Original Article

Physical Activity for Symptom Management in Women With Metastatic Breast Cancer: A Randomized Feasibility Trial on Physical Activity and Breast Metastases

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Abstract

Context. Physical activity for women with early-stage breast cancer is well recognized for managing cancer-related symptoms and improving quality of life. While typically excluded from interventions, women with metastatic breast cancer may also benefit from physical activity.

Objective. To 1) determine the safety and feasibility of a physical activity program for women with metastatic breast cancer and 2) explore the efficacy of the program.

Methods. Fourteen women with metastatic breast cancer were randomized to either a control group or an 8-week home-based physical activity intervention comprising twice weekly supervised resistance training and an unsupervized walking program.

Results. The recruitment rate was 93%. Adherence to the resistance and walking components of the program was 100% and 25%, respectively. No adverse events were reported. When mean change scores from baseline to postintervention were compared, trends in favor of the exercise group over the control group were observed for the Functional Assessment of Chronic Illness Therapy-Fatigue score (+5.6 ± 3.2 vs. −1.8 ± 3.9, respectively), VO_{2max} (+1.6 ml/kg/minute ±1.8 mL/kg/minute vs. −0.2 mL/kg/minute ±0.1 mL/kg/minute, respectively) and six-minute walk test (+40 m ± 23 m vs. −46 m ± 56 m, respectively).

Conclusion. A partially supervised home-based physical activity program for women with metastatic breast cancer is feasible and safe. The dose of the resistance training component was well tolerated and achievable in this population. In contrast, adherence and compliance to the walking program were poor. Preliminary data suggest a physical activity program, comprising predominantly resistance training, may lead to improvements in physical capacity and may help women to live well with their disease. J Pain Symptom Manage 2019;58:929–939.

Key Words

Physical activity, exercise, metastatic cancer, advanced cancer, fatigue, physical function

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Introduction

Owing to advances in the management of metastatic breast cancer, the disease can be viewed as chronic in many women, albeit generally incurable.[1] With survival rate increasing, women may live for several years with a high level of symptom burden, commonly experiencing fatigue, depression, and pain.[2–4] While health-care providers often focus on survival, women living with metastatic breast cancer want more emphasis placed on alleviating symptoms and living well with their disease.[5] One of many strategies identified by women for living well is physical activity.[6,7]

For women with early breast cancer, the benefits of physical activity and exercise have been well documented.[8,9] Programs generally focus on managing symptoms and improving quality of life, with prescription similar to that of a cancer-free population.[9] Women with metastatic disease have traditionally been excluded from physical activity or exercise interventions, with conventional advice to avoid exercise because of fear of pathological fracture and a conservative view that fatigue is best treated with rest.[10,11] However, a recent systematic review of metastatic cancer suggested that exercise interventions may support independence, reduce fatigue, and enhance quality of life.[12]

Preliminary research of exercise programs for individuals with metastatic cancer has been typically conducted in a gymnasium, hospital, or community center.[10,11,13] Programs in these environments require participants to travel and are generally resource-intensive because of the use of specialized equipment, creating potential barriers to translation into clinical practice. A program that can be delivered in the home may not only increase the potential for implementation but has also been identified as a preference for metastatic and palliative patients with cancer.[14,15] Incorporating patient preferences in the design of a physical activity intervention may enhance adherence and retention to the program.

This study evaluated a home-based physical activity intervention in community-dwelling women living with metastatic breast cancer. The primary purpose of this phase I/II study was to evaluate the feasibility and safety of delivering a partially supervised program. In addition, efficacy of the program was explored with respect to patient-reported outcomes, physical performance, and physical activity level.

Methods

Trial Design

This study was a pilot randomized controlled trial (ANZCTR registration: ACTRN12618002019280). Permuted block randomization was performed using a computer-generated random numbers list by an individual external to the study. Participants were stratified according to whether they presented with bone-only or visceral ± bone metastases. Randomization was performed in blocks of 4, 6, and 8 with an allocation ratio of 1:1 to exercise or a control group. Sequentially numbered opaque envelopes containing group allocation were opened by the researcher in the presence of participants after baseline assessment.

Participants

Women with metastatic breast cancer who participated in a previous study investigating physical activity[16] were invited to participate. The researcher who approached potential participants was known to them through the previous project. Fourteen women were enrolled between October 2012 and July 2013. Inclusion criteria included stage IV breast cancer, living in the community, mentally competent to follow instructions, Eastern Cooperative Oncology Group (ECOG) performance status of 0–2,[17] aged over 18 years, and expected survival of at least 4 months. Individuals participating in regular physical activity, determined as "high" activity by the International Physical Activity Questionnaire, were excluded. Other exclusion criteria included inability to communicate in English or experiencing pain or other neuromuscular or musculoskeletal symptoms that limit physical activity.

