ORIGINAL ARTICLE

UDC: 618.19-006-08:[613.73::612.06
DOI:10.2298/VSP101117004B

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

Zorica Brdareski*, Aleksandar Djurović*, Snežana Šušnjar†, Mirjana Životić-Vanović‡, Andjelka Ristić§, Ljubica Konstantinović‖, Ljiljana Vučković-Dekić†, Mirjana Tankosić¶

***Clinic for Physical Medicine and Rehabilitation, ‡Department for Education and Scientific Research, §Clinic for Urgent Internal Medicine, ¶Clinic for Haemathology, Military Medical Academy, Belgrade, Serbia; †Institute for Oncology and Radiology of Serbia, Belgrade, Serbia; ‖Clinic for Physical Medicine and Rehabilitation "dr M. Zotovic", Belgrade, Serbia**

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 ± 7.02% *vs* 55.58 ± 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 tronedeljnog 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 najmenje 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 ± 7,02% *vs* 55,58 ± 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.

Correspondence to: Zorica Brdareski, Military Medical Academy, Clinic for Physical Medicine and Rehabilitation, Crnotravska 17, 11 000 Belgrade, Serbia. Phone: +381 11 3609 455. E-mail: zbrdareski@yahoo.com

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 cooperation [3]. 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 life [4–8]. In addition, it is possible that regular physical activity can reduce the risk of disease relapse and prolong survival [9].

The largest number of studies that investigate physical activity of patients with malignant disease are related to the aerobic, cardiovascular training [10]. Among all patients with malignant diseases, breast cancer patients are the most common studied [11–20]. 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-based [21] or supervised, in the laboratory, on a treadmill [22], or bicycle-ergometer [23]. 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_2max [21, 23], some on maximum heart rate (MHR) [14, 15, 24] or heart rate reserve (RHR) [12] and some on subjective evaluation of efforts, by using the rate percieved exertion (RPE) scale [25, 26]. Maximum aerobic capacity was measured directly, through a progressive maximal tests [23] or estimated from the results of submaximal tests (Modified Canadian Aerobic Fitness Test [21], Astrand-Rhimings protocol [25]. The karvonen formula was the most commonly used to determine the MHR [27]. 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 Wilcox [30] 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_2max) 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 values of VO_2max, 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_2max 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_2max as follows: 30%–35% VO_2max for the period of warming, 45-65% VO_2max for training period and 40%–45% VO_2max for the period of cooling. The conversion of the workload was done based on the measured values of VO_2max and the known energy expenditure of different intensities of the bicycle-ergometer [31], according to the formula:

Workload (W) = $0.08333 \times VO_2$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.

Colecting 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_2max 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 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 accuracy [32].

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 people [35]. 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 differences 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^2test. 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

Basic parameters of the participants before starting the study

Parameter	Patient's groups					
	E1 (n = 10)			E2 (n = 8)		
	$\bar{x}_{av}$ ± SD	median	min–max	$\bar{x}_{av}$ ± SD	median	min–max
Age (year)	51.60 ± 7.47	49	43–63	52.75 ± 7.42	52	42–63
Time after finishig 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)		$p = 0.001$
Radiotherapy [n (%)]	8 (80)			5 (62.5)		
Hormonal therapy [n (%)]	5 (50)			4 (50)		

There were no statistically significant differences 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 (VO_2max), loading and BMI in both groups, before and after a 3-week treaning

Parameters	Patient's groups		p
	E1 (n = 10)	E2 (n = 8)	
	$\bar{x}_{av} \pm SD$	$\bar{x}_{av} \pm SD$	
VO_{2max} (mL/kg/min) before training	20.47 ± 2.28	21.66 ± 4.39	
VO_{2max} (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_2max)	50.47 ± 7.02	55.58 ± 9.58	0.002
BMI (kg/m^2) before training	26.73 ± 2.11	26.19 ± 4.87	
BMI (kg/m^2) after a 3-week treaning	26.77 ± 2.32	26.14 ± 4.72	

BMI – body mass index

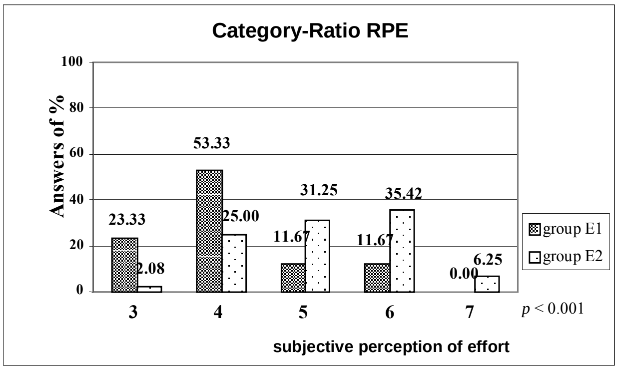

Fig. 1 – Subjective perception of exertion according to the Category-Ratio RPE scale in both groups

