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The effect of a 10-week aerobic exercise on cardiac function among overweight female breast cancer survivors; a randomized clinical trial

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Abstract

Introduction: Breast cancer is the most common and deadliest cancer among women.
Objectives: The aim of this study was to evaluate the effect of 10-week aerobic exercise on cardiac function among overweight female breast cancer survivors.
Patients and Methods: This triple-blinded randomized clinical trial was carried out among 25 overweight female breast cancer survivors (age range; 30-55 years). The aerobic exercise training protocol was performed for 10 weeks with an intensity of 40 to 75% of maximal heart rate. Anthropometric parameters and body composition of patients were measured (pre-test/post-test design). Echocardiography was used to determine the ejection fraction and pulmonary artery pressure of the patients too.
Results: There was no significant difference between anthropometric parameters and body composition of patients in the control and exercise groups. Additionally, there was a significant difference in the ejection fraction (P=0.001), PAP (P = 0.025) and VO2max between patients of control and exercise groups (P=0.001).
Conclusion: A 10-week aerobic exercise leads to an increase in the levels of VO2max, ejection fraction and pulmonary arterial pressure.
Trial Registration: Registration of trial protocol has been approved by Iranian Registry of Clinical Trials (identifier: IRCT20190218042745N1, https://www.irct.ir/trial/37684, ethical code; IR.MUI.REC.1396.2.082).

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Introduction

Breast cancer is the most common cancer in women, which is the second leading cause of death in women, after lung cancer. Breast cancer occurs in one out of every eight women, accounting for almost a third (31%) of all female cases in western countries (1).

The development of technology and the effectiveness of cancer treatment have significantly increased the survival rate. However, the effectiveness of cancer treatment is not only targeting the cancer cells, but also have harmful effects on normal tissues, which can be followed by acute and chronic physiological and mental complications in cancer survivors. For instance, the effect of cancer on the cardiac muscle tissue has led to some abnormalities in the left ventricle, such as an increase in left ventricular filling time, reduced ejection fraction and abnormal contraction of the left ventricle (2). In addition to injuries as well as kidney damage, lung toxicity may occur as a result of cancer treatment, leading to dyspnea, reduced total lung capacity, reduced vital capacity and reduced respiratory capacity, which ultimately leads to disturbances in the transportation of oxygen and removal of carbon dioxide (3). Different treatments of breast cancer such as radiotherapy, chemotherapy and hormone therapy are associated with cardiac diseases. Therefore, these damages, which are caused by radiotherapy, have been developed largely as a cause of death during the last decades (4-6).

Pathophysiologic events, which are associated with cancer treatment, are often secondary to lifestyle changes following physical inactivity and weight gain that lead

Key point

In a study on 25 overweight female breast cancer survivors, we found a 10-week aerobic exercise leads to an increase in the levels of VO2max, ejection fraction and pulmonary arterial pressure.

to cardiovascular damages (7). Therefore, the prevention and management of cardiovascular diseases caused by breast cancer treatment is a very important clinical issue. Several studies have suggested that physical inactivity during cancer treatment may affect the levels of fatigue caused by cancer. Aerobic exercises are addressed as the most effective way to improve cardiorespiratory fitness in normal people. Several studies have investigated the role of exercise in breast cancer survivors and reported a significant relationship between exercise and aerobic capacity, cardiovascular changes, physical activity, and blood pressure (8). Exercise can improve cardiovascular function and increase cardiac output and impulse volume, decrease heart rate and improve ventilation and transportation of oxygen. These benefits reduce the toxicity of cancer and the consequent fatigue (9).