Women in both groups completed the Physical Activity Readiness Questionnaire[18] to screen for cardiovascular, neurological, and musculoskeletal risk factors. Participants who required medical evaluation were granted medical clearance from their oncologist or primary care physician before enrolling.

The study was conducted in accordance with the protocol approved by the Human Research Ethics Committee of the Sydney Local Health District (X11–0344). All participants provided written informed consent.

Intervention

Control group ($n = 6$)

The control group was asked to maintain their habitual level of physical activity. No advice on exercise or physical activity was provided.

Exercise group ($n = 8$)

The intervention comprised an 8-week program of 16 exercise sessions conducted in the participant's home ($n = 6$) or a local park ($n = 2$), supervised by a university-trained exercise specialist. An unsupervised walking program was also prescribed for the duration of the 8-week intervention.

Each supervised session included a brisk walk for 10–15 minutes followed by 30–40 minutes of resistance training. The short walk was monitored via a pedometer and Borg's rating of perceived exertion,

with a target of 11–13 to reflect a moderate intensity.[19] Resistance exercises included chest press, horizontal row, upright row, bicep curl, calf raises, lunges, and sit-to-stands or squats. Each exercise was individualized based on training experience and baseline strength. Upper body exercises were delivered using a portable bar and resistance bands (Smart Stick™ and Smart Toner®; Twist Sport Conditioning Inc, North Vancouver, Canada). Lower body exercises used body weight resistance, with the addition of weights as required. Each resistance exercise involved 2 sets of 10–12 repetitions, with one-minute recovery between each set. Resistance training was performed at a moderate intensity, targeting 6–7 out of 10 on the Adult OMNI Perceived Exertion Scale.[20] Resistance was progressed for each exercise when perceived exertion fell below the target range. Exercise diaries were maintained by the trainer at each session.

The unsupervised walking program was similar to the supervised walk, with steps counted using a pedometer (G-Sensor 2025; Pedometers Australia, Perth, Australia) and a target rating of perceived exertion of 11–13.[19] Women were asked to walk on days they were not seeing the trainer and encouraged to increase the steps taken each week by 10%.

Women in both groups were contacted weekly by a researcher, who documented in a log any physical activity outside the study, appointments with health professionals, and changes to medication.

Primary Outcomes: Feasibility and Safety

Feasibility of the physical activity program was determined through recruitment and retention rates, adherence and compliance to the intervention, and safety. Recruitment rate was determined by the percentage of eligible patients who enrolled, with retention calculated as the percentage of participants who completed the study. Adherence and compliance rates were retrieved from exercise diaries and determined as outlined in Table 1. Adherence was defined as attendance at sessions, with compliance examined in terms of average exercise intensity and volume. Participants were considered adherent or compliant if they achieved at least 90% of the respective prescribed component. Safety was measured by the number of adverse events related to the intervention, as defined by the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0.

Secondary Outcomes: Preliminary Efficacy

The preliminary efficacy outcomes were patient-reported outcomes, physical performance and physical activity level, assessed using standardized tests described previously.[16] Assessments were conducted in the participant's home or at The University of Sydney. All variables were measured before the intervention (baseline), after the intervention (Week 8), and 8 weeks after the intervention (Week 16). All outcome measures were performed by the same assessor who was not blinded to group allocation.

Patient-Reported Outcomes

The Functional Assessment of Chronic Illness Therapy: Fatigue (FACIT-F)[21,22] was used to assess the severity and impact of cancer-related fatigue. A lower score indicates more significant fatigue.

The 30-item European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-30) was also used.[23,24] Items relating to function and symptoms were evaluated, with a higher score representative of better well-being and higher symptom burden, respectively.

Physical Performance

The Modified Canadian Aerobic Fitness Test, a submaximal step test, was used to assess aerobic fitness. Results are reported as VO_{2max} ($ml \cdot kg^{-1} \cdot min^{-1}$) predicted from Modified Canadian Aerobic Fitness Test equations.[25,26] The six-minute walk test (6MWT) was used as a measure of functional capacity.[27] Participants were instructed to walk between two markers 20 m apart as many times as possible in six minutes, and the total distance covered was used for analysis.

A back-leg dynamometer (Back-D; Takei Kiki Kogyo, Tokyo, Japan)[28] was used to evaluate lower limb strength (kg). Handgrip strength (kg) of the dominant limb was measured using a hand dynamometry (Jamar Plus+; Sammons Preston Rolyan, Bolingbrook, IL).[29] Three trials were performed with each dynamometer, with the highest score retained for analysis.

