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Elevated Cardiac Marker Enzymes with the Incidence of Complications in ACS Patients:

Is it Related?

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***Abstract*—Acute coronary syndrome (ACS) is a condition that describes the condition of the heart muscle infarction so that the heart is damaged. Ongoing damage to the heart muscle may result in a new condition known as a complication. Based on this condition, the aim of this study was to determine the relationship between elevated cardiac marker enzymes and the incidence of complications in ACS patients. This study is an observational analytic study based on secondary data, namely medical record data. The subjects of this study were data from medical records of SKA patients who experienced complications recorded in the medical records at the Dustira Cimahi Hospital in 2018. The number of cases found in the Dustira hospital in 2018 was 105 cases, the most age was over 45 years, the sex that often experienced complications was women with a total of 58 people (55.2%), cardiac enzymes both troponin and CKMB in cases experienced a significant increase, patients with troponin increase was 86 people (81.9%) while patients with increased CKMB were 88 people (92.6%), complications were obtained by patients with heart failure as many as 38 cases, cardiogenic shock as many as 16 people, arrhythmia as many as 30 people, as many as 11 people, and cardiac arrest as many as 10 people. In this study, it was concluded that there was a significant relationship between the increase in cardiac marker enzymes both troponin and CKMB (p-value <0.05) on the incidence of complications in ACS patients.**

Keywords—ACS, cardiac marker enzymes, CKMB, complications, troponin

I. INTRODUCTION

Acute coronary syndrome (ACS) is a condition that describes an acute heart muscle ischemia or infarction, which is usually caused by decreased blood flow in the coronary arteries [1]. This syndrome is characterized by three findings that occur in patients, namely typical chest pain which radiating to the left arm, increased cardiac marker enzymes, and changes in electrocardiography (ECG) [2,3]. Based on the history of chest pain, physical examination, ECG examination, and examination of cardiac markers, this syndrome is divided into ST-segment elevation myocardial infarction (STEMI), non-ST segment elevation myocardial infarction (NSTEMI), and unstable angina pectoris (UAP) [2].

Based on the data and information center (Pusdatin) of the Ministry of Health of the Republic of Indonesia, ACS is a disease with the number one cause of death in the world. In 2008, it was estimated that about 17.3 million people worldwide died from ACS. One third of deaths due to cardiovascular diseases came from low to middle income countries. The prevalence of heart disease in Indonesia based on basic health research (Rikesdas) in 2013 was 0.5 percent or about 883.447 people [4,5].

The prevalence of cardiovascular disease is influenced by various risk factors, including hypertension. The prevalence of hypertension in Indonesia, from the results of blood pressure measurements at the age of 18 years and over, was found to be 31.7%, only 7.2% of the population had known hypertension and only 0.4% of cases took hypertension medication. This shows that 76% of cases of hypertension in the community have not been diagnosed or 76% of people do not know that they suffer from hypertension [6]. In West Java in 2016, 790,382 cases of hypertension were found (2.46% of the population over 18 years), As many as 8,029,245 cases were examined, spread over 26 districts / cities, and only one district / city (West Bandung Regency), did not report cases of hypertension. In the city of Cimahi, there are about 5.81% or 13.779 of people are newly diagnosed with hypertension [4,5].

Cardiac markers are proteins released by cardiac muscle cells as they are injured and enter the bloodstream. These markers may help healthcare workers diagnose STEMI, NSTEMI, and unstable angina [7]. There are many types of cardiac marker enzymes that can be checked, including aspartate transaminase (AST), lactate dehydrogenase (LDH), creatine kinase (CK), CKMB - activity assay, CKMB - mass assay, cardiac troponin I (TnI), cardiac troponin T (TnT), and Myoglobin. The increase time of cardiac marker enzymes varies with the beginning of ischemic pain. Among the several cardiac markers that can be tested, troponin I is more often used because it is specific to heart muscle damage [2,8].

Ongoing damage to the heart muscle may result in several complications in ACS patients. ACS patients who receive or do not receive reperfusion therapy may still develop a complication. The most common occurrence of complications in the study was STEMI patients who were not given reperfusion treatment compared to those who were given reperfusion treatment. Complications that occur include heart failure, cardiac arrest, death, and ventricular tachycardia or fibrillation. Meanwhile, the complications that can happen to patients with reperfusion therapy are minor bleeding, heart failure, cardiac arrest, and death. A patient could have more than one complication [9]. In a study conducted by Kusumawati et al., patients with STEMI were four times more likely to develop ventricular arrhythmias that generally occur after the first 48 hours after onset, while in NSTEMI 60% of ventricular arrhythmias occurred after 48 hours [10,11]. The complications depend on the severity of the infarction and the treatment of the disease [10,11].

An increase in cardiac enzymes may be associated with the incidence of complications since an increase in cardiac marker enzymes indicates a lesion in the heart muscle. The more elevated the cardiac marker enzymes, the greater the damage. Based on the study of Kusumawati et al. [11], ACS patients with increased troponin levels could experience major adverse cardiac events (MACE) incidence of 6.5 times than patients with normal troponin levels [10]. In a study conducted at several hospitals in Medan, it was concluded that ACS patients with troponin T were more than 0,1 ng / ml had more severe complications than patients who did not experience an increase in troponin [11].

