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The effects of physical training on cardiovascular parameters, lipid disorders and endothelial function

Uticaj fizičkog treninga na kardiovaskularne parametre, lipidne poremećaje i endotelnu funkciju

Goran Ranković*, Nataša Djindjić*, Gorana Ranković-Nedin*, Saša Marković*, Dragan Nejić†, Branislava Miličić‡, Boris Djindjić*

***Faculty of Medicine, †Faculty of Sport and Physical Education, University of Niš, Niš, Serbia; ‡Clinical Center Maribor, Maribor, Slovenia**

Abstract

Bacground/Aim. Regular physical activity is widely accepted as factor that reduces all-cause mortality and improves a number of health outcomes. The aim of this study was to investigate the effects of aerobic exercise training on cardiovascular parameters, lipid profile and endothelial function in patients with stable coronary artery disease (CAD). **Methods.** The study included seventy patients with stable CAD. All the patients were divided into two groups: the group I – 33 patients with CAD and with regular aerobic physical training during cardiovascular rehabilitation program phase II for 3 weeks in our rehabilitation center and 3 weeks after that in their home setting, and the group II (control) – 37 patients with CAD and sedentary lifestyle. Exercise training consisted of continual aerobic exercise for 45 minutes on a treadmill, room bicycle or walking, three times a week. We determined lipid and cardiovascular parameters and nitric oxide (NO) concentration at the beginning and after a six-week of training. **Results.** There were no significant differences in body weight, waist circumference and waist/hip ratio at the start and at the end of physical training program. Physical training significantly reduced body mass index after six weeks compared to the initial and control values. Physical training significantly reduced systolic and diastolic blood pressure and heart rate after a six-week training period ($p < 0.05$). Heart rate was significantly lower after a training period as compared to the control ($p < 0.05$). A significant reduction of triglyceride and increased high density lipoprotein cholesterol (HDL-C) concentration after cardiovascular rehabilitation were registered ($p < 0.05$). The concentration of triglycerides was significantly lower while NO and HDL-C were higher after six weeks in the exercise training group ($p < 0.05$). **Conclusion.** Dynamic training can improve blood pressure in patients with moderate to severe hypertension and reduce the need for medication. Exercise programs induced favorable adaptations on lipoproteins profile, cardiovascular parameters and endothelial function which are clinically desirable in primary and secondary prevention of CAD.

Key words:
exercise; cardiovascular system; coronary artery disease; blood pressure; risk assessment; obesity; body mass index.

Apstrakt

Uvod/Cilj. Redovna fizička aktivnost je dobro poznati i prihvaćeni faktor koji snižava ukupan mortalitet i poboljšava ishod mnogobrojnih oboljenja. Cilj rada bio je da se ispita efekat umerenog aerobnog fizičkog treninga na kardiovaskularne pokazatelje, lipidni status i endotelnu funkciju kod bolesnika sa stabilnom koronarnom bolešću (SKBS). **Metode.** Istraživanje je obuhvatilo 70 bolesnika od koronarne bolesti podeljenih u dve grupe [33 bolesnika sa SKBS i redovnim aerobnim fizičkim treningom (tri puta nedeljno po 45 minuta hodanja na traci, vožnje bicikla ili hodanja) tokom šest nedelja i kontrola – 37 bolesnika sa SKBS koji u poslednjih 6 meseci, osim osnovnih kućnih fizičkih aktivnosti, nisu upražnjavali fizički trening)]. Kardiovaskularni, lipidni parametri i koncentracija azot-oksida (NO) određivani su na početku i na kraju ispitivanog perioda i upoređivani između grupa. **Rezultati.** Efekat fizičkog treninga nije se odrazio na promenu telesne mase, obima struka i odnosa struk/kuk. Fizički trening značajno je redukovao indeks telesne mase u odnosu na početne vrednosti i kontrolu ($p < 0,05$). U grupi bolesnika sa fizičkim treningom došlo je do značajnog pada sistolnog i dijastolnog krvnog pritiska i srčane frekvencije ($p < 0,05$) nakon programa rehabilitacije sprovedenog fizičkom aktivnošću. Srčana frekvencija u grupi sa fizičkim treningom bila je značajno manja nakon spro-

