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# Assessment of the role of lipoprotein a level in the development of cardiovascular diseases

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**Abstract**

A comparative trial within 2 groups of patients with cardiovascular diseases who have high and normal levels of lipoprotein (a) was conducted to determine the link between high levels of Lp (a) and the nature of the development of cardiovascular events. According to the results of the study, conclusions about the significance of the level of Lp(a), as well as hypolipidemic therapy in patients with cardiovascular pathology were made. The features of the population of patients with an expected increase in Lp(a) and the predominance of lesions of the brachiocephalic arteries among individuals with increased Lp(a) were revealed. Hypolipidemic statin therapy with a passable correction of the lipid spectrum does not always allow to control the increase in Lp(a).

## Introduction

The relevance of the further search for methods of treatment of cardiovascular diseases (CVD) is caused by their predominance in the structure of mortality worldwide. The main cause of cardiovascular catastrophes is an atherosclerotic damage to the arteries. Consequently, the main therapeutic measures are aimed at reducing the level of low-density lipoproteins (LDL). The first-line drugs of lipid-lowering therapy are HMG-CoA reductase inhibitors.

However, in a number of situations, despite optimal control of LDL levels, there is a high risk of cardiovascular complications (CVD)-60-80% [1]. The reason for this may be a high level of lipoprotein (A) (Lp (a)). Studies have demonstrated that the quantitative level of Lp (a) and its low-molecular-weight apo(a) phenotypes are independent risk factors for peripheral and major artery atherosclerosis and coronary atherosclerosis [2,3].

Lp(a) consists of two main components: an LDL-like particle containing ApoV-100, and a specific glycoprotein apo (a) particle, which are interconnected by a disulfide bridge [4]. The apo(a) genotype determines the rate of synthesis, the size of the apo(a) particle in the Lp(a), and the concentration of Lp(a) in the plasma. The level of Lp (a) in plasma is genetically determined, so its indicators in the same person are generally considered constant over time [5]. They are not significantly affected by diet or environmental factors that mediate the risk of cardiovascular disease (CVD) throughout the patient's life.

Lp (a) fixes on plaques and lingers in the arterial wall; it improves the formation of foam cells, generates oxidized radicals in monocytes, promotes the proliferation of smooth muscle cells, and induces monocyte-chemotactic activity in subendothelial spaces [6]. In addition, Lp (a) can stimulate the formation of blood clots due to the inhibition of fibrinolysis.

Blood concentrations of Lp(a) above 50 mg/dl account for up to 20% of the total population and are even more common in patients with CVD and aortic stenosis. The level of Lp (a) greater than 30 mg/ dl is detected in 37-40% of patients at high risk of developing CVD and only in 14% of low-risk individuals. In chronic ischemic heart disease(CHD), the frequency of high Lp (a) levels in men reaches 39%, among women – 48%, while in patients without CHD – 12-15% [7].

## Materials and methods

***Study design:*** a cross-sectional (single-stage) study of patients with manifest CVD who received at least 6 months of combined CVD therapy, including lipid-lowering statin therapy, antiplatelet agents, ACE inhibitors, and B-blockers.

***Inclusion criteria:*** male and female patients aged ≥18 to ≤80 years, the presence of manifest CVD disease, defined as one of the following: a history of myocardial infarction (MI) in the period from ≥ 3 months to ≤ 10 years, a history of ischemic stroke (AI) in the period from ≥ 3

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months to ≤ 10 years, symptomatic peripheral artery disease.

Anamnesis, clinical and demographic data were collected, anthropometric measurement and study of the lipid spectrum of blood plasma were carried out. The anthropometric study included the determination of height (m), body weight (kg), BMI according to the Quetelet formula. The laboratory study included the determination of total cholesterol (TC), triglycerides (TG), high-density lipoproteins (HDL), LDL, and plasma Lp(a). Statistical processing of the results was carried out using the computer program "STATICTICA 10.0". The methods of comparative statistics (Mann-Whitney U-test, Wilcoxon T-test) were used for pair comparisons. The differences were considered statistically significant at p<0,05.

## Research results and their consideration

The study included 52 patients (25 men and 27 women), mean age 67.25±7.8 years, with manifest CVD, who were treated by a cardiologist at the 'Family Clinic' LLC for 1 month. The age and gender structure of the sample corresponds to the natural structure and was not corrected.

The study sample was divided into 2 groups based on the level of Lp(a) based on the results of laboratory data.

