



## Research article

## Effect of exercise on depression and fatigue in breast cancer women undergoing chemotherapy: A randomized controlled trial

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## ABSTRACT

**Background:** Depression and fatigue are common consequences of breast cancer that lead to dysfunction and reduced quality of life of patients. The aim of the present study was to determine the effect of exercise program on depression and fatigue in breast cancer women undergoing chemotherapy.**Methods:** This randomized controlled trial study was performed on 60 breast cancer women undergoing chemotherapy in Kermanshah hospitals from 2017-2018. Participants were selected using convenience sampling and were randomly divided into intervention and control groups. Data collection tools included demographic information form and standard Beck depression inventory (BDI-II) and fatigue severity scale (FSS). The intervention group performed the 20-30-minute indoor exercise program 3 sessions a week for 6 weeks. Questionnaires were completed before, immediately, and one month after the intervention by both groups and data analysis was carried out using SPSS ver.22.**Results:** There was no statistically significant difference between the two groups in terms of the mean fatigue intensity and depression scores before the intervention; however, the mean fatigue intensity scores were significantly decreased in the intervention group as compared to the control group immediately and one month after the intervention ( $P = 0.001$ ). There was no statistically significant difference between the two groups in terms of mean depression score immediately and one month after the intervention ( $p > 0.05$ ).**Conclusion:** Considering that indoor exercises reduced fatigue in breast cancer women undergoing chemotherapy, patients are recommended to perform exercise interventions as a non-pharmacological, safe, easy, and non-invasive solution to improve their physiological capacities and functional abilities as well as Quality of life. On the other hand, since exercise program had no effect on depression among breast cancer women in the present study, longer studies with larger sample size are recommended.

## 1. Introduction

Breast cancer is the most common malignant neoplasm among women and is the second leading cause of cancer-related death. The incidence of breast cancer has increased dramatically in recent years [1, 2]. In Iran, breast cancer is one of the most frequent malignancies in women and accounts for 24.6% of all cancers [3].

Diagnosis and treatment of breast cancer have significant physiological impacts on women [4, 5]. Chemotherapy as one of the oldest and most common treatments for breast cancer is associated with a number of side effects that disrupt the physical, social, and role functions of cancer

patients and have a significant impact on their quality of life (QoL) [6]. Fear of death, frustration, and low QoL due to treatment may increase patients' negative feelings and attitudes [4, 7].

Depression is also one of the most common psychological problems that occurs in most patients with cancer [8, 9]. According to various studies, the prevalence of depression is 9.3%–56% in breast cancer women. Epidemiological studies have shown that depression is associated with dysfunction and decreased patient survival [10]. One third of these women suffered from psychological conditions such as depression [11, 12]. Fatigue is also another common symptom experienced by cancer patients and causes significant impairment in their QoL [13].

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Fatigue is a mental, persistent, and unpleasant feeling in the form of physical, emotional, and cognitive fatigue occurring due to cancer or related therapies [14]. Studies show that 99% of breast cancer women undergoing chemotherapy experience fatigue [15]. Cancer-related fatigue is characterized by symptoms of physical exhaustion, decreased activity, lack of energy, and depressed mood [16].

Considering that women play a vital role in the family, and that the problems caused by breast cancer destabilize not only the individual but also other family members, therefore, it seems important to recognize the moderating factors which may improve physical and mental function and reduce dysfunction [16]. Therapeutic interventions in cancer patients fall into two categories: pharmacological and non-pharmacological [17] and evidence shows that physical activity is a safe, easy, and relatively inexpensive alternative to controlling depression in cancer women and increases survival rate and reduced recurrence of the disease [18]. Physical activity is effective in improving the physical and mental function of cancer patients and thus increasing their QoL during and after treatment by increasing muscle strength, improving cardiopulmonary function, reducing fatigue, anxiety, depression, and increasing bone density [19]. Friedenreich et al. (2016) showed that physical activity reduces cancer-related mortality rate by 37% [20]. Baruth et al. (2015) also showed that walking reduces fatigue and increases QoL of breast cancer women [21].

