Journal of Physical Activity and Hormones

(J Physic Act Horm)

Journal HomePage: *https://sanad.iau.ir/journal/jpah/*

The effect of a period of combined training on the quality of life, cancer markers, aerobic capacity, in type II diabetic patients after breast cancer surgery

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Keywords
Breast Cancer, Diabetes, Quality of Life, Combined Exercise Training, CA15-3.

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Received: 29 Agu 2024; **Revised:** 30 Sept 2024; **Accepted:** 30 Oct 2024

DOI:
https://doi.org/10.71878/jpah.2024.1184722

Abstract

Introduction: The principal aim of this study was to investigate the effect of a period of combined exercise training on the quality of life, cancer markers, and aerobic capacity in type II diabetic patients after breast cancer surgery.

Material & Methods: The subjects were 30 women with cancer and type II diabetes (mean age 50.53 ± 7.62 and weight 69.20 ± 19.14) who were selected for initial screening and were divided into two equal experimental, and control groups. The aerobic-resistance training consisted of three sessions per week for 8 weeks. The resistance training was performed using Pilates and aerobic exercises with a maximum heart rate (HR max) of 50-70% and each intervention session lasted 60 minutes. Tumor markers (CA15-3 and CEA), anthropometry characters (weight, body mass index, and body fat percent), Quality of life, and aerobic power were measured. To compare the pre and post-test results in each group, the statistically correlated t-test, and the independent t-test was used to compare the results of the two groups. The significance level was determined as $P < 0.05$.

Results: The results indicated that there is a significant promotion in quality of life between the two groups and in the experimental group (EG) was higher than the control group (CG) ($P < 0.05$). The results also demonstrated that there was a significant decrease in the cancer markers of CA15-3 among the two research groups and there was a significant decrease in the EG ($P < 0.05$), however, this difference was not significant in CEA markers ($P > 0.05$). No significant differences were observed in other variables. ($P > 0.05$).

Conclusion: It can be concluded that eight weeks of combined exercise training in women with type II diabetes after breast cancer surgery were effective in the promotion of quality of life, and decreased BMI and CA15-3 but it was unchanged in CEA, WHR, aerobic power, weight, and fat%.

1. Introduction

Cancer is a critical global health concern since it is the world's most common non-communicable disease and the second major cause of death (1). Breast cancer is the most common type of cancer with a risk of 8% to 10% in women and includes 25% of all cancers and is the most common cause of cancer death among women. This cancer starts from breast tissue. Some methods such as mammography and needle sampling have increased the rate of diagnosis of this disease (2). It has been known for years that some breast cancers respond to hormonal treatments. Today, it has been proven that about half of breast cancers have estrogen and

