VOLUME-8, ISSUE-8, AUGUST-2019 • PRINT ISSN No. 2277 - 8160

Original Research Paper

Medicine

ASSOCIATION BETWEEN PLATELET-LYMPHOCYTE RATIO (PLR) AND NUMBER OF CORONARY ARTERY LESIONS IN PATIENTS WITH ACUTE CORONARY SYNDROME

Zenith*

Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara, H. Adam Malik General Hospital, Medan, Indonesia
*Corresponding Author

Rahmad Isnanta

Division of Cardiology, Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara, H. Adam Malik General Hospital, Medan, Indonesia

Refli Hasan

Division of Cardiology, Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara, H. Adam Malik General Hospital, Medan, Indonesia

ABSTRACT

Introduction : Acute Coronary Syndrome (ACS) is one of the clinical manifestations of Coronary Heart Disease (CHD) that has high morbidity and mortality. Atherosclerosis is the underlying process of CHD. Inflammation plays an important role in the process of atherosclerosis. Prospective studies suggest that Platelet-to-Lymphocyte ratio (PLR) is one of the predictors of cardiovascular events. Through this study, it is expected to give an illustration of the relationship between PLR value and the number of coronary artery lesions in acute coronary syndrome patients undergoing coronary angiography.

Aim : To determine the relationship between PLR value and the number of coronary artery lesions in patients with Acute Coronary Syndrome

Methods : This was a observational study of 80 consecutive ACS patients who came to Adam Malik General Hospital Medan, from March to June 2019. Evaluation of PLR value, blood tests, and coronary angiography were performed in each subject. The number of coronary artery lesions were assessed by Vessel Score. Furthermore, the calculated PLR values are associated with Vessel scores using Chi-Square analysis.

Results : From 80 research subjects, there were 33 (41.25%) subjects with Simple Vessel Disease (SVD) and 47 (58.75%) subjects with Multi Vessel Disease (MVD). Based on the results of the ROC analysis, it was found that the PLR cut-off point value of the Vessel Score was 109.88 with a sensitivity of 78.7% and specificity of 81.8% with a significant strength ($p < 0.001$). The median of PLR in subjects with SVD was 101.90 (90.67-225.81) while in subjects with MVD was 185.83 (94.74-265.44). In the Chi-Square analysis, there was a significant relationship between PLR value and Vessel score ($p < 0.001$).

Conclusion : There is a significant relationship between PLR value and the number of coronary artery lesions in ACS patients.

KEYWORDS : Acute Coronary Syndrome, PLR, Vessel Score, Angiography

INTRODUCTION

Cardiovascular disease is the leading cause of death globally. Based on data from the World Health Organization (WHO) it is estimated that around 17.7 million people died from cardiovascular disease in 2015, representing 31% of all global deaths. Of these deaths, an estimated 7.4 million are caused by Coronary Heart Disease (CHD) and 6.7 million caused by stroke whereas more than 3/4 of deaths from cardiovascular disease occur in developing countries with low to moderate income.[1]

Among the most common and severe forms of CHD are Acute Coronary Syndrome (ACS), which includes unstable angina pectoris (UAP), acute myocardial infarction without ST-segment elevation (NSTEMI), and acute myocardial infarction with ST segment elevation (STEMI).[2]

It is known that inflammation has played an important role in the initiation and propagation of the atherosclerotic process that underlies cardiovascular disease.[3] The interaction between inflammation and thrombosis has an important factor in the pathogenesis of ACS.[4]

Platelets have a major role in atherothrombotic processes and increased platelet counts are associated with increased infarct size and short and long-term poor prognosis in patients with SKA.[5] Increased platelet activation is known to trigger atherosclerosis and play a major role in its development.[2] In sustained inflammatory conditions it can cause an increase in excessive megacaryocyte proliferation and relative thrombocytosis.[3] Increased platelet counts are strongly associated with severe cardiovascular complications.[2]

