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Correlation between Apolipoprotein B Levels with Coronary Lesion Area Based on the Gensini Scores in Coronary Heart Disease Patients

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ABSTRACT

Background: Coronary heart disease (CHD) is caused by atherosclerosis. apolipoprotein B (Apo B) is a large glycoprotein, that plays a role in lipoprotein metabolism and human lipid transport, reflecting atherogenic cholesterol transport. The Gensini scoring system has the highest correlation with the severity of coronary artery stenosis as assessed by angiography. This study aims to determine the correlation between apolipoprotein B levels with the area of coronary lesions based on the Gensini score in patients with CHD

Methods: This research is an observational study with cross cross-sectional data collection method of 76 coronary heart disease patients who were treated at H. Adam Malik General Hospital Medan (December 2021 – April 2022). Examination of the Apo B value was carried out by the immunoturbidimetry method (Architect). Coronary lesion area calculated from coronary angiography with Gensini score. The research was conducted after obtaining ethical approval and informed consent.

Result: There were 57 male subjects (75 %). The mean age of the subjects was 56.17 years with the youngest age being 24 years and the oldest being 77 years. Most of the subjects who experienced STEMI amounted to 38 people (50 %). The mean Apo B level was 89.18 mg/dL. The mean Gensini score was 62.84. By using the Pearson correlation test, it was found that a significant correlation was found between Apo B and Gensini score, r = 0,288 (p = 0.012)

Conclusions: There was a significant correlation between the levels of Apo B and coronary artery lesions based on the Gensini score. Apo B examination and Gensini score can be used as a risk assessment of severity in CHD patients. Further research is needed to involve a larger number of coronary heart disease patients.

Keywords: Apo B, Coronary heart disease (CHD), Gensini score

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Abstrak

Latar Belakang*: Penyakit jantung koroner (PJK) disebabkan oleh aterosklerosis. Apolipoprotein B (Apo B) adalah glikoprotein yang berperan besar dalam metabolisme lipoprotein dan transportasi lipid, yang mencerminkan transportasi kolesterol aterogenik. Sistem penilaian Gensini memiliki korelasi tinggi dengan tingkat keparahan stenosis arteri koroner yang dinilai dengan angiografi. Penelitian ini bertujuan untuk mengetahui korelasi antara kadar apolipoprotein B dengan area lesi koroner berdasarkan skor Gensini pada pasien PJK*

Metode*: Penelitian ini merupakan penelitian observasional dengan metode pengumpulan data secara potong lintang terhadap 76 pasien penyakit jantung koroner yang dirawat di Rumah Sakit Umum H. Adam Malik Medan dari (Desember 2021 – April 2022). Pemeriksaan nilai Apo B dilakukan dengan metode imunoturbidimetri (Arsitek). Area lesi koroner dihitung dari angiografi koroner dengan skor Gensini. Penelitian dilakukan setelah mendapatkan ethical approval dan informed consent.*

Hasil*: Terdapat 57 subjek laki-laki (75%). Usia rata-rata subjek adalah 56,17 tahun dengan usia termuda adalah 24 tahun dan yang tertua adalah 77 tahun. Sebagian besar subjek yang mengalami STEMI berjumlah 38 orang (50%). Tingkat Apo B rata-rata adalah 89,18 mg / dL. Skor Gensini rata-rata adalah 62,84. Dengan menggunakan uji korelasi Pearson, ditemukan bahwa ditemukan korelasi yang signifikan antara skor Apo B dan Gensini, r = 0,288 (p = 0,012)*

Kesimpulan*: Ada korelasi yang signifikan antara tingkat Apo B dengan lesi arteri koroner berdasarkan skor Gensini. Pemeriksaan Apo B dan skor Gensini dapat digunakan sebagai penilaian risiko keparahan pada pasien PJK.*

