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ASSOCIATION OF PLATELET-TO-LYMPHOCYTE RATIO WITH SEVERITY OF CORONARY ARTERY DISEASE IN PATIENTS WITH ACUTE CORONARY SYNDROMES

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Abstract

Background: Coronary artery disease (CAD) is the leading cause of morbidity and mortality throughout the world. It has a complex pathophysiology, and inflammation seems to play an important role in CAD.Platelet lymphocyte ratio (PLR) is a new prognostic marker that integrates the risk prediction of these 2 parameters into 1. It gives an idea about both the aggregation and inflammation pathways, and it may be more valuable than either platelet or lymphocytecount alone in the prediction of coronary atherosclerotic burden.The SYNTAX score (SXscore) is an anatomic scoring system based on coronary angiography (CA) that not only quantifies lesion severity and complexity. The aim of this study was to investigate the association of PLR with the severity of coronary atherosclerosis as assessed by the SXscore in patients with ACS who underwent urgent CA

Methods: Patients were collected from August to December 2019. A cohort prospective study of 60 ACS patients admitted to the emergency department was studied. Variables such as previous comorbidities, laboratory findings and coronary angiography were evaluated. Admission PLR values were calculated before CA was performed. The PLR were divided into 2 groups, 30 patients with PLR < 116 and 30 with PLR > 116. The SXscore was determined from coronary angiography. The patients were divided into 2 groups, those with low SXscores (<23) and those with intermediate to high SXscores (≥23).

Result: A total of 60 patients with ACS who underwent urgent CA were included in the study fromAugust to Desember 2019. From total 60 patients, there were 25 (42 %) patients had SYNTAX score ≥ 23 and 35 (58%) patients had SYNTAX score < 23. There were significant relation difference between both groups. From chi square analysis, there was significant statistic between platelet lymphocyte ratio and SYNTAX Score (OR: 8,7, p value : 0.001).

Conclusions: In conclusion, theplatelet lymphocyte ratio is significantly associated with the severity of coronary atherosclerosis in patients with ACS

Keywords: Atherosklerosis, Acute Coronary Syndrome, SYNTAX score, platelet-lymphocyte ratio.

Introduction

Cardiovascular disease remains a major burden globally with high morbidity and mortality where 17,5 million deaths are caused by cardiovascular disease every year.[1] In 2014, coronary artery disease was the most comon cause of death after stroke in Indonesia at 12.9%.[2] Acute manifestation of coronary artery disease is acute coronary syndrome, a life threatening condition, consist of Unstable Angina Pectoris (UAP), Non ST-segment Elevation Myocardial Infarction (NSTEMI), ST-Segment Elevation Myocardial Infarction (STEMI).[3]

Inflamation is an essential process in atherosclerosis, and many inflamatory markers have been analyzed in relation with major adverse outcomes in various cardiovascular diseases. Previous studies have shown that higher levels of inflammatory markers are associated with theseverity of CAD and worse cardiovascular outcome. Previous studies have demonstrated an association between high circulating platelet count and major adverse cardiovascular outcomes in patientswith CAD.[4]Platelet tolymphocyte ratio (PLR) is a new prognostic marker that integrates the risk prediction of these two parameters. It gives an idea about both the aggregation and inflammation pathways, and it may be more valuable than either platelet or lymphocyte count alone. [5]

SYNTAX Score is a score system that is comprehensive formulated to describe the complexity of coronaryartery based lesionsan giographic results. A higher SYNTAX score indicates a more complex disease and a worse prognosis. SYNTAX score can be quantifies the complexity of coronary artery lesions by not calculatingonly the number of lesions that is significant and their location, but the complexity of each lesions independently.[6,7]

Because it is well known that inflammatory response is closely associated with the pathogenesis of coronary atherosclerosis, we aimed to investigated the relationship between platelet lymphocyte ratio with in severity of coronary artery as assessed by the SYNTAX score in patients with acute coronay syndrome who underwent coronary angiography.

