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Correlation of platelet distribution width (PDW) with troponin I based on the onset of chest pain in acute myocardial infarction

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Abstract
Coronary artery disease (CAD) is caused by narrowing of the coronary arteries. In the event of acute myocardial infarction (AMI), there will be an increase in heart markers. Several studies have examined the relationship between Platelet Distribution Width (PDW) and AMI, but there is no specific correlation with troponin as the most sensitive and specific cardiac biomarker for AMI. This study aims to see the correlation PDW values with troponin I based on the onsite of chest pain in patients with AMI. This study was a cross-sectional method to determine the correlation between PDW values and troponin I based on the onsite of chest pain in AMI patients. I. In this study, the sample consisted of 64 people. There is a moderate correlation between PDW and troponin I (r2= 0.72, p <0.001). There is a strong correlation with positive direction between PDW and Troponin I in patients with AMI based on the onset of chest pain (<6 hours and > 6 hours: r2 = 0.647 p <0.001and r2 = 0.756, p <0.001).Platelet Distribution Width (PDW) is strongly correlated with Troponin I in patients with AMI, and based on chest pain onset also has a significantly positive correlation.

Keywords: CAD, AMI, Troponin I, PDW

1. Introduction
Coronary Heart Disease (CHD) is the number one cause of death globally. According to the World Health Organization (WHO) in 2017, an estimated 17.9 million people died from heart disease, representing 31% of all global deaths [1]. In Indonesia, according to data from Riset Kesehatan Dasar (Riskesdas) in 2018, it shows that 1.5 percent or 15 of 1,000 Indonesians suffer from CHD [2]. Acute Coronary Syndrome (ACS) is the main clinical manifestation of CHD and the most frequent cause of death. The clinical manifestations of ACS include unstable angina pectoris, non-ST elevation acute myocardial infarction, and acute myocardial infarction with ST segment elevation (IMA-EST) [3]. In the event of acute myocardial infarction (AMI), there will be an increase in cardiac markers, including Myoglobin (MB), Creatine Kinase Muscle Brain (CKMB), Lactate Dehydrogenase (LDH), Serum Glutamate Oxaloacetate Transaminase (SGOT), Cardiac Troponin T (cTnT) or I (cTnI) as a marker of cardiac myocyte necrosis but cannot be used to determine the cause of the myocyte necrosis. Basically troponin T and troponin I provide balanced information on the occurrence of myocyte necrosis, but troponin I has a higher specificity than troponin T in conditions of renal dysfunction [4]. Based on the research, it was found that the highest diagnostic accuracy was with the troponin I test compared to the troponin T test and other cardiac markers. At the time of admission troponin I test, clinical sensitivity was 90.7%, and specificity was 90.2% [5]. The initial release of troponin comes from the cellular cytosol, whereas the persistent increase is the result of a slower dispersion of troponins from a decrease in cardiac myofilaments. Troponin sensitivity increases with time. At 60 minutes after the onset of acute myocardial infarction, the sensitivity is approximately 90%, and the maximum troponin sensitivity (99%) is achieved up to 6 hours or more after the initiation of myocardial necrosis. Elevated troponins can be detected within 3 to 4 hours after the onset of myocardial injury. Serum levels can remain elevated for 7 to 10 days for troponin I and 10 to 14 days for troponin T [6]. Platelet activation and aggregation play an important role in the pathophysiology of CHD. There will be a greater increase in platelet release with denser granules which are highly metabolically and enzymatically active. Platelets with greater prothromotic potential have higher levels of thromboxane A2, beta thromboglobulin, and intracellular and surface procoagulant proteins. More reactive platelets will undergo morphological changes in cells by forming pseudopods, resulting in thrombus ordering. As a result, the platelets will become larger and reactive, thus increasing the platelet volume index; Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) [7].

