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# FATTY ACID METABOLISM DISORDER AS A FACTOR IN ATHEROGENESIS

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## Abstract

***Background and aims:*** *The study aims to analyze of fatty acid (FA) composition of arteries and blood plasma in atherosclerosis.* ***Material and method:*** *The blood plasma in patients with coronary atherosclerosis was studied, the blood from healthy volunteers was used as control. There were also analyzed arteries of patients with severe atherosclerotic lesions and arteries of people with significantly less atherosclerotic changes.* ***Results:*** *The received data indicates that there is a rather active penetration of FA from blood plasma lipoproteins into intima of arteries. Penetration of FA from blood lipoproteins into the depth of atherosclerotic aorta and an atherosclerotic plaque appears to be small and does not effect on their fatty acid composition, which is similar to that of free FA of blood plasma. The evidence of the increased activity of desaturases and fatty acid synthases in atherosclerotic and intact arteries in patients with severe atherosclerotic vascular lesions was obtained. This increase in activity may be related by relatively low content of polyunsaturated linoleic acid in blood plasma in atherosclerosis.* ***Conclusions:*** *The increased activity of desaturases and fatty acid synthases as well as arterial wall hypoxia must promote accumulation of lipids in vascular wall by increasing the synthesis and inhibition of FA oxidation including free FA coming from blood.*

**key words**: *atherosclerosis, coronary heart disease, fatty acids, fatty acid synthase, fatty acid desaturase, fatty acid oxidation.*

## Background and aims

There has been a long-standing interest to the issue of accumulation of lipids in the arterial wall in atherosclerosis. Nevertheless [1,2], there are still a lot of unanswered questions concerning the development of atherogenesis, as well as the reasons for the accumulation of lipids in the arterial vessels. The solution of some problems related to the mechanisms of atherosclerosis may be achieved through the research aimed at studying changes in the composition of fatty acids (FA) in atherogenesis.

## Material and method

The investigation was carried out using fragments of abdominal aortas and common carotid arteries weighing 2-3 g taken from 9 bodies of men (average age at death was 50 ± 6.7 years). It was found out [3] that plaques were most frequently localized in the wall of the abdominal aorta. Common carotid artery in this respect has a greater resistance. In addition,

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scrapings with the help of slides were made from the aortic luminal surface (endothelial and subendothelial layers), thickness about 0.2-0.3 mm. 3-4 ml of blood were also drawn from each body. The experimental group included patients (n = 3) with severe atherosclerotic lesions of the aorta, coronary arteries and other large arteries. The control group (n = 6) included patients with significantly less atherosclerotic changes in the arteries. The tested samples of the abdominal aorta had atherosclerotic lesions of varying degrees (atherosclerotic lesion type evaluation was performed according to the classification by H.C. Stary [3]). Six samples, taken from patients from control group, belonged to type 4 of atherosclerotic lesions (small size atheromas which did not cause clinical symptoms of atherosclerosis). Three samples taken from patients of experimental group represented atherosclerotic lesions of types 5-6 in which there were large plaques, containing considerable amounts of degenerative material and significantly narrowing the lumen of vessel. In these samples atheromas accounted for the greater part of the fragments of the arterial wall taken for examination. All the examined samples of the common carotid artery had no atherosclerotic changes (Figure 1), but considering that the development of atherosclerosis can be affected by systemic processes, they were also divided into control and experimental ones.

Two atherosclerotic lipid-rich cores of plaques were analyzed separately.

