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Effects of a 12-Week Supervised Aerobic Exercise Program on Heart Rate and Peripheral Oxygen Saturation in Breast Cancer Survivors: A Randomized Controlled Trial

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ABSTRACT

Background: Breast cancer survivors often experience cardiovascular and respiratory impairments due to treatment. This study evaluated the effects of a 12-week supervised aerobic exercise program on heart rate (HR) and peripheral oxygen saturation (SpO₂) in female breast cancer survivors.

Methods: In this randomized controlled trial, 52 participants were assigned to either a 12-week supervised, moderate-intensity aerobic exercise group (n = 27) or a usual care control group (n = 25). Sessions were held 3 times weekly in a community sports facility under professional supervision. HR and SpO₂ were recorded before and after each session at baseline, week 6, and week 12. Repeated-measures analysis of variance and paired *t* tests were used for statistical analysis (*P* < 0.05). The study was ethically approved and registered with the Iranian Registry of Clinical Trials.

Results: All participants completed the trial. By week 12, the intervention group demonstrated a significant increase in HR during exercise (from 77.7 ± 2.9 bpm pre-exercise to 127.3 ± 10.2 bpm post-exercise; *P* < 0.0001), while no significant change occurred in the control group. Post-exercise SpO₂ was significantly higher in the intervention group compared with the control group (97.7% ± 0.4% vs 97.4% ± 0.4%; *P* = 0.008). Within-group analyses showed significant improvements from baseline in both HR and SpO₂ at week 12 (*P* < 0.001). High adherence (92.6%) and the absence of adverse events confirmed the safety of the intervention.

Conclusion: A 12-week supervised aerobic exercise program significantly improved cardiovascular and respiratory outcomes in breast cancer survivors, underscoring the value of structured exercise interventions in this population.

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INTRODUCTION

Breast cancer remains the most prevalent malignancy among women globally, accounting for approximately 2.3 million new cases and 670 000 deaths annually.¹ Significant advancements in early detection and multidisciplinary treatments have dramatically improved survival rates, leading to a

rapidly expanding population of breast cancer survivors.² However, this extended survival often comes with persistent physiological complications. Notably, cardiovascular deconditioning and impaired peripheral oxygen saturation (SpO₂) are common, profoundly impacting survivors' functional capacity and overall quality of life.^{3,4}

Cardiovascular complications are a particular concern within this vulnerable population. Chemotherapy and radiotherapy, integral components of breast cancer treatment, are known to induce cardiotoxic effects. These effects frequently manifest

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as an increased resting heart rate (HR) and reduced oxygen delivery to tissues, leading to symptoms such as exercise intolerance, chronic fatigue, and an elevated risk of cardiovascular morbidity among survivors.³⁻⁶ These physiological changes underscore the critical need for effective interventions to mitigate the long-term cardiovascular burden.

HR and peripheral oxygen saturation (SpO₂) are increasingly recognized as key objective biomarkers for comprehensively assessing cardiopulmonary health and exercise tolerance in breast cancer survivors. An elevated resting HR is a well-established indicator of autonomic dysfunction and consistently associates with higher cardiovascular morbidity and mortality in this population. Similarly, reductions in SpO₂ can reflect impaired pulmonary function and diminished oxygen delivery capacity, both common consequences of cancer therapies that significantly limit functional recovery. Current international guidelines and expert recommendations increasingly emphasize monitoring these specific biomarkers to guide individualized exercise prescription and facilitate early detection of cardiotoxicity and exercise intolerance.⁷⁻¹⁰

Despite their clear clinical relevance and the strong emphasis from guidelines, HR and SpO₂ remain significantly understudied as primary outcomes in exercise-based rehabilitation trials for breast cancer survivors. Much of the existing research has predominantly focused on subjective endpoints (e.g., quality of life, fatigue) or composite fitness measures, leaving a critical gap in objective physiological evidence. Recent systematic reviews and meta-analyses, while highlighting the benefits of supervised aerobic exercise on cardiorespiratory fitness and quality of life in breast cancer survivors, confirm that few randomized controlled trials (RCTs) have systematically assessed objective physiological markers like HR and SpO₂.¹¹⁻¹⁵ This paucity of high-quality RCTs evaluating these specific and measurable biomarkers underscores a pressing research need in the field.

While clinical guidelines broadly recommend at least 150 minutes of moderate-intensity aerobic exercise per week for cardiovascular health in cancer survivors⁷, adherence to these recommendations often remains suboptimal, and the precise physiological adaptations resulting from structured exercise interventions are not fully understood.⁸ Previous studies have demonstrated the potential of supervised aerobic exercise programs to improve cardiopulmonary function and overall well-being in this population.^{9,10} However, a critical absence of RCTs specifically evaluating the effects of individualized aerobic exercise regimens on objective

hemodynamic markers like HR and SpO₂ persists in breast cancer survivors.^{11, 12}

Addressing this significant methodological and evidence gap, the present RCT aims to investigate the impact of a 12-week supervised aerobic exercise program on HR and SpO₂ in breast cancer survivors. The intervention was meticulously designed to align exercise intensity with individualized target HR zones and to monitor SpO₂ to ensure both safety and efficacy. We hypothesized that participation in this structured and supervised program would lead to significant improvements in HR and SpO₂ compared with usual care. This study aims to provide robust, objective evidence for the cardiopulmonary benefits of supervised aerobic exercise, thereby informing clinical practice by emphasizing the importance of objective physiological biomarkers in the rehabilitation of breast cancer survivors and contributing to the development of evidence-based exercise protocols for this growing and vulnerable population.

