EFFECT OF A 3-MONTH EXERCISE INTERVENTION ON PHYSICAL PERFORMANCE, BODY COMPOSITION, DEPRESSION AND AUTONOMIC NERVOUS SYSTEM IN BREAST CANCER SURVIVORS: A PILOT STUDY

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ABSTRACT

Purpose: Breast cancer patients are at increased risk of developing comorbidities such as lymphedema, sarcopenia, osteoporosis and cardiovascular disease after breast cancer treatment. These complications contribute to a decrease in quality of life, cardiorespiratory fitness and muscle strength. Regular and long-term physical activity is an effective non-pharmacological strategy that can improve physical, psychological and social outcomes. The aim of our research was to evaluate the effect of various modes of an exercise intervention on *physical performance, body composition, depression and autonomic nervous system in breast cancer survivors.*
Methods: 16 women after surgery with hormonal treatment enter the research. Thirteen of them completed the controlled, quasi-experimental study (54 ± 9 yrs, 164cm ± 6cm, 72 ± 12kg) and were divided into 3 groups according to their place of living: trained under supervision (n=5) (SUPERV), trained at home without supervision by videos (n=7) (HOME) and with no prescribed physical activity (n=4) (CON). Exercise intervention lasted 3 months and comprised of 60 min training units 3 × week (aerobic with resistant exercise in a 2 : 1 mode combined with regular weekly yoga and breathing exercises). The exercise intensity was set individually at 65–75% of HRR based on spiroergometry and was continuously controlled by heart rate monitors. The same principles applied to the HOME group, which, in addition to heart rate monitors, recorded frequency, length, HRmax, HRavg, and Borg scale of intensity perception. VO_{2max}, BMI, fat mass, depression level (Beck's depression inventory) and the power of the autonomic nervous system (total power and sympatho-vagal balance) were analyzed. For data evaluation we used descriptive statistics and Cohens *d* effect size.
Results: 3 women dropped out of research because of medical reason. In all groups VO_{2max} values increased. The largest increase in VO_{2max} values was in SUPERV group by 36%, in HOME group by 20% and in CON group by 2%. Body weight decreased for groups SUPERV (-1.2 kg) and CON (-0.1kg), for HOME group there was an increase (+0.2 kg). Body mass index decreased for SUPERV group (-0.4), for HOME and CON it increased (both +0.1). Total power decreased in SUPERV (-0.6) and HOME group (-0.2), in CON has not changed. The same results were achieved by the sympatho-vagal balance, only the CON group increased. Values from Beck's depression inventory decreased for all groups, most for CON group.
Conclusion: A 3-months of supervised and controlled exercise had a significant effect on physical fitness and body composition in comparison with non-supervised home-based physical intervention. Our results indicate that it is strongly advisable to apply a supervised exercise program to induce positive physiological changes in breast cancer survivors as part of aftercare.

Keywords: cancer; physical activity; anthropometric changes; Beck's depression inventory; spectral analysis of heart rate variability