Group I included 13 (25%) patients with an Lp(a) level of ≥0.3 g / l: 3 men and 10 women, age 70.3±7.6. The analysis of the nosological structure of CVD revealed that in this group, 13 (100%) patients suffered from arterial hypertension (AH), tension angina was detected in 9 (69.2%) patients, MI in the anamnesis was in 4 (30.8%) patients, AI in the anamnesis was in 9 (69.2%) patients, obliterating atherosclerosis of the vessels of the lower extremities (OASNA) was detected in 3 (23.1%) patients, atherosclerosis brachiocephalic arteries (BCA) – in 12 (92.3%) patients, type 2 diabetes mellitus (DM) affected 5 (38.5%) patients. The level of OHS in this group is 4.25 [4.18; 6.31] mmol / l, the level of TG is 1.84 [1.13; 2.3] mmol / l, HDL level-1.4 [1.25; 1.61] mmol/l, LDL level-2.52 [2.07; 4.29] mmol/l, Lp(a) level-0.72 [0.44; 1.21] mmol/l.

Group II included 39(75%) patients with Lp (a) levels <0.3 g/l: 22 men and 17 women, age 66.23±7.7. When analyzing the nosological structure of CVD, it was revealed that in this group, 35 (89.7%) patients suffered from hypertension, 26 (66.7%) patients had angina pectoris, 22 (56.4%) patients had a history of MI, 16 (41%) patients had a history of AI, 18 (46.2%) patients had OASNA, 23 (59%) patients had BCA atherosclerosis, and 17 (43.6%) patients had type 2 diabetes. The level of OHS in this group is 4.35 [3.65; 5.35] mmol / l, the level of TG is 1.63 [1.25; 2.66] mmol / l, HDL level-1.11 [0.91; 1.33] mmol/l, LDL level-2.46 [1.75; 3.15] mmol/l, Lp(a) level – 0.08 [0.04; 0.12] mmol / l.

Table 1 shows the characteristics of the two groups under study.

The analysis of the obtained data showed that in the group I with patients with an increased level of Lp(a), atherosclerotic lesions of the brachiocephalic arteries were detected almost 1.56 times more often than in the group II (Figure 1), which is a statistically significant difference (p<0.025). There was a significant positive weak connection between BCA atherosclerosis and Lp(a) levels (r =0.20, p < 0.025). The data obtained are confirmed by N. Nasr et al. [8]. A retrospective analysis of data from 196 patients (119 men / 77 women), mean age 44.3±8.6 years with a history of ischemic stroke, receiving hypolipidemic therapy was performed. Carotid artery atherosclerosis was assessed using duplex scanning. The sample was divided into 3 groups: group A consisted of 115 people without signs of carotid artery atherosclerosis( CA), the level of Lp(a) 0.26 (0.33) g / l; group B – of 67 people who had atherosclerotic plaques without hemodynamically significant CA stenosis, the level of Lp(a) – 0.44 (0.43) g/l; group C – 14 people with CA stenosis of more than 50%, the level of Lp(a) – 0.73 (0.69) g/l. Multivariate analysis showed an association of Lp(a) concentration with CA atherosclerosis (p<0.001).

***Table 1.*** *Characteristics of the studied groups.*

| Parameter | Group I (n=13) | Group II (n=39) | p |
|---|---|---|---|
| Age (years) | 70,3±7,6 | 66,23±7,7 | 0,054 |
| Sex (M/F) | 3/10 | 22/17 | 0,04* |
| BMI (kg/m$^2$) | 31,96 [28,58;32,25] | 29,5 [27,81;35,85] | 0,89 |
| AH (%) | 13 (100%) | 35 (89,7%) | 0,30 |
| Angina of tension (%) | 9 (69,2%) | 26 (66,7%) | 0,57 |
| Infarction in the anamnesys (%) | 4 (30,8%) | 22 (56,4%) | 0,099 |
| Ischemic stroke in the anamnesys (%) | 9 (69,2%) | 16 (41%) | 0,074 |
| Obliterating atherosclerosis of the vessels of the lower extremities (%)1 | 3 (23,1%) | 18 (46,2%) | 0,12 |
| Atherosclerosis BCA (%) | 12 (92,3%) | 23 (59%) | 0,025* |
| Diabetes II type (%) | 5 (38,5%) | 17 (43,6%) | 0,50 |
| Total cholesterol (mmol/l) | 4,25 [4,18;6,31] | 4,35 [3,65;5,35] | 0,33 |
| Eriglycerides (mmol/l) | 1,84 [1,13;2,3] | 1,63 [1,25;2,66] | 0,75 |
| High-density lipoproteins (mmol/l) | 1,4 [1,25;1,61] | 1,11 [0,91;1,33] | 0,03* |
| Low-density lipoproteins (mmol/l) | 2,52 [2,07;4,29] | 2,46 [1,75;3,15] | 0,38 |
| Lp (a) (grams/l) | 0,72 [0,44;1,21] | 0,08 [0,04; 0,12] | 0,0* |

