



Effects of a short-term differently dosed aerobic exercise on maximum aerobic capacity in breast cancer survivors: a pilot study

Uticaj kratkotrajnog aerobnog vežbanja različitog intenziteta na maksimalni aerobni kapacitet preživelih od karcinoma dojke

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Abstract

Background/Aim. Regular physical activity and exercise improves quality of life and possibly reduces risk of disease relapse and prolongs survival in breast cancer survivors. The aim of this study was to evaluate the impact of a 3-week moderate intensity aerobic training, on aerobic capacity (VO_{2max}) in breast cancer survivors. **Methods.** A prospective, randomized clinical study included 18 female breast cancer survivors in stage I-IIIa, in which the primary treatment was accomplished at least 3 months before the study inclusion. In all the patients VO_{2max} was estimated using the Astrand's protocol on a bicycle-ergometer (before and after 3 weeks of training), while subjective assessment of exertion during training were estimated by the Category-Ratio RPE Scale. Each workout lasted 21 minutes: 3 minutes for warm-up and cool-down each and 15 min of full training, 2 times a week. The workload in the group E1 was predefined at the level of 45% to 65% of individual VO_{2max} , and in the group E2 it was based on subjective evaluation of exertion, at the level marked 4–6. Data on the subjective feeling of exertion were collected after each training course in both groups. **Results.** We recorded a statistically significant improvement in VO_{2max} in both groups (E1 – 11.86%; E2 – 17.72%), with no significant differences between the groups. The workload level, determined by the percent of VO_{2max} , was different between the groups E1 and E2 ($50.47 \pm 7.02\%$ vs $55.58 \pm 9.58\%$), as well as subjective perception of exertion (in the groups E1 and E2, 11.6% and 41.6% of training, respectively, was graded in the mark 6). **Conclusion.** In our group of breast cancer survivors, a 3-week moderate intensity aerobic training significantly improved the level of VO_{2max} .

Key words:

breast neoplasms; physical fitness; exercise.

Apstrakt

Uvod/Cilj. Redovna fizička aktivnost može značajno uticati na kontrolu neželjenih efekata terapije kod žena obolelih od karcinoma dojke, na kvalitet života posle završenog lečenja, pa čak i na smanjivanje rizika od ponovne pojave bolesti. Cilj ovog rada bio je da se provere efekti tronedelnog aerobnog treninga, doziranog na dva načina, na maksimalni aerobni kapacitet (VO_{2max}) bolesnica koje su završile lečenje karcinoma dojke. **Metod.** Prospektivno, randomno kliničko istraživanje uključilo je 18 žena u I-IIIa stadijumu karcinoma dojke, čije je lečenje završeno najmanje tri meseca pre uključivanja u studiju. Maksimalni aerobni kapacitet određen je Astrandovim testom na bicikl-ergometru (na početku i posle tri nedelje treninga), a procena stepena uloženog napora kroz modifikovanu skalu subjektivne procene napora (*Category-Ratio RPE Scale*). Svaki trening trajao je 21 minut: po 3 min za zagrevanje i hlađenje i 15 min punog treninga, dva puta nedeljno. Opterećenje u grupi E1 određeno je na nivou 45–65% individualnog VO_{2max} , a u grupi E2 na osnovu subjektivne procene napora, na nivou ocene 4–6. Podaci o subjektivnom osećaju napora prikupljeni su u obe grupe, posle svakog treninga. **Rezultati.** Registrovana je statistički značajna promena VO_{2max} unutar obe grupe (E1 – 11,86%; E2 – 17,72%), bez značajne razlike između grupa. Nivo opterećenja određen preko % VO_{2max} razlikovao se između grupa ($50,47 \pm 7,02\%$ vs $55,58 \pm 9,58\%$), kao i osećaj napora tokom treninga (ocenu 6 dobilo je 11,6% treninga u grupi E1, a 41,6% treninga u grupi E2). **Zaključak.** U našoj grupi ispitanica 3-nedeljni aerobni trening umerenog intenziteta značajno je povećao nivo VO_{2max} , bez obzira na način određivanja opterećenja.