Table 1

Measures of Adherence and Compliance to the Supervised and Unsupervised Training Components of the Program

Variable	Supervised Resistance Training	Unsupervised Walking Program
Adherence	$\frac{\text{Attended sessions}}{\text{Prescribed sessions}} \times 100\%$	
Compliance		
Exercise intensity	$\frac{\text{Reported OMNI} - \text{RES}}{\text{Prescribed OMNI} - \text{RES}} \times 100\%$	$\frac{\text{Reported RPE}}{\text{Prescribed RPE}} \times 100\%$
Exercise volume	$\frac{\text{Performed repetitions}}{\text{Prescribed repetitions}} \times 100\%$	$\frac{\text{Performed steps}}{\text{Prescribed steps}} \times 100\%$

OMNI-RES = Adult OMNI Perceived Exertion Scale; RPE = Borg's Rating of Perceived Exertion.

Physical Activity

Physical activity was determined from the International Physical Activity Questionnaire,[30] a simple seven-day recall measure commonly used in cancer populations.[31–33] The total score requires the summation of minutes and frequency of physical activity, which is used to score each type of activity by its energy requirements to calculate a score in MET-minutes of activity per week (MET-min·week^{-1}).[30]

Participants also wore an Actiheart™ (Actigraph, Pensacola, FL) physical activity monitor[34] continuously for a period of seven days. The ActiHeart device connects to two electrocardiogram electrodes under the left breast. The ActiHeart combines a uniaxial accelerometer with a heart rate monitor to calculate a range of physical activity variables. The variable used for analysis in this study was daily physical activity energy expenditure (ActiHeart Software, version 4; CamNtech Ltd, Cambridge, U.K.).

Statistical Analyses

Given the exploratory nature of the study, sample size was based on available funding and resources. Group allocation was coded to enable blinded analysis. Measures of feasibility and safety were determined using descriptive statistics. The unadjusted mean change from baseline in physical activity, physical performance, and patient-reported outcomes was compared between the two groups using descriptive statistics. Glass's delta was used to calculate the effect size of the intervention. An effect size of less than 0.2 was considered small, 0.5 considered medium, and more than 0.8 considered large.[35] Probability testing was not used to compare groups because of the small sample size. The mean and standard deviation have been reported unless otherwise stated. IBM SPSS version 20 for Windows (IBM Corp., Somers, NY) was used for statistical analyses.

Results

Recruitment and Retention

Participant disposition through recruitment, assessment, and intervention phases are shown in Figure 1. All 18 women invited to participate expressed interest.

