The Difference of Low Density Lipoprotein Cholesterol Levels on Different Severity of Coronary Artery Disease Patients in Siloam Hospital Lippo Village

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Abstract

Background: Coronary artery disease (CAD) is one of the highest causes of death in the world. Hypercholesterolemia, especially low-density lipoprotein (LDL) levels, is a major risk factor, because it is the main precursor of atherosclerosis. Previous studies showed the relationship between LDL level and the number of vessel disease is still inconsistent, therefore it needs to be observed further. The objective of this study was to know the effect of LDL levels on the number of vessel disease in CAD patients who underwent coronary angiography.
Methods: It was a cross-sectional and retrospective study, where data were taken from medical records of CAD patients who underwent coronary angiography at Siloam Hospital Lippo Village between January to June 2018. Patients with at least one vessel disease were included. The number of vessel disease was categorized into 3 groups: one-vessel, two-vessels, and multi-vessel. The relationship between LDL levels and the number of vessel disease was analyzed using one way ANOVA.
Result: The data includes 90 patients; 70 (77.8%) were male with average age of 56±9 years. There were 32 (35.6%) patients in one-vessel group; 27 (30%) in two-vessel group; and 31 (34.4%) in multi-vessel group with an average LDL levels of 106.43±40.51 mg/dl; 111.15±39.43 mg/dl; and 114.52±32.55 mg/dl respectively. Although it seemed that the increase in LDL cholesterol levels was in line with the number of vessel disease, there was no statistically significant relationship between the two variables (p=0.694).
Conclusions: LDL cholesterol level does not affect the number of vessel disease in CAD patients.

Introduction

Coronary artery disease (CAD) is one of the highest causes of mortality and morbidity in the world[1]. CAD also has the highest prevalence (1.5%)[2] and the second highest cause of mortality (12.9%)[3] in Indonesia for cardiovascular diseases. High concentration of low-density lipoprotein (LDL) is one of the major modifiable risk factors for CAD and has a direct causality for the disease[4, 5, 6] aside from hypertension, smoking, diabetes mellitus, obesity, and sedentary lifestyle[7].

High levels of LDL are the precursor of atherosclerosis. LDL molecules migrate through endothelium, form a buildup of plaque, then narrows the blood vessel overtime. The cap of the plaque then gets thinner and become prone to rupture, causing thrombosis[8]. Atherosclerotic lesions are evaluated using coronary angiography and then classified as obstructive (diameter narrowing of ≥70%; ≥50% for LMCA) or non-obstructive (diameter narrowing of >20% and <70%; >20% and <50% for LMCA). Obstructive lesion is clinically significant and

considered as vessel disease in CAD patients[9].

Several studies have been conducted to find the association between the LDL concentration and the number of vessel disease in CAD. Previous studies by Saito et al.[10] and Chieng et al.[11] have suggested that higher LDL concentration will lead to a more complex and an increase in the number of vessel disease in CAD patients (p<0.01; p<0.05 respectively), which then contradicted by two other studies from Brazil[12] and Iran[13] where neither significance nor correlation is found between the two variables (p=0.1; p=0.73 respectively).

The hypothesis is that the higher the concentration of LDL in the blood, the higher the number of vessel disease in CAD patients. The correlation between the two variables remains inconsistent and contradictory based on the previous studies, therefore this study aimed to know and add more evidence about the effect of LDL on the number of vessel disease in CAD patients.

Material And Methods

Subjects

This retrospective study was conducted in Siloam Hospitals Lippo Village, Tangerang, Indonesia. The data were taken from medical record of patients who underwent coronary angiography within the period of January – June 2018. Subjects were included if they had at least one clinically significant lesion (diameter narrowing of ≥70%; ≥50% for Left Main Coronary Artrery) of coronary arteries. The laboratory result of LDL levels must be taken within 6 months from the time of coronary angiography[14].

The samples were then categorized into three groups: one-vessel; two-vessels; and multivessel based on the number and location of the obstruction. The LDL concentration were compared and analysed along with the other essential variables between these groups. The effect of LDL levels on the number of vessel disease in CAD patients were analysed using one-way ANOVA with a p value of <0.05 to be considered statistically significant. The rest of the confounding variables were presented as descriptive data.

Additional information (if present) such as electrocardiogram (ECG), echocardiogram, diagnosis, and the therapy given were also collected from the medical record and presented in this study as part of the characteristic of subjects. The frequency of the locations of vessel disease such as left main coronary artery (LMCA), right coronary artery (RCA), left anterior descending artery (LAD), and left circumflex artery (LCX) were also presented.

Statistical analysis

The program used for statistical analysis was SPSS 22.0 for Windows (SPSS Inc, USA). The normality and homogeneity test were performed on the data which resulted in normal distribution. The data were then presented by mean ± standard deviation (SD) for variables such as the LDL levels and age, while the rest (male gender; history of hypertension; diabetes; hypertriglyceridemia; and smoking) were presented as frequencies and percentage.

