Feasibility of Exercise Rehabilitation Program During Radiotherapy in Breast Cancer Survivors Based on the American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors

Beom Jun Lee and Mun-Gyu Jun *

Posted Date: 26 February 2026

doi: 10.20944/preprints202602.1735.v1

Keywords: breast cancer survivors; exercise rehabilitation program; cancer-related fatigue; quality of life; axillary lymph node dissection; radiotherapy; chemotherapy

 doi:10.20944/preprints202602.1735.v1

Article

Feasibility of Exercise Rehabilitation Program During Radiotherapy in Breast Cancer Survivors Based on the American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors

Beom Jun Lee [1] and Mun-Gyu Jun [2,*]

[1] St. Mary's Best ENT Clinic, Seoul 08849, Republic of Korea

[2] Department of Professional Sports Instruction, Taegu Science University, Daegu, Republic of Korea

* Correspondence: junmg@tsu.ac.kr; Tel: +82-53-320-1583

Abstract

We conducted this study to identify factors that are associated with the improved clinical benefit of a 6-week exercise rehabilitation (ER) program during radiotherapy (RTx) in breast cancer survivors (BCS). In a total of 95 BCS (n=95), we performed a 6-week course according to the American College of Sports Medicine (ACSM) guidelines. Through a retrospective review of the medical records, we analyzed the clinical and sociodemographic characteristics. We assessed the patient outcomes using the EORTC QLQ-C30, EORTC QLQ-BR23 and Fatigue Severity Scale (FSS) and did the cardiopulmonary functions using a heart rate based, indirect method. We analyzed changes in outcome measures (EORTC QLQ C30 scores, EORTC QLQ BR23 scores, FSS scores and VO_2max) at 6 weeks as compared with baseline. There were significant differences in the EORTC QLQ C30 scores on the QOL and functional scales, the EORTC QLQ BR 23 scores on the functional and symptom scales and the VO_2max between baseline and at 6 weeks. Patients with higher education level undergoing axillary lymph node dissection (ALND) achieved better treatment outcomes of a 6-week ER program. But the age was not associated with the clinical benefit. The exercise program was effective in improving the QOL, cancer-related symptoms and cardiopulmonary functions, but it was not effective in improving the breast cancer-related symptoms. Moreover, the ALND and a higher level of education were associated with the increased clinical benefit of the exercise program during RTx.

Keywords: breast cancer survivors; exercise rehabilitation program; cancer-related fatigue; quality of life; axillary lymph node dissection; radiotherapy; chemotherapy

1. Introduction

Breast cancer (BC) is the most common cancer and the leading cause of cancer death in women worldwide.[1] In the United States (US), 310,720 women are estimated to be diagnosed with BC in 2024.[2] It continues to rank second, after lung cancer, as a cause of cancer death in women in the US, and it is a leading cause of premature mortality for women.[3] BC deaths contribute significantly to years of potential life lost, with an average of approximately 19 years of life lost per death. This suggests that women who die from BC are, on average, losing nearly two decades of their potential lifespan.[4] Even though mortality from BC has declined steadily since 1990, largely due to improvements in early detection and treatment, an estimated 42,250 women are still expected to die from BC in the US in 2024, according to the American Cancer Society.[5] Almost 1.4 million women were diagnosed with BC worldwide in 2008 and approximately 459,000 deaths were recorded.[6] Its prevalence has been reported to be higher in more developed countries compared to less developed ones according to the World Health Organization (WHO) World 2000 Standard Population

 doi:10.20944/preprints202602.1735.v1

(71.7/100,000 *vs*. 29.3/100,000). Moreover, cancer mortality per 100,000 persons was 17.1 and 11.8 in the corresponding order.[7] Due to such factors as the early detection, accessibility to treatment services and cultural background, there is also a difference in the estimated 5-year survival between more developed and less developed ones; it was almost 90% in the US, Australia or Canada and 12% in some African areas. Moreover, with the recent introduction of population-based cancer screening program using a mammography and the systemic use of adjuvant therapies, there have been improvements in BC survival in more developed countries.[7–9]

BC is one of the most common female malignancies. Despite developments in surgical techniques and the prevalent use of breast-conserving surgeries, breast cancer survivors (BCS) remain at risk of developing post-operative complications arising from functional impairment and pain.[10–12] That is, they are vulnerable to sequelae and other health problems on the affected side, which may greatly affect the physical status and quality of life (QOL).[13,14] Recently, there has been an increased interest in the QOL in BCS. It has been reported that their physical status and QOL are subject to adjuvant therapies such as chemotherapy (CTx), hormone therapy (HTx) and radiotherapy (RTx). It remains a great concern, however, that BCS are vulnerable to their complications, such as cancer-related fatigue (CRF) and cardiopulmonary dysfunction (CD), both of which should be reduced for the purposes of improving the physical status and the QOL.[15,16]

According to a Cochrane database review, the exercise rehabilitation (ER) program combined with the postoperative adjuvant therapy was effective in improving the physical fitness and daily activities in BCS.[17] In addition, according to a meta-analysis of published studies, a supervised aerobic exercise program was effective in significantly reducing the CRF.[18]

In patients with BC, their physical status and QOL *as well as* the outcomes of exercise program are also subject to their underlying clinical characteristics such as a past history of taking CTx or HTx and the presence of lymphedema (LE). Moreover, their QOL is also subject to sociodemographic characteristics such as the age, employment status or education level of patients with BC.[19]

Given the above background, we have attempted to perform an ER based on the American College of Sports Medicine (ACSM) Roundtable on Exercise Guidelines for Cancer Survivors in BCS in Korea. In this study, we analyzed the clinical and sociodemographic characteristics improving the feasibility of ER program during RTx in them.

2. Materials and Methods

2.1. Study Patients

Between January 1 and December 31, 2024, a total of 710 BCS received RTx at a tertiary medical institution in Korea. Of these, 456 patients were recommended to undergo ER.

