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ASSOCIATION OF NON CHOLESTEROL HIGH DENSITY LIPOPROTEIN-TO-TOTAL CHOLESTEROL RATIO WITH SEVERITY OF CORONARY ARTERY LESION USING SYNTAX SCORE IN PATIENTS WITH ACUTE CORONARY SYNDROMES

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Abstract

Background: Coronary Artery disease (CAD) is still the leading cause of morbidity and mortality in the world. Many studies centered on the diagnosis or prognosis of CAD suggested dyslipidemia might be associated with severity of atherosclerosis. The ratio of non-HDL cholesterol to total cholesterol (non-HDL-c/TC) is a prognostic marker that combines 2 variables into one. The SYNTAX score is an anatomic scoring system based on coronary artery angiography (CAG) to quantify severity and complexity coronary lesion. The aim of this study was to investigate the association of the non-HDL-c/TC ratio with coronary artery severity using the SYNTAX score in patients with acute coronary syndrome (ACS) who underwent coronary artery angiography.

Methods: Patients were recruited from June to December 2019. This cross-sectional study involved 71 patients who were admitted from the emergency department. Variables such as comorbidities, coronary artery angiography and laboratory finding were evaluated. The non-HDL-c was calculated as total cholesterol (TC) minus HDL-c, while non-HDL-c/TC was the ratio of non-HDL-c and TC. Coronary artery angiography was performed, and the SYNTAX score was calculated in all the subjects divided into two subgroups, those with low SYNTAX score (≤ 22) and those with high SYNTAX score (≥ 23).

Results: a total of 71 patients with ACS who underwent CAG were included in the study from June to December 2019. From total 71 patients, there were 36 patients (50.7%) had a SYNTAX score ≥ 23 and 35 patients (49.3%) had a SYNTAX score ≤ 22 . There were significant relation difference between both groups. From Pearson's analysis, there was significant statistic between ratio of non-HDL/TC and SYNTAX score ($r = 0.299$; P value: < 0.001).

Conclusion: Non-HDL-c/TC ratio is significantly associated with severity of coronary lesion using SYNTAX score in patients with acute coronary syndrome.

Introduction

Cardiovascular disease, especially coronary artery disease (CAD) is the leading cause of morbidity and mortality in the world. Report from World Heart Organization (WHO) in 2013, as many as 17.5 million people died each year from cardiovascular disease¹. In Indonesia, according to Basic Health Research data in 2013, the most common cardiovascular diseases were CAD and heart failure where CAD prevalence was 1.5%, and it increased with age². Wen et al study showed a decrease in high density lipoprotein cholesterol (HDL) and an increase in Low Density Lipoprotein Cholesterol (LDL) are important risk factors CAD³. The study of Huang et al found a novel marker of non cholesterol High Density Lipoprotein (non-HDL-c) to total cholesterol (TC) ratio as an independent risk factor in estimating the severity of coronary artery lesions using Gensini score and correlating with poor outcomes at one year of follow-up. Non-HDL-c was calculated as the difference between TC and HDL-c⁴. The SYNTAX score (SYnergy between percutaneous coronary intervention with TAXus and cardiac surgery) is a score system formulated comprehensively to describe the complexity of the results of coronary angiogram where higher SYNTAX scores, indicate a more complex disease state and a worse prognosis⁵. Based on the above background, this study intends to find a relationship between the ratio of non-HDL cholesterol and total serum cholesterol with the severity of coronary artery lesions as assessed by SYNTAX score in patients with acute coronary syndromes.

