Association Between Lipoprotein(a) and Risk Factors of Atherosclerosis in Russian Population (Data of Observational ESSE-RF study)

Svetlana A. Shalnova1*, Marat V. Ezhov2, Victoria A. Metelskaya1, Svetlana E. Evstifeeva1, Vladimir I. Tarasov3, Galina A. Muromtseva1, Yulia A. Balanova4, Asiai E. Imaeva1, Anna V. Kapustina1, Aleksandra A. Shabunova6, Olga A. Belova4, Irina A. Trubacheva5, Alexey Y. Efano6, Zamira T. Astakhova7, Natalya V. Kulakova8, Sergey A. Boytsov2, Oxana M. Drapkina1 on behalf of ESSE-RF researchers

1 National Medical Research Center for Preventive Medicine. Petroverigsky per. 10, Moscow, 101990 Russia
2 National Medical Research Center of Cardiology. Tretya Cherepkovskaya ul. 15a, Moscow, 121552 Russia
3 Institute of Socio-Economic Development of Territories, Russian Academy of Sciences Gorkogo ul. 56a, Vologda, 160014 Russia
4 Cardiology Clinic. Fridriha Engelsa pr. 22, Ivanovo, 153012 Russia
5 Cardiology Research Institute, Tomsk National Research Medical Centre, Russian Academy of Sciences Kievskaya ul. 111a, Tomsk, 634012 Russia
6 Tyumen State Medical University. Odesskaya ul. 54, Tyumen, 625023 Russia
7 North Ossetia State Medical Academy. Pushkinskaya ul. 40, Vladikavkaz, 362019 Russia
8 Pacific State Medical University. Ostryakova pr. 2, Vladivostok, 690002 Russia

Experimental and clinical data indicate a significant contribution of lipoprotein(a) (Lp[a]) to the atherogenesis. However, the pathophysiological mechanisms of this relationship are not fully understood.

Aim. To investigate the distribution of Lp(a) in the population of the regions participating in the Study "Epidemiology of Cardiovascular Diseases in the Regions of the Russian Federation" (ESSE-RF) and to evaluate its associations with cardiovascular risk factors.

Material and methods. Representative samples of the male and female population of 7 regions of the Russian Federation, aged from 25 to 64 years, enrolled in the multi-center cross-sectional epidemiological study were analyzed. A total of 10332 people were examined, of whom 3732 were men (36.0%) and 6600 were women (64.0%), the average age was equal in both sexes.

Results. The mean value of Lp(a) reached 22.4 mg/dl (standard deviation 21.3 mg/dl) and significantly differed from the median (11.1 mg/dl; interquartile range from 3.9 to 20.2 mg/dl), forming the right-skewed distribution in both male and female population. Lp(a) levels were statistically significantly correlated with the level of low-density lipoproteins cholesterol (LDL-C), apoB/apoAI and total cholesterol. Notably, the odds ratios were growing by quintiles, and increased along with increasing lipid values (p<0.0001). Lp(a) levels were also positively associated with high-sensitivity C-reactive protein (hs-CRP) and negatively correlated with blood concentration of glucose and triglycerides (TG). There were no associations with body mass index, waist circumference and smoking status.

Conclusion. According to the ESSE-RF data, there are significant positive associations of Lp(a) with the LDL-C level, the apoB/apoAI ratio, total cholesterol, and hs-CRP. Negative associations are established with glucose and TG levels. The future studies should be planned with the notion of the Lp(a)’s right-skewed distribution type.

Keywords: coronary heart disease, risk factors, lipoprotein(a), odds ratio, association.

**Lipoprotein(a) and Atherosclerosis Risk Factors**

**Ассоциации липопротеина(а) с факторами риска атеросклероза**

1 Северо-Осетинская государственная медицинская академия. Россия, 362019, Владикавказ, ул. Пушкинская, 40
2 Тихоокеанский государственный медицинский университет. Россия, 690002, Владивосток, пр. Острякова, 2

Экспериментальные и клинические данные свидетельствуют о существенном вкладе в атерогенез липопротеина(а) (Лп[а]), однако патофизиологические механизмы этой связи до конца не ясны.

