



# The Effect of Statin Administration to the Complexity of Coronary Lesions on Acute Coronary Syndrome Patients

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## ABSTRACT

**Introduction:** The severity and prognosis of acute coronary syndrome depend on the complexity of the coronary lesion. The complexity of coronary lesions is influenced by risk factors such as uncontrolled dyslipidemia and unstable coronary plaque conditions. Statin (atorvastatin, fluvastatin, pravastatin, rosuvastatin and simvastatin) is a class of drugs that competitively inhibit the coenzyme 3-hydroxy-3-methylglutaryl (HMG CoA) reductase, an enzyme that plays a role in cholesterol synthesis. Statins can also maintain plaque stability. This study aimed to determine the effect of statin administration to the complexity of coronary lesions on acute coronary syndrome patients.

**Method:** This study is conducted from July to August 2018 at Dr. M. Djamil Hospital Padang. The subjects that are included in the criteria were 109 subjects, and 25 subjects were excluded because of Old age, Diabetes Mellitus, Chronic heart failure, and missing data. The use of statins in subjects was asked about the history of consumption with the type of drug atorvastatin at a dose of 20 mg once a day which is taken regularly in patients with acute coronary syndrome. The complexity of the coronary lesion was assessed based on the percentage of stenosis.

**Result:** This study used the chi square test. There were 60 patients (55%) with complex coronary lesion among 109 patients who regularly took statins. The other 49 subjects (45%) did not have complex coronary lesions. Thus, the result of the statistical analysis found a significant effect of the use of statins on the complexity of coronary lesions with a P value of 0.007.

**Conclusion:** There was a significant effect between statins administration to the the complexity of coronary lesion.

**Keywords:** Acute Coronary Syndrome, Complex Lesions, Dyslipidemia, Statin

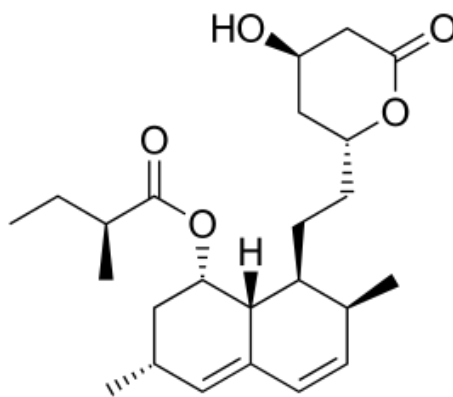
## 1. Introduction

Coronary heart disease (CHD) is one of main problems among all heart diseases. CHD that occurs acutely is known as Acute Myocardial Infarction (AMI) and is one of the main causes of death. Based on the World Health Organization (WHO) report in 2017, around 17.8 million people died due to cardiovascular disease<sup>1</sup>. In Indonesia, based on Basic Health Research (RISKESDAS) in 2018, the prevalence of heart disease was 1.5% of the total Indonesian population, in West Sumatra alone the prevalence of heart disease is higher than the national prevalence figure, namely 1.6%, in 2018<sup>2</sup>. The severity and prognosis of acute coronary syndrome depend on the complexity of the coronary lesion. The complexity of coronary lesions is influenced by risk factors such as uncontrolled dyslipidemia and unstable coronary plaque conditions<sup>3</sup>. Dyslipidemia is a dangerous cholesterol disorder, and there are quite a lot of cases in Indonesia. Prevalence of Indonesian people aged  $\geq 15$  years in 2013 with an increase in abnormal cholesterol ( $\geq 200$  mg/dL) as much as 35.9%; very high LDL levels ( $\geq 190$  mg/dl) with 15.9% percentage; Low HDL as much as 22.9%; and high triglycerides ( $\geq 500$  mg/dl) is 11.9%. Dyslipidemia is known as one of the main risk factors for Atherosclerosis Cardiovascular Disease (ASCVD). The accumulation of cholesterol containing apo B in the intima of arteries at sites of predilection for plaque formation is the basis for initiating atherosclerotic cardiovascular disease and influencing the progression of atherosclerotic plaque<sup>4</sup>.