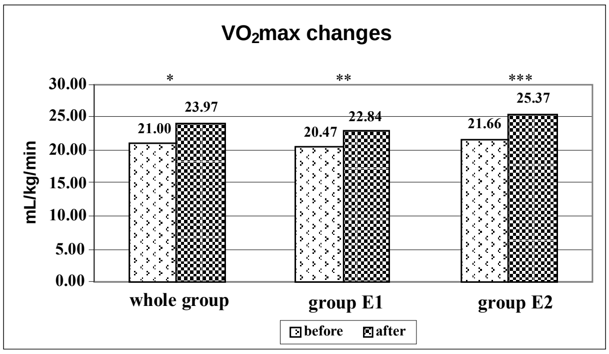

Fig. 2 – Maximum aerobic cepacity (VO_2max) changes after a 3-week training
***p = 0.0001; **p = 0.0002; *p = 0.014**

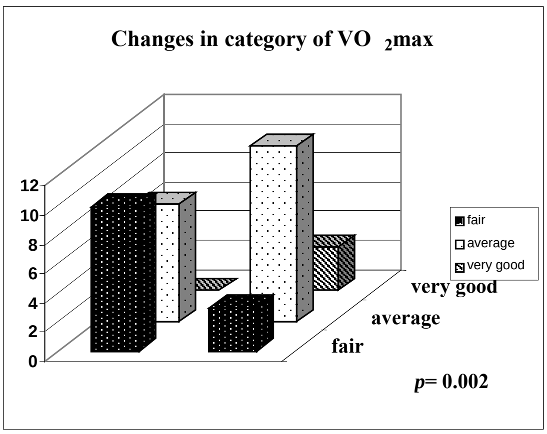

Fig. 3 – Changes in category of maximum aerobic cepacity (VO_2max) in the whole group of participants

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 fitness [37–40]. 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 active [39]. To improve overall health status it is enough to reach and maintain the average level of aerobic capacity [32]. 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 anxiety [41]. 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 (VO_2max), 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% VO_2max) during the first 3 weeks significantly improved VO_2max, submaximal frequency of heart rate, ventilation and lactate production [43]. 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% VO_2max) [40, 44].

Healthy female breast cancer survivors do not differ much than the average sedentary population [45], 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 challenge. 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% VO_2max three times a week for 15 weeks, significantly improved VO_2max 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 period [23].

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 themself, set it at a higher level, which became evident when the level of workload was expressed in the percentage of VO_2max (E2 – 55.58 ± 9.58% *vs* E1 – 50.47 ± 7.02% of VO_2max). 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 results [40], 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 VO_2max 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 VO_2max) or self-determined on the basis of the Category-Ratio RPE Scale.

R E F E R E N C E S

1. *United States Cancer Statistics Working Group*. United States Cancer Statistics: 1999–2006 Incidence and Mortality Web-based Report. Atlanta (GA): Department of Health and Human Services, Centers for Disease Control and Prevention, and National Cancer Institute; 2010. Available from: http://www.cdc.gov/uscs/.
2. *Miljus D, Vukicevic A, Zivkovic S, Mickovski-Katalina N, Rakocevic I, Plavsic S*. The incidence and cancer mortality in central Serbia in 2004. Institute of Public Health of Serbia; 2007. (Serbian)
3. *Robert J Kaplan, James E Van Zandt*. Cancer Rehabilitation. Available from: http://emedicine.medscape.com/article/320261-overview
4. *Irvine DM, Vincent L, Graydon JE, Bubela N*. Fatigue in women with breast cancer receiving radiation therapy. Cancer Nurs 1998; 21(2): 127–35.
5. Dimeo FC. Effects of exercise on cancer-related fatigue. Cancer 2001; 92: 1689–3.
6. *Adamsen L, Midtgaard J, Rorth M, Borregaard N, Andersen C, Quist M*. Feasibility, physical capacity, and health benefits of a multidimensional exercise program for cancer patients undergoing chemotherapy. Support Care Cancer 2003; 11: 707–16.
7. *Jones LW, Eves ND, Courneya KS, Chin BK, Baracos VE, Hanson J*, et al. Effects of exercise training on antitumor efficacy of doxorubicin in MDA-MB-231 breast cancer xenografts. Clin Cancer Res 2005; 11: 6695–8.

