



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

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ABSTRACT

Introduction : Acute coronary syndrome (ACS) is a term used to describe the spectrum of thrombotic coronary artery disease. The basic disorder is atherosclerosis which will cause atheroma plaque. Inflammation has an important role in the process of atherosclerosis. Lower lymphocyte counts and higher monocytes show clinical importance in many cardiovascular conditions. Multivariate analysis showed that LMR was an independent predictor in groups with medium to high syntax scores

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

Methods : This was an observational study of 88 consecutive ACS patients who came to Adam Malik General Hospital Medan, from July 2017 to July 2018. Evaluation of LMR 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 LMR values are associated with Vessel scores using Chi-Square analysis.

Results : From 88 research subjects, there were 35 (39,8%) subjects with Simple Vessel Disease (SVD) and 53 (60,3%) subjects with Multi Vessel Disease (MVD). Based on the results of the ROC analysis, it was found that the LMR cut-off point value of the Vessel Score was 1,221 with a sensitivity of 91,4% and specificity of 79,2% with a significant strength ($p < 0.001$). In the Chi-Square analysis, there was a significant relationship between LMR value and Vessel score ($p < 0.001$).

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

KEYWORDS : Acute Coronary Syndrome, LMR, Vessel Score, Angiography.

INTRODUCTION

Coronary Heart Disease (CHD) is still the leading cause of death in developing countries. In western countries, although the death rate due to CHD has gradually declined in the last few decades, this is still the cause of 1 in 3 deaths in people aged 35 years and over.¹

Atherosclerosis is a chronic inflammatory disease characterized by the accumulation of lipids and leukocytes in the walls of blood vessels. This is caused by the interaction of many factors. Monocytes not only phagocytose and remove metabolites, but also control the inflammatory response by apoptosis of other inflammatory cells. Atherosclerotic plaque formation includes adhesions between monocyte cells and endothelial cells, their displacement into arterial walls and lipid buildup.² Unlike lymphocytes, where the number of lymphocytes is inversely correlated with inflammation, and low lymphocyte counts have a worse prognosis in CHD patients.³

LMR is an easy examination, inexpensive and is a strong inflammatory biomarker, can help predict CHD and evaluate the severity of coronary lesions.⁴ Multivariate analysis showed that LMR values below 3.18 were independent predictors in groups with medium to high syntax values.⁵ The lack of research conducted on LMR and the degree of coronary lesions further research is needed.⁴

METHODS

This study was an observational retrospective study on 88 consecutive acute coronary syndrome patients whom were recruited from Adam Malik General Hospital, Medan, Indonesia between July 2017 and July 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 collagen 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.

Coronary artery stenosis lesions were assessed from the results of the patient's angiography, evaluated and classified based on the vessel scores which translated into: Simple Vessel Disease (SVD) – shows either one or null stenosis on any of the main coronary arteries with stenosis $\geq 50\%$ and Multi Vessel Disease (MVD) – shows 2 or more stenosis on any of the main coronary arteries with stenosis $\geq 50\%$.

Receiver-operating characteristic analyzes will be used to detect cut-offs from Lymphocyte-to-Monocyte Ratio (LMR) values. Chi-Square test was used to see the relationship of Lymphocyte-to-Monocyte Ratio (LMR) in the number of coronary arteries that had stenosis. Data analysis using computer statistical tests with p values < 0.05 were considered statistically significant. To analyze the differences in laboratory parameters between simple vessel disease and multi vessel disease using the Independent T test (normal distribution) or the Mann-Whitney test (abnormal distribution).

Results

This research was participated by 88 subjects. The majority of research subjects were 71 men (80.7%) and 17 women (19.3%).

The mean age of the study subjects was 55.56 years. The comorbid factors of the study subjects were 71 people (80.7%) smoking, 29 people hypertension (33.0%), 43 people (48.9%) diabetes mellitus, and 65 people dyslipidemia (73, 9%). The subjects of this study were 59 people (67.0%) had a BMI ≥ 25 kg /mm².

Based on the results of coronary angiography examination, the most occlusion was obtained occlusion in 3 VD as many as 32 people (36.4%) and 1 VD as many as 28 people (31.8%), while 2 VD were found as many as 21 people (23.9%) and 0 Only 7 people VD (8.0%). The types of acute coronary syndromes suffered by the study subjects were 52 people (59.1%) STEMI, 16 people NSTEMI (18.2%), and 12 people UAP (13.6%).