progesterone receptors on tumor cells, which cause tumor growth in the presence of the above hormones (3). Several studies show that breast cancer patients who are estrogen receptor positive have a longer life span with anti-estrogen treatments than patients without the above-mentioned receptor. Today, measuring the amount of estrogen and progesterone receptors is widely used for therapeutic purposes and determining prognosis in breast cancer (4). Breast cancer is divided into different types based on the origin and the effect it has. The most common type of breast cancer is the invasive cancer of the milk ducts, which originates from the cells of the milk ducts and spreads outside the ducts, i.e. the supporting tissue around them. Over time, cancer cells may spread through the lymphatic system or bloodstream to the lymph nodes or other organs of the body. This type of disease includes approximately 85% of all breast cancer cases. Invasive cancers with the origin of breast lobules start from inside the breast lobes that produce milk when needed, and like the previous type, they can be spread by blood or Lymph to other parts of the body. About 12% of breast cancer cases originate from the lobules or lobes of the breast and are among this group (5). The main causes and factors involved in breast cancer can be sex, age, personal factors, family history (not having children), menopause after 55 years old, geographical difference, inactivity, suffering from other cancers, diet (fat and meat), obesity, alcohol and cigarette consumption, benign breast diseases, type of breast tissue, individual personality, hormonal deficiency, (premature menstruation and under 12 years old), pregnancy at an advanced age, breast density, race, genetic changes and Job mentioned(6, 7). Diabetes or sugar disease is a metabolic disorder in the body. In this disease, the ability to produce insulin hormone in the body is lost or the body becomes resistant to insulin and therefore the produced insulin cannot have its normal function. The main role of insulin is to lower blood sugar by different mechanisms (8, 9). In type 2 diabetes, there is a progressive resistance of the body to insulin, which may eventually lead to the destruction of pancreatic beta cells and complete failure of insulin production. In type 2 diabetes, it is clear that genetic factors, obesity, and inactivity play an important role in a person's disease (10, 11). Symptoms of diabetes include; Thirst, vision changes, fatigue, profuse urination, infection, and hunger. Complications of diabetes include; Peripheral vascular disease, retinopathy, stroke, neuropathy, and nephropathy (1). In people who have breast cancer and their treatment is long, there is a possibility of getting diabetes, even in people who already have diabetes, this disease will increase when they get breast cancer. In addition, statistics have shown that people with diabetes have the possibility of getting breast cancer, and about 20% of these people get breast cancer. Estrogen resistance in the stages of chemotherapy in people with breast cancer is considered one of the causes of diabetes in these people. The use of some drugs such as glucocorticoid in chemotherapy increases the blood sugar of a person, the use of these drugs is to prevent inflammation and nausea. When the body becomes resistant to insulin, it becomes susceptible to the spread of diabetes and various types of cancer, which may occur in people who have breast cancer. Also, in diabetic people, breast tissue changes due to the increase in insulin levels. Which increases the risk of breast cancer. Statistics have shown that people who have advanced breast cancer and diabetes at the same time have larger tumors than other people with breast cancer, and the possibility of spreading the disease (both diabetes and cancer) is higher in these people(12, 13). In research on the relationship between diabetes mellitus and the risk of breast cancer, the results showed that diabetes can be considered a risk factor for breast cancer. In addition, menstrual status and geographical distribution can affect this relationship (12). Breast cancer in Iran is the fifth most common cause of death related to cancer. According to the statistics published in Iran, about 6160 new cases of breast cancer are detected every year, of which 1063 cases lead to death. Also, Iranian women get breast cancer at least 10 years earlier than women in developed countries (14, 15). The occurrence of this cancer can be related to age factor and modernization of lifestyle. Statistics show that only 5% of this type of cancer occurs under the age of 40 (16). Today, in developed countries, new fields have been formed about physical activity, which is known as a therapeutic approach. There is valid evidence that physical activity plays an important role not only in preventing the recurrence of the disease but also in reducing the risk of cancer. In this regard, physical activity is known as an important factor in improving some cancers, including breast cancer (17) It has been shown that exercise can protect the body against harmful substances. Exercise can strengthen mitochondrial activity in all areas of the body, improve oxygen flow, and increase blood pH (17). Breast cancer patients experience many problems in different dimensions of quality of life, including emotional and social functioning, during and after treatment. Examining the quality of life is one of the important indicators of treatment and care all over the world. Quality of life is the degree of people's feelings about their abilities in physical, emotional, and social functions (18). Anxiety and depression reduce the quality of life of people with breast cancer. In general, compared to other women's cancers, patients with breast cancer have longer survival after the diagnosis, but nowadays it is not only the patient's survival that is considered, but patients want a good quality of life. Anxiety, depression, and mental distress are common among most cancer patients (19). Quality of life-related to health and age, marital status, job, income, education, type of breast surgery, duration of disease diagnosis, length of time after breast surgery, duration of completion of chemotherapy and completion of radiotherapy (20). Patients with breast cancer do not have proper aerobic fitness and their physical activities are less than healthy people, so it is necessary to prescribe exercise training activities for these patients. Considering the low level of aerobic capacity of cancer patients and considering the effect of exercise training in this field, it can be concluded that with 24-week, 12-week, 6-week, and even 3-week training, the aerobic capacity of patients can improve inactivity and obesity can be declared as the main reason for the low aerobic fitness of these patients(20).Previously, Koulaei et al. showed that 8 weeks resistance- endurance exercise training can significant reduce body mass index, promotion of glucose homeostasis (attenuate FBS, HOMA_Ir, and HbA1c) and increase the upper limb ROM in women with type II diabetes in BC survivors (21). Hormonal imbalance and high levels of CE 3-15 exist in people with breast cancer. Exercise training reduces this hormone (18). Although the incidence of breast cancer in Iran is slightly lower than neighboring countries, it has significant statistics compared to developed countries. But it has a fast increasing trend that it is necessary to think about it from now on and to determine the factors