**Цель.** Изучить распределение Лп[а] в популяции жителей регионов участников эпидемиологического исследования (Эпидемиология сердечно-сосудистых заболеваний в различных регионах Российской Федерации – ЭССЕ-РФ) и его ассоциаций с сердечно-сосудистыми факторами риска.

**Материал и методы.** Проанализированы представительные выборки из неорганизованного мужского и женского населения в возрасте 25-64 лет из 7 регионов РФ, включенных в многоцентровое эпидемиологическое исследование. Было обследовано 10332 человек, из них — 3732 мужчин (36,0%) и 6600 женщин (64%), средний возраст которых не различался.

**Результаты.** Выявлено, что среднее значение Лп[а] составило 22,4 мг/дл (стандартное отклонение 21,3 мг/дл) и существенно отличалось от медианы (11,1 мг/дл; межквартильный диапазон от 3,9 до 20,2 мг/дл), а его распределение в популяции смещено вправо, что надо учитывать при планировании и интерпретации научных исследований.

**Заключение.** По данным исследования ЭССЕ-РФ отмечаются значимые положительные ассоциации Лп[а] с уровнем ХС ЛНП, величиной отношения ароB/ароА I, ОХС и вчСРБ, отрицательные — с уровнями глюкозы и ТГ. Распределение в популяции смещено вправо, что надо учитывать при планировании и интерпретации научных исследований.

**Лп(а) представляет собой липопротеиновую частицу, подобную частице липопroteидов низкой плотности (ЛНП), апобелок В и др.** Лп(а) обладает и проатерогенным, и протромботическим действием [1, 2]. Этим, по-видимому, и обусловлено значение Лп(а) в механизмах развития атеросклероза.

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*Corresponding Author (Автор, ответственный за переписку): svetlanashalnova@yandex.ru*

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The disorders caused by atherosclerosis continue to dominate mortality from circulatory system diseases in developed countries in the XXI century. The large-scale studies have identified the key risk factors (RF), primary and secondary prevention measures to reduce cardiovascular diseases (CVD) morbidity and mortality. However, in some cases, the prevention remains insufficient or ineffective, forcing the researchers to look for new markers, which allow for early detection of atherosclerosis. Among the most promising ones are the markers of chronic inflammation (high-sensitivity C-reactive protein [hs-CRBl]), markers of myocardial injury (troponin T or troponin I), natriuretic peptide, increased fibrinogen, lipoprotein(a) (Lp[а]), apolipoprotein B (apoB) and others.

Lp(a) is a lipoprotein particle, similar to a particle of low density lipoproteins (LDL), in which the apoB is covalently attached to apolipoprotein(a) (apo[a]). A specific feature of apo(a) is its structural homology with the fibrinolytic proenzyme plasminogen. As a result, Lp(a) has both proatherogenic and prothrombotic effect [1, 2]. This seems to be the reason for the significant contribution of Lp(a) to atherogenesis, as evidenced by the experimental and clinical data, although there are no clear understanding of the pathophysio-

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logical mechanisms of Lp(a)’s association with atherosclerosis. However, there is a sufficient number of studies to consider Lp(a) as an independent RF of CVD. Almost 20 years ago, a meta-analysis of 27 prospective studies showed a correlation of Lp(a) levels above 25-30 mg/dl with a 1.4-1.7 times increased risk of myocardial infarction (MI) and death due to coronary artery disease (CAD), regardless of the level of total cholesterol (TC) both in relatively healthy individuals and in patients with known atherosclerotic lesion [3]. In a later meta-analysis of 11 studies including 18979 patients with CAD there was revealed the relationship of Lp(a) with the risk of cardiovascular complications in the upper quantile of Lp(a) distribution, but with a significant heterogeneity between the studies (p=0.001). When stratified by LDL cholesterol (LDL-C) level, the relationship between Lp(a) and the outcomes was statistically significant only in those studies where the average LDL-C level exceeded 130 mg/dl (<0.001), while in the studies where LDL-C level was lower than 130 mg/dl this correlation did not reach statistical significance [4]. P. Willeit et al. showed that the measurement of Lp(a), especially in patients with intermediate risk (according to the Framingham Risk Score), improved the predictive ability of CVD risk assessment [5].