Introduction

In 2016, breast cancer was the most frequent cause of death of women in the Czech Republic age category 20–54 years („MAMO.CZ: Rakovina prsu", 2018). The annual average of newly diagnosed breast cancer cases is around 7.000 women, with about 1.900 of them dying from the disease (Mužík, Šnajdrová, & Gregor, 2018). The incidence is steadily increasing, with mortality stagnating, even slightly declining, due to early detection and improvement of treatment (Fernández et al., 2018). A common method of treating breast cancer is surgery in combination with chemotherapy, radiation therapy, and hormone therapy („WHO | Cancer country profiles 2014", 2014). Patients who survive breast cancer are at increased risk of developing comorbid conditions such as lymphedema, sarcopenia, osteoporosis (due to hormonal treatment) and cardiovascular disease (Ording et al., 2013) as a result of treatment, thus reducing quality life. Health problems caused by breast cancer treatment include, but are not limited to, persistent psychosocial anxiety, including depression, fatigue (Vigo et al., 2015), sleep disorders (de Jong, Courtens, Abu-Saad, & Schouten, 2002; DeSantis et al., 2014; Knobf, 2011), a reduction in fitness, called deconditioning, which can lead to increased body weight. These side effects can be eliminated through a healthy lifestyle, including a balanced diet and physical activity (Macêdo et al., 2010). Physical activity recommendations for cancer patients report 150 minutes of moderate intensity weekly aerobic activity (walking, ballroom dancing, gardening) or 75 minutes of higher intensity weekly aerobic activity (running, walking uphill). For resistant exercise, 20–30 minutes of moderate intensity at least twice a week is recommended, ideally under supervision (Schmitz et al., 2010). These recommendations concern most types of tumors, more specific recommendations for breast cancer patients are unknown, and it is clear that regular and long-term physical activity is an effective non-pharmacological strategy that can improve results in physical, psychological and social aspects (Goss et al., 2008; Mishra et al., 2012; Peterson & Ligibel, 2018)patients who received placebo (PLAC. Specifically, physical activity performed to a sufficient extent has a positive effect on quality of life (Kramer et al., 2000), physical fitness and cardiovascular system (Rodrigues et al., 2014), body composition (Grabenbauer, Grabenbauer, Lengenfelder, Grabenbauer, & Distel, 2016), fatigue and frequently occurring fatigue syndrome (Radbruch et al., 2008)"container-title":"Palliative Medicine","page":"13-32","volume":"22","issue":"1","source":"PubMed","abstract":"Fatigue is one of the most frequent symptoms in palliative care patients, reported in .80% of cancer patients and in up to 99% of patients following radio- or chemotherapy. Fatigue also plays a major role in palliative care for noncancer patients, with large percentages of patients with HIV, multiple sclerosis, chronic obstructive pulmonary disease or heart failure reporting fatigue. This paper presents the position of an expert working group of the European Association for Palliative Care (EAPC. In addition, physical activity can reduce the risk of breast cancer recurrence while helping to increase patient survival (de Boer, Wörner, Verlaan, & van Leeuwen, 2017; Ferrer, Huedo-Medina, Johnson, Ryan, & Pescatello, 2011; Meneses-Echávez, González-Jiménez, & Ramírez-Vélez, 2015). In view of the results of the above studies, we can assume that the exercise and nutrition program should be a common part of aftercare for breast cancer survivors.

Method

Participants

The group consisted of 16 women (54 ± 9 yrs, min age 42 and max age 70; 164cm ± 6cm, 72 ± 12kg) with breast cancer. For all participants the research started in February 2019. Participants were divided into 3 groups based on deliberate selection based on the distance of individual patients' residence from Brno, while maintaining the homogeneity of the sample (supervised exercises = SUPERV, unattended exercises = HOME, no controlled exercises (usual care) = CON). 3 women dropped out of research because of medical reason.

Inclusion criteria

Inclusion criteria for research were evaluated by doctors from the Masaryk Cancer Institute and are as follows: age over 18, age range 40–70 years; the estimated life expectancy of at least 1 year; 0–III stage of breast cancer; after systematic neoadjuvant or adjuvant chemotherapy, radiation therapy; with ongoing hormone therapy; performance status (PS 0,1); ability to walk 400 meters without sitting, leaning or helping another person.

Exclusion criteria

Exclusion criteria were IV stage of cancer; functional disability impeding exercise; uncontrollable heart, joint or lung disease; untreated hypertension; pregnant or nursing; patients who have not been approved by the oncologist for physical activity and patients who have refused to sign informed consent.

Research design

Participants attend an information meeting where they learn all the important information and receive informed consent. In the case of consent to participate in the research, each participant undergoes an input and output measurement. The SUPERV and HOME groups attended exercise intervention, as described below.

1. Input measurements included:
    - load test on a bicycle ergometer to determine ventilation parameters;
    - body composition measurement using bioelectric impedance;
    - spectral analysis of heart rate variability to determine autonomic nervous system function;
    - Beck's Depression Inventory.
2. Physical intervention according to the attributes of the group, see below.
3. Output measurement was identical to input measurement.

Measures

To gain an appreciation of aerobic capacity (VO_{2max}) we used standardized incremental bicycle ergometer test with a set duration of about 10 (±2) min. The protocol was a continuous ramp exercise where the load increase was 15–20 W/min, until subjects reached a respiratory quotient (RQ) ≥ 1.1. A pedalling frequency of 60/70 rev/min. The maximum of the VO_2 curve was taken as peak. During baseline, exercise and recovery heart rhythm and frequency were monitored from 12 leads ECG. Expired air was collected using a breathing apparatus and analyzed with a metabolic measurement cart (V_{max} Encore, Viasys, CareFusion, San Diego, CA) to determine ventilatory and gas exchange variables on a breath-by-breath basis. Body composition was examined by bioelectric impedance using InBody 230. Contraindications for each participant were excluded. Depressive symptoms were measured by Beck's depression inventory (BDI) (Beck, 1961), which consists of 21 questions about last week's feelings. The filling person has a choice of 4 options (from 0 to 3). The sum of point measures the depth of the depression symptoms: 0–10 points signifies normal mood, 10–20 mild depression, 20–40 moderate depression and 40–60 severe depressive symptoms. DiANS PF8 and Medical DiANS PC software were used to measure heart rate variability. The examination of heart rate variability was performed by changing the position of the body (lie – stand – lie). The investigated person was in every position, with 300 R-R oscillations measured for five-minute interval. All measurement data was transferred to a desktop computer and then analyzed by Medical DiANS PC software. For this work, we chose from the analysis complex indicators, such as a sympatho-vagal balance (SVB) and total score (TS).