related to the occurrence of breast cancer by conducting studies so that the occurrence of this disease can be controlled by informing society, especially women over 45 years old. It is not possible to prevent its occurrence yet, and it is only possible to control and treat this disease with a quick and timely diagnosis (22). Therefore, the present study aims to investigate whether combined resistance- endurance exercise affects quality of life, and cancer markers in breast cancer patients who are scheduled for adjuvant treatment. It was hypothesized that quality of life, cancer markers, insulin resistance, and BMI would be superior after intervention in patients receiving resistance and aerobic exercise as part of adjunctive therapy compared to standard therapy alone.

2. Methodology

2.1. Materials and methods

The current research is a semi-experimental study with a pre and post-test design with 30 females in the range of 35 to 65 years, who volunteered to participate as subjects. These females (with diabetics and a history of breast cancer surgery) were divided into 2 equal experimental groups: EG; who performed combined exercises), and control groups (CG); who did not have any type of intervention, voluntarily cooperated with the researcher for 8 weeks (Table 1). Before the implementation of the exercise protocol, a briefing session was held in the physician's office to explain the risks and benefits of participating in the research, they completed the personal profile forms, exercise training medical record questionnaire, and the written informed consent form. This study was approved by the ethics committee of the Rasht Branch, Islamic Azad University, with code IR.IAU.RASHT.REC.1396.156. To control the diet, the subjects were asked to record their food consumption for 72 hours (one holiday and two non-holiday days) in separate forms. During the study, food notes were repeated three times and the amount of food consumed was recorded. They were advised to avoid overeating. Fruits and vegetables should be consumed at least once per meal, and more grains should be used in meals. From both groups before and after 8 weeks of the training period, measurements of body composition, aerobic capacity test, blood pressure, heart rate, and blood sugar were taken. Also, blood samples were taken from the people of each group 3 days before the start of the training period and 48 hours after the last training session. The inclusion criteria included informed participation in the study, confirmation of breast surgery, completion of chemotherapy, and the ability to do exercise training with the help of an oncologist. Two days before the start of exercise training, both groups visited the Exercise Physiology Laboratory at Islamic Azad University and had taken anthropometry measurements. To measure aerobic power, the Rockport test was performed using a treadmill.

Table 1. *Summary of the research method*

Groups	Exam	intervention	Exam
Experimental (N=15)	pre-test	8 weeks of combined training	post-test
Control (N=15)	pre-test	No intervention	post-test

2.2. Participants

The statistical population of this research consisted of 422 females with breast cancer who visited the Iran Clinic Radiotherapy in Rasht city. Finally, 30 subjects declared their readiness and participated in the relevant tests for 8 weeks until the end of the research. Inclusion criteria were: did not have cardiovascular, skeletal, liver, or blood diseases; did not smoke or drink alcohol, and had no exercise training background, and excluding criteria include: injury during exercise training or change in treatment plan (recurrence of the disease leading to chemotherapy, radiation therapy) or unwillingness to participate in exercise training programs.

2.3. Measurements

Assessment of quality of life: A questionnaire was used to measure the quality of life questionnaire WHO-Qol. This questionnaire consists of three parts of WHO-QoL to measure the quality of life of the subjects. It consists of 26 questions to measure overall quality of life. This scale was created in 1996 by a group of experts of the World Health Organization and by adjusting the items of the 100-question form of this questionnaire.

Measurement of cancer markers: All the subjects went to the laboratory at the same time (8:00 a.m.) while fasting for 12 to 14 hours (23). Five ml of blood was taken from the right brachial vein in a sitting position from each sample. The quantitative diagnosis kit (Monobind Inc, USA) was used to measure Carcinoembryonic Antigen (CEA) and cancerCA15-3) by ELISA method.