Considering that there have been few studies on the effect of exercise on certain diseases such as breast cancer in our country, and most of research have focused on drug and invasive treatments, there is a gap regarding the effect of exercise on this disease. Therefore, the present study aimed to determine the effect of exercise program on depression and fatigue among breast cancer women undergoing chemotherapy. The present study is one of the few studies conducted in Iran to investigate the effect of exercise on anxiety and depression among women with breast cancer, and this is the major novel contribution of this study.

## 2. Methods

### 2.1. Study design and setting

This is a randomized controlled trial with pre- and post-test design (IRCT20130812014333N86), which received an ethics code from the Ethics Committee of Kermanshah University of Medical Sciences (IR.KUMS.REC.1396.508). The research settings included Imam Reza and Ayatollah Taleghani hospitals in Kermanshah.

### 2.2. Participants

The statistical population included women with breast cancer undergoing chemotherapy referred to the Oncology Ward of the clinics of aforementioned hospitals. The researcher undertook available sampling of patients who met the inclusion criteria from two oncology clinics in Kermanshah city. Sample size was calculated based on the formula for comparing a quantitative trait in two groups, taking into account 95% confidence interval ( $1-\alpha$ ), test power 90% ( $1-\beta$ ) and based on the results of the study of Taso et al. [22]. Taking into account the possibility of drop-out among the participants, the sample size was increased by 10% and a total of 60 people ( $N = 30$  people per group) were estimated. Samples were selected using convenience sampling method. The samples were randomly assigned into control and intervention groups. For the random allocation, simple randomization method was used. Briefly, the researcher wrote 60 consecutive numbers on separate papers and placed them inside a container. The selected even numbers were assigned to group A and odd numbers to group B. Next, groups A and B were randomly assigned into either intervention or control groups by the researcher (group A = exercise program, group B = control) (Figure 1).

**Inclusion criteria.** Women with early stage breast cancer (0, 1, 2, and 3), age between 18 and 54 years, undergoing chemotherapy according to the therapeutic protocol (one cycle of chemotherapy is 21 days), not receiving another type of treatment (radiotherapy, hormone

therapy, etc.) concurrent with chemotherapy, literacy of reading and writing, no psychological disorder or dementia, cardiovascular, pulmonary, renal, and hepatic disease, or meta-stasis to the bone and brain, no participation in other group or relevant programs, and no history of doing exercise regularly in the past. The patients whose depression scores ranged from 0 to 13 (minimum score and no depression) as well as from 14 to 19 (mild depression) according to Beck-2 depression questionnaire were included. More importantly, they had the ability and willingness to participate in the study.

**Exclusion criteria.** The patients who had no willingness to participate in the research or continue the exercise activities; those who were not able to perform the activities according to their own statements or a sports physiotherapist; absence in three consecutive sessions or for nonconsecutive sessions of the exercise sessions. In this study, the patients whose depression had scores of 20–28 (moderate depression) and 29–63 (severe depression) according to Beck-2 depression questionnaire did not meet the inclusion criteria.

The purpose of the present study was explained to each patient and patients were assured that their information would be kept confidential and written consent was obtained from them to participate in the study.

### 2.3. Instruments

Beck Depression Inventory (BDI-II) was used to measure depression. This questionnaire consists of 21 items and each item is assigned 0–3 scores. The possible score range is 0 and 63 [23], with scores 0–13, 14–19, 20–28, and 29–63 indicating no depression, mild depression, moderate depression, and severe depression, respectively. Beck et al. (1961) reported that the internal consistency of the instrument for the patient and the non-patient groups was 73–92% (average: 86%) and the reliability value was also  $\alpha = 86\%$  and  $\alpha = 81\%$ , respectively [24]. The reliability of the above instrument was measured in Iran ( $\alpha = 78\%$ ) and had acceptable reliability over time ( $\alpha = 73\%$ ) [25].