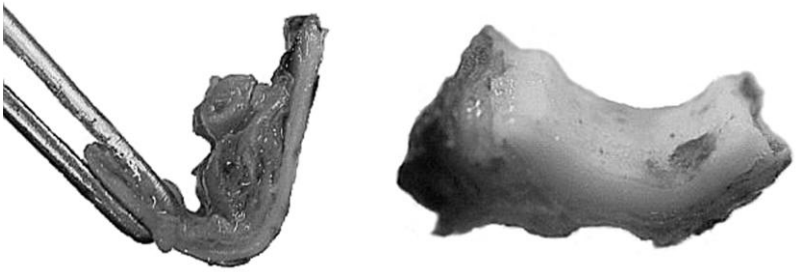

**Figure 1.** *Part of the abdominal aorta with atherosclerotic plaque (left) and the wall of the common carotid artery without any signs of atherosclerosis (right).*

The object of the study were also samples of the blood plasma of 17 patients (age: 56.3 ± 1.5 years) with coronary heart disease (CHD), atherosclerosis of the coronary arteries, stable angina (II–III classes according to Canadian Cardiovascular Society Angina Classification) and arterial hypertension, who were admitted to Mogilev Regional Hospital for treatment and evaluation of indications for coronary stent placement. Blood plasma of 17 apparently healthy volunteers (age: 38.4 ± 3.3 years) served as the control samples. Caucasian men, residents of Mogilev region, participated in the research.

Taking into account the fact that it is impossible to get an adequate model of atherosclerosis with rats, by including in their diet excessive amounts of cholesterol [4], we have studied the composition of FA in the blood plasma of 20 rats and in abdominal aortas of 4 rats.

The study was carried out in accordance with the standards of Good Clinical Practice, the principles of Helsinki Declaration. The study was approved by the Ethical Committee of the Mogilev Regional Hospital, Belarus (President Dr. Gennady M. Karpelev), Protocol No. 2 on 15 September 2016. Subjects signed an informed consent form.

*Fatty acids analysis*

The pre-analytical stage consisted in separating the plasma from cellular components

by centrifugation. In order to obtain ethyl esters of fatty acids of plasma lipids derivatization was performed in 1.5 M solution of HCl in ethanol at the temperature of 60°C for 1 hour. The extraction of the obtained ethyl esters of fatty acids from the reaction mixture was carried out using hexane. The derivatives of FA from the arteries were obtained after extraction of the lipids with ethanol from homogenized samples. Homogenization of the blood vessel fragments was performed, until smooth. The blood vessels were triturated with a porcelain pestle in a mortar with crushed glass while adding small amounts of ethanol. Then, in a similar manner acidic ethanolysis and extraction of ethyl esters of fatty acids with hexane were used. The lipids of the scrapings from the luminal surface of blood vessels have also been subject to ethanolysis. Homogenization was not required for lipid extraction from lipid-rich cores of atherosclerotic plaques, because it was enough to perforate plaque.

The analysis of the FA in the hexane extracts was carried out using the method of gas-liquid chromatography. The measurements were performed on gas chromatographs GC-1000 Chromos and Tsvet-800 (Dzerzhinsk, Russia). Chromatographic analysis the FA was described in detail previously [5,6]. Quantitative evaluation of the content of single FA was done using the method of normalization (the peak area of the chromatogram corresponding to a particular FA was expressed as a percentage of the total area of the peaks of fatty acids). The proportion of the peak of a single FA in the total of fatty acid peak areas corresponded to its weight percentage of the total amount of FA.

*Statistical analysis*

The data was presented as mean for the compared groups and the corresponding values of the confidence interval with the confidence level of 95% (normal distribution was confirmed by the Kolmogorov-Smirnov test), as well as by the use of the median (Me) and interquartile range in the format Me [LQ; UQ], where LQ - lower quartile, UQ - upper quartile of the median. Assessment of the significance of the differences between independent samplings was carried out using the Mann-Whitney U-test, which allowed us to work with samplings consisting of a small number of observations. Assessment of the significance of the differences between dependent samplings (scrapings of aortas luminal layer and fragments of total aortic wall) was performed using the Wilcoxon test [7]. Changes were considered significant at $p < 0.05$.

