



Feasibility of a novel exercise program for patients with breast cancer offering different modalities and based on patient preference

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ARTICLE INFO

Keywords:

Physical exercise
Breast cancer
Patient preference
Feasibility
Supportive care
Quality of life

ABSTRACT

Purpose: Exercise improves quality of life and reduces the side effects of cancer therapies. Nevertheless, attendance to exercise programs remains a challenge for patients. This study explored the feasibility of an exercise program in which women with breast cancer may be allowed to choose among three exercise delivery modalities.

Methods: Forty-seven patients with breast cancer (stage I-IV) participated in a 12-week combined aerobic and resistance training program. The exercise modality was chosen by patients according to their preferences and needs among three options: the *personal training program*, the *home-based program*, or the *group-based program*. Exercise prescription was similar between the three modalities. Whereas the primary endpoint was feasibility, assessed through recruitment rate, attendance, adherence, dropout rate, tolerability, and safety, secondary endpoints included health-related skills and quality of life.

Results: Out of 47 recruited patients, 24 chose the home-based program, 19 the personal training program, and four the group-based program. Six dropouts (13%) were registered, and no severe adverse events were recorded. The median program attendance was 98% for personal training programs, 96% for home-based programs, and 100% for group-based programs, whereas compliance resulted in more than 90% in each modality. At post-intervention, a significant increase in cardiorespiratory fitness, lower body flexibility, and body weight was observed. Different quality-of-life domains were improved following the intervention, including physical and social functioning, fatigue, and appetite loss. No significant changes in other parameters were detected.

Conclusions: An exercise prescription based on a patient-preferred delivery modality showed high feasibility in women with breast cancer.

1. Introduction

Breast cancer is the most common cancer worldwide among women (Arnold et al., 2022). Although early diagnosis and new therapeutical solutions have led to an increased number of survivors (Siegel et al., 2023), breast cancer treatments may produce a series of side effects, seriously impairing patients' quality of life (QoL). Both classical (e.g.,

chemotherapy, radiotherapy, hormone therapy) and innovative (e.g., target therapy) treatments are associated with different adverse events, such as fatigue, peripheral neuropathy, cardiotoxicity, and impaired sexual, cognitive, and bone function, which may persist for years after treatment completion (Di Nardo et al., 2022; Perez et al., 2022). In addition, different physical features may be negatively impacted during the cancer journey. Musculoskeletal toxicities, including joint pain and

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<https://doi.org/10.1016/j.ejon.2024.102554>

Received 10 January 2024; Received in revised form 4 March 2024; Accepted 8 March 2024

Available online 11 March 2024

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muscle weakness, are frequently reported by 48–73% of women undergoing aromatase inhibitors (Ernst et al., 2021; Menas et al., 2012) and are so debilitating that they may lead patients to discontinue or interrupt the therapy (Rosso et al., 2023) with a consequent increased risk of mortality and recurrence (Eliassen et al., 2023). Cardiorespiratory fitness, which is a prognostic factor in breast cancer (Peel et al., 2009), is often compromised in patients; for instance, compared to age-matched healthy women, patients with breast cancer have 31% lower cardiorespiratory fitness during chemotherapy (Jones et al., 2012; Klassen et al., 2017). Therefore, proposing supportive care aiming to ameliorate this symptomatology is essential and may have important clinical implications.

In this light, mounting evidence highlights the use of physical exercise to support patients with breast cancer. Observational researches suggest that postdiagnosis physical activity is associated with a reduction of 26%–45% of breast cancer-specific and 27%–49% of all-cause mortality (Fortner et al., 2023). On the other side, various randomized controlled trials have proved that engaging in a regular exercise program during breast cancer may help to manage symptoms, such as fatigue (Wu et al., 2023), peripheral neuropathy (Brownson-Smith et al., 2023), anxiety/depression (Sun et al., 2023), lymphedema (Hasenoehrl et al., 2020), and, at the same time, can improve health-related skill (e.g., cardiorespiratory fitness, strength, body composition), overall enhancing patient QoL, and potentially prolong patient life (Campbell et al., 2019). For these reasons, different national and international guidelines for physical exercise in cancer have been published (Campbell et al., 2019; Runowicz et al., 2016). These guidelines strongly suggest implementing exercise and avoiding sedentary; nevertheless, despite the recognized benefits, one of the main challenges to date is to increase adherence to the current recommendation. Indeed, less than 40% of patients with breast cancer reported participating in regular physical activity (Gal et al., 2019), and in addition, in patients who participate in a dedicated program, compliance and adherence are often heterogeneous (Singh et al., 2018). Different disease-related (e.g., treatment side effects) and non-disease-related (e.g., weather, distance from facility) barriers may hinder the participation of patients with breast cancer (Doughty et al., 2023; Lavalley et al., 2019; Michael et al., 2021). On the contrary, patient preferences are often reported as facilitators (Avancini et al., 2020). Adapting exercise to the preferences and needs of patients with cancer may be one of the best strategies to encourage participation and adherence to structured exercise programs (Wagoner et al., 2022). In this sense, the preference for the exercise delivery modality may be crucial (Avancini et al., 2020; Schleicher et al., 2023). Some patients may prefer an in-person, individual intervention with the advantage of having a fully personalized and supervised program; others may desire more social support, thus favoring a group-based program (Delrieu et al., 2019), or prefer to exercise at home, especially if they live far from facilities or if they do not feel comfortable exercising with others (Wong et al., 2018). However, the preference in exercise modality, i.e., home-based, individual-supervised, or group-based, is highly heterogeneous, as previously reported (Avancini et al., 2020), suggesting that the “one for all” strategy may disfavor an important percentage of patients. In this sense, an exercise program offering different exercise modalities by encountering patients’ preferences may be an interesting solution to increase compliance and adherence, although, to our knowledge, no research has investigated this kind of intervention. To fill this gap, we designed the present study, aiming to assess the feasibility and the preliminary efficacy of a 12-week exercise program for women with breast cancer based on the patient preference in the delivery modality.