PDW is more reliable because MPV measurement can still be affected by blood collection time, some drugs and a pathological condition, therefore PDW can be used as a marker of platelet activation [8]. PDW is an important and simple marker that increases significantly during platelet activation. PDW shows varying platelet sizes. Large immature platelet counts in patients with AMI occur due to increased bone marrow activity during a process known as thrombocytopoiesis [9]. Several previous studies have examined the relationship between PDW and AMI, but in that study there was no specific correlation with troponin as the most sensitive and specific cardiac biomarker for acute myocardial infarction. Based on the information above, the authors wanted to see the correlation between PDW values and troponin I based on the onsite of chest pain in acute myocardial infarction patients.

2. Methods

This study design is a correlative cross-sectional study with consecutive sampling technique. The data used are secondary data from medical records as research subjects. The study were conducted at Haji Adam Malik General Hospital Medan. Sample data had been carried out in January 2020 using medical record data from January to December 2019. The inclusion criteria included (1) all patients who had been diagnosed with acute myocardial infarction on medical records, in this case either with ST elevation ECG images or without ST elevation, (2) patients whose medical records contained information on the value of platelet distribution width (PDW). Exclusion criteria included (1) incomplete medical record data such as time recording of chest pain onset and time of blood sampling, (2) patients diagnosed with other heart disease apart from acute myocardial infarction on medical records, (3) patients with active autoimmune disease, inflammatory disease, and active infection, (4) history of blood transfusions, (5) patients with hematological disorders such as ITP, aplastic anemia, or other diseases that directly affect platelet size and volume, patients with end-stage renal disease undergoing hemodialysis, patients with malignancy.

The data analysis used was univariate analysis to determine the demographic characteristics of this study. Bivariate analysis is an analysis of the variables under study (independent) which are suspected of having a relationship with the dependent variable (dependent). Bivariate analysis used the Pearson correlation test if the distribution was normal and the Spearman correlation test if the distribution was not normal. Data analysis was performed on the correlation of the independent variable (Platelet Distribution Width) with the dependent variable (Troponin I). This analysis is to determine the direction of the correlation between the independent variable and the dependent variable whether it is positive or negative and to predict the value of the dependent variable if the value of the independent variable has increased or decreased.

3. Results and discussions

From the overall medical record data of AMI patients seeking treatment at H. Adam Malik General Hospital Medan in the January-December 2019 period, 64 samples were found that met the inclusion criteria. The characteristics of respondents are listed in the table 1.

Table 1: Characteristics of respondents in acute myocardial infarction

Characteristics	**n = 64 (%)**
Sex	
M	57 (89,1%)
F	7 (10.9%)
Age (Mean ± SD)	55.02 ± 11.02
Hypertension	
Yes	39 (60.9%)
No	25 (39.1%)
Diabetes Mellitus	
Yes	37 (57.8%)
No	27 (42.2%)
Smoking	
Yes	51 (79.7%)
No	13 (20.3%)
Dyslipidemia	
Yes	36 (56.3%)
No	28 (43.8%)
BMI	
< 25	28 (43.8%)
> 25	36 (56.3%)
AMI-type	
AMI-NEST	16 (25%)
AMI-EST	48 (75%)
Laboratory Parameter	**Median (Range)**
Hb (g/dL) (Median (min-max))	(14.3(9.8-17.5))
Leukocytes (Median (min-max))	(10.106(6.670 - 10.980))
Platelet (Median (min-max))	(240.500(156.000-448.000))
PDW (mean ± SD)	13.3 ± 3.04
Troponin I (ng/mL) (Median (min-max))	(4.84(0.58-30.3))
Creatinin (mg/dL) (Median (min-max))	(0.81(0.45 - 1.30))
Blood glucose level (mg/dL) (Median (min-max))	(154(84-293))

Based on the 64 samples above, the researchers divided 32 study samples for each group divided according to the onset of chest pain that is < 6 hours and > 6 hours. The characteristics of the two groups can be seen in the table 2.