Kata kunci*: Apo B, Penyakit jantung koroner (PJK), skor Gensini*

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1 Introduction

Coronary Heart Disease (CHD) is one of the most common causes of death,[1] and acute coronary syndrome (ACS) is one of the major clinical manifestations of CHD.[2] CHD is generally divided into 2 groups, namely stable angina pectoris and ACS, which includes unstable angina, myocardial infarction, and sudden death, where heart muscle damage occurs characterized by increased cardiac enzyme activity and typical ECG features, both ST-elevation myocardial infarction, and non-ST-segment elevation myocardial infarction.[3] There are many risk factors (multifactorial) that play a role in CHD, among which the most important are lipids/lipoproteins.[4]

Apolipoprotein B (Apo B) is a large glycoprotein, which plays a role in lipoprotein metabolism and human lipid transport. Apo B is a major component of very low-density lipoproteins (VLDL),

intermediate-density lipoproteins (IDL), low-density lipoproteins (LDL), and lipoprotein (a).[1] Apo B consists of Apo B-100 and Apo B-48. Apo B-100 is produced in the liver (liver) and Apo B-48 is made in the intestine. Apo B-100 in plasma is more abundant than Apo B-48, although it is measured after meals. The total amount of Apo B describes the number of particles that have a strong atherogenic effect.[5] Apo B is an independent risk predictor of coronary artery disease severity.[6]

Currently, there are various scoring systems used for the quantitative analysis of coronary artery lesions and the Gensini score assessment is more commonly used in clinical practice. The Gensini score is an effective tool for evaluating the severity of coronary artery disease.[7] The Gensini score fully considers the number, location, and degree of stenosis of coronary artery lesions, which is a more scientific evaluation standard for coronary artery lesions. Gensini developed a scoring system to determine the severity of coronary artery disease based on the degree of stenosis of the luminal coronary arteries through coronary artery angiography. This scoring system was designed to geometrically assess the severity of coronary lesions (diameter reductions of 25, 50, 75, 90, 99, and 100% and the cumulative effect of multiple lesions, as well as the effect of lesion location. [8,9] This study aims to determine the correlation between Apo B levels with the area of coronary lesions based on the Gensini score in patients with coronary heart disease

2 Method

This research is an observational study with a cross-sectional data collection method. This research was conducted at the Department of Clinical Pathology, USU Medical Faculty/H. Adam Malik Hospital, Medan in collaboration with the Department of Cardiology, USU Medical Faculty/H. Adam Malik Hospital in the selection of coronary heart disease patients starting from December 2021 until April 2022. The study sample was patients with coronary heart disease who had been diagnosed by the Department of Cardiology at H. Adam Malik Hospital, Medan. The study was conducted after obtaining approval (ethical clearance) from the Health Research Committee, Faculty of Medicine, University of North Sumatra, and research permission from the Research and Development Installation of Haji Adam Malik Hospital, Medan.

The sample size in this study was 76 samples. Apo B examination was carried out at the Department of Clinical Pathology and the Gensini score was calculated at the Department of Cardiology, H. Adam Malik Hospital, Medan. The inclusion criteria in this study were coronary heart disease patients who underwent coronary angiography. Exclusion criteria in this study were pregnant women, liver disease patients, sepsis patients, nephrotic syndrome patients, patients with post-CABG history, and patients with PCI history.

Blood samples were taken for Apo B examination using a vacutainer tube taken from the median cubital vein as much as 5 mL, then the blood in the tube was centrifuged at 3000 rpm for 15

minutes, then the serum was taken. Apo B examination was carried out using the Abbot Architect automatic cell analyzer. The Apo B assay was performed by an immunoturbidimetric procedure which measures the increase in sample turbidity caused by the formation of insoluble immune complexes when antibodies to Apo B are added to the sample. Samples containing Apo B were incubated with buffer and the determination of sample blanks was carried out before the addition of Apo B antibody. Due to the presence of an excess of appropriate antibodies, Apo B concentration was measured as a function of turbidity.

