УДК 616.1-085.835
https://doi.org/10.20538/1682-0363-2025-2-162-168

Modern Ideas about the Mechanisms of Intermittent Hypoxia Hyperoxia Training and the Possibility of its Use in Cardiovascular Diseases (Literature Review)

Lebedeva N.B.[1], Egle A.P.[2], Sacharchuk A.Yu.[1], Argunova Yu.A.[1], Barbarash O.L.[1]

Research Institute for Complex Problems of Cardiovascular Diseases
6 Academician L.S. Barbarash Blvd., 650002 Kemerovo, Russian Federation

[2] *Kuzbass Clinical Cardiology Dispensary named after Academician L.S. Barbarash*
6 Academician L.S. Barbarash Blvd., 650002 Kemerovo, Russian Federation

ABSTRACT

Intermittent hypoxia–hyperoxia therapy with individually dosed gas levels (ReOxy therapy) is a modification of the long-known method of intermittent normobaric hypoxia training. Currently, ReOxy therapy can be considered as an addition to physical training in programs of cardiological rehabilitation, primary and secondary prevention of a wide range of cardiovascular diseases, as well as an alternative to physical exercises if it is impossible to perform them.

This review examines the pathogenetic rationale, differences from traditional intermittent hypoxia training, and clinical prospects for the use of intermittent hypoxia–hyperoxia therapy in cardiovascular diseases.

Keywords: hypoxia–hyperoxia therapy, cardiovascular diseases, ReOxy therapy, rehabilitation

Conflict of interest. The authors declare the absence of obvious or potential conflict of interest related to the publication of this article.

Source of financing. The study was performed within the basic research topic of Research Institute for Complex Problems of Cardiovascular Diseases No. 0419-2022-0002.

For citation: Lebedeva N.B., Egle A.P., Sacharchuk A.Yu., Argunova Yu.A., Barbarash O.L. Modern Ideas about the Mechanisms of Intermittent Hypoxia Hyperoxia Training and the Possibility of its Use in Cardiovascular Diseases (Literature Review). *Bulletin of Siberian Medicine.* 2025;24(2):162–168. https://doi.org/10.20538/1682-0363-2025-2-162-168.

Современные представления о механизмах гипоксически-гипероксических тренировок и возможности их применения при сердечно-сосудистых заболеваниях (обзор литературы)

Лебедева Н.Б.[1], Егле А.П.[2], Сахарчук А.Ю.[1], Аргунова Ю.А.[1], Барбараш О.Л.[1]

[1] *Научно-исследовательский институт комплексных проблем сердечно-сосудистых заболеваний (НИИ КПССЗ)*
Россия, 650002, г. Кемерово, бульвар им. академика Л.С. Барбараша, 6

[2] *Кузбасский клинический кардиологический диспансер(КККД) им. академика Л.С. Барбараша*
Россия, 650002, г. Кемерово, бульвар им. академика Л.С. Барбараша, 6

✉ *Lebedeva Nataliya B.,* lebenb@mail.ru

РЕЗЮМЕ

Интервальная гипокси-гиперокситерапия с персонализированным дозированием нагрузки (ре-окси терапия) является результатом совершенствования давно известного метода интервальных нормобарических гипоксических тренировок. В настоящее время ре-окси терапия может рассматриваться как дополнение к физическим тренировкам в программах кардиологической реабилитации, первичной и вторичной профилактики многочисленного спектра сердечно-сосудистых заболеваний, а также в качестве альтернативы физическим тренировкам при невозможности их выполнения.

В обзоре рассматриваются патогенетическое обоснование, отличия от традиционного метода гипоксически-нормоксического воздействия и клинические перспективы применения метода интервальной гипокси-гипероксितерапии при сердечно-сосудистых заболеваниях.

Ключевые слова: гипоксически-гипероксические тренировки, сердечно-сосудистые заболевания, ре-окси терапия, реабилитация

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Работа выполнена в рамках фундаментальной темы НИИ КПССЗ № 0419-2022-0002.