Correspondence to: Goran Ranović, Institute of Physiology, Faculty of Medicine University of Niš, Bul. Dr Zorana Djindjica 81, 18 000 Niš, Serbia. E-mail: boris_dj@medfak.ni.ac.rs; drg.rankovic@gmail.com

vedenog programa ($p < 0,05$) nego u kontrolnoj grupi. Efekat šestonedeljnog programa kardiovaskularne rehabilitacije na lipidne parametre ogledao se u značajnoj redukciji triglicerida i u porastu NO i lipoproteina velike gustine u grupi sa fizičkim treningom u odnosu na početne vrednosti i vrednosti u kontroloj grupi ($p < 0,05$). **Zaključak.** Fizička aktivnost izaziva povoljne promene kardiovaskualrnih i lipidnih pokazatelja i popravlja parametare endotelne funkcije u sekundarnoj prevenciji koronarne bolesti.

Ključne reči:
vežbanje; kardiovaskularni sistem; koronarna bolest; krvni pritisak; rizik, procena; gojaznost; indeks telesne mase.

Introduction

Regular physical activity and good physical fitness are widely accepted as factors that reduce all-cause mortality and improve a number of health outcomes [1]. Exercise training, major component of cardiac rehabilitation, reduces risk factors, improves functional capacity and prognosis, and enhances psychosocial well-being and quality of life in patients suffering from coronary artery disease (CAD) [2]. It has been shown that low maximal aerobic capacity is closely related to an increase of untoward cardiac events [3]. Therefore, physical training has been proposed to reduce these events by improving aerobic capacity. Nevertheless, a paradox seems to arise when considering that aerobic exercise is closely related to higher oxygen consumption and, thus, more pronounced oxidative stress which can be defined as an increase in the intracellular steady state concentration of oxidants over physiological values [4].

In the groups of well-trained persons, the prooxidant state was counteracted by an increase in hydrosoluble, liposoluble and enzymatic antioxidants. The other observed change was the increase in high density lipoproteins (HDL) capacity to inhibit low density hipoproteins (LDL) oxidation. These change were attributed to an adaptative response, to the deleterious effect associated to aerobic physical activity [5].

However, the association of training response and cardiovascular autonomic function is largely unknown. Laitinen et al. [6] have shown that blood pressure (BP) variability (BPV) represents predominantly sympathetic modulation of cardiovascular regulation. In addition, they found that age, gender, body mass index (BMI) and BP are significant independent determinants of BPV. BPV and heart rate variability are shown to be an independent predictors of cardiovascular mortality and indicators of autonomic cardiovascular function [6].

In assessing exercise, both the frequency and the intensity of exercise are important. Exercise training is generally categorized as being of: low intensity (less than 45% of maximal oxygen uptake), moderate intensity (45%–60% of maximal oxygen uptake), vigorous intensity (61%–75% of maximal oxygen uptake) and strenuous intensity (greater than 75% of maximal oxygen uptake). Moderate-intensity exercise, for example, corresponds to an exercise that elicits 60%–70% of maximal heart rate (about 110 to 125 beats/min) [7].

With the growing knowledge of the endothelial function importance, the endothelium has become a major target for therapeutic interventions. Apart from pharmacological interventions with ACE inhibitors and statins, exercise training has evolved as an accepted therapy to improve endothelial function. The results show that only regular moderate physical activity promotes an antioxidant state and preserves endothelial function. Thus, exercise may have a beneficial effect on the development of cardiovascular disease through preserving endothelial function [8].

Impaired endothelial function is detectable in patients with diseases associated with vascular complications. An important functional consequence of endothelial dysfunction is the inability to release nitric oxide (NO), the vasodilator of the underlying vascular smooth muscle cells [9].