The results of previous studies in women with breast cancer showed that aerobic exercise is accompanied by an improvement in the VO2 max. Exercise can be effective in the treatment of breast cancer patients due to weight loss, body mass index, body fat and some physical measurements, as well as improving the cardiorespiratory fitness (8,10). Typically, the positive effects of exercise on cardiac function include increased the skeletal muscle function, improved endothelial function, increased the autonomic nervous system function, reduced inflammatory cytokines, increased muscle strength and reduced mortality rate (11). Furthermore, studies have shown that aerobic exercise can increase the red cell mass. It also alters the number and distribution of leukocytes and platelets in the blood, and the proliferation and number of lymphocytes. However, changes in the number, distribution, and proliferation of white blood cells caused by exercise are temporary (12). Study reported that aerobic exercises improve the amount of hemoglobin during and after chemotherapy (13). It is believed that physical activity and exercise are safe and effective alternative methods to treat breast cancer and other cancers. This is only possible when the effective pathways of physical activity identified in breast cancer treatment, however. Some studies about the effect of aerobic exercise on cardiac function in women with breast cancer for example Schneider et al showed that moderate intensity, individualized and prescriptive exercise maintains, or improves cardiovascular and pulmonary function with concomitant reduction in fatigue during and after cancer treatment (3).

Objectives

The fundamental characteristic of our study is the selection of overweight women breast cancer survivors and considering the association of aerobic exercises with increased cardiovascular fitness. Furthermore, aerobic with music is a fun sport and prevents treatment side effects such as fatigue due to exercise and depression and also leads to high tolerance in the participants during the study. Therefore, the aim of this study is to evaluate the effect of a 10-week aerobic exercise on cardiac function among overweight female breast cancer survivors.

Patients and Methods

Protocol

In this triple-blinded randomized clinical trial study, the study population consisted of women with breast cancer admitted to Omid hospital, Isfahan, Iran. Twenty-five patients (age range; 30-55 years) were randomly assigned to one of the two groups of exercise (n = 15) and control (n = 10). During the study, one patient in the control group (n = 9) and one in the exercise group (n = 14) withdrew from continuing the study. After obtaining an approval from the medical ethics committee, eligible patients, who met the inclusion criteria, were recruited. Patients' informed consent was obtained prior to the study. The subjects, the person administering the treatment and the person evaluating the response to treatment were not aware of which subjects are in which group (triple blind).

The inclusion criteria were lack of regular physical activity during the past six months, lack of smoking history, lack of other symptomatic diseases such as hypertension, diabetes, cardiopulmonary disease, overweight, history of surgery, chemotherapy and diagnosed at the same stage of the disease [all of the patients were in the 1 and 2 stages of breast cancer (no metastasis) and passed through their treatment for 2 to 12 months while they were undertake tamoxifen medication]. The exercise group regularly did aerobic exercise for 10 weeks. The exclusion criteria were any conditions that make the patient's current condition worse, not attending training sessions more than five sessions, failure to participate in programs such as echo and instrumentation and blood sampling.

Body composition measurement

In order to assess the body composition of the patients, the height was measured to the nearest of 5 mm using Seca stadiometer, waist and hip girth was measured using Mabis strip and the weight was measured using Beurer digital scale. By dividing waist to hip girth, waist to hip ratio (WHR) was calculated, and from height (m) and weight (kg), each patient's BMI (kg/m^2) was calculated. Weight, fat and BMI of the participants were measured using body composition analyzer (TINA, Japan). Modified Bruce treadmill test was used to measure the maximal aerobic power. The total recorded time for each participant was put in the following formula and VO2 max was calculated.

$VO2max = 2.327 \times Time\ (min) + 9.48$

Complete blood cell parameters

Prior to the measurements, 10 milliliters of blood, after 12 hours of fasting, were taken from the participants' cubital vein in the sitting position (before and after the procedure) and red blood cells (RBCs), white blood cells (WBCs), and hemoglobin were measured using an automated Cell Counters (Sysmax-KXn21, Japan).

Cardiac function measurement

Before the procedure and immediately after the end of eight weeks of exercise program, the ejection fraction (EF) and pulmonary artery pressure (PAP) of patients were measured at rest position based on one-dimensional and two-dimensional methods using echocardiography (Esaote, s.p.d. GE, P8000, USA) (Probe Frequency: 3.5 MHz) by cardiologist in order to evaluate the cardiorespiratory function of the participants. The ejection fraction was calculated using the Composite Simpson's Rule in apical 4 chamber view. Diastolic heart rate was recorded at the end of echocardiography in both rest and supine position. All measurements were carried out 48 hours before the onset of the program and 48 hours after the session (14).