Для цитирования: Лебедева Н.Б., Егле А.П., Сахарчук А.Ю., Аргунова Ю.А., Барбараш О.Л. Современные представления о механизмах гипоксически-гипероксических тренировок и возможности их применения при сердечно-сосудистых заболеваниях (обзор литературы). *Бюллетень сибирской медицины*. 2025;24(2):162–168. https://doi.org/10.20538/1682-0363-2025-2-162-168.

INTRODUCTION

The issues of treatment, prevention, and rehabilitation after cardiovascular diseases remain important in modern medicine. Various methods of non-drug therapies are a key component of secondary prevention and cardiac rehabilitation programs aimed at restoring physical and social wellness, improving the quality of life in the short term, and reducing the risk of recurrent cardiovascular events, while increasing life expectancy in the long term [1].

The most heavily researched and proven method of cardiac rehabilitation is physical training (PT). The indications for PT have evolved over time from increasing exercise tolerance to the main method of secondary prevention (evidence level IA) [2, 3]. The evidence base for PT as a method of cardiac rehabilitation is based on the study of the mechanisms that increase physical tolerance and improve adaptation to ischemia, as well as on the proven long-term effect of reducing the risk of adverse cardiovascular events. However, the implementation of rehabilitation programs based on PT can be complicated.

The main problem is related to low adherence of patients to PT. Recent studies have revealed that only 18% of patients are compliant with physical rehabilitation programs [4]. Moreover, current advances in the treatment of cardiovascular diseases have led to a change in the profile of a patient. The number of patients with heart failure, multifocal atherosclerosis, who underwent heart surgery, and elderly patients with severe concomitant pathology, including musculoskeletal disorders, has increased, which significantly lowers their active participation in physical rehabilitation programs [5]. These facts indicate the need to find new effective and safe methods of cardiac rehabilitation as an addition or alternative to PT with a similar mechanism of action and comparable clinical and prognostic efficacy.

As such, researchers are engaged in the study of hypoxia training which has been used to increase the endurance of healthy individuals and later became a method of prevention and rehabilitation after various diseases in which hypoxia plays a key role [6–12]. The results of experimental and clinical studies showed that enhanced exercise tolerance can be observed upon exposing a patient to short episodes of hypoxia that do not exceed the physiological threshold. This resulted in the development of intermittent hypoxia training (IHT) [9, 10]. IHT consists in alternating inspiration of hypoxic gas mixture and normal air for an average of 5 minutes for 20-40 minutes [6]. Intermittent hypoxia–hyperoxia therapy with individually dosed gas levels (IHHT, ReOxy therapy) is the improvement of the long-known IHT method.

Aim. To substantiate the use of IHHT in the rehabilitation of patients with cardiovascular diseases based on the analysis of the best practices of using IHT in cardiology and the mechanisms of its therapeutic effect.

Methods. The authors carried out the analysis of publications in eLIBRARY.ru and PubMed databases, published from 2014 to 2024, using the following keywords: hypoxic effects, intermittent hypoxic training, hypoxia–hyperoxia therapy, ReOxy therapy, pathophysiological mechanisms of hypoxia, hypoxic preconditioning, and cardiac rehabilitation. The inclusion criteria were the results of randomized trials, systematic reviews, and original articles including a control group.

MECHANISMS OF EFFECTS OF HYPOXIA TRAINING

A number of studies have shown that hypoxia increases body adaptive capabilities to hypoxic conditions by activating numerous pathophysiological mechanisms, including modulation of sympathoadrenal reactivity, chemoreceptor sensitivity, anaerobic and aerobic energy production pathways, increased tissue resistance to hypoxia, activation of antioxidant defense systems, and many others [7, 13–17].

Essentially, IHT is one of the methods of hypoxic preconditioning that consists of short episodes of hypoxia. Such training increases the activity of the antioxidant system and trains the metabolic mitochondrial systems of cells, which subsequently prevents structural and functional damage to tissues, including the heart and brain, in severe or acute hypoxia [9, 18]. In terms of the action and end result, IHT is very similar to PT, triggering numerous hematological and non-hematological adaptation mechanisms [13–17, 19].