The Gensini score was calculated based on the results of coronary angiography. Angiography was performed on both the left and right coronary arteries and each arterial segment was also analyzed. Scores are assigned based on the degree of obstruction of the luminal coronary arteries. An assessment of the reduction in coronary diameter was made, namely 0-25-50-75-90-99-100%. Then a value is given to the degree of reduction with values in the order 0-1-2-4-8-16-32. Then multiplied according to the location of the affected coronary segment.

Statistical Analysis

Data analysis using SPSS (*Statistical Package for Social Sciences*, Chicago, IL, USA) software for Windows. The description of the characteristics of the research subjects is presented in tabulated form and described. Correlation of Apo B levels with lesion area based on the Gensini score in patients with coronary heart disease using the Pearson correlation test, because the data were normal. All statistical tests with p-values < 0.05 were considered significant.

3 Result

There were 57 male subjects (75 %). The mean age of the subjects was 56.17 years with the youngest age being 24 years and the oldest being 77 years. A total of 32 subjects (42,1 %) had a habit smoke. A history of hypertension was found in 41 subjects (53.9%) and 35 subjects (46.1%) with a history of DM. Based on the results of the examination showed most of the subjects experienced STEMI amounted to 38 people (50%). The complete characteristics of the subject are presented in Table 1.

Table 1 Characteristics of Research Subjects

Characteristics Subject	n = 76
Sex, n (%)	
Male	57 (75)
Female	19 (25)
Age, years	
Mean (SD)	56.17 (9.42)
Median (Min-Max)	56 (24 – 77)
Smoking, n (%)	
Yes	32 (42.1)
No	44 (57.9)
Hipertension, n (%)	
Yes	41 (53.9)
No	35 (46.1)
Diabetes Mellitus, n %)	
Yes	35 (46.1)
No	41 (53.9)
Diagnosis n (%)	
APS	18 (23.69)
NSTEACS (NSTEMI)	14 (18.42)
NSTEACS (UAP)	6 (7.89)
STEMI	38 (50)

Table 2 shows Apo B levels and Gensini score to assess the extent of coronary lesions in patients with coronary heart disease. The mean level of Apo B was 89.18 mg/dL with the lowest level at 37 mg/dL and the highest level at 141 mg/dL. Gensini's average score is 62.84 with the lowest score of 1 and the highest score of 171. Based on score categorization Gensini showed as many as 67 people (88.2%) with severe atherosclerosis and 9 people (11.8%) with mild atherosclerosis.

Table 2 Apolipoprotein B Level and Gensini Score

Variable	n = 76
Apo B levels, mg/dL	
Mean (SD)	89.18 (25.07)
Median (Min-Max)	87 (37 – 141)
Gensini's score	
Mean (SD)	62.84 (36.4)
Median (Min-Max)	60 (1 – 171)
Severe atherosclerosis	67 (88.2)
Mild atherosclerosis	9 (11.8)

Table 3 shows the correlation between cardiovascular risk factors (Apo B, LDL-cholesterol, fasting plasma glucose) with coronary lesion area based on Gensini score. Using the Pearson correlation test shows a significant correlation between Apo B and the Gensini score ($p = 0.012$). The correlation value (r) obtained is 0.288, which means that there is a level of correlation is a positive value, the higher Apo B, will be followed by a higher area of coronary lesions based on the Gensini score in patients with coronary heart disease. The correlation between LDL-Cholesterol with coronary lesion area based on the Gensini score, using

the Pearson correlation test in this study showed that r= 0.270 (p= 0.019). In this study, using Spearman correlation, there is no positive relationship between Fasting Plasma Glucose (FPG) and the area of coronary lesions based on the Gensini Score, r= 0.043 (p= 0.715).