8. *McKenzie DC, Kalda AL.* Effect of upper extremity exercise on secondary lymphedema in breast cancer patients: a pilot study. J Clin Oncol 2003; 21: 463–6.
9. *Holmes MD, Chen WY, Feskanich D, Kroenke CH, Colditz GA*, et al. Physical activity and survival after breast cancer diagnosis. JAMA 2005; 293: 2479–86.
10. *Galvão DA, Newton RU.* Review of Exercise Intervention Studies in Cancer Patients. J Clin Oncol 2005; 23(4): 899–909.
11. *Mock V, Dow KH, Meares CJ, Grimm PM, Eienemann JA, Haisfield-Wolfe ME,* et al: Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. Oncol Nurs Forum 1997; 24: 991–1000.
12. *MacVicar MG, Winningham ML, Nickel JL.* Effects of aerobic interval training on cancer patients functional capacity. Nurs Res 1989; 38: 348–51.
13. *Mock V, Pickett M, Ropka ME,,Unscari Lin E, Stewart KJ, Rhodes VA,* et al: Fatigue and quality of life outcomes of exercise during cancer treatment. Cancer Practice 2001; 9: 119–27.
14. *Winningham ML, MacVicar MG, Bondoc M, Anderson JI, Minton JP.* Effect of aerobic exercise on body weight and composition in patients with breast cancer on adjuvant chemotherapy. Oncol Nurs Forum 1989; 16: 683–9.
15. *Winningham ML, MacVicar MG.* The effect of aerobic exercise on patient reports of nausea. Oncol Nurs Forum 1988; 15: 447–50.
16. *Schwartz AL, Mori M, Gao R, Nail LM, King ME.* Exercise reduces daily fatigue in women with breast cancer receiving chemotherapy. Med Sci Sports Exerc 2001; 33(5): 718–23.
17. *Dimeo FC, Stieglitz RD, Novelli-Fischer U, Fetscher S, Keul J.* Effects of physical activity on the fatigue and psychologic status of cancer patients during chemotherapy. Cancer 1999; 85(10): 2273–7.
18. *Dimeo F, Rumberger BG, Keul J.* Aerobic exercise as therapy for cancer fatigue. Med Sci Sports Exerc 1998; 30(4): 475–8.
19. *Dimeo F, Fetscher S, Lange W, Mertersmann R, Kenl J.* Effects of aerobic exercise on the physical performance and incidence of treatment-related complications after high-dose chemotherapy. Blood 1997; 90(9): 3390–4.
20. *Berard A, Bravo G, Gauthier P.* Meta-analysis of the effectiveness of physical activity for the prevention of bone loss in postmenopausal women. Osteoporos Int 1997; 7: 331–7.
21. *Segal R, Evans W, Johnson D, Smith J, Colletta S, Gayton J,* et al. Structured Exercise Improves Physical Functioning inWomen With Stages I and II Breast Cancer: Results of a Randomized Controlled Trial. J Clin Oncol, 2001; 19(3): 657–65.
22. *Dimeo F, Tilman MH, Bertz H, Kanc L, Metelsmann R, Kenl I.* Aerobic exercise in the rehabilitation of cancer patients after high dose chemotherapy and autologous stem cell transplantation. Cancer 1997; 79: 1717–22.
23. *Courneya KS, Mackey JR, Bell GJ, Jones LW, Field FJ, Fairey AS.* Randomized Controlled Trial of Exercise Training in Postmenopausal Breast Cancer Survivors: Cardiopulmonary and Quality of Life Outcomes. J Clin Oncol, 2003; 21(9): 1660–8.
24. *Pinto BM, Frierson GM, Rabin C, Trunzo JJ, Marcus BH.* Home-Based Physical Activity Intervention for Breast Cancer Patients J Clin Oncol 2005; 23: 3577–87.
25. *Thorsen L, Skovlund E, Strømme SB, Hornslien K, Dahl AA, Fosså SD.* Effectiveness of Physical Activity on Cardiorespiratory Fitness and Health-Related Quality of Life in Young and Middle-Aged Cancer Patients Shortly After Chemotherapy. J Clin Oncol. 2005; 23(10): 2378–88.
26. *Nikander R, Sievänen H, Ojala K, Oivanen T, Kellokumpu-Lehtinen PL, Saarto T.* Effect of a vigorous aerobic regimen on physical performance in breast cancer patients - a randomized controlled pilot trial. Acta Oncologica, 2007; 46(2): 181–6.
27. *Karvonen M, Kentala E, Mustala O.* The effects of training on heart rate. A longitudinal study. Ann Med Exp Biol Fenn 1957; 35: 307–15.
28. *Schmitz HK, Holtzman J, Courneya KS, Mâsse LC, Duval S, Kane R.* Controlled Physical Activity Trials in Cancer Survivors: A Systematic Review and Meta-analysis. Cancer Epidemiol Biomarkers Prev 2005; 14(7): 1588–95.