Although most researchers agree that the elevated Lp(a) level is an independent CVD RF [2,6,7], the relationships of Lp(a) with LDL-C and other lipid parameters, as well as classical RFs of atherosclerosis, remain unclarified and need to be examined or confirmed in future large-scale epidemiological studies. In Russia, the Lp(a) has not been studied in nationwide projects. Some clinical studies are known, which demonstrate both the unfavorable role of Lp(a) in the prognosis of patients with CAD, and the associations of Lp(a) levels with RF in patients without clinical manifestations of atherosclerosis [8-10].

The aim of this paper is to evaluate the distribution of Lp(a) in the Russian population and its associations with CVD RF, on the basis of the ESSE-RF study.

Material and methods

The subjects of the multi-center cross-sectional epidemiological ESSE-RF study (Study on Epidemiology of Cardiovascular Diseases in the Russian Federation) were the representative samples of the male and female population, aged from 25 to 64 years, of 7 regions of the Russian Federation (Ivanovo, Vologda, Tyumen regions, Primorsky Krai, Republic of North Ossetia-Alania, Tomsk), with detected level of Lp(a) in the blood serum. The analysis included 3732 men and 6600 women, in total 10332 persons. Lp(a) distribution curves were created. In the representative samples the Lp(a) level is an independent CVD RF [2,6,7], the relationships of Lp(a) with the risk of cardiovascular complications in the upper quantile of Lp(a) distribution, but with a significant heterogeneity between the studies (p=0.001). When stratified by LDL cholesterol (LDL-C) level, the relationship between Lp(a) and the outcomes was statistically significant only in those studies where the average LDL-C level exceeded 130 mg/dl (<0.001), while in the studies where LDL-C level was lower than 130 mg/dl this correlation did not reach statistical significance [4]. P. Willeit et al. showed that the measurement of Lp(a), especially in patients with intermediate risk (according to the Framingham Risk Score), improved the predictive ability of CVD risk assessment [5].
Lp(a) associations were examined according to participants’ gender, age, level of education (under secondary education, secondary and higher education), urban or rural settlement type, smoking status.

The study received the approval of the Ethics Committees of National Medical Research Center for Preventive Medicine, National Medical Research Center of Cardiology, Almazov National Medical Research Centre and the local Ethics Committees of the study sites. All participants have signed an informed consent. The overall response rate to the survey was about 80%. The detailed ESSE-RF study protocol was published [11].

The questionnaire for the participants was based on the adapted international methodologies and comprised the information on their socio-demographic characteristics, behavioral habits, medical history, economic living conditions, etc.

The standard instrumental methods of examination were used for measurement of blood pressure (BP), height, weight, waist circumference (WC). The body mass index (BMI) was calculated according to the formula: BMI=weight (kg)/[height (m)]². Obesity was registered in persons with the BMI ≥30 kg/m², the abdominal obesity – with the waist circumference >102 cm in men and >88 cm in women. BP was measured on the right hand in sitting position with the automatic tonometer OMRON M3 Expert (Japan).

In all sites the blood samples were taken from the ulnar veins of the patients on an empty stomach, after 12 hours of fasting. The blood serum was obtained by centrifugation at 900 g for 20 minutes at a temperature of +4°C. The samples of biological material were frozen and stored at temperatures not exceeding -20°C until they were sent to the federal medical centre for analysis. Biomaterials were transported by specialized services. The lipid panel analysis, including the levels of total cholesterol, triglycerides (TG), LDL-C and high-density lipoprotein cholesterol (HDL-C), Lp(a), apoB/apoAI, was performed by Abbott Architect c8000 autoanalyzer with “Abbott Diagnostic” diagnostic kits (USA). Standardization and quality control of the analysis was carried out in accordance with the requirements of the Federal System of the External Evaluation of the Quality of Clinical Laboratory Analysis (FSVOK; http://www.fsvok.ru).

Statistical data analysis was performed using the Statistical Analysis System (SAS), version 6.12. The mean values, standard deviation (M±δ), quintiles and ranking were calculated. Analytical statistics were used – the method of logistic regression, including the multivariable logistic regression analysis adjusted to gender, age, place of residence, region, education level. The statistically significant p value was determined as p<0.05.
Results

Among the 10332 people included in the study, men accounted for 36% and mainly they were the urban residents (79%). The average age of men and women (43.59±0.02 and 43.62±0.01 years, respectively) was not statistically different. Tab. 1 presents the main characteristics of the Lp(a) distribution in the Russian population, both in male and female. The distribution of Lp(a) in the total cohort was right-skewed, with the median 11.1 mg/dl (interquartile range [IQR] from 3.9 to 20.2 mg/dl) and the mean value of Lp(a) 22.4 mg/dl (standard deviation [SD] 21.3 mg/dl). There was no statistically significant gender difference in the distributions, but the slight predominance of Lp(a) in women was registered.

