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Effect of Six Weeks Endurance Training on Some Hemodynamic Factors in High-fat Diet-Fed Male Rats

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ABSTRACT

Introduction: Hypertension is a pivotal modifiable risk factor for global cardiovascular diseases and premature mortality, often associated with a high-fat diet. This study aimed to explore the impact of endurance training on selected hemodynamic factors in rats subjected to a high-fat diet.

Material & Methods: In this experimental research, 21 male Wistar rats (weighing 200-250 g) were randomly assigned to three groups: high-fat diet (HF), normal diet (C), and high-fat diet with endurance training (HF+T), each comprising seven rats. The HF and HF+T groups were exposed to a high-fat diet (60% calories from fat) for 12 weeks. Subsequently, the HF+T group underwent a six-week, five-sessions-per-week endurance training program. Cardiac parameters were recorded using physiography, and data analysis was performed with SPSS software version 24, utilizing one-way ANOVA.

Results: The one-way ANOVA results showed no significant difference between groups in heart rate (p=0.143). However, systolic blood pressure was significantly higher in the HF+T group compared to C (p=0.001) and HF (p=0.045) groups. The HF group also exhibited significantly elevated systolic blood pressure compared to the C group (p=0.044). Additionally, diastolic blood pressure was significantly higher in both the HF (p=0.021) and HF+T (p=0.009) groups compared to the C group.

Conclusion: This study suggests that a high-fat diet, particularly when combined with endurance training, leads to an increase in blood pressure in rats compared to those fed a normal diet, emphasizing the complex relationship between diet, exercise, and cardiovascular health. The findings underscore the importance of understanding these interactions for comprehensive cardiovascular risk management. The identified hemodynamic changes contribute valuable insights for future interventions aimed at mitigating the impact of high-fat diets on cardiovascular health.

Keywords: Hemodynamics, Exercise Training, Blood Pressure Regulation

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Introduction

Hypertension has been identified by the World Health Organization (WHO) as one of the important risk factors for enhancing morbidity and mortality worldwide and is responsible for 9 million deaths annually worldwide (1). Hypertension is defined as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg (2), with its prevalence dramatically increasing in different countries, affecting 1.4 billion of the world population (3). Hypertension is recognized as the main modifiable risk factor for cardiovascular disease and is associated with adverse cardiovascular outcomes, such as heart failure, stroke, myocardial infarction, and death (4). High sodium and low potassium ingestion, sedentary lifestyle, obesity, alcohol consumption, and an unhealthy diet play an important role in hypertension pathogenesis, and the reduction of these risk factors is recommended for the prevention and control of hypertension disease (5).

Almost one-third of the world population is overweight or obese, which, in turn, is a significant risk factor for different conditions such as hypertension, non-alcoholic fatty liver disease (NAFLD), cardiovascular diseases, metabolic syndrome, certain types of cancer, hypercholesterolemia, musculoskeletal disorders, and type 2 diabetes (6). Excess body weight, especially enhancing visceral fat, is the main risk factor for hypertension, accounting for 65% to 75% of the risk of essential hypertension in humans, and an increase in body mass index (BMI) causes an increase in the risk of hypertension (7). On the other hand, animal studies have suggested that hypertension results from obesity induced by a high-fat diet (8), emphasizing the pathological effects of obesity on blood pressure in animal samples.

Despite the role of obesity and a high-fat diet in promoting blood pressure, lifestyle intervention, including weight loss, should be considered the first step in hypertension management, especially in overweight and obese individuals. Weight loss induced by dietary intervention alone or with exercise training, drugs, or bariatric surgery can lower blood pressure in hypertensive patients in a dose-dependent manner (9). Therefore, nonpharmacological interventions such as exercise training have attracted a lot of attention for the treatment of hypertension (10, 11). Conducted research indicates that exercise training decreases blood pressure in approximately 75% of hypertension subjects, with systolic and diastolic BP reductions averaging approximately 11- and 8-mm Hg, respectively. Moreover, the decrease in blood pressure with exercise training may be more pronounced in women than men, and exercise training can be associated with further benefits in middle-aged people with hypertension compared to young or older people (12). However, identifying the mechanisms of blood pressure reduction with exercise training in hypertensive patients needs further research. Due to the high-fat diet's role in inducing hypertension in rodents, cardiac parameters in high-fat-fed rats were recorded in this study after a six-week endurance training program.