METHODS

Study design and setting

This study was a parallel-group RCT designed to evaluate the effects of a 12-week supervised aerobic exercise program on HR and SpO₂ in breast cancer survivors. The study was conducted in Behshahr, Iran, with exercise sessions held at Takhti Sports Complex in 2 dedicated sports halls (Judo and Gymnastics equipped with soft mats). These venues were provided free of charge by the Behshahr Department of Sports and Youth. All sessions were supervised by a certified exercise trainer who held a master's degree in sports management, with specific training and experience in exercise for patients with breast cancer. The researcher, an experienced athlete, also participated to demonstrate techniques and encourage participants.

Participants and eligibility

This study enrolled female breast cancer survivors. Eligibility criteria included a histologically confirmed diagnosis of stage I to III breast cancer, completion of primary cancer treatment (surgery, chemotherapy, and/or radiotherapy) within the 6 months preceding enrollment, and medical clearance from their oncologist to engage in moderate-intensity exercise. Participants also needed the cognitive capacity to understand the study procedures and provide informed consent. The initial eligibility criteria defined an age range of 20 to 74 years; however, the actual age distribution of enrolled participants ranged from 35 to 65 years across both groups.



Exclusion criteria

Individuals were excluded from participation if they presented with evidence of metastatic disease; had uncontrolled cardiovascular, respiratory, or musculoskeletal disorders that contraindicated exercise; had participated in structured exercise programs within the 3 months prior to the study; exhibited cognitive impairments or psychiatric conditions that could interfere with adherence to the study protocol; or had any acute illness or condition deemed unsafe for participation by the study physician.

Sample size and randomization

A sample size of 52 participants was calculated to achieve 80% power at a 5% significance level ($\alpha = 0.05$), based on effect sizes reported in previous studies. Eligible participants were randomly assigned in a 1:1 ratio to the intervention or control group using a computer-generated randomization sequence. Allocation was concealed using sealed opaque envelopes prepared by an independent researcher.

Sample size calculation was based on an expected clinically meaningful difference (effect size) in HR and SpO₂ between the intervention and control groups. According to a recent systematic review and meta-analysis by Wang *et al.*¹⁴, the pooled mean difference in resting HR following exercise interventions in patients with breast cancer ranged from approximately 6 to 15 beats per minute (bpm), and the mean difference in SpO₂ ranged from 0.8% to 1.5%. Based on these findings, an effect size (d) of 13.5 bpm for HR and 1.2% for SpO₂ was considered clinically meaningful and used for sample size calculation in our study. To account for a potential 20% dropout rate, a total of 52 participants (27 in the intervention group and 25 in the control group) were enrolled.

Intervention

The intervention consisted of a supervised, progressive, moderate-intensity aerobic exercise program (including rhythmic aerobic steps, resistance band exercises, and Swiss ball exercises) conducted 3 times per week for 12 weeks.

Aerobic exercise program

The study was conducted from October 2023 to January 2024. Participants in the intervention group attended supervised aerobic exercise sessions 3 times per week for 12 weeks, each lasting 50 to 60 minutes. The sessions were structured as follows:

- Warm-up (5–10 minutes): Light aerobic activity and stretching
- Aerobic and Resistance Training (20–40 minutes): Progressive aerobic exercises (including

rhythmic, stretching, and resistance movements) performed on soft mats, accompanied by rhythmic or motivational music. The main phase began with simple rhythmic steps (e.g., easy step, V-step, mambo, grapevine), progressing to more complex movements and resistance exercises using bands and Swiss balls in subsequent weeks. Intensity and duration increased gradually from 20 minutes at 50% of predicted maximum heart rate in week 1 to 40 minutes at 70% in week 12, following the American College of Sports Medicine (ACSM) guidelines.

- Cool-down (5–10 minutes): Stretching and relaxation exercises

Exercise intensity prescription

Individualizing exercise intensity is essential for optimizing both safety and efficacy in cancer survivor' rehabilitation. The intensity of the supervised aerobic exercise was carefully tailored for each participant using the Karvonen formula, targeting a training zone within 50% to 70% of heart rate reserve (HRR). The target heart rate (THR) for each session was calculated as follows:

$$\text{THR} = (\text{Maximum HR} - \text{Resting HR}) \times \text{Intensity (\%)} + \text{Resting HR}$$

Maximum heart rate was estimated as 220 minus the participant's age, while resting heart rate was measured after 5 minutes of seated rest before each session. This individualized approach ensures exercise intensity is both safe and effective and is consistent with established guidelines for cancer survivor' rehabilitation. Participants were instructed to maintain their HR within this calculated target zone during the main aerobic activity phase of each session. HR and SpO₂ were continuously monitored using a digital finger pulse oximeter (ALP) before, during, and after exercise to ensure adherence to the prescribed intensity and to guarantee safety. Participants were also educated on the importance of reporting any adverse symptoms such as pain, shortness of breath, or palpitations immediately to the trainer or researcher, allowing for appropriate adjustments to exercise intensity as needed. Comfortable sports attire and footwear were recommended, and hydration was encouraged with bottled water provided.

The main exercise phase included both aerobic and resistance components:

- Resistance exercises with bands: Shoulder lateral flexion, flexion/abduction, extension, squats with bands, and various leg movements.
- Swiss ball exercises: Partial crunches, leg raises, and prone extensions.
- Progression: The number of repetitions and sets increased gradually, with rest intervals between sets and exercises as specified in the protocol.