The aim of this study was to investigate the effects of aerobic exercise training on cardiovascular parameters, lipid profile and endothelial function in patients with stable CAD participating in a cardiovascular rehabilitation exercise program.

Methods

The study included 70 patients with stable coronary heart disease who had been accepted into the outpatient phase II cardiovascular rehabilitation program at the Institute for Treatment and Rehabilitation of Cardiovascular Diseases Niška Banja, Niš, Serbia. All the patients were divided into two groups: the group I – 33 patients with stable coronary heart disease who had regular aerobic physical training during 3 weeks of cardiovascular rehabilitation program phase II in cardiovascular rehabilitation center and 3 weeks after that at their homes; the group II (control) – 37 patients with stable coronary heart disease who practiced only usual housework without recommended aerobic physical training 6 weeks before examination.

The patients participated in the study if they had a history of any of the following: myocardial infarction (MI), coronary revascularization, angiographic evidence of more than 50% stenosis in one or more coronary vessels. The subjects were excluded from the study if they had uncontrolled arrhythmias, hypertension (systolic BP >180 mmHg or diastolic BP >100 mmHg), unstable angina pectoris, poorly controlled congestive heart failure, abnormal hemodynamic response or ischemic electrocardiogram changes during stage 1 of the exercise tolerance test (Bruce protocol), or uncontrolled metabolic disease (e.g. uncontrolled diabetes or thyroid disease).

All cardiac-related medication doses were kept constant throughout the study. All the subjects used beta-blockers, ACE inhibitors and statins in their therapy. The patients were required to refrain from any change in their habitual diet.

Exercise training protocol

The patients underwent 6 weeks of aerobic exercise training consisting of 45 min sessions of continuous aerobic

exercise on a treadmill, ergo bicycle or walking. The intensity was maintained at 70%–80% of the individual maximum heart rate obtained in the pre-study graded exercise test. All the patients trained 3 times a week for 6 weeks.

Biochemical examinations were done at the beginning and after 6 weeks of physical exercise training and compared with the control group. In the first group blood samples were collected at least 24 h after the last bout of exercise in order to avoid immediate effects of exercise. The lipids status comprised determination of total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides.

Cardiovascular parameters comprised measuring of systolic and diastolic arterial tension. Upon arrival, the subjects remained in sitting position for 5 min before the start of measuring. BP was measured in the left upper arm by auscultation (sphygmomanometer and stethoscope, Becton Dickinson, USA) three times accordingly to the American Heart Association procedure and the average values were adopted [6].

Besides arterial tension, measurements simultaneously determined heart rate.

Anthropometry

Fasting body weight, body height, waist circumference and hip circumference were measured. BMI was calculated as kg/m^2. We also calculated waist/hip ratio.

Endothelial function

NO release was determined spectrophotometrically by measuring the accumulation of its stable degradation products nitrite and nitrate. Total nitrite was then determined spectrophotometrically by using the Navarro-Gonzalvez et al, reaction based on Griess reaction [10]. A total nitrate and nitrite concentration was given in nmol/mg protein.

The data were analyzed by standard descriptive methods (mean, standard deviation and percent frequency). The results were analyzed by using the Student's *t*-test, χ^2 test and Fisher test depending on specimens and the type of data. Statistical analyzes were done by the software package SPSS 11.0.

Results

The patients in both groups had similar age, gender distribution and risk factors profile (Table 1).

There were no significant changes in body weight, waist circumference and waist/hip ratio before and after the exercise training program as well as in their values between the groups. Physical training significantly reduced BMI after 6 weeks compared to the initial and control values ($p < 0.05$) (Table 2).