Lymphocytes have been shown to modulate immunological responses at all stages of the atherosclerotic process.[2] Lymphocyte counts are inversely correlated with inflammation.[6] Low lymphocyte counts have also been shown to be associated with worse cardiovascular complications in patients with cardiovascular disease and chronic heart failure.[3] Low lymphocyte counts are worse prognostic markers in patients with CHD.[5] In cases of sustained inflammation, the number of lymphocytes decreases due to increased lymphocyte apoptosis.[3]

Platelet-to-Lymphocyte Ratio (PLR) is a new prognostic marker that integrates risk predictions from these 2 parameters (platelets and lymphocytes) into 1. This PLR provides an overview of aggregation and inflammatory pathways, and may be more valuable than platelet or lymphocyte counts individually in predicting coronary atherosclerotic load.[3] Platelet-to-Lymphocyte Ratio (PLR) is calculated as the ratio of platelet counts to lymphocytes (obtained from the same blood sample) and can be obtained from a complete blood examination where the test is classified as routine, automatic, inexpensive and easy which provides information about erythrocytes, leukocytes and platelets.[7]

Platelet-to-Lymphocyte Ratio (PLR) has recently been investigated as a new marker of inflammation and a major prognostic predictor in a variety of cardiovascular diseases.[8] PLR value, as an indicator of interactions between platelets and lymphocytes, seems to be a new marker for prothrombotic

and inflammatory status and can predict long-term hospital and major adverse cardiovascular events (MACE) in populations with IMA-EST.[9]

Platelet-to-Lymphocyte Ratio (PLR) can predict the development of no-reflow, and severity of CHD and hospital mortality in patients undergoing primary Percutaneous Coronary Intervention (pPCI).[5,10,11]

PLR is significantly related to the severity and complexity of coronary atherosclerosis in patients with SKA who undergo urgent Coronary Angiography (CA) so that it can be used for risk stratification in patients with CHD.[8]

So, based on the description in the background above, the researchers tried to prove whether there was a relationship between PLR values and the number of coronary artery lesions in acute coronary syndrome (ACS) assessed through angiography.

METHODS

This study was an observasional retrospective study on 80 consecutive acute coronary syndrome patients whom were recruited from Adam Malik General Hospital, Medan, Indonesia between November 2017 and October 2018. Acute coronary syndrome was confirmed by a cardiologist using angiography. Exclusion criteria were acute coronary syndrome patients with any history of; Percutaneous Transluminal Coronary Angioplasty (PTCA), Coronary Artery Bypass Grafting (CABG), chronic liver disease, chronic renal disease, malignancies, systemic colagen disease, infection, or acute coronary syndrome patients with history of trauma, surgery, and burns. This study was approved by the Institutional Review Board of Universitas Sumatera Utara.

The number of coronary arterial lession was assessed by angiography and classified according to Vessel Score which translated into: Simple Vessel Disease (SVD) – shows either one or null stenosis on any of the main coronary arteries with stenosis ≥ 50 % and Multi Vessel Disease (MVD) – shows 2 or more stenosis on any of the main coronary arteries with stenosis ≥ 50 %.

All basic data such as age, sex, risk factors, routine blood examination, angiography, Vessel Score were tabulated, described and processed using statistical software. Receiver-operating characteristic (ROC) analysis will be used to detect the cut-off of the Platelet-Lymphocyte Ratio (PLR) value. Chi-Square test was used to determine the relationship of Platelet-Lymphocyte Ratio (PLR) on the number of stenosed coronary arteries. Data were analysed using computer statistical tests with p values <0.05 were considered statistically significant. Independent T test (normal distribution) or Mann-Whitney test (abnormal distribution) were used to analyze the differences in laboratory parameters between SVD and MVD.

