DOI: https://doi.org/10.17816/medjrf643283

Vascular remodeling and endothelial dysfunction in patients with occupational chronic obstructive pulmonary disease caused by exposure to industrial aerosol nanoparticles

Lyubov A. Shpagina[1], Marina A. Zenkova[2], Anatoly I. Saprykin[3], Evgeniya B. Logashenko[2], Ilya S. Shpagin[1], Olga S. Kotova[1], Alphiya R. Tsygankova[3], Elena G. Kondyurina[1], Vera V. Zelenskaia[1], Galina V. Kuznetsova[1], Ekaterina V. Anikina[1], Natalya V. Kamneva[1], Valerij A. Sergeev[1], Tatyana N. Surovenko[4]

[1] Novosibirsk State Medical University, Novosibirsk, Russia;
[2] Institute of Chemical Biology and Fundamental Medicine, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russia;
[3] Nikolaev Institute of Inorganic Chemistry, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russia;
[4] Pacific State Medical University, Vladivostok, Russia

ABSTRACT

BACKGROUND: The characteristics of vascular pathology in different phenotypes of occupational chronic obstructive pulmonary disease (COPD), as well as the causal role of various industrial aerosol components, especially nanoparticles, are poorly understood.

AIM: To determine the characteristics of arterial remodeling and endothelial function in patients with occupational COPD caused by exposure to aerosol nanoparticles.

METHODS: An observational, cohort cross-sectional study was performed in patients with occupational COPD caused by exposure to aerosols containing metal (n = 48) or silicon (n = 55) nanoparticles, compared with COPD caused by tobacco smoking (n = 50). Scanning electron microscopy and inductively coupled plasma atomic emission spectroscopy were used to measure the size and chemical composition of particles, respectively. The procedures used in the study included color-flow duplex scanning of the brachiocephalic arteries, brachial arteries, and aorta; flow-mediated dilation test of the brachial arteries; and enzyme-linked immunosorbent assay of molecular markers. Linear regression was used to determine relationships.

RESULTS: The group of occupational COPD caused by aerosols with silicon nanoparticles had the highest values of carotid intima-media thickness: 1.2 [0.9; 1.5] mm; in the group of occupational COPD caused by aerosols with metal nanoparticles and the control group, these values were 0.9 [0.7; 1.0] mm and 0.8 [0.7; 0.9] mm, respectively (p = 0.009). Moreover, the group of occupational COPD caused by aerosols with silicon nanoparticles had the highest incidence of atherosclerosis compared to the group of occupational COPD caused by aerosols with metal nanoparticles and the control group (41.8% vs. 22.9% and 18.0%, respectively; p = 0.003). The aortic pulse wave velocity in the three groups was 12.6 [11.2; 14.1], 9.3 [8.9; 10.7], and 7.2 [6.9; 8.4] m/s, respectively (p = 0.001). The minimum flow-mediated dilation of the brachial arteries was 2.5 [2.1; 3.4], 3.8 [3.3; 4.6], and 4.7 [4.5; 5.3]%, respectively (p = 0.001). Occupational COPD caused by aerosols with silicon nanoparticles was associated with the highest serum levels of vascular cell adhesion molecule 1, von Willebrand factor, transforming growth factor β1, procollagen III N-terminal propeptide, and fibroblast growth factor 2. Regression relationships were found between the intima-media thickness and the concentration of metal (adjusted R-squared [R^2]: 0.36) and silicon (adjusted R^2: 0.47) nanoparticles, as well as the length of employment (adjusted R^2: 0.27). Moreover, regression relationships were found between the flow-mediated dilation of the brachial arteries and the concentration of metal (adjusted R^2: 0.51) and silicon (adjusted R^2: 0.71) nanoparticles, the length of employment (adjusted R^2: 0.68), and the total concentration of silicon-containing dust (adjusted R^2: 0.55).

CONCLUSION: Occupational COPD caused by exposure to aerosol nanoparticles (especially silicon-containing ones) is associated with significant vascular remodeling and endothelial dysfunction, which must be considered during follow-up care.

Keywords: nanoparticles; occupational chronic obstructive pulmonary disease; vascular remodeling; endothelial dysfunction.

To cite this article:
Shpagina LA, Zenkova MA, Saprykin AI, Logashenko EB, Shpagin IS, Kotova OS, Tsygankova AR, Kondyurina EG, Zelenskaia VV, Kuznetsova GV, Anikina EV, Kamneva NV, Sergeev VA, Surovenko TN. Vascular remodeling and endothelial dysfunction in patients with occupational chronic obstructive pulmonary disease caused by exposure to industrial aerosol nanoparticles. *Russian Medicine.* 2025;31(2):127–138. DOI: https://doi.org/10.17816/medjrf643283

Submitted: 22.12.2024 **Accepted:** 30.01.2025 **Published online:** 20.03.2025

DOI: https://doi.org/10.17816/medjrf643283

Ремоделирование сосудов и эндотелиальная дисфункция у больных профессиональной хронической обструктивной болезнью лёгких, связанной с воздействием промышленных аэрозолей с наночастицами

Л.А. Шпагина[1], М.А. Зенкова[2], А.И. Сапрыкин[3], Е.Б. Логашенко[2], И.С. Шпагин[1], О.С. Котова[1], А.Р. Цыганкова[3], Е.Г. Кондюрина[1], В.В. Зеленская[1], Г.В. Кузнецова[1], Е.В. Аникина[1], Н.В. Камнева[1], В.А. Сергеев[1], Т.Н. Суровенко[4]

[1] Новосибирский государственный медицинский университет, Новосибирск, Россия;
[2] Институт химической биологии и фундаментальной медицины Сибирского отделения Российской академии наук, Новосибирск, Россия;
[3] Институт неорганической химии имени А.В. Николаева Сибирского отделения Российской академии наук, Новосибирск, Россия;
[4] Тихоокеанский государственный медицинский университет, Владивосток, Россия

АННОТАЦИЯ

Обоснование. Особенности патологии сосудов при фенотипах профессиональной хронической обструктивной болезни лёгких (ПХОБЛ), а также роль в их формировании компонентов промышленных аэрозолей, особенно наночастиц, изучены недостаточно.

Цель. Определить особенности ремоделирования артерий и функции эндотелия у больных ПХОБЛ, развившейся от воздействия аэрозолей, содержащих наночастицы.

Методы. Выполнено наблюдательное когортное одномоментное исследование больных ПХОБЛ, развившейся от воздействия аэрозолей с наночастицами металлов (n=48) или кремния (n=55), в сравнении с ХОБЛ вследствие табакокурения (n=50). Размеры частиц определены с использованием сканирующей электронной микроскопии, химический состав — атомно-эмиссионной спектрометрии с индуктивно связанной плазмой. Проведены дуплексное сканирование с цветным допплеровским картированием кровотока брахиоцефальных, плечевых артерий, аорты; оценка поток-опосредованной дилатации плечевых артерий; исследование молекулярных маркеров твердофазным иммуноферментным методом. Взаимосвязи определяли с помощью линейной регрессии.