*when calculating the Mann-Whitney U-test, the difference is statistically significant.
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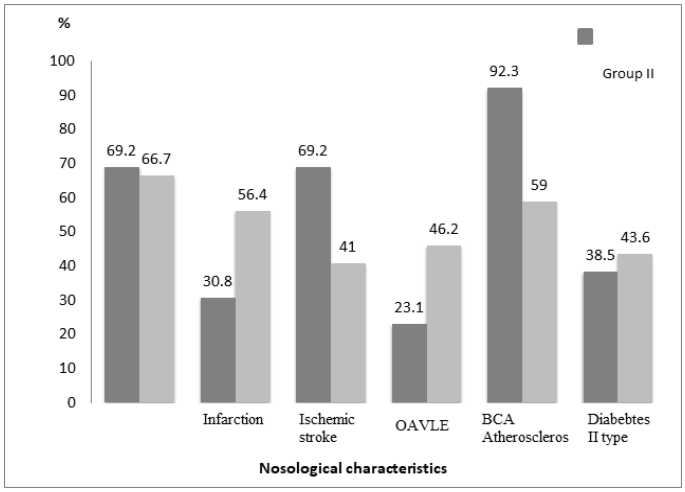


***Figure 1.*** *Comparison of nosological characteristics of the studied groups.*

It is worth noting that the number of ischemic strokes in group I exceeded it in group II by 1.68 times (Figure 1), this difference was not statistically significant, but the sample size was small. According to the study of Tmoyan N. A. et al. , in the main group, which included 89 patients with stenosing atherosclerosis SA, 19 (21%) people had AI, among them the average level of Lp(a) was higher than 0.43±0.38 g/l, than in patients of the main group without stroke – 0.31±0.26 g/l (p=0.03). There were no differences in other CVD risk factors between subgroups of patients, depending on the transferred AI. These data confirm that elevated Lp(a) levels are associated with the risk of developing BCA and AI atherosclerosis [9].

When comparing the study groups, there was a significant moderate positive relationship between female sex and the level of Lp (a) ($r = 0.49$, $p < 0.05$), as well as a moderate positive relationship between age and the level of Lp(a) ($r = 0.35$, $p=0.054$). Reviewing the literature, there were no studies confirming or refuting the relationship between age and sex with the level of Lp (a).

## Conclusions

High levels of lipoprotein (a) may be associated with atherosclerotic lesions of the brachiocephalic arteries and ischemic stroke.

Women and the older age group are at high risk of developing cardiovascular diseases, which makes it possible to increase an alertness to patients with such characteristics for additional laboratory screening for lipoprotein (a).

With a satisfactory correction of the lipid profile, it is not always necessary to count on a decrease in the level of lipoprotein (a) during statin therapy, which poses new challenges for medicine in the development of drugs and the ability to control the level of lipoprotein (a).

## References

1. Zueva IB, Baratashvili GG, Krivonosov DS, Buch AV, Sidorkevich SV. The role of lipoprotein (a) in the development of cardiovascular events and the therapeutic potential. Arterial Hypertension. 2016;22(3):232-242.
2. Zueva IB, Baratashvili GG, Krivonosov DS, Buch AV, Sidorkevich SV. Lipoprotein (a) as a factor of cardiovascular risk. Current state of the problem. Bulletin of the Russian Military Medical Academy. 2017;1(57):219-225.
3. Tmoyan NA, Ezhov MV, Afanas'eva OI, et al. The association of lipoprotein(a) and apolipoprotein(a) phenotypes with peripheral artery disease]. Therapeutic archive. 2018;90(9):31-36.
4. Schmidt K, Noureen A, Kronenberg F, Utermann G. Structure, function, and genetics of lipoprotein (a). J Lipid Res. 2016;57(8):1339-1359.
5. Pizov NA, Pizova NV. Role of lipoprotein (a) in the development of ischemic stroke and other cardiovascular diseases. Neurology, neuropsychiatry, psychosomatics]. 2016;(8)1: 90–95.
6. van der Valk FM, Bekkering S, Kroon J, et al. Oxidized Phospholipids on Lipoprotein(a) Elicit Arterial Wall Inflammation and an Inflammatory Monocyte Response in Humans. Circulation. 2016;134(8):611-624.
7. Graham MJ, Viney N, Crooke RM, Tsimikas S. Antisense inhibition of apolipoprotein (a) to lower plasma lipoprotein (a) levels in humans [published correction appears in J Lipid Res. 2016 Dec;57(12 ):2235]. J Lipid Res. 2016;57(3):340-351.
8. Nasr N, Ruidavets JB, Farghali A, Guidolin B, Perret B, Larrue V. Lipoprotein (a) and carotid atherosclerosis in young patients with stroke. Stroke. 2011;42(12):3616-3618.
9. Tmoyan NA, Ezhov MV, Afanas'eva OI, Balahonova TV, Pokrovskij SN. Lipoprotein (a) - a risk factor for the development of atherosclerosis of the carotid arteries and ischemic stroke. Kardiologiya 2017: lechit' ne bolezn', a bol'nogo. – 2017. – S. 41-41.