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Original research

STUDYING VARIABLE IN SERUM APOLIPOPROTEIN B LEVELS IN DAMAGED CORONARY ARTERY PATIENTS

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ABSTRACT

Introduction: *Atherosclerosis is the most important cause of increasing coronary heart disease. When cholesterol LDL-C levels are low, an increase in Apo B is associated with 60% of the cardiovascular risk factors. This study find out the association between serum Apolipoprotein B levels with the degree of coronary artery lesions*

Methods: *The study consists of 110 patients who were diagnosed with a meaningful damaged coronary artery through angiography at Hoan My Da Nang hospital, from March 2018 to September 2019. Research method: cross-sectional description.*

Results: *The average value of serum Apo B in group 1 was 133.67 ± 17.56 mg/dl, and in group 2 it was 113.92 ± 16.78 mg/dl. The difference is statistically significant, p < 0.01. Cardiovascular risk factors in the study did not have a meaningful effect on serum Apo B levels. Dyslipidemia does not have a strong correlation with serum Apo B levels. Thereby, it is possible to recognize serum Apo B as an independent indicator along with other cardiovascular risk factors. Serum Apo B levels increase linearly according to the number of damaged coronary artery branches. There is a proportional correlation between serum Apo B levels and the degree of coronary artery lesions (r = 0.48, p < 0.01).*

Conclusion: *Apo B is associated with the degree of coronary artery lesions.*

Keywords: *Apolipoprotein B, coronary heart disease, atherosclerosis*

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I. INTRODUCTION

Currently, there are 422 million cardiovascular patients in the world and more than 4 million patients die annually in Europe, accounting for 45% of all deaths [1]. In Vietnam, through the development of economic society, coronary artery disease is becoming more and more prevalent and it becomes a topical question.

Atherosclerosis is the most important cause of increasing coronary artery disease. There are a lot of risk factors that form and develop coronary atherosclerosis. One of the important risk factors is dyslipidemia. Over the past three decades, it has been recognized that cholesterol total and specific LDL - cholesterol levels are the main risk factors for coronary artery disease. However, a proportion of patients have atherosclerosis but have normal HDL-C, and LDL-C levels and a proportion of coronary artery patients are still progressing even though they control their risk factors well [2]. Apolipoprotein B is the main component that constitutes lipoproteins (chylomicron, VLDL, IDL, LDL, small concentrated LDL) with a constant ratio of 1:1, so it is possible to quantify the number of atherosclerosis molecules and is very valuable in cases of increasing the small concentrated LDL predominantly [3]. In 2009, a study in Quebec, Canada, showed that Apo B is a very strong factor

in predicting cardiovascular events. It's independent of age, blood pressure, diabetes, smoking, etc. When cholesterol and LDL-C levels are low, an increase in Apo B is associated with 60% of the cardiovascular risk factors. High LDL-C and low Apo B have an increasing 1.5 - fold cardiovascular risk, but when both of them are high, the cardiovascular risk increases more than 2.2 - fold [3]. Desiring to study serum Apo B levels and their value in the diagnosis of the damaged coronary artery so as to determine the prognosis and have an appropriate treatment strategy. We carried out this study explore the association between serum Apolipoprotein B levels and the degree of coronary artery lesions

II. Materials and methods

2.1. Study subjects

There were 110 patients diagnosed with significant coronary artery damage through percutaneous coronary artery angiography at Hoan My Da Nang Hospital, from March 2018 to September 2019.

Based on the results of percutaneous coronary artery angiography, the patients were divided into two groups following ESC 2018 recommendations on the diagnosis and management of chronic coronary artery disease [4], and JAS (Japan Atherosclerosis Society) 2017 [5].

Group 1: Including patients with results of angiography that show stenosis ≥ 70% of the coronary artery diameter

Group 2: Including patients with results of angiography that show stenosis < 70% of the coronary artery diameter

Inclusion criteria: Patients are diagnosed with coronary artery disease through percutaneous coronary artery angiography. The patient agreed to participate in the study. Patient cardiovascular risk stratification is based on the ESC/EAS 2016 recommended treatment of dyslipidemia [6].

Exclusion criteria: Congenital malformations the of coronary artery (fistula, left artery originating from the right coronary artery). Systemic diseases (Kawasaki disease, Takayasu, systemic lupus erythematosus, ...). Radiation-induced coronary artery disease. Severe heart valve diseases. Life - threatening arrhythmias. Injury or stroke in less than 3 months; acute infections. Patients who have fever or are suspected of having combined surgical diseases. Patients with acute or chronic liver disease or kidney failure. The patient is taking medicine to lower lipidemia. The patient did not agree to participate in the study.