Результаты. В группе ПХОБЛ, развившейся от аэрозолей с наночастицами кремния, выявлены максимальные значения толщины комплекса интима-медиа общей сонной артерии — 1,2 [0,9; 1,5] мм; в группе ПХОБЛ, развившейся от аэрозолей с наночастицами металлов, — 0,9 [0,7; 1,0] мм; в группе сравнения — 0,8 [0,7; 0,9] мм (p=0,009). В этой же группе установлены наибольшие значения частоты атеросклероза (41,8% в сравнении с 22,9% в группе ПХОБЛ, развившейся от аэрозолей с наночастицами металлов; и 18,0% в группе сравнения, p=0,003); скорости распространения пульсовой волны в аорте (12,6 [11,2; 14,1]; 9,3 [8,9; 10,7]; и 7,2 [6,9; 8,4] м/с соответственно, p=0,001); минимальные значения поток-опосредованной дилатации плечевых артерий (2,5 [2,1; 3,4]; 3,8 [3,3; 4,6] и 4,7 [4,5; 5,3]% соответственно, p=0,001). При ПХОБЛ от аэрозолей с наночастицами кремния были максимальными сывороточные концентрации сосудистой молекулы адгезии 1, фактора фон Виллебранда, трансформирующего фактора роста β1, N-терминального пропептида проколлагена III, фактора роста фибробластов 2. Выявлены регрессионные взаимосвязи толщины комплекса интима-медиа с концентрацией наночастиц металлов (корректированный квадрат коэффициента детерминации — $R^2_{корр}$ — равен 0,36) и кремния ($R^2_{корр}$ 0,47), стажем работы ($R^2_{корр}$ 0,27); поток-опосредованной дилатации плечевых артерий с концентрацией наночастиц металлов ($R^2_{корр}$ 0,51), кремния ($R^2_{корр}$ 0,71), стажем работы ($R^2_{корр}$ 0,68), общей концентрацией кремнийсодержащей пыли ($R^2_{корр}$ 0,55).

Заключение. ПХОБЛ в условиях воздействия аэрозолей с наночастицами (особенно кремнийсодержащими) отличается выраженностью ремоделирования сосудов и дисфункции эндотелия, что необходимо учитывать при диспансерном наблюдении.

Ключевые слова: наночастицы; профессиональная хроническая обструктивная болезнь лёгких; ремоделирование сосудов; эндотелиальная дисфункция.

Как цитировать:
Шпагина Л.А., Зенкова М.А., Сапрыкин А.И., Логашенко Е.Б., Шпагин И.С., Котова О.С., Цыганкова А.Р., Кондюрина Е.Г., Зеленская В.В., Кузнецова Г.В., Аникина Е.В., Камнева Н.В., Сергеев В.А., Суровенко Т.Н. Ремоделирование сосудов и эндотелиальная дисфункция у больных профессиональной хронической обструктивной болезнью лёгких, связанной с воздействием промышленных аэрозолей с наночастицами // Российский медицинский журнал. 2025. Т. 31, № 2. С. 127–138. DOI: https://doi.org/10.17816/medjrf643283

Рукопись получена: 22.12.2024 **Рукопись одобрена:** 30.01.2025 **Опубликована online:** 20.03.2025

BACKGROUND

The significance of chronic obstructive pulmonary disease (COPD) is determined by its high prevalence (ranking second among chronic non-communicable respiratory diseases [1]), associated disability, and premature mortality (ranking third among chronic non-communicable diseases).[1] The projected economic burden of COPD in Russia is 378.9 billion rubles (as of 2022) [2]. The disease significantly reduces the workforce, directly impacting the country's economic security. Mortality among the working-age population (18–65 years) is 22.5 per 100,000 people or 4% [3].

Occupational chronic obstructive pulmonary disease (O-COPD) is a progressively worsening severe disease caused by exposure to harmful particles and gases in the workplace environment. In the structure of occupational diseases caused by chemical exposure, O-COPD ranks second, accounting for 19.2%.[2]

The burden of COPD is associated not only with progressive respiratory failure. Cardiovascular comorbidities are the cause of at least 50% of deaths in patients with COPD [4]. COPD increases the risk of heart failure [5], ischemic heart disease [6], hypertension [7], and atrial fibrillation [8]. Within 6 months after a moderate COPD exacerbation, the risk of acute myocardial infarction increases by 50%, while after a severe exacerbation, it is 6.4 times higher [9]. Cardiovascular diseases and COPD have a mutually aggravating effect, increasing the risk of death and reducing disease control effectiveness [7, 10]. The high comorbidity rate of COPD and cardiac pathology is associated with the impact of pro-inflammatory regulatory molecules on the vascular wall and myocardium, which enter the bloodstream from the lungs and bronchi.

In the case of O-COPD, the development of comorbidities is likely influenced by both the specific pattern of systemic inflammation and the direct impact of industrial aerosol components [11–13]. For example, the prevalence of atherosclerosis is higher in patients with occupational dust-related pathology than in non-exposed individuals [12]. Additionally, clinical and functional differences in heart failure have been observed [13]. Exposure to metals, silica dust, and toxic gases increases the risk of hypertension, atherosclerosis, and atherosclerosis-associated diseases [13].

Many industrial aerosols contain nanoparticles—particles measuring less than 100 nm in at least one dimension. The unique physical properties determined by their size contribute to the high biological activity of these particles and their potential health risks [14]. Nanoparticles can induce damage and inflammation in the bronchopulmonary system and modify the phenotype of O-COPD. Additionally, nanoparticles penetrate the bloodstream through the alveoli and directly interact with the vascular wall [15]. The mechanisms of this interaction remain understudied. At the same time, the known properties of nanoparticles suggest their independent role in the development of vascular pathology in O-COPD, highlighting the relevance of research in this field.

AIM

To determine the characteristics of arterial remodeling and endothelial function in patients with O-COPD resulting from exposure to nanoparticle-containing aerosols.

MATERIALS AND METHODS

Study Design

It was a single-center, observational, cross-sectional cohort study. Patients with O-COPD were examined as the main groups, while patients with COPD due to tobacco smoking constituted the reference group. COPD was diagnosed based on the spirometric criterion: a post-bronchodilator forced expiratory volume in 1th s to forced vital capacity ratio of less than 70% [16].

Eligibility Criteria

The patients included in the study met the following criteria: age 40 to 65 years, both men and women, and signed informed consent to participate.

Inclusion criteria for the main groups (O-COPD): workers from a mechanical engineering enterprise (the All-Russian Classifier of Types of Economic Activity (OKVED) code 30.30.32) exposed to industrial aerosols containing incidental nanoparticles; workers from other enterprises engaged in similar production processes and materials; a minimum work experience of 10 years under these conditions; and chronic respiratory symptoms for at least 5 years while working under these conditions.

Inclusion criteria for the reference group (COPD in tobacco smokers): no exposure to industrial aerosols throughout the entire work history; a minimum of 10 years of tobacco smoking (traditional cigarettes); and a pack-year index of at least 10.

Exclusion criteria: individuals with other chronic bronchopulmonary diseases (simple bronchitis and bronchial asthma were allowed); inflammatory diseases other than COPD; malignant neoplasms regardless of localization; vibration disease; stages IIA–III left ventricular heart failure;

[1] Global burden of disease study 2021. Available from: https://vizhub.healthdata.org/gbd-compare/ Accessed on July 27, 2024.