2. Materials and methods

2.1. Study design

This prospective single-arm study was conducted at the University of

Verona to explore the feasibility and safety of a combined exercise program in women with breast cancer. The present study adhered to Good Clinical Practice principles; all the procedures were conducted in compliance with the Helsinki and Oviedo declarations, and the protocol was registered at [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT04226508). The Verona University Ethics Committee for Clinical Trials has reviewed and approved the project (Prot. N. 33320). Written informed consent was obtained before starting baseline assessments or any study procedures. The study is reported following the CONSORT Statement: extension to randomized pilot and feasibility trials (Eldridge et al., 2016).

2.2. Participants and procedures

Between November 2019 and January 2021, women with breast cancer were invited to participate in the study at the Oncology Unit of the University of Verona Hospital Trust. Eligibility criteria were: (i) ≥ 18 years old, (ii) a histologically/cytologically confirmed diagnosis of breast cancer at any stage, (iii) at least eight weeks from surgical resection, (iv) medical clearance for study participation, and (v) written informed consent signed. Patients were excluded if they had surgery scheduled within 12 weeks and had absolute contraindications for exercise participation. Oncology healthcare providers proposed the study to patients during the visits, and if patients were interested in participating, they were contacted by the research staff to explain in detail the program’s features and to fix a first appointment at the Departments of Sport Science facilities.

2.3. Exercise intervention

The exercise intervention included a 12-week combined aerobic and resistance training program designed following the American College of Sports Medicine exercise guidelines for cancer (Campbell et al., 2019) and adapted to the patient’s condition, with special attention for bone metastatic disease. Following the recent exercise recommendations for bone metastasis, potential risks deriving from exercise were prevented by: i) avoiding exercises or loads that excessively stressed the lesion site; ii) starting with light loads or free-body exercises and slowly progressing with intensity throughout the program; iii) avoiding exercise in the presence of pain, especially at the metastatic site; iv) avoiding rapid or loaded end-range movements like rotations, extensions, and flexions at the area of bone lesions; v) educating patients about the correct technique and posture of exercises; vi) constantly monitoring the patient’s response to exercise and adapting it as needed (Campbell et al., 2022).

During the baseline evaluation, patients were asked to choose the exercise modality according to their preferences and needs among three options (Fig. 1): (i) the personal training program, (ii) the home-based program, or (iii) the group-based program. Each program modality involved a patient-centered exercise prescription based on clinical history and functional assessments of women, requiring the same amount of time for participating. The first modality was delivered at the Department of Sport Science facility and comprised 24 exercise sessions fully supervised and guided directly by an expert kinesiologist (with a master’s degree) in a one-to-one mode. The second delivery modality included a tailored written exercise program to perform independently. About one week after initial assessments, patients meet the trainers at the Department of Sport Science to receive the program and the equipment (an elastic band). Patients tried the exercises under the supervision of the kinesiologists in order to learn the correct exercise technique and were educated to self-monitor the exercise intensity using the 10-point Borg Rating of the Perceived Exertion Scale (RPE). Periodical meetings at the facility were scheduled every two, four, and six weeks to hand out the new part of the program and try the activities. In addition, weekly telephone contacts to continuously monitor and support the patient were administered by the kinesiologist, and patients were asked to complete an exercise diary after each session, reporting the adherence and the intensity perceived for each exercise component.






Exercise program: modalities and prescription		
 Home-based modality	 Personal training modality	 Group-based modality
<ul style="list-style-type: none"> • Written exercise program; • Periodic meeting every 2, 4 and 6 weeks; • Weekly telephone contacts; 	<ul style="list-style-type: none"> • 1:1 ratio patient-kinesiologist; • Performed at the facilities ; 	<ul style="list-style-type: none"> • Group of 4-6 patients; • Supervision of kinesiologist • Performed at the facilities ;
 Aerobic training	<p>Type: walking, cycling Frequency: 2 times per week Duration: 15 minutes up to 30 minutes Intensity: moderate, i.e., 3-5 rate of perceived exertion (C-10) Progression: Yes</p>	
 Strength training	<p>Type: body-weight or with elastic bands exercises Frequency: 2 times per week Duration: 2-3 sets, 8-12 repetitions Intensity: moderate, i.e., 3-5 rate of perceived exertion (C-10) Progression: Yes</p>	

Fig. 1. Exercise program modalities and prescription.