In these patients, we analyzed clinical and sociodemographic characteristics such as education level (low level [≤ high school graduate] or high level [≥ college or university graduate]), employment status, marital status, the type of axillary surgery (axillary lymph node dissection [ALND], sentinel node biopsy [SNB]) or lymph node dissection) and the involvement of dominant side (dominant or non-dominant side).

Inclusion criteria for the current study are as follows:

(1) Adult women aged 18 years or older

(2) The patients with BC who underwent surgery

(3) The patients who started adjuvant radiotherapy

(4) The patients who wanted to regain or improve physical functions, aerobic capacity, strength, flexibility, body image, body composition and QOL

(5) The patients who wanted to physically or psychologically tolerate any current and/or future cancer treatments or anxiety due to living with current or recurrent disease

(6) The patients who were in need of the reduction of long-term and late effects of cancer treatment

 doi:10.20944/preprints202602.1735.v1

(7) The patients who were in need of the potential delay in any recurrence or progress of the disease.

Exclusion criteria for the current study are as follows:

(1) The patients who concurrently had major health problems that may affect the study participation

(2) The patients with uncontrolled hypertension or other cardiovascular diseases

(3) The patients with acute or chronic respiratory diseases

(4) The patients with acute arm and shoulder problems for upper body exercises

(5) The patients with extreme fatigue, anemia or ataxia

(6) The patients with cognitive dysfunction

(7) The patients who are deemed to be ineligible for study participation according to our judgment.

We finally enrolled a total of 95 BCS (n=95), all of whom submitted a written informed consent. The current study was approved by the Internal Institutional Review Board (IRB) of the Public Institutional Bioethics Committee designated by the Korean Ministry of Health and Welfare.

2.2. ER Program

According to the ACSM guidelines, the patients received a 6-week course of a 1-hr exercise program, comprising a 5-min warm-up, 5-min stretching, a 30-min aerobic exercise using an a bicycle ergometer (Ergoselect 200K, Ergoline, Bitz, Germany), a 15-min resistance exercise using a latex exercise band (Thera-band®, Hygenic co., Ohio) and a 5-min cool-down, five times/week for 60 minutes/day.[20,21] The patients were initially recommended to perform aerobic exercise with 40% of peak oxygen uptake (VO_2max) followed by a progressive increase in it up to 75%. In addition, the resistance exercise consists of six different exercises, each of which was repeated 8-12 times.

2.3. Patients' Self-Reporting Questionnaire Survey

2.3.1. European Organization for Research and Treatment of Cancer Quality of Life Questionnaire core (EORTC QLQ-C30) and breast module (EORTC QLQ-BR23)

We used both the EORTC QLQ-C30 and EORTC QLQ-BR23 in assessing the QOL in our clinical series of patients.

The EORTC QLQ-C30 include the following items:

(1) A global health and quality-of-life scale

(2) Functional scales (physical, role, cognitive, emotional and social functions)

(3) Symptom scales (fatigue, pain, nausea and vomiting).

In addition, the EORTC QLQ-BR23 include the following items:

(1) Functional scales (body image and sexual function)

(2) Symptom scales (arm and breast symptoms *and* systemic adverse effects).

2.3.2. Fatigue Severity Scale (FSS)

We used the FSS in assessing the severity of CRF that is measured using nine items on a 7-point scale. Thus, we attempted to evaluate the patients' conditions during the past week.

2.4. Evaluation of Cardiopulmonary Functions

We used the submaximal exercise test with a heart rate based, indirect method to assess the cardiopulmonary functions based on a step-incremental continuous test protocol. Thus, we attempted to control the patients' heart rate within 10 BPM of 85% of the mean maximal heart rate (MHR), for which we used both a bicycle ergometer (Ergoselect 200K, Ergoline, Bitz, Germany) and a heart rate monitor (Polar sport tester, Polar, Finland). We evaluated the patients' cardiopulmonary functions based on the VO_2max.

 doi:10.20944/preprints202602.1735.v1

2.5. Outcome Measures

We analyzed changes in outcome measures (EORTC QLQ C30 scores, EORTC QLQ BR23 scores, FSS scores and VO_2max) at 6 weeks as compared with baseline.

2.6. Subgroup Analysis

Based on a cut-off value of 50 years old, we divided our clinical series of patients into two subgroups: the 50 years or older group and the 50 years or younger group.

2.7. Statistical Analysis

Statistical analysis was done using the SPSS version 16.0 (SPSS, Inc., Chicago, IL). All data was expressed as mean±SD (SD: standard deviation). We used the paired *t*-test to analyze changes in outcome measures at six weeks as compared with baseline. In addition, we also used the independent *t*-test for univariate analysis to analyze the difference in outcome measures depending on underlying clinical or sociodemographic variables. Furthermore, we also used the analysis of covariance (ANCOVA) after the adjustment of underlying clinical or sociodemographic variables, thus attempting to estimate differences in outcome measures depending on such variables. Finally, we performed a multivariate analysis using the Cox regression model. A *P*-value of <0.05 was considered statistically significant.

3. Results

3.1. Baseline Characteristics

We enrolled a total of 95 BCS (n=95), all of whom were women. The mean age of the patients was 44.5±9.11 years old. The study flow chart is shown in Figure 1. Moreover, baseline characteristics of the BCS are presented in Table 1.