Table 1

Characteristics of the patients

Parameters	The exercise training group	The control group	*p*
Male/female (n)	14/19	18/19	ns
Age (years)	57.2 ± 5.9	59.3 ± 7.1	ns
MI, n (%)	22 (66)	26 (70)	ns
CAB, n (%)	5 (15)	4 (11)	ns
PTCA, n (%)	6 (19)	7 (19)	ns
Risk factors for CAD, n (%)			
smokers	13 (39.4)	16 (43.2)	ns
hypertension	28 (84.8)	30 (81.1)	ns
dyslipidemia	14 (42.4)	15 (40.5)	ns
diabetes mellitus	11 (33.3)	13 (35.1)	ns
obesity	10 (30.3)	10 (27.0)	ns
family history for CAD	14 (42.4)	15 (40.5)	ns

Data are presented as the mean ± SD or n (%); MI – myocardial infarct; PTCA – percutaneous transluminal coronary angioplasty; CAB – coronary artery bypass; CAD – coronary artery disease; ns – non significant

Table 2

Anthropometric data, cardiovascular lipid parameters and NO concentrations

Parameters	The exercise training group ($\bar{x}$ ± SD)		The control group ($\bar{x}$ ± SD)	
	before	after	before	after
Body weight (kg)	79.1 ± 12.1	74.7 ± 11.3	73.3 ± 10.6	68.9 ± 10.3
Body hight (cm)	163.5 ± 7.1	-	165.9 ± 5.4	-
Body mass index (kg/m^2)	29.7 ± 5.2	28.2 ± 4.4*†	26.3 ± 4.7	24.8 ± 3.2
Waist circumference (cm)	94.9 ± 10.4	93.7 ± 9.6	88.2 ± 7.6	88.8 ± 6.5
WHR	0.88 ± 0.04	0.87 ± 0.04	0.89 ± 0.05	0.88 ± 0.04
Sistolic arterial tension (mmHg)	143.4 ± 5.6	135.7 ± 4.2†	138.8 ± 4.3	134.1 ± 6.2
Diastolic arterial tension (mmHg)	90.2 ± 6.5	82.8 ± 5.1†	87.3 ± 6.3	84.7 ± 7.1
Heart rate (/min)	78.6 ± 11	72.3 ± 5.6*†	76.1 ± 9.2	77.4 ± 6.8
Total cholesterol (mmol/L)	5.4 ± 0.8	5.2 ± 0.7	5.3 ± 0.4	5.1 ± 0.9
LDL-C (mmol/L)	3.3 ± 0.6	3.0 ± 0.28	3.6 ± 0.3	3.4 ± 0.6
HDL-C (mmol/L)	0.98 ± 0.2	1.21 ± 0.2*†	1.0 ± 0.3	0.99 ± 0.2
Triglicerides (mmol/L)	1.78 ± 0.5	1.58 ± 0.3*†	1.7 ± 0.2	1.8 ± 0.4
NO (nmoL/mg prot.)	64.95 ± 23.15	72.43 ± 28.65*†	68.5 ± 17.9	65.7 ± 19.6

***$p < 0.05$ *vs* control; †$p < 0.05$ *vs* initial values; WHR – waist/hip ratio; LDL-C – low density lipoprotein cholesterol; HDL-C – high density lipoprotein cholesterol; NO – nitric oxide**

Exercise training induced significant reduction in systolic and diastolic BP and heart rate after 6 weeks of cardiovascular rehabilitation ($p < 0.05$). Similar trends were not registered in the control group. In the patients with moderate aerobic physical training significantly lower heart rate was registered after a 6-week follow-up compared to the group with sedentary lifestyle ($p < 0.05$) (Table 2).

The effects of a 6-week cardiovascular rehabilitation on lipid parameters were visible in a significant reduction in triglycerides and significant increase in HDL cholesterol concentration ($p < 0.05$). The concentrations of triglycerides were significantly lower and HDL cholesterol significantly higher after a 6-week follow-up in the exercise training group as compared to sedentary patients ($p < 0.05$) (Table 2).

Regular moderate exercise training within 6 weeks induced favorable increase in NO compared with its initial level and the level in the sedentary control group (Table 2).

