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Влияние факторов риска развития сердечно-сосудистых заболеваний на параметры жесткости артерий у пациентов с артериальной гипертензией и атеросклерозом разной степени выраженности

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Обоснование. Артериальная гипертензия имеет широкое распространение в популяции, ведет к развитию артериосклероза, увеличению жесткости артерий и является основным нелипидным фактором риска развития атеросклероза. Во множестве исследований показано, что повышение жесткости артерий — это независимый фактор риска развития сердечно-сосудистых событий. Однако влияние традиционных факторов сердечно-сосудистого риска на жесткость артерий при артериальной гипертензии и разной степени выраженности атеросклеротического процесса недостаточно изучено.

Цель исследования — оценить влияние традиционных факторов риска развития сердечно-сосудистых заболеваний на параметры жесткости артерий у пациентов с артериальной гипертензией и атеросклерозом разной степени выраженности.

Материалы и методы. 133 больных артериальной гипертензией распределены в три группы в зависимости от степени выраженности атеросклероза. В группу контроля вошли 33 пациента без известных сердечно-сосудистых заболеваний. Всем пациентам выполнены стандартное клиническое и лабораторное обследования, суточное мониторирование артериального давления с оценкой параметров жесткости артерий. Проанализировано влияние традиционных факторов риска развития сердечно-сосудистых заболеваний на параметры артериальной жесткости.

Результаты. В группе больных только артериальной гипертензией рост индекса ригидности артерий связан с повышением возраста и уровня систолического артериального давления, а индекс аугментации, нормированный по частоте сердечных сокращений 75 в минуту, повышается с возрастом, уровнем систолического артериального давления и выше у женщин. У пациентов с артериальной гипертензией и субклиническим атеросклерозом скорость распространения пульсовой волны в аорте наиболее зависит от возраста, курения и отягощенного семейного анамнеза, индекс аугментации — от возраста и выше у женщин, а индекс ригидности артерий — от возраста и уровня систолического артериального давления. В группе больных артериальной гипертензией и ишемической болезнью сердца скорость распространения пульсовой волны в аорте зависит от индекса массы тела и выше у мужчин, а рост индекса ригидности артерий связан с женским полом, повышением возраста и уровня систолического артериального давления. У пациентов без артериальной гипертензии и признаков атеросклероза при наличии сердечно-сосудистых заболеваний в семейном анамнезе скорость распространения пульсовой волны в аорте выше, чем у пациентов без отягощенного семейного анамнеза.

Выводы. Женский пол, курение, повышение возраста, уровня систолического артериального давления и индекса массы тела связаны с увеличением параметров артериальной жесткости. Влияние факторов риска развития сердечно-сосудистых заболеваний на параметры жесткости артерий зависит от степени выраженности атеросклеротического процесса.

Ключевые слова: артериальная гипертензия; артериальная жесткость; субклинический атеросклероз; ишемическая болезнь сердца.

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Influence of risk factors for the development of cardiovascular diseases on the parameters of arterial stiffness in patients with arterial hypertension and atherosclerosis of different degrees of severity

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BACKGROUND: Arterial hypertension is widespread in the population, leads to the development of arteriosclerosis and increase of arterial stiffness, and is the main non-lipid risk factor of atherosclerosis development. Multiple studies have shown that increase of arterial stiffness is an independent risk factor for the development of cardiovascular events. However, the influence of traditional cardiovascular risk factors on arterial stiffness in arterial hypertension and atherosclerotic process of different degrees of severity has not been sufficiently studied.

AIM: To assess the influence of traditional risk factors on the parameters of arterial stiffness in patients with arterial hypertension (AH) and atherosclerotic process of varying degrees of severity.

MATERIALS AND METHODS: 133 subjects with AH have been divided into 3 groups depending on the severity of the atherosclerotic process. The control group included 33 individuals without known cardiovascular diseases. All the participants have undergone a standard clinical and laboratory examination, 24hr blood pressure monitoring with assessment of arterial stiffness (AS) parameters. The influence of risk factors on AS parameters has been analyzed for all the participants and separately by groups.

RESULTS: In the AH patients, an increase in the arterial stiffness index (ASI) is associated with an older age and an increase in systolic blood pressure (SBP); an increase in the augmentation index (AIx_{75}) is associated with age; SBP in higher in women. Pulse wave velocity in the aorta (PWVao) is most associated with age, smoking, and family history in patients with hypertension and subclinical atherosclerosis. An increase in AIx_{75} is associated with an older age and is higher in women, while ASI has a positive relationship with age and SBP. In patients with hypertension and coronary artery disease, there is a positive correlation between male body mass index and PWVao. The increase in ASI in this group is associated with female gender, SBP and age. In individuals without hypertension and signs of atherosclerosis with a family history of CVD, PWVao values are higher than in similar individuals without a family history of CVD.

