Exercise therapy for resistant hypertension: a narrative review

Konstantinos Athanasios Volaklis[1, 2], Dennis Freuer[3], Christa Meisinger[3]

[1]TU Munich, Munich, Germany
[2]7FIT, Cardiac Rehabilitation Center, Augsburg, Germany
[3]Department of Epidemiology, Medical Faculty, University of Augsburg, Augsburg, Germany

Abstract

Resistant hypertension (RH), defined as a high blood pressure that remains uncontrolled despite treatment, is still a major medical challenge. During the last decade, several studies have demonstrated the promising effects of exercise on the category of hypertensives. This review summarizes the existing literature on the effects of exercise therapy on patients with RH. From the literature search conducted in PubMed (January 1980 – December 2023), 12 papers (6 with acute- and 6 with chronic exercise) were selected. Despite the few studies, the acute hemodynamic burden and the post-exercise response in patients with RH were within clinically acceptable limits and may vary according to the intensity and duration of the exercise protocols. Chronic exercise, especially warm-water exercise, effectively lowers blood pressure in patients with RH without serious adverse events or complications. Based on recent scientific evidence, patients with RH need to change their lifestyle by adopting systematic exercise for the optimal treatment of their disease. Future investigations are required to explore the exact exercise mechanisms that benefit patients with RH.

Key words: resistant hypertension; exercise; acute; chronic

Arterial Hypertens. 2024, vol. 28, pages: 71–77
DOI: 10.5603/ah.99228

Introduction

Physical exercise has been established as an effective means (complementary to medication) in the treatment of elevated blood pressure. This scientific knowledge is regularly updated by several scientific organizations [1, 2]. For patients with mild (stage I) hypertension, defined as a systolic blood pressure (SBP) reading that falls between 130 and 139 mm Hg or a diastolic reading (DBP) that is between 80 and 89 mm Hg, exercise is recommended as the first-line therapy of a healthy lifestyle approach to regulate their disease [3] sufficiently. Interestingly, the results of a recent meta-analysis (391 randomized trials with 39742 participants) showed comparable SBP-lowering effects between anti-hypertensive drugs and various exercise interventions [4].

However, it has to be clarified yet whether physical exercise is also effective for those with poor responsiveness to medication, such as patients with resistant hypertension (RH). The latter is defined as the failure to regulate blood pressure below 140/90 mm Hg despite taking three antihypertensive medications, one of which is a diuretic [5]. Despite the recent progress in the management of RH (drug optimization, sympathetic denervation of renal arteries), the disease`s prevalence remains high

Address for correspondence: Konstantinos Athanasios Volaklis, TU Munich, Georg Brauchle Ring 56, 80333 Munich, Germany;
e-mail: konstantinosvolaklis@gmail.com

among hypertensive patients (ranging between 10 and 30%), increasing the risk of cardiovascular mortality [6].

During the last decade several studies have demonstrated the therapeutic effect of exercise in this category of hypertensive patients [7–13]. This review will briefly discuss the positive acute exercise alterations as well as the favorable chronic adaptations after systematic training in patients with resistant hypertension, providing recent scientific knowledge.

Material and methods

A literature search in the electronic PubMed database was conducted to identify studies on the association between resistant hypertension and exercise. To search for relevant studies, the following keywords in different combinations were used: "resistant hypertension", "acute exercise", "exercise response", "exercise therapy", "physical exercise", "regular exercise", "treatment", and "training adaptations". Only non-duplicated research articles published in English between January 1980 and December 2023 were selected. Case reports, letters to the editor, conference papers, dissertations, commentaries, and review papers were excluded. In total, 816 studies were yielded from the medical database search. After the initial screening of titles, 156 studies were selected for reading the abstract; after reading the abstracts, 18 were chosen for full-text reading. Only 10 met the inclusion criteria, and in addition, 2 studies identified from reference lists were included, resulting in a total number of 12 articles (Fig. 1).