Aerobic exercise program

The aerobic exercise program was performed with an intensity of 40% to 75% of maximal heart rate, and included warming up (tensile, smooth exercise and slow running) for five minutes. Main program was the coordination between arm and leg movements (rhythmic aerobics exercises then, performing simple series of rhythmic aerobic exercises) for 30 minutes and the cooling down (tensile and smooth exercise) for 10 minutes in a form of block. After the program started, the number of blocks, the time and intensity of the exercises to reach the appropriate time (40 minutes) were added according to the following table twice in a week. Participants were asked not to participate in any other sport program during this study. The intensity of exercise was calculated based on the maximal heart rate of each patient using the heart rate monitor (POLAR, Finland) and patients' heart rate was monitored every session. After the program started, the number of blocks, the time and intensity of the exercise to reach the appropriate time (40 minutes) was added according to Table 1, twice in a week. Then, all the measurements and tests were calculated 48 hours after the last session (15).

Statistical analysis

Descriptive statistics were used to determine the central and dispersion indicators (mean and standard deviation). Before the analysis, the normal distribution among variables was measured by Kolmogorov-Smirnov test. ANCOVA test was used to compare the variables before and after test. All statistical methods were analyzed using SPSS (version 20). The significant level for all tests was considered as $P<0.05$.

Results

This study was conducted to evaluate the effect of a 10-week aerobic exercise on cardiac function among overweight female breast cancer survivors. Of all the 250 eligible patients, 14 were assigned to the exercise group and 9 to the control group (Figure 1). The data relating to the treatment method, grade, and stage of cancer among the participants in the control and exercise groups are presented in Table 2. The majorities of participants were in stage 2 and had a moderate degree of cancer and were treated with chemotherapy and radiotherapy as well.

Anthropometric parameters and body composition of the participants in the control and exercise groups are presented in Table 3. The results of this study showed that there were no significant differences between BMI ($P=0.114$), WHR ($P=0.992$) and body fat ($P=0.052$) of patients in the control and exercise groups after 10 weeks of exercise program. However, there was a significant difference in weight ($P=0.033$) between the two groups (Table 3, Figure 2A-D).

Hematological parameters showed, no significant differences in the level of RBCs ($P=0.192$), WBCs ($P=0.899$) and hemoglobin ($P=0.546$) between the exercise and control groups after 10 weeks of exercise program. Additionally, our results showed a significant difference in the ejection fraction ($P=0.001$), PAP ($P=0.025$) and VO2max ($P=0.001$; Table 3, Figures 3A-3E) among the groups.

Discussion

In this study, no significant differences were found between anthropometric parameters, body composition and hematological parameters in the control and exercise groups. However, there was a significant difference in patients' weight between the groups. After 10 weeks of aerobic exercise, the level of VO2max was increased between the control and exercise groups. Moreover, a significant difference in the cardiorespiratory functions of patients in exercise and control groups after 10 weeks of aerobic exercise was found. Several studies have shown that moderate-intensity physical activity can reduce 34%mortality rate caused by different types of cancers including breast cancer in women. This condition is mostly related to the effect of exercise on physical functioning,

Table 1. Participants' 10 weeks' aerobic exercise program

Weeks	Main exercise time (cooling down and warming up time were not considered)	Intensity	Numbers of the chains
The first two weeks	20 min	40-50% of maximal heart rate	One block of 16 beat
The second two weeks	25 min	50-60% of maximal heart rate	Two block of 32 beat
The third two weeks	30 min	60-70% of maximal heart rate	Three block of 32 beat
The fourth two weeks	40 min	70-75% of maximal heart rate	Four block of 32 beat