Currently, changes in the rate of reactive oxygen species (ROS) generation and redox signaling in the form of intracellular and intercellular electron transport chains that provide a balance between oxidative stress and antioxidant defense in the aerobic body are considered as the main mechanism through which therapeutic, modifying, and pathological effects of hypoxia are implemented [20, 21]. ROS, including free radicals and hydrogen peroxide, are generated in all major biological aerobic systems and play an important role in regulating vital processes and forming a cellular response to external stimuli. During hypoxia, a specific regulatory protein, the hypoxia-inducible factor (HIF), is activated through ROS, which plays a key role in body adaptation to hypoxia.

Currently, three types of HIF have been discovered: HIF-1 (several subtypes), HIF-2, and HIF-3. While HIF-1 and HIF-2 regulate multidirectional processes, HIF-3 is possibly associated with negative effects of hypoxia. HIF-1α increases the expression of more than 100 genes necessary for survival in conditions of oxygen deficiency, including those that activate endothelium-dependent vasodilation, angiogenesis and angioedema, energy metabolism, mitochondrial metabolism, cell division processes, erythropoiesis, iron metabolism, and many others [22, 23]. Following IHT, increased expression of HIF-1α initiates metabolic processes necessary for regeneration of damaged myocardium and improvement of cardiac functions after episodes of ischemia [23].

In 2017, the understanding of the pathophysiology of hypoxia was expanded by C.W. Pugh and P. J. Ratcliffe. They discovered that cells have a unique mechanism of direct perception of oxygen fluctuations in the blood, in which an oxygen-sensitive signal ultimately increases the level of HIF-1α through the catalytic action of a number of 2-oxoglutarate-dependent oxygenases [24]. Further in-depth studies of the pathophysiological mechanisms and the boundary between adaptive and pathological effects of hypoxia have continued to this day. Their findings will help us understand the effects of different IHT and IHHT regimens depending on the severity, duration, and intermittent regimen of hypoxia [25].

FEATURES AND MECHANISMS OF HYPOXIA – HYPEROXIA TRAINING EFFECTS

Biofeedback-controlled IHHT represents the next step in the development of IHT. ReOxy therapy is a unique treatment that has two fundamental differences compared to IHT: 1) the principle of hypoxia–hyperoxia is used instead of hypoxia–normoxia; 2) individual selection of a hypoxia regimen is based on a hypoxic test and collected biofeedback [26].

ReOxy therapy involves changing the oxygen concentration in the gas mixture (ranging from 10 to 40% O_2 max) under the control of blood oxygen saturation using pulse oximetry. The addition of hyperoxia episodes (up to 40% oxygen in the gas mixture) during the reoxygenation period makes it possible to increase the dose of oxygen free radicals without increasing hypoxia and is the main difference from the IHT method. Moreover, the hypoxia–

hyperoxia paradox serves as the physiological basis for the combination of hypoxia and hyperoxia episodes in one procedure. Cells perceive fluctuations in the concentration of free oxygen (not its absolute level) as hypoxia.

Thus, repetitive intermittent hyperoxia can induce many molecular cascades and cellular mechanisms that are normally induced by hypoxia. Hyperoxic stimuli activate angiogenesis, mitogenesis, oxygen consumption efficiency, and metabolic activity in different tissues in the same way as hypoxia, but without adverse consequences [11].

A number of studies have shown that ReOxy therapy provides more significant activation of the antioxidant enzyme system in response to a moderate increase in the concentration of free radicals compared to conventional IHT. As a result, the body tissue resistance to hypoxia is more pronounced and achieved faster [11, 27].

Personalized hypoxic load chosen after a hypoxic test and biofeedback are other important differences between ReOxy therapy and conventional IHT. The selection of an adequate hypoxic and hypoxemic load within one IHHT course is based on an individual physiological response (SpO_2 level and heart rate) to a hypoxic stimulus. It ensures high effectiveness and safety of the procedure. Biological feedback is collected by constant monitoring of the degree of oxygen saturation in the blood, which allows specialists to maintain an individually adjusted level of hypoxemia.