CONCLUSIONS: In the group of all the participants, female gender, smoking, an older age, SBP, and body mass index are associated with increased AS parameters. The association between risk factors and parameters of arterial stiffness has peculiarities in patients with hypertension with varying degrees of severity of the atherosclerotic process.

Keywords: arterial hypertension; arterial stiffness; subclinical atherosclerosis; coronary artery disease.

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ECO•VECTOR

BACKGROUND

Cardiovascular diseases represent the main problem of modern medicine and the key cause of mortality worldwide [1, 2]. According to the American Heart Association, 40.6% of lethal outcomes from cardiovascular causes are associated with arterial hypertension (AH) [3].

In AH, vascular wall damage and endothelial dysfunction lead to the progression of the atherosclerotic process and an increase in arterial stiffness (AS), which causes the deterioration in intravascular hemodynamics and tissue perfusion. The pulse wave velocity in the aorta (PWVao) is one of the most studied indicators characterizing AS. It enables the prediction of cardiovascular morbidity and mortality and all-cause mortality [4].

Arteriosclerosis and atherosclerosis are two processes that often coexist due to common risk factors for development. An increase in AS may be a better predictor of cardiovascular events than traditional risk factors, such as increased systolic blood pressure (SBP) and glucose levels, lipid metabolism disorders, and smoking, since it reflects their cumulative effect on the arterial wall [5]. In the study, we revealed traditional risk factors and the extent they affect AS in patients with AH accompanied by atherosclerosis of varying severity.

The study aimed to evaluate the influence of traditional risk factors for the development of cardiovascular diseases on the parameters of AS in patients with AH and atherosclerosis of varying severity.

MATERIALS AND METHODS

The study included 166 patients (123 men aged 40–70 years and 43 women aged 55–70 years in the postmenopausal period) who underwent examination and treatment at the City Pokrovskaya Hospital of St. Petersburg. They were distributed into the following four groups:

- Group 1 (control) included 33 patients without known cardiovascular diseases (23 men and 10 women; mean age, 54.6 ± 8.4 years).
- Group 2 included 42 patients with AH without coronary heart disease and subclinical atherosclerosis (30 men and 12 women; mean age, 53.3 ± 7.6 years).
- Group 3 consisted of 52 patients with AH and subclinical atherosclerosis (37 men and 15 women; mean age, 56.5 ± 7.95 years).
- Group 4 included 39 patients with AH and confirmed coronary heart disease (33 men and 6 women; mean age, 57.4 ± 6.8 years).

The inclusion criteria were the absence of diabetes mellitus, presence of confirmed AH in the main groups, and signed voluntary informed consent for inclusion in the study. The study was approved by the local ethics committee of the North-Western State Medical University named after I.I. Mechnikov.

All patients underwent clinical, laboratory, and instrumental examinations, including complaints and history taking, determination of risk factors for the development of cardiovascular diseases, measurement of anthropometric parameters (height, weight, and body mass index), assessment of lipid and carbohydrate metabolism, and ultrasound examination of extracranial segments of the carotid arteries.

AS parameters were estimated from the shape of the oscillometric curve using mathematical formulas in Vasotens 24 of the BPLab blood pressure monitor (Russia). PWVao was automatically calculated and normalized to an arterial pressure of 100 mm Hg and a heart rate of 60 per minute ($PWVao_{100–60}$), the augmentation index was normalized to a heart rate of 75 per minute (AIx_{75}), and an AS index (ASI).

Statistical data processing was performed using Statistica 10 (USA) and StatTech v. 2.4.8 (Russia). For qualitative variables, the absolute values of cases and frequencies were compared using χ^2 and Fisher's exact test. Quantitative parameters with a normal distribution were defined as the mean value of the attribute and the mean-square deviation. In the absence of a normal distribution, quantitative data were described using the median and the lower and upper quartiles. For comparison, Student's *t*-test was used. The relationship between variables was described using Spearman's rank correlation coefficient. A significant threshold difference was defined as $p < 0.05$.