Fatigue severity scale (FSS) was used to measure patients' fatigue. This instrument measures general fatigue quickly in patients and the score is completely proportional to the patient fatigue intensity [26]. This scale consists of 9 items scored based on an 8-point Likert scale, ranging from absence of fatigue = zero to severe fatigue = 7. Severe and mild fatigue are represented by scores  $>40$  and  $\leq 40$ , respectively. The validity and reliability of this instrument have been confirmed in Iran [27, 28]. Demographic data were collected by reviewing patients' clinical cases and using a demographic information questionnaire.

### 2.4. Intervention

Before starting the intervention, in order to ensure that exercises are performed correctly, intervention group patients ( $n = 5-10$  per group) attended face-to-face sessions at Razi University of Physical Education in Kermanshah, Iran. The researcher, an exercise physiologist, and a physiotherapist also attended these sessions. The exercise videos and a brochure containing exercises were given to patients to watch them at home, and then perform 30-minute exercises 3 days a week for 6 weeks 72 h after each chemotherapy course (2 chemotherapy cycles). The exercise program along with a slow-rhythm music in the form of a video and an educational brochure was prepared in collaboration with an exercise physiologist and a physiotherapist in accordance with the patients' physical conditions. In each 30-minute training session, exercises included 5-minute warm-up and stretching exercises, dynamic exercises (walking, running, and jumping jacks) and resistance band exercises and balance exercises for 20 min, and cool down exercises for 5 min. The movement chains included very simple and gentle movements.

During the exercise program, the researcher contacted the subjects by phone and also held a face-to-face session for the patients in the intervention group (a total of three face-to-face sessions for the patients in the intervention group. And finally each patient in the intervention group attended one face-to-face session). Patients in the control group did not