Methods

Patients were recruited from June to December 2019. This cross-sectional study involved 71 acute coronary syndrome patients who were admitted from the emergency department. Persons were included in the study if (1)



INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

patient with acute coronary syndrome. (2) the patient had coronary artery angiography performed; and (3) test of lipid metabolism including TC, HDL, LDL, triglyceride. Exclusion criteria included (1) prior PCI therapy, (2) unavailable clinical data especially TC or HDL-c, and (3) comorbidity of severe liver dysfunction, and/or renal insufficiency or malignant tumor. Variables such as comorbidities, coronary artery angiography and laboratory finding were evaluated. The non-HDL-c was calculated as total cholesterol (TC) minus HDL-c, while non-HDL-c/TC was the ratio of non-HDL-c and TC. Coronary artery angiography was performed, and the SYNTAX score was calculated in all the subjects divided into two subgroups, those with low SYNTAX score (≤ 22) and those with high SYNTAX score (≥ 23). Bivariate analysis was carried out to find the relationship between non-HDL/TC ratio and SYNTAX score. P values < 0.05 were considered statistically significant. Ethical Committee Board of Faculty of Medicine, University of North Sumatera and Adam Malik General Hospital approved this study protocol.

Procedure Study

All patients in this study were patients suffering from acute coronary syndrome based on clinical, ECG, and cardiac enzymes. Researchers examine and record patient complaints, physical examination, ECG, and laboratory results and comorbidities obtained from medical records. Patients with acute coronary syndromes will be examined for lipid profile and non-HDL-c and TC ratio were calculated. Non-HDL-c is obtained from serum TC values minus serum HDL values. Then patients with acute coronary syndromes will undergo coronary angiography to assess coronary artery lesions. The severity of coronary artery lesions will be assessed using a SYNTAX score. The SYNTAX score will be divided into two subgroups, those with low SYNTAX score (≤ 22) and high SYNTAX score (≥ 23).

Statistical Analysis

Data processing and analysis of statistical data using statistical computer tools. Categorical variables are represented by the number or frequency (n) and percentage (%). Data normality test uses Kolmogorov-Smirnoff. To test the hypothesis, assess whether there is a relationship between the non-HDL-c ratio and the SYNTAX score using the t test. But if the distribution is not normal then Mann Withney is used. Data were analyzed statistically using statistical tools with p value is less than 0.05 was statistically significant.

Results

A total of 71 patients in this study with most of the subjects were men (84%) compared with 11 women (16%) with an average age of 55 years. Smoking is the most dominant risk factor (74%) compared to diabetes and hypertension. NSTEMI is the most ACS presentation (36%) compared to STEMI (24%) and unstable angina (21%). The first group were patients with a SYNTAX score ≤ 22 , amounting to 35 people (49.3%), and the second group were patients with a SYNTAX score ≥ 23 of 36 people (50.7%). (table 1)

Table 1. Baseline Characteristics

Variables	(n:71)
Age, year	54 \pm 8,48
Sex	
Male	60 (84%)
Female	11 (16%)
BMI, kg/m ²	26,5 (21,2-33,9)
Unstable angina	21 (29,5%)
NSTEMI	26 (36,6%)
STEMI	24 (33,8%)
Diabetes melitus	33 (46,4%)
Hypertension	44 (61,9%)
Smoker	53 (74,6%)
Laboratory finding	
Hemoglobin	13,4 \pm 1,60



INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

Hematocrit	39±4,75
Leukocyte	108.000 (6.200-21.550)
Platelet	249.000 (140.000-489.000)
Fasting glucose	117 (70-281)
2 PP glucose	142 (78-328)
HbA1c	5,9 (4,4-11,2)
Ureum	30 (17-73)
Creatinine	1,12 (0,4-2,2)
Total cholesterol	117 (81-271)
Triglyceride	134 (58-364)
High Density Lipoprotein	38±8,84
Low Density Lipoprotein	115±41,33
Non-HDL-c	138 (52-234)
Non-HDL-c/TC ratio	0,77±0,80

From the bivariate analysis, there was statistically significant in group with a SYNTAX score ≥ 23 such as hypertension (p value=0.002), total cholesterol (p value=0.001), LDL (p value = 0.012), non-HDL-c (p value=0.001). There were also significant differences for the non-HDL-c/TC ratio in the two groups. Patients with a SYNTAX score ≥ 23 had a mean value of 0.820 ± 0.530 , while those in the SYNTAX group ≤ 22 had a non-HDL-c/TC ratio of 0.737 ± 0.083 (p value=0.001)(table 2).