Results

Acute exercise responses

Few studies have examined the acute hemodynamic and post-exercise responses in patients with

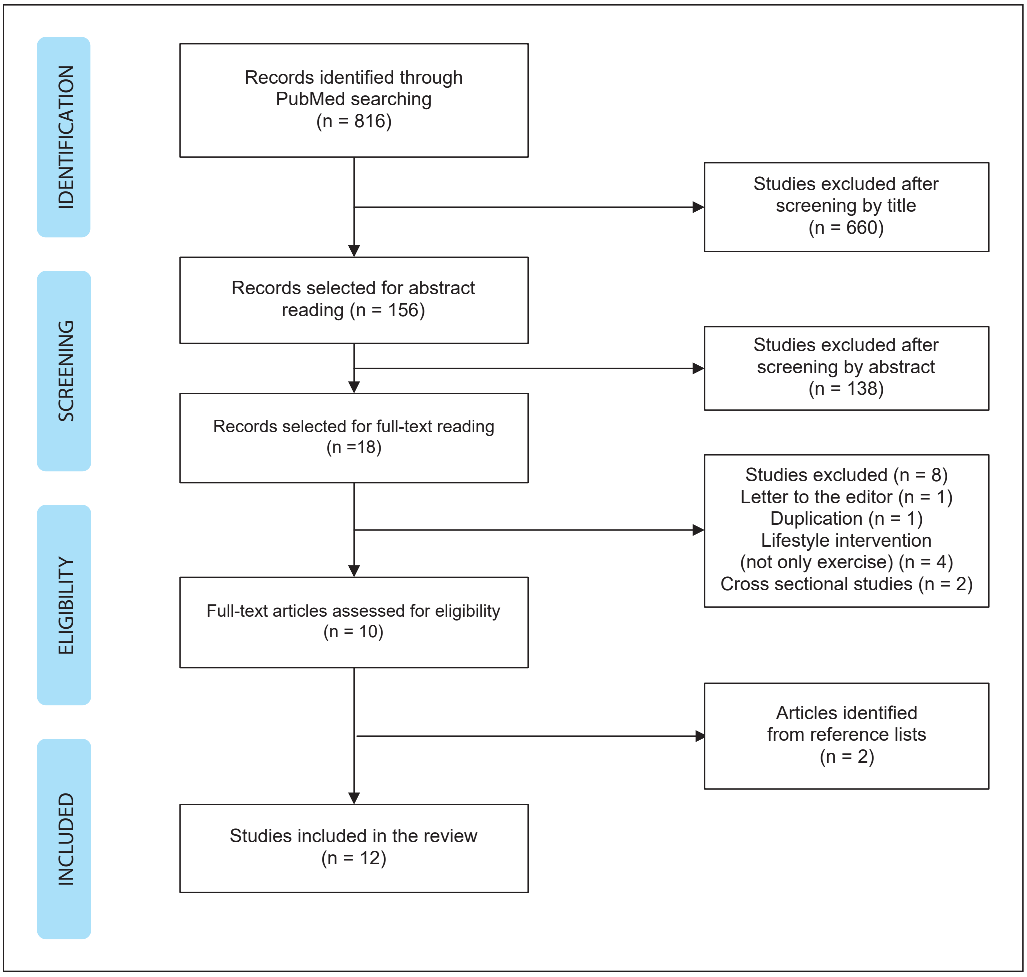

Figure 1. Flow chart of the studies selection strategy

RH with promising results. Ribeiro et al. [7] analyzed the effects of a single session of light-intensity aerobic exercise (10 min walking at 3 km/h) on the central and peripheral blood pressure and the carotid-femoral pulse wave velocity (PWV) in 19 RH patients (age: 58.7 years, 53% men). The central (150.5 to 156.6 mm Hg, p = 0.023) and peripheral (163.1 to 173.4 mm Hg, p = 0.002) SBP were increased immediately after exercise, while normal PWV alterations were observed.