Methods

This study is an observational cohort study which perfomed at Haji Adam Malik General Hospital Medan with permisson from Research Ethics Commitee of Faculty of Medicine, Universitas Sumatera Utara-RSHAM. Subjects were recruited from August to December 2019. The inclusion criteria were patients who were clinically confirmed as acute myocardial infarction and undergoing coronary angiography procedure and never had revascularization either Percutaneuous Coronay Intervention (PCI) or Coronry Artery Bypass Graft (CABG) procedure before. While exclusion criteria were missing medical record, patients with blood disorders, liver disease, or malignancies, such as leukemia, lymphoma, idiopathic thrombocytopenic purpura, hemophilia, sepsis, liver cirrhosis and cancer.

Study Procedure

Subjects clinical and demographic charcteristics who admitted in the ER with acute myocardial infarction as working diagnose were recorded. Blood samples were taken from all subjects upon admisson. the ratio of platelet lymphocytes was calculated. The lymphocyte platelet ratio was from the calculation of the platelet value divided by the lymphocyte value. The patients were performed coronary angiography to assess coronary artery lesions. The severity of coronary artery lesions will be assessed using a SYNTAX score.

Statistical Analysis

Categorical variables are presented by number or frequency (n) and percentage (%). Numerical variables are represented by mean and standard deviation for normally distributed data, if data not normally distributed, the data shown by median. For bivariat analysis, Chi Square test was conducted between Platelet Lymphocyte Ratio and SYNTAX Score

Result

A total of 60 patients ith acute myocardial infarction were included in this study. Most of the subjects were men (85%) with average age of years old. Subjects with majority of traditional cardiovascular risk factors were seen in this study, such obesity with median BMI of 26,3 ± 3,05, 58,3% with history of hypertension, 46,7% with history of diabetes mellitus and 61,7% were smoker. Subject with ST- segment elevation myocardial infarction (STEMI) were 35%, subject with Non ST- segment elevation (NSTEMI) were 33%, and the rest were diagnosed with Unstable Angina Pectoris. The PLR were divided into 2 groups, 30 patients with PLR < 116 and 30 with PLR > 116. The SXscore was determined from coronary angiography. The patients were divided into 2 groups, those with low SXscores (<23) and those with intermediate to high SXscores (≥23)

Table 1. Baseline Characteristics

Variables	(n:60)
Age, (years)	52,8 ± 8,4
Gender (n,%)	
Male	51 (85%)
Female	9 (15%)
BMI, kg/m2	26,3 ± 3,05
UAP	19 (32%)
NSTEMI	20 (33%)

STEMI	21 (35%)
Family History	
DM	28 (46.7%)
Hypertension	35 (58.3%)
Smoker	37 (61.7%)
Laboratory	
Hb	13,6 ± 1,6
Ht	39,5 ± 4,8
Leukocyte	11.085 (6260-16.340)
Lymphocyte	2,0 ± 0,75
Platelet	240 (140-489)
Glucose ad random	120 (70-337)
Fasting blood glucose	140 (78—328)
HbA1c	5,9 (4,4-11,2)
Ureum	30 (17-73),
Creatinine	1,05 (0,4-2,2)
Cholesterol Total	166 ± 43,7
Trigliserida	127 (58-364)
HDL	39,2 ± 8,8
LDL	109 ± 37

All the subjects were divided into two groups, patients with SYNTAX Score < 23 were 35 patients, and patient with SYNTAX Score > 23 were 25 patients.

Table 2. Baseline Characteristics based on SYNTAX Score

Variables	**SYNTAX**		
	<23 (n= 35)	**≥23 (n= 25)**	**P value**
Age	51 ± 9	55 ± 7,5	0,096
Hypertension	17 (48%)	18 (72%)	0,070
Smoker	20 (57%)	19 (76%)	0,131
DM	12 (34%)	16 (64%)	0,023
Dislipidemia	9 (52%)	8 (47%)	0,594
Gender			
Male	30 (85%)	21(84%)	0,855
Female	5 (15%)	4 (16%)	
BMI	26,15 ± 3,02	26,52 ± 3,15	0, 648
Glucose ad Random	113 (70-337)	152 (83-268)	0,002
Fasting Blood Glucose	104 (70-246)	131 (85-281)	0,011
Postprandial Blood Glucose	122 (78-283)	172 (102-328)	0,016
HbA1c	5,8 (4,4-11,2)	6,4 (5,1-10,4)	0,031
Hb	13,59 ± 1,72	13,62 ± 1,45	0,957
Ht	39,6 ± 5,20	39,4 ± 4,37	0,876
Leukocyte	10110 (7370-16340)	11.440 (6260-16240)	0,170
Platelet	251 (140-489)	213 (140-419)	0,397
Lymphocyte	2,30 ± 0,72	1,68 ± 0,66	0,002
PlateletLymphocyte Ratio	107 (51,5-337)	144 (58-405)	0,002
Creatinine	1,02 (0,43-2,1)	1,13 (0,4-2,2)	0,348
Cholesterol total	170,77 ± 39,85	160,40 ± 48,90	0,370
Trigliserida	139,7 (69-364)	137,3 (58-302)	0,857
HDL	39,77 ± 9,24	38,48 ± 8,38	0,582
LDL	116,94 ± 33,38	99,96 ± 41,29	0,048
Diagnosis			