BEST PRACTICES AND PROSPECTS OF REOXY THERAPY IN CARDIOVASCULAR DISEASES

The safety and effectiveness of IHHT in various cardiovascular diseases has been actively studied. Studies highlighting the effects of ReOxy therapy in arterial hypertension [26], metabolic syndrome [12, 28], acute and chronic coronary artery disease, including after coronary bypass surgery [2, 29, 30], in elderly patients and patients with comorbidities [31–33], and chronic heart failure (CHF) have been already published [34]. All these studies have proven the safety of the method and demonstrated the positive effect of IHHT on exercise tolerance [29, 30], lipid and carbohydrate metabolism [12, 28], cognitive functions [34], blood pressure levels and normalization of its daily profile [26], and reduction of depression [26, 31].

After IHHT, patients with hypertension present with blood pressure stabilization and a significant systolic blood pressure decrease by 15–17% compared to baseline [12, 26, 29]. ReOxy therapy in patients with coronary heart disease improves physical tolerance and lipid profile [7, 17, 29]. Moreover, there is evidence that IHHT impacts all pathological components of the metabolic syndrome: it mediates weight loss due to a decrease in fat mass, increases physical endurance in obese patients, lowers blood pressure, glucose levels, cholesterol, triglycerides, and low-density lipoproteins [12, 28]. The findings indicate that ReOxy therapy is an effective way of reducing cardiovascular risk factors in patients with metabolic syndrome, even in the absence of physical training [28].

In addition to the clinical and metabolic effects of IHHT, there is evidence of a positive effect of IHHT on myocardial remodeling and biochemical markers in blood plasma, which explains the mechanisms of the positive cardiological effects of ReOxy therapy [29, 30]. Thus, arranging an IHHT course for patients with myocardial infarction at the inpatient stage of rehabilitation helped increase exercise tolerance, significantly decrease the volume of the left ventricle, and increase left ventricular ejection fraction by 12% compared to the controls ($p < 0.05$) [30]. In another study, patients with stable coronary heart disease presented with an improvement in physical tolerance, an increase in hemoglobin levels, a decrease in cardiovascular reactions, and an increase in oxygen saturation during exercise [29]. Patients with hypertension exhibited normalization of blood pressure during ReOxy therapy due to increased levels of nitric oxide and HIF-1 in plasma [26]. Studies focusing on patients with CHF indicate an increase in cardiopulmonary reserve due to IHHT, which was confirmed by cardiopulmonary stress test results, and a decrease in biochemical prognostic markers, such as sodium uretic peptide, tumor necrosis factor (TNF) α, and homocysteine, thus making this method quite promising for management of patients with chronic heart failure [34].

In patients with metabolic syndrome, IHHT contributed to an improvement in the proinflammatory status by lowering the level of CRP and heat shock protein (Hsp70) [28]. Some studies show that moderate IHHT protocols enhance the innate immune system, while simultaneously exerting an overall anti-inflammatory effect by suppressing TNFα and IL-4 by more than 90% [30].

All abovementioned studies emphasize safety of the method ensured by an individual hypoxic test and biofeedback and indicate the possibility of studying its effects in patients with severe coronary artery disease after surgical interventions on the heart and blood vessels and in the postoperative period, in patients with low left ventricular ejection fraction and acute decompensated heart failure.

In addition, ReOxy therapy has a great potential in neurology as a method of rehabilitation after ischemic stroke, transient cerebral circulation arrest, vascular dementia, Alzheimer`s disease, chronic progressive cerebral circulation insufficiency, and rehabilitation after spinal cord injuries. Presumably, this is due to mechanisms that are involved in influencing neurophysiological biomarkers and electrophysiological properties of the neural network, and not only due to the mechanisms that are involved in myocardial pathology [35–38].

CONCLUSION

According to the results of the conducted studies, IHHT proved to be a very promising method of cardiac rehabilitation, as an alternative to PT and as an addition to it, aimed at increasing exercise tolerance, reducing symptoms and improving the functional status of angina pectoris and CHF, as well as improving myocardial perfusion and metabolic status. ReOxy therapy has a clinical and pathophysiological potential to optimize long-term prognosis in cardiovascular diseases. However, to confirm this, further studies are required.