Santos and coworkers (8) compared the effects of two different exercise intensities (45 minutes at 50% and 75% of maximum heart rate) in 20 patients with RH (mean age: 54 years). Both exercise protocols (light and moderate) reduced the systolic ambulatory pressure over 5 hours (light: –7.7 ± 2.4 mm Hg and moderate: –9.4 ± 2.8 mm Hg), but only light intensity exercise reduced diastolic pressure (–5.7 ± 2.2 mm Hg), compared to controls. Forearm blood flow, as an index of vascular reactivity, decreased only after light exercise, suggesting that the expected exercise alterations are intensity-dependent.

In another study, Pires et al. [9] compared the postexercise hypotension phenomenon after three different exercise programs (aerobic, resistance, and combined) in patients with RH. In their study, more prolonged reductions in systolic and diastolic blood pressure were observed after combined (~12 h) relative to aerobic (~6 h) and resistance (~3 h) exercise, suggesting that exercise modality can affect the blood pressure responses post-exercise.

Patients with RH experience excessive blood pressure elevation during exercise, so some researchers have also investigated whether systemic renal denervation improves exercise blood pressure, an established predictor for future cardiovascular events [10]. Ukena et al. [11] examined the effects of this intervention on the cardiopulmonary response to acute exercise in 46 patients (70% male) with therapy-resistant hypertension. Systolic blood pressure at rest and maximum exercise after 3 months was significantly reduced by 31 mm Hg and 21 mm Hg, respectively, compared to baseline, as well as the recovery of systolic blood pressure by 29 mm Hg. Interestingly, these impressive alterations occurred without affecting the chronotropic competence of the heart.

Significant blood pressure reductions at rest (158/90 mm Hg *vs.* 141/84 mm Hg) and during maximal exercise (201/95 mm Hg *vs.* 188/86 mm Hg) were also reported by Ewen et al. [12] after 12 months of applying renal denervation in 60 patients (mean age 64.7 years, 78% men) with RH with simultaneous improvement in mean exercise time (from 6.6 to 9.0 minutes) and mean workload (from 93 to 101 Watt).

The above data suggest that the acute hemodynamic burden and the post-exercise response in patients with RH may vary according to the intensity and duration of the exercise protocols and whether patients had successfully undergone renal sympathetic denervation or not. Most existing studies applied low-moderate intensity aerobic exercise (up to 75% of HRmax), and acceptable hemodynamic responses were found.

However, more research is needed to confirm this preliminary evidence further and establish the safety application of other exercise modalities (such as resistance or interval exercise) as an alternative therapy. The magnitude and duration of the post-exercise phenomenon must also be further investigated since this knowledge will allow the implementation of the most appropriate exercise program for hypertensive patients with low responsiveness to drug treatment.

Chronic exercise adaptations

During the last decade, several studies have examined the adaptations as a result of long-term exercise in patients with RH. Dimeo et al. [13] were among the first to investigate the cardiovascular effects of aerobic exercise on RH in a randomized controlled trial (n = 50, 46% male, mean age 62.8 yrs). After 8 to 12 weeks of treadmill exercise with a target lactate of 2 mmol/l, systolic and diastolic daytime ambulatory blood pressure decreased by 6 and 3 mmHg, respectively. However, arterial compliance and cardiac index (relating cardiac output to body size) remained unchanged after training.

In another randomized controlled clinical trial (EnRich, exercise training in the treatment of resistant hypertension) with the same characteristics (53 patients, 54% male, mean age: 59.3 yrs 12-weeks training duration), Lopes et al. [14] reported significant reductions in 24-hour and daytime ambulatory systolic and diastolic blood pressure (by 7.1 and 5.1 mm Hg, respectively). In the above study, training intensity was set at 50-70% of VO-2max, which contributed to an improvement in cardiorespiratory fitness by 14%. The analysis of the secondary endpoints in the EnRicH trial further suggested that exercise training improved central BP and BP variability and some cardiovascular disease risk biomarkers associated with target organ damage and increased CVD risk and mortality in this population [15].