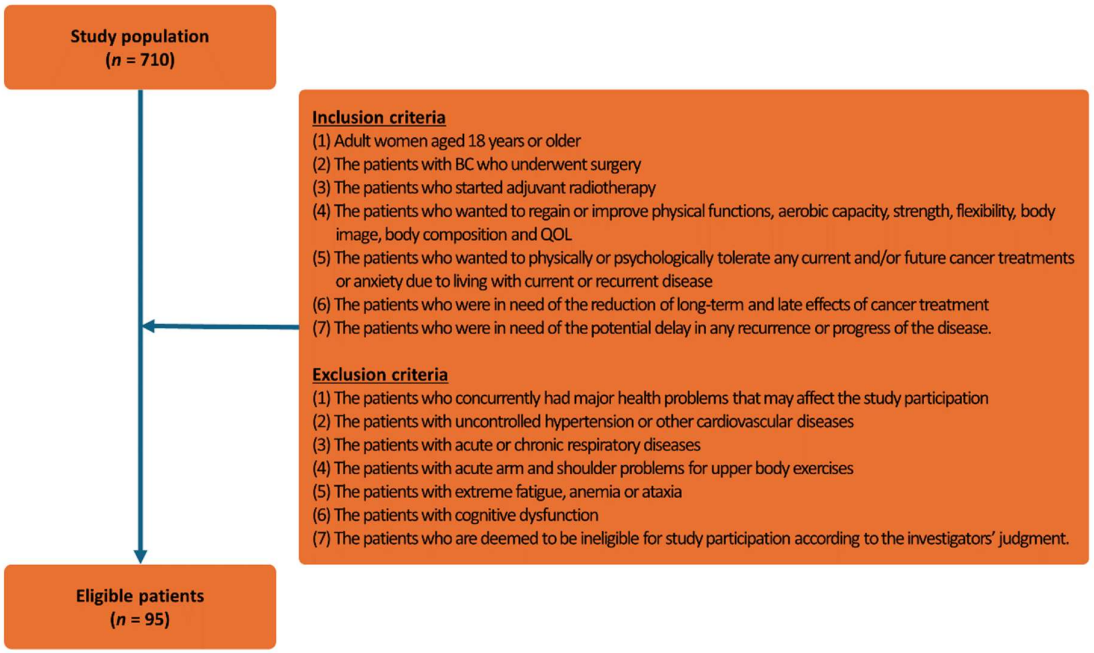

Figure 1. Study flow chart.

 doi:10.20944/preprints202602.1735.v1

Table 1. Baseline characteristics.

		Value (%)
Age	≤39	29 (30.5)
	40-49	43 (45.3)
	≥50	23 (24.2)
Gender	Male	0 (0)
	Female	95 (100)
Level of education	≤ High school graduate	42 (44.2)
	≥ College or university graduate	53 (55.8)
Marital status	Married	76 (80)
	Unmarried	19 (20)
Employment status	Employed	33 (34.7)
	Unemployed	62 (65.3)
Chemotherapy	(+)	42 (44.2)
	(-)	53 (55.8)
Hormone therapy	(+)	77 (81.1)
	(-)	18 (18.9)
Lymphedema	(+)	25 (26.3)
	(-)	70 (73.7)
Type of axillary lymph node surgery	SNB	48 (50.5)
	ALND	42 (44.2)
	LN dissection (-)	5 (5.3)

Abbreviations: SNB, sentinel node biopsy; ALND, axillary lymph node dissection; LN, lymph node.

3.2. Outcome Measures

As shown in Table 2, there were significant differences in the EORTC QLQ C30 scores on the QOL and functional scales, the EORTC QLQ BR 23 scores on the functional and symptom scales and the VO_2max between baseline and at 6 weeks (P<0.05).

Table 2. The quality of life, cancer-related fatigue and cardiopulmonary functions.

		Baseline	6 weeks	Change at 6 weeks from baseline
EORTC QLQ C30	Global health/QOL scale	55.7±18.6	**65.0±19.0***	9.3±17.3
	Functional scales	71.5±13.4	**74.3±13.4***	2.8±10.1
	Symptom scales	23.0±10.7	**21.7±12.4**	-1.3±10.8
EORTC QLQ BR 23	Functional scales	72.8±16.6	**79.2±15.8***	6.5±14.4
	Symptom scales	24.9±14.8	**33.9±22.1***	9.0±21.1
	FSS	13.6±16.3	13.3±16.6	-0.2±8.2
	VO_2max	24.6±6.4	**30.1±9.4***	5.5±8.8

Abbreviations: EORTC QLQ C30, European Organization for Research and Treatment of Cancer 30-item core quality of life questionnaire; QOL, quality of life; EORTC QLQ BR 23, EORTC breast cancer-

 doi:10.20944/preprints202602.1735.v1

specific quality of life questionnaire; FSS, Fatigue Severity Scale. Values are mean±standard deviation. *Bold numbers represent significant differences at *P*-value of < 0.05 by paired t-test.

3.3. Correlations Between Outcome Measures and Clinical/Sociodemographic Characteristics on Univariate Analysis

There was a significant difference in the EORTC QLQ BR 23 scores on the symptom scale between baseline and at 6 weeks in the patients who did not undergo CTx. There was a significant difference in the FSS scores between baseline and at 6 weeks in the patients who underwent ALND. There were significant differences in the EORTC QLQ C30 scores on the QOL and symptom scales in the patients with a higher level of education. There was a significant difference in the EORTC QLQ C30 scores on the symptom scale between baseline and at 6 weeks in the employed patients (Tables 3–10).

Table 3. Correlations between outcome measures and chemotherapy on univariate analysis.