Table 2: Characteristics of respondents based on chest pain onset

Characteristics	Onset Chest Pain < 6 hours n = 32 (%)	Onset Chest Pain > 6 hours n = 32 (%)
Sex		
M	27 (84%)	30 (93.8%)
F	5 (15.6%)	2 (6.3%)
Age (Mean ± SD)	56.56 ± 11.05	53.47 ± 10.41
Hypertension		
Yes	18 (56.3%)	21 (65.6%)
No	14 (43.8%)	11 (34.4%)
Diabetes Mellitus		
Yes	19 (59.4%)	18 (56.3%)
No	13 (40.6%)	14 (43.8%)
Smoking		
Yes	27 (84.4%)	26 (81.3%)
No	5 (15.6%)	6 (18.8%)
Dyslipidemia		
Yes	17 (53.1%)	19 (59.4%)
No	15 (46.9%)	13 (40.6 %)
BMI		
< 25	28 (43.8%)	13 (40.6%)
> 25	36 (56.3%)	19 (59.4%)
AMI-type		
AMI-NEST	16 (50%)	8 (25%)
AMI-EST	16 (50%)	24 (75%)
Laboratory Parameter		
Hb (g/dL) (Median (min-max))	(14.55(9.8-17))	(13.9(4.94-19.8))
Leukocytes (Median (min-max))	(10.015(6.670-10.980))	(10.305(6950-11.090)
Platelet (Median (min-max))	245656 ± 56778	256178 ± 67574
PDW (mean ± SD)	12.13 ± 1.33	14.59 ± 3.72
Troponin I (ng/mL) (Median (min-max))	2.04 ± 1.04	18.3 ± 7.78
Creatinin (mg/dL) (Median (min-max))	(0.81(0.45-1.29))	(0.82(0.56-1.30)
Current blood glucose (mean ± SD)	173 ± 61.4	167 ± 59.8

In this study, the Pearson test was conducted to find the correlation between PDW and Troponin I in 32 samples of each group. The results show that there is a significant correlation with the positive direction between PDW and Troponin I in patients with AMI based on the onset of chest pain.