Kruk et al. [16] assessed the effects of a physical activity program intensified by educational sessions on blood pressure control in subjects with RH in a primary care unit. Patients experienced significant decreases in office SBP and DBP as well as in ambulatory BP after three months. Still, these improvements did not persist at the end of the intervention (after 6 months). On the other hand, in the study of Mandini et al. [17], seventy-nine patients with RH (mean age: 66.6 yrs, 5.19% men) who participated in supervised walking and experienced clinically significant reductions of systolic blood pressure after one year of training. Thus, it seems that more extended periods and training supervision are needed to achieve effective blood pressure reduction in patients with RH.

Significant reductions in blood pressure have also been reported after applying water-based exercise [18]. Such an exercise protocol, which consisted of gymnastics and walking inside the pool at a temperature of 30–32°C, resulted in significant blood pressure reductions (daytime: –11.6 and –6.4 mm Hg and nighttime: –9.6 and –7.4 mm Hg, for systolic and diastolic pressure respectively). In the same study (19), even more significant improvements were observed after 3 months of daytime training (SBP: –22.3 mm Hg and DBP: –13.0 mm Hg) and nighttime blood pressure (SBP: 17.4 ± 9.1 mm Hg and DBP: 8.5 ± 2.1 mm Hg).

These data suggest that exercise training effectively lowers blood pressure in patients with RH. The mentioned studies showed a high compliance rate without serious adverse events or complications. Warm water acts as a thermal vasodilation therapy for these patients, providing even more significant benefits compared to land exercise. Positive vasodilatory effects in endothelial function have also been reported after repeated sauna therapy (15 min at 60ofor 3 weeks) in patients with coronary risk factors and heart failure [20, 21].

Mechanisms of exercise

Several different mechanisms have been proposed to explain the exercise-induced adaptations in patients with RH. Regular exercise reduces sympathetic nervous activity while increasing parasympathetic tone and baroreceptor sensitivity [22]. Furthermore, exercise regulates the renin-angiotensin-aldosterone system to produce less angiotensin II, reducing peripheral vascular resistance [23, 24].

The increase in shear stress and the subsequent release of nitric oxide (NO) that occurs during exercise have therapeutic effects [25] since decreased NO bioavailability and endothelial dysfunction are critical factors involved in the pathogenesis of hypertension [26]. In addition, exercise helps regulate body weight and blood lipids and reduces chronic low-grade inflammation, which are further significant factors associated with elevated blood pressure [27].

The above mechanisms are further optimized when exercise takes place in an aquatic, warm environment. This is attributed to the hydrostatic pressure favoring venous return and the high water temperature, which positively affect the sympathetic activity and, thus, vascular resistance [28, 29]. Another advantage of water-based exercise is the principle of buoyancy, which significantly reduces body weight sensation with increased immersion depth [30]. Thus, water exercise supports the body and decreases joint and muscle stress, allowing, in this way, appropriate blood pressure responses since several of the RH patients are overweight or obese [31].

Clinical implications

The reduction in blood pressure after exercise (post-exercise hypotension) lasts for several hours throughout the day, which is of great clinical importance given the better predictive value of ambulatory versus resting blood pressure measurements [32]. When exercise is done regularly, a permanent down-regulation of the blood pressure takes place, and this is very important for those patients having RH because the exercise-induced blood pressure reductions are comparable to those observed after the sympathetic denervation of renal arteries (e.g., 7.4 and 4.2 mm Hg for systolic and diastolic pressure, respectively in the SPYRAL-HTN study) [33]. This may affect outcome since improving systolic by 10 mm Hg (or diastolic by 4 mm Hg) reduces the risk of stroke by 30% and myocardial infarction risk by 20% [34].