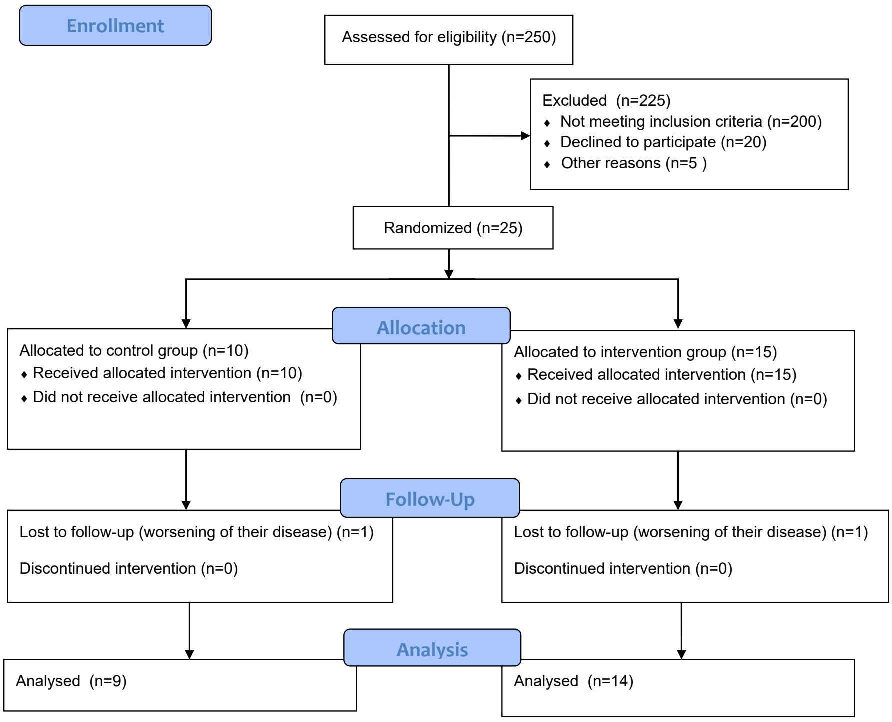

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) chart for study.

weight loss and the relevant complications (16). The American Cancer Society reported that walking, which is an aerobic exercise, can reduce 14% risk of developing breast cancer (17).

The results of this study showed that there were no significant differences between BMI, WHR and body fat of patients in the control and exercise groups after 10 weeks of exercise program. However, a significant difference in patients' weight between the two groups appears to be not in line with the results of the study by Nuri et al (18). Their study showed that 15 weeks of combined exercise (aerobic and resistance training) led to a reduction in body mass and weight of women with breast cancer (18). Mock et al reported that aerobic exercise can reduce body fat; however, Kolden et al showed that fat loss can be achieved with the combination of aerobic and resistance training (19, 20). The results of a study showed that eight weeks of aerobic and resistive training in breast cancer survivors reduced the fat on waist and neck without any significant changes

Table 2. Treatment method, grade, and stage of cancer among the participants in the control and exercise groups

Variables	Control Group (n = 9)		Exercise Group (n = 14)	
	No.	%	No.	%
Tumor grade				
Well	1	11.11	2	14.28
Moderate	8	88.88	12	85.71
Poor	0	0	0	0
Tumor stage				
T1	0	0	0	0
T2	7	77.77	11	78.57
T3	2	22.22	3	21.42
T4	0	0	0	0
Treatment				
Mastectomy	2	22.22	4	28.57
Chemotherapy	9	100	12	85.71
Radiotherapy	8	88.88	13	92.85

Table 3. Anthropometric parameters, body composition, hematological parameters and cardiopulmonary tests of the participants in the control and exercise groups

Variable	Control group Mean±SD	Training group Mean±SD	P value
Age (year)	41.44 ± 4.18	42.79 ± 7.01	0.612
Height (cm)	157.50 ± 4.96	160.92 ± 5.72	0.155
Weight (kg)	73.50 ± 23.33	74.10 ± 13.24	0.033*
BMI (kg/m^2)	28.78 ± 7.70	28.60 ± 4.96	0.114
Body fat (%)	26.41 ± 12.36	26.66 ± 7.54	0.052
WHR (m)	0. 86 ± 0.09	0.86 ± 0.05	0.992
WBC	4.10 ± 1.39	4.33 ± 1.16	0.899
RBC	4.12 ± 0.42	4.22 ± 0.26	0.198
Hemoglobin (g/dL)	11.46 ± 0.84	12.06 ± 1.033	0.546
PAP (mm Hg)	20.88 ± 2.42	20.78 ± 2.391	0.025*
EF (%)	57.22 ± 3.63	59.28 ± 2.67	0.001*
VO2Max (mL/kg/min)	39.75 ± 8.17	46.76 ± 6.52	0.001*

BMI: body mass index, WHR: waist-hip ratio, WBC: white blood cell, RBC: red blood cell, PAP: pulmonary artery pressure, EF: ejection fraction, VO2Max: maximum volume of oxygen.