Table 2. Basic Characteristics Based on Severity of Coronary Artery Lesions

Variables	SYNTAX Score		P Value
	≤ 22 (n =35)	≥ 23 (n=36)	
Age, year	52,8 ± 8,91	54,8 ± 7,94	0,175
Sex			
Male	29 (82%)	32 (88%)	
Female	6 (18%)	4 (12%)	0,575
BMI, kg/m ²	26,7±3,28	26,3±2,52	0,575
Unstable angina	13 (37%)	8 (22%)	
NSTEMI	11 (31%)	15 (41%)	0,125
STEMI	11 (31%)	13 (36%)	
Diabetes melitus	15 (42,8%)	18 (50%)	0,715
Hypertension	15 (42%)	29 (80%)	0,002
Smoker	26 (74%)	27 (75%)	0,999
Hemoglobin	13,52±1,40	13,32±1,78	0,605
Hematocrit	39,80±4,56	38,30±4,89	0,188
Leukocyte	9830 (6840-21550)	11190 (6260-20550)	0,382
Platelet	253k(140k-489k)	219k (140k-478k)	0,613
Fasting glucose	111 (70-246)	117 (84-281)	0,831
2 PP glucose	157 (78-294)	137(85-328)	0,915
HbA1c	5,90 (4,40-11,2)	5,95 (5,10-10,41)	0,692
Ureum	31,2±10,77	33,0±15,55	0,181
Creatinine	1,06±0,368	1,17±0,396	0,401
Total Cholesterol	141±37,45	195±49,99	0,001
Triglyceride	127 (58-331)	148,5 (73-364)	0,32
HDL	39,3±8,652	36,47±8,923	0,177
LDL	103±34,29	127,6±44,6	0,012
Non-HDL-c	121,3±38,94	167,3± 41,27	0,001
Non-HDL-c/TC ratio	0,737±0,083	0,820±0,530	0,001

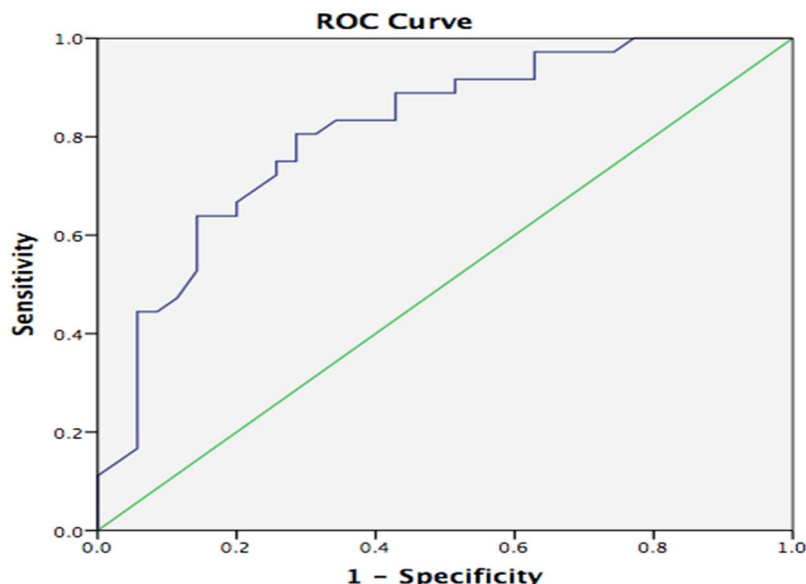


Figure 1. ROC Curves Optimal Point Intersection Non-HDL-c/TC Ratio To Severity of Coronary Lesions

Table 3. Area Under The Curve Prognostic Model

Parameter	Area Under The Curve (AUC)	p
Rasio non-HDL-c/TC	0,812	<0.001

In table 3, ratio above 0.812 can predict a SYNTAX Score ≥ 23 . Based on the table, the clinically optimal non-HDL-c / TC ratio to the severity of coronary lesions is determined by 0.778 with a sensitivity of 80% and a specificity of 69% (figure 1). Pearson correlation analysis results the value of the ratio of non-HDL-c/TC with a SYNTAX score showed a significant difference (p: 0.011) with a weak correlation level (r: 0.299) (table 4).