UAP	13 (37%)	6 (24%)	0,125
NSTEMI	8 (23%)	12 (48%)	
STEMI	14 (40%)	7 (28%)	

From table 2, we can see statistically significant different between two groups in terms of some parameters, namely age, hypertension, DM, glucose ad random, platelet lymphocyte ratio, etc. The average age of the SYNTAX score ≥ 23 was higher than the group with SYNTAX score < 23. The median of platelet lymphocyte ratio of the SYNTAX Score ≥23 was higher than the group with SYNTAX score < 23. The diagnosis of NSTEMI was more common in the group with SYNTAX score ≥ 23

(12 people, 48%), while STEMI was more common in the group with SYNTAX score < 23 (14 people, 40%).

Table 3. Association between Platelet Lymphocyte Ratio with SYNTAX Score

PLR	SYNTAX		Total	P	OR
	< 23	**≥23**			
< 116	24	5	29		
> 116	11	20	31	0,001	8,7
Total	35	25	60		

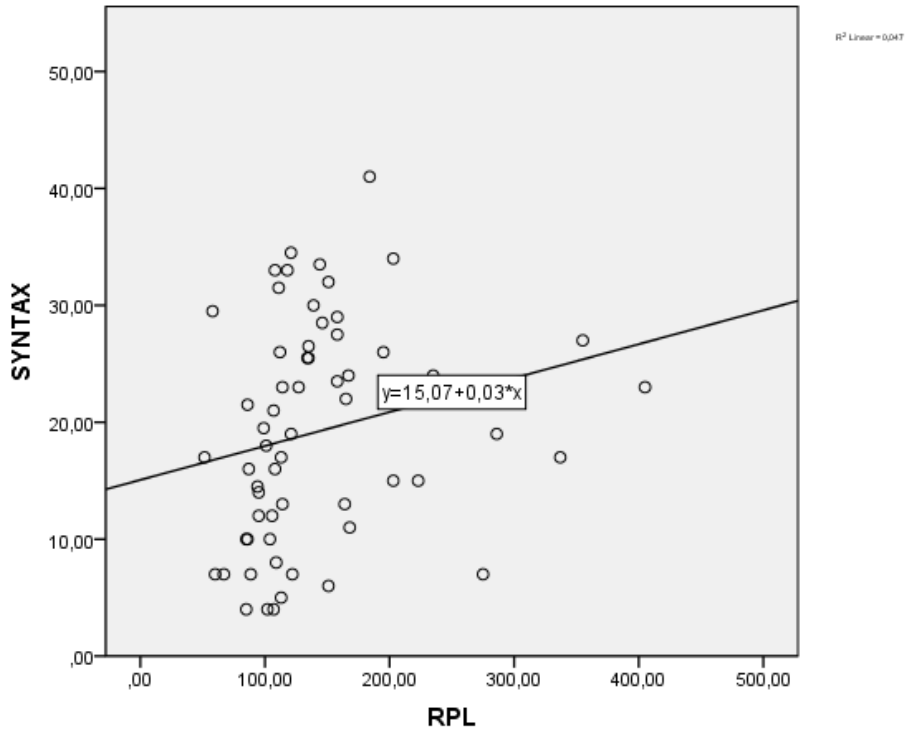

Figure 1. Correlation between Platelet Lymphocyte Ratio with SYNTAX Score

From the bivariate analysis, we found that platelet lymphocyte ratio was significantly associate with SYNTAX score, with moderate correlation (p : 0,001 ; r : 0,42)

Discussion

This research is a cross sectional to find out relationship between platelet lymphocyte ratio with severity of coronary lesion in patient with acute myocardial infarction. This research was conducted at RSUP Adam Malik Medan from August to November 2019 and involved 60 subjects that met inclusion and exclusion criteria.

