

Association between Mean Platelet Volume (MPV) and Mayor Cardiovascular Incidence among Inpatient Acute Myocardial Infraction with ST-Elevation

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Abstract.

MPV value is an index of platelet associated with platelet activity. A larger platelet size shows a hyper-reactive platelet and accelerates thrombus formation with coronary circulation, leading to major cardiovascular events. Hence, this study was designed to investigate the relationship between MPV value and each type of major cardiovascular event in General Hospital Haji Adam Malik. This study was observational research with a cross-sectional design in General Hospital Haji Adam Malik in October 2014-January 2015 among sixty-nine ACS inpatients with ST-Elevation. The evaluated major cardiovascular events were death, heart failure, arrhythmia, and cardiogenic shock. The average MPV value of ACS patients with heart failure, cardiogenic shock, arrhythmia, death, and all major cardiovascular events was 10.08 fL, 10.40 fL, 10.00 fL, 9.76 fL, and 10.00 fL, respectively. Either major cardiovascular event did not show any significant difference in the average MPV value due to these P-Values > 0.05. Hence, it can be concluded that the MPV value cannot be used to predict the incidence of either major cardiovascular event in ACS patients.

Keywords: ACS, MPV, Major, Cardiovascular, Events.

I. INTRODUCTION

World Health Organization (WHO) reported that non-communicable diseases were the most common cause of death in low- and middle-income countries (77%). Cardiovascular diseases (CVDs), a non-communicable disease, are the leading cause of death globally, followed by cancers, respiratory diseases, and diabetes [1]. Coronary artery disease in the emergency condition is shown as an acute coronary syndrome (ACS) that affects the coronary artery blood flow and partially or fully obstructs the coronary artery. Moreover, ACS is classified as Unstable Angina Pectoris (UAP), Acute Myocardium Infarct with ST-Elevation, and Acute Myocardium Infraction without ST-Elevation [2]. Coronary heart disease is a common health problem predicted to increase over time. American Heart Association (AHA) reported that an estimated 18.2 million people aged more than 20 years old suffered from coronary heart disease in the United States, and the prevalence of coronary heart disease was more common in females than males. Moreover, AHA also reported that around 720,000 cases were new coronary events and around 335,000 cases were recurrent [3]. In June 2021, also reported that there were 17 million premature death (under the age of 70 years old) due to non-communicable disease in 2019 and amount of 39% cases were caused by cardiovascular disease; these deaths represented 32% of all global deaths [4]. Coronary heart disease has also become a health problem in Indonesia. An annual report from Indonesia Health Ministry was reported into Basic Health Research.

This report reported that coronary heart disease incidence rate in 2007 was 9.3%, which was also the third cause of death after stroke and hypertension. Moreover, this report also reported that the incidence of cardiac disease in Indonesia was 1.5% (95% CI: 1.4-1.5) in 2018; however, these cases were mixed between congenital or acquired causes [5]. The basic mechanism of coronary artery disease was the formation of atherosclerosis. Atherosclerosis accumulates fatty and various substances into the coronary artery, disturbing blood flow and injuring blood vessels. After that, the injured site forms a thrombus clot that partially or fully obstructs the coronary artery, and this obstruction ends as the necrosis of myocardium tissue and activates more platelets [6]. The activated platelet secretes various mediators that affect platelet adhesion, aggregation, or size. Larger platelets have more adhesion and aggregation ability because they secrete more mediators, especially Thromboxane A₂. Hence, the larger platelet may increase thrombus size and correlate with UAP and Acute Myocardium Infarct. In the clinical settings, the larger platelet has a higher Mean Platelet Volume

(MPV), the average platelet size in the peripheral circulation [7], [8]. Some previous study has been performed to investigate the relationship between prolonged effects of Acute Coronary Syndrome against the structural changes of platelets. Sun et al. (2016) reported that the increase of MPV value significantly increased the mortality among ACS patients with ST-Elevation in Xuanwu Hospital, and this MPV value might be used as a marker for risk stratification. Moreover, Mumpuni et al. (2016) also reported that the increase in MPV could predict major cardiovascular disease in patients suffering from ACS [9], [10]. The major cardiovascular event in the ACS setting is one complication in patients with AMI with ST-Elevation that includes heart failure, arrhythmia, sudden death, or cardiogenic shock.