Furthermore, exercise training increases cardiorespiratory fitness (CRF), low levels of which are independently associated with mortality in hypertensives. Indeed, in a large cohort of RH patients (n = 1276), those stratified into the highest quartile of CRF had a 62% lower risk of all-cause mortality compared to the lowest fit group (8.8 versus 4.5 METs). For each 1-MET increment in exercise capacity, the mortality risk reduction was 18% [35].

In another study, higher levels of physical activity were significantly associated with lower risk for cardiovascular events among 2043 RH patients (mean age: 58.8 yrs, 50.9% men) over a mean follow-up of 4.5 years, whereas higher daily levels of light-intensity and total physical activity were also associated with lower arterial stiffness [36]. All the above results are of great clinical interest since the majority of RH patients lead a sedentary lifestyle, and even modest amounts of physical activity may be beneficial in reducing cardiovascular events and all-cause mortality [37].

Conclusions and future directions

Outside the sympathetic denervation of renal arteries, several lifestyle interventions have been proposed to manage RH. In recent years, the progress in the therapeutic application of exercise in patients with RH has been impressive. Based on recent scientific evidence, these patients need to change their lifestyle by adopting systematic training for the optimal treatment of their disease.

However, several issues must be further clarified. In some acute studies, the participants underwent maximal exercise testing (which does not reflect real training routines), or the intensity was not controlled. There is a need, however, for exact information regarding intensity during exercise since this factor is the most important determinant of the blood pressure response and, thus, safety. From the follow-up studies, the duration of the programs was short (ranging from 8 to 12 weeks), and the effects of long-term exercise training are unknown. Heterogeneity also exists regarding other research variables (training intensity, mode of exercise, age and gender of the participants, use of medications, monitoring strategies), and more studies are needed to identify the most effective exercise modality and dose and to fully establish the applicability of exercise therapy as an alternative intervention in these patients. It should also be clarified whether the effects of exercise could be maintained since none of the referred studies provided a follow-up evaluation period.

Given that the optimal treatment of patients in any stage of hypertension requires both lifestyle and pharmacological interventions [38] and that two recent metanalyses further demonstrated similar efficacy by comparing exercise and medications [4, 39], it is of vital importance for patients with RH to exercise systematically and uninterrupted throughout life to reduce their hemodynamic burden and to improve exercise tolerance, clinical status, and prognosis. Due to the small number of the included studies and their high heterogeneity, further research is needed to confirm this preliminary evidence.

Conflict of interest:
The authors declare no conflict of interest.

Funding

None declared.

Acknowledgments

None.

References

1. Reboussin DM, Allen NB, Griswold ME, et al. Systematic Review for the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018; 71(19): 2176–2198, doi: 10.1016/j.jacc.2017.11.004, indexed in Pubmed: 29146534.
2. Pescatello LS, Buchner DM, Jakicic JM, et al. 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE*. Physical Activity to Prevent and Treat Hypertension: A Systematic Review. Med Sci Sports Exerc. 2019; 51(6): 1314–1323, doi: 10.1249/MSS.0000000000001943, indexed in Pubmed: 31095088.
3. Barone Gibbs B, Hivert MF, Jerome GJ, et al. American Heart Association Council on Lifestyle and Cardiometabolic Health; Council on Cardiovascular and Stroke Nursing; and Council on Clinical Cardiology. Physical Activity as a Critical Component of First-Line Treatment for Elevated Blood Pressure or Cholesterol: Who, What, and How?: A Scientific Statement From the American Heart Association. Hypertension. 2021; 78(2): e26–e37, doi: 10.1161/HYP.0000000000000196, indexed in Pubmed: 34074137.
4. Naci H, Salcher-Konrad M, Dias S, et al. How does exercise treatment compare with antihypertensive medications? A network meta-analysis of 391 randomised controlled trials assessing exercise and medication effects on systolic blood pressure. Br J Sports Med. 2019; 53(14): 859–869, doi: 10.1136/bjsports-2018-099921, indexed in Pubmed: 30563873.
5. Carey RM, Calhoun DA, Bakris GL, et al. American Heart Association Professional/Public Education and Publications Committee of the Council on Hypertension; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Genomic and Precision Medicine; Council on Peripheral Vascular Disease; Council on Quality of Care and Outcomes Research; and Stroke Council, American Heart Association Professional Education Committee. Resistant hypertension: diagnosis, evaluation, and treatment. A scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. Hypertension. 2008; 51(6): 1403–1419, doi: 10.1161/HYPERTENSIONAHA.108.189141, indexed in Pubmed: 18391085.
6. Carey RM, Whelton PK, Carey RM, et al. American Heart Association Professional/Public Education and Publications Committee of the Council on Hypertension; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Genomic and Precision Medicine; Council on Peripheral Vascular Disease; Council on Quality of Care and Outcomes Research; and Stroke Council. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018; 71(6): 1269–1324, doi: 10.1161/HYP.0000000000000066, indexed in Pubmed: 29133354.