Exercises intervention

The duration of the intervention was 3 months and included 60min of training unit 3 times a week (aerobic exercise with strength training elements combined with 2 : 1 yoga and breathing exercises). The intensity of the exercise was continuously monitored by heart rate monitors and was gradually increase as shown below. These principles applied to the SUPERV group and HOME group. HOME group performed exercises at home according to instructional videos. There was a regular educational meeting with the HOME group where we will explain the new exercise videos for the next month and check the heart rate monitors. The control group (CON) did not perform any controlled physical activity.

Content of training unit:

1. Warm-up (10min): 40–50% of HRR.
2. Main part of TJ (40min): combination of aerobic and resistant exercise:

    - **Aerobic exercise** – walking on a belt, spinning bike and elliptical trainer. Individually set training zone from spiroergometry results: 1st month, 30 min, 55–70% of HRR; 2nd month 25 min, 70–80% of HRR; month 25 min, 70–85% of HRR.
    - **Resistant exercises** – free squat, lunges, pelvic bridge, sit-ups, exercise with strength rubber: rowing in a sitting position, tightening behind the head, tightening, biceps strokes and triceps extensions. 1st month 10min – 10 reps, 2 series; 2nd month 15min – 12 reps, 2 series; 3rd month 15min – 15 reps, 2 series.

    3. Cooldown and stretching (10min) – 40–50% of HRR.

Yoga: Asanas – training of individual positions at the beginner level (stretching techniques for warming up, standing, lying, side and sitting positions), each stance last 10–30s, rest between 30s to 1 minute Pranayama – work with breathing, breathing techniques. At the end of training there were meditation and relaxation on the back side.

Statistical analysis

To evaluate data, we used descriptive (mean, standard deviation, maximum and minimum) and analytical statistics (paired T-test) and Cohen's d (effect size). Data were calculated in the program Statistica 13.2.

Results

The comparison between the physical activity, body composition, depression level and autonomic nervous system is presented in Tab. 1. The most significant changes among the tested groups are changes in physical fitness (VO_{2max}) of the SUPERV ($p = 0.047$) and HOME ($p=0.002$) groups as evidenced by the high level of effect size (SUPERV $d = 1.211$, HOME $d = 1.034$). Average values of body mass index decreased in SUPERV group, slightly in CON group. HOME group has seen an increased in BMI values. Depression level and total score decreased in all study group. All these changes are not statistically significant and there was no effect size. Other significant changes were noted in the post-intervention SVB values ($p = 0.004$), where there is a medium level of effect size (d = 0.531). A high effect size value was also measured for the SVB values of the control group (CON $d = 0.523$).

Table 1 *Changes in examined variables in breast cancer patients after physical intervention*

	Baseline Mean (SD)	Post-intervention Mean (SD)	P value	Effect size (Cohen's d)
Physical fitness (VO_{2max})				
SUPERV (n=4)	20.2 (5.6)	26.8 (5.3)	0.047	1.211
HOME (n=7)	21.6 (3.4)	25.9 (4.8)	0.002	1.034
CON (n=2)	18.3 (0.8)	18.7 (2.0)	0.744	0.263
Body composition (BMI)				
SUPERV (n=4)	25.3 (3.3)	24.9 (3.4)	0.094	0.120
HOME (n=7)	26.3 (4.9)	26.4 (4.6)	0.737	0.021
CON (n=2)	30.1 (3.7)	30.0 (4.2)	0.844	0.025
Depression level				
SUPERV (n=4)	8.5 (2.9)	7.3 (4.3)	0.312	0.327
HOME (n=7)	10.7 (6.2)	9.1 (5.0)	0.494	0.284
CON (n=2)	20.5 (7.8)	17.0 (8.5)	0.090	0.430
Autonomic nervous system (TS)				
SUPERV (n=4)	´-1.8 (3.0)	´-2.4 (2.8)	0.292	0.207
HOME (n=7)	´-2.0 (3.1)	´-2.2 (2.6)	0.767	0.070
CON (n=2)	´-4.8 (0.2)	´-4.9 (0.1)	0.832	0.632
Autonomic nervous system (SVB)				
SUPERV (n=4)	1.5 (2.4)	1.2 (1.3)	0.837	0.155
HOME (n=7)	0.4 (2.4)	´-0.9 (2.5)	0.004	0.531
CON (n=2)	1.3 (1.2)	2.1 (1.8)	0.322	0.523