RESULTS

This study was attended by 80 research subjects. There were 65 male (81.3%) and 15 female (18.8%) research subjects. The mean of the research subjects' age was 55.56 years. The risk factors of the study subjects were 65 subjects (81.3%) smoke, 24 subjects (30.0%) have hypertension, 43 subjects (53.8%) have Diabetes mellitus, and 64 subjects (80%) have dyslipidemia. There were 55 subjects (68.8%) who have BMI ≥ 25 kg / mm^2.

Based on the results of coronary angiography examination, the most occlusions were obtained in 29 people (36.3%) of 3 VD and 26 people (32.5%) of 1 VD, while 2 VD were found in 18 people (22.5%) and there is only 7 people (8.8%) in 0 VD. The types of acute coronary syndrome suffered by the most research subjects were STEMI as many as 52 people (65.0%), NSTEMI as many as 16 people (20.0%), and UAP as many as 12 people (15.0%).

Table 1. Basic and Clinical characteristics of subjects

Characteristics	n (%)
Sex	
Male	65 (81,3%)
Female	15 (18,8%)
Age (years), (Mean ± SD)	55,56 ± 7,974
Risk Factors	
Smoking	65 (81,3%)
Hypertension	24 (30,0%)
Diabetes mellitus	43 (53,8%)
Dyslipidemia	64 (80,0%)
BMI (kg/m^2)	
<25	25 (31,3%)
≥25	55 (68,8%)
Coronary Angiography (*Vessel Score*)	
0 VD	7 (8,8%)
1 VD	26 (32,5%)
2 VD	18 (22,5%)
3 VD	29 (36,3%)
Type of Acute Coronary Syndrome	
STEMI	52 (65,0%)
NSTEMI	16 (20,0%)
UAP	12 (15,0%)
Laboratory Examination, (Mean ± SD)	
Hemoglobin (g/dl)	13,91 ± 1,969
Leucocyte (sel/mm^3)	12.176,53 ± 5.111,71
Lymphocyte (sel/mm^3)	1.802,0 ± 639,55
Thrombocyte (sel/mm^3)	256.875 ± 89.305,247
PLR (Mean ± SD)	151,076 ± 52,030
Troponin I (μg/L)	7,98 ± 9,620
CKMB (U/L)	206,66 ± 159,516
Random PG (mg/dl)	163,63 ± 97,046
Fasting PG (mg/dl)	133,70 ± 72,147
2-h PG (mg/dl)	170,59 ± 76,879
A1c	8,80 ± 9,735
Total Cholesterol (mg/dl)	175,31 ± 44,47
Triglycerides (mg/dl)	164,73 ± 133,97
HDL (mg/dl)	35,35 ± 9,59
LDL (mg/dl)	115,44 ± 34,09

Based on the results of routine blood tests, we obtained an average hemoglobin of 13.91 ± 1.969 g/dl, an average of leukocyte counts of 12,176.53 ± 5,111.71 cells/mm^3, lymphocyte counts 1,802.0 ± 639.55 cells/mm^3, platelets 256,875 ± 89,305,247 cells/mm^3, Platelet-Lymphocytes Ratio (PLR) values 151.076 ± 52.030. On examination of cardiac enzymes, the average level of Troponin I was 7.98 ± 9,620 μg/L and CKMB level was 206.66 ± 159.516 U/L. On examination of blood glucose, we obtained an average random PG of 163.63 ± 97.046 mg/dl, fasting PG 133.70 ± 72.147 mg/dl, 2h-PG of 170.59 ± 76.887 mg/dl, $HbA1_c$ 8.80 ± 9.735%. On examination of the lipid profile, we obtained an average level of total cholesterol 175.31 ± 44.47 mg/dl, triglycerides 164.73 ± 133.97 mg/dl, HDL cholesterol 35.35 ± 9.59 mg/dl, and LDL cholesterol 115 , 44 ± 34.09 mg/dl.