		Baseline		6 weeks		Change at 6 weeks from baseline	
		CTx (+)	CTx(-)	CTx (+)	CTx(-)	CTx (+)	CTx(-)
EORTC QLQ C30	Global health /QOL	54.0±20.1	57.9±15.4	62.2±20.9	**70.7±13.4***	8.2±19.7	12.8±10.9
	Functional	69.1±14.2	**76.1±9.9***	71.3±13.9	80.1±10.4	2.2±11.5	3.9±6.7
	Symptom	23.5±10.6	21.3±10.1	23.5±12.4	**17.3±10.4***	-0.1±12.2	-4.0±7.1
EORTC QLQ BR 23	Functional	72.1±18.1	74.5±13.9	76.7±15.3	82.9±16.6	4.6±14.9	8.5±12.4
	Symptom	26.2±15.9	22.47±12.3	39.9±23.5	**22.5±12.7***	13.8±22.9	**0.2±12.1*†**
FSS		18.6±17.8	**3.4±3.0***	17.9±17.9	**4.3±7.6***	-0.7±9.5	0.9±4.9
VO_2max		23.4±6.9	**26.8±4.5***	29.5±10.7	31.0±5.8	6.0±10.4	4.2±3.8

Abbreviations: CTx, chemotherapy; EORTC QLQ C30, European Organization for Research and Treatment of Cancer 30- item core quality of life questionnaire; QOL, quality of life; EORTC QLQ BR 23, EORTC breast cancer-specific quality of life questionnaire; FSS, Fatigue Severity Scale. Values are mean±standard deviation. *Bold numbers represent significant differences at *P*-value of < 0.05 by paired t-test. † Bold numbers represent significant differences at *P*-value of < 0.05 by ANCOVA adjusting for baseline measures.

Table 4. Correlations between outcome measures and hormone therapy on univariate analysis.

		Baseline		6 weeks		Change at 6 weeks from baseline	
		HTx (+)	HTx(-)	HTx (+)	HTx(-)	HTx (+)	HTx(-)
EORTC QLQ C30	Global health/QOL	53.9±19.3	59.3±17.2	61.7±19.5	**74.7±15.1***	7.8±18.1	15.4±15.4
	Functional	70.0±13.3	75.4±14.1	72.4±13.5	79.1±12.6	2.1±10.7	3.7±9.0
	Symptom	23.8±10.8	19.7±8.7	23.4±12.4	**15.2±8.9***	-0.4±11.8	-4.5±7.0
EORTC QLQ BR 23	Functional	71.4±16.5	76.4±17.7	77.1±15.7	83.6±16.2	5.7±14.5	7.2±13.8
	Symptom	26.4 ±15.1	20.9±13.8	37.3±22.9	26.7±17.1	10.9±22.6	5.9±16.9
FSS		15.9±17.3	**14.7±17.2***	14.7±17.2	10.2±15.0	-1.2±8.1	2.1±7.3
VO_2max		23.7±27.4	**27.4±6.7***	29.4±10.2	31.9±6.2	5.7±9.8	4.5±4.4

Abbreviations: HTx, hormone therapy; EORTC QLQ C30, European Organization for Research and Treatment of Cancer 30- item core quality of life questionnaire; QOL, quality of life; EORTC QLQ BR

 doi:10.20944/preprints202602.1735.v1

23, EORTC breast cancer-specific quality of life questionnaire; FSS, Fatigue Severity Scale. Values are mean±standard deviation. *Bold numbers represent significant differences at *P*-value of < 0.05 by paired t-test.

Table 5. Correlations between outcome measures and the type of axillary lymph node surgery on univariate analysis.

		Baseline		6 weeks		Change at 6 weeks from baseline	
		ALND	SNB	ALND	SNB	ALND	SNB
EORTC QLQ C30	Global health/QOL	52.7±19.5	57.2±18.2	59.6±20.6	**68.3±18.2***	6.9±19.9	11.1±15.1
	Functional	67.4±16.5	73.6±9.7	69.9±14.1	**75.6±11.9***	2.5±10.6	1.9±10.3
	Symptom	23.9±11.3	22.7±9.9	22.7±11.1	21.7±13.2	-1.2±7.9	-1.1±13.7
EORTC QLQ BR 23	Functional	69.2±18.8	75.2±15.3	75.8±14.9	**79.5±16.7***	6.7±11.9	4.3±16.4
	Symptom	29.9±16.4	21.9±12.8	40.2±22.2	**32.4±21.8***	10.3±20.7	10.4±23.0
FSS		17.9±18.0	12.1±15.1	15.5±16.4	13.8±17.6	**-2.4±7.8*†**	1.7±8.9
VO_2max		23.5±6.9	24.9±6.2	30.1±12.8	29.4±5.4	6.6±12.2	4.5±5.3

Abbreviations: ALND, axillary lymph node dissection; SNB, sentinel node biopsy; EORTC QLQ C30, European Organization for Research and Treatment of Cancer 30- item core quality of life questionnaire; QOL, quality of life; EORTC QLQ BR 23, EORTC breast cancer-specific quality of life questionnaire; FSS, Fatigue Severity Scale. Values are mean±standard deviation. *Bold numbers represent significant differences at *P*-value of < 0.05 by paired t-test.

Table 6. Correlations between outcome measures and lymphedema on univariate analysis.

		Baseline		6 weeks		Change at 6 weeks from baseline	
		LE (+)	LE (-)	LE (+)	LE (-)	LE (+)	LE (-)
EORTC QLQ C30	Global health/QOL	52.2±20.5	56.2±18.2	59.7±24.8	66.5±16.9	7.5±20.4	10.3±16.7
	Functional	66.4±15.5	72.9±12.3	68.1±15.7	75.9±12.1	1.8±10.5	3.0±10.3
	Symptom	24.6±11.8	22.2±9.9	21.9±12.9	21.5±11.9	-2.7±10.8	-0.7±11.2
EORTC QLQ BR 23	Functional	68.4±20.5	74.4±15.4	76.4±17.3	79.3±15.4	8.0±13.9	4.9±14.4
	Symptom	28.7±15.2	23.8±14.8	40.1±26.1	32.9±20.6	11.5±24.2	9.2±20.4
FSS		17.3±18.8	**13.0±15.6***	14.8±16.6	**13.6±16.9***	-2.5±6.1	0.6±9.0
VO_2max		23.4±5.7	30.3±16.2	30.3±16.2	29.8±5.6	6.9±14.6	5.0±5.8

Abbreviations: LE, lymphedema; EORTC QLQ C30, European Organization for Research and Treatment of Cancer 30- item core quality of life questionnaire; QOL, quality of life; EORTC QLQ BR 23, EORTC breast cancer-specific quality of life questionnaire; FSS, Fatigue Severity Scale. Values are mean±standard deviation. *Bold numbers represent significant differences at *P*-value of < 0.05 by paired t-test.

 doi:10.20944/preprints202602.1735.v1

Table 7. Correlations between outcome measures and the level of education on univariate analysis.