**Results and discussion**

The analysis of the test samples showed that the FA composition of blood plasma total lipids (practically completely in the form of esters with glycerol and cholesterol within lipoproteins [8]) in both healthy volunteers and patients with stable angina and arteriosclerosis is significantly different from that of the FA of intact and atherosclerotic arterial vessels. The differences in the FA composition between the vessels with atherosclerosis and vessels without any signs of atherosclerosis are insignificant compared to the differences between the FA composition of these vessels and the FA composition of total lipids in blood plasma (Tables 1 and 2).

The fatty acid composition of lipid-rich cores of plaques is also appreciably similar to FA composition of fragments taken from the same vessels, but having normal consistence and FA composition of intact arteries. At the same time, the fatty acid composition of cores of large atherosclerotic plaques differs significantly from FA composition of plasma total lipids in both healthy people and people with pathology (Figure 2). Thus, the results of the study suggest that the effect of fatty acids of blood lipoproteins on the FA composition of the total aortic wall thickness and atherosclerotic plaques is small.

**Table 1.** FA composition of atherosclerotic abdominal aorta and intact common carotid artery in severe atherosclerotic vascular lesions (1); and in significantly less atherosclerotic changes in arteries (2).

| Fatty acids, % | (1) n=6 | | (2) n=3 | |
|---|---|---|---|---|
| | carotid artery | abdominal aorta | carotid artery | abdominal aorta |
| lauric ($C_{12:0}$) | 0.30 [0.26; 0.36] | 0.34 [0.26; 0.37] | 0.35 [0.32; 0.39] | 0.60 [0.50; 0.62] |
| myristic ($C_{14:0}$) | 2.48 [2.40; 3.09] | 2.65 [2.60; 2.91] | 2.80 [2.58; 3.08] | 3.73 [3.50; 3.89] |
| palmitic ($C_{16:0}$) | 26.90 [25.71; 27.56] | 27.12 [25.80; 29.04] | 23.45 [21.68; 23.51] | 24.15 [22.41; 24.44]* |
| margaric ($C_{17:0}$) | 0.22 [0.18; 0.25] | 0.29 [0.24; 0.30] | 0.16 [0.12; 0.21] | 0.23 [0.17; 0.24] |
| stearic ($C_{18:0}$) | 7.01 [6.29; 7.54] | 7.35 [6.77; 8.04] | 5.34 [5.03; 5.57]* | 4.88 [3.99; 5.55]* |
| arachidic ($C_{20:0}$) | 0.86 [0.69; 1.03] | 0.78 [0.75; 0.91] | 0.74 [0.72; 0.74] | 0.55 [0.53; 0.61]* |
| myristoleic ($C_{14:1}$) | 0.18 [0.15; 0.20] | 0.20 [0.15; 0.21] | 0.30 [0.30; 0.34]* | 0.44 [0.43; 0.49]* |
| palmitoleic ($C_{16:1}$) | 5.25 [5.06; 6.44] | 5.50 [4.65; 6.09] | 7.94 [7.54; 8.26]* | 8.29 [8.06; 10.13]* |
| oleic ($C_{18:1}$) | 42.18 [41.42; 43.18] | 41.15 [36.89; 43.60] | 43.73 [43.51; 44.13] | 40.26 [39.99; 40.37] |
| linoleic ($C_{18:2}$) | 9.08 [8.89; 9.87] | 9.58 [9.01; 10.46] | 9.28 [9.10; 12.63] | 10.52 [10.13; 13.45] |
| dihomo-γ-linolenic ($C_{20:3}$) | 0.00 [0.00; 0.04] | 0.15 [0.09; 0.20] | 0.19 [0.16; 0.32]* | 0.26 [0.25; 0.28] |
| arachidonic ($C_{20:4}$) | 0.24 [0.10; 0.31] | 0.51 [0.44; 1.00] | 0.51 [0.49; 0.71] | 1.29 [0.91; 1.32] |
| docosahexaenoic ($C_{22:6}$) | 0.12 [0.09; 0.27] | 0.24 [0.15; 0.29] | 0.25 [0.21; 0.38] | 0.24 [0.23; 0.24] |

Note. The differences were significant between control and experimental groups * – $p < 0.05$.

