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Exercise adherence in a randomized trial of exercise on aromatase inhibitor arthralgias in breast cancer survivors: The Hormones and Physical Exercise (HOPE) Study

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Abstract

Purpose—Up to 50% of postmenopausal breast cancer survivors taking aromatase inhibitors (AIs) experience AI-associated arthralgias, or joint pain, which causes many to stop taking AIs and may inhibit exercise, despite known health benefits. We thus evaluated exercise adherence and factors associated with better exercise adherence in breast cancer survivors experiencing AI-induced arthralgia in the Hormones and Physical Exercise (HOPE) year-long randomized controlled trial.

Methods—We included the 61 HOPE women randomized to exercise (150 min/wk of moderate-intensity aerobic exercise and twice-weekly supervised strength training). Our main outcomes were aerobic exercise measured with daily activity logs, attendance at supervised exercise sessions, and changes in cardiorespiratory fitness, measured maximal oxygen consumption (VO₂max). We examined means and standard deviations (SD) for exercise adherence by demographic and medical characteristics and used the t-test for mean differences. We also examined predictors of adherence using linear regression.

Results—On average, at the end of the year-long trial, women reported 119 (SD 78) min/wk of moderate-intensity aerobic exercise and participated in 70% of supervised exercise training sessions. After adjustment for other factors that influence adherence, at 6-months post-

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Informed consent: Informed consent was obtained from all individual participants included in the study.

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randomization only baseline VO₂max was associated with higher aerobic exercise levels and at 12-months only older age predicted better supervised exercise training attendance.

Conclusions—Breast cancer survivors taking AIs and experiencing arthralgia are able to initiate and maintain a yearlong exercise program, regardless of other factors that influence activity levels.

Implications—Breast cancer survivors can exercise at levels that have been shown to improve AI-associated arthralgia.

Keywords

physical activity; exercise; breast cancer; aromatase inhibitors; arthralgia

Introduction

There are an estimated 2.8 million breast cancer survivors in the U.S. [2]. In 2004 aromatase inhibitors (AIs) became standard of care for postmenopausal women with hormone receptor positive breast cancer [7], but recent studies have found that approximately 20% of these women discontinue AI therapy within the first year of use and up to 50% do not take AIs regularly, primarily because of side effects [10, 18]. The most common AI side effect is arthralgia, defined as pain or stiffness in the joints [10]. Both non-adherence to and early discontinuation of AIs have been shown to be independent predictors of mortality [12], and there are few established effective treatments for AI-induced arthralgia [8]. Thus, it is essential to identify effective interventions that alleviate arthralgia, which may in turn improve AI adherence.

The American College of Sports Medicine, the American Cancer Society, and the US Department of Health and Human Services issued exercise guidelines recommending 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity aerobic physical activity weekly based on findings that activity is associated with lower risks of all-cause and cancerspecific mortality, health-related fitness, patient-reported outcomes, lymphedema and comorbid conditions [1, 3, 21]. Physical activity in the breast cancer survivor population, and specifically among women on AIs, is paramount to improving health outcomes in this population. However, few breast cancer survivors engage in recommended levels of physical activity [5, 14]. Objective measures of cardiovascular disease mortality [11], cancer mortality [22], and in cross-sectional studies of cardiovascular function. At diagnosis, cancer survivors showed an approximately 30% lower VO₂max, compared with age- and sex-matched sedentary controls without a history of cancer [15, 16].

The recently completed Hormones and Physical Exercise (HOPE) Study examined the effect of a yearlong exercise intervention vs. usual care on severity of AI-induced arthralgia in 121 women taking AIs and experiencing arthralgia [13]. At 12-months, AI-induced arthralgia, assessed via the Brief Pain Inventory worst joint pain score, decreased by 29% among breast cancer survivors randomized to exercise vs. a 3% increase among breast cancer survivors randomized to usual care (p < .0001).

The HOPE study was the first randomized trial of exercise in breast cancer survivors experiencing AI-induced arthralgia, making it an ideal population for describing exercise adherence, fitness and exercise predictors. Thus, the aims of this paper were to: 1) describe the HOPE exercise intervention conducted in breast cancer survivors taking AIs and experiencing AI-induced arthralgia; 2) report 6- and 12-month HOPE exercise adherence and cardiorespiratory fitness changes; and 3) identify predictors of exercise adherence.

Methods

Eligibility and Recruitment

The details of this trial have been previously described [13]. In short, breast cancer survivors were recruited between June 1, 2010 and December 30, 2012 from 5 hospitals in Connecticut (CT) through the Rapid Case Ascertainment Shared Resource of the Yale Cancer Center (RCA), a field arm of the CT Tumor Registry.