		Baseline		6 weeks		Change at 6 weeks from baseline	
		Higher	Lower	Higher	Lower	Higher	Lower
EORTC QLQ C30	Global health/QOL	54.9±17.6	55.4±20.5	**69.9±17.7***	58.1±19.7	**14.9±15.2*†**	2.7±18.4
	Functional	73.4±12.4	68.4±14.4	**77.4±11.4***	69.4±14.7	4.0±8.4	0.9±12.3
	Symptom	21.5±9.2	24.6±11.7	**17.6±8.6***	26.7±14.0	**-3.9±7.2*†**	2.1±13.9
EORTC QLQ BR 23	Functional	74.8±16.9	70.4±16.9	80.7±15.1	75.8±16.6	6.0±11.3	5.5±17.4
	Symptom	23.2±14.1	27.3±15.9	**29.8±19.6***	41.1±24.1	6.6±17.8	13.8±24.9
FSS		11.5±14.9	17.6±18.0	11.8±15.0	16.6±18.6	0.3±8.9	-0.9±7.8
VO_2max		25.0±7.2	23.6±5.5	**31.7±11.8***	27.7±4.6	6.6±11.1	4.1±4.9

Abbreviations: EORTC QLQ C30, European Organization for Research and Treatment of Cancer 30-item core quality of life questionnaire; QOL, quality of life; EORTC QLQ BR 23, EORTC breast cancer-specific quality of life questionnaire; FSS, Fatigue Severity Scale. Values are mean±standard deviation. *Bold numbers represent significant differences at *P*-value of < 0.05 by paired t-test.

Table 8. Correlations between outcome measures and employment status on univariate analysis.

		Baseline		6 weeks		Change at 6 weeks from baseline	
		Employed	Unemployed	Employed	Unemployed	Employed	Unemployed
EORTC QLQ C30	Global health/QOL	52.0±19.8	56.8±18.3	64.0±18.8	65.1±19.8	12.1±15.0	8.3±18.8
	Functional	70.8±13.6	71.4±13.5	74.4±13.2	73.6±12.7	3.6±9.2	2.2±10.9
	Symptom	22.5±10.2	23.1±10.6	**17.7±9.5***	23.7±12.9	**-4.8±8.3*†**	0.6±11.9
EORTC QLQ BR 23	Functional	72.9±17.3	72.8±17.0	78.7±17.2	78.5±75.3	5.8±12.5	5.8±15.1
	Symptom	22.9±12.6	26.1±16.1	29.4±19.3	37.5±23.3	6.5±20.1	11.4±22.0
FSS		10.2±14.6	16.2±17.1	10.1±14.9	15.9±17.4	-0.1±4.8	-0.3±9.8
VO_2max		25.8±6.4	23.7±6.5	30.3±6.2	29.7±10.8	4.5±3.7	6.0±10.7

Abbreviations: EORTC QLQ C30, European Organization for Research and Treatment of Cancer 30-item core quality of life questionnaire; QOL, quality of life; EORTC QLQ BR 23, EORTC breast cancer-specific quality of life questionnaire; FSS, Fatigue Severity Scale. Values are mean±standard deviation. *Bold numbers represent significant differences at *P*-value of < 0.05 by paired t-test. † Bold numbers represent significant differences at *P*-value of < 0.05 by ANCOVA adjusting for baseline measures.

 doi:10.20944/preprints202602.1735.v1

Table 9. Correlations between outcome measures and marital status on univariate analysis.

		Baseline		6 weeks		Change at 6 weeks from baseline	
		Married	Unmarried	Married	Unmarried	Married	Unmarried
EORTC QLQ C30	Global health/QOL	54.0±19.0	60.6±18.0	62.8±19.7	72.5±17.0	8.8±18.1	11.9±16.2
	Functional	70.9±12.3	72.7±17.8	78.8±13.4	78.6±13.1	1.9±10.7	5.9±8.4
	Symptom	23.0±10.1	21.9±12.0	22.6±12.2	21.92±12.0	0.4±12.0	-3.9±5.0
EORTC QLQ BR 23	Functional	71.5±19.2	79.4±19.2	77.1±15.7	**86.2±12.9***	5.6±14.4	6.8±14.0
	Symptom	25.2±13.8	24.0±19.5	36.8±22.8	27.5±19.5	11.6±21.8	3.5±18.8
FSS		14.8±16.8	12.0±15.8	14.6±17.2	12.0±15.6	-0.3±8.7	0.0±7.4
VO_2max		24.5±5.8	24.2±9.2	30.0±10.1	30.4±6.7	5.4±9.3	6.2±7.7

Abbreviations: EORTC QLQ C30, European Organization for Research and Treatment of Cancer 30-item core quality of life questionnaire; QOL, quality of life; EORTC QLQ BR 23, EORTC breast cancer-specific quality of life questionnaire; FSS, Fatigue Severity Scale. Values are mean±standard deviation. *Bold numbers represent significant differences at *P*-value of < 0.05 by paired t-test.

Table 10. Correlations between outcome measures and dominant side on univariate analysis.