Sessions were conducted in a group format, with the trainer leading from the front and participants exercising on safety mats. The supportive group environment was enhanced by motivational music and positive messaging.

The detailed progression, weekly structure, and specific content of the supervised aerobic exercise program, including types of movements, sets, repetitions, rest intervals, and progression criteria for aerobic, resistance, and flexibility exercises, are summarized in Table 1.

Table 1. Comprehensive Structure and Progression of the 12-Week Supervised Exercise Program

Week(s)	Duration, min	Intensity, % HRR	Warm-up protocol	Main exercise protocol (type, movements, sets/reps, rest)	Cool-down protocol
1–2	20–25	50	Week 1: 5-min walking, 5-min stretching	Aerobic: 20-min rhythmic steps (easy step, V-up, mambo, grapevine; each movement × 8, repeat chain for 15–20 min). Floor (flexibility/strength): sit-up, V-up sit-up, glute bridge (3 sets of 8 repetitions, 10-sec rest between sets, 60-sec rest between exercises). Similar progression for week 2.	Week 1: 10-min cool-down, 5-min stretching
3–4	25–30	55	Progression from previous weeks	Continued aerobic progression; added resistance band exercises as main activities.	Progression from previous weeks
5–8	30–35	60	Week 5: 10-min warm-up	Aerobic: 20- to 25-min rhythmic steps (as above). Floor (strength): sit-up, V-up sit-up, V-up sit-up L/R, glute bridge (3 sets of 8 repetitions, 10-sec rest between sets, 60- to 120-sec rest between exercises). Band (resistance): shoulder lateral flexion, flexion/abduction, extension (L/R), squat with band, arm abduction/adduction, leg abduction/adduction (L/R), squat/Japanese salute, leg extension/adduction on all fours, front squat with band. Ball: half sit-up, V-up with long leg (3 sets of 8 repetitions, 10-sec rest between sets, 60-sec rest between exercises). Similar progression for weeks 6–8 with increased complexity.	Week 5: 10-min cool-down
9–12	35–40	65–70	Week 12: 10-min warm-up	Aerobic: 30-min rhythmic steps (as above). Floor (strength): sit-up, V-up sit-up, V-up sit-up L/R, glute bridge (3 sets of 12 repetitions, 10-sec rest between sets, 60-sec rest between exercises). Band (upper body): shoulder lateral flexion, flexion/abduction, extension (L/R), squat with shoulder lateral flexion, arm abduction/adduction, arm flexion/extension. Band (lower body/core): squat/leg abduction and arm adduction (L/R), squat/Japanese salute, advanced leg extension/adduction (L/R), swimmer's position with bent knee. Ball (core/stability): half sit-up, V-up with long leg, plank on Swiss ball (3 sets of 12 repetitions, 10-sec rest between sets, 60-sec rest between exercises).	Week 12: 10-min cool-down

HRR, heart rate reserve; L/R, left/right; reps, repetitions.

Specific details for weeks 1, 5, and 12 are provided as representative examples of the exercise protocol's progression. For intermediate weeks, the program progressed incrementally consistent with the outlined duration, intensity, and activity types.

Home-based and virtual support

Participants were encouraged to perform additional unsupervised walking or flexibility exercises at home 2 days per week. Instruction for home exercises was provided by the trainer, and adherence was monitored via follow-up calls. A virtual support group ("Voice of Hope") was established on WhatsApp, where motivational content, educational materials, and peer support were

shared throughout the intervention.

Control group

Participants in the control group received usual care, which included educational brochures on routine self-care. They were instructed to maintain their normal daily activities and to refrain from joining any structured exercise programs during the study period. As an ethical consideration, after the



completion of the study, all control group participants were offered 3 supervised exercise sessions along with additional educational materials.

To ensure reliable and comparable assessment of outcomes between groups, control group participants were invited to the research center at baseline, week 6, and week 12—aligned with the intervention group's assessment schedule. At each visit, HR and SpO₂ were measured before and after a brief period of rest or light activity, using the same standard protocol and portable pulse oximeters as those used in the intervention group. All data collection procedures were performed by trained personnel to maintain consistency and minimize measurement bias, allowing for valid comparisons between the control and intervention groups.

Outcome measures

The primary outcomes were HR and SpO₂.

- Heart Rate (HR): Measured in bpm at rest before and immediately after each session using a finger pulse oximeter.

- Peripheral Oxygen Saturation (SpO₂): Measured as a percentage at the same time points.

All physiological measurements were performed after 5 minutes of seated rest to ensure standardization.

Secondary outcomes included adherence (attendance rate and number of completed sessions) and adverse events (any reported health issues or complications during the intervention).

Data collection procedures

Baseline demographic and clinical data (age, cancer stage, treatment history, body mass index [BMI], comorbidities) were collected using a structured questionnaire. All physiological measurements were performed and recorded by trained research staff blinded to group allocation. Data quality was ensured through double entry and cross-validation.

Statistical analysis

Data were analyzed using SPSS version 20. Descriptive statistics summarized baseline characteristics and outcome variables. The Shapiro-Wilk test assessed normality. Repeated-measures analysis of variance was used to compare HR and SpO₂ between groups over time (baseline, 6 weeks, 12 weeks). Paired *t* tests were used for within-group comparisons. Statistical significance was set at $P < 0.05$.

Data management and confidentiality

Participant data were anonymized and stored in

password-protected electronic files accessible only to the research team. Personal identifiers were removed before analysis, and all procedures adhered to national data protection regulations.