Primorsky Krai and Tomsk showed the lowest mean level of Lp(a) – 20.4 mg/dl. The highest Lp(a) mean values were in Tyumen and Ossetia – 25.8 mg/dl and 22.4 mg/dl (standard deviation 21.3 mg/dl). There was no statistically significant gender difference in the distributions, but the slight predominance of Lp(a) in women was registered.

Table 1. Lp(a) characteristics in the population of the ESSE-RF study regions
Таблица 1. Характеристика Лп(а) в популяции регионов ЭССЕ-РФ

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Lp(a) – lipoprotein(a)
Лп(а) – липопротеин(а)

Lipoprotein(a) and Atherosclerosis Risk Factors
Ассоциация липопротеида(а) с факторами риска атеросклероза
Lipoprotein(a) and Atherosclerosis Risk Factors
Ассоциации липопротеина(а) с факторами риска атеросклероза

25.3 mg/dl, respectively. It should be noted, however, that the high level of Lp(a) in these regions is largely due to its higher values in the female cohort. At the same time, the median ranged from 7.8 mg/dl in Tomsk to 13.3 mg/dl in Ossetia; in men it was the lowest in Tomsk and the highest in Ossetia; in women the lowest median was registered in Tomsk and the highest in Primorsky Krai.

Associations with the RF were studied in the Lp(a) distribution quintiles. A gradual increase of the lipid levels (total cholesterol, LDL-C, apoB/apoAI) in the Lp(a) quintiles was observed both in men and women. There were no statistically significant correlations between hemodynamic parameters (systolic BP [SBP], diastolic BP [DBP], heart rate), metabolic parameters (BMI, WC, glucose), and nonspecific inflammation (hs-CRP) (Tab. 2).

In order to identify the influence of the confounding factors, the correction was done depending on gender, age, education, place of residence and region, as well as marital status. Tab. 3 presents the analysis of these associations. Lp(a) levels had significant positive correlation with the LDL-C, apoB/apoAI and total cholesterol, notable is the gradient increase of the odds ratios. The positive associations of the quintiles were not observed. It is worth noting the absence of statistically significant correlation between the Lp(a) and the RF.

Associations with other RF were studied in the Lp(a) distribution quintiles. A gradual increase of the lipid levels (total cholesterol, LDL-C, apoB/apoAI) in the Lp(a) quintiles was observed both in men and women. There were no statistically significant correlations between hemodynamic parameters (systolic BP [SBP], diastolic BP [DBP], heart rate), metabolic parameters (BMI, WC, glucose), and nonspecific inflammation (hs-CRP) (Tab. 2).

In order to identify the influence of the confounding factors, the correction was done depending on gender, age, education, place of residence and region, as well as marital status. Tab. 3 presents the analysis of these associations. Lp(a) levels had significant positive correlation with the LDL-C, apoB/apoAI and total cholesterol, notable is the gradient increase of the odds ratios. The positive associations of the quintiles were not observed. It is worth noting the absence of statistically significant correlation between the Lp(a) and the RF.

Table 2. The mean values of risk factors in Lp(a) quintiles
Таблица 2. Средние характеристики факторов риска в квинтилях Лп(а)