**Table 2.** FA composition of two lipid-rich cores of plaques (1), blood plasma total lipids of healthy volunteers (2) and of patients with stable angina and atherosclerosis (3).

| Fatty acids, % | (1) $x_1$; $x_2$ | (2) n=17 | (3) n=17 |
|---|---|---|---|
| lauric ($C_{12:0}$) | 0.44; 0.68 | - | - |
| myristic ($C_{14:0}$) | 3.26; 4.11 | 0.64±0.12 | 1.27±0.33*** |
| palmitic ($C_{16:0}$) | 24.98; 24.41 | 26.82±1.55 | 31.65±1.07*** |
| margaric ($C_{17:0}$) | 0.12; 0.28 | 0.32±0.04 | 0.40±0.04** |
| stearic ($C_{18:0}$) | 3.58; 5.41 | 11.98±0.67 | 14.28±0.75*** |
| arachidic ($C_{20:0}$) | 0.50; 0.72 | - | - |
| myristoleic ($C_{14:1}$) | 0.42; 0.50 | - | - |
| palmitoleic ($C_{16:1}$) | 11.26; 8.67 | 1.55±0.29 | 1.45±0.36 |
| oleic ($C_{18:1}$) | 40.19; 42.33 | 16.55±1.17 | 16.60±1.21 |
| linoleic ($C_{18:2}$) | 10.21; 8.84 | 30.37±2.22 | 21.03±2.37*** |
| dihomo-γ-linolenic ($C_{20:3}$) | 0.24; 0.15 | 1.14±0.17 | 1.86±0.30*** |
| arachidonic ($C_{20:4}$) | 0.45; 0.55 | 6.17±0.64 | 6.82±0.52 |
| docosahexaenoic ($C_{22:6}$) | 0.25; 0.24 | 2.23±0.43 | 2.67±0.34* |

Note. The differences were significant between the blood plasma of healthy volunteers and blood plasma of patients with stable angina and atherosclerosis * – $p < 0.05$, ** – $p < 0.01$, *** – $p < 0.001$.

According to the experimental data, a certain similarity is observed between the FA composition of total plasma lipids and the corresponding composition of the luminal surface of the aorta (Figure 2). This part of the aorta has higher proportions of PUFA, saturated stearic ($C_{18:0}$) acid, and lower proportions of monounsaturated FA and saturated myristic ($C_{14:0}$) acids, than in the aortic wall as a whole, which suggests a convergence of the FA composition in the luminal layer of the aorta and the FA composition of total lipids in blood plasma (Tables 2 and 3). This indicates an active penetration of FA from plasma lipoproteins into the intima of arterial blood vessels. Consequently, this fact also reflects the ability of the intima of blood vessels to accumulate blood plasma lipoproteins. Indeed, in a number of

papers attention was drawn to the increased level of low density lipoproteins in the intercellular space of the arterial intima as compared to other connective tissues. It was noted that this fact is caused by the interaction of LDLs with proteoglycans and elastin in the intimal layer of arteries. This feature of the intima is viewed by some researchers as the main factor of accumulation of extracellular lipids in atherogenesis [2].

