquet. The measurement materials for CK-MB were CK-MB FS reagent and Siemens Flex reagent cartridge. CK-MB values were measured by TMS Biolis and Dimension RXL max (siemens) using enzymatic immunoassay method. The measurement material for Troponin I was vidas. Troponin I values were measured by vidas using immunochromatography method. The blood sampling for troponin I and CK-MB examination was done less than 24 hours after the patient was admitted to the hospital and blood sampling was not repeated.

The data were processed and analyzed using computer software. Data analysis includes descriptive analysis and hypothesis testing. Univariate analysis was performed on each variable to determine the characteristics of the sample. The research subjects were divided into two unpaired groups with one measurement. The data normality test used Shapiro-Wilk test and the comparative test used Mann-Whitney test after transforming the data.

The study has received ethical clearance from the Medical and Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University with Number 106/ EC / KEPK / FK-UNDIP / VI / 2020.

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RESULTS

This study involved 48 respondents who were patients at the Dr. Kariadi General Hospital and Diponegoro National Hospital. These patients were diagnosed with AMI was characterized by chest pain and elevated Troponin I and CK-MB measured in less than 24 hours. From the results of the ECG examination, the patients were grouped into 25 STEMI patients and 23 NSTEMI patients

Characteristics of Research Subjects

The distribution of subject characteristics in the two groups was presented in table 1.

Table 1. Characteristics of Research Subjects

Variable	Mean ± SD	Median (min-max)	p
Age (years)			
- STEMI	55.80 ± 7.84	57(40 - 67)	0.31
- NSTEMI	58.22 ± 10.22	56 (35 – 83)	0.42
Gender			
- Male n=33 (68.8%)			
- Female n=15 (31.3%)			

Based on table 1 the mean age of STEMI patients was 55.80 ± 7.84 and the mean age of NSTEMI patients was 58.22 ± 10.22. . The percentage of male patients in this study is more than female patients.

Analysis of Differences in Troponin I and CK-MB Values between STEMI and NSTEMI Patients

The data obtained from the examination of troponin I and CK-MB values were ratio numerical data. The characteristics of the troponin I and CK-MB values were presented in table 2.

Table 2. Characteristics of the Troponin I and CK-MB Values

Variable	Mean ± SD	Median (min-max)	Shapiro-Wilk (p)
Troponin I (ng/mL)			
- STEMI	30.40 ± 20.79	40.00 (0.04 – 50.00)	0.00
- NSTEMI	1.38 ± 1.76	0.43 (0.02 – 5.85)	0.00
CK-MB (U/L)			
- STEMI	386,12 ± 319,70	454 (15 – 1067)	0.03
- NSTEMI	42,39 ± 27,54	34 (12 – 116)	0.00

* Normal data distribution (p>0.05)

Based on table 2, the mean troponin I value and the mean CK-MB value in the STEMI patient group was higher than the NSTEMI patient group. The data normality test used Shapiro-Wilk test because the sample size was less than 50. The Shapiro-Wilk normality test performed on troponin I and CK-MB values from 2 groups (STEMI and NSTEMI patients) showed abnormal data distribution in both groups ($p < 0.05$). Data transformation has been carried out but the data distribution is still not normal.

Furthermore, Mann-Whitney test was used to determine whether there were significant differences in troponin I and CK-MB values between STEMI and NSTEMI patients. The results of the Mann-Whitney test were presented in table 3

Table 3. Mann-Whitney Test Results

Variable	N	Mean Rank	p
Troponin I (ng/mL)			
- STEMI	25	32.02	
- NSTEMI	23	16.33	0.00*
CK-MB (U/L)			
- STEMI	25	31.24	
- NSTEMI	23	17.17	0.00*

* Significant difference (p<0.05)

Based on table 3, there were significant differences in troponin I and CK-MB values between STEMI and NSTEMI patients ($p < 0.05$).