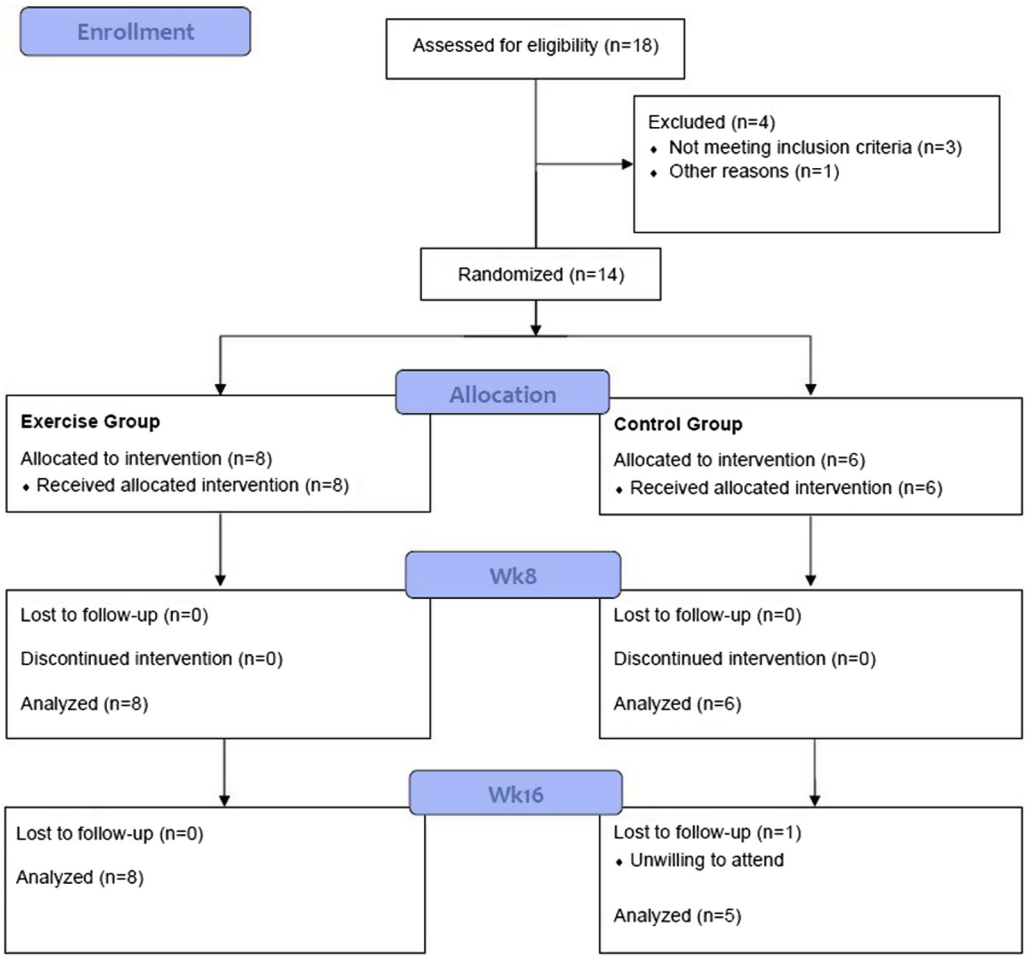

Fig. 1. Flow of participants through study.

Three women were ineligible because of already participating in regular exercise ($n = 2$) or moving out of the area ($n = 1$). Fifteen were eligible to participate; however, one was not able to commit at the time of initial contact. Fourteen women were therefore enrolled into the study, generating a recruitment rate of 93%. Eight women were allocated to the exercise group and six to the control group. Retention was good in both exercise and control groups (100% and 83%, respectively), with one control lost to follow-up at week 16.

Participant Characteristics

Participant characteristics are shown in Table 2. Notably, 67% in the control group were receiving chemotherapy compared with 13% in the exercise group.

Adherence and Safety

Adherence and compliance to the supervised resistance training component of the physical activity program was high (Table 3). All eight women attended 100% of the 16 supervised sessions with all sessions completed at the prescribed intensity and volume. In contrast, only 2 women adhered to the walking program. Compliance with walking intensity was found in 71% of participants; however, no participants achieved the desired volume of walking. No adverse events or safety concerns related to the intervention occurred.

Preliminary Efficacy Outcomes

Patient-reported outcome data are presented in Figure 2 and Table 4. A large effect was observed in the reduction of fatigue in the exercise group as

Table 2
Demographic and Baseline Physical Characteristics of the Control and Exercise Groups

Variable	All, $n = 14$	Control Group, $n = 6$	Exercise Group, $n = 8$
Age (y)	62.2 ± 10.6	65.0 ± 6.9	60.1 ± 12.7
Height (m)	1.63 ± .07	1.62 ± .05	1.64 ± .08
Body mass (kg)	75.2 ± 16.3	74.1 ± 16.9	76.1 ± 17.0
BMI ($kg \cdot m^{-2}$)	28.3 ± 5.7	28.1 ± 5.6	28.4 ± 6.2
Time since primary breast cancer diagnosis (y)	9.8 ± 6.5	11.0 ± 5.5	8.9 ± 7.4
Time since metastatic breast cancer diagnosis (y)	3.5 ± 4.2	4.8 ± 4.6	2.6 ± 3.9
Number of comorbid conditions	3.0 ± 2.5	3.3 ± 2.6	2.8 ± 2.6
ECOG			
0	4 (29)	2 (33)	2 (25)
1	8 (57)	3 (50)	5 (63)
2	2 (14)	1 (17)	1 (13)
Location of metastasis			
Bone only	4 (29)	1 (17)	3 (38)
Visceral involvement	10 (71)	5 (83)	5 (63)
Current treatment			
Hormone therapy	7 (50)	1 (17)	6 (75)
Chemotherapy	5 (36)	4 (67)	1 (13)
No current treatment	2 (14)	1 (17)	1 (13)
Education			
School certificate	5 (36)	3 (50)	2 (25)
University degree	9 (64)	3 (50)	6 (75)
Marital Status			
Married	6 (43)	2 (33)	4 (50)
Other	8 (57)	4 (67)	4 (50)
Employment			
Not working	10 (71)	3 (50)	7 (88)
Income			
≤$52,000	8 (57)	4 (67)	4 (50)
Menopausal status			
Perimenopausal	2 (14)	0 (0)	2 (25)
Postmenopausal	12 (86)	6 (100)	6 (75)
Physical performance			
O_{2max} ($ml \cdot kg^{-1} \cdot minute^{-1}$)	23.4 ± 6.3	21.9 ± 4.6	24.3 ± 7.4
6MWT (m)	520.6 ± 116.4	506.3 ± 93.9	531.4 ± 136.2
Leg strength (kg)	59.6 ± 17.0	62.3 ± 15.8	56.6 ± 18.6
Hand strength (kg)	26.7 ± 5.7	26.5 ± 2.8	26.8 ± 7.4
Physical activity			
PAEE (kJ)	2829 ± 1887	2714 ± 814	3143 ± 2362
IPAQ ($MET\text{-}min \cdot week^{-1}$)	1790 ± 2018	1898 ± 2471	1709 ± 1785

BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; 6MWT = six-minute walk test; PAEE = physical activity energy expenditure; IPAQ = International Physical Activity Questionnaire; SD = standard deviation.
Values are presented as mean ± SD or n (%).