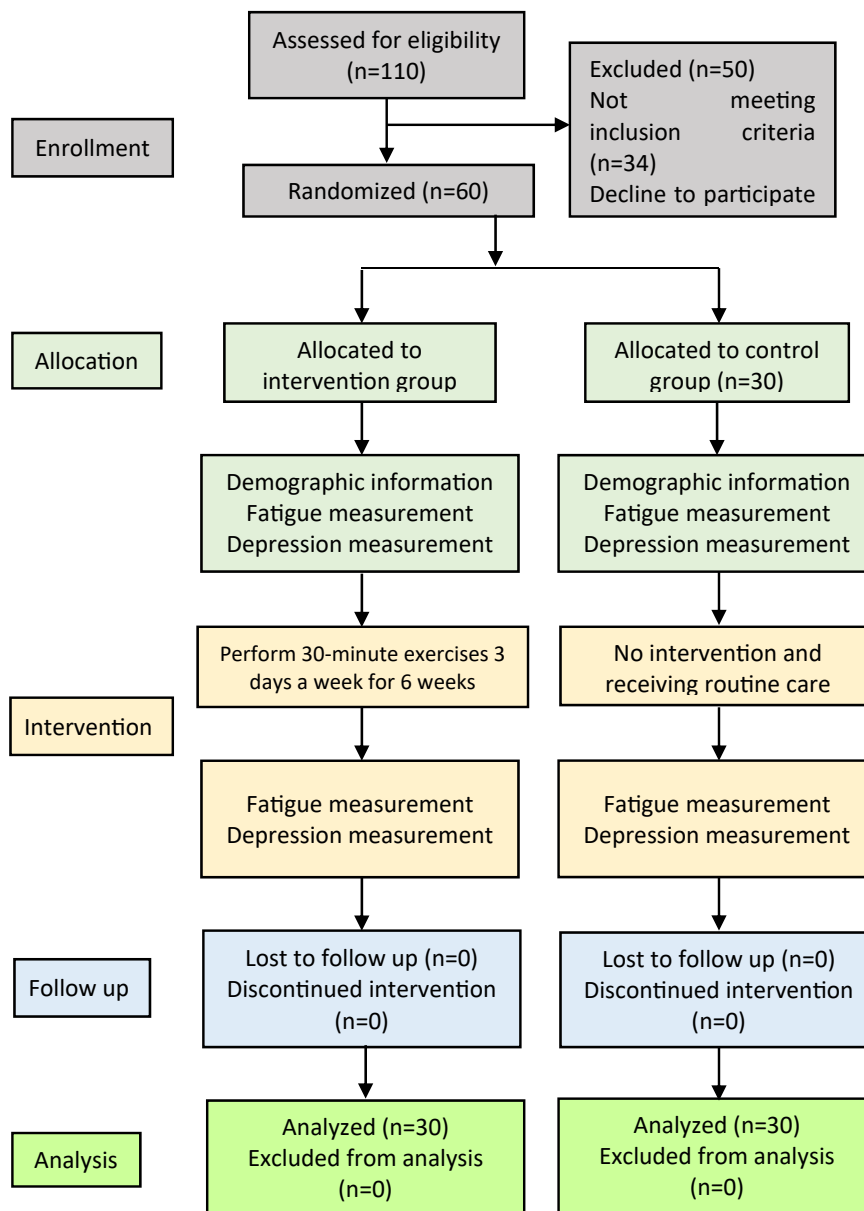


Figure 1. Consort flow diagram of the study.

exercise at this time. Questionnaires were distributed among the two groups by a researcher colleague before, immediately, and one month after the intervention. The control group received routine care and no phone contact was made for this group. In order to observe the ethical principles, educational videos, and brochures were provided to the control group after the research.

All subjects in both groups remained until the end of study and none of them quit the research process. In order to make sure the subjects would follow the study guidelines and conduct the exercises at home, in addition to phone monitoring by the researcher, a checklist was provided to the patients in the intervention group which would record their activity including tables covering seven days of the week. They could record the frequency of doing exercises over the week as well as the hour of beginning and finishing the exercise. Thereafter, the researcher checked and recorded all these through phone and by receiving images of the checklist from the patients. In this study, all participants in the intervention group performed three sessions of exercise completely per week, each week 20–30 min for 6 weeks.

2.5. Data analysis

Data analysis was carried out using SPSS ver. 22. Quantitative variables were expressed as mean and qualitative variables were expressed as frequency (number and percentage). First, the Kolmogorov-Smirnov test was used to evaluate the normality of quantitative data distribution. Analytical tests (Mann–Whitney U-test, Friedman, and repeated measures ANOVA) were used to analyze and compare data obtained in two stages after the intervention (immediately and one month after the intervention).

2.6. Ethical considerations

This study was approved by the Ethical Committee of the Kermanshah University of Medicine Science (approval number KUMS.REC.1396.508) and was recorded in the Iranian Registry of Clinical Trials (IRCT20130812014333N86). Written informed consent was provided by all participants.

### 3. Results

There was no significant difference between the intervention and control groups in terms of demographic characteristics before the intervention (Table 1).

The effect of exercise on fatigue was evaluated as the primary outcome, while the impact of exercise on depression was assessed as the secondary outcome. There was no significant difference between the intervention and control groups in terms of the mean fatigue intensity scores before exercise intervention ( $47.23 \pm 9.43$  versus  $49 \pm 7.28$ ,  $P = 0.59$ ); however, a significant difference was observed between the two groups in terms of the mean fatigue intensity score immediately ( $41.3 \pm 9.40$  versus  $50.16 \pm 9.96$ ,  $P = 0.001$ ) and one month after the exercise intervention ( $40.90 \pm 9.20$  versus  $50.40 \pm 9.83$ ,  $P = 0.001$ ). Data analysis showed that exercise program statistically reduced the mean fatigue intensity score immediately and one month after the intervention in the intervention group (95 % CI,  $P = 0.001$ ). There were also no significant changes in the mean fatigue intensity score in the control group ( $P = 0.07$ ) (Table 2).