Materials and methods

Animal Allocation

In this experimental study, 21 male Wistar rats weighing 200-250 g were procured from Kerman Medical University. All animals were housed in the Laboratory Animal Care Center, with four rats in each separate cage, maintained at an ambient temperature of 23 °C, humidity between 45 to 60%, and under a 12:12 h light–dark cycle.

The animals were acclimated to the new environmental conditions for one week. Subsequently, the rats were assigned to three equal groups: normal diet (C), high-fat diet group (HF), and high-fat diet + endurance training group (HF+T). Fourteen rats were initially fed a high-fat diet (60% calories from fat) for 12 weeks and were then randomly divided into the HF and HF+T groups. Meanwhile, the seven rats in the normal diet group were fed a standard diet for the entire 12-week period.

In the next phase, a six-week intervention (exercise training or a sedentary lifestyle) was implemented, and animals continued their previous diet (normal diet or high-fat diet) during this period. Throughout the intervention, all animals had unrestricted access to rat-specific water and food (high-fat diet for HF and HF+T groups, and normal diet for the C group).

Exercise Training Protocol

The exercise training program in the present study was of the endurance type and conducted on a rodent-specific treadmill with a zero-degree slope. The regimen involved sessions held 5 days per week over a six-week period, with each session lasting 70 minutes. The treadmill speed initiated at 15-18 meters per minute (m.min-1) in the first week and progressively increased throughout the training program, reaching 26 m.min-1 in the final week.

Each training session comprised a 10-minute warm-up phase at 10-12 m.min-1, followed by a 50-minute main part of the endurance training session, ranging from 15-26 m.min-1, and concluding with a 10-minute cooldown at 10 m.min-1 (13). The properties of the endurance training protocol over the six weeks are detailed in Table 1.

Table 1. Endurance Training Program for Rats during Weeks 1-6.

	10 minutes of warming up (meters per minute)	50 minutes main part of training (meters per minute)	10 minutes of cooling down (meters per minute)
Week 1	10	15-18	**10**
Week 2	10	18-22	**10**
Week 3	12	23-25	**10**
Week 4	12	26	**10**
Week 5	12	26	**10**
Week 6	12	26	**10**

High Fat Diet

The normal diet group was provided with a pelletized diet (Laboratory Rodent Base Food) purchased from the Laboratory Animal Care. In contrast, the high-fat diet used in this study comprised animal pelletized rodent diet consisting of 60 percent fat, sourced from the Royan Research Institute. The high-fat diet was consumed by the HF and HFE groups for 12 weeks before the initiation of endurance training and continued for six weeks during the exercise training program. Throughout the study duration, all research groups had ad libitum access to either the normal diet or the high-fat diet, ensuring unrestricted availability of food and water.

Recording of Hemodynamic Factors

Animals were anesthetized with sodium thiopental (50 mg/kg). If necessary, complementary anesthesia by gas method, involving a mixture of 1% halothane, 30% oxygen, and 69% $N2O$ through the endotracheal cannula, was administered during surgery. A polyethylene catheter filled with heparin serum (70.00) was then carefully directed to the left ventricle through the right carotid artery. Left ventricular systolic pressure and diastolic pressure indices were recorded using a Power Lab physiography system. Following the placement of the cannulas, a ten-minute waiting period was observed to allow the pressures to stabilize, during which hemodynamic indices were continuously recorded.

Statistical Analysis

The data from the present study were analyzed using SPSS software version 24. To evaluate the normality of data distribution, the Shapiro-Wilk test was employed, indicating a normal distribution of the data. Between-group analyses were conducted using one-way ANOVA, complemented by the Tukey post hoc test ($P < 0.05$).