Table 3
Rates of Adherence and Compliance to the Supervised and Unsupervised Training Components of the Program

Variable	Supervised Resistance Training	Unsupervised Walking Program
Adherence to prescribed sessions		
90%–100%	8 (100)	2 (25)
75%–89%	0 (0)	1 (13)
50%–74%	0 (0)	3 (38)
25%–49%	0 (0)	1 (13)
0%–24%	0 (0)	1 (13)
Compliance with exercise intensity[a]		
90%–100%	8 (100)	5 (71)
75%–89%	0 (0)	2 (29)
50%–74%	0 (0)	0 (0)
25%–49%	0 (0)	0 (0)
0%–24%	0 (0)	0 (0)
Compliance with exercise volume[a]		
90%–100%	8 (100)	0 (0)
75%–89%	0 (0)	0 (0)
50%–74%	0 (0)	2 (29)
25%–49%	0 (0)	5 (29)
0%–24%	0 (0)	0 (0)

Values are given as n (%).
[a]Data missing for unsupervised component ($n = 1$).

measured by the EORTC QLQ-C30 (effect size [ES] = 0.99) and FACIT-F (ES = 1.92). There was a reduction in pain (ES = 1.61) in the exercise group immediately after the intervention. A consistent trend in favor of exercise was also observed across physical (ES = 1.71), role (ES = 0.96), emotional (ES = 1.46), and social function (ES = 1.49) scales of the EORTC QLQ-C30.

Physical and activity measures are reported in Table 5. A large effect size was observed in the exercise group for 6MWT (ES = 1.54), leg strength (ES = 1.87), and body mass (ES = 1.45) at both time points. Measures of physical activity show a consistent trend in favor of the exercise group.

Discussion

This study investigated the safety and feasibility of a partially supervised home-based physical activity program for community-dwelling women living with metastatic breast cancer. The program was well accepted and feasible, with positive preliminary findings warranting further investigation as a potentially effective intervention for improving well-being in this population.

Feasibility

This study demonstrated feasibility to recruit and retain patients with metastatic breast cancer into a longitudinal exercise intervention. Recruitment rates for resistance exercise trials in early breast cancer are typically lower than those observed in this study.[36–38] This may be the result of women in the present study previously expressing interest in increasing physical activity, after participation in a cross-sectional study of physical activity and fitness.[16] Recruitment into this earlier study was also high, with 88% of women invited to take part enrolling in the trial. These high rates of recruitment may also indicate clinician bias, whereby those referred were higher functioning and more motivated to be physically active than the average metastatic population. Excellent retention in the study may be due to the implementation of a home-based program, which has been identified as a preference for physical activity in palliative patients with cancer.[14] This is further supported by a recent study of an aerobic intervention in a metastatic breast cancer population, which found that although participants were provided with a gym membership, they primarily completed the intervention at home.[39]

Adherence to the supervised component of the physical activity intervention was excellent, with 100% of prescribed resistance training sessions attended by participants. Within these sessions, compliance with prescribed intensity and volume was also high. The high adherence and compliance rates of resistance training may be due to the supervision of these sessions by an exercise specialist, promoting participation and motivation.

Despite both the resistance and walking components of the program being home-based, adherence to the unsupervized walking program was poor. The low adherence highlights the importance of the role of the exercise specialist as an external motivator and indicates the need for strategies to promote adherence in the absence of a trainer. Given that walking does not require supervision, one approach may be to facilitate social support by encouraging women to walk with family or friends. While none of the women successfully increased their walking volume as prescribed, it was encouraging that the majority were compliant with walking at a moderate intensity. This finding is important as it indicates that women were able to achieve the desired level of intensity without the supervision of a trainer or sophisticated equipment. These findings support the implementation of a home-based training program but emphasize the need for strategies to foster adherence to unsupervized exercise.

Although the physical activity program was home-based, the resistance training sessions were supervised by an exercise specialist. This level of supervision may have contributed to the lack of any adverse events related to the intervention, a finding similar to previous studies of individuals with metastatic disease.[11,40,41] However, given the large number of resources required to run this component of the program, it has a number of barriers for integration into care. With the high level of adherence and