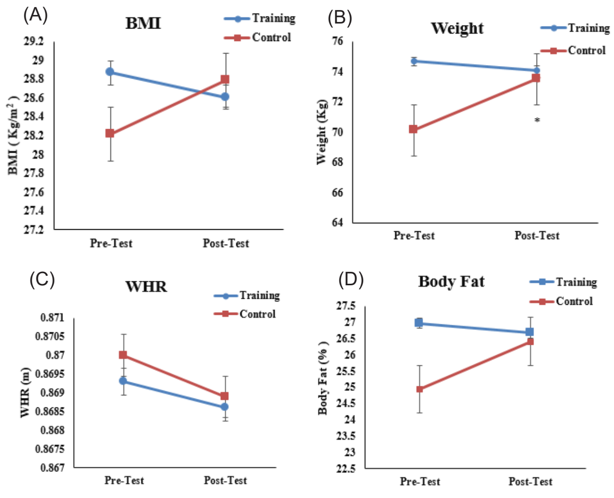

Figure 2. Participant of (A) BMI, (B) weight, (C) WHR, and (D) body fat in the control and exercise groups before and after intervention.

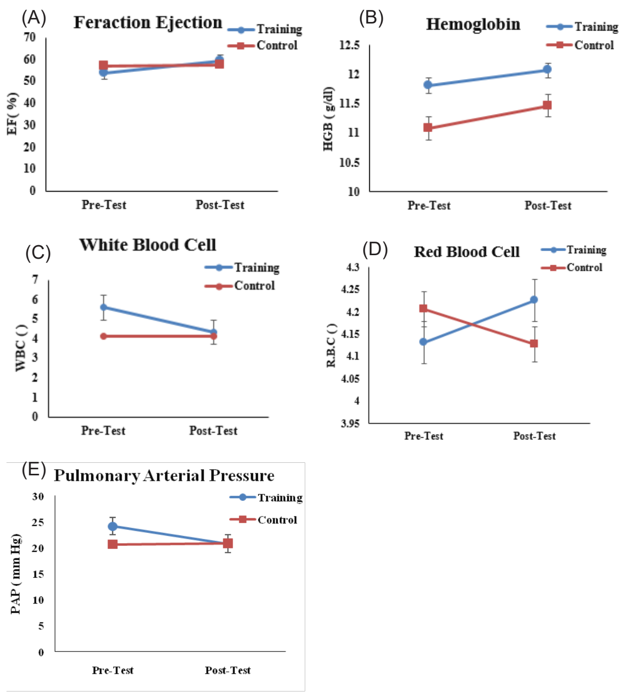

Figure 3. Participant of (A) ejection fraction, (B) hemoglobin, (C) WBC, (D) RBC and (E) PAP levels in the control and exercise groups before and after intervention.

in body weight (21). Similar to our study, Matthews et al evaluated the effect of a 12-week home-based walking intervention for breast cancer survivors. They reported an increase in the level of physical activity in the intervention group; however no significant difference in weight and body composition was detected. Physical fitness indicators are addressed as the indicators of individuals' health status, and cardiorespiratory fitness is an important matter that most people are looking forward to achieving it through physical activities (22).

Recently, many cancer survivors are at high risk of cardiovascular diseases. The treatment options for cancer are drug therapy and radiotherapy that many of these treatments have their side effects on the cardiovascular system and lead to changes in cardiac function such as changes in ejection fraction (23).