The group-based modality consisted of kinesiologist-supervised activities conducted at the facilities of the Department of Sport Science in a group of 4–6 patients each session.

The exercise prescription was similar between the three modalities (Fig. 1). Exercise sessions were undertaken two times a week for approximately 60 min and included a warm-up, an aerobic part, resistance exercise, and stretching activities. The warm-up included dynamic stretching exercises starting from the neck to the ankles. The aerobic component was performed using the treadmill, cycle ergometer, or arm ergometer for the personal training and group-based programs, while patients who chose the home-based program were asked to select their preferred activities among walking, running, cycling, and swimming. The intensity was moderate according to the RPE scale. The aerobic part started from 15 to 20 min based on the patient's initial status and progressively increased over the weeks, about 5 min every two weeks, up to 30 min at the end of the program. The resistance part included six body-weight or elastic band exercises that targeted the major upper and lower body muscles and had a gradual increase in volume over the weeks. Exercises were adapted to the patient's capacity, for example, increasing/decreasing the intensity of the elastic band or changing the position like sitting or standing. Each exercise was performed at a moderate intensity (3–5 RPE) in 2–3 sets of 8–12 repetitions. Cool-down was composed of five stretching exercises for the major muscle groups.

2.4. Outcomes

The primary study outcome was the feasibility of the intervention. The exercise program was considered feasible if do not occur severe or

life-threatening adverse events (Dittus et al., 2017) and almost three of the following criteria were met: recruitment rate $\geq 50\%$ (Dittus et al., 2017), completion rate $\geq 80\%$, program attendance $\geq 80\%$ (resistance and aerobic), program compliance $\geq 75\%$ (Singh et al., 2018) and program tolerance $\geq 70\%$ (Crosby et al., 2023)%. Feasibility was checked during the program by the research staff and assessed with: 1) *recruitment and completion rates*, determined by the ratio of patients enrolled compared with the number of eligible patients and the ratio of patients who completed the intervention and withdrawals, 2) *program attendance*, calculated as the number of exercise sessions (divided in aerobic and resistance components) attended out of the scheduled sessions; attendance was also evaluated in missed session (i.e., 1 or 2 missed sessions consecutively), interruption (i.e., 3 or more missed consecutive sessions) and permanent discontinuation (i.e., loss to follow-up), 3) *program compliance*, defined as the ratio of the total volume completed compared with the prescribed one; compliance was also determined by dose modification, which is the number of sessions requiring a decrease or increase in load and 4) *program tolerance*, which corresponds to the RPE perceived by the patients compared with the prescribed intensity. Safety of the program was obtained by calculating the number of adverse events linked to exercise intervention according to the Common Terminology Criteria for Adverse Events, version 5.0 (National Cancer Institute, 2022). Adverse events were continuously monitored for each program modality.

Secondary endpoints of the study included the evaluation of the effects of the exercise program on physical fitness, QoL and amount of physical activity. Functional assessments were performed at the Department of Sport Science following standardized guidelines. Before

starting physical tests, blood pressure and saturation were recorded. According to standardized protocols, anthropometric parameters included height, weight, waist and hip circumferences were evaluated (de Onis et al., 2004) and through these measures, body mass index (kg/m^2) and the waist-hip ratio were calculated. Cardiorespiratory fitness was estimated using the 6-min walking test, which has been largely tested in clinical populations, according to the procedures proposed by the American Thoracic Society guidelines (ATS, 2002). The handgrip strength test was used for evaluating the maximum isometric strength of the hand and forearm muscles (Innes, 1999), whereas for lower limbs, the isometric leg press test (Impellizzeri et al., 2007) was performed. Five trials for each arm and lower limbs were performed and the contractions were held for 2–4 s. Flexibility was measured using the sit and reach test and the back scratch test, using standardized procedures (Rikli and Jones, 2013). QoL was measured using the Italian version of the European Organization for Research and Treatment of Cancer Quality of Life and Core Questionnaire (EORTC QLQ C-30), designed to evaluate cancer-specific QoL, symptoms burden and functional scales with 30 items (Neil et al., 1993). Current physical exercise behavior was assessed using Godin's Shepard Leisure Time Exercise Questionnaire. It consists of 3 items, in which the patients were asked to indicate the frequency and duration of vigorous, moderate, or light activities in a typical week (Amireault et al., 2015). Socio-demographic information were collected using a dedicated questionnaire, investigating age, gender, education, marital status, and employment, while medical variables were checked through medical charts during the baseline evaluation and included cancer type and stage, date of diagnosis, type and duration of prior and ongoing treatments, presence of comorbidities, and use of medications.