<table>
<thead>
<tr>
<th>Q1&lt;4 (0)</th>
<th>4≤Q2&lt;8 (1)</th>
<th>8≤Q3&lt;15 (2)</th>
<th>15≤Q4&lt;35 (3)</th>
<th>Q5≥35 (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC, mmol/l</td>
<td>5.28±1.2</td>
<td>5.37±1.13</td>
<td>5.53±1.15</td>
<td>5.67±1.2</td>
</tr>
<tr>
<td>LDL-C, mmol/l</td>
<td>3.21±1</td>
<td>3.33±0.99</td>
<td>3.51±1.01</td>
<td>3.67±1.07</td>
</tr>
<tr>
<td>apoB, g/l</td>
<td>0.69±0.4</td>
<td>0.77±0.37</td>
<td>0.79±0.38</td>
<td>0.77±0.42</td>
</tr>
<tr>
<td>apoAI, g/l</td>
<td>1.22±0.67</td>
<td>1.31±0.6</td>
<td>1.31±0.59</td>
<td>1.27±0.67</td>
</tr>
<tr>
<td>apoB/AI</td>
<td>2.09±7.4</td>
<td>2.52±5.57</td>
<td>2.59±4.72</td>
<td>3.04±7.3</td>
</tr>
<tr>
<td>HDL-C, mmol/l</td>
<td>1.39±0.35</td>
<td>1.41±1.34</td>
<td>1.42±0.33</td>
<td>1.41±0.33</td>
</tr>
<tr>
<td>TG, mmol/l</td>
<td>1.53±1.4</td>
<td>1.44±1.02</td>
<td>1.42±0.94</td>
<td>1.44±0.89</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>133.8±19.86</td>
<td>133.68±8.97</td>
<td>134.86±0.8</td>
<td>135.29±0.46</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>82.19±11.64</td>
<td>82.26±10.92</td>
<td>82.46±11.19</td>
<td>82.34±11.32</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>73.66±10.99</td>
<td>73.4±10.64</td>
<td>73.85±1.08</td>
<td>74.01±10.69</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>2.76±0.59</td>
<td>2.84±0.6</td>
<td>2.84±0.58</td>
<td>2.87±0.59</td>
</tr>
<tr>
<td>WC, cm</td>
<td>87.59±15.06</td>
<td>88.21±14.99</td>
<td>88.39±14.94</td>
<td>89.1±114.83</td>
</tr>
<tr>
<td>Glucose, mmol/l</td>
<td>5.28±1.2</td>
<td>5.37±1.13</td>
<td>5.53±1.15</td>
<td>5.67±1.2</td>
</tr>
</tbody>
</table>