Table 3 Correlation between Cardiovascular Risk Factors (Apo B, Fasting plasma glucose, and LDL Cholesterol) with coronary lesion area based on Gensini score

		Coronary lesion area based on Gensini score	
Parameter		**r**	**p**
Apo B	mg/dL	0.288	0.012 *a
LDL-Cholesterol	mg/dL	0.270	0.019 *a
Fasting plasma glucose	mg/dL	0.043	0.715 *b

Significant : 'p' < 0.05; *a Pearson Correlation Test; *b Spearman Correlation Test

4 Discussion

The study Ghodsi et al 2021 conducted a retrospective cohort study of 2259 STEMI patients who were to undergo PCI and examined for Apo B and Lipid profile. Most of the subjects were male 1759 people (77.9%), mean age of 59.54 years with the youngest being 46 years, the oldest being 70 years old, and 611 subjects (45.1%) had a smoking habit.[10] The research conducted by Bodde et al, 2019, conducted a retrospective cohort study of 220 STEMI patients who were to undergo PCI. From the character of the research subjects obtained, most of the subjects were male, amounting to 173 people (78.6%), The mean age of the subjects was 55 years with the youngest 46 years old and the oldest 64 years old and 139 subjects (63.2%) had a smoking habit.[11] The study is in line with this study with male subjects (75 %), the mean age of the subjects was 56.17 years with the youngest age being 24 years and the oldest being 77 years. A total of 32 subjects (42,1 %) had a habit smoke.

The risk factors for coronary heart disease include age and gender, with the incidence in men much more than in women, but the incidence in women will increase after menopause around the age of 50 years. This is because the hormone estrogen has a protective effect against the occurrence of atherosclerosis, where in people aged > 65 years 20% of CHD in men and 12% in women. Increasing age will cause an increase in patients with CHD because blood vessels undergo progressive changes and last for a long time. The earliest changes begin at age 20 in the coronary arteries. Other arteries begin to modify only after the age of 40 years, occur in men aged 35-44 years, and increase with age.[12] Smoking, whether active or passive, can cause cardiovascular disease through a series of interdependent processes, such as enhanced oxidative stress, hemodynamic and autonomic changes, endothelial dysfunction, thrombosis, inflammation, and hyperlipidemia. Individuals who smoked about one cigarette per day had a 48% higher risk of coronary heart disease than nonsmokers. Several chemicals in tobacco smoke can cause

excessive reactive oxygen species (ROS) formation which results in smooth muscle cell proliferation, DNA damage, and inflammation, all of which lead to coronary heart disease.[13]

Type 2 diabetes mellitus (T2DM) is a risk factor for CHD if it is not managed properly will cause various chronic complications, both microangiopathy such as retinopathy, and nephropathy and macroangiopathy such as coronary heart disease. The main cause of mortality and morbidity in T2DM patients is CHD.[14] The results of this study show that hypertension is a risk factor for the occurrence of CHD, which means that respondents who have hypertension have a risk of 4.048 times experiencing CHD events compared to those without hypertension. Blood pressure that continues to increase in the long term will cause the formation of plaque that will narrow the blood vessels, and in certain circumstances where high blood pressure can crack plaque so that plaque fragments can clog blood vessels, where it is known that blood vessels are the entry route for oxygen and energy. to the heart. In addition, increased blood pressure due to hypertension can increase resistance to pumping blood, so the workload of the heart will increase.[15]

In this study, the mean level of Apo B was 89.18 mg/dL with the lowest being 37 mg/dL and the highest level being 141 mg/dL. Gensini's average score is 62.84 with the lowest score of 1 and the highest score of 171. Based on categorization Gensini's score showed as many as 67 people (88.2%) with severe atherosclerosis and 9 people (11.8%) with mild atherosclerosis. Study results from research conducted by Hua et al, 2021, conducted a cross-sectional study of 6956 CAD patients who would undergo PCI, then all study subjects were examined for Apo B and Gensini scores. There are differences in results from this study showed the mean level of Apo B was 72 mg/dL with the lowest level of 59 mg/dL and the highest level of 88 mg/dL. Gensini's average score is 40 with the lowest score of 20 and the highest score of 70.[1] : Both Apo B and Apo B/Apo A1 ratio correlated significantly with Gensini scores (p-value scores $p < 0.001$)