2.2. Research methods

Research design: Cross-sectional description. Choose a convenient template.

Testing methods:

Quantity of serum Apo B levels

Quantitative method: Quantifying Apo B levels using the immunity method of measuring turbidity on Beckman Coulter's AU 680 machine.

Normal values (according to Beckman Coulter 1 and 2) [7]: Male: 60 - 140 mg/dl; Female: 55 - 130 mg/dl

Quantity of bilan lipid:

- Total cholesterol: Quantified by the enzyme color comparison method, CHOP - PAP technique (cholesterol oxidase phenazone amino peroxidase).

- Triglyceride: Quantified by GPO - PAP enzyme color comparison (glycerol phosphate oxidase phenazone amino peroxidase).

- HDL - cholesterol: Quantified by the Burstein and Lopes - Virella method with the CHO - PAP technique after being made with phosphotungstic acid and Mg++.

- LDL - cholesterol: calculated according to the Formula Friedelwald LDL = CT - (HDL + TG / 2.2).

Quantity of glycemia: Quantifying blood glucose according to enzyme color comparison (hexokinase method).

Quantity of blood creatinine: Creatinine is measured using non-decaliculating kinetic method, normal value: 62 - 115 μmol/l

The quantitative variables of total cholesterol, triglycerides, HDL-C, LDL-C, non - HDL-C, and Apo B are evaluated according to the AHA/ACC 2018 dyslipidemia recommendations [8].

2.3. Stratification of cardiovascular risk and treatment of dyslipidemia

Based on ESC/EAS's 2016 recommendations for dyslipidemia, stratification of the risk of cardiovascular diseases [6].

Classification of dyslipidemia levels according to the AACE 2017 [9].

Table 1: Levels of dyslipidemia

Blood lipids	Disorder value (mmol/l)
Cholesterol (mmol/l)	≥ 5.2
Triglyceride (mmol/l)	≥ 1.4
HDL-C (mmol/l)	< 1
LDL-C (mmol/l)	≥ 3.4
Non - HDL-C (mmol/l)	≥ 3.7

2.4. Variable study in coronary angiography

- Number of damaged branches: 1, 2 or 3 branches.

- The degree of stenosis: Coronary stenosis is significant if it's ≥ 50% of the diameter of the vessel, as evaluated by the software to quantify the degree of coronary stenosis of the DSA Artis One Siemen machine.

- Assess coronary damage by Gensini scale [10]

2.5. The severity of the damage is calculated on the GENSINI scale

Severity of injury = number of damaged points x coefficient.

The patient's Gensini score is the total Gensini score of the narrow segments on the circuit. The severity of damage on the Gensini scale: Mild: ≤ 23 points; average: 24 - 54 points, severity: > 54 points [10].

2.6. Data processing

The data of the study is handled by SPSS 22.0

III. Results

Table 2: Serum Apolipoprotein B levels

Stenosis group	Group 1 (n = 70)	Group 2 (n = 40)	p
Apo B (mg/dl)	133.67 ± 17.56	113.92 ± 16.78	< 0.01

The average value of serum Apo B in group 1 is higher than in group 2 with a statistically significant, p < 0.01.

Table 3: Correlation between Apo B and Cardiovascular Risk Factors

Characteristic		n	Apo B (mg/dl)	p
Age	< 60	41	126.73 ± 19.69	> 0.05
	≥ 60	69	126.34 ± 19.79	
Sex	Male	62	125.48 ± 18.27	> 0.05
	Female	48	127.78 ± 21.47	
Hypertension	Yes	76	127.09 ± 20.66	> 0.05
	No	34	125.13 ± 17.46	
Diabetes	Yes	34	129.91 ± 18.94	> 0.05
	No	76	124.95 ± 19.92	
Dyslipidemia	Yes	60	126.91 ± 18.99	> 0.05
	No	50	125.97 ± 20.63	

Characteristic		n	Apo B (mg/dl)	p
Smoking	Yes	27	126.47 ± 18.07	> 0.05
	No	83	126.49 ± 20.27	
BMI	< 23	59	126.08 ± 19.84	> 0.05
	≥ 23	51	126.95 ± 19.66	

Serum Apo B levels have no difference between subtypes of cardiovascular risk factors. Factors such as hypertension, diabetes, smoking, and BMI did not have an effect on serum Apo B levels in the study group.