Furthermore, evidence suggests that aerobic exercise is addressed as a strong indicator for early death in normal people and patients with cardiovascular disease (22). In the present study, 10 weeks of aerobic exercise resulted in the improvement of cardiorespiratory fitness indicators, which are the ejection fraction and PAP. Then, the amount of ejection fraction was significantly increased as an indicator of heart's pumping ability. A study reported that 12 weeks of high-intensity interval training versus moderate-intensity continuous training increase the rate of left ventricular ejection fraction (24). Similar to the results of our study, Dias Reis et al evaluated the effect of exercise training and detraining in autonomic modulation and cardiorespiratory fitness in 18 breast cancer survivors. The results demonstrated that exercise can be used to prevent autonomic dysfunction in breast cancer patients, but detraining promotes loss of all autonomic benefits. Likewise, Rogers et al evaluated the effect of physical activity intervention on breast cancer survivors in a randomized clinical trial. In this study, cardiovascular fitness was significantly improved in the intervention group compared to the control group (25).

A significant improvement in the quality of life, physical fitness, oxygen consumption, and the symptoms of fatigue was observed in a study evaluating the effects of physical activity among patients with breast cancer and survivors of this disease. Therefore, exercise is considered as an effective intervention to improve the quality of life, physical fitness, physical activity and fatigue in patients with breast cancer and survivors of this disease. Studies suggest that regular exercise can increase the red cell mass and plasma volume, increase end-diastolic volume and increase intracellular and extracellular fluids, which finally leads to an increase in myocardial contractility and ejection fraction (26).

Burnham et al evaluated the effects of exercise on physiological and psychological variables in cancer survivors. The results revealed statistically significant increases in aerobic capacity, quality of life and body flexibility, and a significant decrease in body fat in the exercise group. Low- and moderate-intensity aerobic-exercise programs were equally effective in improving physiological and psychological function in this population of cancer survivors. Aerobic exercise appears to be a valuable and well-tolerated component of the cancer-rehabilitation process. Therefore, moderate-intensity aerobic exercise can be effective in the cardiorespiratory fitness among women with breast cancer (3).

Jones et al assessed the cardiovascular function (stroke volume, cardiac output, cardiac power output and cardiac reserve), BMI, lipid profile, insulin and fasting blood sugar, the levels of C-reactive protein and brain natriuretic peptide as risk factors for cardiovascular disease in postmenopausal women with breast cancer after chemotherapy and normal people at the same age as patients. The results of this study showed that cardiac output, cardiac power output and VO2 max were significantly lower in patients treated with chemotherapy rather than controls and as a result, chemotherapy will cause cardiovascular complications and loss of heart function in cancer patients (4).

Exercise generally improves the cardiovascular and respiratory systems' functions, strength, fatigue, depression and quality of life of the patient. Patient education about exercise is very effective among breast cancer patients, and participating in regular exercise can improve physiological, psychological and functional parameters (27).

Conclusion

Our study showed, that a 10-week aerobic exercise leads to an increase in VO2max. We also found that no significant changes in anthropometric parameters, body composition and hematological parameters of participants were observed after aerobic exercise. These exercises also improved the cardiac function of overweight female breast cancer survivors. Exercise also increases physical fitness and leads to positive perspective about physical conditions in the person. Therefore, it is suggested that aerobic exercises be used to improve cardiorespiratory function and increase physical activity in breast cancer survivors.

Study limitations

Our study was conducted on a limited number of patients; therefore, we suggest further studies on this subject.

Authors' contribution

Conceptualization: MKF and MS. Methodology: MKF and MS. Validation: MKF and MS. Formal Analysis: MKF and MS. Investigation: MKF and MS. Resources: MKF. Data Curation: MKF. Writing—Original Draft Preparation: MKF and MS. Writing—Review and Editing: MKF and MS. Visualization: MKF. Supervision: MKF. Project Administration: MKF & MS. Funding Acquisition: MKF.

Conflicts of interest

There are no conflicts of interest.

Ethical issues

This study was registered by the Iranian Registry of Clinical Trials website (identifier: IRCT20190218042745N1, https://www.irct.ir/trial/37684). The study was reviewed and approved by the ethical committee of Isfahan University of Medical Sciences (IR.MUI.REC.1396.2.082). Additionally, this study was extracted from M.D, thesis of Mahnaz Sourani, at the department of exercise physiology of Shahed University. Accordingly, written informed consent was taken from all participants before any intervention. Ethical issues (including plagiarism, double publication) have been completely considered by the authors.

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