This condition is frequently found in the early patient care phase among inpatients patient. Some factors that affect the incidence of major cardiovascular events included age, sex, family history with coronary artery disease, diabetes, low haemoglobin concentration, higher white blood cells count, low blood pressure, platelet profile, cardiac enzymes, heart rate, cardiogenic shock, ST-Segment deviation, and Killip classification [11], [12]. According to the information above, preventing major cardiovascular events incidence among ACS patients becomes important. Some previous studies have been performed to investigate the relationship between MPV value against major cardiovascular events because the MPV value is part of a routine blood count test and a simple and low cost to be performed. Pal et al. (2014) reported that there was a significant difference between ACS patients with and without major cardiovascular events (P-Value < 0.001), it can be seen from the average MPV value in ACS patients with and without major cardiovascular events that were 9.91 fl and 11.44 fl, respectively. Moreover, Pal et al. (2014) also reported that the positive and negative predicted value of MPV was 61.18% and 82.53%, respectively [13]. These previous studies have looked for the relationship between MPV and major cardiovascular events. However, these studies were not be performed in Indonesia, and none of these studies simultaneously investigated the relationship between MPV and each type of Major Cardiovascular Event. Hence, this study was performed to investigate the relationship between MPV value and each type of major cardiovascular event in General Hospital Haji Adam Malik.

II. METHODS

This study was an observational study with a cross-sectional design in General Hospital Haji Adam Malik in October 2014-January 2015. The research protocol has been approved by the Health Research Ethics Committee from Universitas Sumatera Utara with a letter of no. This study's target population was all inpatients suffering from acute myocardial infarction with ST-Elevation. Meanwhile, the study population was all inpatients suffering from acute myocardial infarction with ST-Elevation in the emergency room of General Hospital Haji Adam Malik. According to this population, this study was determined the number of samples by the following formulation:

$$n = \left\{ \frac{Z\alpha\sqrt{PoQo} + Z\beta\sqrt{PaQa}}{Pa - Po} \right\}^2$$

n = number of samples

Z α = Z-Score for alpha= 1,96

Z β = Z-Score for beta = 0,84

Po = Proportion of Acute Coronary Syndrome Death = 17,5%

Pa = 0,38

Qo = 1 – Po

Based on the formulation above, the number of samples used in this study was up to 32 patients. These patients were selected by purposive sampling methods limited by inclusion and exclusion criteria. This study was performed by evaluating medical records from inpatients who came to the emergency room of General Hospital Haji Adam Malik between October 2014-January 2015. After that, these inpatients must fulfil inclusion criteria viz. acute coronary syndrome with ST-Elevation and aged between 18-75 years old. Moreover, these inpatients were excluded if these inpatients fulfil exclusion criteria viz. acute coronary syndrome patients with ST-Elevation with one of the comorbid coagulation conditions (either severe kidney

or liver diseases, malignancy, some abnormalities of platelet function like thrombocytopenia or thrombocytosis, or bleeding), history of either coronary artery disease or stroke, occupied by sepsis, or suffered from critical diseases. This study has independent and dependent variables.

The independent variable of this study was mean platelet volume (MPV) which was expressed as femtoliters (fL); meanwhile, the dependent variable was major cardiovascular incidences like heart failure, cardiogenic shock, arrhythmia, and sudden death. An acute myocardial infarction with ST-Elevation was diagnosed by evaluating clinical presentations, ECG findings, complete blood count, and cardiac enzymes from medical records. MPV was obtained from a complete blood count analyzed from whole blood (EDTA Blood Tube) by SYSMEX XT-4000 machine. Moreover, this study also analyzed the characteristics of patients, including age, sex, smoking, history of similar disease in the family, comorbid conditions (Diabetes Mellitus, Hypertension, and obesity), vital signs (Systolic Blood Pressure, Diastolic Blood Pressure, and Pulse Rate), haematology parameters (White Blood Count and Platelet Count), blood chemistry test (Random Blood Glucose Level, Total Cholesterol, Blood Urea Nitrogen (BUN), Creatinine, and Potassium Level), the onset of diseases, and location of the infraction. Initially, all data were analyzed by the descriptive statistic. All numeric data was expressed Mean (SD), and Mann-Whitney Test analyzed the differences. Meanwhile, categorical data were expressed as frequency (percentage).