Table 4: Correlation coefficients between serum Apolipoprotein B levels and blood lipid parameters in the study

Element	r	p
Cholesterol (mmol/l)	0,21	< 0.05
Triglyceride (mmol/l)	0,04	> 0.05
HDL-C (mmol/l)	0,05	> 0.05
LDL-C (mmol/l)	0,06	> 0.05
Non - HDL-C (mmol/l)	0,25	< 0.05

Serum Apo B has a weak correlation with cholesterol levels, non - HDL-C.

Serum Apo B does not correlate with the following factors: LDL-C, HDL-C, Triglycerides.

Table 5: Serum Apolipoprotein B levels according to the number of narrowing branches

Number of damaged coronary branches	n	Apo B levels (mg/dl) (X ± SD)	p
1 branch	31	120.01 ± 19.13	< 0.01
2 branches	44	121.59 ± 16.62	
3 branches	35	138.36 ± 18.81	

The average serum Apo B levels between the 3 groups differed with p < 0.01.

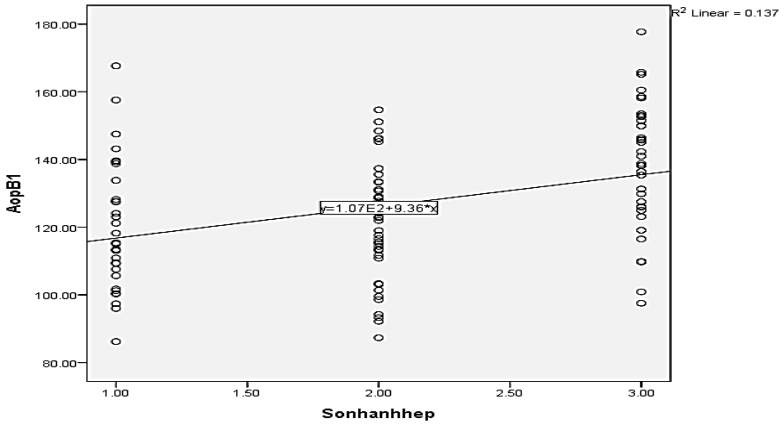

Figure 1: Point distribution chart of Apo Lipoprotein B and the number of damaged branches. The linear regression equation between Apo B and the number of damaged coronary artery branches. Linear regression equation: Apo B = a + b number of narrowing branches. Correlation coefficient r = 0.37. The blocker is: 107.43 mg/dl. Regression coefficient b = 9.36; confidence interval 95%, p < 0.01. Equation: Apo B = 107.43 + 9.36, number of narrowing branches

Table 6: Apo Lipoprotein B levels and Gensini scale

Gensini scale	n	Apo B (mg/ml) (X ± SD)	p
Gensini score ≤ 23	42	116.50 ± 17.32	< 0.01
Gensini score 24 - 54	38	126.98 ± 17.53	
Gensini score > 54	30	139.84 ± 17.58	

Serum Apo B levels between Gensini point groups differed with a 95% reliability.

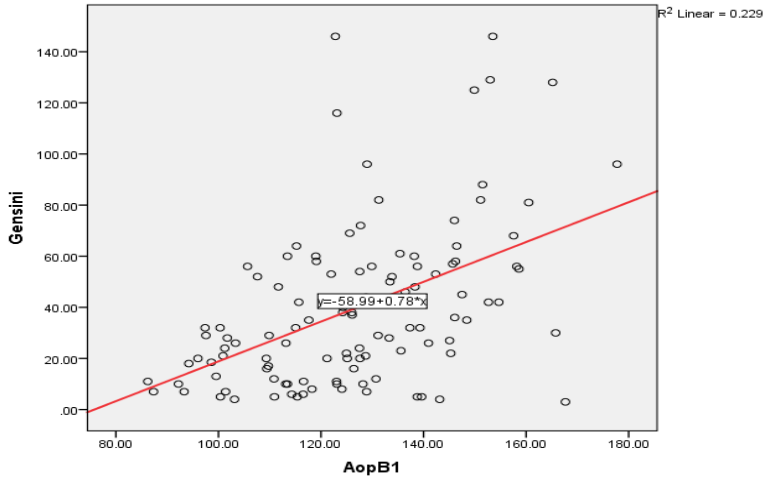

Figure 2: Distribution dot chart of Gensini point

Linear regression equation between Apo B and Gensini scale. Linear regression equation: Gensini score = a + b Apo B. Correlation coefficient r = 0.48, p < 0.01. The block point is: - 58.99. Regression coefficient b = 0.778. Confidence interval 95% (0.506 - 1.051). Meaning level p < 0.01. Equation: Gensini score = 0.778 Apo B - 58.99

Through the regression equation, we can estimate the Gensini scale of coronary damage based on the patient's serum Apo B level.