Results

Cardiac parameters, encompassing heart rate, systolic, and diastolic blood pressure, were recorded following 12 weeks of a high-fat diet and a subsequent six-week endurance training program, either with a high-fat or normal diet. Findings from the one-way ANOVA test revealed no significant difference between groups for heart rate ($p=0.143$). Consequently, it can be inferred that neither exercise training nor a high-fat diet significantly affects heart rate. The graphical representation of the rat's heart in the different groups is illustrated in Figure 1.

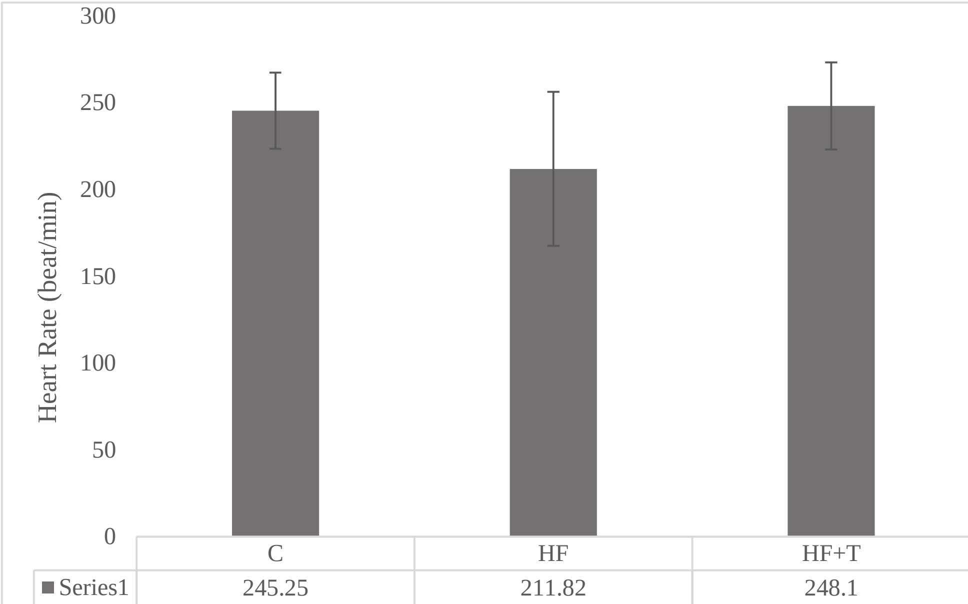

Figure 1. Heart Rate in Various Groups (Mean±SD). **C**: Control, **HF**: High Fat Diet, **HF+T**: High-Fat Diet + Endurance Training Groups

According to the results of the one-way ANOVA test, a significant difference between groups for systolic blood pressure (SBP) was observed (p=0.003). The Tukey post hoc test indicated that SBP in the HF+T group, when compared to the C (p=0.001) and HF (p=0.045) groups, and in the HF, group compared to the C group (p=0.044), was significantly higher. Figure 2 presents SBP reported as mean ± standard deviation for the various research groups.