RESULTS

Table 1 presents the main data of the studied groups. Men predominated in all groups. Participants of the control group smoked significantly less frequently and had a lower body mass index than patients from other groups ($p < 0.05$), but no differences in these parameters were found in different groups of patients with AH. The study of lipid metabolism indicators revealed that the levels of total cholesterol and low- and high-density lipoproteins were significantly lower in groups 2 and 4 than in the control group ($p < 0.05$). No differences in these parameters were observed between groups 2 and 3. Group 4 had the lowest values of total cholesterol and low-density lipoproteins ($p < 0.05$) probably due to the more frequent use of inhibitors of 3-hydroxy-3-methylglutaryl-coenzyme A reductase ($p < 0.001$) than in other groups.

An analysis of the relationship between AS parameters and traditional risk factors for the development of cardiovascular diseases is presented in Table 2. All patients had moderate dependences of AIx_{75} and ASI on age ($r = 0.4$ and $r = 0.4$, respectively; $p < 0.001$) and a relationship between the level of SBP and ASI ($r = 0.7$; $p < 0.001$). Weak positive correlations were found between age and $PWVao_{100–60}$ ($r = 0.3$; $p = 0.02$),

Table 1. Characteristics of the studied groups

Таблица 1. Характеристика исследуемых групп

Indicator		Group 1 (*n* = 33)	Group 2 (*n* = 42)	Group 3 (*n* = 52)	Group 4 (*n* = 39)
Sex	male, *n* (%)	23 (69.7)	30 (71.4)	37 (71.2)	33 (84.6)
	female, *n* (%)	10 (30.3)	12 (28.6)	15 (28.9)	6 (15.4)
Age, years		54.6 ± 8.4	53.3 ± 7.6	56.5 ± 8	57.4 ± 6.8
Smoking, *n* (%)		5 (15.2)	17 (40.5)**	15 (29.9)**	18 (46.2)**
Total cholesterol, mmol/L		5.9 ± 1.2	5.3 ± 1.1*	5.6 ± 1.5	4.6 ± 1.4*, #, ∞
Low-density lipoproteins, mmol/L		4.0 ± 0.9	3.5 ± 0.9*	4.0 ± 1.2	3 ± 1.2*, #, ∞
High-density lipoproteins, mmol/L		1.4 ± 0.3	1.36 ± 0.3**	1.3 ± 0.3	1.2 ± 0.3**, #
Triglycerides, mmol/L		1.3 (1; 2.2)	1.2 (1.1; 1.6)	1.4 (1.1; 2)	1.5 (1.2; 2.3)
Glucose, mmol/L		5.1 ± 0.6	5.1 ± 0.6	5.0 ± 0.6	5.0 ± 0.6
Body mass index, kg/m^2		26.8 ± 3.8	30.1 ± 4.5**	29.9 ± 4.6**	29.9 ± 4.6**

Note. * $p < 0.001$ compared with group 1; ** $p < 0.05$ compared with group 1; # $p < 0.05$ compared with group 2; ∞ $p < 0.05$ compared with group 3.

Table 2. Correlation between risk factors of cardiovascular disease development and parameters of arterial stiffness in the general population group

Таблица 2. Взаимосвязь факторов риска развития сердечно-сосудистых заболеваний и параметров артериальной жесткости в общей группе

Indicator	PWVao, m/s	$PWVao_{100–60}$, m/s	AIx_{75}, %	ASI, mmHg
Age, years	0.01 (ns)	0.3 ($p = 0.02$)	0.4 ($p < 0.001$)	0.4 ($p < 0.001$)
Systolic blood pressure, mm Hg	0.2 ($p = 0.03$)	0.1 (ns)	0.1 (ns)	0.7 ($p < 0.001$)
Total cholesterol, mmol/L	0 (ns)	0.01 (ns)	–0.03 (ns)	0.04 (ns)
Low-density lipoproteins, mmol/L	0.03 (ns)	–0.02 (ns)	–0.1 (ns)	0.01 (ns)
High-density lipoproteins, mmol/L	–0.1 (ns)	–0.01 (ns)	–0.01 (ns)	–0.04 (ns)
Triglycerides, mmol/L	0.1 (ns)	0.1 (ns)	–0.02 (ns)	0.1 (ns)
Body mass index, kg/m^2	0.3 ($p < 0.001$)	0.2 ($p = 0.03$)	–0.1 (ns)	0.14 (ns)

Note. PWVao, pulse wave velocity in the aorta; $PWVao_{100–60,}$ pulse wave velocity in the aorta normalized to a systolic blood pressure of 100 mm Hg and heart rate of 60 beats per minute; AIx_{75}, augmentation index normalized to heart rate of 75 beats per minute; ASI, arterial stiffness index; ns, statistically insignificant.