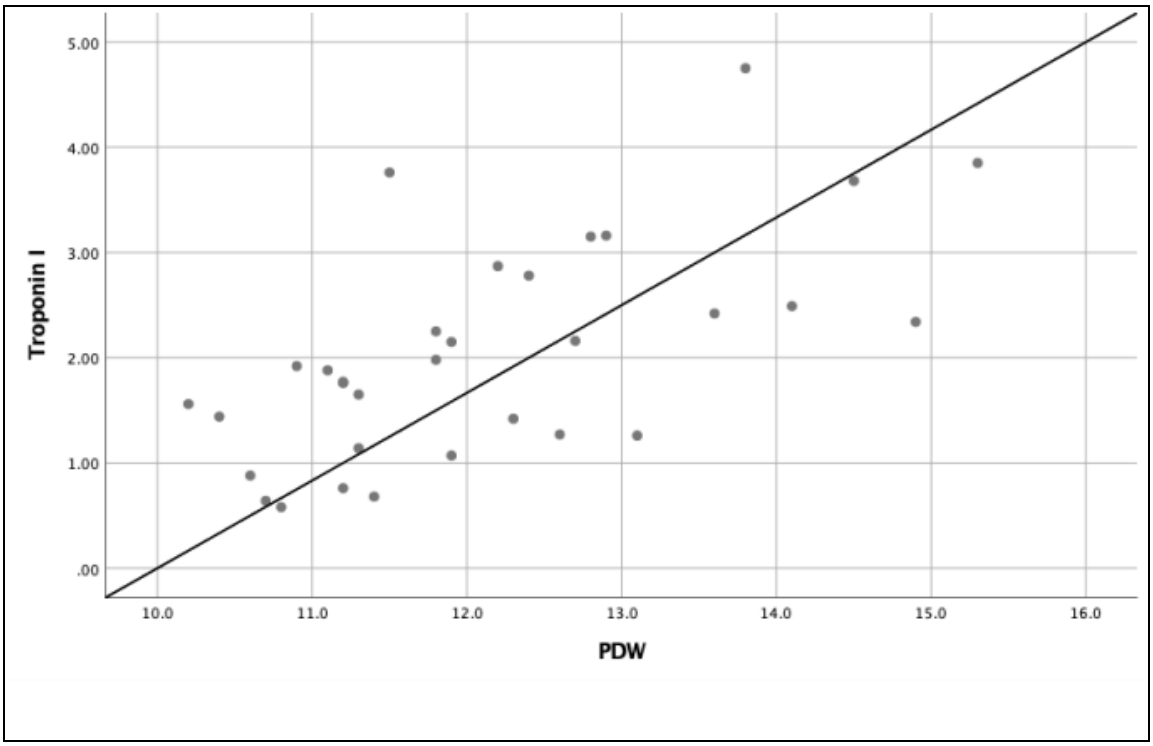

Fig 1: Scatter Plot correlation of PDW with Troponin I based on Chest Pain Onset <6 hours (r =0.647, p < 0.001) in patients with AMI

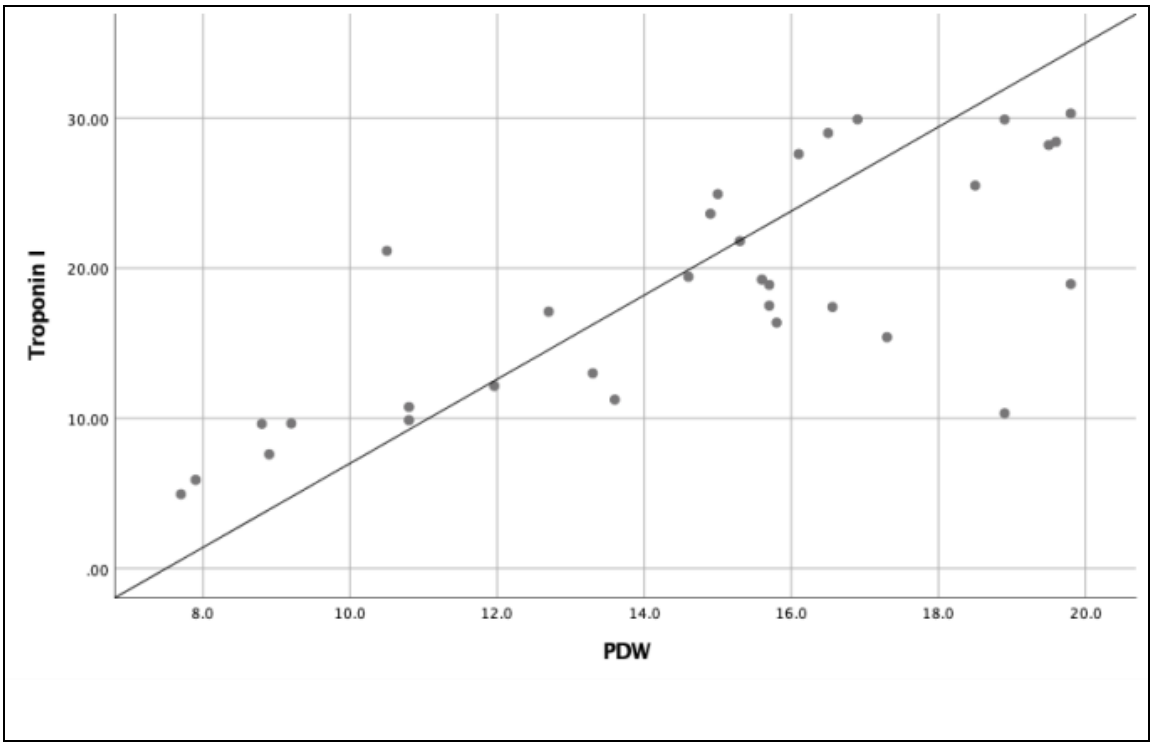

Fig 2: Scatter Plot correlation of PDW with Troponin I based on Chest Pain Onset >6 hours (r =0.756, p < 0.001) in patients with AMI