[2] On the State of Sanitary and Epidemiological Well-Being of the Population in the Russian Federation in 2023: State Report. Moscow: Federal Service for Surveillance on Consumer Rights Protection and Human Well-Being, 2024. Available from: https://rospotrebnadzor.ru/documents/details.php?ELEMENT_ID=27779 Accessed on July 27, 2024.

stage C5 chronic kidney disease; Child–Pugh class B–C liver cirrhosis; individuals unable to understand and comply with the study protocol; and contraindications to the study diagnostic procedures.

Study Conditions and Investigation of External (Occupational) Environmental Factors

Initially, an air quality study was conducted in the working area of a mechanical engineering enterprise (OKVED code 30.30.32). Air sampling with a volume of 200–600 L was performed using the PU-4E electric aspirator (NIKI MLT, Russia). The sample was passed through a Drechsel bottle filled with an absorbent solution (50 mL of deionized water). The nanoscale particle fraction was isolated by centrifuging the solution in a planetary centrifuge for 10 min at 1500 rpm. The particle sizes in the upper fraction of the solution were determined using scanning electron microscopy combined with an energy-dispersive analyzer (scanning electron microscope Zeiss EVO MA 15; Carl Zeiss, Germany) at magnifications ranging from 2000× to 8000×. The overall chemical (elemental) composition was determined using inductively coupled plasma atomic emission spectrometry on a high-resolution iCAP-6500 spectrometer (Thermo Scientific, USA).

The concentration of nanoparticles ranged from 5 to 625 ng/L. At the workstations of smelters and welders, metal nanoparticles predominated, with the highest mass concentrations recorded for aluminum (0.0031 μg/mL), iron (0.0042 μg/mL), and chromium (0.00021 μg/mL), while the concentration of silicon nanoparticles was minimal. Subsequently, the total concentration of metal nanoparticles was used for calculations. At the workstations of charge workers, molders, chippers, and grinders, the highest mass concentration was observed for silicon nanoparticles (0.035 μg/mL), whereas the concentration of metal nanoparticles was minimal. Based on these results, two study groups of patients with O-COPD were formed, depending on the predominant content of metal or silicon nanoparticles in the aerosols.

Data on gas and dust concentrations in the occupational environment, excluding particle size fractions, were obtained from hygienic assessments of working conditions conducted by experts from the Department of Occupational Hygiene and Community Hygiene of the Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing (Rospotrebnadzor) in the Novosibirsk Region. These assessments were carried out as part of an occupational disease investigation at the Center for Occupational Pathology, State Budgetary Healthcare Institution of the Novosibirsk Region, City Clinical Hospital No. 2. At the workstations of the examined individuals, the maximum allowable concentrations were exceeded for copper (maximum single exposure by 1.5 times, time-weighted average by 2.9 times); manganese (maximum single exposure by 5.5 times, time-weighted average by 2.7 times); and silicon dioxide-containing dust (maximum single exposures by 1.5–10.2 times, time-weighted average by 6.5–16.1 times).

All subjects worked under conditions of physical overexertion, exposure to noise exceeding maximum permissible levels by 1.1–1.3 times. A total of 90.9% of patients with COPD developed from aerosols with silicon nanoparticles were exposed to local and/or general vibration exceeding maximum permissible levels by 10%–15%. A total of 60.4% of patients with O-COPD developed from aerosols with metal nanoparticles were exposed to a heating microclimate.

Study Duration

The study of patients was conducted from 2019 to 2023.

Main Study Outcome

Differences in parameters characterizing vascular wall morphology, blood flow, and vascular tone were evaluated between etiologically distinct O-COPD groups.

Methods for Registration of Outcomes

All diagnostic procedures were performed during the stable phase of O-COPD, in the absence of any acute or emergency conditions or acute infections.

To assess the structural characteristics of arterial vessels, duplex scanning of the brachiocephalic and brachial arteries, as well as the aorta, was performed with color Doppler flow mapping using the Vivid S70N system (GE Healthcare, USA). The system included an electrocardiogram recording module and a linear transducer with a frequency range of 3–9 MHz, applied in longitudinal anterior, longitudinal lateral, and transverse sections. An atherosclerotic plaque was detected by visualizing a structure protruding into the arterial lumen by 0.5 mm or 50% of the intima-media thickness (IMT) or a structure extending into the vessel lumen by 1.5 mm or more. IMT was measured in the distal part of the common carotid artery. Measurements were taken at end-diastole. In Doppler mode, arterial stiffness of the neck was assessed by evaluating the pulsatility and resistive indices of the common carotid artery. Pulse wave velocity was analyzed using Doppler ultrasonography with color Doppler flow mapping from the descending aortic arch to the aortic bifurcation [17].

Endothelial function was assessed by measuring flow-mediated dilation of the brachial artery. Baseline duplex scanning of the brachial artery was performed, followed by inflation of a cuff placed on the distal third of the upper arm to 50 mmHg above the systolic arterial pressure for 3 min. The cuff was then slowly decompressed, and after 1 min, the brachial artery diameter and its percentage increase were assessed [18]. Molecular markers of endothelial function were evaluated, including soluble vascular cell adhesion molecule-1 (sVCAM-1) and von Willebrand factor, as well as fibrosis markers: transforming growth factor beta 1 (TGF-β1), procollagen type III N-terminal propeptide (PIIINP),

and fibroblast growth factor 2 (FGF-2). For marker analysis, a solid-phase "sandwich" enzyme-linked immunosorbent assay (ELISA) was used on an ExpertPlus 8-channel microplate photometer (ASYS HITECH, Austria). The serum concentration of low-density lipoproteins was determined using a standard colorimetric method.

Additionally, a comprehensive lung function assessment was performed, including spirometry with a bronchodilator test using a MAS2-C spirometer (Belintelmed, Belarus), body plethysmography, and measurement of lung diffusion capacity for carbon monoxide using the single-breath method (PowerCube Body plethysmograph; Schiller, Germany).

Statistical Analysis

Sample size calculation principles: The required number of patients for inclusion in the study was estimated using Altman's nomogram, based on a study power of 0.75.

Methods of statistical data analysis: The statistical analysis was performed using SPSS Statistics 29 (IBM, USA). The level of statistical significance for rejecting the null hypothesis was set at $p = 0.017$, accounting for the Bonferroni correction.

Standard descriptive statistical methods were applied. Results are presented as the median and interquartile range (Me [Q1; Q3]) for continuous variables and as percentages/proportions for ordinal variables. Independent sample comparisons for continuous variables were performed using the Kruskal–Wallis test, while ordinal variables were analyzed using Pearson's χ^2 test, provided that the total number of observations was at least 50 and each category contained at least 5 observations. Associations were determined within each study group using linear regression analysis. IMT and flow-mediated dilation of the brachial artery were used as dependent variables. To control for confounding factors, the regression models included the following parameters: forced expiratory volume in 1th s, smoking status, hypertension, and vibration exposure. Continuous variables were dichotomized.