29. *McNeely ML, Campbell KL, Rowe BH, Klassen TP, Mackey JR, Courneya KR.* Efects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. CMAJ 2006; 175(1): 34–41.
30. *Burnham TR, Wilcox A.* Effects of exercise on physiological and psychological variables in cancer survivors. Med Sci Sports Exerc 2002; 34(12): 1863–7.
31. American College of Sports Medicine. ACSM's Guidelines for Graded Exercise Training and Proscription (3rd ed.). Philadelphia: Lea and Febinger, 1986.
32. *Zivanic S, Zivotic-Vanovic M, Mijic R, Dragojevic R.* Maximal oxygen intake (VO_{2max}) and it's predicting by Astrand's test on bicycle-ergometer. Belgrade: Sports Medicine Association of Serbia & Zelnid; 1999. (Serbian)
33. *Borg GAV.* Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982; 14(5): 377–81.
34. *Noble BJ, Borg GAV, Jacobs I, Ceci R, Kaiser P.* A category-ratio perceived exertion scale: relationship to blood and muscle lactates and heart rate. Med Sci Sports Exerc 1983; 15(6): 523–8.
35. *Stoudemire NM, Wideman L, Pass KA, McGinnes CL, Gaesser GA, Weltman A.* The validity of regulating blood lactate concentration during running by ratings of perceived exertion. Med Sci Sports Exerc 1996; 28: 490–5.
36. *Petz B.* The basic of statistical methods for nonmathematicians. Zagreb: University Press Liber, 1985. (Croatian)
37. *Kesaniemi YA, Danforth E, Jensen MD, Kopelman PG, Lefebvre P, Reeder BA.* Dose–response issues concerning physical activity and health: an evidence based symposium. Med Sci Sports Exerc 2001; 33(suppl): S351–8.
38. *Phillips WT, Pruitt LA, King AC.* Lifestyle activity: current recommendations. Sports Med 1996; 22: 1–7.
39. *Balir SN, Booth M, Gyarfas I, Iwane H, Marti B, Matsudo V,* et al. Development of public policy and physical activity initiatives internationally. Sports Med 1996; 21: 157–63.
40. *U.S. Department of Health and Human Services.* Physical Activity and Health: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996.
41. *Blacklock R, Rhodes R, Blanchard C, Gaul C.* Effects of Exercise Intensity and Self-Efficacy on State Anxiety with Breast Cancer Survivors. Oncology Nursing Forum 2010; 37(2): 206–12.
42. *Smith TP, McNaughton LR, Marshall KJ.* Effects of 4-wk training using V_{max}/T_{max} on VO_2max and performance in athletes. Med Sci Sports Exerc 1999; 31: 892–6.
43. *Hikson RC.* Time course of the adaptive responses of aerobic power and heart rate to training. Med Sci Sports Exerc 1981; 13: 17–20.
44. *American College of Sports Medicine.* ACSM's Guidelines for Graded Exercise Training and Proscription (6th ed.). Philadelphia: Lippincott Williams&Wilkins; 2000.
45. *Brown J, Byers T, Doyle C, Courneya K, Demark-Wahenfried W, Kushi L.* Nutrition and physical activity during and after cancer treatment: an American Cancer Society guide for informed choices. CA Cancer J Clin 2003; 53: 268–91.
46. *Ewer MS, Gluck S.* A Woman's Heart: The Impact of Adjuvant Endocrine Therapy on Cardiovascular Health. Cancer 2009; 115: 1813–26.
47. *Lenihan DJ, Esteva FJ.* Multidisciplinary Strategy for Managing Cardiovascular Risks When Treating Patients with Early Breast Cancer. The Oncologist 2008; 13: 1224–34.
48. *Courneya KS.* Coping with cancer: can exercise help? The Physician and Sports Medicine 2000; 28: 49–73.
49. *Nyikos I, Malone LA, Vogtle LK, O'Nihill AE.* Self-directed Exercise and Quality of Life in Breast Cancer Survivors Using Aromatase Inhibitors. Med Sci Sports Exerc 2010; 42(5): 317–8.
50. *Korstjens I, May AM, van Weert E, Mesters I, Tan F, Ros WJG*, et al. Quality of Life After Self-Management Cancer Rehabilitation: A Randomized Controlled Trial Comparing Physical and Cognitive-Behavioral Training Versus Physical Training. Psychosomatic Medicine 2008; 70: 422–9.

Received on November 17, 2010.
Revised on March 10, 2011.
Accepted on March 14, 2011.
OnLine-first, December, 2011.