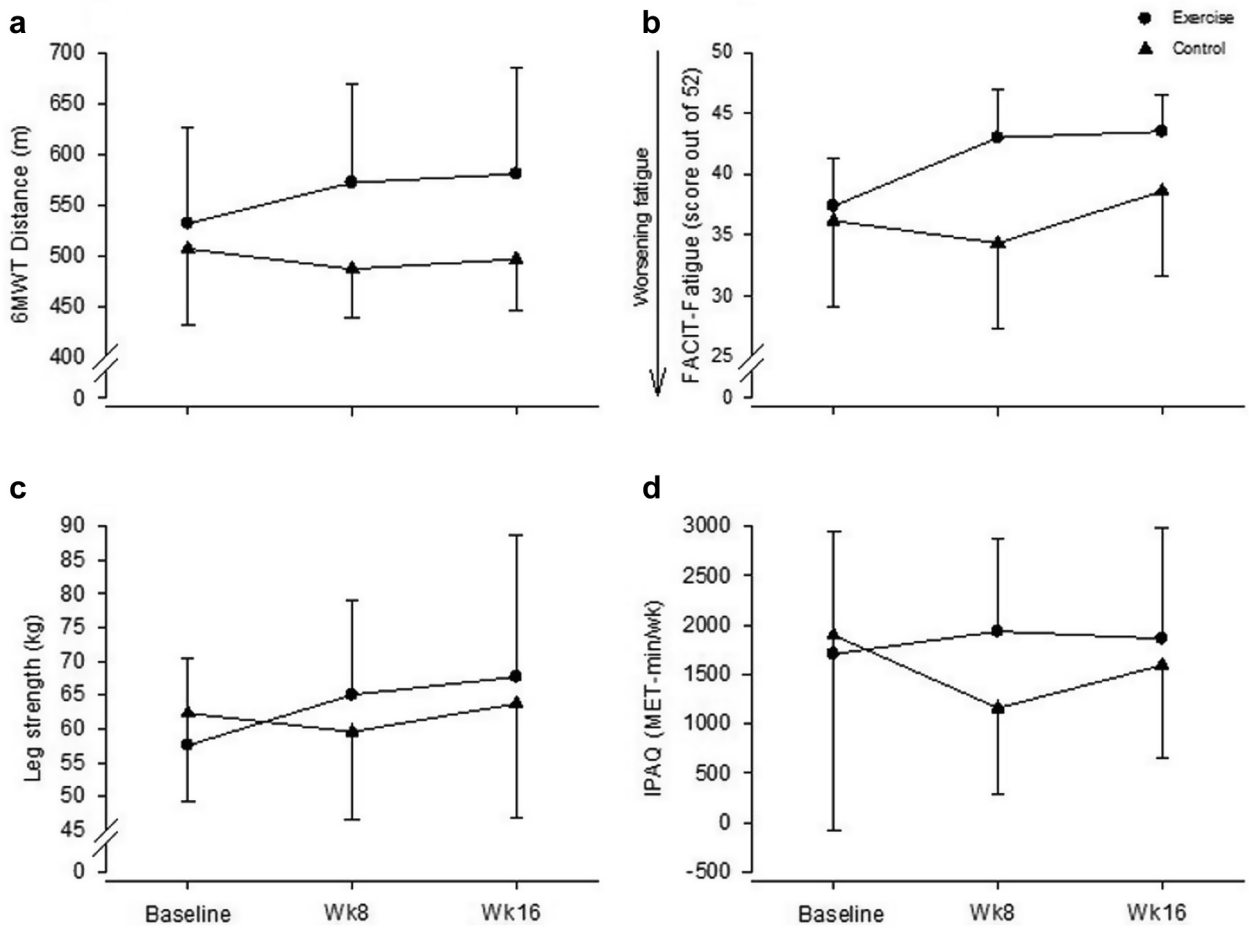

Fig. 2. Result of a) 6MWT, b) FACIT-F, c) leg strength, and d) IPAQ in each group at each assessment value with mean and 95% confidence interval. 6WMT = six-minute walk test; FACIT-F = Functional Assessment of Chronic Illness Therapy: Fatigue; IPAQ = International Physical Activity Questionnaire.

compliance to the resistance training sessions, it appears reasonable for supervision to taper off with appropriate mechanisms in place for maintaining adherence. One approach that could be adopted is the use of commercial wearable devices, such as the Fitbit® (Fitbit Inc., San Francisco, CA), which provide a fun and interactive way of monitoring and providing motivation for physical activity. Findings from this study suggest that an appropriately designed and partially supervised moderate-intensity physical activity program is well tolerated and safe for women with metastatic breast cancer.

Efficacy Outcomes

The between-group differences observed in measures of quality of life, symptom burden, physical performance, and physical activity can be used to inform the design of a larger randomized controlled trial. The intervention used in the present study was not only well tolerated but also there was a large effect in favor of the exercise group for symptoms such as fatigue and pain. A medium-to-large effect was also evident for all physical performance and physical activity measures in the exercise group. Given the poor adherence to the walking program, it is likely that these improvements were predominantly caused by the resistance training component. These findings align with a systematic review of exercise for individuals with metastatic disease,[12] suggesting exercise and physical activity may help women living with metastatic breast cancer to live well and to manage their condition.