RESULTS

Participant Characteristics

The O-COPD group exposed to aerosols containing metal nanoparticles included 48 patients, comprising foundry workers ($n = 29$) and welders ($n = 19$). The O-COPD group exposed to aerosols containing silicon nanoparticles included 55 patients, consisting of charge workers ($n = 5$), molders ($n = 22$), chippers ($n = 10$), and grinders ($n = 18$). The reference group consisted of 50 tobacco-smoking patients. The main characteristics of the study participants are presented in Table 1. The groups were comparable in terms of sex, age, and COPD duration, while the occupational disease groups were also matched for work experience. The proportion of patients with comorbid hypertension (both controlled and uncontrolled), obesity, and diabetes mellitus—potential causes of vascular remodeling—was similar across the groups. However, ischemic heart disease, atrial fibrillation, and chronic kidney disease—potential consequences of vascular remodeling—were more prevalent in the O-COPD groups.

Primary Findings

Ultrasound evaluation of the vascular wall revealed the greatest increase in IMT, as well as a higher prevalence of carotid artery atherosclerosis and a greater percentage of arterial lumen narrowing due to atherosclerotic plaque, in the O-COPD group exposed to aerosols containing silicon nanoparticles (Table 2). This group also demonstrated higher systolic and lower mean linear blood flow velocities. The increase in the pulsatility index, resistive index of the brachiocephalic arteries, and pulse wave velocity in the aorta in patients with O-COPD due to nanoparticle aerosol exposure indicates increased arterial stiffness.

In the O-COPD group exposed to aerosols containing metal nanoparticles, compared with the smoking-related COPD group, there was a decrease in the mean linear blood flow velocity in the common and external carotid arteries, an increase in the resistive index in the common, external carotid, and vertebral arteries, and an increase in the pulsatility index in the external carotid arteries. These findings also indicate a greater degree of vascular remodeling and increased arterial stiffness.

Statistically significant differences in pulse wave velocity in the aorta were identified between the study groups. The highest values were observed in the O-COPD group exposed to aerosols containing silicon nanoparticles, intermediate values were observed in the group exposed to metal nanoparticles, and the lowest values were observed in the tobacco-smoking COPD group.

Thus, ultrasound characteristics reflecting vascular remodeling (fibrosis and atherosclerosis) were more pronounced in O-COPD compared to smoking-related COPD, particularly in O-COPD caused by exposure to aerosols containing silicon nanoparticles.

The analysis of molecular factors revealed a profibrotic cytokine profile in the blood of patients with O-COPD exposed to silicon nanoparticle aerosols, along with the highest levels of active fibroproliferation markers. Specifically, TGF-β1 concentration was 944.6 [864.5; 966.7] pg/mL, FGF-2 was 16.3 [13.0; 19.6] pg/mL, and PIIINP was 92.1 [82.8; 101.4] ng/mL. For comparison, in O-COPD due to exposure to aerosols containing metal nanoparticles, the concentrations of these molecules were 713.0 [688.2; 736.6] pg/mL, 1.5 [1.41; 1.62] pg/mL, and 156.7 [141.5; 171.9] ng/mL, respectively. In the reference group, the values were 732.8 [654.4; 811.6] pg/mL, 8.3 [5.7; 11.3] pg/mL, and 28.5 [16.6; 42.3] ng/mL, respectively ($p < 0.017$); differences were statistically significant among all groups.

Table 1. Patients' characteristics

Parameter	O-COPD (*n* = 103)		Smoking-related COPD (*n* = 50)	*p*
	Metal nanoparticles (*n* = 48)	Silicon nanoparticles (*n* = 55)		
Work experience, years, Me [Q1; Q3]	23 [19; 26]	22 [20; 25]	N/A	0.316
Men, *n* (%)	45/93.8	52/94.5	46/92.0	0.442
Women, *n* (%)	3/6.2	3/5.5	4/8.0	0.439
Age, years, Me [Q1; Q3]	57 [55; 63]	59 [54; 64]	60 [55; 63]	0.318
Percentage of smokers, *n* (%)	15/31.2[3]	18/32.7[3]	50/100[1, 2]	0.001
Pack-year index, Me [Q1; Q3]	13 [11; 17]	14 [12; 16]	17 [13; 19]	0.142
Smoking duration, years, Me [Q1; Q3]	25 [20; 27]	24 [21; 26]	25 [21; 26]	0.225
COPD duration, years, Me [Q1; Q3]	12 [7; 15]	13 [9; 16]	14 [10; 16]	0.496
Work experience at the onset of O-COPD symptoms, years, Me [Q1; Q3]	11.0 [9.0; 14.5]	10 [8; 13]	N/A	0.233
FEV_1/FVC, %, Me [Q1; Q3]	65 [63; 67][2, 3]	69 [66; 68][1, 3]	62 [58; 68][1, 2]	0.011
FRC, %, Me [Q1; Q3]	195 [180; 210][2, 3]	164 [155; 173][1, 3]	172 [166; 182][1, 2]	0.001
DLCO/Va, %, Me [Q1; Q3]	33 [30; 37][2, 3]	46 [42; 55][1, 3]	57 [52; 66][1, 2]	0.001
LDL-C, mmol/L, Me [Q1; Q3]	2.5 [2.1; 2.9]	2.3 [2.0; 2.8]	2.6 [2.0; 2.9]	0.437
Comorbidity, *n* (%):				
• Controlled hypertension	12/25.0	16/29.1	15/30.0	0.260
• Uncontrolled hypertension	9/18.8	9/16.4	8/16.0	0.312
• Ischemic heart disease	5/10.4[3]	9/16.4[3]	3/6.0[1, 2]	0.015
• Heart failure	25/52.1[3]	30/54.5[3]	17/34.0[1, 2]	0.009
• Atrial fibrillation	7/14.6[3]	7/12.7[3]	3/6.0[1, 2]	0.010
• Stages II–IV chronic kidney disease	31/64.6[2, 3]	29/52.71[3]	19/38.0[1, 2]	0.009
• Lower extremity atherosclerosis	2/4.2	4/7.2	2/4.0	N/A
• Obesity	5/10.4	6/10.9	6/12.0	0.142
• Diabetes mellitus	3/6.3	3/5.5	4/8.0	0.155

Note: COPD, chronic obstructive pulmonary disease. Statistical significance of differences in values relative to the groups: [1], O-COPD due to exposure to aerosols primarily containing metal nanoparticles, [2], O-COPD due to exposure to aerosols primarily containing silicon nanoparticles, [3], Smoking-related COPD; N/A, not applicable. FEV_1, forced expiratory volume in one second, FVC, forced vital capacity, FRC, functional residual capacity, DLCO/Va, diffusing capacity of the lungs adjusted for alveolar volume, LDL-C, low-density lipoprotein cholesterol in blood serum.

Flow-mediated dilation of the brachial artery was lowest in patients with O-COPD caused by exposure to silicon nanoparticle aerosols, indicating the highest degree of endothelial dysfunction. Intermediate values were recorded in the second O-COPD group (exposed to metal nanoparticles), while the highest values were observed in the reference group. Molecular factor analysis also revealed the highest concentrations of endothelial dysfunction and injury markers, including sVCAM-1 and von Willebrand factor, in O-COPD due to exposure to silicon nanoparticle aerosols.

According to regression analysis, the mass concentrations of nanoparticles in industrial aerosols and work experience were associated with vascular remodeling characteristics and endothelial function. With increasing nanoparticle concentrations, IMT increased, while the flow-mediated dilation of the brachial artery decreased. The strongest associations were observed for silicon nanoparticles (Tables 3 and 4).