Based on the onset of chest pain < 6 hours, the men who experienced AMI were bigger than women, namely men 27 (84.4%), women 5 (15.6%). The results were similar at the onset of chest pain> 6 hours in men 30 (93.8%) and women 2 (6.3%). These results are consistent with previous studies. From a research conducted at RSUP Dr. M. Djamil Padang in 2017 found that the prevalence of AMIwas higher in men (70.8%) compared to women (29.2%)[10].Similar to research at RSUP H. Adam Malik Medan in 2018, the prevalence of AMIin men (87.4%) compared to women (12.6%) [11]. AMI is mostly found in men than women. This is caused by the female hormone estrogen which is thought to have a protective effect on vascular endothelium. This hypothesis is based on the increased incidence of AMI in postmenopausal women. The hormone estrogen will increase the release of nitric oxide (NO) which can cause vasodilation, regulation of prostaglandin production, and inhibition of smooth muscle proliferation [12]. Another risk factor that can also influence is smoking habits, which are generally mostly in men than women [13].

The mean age of patients with AMI in this study was 55.02 (± 11.02) years and the mean age of patients who had an onset of chest pain < 6 hours was 56.56 (11.570) years and patients who had an onset of chest pain > 6 hours were 53.47. (10,411) years. These results are also consistent with previous studies. The research conducted at Dr. M. Djamil Padang in 2017, it was found that the average age of patients with AMI was 56.75 (9.34) years [10]. The incidence of AMI increases with age, which is associated with an increase in risk factors such as hypertension, diabetes mellitus, dyslipidemia [14]. The incidence of AMI is up to fivefold in the population aged 40-60 years [13]. Based on the onset of chest pain < 6 hours, 18 people had hypertension risk factors (56.3%), while 14 people did not have hypertension risk factors (43.8%). 21 patients (65.6%) had chest pain on set> 6 hours and 11 (34.4%) had no hypertension risk factors. These results are consistent with previous studies. Research at the Dr. Wahidin Sudirohusodo, Makassar, in 2016, 58.73% of patients who experienced acute myocardial infarction with hypertension were found while those without hypertension were 41.26% [15]. The same thing was also obtained from the results of research conducted at Dr. M. Djamil Padang in 2017, where this study found that most AMI-EST patients had a history of hypertension, as many as 95 people (52.5%) [16]. Increased blood pressure is a heavy burden on the heart, causing left ventricular hypertrophy, this condition depends on the weight and duration of hypertension. High and persistent blood pressure will also cause direct trauma to the walls of the coronary arteries, making it easier to develop atherosclerosis. The more severe the hypertension is, the greater the risk of developing CAD. Based on the onset of chest pain < 6 hours, there were 19 people (59.4%) who had diabetes mellitus risk factors, while 13 people (40.6%) had no diabetes mellitus risk factors. 18 patients with the onset of chest pain> 6 hours had risk factors for diabetes mellitus (56.3%), while 14 people who did not have risk factors for diabetes mellitus (43.8%). These results are consistent with previous studies. Research at RSUD '45 Kuningan in 2014, found that more diabetes cases occurred in cases of acute myocardial infarction, namely 63 people (88.7%) were obtained [17]. Diabetes mellitus is one of the main factors for coronary artery disease and more than 40% of patients with acute coronary syndrome have DM [18]. The increased risk of developing atherosclerosis and further complications in patients with DM is caused by different mechanisms including endothelial dysfunction and abnormal platelet activity as well as impaired coagulation-fibrinolysis balance [19]. Platelet activation is one of the key mechanisms underlying atherothrombosis in acute myocardial infarction, where platelets in diabetic patients are dysregulated by several signaling pathways, which leads to increased platelet reactivity [29]. A number of mechanisms in DM, some are still not known with certainty, are associated with impaired platelet function, activity, adhesion and aggregation [19]. Based on the onset of chest pain < 6 hours, 27 people (84.4%) had risk factors for smoking, while 5 people (15.6%) had no risk factors for smoking. Patients with the onset of chest pain > 6 hours who had risk factors for smoking were 26 people (81.3%), while those who had no risk factors for smoking