Discussion

Breast cancer treatment is challenging for the body and can lead to various disorders including decreased bone density (Chen, 2005) and cardiometabolic profile (Caro-Morán et al., 2016)controlling for known confounders. This descriptive case-controlled study included 22 breast cancer survivors and 22 healthy age- and sex-matched controls. Short-term HRV was measured using an accepted methodology to assess the cardiac autonomic balance. One-way analysis of covariance results revealed that heart rate was significantly higher ($F = 15.86$, $p < .001$, persistent psychosocial anxiety including depression, fatigue (Vigo et al., 2015), sleep disorders (de Jong et al., 2002; DeSantis et al., 2014; Knobf, 2011), decreased physical fitness. Regular and long-term physical activity can improve the results in physical, mental and social aspects of breast cancer patients (Mishra et al., 2012; Peterson & Ligibel, 2018).

Currently, physical activity is an important part of aftercare in breast cancer patients, but it is not still performed as a standard. The aim of our research was to evaluate the effect of various modes of 3 months exercise intervention on physical performance, body composition, depression and autonomic nervous system in breast cancer survivors. The project was completed by 16 participants with diagnosed breast cancer, of which 4 patients underwent a movement program under supervision, 7 patients exercised without supervision and 2 patients were in the control group. Due to the deliberate selection of probands and the consequent low number of probands who completed the physical intervention, we evaluated that statistical significance is not a suitable tool for evaluating changes in the variables examined and therefore we decided to mention especially those results that had at least effect size.

The results show that the most significant changes before and after exercise intervention were with VO_{2max} values, namely in the group under supervision and without supervision at home while for

supervised group, the change was more significant. This result is consistent with the study result from Casla et al., (2015). They experienced significant changes in VO_{2max} values by the 12 weeks combination training, twice a week against the control group with usual care. (Dieli-Conwright et al., 2018) also noted a significant decrease in VO_{2max}, which is an indicator of cardiorespiratory fitness in the exercise group (16 weeks, 3 times per week) compared to baseline and the usual care group. Our results of sympatho-agal balance values indicate significant decrease with effect size after exercise intervention, but the values are still within normal limits (Stejskal, Šlachta, Elfmark, Salinger, & Gaul-Aláčová, 2002). (Dias Reis et al., 2017) becoming thus an ultimate importance tool in both clinical and research setting, being a good predictor of cardiac events and mortality risk and also used in physical exercise and sports in general. The aim of the present study was to evaluate 12 weeks of exercise training and six weeks of detraining in cardiorespiratory capacity, and autonomic modulation in breast cancer patients.\nMETHODS: The sample was composed of 18 females (9 controls and 9 exercised did not reach the same results. They investigated that after 12 weeks exercise intervention with combined training values of LF/HF, which is sympatho-vagal balance indicator, significant increased, which may be due to age or gender (Li, Rüdiger, & Ziemssen, 2019).

Our results support the proposition that physical activity in breast cancer patients has positive effects on physical fitness, but we have not confirmed a positive effect on autonomic nervous system function. However, the complications that occur during and after treatment of the patient put further demands on research into improving the quality of life of patients in remission. Further research could focus on the most effective exercise protocol or the creation of appropriate educational materials for patients who cannot or do not want to commute to exercise for a variety of reasons, but could also carry out exercise at home.

The study limitations

Baseline values may be affected by ignorance of the tests. Furthermore, the probands showed a different level of motivation to exercise. This can be influenced by the current mental or physical condition. The data may have been influenced by the socio-economic factor and the period during which the intervention took place. It would certainly be advisable to monitor the adherence of the patients to exercise, whether it was higher in the group exercising under supervision or without it.

Conclusion

The pilot study examined changes in physical condition, body composition, depression levels and autonomic nervous system in breast cancer patients who had undergone 3 months exercise intervention. Sixteen patients participated in the research and completed the physical intervention. Slight statistically significant changes and high level of effect size were recorded only for the values of the physical fitness, namely in the group exercise under supervision and non-supervised group. Other significant changes were observed in the sympatho-vagal balance before and after the intervention in the non-supervised group (HOME). The measured data cannot be generalized due to the small number of participants. For a possible generalization, confirmed and deeper interpretation of the results, it is necessary to expand the research file and carry out further studies to confirm our data from the pilot project.

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