Table 4. Pearson Correlation Analysis

Non HDL-c/TC ratio	Skor SYNTAX
	r = 0,299
	p < 0,001
	n = 71

Discussion

Acute coronary syndrome is caused by rupture of unstable atherosclerotic lesions. It is well known that the role of cholesterol is related to the severity of coronary lesions. One of them is the ratio of non-HDL-c to total cholesterol. Increasing of this marker has been shown an increase in poor outcomes⁴. In this study, the majority of the samples have male sex and an average age of 54 years with an age range in the 5th to 7th decade. Subjects with a SYNTAX score ≥ 23 have an older age compared to subjects with a SYNTAX score ≤ 22 . It was correlated with the study from Kurtul et al and Cimen et al where the frequency of male subjects was higher than women with a ratio of 1.6: 1^{6,7}. In this study, Diabetes melitus population at NSTEMI was higher in the population with a SYNTAX score ≥ 23 compared to a SYNTAX score ≤ 22 . This study also found patients with SYNTAX score ≥ 23 have a higher percentage of hypertension history compared to subjects with a SYNTAX score ≤ 22 . This research was conducted by Nakanishi et al in hypertensive and non-hypertensive populations proving that hypertension is associated with coronary atherosclerosis with CT angiography⁸. This is also in line with the study of Cimen et al, that subjects with higher coronary artery severity have a greater percentage of high blood pressure when compared to low coronary artery severity⁷. The theory also supports that hypertension is one of the risk factors for acute coronary syndrome or factors that influence the process of atherosclerosis. In this



INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

study also showed that subjects with a SYNTAX score ≥ 23 had a greater percentage of total cholesterol when compared with a SYNTAX score ≤ 22 . Previous study Dyer et al, which proved the relationship of total cholesterol with coronary artery disease and mortality⁹. In this study also showed that subjects with SYNTAX score ≥ 23 had higher LDL levels than those in the SYNTAX score group ≤ 22 . This is in line with the study of Abdelrazik et al which proved that high LDL values had a risk of coronary artery disease and increased coronary lesion severity by using the SYNTAX score¹⁰. Subjects with a SYNTAX score ≥ 23 had higher non-HDL-c scores compared to the SYNTAX score group ≤ 22 . This is in line with the study of Zhang et al, which proved that non-HDL-c as a predictor for severity of coronary lesions compared to with LDL in CAD populations receiving coronary angiography¹¹. Non-HDL-c itself has been recommended as a secondary target in the 2019 European Society of Cardiology on the management of dyslipidemia in reducing cardiovascular risk¹². This study also shows that subjects with a SYNTAX score ≥ 23 have a higher non-HDL-c/TC ratio compared to the SYNTAX score group ≤ 22 . This is in line with research by Huang et al which has proven that an increase in the non-HDL ratio HDL-c/TC can predict an increase in severity of coronary lesions using Gensini score and an poor outcomes in CAD populations receiving statin therapy⁴.

The SYNTAX score has many potential applications and presents a very powerful stratification tool as a standardized assessment of the severity and complexity of coronary artery lesions⁵. Several studies have also shown that hypertension, smoking and dyslipidemia are associated with severity of coronary artery lesions and measuring SYNTAX score has been recommended for the revascularization plan^{5,13}. The underlying mechanism the relationship between the ratio of non-HDL-c/TC to the severity of coronary lesions is still unknown. Maybe one mechanism is the role of apolipoprotein B, which has been proven that apolipoprotein B is a transport lipoprotein in triglyceride, VLDL, IDL and chylomicrons. Continuous exposure to lipoproteins containing ApoB causes development of atherosclerotic plaque.^{12,13} There are some limitation of this study such as observational study, single center with limited study subjects.

Conclusion

The aim of the this study is to determine the relationship of non-HDL-c/TC ratio with severity of coronary artery lesions using SYNTAX scores in patients with acute coronary syndrome. Based on the results, it can be concluded that the ratio of non-HDL-c/TC has a significant relationship with severity of coronary artery lesions in patients with acute coronary syndrome in Adam Malik General Hospital with a low correlation value.

Conflict of interest

The authors declare that there is no conflict of interest

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INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

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