		Baseline		6 weeks		Change at 6 weeks from baseline	
		Dominant	Non-dominant	Dominant	Non-dominant	Dominant	Non-dominant
EORTC QLQ C30	Global health/QOL	54.9±17.9	55.2±20.0	65.3±19.5	64.2±19.7	10.4±17.3	8.9±18.3
	Functional	69.3±12.1	72.9±14.6	72.6±11.8	74.8±14.9	3.3±8.9	1.9±11.6
	Symptom	23.3±10.0	22.6±11.0	21.0±9.8	22.4±14.1	-2.2±6.9	-0.2±13.9
EORTC QLQ BR 23	Functional	69.5±16.9	75.8±16.8	77.2±14.6	79.7±17.2	7.7±12.0	3.9±16.1
	Symptom	25.8±15.3	24.5±14.9	32.9±20.5	36.9±23.9	7.1±18.4	12.4±24.0
FSS		12.9±16.0	15.6±17.1	14.0±17.0	14.1±16.8	1.1±8.8	-1.5±8.0
VO_2max		24.6±6.0	24.2±7.1	30.3±12.2	30.0±6.1	5.7±11.3	5.4±6.1

Abbreviations: EORTC QLQ C30, European Organization for Research and Treatment of Cancer 30-item core quality of life questionnaire; QOL, quality of life; EORTC QLQ BR 23, EORTC breast cancer-specific quality of life questionnaire; FSS, Fatigue Severity Scale. Values are mean±standard deviation.

3.4. Correlations Between Outcome Measures and Clinical/Sociodemographic Characteristics on Multivariate Analysis

There were significant differences in the EORTC QLQ-C30 scores on the QOL and symptom scales between baseline and at 6 weeks in the patients with a higher level of education. In addition, there were also significant differences in the EORTC QLQ-BR23 scores on the symptom scale between baseline and at 6 weeks in the patients who did not undergo CTx. Furthermore, there were also significant differences in the FSS scores between baseline and at 6 weeks in the patients who underwent ALND (Table 11).

 doi:10.20944/preprints202602.1735.v1

Table 11. Correlations between outcome measures and clinical/sociodemographic characteristics on multivariate analysis.

		Significant outcome measures
EORTC QLQ C30	Global health / QOL	**Education level** (**Higher** > Lower)*
	Functional	None
	Symptom	**Education level** (**Higher** > Lower)*
EORTC QLQ BR 23	Functional	None
	Symptom	**History of CTx** (**CTx(-)** > CTx(+))*
FSS		**Type of axillary lymph node surgery** (**ALND** > SNB)*
VO_2max		None

Abbreviations: EORTC QLQ C30, European Organization for Research and Treatment of Cancer 30-item core quality of life questionnaire; QOL, quality of life; EORTC QLQ BR 23, EORTC breast cancer-specific quality of life questionnaire; FSS, Fatigue Severity Scale; CTx, chemotherapy; ALND, axillary lymph node dissection; SNB, sentinel node biopsy. Values are mean±standard deviation. *Bold numbers represent significant differences at *P*-value of < 0.05 by paired t-test. † Bold numbers represent significant differences at *P*-value of < 0.05 by ANCOVA adjusting for baseline measures.

3.5. Subgroup Analysis

There were no significant differences in outcome measures between the two subgroups. That is, the age was not associated with the clinical benefit of the ER program (Table 12).

Table 12. Results of the subgroup analysis.

		Baseline		6 weeks		Change at 6 weeks from baseline	
		< 50 yrs	≥ 50 yrs	< 50 yrs	≥ 50 yrs	< 50 yrs	≥ 50 yrs
EORTC QLQ C30	Global health/QOL	58.8±12.2	52.0±22.0	72.3±17.1	58.6±22.7	13.5±16.0	6.6±16.3
	Functional	74.4±12.6	68.5±16.8	78.8±11.1	70.6±16.5	4.5±7.2	2.0±10.9
	Symptom	21.1±10.3	23.1±12.7	17.2±10.5	24.2±14.9	-3.9±7.0	1.1±14.6
EORTC QLQ BR 23	Functional	74.9±17.0	74.4±18.9	79.6±15.7	79.2±17.8	4.7±10.3	4.8±18.3
	Symptom	22.6±13.3	22.1±14.5	26.2±17.6	37.2±27.4	3.6±14.4	15.1±22.9
FSS		12.9±17.8	12.8±15.7	12.2±16.1	11.9±15.8	-0.7±9.2	-1.0±4.3
VO_2max		24.9±7.5	22.9±5.8	30.2±6.3	30.2±17.0	5.3±4.9	7.3±15.2

Abbreviations: EORTC QLQ C30, European Organization for Research and Treatment of Cancer 30-item core quality of life questionnaire; QOL, quality of life; EORTC QLQ BR 23, EORTC breast cancer-specific quality of life questionnaire; FSS, Fatigue Severity Scale. Values are mean±standard deviation.

4. Discussion

To date, several randomized controlled studies have demonstrated the effects of exercise programs in improving the QOL, CRF and the physical and psychological status in BCS.[16,22] We conducted the current study to identify the clinical and sociodemographic characteristics that contribute to improving the treatment outcomes of ER program in them. Our results showed that our exercise program was effective in improving the QOL, cancer-related symptoms and cardiopulmonary functions in our clinical series of patients. But it was not effective in improving the BC-related symptoms such as pain and skin problems on the affected side. Presumably, this might be because our patients are at risk of worsening BC-related symptoms during a 6-week exercise program combined with RTx, as previously described.[23]

On both univariate and multivariate analysis, the severity of BC-related symptoms was significantly greater in the patients who underwent CTx as compared with those who did not

 doi:10.20944/preprints202602.1735.v1

undergo it. But it was relatively lower in the patients who did not undergo CTx. These results indicate that patients with a past history of CTx are at an increased risk of worsening BC-related symptoms during RTx. Such patients are vulnerable to systemic adverse effects. It can therefore be inferred that they are also vulnerable to local damage during RTx. But we could not confirm whether this is due to the effects of exercise program because we did not serve the control group in the current study. This indicates that it would be mandatory to consider the possibility that BC-related symptoms might be worsened during RTx in patients with a past history of CTx. As shown in Table 3, the QOL, CRF and cardiopulmonary functions were poor at both baseline and 6 weeks in the patients who underwent CTx. This indicates that patients with a past history of CTx presented with a greater severity of BC-related symptoms. It can therefore be inferred that they should receive exercise program to improve their aggravated symptoms.