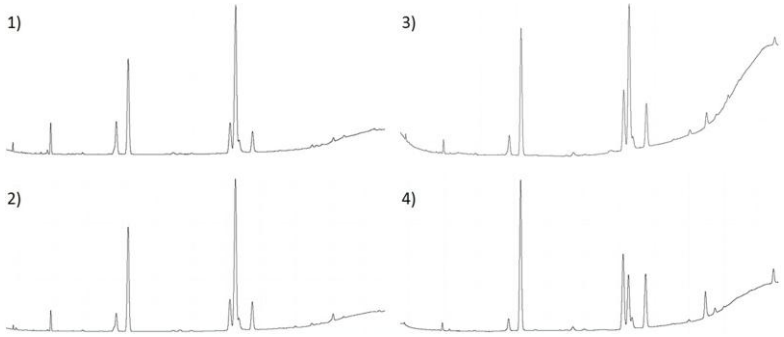


**Figure 2.** *Chromatograms of fatty acids: (1) – a large atherosclerotic plaque (mostly core), (2) – an intact common carotid artery, (3) – the luminal layer of the aorta, (4) – blood plasma of a patient with atherosclerosis and stable angina.* Note. There is a close similarity in the FA profile between chromatograms 1 and 2; chromatogram 4 is significantly different from chromatograms 1 and 2; the FA profile of chromatogram 3 has a number of features in common with both chromatogram 1 and 2 and with the FA profile of chromatogram 4.

So, based on the study, we can make a conclusion that fatty acids from blood plasma lipoproteins penetrate into the aortic intima relatively actively; but, the penetration of these FA into the depth of atherosclerotic aorta and an atherosclerotic plaque appears to be small.

The data on the FA composition of lipid-rich cores of atherosclerotic plaques, atherosclerotic and intact vessels suggests that their composition has a substantial degree of similarity to the composition of free fatty acids (FFA) in blood plasma described in the science publications [9,10]. FFA composition of blood plasma as well as the FA composition of the analyzed arteries, unlike the FA composition of lipids of blood plasma is rich in oleic ($C_{18:1}$) acid, there is a relatively high content of myristic ($C_{14:0}$) and palmitoleic ($C_{16:1}$) acids. The content of linoleic ($C_{18:2}$) FA is relatively small; extremely small was also the proportion of polyunsaturated fatty acids (PUFA) with 3 or more double bonds. Furthermore, the FA composition of blood vessels has similarities with the FA composition of the tissues actively involved in the metabolism of free fatty acids and capable of accumulating neutral lipids. This is evidenced by the proximity of the FA composition of the analyzed vessels with the described in science resources FA composition of adipose tissue [9,11] and bone marrow [12] (significant fat depot) and the FA composition of triglycerides of striated muscle tissue [13] (triglycerides make up the overwhelming part of lipids in this tissue [14]). The FA composition of arteries differs from the corresponding composition of other tissues, especially those with low triglyceride levels as compared to other lipids (brain tissue [15]), and to a lesser extent (mainly due to the lower content of most PUFA) from tissues with high triglyceride levels (liver tissue [11]). Consequently, the main effect on the FA composition and their accumulation in atherosclerotic vessels must be produced by FFA of blood plasma, which did not undergo oxidation and are used by smooth muscle cells for the synthesis of structurally more complex lipids. The accumulation of these lipids can significantly affect the formation and growth of an atherosclerotic plaque. This conclusion can be confirmed by the fact that atherosclerotic

plaques accumulate not only cholesterol, but also a significant amount of triglycerides [16]. Furthermore, in the event when free cholesterol appears in an atherosclerotic plaque, its cells apparently use oleic acid which is predominant in the spectrum of FFA for the sake of esterification of cholesterol and its storage. This may explain the high proportion of cholesterol oleate in the cells of plaques [2,17].

**Table 3.** FA composition of the total aortic walls in its abdominal part (1), the luminal layers of the analyzed aortas (2).