Table 3. Significance of relationships among age, systolic blood pressure, body mass index, and arterial stiffness parameters in the study groups

Таблица 3. Статистическая значимость связей возраста, систолического артериального давления, индекса массы тела и параметров артериальной жесткости в группах

Indicator	Group 1			Group 2			Group 3			Group 4		
	Age	SBP	BMI	Age	SBP	BMI	Age	SBP	BMI	Age	SBP	BMI
PWVao	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
$PWVao_{100–60}$	ns	ns	ns	ns	ns	ns	0.4	ns	ns	ns	ns	0.4
AIx_{75}	0.6	ns	ns	0.4	0.4	–0.5	0.3	ns	ns	ns	ns	ns
ASI	0.4	0.5	ns	0.6	0.6	ns	0.4	0.6	ns	0.4	0.7	ns

Note. SBP, systolic blood pressure; BMI, body mass index; PWVao, pulse wave velocity in the aorta; $PWVao_{100–60}$, pulse wave velocity in the aorta normalized to a systolic blood pressure of 100 mm Hg and heart rate of 60 beats per minute; AIx_{75}, augmentation index normalized to a heart rate of 75 beats per minute; ASI, arterial stiffness index; ns, statistically insignificant.

SBP and PWVao (r = 0.2; p = 0.03), body mass index and PWVao (r = 0.03, p < 0.001), and body mass index and $PWVao_{100–60}$ (r = 0.2; p = 0.03). No relationship was detected between AS parameters and lipid metabolism parameters.

The assessment of the influence of traditional risk factors on the development of cardiovascular diseases within groups revealed that an increase in age was associated with an increase in ASI in all groups, AIx_{75} in groups 1, 2, and 3, and $PWVao_{100–60}$ in group 3 (Table 3).

The increase in SBP was associated with an increase in ASI in all groups and an increase in AIx_{75} in group 2. In group 4, a positive moderate correlation was identified between body mass index and $PWVao_{100–60}$. In group 2, a negative correlation was noted between body mass index and AIx_{75} (Table 3).

When studying the effect of sex on AS parameters in female patients, higher values of ASI and AIx_{75} were revealed, that is, 152 (135; 171) at p = 0.01 and –9 (–21; –0.5) at p < 0.001, respectively. No sex-related differences were found in other indicators of AS. In groups 1–3, women had significantly higher AIx_{75} values (p < 0.001). In group 4, higher ASI values were detected in female patients (p = 0.04) and higher PWVao values were noted in male patients (p = 0.048).

Patients with a history of smoking had significantly higher PWVao and $PWVao_{100–60}$ values (p = 0.008 and p = 0.02, respectively) (Fig. 1). However, in the within-group analysis, significant differences were revealed only in the PWVao value in group 3 (p = 0.03).

The influence of a family history of cardiovascular diseases on PWVao was registered in all patients (p = 0.001) (Fig. 2). The within-group analysis revealed significant differences in this indicator only in group 1 (p = 0.005) and group 3 (p = 0.013).

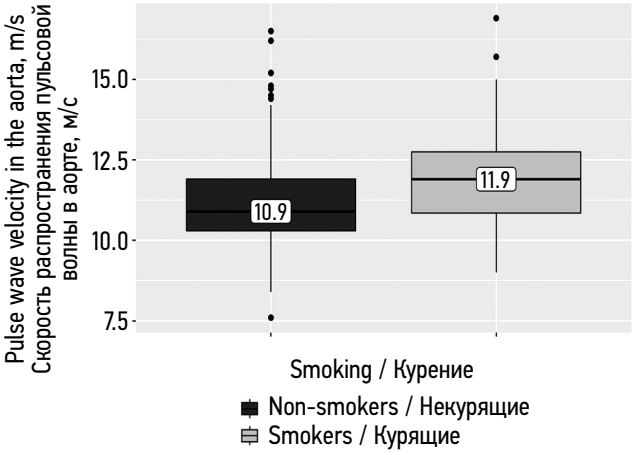

Fig. 1. Analysis of pulse wave velocity in aorta depending on the status of smoking
Рис. 1. Анализ скорости распространения пульсовой волны в аорте в зависимости от статуса курения