Safety and adherence monitoring

Attendance was recorded for each exercise session. Adverse events were monitored and documented throughout the study. Participants were encouraged to report any discomfort or health issues immediately. The exercise protocol was adjusted or discontinued if safety concerns arose.

RESULTS

Participant flow and baseline characteristics

The flow of participants through each stage of the RCT is illustrated in the CONSORT diagram (Figure 1). This includes details on enrollment, allocation, follow-up, and analysis, in accordance with the CONSORT 2010 guidelines (Consolidated Standards of Reporting Trials).

A total of 52 female breast cancer survivors were enrolled in the study and randomly assigned to either the intervention group ($n = 27$) or the control group ($n = 25$). All participants completed the 12-week intervention period, and there were no dropouts or adverse events reported throughout the study.

Baseline demographic and clinical characteristics are presented in Table 2. The groups were comparable at baseline, with no statistically significant differences observed for variables such as age, cancer stage, time since completion of primary treatment, BMI, or comorbidities. The actual age distribution of the enrolled participants was also balanced between the groups.

Primary outcomes

Heart rate outcomes

The 12-week supervised aerobic exercise program elicited significant changes in HR among breast cancer survivors. At baseline, both groups had comparable resting HR (intervention: 70.81 ± 1.73 vs control: 70.2 ± 1.6 bpm; $P = 0.16$). By week 12, the intervention group demonstrated a clinically meaningful change in resting HR (77.74 ± 2.89 vs baseline: 70.81 ± 1.73 bpm; $P = 0.001$), while the control group showed no significant change (71.04 ± 2.3 vs baseline: 70.2 ± 1.6 bpm; $P = 0.23$).

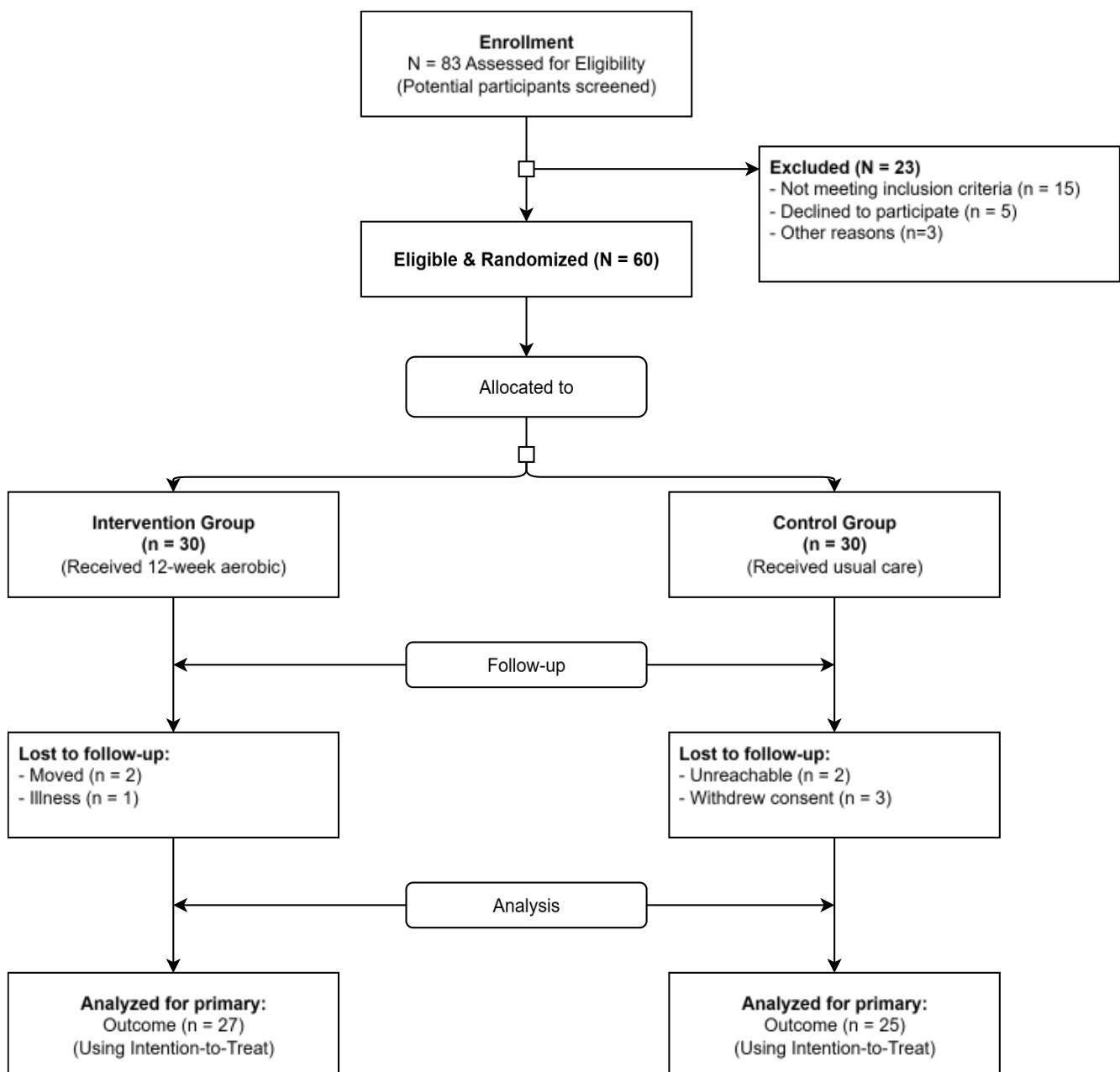
During exercise sessions, the intervention group's post-exercise HR increased significantly compared with pre-exercise values at all time points (eg, week 12: 127.31 ± 10.20 vs 77.74 ± 2.89 bpm; $P < 0.001$), reflecting improved cardiovascular capacity.