III. RESULT AND DISCUSSION

In the beginning, this study evaluated the characteristics of ACS patients in General Hospital Haji Adam Malik that were sex, age, smoking history, hypertension, diabetes mellitus, obesity, history of ACS in the family, the onset of ACS, vital signs, site of infarct, random blood glucose level, number of white blood cells, platelets, BUN, creatinine, and potassium level. These characteristics are described in Table 1.

Table 1. Characteristics of ACS Patients in General Hospital Haji Adam Malik

Characteristics	Frequency (n=69)
Sex	
Male	55 (79.7)
Female	14 (20.3)
Age (Years), Mean (SD)	54.7 (11.11)
Smoking, n (%)	
Yes	49 (71.00)
No	20 (29.00)
Hypertension, n (%)	
Yes	28 (40.60)
No	41 (59.40)
Diabetes Mellitus, n (%)	
Yes	14 (20.30)
No	55 (79.70)
Obesity, n (%)	
Yes	1 (1.40)
No	68 (98.60)
History of Family with ACS, n (%)	
Yes	7 (10.10)
No	62 (89.90)
Onset, Mean (SD)	32.59 (32.66)
SBP, Mean (SD), mmHg	128.12 (27.29)
DBP, Mean (SD), mmHg	80.58 (14.23)
Pulse (BPM), Mean (SD)	83.07 (18.25)
Site of Infarct, n (%)	
Antero septal	21 (30.4)
Antero lateral	10 (14.5)
Antero Extensive	12 (17.4)
Inferior	26 (37.7)
MPV (fL), Mean (SD)	9.99 (0.9)
White Blood Cells ($\times 10^3$ cells/ mm^3), Mean (SD)	13.45 (3.79)
Platelets ($\times 10^3$ cells/ mm^3), Mean (SD)	241.3 (70.56)
Random Blood Glucose Level (mg/ dL), Mean (SD)	168.52 (118.75)
Total Cholesterol (mg/ dL), Mean (SD)	201.9 (43.91)

BUN (mg/ dL), Mean (SD)	27.36 (11.3)
Creatinine (mg/ dL), Mean (SD)	1.02 (0.4)
Potassium (mEq/ L), Mean (SD)	4.49 (5.1)
Troponin-T (ng/ mL), Mean (SD)	1.16 (0.71)
CKMB (ng/mL), Mean (SD)	114.16 (104.92)
Ejection Fraction (%), Mean (SD)	46.30 (13.07)

Based on Table 1, it can be seen that most of the ACS patients in General Hospital Haji Adam Malik were male (55 patients) that had an average age of 54.7 years olds. Most of these patients did not have any comorbid conditions like hypertension (59.40%), diabetes mellitus (79.70%), or obesity (98.60%). However, Most of these patients had a history of ACS in their family (89.90%). Meanwhile, the ACS patients in General Hospital Haji Adam Malik had an average ACS onset of 32.59 hours, and the most common infarct site was inferior (37.7%), followed by anteroseptal (30.4%), extensive anterior (17.4%), and the lowest infarct site was anterolateral (14.5%). The routine blood count of ACS patients in the General Hospital of Haji Adam Malik showed the average of white blood cells, platelets, and MPV value was 13.45×10^3 cells/ mm³, 241.3×10^3 cells/ mm³, and 9.99 fL, respectively. Other parameters, the biochemical parameters, were also evaluated in this study. Average of random blood glucose level, total cholesterol, BUN, creatinine, and potassium level as biochemical parameters were 168.52 mg/ dL, 201.9 mg/ dL, 27.36 mg/ dL, 1.02 mg/ dL, and 4.49 mEq/ L, respectively. On the other hand, this study also looked for the cardiac marker and function in ACS patients, including Troponin T, CKMB, and ejection fraction. The average of Troponin-T, CKMB, and ejection fraction were 1.16 ng/ mL, 114.16 ng/ mL, and 46.30%, respectively. Furthermore, the analysis was continued to look for the relationship between these numeric characteristics against the incidence of major cardiovascular events, and the analysis result was described in Table 2.