REFERENCES

1. Cardiac rehabilitation and secondary prevention. Ed. by Aronov D.M. M.: GEOTAR-Media, 2021: 337. (In Russ.). DOI: 110.33029/9704-6218-8-CAR-2021-1-464.
2. Aronov D.M., Ioseliani D.G., Bubnova M.G., Krasnitskiy V.B., Novikova N.K. The clinical efficacy of a comprehensive program of rehabilitation after coronary artery bypass grafting in patients with coronary artery disease in the outpatient cardiac rehabilitation unit – stage III of rehabilitation. *CardioSomatika*. 2015;6(3)6–14. (In Russ.).
3. Dibben G., Faulkner J., Oldridge N., Rees K., Thompson D.R., Zwisler A.D. et al. Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database Syst. Rev.* 2021;6:11(11):CD001800. DOI: 10.1002/14651858.CD001800.pub4.
4. Patnode C.D., Redmond N., Iacocca M.O., Henninger M. Behavioral Counseling Interventions to Promote a Healthy Diet and Physical Activity for Cardiovascular Disease Prevention in Adults Without Known Cardiovascular Disease Risk Factors: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA.* 2022;328(4):375–388. DOI: 10.1001/jama.2022.7408
5. Suaya J.A., Stason W.B., Ades P.A., Normand S.L., Shepard D.S. Cardiac rehabilitation and survival in older coronary patients. *J. Am. Coll. Cardiol.* 2009;54(1):25–33. DOI: 10.1016/j.jacc.2009.01.078.
6. Meerson F.Z. Adaptive medicine: mechanisms and protective effects of adaptation. M.: Hypoxia Medical, 1993:331. (In Russ.).
7. Glazachev O.S., Lyamina N.P., Spirina G.K. Intermittent hypoxic conditioning: experience and potential in cardiac rehabilitation programs. *Russian Journal of Cardiology.* 2021;26(5):4426. (In Russ.). DOI: 10.15829/1560-4071-2021-4426.
8. West J.B. High-altitude medicine. *Lancet Respir. Med.* 2015;3(1):12–13. DOI: 10.1016/S2213-2600(14)70238-3.
9. Faeh D., Gutzwiller F., Bopp M. Lower mortality from coronary heart disease and stroke at higher altitudes in Switzerland. *Circulation.* 2009;120(6):495–501. DOI: 10.1161/circulationaha.108.819250.
10. Richalet J.P., Hermand E., Lhuissier F.J. Cardiovascular physiology and pathophysiology at high altitude. *Nat. Rev. Cardiol*. 2024;21(2):75–88. DOI: 10.1038/s41569-023-00924-9.
11. Glazachev O.S., Pozdnyakov Yu.M., Urinskyi A.M., Zabashta S.P. Hypoxia–hyperoxia adaptation and increased exercise capacity in patients with coronary heart disease. *Cardiovascular Therapy and Prevention*. 2014;13(1):16–21. (In Russ.). DOI: 10.15829/1728-8800-2014-1-16-21.
12. Zhang Q., Zhao W., Li S., Ding Y., Wang Y., Ji X. Intermittent hypoxia conditioning: a potential multi-organ protective therapeutic strategy. *Int. J. Med. Sci*. 2023;20(12):1551–1561. DOI: 10.7150/ijms.86622.
13. Wadley A.J., Veldhuijzen van Zanten J.J., Aldred S. The interactions of oxidative stress and inflammation with vascular dysfunction in ageing: the vascular health triad. *Age (Dordr.).* 2013;35(3):705–718. DOI: 10.1007/s11357-012-9402-1.
14. Sies H., Jones D.P. Reactive oxygen species (ROS) as pleiotropic physiological signalling agents. *Nat. Rev. Mol. Cell. Biol.* 2020;21(7):363–383. DOI: 10.1038/s41580-020-0230-3.
15. Richalet J.P., Hermand E., Lhuissier F.J. Cardiovascular physiology and pathophysiology at high altitude. *Nat. Rev. Cardiol.* 2024;21(2):75–88. DOI: 10.1038/s41569-023-00924-9.
16. Tuter D.S., Komarov R.N., Glazachev O.S., Syrkin A.L., Severova L.P., Ivanova E.V. et al. The use of intermittent hypoxia – hyperoxia training for the prevention of intraoperative and early postoperative complications during coronary artery bypass grafting. *Russian Journal of Cardiology*. 2018;23(6):166–172. (In Russ.). DOI: 10.15829/1560-4071-2018-6-166-172.
17. Haji Mohd Yasin N.A., Herbison P., Saxena P., Praporski S., Konstantinov I.E. The role of remote ischemic preconditioning in organ protection after cardiac surgery: a meta-analysis. *J. Surg. Res*. 2014;186(1):207–216. DOI: 10.1016/j.jss.2013.09.006.
18. Ara J., Fekete S., Frank M., Golden J.A., Pleasure D., Valencia I. Hypoxic-preconditioning induces neuropro-

tection against hypoxia-ischemia in newborn piglet brain. *Neurobiol. Dis.* 2011;43(2):473–485. DOI: 10.1016/j.nbd.2011.04.021.