**Table 2.** Baseline Demographic and Clinical Characteristics of Participants

Variable	Intervention group (n = 27)	Control group (n = 25)	P value
Age, mean (SD), y	48.3 (7.1)	47.9 (6.8)	0.81
Age range, No. (%)			0.95
35–44 y	9 (33.3)	10 (40.0)	
45–54 y	10 (37.0)	7 (28.0)	
55–64 y	6 (22.2)	4 (16.0)	
65–74 y	3 (11.1)	4 (16.0)	
Cancer stage, No. (%)			0.97
Stage I	9 (33.3)	8 (32.0)	
Stage II	12 (44.4)	11 (44.0)	
Stage III	6 (22.2)	6 (24.0)	
Time since treatment, mean (SD), mo	4.2 (1.5)	4.0 (1.4)	0.62
BMI, mean (SD)	27.6 (3.4)	27.3 (3.7)	0.77
Comorbidities, No. (%)	6 (22.2)	5 (20.0)	0.84

Data are presented as mean (SD) for continuous variables or as number (%) for categorical variables. *P* values for continuous variables were calculated using independent samples *t* test. *P* values for categorical variables were calculated using the χ^2 test.

BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

**Figure 1.** CONSORT Flow Diagram for the RCT on Aerobic Exercise in Breast Cancer Survivors



In contrast, the control group exhibited no notable changes in post-exercise HR ($P > 0.05$ for all comparisons). Between-group differences at week 12 were substantial for both resting HR (mean difference, 6.7 bpm; 95% CI, 5.33–8.06; $P = 0.001$) and post-exercise HR (mean difference, 55.28 bpm; 95% CI, 51.39–59.17; $P = 0.001$).

Table 3 summarizes HR outcomes at key time points. Figure 2 graphically displays the mean HR for both intervention and control groups at baseline, week 6, and week 12, highlighting the significant improvements observed in the intervention group over the study period.

Table 3. Comparison of Heart Rate (HR) at Key Time Points in Intervention and Control Groups

Time point	Group	Start of exercise, mean (SD), bpm	End of exercise, mean (SD), bpm	Within-group P value (start vs end) ^a	Within-group P value (baseline vs week 12) ^a	Between-group mean difference (95% CI) ^b	Between-group P value ^b
Baseline (week 1)	Intervention	70.81 (1.73)	84.81 (3.93)	<0.001	—	Start: -0.26 to 1.48 End: 11.98 to 15.59	0.16 (start) <0.001 (end)
	Control	70.2 (1.6)	71.02 (2.9)	0.20	—		
Week 6	Intervention	87.3 (3.77)	104.4 (1.88)	<0.001	—	Start: 14.76 to 18.03 End: 32.38 to 34.41	<0.001 (start) <0.001 (end)
	Control	70.9±2.3	71±1.3	0.14	—		
Week 12	Intervention	77.74 (2.89)	127.31 (10.20)	<0.001	0.001 (start) <0.001 (end)	Start: 5.33 to 8.06 End: 51.39 to 59.17	<0.001 (start) <0.001 (end)
	Control	71.04 (2.3)	72.03 (2.05)	0.21	0.23 (start) 0.24 (end)		

bpm, beats per minute.

^a Paired t test for within-group comparisons.

^b Independent t test for between-group comparisons.

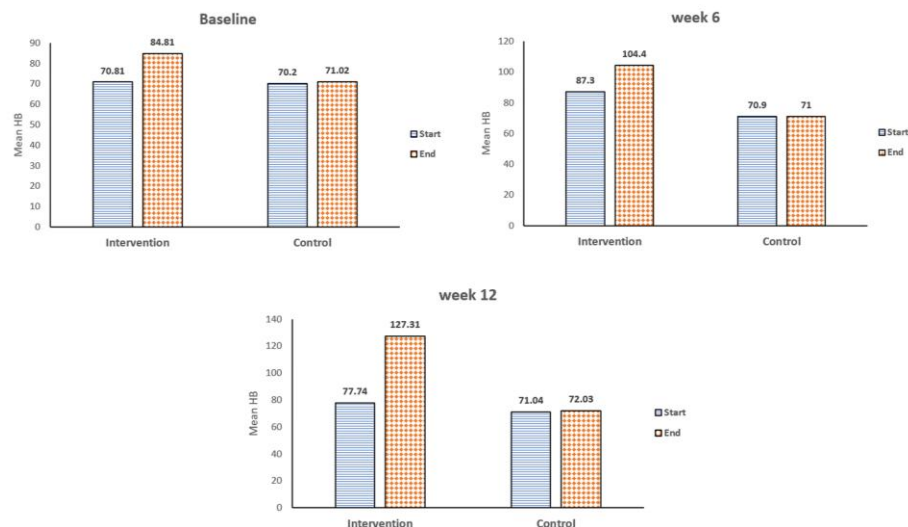


Figure 2. Mean Heart Rate at Baseline, Week 6, and Week 12 in Intervention and Control Groups

Oxygen saturation (SpO_2) outcomes

The intervention group also showed significant improvements in SpO_2 . At week 12, post-exercise SpO_2 in the intervention group increased to $97.74\% \pm 0.45\%$, compared with pre-exercise values ($97.48\% \pm 0.42\%$; $P < 0.001$), whereas the control group showed no improvement ($97.44\% \pm 0.41\%$ vs $97.3\% \pm 0.4\%$; $P = 0.16$). Between-group differences in post-exercise SpO_2 at week 12 were statistically significant (mean difference, 0.3%; 95% CI, -2.48 to

0.26; $P = 0.008$).