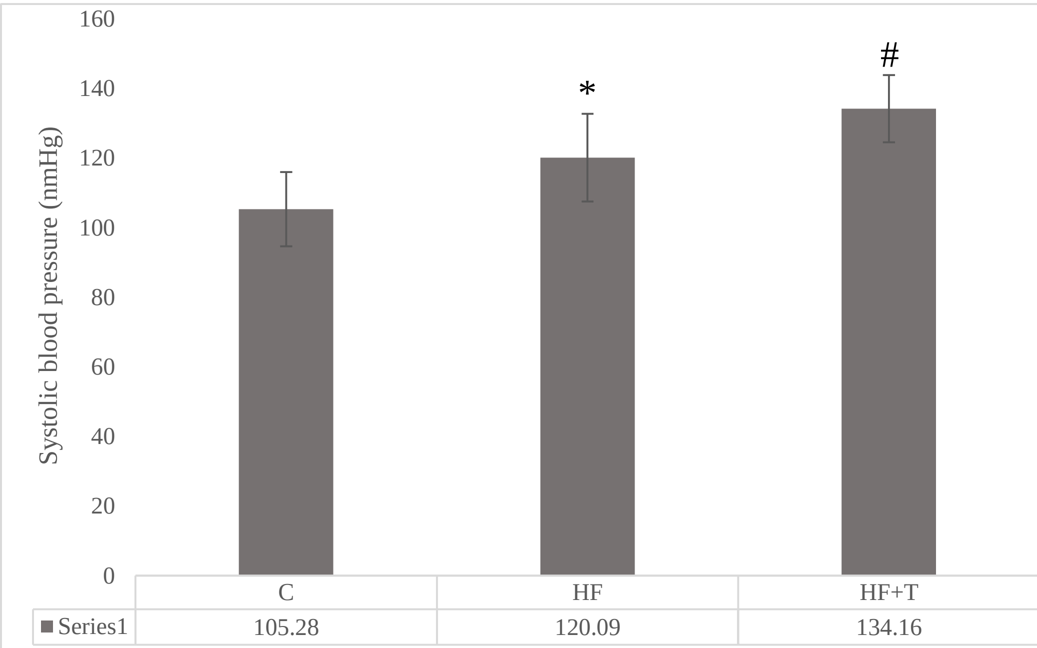

Figure 2. Systolic Blood Pressure in Various Groups (Mean±SD). **C**: Control, **HF**: High Fat Diet, **HF+T**: High-Fat Diet + Endurance Training Groups. * Significant difference compared to the C group, # Significant difference compared to the HF group.

Based on the results of the one-way ANOVA test, another notable finding in the present study was the statistically significant difference between groups for diastolic blood pressure (DBP) (p=0.019). The Tukey post hoc test results indicated that DBP was significantly higher in the HF (p=0.021) and HF+T (p=0.009) groups compared to the C group. However, no significant difference was observed between the HF+T and HF groups (p=0.647). The mean ± standard deviation of DBP for the C, HF, and HF+T groups is reported in Figure 3.

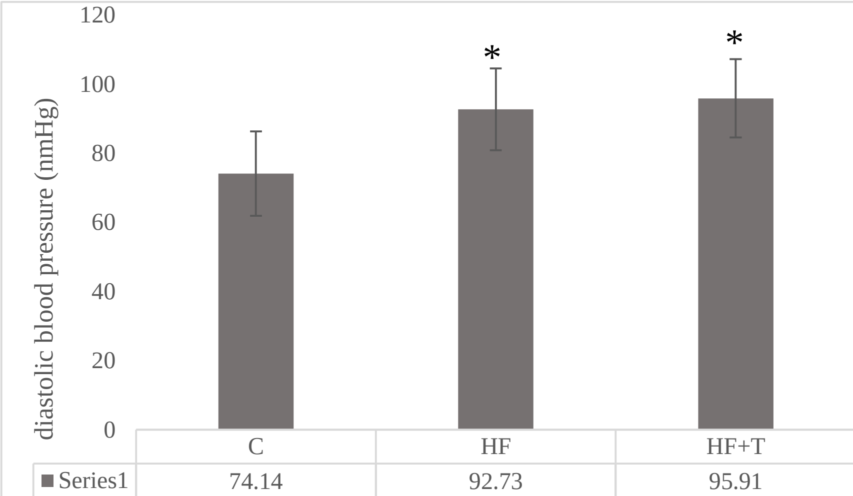

Figure 3. Diastolic Blood Pressure in Various Groups (Mean±SD). **C**: Control, **HF**: High Fat Diet, **HF+T**: High-Fat Diet + Endurance Training Groups.*Significant difference compared to the C group.

Discussion

The present study aimed to investigate the effect of six weeks of endurance training on some hemodynamic factors in high-fat diet-fed male rats. The main findings of this research indicate that systolic blood pressure (SBP) and diastolic blood pressure (DBP) significantly increased after receiving the high-fat diet. Moreover, the enhancement of SBP after endurance training with a high-fat diet was statistically significant compared to high-fat diet ingestion alone. However, neither the high-fat diet alone nor combined with the endurance training program had an impact on the heart rate in the rats.