Measurement of aerobic power: The subjects covered a distance of 1609 meters using a treadmill model Turbo 2200 made in Taiwan. Participants were taught the walking test, which required them to walk a mile as fast as possible. Taking the pulse of the participants in the test for one minute and using the pulse, the heart rate of the subjects was determined and recorded. Aerobic power for females was calculated using the following equation:

Maximum oxygen consumption (VO2max) = 88/768+8/892 - 0/0957 × body weight-1/37/45 × time – 0/1194× heartbeat.

2.4. Intervention

Exercises for patients include 10 minutes of warming up in the form of stretching and softening of different parts of the body, then using a treadmill and exercise bike with an intensity of 50-70%, and then using yellow and red elastic bands, size 15x20 cm, which starts with the yellow band. which is equivalent to 1 kg with an elasticity of 40 cm and the red elastic band which is equivalent to 1.6 kg with an elasticity of 42 cm from the first to the fourth week and an increase in the number of 10-15 repetitions in 3-5 sets of movements from 4 movements to 9 movements and a rest time of 30 to 60 seconds and a duration of movements of 20 minutes.

Resistance exercises: Exercises were done with yellow elastic bands while standing and sitting on a chair and the wall. These exercises were done with a focus on the stability of the spine and increasing the lymph flow through the continuous contraction of the muscles in the lymph nodes, and hand and arm movements in all positions slowly and activities that caused rapid pumping of the lymph flow (to The arm face, closing the hands and moving the wrists) done (24). They are given recommendations such as walking for a day between 30-60 minutes and movements that increase the range of motion of the hands and pump more lymph. The types of movements include opening the elastic band in front of the chest, above the head, and on the sides, stretching the

triceps muscle and lateral stretching of the scapula muscle, and stretching the arm muscle with a gym band and push-ups on the wall, squat movement, and then from Week five to eight. The number of repetitions of the movements started from 10 repetitions and gradually increased to 15 repetitions with a red elastic band. These movements were performed standing, sitting, and lying down. The last 10 minutes of the exercise were devoted to cooling down with stretching movements such as stretching the arms to the sides, stretching the hands above the head, and stretching the quadriceps.

Aerobic exercises: After the resistance training, the program of aerobic exercises including 20 minutes using a treadmill and exercise bike was performed. Aerobic exercise stress tolerance was measured using the 6-20 Borg scale. The members of EG used treadmill and stationary bikes as aerobic exercise three times a week for 8 weeks with moderate intensity (50-70% of HR $_{max}$). In the first to fourth week of the study, each training session included 20 minutes of exercise training (50% HR_{max}), and then its intensity increased to 60% in the fourth week. From the fourth to eighth weeks, the intensity of exercise promoted to 70% of HR_{max}. The daily activities of the subjects remained constant in the control group Table 2.

Table 2. *Resistance and aerobic exercise program*

Aerobic exercises						Resistance exercises		
duration (min)	intensity (%HR_{max})	seconds	rest_sec	Number of rep	set number	Number of movement	Band paint	week
20	50-60	20	60-30	15-9	5-3	4-7	Yellow	1-4
20	70-60	20	60-30	15-9	5-3	4-7	red	4-8

2.5. Statistical Methods

In this research, descriptive statistics and inferential statistics were used. In addition to the mean, standard deviation and graph, the Shapiro-Wilk was used to determine the normality of the data distribution. To determine the significance of the intra-group mean difference between groups, the paired t- test was used, and the independent t-test was used to compare the differences between groups. All statistical analysis in this research was done with SPSS statistical software (version 21) and at a significance level $\leqslant$ 0.05.

3. Results

Table 3 presents the values before and after 8 weeks of exercise training for body composition and blood markers.