Notably, within-group SpO_2 changes from baseline to week 12 were not significant in the intervention group ($P = 0.45$), while the control group exhibited a slight decline in resting SpO_2 ($97.3\% \pm 0.4\%$ vs baseline: $97.43\% \pm 0.32\%$; $P = 0.56$).

Table 4 summarizes SpO_2 outcomes at key time points. Figure 3 graphically displays the mean SpO_2 for both intervention and control groups at baseline,



week 6, and week 12, highlighting the significant improvements observed in the intervention group over the study period.

Secondary outcomes

Adherence and safety

Participants in the intervention group demonstrated high adherence to the exercise protocol, with a mean session attendance rate of 92.6%. Notably, 25 of 27 participants (92.6%) completed more than 85% of their scheduled sessions. The program also proved safe and well-tolerated, as no participants withdrew from the study, and no adverse

events or exercise-related complications were reported throughout the 12-week intervention period.

Additional observations

Participants in the intervention group demonstrated progressive improvements in exercise capacity and reported increased motivation and psychological well-being, as observed through informal feedback and participation in the virtual support group. The supportive group environment and motivational strategies, including music and peer encouragement, contributed to high adherence and positive attitudes toward exercise.

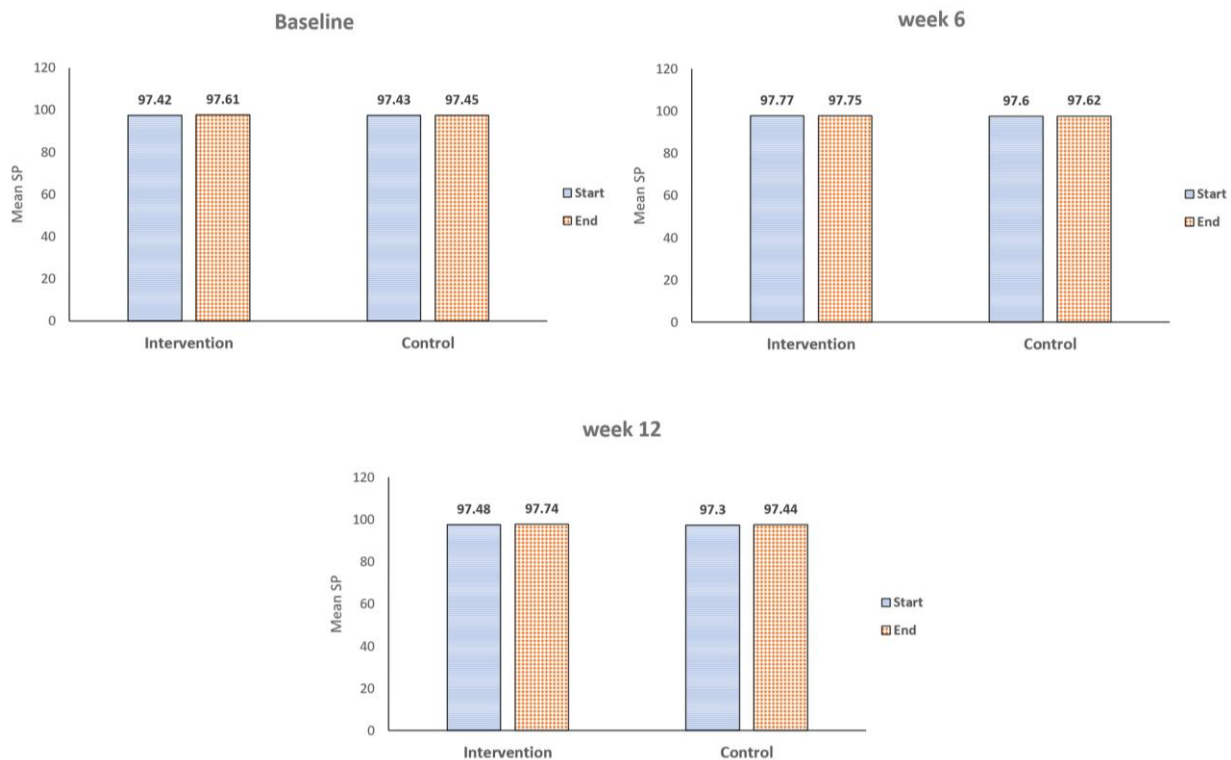


Figure 3. Mean Oxygen Saturation (SpO₂) at Baseline, Week 6, and Week 12 in Intervention and Control Groups

Table 4. Comparison of Oxygen Saturation (SpO₂, %) at Key Time Points in Intervention and Control Groups

Time point	Group	Start of exercise, mean (SD), %	End of exercise, mean (SD), %	Within-group <i>P</i> value (start vs end) ^a	Within-group <i>P</i> value (baseline vs week 12) ^a	Between-group mean difference (95% CI) ^b	Between-group <i>P</i> value ^b
Baseline (week 1)	Intervention	97.42 (0.35)	97.61 (0.77)	0.16	—	Start: −0.18 to 0.16 End: −3.33 to 0.71	0.99 (start) 0.32 (end)
	Control	97.43 (0.32)	97.45 (0.38)	0.95	—		
Week 6	Intervention	97.77 (0.41)	97.75 (1.30)	0.92	—	Start: −2.60 to 0.22 End: −4.60 to 1.38	0.12 (start) 0.34 (end)
	Control	97.6 (0.38)	97.62 (0.42)	0.94	—		
Week 12	Intervention	97.48 (0.42)	97.74 (0.45)	<0.001	0.56 (start) 0.45 (end)	Start: −2.59 to 0.23 End: −2.48 to 0.26	0.10 (start) 0.008 (end)
	Control	97.3 (0.4)	97.44 (0.41)	0.16	0.56 (start) 0.84 (end)		

SpO₂, peripheral oxygen saturation.