Silicon-containing dust concentrations in workplace air, measured without consideration of particle size fractions, were associated with signs of endothelial dysfunction but did not affect vascular structural remodeling parameters. Metal concentrations in workplace air were not associated with the vascular parameters studied.

Additionally, a significant association was found between silicon nanoparticle concentrations and the molecular marker of fibrosis, PIIINP [regression coefficient (B) 2.1; coefficient of determination (R^2) 0.92; $p < 0.001$], as well as markers of endothelial inflammation, sVCAM-1 (B = 1.6, R^2 = 0.85, $p = 0.001$). When dust concentrations were analyzed without considering particle size fractions, these patterns were not observed ($p > 0.05$).

Table 2. Vascular remodeling and endothelial function parameters depending on the etiology of chronic obstructive pulmonary disease

Parameter	O-COPD (*n* = 103)		Smoking-related COPD (*n* = 50)	*p*
	Metal nanoparticles (*n* = 48)	Silicon nanoparticles (*n* = 55)		
CIMT of the CCA, mm, Me [Q1; Q3]	0.9 [0.7; 1.0][2]	1.2 [0.9; 1.5][1, 3]	0.8 [0.7; 0.9][2]	0.009
Percentage of patients with CIMT of the CCA > 0.9 mm, *n* (%)	21/43.9[2]	39/70.9[1, 3]	19/38.0[2]	0.005
Atherosclerotic plaque in the brachiocephalic arteries, *n* (%)	11/22.9[2]	23/41.8[1, 3]	9/18.0[2]	0.003
Hemodynamically significant atherosclerotic plaque in the brachiocephalic arteries, *n* (%)	3/6.3	5/9.0	2/4.0	н/п
Degree of stenosis in the brachiocephalic arteries at the site of the atherosclerotic plaque, %, Me [Q1; Q3]	35 [29; 41][2]	55 [49; 61][1, 3]	30 [25; 42][2]	0.001
Systolic linear blood flow velocity in the CCA, cm/s, Me [Q1; Q3]	67.7 [52.6; 69.4][2]	72.1 [70.3; 79.1][1, 3]	68.9 [55.3; 70.6][2]	0.001
Mean linear blood flow velocity in the CCA, cm/s, Me [Q1; Q3]	38.5 [35.8; 41.2][2, 3]	31.1 [27.4; 36.2][1, 3]	42.6 [39.2; 47.5][1, 2]	0.005
PI CCA, Me [Q1; Q3]	1.2 [1.1; 1.4][2]	1.5 [1.3; 1.7][1, 3]	1.1 [1.1; 1.3][2]	0.001
RI CCA, Me [Q1; Q3]	0.64 [0.60; 0.66][2, 3]	0.69 [0.65; 0.70][1, 3]	0.61 [0.56; 0.64][2, 3]	0.010
Systolic linear blood flow velocity in the ECA, cm/s, Me [Q1; Q3]	66.2 [63.8; 68.1][2]	70.3 [68.6; 74.9][1, 3]	65.4 [62.7; 67.9][2]	0.001
Mean linear blood flow velocity in the ECA, cm/s, Me [Q1; Q3]	28 [24.6; 31.5][2, 3]	24 [20.3; 27.1][1, 3]	30.4 [27.9; 35.3][1, 2]	0.009
PI ECA, Me [Q1; Q3]	1.3 [1.2; 1.4][2, 3]	1.6 [1.4; 1.8][1, 3]	1.2 [1.1; 1.2][1, 2]	0.002
RI ECA, Me [Q1; Q3]	0.69 [0.64; 0.74][2, 3]	0.73 [0.70; 0.79][1, 3]	0.66 [0.60; 0.69][2, 3]	0.009
Systolic linear blood flow velocity in the ICA, cm/s, Me [Q1; Q3]	65.2 [60.7; 68.1][2]	68.4 [65.0; 74.1][1, 3]	65.9 [62.4; 67.7][2]	0.010
Mean linear blood flow velocity in the ICA, cm/s, Me [Q1; Q3]	30.6 [27.4; 36.2][2]	25.1 [21.7; 29.3][1, 3]	31.2 [26.8; 35.5][2]	0.009
PI ICA, Me [Q1; Q3]	1.3 [1.2; 1.4][2]	1.7 [1.5; 1.8][1, 3]	1.3 [1.2; 1.3][2]	0.001
RI ICA, Me [Q1; Q3]	0.69 [0.65; 0.71][2]	0.72 [0.70; 0.78][1, 3]	0.68 [0.66; 0.70][2]	0.009
Systolic linear blood flow velocity in the vertebral artery, cm/s, Me [Q1; Q3]	42.1 [40.5; 43.9][2]	45.4 [42.6; 47.1][1, 3]	41.0 [39.3; 43.2][2]	0.003
Mean linear blood flow velocity in the vertebral artery, Me [Q1; Q3]	19.3 [18.1; 21.4][2]	17.7 [16.4; 18.5][1, 3]	21.7 [19.6; 23.3][2]	0.001
PI of the vertebral artery, Me [Q1; Q3]	1.2 [1.1; 1.3][2]	1.5 [1.3; 1.6][1, 3]	1.2 [1.1; 1.2][2]	0.001
RI of the vertebral artery, Me [Q1; Q3]	0.72 [0.68; 0.76][2, 3]	0.78 [0.74; 0.81][1, 3]	0.75 [0.70; 0.77][1, 2]	0.009
Pulse wave velocity in the aorta, m/s, Me [Q1; Q3]	9.3 [8.9; 10.7][2, 3]	12.6 [11.2; 14.1][1, 3]	7.2 [6.9; 8.4][1, 2]	0.001
Flow-mediated dilation of the brachial artery, %, Me [Q1; Q3]	3.8 [3.3; 4.6][2, 3]	2.5 [2.1; 3.4][1, 3]	4.7 [4.5; 5.3][1, 2]	0.001
Soluble vascular cell adhesion molecule-1, pg/mL, Me [Q1; Q3]	18.5 [13.3; 23.1][2, 3]	46.1 [37.8; 55.2][1, 3]	12.9 [6.28; 17.6][1, 2]	0.001
Von Willebrand factor, IU/L, Me [Q1; Q3]	4.9 [3.7; 6.2][2, 3]	7.5 [6.0; 7.3][1, 3]	3.1 [2.3; 3.8][1, 2]	0.001

Note. Statistical significance of differences in values relative to the groups: [1], O-COPD due to exposure to aerosols primarily containing metal nanoparticles, [2], O-COPD due to exposure to aerosols primarily containing silicon nanoparticles, [3], smoking-related COPD. O-COPD, occupational chronic obstructive pulmonary disease, CIMT, carotid intima-media thickness, CCA, common carotid artery, ICA, internal carotid artery, ECA, external carotid artery, PI, pulsatility index, RI, resistive index.

DISCUSSION

Summary of the Primary Study Results

Differences in vascular remodeling and endothelial dysfunction were identified among the etiologically distinct COPD groups, as well as between occupational COPD and smoking-related COPD. Regression analysis revealed associations between vascular syndrome and occupational exposure characteristics, including mass concentrations of nanoparticles.