Table 2. Association between Characteristics of ACS Patients and Major Cardiovascular Event in General Hospital Haji Adam Malik

Characteristics	Major Cardiovascular Event		P-Value
	Yes (n=34)	No (n=35)	
Age (Years), Mean (SD)	58.79 (9.18)	50.89 (11.56)	0.265 ^a
Onset, Mean (SD)	36.75 (35.32)	28.54 (29.8)	0.279 ^b
White Blood Cells ($\times 10^3$ cells/ mm ³), Mean (SD)	14.55 (3.98)	12.48 (3.37)	0.383 ^a
Platelets ($\times 10^3$ / mm ³), Mean (SD)	238.97 (77.72)	243.57 (63.91)	0.769 ^b
Random Blood Glucose Level (mg/ dL), Mean (SD)	172.42 (100.74)	165.32 (135.38)	0.374 ^b
Total Cholesterol, Mean (SD)	206.24 (47.55)	197.69 (40.32)	0.755 ^b
Creatinine (mg/ dL), Mean (SD)	0.99 (0.38)	1.04 (0.42)	0.644 ^b
Potassium (mEq/ L), Mean (SD)	3.78 (0.58)	5.18 (7.12)	0.108 ^b
Troponin-T (ng/ mL), Mean (SD)	1.27 (0.72)	1.06 (0.78)	0.357 ^b
CKMB (ng/mL), Mean (SD)	143.29 (128.4)	85.87 (75.32)	0.264 ^b
Ejection Fraction (%), Mean (SD)	44.48 (13.38)	48.07 (12.77)	0.186 ^b

^aP-Value obtained from T-independent; ^bP-Value obtained from Mann-Whitney.

Based on Table 2, it can be seen that all characteristics of ACS patients were not associated with the incidence of major cardiovascular events. It can be seen from the P-Values of all parameters that were higher than 0.05. Furthermore, the analysis was continued to compare the MPV value in each type of major cardiovascular event, and the comparison was described in Table 3.

Table 3. Comparison of Mean Platelet Volume (MPV) in Some Major Cardiovascular Incidence

Major Cardiovascular Event	Mean Platelet Volume	P-Value
Heart Failure		
Yes	10.08 (0.85)	0.280
No	9.93 (0.93)	
Cardiogenic Shock		
Yes	10.40 (1.27)	0.464
No	9.96 (0.88)	
Arrhythmia		
Yes	10.00 (1.23)	0.521
No	9.98 (0.83)	
Death		

Yes	9.76 (1.42)	0.521
No	10.00 (0.86)	
All Major Cardiovascular Events		
Yes	10.00 (0.94)	0.876
No	9.97 (0.88)	

Based on Table 3, the MPV value did not show any significance in each type of major cardiovascular event; it can be seen from P-Values that are higher than 0.05. P-value of heart failure, cardiogenic shock, arrhythmia, death, and all major cardiovascular events were 0.280, 0.464, 0.521, 0.521, and 0.876, respectively. As one of major cardiovascular events, heart failure was found in 25 patients (36.23%) with ACS in General Hospital Haji Adam Malik. The average MPV value of ACS patients with heart failure (10.08 fL) was higher than the ACS patients without heart failure (9.93 fL), and these MPV values did not show any significant differences; it can be seen from P-Value that higher than 0.05 (P-Value: 0.280). Another major cardiovascular event, arrhythmia, was found in 12 patients with ACS in the General Hospital of Haji Adam Malik. The average MPV value of ACS patients with arrhythmia was higher than the ACS patients without arrhythmia, and these MPV values also did not show any significant differences; it can be seen from the P-Value that higher than 0.05 (P-Value: 0.521). On the other hand, this study also compared the MPV value in another major cardiovascular event that was a cardiogenic shock. There are four patients (5.80%) with cardiogenic shock among ACS patients in General Hospital Haji Adam Malik. The average MPV value in the ACS patients with cardiogenic shock (10.40 fL) was higher than the average of MPV value in ACS patients without cardiogenic shock (9.96 fL), and these MPV values did not show any significant differences, it can be seen from the P-Value that was higher than 0.05 (P-Value: 0.464). All major cardiovascular events may end in death.