Although this study was not powered to detect statistical significance, the consideration of clinical relevance provides further insight into the findings. For the measures adopted, the magnitude of clinically meaningful change has not been established for individuals with metastatic disease. However, the minimal clinically important difference for fatigue, measured by FACIT-F, has been established as 3 points in a mixed cancer population.[42] With respect to physical function, one study of the 6MWT in older adults with mild-to-moderate mobility limitations described a small meaningful change with an increase of 19 m

Table 4

Change in Patient-Reported Measures From Baseline at Week 8 and Week 16

Variable	Week 8—Baseline				Week 16—Baseline			
	Control, Mean (SD)	Exercise, Mean (SD)	Between-Group Difference (95% CI)	Effect Size	Control, Mean (SD)	Exercise, Mean (SD)	Between-Group Difference (95% CI)	Effect Size
FACIT-F	−1.8 (3.9)	5.6 (3.2)	7.5 (3.3 to 11.6)	1.92[a]	0.8 (5.7)	6.1 (3.6)	5.3 (−0.3 to 10.9)	0.93[a]
EORTC QLQ-C30								
Function scales								
Global health	−2.8 (14.6)	5.2 (15.4)	8.0 (−9.7 to 25.7)	0.55	−6.7 (10.9)	7.3 (21.6)	14.0 (−9.1 to 37.1)	1.28[a]
Physical	−6.7 (7.3)	5.8 (6.6)	12.5 (4.4 to 20.6)	1.71[a]	1.3 (9.9)	4.2 (8.7)	2.8 (−8.6 to 14.3)	0.29
Role	−11.1 (20.2)	8.3 (8.9)	19.4 (2.1 to 36.7)	0.96[a]	−16.7 (20.4)	8.3 (12.4)	25.0 (3.2 to 46.8)	1.22[a]
Emotional	−6.9 (9.7)	7.3 (13.7)	14.2 (−0.1 to −28.6)	1.46[a]	5.0 (4.6)	7.3 (10.4)	2.3 (−8.7 to 13.2)	0.50
Cognitive	2.8 (16.4)	2.1 (5.9)	−0.7 (−14.2 to 12.8)	0.04	6.7 (15.0)	0 (12.6)	−6.7 (−23.6 to 10.3)	0.45
Social	−8.3 (14.0)	12.5 (17.3)	20.8 (2.1 to 39.6)	1.49[a]	−3.3 (7.5)	4.2 (21.4)	7.5 (−14.6 to 29.6)	1.01[a]
Symptoms								
Fatigue	0.0 (7.0)	−6.9 (13.2)	−6.9 (−20 to 6.1)	0.99[a]	2.2 (9.3)	−5.6 (17.8)	−7.8 (−26.9 to 11.4)	0.85[a]
Nausea/vomiting	0.0 (10.5)	−4.2 (11.8)	−4.2 (−17.4 to 9.1)	0.40	−10.0 (14.9)	2.1 (18.8)	12.1 (−9.8 to 34.0)	0.81[a]
Pain	5.6 (8.6)	−8.3 (19.9)	−13.9 (−31.4 to 3.6)	1.61[a]	−6.7 (36.5)	−14.6 (13.9)	−7.9 (−38.9 to 23.0)	0.22
Dyspnea	5.6 (13.6)	0 (17.8)	−5.6 (−24.6 to 13.5)	0.41	6.7 (14.9)	0 (17.8)	−6.7 (−27.8 to 14.4)	0.45
Insomnia	5.6 (25.1)	0 (17.8)	−5.6 (−30.4 to 19.3)	0.22	6.7 (14.9)	−4.2 (11.8)	−10.8 (−27.2 to 5.5)	0.73
Appetite loss	11.1 (17.2)	0 (0)	−11.1 (−29.2 to 7.0)	0.65	0 (0)	0 (0)	0 (0)	0
Constipation	−5.6 (13.6)	0 (17.8)	5.6 (−13.5 to 24.6)	0.41	−13.3 (18.3)	0 (17.8)	13.3 (−9.2 to 35.9)	0.73
Diarrhea	11.1 (27.2)	0 (0)	−11.1 (−39.7 to 17.5)	0.41	6.7 (14.9)	8.3 (23.6)	1.7 (−24.5 to 27.8)	0.11
Financial difficulties	5.6 (25.1)	0 (17.8)	−5.6 (−32.9 to 21.8)	0.22	6.7 (14.9)	−4.2 (11.8)	−10.8 (−27.2 to 5.5)	0.73

SD = standard deviation; CI = confidence interval; FACIT-F = Functional Assessment of Chronic Illness Therapy: Fatigue; EORTC QLQ-C30 = 30-item European Organization for Research and Treatment of Cancer Quality of Life Questionnaire.

[a]Large effect size based on Glass's delta >0.8.