| Fatty acids, % | (1) n=9 | (2) n=9 |
|---|---|---|
| lauric ($C_{12:0}$) | 0.38 [0.34; 0.60] | 0.32 [0.23; 0.36] |
| myristic ($C_{14:0}$) | 2.98 [2.61; 3.73] | 1.78 [1.44; 2.12]* |
| palmitic ($C_{16:0}$) | 25.74 [24.73; 28.25] | 24.48 [22.60; 26.76] |
| margaric ($C_{17:0}$) | 0.25 [0.23; 0.29] | 0.30 [0.24; 0.39] |
| stearic ($C_{18:0}$) | 6.74 [6.19; 7.84] | 9.49 [8.44; 10.46]* |
| arachidic ($C_{20:0}$) | 0.74 [0.67; 0.79] | 0.63 [0.55; 0.75]* |
| myristoleic ($C_{14:1}$) | 0.21 [0.20; 0.41] | 0.13 [0.09; 0.16]* |
| palmitoleic ($C_{16:1}$) | 6.22 [5.27; 7.83] | 4.34 [3.64; 5.07]* |
| oleic ($C_{18:1}$) | 40.26 [38.96; 43.33] | 35.56 [33.63; 38.81]* |
| linoleic ($C_{18:2}$) | 9.74 [9.41; 10.70] | 13.80 [13.15; 14.42]* |
| dihomo-γ-linolenic ($C_{20:3}$) | 0.20 [0.11; 0.26] | 0.45 [0.41; 0.88]* |
| arachidonic ($C_{20:4}$) | 0.55 [0.47; 1.29] | 2.86 [2.28; 4.89]* |
| docosahexaenoic ($C_{22:6}$) | 0.24 [0.21; 0.26] | 1.18 [0.85; 1.56]* |

Note. The differences were significant between the analyzed total aortic walls and luminal layers of aortas * – $p < 0.05$.

An important reason for the changes in lipid metabolism and lipid accumulation in arterial walls can be local hypoxia which is developing under the influence of intimal hyperplasia [18]. Lack of oxygen, apparently, causes arterial smooth muscle cells to synthesize additional neutral lipids from free fatty acids of blood instead of using FFA in oxidation processes in a full volume. Accumulating in lipid vacuoles (in conditions of oxygen deficiency or high level receipts FFA) these lipids will promote degeneration of cells. This view on atherogenesis may explain accelerated development of atherosclerosis in a number of conditions, accompanied by an increase in the content of free fatty acids in blood plasma, such as obesity, metabolic syndrome, diabetes mellitus and chronic stress [19-22].

Another reason for the accumulation of lipids in blood vessels with atherosclerosis can be an increased activity of fatty acid synthase. It was shown that saturated fatty acids with a hydrocarbon chain length less than 18 carbon atoms are synthesized through fatty acid synthase. The overwhelming part of FA with a number of carbon atoms in the hydrocarbon chain greater than 16 are formed by the elongation of palmitic ($C_{16:0}$) and palmitoleic ($C_{16:1}$) acids. Under normal fatty acid synthase activity, a significant portion of these FA is then converted to acids with a longer hydrocarbon chain [23,24]. A sign of increased activity of FA synthase in the arterial walls in severe atherosclerosis may be the enlarged proportion of monounsaturated myristoleic ($C_{14:1}$) and ($C_{16:1}$) palmytholeic FA towards monounsaturated oleic ($C_{18:1}$) acid as in experimental aortas (21.49 [21.27; 26.16]% versus 13.91 [11.81; 15.65]% ($p < 0.05$) in the control) and in experimental carotid arteries (18.84 [18.11; 19.39]% versus 12.70 [11.55; 16.05]% in the control, $p < 0.05$).

Increased activity of fatty acid synthase and increased FA synthesis in cells of vessels can simultaneously contribute to the inhibition of FFA oxidation in these vessels because malonyl-CoA which is formed during FA synthesis is an inhibitor of FA β-oxidation [25].

In addition, overexpression of fatty acid synthase observed in actively proliferating tissues and cells with a high level of lipid metabolism [26,27]. It has been established that some substances, due to their ability to inhibit the synthesis of fatty acids, can block proliferation of tumor cells and inhibit angiogenesis [26]. At the same time, formation of new blood vessels in atherosclerotic plaques is a major cause of their destabilization [28], and

proliferation of smooth muscle cells of the plaque is a cause of vascular restenosis [29].