Table 3. *Body composition, Cancer marker, Quality of life, aerobic power values in EG and CG (n=15 in each group)*

variable	group	Pre-test M±SD	Post-test M±SD
body weight (kg)	EG	69.66±19.14	67.73 ± 9.66
	CG	67.88 ±15.23	68.06 ± 15.03
BMI(Kg/m^2)	EG	27.13 ± 2.51	26.60 ± 2.46
	CG	27.54 ± 2.85	27.76 ± 2.87
Fat (%)	EG	37.30 ± 5.10	36.92 ± 4.96
	CG	36.90 ± 4.84	36.90 ± 4.90
WHR	EG	0.81 ± 0.06	0.81± 0.05
	CG	0.83 ± 0.12	0.83 ± 0.11
CA15-3	EG	20.52 ± 8.65	22.52 ± 8.47
(micrograms /mil)	CG	22.39 ± 8.18	22.19 ± 8.03
CEA	EG	1.09 ± 0.40	1.39 ± 0.22
(micrograms/ mil)	CG	1.36 ± 0.38	1.32 ± 0.33
quality of life	EG	56.60 ± 5.12	51.00 ± 3.38
	CG	50.67 ± 3.37	50.61 ± 3.38
aerobic power	EG	28.07 ± 4.73	28.00 ± 4.49
(ml/kg/min)	CG	28.00 ± 4.32	28.00 ± 4.13

WHR, waist to hip circumference; BMI, Body Mass Index; experimental group, EG; control group, CG

Since the Shapiro-Wilk test showed a normal data distribution, paired and independent t-tests were used to test the research hypotheses (Table 4).

Table 4. *Paired t-test results of body composition values, Cancer marker, Quality of life, and aerobic power values in EG and CG (n=15 in each group)*

variable	**Group**	**Pre-test M±SD**	**Post-test M±SD**	**t**	**sig**
weight(kg)	EG	69.66±19.14	67.73±9.66	1/51	0.153
	CG	67.88±15.23	68.06±15.03	-1.01	0.396
WHR	EG	0.81±0.06	0.81±0.05	1.09	0.294
	CG	0.83±0.12	0.83±0.11	-0.26	0.797
fat %	EG	37.30±5.10	36.92±4.96	3.13	0.797
	CG	36.90±4.84	36.90±4.90	0.02	1.00
BMI(kg/m^2)	EG	27.13±2.51	26.60±2.46	5.35	0.001*
	CG	27.54±2.85	27.76±2.87	1.63	0.123
CA15-3(U/ml)	EG	22.52±8.47	20.53±8.65	0.319	0.006*
	CG	22.19±8.03	22.39±8.18	-1.38	0.189
CEA(ng/ml)	EG	1.39±0.22	1.09±0.40	2.55	0.023*
	CG	1.32±0.33	1.36±0.38	-1.02	0.323
quality of life	EG	51.00±3.38	56.60±5.12	-5.07	0.001*
	CG	50.61±3.38	50.67±3.38	-0/43	0.670
aerobic power	EG	15.20±0.87	21.62±1.43	-0.435	0.052
(ml/kg/min)	CG	20.00±4.13	20.23±4.32	0.00	1.00

The results of the above table showed that compared to the experimental group's pre-test, QOL increased significantly, and BMI, CA15-3, and CEA decreased significantly.

The results of the independent t-test between groups are presented in Table 5.

Table 5. *Independent t-test results in pre and post-test of body composition, Cancer marker, Quality of life, aerobic power values in EG and CG (n=15 in each group)*

variable	Pre-test			Post- test		
	Difference of means	T	sig	Difference of means	t	sig
Weight (kg)	0.713	0.394	0.697	0.713	1.811	0.081
WHR	0.04	0.220	0.828	0.74	1.87	0.08
fat %	0.003	-0.421	0.308	0.003	1.04	0.308
BMI(kg/m^2)	0.015	-0.421	0.671	0.740	1.815	0.001*
CA15-3(U/ml)	0.333	0.111	0.913	2.20	3.42	0.004*
CEA(ng/ml)	0.069	0.578	0.568	0.264	1.85	0.082
quality of life	0.392	0.317	0.392	5.92	3.73	0.001*
aerobic power (ml/kg/min)	-1.47	3.23	1.00	-1.47	-1.00	0.3

The results of the independent t-test showed no significant difference in all variable in the pre-test. However, the results of the independent t-test in the post-test indicated a significant decrease in the EG compared to the CG in BMI, CA15-3, and QOL.