Table 5
Change in Physical and Activity Measures From Baseline at Week 8 and Week 16

Variable	Week 8—Baseline				Week 16—Baseline			
	Control, Mean (SD)	Exercise, Mean (SD)	Between-Group Difference (95% CI)	Effect Size	Control, Mean (SD)	Exercise, Mean (SD)	Between-Group Difference (95% CI)	Effect Size
Body mass (kg)	0.9 (.8)	2.1 (2.8)	1.1 (−1.3 to 3.5)	1.45[a]	−0.4 (1.7)	3.1 (2.3)	3.4 (0.8 to 6.1)	2.07[a]
Physical performance								
VO_{2max} ($ml \cdot kg^{-1} \cdot minute^{-1}$)	−0.2 (.1)	1.6 (1.8)	1.8 (0.3 to 3.3)	14.85[a]	−0.2 (.2)	0.1 (1.0)	0.2 (−1.0 to 1.3)	0.71
6MWT (m)	−46 (56)	40 (23)	86 (38 to 134)	1.54[a]	−11 (26)	49 (35)	59 (15 to 104)	2.26[a]
Leg strength (kg)	−2.8 (5.5)	7.5 (11.3)	10.3 (−0.7 to 21.2)	1.87[a]	1.7 (6.1)	13.5 (15.6)	11.8 (−3.1 to 26.6)	1.92[a]
Hand strength (kg)	0.1 (2.2)	1.8 (1.3)	1.7 (−0.7 to 4.1)	0.76	−0.4 (1.5)	1.6 (2.2)	2.0 (−0.5 to 4.4)	1.29[a]
Physical activity								
PAEE (kJ)	−746 (1177)	−129 (657)	494 (−561 to 1549)	0.56	−569 (1171)	293 (700)	862 (−336 to 2060)	0.74
IPAQ ($MET \cdot min \cdot week^{-1}$)	−738 (1622)	228 (915)	966 (−514 to 2447)	0.60	−611 (2046)	155 (1051)	767 (−1106 to 2638)	0.37

SD = standard deviation; CI = confidence interval; VO_{2max} = maximal oxygen consumption; 6WMT = six-minute walk test; PAEE = physical activity energy expenditure; IPAQ = International Physical Activity Questionnaire.
[a]Large effect size based on Glass's delta >0.8.

and a substantial change with 47 m.[43] Using these as indicators, the exercise group demonstrated clinically meaningful improvements in fatigue and physical function both immediately after intervention and 8 weeks after intervention. Patient-reported outcomes in the exercise group may be influenced by the additional attention provided by the trainer or a placebo effect, which may be overcome in future trials by having a placebo control such as stretching. Nonetheless, the preliminary evidence is promising and supports the need for further research to explore the most efficacious frequency, intensity, duration, and mode of intervention in this population.

An increase in body mass was observed in the exercise group. While not measured in this study, this may be explained by alterations to nutritional intake or an increase in lean muscle mass, which is typically associated with resistance training.[44] With a strong link between cancer cachexia and morbidity and mortality,[44] future research should consider incorporating evaluation of lean body mass for further understanding of the role of exercise in cachexia prevention.

Study Limitations

As a phase I/II study examining the effects of exercise in women with metastatic breast cancer, certain limitations should be considered when interpreting these findings. Our recruitment strategy targeted women who were high functioning and excluded those with ECOG 3−4. However, some women were low functioning, with three women covering ≤400m in the 6MWT. Although the intervention in this present study was found to be feasible and safe, it may not be feasible for women who spend the majority of their time confined to a bed or chair (i.e., ECOG 3−4). Similarly, it may not be sufficiently challenging for women who are high functioning and active. A higher proportion of women in the control group were receiving chemotherapy compared with the exercise group, which may have impacted findings. As previously established, physical capabilities are highly variable in women living with metastatic breast cancer.[16] Given the disparate physical function and breadth of treatment observed, future interventions could be designed to target or carefully stratify subgroups of the metastatic population, such as on the basis of ECOG or current treatment. While the benefits of exercise are well understood for women with early breast cancer,[45−47] there is a need to address gaps in knowledge with respect to exercise and metastatic breast cancer. Appropriately powered randomized controlled trials are required to confirm the safety and efficacy of physical activity programs in this population.

Conclusion

Preliminary evidence from this randomized controlled trial suggests that a partially supervised physical activity program for women with metastatic breast cancer is feasible and safe. The dose of the supervised resistance training component was well tolerated and achievable in this population. However, issues with adherence and compliance to the walking program were evident. Initial efficacy data suggest that a physical activity program, comprising predominantly resistance training, may lead to improvements in physical activity, physical fitness, and functional capacity and may help women to live well with their disease. These preliminary findings justify the need for future research to identify safe and optimal exercise parameters for women living with metastatic breast cancer.

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