Original article

Correlation of Lipoprotein (a) Level with Complexity of Coronary Lesion in Coronary Heart Disease Patient at RSUP Dr. Sardjito Yogyakarta

Mahmuda INN[1], Dinarti LK[2], Taufiq N[3]

Abstract:

Background: In 2020 there were estimated to be 25 million deaths each year from cardiovascular disease; most of them being coronary heart disease. Traditional risk factors such as smoking, hypertension, diabetes, dyslipidemia reported to affect only 50% of the prevalence and degree of coronary heart disease. It pushes a lot of research on non-traditional risk factors one of which is lipoprotein (a). Levels of Lp (a) also reflects the degree of severity and is associated with the number of coronary arteries involved. The purpose of this study was to determine the relationship of Lp (a) level with the complexity of coronary artery lesion. ***Methods***: This was a cross-sectional study. Subjects were male and women patients aged between 20 to 60 years who underwent coronary angiography for theirs STEMI, NSTEMI, unstable angina pectoris, and stable angina pectoris. Correlation between elevated Lp (a) with the complexity of coronary artery lesion was performed by Pearson test. If the distribution was abnormal we used Spearman test. ***Result***: Number of samples was 64 subjects (49 men and 15 women). The result showed a significant positive correlation between Lp (a) level and complexity of coronary vessel lesion that counted by SYNTAX score (p 0,004) even though the coefficient correlation is weak (r 0, 33). ***Conclusion***: The higher Lp (a) level shows bigger SYNTAX score which means the coronary vessel lesion more complex.

Key Words: coronary heart disease; lipoprotein (a); complexity coronary vessel lesion; SYNTAX Score; correlation

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Background:

Cardiovascular disease is the leading cause of death in developed countries[1]. In 2020 there were estimated to be 25 million deaths each year from cardiovascular disease almost half of them due to coronary heart disease[2,3].

Traditional risk factors such as smoking, hypertension, diabetes, dyslipidemia reported to affect only 50% of the prevalence and degree of coronary heart disease. Many of coronary heart disease patients who have normal levels of dyslipidemia or slightly increase. It pushes a lot of research on non-traditional risk factors such as fibrinogen, homocysteine, tissue plasminogen activator (t-PA), and lipoprotein (a)[4].

Correlation of Lp (a) with atherosclerosis and acute coronary syndrome (ACS) is mediated by: 1) a partial homology between apo (a) with plasminogen, compete for binding to fibrin and plasminogen receptor in endothelium[5, 2] the oxidation of Lp (a) and uptake of Lp (a) by macrophages in the arterial wall as a process that occurs in the Low Density Lipoprotein (LDL)[6].Research has shown that Lp (a) is a risk factor ACS. Another interesting thing is the level of Lp (a) also reflects the degree of severity and is associated with the number of coronary arteries that terlibat[7, 8, 9]. Other studies have also shown consistent results in which the levels of Lp (a) in patients with three vessels disease two times higher than patients with one or two blood vessels

1. Iin Novita Nurhidayati Mahmuda, Department Internal medicine, Faculty of Medicine Muhammadiyah University of Surakarta

2. Lucia Kris Dinarti, Department of Cardiologi-Internal Medicine, Faculty of Medicine Gadjah Mada University

3. Nahar Taufiq, Department of Cardiologi-Internal Medicine, Faculty of Medicine Gadjah Mada University

Corresponds to: Iin Novita Nurhidayati Mahmuda. Fakultas Kedokteran UMS, Kompleks Kampus 4 UMS Gonilan Surakarta, Jl. A. Yani Tromol Pos I Pabelan Kartasura. **E-mail:** innm209@ums.ac.id

Table 1. Baseline characteristic

Characteristic	n (%) or mean ± SD
Age (year)	54,48 ± 7,63
Gender	
Male	49 (76,6)
Female	15 (23,4)
Ethnic	
Javaness	63 (98,4)
Other	1 (1,6)
Clinical presentation	
STEMI	7 (10,9)
NSTEMI	5 (7,8)
UAP	5 (7,8)
APS	38 (59,4)
RECENT	9 (14,1)
MCI	
BMI (kg/m^2)	25,03± 3,32
< 18,5	0
18,5 – 22,9	18 (28,1)
23 – 24,9	17 (26,6)
25 – 29,9	25 (39,1)
>30	4 (6,2)
Diabetes	
Yes	16 (25)
No	48 (75)
Hypertension	
Yes	37 (57,8)
No	27 (42,2)
Dyslipidemia	
Ya	32 (50)
Tidak	32 (50)
Lipid profile	
HDL	44,21 ± 17,32
LDL	121,82 ± 32,94
TG	156,09 ± 73,33
Cholesterol	185,75 ± 39,21
Smoking	
Active Smoker	13 (20,30)
Ex-smoker	26 (40,60)
No	25 (39,10)
Family history of	
CAD	18 (28,10)
Yes	46 (71,90)
No	
Lp(a) level	32,78 ± 11,28
< 20 mg/dl	9 (14,10)
>20 mg/dl	55 (85,90)
SYNTAX score	17,23 ± 14
Low < 22	45 (70,30)
Intermediate	13 (20,30)
23-32	6 (9,40)
High > 32	

involved [2,10,11,12].