Ključne reči:

dojka, neoplazme; sposobnost, fizička; vežbanje.

Introduction

Breast cancer is the most common female cancer and the second leading cause of death from malignancy in women^{1,2}. The treatment of early breast cancer usually involves a combination of surgery, chemo- and radiotherapy, often with a prolonged hormonal and biological therapy. Besides the problems of acute and chronic adverse effects of treatment, these women also are challenged with other diseases common for their age. Their rehabilitation is a complex process and requires multidisciplinary team cooperation³. Previous studies have shown that physical activity and exercise are associated with a lower sense of fatigue during and after the treatment, improve muscle status, physical strength, aerobic fitness and have a positive effect on confidence and quality of life⁴⁻⁸. In addition, it is possible that regular physical activity can reduce the risk of disease relapse and prolong survival⁹.

The largest number of studies that investigate physical activity of patients with malignant disease are related to the aerobic, cardiovascular training¹⁰. Among all patients with malignant diseases, breast cancer patients are the most common studied¹¹⁻²⁰. However, there are still no standardized protocols with regards neither to the exercise modalities, nor the intensity and frequency of exercise.

The most common aerobic activities investigated are walking, whether home-based²¹ or supervised, in the laboratory, on a treadmill²², or bicycle-ergometer²³. Duration and frequencies of the training also varies (usually 3–5 times a week, 10 to 30 minutes). The intensity was determined in different ways. Some are based on $VO_2\text{max}$ ^{21,23}, some on maximum heart rate (MHR)^{14,15,24} or heart rate reserve (HRR)¹² and some on subjective evaluation of efforts, by using the rate perceived exertion (RPE) scale^{25,26}. Maximum aerobic capacity was measured directly, through a progressive maximal tests²³ or estimated from the results of submaximal tests (Modified Canadian Aerobic Fitness Test²¹, Astrand-Rhimmings protocol²⁵). The karvonen formula was the most commonly used to determine the MHR²⁷. Exercise program in most studies lasts between 5 weeks and 6 months^{28,29}, and they show that a regular physical activity improves aerobic capacity and quality of life (QOL) of these patients and alleviates many side effects of the treatment (nausea, fatigue, depression and anxiety), as well^{10,28}. Burnham and Wilcox³⁰ showed the positive effects of a 10-week of lasting aerobic training on aerobic capacity, body fat percentage and QOL in cancer survivors, regardless of loading during exercise – small (23%–35% HRR) vs moderately high (40%–50% HRR).

However, to our best knowledge there is no study which compares the effects of a controlled aerobic training of relatively short duration and dosed in two ways – objectively (based on measured values of $VO_2\text{max}$) and subjectively (based on subjective feelings of fatigue, estimated through RPE or Category–Ratio RPE Scale).

The aim of this study was to evaluate the impact of a 3-week moderate intensity aerobic training on aerobic capacity in breast cancer survivors, regardless of the method for determining the workload (objectively, based on measured val-

ues of $VO_2\text{max}$, or subjectively, based on the subjective feeling of exertion, measured through the Category-Ratio RPE scale).

Methods

Participants, recruitment strategies, and eligibility

Inclusion criteria were: female breast cancer survivors without disease relapse, diagnosed in stage I-IIIa, in which the primary treatment (radical surgery and/or postoperative radiotherapy and/or adjuvant systemic therapy) was accomplished at least 3 months before the investigation. The recruitment strategy included the treating oncologist who identified potentially eligible patients during a regular clinical control. Exclusion criteria were: disseminated breast cancer, cardiorespiratory disease (uncontrolled hypertension, heart failure, cardiac arrhythmia, chronic obstructive pulmonary disease and pulmonary fibrosis) and age over 65 years.