The data is represented as mean±SD

The reference quintile: odds ratio = 1


Table 2. The mean values of risk factors in Lp(a) quintiles
Таблица 2. Средние характеристики факторов риска в квинтилях Лп(а)
mg/dl, respectively). The only gender specific associ-
Lp(a) (11.1 [IQR 4.8-26.8] mg/dl and 22.4±26.2
is not unique. The majority of researchers reported the
same phenomenon. In particular, the results of Bio -
was about two times lower than the mean value of
skewed distribution of Lp(a) level in the Russian po-
Discussion
Table 3. Analysis of associations of risk factors in quintiles of Lp(a) adjusted for gender, age, and region
(данные ЭССЕ-РФ)
<table>
<thead>
<tr>
<th>Indicators / Показатели</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol, mmol/l / ОХС, ммоль/л</td>
<td>1.08(0.95-1.23), 0.25</td>
<td>1.31(1.14-1.45), 0.0001</td>
<td>1.60(1.40-1.84), 0.0001</td>
<td>1.95(1.67-2.21), 0.0001</td>
</tr>
<tr>
<td>LDL-C, mmol/l / ХС-ЛНП, ммоль/л</td>
<td>1.25(1.10-1.43), 0.0008</td>
<td>1.60(1.40-1.83), 0.0001</td>
<td>1.90(1.66-2.18), 0.0001</td>
<td>2.41(2.06-2.73), 0.0001</td>
</tr>
<tr>
<td>HDL-C, mmol/l / ХС-ЛВП, ммоль/л</td>
<td>0.82(0.70-0.96), 0.0148</td>
<td>0.81(0.69-0.95), 0.0083</td>
<td>0.778(0.66-0.91), 0.0018</td>
<td>0.720(0.61-0.84), 0.0001</td>
</tr>
<tr>
<td>TG, mmol/l / ТГ, ммоль/л</td>
<td>0.88(0.76-1.01), 0.0776</td>
<td>0.780(0.68-0.90), 0.0007</td>
<td>0.78(0.67-0.90), 0.0006</td>
<td>0.80(0.69-0.92), 0.0023</td>
</tr>
<tr>
<td>apoB/apoAI / ароБ/ароАI</td>
<td>0.99(0.79-1.25), 0.9644</td>
<td>1.11(0.88-1.38), 0.3954</td>
<td>1.33(1.10-1.67), 0.0123</td>
<td>1.56(1.26-1.93), 0.0001</td>
</tr>
<tr>
<td>hs-CRP, mg/l / вчСРБ, мг/л</td>
<td>1.13(0.96-1.33), 0.1297</td>
<td>1.15(0.98-1.35), 0.0889</td>
<td>1.29(1.11-1.50), 0.0125</td>
<td>1.50(1.30-1.71), 0.0211</td>
</tr>
<tr>
<td>Smoking, % / Курение, %</td>
<td>0.94(0.80-1.10), 0.4466</td>
<td>0.92(0.78-1.08), 0.3258</td>
<td>0.93(0.81-1.11), 0.5156</td>
<td>0.86(0.73-1.01), 0.0678</td>
</tr>
<tr>
<td>BMI, kg/m² / ИМТ, кг/м²</td>
<td>1.12(0.98-1.29), 0.1013</td>
<td>0.97(0.84-1.11), 0.6381</td>
<td>1.05(0.92-1.21), 0.4623</td>
<td>0.88(0.77-1.17), 0.0859</td>
</tr>
<tr>
<td>WC, cm / OT, см</td>
<td>1.00(0.87-1.15), 0.9633</td>
<td>0.94(0.82-1.08), 0.3909</td>
<td>1.04(0.91-1.20), 0.5449</td>
<td>0.86(0.75-0.99), 0.0365</td>
</tr>
<tr>
<td>BP 140/90, mm Hg / АД 140/90, мм рт. ст</td>
<td>0.86(0.75-0.99), 0.0333</td>
<td>0.91(0.79-1.05), 0.2008</td>
<td>0.86(0.75-0.99), 0.0372</td>
<td>0.83(0.72-0.95), 0.0075</td>
</tr>
<tr>
<td>HR, bpm / ЧСС, уд/мин</td>
<td>0.85(0.73-0.99), 0.0363</td>
<td>0.93(0.80-1.08), 0.3677</td>
<td>0.82(0.71-0.95), 0.0098</td>
<td>0.82(0.71-0.96), 0.0125</td>
</tr>
<tr>
<td>Glucose, mmol/l / Глюкоза, ммоль/л</td>
<td>0.98(0.64-1.14), 0.8027</td>
<td>0.83(0.71-0.97), 0.0192</td>
<td>0.75(0.64-0.88), 0.0004</td>
<td>0.84(0.72-0.98), 0.0305</td>
</tr>
</tbody>
</table>

Q1 – reference quintile: Odds ratio = 1

The present study revealed the strongly right-skewed distribution of Lp(a) level in the Russian population included in the ESSE-RF project. The median was about two times lower than the mean value of Lp(a) (11.1 [IQR 4.8-26.8] mg/dl and 22.4±26.2 mg/dl, respectively). The only gender specific association was the gradient growth of distribution in women. It should be noted that this form of distribution is not unique. The majority of researchers reported the same phenomenon. In particular, the results of BiomarCare meta-analysis comprising the data from the European studies (7 cohorts from 5 countries) indicated that the median of Lp(a) was 8.7 [IQR 3.9-19.1] mg/dl, while the mean level was 15.8±18 mg/dl (SD). Moreover, the researchers found an increase of the median of Lp(a) from north to south from 4.6 to 10.9 mg/dl. Thus, both the median and the mean of Lp(a) giyonu, а также семейному положению. В табл. 3 пред-
ставлен анализ этих ассоциаций. Lp(a) был статистиче-
ски значимо положительно связан с ХС ЛНП, ароБ/ароАI и ОХС, причем отношение шансов увеличивалось гра-
диентно. В 4 и 5 квинтилях выявлены положительные
ассоциации с вчСРБ. Значимых ассоциаций Lp(a) с ИМТ,
ОТ и статусом курения обнаружено не было. Отрцат-
ельные ассоциации были продемонстрированы между
Lp(a) и ХС ЛВП, глюкозой и ТГ. Слабо выраженные от-
рицательные ассоциации были выявлены с повышен-
ным АД и ЧСС.