Result

Out of 427 patients who underwent coronary angiography in Siloam Hospitals Lippo Village, 162 were excluded due to non-existent significant lesion, 175 were excluded because of insufficient data, resulting in the final sample of 90 patients. Baseline characteristics were shown in Table 1. The predominant samples in this study were male (77.8%) with average age was 56 ± 9 years. There were 32 samples (35.6%) in the one-vessel group, 27 samples (30%) in the two-vessels group, and 31 samples (34.4%) in the multivessel group. Left Anterior Descending was the most affected coronary artery in this study (80%).

The average LDL cholesterol level was 110.63 ± 37.34 mg/dl, with majority of samples in the <100 mg/dl category (n=36;

40%). A total of 77 patients (85.6%) had a history of hypertension, 47 patients (52.2%) had a history of diabetes, and 59 patients (65.6%) had a history of smoking.

Table 1. Baseline Characteristics

Characteristic	Frequency (n=90)	Percentage (%)
Gender		
Male	70	77,8
Female	20	22,2
Age (years)	56 ± 9*	
< 40	3	3,3
40-49	23	25,6
50-59	30	33,3
60-69	28	31,1
70-79	5	5,6
>80	1	1,1
Number of vessel disease		
One-vessel	32	35,6
Two-vessels	27	30,0
Multivessel	31	34,4
Location of vessel disease		
LMCA	9	10,0
LAD	72	80,0
LCX	53	58,9
RCA	53	58,9
Diagnosis		
ACS (without further explanation)	14	15,6
STEMI	19	21,1
NSTEMI	16	17,8
UAP	9	10,0
SAP	10	11,1
N/A	22	24,4
LDL-c levels (mg/dl)	110,63±37*	
<100	36	40,0
100-129	32	35,6
130-159	12	13,2
160-189	7	7,8
≥190	3	3,3
Risk factors		
Hypertension	77	85,6
Diabetes	47	52,2
Hyper TG	29	32,2
Smoking	59	65,6
Therapy		
Antiplatelet	84	93,3
Anticoagulant	21	23,3
Beta blocker	48	55,6
ACEI/ARB	34	37,8
Nitrate	43	47,8
Statin	81	90,0
Spironolactone	4	4,4
CCB	24	26,7
ECG		
Sinus rhythm	51	56,7
Atrial rhythm	3	3,4
ST elevation	19	21,1
ST depression	14	15,6
T inversion	10	11,1
Q wave	13	14,4
LVH	8	8,9
N/A	27	30,0
Echocardiogram		
Dilated LV	8	8,9
EF (≥ 50%)	20	22,2
RWMA	13	14,4
N/A	62	68,9

*Mean ± standard deviation

ACEI/ARB - angiotensin converting enzyme inhibitor/angiotensin receptor blocker; ACS - acute coronary syndrome; CCB - calcium chanel blocker; EF - ejection fraction; LAD - left anterior descending; LCX - left circumflex artery; LDL – low density lipoprotein; LMCA - left main coronary artery; LV – left ventricle; LVH – left ventricle hypertrophy; N/A – not available; NSTEMI - non ST elevation myocardial infarction; RCA - right coronary artery; RWMA: regional wall motion abnormality; SAP – stable angina pectoris; STEMI - ST elevation myocardial infarction; UAP - unstable angina pectoris.

Most of them were given antiplatelet therapy (93.3%) and statins (90%). ECG results found from samples showed sinus rhythm for 51 patients (56.7%) and most of them experienced myocardial infarction with the presence of ST elevation (21.1%). Samples with echocardiogram results showed that there was no significant ventricular dilatation of the heart (21.1%) with the ejection fraction of ≥50% (22.2%) for most patients.

The predominant samples in this study were male (77.8%) with average age was 56 ± 9 years. There were 32 samples (35.6%) in the one-vessel group, 27 samples (30%) in the two-vessels group, and 31 samples (34.4%) in the multivessel group. Left Anterior Descending was the most affected coronary artery in this study (80%).

The average LDL cholesterol level was 110.63 ± 37.34 mg/dl, with majority of samples in the <100 mg/dl category (*n*=36; 40%). A total of 77 patients (85.6%) had a history of hypertension, 47 patients (52.2%) had a history of diabetes, and 59 patients

(65.6%) had a history of smoking. Most of them were given antiplatelet therapy (93.3%) and statins (90%). ECG results found from samples showed sinus rhythm for 51 patients (56.7%) and most of them experienced myocardial infarction with the presence of ST elevation (21.1%). Samples with echocardiogram results showed that there was no significant ventricular dilatation of the heart (21.1%) with the ejection fraction of ≥50% (22.2%) for most patients.