High Gensini score patients had a significantly high Apo B/Apo A1 ratio with the best cutoff value of 0.8 with sensitivity of 90% and specificity of 70%. [17]

Apolipoproteins are important components of lipoprotein particles, and measurement of various forms of apolipoproteins can improve the prediction of cardiovascular disease risk. In the study conducted by Hua et al, 2021 on 6956 CAD patients who will undergo PCI, then all study subjects were examined for Apo B and Gensini scores. The results of their study showed that there was a significant relationship between Apo B and CAD and a significant relationship with Gensini's score ($P < 0.001$), [1] similar to this study

By using the Pearson correlation test in this study showed that a significant correlation was found between Apo B with the area of coronary lesions based on the Gensini score ($p = 0.012$). The correlation value (r) obtained is 0.288. The correlation between LDL-Cholesterol with coronary lesion area based on the Gensini score, using the Pearson correlation test in this study showed that

r= 0.270 (p= 0.019). In this study, the correlation between Apo B with coronary lesion area based on the Gensini score is higher than the correlation between LDL- cholesterol with coronary lesion area based on the Gensini score. In this study, using Spearman correlation, there is no positive relationship between Fasting Plasma Glucose (FPG) and the area of coronary lesions based on the Gensini Score, r= 0.043 (p= 0.715). Thus, an increase in Fasting Plasma Glucose will not followed by an increase in the area of coronary lesions based on the Gensini Score.

In line with the cross-sectional study conducted by Yaseen et al, 2021 on 90 ACS patients, they obtained the results that Apo B levels were significantly correlated with Gensini score (r= 0.32, P value < 0.001). This is also in line with the case-control study conducted by Mashayekhi et al, 2014 on 271 CAD patients, they obtained a significant correlation between Apo B and Gensini score (r = 0.127, with p = 0.047).[16] This is also in line with the study of Hua et al, 2021. Researchers conducted a cross-sectional study of 6956 CAD patients undergoing PCI, then all research subjects were examined for Apo B and Gensini scores. The results of their study show that there is a significant relationship between Apo B and CAD and there is also a significant relationship with the Gensini score (P < 0.001). An important implication of this study is that ApoB was identified as a serum predictor for the severity of the lesion cardiovascular disease in CAD patients. Shows a positive linear correlation between Apo B and Gensini scores in patients with CAD but not in non-CAD patients, suggesting that Apo B has a potential mechanism for the progression of coronary lesions in CAD patients.[1]

Moreover, it implies that Apo B monitoring is associated with pathology inflammation in CAD. A previous study showed that Apo B can predict CAD plaque susceptibility. Apo B also predicts the severity of CAD and provides more prognostic information than routine lipid profiles. However, several studies have answered that Apo B is associated with levels of coronary disease severity using a complex approach and systemic score, that is, the Gensini score or the SYNTAX score to predict the severity of coronary artery stenosis more accurately.[1]

The strength of this study is that Apo B is a new biomarker whose cardiovascular risk factor is more accurate and updated. The use of Apo B also has several advantages in CAD patients, e.g. non-invasive, simpler, and more inexpensive compared to coronary angiography. This still applies to some patients with contraindications to coronary angiography. The limitations of this study that must be addressed: are (1) the small number of study population. (2) Apo B is not yet widely used because it is not covered by national insurance.

5 Conclusion

In this study, from the characteristics of the subjects in patients with coronary heart disease, it was found that based on gender, male was more than female as much as 75 %, based on age there was a mean age of 56,17 years, based on risk factors for the disease, smoking was 42.1 %,

hypertension was 53.9 %, DM was 46.1 %. The mean level of Apo B was 89.18 mg/dL. Gensini's average score is 62.84 years. By using the Pearson correlation test, it was found that a significant correlation was found between Apo B and Gensini score.

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