It has been previously reported that high-fat diet feeding in rats induces cardiovascular remodeling, especially hypertension, hypertrophy, ventricular fibrosis, and endothelial dysfunction. Additionally, metabolic syndrome and its related disorders are known as other health consequences of receiving a high-fat diet (14). Some researchers found that a rat model of diet-induced obesity with even 32% kcal as fat leads to hypertension (15), emphasizing the importance of a high-fat diet in enhancing blood pressure. In line with these reported findings, we confirmed a significant increase in SBP and DBP after a 60% high-fat diet.

According to previous research findings, it is hypothesized that high-fat diet-induced hypertension involves increases in vascular smooth muscle cells (VSMCs) membrane levels of long-chain fatty acids (FAs), contributing to increased membrane Ca^{2+} influx through the augmentation of L-type Ca^{2+} channel current (25).

Furthermore, some researchers have noted that obesity-induced hypertension mechanisms are complex and multifaceted, possibly related to renin-angiotensin-aldosterone system/sympathetic nervous system overactivation, overstimulation of adipokines, insulin resistance, immune dysfunction, and structural/functional changes in renal, cardiac, and adipocyte tissues. Therefore, weight loss is considered an effective strategy for improving obesity-related hypertension (16). Supporting the role of weight loss in hypertension treatment, there is sufficient evidence to endorse the role of aerobic and resistance training (as effective anti-obesity interventions) in the management of hypertension, contributing to the lowering of both systolic and diastolic blood pressures (17).

In contrast to our findings, Batista et al (2023) indicated a significant decrease in SBP after eight weeks of high-intensity interval training (HIIT) in spontaneously hypertensive rats. The anti-hypertensive effect of HIIT was associated with increased antioxidant capacity and attenuation of inflammatory mediators (IL-6, TNF-α) (18). The contradictory findings compared to our research may be partly related to the different types of exerted training programs and the shorter training period (six compared to 8 weeks) in the present study.

Some researchers attribute the anti-hypertensive effect of endurance training to the reduction of systemic vascular resistance in patients with hypertension or prehypertension (19). Mechanisms such as a decrease in body weight and fat mass, down-regulation of catecholamines, improved insulin sensitivity, and alterations in vasodilators and vasoconstrictors have been suggested to explain the antihypertensive effects of exercise training (20).

Despite the approved antihypertensive effect of exercise training, the findings of the present study suggest that endurance training cannot modulate high-fat diet-induced hypertension. Surprisingly, an elevation of SBP in the trained group compared to the high-fat diet group was observed. Consistent with our research, Moraska et al (2000) found that exercise training doesn't solely have positive effects for rodents, and both positive and negative physiological adaptations were observed in rats after treadmill running for eight weeks (21). In another study, Church et al (2007) confirmed our findings and observed no significant changes in systolic or diastolic blood pressure after 6 months of exercise training with 50 percent of VO2peak in sedentary, overweight, or obese postmenopausal women with elevated blood pressure (22).

Researchers have suggested that exercise training may not improve blood pressure for several reasons: 1) the intensity of the training program was low, and training at a higher intensity may have elicited a greater blood pressure response, 2) the conducted training program did not result in changes in participants' body weight, which might have blunted the benefits to blood pressure (22). Despite similar findings, the participants in the present study were rats, and the duration of the conducted training program was too short compared to the research by Church et al (2007).

Collectively, it has been reported that the effects of exercise training on blood pressure may vary depending on exercise modalities (e.g., endurance or resistance) and dose parameters, specifically program length, session duration, frequency, and workload or intensity (23). Therefore, the optimal exercise training prescription for improving blood pressure remains unclear. Although acute exercise can cause a significant increase in systolic blood pressure (24), there is limited research on chronic exercise training leading to an increase in blood pressure. Given that a high-fat diet, typically rich in saturated fatty acids and cholesterol, is associated with increased cardiovascular risk, in part due to an abnormal increase in plasma cholesterol and arterial wall thickness (25), an increase in blood pressure was expected in the animals that received a high-fat diet in this research. However, the observed endurance training program did not produce stimulation to lower blood pressure or attenuate the high-fat diet-induced hypertension. Therefore, identifying the mechanisms behind the inability of exercise training to reduce blood pressure and even increase blood pressure in hypertensive samples requires further investigation.