To determine the effect of LDL levels on the number of vessel disease, one-way ANOVA test were performed and shown on the table (Table 2). The average LDL cholesterol level in one-vessel, two-vessels, and multivessel group respectively was 106.43 ± 40.51 mg/dl, 111.15 ± 39.43 mg/dl, and 114.52 ± 32.55 mg/dl. Although LDL levels were directly proportional to the number of vessel disease, there was no statistically significant relationship between the two variables (p=0.694).

Other collected variables (risk factors for CAD) were compared descriptively between each vessel group (Table 3). The average age tends to be higher as the number of vessel disease increases. The percentage of samples who had hypertension, diabetes, and had a history of smoking are also increased in the two-vessels and multivessel group. In contrast, male gender and hypertriglyceridemia did not show any relationship to the number of vessel disease.

Table 2. Relationship Between Number of Vessel Disease and LDL Cholesterol Levels

	N (%)	LDL level (mg/dl)	P value
One-vessel	32 (35,6%)	106,43 ± 40,51	0,694
Two-vessel	27 (30%)	111,15 ± 39,43	
Multivessel	31 (34,4%)	114,52 ± 32,55	

Table 3. Descriptive comparison between risk factors to the number of vessel disease in CAD patients

Risk factor	One (n=32)	Two (n=27)	Multi (n=31)
Age (years)	54 ± 7	55 ± 10	58 ± 11
Male gender	25 (78,1%)	22 (81,5%)	23 (74,2%)
Hypertension	25 (78,1%)	22 (81,5%)	30 (96,8%)
Diabetes	13 (40,6%)	13 (48,1%)	21 (67,7%)

Discussion

Most patients in this study belong in the one-vessel group, which consists of 32 samples (35.6%), followed by multivessel group with 31 samples (34.4%), and two-vessels group with 27 samples (30%). The most frequently affected artery was LAD (n = 72, 80%), followed by LCX and RCA arteries with the same frequency (n = 53, 58.9%), then LMCA (n = 9, 10%). This is consistent with the theory and research described by Wasilewski et al, where the septal perforator in LAD tends to have a "milking effect" which causes the distribution of atherosclerotic plaque to be more dominant in this artery than the others.[15, 16]

The LDL cholesterol levels were shown to be increased in the two-vessels group and multivessel group. LDL levels had an average of 106.43 ± 40.51 mg/dl in one-vessel group, 111.15 ± 39.43 mg/dl in two-vessels group, and 114.52 ± 32.55 mg/dl in multivessel group. There was no statistical significance found after the data was analysed with one-way ANOVA (p = 0.694). The result of this study was similar with another study conducted by Penalva et al, in which LDL levels and the number of vessel disease does not have statistically significant relationship, although the data similarly showed that the increase in LDL levels was also consistent with the increase of the number of vessel disease. The researcher assumed that his sample of 107 patients was still relatively

small in order to obtain any statistical significance in his research[14]. This could also be one of the factors that caused no statistical difference in this study because of the relatively small number of samples (*n* = 90 samples). A study conducted by Khashayar et al, described that there was no correlation between the two variables at all. According to their study, there was other factor that affects the number of vessel disease besides LDL levels, which is the high-density lipoprotein (HDL)[13]. HDL levels were not included in this study and it was unknown whether it had any influence on the outcome and the number of vessel disease.

In contrast, a study by Gruzdeva et al. found a significant effect between LDL levels and the number vessel disease in CAD patients. Their method was that angiography procedure and the laboratory examination are carried out strictly and only within a few hours after the onset of the disease, with the number of samples as many as 400 samples[17]. In this study the data were obtained retrospectively from medical records and the time between the LDL examination and angiography procedure was not necessarily uniform between one sample to another. These difference of time period between each sample might be a factor for a less representative data, which then affected the outcome of this study to be statistically insignificant.

In theory, a high level of blood LDL will cause more lesions in coronary arteries because the process of atherosclerosis is initiated by a high number of LDL molecules that invades the endothelium. High LDL levels can also form free radicals that also damage the function of endothelial cells, making LDL particles penetrate more easily through endothelial cells. Although the results obtained in this study were not statistically significant, high LDL levels remain as the major precursor of plaque formation in coronary artery disease. Therefore, LDL levels is still considered for estimating the severity of lesions in CAD.

Limitation of study

The design of this study is cross-sectional retrospective, which includes some limitations such as: time of examination of LDL levels that are not uniform between one sample to another; and lack of information whether the patient's LDL cholesterol level is controlled. The assessment of complexity and severity of lesion in this study was only qualitative in nature and did not use standardized scores such as SYNTAX, hence another limitation that can be improved in the future. Besides, this study did not analyze other risk factors for coronary artery disease. Hypertension, diabetes, smoking, and family history are traditonal risk factors that may influence severity of coronary artery disease. Further studies are needed to evaluate those factors together with LDL levels to predict the outcome in coronary artery disease population.

Conclusion

In conclusion, LDL cholesterol levels have no effect on the number of vessel disease in patients with CAD. Patients in the higher vessel group tend to be older, have a history of hypertension, diabetes, and smoking.

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