Discussion of the Primary Study Results

The clinical significance of endothelial dysfunction and arterial remodeling (IMT, vascular stiffness, etc.) is determined by their association with adverse cardiovascular events and hypertension [19, 20]. Studies of the general COPD population (regardless of phenotype) have demonstrated the presence of vascular remodeling, which is statistically significantly dependent on lung function [21, 22]. The most compelling evidence supports increased vascular stiffness and IMT [21–23]. Additionally, endothelial dysfunction is recognized as a key

Table 3. Relationships between environmental factors and carotid intima-media thickness

Independent variable (environmental factor)	B	Standard error of B	R	R^2	Adjusted R^2	*p*
O-COPD due to exposure to aerosols containing metal nanoparticles						
Concentration of metal nanoparticles, mg/mL	0.008	0.001	0.61	0.37	0.36	0.001
Maximum one-time copper concentration, mg/m^3	0.002	0.001	0.16	0.03	0.03	0.327
Time-weighted average copper concentration, mg/m^3	0.001	0.001	0.18	0.03	0.03	0.322
Maximum one-time manganese concentration, mg/m^3	0.003	0.002	0.15	0.02	0.02	0.406
Time-weighted average manganese concentration, mg/m^3	0.002	0.001	0.19	0.04	0.03	0.185
Work experience, years	0.009	0.002	0.53	0.28	0.27	0.002
Pack-year index	0.008	0.001	0.20	0.04	0.03	0.192
O-COPD due to exposure to aerosols containing silicon nanoparticles						
Concentration of silicon nanoparticles, mg/mL	0.005	0.001	0.70	0.49	0.47	0.001
Maximum one-time silica dust concentration, mg/m^3	0.003	0.002	0.18	0.032	0.031	0.207
Time-weighted average silica dust concentration, mg/m^3	0.004	0.002	0.21	0.044	0.043	0.170
Work experience, years	0.025	0.008	0.40	0.16	0.14	0.002
Pack-year index	0.003	0.001	0.23	0.06	0.04	0.296

Note: O-COPD, occupational chronic obstructive pulmonary disease. B, regression coefficient, R, coefficient of determination, R^2, coefficient of determination squared, adjusted R^2, adjusted coefficient of determination squared.

Table 4. Relationships between environmental factors and brachial artery flow-mediated dilation

Independent variable (environmental factor)	B	Standard error of B	R	R^2	Adjusted R^2	*p*
O-COPD due to exposure to aerosols containing metal nanoparticles						
Concentration of metal nanoparticles, mg/mL	–0.010	0.003	0.72	0.52	0.51	0.001
Maximum one-time copper concentration, mg/m^3	–0.001	0.001	0.09	0.008	0.007	0.762
Time-weighted average copper concentration, mg/m^3	–0.002	0.001	0.15	0.023	0.022	0.412
Maximum one-time manganese concentration, mg/m^3	–0.003	0.002	0.14	0.020	0.019	0.395
Time-weighted average manganese concentration, mg/m^3	–0.001	0.001	0.11	0.012	0.011	0.429
Work experience, years	–0.012	0.002	0.75	0.56	0.55	0.001
Pack-year index	–0.025	0.004	0.70	0.49	0.48	0.001
O-COPD due to exposure to aerosols containing silicon nanoparticles						
Concentration of silicon nanoparticles, mg/mL	–0.029	0.003	0.85	0.72	0.71	0.001
Maximum one-time silica dust concentration, mg/m^3	–0.015	0.002	0.54	0.29	0.28	0.001
Time-weighted average silica dust concentration, mg/m^3	–0.021	0.001	0.75	0.56	0.55	0.001
Work experience, years	–0.015	0.005	0.83	0.69	0.68	0.001
Pack-year index	–0.023	0.003	0.71	0.50	0.50	0.001

Note: O-COPD, occupational chronic obstructive pulmonary disease. B, regression coefficient, R, coefficient of determination, R^2, coefficient of determination squared, adjusted R^2, adjusted coefficient of determination squared.

factor in the pathogenesis of COPD [18, 24]. For instance, reduced FMD of the brachial artery is associated with pulmonary hypertension and impaired lung function [16, 25].

This study further established that etiologically distinct O-COPD phenotypes caused by exposure to aerosols containing metal or silicon nanoparticles exhibit varying degrees of vascular remodeling and endothelial dysfunction, differing from smoking-related COPD. A correlation was identified with the intensity and duration of exposure to incidental nanoparticles. The associations observed for nanoparticles differed from those for the total aerosol mass. Thus, vascular remodeling and endothelial dysfunction in patients with O-COPD due to occupational aerosol exposure are likely associated, at least in part,

with the impact of nanoparticles. For effective occupational health risk management, it is advisable to monitor not only the total concentrations of hazardous substances but also nanoparticle concentrations, particularly for assessing cardiovascular risk. Further development of respiratory protective equipment capable of reducing nanoparticle exposure intensity is necessary.

The most pronounced structural vascular changes (IMT, pulsatility index, and resistive index, indirectly reflecting arterial stiffness) and endothelial dysfunction were observed in cases of O-COPD caused by exposure to silicon nanoparticle aerosols. Given the elevated serum concentrations of TGF-β1, FGF-2, and PIIINP in this group, it can be hypothesized that fibroproliferation plays a significant role in the vascular remodeling process associated with exposure to silicon nanoparticles. The maximum increase in von Willebrand factor and sVCAM-1 blood concentrations further confirms endothelial cell activation [26]. The identified differences and associations may be explained by either the direct impact of nanoparticles on the vascular wall or an indirect effect mediated by the specific endotype of O-COPD, which is also influenced by aerosol properties [15].

The observed severity of vascular involvement underscores the need to consider patients with O-COPD due to exposure to silicon-containing dust as a high cardiovascular risk group. Regular ultrasound monitoring of the carotid arteries is essential for the early diagnosis and management of vascular damage. The established correlation with the intensity and duration of nanoparticle exposure raises the question of incorporating duplex vascular scanning into routine occupational health assessments for workers exposed to nanoparticles during industrial processes.

Study Limitations

The main limitations of this study include its single-center design and the use of a limited number of hygienic characteristics of nanoparticles. Further multicenter studies across various industries with unintended nanoparticle emissions in workplace air are advisable.

CONCLUSION

In the development of O-COPD due to exposure to nanoparticle-containing aerosols, the severity of vascular remodeling and endothelial dysfunction increases, with more pronounced effects observed with silicon nanoparticle exposure. This should be considered in occupational health surveillance programs.

ADDITIONAL INFORMATION

Author contributions. L.A. Shpagina, M.A. Zenkova, A.I. Saprykin, I.S. Shpagin, E.B. Logashenko, O.S. Kotova, E.V. Anikina — concept and design; L.A. Shpagina, M.A. Zenkova, A.I. Saprykin, E.B. Logashenko, I.S. Shpagin, O.S. Kotova, A.R. Tsygankova, G.V. Kuznetsova, E.G. Kondyurina, V.V. Zelenskaia, E.V. Anikina, N.V. Kamneva, V.A. Sergeev, T.N. Surovenko — data collection analysis and interpretation; L.A. Shpagina, E.B. Logashenko, I.S. Shpagin, O.S. Kotova, V.A. Sergeev — preparation of manuscript. All authors have approved the manuscript (version for publication) and have also agreed to be responsible for all aspects of the work, ensuring that issues related to the accuracy and integrity of any part of it are properly addressed and resolved.