2.5. Statistical analysis

Descriptive statistics was used to analyze the intervention's feasibility and participants' baseline characteristics (sociodemographic and clinical variables). Aerobic and resistance components were considered and analyzed as separated, even if performed in a single training session. To calculate the difference between baseline and post-intervention values, a paired *t*-test or Wilcoxon signed-ranked test was performed using SigmaStat v. 4.0 (Systat Software Inc.). Shapiro-Wilk test was used to test the normal distribution of secondary outcomes data. Data were presented as mean and standard deviation if they were distributed normally or as median and interquartile range if they were not. *P*-values <0.05 were considered statistically significant. An exploratory analysis was performed to investigate changes in patients' reported outcomes and functional assessment according to the training delivery modality and cancer stage. A formal sample size analysis was not done since this was a feasibility study. The sample size was chosen considering the access of patients at the Oncology Unit, and a sample of 47 women was considered adapted to evaluate the study's feasibility and explore the efficacy (Kaye et al., 2020).

3. Results

The flow of patients through the study is reported in Fig. 2. Of the 55 women referred by clinicians, 47 consented to participate and underwent baseline assessments. A total of 47 patients participated in the study. Baseline characteristics are presented in Table 1. Women had a mean age of 54.24 ± 9.21 years old, 53.2% had a high school degree, and 80.9% were married. The majority of patients were diagnosed with stage I breast cancer (44.7%). The majority of patients were diagnosed with stage I breast cancer (44.7%), the mean time since diagnosis was 24.74 ± 29.24 months, and 87% had undergone surgery. All the patients underwent anticancer treatments during the study, mainly chemotherapy (57.4%) and hormone therapy (80.9%). Regarding program delivery mode, 24 patients chose the home-based program, 19 the personal training program, and 4 the group-based program.

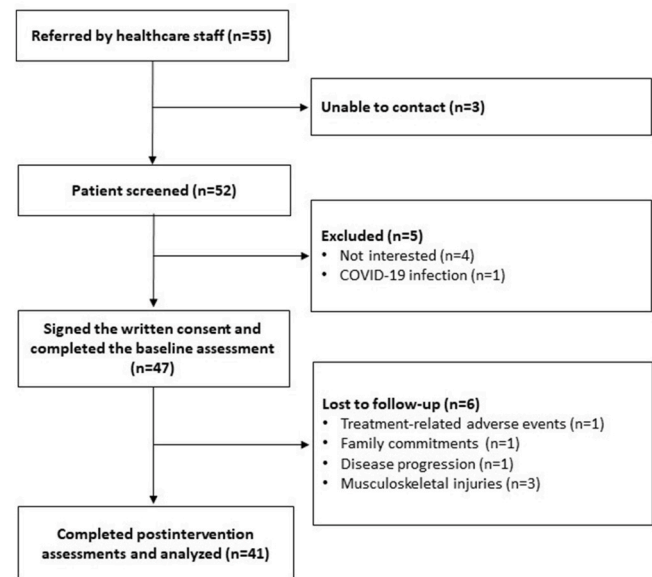


Fig. 2. Study flow diagram.

3.1. Feasibility and safety

Feasibility outcomes are reported in Table 2. The study recruitment rate was 85.4%. Throughout the study, 6 (13%) dropouts occurred, 3 (19%) in the personal training program and 3 (14%) in the home-based program. Differences in baseline assessments for completers vs. non-completers are presented in Supplementary Materials. The median program attendance for the entire cohort was 100% (IQR: 88–100%), 100% for aerobic training (IQR: 91–100%), and 96% for resistance training (IQR: 87–100%). The median program attendance was >95% for all three exercise modalities. Participants completed 811 sessions out of the 984 sessions scheduled, and missed sessions occurred mainly for the resistance component. Disease-related, such as lymphedema exacerbation and shoulder pain, were the most common frequent reasons for missed sessions. Details for missed sessions are reported in Supplementary Materials. Six patients, 2 in the personal training program and 4 in the home-based group, had treatment interruptions due to work problems ($n = 4$), lymphedema exacerbation ($n = 1$), and treatment-related symptoms ($n = 1$). Four patients permanently discontinued the program due to lack of motivation, lymphedema, hormone therapy side effects, and frozen shoulder.

The median program compliance was 100% (IQR: 67–100%) and 96% (IQR: 78–100%) for aerobic and resistance training sessions, respectively. Median compliance among the three exercise modalities resulted high, >90%.

The overall volume of each resistance training session (i.e., sets and repetitions) required adjustments exceeding 10% for six patients. In two patients attending the personal training program, the resistance volume needed reduction due to joint pain, while in four patients participating in the home-based program, adjustments were made due to lymphedema in the upper arm, arthralgias, and fatigue. Regarding program tolerance, 761 out of the 811 sessions completed were performed at the prescribed intensity. In the personal training group, 10 aerobic sessions (3%) and 10 resistance sessions (3%) were completed at a lower RPE than that prescribed (2 RPE). In the home-based group 8 sessions were performed at a lower intensity (2%) while 22 were perceived as too strenuous (6%) and exceeded the target RPE (6–8 RPE). No severe or life-threatening adverse events were registered throughout the study. In total, 18 adverse events occurred, 8 in the personal training program and 10 in the home-based, as reported in Fig. 3. Patients experienced mild (Grade 1) adverse events like fatigue and dizziness, which were related

Table 1
Baseline characteristics of the participants.