Table 1. Basic and Clinical characteristics of subjects Characteristics

Characteristics	n (%)
Sex	
Male	71 (80,7%)
Female	17 (19,3%)
Age (years), (Mean \pm SD)	55,56 \pm 7,974
Risk Factors	
Smoking	71 (80,7%)
Hypertension	29 (33,0%)
Diabetes mellitus	43 (48,9%)
Dyslipidemia	65 (73,9%)
BMI (kg/m ²)	
<25	29 (33,0%)
≥ 25	59 (67,0%)
Coronary Angiography (Vessel Score)	
0 VD	7 (8,0%)
1 VD	28 (31,8%)
2 VD	21 (23,9%)
3 VD	32 (36,4%)
Type of Acute Coronary Syndrome	
STEMI	52 (59,1%)
NSTEMI	16 (18,2%)
UAP Laboratory Examination	12 (13,6%)
Hemoglobin (g/dl)	14,1 (7,90-17,60)
Leucocyte (sel/mm ³)	11.961 \pm 4.971
Lymphocyte (sel/mm ³)	1925(930-4850)
Monocyte (sel/mm ³)	1610(870-4860)
LMR	1,19(0,38-3,97)
Troponin I (μ g/L)	3,18(0,00-49,0)
CKMB (U/L)	84,50(12-872)
Random PG (mg/dl)	128,50(64-559)
Fasting PG (mg/dl)	107(81-457)
2-h PG (mg/dl)	149(87-430)
A1c	6(4,9-13,9)
Total Cholesterol (mg/dl)	179,60 \pm 43,43
Triglycerides (mg/dl)	135,50(63-1158)
HDL (mg/dl)	34,94 \pm 9,554
LDL (mg/dl)	115,24 \pm 33,52
Ureum	28,50(15-248)
Creatinin	0,94(0,57-4,10)

Based on the results of routine blood tests, the average leukocyte level is more increased in study subjects who suffer from multi vessel disease 12,980.68 \pm 5,641.44 cells / mm³ compared to the average leukocyte level that suffer from single vessel disease 10,418,17 \pm 3,241,71 cells / mm³. There was a significant difference between leukocyte levels and vessel score (p = 0.017).

Based on the results of lymphocyte examination, the average lymphocyte level was lower in the study subjects who suffered from multi vessel disease 1,683.58 \pm 377.67 cells / mm³ compared to the median levels of lymphocytes suffering from

single vessel disease 2524.34 \pm 651.23 cells / mm³. There was a significant difference between lymphocyte levels and vessel score (p <0.001).

Based on the results of leukocyte examination, the median monocyte level increased more in study subjects suffering from multi vessel disease 1960 (950-2980) cells / mm³ compared to the median levels of monocytes suffering from single vessel disease 1190 (870-4860) cells / mm³. There was a significant difference between platelet levels and vessel scores (p <0.001).

Based on LMR examination results, the mean LMR levels were more increased in the study subjects who suffered from single vessel disease 1,964 \pm 0.680 compared to the average LMR levels which suffered from multi vessel disease 0.941 \pm 0.373. There was a significant difference between LMR levels and vessel scores (p <0.001) (table 2).

Table 2. Association between subjects' characteristics and Vessel Score

Characteristics	Simple Vessel Disease (n=33)	Multi Vessel Disease (n=47)	p
Sex			
Male	28 (80,0%)	43 (81,1%)	0,895
Female	7 (20,0%)	10 (18,9%)	
Age	53,77 \pm 6,165	56,74 \pm 8,749	0,086
Smoking			
Yes	26 (80,0%)	43 (81,1%)	0,895
No	7 (20,0%)	10 (18,9%)	
Hypertension			
Yes	11 (31,4%)	18 (34,0%)	0,805
No	24 (68,6%)	35 (66,0%)	
Diabetes mellitus			
Yes	12 (34,3%)	31(58,5%)	0,026
No	23 (65,7%)	22 (41,5%)	
Dyslipidemia			
Yes	23 (65,7%)	42(79,2%)	0,157
No	12 (34,3%)	11 (20,8%)	
BMI			
<25	13(37,1%)	16 (30,2%)	0,497
≥ 25	22 (62,9%)	37 (69,8%)	
Hemoglobin	14,30 (9,70-17,40)	14,10 (7,90-17,60)	0,471
Leucocyte	10.418,17 \pm 3.241,71	12.980,68 \pm 5.641,44	0,017
Lymphocyte	2524,34 \pm 651,23	1.683,58 \pm 377,67	<0,001
Monocyte	1190(870-4860)	1960(950-2980)	<0,001
LMR	1,964 \pm 0,680	0,941 \pm 0,373	<0,001
Troponin I/T	1,36(0,00-29,41)	4,19(0,00-49,00)	0,103
CKMB	79 (12-872)	86 (22-814)	0,224
Random PG	122 (79-407)	131 (64-559)	0,273
Fasting PG	103 (81-430)	109 (82-457)	0,466
2-h PG	132 (93-360)	159 (87-430)	0,294
A1c	6,4(5,0-10,2)	6,9(4,9-13,9)	0,019
Total Cholesterol	174 (111-307)	176 (113-283)	0,736
Triglycerides	138 (63-1158)	134 (62-360)	0,861
HDL	35,77 \pm 9,023	34,40 \pm 9,935	0,512
LDL	110,63 \pm 36,850	118,28 \pm 31,115	0,297
Ureum	26 (15-64)	30(15-248)	0,033
Creatinin	0,83(0,57-2,95)	1,07(0,64-4,10)	0,005