Our results showed that there were significant differences in the cancer-related QOL and symptoms between baseline and at 6 weeks in the patients with a higher level of education. These variables showed no significant difference at baseline between the patients with a higher level of education and those with a lower one. At 6 weeks, however, the patients with a higher level of education achieved an improvement in the cancer-related functions, BC-related symptoms and cardiopulmonary functions. Based on these results, it can be inferred that the education level may affect the effects of exercise program because the patients with a higher level of education are more inclined to participate in the exercise program and have a better understanding of it. In the current study, we encouraged the patients to perform exercise at home. It is therefore probable that the patients with a higher level of education had a better understanding of exercise program and this may have affected the results.

Our results also showed that the employment status had a significant correlation with cancer-related symptoms on univariate analysis. But there was no such correlation on multivariate analysis. On multivariate analysis, the education level was the only variable with a significant correlation with cancer-related symptoms. There was a positive correlation between the employment status and education level. It can therefore be inferred that the above results might be because the patients with a higher level of education are more inclined to be employed; such results might not be due to the employment status itself.

Pinto e Silva MP, et al. reported that the rehabilitation program was effective in improving the QOL in patients undergoing ALND as compared with those doing SNB.[24] Our results showed that the exercise program was effective in improving the CRF in the patients who underwent ALND as compared with those who did SNB. Presumably, this might be because ALND is a more invasive modality than SNB and the patients undergoing ALND might have suffered from a greater severity of CRF. It can therefore be inferred that the exercise program might be more beneficial for the patients undergoing ALND. Nevertheless, the FSS scores remained higher in the patients undergoing SNB. This indicates that the exercise program would be more effective in improving the CRF in the patients undergoing ANLD because their systemic conditions were poorer and their outcomes were better as compared with those doing SNB.

With regard to the relationship between the age and the effects of exercise program, Harrison SA, et al. reported that the age has a potential effect in improving the QOL because of the age-related physical activity.[25] We have therefore hypothesized that the age would have a significant effect on the treatment outcomes of exercise program. Accordingly, in the current study, we served two age subgroups based on a cut-off value of 50 years. But we found that the age was not associated with the clinical benefit. Further large-scale studies are therefore warranted to examine the effects of ER program depending on the age in patients with a diffuse, wide age distribution.

The aerobic and resistance exercise is an important, effective intervention for patients with BC undergoing RTx. It is neither easy nor cost-effective, however, to perform the exercise program for such patients. It would therefore be mandatory to screen patients with BC who are eligible for the participation in the exercise program.[26]

 doi:10.20944/preprints202602.1735.v1

There are two limitations of the current study as shown below: First, we failed to serve the control group for the current study. Second, we enrolled only the patients with BC from a single tertiary medical institution in Korea. Therefore, the possibility of selection bias could not be completely ruled out.

To summarize, our results are as follows:

(1) There were significant differences in the EORTC QLQ C30 scores on the QOL and functional scales, the EORTC QLQ BR 23 scores on the functional and symptom scales and the VO_2max between baseline and at 6 weeks.

(2) There were no effects in improving the BC-related symptoms.

(3) The patients with higher education level undergoing ALND achieved better treatment outcomes of a 6-week ER program.

(4) The age was not associated with the clinical benefit.

5. Conclusion

In conclusion, our results indicate that the patients with higher education level undergoing ALND might achieve better treatment outcomes of a 6-week ER program. Our results are of significance in that we have identified the patients' demographic and clinical factors affecting its feasibility during RTx where their conditions might be worsened. But further randomized controlled studies with long-term follow-up are warranted to assess the feasibility of exercise program in improving the QOL, CRF and CD in the patients with BC who underwent postoperative adjuvant therapies.

Author Contributions: Conceptualization, M.-G. J.; Methodology, M.-G. J.; Software, M.-G. J.; Validation, M.-G. J.; Formal analysis, M.-G. J.; Investigation, M.-G. J.; Resources, M.-G. J.; Data curation, M.-G. J.; Writing—original draft preparation, B. J. L. and M.-G. J.; Writing—review and editing, B. J. L. and M.-G. J.; Visualization, M.-G. J.; Supervision, M.-G. J.; Project administration, M.-G. J.; Funding acquisition, M.-G. J. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement: The ethical approval of the current study was obtained from the Internal Institutional Review Board (IRB) of the Public Institutional Bioethics Committee designated by the Korean Ministry of Health and Welfare (IRB approval #: P01-202208-03-004) and conducted it in compliance with the relevant guidelines and applicable laws.

Informed Consent Statement: Informed consent was obtained from all individual patients included in the study.

Data Availability Statement: Data is provided within the manuscript.