Patients' characteristics	(N = 47)
Age, mean (SD)	54,24 (9,21)
BMI, mean (SD)	27,33 (6,20)
Education, n (%)	
Elementary	1 (2,1%)
Secondary	8 (17,0%)
High school degree	25 (53,2%)
Undergraduate degree	8 (17,0%)
Postgraduate degree	5 (10,6%)
Marital status, n (%)	
Married	38 (80,9%)
Divorced	2 (4,3%)
Single	7 (14,9%)
Employment, n (%)	
Part-time employed	10 (21,3%)
Full-time employed	14 (29,8%)
Retired	10 (21,3%)
Sick leave	7 (14,9%)
Homemaker	3 (6,4%)
Unemployed	3 (6,4%)
Family income, n (%)	
Barely adequate	8 (17,0%)
Adequate	28 (59,6%)
More than adequate	11 (23,4%)
Stage, n (%)	
I	21 (44,7%)
II	11 (23,4%)
III	5 (10,6%)
IV	10 (21,3%)
Metastases sites, n (%)	
Bone	6 (12,8%)
Other sites ^a	4 (8,5%)
Time since diagnosis, mean in months (SD)	24,74 (29,24)
Type of treatment, n (%)	
Chemotherapy	27 (57,4%)
Radiotherapy	9 (19,1%)
Surgery	41 (87,2%)
Target therapy	9 (19,1%)
Hormone therapy	38 (80,9%)
Current treatments status, n (%)	
Ongoing	47 (100%)
Concomitant comorbidities, n (%)	
Yes ^b	22 (46,8%)
No	25 (53,2%)
Exercise program modality	
Home-based program	24 (51,1%)
Personal training program	19 (40,4%)
Group-based program	4 (8,5%)

Notes.

^a metastasis sites: lung (2,1%), liver (2,1%), brain (2,1%) and lymph nodes (4,3%).

^b Types of comorbidities: hypertension (19,1%), diabetes (2,1%), osteoporosis/osteopenia (19,1%), hypercholesterolemia (12,8%), obesity (2,1%), asthma (4,3%), cardiopathy (4,3%), hypothyroidism (2,1%), arthritis (2,1%), Sjogren's syndrome (2,1%), Hashimoto's thyroiditis (2,1%), labyrinthitis (2,1%).

to anticancer therapies, but also moderate (Grade 2) adverse events like lymphedema and arm or shoulder pain, which limited the program participation.

3.2. Physical fitness and patient-reported outcomes

Functional assessments outcomes are reported in Table 3. At post-intervention, cardiorespiratory fitness (519.5 ± 67.7 vs. 544.9 ± 67.8 m; $p < 0.001$) and lower body flexibility (-2.5 [IQR: 14.5–1.43] vs. -1.0 [IQR: 7.25–5.0] centimeters; $p < 0.001$) significantly improved, whereas a significant gain in BMI (26.7 [IQR: 22.9–30.3] vs. 27.2 [IQR: 23.1–30.3] kg/m²; $p = 0.041$) and body weight (73.5 [IQR: 61.9–81.7] vs. 73.0 [IQR: 62.7–82.5] kg; $p = 0.042$) were detected. No changes occurred for waist-hip ratio or upper and lower limb strength. Regarding patient-reported outcomes (Table 4), there were improvements in

Table 2
Feasibility results of the entire cohort, and according to the exercise modality.

Variable	Total cohort			Personal training program			Home-based program			Group-based program		
	Overall	Aerobic training	Resistance training	Overall	Aerobic training	Resistance training	Overall	Aerobic training	Resistance training	Overall	Aerobic training	Resistance training
Lost to follow-up, n (%)	6 (13)	–	–	3 (19)	–	–	3 (14)	–	–	0	–	–
Attendance, median (IQR)	100% (88%–100%)	100% (91%–100%)	96% (87%–100%)	98% (90%–100%)	98% (90%–100%)	98% (90%–100%)	96% (83%–100%)	96% (86%–100%)	92% (74%–100%)	100% (100%–100%)	100% (100%–100%)	100% (100%–100%)
Treatment interruption, n (%)	6 (15)	5 (12)	6 (15)	2 (13)	2 (13)	2 (13)	4 (19)	3 (14)	4 (19)	0	–	–
Missed session, n (%)	173 (100)	63 (36)	110 (64)	32 (100)	16 (50)	16 (50)	141 (100)	47 (33)	94 (67)	0	–	–
Compliance, median (IQR)	96% (88%–100%)	100% (67%–100%)	96% (78%–100%)	96% (92%–100%)	100% (92%–100%)	96% (90%–100%)	94% (79%–100%)	96% (86%–100%)	92% (71%–100%)	100% (100%–100%)	100% (100%–100%)	100% (100%–100%)
Dose modification, n (%)	6 (15)	0	6 (15)	2 (10)	0	2 (10)	4 (25)	0	4 (25)	0	–	–
Early session termination, n (%)	–	–	–	–	–	–	–	–	–	–	–	–
Tolerability, n (%)	761/811 (94)	780/811 (96)	792/811 (98)	332/352 (94)	342/352 (97)	342/352 (97)	333/363 (92)	342/363 (94)	354/363 (98)	96/96 (100)	96/96 (100)	96/96 (100)

Definition: Lost to follow-up, number of patients who did not complete the study; Attendance, number of attended sessions compared to the total; Treatment interruption, number of patients who missed ≥ 3 continuous sessions; missed session, number of sessions not attended by the patients; compliance, number of completed planned exercise dosage compared to the total programmed; dose modification, number of patients that required $\geq 10\%$ of sessions dose escalation/reduction; early session termination, number of sessions interrupted before the planned intensity/duration; tolerability, number sessions performed at the planned intensity.