the percentage of research subjects with STEMI was more commonly found to have Multi vessel disease as many as 35 people (68.6%) than experienced Single vessel disease as many as 17 people (58.6%). The percentage of research subjects with NSTEMI was also found to be more likely to have Multi vessel disease by 9 people (17.6%) than to experience Single vessel disease by 7 people (24.1%). The percentage of research subjects with UAP was also more found to have Multi

vessel disease by 7 people (13.7%) than to experience Single vessel disease by 5 people (17.2%). There was no significant relationship between acute coronary syndrome and vessel score $p = 0.661$ (table 3).

Table 3. Relationship of Acute Coronary Syndrome and Vessel Score

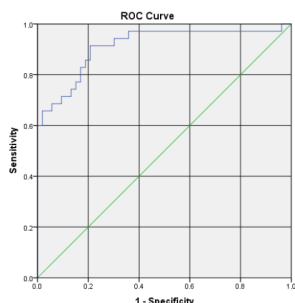
		Vessel score		P*
		Single vessel disease	Multi vessel disease	
Sindrom Koroner Akut	STEMI	17 (58,6%)	35 (68,6%)	0,661
	NSTEMI	7 (24,1%)	9 (17,6%)	
	UAP	5(17,2%)	7(13,7%)	

Based on the results of the ROC analysis, it was found that the cut off point value of LMR levels against the vessel score was 1.221 with a sensitivity of 91.4% and a specificity of 79.2% having a very strong strength that was statistically significant ($p < 0.001$) expressed by the area under the curve (AUC = 0.913; CI: 0.847-0.979).

Table 4. Cut-off point for LMR (Lymphocyte-Monocyte Ratio) to Vessel Score

AUC	Cut off	P	Confidence Interval 95%	
0,913	1,221 Sens: 91,4% Spes : 79,2%	<0,001	0,847	0,979

Figure 1. ROC Curve for LMR (Lymphocyte Monocyte Ratio) to Vessel Score



DISCUSSIONS

In this study it was found that there was no relationship between risk factors such as age, sex, smoking habits, comorbid dyslipidemia, hemoglobin levels, erythrocyte levels, troponin I / T levels, CKMB levels, ad random KGDD, fasting or 2PP, levels total cholesterol, triglycerides, HDL, and LDL against the vessel score.

Based on the results of the ROC analysis, it was found that the cut off point value of LMR levels to the vessel score was 1.221 with a sensitivity of 91.4% and specificity of 79.2%, and a significant relationship was obtained between the LMR value and the vessel score. Another study by Gong et.al showed that the cut-off value of LMR 5.06 could predict the presence of atherosclerosis before coronary angiography with a sensitivity of 57.1% and specificity of 69.7%.^{6,7} In a study conducted by Ji Hanhua et.al, found that LMR became an independent risk factor for CAD (OR: 3.94, 95% CI: 1.20-12.95) and predictors of lesion severity (OR: 2.05, 95% CI: 1, 15-3.66). In addition to that study, LMR was positively correlated with the syntax score, which is a score that describes the severity of coronary lesions ($r = 0.437, p < 0.001$).⁸ In ROC analysis, LMR with an optimal cut-off value of 0.25 can estimate severe coronary lesions with a sensitivity of 60.26% and specificity of 78.49%.

CONCLUSION

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

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