Discussion

Anthropometric parameters did not show any significant difference in the groups of patients with similar age and gender distribution. Meanwhile, comparison of the initial values with those at the end of a 6-week follow-up showed a significant reduction in obesity without changes in the degree of visceral obesity. Similar findings of anthropometric parameters value after 6 weeks of physical training are presented by other authors [11], showing no important reduction in the degree of visceral obesity measured by waist circumference and waist/hip ratio.

Moderate aerobic physical training reduced systolic and diastolic BP. The BP values were very similar between the examined groups at the start of examination. Only significantly lower heart rate was registered in the group with physical training. BP reduction trend was obvious in both groups but a significant reduction was registered only in the group with physical training.

There is consistent evidence that regular rhythmic physical exercise of the lower extremities decreases both systolic and diastolic BP by 5–7 mmHg independently of weight loss, alcohol intake or salt intake [12]. These results of exercise training did not seem to be affected by the type of aerobic training because several studies that used home training programs found reductions in BP comparable to those in which subjects trained under staff supervision [13].

Thus, it appears that antihypertensive effects of exercise were additive with those of most used antihypertensive medications [14]. It has been shown that chronic NO-deficient hypertension is associated with depletion of antioxidants and oxidative injury of the cardiovascular system. Exercise training normalizes BP by scavenging free radicals/reactive oxygen species (ROS), through up-regulation of cardiac NO and antioxidant systems [15]. It is hypothesized that interaction of exercise training and chronic nitroglycerin treatment would maintain BP through the up-regulation of NO and cardiac antioxidant system in rat [16].

Heart rate was lower in the group with moderate aerobic physical training after 6 weeks compared to starting values and the control group. One similar study conducted by Anton et al. [17] found a reduction of BP and decrease of heart rate in physically-active smokers compared to sedentary ones.

Slight reduction in triglyceride concentration and HDL cholesterol level rising in the group with physical training are in concordance with literature results. Training programs revealed positive adaptations of body composition and lipid profile total cholesterol and triglycerides. Literature data showed decrease in body weight by 1.7%–2.0% after 16 weeks of physical training. Also, exercise groups showed a significantly reduced total cholesterol (-7.0 mg%) and triglycerides (-14.5 mg%) [18]. Similar findings are registred in diabetics with physical acitvity [19].

LDL oxidation is a crucial step in atherosclerosis, process which can be inhibited by HDL by its ROS capable components or associated enzymes like paraoxonase [5].

Exercise training consistently improves NO bioavailability, and the number of endothelial progenitor cells. It also diminishes the level of inflammatory markers, namely proinflammatory cytokines and C-reactive protein [20]. A significantly higher NO concentration in the exercise training group found in this study indicates an improvement in endothelial function. Knowing that exercise and statins therapy reduce inflammatory response and improve other indicators of endothelial function [21] obtained results pushed exercise training programe in front of other therapy modalities in secondary prevention.

Conclusion

Dynamic training can improve BP in patients with moderate to severe hypertension and reduce the need for medication.

Exercise programs induced favorable adaptations to HDL cholesterol, triglycerides, and NO bioavailability.

This study adds an important piece of evidence to the rationale for exercise training in patients with stable CAD: it documents that an optimized medical therapy, along with exercise training as a lifestyle intervention, can be an alternative approach to an interventional strategy in selected motivated patients with stable CAD.

R E F E R E N C E S

1. *Ascensão A, Ferreira R, Magalhães J.* Exercise-induced cardioprotection--biochemical, morphological and functional evidence in whole tissue and isolated mitochondria. Int J Cardiol 2007; 117(1): 16−30.

2. *Leon AS, Franklin BA, Costa F, Balady GJ, Berra KA, Stewart KJ,* et al. Cardiac rehabilitation and secondary prevention of coronary heart disease: an American Heart Association scientific statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention)

and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity), in collaboration with the American association of Cardiovascular and Pulmonary Rehabilitation. Circulation 2005; 111(3): 369−76.