Acknowledgments: The authors thank Laon Medi Solution Inc. (Seoul, Republic of Korea) and KDH Medical Inc. (Gwangmyeong, Gyeonggi, Republic of Korea) for additional support of this study.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

The following abbreviations are used in this manuscript:

ACSM	American College of Sports Medicine
ALND	axillary lymph node dissection
ANCOVA	analysis of covariance
BS	breast cancer
BCS	breast cancer survivors
CD	cardiopulmonary dysfunction

 doi:10.20944/preprints202602.1735.v1

CRF	cancer-related fatigue
CTx	chemotherapy
EORTC QLQ-C30	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire core
EORTC QLQ-BR23	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Breast Cancer Module
ER	exercise rehabilitation
FSS	Fatigue Severity Scale
HTx	hormone therapy
IRB	Institutional Review Board
LE	lymphedema
MHR	maximal heart rate
QOL	quality of life
RTx	radiotherapy
SNB	sentinel node biopsy
SD	standard deviation
US	United States
VO_2max	peak oxygen uptake
WHO	World Health Organization

References

1. Arnold M, Morgan E, Rumgay H, et al. Current and future burden of breast cancer: global statistics for 2020 and 2040. Breast. 2022;66:15–23.
2. Akkala S, Zuber M, Atta JA, Mzizi NO, Akkula J. Socioeconomic status and breast cancer treatment in the United States: results from a systematic literature review. Cancer Control. 2025;32:10732748251341520.
3. Huang Y, Lin JJ, Wisnivesky JP, Kong CY, Sigel K. Assessing the risk of second primary lung cancer in women after previous breast cancer. BJC Reports. 2025;3:33.
4. Kihn-Alarcón AJ, Peralta A, Torres-Ruiz J, et al. Years of potential life lost because of breast and cervical cancers in Guatemala. JCO Global Oncology. 2020;6:761–765.
5. American Cancer Society. Breast Cancer Facts & Figures 2024–2025 [Internet]. Available from: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/2024/breast-cancer-facts-and-figures-2024.pdf. (Accessed June 3, 2025)
6. Heer E, Harper A, Escandor N, et al. Global burden and trends in premenopausal and postmenopausal breast cancer: a population-based study. The Lancet Global Health. 2020;8:e1027–e1037.
7. Youlden DR, Cramb SM, Yip CH, Baade PD. The descriptive epidemiology of female breast cancer: an international comparison of screening, incidence, survival and mortality. Cancer Epidemiology. 2012;36:237–248.
8. Francies FZ, Hull R, Khanyile R, Dlamini Z. Breast cancer in low-middle income countries: abnormality in splicing and lack of targeted treatment options. American Journal of Cancer Research. 2020;10:1568–1591.
9. Harford JB. Breast-cancer early detection in low-income and middle-income countries: do what you can versus one size fits all. The Lancet Oncology. 2011;12:306–312.
10. Guo G, Li J, Zheng Y, Liu ZX, Lin H. Breast-conserving surgery is associated with a lower incidence of suicide among females with breast cancer in the United States: a population-based retrospective cohort study. International Journal of Surgery. 2024;110:1392–1401.
11. Mohamedahmed AYY, Elamin AM, Ahmed EA, et al. Comparison of surgical and oncological outcomes between oncoplastic breast-conserving surgery versus conventional breast-conserving surgery for treatment of breast cancer: a systematic review and meta-analysis of 31 studies. Surgical Oncology. 2022;42:101779.

 doi:10.20944/preprints202602.1735.v1

12. Ren Y, Deng J, Zhao J, et al. Incidence, risk factors, prevention and treatment of postmastectomy pain syndrome in breast cancer: a multicenter study. International Journal of Surgery. 2022;106:106937.
13. de Ligt KM, Heins M, Verloop J, et al. The impact of health symptoms on health-related quality of life in early-stage breast cancer survivors. Breast Cancer Research and Treatment. 2019;178:703–711.
14. Paraskevi T. Quality of life outcomes in patients with breast cancer. Oncology Reviews. 2012;6:e2.
15. Kröz M, Girke M, Bruns F, et al. Predictors of fatigue improvement in multimodal, multimodal-aerobic and aerobic exercise intervention studies in breast cancer survivors with cancer-related fatigue. Scientific Reports. 2025;15:20690.
16. Chen X, Li Q, Wang Y, et al. Effects of exercise interventions on cancer-related fatigue and quality of life among cancer patients: a meta-analysis. BMC Nursing. 2023;22:200.
17. Markes M, Brockow T, Resch KL. Exercise for women receiving adjuvant therapy for breast cancer. Cochrane Database of Systematic Reviews. 2006;4:CD005001.
18. Velthuis MJ, Agasi-Idenburg SC, Aufdemkampe G, Wittink HM. The effect of physical exercise on cancer-related fatigue during cancer treatment: a meta-analysis of randomised controlled trials. Clinical Oncology. 2010;22:208–221.
19. Devoogdt N, Van Kampen M, Geraerts I, et al. Physical activity levels after treatment for breast cancer: one-year follow-up. Breast Cancer Research and Treatment. 2010;123:417–425.
20. Schmitz KH, Courneya KS, Matthews C, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Medicine and Science in Sports and Exercise. 2010;42:1409–1426.
21. Wolin KY, Schwartz AL, Matthews CE, Courneya KS, Schmitz KH. Implementing the exercise guidelines for cancer survivors. Journal of Supportive Oncology. 2012;10:171–177.
22. Ficarra S, Bisignano G, Laganà AS, et al. Impact of exercise interventions on physical fitness in breast cancer patients and survivors: a systematic review. Breast Cancer. 2022;29:402–418.
23. Imayama I, Alfano CM, Neuhouser ML, et al. Weight, inflammation, cancer-related symptoms and health-related quality of life among breast cancer survivors. Breast Cancer Research and Treatment. 2013;140:159–176.
24. Pinto e Silva MP, Borges CM, Ferreira EB, et al. Implications of a postoperative rehabilitation program on quality of life in women with primary breast cancer treated with sentinel lymph node biopsy or complete axillary lymph node dissection. Annals of Surgical Oncology. 2008;15:3342–3349.
25. Harrison SA, Hayes SC, Newman B. Age-related differences in exercise and quality of life among breast cancer survivors. Medicine and Science in Sports and Exercise. 2010;42:67–74.
26. Astari YK, Fajriyah SN, Rachmawati IN, et al. Feasibility, acceptability, and preliminary effectiveness of implementing a 12-week home-based aerobic and resistance exercise program for breast cancer patients receiving endocrine treatment in Indonesia: a mixed methods study. SAGE Open Medicine. 2024;12:20503121241272706.