Patients were informed about the goals and methods of research, and after written consent, they were randomly divided into two experimental groups: the group E1 (10 woman), whose workload level was determined by the examiner based on the measured values of $VO_2\text{max}$ and the group E2 (8 woman), in which the participants self-determined the workload level according to a subjective feeling of the exertion. The Military Medical Academy Belgrade Ethics Committee provided the approval for this study.

Procedures

The program consisted of three weeks of aerobic training on a bicycle-ergometer (ERG Bosh 550), two times a week. Each workout lasted 21 minutes, and the structure of the training was as follows: 3 min of warming-up and cooling-down period each and 15 min training period. All the participants were introduced with the Category-Ratio RPE Scale. The intensity of the workload, expressed in Watts (W), was determined in two ways. In the group E1 it was determined on the basis of the estimated values of $VO_2\text{max}$ as follows: 30%–35% $VO_2\text{max}$ for the period of warming, 45–65% $VO_2\text{max}$ for training period and 40%–45% $VO_2\text{max}$ for the period of cooling. The conversion of the workload was done based on the measured values of $VO_2\text{max}$ and the known energy expenditure of different intensities of the bicycle-ergometer³¹, according to the formula:

$$\text{Workload (W)} = 0.08333 \times VO_2\text{max (mL/min)} - 25.$$

In the group E2, after being informed about the structure of the training and the Category-Ratio RPE scale, the patients themselves determined workload level. The recommended level of exertion was rating between 4 and 6. The participants were asked not to change their habits of regular physical engagement nor the nutrition habits during the research period.

Collecting data and measurement

General information was collected at the beginning of the study using a questionnaire that the patients filled in themselves. Body weight and $VO_2\text{max}$ were determined at

baseline and after a 3-week training period. Subjective assessment of exertion with the Category-Ratio RPE Scale was performed after each training course, in both groups.

Height and weight were measured on the standing balance (TTM Zagreb), and the values of BMI were calculated. Heart rate during testing and training was continuously monitored and recorded using a Polar Cycling Computer S725X Pro Team, while the measurement of arterial blood pressure was done using a manometer with a cuff (Dosh Heidelberg).

For the estimation of VO_2max in all participants, we used the Astrand's protocol on a bicycle-ergometer. It is a progressive, continuous exercise test during which a patient is encumbered to submaximal levels (to reach steady state). Each level of the workload lasted 6 minutes. Levels of workload for women 50W–125W, with the progression of 25 W between the levels. Steady-state reached when the heart rate was between 120 and 170 beats per minute (bpm), and

ences between initial and posttraining values within groups, we used the paired *t*-test for parametric and Fisher's exact test and χ^2 test for nonparametric categories. Significant difference between groups was tested by unpaired *t*-test and χ^2 test. Statistical significance was accepted at the level of $p < 0.05$ ³⁶.

Results

There were no significant differences between the groups according to age and time from the end of breast cancer treatment, but there were differences according to the type of therapy: all the participants in the group E1 were treated with adjuvant chemotherapy (100%) while in the group E2 adjuvant chemotherapy received only 3/8 (37.5%) patients. Basic characteristics of patients prior entering the study are shown in Table 1.

Table 1

Parameter	Patient's groups					
	E1 (n = 10)			E2 (n = 8)		
	$\bar{x}_{av} \pm SD$	median	min–max	$\bar{x}_{av} \pm SD$	median	min–max
Age (year)	51.60 ± 7.47	49	43–63	52.75 ± 7.42	52	42–63
Time after finishing treatment (year)	5.10 ± 4.45	3.5	0.5–12	3.43 ± 2.57	3	1–7
Surgery [n (%)]		10 (100)			8 (100)	
Chemotherapy [n (%)]		10 (100)			3 (37.5)	<i>p</i> = 0.001
Radiotherapy [n (%)]		8 (80)			5 (62.5)	
Hormonal therapy [n (%)]		5 (50)			4 (50)	

the difference between the 5th and 6th minutes no more than 5 bpm. The value of VO_2max was determined by a table data, based on the reached pulse value of a certain load levels and patient's age. The participants were divided according to VO_2max levels using the classification aerobic fitness World Health Organization (low, fair, average, very good, high), that was mathematically modified to improve accuracy³².