Research also shows that levels of Lp (a) increases in patients with acute coronary syndrome and higher in patients with significant coronary lesions (≥ 50%) but had a weak correlation (r = 0.106) with the degree of severity of lesion[13]. The results of a research in Japan shows that there are differences in the levels of Lp (a) and significant association between patients with angiography results were normal, mild-moderate stenosis (30-70%) and severe stenosis (>70%)[14].

Although most studies support the concept of Lp (a) as a risk factor for coronary atherosclerosis, several studies reported no difference between patients with or without coronary lesion and patients with involvement of one, two or three blood vessels[13]. Research also shows that variation in the levels of Lp (a) is quite large (19-70%) in seven different ethnic populations. So the results of research conducted in one country can notautomaticcaly be applied in other countries that ethnically different[15]. Currently, there was not any data showed the correlation between the level of Lp(a) and complexity of coronary lesion in coronary heart disease patient, especially in Yogyakarta. This study aimed to find the correlation the level of Lp(a) and complexity of coronary lesion in coronary heart disease patient at RSUP Dr. Sardjito Yogyakarta. We hypothesized that the increased of Lp(a) level positively associated with the more complex lesion of coroner.

Materials and methods:

This study is a cross-sectional study conducted in Internal Medicine Dr. Sardjito Yogyakarta in April-Juni 2013. Subjects were patients with clinical coronary heart disease including acute coronary syndrome (STEMI, NSTEMI, UAP) admitted to the ICCU Dr Dr. Sardjito and APS patients who were treated in the internal medicine ward of Dr. Sardjito who underwent coronary angiography.

Study inclusion criteria men and women aged between 20 years to 60 years, with a diagnosis of STEMI, NSTEACS which includes NSTEMI and unstable angina pectoris, also stable angina pectoris patient, underwent coronongiografi, willing to follow the study with informed consent approved. Exclusion criteria in this study are: patients suffering from chronic renal failure requiring renal replacement therapy, severe congestive heart failure (NYHA class III-IV), liver cirrhosis, previous heart valve disease, acute stroke, acute complications of diabetes mellitus (KAD and HHS), acute

exacerbation of COPD and pneumonia, sepsis, chronic inflammatory disease, malignancy, blood coagulation disorders, and autoimmune diseases as well as patients who are pregnant.

All patients who meet the inclusion and exclusion criteria will be enrolled in the study, blood samples were taken for subsequent serum and performed pooling. All patients then underwent coronary angiography. And the complexity of coronary lesions assessed by SYNTAX Score. Searches related to previous medical history, risk factors, and other data taken from patient interviews and medical records.

Examination of the levels of lipoprotein (a) serum was conducted by immunohistochemistry. Assessment of coronary lesion complexity with SYNTAX Score. Data presented in the form of mean and standard deviations. To view the data distribution Kolmogorov-Smirnov test was done to see if the variable distribution is normal or not.

Table 2. Univariate analysis baseline characteristic

Characteristic	Lipoprotein(a) n or mean ± SD		p
	≥ 20 mg/dl n = 55	< 20 mg/dl n = 9	
Age (year)	54,78 ± 7,58	52,67 ± 8,12	0,481
Gender			
Male	41	8	0,320
Female	14	1	
Ethnic			
Javaness	55	8	0,141
Other	0	1	
Clinical Presentation			
STEMI	7	0	
NSTEMI	5	0	
UAP	5	0	0,288*
APS	33	5	
RECENT	5	4	
MCI			
BMI (kg/m^2)	24,99 ± 3,36	25,30 ± 3,29	
< 18,5	0	0	
18,5 – 22,9	15	3	
23 – 24,9	17	0	0,801
25 – 29,9	19	6	
>30	4	0	
Diabetes			
Yes	16	0	0,610
No	39	9	
Hypertension			
Yes	30	7	0,174
No	25	2	
Dyslipidemia			
Yes	31	1	0,013
No	24	8	