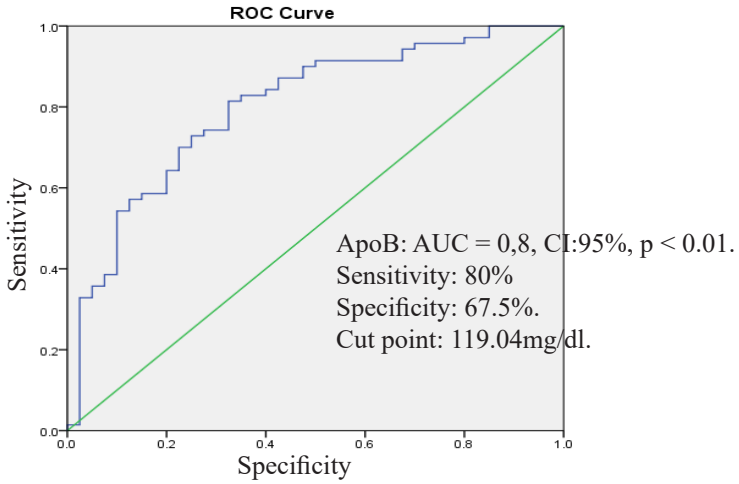

Figure 3: ROC curve of serum Apo Lipoprotein B level predicts the degree of coronary stenosis

Increased Apo B concentration has an area below the AUC curve = 0.8, p < 0.01 has a predictive value of coronary artery stenosis with a cutting value of 119.04 mg/dl with a sensitivity of 80%, specificity of 67.5%.

IV. DISCUSSION

Cardiovascular disease in general and coronary heart disease in particular are the enemies of humanity in the modern world with numerous risk factors for this disease. It is currently the leading cause of death from all diseases. Coronary atherosclerosis is considered the main cause. Initially, blood lipid indices such as cholesterol, triglyceride, HDL-C, and LDL-C were used to assess the risk and evaluate coronary artery damage. However, there is a contradiction in the correlation between blood lipid parameters and coronary artery damage, leading researchers and contemporary medical systems to find new and more valuable parameters. New studies on the mechanism of atherosclerosis have found that an increase in the amount of small dense LDL-C associated with atherogenic dyslipidemia is reflected in increased levels of Apo B - an indicator reflecting lipoprotein production better. Comparing between the two study groups on Apo B concentration, we found that: group 1 had an average Apo B of 133.67 ± 17.56 mg/dl; group 2 had an average Apo B of 113.93 ± 16.78 mg/dl. This difference was statistically significant with $p < 0.01$. Thereby we see that the level of Apo B is directly proportional to the degree of coronary stenosis. According to Nguyen Thi Binh Minh (2016), the mean serum Apo B level in coronary artery stenosis was 110.7 ± 25.1 mg/dl, while it was 86.8 ± 12 mg /dl in non - stenotic group, $p < 0.01$ [11]. The study of H. Tineke Westerveld (n = 117, 1997) had similar results: 121 ± 20 mg/dl and 108 ± 28 mg/dl, $p < 0.01$ [13].

The value of Apo B in coronary stenosis has been scientifically proven. The above studies all showed that the Apo B level of the coronary artery lesion group was significantly higher than the non-injured group. In the study, we evaluated the level between the 2 groups of severe and mild coronary stenosis to find out, in addition to the role of an indicator for medical assessment of coronary artery disease, what value it has to assess the extent of coronary artery disease. Our research results are similar to Nguyen Thi Binh Minh's and higher than other authors. All the subjects in the study were probably patients with coronary stenosis. Therefore, the value of Apo B is more closely associated with the prognosis of the lesion.

The study's results showed that serum Apo B level was associated with the number of damaged coronary artery branches. The Apo B level increased corresponding to the number of main damaged branches: 120.01 ± 19.13 mg/dl; 121.59 ± 16.62 mg/dl; 138.36 ± 18.81 mg/dl with 1, 2, and 3 narrow branches, respectively. This result is also consistent with the study of Nguyen Thi Binh Minh (2016) with the average serum Apo B level according to the corresponding narrow branches: 1 - branch stenosis 96.5 ± 21.2 mg/ dl, 2 - branches are 110.3 ± 20.8 mg/dl, 3 - branch stenosis are 136.4 ± 16 mg/dl, $p < 0.01$ [11]. Study of H Tineke Westerveld (n = 160, 1997) were respectively 139 ± 29 mg/dl, 155 ± 33 mg/dl, 164 ± 34 mg/dl, $p < 0.001$ [12]. Research by N. S. Dange (n = 234, 2011) showed similar results: 143.36 ± 10.16 mg/dl; 148.75 ± 13.28 mg/dl; 149.84 ± 1.92 mg/dl, $p < 0.001$ [13].