There was no statistically significant difference between intervention in the intervention and control groups in terms of the mean depression score before exercise ( $16.43 \pm 2.04$  versus  $16.13 \pm 1.99$ ,  $P = 0.45$ ) and immediately after exercise intervention ( $15.93 \pm 2.22$  versus  $16.46 \pm 1.94$ ,  $P = 0.44$ ) one month after the intervention ( $16.10 \pm 2.02$  versus  $16.33 \pm 1.80$ ,  $P = 0.63$ ). In the intervention group, there were no significant changes in the mean depression score immediately and one month after the intervention ( $P = 0.05$ ). Also, there were no significant changes in the mean depression score in the control group ( $P = 0.22$ ) (Table 2).

### 4. Discussion

Physical inactivity is a major risk factor for the development of breast cancer and its prevalence is higher in women than men [29, 30, 31]. Decreased levels of physical preparedness, treatment side effects, and stress from being diagnosed with cancer all play a role in exacerbating the clinical conditions of a breast cancer person [31, 32]. Studies have shown that exercise as a non-invasive and non-pharmacological treatment directly affects the components of breast cancer and improves the QoL of patients [33]. Exercise ultimately reduces fatigue by increasing muscle mass, increasing plasma volume, increasing ventilation and blood flow to the lungs, and increasing cardiac capacity [17]. The aim of the present study was to investigate the effect of exercise program on

**Table 1.** Comparison of demographic information of two intervention and control groups before the intervention.

Variables	Dimensions	Intervention group n (%)	Control group n (%)	P value
Marital Status	Married	25 (49)	26 (51)	0.50 <sup>a</sup>
	Single & Divorced	5 (55.6)	4 (44.4)	
Education	Under diploma	9 (37.5)	15 (62.5)	0.27 <sup>b</sup>
	Diploma	15 (60)	10 (40)	
	University	6 (54.5)	5 (45.5)	
Job	Housewife	15 (60)	10 (40)	0.14 <sup>c</sup>
	Other	15 (42.9)	20 (57.1)	
Income (million Tomans)	<1	8 (53.3)	7 (46.7)	0.47 <sup>b</sup>
	1–2	17 (54.8)	14 (45.2)	
	>2	5 (37.5)	9 (64.3)	
Residency	City	19 (47.5)	21 (52.5)	0.39 <sup>c</sup>
	Rural	11 (55)	9 (45)	
Age	Mean ± SD	48.46 ± 5.72	49.60 ± 7.48	0.58 <sup>d</sup>

<sup>a</sup>Fishers exact test, <sup>b</sup>Chi-Squared test, <sup>c</sup>Yates Correction Test, <sup>d</sup>Mann-Whitney U, P value significant at  $P < 0.05$ , SD = Standard deviation.

**Table 2.** Mean and standard deviation of the variables in the control and intervention groups before, after, and 1 months after the intervention.

Variables	Stages	Mean ± SD		P value
		Intervention group	Control group	
Fatigue Severity	Before intervention	47.23 ± 9.43	49 ± 7.28	0.59 <sup>a</sup>
	After intervention	41.3 ± 9.40	50.16 ± 9.96	0.001 <sup>a</sup>
	1 month after intervention	40.90 ± 9.20	50.40 ± 9.83	0.001 <sup>a</sup>
	P value	0.001 <sup>b</sup>	0.07 <sup>c</sup>	-
Depression	Before intervention	16.43 ± 2.04	16.13 ± 1.99	0.45 <sup>a</sup>
	After intervention	15.93 ± 2.22	16.46 ± 1.94	0.44 <sup>a</sup>
	1 month after intervention	16.10 ± 2.02	16.33 ± 1.80	0.63 <sup>a</sup>
	P value	0.05 <sup>b</sup>	0.22 <sup>c</sup>	-

<sup>a</sup>Mann-Whitney U, <sup>b</sup>Friedman Test, <sup>c</sup>Repeated measurements test. P value significant at  $P < 0.05$ . SD = Standard deviation.

depression and fatigue in breast cancer women undergoing chemotherapy.