Ethics approval. The present study was approved by the local Ethics Committee of the Novosibirsk State Medical University (protocol No. 121 by 21.11.2019).

Funding sources. The study was founded by Russian Science Foundation, grant No. 19-74-30011.

Disclosure of interests. The authors have no relationships, activities or interests for the last three years related with for-profit or not-for-profit third parties whose interests may be affected by the content of the article.

Statement of originality. The authors did not use previously published information (text, illustrations, data) to create this paper.

Data availability statement. All data obtained in the present study are available in the article.

Generative AI. Generative AI technologies were not used for this article creation.

Provenance and peer-review. This paper was submitted to the journal on an initiative basis and reviewed according to the usual procedure. The review process involved an external reviewer, a member of the editorial board and the scientific editor of the publication.

REFERENCES | СПИСОК ЛИТЕРАТУРЫ

1. Bystritskaya EV, Bilichenko TN. The morbidity, disability, and mortality associated with respiratory diseases in the Russian Federation (2015–2019). *Pulmonologiya.* 2021;31(5):551–561. doi: 10.18093/0869-0189-2021-31-5-551-561 EDN: KXDQEV

2. Drapkina OM, Kontsevaya AV, Mukaneeva DK, et al. Forecast of the socioeconomic burden of COPD in the Russian Federation in 2022. *Pulmonologiya.* 2022;32(4):507–516. doi: 10.18093/0869-0189-2022-32-4-507-516 EDN: MZWUQY

3. Egorenko SN, editor. *Russian Statistical Yearbook.* Moscow: Rosstat; 2023.

4. Halpin DMG, Martinez FJ. Pharmacotherapy and mortality in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2022;206(10):1201–1207. doi: 10.1164/rccm.202205-1000PP EDN: ICYMFU

5. Jiang R, Sun C, Yang Y, et al. Causal relationship between chronic obstructive pulmonary disease and heart failure: A Mendelian randomization study. *Heart Lung.* 2024;67:12–18. doi: 10.1016/j.hrtlng.2024.04.007 EDN: YRXATG

6. Ingebrigtsen TS, Marott JL, Vestbo J, et al. Coronary heart disease and heart failure in asthma, COPD and asthma-COPD overlap. *BMJ Open Respir Res.* 2020;7(1):e000470. doi: 10.1136/bmjresp-2019-000470 EDN: TSOTJX

7. Almagro P, Soler-Cataluña JJ, Huerta A, et al. Impact of comorbidities in COPD clinical control criteria. The CLAVE Study. *BMC Pulm Med.* 2024;24(1):6. doi: 10.1186/s12890-023-02758-0 EDN: TLJAXG

8. Xue Z, Guo S, Liu X, et al. Impact of COPD or asthma on the risk of atrial fibrillation: a systematic review and meta-analysis. *Front Cardiovasc Med.* 2022;9:872446. doi: 10.3389/fcvm.2022.872446 EDN: SWAPQA

9. Løkke A, Hilberg O, Lange P, et al. Exacerbations predict severe cardiovascular events in patients with COPD and stable cardiovascular disease — a nationwide, population-based cohort study. *Int J Chron Obstruct Pulmon Dis.* 2023;18:419–429. doi: 10.2147/COPD.S396790 EDN: KKVGHX

10. Xu S, Gu Z, Zhu W, Feng S. Association of COPD with adverse outcomes in heart failure patients with preserved ejection fraction. *ESC Heart Fail.* 2024. doi: 10.1002/ehf2.14958 EDN: IKIZRO

11. Shpagina LA, Kamneva NV, Shpagin IS, et al. Molecular markers in occupational chronic obstructive pulmonary disease comorbid with heart failure.

Annals of the Russian Academy of Medical Sciences. 2020;75(5):541–551. doi: 10.15690/vramn1381 EDN: UARRQV
12. Panev NI, Evseeva NA, Filimonov SN, et al. Risk factors for coronary heart disease in miners with anthracosilicosis. *Russian Journal of Occupational Health and Industrial Ecology.* 2021;61(3):161–167. doi: 10.31089/1026-9428-2021-61-3-161-167 EDN: WFOOKG
13. Sorkina NS, Kuzmina LP, Artemova LV, Bezrukavnikova LM. Issues of the effects of lead on circulatory and respiratory diseases. *Russian Journal of Occupational Health and Industrial Ecology.* 2019;(12):983–988. doi: 10.31089/1026-9428-2019-59-12-983-988 EDN: FVGJXT
14. Popova AYu, Onishchenko GG, Rakitskii VN. Hygiene in supporting scientific and technological development of the country and sanitary and epidemiological welfare of the population (to the 130th anniversary of the Federal Scientific Centre of Hygiene named after F.F. Erisman). *Hygiene and Sanitation, Russian Journal.* 2021;100(9):882–889. doi: 10.47470/0016-9900-2021-100-9-882-889 EDN: OXJKGH
15. Shpagina LA, Zenkova MA, Saprykin AI, et al. The role of nanoparticles of industrial aerosols in the formation of occupational bronchopulmonary pathology. *Russian Journal of Occupational Health and Industrial Ecology.* 2024;64(2):111–120. doi: 10.31089/1026-9428-2024-64-2-111-120 EDN: DBXTZJ
16. Chuchalin AG, Avdeev SN, Aisanov ZR, et al. Federal guidelines on diagnosis and treatment of chronic obstructive pulmonary disease. *Pulmonologiya.* 2022;32(3):356–392. doi: 10.18093/0869-0189-2022-32-3-356-392 EDN: ANYVUN
17. Aboyans V, Ricco JB, Bartelink MEL, et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries endorsed by: the European Stroke Organization (ESO) The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). *Eur Heart J.* 2018;39(9):763–816. doi: 10.1093/eurheartj/ehx095 EDN: VFJGYP
18. Vaes AW, De Boever P, Franssen FME, et al. Endothelial function in patients with COPD: an updated systematic review of studies using flow-mediated dilatation. *Expert Rev Respir Med.* 2023;17(1):53–69. doi: 10.1080/17476348.2023.2176845 EDN: XULOKC
19. Georgiopoulos G, Mavraganis G, Delialis D, et al. Carotid ultrasonography improves residual risk stratification in guidelines-defined high cardiovascular risk patients. *Eur J Prev Cardiol.* 2022;29(13):1773–1784. doi: 10.1093/eurjpc/zwac095 EDN: ULONSP
20. Malyutina NN, Yuy ND, Luzina SV, et al. Prognosis of forming phenotype of comorbidity of arterial hypertension and erosive-ulcerative lesions of gastroduodenal zone in railway transport workers. *Perm Medical Journal.* 2022;39(6):17–27. doi: 10.17816/pmj39617-27 EDN: ZMAHMW
21. Mancusi C, Manzi MV, de Simone G, et al. Carotid atherosclerosis predicts blood pressure control in patients with hypertension: the Campania Salute Network Registry. *J Am Heart Assoc.* 2022;11(5):e022345. doi: 10.1161/JAHA.121.022345 EDN: MQPFMP
22. Nevzorova VA, Zakharchuk NV, Shapkina EU, et al. COPD and preclinical cardiovascular disease. *South Russian Journal of Therapeutic Practice.* 2021;2(2):70–79. doi: 10.21886/2712-8156-2021-2-2-70-79 EDN: BIEKCD
23. Watanabe K, Onoue A, Omori H, et al. Association between airflow limitation and carotid intima-media thickness in the Japanese population. *Int J Chron Obstruct Pulmon Dis.* 2021;16:715–726. doi: 10.2147/COPD.S291477 EDN: ROTOMG
24. Zhang X, Zhang S, Huang Q, et al. Comparison of arterial stiffness and ultrasound indices in patients with and without chronic obstructive pulmonary disease. *Rev Assoc Med Bras (1992).* 2022;68(5):605–609. doi: 10.1590/1806-9282.2021203 EDN: JYMWCW
25. Screm G, Mondini L, Salton F, et al. Vascular endothelial damage in COPD: where are we now, where will we go? *Diagnostics (Basel).* 2024;14(9):950. doi: 10.3390/diagnostics14090950 EDN: LABQLL
26. Yu GH, Fang Y. Resveratrol attenuates atherosclerotic endothelial injury through the Pin1/Notch1 pathway. *Toxicol Appl Pharmacol.* 2022;446:116047. doi: 10.1016/j.taap.2022.116047 EDN: DOLRDO