3. *Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE.* Exercise capacity and mortality among men referred for exercise testing. N Engl J Med 2002; 346(11): 793−801.
4. *Banerjee AK, Mandal A, Chanda D, Chakraborti S.* Oxidant, antioxidant and physical exercise. Mol Cell Biochem 2003; 253(1−2): 307−12.
5. *Brites F, Zago V, Verona J, Muzzio ML, Wikinski R, Schreier L.* HDL capacity to inhibit LDL oxidation in well-trained triathletes. Life Sci 2006; 78(26): 3074−81.
6. *Laitinen T, Hartikainen J, Niskanen L, Geelen G, Länsimies E.* Sympathovagal balance is major determinant of short-term blood pressure variability in healthy subjects. Am J Physiol 1999; 276(4 Pt 2): H1245−52.
7. *Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN,* et al. Recommendations for blood pressure measurement in humans and experimental animals: Part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Hypertension 2005; 45(1): 142−61.
8. *Di Francescomarino S, Sciartilli A, Di Valerio V, Di Baldassarre A, Gallina S.* The effect of physical exercise on endothelial function. Sports Med 2009; 39(10): 797−812.
9. *Fuchsjäger-Mayrl G, Pleiner J, Wiesinger G, Sieder EA, Quittan M, Nuhr MJ,* et al. Exercise training improves vascular endothelial function in patients with type 1 diabetes. Diabetes Care 2002; 25(10): 1795−801.
10. *Navarro-Gonzalvez AJ, Garcia-Benayas C, Arenas J.* Semiautomated Measurement of Nitrate in Biological Fluids. Clin Chem 1998; 44(3): 679−81.
11. *Uusitalo A, Laitinen T, Väisänen S, Länsimies E, Rauramaa R.* Physical training and heart rate and blood pressure variability: a 5-yr randomized trial. Am J Physiol Heart Circ Physiol 2004; 286(5): H1821−6.
12. *Whelton SP, Chin A, Xin X, He J.* Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. Ann Intern Med 2002; 136(7): 493−503.
13. *Nemoto K, Genno H, Masuki S, Okazaki K, Nose H.* Effects of high-intensity interval Walking training on physical fitness and blood pressure in middle-aged and older people. Mayo Clin Proc 2007; 82(7): 803−11.
14. *Nelson ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC,* et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. Circulation 2007; 116(9): 1094−105.
15. *Husain K.* Exercise conditioning attenuates the hypertensive effects of nitric oxide synthase inhibitor in rat. Mol Cell Biochem 2002; 231(1−2): 129−37.
16. *Husain K, Hazelrigg SR.* Oxidative injury due to chronic nitric oxide synthase inhibition in rat: effect of regular exercise on the heart. Biochim Biophys Acta 2002; 1587(1): 75−82.
17. *Anton MM, Cortez-Cooper MY, DeVan AE, Neidre DB, Cook JN, Tanaka H.* Cigarette smoking, regular exercise, and peripheral blood flow. Atherosclerosis 2006; 185(1): 201−5.
18. *Volaklis KA, Spassis AT, Tokmakidis SP.* Land versus water exercise in patients with coronary artery disease: effects on body composition, blood lipids, and physical fitness. Am Heart J 2007; 154(3): 560.e1−6.
19. *Đinđić B, Janković R, Savić T, Bojanić V.* Antilipemic therapy and low total cholesterol problems. Acta Medica Medianae 2004; 43(1): 43−7. (Serbian)
20. *Ribeiro F, Alves AJ, Duarte JA, Oliveira J.* Is exercise training an effective therapy targeting endothelial dysfunction and vascular wall inflammation? Int J Cardiol 2010; 141(3): 214−21.
21. *Djindjić B, Ranković G, Zivić M, Savić T, Spasić M, Bubanj M.* Gender difference in hipolipemic and anti-inflammatory effects of statins in diabetics with coronary artery disease. Vojnosanit Pregl 2009; 66(12): 966−72. (Serbian)

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