The results of the present study showed that exercise program reduced fatigue among women of the intervention group and remained stable for one month after the intervention, which is consistent with results of various studies. Ajam et al. (2014) showed that 12-week aerobic exercises prevented the reduction of white blood cell and red blood cell levels and thus strengthened the immune system, improved general health status and reduced fatigue in breast cancer women undergoing chemotherapy [34]. Huang et al. (2019) showed that a 12-week walking program reduced fatigue among breast cancer women undergoing chemotherapy [35]. Do et al. (2015) found that aerobic and stretching exercises reduced fatigue, improved QoL, and cardiopulmonary function among breast cancer women [36]. However, Al-Majid et al. (2015) reported that treadmill exercises did not have a significant effect on fatigue and QoL of breast cancer women undergoing chemotherapy, which is not consistent with the results of the present study [37]. Husebø et al. (2014) also concluded that aerobic and endurance exercises did not have a significant effect in reducing fatigue in breast cancer women [38]. The reasons for this difference may be due to differences in the type of exercise and training exercises and the duration of the intervention.

The present study also revealed that exercise program had no significant effect on depression among patients of the intervention group. These results are consistent with the findings of a study by Travier et al. (2015), which showed that aerobic and endurance exercise had no significant effect on fatigue, QoL, anxiety, depression, and physical fitness of breast cancer women undergoing chemotherapy [39]. Inconsistent with the present study, other studies have shown the effect of exercise on reducing depression in cancer women. Zareian & Rahmati (2015) showed that aerobic exercises reduce anxiety, depression, and improves QoL of breast cancer patients undergoing chemotherapy [40]. Rogers et al. (2016) also found that 12-session indoor physical exercises reduced fatigue, anxiety, and depression among breast cancer women [41]. This difference may be due to different in sample sizes, intervention durations, and the exercise techniques used.

### 5. Strengths and limitations

Strengths of the present study include gentle exercises, which were selected considering the patients' level of tolerance by the exercise physiotherapist and had lower costs on the patients compared to outdoor exercises, the telephone follow-up of patients throughout the study, and face-to-face sessions. Since the patients had some degree of fatigue, thus exercise at home and no need to leave home as well as performing exercises at hours desired by the patient could be the advantages of exercise at home. However, the present study had some limitations. Some patients did not perform exercises and the researcher, physiotherapist, exercise physiologist, and oncologist made attempts to encourage patients to

perform the intervention. Another limitation of the present study was the fact that patient might perform the exercises incorrectly and not according to the instructions. The researcher guided the patients to perform the exercises correctly through regular telephone follow-ups and face-to-face visits at their homes. In the present study, the aim was to explore the effect of exercise on depression of patients after six weeks of exercise as well as one month after. One of the limitations of the present study was short-term follow-up, whereby longer follow-ups may change the outcomes.

## 6. Conclusion

The results of the present study showed that indoor exercise reduces fatigue among breast cancer women undergoing chemotherapy. According to the results of the present study and almost similar research, it can be concluded that exercise and physical activity have a positive effect on reduce fatigue of patients. Therefore, exercise interventions are recommended as a non-pharmacological, safe, easy, comfortable, and non-invasive solution to improve physiological capacities and functional abilities and improve QoL of patients. On the other hand, since exercise program had no effect on depression among breast cancer women in the present study, longer studies with larger sample size are recommended. It is also recommended to evaluate the effect of exercises along with psychological counseling on the depression level in these patients.

## Declarations

### Author contribution statement

Fatemeh Mostafaei: Conceived and designed the experiments; Wrote the paper.

Mohammad Azizi: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

Amir Jalali: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Nader Salari: Performed the experiments; Contributed reagents, materials, analysis tools or data.

Parvin Abbasi: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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### Data availability statement

Data will be made available on request.

### Declaration of interests statement

The authors declare no conflict of interest.

### Additional information

The clinical trial described in this paper was registered at the Iranian Registry of Clinical Trials under the registration number IRCT20130812014333N86.

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