This study also compared the MPV value among ACS patients that died. This study also reported that five patients (7.25%) with ACS died. The average MPV value in death ACS patients (9.76 fL) was lower than the patients that did not die (10.00 fL), and these MPV values also did not show any significant differences, it can be seen from P-Value that higher than 0.05 (P-Value: 0.521). Moreover, this study also compared the MPV value in all ACS patients without grouping the type of cardiovascular events. Either type of cardiovascular event was found in 34 patients with ACS in General Hospital Haji Adam Malik. The average MPV value of ACS patients with either major cardiovascular event (10.00 fL) was higher than the ACS patients without either major cardiovascular event (9.97 fL), and these MPV values also did not show any significant differences, it can be seen from P-Value that was higher than 0.05 (P-Value: 0.876). This study evaluated the association between MPV value and major cardiovascular events among AMI patients with ST-Elevation. The major cardiovascular events evaluated in this study included heart failure, cardiogenic shock, arrhythmia, and sudden death. The result of this study may become important to improve the length of stay in hospital. Moreover, the result of this study also showed that MPV value was not significantly associated with major cardiovascular events among AMI patients with ST-Elevation. It can be seen from the P-Value (P-Value > 0.05) that heart failure, cardiogenic shock, arrhythmia, death, and all major cardiovascular events were 0.280, 0.464, 0.521, 0.521, and 0.876, respectively.

Mean Platelet Volume (MPV) value is an average platelet volume in the peripheral circulation. The increase of MPV value increases thrombus formation in thrombus in coronary circulation in ACS patients, which is due to the increase of platelet activation, aggregation, adhesion, and secretion of thromboxane. As long as the disease progresses, ACS patients show various major cardiovascular events like heart failure, arrhythmia, and cardiogenic shock as the complications of AMI; it can also end as sudden death [14], [15]. This recent study showed that the ACS patients with ST-Elevation in General Hospital Haji Adam Malik were male (55 patients) that had an average age of 54.7 years old. This recent study showed a similar result against the result of the study from Indriastuti (2020), who was reported that the ACS patients with ST-Elevation had an average age of 60.8 years old. Moreover, Indriastuti (2020) also reported an inline tendency of MPV value. This recent study reported that the tendency of MPV value of ACS patients with ST-Elevation was 9.99 fL. Meanwhile, Indriastuti et al. (2020) reported that the tendency of MPV value was 10.6 fL [16]. Some previous studies also show a similar result. However, none of these previous studies looked for each type of cardiovascular event. Nozari et al. (2013) reported that MPV value did not

significantly associate with any major cardiovascular events; it can be seen from the P-Value > 0.05 (P-Value: 0.562).

However, the MPV value may predict the incidence of major cardiovascular events in ACS patients with diabetes mellitus that did not receive elective percutaneous intervention within one year. Another study showed the opposite result; Tian et al. (2018) reported that the MPV could be used as a prognostic predictor, it can be seen from the P-Value in Receiver-Operating Characteristic Curves that was 0.002 (P-Value < 0.05). However, the Tian et al. also reported that the MPV/PC ration was better than the MPV alone, based on the difference of width area under the curve (P-Value < 0.001 ; Difference: 0.163). Most of these previous studies did not specifically compare the MPV value within each type of major cardiovascular event [17], [18]. The variation in results of the recent and previous study was due to fewer samples in the recent study than the previous study, the distance time between blood withdrawal and analysis, none of defining normal MPV value, and the tendency of lower MPV value in the recent study than the previous study. Moreover, some comorbid conditions may also act as confounder factors. One of these comorbid conditions was diabetes mellitus. Supel et al. (2013) also reported that blood glucose level and cardiogenic shock were significantly associated; it can be seen from P-Value < 0.001 . Tekbas also reported that other parameters like the white blood cell and platelet number, creatinine level, and left ventricle function were significantly associated with death in ACS patients. Furthermore, Cuenca et al. (2012) also reported that the MPV value might predict the occurrence of death in ACS patients within six months; it can be seen from P-Value < 0.05 (P-Value: 0.018) [19], [20].

IV. CONCLUSION

Overall, it can be concluded that there was no significant difference in the average MPV value among either type of major cardiovascular event. Thus, the MPV value can not predict either type of major cardiovascular event incidence among ACS patients in General Hospital Haji Adam Malik.

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