19. Sementsov A.S., Maslov L.N., Naryzhnaya N.V., Bushov Yu.V., Lishmanov Yu.B. The role of reactive oxygen species in the heart attack-limiting effect of early hypoxic preconditioning. *Ros. Fiziol. Zhurn. Im. I.M. Sechenova*. 2019;105(5):650–656. (In Russ.). DOI: 10.1134/S0869813919050091.
20. Sasidharan R., Schippers J.H.M., Schmidt R.R. Redox and low-oxygen stress: signal integration and interplay. *Plant. Physiol.* 2021;186(1):66–78. DOI: 10.1093/plphys/kiaa081.
21. Liu W., Fan X., Jian B., Wen D., Wang H., Liu Z. et al. The signaling pathway of hypoxia inducible factor in regulating gut homeostasis. *Front. Microbiol.* 2023; 14:1289102. DOI: 10.3389/fmicb.2023.1289102.
22. Yang C., Zhong Z., Wang S., Vong C., Yu B., Wang Y.T. HIF-1: structure, biology and natural modulators. *Chin. J. Nat. Med*. 2021;19(7):521–527. DOI: 10.1016/S1875-5364(21)60051-1.
23. Pugh C.W., Ratcliffe P.J. New horizons in hypoxia signaling pathways. *Exp. Cell. Res.* 2017;356(2):116–121. DOI: 10.1016/j.yexcr.2017.03.008 .
24. D'Aiuto N., Hochmann J., Millán M., Di Paolo A., Bologna-Molina R., Sotelo Silveira J. et al. Hypoxia, acidification and oxidative stress in cells cultured at large distances from an oxygen source. *Sci. Rep.* 2022;12(1):21699. DOI: 10.1038/s41598-022-26205-y.
25. Muangritdech N., Hamlin M.J., Sawanyawisuth K., Prajumwongs P., Saengjan W., Wonnabussapawich P. et al. Hypoxic training improves blood pressure, nitric oxide and hypoxia-inducible 7 factor-1 alpha in hypertensive patients. *European Journal of Applied Physiology*. 2020;120:1815–1826. DOI: 10.1007/s00421-020-04410-9 .
26. Hadanny A., Efrati S. The hyperoxic-hypoxic paradox. *Biomolecules.* 2020;10(6):958. DOI: 10.3390/biom10060958.
27. Burtscher M., Gatterer H., Szubski C., Pierantozzi E., Faulhaber M. Effects of interval hypoxia on exercise tolerance: special focus on patients with CAD or COPD. *Sleep Breath.* 2010;14(3):209–220. DOI: 10.1007/s11325-009-0289-8.
28. Afina A.B., Oleg S.G., Alexander A.B., Ines D., Alexander Yu.S., Nikita V.V. et al. The effects of intermittent hypoxic-hyperoxic exposures on lipid profile and inflammation in patients with metabolic syndrome. *Front. Cardiovasc. Med.* 2021;8:700826. DOI: 10.3389/fcvm.2021.700826.
29. Bestavashvili A., Glazachev O., Bestavashvili A., Suvorov A., Zhang Y., Zhang X. et al. Intermittent hypoxic-hyperoxic exposures effects in patients with metabolic syndrome: correction of cardiovascular and metabolic profile. *Biomedicines.* 2022;10(3):566. DOI: 10.3390/biomedicines10030566.
30. Valle M., García-Godos F., Woolcott O.O., Marticorena J.M., Rodríguez V., Gutiérrez I. et al. Improvement of myocardial perfusion in coronary patients after intermittent hypobaric hypoxia. *J. Nucl. Cardiol.* 2006;13:6974. DOI: 10.1016/j.nuclcard.2005.11.008.
31. Karamova I.M., Kuzmina Z.S., Gazizova N.R., Abdyukova E.R., Stolyarova T.V. The use of interval hypoxic training at the second inpatient stage of rehabilitation of patients with myocardial infarction without Q wave in the subacute period. *CardioSomatika*. 2017;1:40–41. (In Russ.).