Обсуждение
Настоящее исследование показало, что распределе-
ние Lp(a) в российской популяции, включенной в
ЭССЕ-РФ, сильно скошено вправо таким образом, что
медiana распределения почти в два раза меньше, чем
средняя (11.1; IQR 4.8-26.8 мг/дл и 22.4±26.2 мг/дл,
соответственно). Гендерных отличий, кроме равномер-
ного увеличения показателей распределения у женщин,
обнаружено не было. Следует отметить, что подобное
распределение не является уникальным, большинство
исследователей об этом сообщали. В частности, резуль-
tаты мета-анализа BiomareCare указали, что медиана
Lp(a) в Европейских исследованиях (7 когорт из 5 стран)
Lipoprotein(a) and Atherosclerosis Risk Factors

Ассоциации липопротеина(а) с факторами риска атеросклероза

in the Russian population in general is higher than in Europe [12].

In our study, Lp(a) positively correlated to the lipoproteins values (total cholesterol, LDL-C and apoB/apoAI). Positive associations of Lp(a) with total cholesterol, LDL-C, as well as with apoB/apoAI, have been noted by other researchers [12]. The level of Lp(a) associated negatively with HDL-C, and positively with hs-CRP level.

Negative associations were detected with glucose and TG levels. No significant associations of Lp(a) with smoking status, BMI, and WC were found. The similar data was obtained by another Russian clinical study, including patients with CAD. No associations of Lp(a) with age, family history of CAD, arterial hypertension, fibrinogen and hs-CRP levels, smoking status and obesity (BMI) were identified, but a relationship of high Lp(a) values with LDL-C was shown [8,9].

The negative relationship between TG and Lp(a), presented in our study, was also detected earlier. The Consensus Statement of the European Atherosclerosis Society, published in 2010 and devoted to Lp(a) as a risk factor for CVD, testified that most researchers found the positive association of Lp(a) level with total cholesterol, non-high-density lipoprotein cholesterol (non-HDL-C), apoB100; and negative one – with TG. Similar to the results of our study, the level of Lp(a) in blood in women was 12% higher than in men (95%CI 8-16%); and in patients with diabetes mellitus (DM) the Lp(a) was 11% lower when compared to individuals without diabetes [13].

However, the studies show a significant heterogeneity of associations between Lp(a) and RF. Thus, the results of the above mentioned BiomarCare consortium study, obtained from 52131 participants from Central, Northern and Western Europe, revealed that total cholesterol and age were positively related to Lp(a) levels; while male gender, DM and BMI – negatively. All associations were rather weak. Hypertension and smoking status did not correlate with Lp(a) levels [12]. In our study, blood glucose concentration, as a surrogate marker for diabetes mellitus, was also negatively associated with Lp(a), but no correlations with smoking status and BMI were found. Another prospective study, EPIC-Norfolk, also revealed no associations between Lp(a) and BMI and smoking, but detected significant positive relation to hs-CRP level, which is completely consistent with our data. At the same time, the EPIC-Norfolk study obtained the weakly positive relationships with SBP, but not with DBP [14], while in our study, a weak negative relationship between elevated BP and Lp(a) was noted.

The limitations of this study include its instantaneous nature.
Conclusion

The distribution of Lp(a) in the Russian population is right-skewed, which should be taken into account when analyzing the results. The data confirm the statistically significant positive associations between Lp(a) and LDL-C, apoB/apoAI, total cholesterol, hs-CRP; and the negative associations with HDL-C, glucose and TG. The heterogeneity of associations between Lp(a) and risk factors requires further investigation.

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About the Authors:

Svetlana A. Shalnova – MD, PhD, Professor, Head of Department of Epidemiology of Chronic Non-Communicable Diseases, National Medical Research Center for Preventive Medicine

Marat V. Ezov – MD, PhD, Leading Researcher, Department of Atherosclerosis, National Medical Research Center of Cardiology

Victoria A. Metelskaya – PhD (in Biology), Professor, Head of Department of Biochemical Markers of Chronic Non-Communicable Diseases Risk, National Medical Research Center for Preventive Medicine

Svetlana E. Evstifeeva – MD, PhD, Senior Researcher, Department of Epidemiology of Chronic Non-Communicable Diseases, National Medical Research Center for Preventive Medicine