were 6 people (18.8%). These results are consistent with previous research studies. Research at the dr. Wahidin Sudirohusodo, Makassar in 2016, it was found that patients who experienced acute myocardial infarction with smoking risk factors were 76.12%, while those who did not smoke were 23.80% [15]. The same thing was also obtained from the results of research conducted at Dr. M. Djamil Padang in 2017, where this study found that most AMI-EST patients had a history of smoking, as many as 122 people (67.4%) [16]. The most traditional risk factor for AMI patients in the study by Amaliah R, Yaswir R, and Prihandani T in 2017 was smoking (41.7%). This result is in accordance with the existing theory, namely smoking is a risk factor that affects the increase in the incidence of coronary heart disease because smoking increases the effects of other risk factors, such as increasing the incidence of hyperlipidemia, hypertension, and diabetes mellitus, which both increase the incidence. Coronary heart disease, and even other heart diseases. Smoking can cause inflammation of blood vessels which results in narrowing of blood vessels, reducing blood flow and oxygen supply to organs including the heart which can lead to myocardial infarction. Smoking causes endothelial injury and dysfunction of the coronary and peripheral arteries, a chronic inflammatory state that contributes to the atherogenic disease process and increases levels of inflammatory biomarkers, which are known to be strong predictors of cardiovascular events. Based on the onset of chest pain < 6 hours, 17 people (53.1%) had risk factors for dyslipidemia, while 15 people (46.9%) had no risk factors for dyslipidemia. Patients with chest pain onset > 6 hours had risk factors for dyslipidemia as many as 19 people (59.4%), while those who did not have risk factors for dyslipidemia were 13 people (40.6%). These results are consistent with previous studies. Research at RSUD '45 Kuningan in 2014, where 56 patients had acute myocardial infarction with dyslipidemia (78.8%) [17]. This case of dyslipidemia simply can be a risk factor for acute myocardial infarction because in the process of disruption of the lipid profile in the blood there is accumulation of fat in the lining of the blood vessels which ultimately reduces the lumen diameter of the blood vessels as a result of which ischemia occurs with subsequent manifestation of infarction. Abnormalities in the lipid profile are a factor in atherosclerosis. Atherosclerosis is a change in the arterial wall characterized by the accumulation of extra cell lipids, causing thickening and stiffness of the arteries. The thickening of the arteries caused by fat deposits due to extra cells causes ischemia in the tissues leading to infarction. High levels of fat in the blood will affect the fat metabolism cycle, so this causes dyslipidemia. The occurrence of dyslipidemia in the body results in atrerokslerosis in the arteries, this process causes the arteries to become blocked. Seventeen patients (53.1%) had chest pain onset <6 hours with a BMI> 25, while 15 (46.9%) had a BMI <25. There were 19 patients with chest pain onset> 6 hours with a BMI> 25 (59.4%), while 13 patients (40.6%) had a BMI <25. High body mass index (BMI) is an independent risk factor for an increased incidence of myocardial infarction and ischemic heart disease [21]. Obesity is associated with a higher incidence of components of the metabolic syndrome, which significantly increases the risk of coronary atherosclerosis. Indeed, risk factors for coronary atherosclerosis (including hypertension, diabetes, and dyslipidemia) are more common in obese individuals than in non-obese subjects [22]. In this study, AMI in the patient group was divided into two groups, AMI with ST-elevation and AMI without ST elevation. In the comparison of the number of patients, the group of patients with ST-elevation was higher than the group of patients without ST-elevation with a ratio of 40 cases (62.5%) for AMI with ST-elevation and 24 cases (37.5%) for AMI without ST elevation. In the comparison of the number of patients, the group of patients with ST-elevation was higher than the group of patients without ST-elevation with a comparison of 16 cases (50%) for AMI with ST-elevation and 16 cases (50%) for AMI without ST elevation at the onset of chest pain <6 hours while ST elevation was also more than the group of patients without ST elevation with a comparison of 24 cases (75%) for AMI with ST-elevation and 8 cases (25%) for AMI without ST elevation at the onset of chest pain> 6 hours. These