Additionally, in experimental aortas the ratio of lauric ($C_{12:0}$) and myristic ($C_{14:0}$) fatty acids is 17.70 [16.45; 20.10] % to palmitic ($C_{16:0}$) acid, whereas in control aortas the figure is 11.33 [11.18; 11.56] %. This indicates that in severe aortic atherosclerotic lesions the elongation of hydrocarbon chains of fatty acids formed with the help of FA synthase is more often terminated prematurely (the end product of the enzyme is considered to be the formation of palmitic acid [24,27]). Synthesis stops at the formation of fatty acids with the hydrocarbon chains shorter than that of $C_{16:0}$ acid, (such as lauric and myristic acids).

The aortas of the experimental group as compared to the control group aortas have a higher content of monounsaturated fatty acids in comparison with saturated fatty acids with the same number of carbon atoms. The ratio of myristoleic ($C_{14:1}$) FA in them constitutes 13.08 [12.09; 13.30] % to the content of myristic ($C_{14:0}$) acid, in contrast to the control aortas, wherein the ratio of $C_{14:1}$ is 6.86 [5.52; 7.40] % to $C_{14:0}$ ($p < 0.05$). The ratio of palmitoleic ($C_{16:1}$) FA to palmitic ($C_{16:0}$) acid in the experimental aortas constitutes 37.86 [35.69; 43.71] % while in the control aortas this value is 19.42 [17.32; 21.88] % ($p < 0.05$). The ratio of oleic ($C_{18:1}$) fatty acid is 814.3 [732.3; 1056] % to stearic ($C_{18:0}$) FA in the experimental group and 567.6 [476.9; 628.1] % in the control group ($p < 0.05$).

Common carotid arteries of the experimental group (in spite of the absence of signs of atherosclerosis), in contrast to the control carotid arteries, also have an increased content of monounsaturated FA with respect to the corresponding saturated acids ($p < 0.05$). Thus, the content of $C_{14:1}$ in them is 11.45 [11.12; 11.88]% to $C_{14:0}$, the content of $C_{16:1}$ is 35.85 [34.85; 36.15]% to $C_{16:0}$; the $C_{18:1}$ content is 834.2 [794.1; 875.9]% to $C_{18:0}$. In the control carotid arteries, the corresponding values are 6.69 [6.24; 7.38]%, 21.55 [19.33; 24.34]% and 622.8 [568.9; 674.7] %.

The findings suggest that there is an activation of 9-desaturase, which catalyzes the formation of monounsaturated acids from saturated acids. It is involved in the regulation of the response to changing conditions by maintaining the fluidity of cell membranes [30]. It was shown [31] that the presence of the sufficient amounts of PUFA in food inhibits the expression of 9-desaturase. Given this, it can be assumed that the deficiency of linoleic ($C_{18:2}$) PUFA in blood plasma in atherosclerosis may be a factor that stimulates the expression of desaturases in smooth muscle cells. The patients with CHD and atherosclerosis as compared with healthy volunteers have a reduced proportion of polyunsaturated fatty acids due to linoleic ($C_{18:2}$) acid (Table 2). The shortage of PUFA in CHD and atherosclerosis patients is also prompted by an increase of the proportion of dihomo-γ-linolenic ($C_{20:3}$) acid in blood plasma (Table 2), the synthesis of which in the body can significantly increase under conditions when there is a lack of essential polyunsaturated fatty acids. There is also a confirmed increase in the proportion of $C_{20:3}$ acid in the experimental carotid arteries (Table 1), as well as a tendency to an increased proportion of this polyunsaturated fatty acid in the experimental aortas. It should be noted that PUFA may also inhibit the activity of fatty acid synthase [32]. Thus, we can talk about systemic changes in fatty acid composition in the organism in atherosclerosis, affecting both blood plasma and arterial vessels.

The participation of linoleic ($C_{18:2}$) FA in atherogenesis is confirmed by the test results of postmortem blood plasma samples. In the cases

where the abdominal aorta had significant atherosclerotic lesions, the level of $C_{18:2}$ acid was 14.98 [14.84; 16.16] %. If there were only small atheromas, the level of linoleic ($C_{18:2}$) FA was 21.01 [18.36; 21.99] % ($p < 0.05$). It should be mentioned that a decrease in the proportion of $C_{18:2}$ acid (and other PUFA) in blood plasma was observed in critical for the body conditions [5]. This accounts for a lower share of PUFA in postmortem samples in comparison with samples of healthy volunteers.