Vladimir I. Tarasov – PhD (in Biology), Researcher, Department of Epidemiology of Chronic Non-Communicable Diseases, National Medical Research Center for Preventive Medicine

Galina A. Muromtseva – PhD (in Biology), Leading Researcher, Department of Epidemiology of Chronic Non-Communicable Diseases, National Medical Research Center for Preventive Medicine

Yulia A. Balanova – MD, PhD, Leading Researcher, Department of Epidemiology of Chronic Non-Communicable Diseases, National Medical Research Center for Preventive Medicine

Asiya E. Imaeva – MD, PhD, Senior Researcher, Department of Epidemiology of Chronic Non-Communicable Diseases, National Medical Research Center for Preventive Medicine

Anna V. Kapustina – MD, Senior Researcher, Department of Epidemiology of Chronic Non-Communicable Diseases, National Medical Research Center for Preventive Medicine

Aleksandra A. Shabunova – PhD (in Economics), Professor, Director, Institute of Socio-Economic Development of Territories, Russian Academy of Sciences

Olga A. Belova – MD, Head Physician, Cardiology Clinic

Irina A. Trubacheva – MD, PhD, Head of the Department of Population Cardiology with a Group of Scientific and Medical Information, Patent Science and International Relations, Cardiology Research Institute, Tomsk National Research Medical Centre, Russian Academy of Sciences

Alexey Y. Efanov – MD, PhD, Associate Professor, Chair of Preventive and Restorative Medicine, Tyumen State Medical University

Zamira T. Astakhova – MD, PhD, Professor, Head of Chair of Hospital Therapy, North Ossetia State Medical Academy

Natalya V. Kulakova – MD, PhD, Associate Professor, Institute of Therapy and Instrumental Diagnostics, Pacific State Medical University

Sergey A. Boytsov – MD, PhD, Professor, Corresponding Member of the Russian Academy of Sciences, Director, National Medical Research Center of Cardiology

Oxana M. Drapkina – MD, PhD, Professor, Corresponding Member of the Russian Academy of Sciences, Director, National Medical Research Center for Preventive Medicine

Sведения об авторах:

Шалнова Светлана Анатольевна – д.м.н., профессор, руководитель отдела эпидемиологии хронических неинфекционных заболеваний, НМИЦ ПМ

Ежов Марат Владиславович – д.м.н., в.н.с., отдел проблем атеросклероза, НМИЦ кардиологии

Метельская Виктория Алексеевна – д.б.н., профессор, руководитель отдела изучения биохимических маркеров риска хронических неинфекционных заболеваний, НМИЦ ПМ

Евстифеева Светлана Евгеньевна – к.м.н., с.н.с., отдел эпидемиологии хронических неинфекционных заболеваний, НМИЦ ПМ

Тарасов Владимир Ильич – к.б.н., в.н.с., отдел эпидемиологии хронических неинфекционных заболеваний, НМИЦ ПМ

Имаева Асия Эмверовна – к.м.н., с.н.с., отдел эпидемиологии хронических неинфекционных заболеваний, НМИЦ ПМ

Каустина Анна Владимировна – к.м.н., с.н.с., отдел эпидемиологии хронических неинфекционных заболеваний, НМИЦ ПМ

Шабунова Александра Анатольевна – д.э.н., профессор, директор, Институт социально-экономического развития территорий РАН

Белова Ольга Анатольевна – главный врач, кардиологический диспансер

Трубачева Ирина Анатольевна – д.м.н., руководитель отделения популяционной кардиологии с группой научно-медицинской информации, патентоведения и международных связей, НИИ кардиологии, Томский национальный исследовательский медицинский центр РАН

Ефанов Алексей Юрьевич – к.м.н., доцент, кафедра профилактической и восстановительной медицины, ТомГМУ

Астахова Замира Татарбековна – д.м.н., профессор, зав. кафедрой госпитальной терапии, Северо-Осетинская ГМА

Кулахова Наталия Валентиновна – к.м.н., доцент, институт терапии и инструментальной диагностики, Тихоокеанский государственный медицинский университет

Бойцов Сергей Анатольевич – д.м.н., профессор, чл.корр. РАН, генеральный директор НМИЦ кардиологии

Драпкина Оксана Михайловна – д.м.н., профессор, чл.корр. РАН, директор НМИЦ ПМ