Conclusion

In summary, this study underscores the significant impact of a high-fat diet on elevating systolic and diastolic blood pressure in male rats, with an unexpected exacerbation of hypertension observed when combined with a six-week endurance training program. Contrary to prior research reporting antihypertensive effects of exercise, this study suggests that the specific endurance training regimen employed did not mitigate high-fat diet-induced hypertension and, surprisingly, led to an increase in systolic blood pressure. The complex interplay between diet, exercise, and blood pressure regulation highlights the need for further investigations into the underlying mechanisms and optimal exercise prescriptions for effective cardiovascular risk management in the context of high-fat diet-induced hypertension.

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Conflict of interest

The authors declare that no conflict of interest exists.

Authors’ contributions

This study's design and initial research studies were conducted by N. A and F. GH, the training protocol, monitoring, and laboratory assessment were performed by H. N, N. A, and H. AN. Additionally, F. GH analyzed data and prepared the article draft. All authors were involved in data collection, and the final version of the article was edited and confirmed by all authors.

References

1. Kitt J, Fox R, Tucker KL, McManus RJ. New approaches in hypertension management: a review of current and developing technologies and their potential impact on hypertension care. Curr Hypertens Rep. 2019; 21(6):1-8. doi: 10.1007/s11906-019-0949-4.
2. DeGuire J, Clarke J, Rouleau K, Roy J, Bushnik T. Blood pressure and hypertension. Health Rep. 2019; 30(2):14-21. doi: 10.25318/82-003-x201900200002.
3. Santo Cestário EDE, Santim AA, Alves BB, Alcarde BP, Rodrigues BS, de Souza Nascimento C, et al. Prevalence, knowledge and treatment of systemic arterial hypertension in a campaign day. EJMED. 2022; 4(1):14-20. doi: 10.24018/ejmed.2022.4.1.1126
4. Oliveros E, Patel H, Kyung S, Fugar S, Goldberg A, Madan N, Williams KA. Hypertension in older adults: Assessment, management, and challenges. Clin cardiol. 2020; 43(2):99-107. doi: doi: 10.1002/clc.23303.
5. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol. 2020; 16(4):223-37. doi: 10.1038/s41581-019-0244-2.
6. Mohajan D, Mohajan HK. Obesity and Its Related Diseases: A New Escalating Alarming in Global Health. Int j innov res med sci. 2023; 2(3):12-23. doi: 10.56397/JIMR/2023.03.04.
7. Tang N, Ma J, Tao R, Chen Z, Yang Y, He Q, et al. The effects of the interaction between BMI and dyslipidemia on hypertension in adults. Sci Rep. 2022; 12(1):927. doi: 10.1038/s41598-022-04968-8.
8. Chaar LJ, Coelho A, Silva NM, Festuccia WL, Antunes VR. High-fat diet-induced hypertension and autonomic imbalance are associated with an upregulation of CART in the dorsomedial hypothalamus of mice. Physiol Rep. 2016; 4(11): e12811. doi: 10.14814/phy2.12811.
9. Fantin F, Giani A, Zoico E, Rossi AP, Mazzali G, Zamboni M. Weight loss and hypertension in obese subjects. Nutrients. 2019; 11(7):1667. doi: 10.3390/nu11071667.
10. Tsai JC, Yang HY, Wang WH, Hsieh MH, Chen PT, Kao CC, et al. The beneficial effect of regular endurance exercise training on blood pressure and quality of life in patients with hypertension. Clin Exp Hypertens. 2004; 26(3):255-65. doi: 10.1081/ceh-120030234.