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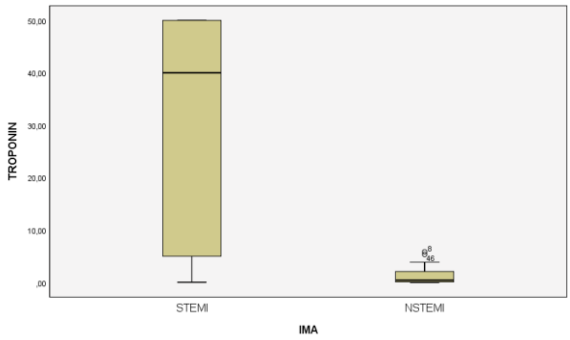

Figure 1. The difference in Troponin I Values Boxplot

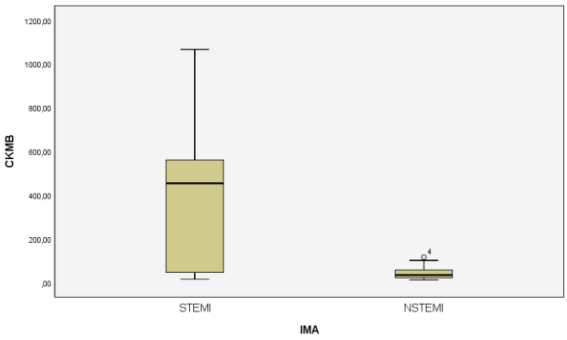

Figure 2. The difference in CK-MB Values Boxplot

DISCUSSION

Characteristics Data

This study involved 48 AMI patients consists of 33 men (68.8%) and 15 women (31.3%) who had met the inclusion and exclusion criteria. The percentage of male patients in this study is more than female patients. It is supported by previous research which describes the number of samples of AMI patients dominated by men.[13] Male gender is a major risk factor for AMI apart from smoking, hypertension, high cholesterol levels, and diabetes mellitus. Women have a lower risk due to the presence of the endogenous hormone estrogen (17-β-estradiol which is biologically active) and have been shown to be cardioprotective that protects against apoptosis of heart cells. However, these endogenous estrogens only provide benefits to women before menopause.[14,15]

The mean age of STEMI patients was 55.80 ± 7.84 and the mean age of NSTEMI patients was 58.22 ± 10.22. It is supported by previous research that there is a significant increase in the relative proportion of AMI patients between the ages of 45 and 65 years.[16] Women can experience a delay of up to 9 years to be suffered from AMI compared to men because men under 65 years have a higher risk factor than women under 65 years.[17]

Troponin I Values in STEMI and NSTEMI Patients

The results showed that the mean troponin I value in the STEMI patient group was higher than the NSTEMI patient group. These results are supported by previous research which showed that the velocity of increasing cTnI in STEMI patients was higher than NSTEMI patients, thus allowing higher troponin I value in STEMI patients.[12] The results of Mann-Whitney test for troponin I values between STEMI and NSTEMI patients obtained p = 0.00, which indicates that there is a significant difference in troponin I values between STEMI and NSTEMI patients.

The difference in troponin I values between STEMI and NSTEMI patients can be caused by the pathophysiology of STEMI. There is total occlusion of the coronary arteries in STEMI caused by thrombus formed due to atherosclerotic plaques rupture. In contrast to STEMI, NSTEMI only partially blocks the coronary arteries.[18,19] STEMI patients have a wider myocardial risk. Total occlusion in STEMI patients will result in a greater decrease in oxygen supply to cardiac muscle cells compared to NSTEMI patients.[20] The decrease in oxygen supply will result in a large reduction in ATP due to compensatory anaerobic glycolysis metabolism. Anaerobic glycolysis will cause the accumulation of hydrogen and lactate ions resulting in intracellular acidosis. With this, there is an ionic and osmotic imbalance in the cells that can cause necrosis.[21] Necrosis will disrupt the sarcolemma membrane of the cardiomyocytes which causes proteolytic degradation of the troponin-tropomyosin protein complex so that troponin from the cytoplasmic will be released first followed by more excretion from myofilament.[22] Therefore, more troponins are released in STEMI patients due to the higher number of cell damage. The wider the myocardial infarction, the higher the troponin I value.[23]