For subjective assessment of exertion during training we used the Category-Ratio RPE Scale^{33, 34}. This is a 10-level scale for subjective assessment of exertion, where the grade 0 means "absolutely no exertion" and the grade 10 "maximal exertion that one can still submit a short time". It is shown that the level of grade 4 (moderate) is the level of lactate threshold for most people³⁵. Exercising below this level is not strong enough to increase cardiorespiratory endurance. The recommended level of subjective feeling of effort for our participants was moderate, "somewhat strong" degree (grade 4 to 6).

The primary objective was to investigate the differences in the VO_2max expressed in mL/kg/min after a 3-week aerobic training in the whole group, in the groups E1 and E2 as well as between the groups E1 and E2. A secondary goal was to test changes in VO_2max level categories, and changes in BMI.

The statistical package GraphPad Prism 5th was used for statistical analysis. For parametric categories of the observation we calculated the mean ± SD, median and range, and for nonparametric categories the distributions of frequency were calculated. To test the significance of differ-

ences between the groups in the VO_2max expressed in mL/kg/min before starting the training. According to the WHO classification level of aerobic fitness, 10 woman (55.55%) had fair levels of VO_2max (6/10 in the the group E1 and 4/8 in the group E2), while 8/18 woman (44.45%) had an average level of VO_2max (4 women in each group). The groups did not differ in the size of the workload expressed in Wats (W) but the significant differences were noted with the workload expressed in percent of VO_2max (Table 2). The groups also differed in the subjective perception of exertion by percent of Category-Ratio RPE scale: 76% of training in the group E1 was marked by 4, compared to 27% in the group E2. On the other hand, only 11.6% of training in the group E1 was marked 6 or higher, while this percentage in the group E2 was 41.6% (Figure 1).

After 3 weeks of training, the value of VO_2max significantly increased (14.46%) in both groups (Figure 2). Percentages of increasing in VO_2max for the groups E1 and E2 were 11.86% and 17.72%, respectively. The values of VO_2max between the groups still did not differ significantly (Table 2).

According to WHO categories of aerobic capacity, 3/18 patients remained in the fair category (2/10 in the group E1 and 1/8 in the E2 group), 12/18 were classified as average (8/10 in the E1 and 4/8 in the group E2), and 3/8 patients in the group E2 had entered into the very good category level of VO_2max . Although category changes in each group were not statistically significant, the overall change was statistically significant (Figure 3).

Table 2
Maximum aerobic capacity (VO₂max), loading and BMI in both groups, before and after a 3-week training

Parameters	Patient's groups		p
	E1 (n = 10)	E2 (n = 8)	
	$\bar{x}_{av} \pm SD$	$\bar{x}_{av} \pm SD$	
VO ₂ max (mL/kg/min) before training	20.47 ± 2.28	21.66 ± 4.39	0.002
VO ₂ max (mL/kg/min) after a 3-week training	22.85 ± 2.26	24.90 ± 5.26	
Workload (W)	50.65 ± 9.11	53.05 ± 7.87	
Workload (% VO ₂ max)	50.47 ± 7.02	55.58 ± 9.58	
BMI (kg/m ²) before training	26.73 ± 2.11	26.19 ± 4.87	
BMI (kg/m ²) after a 3-week training	26.77 ± 2.32	26.14 ± 4.72	

BMI – body mass index

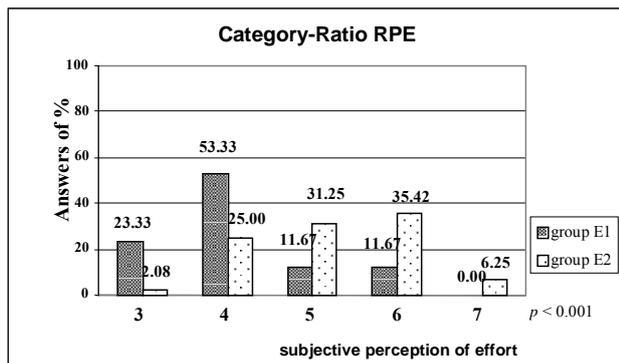


Fig. 1 – Subjective perception of exertion according to the Category-Ratio RPE scale in both groups