4. Discussion

Breast cancer is considered the most common cancer in women (25).Physical activity has been considered an approach to limit adverse outcomes and improve quality of life for patients with breast cancer (26). As the most common form of cancer in women worldwide, BC is often treated with a variety of approaches, including surgery, radiotherapy, chemotherapy, and targeted therapy. As the clinical field has evolved, survival rates for BCS have improved dramatically.

Our research was carried out with the aim of the effect of combined exercise training on the QOL, cancer markers, and aerobic capacity of type 2 diabetic patients after breast cancer surgery. This research was a clinical trial study with a pre and post-test design in which 30 patients with an age range of 35 to 65 years old participant volunteered.

The findings of the present study indicated that eight weeks of combined aerobic-resistance training exercise was effective in reducing BMI, CA15-3, and QOL in type 2 diabetic patients after mastectomy surgery. These results were consistent with the results of Bukan et al. (2016) and inconsistent with the findings of Ochalek et al. (2018). The reason for the contradiction is that it was done on people with cancer, while the subjects of our research were studied after completing the treatment process, which in itself can be effective in reducing cancer markers of type 2 diabetic patients after breast cancer surgery, the results obtained from the statistical analysis showed that CA15-3 variable had a significant decrease under the influence of combined exercises But concerning the CEA marker changes were not significant. The current research on the CA15-3 marker was consistent with the research of Esfahabdi et al. (2018). The effect of combined exercises (aerobic-resistance) on the aerobic capacity of type 2 diabetic patients after breast cancer surgery the findings related to aerobic endurance showed that this variable did not change significantly in the research subjects after 8 weeks of combined training. While there was a significant difference in the research of Esfahabdi et al. 2016. Among the possible reasons for the disparity, we can point out the duration and intensity of the exercises, and the method of exercises in our studies, which mostly focused on aerobic exercises. Schneider 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 cardiorespiratory fitness among women with breast cancer (27).

Physical exercise also contributes to improving the general health, QoL, mental health, and physical function of cancer survivors (28). It is effective in reducing and preventing adverse effects of breast cancer treatment with HT, such as anxiety, depressive symptoms, fatigue, health-related quality of life, lymphedema (without worsening) physical function, bone health, and sleep(29).

The potential benefits of exercise in improving the quality of life of breast cancer survivors have been reported in studies (30). In a systematic review based on 26 RCTs, Hong et al. concluded that exercise intervention substantially improved the quality of life of breast cancer survivors, and the improved quality of life was associated with “time of session” (31). Another meta-analyses also found that exercise intervention improved the quality of life in breast cancer survivors, including social well-being, functional well-being, emotional well-being, physical well-being (32), mental health, and general health. However, this meta-analysis indicated that exercise intervention tended to increase the physical health summary score (PHS) or the mental health summary score (MHS) of overweight/obese breast cancer survivors, but did not reach statistical significance. The differences in the number of included studies might partly explain such inconsistent conclusions as only two studies reporting the differences in PHS or MHS of overweight/obese breast cancer survivors between exercise and control groups were included (33). On the other hand, the quality of life of breast cancer survivors is heavily influenced by the treatment (e.g., selective estrogen receptor modulator), which may cause a series of physical and psychological impairments (34). The relatively small sample size are limitation of the present study, and didn’t evaluate spontaneous PA with accelerometry.

5. Conclusion

The results of the present research showed that 8 weeks of combined training in women with type 2 diabetes after breast cancer surgery was able to affect the quality of life variable and concerning cancer markers, the decrease variable and CA15-3 marker were unchanged. No significant change was observed in aerobic endurance after these exercises. Overall, the results of this research showed that 8 weeks of combined exercises can be beneficial to lifestyle and CA15-3 cancer markers in women with diabetes after breast cancer surgery.

6. Acknowledgment

Researchers hereby thank and appreciate all the women for their participation in this research.

Conflict of interests: The authors declare that they have no conflict of interest relating to the publication of this manuscript.

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