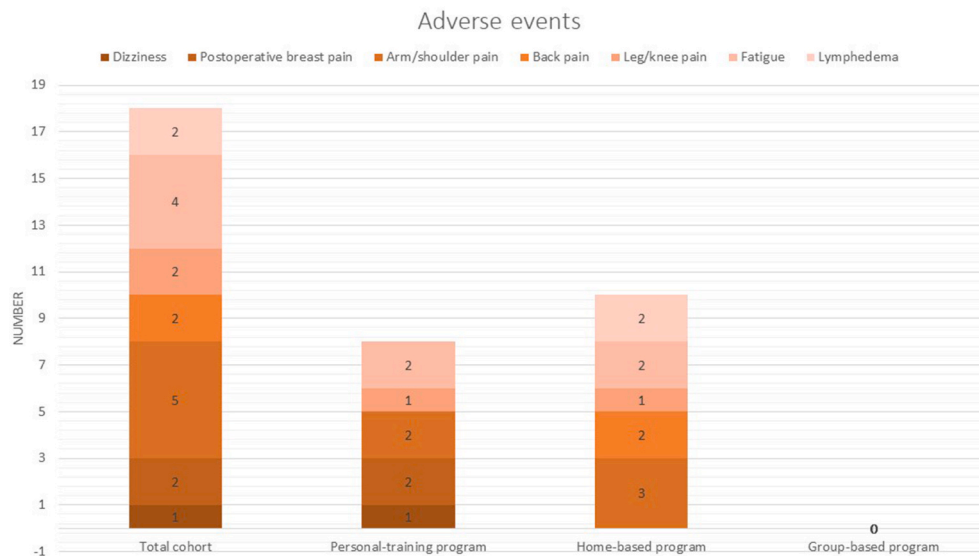


Fig. 3. Adverse events during the exercise program.

Table 3 Health-related skills assessment before and after exercise intervention.

Variables	Baseline, median (IQR)	Postintervention, median (IQR)	p-value
Anthropometric measures			
Body weight (kg)	73.50 (61.87–81.75)	73.00 (62.75–82.50)	0.042
Body mass index (kg/m ²)	26.67 (22.99–30.29)	27.20 (23.08–30.29)	0.041
Waist (cm)	92.0 (78.75–102.0)	88.0 (78.75–98.62)	0.803
Hip (cm)	106.0 (99.75–115.0)	108.0 (98.75–114.12)	0.831
Waist-hip ratio (cm)	0.83 (0.77–0.91)	0.82 (0.77–0.89)	0.764
Sit and reach (cm)	−2.50 (−14.50–1.43)	−1.00 (−7.25–5.0)	<0.001
Back scratch (cm)			
Right arm	0.00 (−8.00–3.62)	0.00 (−11.37–3.87)	0.200
Left arm*	−6.89 (9.41)	−6.12 (9.80)	0.802
Handgrip (kg)			
Right arm*	25.07 (5.17)	25.55 (5.22)	0.078
Left arm	24.00 (20.00–28.00)	26.00 (21.50–29.00)	0.071
Leg press (kg)*	81.29 (47.50)	81.25 (47.04)	0.277
Six minutes walking test (m)*	519.49 (67.67)	544.95 (67.88)	<0.001

Notes: * Data presented as mean and standard deviation.

physical (86.7 [IQR: 78.33–93.33] vs. 86.7 [IQR: 85.00–93.33]; $p = 0.005$) and social functioning (66.7 [IQR: 66.67–83.33] vs. 83.3 [IQR: 66.67–100.00]; $p = 0.006$), fatigue (33.3 [IQR: 22.22–44.44] vs. 33.3 [IQR: 11.11–33.33]; $p = 0.004$) and appetite loss (0.0 [IQR: 0.00–16.67] vs. 0.0 [IQR: 0.00–0.00]; $p = 0.049$). Significant increases in the total amount of physical activity (240.0 [IQR: 11.2–457.5] vs. 420.0 [IQR: 180.0–562.5] minutes; $p = 0.031$) and activities performed at vigorous (0.0 [IQR: 0.0–0.0] vs. 0.0 [IQR: 0.0–67.5] minutes; $p = 0.044$) and moderate (90.0 [IQR: 0.0–240.0] vs. 180.0 [IQR: 60.0–323.7]; $p = 0.015$) intensity were also observed.

An exploratory analysis of changes in health-related physical fitness and QoL according to exercise delivery modalities and cancer stage is presented in the Supplementary Materials. The home-based and personal training groups found a significant increase in lower limb flexibility and cardiorespiratory fitness. Patients in the home-based group reported a significant gain in body weight. In contrast, those in the

Table 4 Patient-reported outcomes before and after exercise intervention.