Based on the previous study, we aimed to identify the relationship between increased cardiac marker enzymes and the incidence of complications in ACS patients at Dustira Hospital. The purpose of this study is to provide health workers with information on the amount of elevated cardiac marker enzymes that must be considered and that will become a complication when handling STEMI and NSTEMI cases.

II. METHODS

This study was an observational analytical study with the case-control design. These methods were used to determine the relationship between elevated cardiac marker enzymes and the incidence of complications of ACS at Dustira Hospital. The population in this study was all ACS patients. Data was collected from 96 medical recrods. The study used retrospective cross-sectional design. The sample was taken by consecutive random sampling.

The population in this study was all ACS patients, while the research subjects were ACS patients who suffered complications which were documented in the medical records and treated at Dustira Cimahi Hospital in 2018. The inclusion criteria for the study were ACS patients who experienced complications at the Dustira Hospital in 2018 and underwent a quantitative CKMB and Troponin examination. Exclusion criteria was the incomplete medical records.

III. RESULTS AND DISCUSSION

A. Subject Characteristics

We identified 96 ACS patients based on the medical record which fulfilled inclusion criteria. Table 1 shows that the age description of patients with ACS shows that the youngest is 26 years old and the oldest is 96 years old. The mean patient with ACS was 63 years.

In the present study we found that ACS patients were more likely to suffer in older age. These results are consistent with previous studies where ACS patients were more likely to suffer from people over the age of 45. Elderly patients tend to experience complications due to vascular risk factors such as age-related weakness of the blood vessels. In addition, the mortality rate in the elderly is higher than that of young patients [12]. Based on the Journal of Geriatric Cardiology conducted in America, it was found that about 60% of ACS patients who entered the hospital were more than 65 years old, this was related to the aging process. In the aging process, there is more extensive calcification of blood vessels compared to a young age. The flexibility of the blood vessels diminishes with age, making it easier to form plaques [13]. The incidence of ACS increases fivefold at the age of 40 to 60 years due to decrease in the function of internal organs including the heart. Decreased heart function causes coronary arteries to experience vasoconstriction leading to an impaired blood perfusion that causes ACS [14].

In the present study showed that ACS cases in women are more frequent than men. The results of this study were inversely proportional to a study conducted at the Gatot Soebroto Army Hospital, Jakarta by Indrawati, which showed that the risk of CHD was greater in men, amounting to 52.5% [15]. The present study was also inversely proportional to a study conducted at RSUP Prof. Dr. R.D. Kanoo Manado which shows the ratio of the incidence of ACS between men and women was 7: 3. Based on the results of their study, men are more susceptible to ACS due to the risk factors such as smoking and hypercholesterolemia [16].

TABLE I. DEMOGRAPHIC OF SUBJECTS

Variable	n=96	Percentage (%)
Age (years)		
Mean ±SD	63±14.095	
Median	65	
Range	26 – 96	
Sex		
Male	43	44.8
Female	52	55.2

B. Cardiac Marker Levels

Based on Table 2, most of the ACS patients experienced an increase in troponin values ≥ 0.01 ng/ml as many as 86 people or 89.6% and the rest did not experience an increase in troponin. The normal troponin threshold value set by the Dustira Hospital laboratory is ≤0.01 ng/ml, therefore it can be concluded that 80% of patients showed a significant increase in troponin in the blood.

Based on the table 2, it is found that the mean troponin in patients is 0.06 ng/ml (95% CI: 0.03-0.08). The lowest tropoinin was 0 ng / ml and the highest was 1 ng / ml. This study was in line with previous study which found that damage to the myocardium in the case of ACS will increase the levels of heart enzymes in the body. In myocardial ischemia, the cell membrane becomes more permeable so that intracellular components such as cardiac troponins leave the tissue and enter the interstitial and intravascular space [17]. The results of this study were also the same as Ang's study which stated that patients with increased troponin have a 6-fold risk of developing complications greater than that of patients who had normal troponin levels [18].

Meanwhile, based on the Table 2, it can be concluded that most of the ACS patients experienced an increase in the CKMB value ≥ 24 U/L as many as 86 people or 89.6%, and the rest did not experience an increase in CKMB.

The mean levels of CKMB in patients were 30.84 U/mL (95% CI: 26.39-44.30). The lowest CKMB was 10 U/mL and the highest was 65 U/mL. This study was in line with the literature which stated that CKMB is a protein that will come out when an injury occurs that damages the components of the cells located in the heart muscle tissue [8]. CKMB levels >24 U/L were a sign that myocardial injury has occurred. This was in line with the study conducted by Ahmad released in The Indonesian Journal of Health Science which stated that ACS patients with increased CKMB results have a 4.3 times greater risk of mortality compared to ACS patients with normal CKMB values [19].