Acute myocardial infarction patients in this study consisted of UAP, NSTEMI and STEMI. The number of ST elevation myocardial infarction (STEMI) cases in our study was higher in patients with SYNTAX score < 23 compared to SYNTAX score ≥ 23. (40% vs 28%). Overall, the STEMI incidence in our study was higher than the other types of acute coronary syndrome.

From 60 subjects, there were51 male (85%) and 9 female (15%) patients. Our data was similar with previous studies by Kurtul 2014, in which higher incidence of acute coronary syndrome was found in men than women. We found that subjects with SYNTAX score ≥ 23 had a higher precentage of diabetes mellitus than subjects with SYNTAX score < 23 (64% vs 34%). This is in accordance with research conducted by Kurtul (2014), where higher SYNTAX score associate with higher incidence diabetes mellitus. Diabetes melitus is a associated with micro or macro complications of blood vessels, which initiate the process of atherosclerosis, such as endothelial dysfunction of blood vessels.[4,5]

Our study showed that subjects with a SYNTAX score ≥ 23 had a greater percentage of high blood pressure history compared to a SYNTAX score <23 (72% vs 48%).This is in accordance with research conducted by Yuksel2015, that subjects with high coronary artery severity have a higher percentage of high blood pressure when compared to low coronary artery severity. The theory also supports that high blood pressure is one of the risk factors for acute coronary syndrome.[4]

Another factor was smoking, which in this study found a significant difference between both groups (p : 0,131). Subjects with a SYNTAX score ≥23 had a percentage of 76% and subjects with a SYNTAX score <23 had a percentage of 57%. This is accordance conducted by Kurtul (2014)where research subjects with a SYNTAXscore ≥ 23 have a higher percentage of smoking history compared to a SYNTAX score <23.[4]

The median of platelet lymphocyte ratio in subjects with SYNTAX score ≥ 23 was higher than subject on SYNTAX score < 23 (144 vs 107). This fact supports a theory the pathophysiology of acute coronary syndrome, which suggest that inflamatory process is correlated with severity of the lesion. Several previous studies have demonstrated that there is a correlation between increase platelet lymphocyte ratio and the severity of coronary lesion. Platelets and inflammation play an important role in the pathophysiology of CAD. In cases of sustained inflammation, lymphocyte counts decrease due to increased lymphocyte apoptosis. Also, ongoing inflammatory conditions lead to increased proliferation in megakaryocytic series and relative thrombocytosis.[5]Previously platelet lymphocyte ratio were also used as predictors in the assessment of major cardiovascular events. Like a meta-analysis study conducted by Li et al (2017). From the results of the study concluded that the high platelet lymphocyte ratio can be an independent factor in determining mortality or major cardiovascular events in patients with acute coronary syndrome.[8]

The advantage of platelet lymphocyte ratio calculation could be that it reflects the condition of both aggregation and inflammatory pathways, and it may be more valuable than either platelet or lymphocyte count alone in the prediction of coronary atherosclerotic burden. In a study conducted by Reddy (2014) also found a significant correlation between the platelet lymphocytes ratio to the severity of coronary artery lesions. In a study conducted by Yuksel(2015) and Wahyuni (2018) also concluded that platelet lymphocytes ratio can be used as a predictor of severity of coronary artery lesions. [9,10]

There is some limitation of this study such as limited sample, this study investigated the relationship between platelet lymphocyte ratio 116 as a cut off point with severity of coronary artery as assessed by the SYNTAX score. This research is an observational analytic study so the causal relationship cannot be ascertained. Future studies are expected to be carried out by involving many hospitals and more samples, and needed to determine the new cut off point.

Conclusion

The platelet lymphocyte ratio was significantly associate with SYNTAX score, with moderate correlation

Conflict of Interest

The authors declare that there is no conflict of interest.

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