7. Ribeiro F, Almeida N, Ferreira R, et al. Central and peripheral blood pressure response to a single bout of an exercise session in patients with resistant hypertension. Hypertens Res. 2019; 42(1): 114–116, doi: 10.1038/s41440-018-0100-y, indexed in Pubmed: 30206324.
8. Santos LP, Moraes RS, Vieira PJC, et al. Effects of aerobic exercise intensity on ambulatory blood pressure and vascular responses in resistant hypertension: a crossover trial. J Hypertens. 2016; 34(7): 1317–1324, doi: 10.1097/HJH.0000000000000961, indexed in Pubmed: 27137175.
9. Pires NF, Coelho-Júnior HJ, Gambassi BB, et al. Combined Aerobic and Resistance Exercises Evokes Longer Reductions on Ambulatory Blood Pressure in Resistant Hypertension: A Randomized Crossover Trial. Cardiovasc Ther. 2020; 2020: 8157858, doi: 10.1155/2020/8157858, indexed in Pubmed: 32821284.
10. Schultz MG, Otahal P, Cleland VJ, et al. Exercise-induced hypertension, cardiovascular events, and mortality in patients undergoing exercise stress testing: a systematic review and meta-analysis. Am J Hypertens. 2013; 26(3): 357–366, doi: 10.1093/ajh/hps053, indexed in Pubmed: 23382486.
11. Ukena C, Mahfoud F, Kindermann I, et al. Cardiorespiratory response to exercise after renal sympathetic denervation in patients with resistant hypertension. J Am Coll Cardiol 2011; 58: 1176–82. J Am Coll Cardiol. 2011; 58(11): 839–845, doi: 10.1016/j.jacc.2011.05.036, indexed in Pubmed: 21884958.
12. Ewen S, Mahfoud F, Linz D, et al. Effects of renal sympathetic denervation on exercise blood pressure, heart rate, and capacity in patients with resistant hypertension. Hypertension. 2014; 63(4): 839–845, doi: 10.1161/HYPERTENSIONAHA.113.01985, indexed in Pubmed: 24420550.
13. Dimeo F, Pagonas N, Seibert F, et al. Aerobic exercise reduces blood pressure in resistant hypertension. Hypertension. 2012; 60(3): 653–658, doi: 10.1161/HYPERTENSIONAHA.112.197780, indexed in Pubmed: 22802220.
14. Lopes S, Mesquita-Bastos J, Garcia C, et al. Effect of Exercise Training on Ambulatory Blood Pressure Among Patients With Resistant Hypertension: A Randomized Clinical Trial. JAMA Cardiol. 2021; 6(11): 1317–1323, doi: 10.1001/jamacardio.2021.2735, indexed in Pubmed: 34347008.
15. Lopes S, Mesquita-Bastos J, Garcia C, et al. Aerobic exercise improves central blood pressure and blood pressure variability among patients with resistant hypertension: results of the EnRicH trial. Hypertens Res. 2023; 46(6): 1547–1557, doi: 10.1038/s41440-023-01229-7, indexed in Pubmed: 36813985.
16. Kruk PJ, Nowicki M. Effect of the physical activity program on the treatment of resistant hypertension in primary care. Prim Health Care Res Dev. 2018; 19(6): 575–583, doi: 10.1017/S1463423618000154, indexed in Pubmed: 29564997.