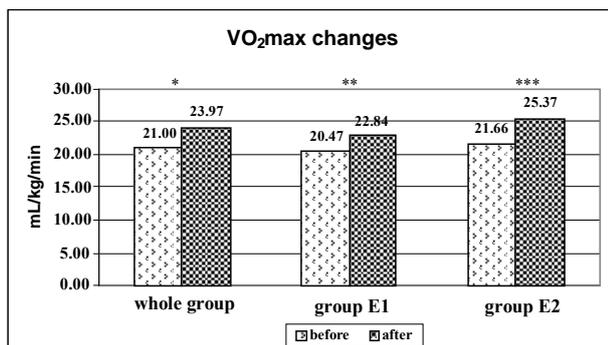


Fig. 2 – Maximum aerobic capacity (VO₂max) changes after a 3-week training
 p* = 0.0001; *p* = 0.0002; ****p* = 0.014

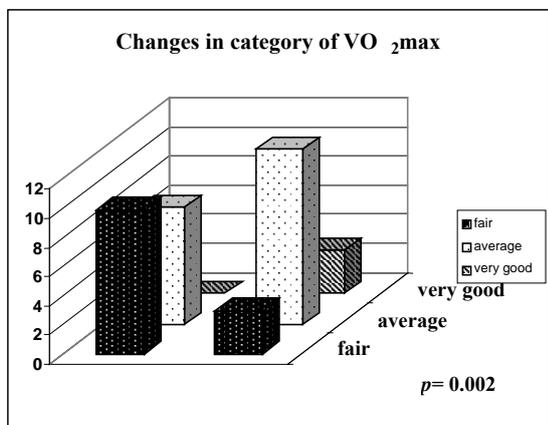


Fig. 3 – Changes in category of maximum aerobic capacity (VO₂max) in the whole group of participants

There were no differences in BMI, both within each group and between the groups, as well (Table 2).

Discussion

Epidemiological studies in the second half of the 20th century confirmed a dose dependent link between physical activity and physical fitness³⁷⁻⁴⁰. The greatest difference in mortality due to cardiovascular disease and some types of cancer recorded between categories of sedentary (little or no physically active persons) and the first following categories of physically active, or when sedentary people become moderately physically active³⁹. To improve overall health status it is enough to reach and maintain the average level of aerobic capacity³². Any physical engagement of the appropriate intensity causes an acute adaptive response (change in arterial pressure, heart rate, stroke volume and cardiac output, blood distribution, ventilation). One of the latest researches suggests that it may also influence the level of anxiety⁴¹. If done regularly, physical training leads to chronic adaptability reactions (central and peripheral). The size of chronic adaptation to regular physical training depends on the frequency, intensity and duration of training, types of activities and previous physical status. Some of cardiorespiratory and metabolic responses to workload develop relatively quickly during exercise (VO₂max), while others require more time (e.g. changes in capillary density)^{42, 43}. Cardiorespiratory intensive training of young healthy subjects (6 days a week, 40 min–60 min a day, the intensity of 70% to 90% VO₂max) during the first 3 weeks significantly improved VO₂max, submaximal frequency of heart rate, ventilation and lactate production⁴³. It is shown that middle-aged and elderly people, obese patients and those with low aerobic capacity, over several months of regular aerobic training may, with the loss of weight, dramatically improve their cardiorespiratory fitness^{42, 43} and reduce the risk of illness even when they practice at the level lower than the American College of Sports Medicine (ACSM) recommended (less than 50% VO₂max)^{40, 44}.