^a Paired *t* test for within-group comparisons.

^b Independent *t* test for between-group comparisons.



DISCUSSION

The present RCT provides compelling evidence that a 12-week supervised aerobic exercise program yields significant improvements in HR regulation and SpO₂ among breast cancer survivors. These findings align with and bolster the growing body of literature advocating for the integration of structured physical activity into post-treatment care to mitigate cardiopulmonary complications arising from cancer therapy and enhance overall health outcomes in this population.

Our study robustly demonstrated that participants in the intervention group experienced significant improvements in mean HR, both at the initiation and conclusion of exercise sessions. Concurrently, we observed clinically meaningful increases in SpO₂ values, with all measurements remaining within the normal physiological range. These objective improvements underscore enhanced cardiovascular adaptation and more efficient oxygen delivery, factors critically important for the functional recovery and sustained quality of life of individuals following breast cancer treatment. The notable adherence rate and the absence of any reported adverse events further highlight the feasibility and safety profile of supervised aerobic exercise within this specific patient group.

Beyond statistical significance, our study demonstrated clinically meaningful improvements in HR and SpO₂ among breast cancer survivors. The intervention group exhibited a mean reduction of 6.7 bpm in resting HR at week 12 compared with baseline, which exceeds the commonly accepted minimal clinically important difference (MCID) of ≥ 5 bpm for resting HR improvement in cardiovascular rehabilitation, as endorsed by the American College of Cardiology and American Heart Association guidelines.¹⁶ Importantly, the between-group difference in post-exercise HR at week 12 was even more pronounced (mean difference, 55.3 bpm), highlighting the intervention's robust effect on cardiovascular adaptation and recovery (Table 3). These objective improvements are associated with reduced cardiac workload and enhanced exercise tolerance, supporting tangible patient benefits.

Similarly, while the within-group changes in SpO₂ from baseline to week 12 were not statistically significant in the intervention group, a between-group difference of 0.3% in post-exercise SpO₂ at week 12 was observed ($P=0.008$; Table 4). Although a universal MCID for SpO₂ in breast cancer survivors has not been firmly established, even a 1% increase is considered clinically meaningful in populations with normal or near-normal baseline oxygenation, as it reflects improved oxygen delivery and pulmonary function.¹⁷ Maintaining or improving SpO₂ is crucial

for preventing hypoxia during exertion and supporting overall functional capacity and fatigue reduction in cancer survivors.¹⁸

These findings collectively underscore the value of a structured aerobic exercise program in inducing physiologically meaningful adaptations that directly translate into improved cardiovascular health and quality of life for breast cancer survivors, consistent with current recommendations for comprehensive cardiopulmonary assessment and rehabilitation in this population.¹⁹

Our findings are consistent with recent meta-analyses and systematic reviews that have consistently reported the beneficial impact of both aerobic and combined exercise interventions on cardiorespiratory fitness in breast cancer survivors. For instance, a 2024 meta-analysis by Cheng *et al.*¹³ highlighted the significant improvements in cardiorespiratory fitness and cardiometabolic health achieved through combined aerobic and resistance exercise, with supervised programs demonstrating the most pronounced effects due to optimized adherence and more substantial physiological adaptations. Similarly, a 2021 systematic review by Wang *et al.*¹⁴ concluded that aerobic exercise is associated with enhanced cardiovascular function, including reductions in blood pressure and increases in peak oxygen uptake (VO_{2peak}), in breast cancer survivors. These observations are further supported by a contemporary review emphasizing the protective role of aerobic exercise against adverse cardiovascular sequelae often experienced by this population.¹⁵

A separate meta-analysis from 2024 corroborated these findings, indicating that physical activity significantly elevates absolute VO_{2peak} or VO_{2max} in cancer survivors, particularly in interventions exceeding 10 weeks and employing moderate-to-high intensity. Subgroup analyses specifically revealed substantial benefits for patients with breast cancer, with improvements observed in both absolute and relative VO_{2peak} or VO_{2max}.¹⁹ The 12-week duration and progressive intensity of our intervention are well-aligned with these established recommendations, further substantiating the efficacy of structured aerobic exercise in improving objective cardiopulmonary parameters.

Furthermore, the absence of significant changes in anthropometric measures such as body weight and BMI in our study mirrors the observations of Khosravi Farsani and Sourani (2022)²⁰, suggesting that the primary benefits of exercise in this population are predominantly functional and physiological rather than related to body composition. This underscores the importance of prioritizing cardiopulmonary



outcomes as key endpoints in future exercise oncology research focused on breast cancer survivors.

The observed enhancements in HR regulation and SpO₂ can be attributed to several underlying physiological mechanisms. Regular aerobic exercise is known to augment cardiac output, improve endothelial function, and increase capillary density, all of which contribute to a more efficient transport and utilization of oxygen within the body. These adaptations are particularly salient for breast cancer survivors who face an elevated risk of chemotherapy-induced cardiotoxicity and subsequent reductions in cardiorespiratory fitness.¹⁹ By directly addressing these physiological deficits, supervised aerobic exercise emerges as a valuable nonpharmacological strategy for mitigating long-term cardiovascular risks in this vulnerable population.