17. Mandini S, Conconi F, Mori E, et al. Guided walking reduces blood pressure in hypertensive sedentary subjects including those with resistant hypertension. J Hum Hypertens. 2021; 35(3): 226–231, doi: 10.1038/s41371-020-0324-6, indexed in Pubmed: 32152454.
18. Guimarães GV, Cruz LGB, Tavares AC, et al. Effects of short-term heated water-based exercise training on systemic blood pressure in patients with resistant hypertension: a pilot study. Blood Press Monit. 2013; 18(6): 342–345, doi: 10.1097/MBP.0000000000000000, indexed in Pubmed: 24192849.
19. Guimaraes GV, de Barros Cruz LG, Fernandes-Silva MM, et al. Heated water-based exercise training reduces 24-hour ambulatory blood pressure levels in resistant hypertensive patients: a randomized controlled trial (HEx trial). Int J Cardiol. 2014; 172(2): 434–441, doi: 10.1016/j.ijcard.2014.01.100, indexed in Pubmed: 24491874.
20. Imamura M, Biro S, Kihara T, et al. Repeated thermal therapy improves impaired vascular endothelial function in patients with coronary risk factors. J Am Coll Cardiol. 2001; 38(4): 1083–1088, doi: 10.1016/s0735-1097(01)01467-x, indexed in Pubmed: 11583886.
21. Ohori T, Nozawa T, Ihori H, et al. Effect of repeated sauna treatment on exercise tolerance and endothelial function in patients with chronic heart failure. Am J Cardiol. 2012; 109(1): 100–104, doi: 10.1016/j.amjcard.2011.08.014, indexed in Pubmed: 21944673.
22. Krieger EM, Da Silva GJ, Negrão CE. Effects of exercise training on baroreflex control of the cardiovascular system. Ann N Y Acad Sci. 2001; 940: 338–347, doi: 10.1111/j.1749-6632.2001.tb03689.x, indexed in Pubmed: 11458691.
23. Fallo F. Renin-angiotensin-aldosterone system and physical exercise. J Sports Med Phys Fitness. 1993; 33(3): 306–312, indexed in Pubmed: 8107485.
24. Peng WW, Hong L, Liu GY, et al. Prehypertension exercise training attenuates hypertension and cardiac hypertrophy accompanied by temporal changes in the levels of angiotensin II and angiotensin (1-7). Hypertens Res. 2019; 42(11): 1745–1756, doi: 10.1038/s41440-019-0297-4, indexed in Pubmed: 31273339.
25. Volaklis KA, Tokmakidis SP, Halle M. Acute and chronic effects of exercise on circulating endothelial progenitor cells in healthy and diseased patients. Clin Res Cardiol. 2013; 102(4): 249–257, doi: 10.1007/s00392-012-0517-2, indexed in Pubmed: 23117697.
26. Li Q, Youn JY, Cai H. Mechanisms and consequences of endothelial nitric oxide synthase dysfunction in hypertension. J Hypertens. 2015; 33(6): 1128–1136, doi: 10.1097/hjh.0000000000000587, indexed in Pubmed: 25882860.
27. Crea F. Physical exercise, inflammation, and hypertension: how to improve cardiovascular prevention. Eur Heart J. 2022; 43(46): 4763–4766, doi: 10.1093/eurheartj/ehac695, indexed in Pubmed: 36473697.
28. Cui J, Gao Z, Leuenberger UA, et al. Repeated warm water baths decrease sympathetic activity in humans. J Appl Physiol (1985). 2022; 133(1): 234–245, doi: 10.1152/japplphysiol.00684.2021, indexed in Pubmed: 35736952.