Table 2. Association between subjects' characteristics and Vessel Score

Characteristics	*Simple Vessel Disease* (n=33)	*Multi Vessel Disease* (n=47)	p
Sex			
Male	26 (78,8%)	39 (83,0%)	0,773[c]
Female	7 (21,2%)	8 (17,0%)	
Age	53,67 ± 6,278	56,89 ± 8,798	0,075[a]
Smoking			

Yes	26 (78,8%)	39 (83,0%)	0,773[c]
No	7 (21,2%)	8 (17,0%)	
Hypertension			
Yes	10 (30,3%)	14 (29,8%)	1,000[c]
No	23 (69,3%)	33 (70,2%)	
Diabetes mellitus			
Yes	12 (36,4%)	31(66,0%)	0,012[c]
No	21 (63,6%)	16 (34,0%)	
Dyslipidemia			
Yes	23 (69,7%)	41(87,2%)	0,087[c]
No	10 (30,3%)	6 (12,8%)	
BMI			
<25	12 (36,4%)	13 (27,7%)	0,467[c]
≥25	21 (63,6%)	34 (72,3%)	
Hemoglobin	14,20 (9,70-17,40)	14,20 (7,90-17,60)	0,762[b]
Leucocyte	10.500,48 ± 3.301,62	13.353,32 ± 5.819,06	0,013[a]
Lymphocyte	1.950 (850-3.880)	1.690 (450-3.560)	0,007[b]
Thrombocyte	203.000 (94.000-420.000)	274.000 (102.000-450.000)	0,005[b]
PLR	101,90 (90,67-225,81)	185,83 (94,74-265,44)	<0,001[b]
Troponin I	4,19 (0,00-29,41)	4,60 (0,00-49,00)	0,338[b]
CKMB	181,06 ± 128,86	224,64 ± 177,05	0,231[a]
Random PG	116 (79-407)	136 (64-559)	0,054[b]
Fasting PG	101 (81-430)	105 (82-457)	0,457[b]
2-h PG	129 (93-360)	158 (87-430)	0,159[b]
A1c	6,2 (5,0-75,0)	6,9 (4,9-59,0)	0,006[b]
Total Cholesterol	160 (111-307)	169 (85-283)	0,440[b]
Triglycerides	135 (63-1158)	133 (57-360)	0,685[b]
HDL	36,21 ± 9,00	34,74 ± 10,03	0,504[a]
LDL	112,97 ± 33,93	117,17 ± 34,45	0,591[a]

[a]Independent T [b]*Mann-Whitney* [c]*Chi Square*

Subjects with Diabetes mellitus experienced more MVD compared to SVD by 31 people (66.0%) and 12 people (36.4%) respectively. There was a significant relationship between Diabetes mellitus and Vessel Score (p = 0.012). the median levels of $A1_c$ were higher in subjects suffering from MVD 6.9 (4.9-59.0)% compared to median levels of SVD subjects 6.2 (5.0- 75.0)%. There was a statistically significant difference between $A1_c$ levels and Vessel Score (p = 0.006).

The average leukocyte counts were higher in subjects suffering from MVD 13,353.32 ± 5,819.06 cells/mm^3 compared to counts in SVD subjects 10,500.48 ± 3,301.62 cells/mm^3. There was a statistically significant difference between leukocyte count and Vessel Score (p = 0.013).

The median lymphocyte counts were lower in subjects suffering from MVD 1,690 (450-3,560) cells/mm^3 compared to counts in SVD subjects 1,950 (850-3,880) cells/mm^3. There was a statistically significant difference between lymphocyte count and Vessel Score (p = 0.007).

The median platelet counts were higher in subjects suffering from MVD 274,000 (102,000-450,000) cells/mm^3 compared to counts in SVD subjects 203,000 (94,000-420,000) cells/mm^3. There was a statistically significant difference between platelets count and Vessel Score (p = 0.005).