Healthy female breast cancer survivors do not differ much than the average sedentary population⁴⁵, so the mechanisms by which regular physical activity (exercise) improves aerobic capacity are identical. In our country women treated from breast cancer are generally of low physical activity and often unprepared to cope with any serious physical chal-

lenge. Although all our participants indicated that they occasionally practiced exercise at home or go for a walk, the majority of them (55.5%) did not have enough physical activity to reach the average level of baseline aerobic capacity. Guided by this, and bearing in mind the potential cardiotoxicity of the applied antineoplastic therapy^{46,47}, we decided to lower the levels and shorten the duration of training workload compared to general recommendations^{44,48}.

The work of Pinto et al.²⁴ shows that regular home-based aerobic exercise (fast walking, biking, swimming or exercise at home) of moderate intensity (55% to 65% HRmax) lasting 12 weeks, has positive effects on psychological well-being, level of fatigue and physical ability of female breast cancer survivor. The frequency of the training was initially 2 times per week, with progressive increase to 5 times per week, and physical ability was assessed through one-mile walk test. Corneya et al.²³ showed that aerobic training intensity of 70%–75% VO₂max three times a week for 15 weeks, significantly improved VO₂max and QOL. Peak oxygen consumption was assessed by a graded exercise test using gas exchange analysis at the beginning and at the end of training period²³.

Our research shows that training involvement two times a week with moderate intensity (45% to 65% VO₂max or 4–6 on Category-Ratio RPE Scale) for 15 minutes (plus 3 minutes for warm-up and cool-down each) is enough to achieve some improvements in aerobic capacity (2.97 mL/kg/min, 14.46%). The subjects in the group E2, who determined the workload by themselves, set it at a higher level, which became evident when the level of workload was expressed in the percentage of VO₂max (E2 – 55.58 ± 9.58% vs E1 – 50.47 ± 7.02% of VO₂max). Change in categories of aerobic capacity levels in the group E2 is also indicative (3/8 patients were switched to the category of very good). When people with low level of physical activity become active, they fairly quickly can achieve very impressive results⁴⁰, but in order to improve good results they need more time for exercise and, in particular, a larger workload.

It is possible that self-determination of exercise intensity within recommended limits results in more active participation in training. This is supported by the research of Nyikos et al.⁴⁹, who showed that moderate physical activity may have beneficial effects on some of the components of

physical and mental health and pain relief in cancer survivors treated with aromatase inhibitors. The program lasted 12 weeks, with the recommendation of at least 30 minutes of moderate physical training two times a week. Similar to our participants, the woman in that study, by its own sense, opted for the greater workload (137.9 ± 67.6 min moderate, and 52.5 ± 43.6 min vigorous exercise weekly). A similar result was reported by Segal et al.²¹ in a group with a self-determined load of physical activity at home which achieved better results in physical status than the group that practiced under supervision. The work of Korstjens et al.⁵⁰, points that self-defining level of physical involvement has beneficial effects on QOL with no other intervention. They examined the effects of a 12-week self-determined physical activity of breast cancer survivors, comparing a group that had only two times physical training a week and a group that, in addition to physical training, also had once a cognitive-behavioral training week. At the end of the training period, there were no significant differences between those two groups.

Our results show that for the improvement of aerobic metabolism of breast cancer survivors it is sufficient to start with relatively little exertion, and that they are ready for greater exertion if they are responsible for their training. Improvement that is achieved in this way can be very supportive in terms of changes in habits related to physical activity over long period of time.

Our results obtained in this study are encouraging. However, there are several caveats of this investigation that we consider important. First, the number of patients included was relatively small. Second, the groups were not well balanced in regard to adjuvant chemotherapy received, although there was enough time elapsed between the completion of adjuvant chemotherapy and study beginning (months to years) in all the included patients.

Conclusion

In our group of patients, the VO₂max determined using the Astrand's test on a bicycle-ergometer was significantly improved after only three weeks of moderate aerobic exercise, regardless of whether the workload is given on the basis of objective parameters (size of VO₂max) or self-determined on the basis of the Category-Ratio RPE Scale.

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