29. Ngomane AY, Fernandes B, Guimarães GV, et al. Hypotensive Effect of Heated Water-based Exercise in Older Individuals with Hypertension. Int J Sports Med. 2019; 40(4): 283–291, doi: 10.1055/a-0828-8017, indexed in Pubmed: 30791079.
30. Orselli MI, Duarte M. Joint forces and torques when walking in shallow water. J Biomech. 2011; 44(6): 1170–1175, doi: 10.1016/j.jbiomech.2011.01.017, indexed in Pubmed: 21334630.
31. Shimbo D, Levitan EB, Booth JN, et al. The contributions of unhealthy lifestyle factors to apparent resistant hypertension: findings from the Reasons for Geographic And Racial Differences in Stroke (REGARDS) study. J Hypertens. 2013; 31(2): 370–376, doi: 10.1097/HJH.0b013e32835b6be7, indexed in Pubmed: 23303356.
32. Banegas J, Ruilope L, Sierra Ad, et al. Relationship between Clinic and Ambulatory Blood-Pressure Measurements and Mortality. New Engl J M. 2018; 378(16): 1509–1520, doi: 10.1056/nejmoa1712231, indexed in Pubmed: 29669232.
33. Kandzari D, Böhm M, Mahfoud F, et al. Effect of renal denervation on blood pressure in the presence of antihypertensive drugs: 6-month efficacy and safety results from the SPYRAL HTN-ON MED proof-of-concept randomised trial. Lancet. 2018; 391(10137): 2346–2355, doi: 10.1016/s0140-6736(18)30951-6, indexed in Pubmed: 29803589.
34. Staessen JA, Wang JG, Thijs L. Cardiovascular protection and blood pressure reduction: a meta-analysis. Lancet. 2001; 358(9290): 1305–1315, doi: 10.1016/S0140-6736(01)06411-X, indexed in Pubmed: 11684211.
35. Narayan P, Doumas M, Kumar A, et al. Impact of Cardiorespiratory Fitness on Mortality in Black Male Veterans With Resistant Systemic Hypertension. Am J Cardiol. 2017; 120(9): 1568–1571, doi: 10.1016/j.amjcard.2017.07.055, indexed in Pubmed: 28886854.
36. Lopes S, Mesquita-Bastos J, Garcia C, et al. Physical Activity is Associated With Lower Arterial Stiffness in Patients With Resistant Hypertension. Heart Lung Circ. 2021; 30(11): 1762–1768, doi: 10.1016/j.hlc.2021.06.532, indexed in Pubmed: 34417116.

37. Diaz KM, Booth JN, Calhoun DA, et al. Healthy lifestyle factors and risk of cardiovascular events and mortality in treatment-resistant hypertension: the Reasons for Geographic and Racial Differences in Stroke study. Hypertension. 2014; 64(3): 465–471, doi: 10.1161/HYPERTENSIONAHA.114.03565, indexed in Pubmed: 24914189.
38. Valenzuela P, Carrera-Bastos P, Gálvez B, et al. Lifestyle interventions for the prevention and treatment of hypertension. Nat Rev Cardiol. 2020; 18(4): 251–275, doi: 10.1038/s41569-020-00437-9, indexed in Pubmed: 33037326.
39. Noone C, Leahy J, Morrissey EC, et al. Comparative efficacy of exercise and anti-hypertensive pharmacological interventions in reducing blood pressure in people with hypertension: A network meta-analysis. Eur J Prev Cardiol. 2020; 27(3): 247–255, doi: 10.1177/2047487319879786, indexed in Pubmed: 31615283.