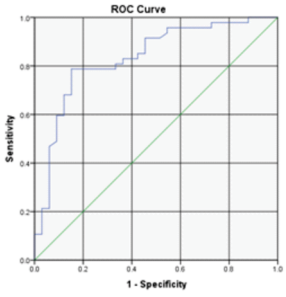
Based on the results of PLR calculations, the median PLR values were higher in subjects suffering from MVD 185.83 (94.74-265.44) compared to the median PLR values suffering from SVD 101.90 (90.67-225.81). There was a statistically significant difference between the PLR values and the Vessel Score (p <0.001).

Based on the results of the ROC analysis (Figure 1.), we found that the cut-off point for PLR value of the Vessel Score was 109.88 with a sensitivity of 78.7% and a specificity of 81.8% and had a significant strength (p <0.001) expressed by the area under the curve (AUC = 0.834 CI: 0.741-0.926). (Table 3.)

Table 3. Cut-off point for PLR (Platelet-Lymphocyte Ratio) to Vessel Score

AUC		*Cut-off*	p	*Confidence Interval* 95%
0,834		109.8850	<0,001	0,741	0,926
Sens = 78,7%	Spec = 81,8%	PPV = 86%	NPV = 73 %	PLR = 4,32	NLR = 0,26

Figure 1. ROC Curve for PLR (Platelet-Lymphocyte Ratio) to Vessel Score



After conducting an ROC analysis to find the cut off point of the PLR value against the Vessel Score, in Table 4 shows the relationship between the cut off of the PLR and the Vessel Score. The percentage of research subjects who had high PLR values were found to have suffered from MVD than SVD which is 37 subjects (86%) and 6 subjects (14%) respectively. There was a statistically significant difference between the PLR scores and the Vessel Score (p <0.001).

Table 4. Association between PLR *(Platelet-Lymphocyte Ratio)* and *Vessel Score*

		Vessel Score		p*	*Prevalance RatioPrevalance Ratio*
		Multi vessel disease	*Simple vessel disease*		
PLR Cut-off	High PLR	37 (86%)	6 (14%)	<0,001	3,184 (1,85 - 5,48)
	Low PLR	10 (27%)	27 (73%)		
	Total	47 (100,0%)	33 (100,0%)		

DISCUSSIONS

In this study, we found association between Diabetes mellitus and Vessel Score, association between A1c with Vessel Score. Increased blood glucose levels in patients with Diabetes mellitus are risk factors for the occurrence of acute coronary syndrome, this can be explained through the pathogenesis of ACS through the process of atherosclerosis and inflammation of the endothelium which will affect the elasticity of blood vessels.

In this study, low PLR values were found to be more likely to have SVD than to have MVD, whereas the percentage of research subjects who had high PLR values were more likely to have MVD. There is a statistically significant difference between PLR value and Vessel Score. The results of this study have also been reported by Kurtul et al. that multi vessel disease and total chronic occlusion are more common in patients with high-intermediate SX scores and is significantly related to PLR levels.[8] In conjunction with our study, Ayca et al. also reported that High Platelet-Lymphocyte Ratio (PLR) values are also associated with high No Reflow events, high Syntax score (SXS), and high mortality rates in patients undergoing pPCI.[5]

In this study, we found statistically significant difference between leukocyte counts and Vessel Score, as well as lymphocyte counts and platelet counts. This is in accordance with the ACS pathogenesis theory that activation of inflammatory cells has a key role in the mechanism leading to plaque instability and erosion, or functional changes in epicardial coronary arteries. Increased levels of leukocytes can reflect the process of atherosclerosis and the extent of occlusion in SKA patients.[13] Lymphocyte count is inversely correlated with inflammation.[6] Low blood lymphocyte counts have also been associated with worse cardiovascular complications in patients with cardiovascular disease and chronic heart failure.[3] In STEMI patients, high platelet counts at hospital admission is independently associated with worse clinical outcomes, whereas a greater decrease in platelet count is subsequently associated with an increased risk of higher reinfarction.[14]

Yayla also reported that the value of Platelet-Lymphocyte Ratio (PLR) at hospital admission was significantly related to the severity and complexity of atherosclerosis in SKA patients as a strong predictor and independent of Infarct-Related Artery (IRA) Patency in patients with IMA-EST before pPCI.[12] High Platelet-Lymphocyte Ratio (PLR) values are also associated with recurrent myocardial infarction, heart failure, ischemic stroke, and are also at risk for long-term complications.[4,15]

CONCLUSION

There is a significant relationship between PLR value and the number of coronary artery lesions in ACS patients.