Variables	Baseline, median (IQR)	Postintervention, Median (IQR)	p-value
EORTC QLQ-C30			
Physical functioning	86.67 (78.33–93.33)	86.67 (85.00–93.33)	0.005
Role functioning	83.33 (66.67–100.00)	83.33 (83.33–100.00)	0.109
Emotional functioning	75.00 (66.67–91.67)	83.33 (66.67–91.67)	0.122
Cognitive functioning	83.33 (79.17–100.00)	83.33 (83.33–100.00)	0.190
Social functioning	66.67 (66.67–83.33)	83.33 (66.67–100.00)	0.006
Global health status*	66.4 (15.97)	68.3 (17.89)	0.573
Fatigue	33.33 (22.22–44.44)	33.33 (11.11–33.33)	0.004
Nausea/vomiting	0.00 (0.00–16.67)	0.00 (0.00–0.00)	0.042
Pain	16.67 (0.00–33.33)	16.67 (0.00–33.33)	0.576
Dyspnea	0.00 (0.00–33.33)	0.00 (0.00–33.33)	0.265
Insomnia	33.33 (0.00–33.33)	33.33 (0.00–33.33)	0.860
Appetite loss	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.049
Constipation	0.00 (0.00–33.33)	0.00 (0.00–33.33)	0.252
Diarrhea	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.831
Financial problems	0.00 (0.00–33.33)	0.00 (0.00–33.33)	0.945
Physical activity level (min/week)			
Vigorous	0.00 (0.00–0.00)	0.00 (0.00–67.50)	0.044
Moderate	90.00 (0.00–240.00)	180.00 (60.00–323.75)	0.015
Light	0.00 (0.00–150.00)	90.00 (0.00–240.00)	0.181
Total	240.00 (11.25–457.50)	420.00 (180.00–562.50)	0.031

Notes: * Data presented as mean and standard deviation.

personal-training modality reported significant improvements in the total amount of physical activity and light-intensity physical activity. The group-based intervention showed significant results in the strength of the left arm. According to cancer stage analysis, women with early-stage breast cancer exhibited a significant improvement in the sit-and-reach test and in the 6-min walking test, while in patients with metastatic disease, these increases did not result in statistical significance. Regarding QoL, statistically positive effects on physical, cognitive, and social functioning, and fatigue were detected as well as in the vigorous, moderate, and total amount of physical activity.

4. Discussion

The key study finding is that an exercise program based on the preferred delivery modality is feasible in patients with breast cancer. Notably, we found a recruitment rate of 85%, a dropout rate of 13.6%, no severe adverse events, and high attendance and compliance among the three exercise modalities. These results are particularly crucial in the context of lifestyle intervention, since adherence and compliance are essential to obtaining health benefits (Kampshoff et al., 2016), as reported by the World Health Organization (De Geest and Sabate, 2003). Additionally, our findings become even more significant if it is considered that attendance and compliance to exercise programs are often hindered in patients with breast cancer, especially due to treatment-related side effects, low motivation, kinesophobia, low social support, time pressures and inaccessible fitness facilities (Courneya et al., 2008; Goldschmidt et al., 2024; Hardcastle et al., 2018; Kampshoff, 2014; Wurz et al., 2015). On the contrary, effective symptom management strategies, perceived health benefits, social support, and guidance are powerful facilitators (Borsati et al., 2023; Courneya et al., 2008; Kampshoff, 2014; Lavallee et al., 2019). In our study, all three exercise modalities reached $\geq 90\%$ of attendance and adherence to the intervention. However, the literature reports mixed findings and often lower feasibility levels compared to ours. For instance, in the study of Naumann et al., adherence to a 9-week individual-based exercise program for patients with breast cancer was higher compared to a group-based program (74% vs. 84%) (Naumann et al., 2012), and in another research in adherence was higher in home-based activities compared to supervised activities (62% vs. 59%) (van Waart et al., 2020). A possible explanation for these discrepancies could be related to the intervention design; indeed, offering a multimodal delivery modality could be an effective strategy to empower patients and make them proactive in managing their lifestyles. The main reasons for missed sessions in our study were predominantly related to treatment side effects, especially arm or shoulder pain, arthralgias, and lymphedema, and prevalently interfered with resistance exercises and in the home-based program. Although these impairments are common in patients with breast cancer (DiSipio et al., 2013; Lin et al., 2023), aerobic but also resistance training, if correctly adapted, are safe and able to improve shoulder range of motion, arthralgias and lymphedema (Hasenoehrl et al., 2020). However, despite the potential benefits, the literature frequently reports treatment-related illness (33%), surgery restrictions (22%), and treatment symptoms (12%) as factors interfering with adherence to resistance programs (Kirkham et al., 2018). To overcome these barriers, the support of brochures and electronic materials may be positive instruments to ensure the safety of the exercises and enhance motivation to practice. For instance, in our participants, direct supervision by kinesiologists may have facilitated the training session by adjusting the intensity and type of exercises and educating the patients. This aspect underlines the importance of tailoring exercise day by day in the cancer population and motivating patients to maintain regular exercise by educating them that regular exercise participation can help manage pain symptoms and that exercises can be modified so that the pain symptoms do not worsen.