Hypertension is a risk factor for cardiovascular disease and particularly for coronary artery disease. Hypertension often co - exists with other risk factors, synergistically affecting the pathology, especially dyslipidemia. In the study, the results of serum Apo B level in the group without hypertension were 125,13 ± 17.46. There was no difference with the group with hypertension 127.09 ± 20.66 mg/dl, $p > 0.05$. This result is different from some results of domestic and international studies, because the subjects in the selected study group all had coronary artery lesions, and because of the mixing of many other factors in the structure of risk factors, they elevated serum Apo B levels in the non-hypertensive group. Research by Nguyen Thi Binh Minh on 102 patients (2016) showed that the group with hypertension was 117.4 ± 23.5 mg/dl higher than the group without hypertension, which was 97 ± 23.2 mg/dl, $p < 0.05$ [11].

In the study, we evaluated in more detail the role of Apo B in coronary injury through the following parameters: location, number of branches, and Gensini scale. The results showed that Apo B level was related to the number of damaged coronary branches. The level of Apo B increased correspondingly to the number of main branches of lesions: 120.01 ± 19.13 mg/dl; 121.59 ± 16.62 mg/dl; 138, 36 ± 18.81 mg/dl with 1, 2, and 3 narrow branches, respectively. Research

by Nguyen Thi Binh Minh (2016) has the results of mean serum Apo B level according to the corresponding narrow branches: narrowing of 1 branch 96.5 ± 21.2 mg/dl, 2 branches being 110.3 ± 20, 8 mg/dl, 3 branches are 136.4 ± 16 mg/dl, $p < 0.01$ [11]. Research by H Tineke Westerveld (1997) are 139 ± 29 mg/dl, 155 ± 33 mg/dl, 164 ± 34 mg/dl, $p < 0.001$ [12], respectively. Research by N. S. Dange (2011) were similar results 143.36 ± 10.16 mg/dl; 148.75 ± 13.28 mg/dl; 149.84 ± 1.92 mg/dl, $p < 0.001$ [13].

Research shows that serum Apo B is an independent biochemical indicator that can be used clinically to predict the number of damaged coronary artery branches for patients. Through the analysis of linear regression between Apo B level and the number of narrowing coronary branches: we see a favorable correlation between Apo B and the number of narrow branches ($r = 0.37$, $p < 0.01$) and we write the linear regression equation between the number of narrowing coronary branches and Apo B: Apo B (mg/dl) = 107.43 + 9.36 number of narrowing branches.

Previously, there were many evaluations of Apo B with coronary artery lesions, but mostly based on the number of narrow branches and the degree of stenosis, so many different judgments were made. The study used the Gensini scale to assess coronary lesions on the results of percutaneous coronary angiography. The Syntax scale assessed the degree of stenosis starting at a narrowing of 50% of the lumen diameter. Lesions < 50% have not been evaluated well, especially lesions formed in a multi - lesion coronary system, so the study chose the Gensini scale. The Gensini scale assesses lesions of 25% or more of vascular stenosis.

When considering the correlation between serum Apo B levels and the Gensini scale in the study, it was found that there was a proportional correlation: $r = 0.48$, $p < 0.01$. This result is equivalent to Nguyen Thi Binh Minh, which has a correlation coefficient $r = 0.491$, $p < 0.001$ [11].

Apo B cutting point at the time of diagnosis of coronary heart disease by percutaneous coronary angiography with a cutting point threshold of 119.04 mg/dl, sensitivity is 80%, specificity is 67.5%, area below the curve (AUC) is 0.8 with $p < 0.01$. Thereby we can rely on the value of the cutting point to assess the prognosis of the degree of damaged coronary artery.

V. CONCLUSION

Cardiovascular risk factors in the study did not have a meaningful effect on serum Apo B levels. Dyslipidemia does not have a strong correlation with serum Apo B levels. Thereby, it is possible to recognize serum Apo B as an indicator independent of other cardiovascular risk factors. Serum Apo B levels increase linearly according to the number of damaged coronary artery branches. There is a proportional correlation between serum Apo B levels and levels of coronary artery damage ($r = 0.48$, $p < 0.01$).

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