REFERENCES

1. World Health Organization. 2015. WHO Cardiovascular diseases fact sheets. Available from: http://www.who.int/mediacentre/factsheets/fs317/en/ [25 April 2018].
2. Oylumlu M, Yildiz A, Oylumlu M, et al. Platelet-to-lymphocyte ratio is a predictor of in-hospital mortality patients with acute coronary syndrome. Anatolian journal of cardiology. 2015;15(4):277-283.
3. Yuksel M, Yildiz A, Oylumlu M, et al. The association between platelet/lymphocyte ratio and coronary artery disease severity. Anatolian journal of cardiology. 2015;15(8):640-647.
4. Li W, Liu Q, Tang Y. Platelet to lymphocyte ratio in the prediction of adverse outcomes after acute coronary syndrome: A meta-analysis. Vol 72017.
5. Ayca B, Akin F, Celik O, et al. Platelet to lymphocyte ratio as a prognostic marker in primary percutaneous coronary intervention. Platelets. 2015;26(7):638-644.
6. Crea F, Libby P. Acute Coronary Syndromes. Circulation. 2017;136(12):1155.
7. Balta S, Ozturk C. The platelet-lymphocyte ratio: A simple, inexpensive and rapid prognostic marker for cardiovascular events. Platelets. 2015;26(7):680-681.
8. Kurtul A, Murat SN, Yarlioglues M, et al. Association of Platelet-to-Lymphocyte Ratio With Severity and Complexity of Coronary Artery Disease in Patients With Acute Coronary Syndromes. The American Journal of Cardiology. 2014;114(7):972-978.
9. Ozcan Cetin EH, Cetin MS, Aras D, et al. Platelet to Lymphocyte Ratio as a Prognostic Marker of In-Hospital and Long-Term Major Adverse Cardiovascular Events in ST-Segment Elevation Myocardial Infarction. Angiology. 2016;67(4):336-345.
10. Yildiz A, Yuksel M, Oylumlu M, et al. The Utility of the Platelet–Lymphocyte Ratio for Predicting No Reflow in Patients With ST-Segment Elevation Myocardial Infarction. Clinical and Applied Thrombosis/Hemostasis. 2015;21(3):223-228.
11. Temiz A, Gazi E, Güngör Ö, et al. Platelet/lymphocyte ratio and risk of in-hospital mortality in patients with ST-elevated myocardial infarction. Medical Science Monitor : International Medical Journal of Experimental and Clinical Research. 2014;20:660-665.
12. Yayla Ç, Akboğa MK, Canpolat U, et al. Platelet to Lymphocyte Ratio Can be a Predictor of Infarct-Related Artery Patency in Patients With ST-Segment Elevation Myocardial Infarction. Angiology. 2015;66(9):831-836.
13. Crea F, Binder RK, Luscher TF. The year in cardiology 2016: acute coronary syndromes. European heart journal. 2017;38(3):154-164.
14. Ly HQ, Kirtane AJ, Murphy SA, et al. Association of Platelet Counts on Presentation and Clinical Outcomes in ST-Elevation Myocardial Infarction (from the TIMI Trials). American Journal of Cardiology. 2006;98(1):1-5
15. Sun XP, Li J, Zhu WW, et al. Impact of Platelet-to-Lymphocyte Ratio on Clinical Outcomes in Patients With ST-Segment Elevation Myocardial Infarction. Angiology. 2017;68(4):346-353.