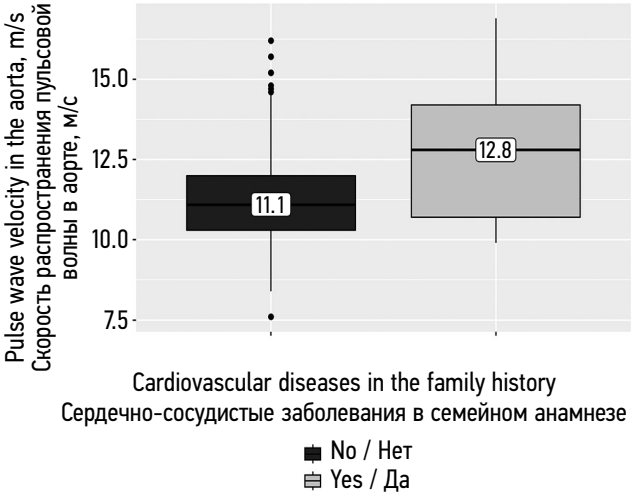

Fig. 2. Analysis of pulse wave velocity in the aorta depending on the presence of cardiovascular diseases in the family history
Рис. 2. Анализ скорости распространения пульсовой волны в аорте в зависимости от наличия сердечно-сосудистых заболеваний в семейном анамнезе

DISCUSSION

Most studies have shown that an increase in SBP and age are the main causes of an increase in AS [6], and the present study confirms these findings. In groups, age correlated with more AS parameters than SBP, which may be associated with effective antihypertensive therapy in patients. The largest number of AS parameters significantly associated with age was noted in patients with AH and subclinical atherosclerosis.

Interesting data were obtained on the effect of body mass index on AS. Its positive correlation with PWVao was obtained in the general population group and AH and coronary heart disease group, and an increase in body mass index was associated with a decrease in AIx_{75} only in the AH group. The results of studies on the relationship between body mass index and AS in various populations, including patients with AH, are contradictory, probably due to the influence of additional risk factors, nature of the adipose tissue distribution, and concentration of adipokines in blood serum [7, 8].

Reproductive hormones have a direct effect on the arterial wall. Estrogens increase the ratio of elastin and collagen, reduce overall vascular resistance and metalloproteinase activity, and improve endothelial function. Women in the postmenopausal period have higher AS than men of the same age, which is associated with a decrease in arterial elasticity in the presence of hormonal changes [9].

Smoking is one of the most significant risk factors for cardiovascular diseases. The degree of the influence of smoking on AS remains the subject of discussion [10]. In our study, higher PWVao values were observed in patients with smoking habits, but when assessed within groups, the relationship between AS and smoking was

significant only in patients with AH and subclinical atherosclerosis. Under the influence of smoking, endothelial dysfunction occurs, normal lipid metabolism is impaired, and remodeling and calcification of arteries occur, which induces the development of not only atherosclerosis but also arteriosclerosis [11]. The incidence of AS is higher in patients with a burdened family history and normal blood pressure who consider themselves healthy than in people without a family history of cardiovascular events. This confirms again the influence of hereditary factors on the development of arteriosclerosis [12].

Higher AS rates were noted in patients with subclinical atherosclerosis than in individuals without this pathology [13]. In these patients, the main risk factors for the development of cardiovascular diseases have the maximum effect on AS. An increase in AS, as an independent risk factor, may be a more significant predictor of the development of cardiovascular events than traditional risk factors [4]. Subclinical atherosclerosis is widespread. In the PESA study, 63% of 4184 asymptomatic patients aged 40–54 years had subclinical atherosclerosis on carotid ultrasonography [14]. It precedes most cardiovascular events, but its diagnostics is still complicated. The study demonstrated that in the presence of a carotid atherosclerotic plaque that narrows the lumen by more than 50%, the risk of cardiovascular events increases by two times [15]. Reducing the severity of modifiable risk factors can reduce significantly the incidence of cardiovascular events [16], which is especially important for patients with AH associated with subclinical atherosclerosis.

CONCLUSIONS

The influence of traditional risk factors for the development of cardiovascular diseases on AS parameters in patients with AH depends on the severity of the atherosclerotic process.

In AH patients without atherosclerosis, an increase in ASI is associated with an increase in age and SBP, and an increase in AIx_{75} is associated with age, SBP, and female sex.

PWVao is most associated with age, smoking, and positive family history in patients with AH and subclinical atherosclerosis. An increase in AIx_{75} in them is associated with an increase in age and female sex, and ASI is positively correlated with age and SBP.

In the group with AH and coronary heart disease, the PWVao value correlated with body mass index and male sex, and the increase in ASI correlated with female sex, SBP level, and age.

PWVao values were higher in patients without AH or signs of atherosclerosis with a family history of cardiovascular diseases than in people without a positive family history.

ADDITIONAL INFORMATION

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Author contributions. *S.A. Sayganov* — idea formation, formulation of goals and objectives; *V.E. Gumerova* — conducting research, preparing and editing text; *V.V. Gomonova* — conducting research.

All authors made a significant contribution to the study and preparation of the article and read and approved the final version before its publication.

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