32. Klyuchnikova E.A., Abbazova L.V., Lokhannikova M.A., Ananyev S.S., Pavlov D.A., Balykin M.V. The influence of intermittent normobaric hypoxia on systemic hemodynamics, biochemical composition of blood, and physical performance of elderly people. *Uljanovsk Journal of Medical Biology*. 2017;4:155–160. (In Russ.). DOI: 10.23648/UMBJ.2017.28.8755.
33. Behrendt T., Altorjay A.C., Bielitzki R., Behrens M., Glazachev O.S., Schega L. Influence of acute and chronic intermittent hypoxic-hyperoxic exposure prior to aerobic exercise on cardiovascular risk factors in geriatric patients-a randomized controlled trial. *Front. Physiol.* 2022;13:1043536. DOI: 10.3389/fphys.2022.1043536.
34. Bayer U., Likar R., Pinter G., Stettner H., Demschar S., Trummer B., et al. Effects of intermittent hypoxia-hyperoxia on mobility and perceived health in geriatric patients performing a multimodal training intervention: a randomized controlled trial. *BMC Geriatr.* 2019;14:19(1):167. DOI: 10.1186/s12877-019-1184-1.
35. Dushina A.G., Libis R.A. New opportunities in treatment of chronic heart failure with normal ejection fraction. *Cardiovascular Therapy and Prevention.* 2015;14(4):52–58. (In Russ.). DOI: 10.15829/1728-8800-2015-4-52-58.
36. Yi L., Wu J., Yan B., Wang Y., Zou M., Zhang Y., et al. Effects of three weeks base training at moderate simulated altitude with or without hypoxic residence on exercise capacity and physiological adaptations in well-trained male runners. *Peer J.* 2024;12:e17166. DOI: 10.7717/peerj.17166.
37. Serebrovska Z.O., Serebrovska T.V., Kholin V.A., Tumanovska L.V., Shysh A.M., Pashevin D.A. et al. Intermittent Hypoxia-Hyperoxia Training Improves Cognitive Function and Decreases Circulating Biomarkers of Alzheimer's Disease in Patients with Mild Cognitive Impairment: A Pilot Study. *Int. J. Mol. Sci.* 2019;20(21):5405. DOI: 10.3390/ijms20215405.
38. Yuan H., Liu J., Gu Y., Ji X., Nan G. Intermittent hypoxia conditioning as a potential prevention and treatment strategy for ischemic stroke: Current evidence and future directions. *Front. Neurosci*. 2022;16:1067411. DOI: 10.3389/fnins.2022.1067411.

Author information

Lebedeva Nataliya B. – Dr. Sc. (Medicine), Associate Professor, Leading Researcher, Laboratory of Rehabilitation, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, lebenb@mail.ru, https://orcid.org/0000-0003-2769-3807

Egle Albert P. – Cardiologist, Kuzbass Clinical Cardiology Dispensary named after Academician L.S. Barbarash, Kemerovo, albert_egle@mail.ru, https://orcid.org/0009-0009-2547-0782

Sakharchuk Alexey Yu. – Cardiology Resident, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, alex90s03kemerovo@mail.ru, https://orcid.org/0009-0007-2788-0748

Argunova Yulia A. – Dr. Sc. (Medicine), Head of the Laboratory of Rehabilitation, Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, argunova-u@mail.ru, https://orcid.org/0000-0002-8079-5397

Barbarash Olga L. – Dr. Sc. (Medicine), Professor, Full Member of the Russian Academy of Sciences, Director of Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, olb61@mail.ru, https://orcid.org/0000-0002-4642-3610

(✉) **Lebedeva Nataliya B.,** lebenb@mail.ru

Received 24.12.2024;
approved after peer review 14.01.2025;
accepted 21.01.2025