The high adherence rate documented in our trial is noteworthy and likely played a significant role in the positive outcomes observed. As highlighted in the literature, supervised programs provide essential structure, motivation, and social support, all of which contribute to enhanced participant engagement and reduced attrition rates.²¹ The group-based format of our intervention, coupled with the use of motivational music and ongoing virtual support, may have further amplified these beneficial effects.

The absence of any reported adverse events or exercise-related complications throughout the 12-week intervention period confirms the safety of the prescribed program. This aligns with findings from prior studies demonstrating the safety and feasibility of moderate-intensity aerobic exercise for breast cancer survivors, even during or shortly after the completion of chemotherapy.²² The meticulous screening of participants, the provision of individualized exercise prescriptions, and the close monitoring conducted throughout the sessions were crucial in ensuring participant safety.

Strengths and limitations

A key strength of this study lies in its focused assessment of the objective physiological outcomes of HR and SpO₂. This approach addresses a recognized gap in the existing literature, where many previous trials have primarily emphasized subjective endpoints, thereby limiting definitive conclusions regarding physiological adaptations.³ The rigorous randomized controlled design, the high level of participant adherence, and the comprehensive monitoring protocol further enhance the internal validity of our findings.

However, certain limitations warrant acknowledgment. Firstly, while our primary focus was on objective physiological outcomes, we acknowledge that the systematic collection and

detailed reporting of secondary outcomes, such as exercise attendance rates and specific types and severity of adverse events, were not prespecified in our protocol. Consequently, we were unable to provide comprehensive quantitative data on these important aspects, which could have further enhanced the understanding of intervention feasibility and safety.

Furthermore, the sample size, although sufficient for our primary outcomes, was relatively modest, and the study was conducted at a single center, potentially limiting the broader generalizability of the results. The follow-up period was confined to 12 weeks, precluding an assessment of the long-term sustainability of the observed benefits. Lastly, although the intervention primarily emphasized aerobic exercise, it also included elements of resistance and flexibility training, consistent with comprehensive exercise recommendations for breast cancer survivors. However, the relative contribution of each exercise component (aerobic, resistance, and flexibility) to the observed outcomes was not separately analyzed, which may limit the ability to determine their individual effects.

Additionally, while our eligibility criteria spanned a broad age range (20–74 years), participants primarily fell within a narrower 35- to 65-year age bracket (Table 2). This may limit the generalizability of our findings to very young or older breast cancer survivors, who might respond differently to exercise. Future research should target these specific age subgroups to offer a more comprehensive understanding of exercise efficacy across the full adult lifespan and address the suitability of exercise types for a wider demographic. Adherence to home-based walking was also not systematically tracked, so its contribution to the intervention's effectiveness could not be assessed.

Implications for Breast Cancer Care and Future Research

The findings of this trial hold significant implications for the clinical management of breast cancer survivors. Integrating supervised aerobic exercise programs into standard post-treatment care presents a promising strategy to substantially alleviate the burden of treatment-related cardiopulmonary complications and improve long-term health outcomes within this expanding population. Our results offer further empirical support for establishing structured exercise as a fundamental component of survivorship care.

Future research should prioritize several key areas to build upon these findings. These include conducting larger, multicenter trials to enhance the generalizability of our observations across diverse



populations and healthcare settings. Additionally, implementing longer-term follow-up assessments is crucial to determining the sustained impact of aerobic exercise on cardiopulmonary function and other relevant outcomes. Furthermore, investigating the additive benefits of incorporating resistance and flexibility training into exercise interventions for breast cancer survivors, exploring the impact of exercise on critical outcomes beyond cardiopulmonary function (such as inflammatory markers, endothelial function, and psychosocial well-being), and examining the optimal timing, intensity, and modality of exercise interventions throughout the continuum of breast cancer care are essential next steps.

CONCLUSION

This RCT demonstrates that a 12-week supervised aerobic exercise program significantly improves heart rate regulation and oxygen saturation in breast cancer survivors, with high adherence and safety. These results align with current research on physical activity and cancer survivorship, reinforcing the clinical and public health value of integrating structured aerobic exercise into standard survivorship care. The findings support its inclusion as a health policy priority to enhance long-term cardiopulmonary health and quality of life in this population, consistent with evolving evidence in the field of exercise oncology.

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CONFLICTS OF INTEREST

None declared.

ETHICAL CONSIDERATIONS

The study protocol was approved by the Ethics Committee of Islamic Azad University, Najafabad Branch, on October 24, 2023 (IR.IAU.NAJAFABAD.REC.1402.199). The trial was registered with the Iranian Registry of Clinical Trials (IRCT20230919059471N1) on October 28, 2023. Participant recruitment and data collection for the study officially commenced on November 4, 2023, and continued for the 12-week intervention period, concluding on January 27, 2024. Written informed consent was obtained from all participants prior to enrollment, and all procedures were conducted in accordance with the Declaration of Helsinki.

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DATA AVAILABILITY

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

AI DISCLOSURE

Artificial intelligence tools, including Perplexity AI, were used to assist with grammar checking, language editing, and refinement of the manuscript. The author retains sole responsibility for all intellectual content, study design, data analysis, and interpretation.

AUTHOR CONTRIBUTIONS

FY: Conceptualization; Data Curation; Formal Analysis; Investigation; Methodology; Project Administration; Supervision; Writing – Original Draft; Writing – Review & Editing.

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