Various epidemiological studies, Mendelian randomization studies, and randomized controlled clinical trials consistently show a strong association between high LDL levels and cardiovascular events. Therefore, reducing LDL levels is the main target in preventing cardiovascular disease. This is also supported by various studies which show that reducing LDL levels is directly proportional to reducing cardiovascular events. Statins are the drug of choice for lowering LDL-C cholesterol. Statins reduce cholesterol synthesis by hepatocytes through inhibition of hydroxymethylglutaryl (HMG) CoA reductase. Reducing intracellular cholesterol will increase hepatocyte LDL receptor expression, thereby increasing LDL-C uptake from the blood<sup>4,5</sup>.

Statin (atorvastatin, fluvastatin, pravastatin, rosuvastatin and simvastatin) is a class of drugs that competitively inhibit the coenzyme 3-hydroxy-3-methylglutaryl (HMG CoA) reductase, an enzyme that plays a role in cholesterol synthesis. Statins can also maintain plaque stability. The meta-analysis of Chou et al. of 71,344 participants reported that the use of statins in adults who were at risk of cardiovascular disease but had never experienced a

cardiovascular event was able to reduce the risk of mortality from all causes, reduce cardiovascular mortality, and reduce cardiovascular events. The use of these statins is reported to have greater absolute benefit in patients with greater cardiovascular risk. Another study by Li et al. which involved 16 randomized clinical trials involving 69,159 participants also found that statins effectively reduced the incidence of angina, fatal myocardial infarction, coronary revascularization and other cardiovascular events. This study aimed to determine the effect of statin administration to the complexity of coronary lesions on acute coronary syndrome patients<sup>4,5</sup>.



**Figure 1. Statin Components.** Statins work competitively with 3-hydroxy-3-methylglutaryl coenzyme (HMG CoA) reductase, an enzyme that plays a role in cholesterol synthesis, especially in the liver.

## 2. Methodology

This study used data from a cohort of patient medical records at the Department of Cardiology and This study is conducted from July to August 2018 at Dr. M. Djamil Hospital Padang. The population of this study was all acute coronary syndrome patients who underwent coronary angiography in the cardiac catheterization laboratory at Dr. Hospital. M. Djamil Padang. The subjects that were included in the inclusion criteria were 109 subjects, and 25 subjects were excluded because of Old age, Diabetes Mellitus, Chronic heart failure, and missing data. The use of statins in subjects was asked about the history of consumption with the type of drug atorvastatin at a dose of 20 mg once a day which is taken regularly in patients with acute coronary syndrome.

The complexity of the coronary lesion was assessed based on the percentage of stenosis. Coronary lesions are complex lesions if the stenosis in the main blood vessels (LM) is 50%, or stenosis in the ostial/proximal Left Anterior Descending (LAD) > 50%, or stenosis in the mid-distal LAD  $\geq$  70%, stenosis in the LCx  $\geq$  70% , or stenosis in the RCA  $\geq$  70%. Meanwhile, if the stenosis in the main blood vessels (LM) is < 50%, or stenosis in the ostial/proximal Left Anterior Descending (LAD)  $\leq$  50%, or stenosis in the mid-distal LAD < 70%, or stenosis in the LCx < 70%, or stenosis in the RCA is <70%, then the coronary lesion is referred to as a non-complex lesion<sup>1</sup>. The assessment of stenosis is carried out through angiography. This study used the chi square test.

## 3. Result

### Baseline Characteristics of Acute Coronary Syndrome (ACS) Patients with complex coronary lesion based on Angiography result

The characteristics of the research subjects are presented in table 1. The group with significant lesions was mainly men with an average age of  $53.0 \pm 6.39$  years, and had risk factors for smoking, dyslipidemia and hypertension. Meanwhile, women are more likely to have insignificant lesions.