results are consistent with the study of Bacci *et al*. in Sri Lanka who found the prevalence of STEMI patients to be greater than NSTEMI and UA patients (57.2%; 22.1% and 20.6%) [23]. Research in Indonesia shows the same results as this study, namely the prevalence of AMI patients with ST-elevation is higher than AMI without ST elevation with a ratio of 61% and 39% [24]. The prevalence of AMI with high ST elevation can be caused by the lack of prevention efforts on several risk factors in previous health facilities so that the number of AMI patients with ST-elevation is high [23]. This study found that there was a significant correlation between PDW and Troponin I in acute myocardial infarction patients. With p value and correlation coefficient p <0.001, r = 0.713. This shows that the higher the PDW value, the higher the Troponin I level in patients with acute myocardial infarction. Based on the onset of chest pain, it turned out to have a significant correlation between PDW and troponin I with the correlation value for each group of chest pain onset <6 hours (p<0.001, r = 0.647) and chest pain onset> 6 hours (p<0.001, r = 0.756). Until now there has been no research that directly assesses the correlation between PDW and Troponin I according to the onset of chest pain experienced by patients. Research by Reddy *et al*. regarding changes in platelet volume in STEMI patients comparing the STEMI group with the control group found that the PDW value was significantly higher statistically in the group with STEMI compared to the control group ((17.8 ± 2.2 vs 16.3 ± 0.7)) with a value p <0.001. In the study, there was no direct statistical test between PDW and Troponin I, but the diagnosis of STEMI was adjusted according to the criteria of The Third Universal Definition of Myocardial Infarction, namely an increase in cardiac biomarkers that was very sensitive and specific, namely cardiac troponin I accompanied by one of the symptoms of ischemia, changes in the description of the picture electrocardiography, changes in imaging features and/or identification of intracoronary thrombus on angiographic examination or autopsy [25]. Another study in Sri Lanka in 2018 conducted by Alvitigala *et al*. regarding the relationship between platelet volume parameters and STEMI also found a statistically significant relationship between PDW levels with a cut off of 15.55fL and the occurrence of STEMI (p = 0.000) and a positive correlation with value. r = 0.556, but in this study the diagnosis of STEMI was not specifically explained by examining troponin I levels [7]. PDW reflects a variant in platelet size due to active platelet release. PDW increases when there is an increase in the number of larger platelets as well as smaller platelets in the circulation. This shows the heterogeneity of platelet size by providing the relative width of the distribution of platelets by volume [7]. The most common cause of coronary thrombosis is the rupture of the plaque which allows the platelets to contact the necrotic nucleus which is highly thrombogenic. Larger platelets are

metabolically and enzymatically more active than smaller ones. Larger platelets contain more prothrombotic material, release an increase in thromboxane A2 per unit volume, and exhibit greater glycoprotein IIb-IIIa receptors. PDW increases significantly in patients with STEMI and is an independent predictor of acute STEMI [26]. Troponin is one of the most sensitive and specific biomarkers for detecting damage to the heart muscles. Under normal circumstances troponin T and troponin I am not found in the circulation. Troponins will be released into the circulation when there is necrosis of the heart muscles which is an indicator of damage to the heart muscles [27].Increased levels of cardiac troponin begin at the onset of myocardial infarction 2-3 hours and almost 100% increase in troponin levels in myocardial infarction onset 6 hours to a peak of 24 hours and troponin levels will continue to show an increase in results for up to 1-2 weeks [28]. Limitations in this study were not conducted assessments of outcome outcomes and mortality in the two AMI groups with the onset of chest pain <6 hours and AMI with the onset of chest pain >6 hours so that the average PDW values found in this study cannot be used to determine the prognosis in both groups.

4. Conclusion

Platelet Distribution Width (PDW) is moderately correlated with Troponin I based on chest onset in acute myocardial infarction has a significantly positive correlation.

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