Beyond the feasibility, we observed a positive effect on cardiorespiratory fitness among the entire cohort of patients and in patients attending the personal training program and the home-based program, which will need to be further confirmed in a future randomized controlled trial. The improvement in cardiorespiratory fitness following an exercise intervention is well-established in the breast cancer population. A meta-analysis including 214 women with breast cancer undergoing hormone therapy found that patients allocated in the exercise group, comprising supervised and home-based interventions, reported a significant increase in cardiorespiratory fitness compared to the controls (SMD = 0.37; 95% CI: 0.11; 0.63; I² = 93%) (Boing et al., 2020). These results are encouraging because adjuvant treatments can negatively impact cardiorespiratory fitness in breast cancer patients. Impaired

cardiorespiratory fitness likely predisposes to noncancer competing morbidity and mortality as well as its attendant symptom burden. In our study, upper and lower body muscle strength did not significantly change. Similarly, the systematic review of Correia and colleagues, evaluating home-based interventions in women with breast cancer undergoing systemic treatments, did not find improvements in terms of strength (Correia et al., 2023), whereas several other research report positive results. Although the precise reasons remain unclear, the large number of missed resistance sessions and the type of activities, i.e., with elastic bands and using body weight, may be possible explanations.

Regarding anthropometric assessments, we found a significant increase in weight and BMI on one side, but on the other, no changes in waist-hip ratio were detected. Although taken together, these findings may appear opposite; it is possible to speculate that they may be the result of body composition optimization by gaining muscle mass and reducing body fat, and since muscle has a greater density than fat, meaning it takes up less volume than an equal amount of fat, it may have been translated into a reduction of the circumferences. However, our cohort was overall overweight. Reducing BMI is essential for patients with breast cancer due to its negative effect on prognosis (Thomas et al., 2017; Wang et al., 2019). Obese patients had a 46% higher risk of developing distant metastases after 10-year follow-up and a high mortality risk compared with normal-weight women (Barone et al., 2020). In this sense, combining exercise with a nutritional intervention may be an optimal strategy to take control the weight.

Even if the beneficial effect of exercise on QoL is well-recognized, not all the research agrees. For instance, in a systematic review including 22 studies evaluating the impact of exercise on breast cancer, 21 of them reported improvements in QoL, while one found a reduction in QoL, probably due to chemotherapy side effects (Ficarra et al., 2022). Although these findings necessitate being consolidated in a future randomized study, we observed enhancements in different domains of QoL, including physical and social functioning, fatigue, nausea, and appetite loss, suggesting a possible influence in attenuating treatment side-effects.

Limitations of the present study should be noted. Firstly, the heterogeneity of the study population, including disease stage and type of treatment, may limit the interpretation of our results. Nevertheless, our purpose was to test such exercise intervention in the breast cancer population, which by definition includes women affected by different stages of disease and undergoing various treatments. Secondly, a single-arm study design is appropriate to explore the feasibility of an exercise program; however, the effect of exercise intervention should be interpreted cautiously due to the lack of a control group. In this sense, a future randomized controlled trial may help to define better the real impact of this exercise program in patients with breast cancer.

5. Conclusion

In the era of personalized medicine, no standard and ideal exercise prescription that suits all exists, and its targeting also passes through the personalization of the delivery modality. All the exercise modalities we have proposed have pros and cons regarding supervision degree, spatial, and time constraints. Our goal was to meet patients' needs without bypassing the fundamental exercise prescription principles to deliver a feasible, effective, and beneficial exercise program. In this sense, we found that a 12-week combined exercise program, in which its delivery was based on the patient's preference, is feasible and probably able to produce psycho-physical improvements in patients with breast cancer undergoing systemic treatments.

CRediT authorship contribution statement

Anita Borsati: Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Linda Toniolo:**

Writing – review & editing, Visualization, Investigation, Data curation. **Iliaria Trestini**: Writing – review & editing, Visualization, Resources. **Daniela Tregnago**: Writing – review & editing, Visualization, Resources. **Lorenzo Belluomini**: Writing – review & editing, Visualization, Resources. **Elena Fiorio**: Writing – review & editing, Visualization, Resources. **Massimo Lanza**: Writing – review & editing, Visualization, Resources. **Federico Schena**: Writing – review & editing, Visualization, Resources. **Sara Pilotto**: Writing – review & editing, Visualization, Supervision, Resources, Project administration. **Michele Milella**: Writing – review & editing, Visualization, Supervision, Project administration, Methodology, Investigation, Conceptualization. **Alice Avancini**: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Michele Milella reports personal fees from Pfizer, EUSA Pharma and Astra Zeneca, outside the submitted manuscript. Sara Pilotto received honoraria or speakers' fee from Astra-Zeneca, Eli-Lilly, BMS, Boehringer Ingelheim, MSD and Roche, outside the submitted manuscript. All remaining authors declare that they have no competing interests.

Acknowledgments

The authors thank the participants in this study. This work was supported by grants from Associazione Pietro Casagrande ONLUS. M.M. and A.A. are currently supported by PRIN (CUP B39J21037270006).

Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejon.2024.102554>.

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