**Table 1. Characteristics of Research Subjects**

Variables	Coronary Lesion		p-value
	Complex (n=60)	Non-complex (n=49)	
Age (years), mean $\pm$ SD	53,0 $\pm$ 6,39	50,98 $\pm$ 8,84	0,057
Gender			
Male	51 (85,0)	26 (53,1)	0,000
Female	9 (15,0)	23 (46,9)	

Risk factors of CHD, n (%)			
Family History	7 (11,7)	3 (6,1)	0,507
Smoking	47 (78,3)	23 (46,9)	0,001
Dyslipidemia	30 (50,0)	14 (28,6)	0,038
Hypertension	38 (63,3)	26 (53,1)	0,375
Menopause	4 (6,7)	5 (10,2)	0,729

As seen in Table 2, there were 49 patients (100%) patients who regularly took statins among 60 patients with non-complex coronary lesion. On the other hand, only 43 subjects (71%) among subjects with complex coronary lesions who took statin regularly. Thus, the result of the statistical analysis found a significant effect of the use of statins on the complexity of coronary lesions with a P value of 0.007.

**Table 2. The effect of statin administration to the complexity of coronary lesions on acute coronary syndrome patients**

Variables	Coronary Lesion		P-value
	Complex (n=60)	Non-complex (n=49)	
Statin Administration	43 (71%)	49 (100%)	0,007

#### 4. Discussion

The group with significant lesions was more common in men, while the group with non-significant lesions were more common in women. This is in line with a population study conducted by Cheng, that men with typical angina had a greater risk of suffering from coronary heart disease with more severe lesions than women (19% compared to 11% with  $p < 0.001$ ). In a population study involving 14,786 male and female subjects in Finland, it was also found that men had a 3 times greater risk of suffering from CHD than women, with a 5 times greater risk of mortality. 51 More men were affected by CHD, associated with unhealthy behaviors, such as smoking, alcohol consumption, and exposure to physical stressors. Meanwhile, the cardio-protective effect of estrogen plays an important role in the low number of female subjects suffering from CHD<sup>6,7</sup>.

The most traditional risk factors for cardiovascular disease in this study were smoking and dyslipidemia, and these results were statistically significant. This is in line with research conducted by Kannel, that in patients studied in the Framingham Heart Study, the relative risk of CHD was three times higher in smokers compared to non-smokers. Smoking can cause endothelial dysfunction, increase systemic blood pressure, increase peripheral vascular resistance, heart rate and change heart rate variability parameters. Meanwhile, dyslipidemia has a prevalence of 33.9%<sup>7</sup>. Age is a cardiovascular risk factor that cannot be modified. This is related to the aging process which causes a decrease in body organ function and the incidence of cardiovascular disease significantly increases at ages over 55 years. However, this is not in line with the results of the study where in the group of ACS patients with complex or non-complex coronary lesions, both groups were under 55 years of age<sup>8,9</sup>.

The Scandinavian Simvastatin Survival Study (4S) was the first large-scale study showing that using statins reduced major cardiovascular events, cardiovascular mortality, and total mortality in patients with coronary artery disease and high blood cholesterol levels. The Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering study reported that 80 mg atorvastatin within 24 to 96 hours after hospital admission reduced the risk of the composite primary endpoint of death, myocardial infarction, cardiac arrest, and recurrent ischemia by 16% compared with placebo. The study above is in line with the result of this study that patients who receive regular statin therapy tend to have fewer complex coronary lesions when they suffer from coronary heart disease<sup>10,11</sup>.

#### 5. Conclusion

There was a significant effect between statins administration to the the complexity of coronary lesion. However, further research is needed with a larger sample size, and the use of follow-up research methods to see the impact of statin administrations for 3 months, 6 months, 1 year and 3 years, in the patients, so that the results obtained can be more representative.

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