CK-MB Values in STEMI and NSTEMI Patients

The results showed that the mean CK-MB value in the STEMI patient group was higher than the NSTEMI patient group. These results are supported by previous research which showed that the velocity of increasing cTnI in STEMI patients

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was higher than NSTEMI patients, thus allowing higher levels of other cardiac biomarkers in STEMI patients.[12] The results of Mann-Whitney test for CK-MB values between patients STEMI and NSTEMI obtained p = 0.00, which indicates that there is a significant difference in the CK-MB values between STEMI and NSTEMI patients.

Creatine kinase (CK) is an intracellular enzyme present in large amounts in skeletal muscle, myocardium, and brain. CK is a dimeric molecule consisting of two subunits, namely M and B. The combination of these subunits forms the isoenzymes CK-MM, CK-MB, and CK-BB. Significant concentrations of the CK-MB isoenzyme are found exclusively in the myocardium.[24] CK is an enzyme that catalyzes the reversible reaction of creatine and ATP to creatine phosphate and ADP. The creatine phosphate created from this reaction is used to supply ATP to tissues and cells that need large amounts of ATP. During the ischemic process in myocardial infarction, oxygen supply is interrupted so that mitochondrial oxidative phosphorylation is rapidly stopped. This causes a massive reduction in the production of ATP from energy metabolism resulting in compensation for anaerobic glycolysis for ATP production which can lead to accumulation of hydrogen and lactate ions and induces intracellular acidosis and inhibition of glycolysis. It will cause changes in the ion transport system in the sarcolemma and organellar membranes which will result in increased DNA damage that leads to cell death. Disruption of the sarcolemma membrane causes intracellular macromolecules to leak into the heart interstitium and eventually into the bloodstream. One such macromolecule is CK-MB.[21,25]

The difference in CK-MB values between STEMI and NSTEMI patients can be caused by the different pathophysiology between STEMI and NSTEMI. There is total occlusion of the coronary arteries in STEMI caused by thrombus formed due to atherosclerotic plaques rupture. In contrast to STEMI, NSTEMI only partially blocks the coronary arteries.[18,19] STEMI patients have a wider myocardial risk. Total occlusion in STEMI patients will result in a greater decrease in oxygen supply to cardiac muscle cells compared to NSTEMI patients. This can cause greater disruption of the sarcolemma membrane so that more CK-MB will be released into the bloodstream.[20]

This study has limitations on the determination of inclusion and exclusion criteria. The increase in troponin I and CK-MB was influenced by the time the patient's blood sample was examined and the patient's symptom onset. In this study, the patient's blood sampling for troponin I and CK-MB examination was done less than 24 hours after the patient was admitted to the hospital with different symptom onset. The difference in blood sampling time within 24 hours and symptom onset between patients may affect the troponin I and CK-MB values examined. Patients can be diagnosed with AMI if one of the cardiac biomarkers is elevated. In this study, there were patients diagnosed with AMI only with an increase in one of the biomarkers. Researcher did not consider gender, age, patients with diabetes, hypertension, and obesity as inclusion criteria. This may affect the results of the study.[5]

Troponin I and CK-MB values can be affected by hemolysis in blood samples, patients taking supplements that can increase ATP, patients with previous excessive activity, and patients with a history of heart attack 2 weeks before, abnormalities in the skeletal muscles, consumption of certain drugs, history of ACS, and history of surgery or other heart procedures. In this study, the researchers did not consider those things as exclusion criteria so that they might affect the results of the study. The results of this study are still not completely correct due to those limitations. It is necessary to do further research that considers those inclusion and exclusion criteria for more accurate results.[26,27]

CONCLUSION

There are differences in troponin I and CK-MB values between STEMI and NSTEMI patients. The troponin I and CK-MB values in STEMI patients are higher than in NSTEMI patients. This article provides knowledge about the differences in troponin I and CK-MB values in acute myocardial infarction patients.

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