Lipid profile			
HDL	44,08 ± 18,38	45,02 ± 9,06	0,390**
LDL	125,15 ± 33,00	101,44 ± 25,33	0,028
TG	160,88 ± 76,85	126,22 ± 36,30	0,271**
Cholesterol	188,56 ± 39,47	168, 56 ± 34,71	0,143
Smoking			
Active Smoker	10	3	0,928*
Ex-smoker	22	4	
No	23	2	
History of family CAD			
Yes	16	2	0,508
No	39	7	

To assess whether there is a correlation between elevated Lp (a) with the complexity of coronary artery lesions pearson test performed when the data distribution is normal and if its spread is abnormal used spearman test[17] .

This study was approved by ethics committee.

Result and Discussion:

The subjects of this study consisted of 49(76.6%) men and 15(23.4%) women. Table 1shows the basic characteristics of the subjects, including percentage or mean and standard deviations of age, sex, clinical presentation, race, body mass index (BMI), comorbid diabetes, hypertension, dyslipidemia, HDL, LDL cholesterol, cholesterol, triglyceride levels, family history of coronary heart disease, levels of Lipoprotein(a) and the SYNTAX score.

Note : STEMI: ST Elevation MiocardInfarc; NSTEMI : Non ST Elevation MiocardInfarc; UAP : Unstable Angina Pectoris ; APS : Stable Angina Pectoris ; RECENT AMI : History of Acute Coronary Syndrome in 28 days ; BMI : Body Mass Index ; HDL : High Density Lipoprotein ; LDL : Low Density Lipoprotein ; TG : Triglyserid.

The results of the univariate analysis of the basic characteristics ofthe study subjects are shown in Table 2. Factors baseline characteristics were not statistically significantly different in age, gender, race, clinical presentation, BMI, comorbidities diabetes, hypertension, mean levels of HDL, cholesterol and triglycerides, smoking history, and family history of coronary heart disease ($p > 0.05$). Levels of Lipoprotein (a) is varied and differ between populations, the black population had higher levels of Lp(a) higher than whitesand Asians. Apo(a) polymorphism affects the levels of Lp(a). Lp(a) is strongly influenced by the synthesis of apo(a) which is predominantly genetically influenced. Various studies have also set a different cut-off, Frolkis[18], Willeit etal.,[19], Buldasarreetal., [20] Jurgensetal.,[21] respectively set the cut off for Lp(a) is 32mg/dl, 30mg/dl, >24mg/dl and 20mg/dl. In this study, the cut-off for Lp(a) refers to research Shokanvaretal.,[12]in which the levels of Lp(a) which shows the relationship with coronary stenosis ≥20mg/dl.

*= Kolmogorov-Smirnov test (Alternative test of Chi-Square test), ** = Mann-Whitney test (Alternatifof un paired t-test). Note : STEMI: ST Elevation Miocard Infarc; NSTEMI : Non ST Elevation Miocard Infarc; UAP : Unstable Angina Pectoris ; APS : Stable Angina Pectoris ; RECENT AMI : History of Acute Coronary Syndrome in 28 days ; BMI : Body Mass Index ; HDL : High Density Lipoprotein ; LDL : Low Density Lipoprotein ; TG : Triglyserid.

The results of correlation analysis showed a positive relationship between levels of Lipoprotein (a) the SYNTAX score (p 0.004) despite the strength of the weak correlation (r 0.33). The results of the

Table 3. Correlation Lp(a) level with SYNTAX Score

		Lp(a) level	SYNTAX score
Lp(a) level	Pearson Correlation	1	.333**
	Sig. (2-tailed)		.004
	N	64	64
SYNTAX score	Pearson Correlation	.333**	1
	Sig. (2-tailed)	.004	
	N	64	Lk;64

**. Correlation is significant at the 0.01 level (1-tailed).

correlation analysis are shown in Table3.

The positive correlation levels of Lp(a) with a SYNTAX score showed a positive relationship between levels of Lp (a) with a SYNTAX score. In line with the research Momiyama *et al.*,[22]the concentration of Lp(a) plasma also showed a correlation with the progression of stenosis >25%, despite a weak correlation (r 0.18). Lp(a) is also an independent factor for atherosclerotic aorta(r 0.18). While research Moliternoetal., [23]on the African American population suggests other wise there is no relationship between the levels of Lp (a) with the incidence of coronary stenosis.

Conclusion:

Lp(a) can be recommended as an alternative non-invasive diagnostic tool to predict the complexity of the blockage of the coronary arteries that can be performed before other invasive procedures.

Conflict of interest: None

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