It should be noted that the FA composition of the abdominal aortas of rats is different from that of human abdominal aortas in terms of the content of monounsaturated fatty acids. For example, the proportion of monounsaturated oleic ($C_{18:1}$) acid in these animals is lower than the corresponding value in humans and constitutes 32.79 [31.61; 34.84] % ($p < 0.05$). At the same time in blood plasma of rats when compared to both healthy humans and patients with CHD and atherosclerosis (Table 2), there is a high proportion of arachidonic ($C_{20:4}$) PUFA (11.53 ± 1.08%, $p < 0.001$). Thus, a lower, in comparison with humans' proportion of $C_{18:1}$ FA in the aortas of rats may be due to a high content of polyunsaturated $C_{20:4}$ acid in their blood plasma. A low proportion (0.47 ± 0.08%, $p < 0.001$) of dihomo-γ-linolenic ($C_{20:3}$) FA in blood plasma of these animals is also an indication of that. It should be noted that the specific FA composition of rat arteries may provide the key to a better understanding of the causes of the resistance of these animals to the development of experimental atherosclerosis.

Increased activity of Δ9-desaturase in arterial smooth muscle cells and, consequently, an increased synthesis of monounsaturated fatty acids from saturated fatty acids may also promote atherogenesis. The evidence in favor of this assumption may be found in some research works [30], pointing to the low activity of Δ9-desaturase as one of the reasons for an increase of FA oxidation and inhibition of lipid synthesis.

This point to the need to find measures aimed at strengthening the processes of FA oxidation in smooth muscle cells of the vessels with developing atherosclerosis. Additionally, an increased content of unsaturated fatty acids with simultaneous reduction in the content of saturated fatty acids, should lead to a decrease in the viscosity of lipids in blood vessels. It can be assumed that the decrease of lipid viscosity, in its turn, makes the plaques softer and contributes to their destabilization under the influence of blood flow. Some researchers [33] concluded that the mechanical conditions around vasa vasorum inside a plaque (the tendency of plaques to deformation and hemodynamic load) lead to their rupture, resulting in intraplaque hemorrhages. So, the lipid transformation of smooth muscle cells associated with a metabolic disorder of fatty acids, may favor the appearance of hemorrhages and penetration of cholesterol into an emerging atherosclerotic plaque. It is also interesting to note, that in Duchenne muscular dystrophy [34], as a result of decreased ability of myocytes to oxidize FFA, not only increase of triglycerides content is observed, but cholesterol level grows either. In addition, it should be noted that penetration of erythrocyte iron into the plaque with hemorrhages may explain the high ability of plaque homogenate to cause lipid peroxidation.

## Conclusions

Based on the study we can make a conclusion that fatty acids from blood plasma lipoproteins penetrate into the aortic intima relatively actively; but, the penetration of these FA into the depth of the atherosclerotic aorta and an atherosclerotic plaque appears to be small. The main effect on accumulation of these FA in atherosclerotic vessels is probably due to FFA of

blood plasma, not subjected to oxidation and using in cells for the synthesis of more complex lipids.

The evidence of the increased activity of desaturases and fatty acid synthases in atherosclerotic and intact arteries in patients with severe atherosclerotic vascular lesions was obtained. This can promote accumulation of lipids in cells of arterial wall by increasing the synthesis and inhibition of FA oxidation. The increased activity of these enzymes, in turn, may be caused by relatively low content of linoleic PUFA in blood plasma in atherosclerosis.

In general, we can conclude, that the factors contributing to insufficient oxidation of fatty acids in arterial vessels (increased activity of desaturases and fatty acid synthases in arteries, arterial wall hypoxia, and chronically elevated content of free fatty acids in the blood plasma) contribute to the formation of atherosclerotic lesions.

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