11. Alpsoy Ş. Exercise and hypertension. Adv Exp Med Biol. 2020; 1228: 153-67. doi: 10.1007/978-981-15-1792-1_10.
12. Hagberg JM, Park J-J, Brown MD. The role of exercise training in the treatment of hypertension: an update. Sports medicine. 2000; 3(3):193-206. doi: 10.2165/00007256-200030030-00004.
13. de Bem GF, Costa CA, Santos IB, Cristino Cordeiro VdS, de Carvalho LCRM, de Souza MAV, et al. Antidiabetic effect of Euterpe oleracea Mart.(açaí) extract and exercise training on high-fat diet and streptozotocin-induced diabetic rats: A positive interaction. PLoS One. 2018; 13(6): e0199207. doi: 10.1371/journal.pone.0199207.
14. Panchal SK, Poudyal H, Iyer A, Nazer R, Alam A, Diwan V, et al. High-carbohydrate, high-fat diet–induced metabolic syndrome and cardiovascular remodeling in rats. J Cardiovasc Pharmacol. 2011; 57(5):611-24. doi: 10.1097/FJC.0b013e31821b1379.
15. Dobrian AD, Davies MJ, Prewitt RL, Lauterio TJ. Development of hypertension in a rat model of diet-induced obesity. Hypertension. 2000; 35(4):1009-15. doi: 10.1161/01.hyp.35.4.1009.
16. Shams E, Kamalumpundi V, Peterson J, Gismondi RA, Oigman W, de Gusmão Correia ML. Highlights of mechanisms and treatment of obesity-related hypertension. J Hum Hypertens. 2022; 36(9):785-93. doi: 10.1038/s41371-021-00644-y.
17. Ghadieh AS, Saab B. Evidence for exercise training in the management of hypertension in adults. Can Fam Physician. 2015; 61(3):233-9.
18. Batista VRG, Correia RR, Fernandes VS, Veras ASC, Tavares MEA, Chaves-Neto AH, et al. High-Intensity Interval Training Minimizes the Deleterious Effects of Arterial Hypertension on the Urinary Bladder of Spontaneously Hypertensive Rats. Oxid Med Cell Longev. 2023; 9979397. doi: 10.1155/2023/9979397.
19. Cornelissen VA, Fagard RH. Effects of endurance training on blood pressure, blood pressure–regulating mechanisms, and cardiovascular risk factors. Hypertension. 2005; 46(4):667-75. doi: 10.1161/01.HYP.0000184225.05629.51.
20. Pescatello LS, Franklin BA, Fagard R, Farquhar WB, Kelley GA, Ray CA. Exercise and hypertension. Med Sci Sports Exerc. 2004; 36(3):533-53. doi: 10.1249/01.mss.0000115224.88514.3a.
21. Moraska A, Deak T, Spencer RL, Roth D, Fleshner M. Treadmill running produces both positive and negative physiological

adaptations in Sprague-Dawley rats. Am J Physiol Regul Integr Comp Physiol. 2000; 279(4): 1321-R9. doi: 10.1152/ajpregu.2000.279.4. R1321.
22. Church TS, Earnest CP, Skinner JS, Blair SN. Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: a randomized controlled trial. JAMA. 2007; 297(19):2081-91. doi: 10.1001/jama.297.19.2081.
23. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. J Am Heart Assoc. 2013; 2(1): e004473. doi: 10.1161/JAHA.112.004473.
24. Gupta MP, Polena S, Coplan N, Panagopoulos G, Dhingra C, Myers J, Froelicher V. Prognostic significance of systolic blood pressure increases in men during exercise stress testing. Am J Cardiol. 2007; 100(11):1609-13. doi: 10.1016/j.amjcard.2007.06.070.
25. Stephanie D, Carole R, Ségolène G, Jean-Claude G, Catherine V, Patrick D, et al. Impact of high-fat diet on antioxidant status, vascular wall thickening and cardiac function in adult female LDLR–/–mice. World Journal of Cardiovascular Diseases. 2012; 2(3)184-192. doi: 10.4236/wjcd.2012.23031.