AUTHORS' INFO

*** Lyubov A. Shpagina,** MD, Dr. Sci. (Medicine), Professor;
address: 8 Akademika Lavrent'eva ave, Novosibirsk, Russia, 630090;
ORCID: 0000-0003-0871-7551;
eLibrary SPIN: 5773-6649;
e-mail: lashpagina@gmail.com

Marina A. Zenkova, Dr. Sci. (Biology), Professor, Corresponding Member of the Russian Academy of Sciences;
ORCID: 0000-0003-4044-1049;
eLibrary SPIN: 2284-2692;
e-mail: marzen@niboch.nsc.ru

Anatoly I. Saprykin, Dr. Sci. (Engineering);
ORCID: 0000-0002-8999-8457;
eLibrary SPIN: 4688-9801;
e-mail: saprykin@niic.nsc.ru

Evgeniya B. Logashenko, Cand. Sci. (Biology);
ORCID: 0000-0001-8977-5395;
eLibrary SPIN: 7408-9400;
e-mail: evg.log@gmail.com

Ilya S. Shpagin, MD, Dr. Sci. (Medicine), Associate Professor;
ORCID: 0000-0002-3109-9811;
eLibrary SPIN: 2892-6184;
e-mail: doctor_ilya@mail.ru

ОБ АВТОРАХ

*** Шпагина Любовь Анатольевна,** д-р мед. наук, профессор;
адрес: Россия, 630090, Новосибирск, пр-кт Академика Лаврентьева, д. 8;
ORCID: 0000-0003-0871-7551;
eLibrary SPIN: 5773-6649;
e-mail: lashpagina@gmail.com

Зенкова Марина Аркадьевна, д-р биол. наук, профессор, член-корреспондент РАН;
ORCID: 0000-0003-4044-1049;
eLibrary SPIN: 2284-2692;
e-mail: marzen@niboch.nsc.ru

Сапрыкин Анатолий Ильич, д-р техн. наук;
ORCID: 0000-0002-8999-8457;
eLibrary SPIN: 4688-9801;
e-mail: saprykin@niic.nsc.ru

Логашенко Евгения Борисовна, канд. биол. наук;
ORCID: 0000-0001-8977-5395;
eLibrary SPIN: 7408-9400;
e-mail: evg.log@gmail.com

Шпагин Илья Семенович, д-р мед. наук, доцент;
ORCID: 0000-0002-3109-9811;
eLibrary SPIN: 2892-6184;
e-mail: doctor_ilya@mail.ru

Olga S. Kotova, MD, Dr. Sci. (Medicine), Associate Professor;
ORCID: 0000-0003-0724-1539;
eLibrary SPIN: 2488-0659;
e-mail: ok526@yandex.ru

Alphiya R. Tsygankova, Cand. Sci. (Chemistry);
ORCID: 0000-0001-7126-276X;
eLibrary SPIN: 6619-9694;
e-mail: mkb-2@yandex.ru

Elena G. Kondyurina, MD, Dr. Sci. (Medicine), Professor;
ORCID: 0000-0003-3250-3107;
eLibrary SPIN: 8665-9138;
e-mail: econdur@yandex.ru

Vera V. Zelenskaia, MD, Dr. Sci. (Medicine), Associate Professor;
ORCID: 0000-0003-0344-9412;
eLibrary SPIN: 9151-5099;
e-mail: v.zelenskaya@mail.ru

Galina V. Kuznetsova, MD, Cand. Sci. (Medicine);
ORCID: 0000-0001-7428-9159;
e-mail: doktor67@list.ru

Ekaterina V. Anikina;
ORCID: 0000-0002-6047-1707;
eLibrary SPIN: 3847-0025;
e-mail: mkb-2@yandex.ru

Natalya V. Kamneva, MD, Cand. Sci. (Medicine);
ORCID: 0000-0003-3251-0315;
eLibrary SPIN: 8868-3043;
e-mail: natali.spor@yandex.ru

Valerij A. Sergeev;
ORCID: 0009-0007-6984-4294;
e-mail: valerasergeev030197@yandex.ru

Tatyana N. Surovenko, MD, Dr. Sci. (Medicine);
ORCID: 0000-0001-7676-3213;
eLibrary SPIN: 6169-4476;
e-mail: mkb-2@yandex.ru

Котова Ольга Сергеевна, д-р мед. наук, доцент;
ORCID: 0000-0003-0724-1539;
eLibrary SPIN: 2488-0659;
e-mail: ok526@yandex.ru

Цыганкова Альфия Рафаэльевна, канд. хим. наук;
ORCID: 0000-0001-7126-276X;
eLibrary SPIN: 6619-9694;
e-mail: mkb-2@yandex.ru

Кондюрина Елена Геннадьевна, д-р мед. наук, профессор,
ORCID: 0000-0003-3250-3107;
eLibrary SPIN: 8665-9138;
e-mail: econdur@yandex.ru

Зеленская Вера Викторовна, д-р мед. наук, доцент;
ORCID: 0000-0003-0344-9412;
eLibrary SPIN: 9151-5099;
e-mail: v.zelenskaya@mail.ru

Кузнецова Галина Владимировна, канд. мед. наук;
ORCID: 0000-0001-7428-9159;
e-mail: doktor67@list.ru

Аникина Екатерина Валентиновна;
ORCID: 0000-0002-6047-1707;
eLibrary SPIN: 3847-0025;
e-mail: mkb-2@yandex.ru

Камнева Наталья Вадимовна, канд. мед. наук;
ORCID: 0000-0003-3251-0315;
eLibrary SPIN: 8868-3043;
e-mail: natali.spor@yandex.ru

Сергеев Валерий Алексеевич;
ORCID: 0009-0007-6984-4294;
e-mail: valerasergeev030197@yandex.ru

Суровенко Татьяна Николаевна, д-р мед. наук;
ORCID: 0000-0001-7676-3213;
eLibrary SPIN: 6169-4476;
e-mail: mkb-2@yandex.ru

* Corresponding author / Автор, ответственный за переписку