TABLE II. TROPONIN LEVELS

Variable	n=96	%
Troponin		
Mean ±SD	0.06±0.126	
Median	0.04	
Range	0 – 1	
Normal	10	10.4
Elevated	86	89.6
CMB		
Mean ±SD	30.84±9.268	
Median	28	
Range	10 – 65	
Normal	10	10.4
Elevated	86	89.6

C. Complications of ACS Patients

The description of complications among ACS patients at Dustira Hospital was quite diverse. A patient may have single or multiple complications. Complications were categorized into five groups: cardiogenic shock, arrhythmia, acute pulmonary oedema, heart failure, and cardiac arrest.

Table 3 shows that most complications in ACS patients are arrhythmias and the least complications are heart attacks. The occurrence of this complication is related to the formation of plaque in the blood vessels resulting in damage to the heart muscle, which will cause structural and functional disorders of the heart muscle. These disorders cause a medical condition that may lead to several complications for the patient.

TABLE III. COMPLICATIONS OF ACS PATIENTS

Complications	n	Percentage (%)
Cardiogenic Shock	16	15.2
Arrhythmia	30	28.6
Acute Pulmonary Oedema	11	10.5
Acute Heart Failure	29	36.2
Cardiac Arrest and Death	10	9.5
Total	96	100

Most complications were arrhythmias as many as 30 people (28.6%). Arrhythmias that occur in patients in this study can be seen in Table 4. In the study, the most common arrhythmia was atrial fibrillation with 19 cases (63%), while the rarest was LBBB in 1 person (3%).

Arrhythmias can occur because of 3 things, namely impulse formation disorders, impulse conduction disorders, and a combination of both. In the case of ACS, it is very likely that arrhythmias occur because the electrical conduction pathway of the heart is disturbed due to plaque formation which can disrupt the flow of electricity resulting in contraction disorders [10,21]. Based on the guidelines for AF management by PERKI, AF may increase mortality and morbidity in ACS and stroke patients [2]. Patients with AF have a 5 times higher risk of stroke and a 3 times higher risk of heart failure than patients without AF [21].

TABLE IV. ARRHYTHMIA FEATURES

Types	N=96	Percentage (%)
Left Bundle Branch Block (LBBB)	1	3
Right Bundle Branch Block (RBBB)	3	10
Atrial Fibrilation (AF)	19	63
Supraventricular Tachycardia (SVT)	4	14
Total AV Block	3	10
Total	30	100

D. Relationship of Increased Troponin Levels to Complications in ACS Patients

This study demonstrated that an increase in the troponin level was more likely to cause a complication than a normal troponin concentration. As in arrhythmias, there were 29 patients with elevated troponin levels and only 1 patient had normal troponin levels. Statistical test results showed a significant relationship between increased troponin levels and the incidence of complications in patients with ACS.

The relationship of increased toponin levels can be seen at Table 5.

TABLE V. RELATIONSHIP OF INCREASED TROPONIN LEVELS TO COMPLICATIONS IN ACS PATIENTS

Complications	Troponin Levels		Total	P- Value
	Normal	*Elevated*		
Cardiogenic Shock	0	16	16	0.012
Arrhythmia	1	29	30	
Acute Pulmonary Oedema	2	9	11	
Heart Failure	7	22	29	
Cardiac Arrest	0	10	10	
Total	10	86	96	

E. Relationship of Increased CKMB Levels to Complications in ACS Patients

TABLE VI. RELATIONSHIP OF INCREASED TROPONIN LEVELS TO COMPLICATIONS IN ACS PATIENTS

Complications	CKMB Levels		Total	P- Value
	Normal	*Elevated*		
Cardiogenic Shock	0	16	16	0.001
Arrhythmia	1	29	30	
Acute Pulmonary Oedema	0	11	11	
Heart Failure	9	20	29	
Cardiac Arrest	0	10	10	
Total	10	86	96	

The present study showed that the increased CKMB level was more likely to have a complication than the normal CKMB level (Table 6). In acute pulmonary edema, 11 patients had an increase in CKMB, and no patients had a normal CKMB. Statistical test results indicated that there was a significant relationship between the increase in CKMB level and the incidence of complications in ACS patients.

A limitation of the study was that the examination of troponin and CKMB which depends on the onset of the chest pain, so the examination results may show normal results or not increase yet even though the damage that occurs is extensive this was due to the time the examination was too short to the onset of chest pain. Another our limitation of the study was that the examination of troponin and CKMB was not at the same time, so there would be have a different result.

IV. CONCLUSION

Overall, 89.6% of patients had troponin levels over 0.01 ng/L with an average troponin of 0.06 ng/ml. A total of 89.6% of patients showed an increase in CKMB levels of more than 24 U/mL, with mean CKMB levels of 30.84 U/mL. The most complications that occur in ACS patients were arrhythmias with 30 cases. Other complications include cardiogenic shock, acute heart failure, acute pulmonary edema, and cardiac arrest. There was a significant relationship between the increase in cardiac marker enzymes both troponin and CKMB and the incidence of complications in ACS patients.

It is recommended that the hospital check for troponin and CKMB at the same time in ACS patients. Further research is needed regarding the relationship of troponin and CKMB with the complications of ACS that were examined at the time of the incidence of complications. We also suggest further research to examine the relationship between increased cardiac markers and the incidence of chronic complications in ACS patients.

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