Eligible participants were physically inactive (< 90 min/wk of physical activity in the past six months and no strength training in the past year), postmenopausal women, diagnosed 0.5-4.0 years prior to enrollment with hormone receptor positive Stage I to III breast cancer, and taking an AI for at least six months. Participants had to be experiencing arthralgias for at least two months that were at least mild in severity (i.e., a score of at least 3 out of 10 on the worst pain item of the Brief Pain Inventory (BPI)) [6]. Women were eligible if their arthralgias started after initiation of an AI or if they had pre-existing joint pain that was exacerbated by AI use.

A total of 121 women were randomized, with 61 randomized to exercise and 60 randomized to usual care. However, given funding cuts in the final year, the last 25 women (13 exercisers and 12 usual care) of the 121 women recruited were enrolled into a 6-month rather than a 12-month trial. Thus, their study compliance is based on 6-month data (see Figure 1).

All study procedures, including written informed consent, were approved by the Yale School of Medicine Human Investigation Committee and Connecticut Department of Public Health Human Investigation Committee.

Exercise Intervention

The yearlong exercise intervention was a combination of a twice-weekly supervised aerobic and resistance training program (under the supervision of an American College of Sports Medicine certified cancer exercise trainer) at a local health club and a home-based aerobic exercise program [23]. Participants wore heart rate monitors during each workout. Following each exercise session, participants recorded the type, duration, and average heart rate during exercise, in daily physical activity logs, as a measure of exercise adherence [4]. Participants returned logs to the exercise trainers at the end of each week. Exercise trainers recorded attendance (yes/no) to the supervised sessions.

The aerobic exercise intervention consisted primarily of brisk walking (treadmill or outside), although participants could choose other aerobic exercise such as stationary bicycling, and was performed during the twice-weekly supervised exercise sessions as well as at home. The

goal was to participate in at least 150 min/wk of aerobic exercise, in accordance with current exercise recommendations for cancer survivors. Exercise started at 50% of maximal heart rate (determined from VO₂max testing) and increased over the first month to 60-80% of maximal heart rate for the study duration. The strength training protocol consisted of six exercises (e.g., bench press, latissimus pull down, seated row, leg press, leg extension, and leg curl) performed for 8-12 repetitions for three sets. Participants progressed up to three sets per exercise over the first month. After two sessions during which a participant lifted the same weight 12 times during each set, the weight was then increased by the smallest possible increment. There were no adverse events associated with the exercise program.

Outcome Measures

Exercise Adherence—Our primary outcome measures were 6- and 12-month adherence to the exercise intervention goal of 150 min/wk of aerobic exercise measured via the daily activity logs and participation in the twice-weekly supervised exercise sessions.

Cardiorespiratory Fitness—Change in cardiorespiratory fitness from baseline to end of study was examined as a secondary outcome measure. Cardiorespiratory fitness was measured at baseline and end of study with a standard VO_2 max treadmill test (including 12-lead electrocardiogram). Expired gases were analyzed using a metabolic measurement cart (CPX-D; Medical Graphics, St Paul, MN). Peak oxygen consumption was determined by taking the highest values during a 15-second period. We used a modified "Branching Treadmill Protocol" whereby participants began at a 3.0 mph walking speed and 0% grade. After two minutes the speed was increased to 3.5 mph with no change in grade. Thereafter, the grade was increased by 3% every two min. Oxygen consumption (VO₂), carbon dioxide production (VCO₂), and flow rate were measured continuously. Efforts were made to have participants safely exercise to maximal levels (e.g., Respiratory exchange ratio (RER) > 1.0). The test was ended when the participant indicated that she could not continue any further, or if the supervising physician recommended halting the exercise for medical concerns. Maximal heart rate and reasons for stopping the test were recorded, and cardiorespiratory measures (VO₂max, VCO₂max, RER, and MET) were recorded.

Covariate Measures

Demographics and Medical History—Medical record reviews and an interviewer-administered questionnaire were used to determine disease stage, surgery, adjuvant therapy, endocrine therapy and comorbidities. To determine eligibility based on baseline physical activity levels, an interviewer-administered questionnaire assessing the duration, frequency and intensity of 20 recreational activities over the prior 6 months was completed [13].

Height and Weight—Height (stadiometer) and weight (digital scale, no shoes) were measured at baseline, 6-, and 12-months. All measurements were taken twice and averaged. Body mass index (BMI) was calculated as kg/m².

Brief Pain Inventory (BPI)—The BPI is a 14-item questionnaire, developed for use in cancer patients, that assesses pain over the past week, reported on a 0-10 scale [6]. Worst pain is categorized as mild pain (score of 3-4), moderate pain (score of 5-7) or severe pain

(score of 8-10). The BPI is the most common, valid and reliable measure to assess pain in cancer survivors (Cronbach alpha and test-retest reliability scores both greater than 0.80) [6]. The BPI was modified to capture joint pain and stiffness by adding the term "joint pain/stiffness" rather than just the word "pain" throughout the questionnaire.

Statistical analysis

This analysis included the 61 women randomized to exercise, with 6-month intent-to-treat exercise adherence reported for 61 women, and 12-month intent-to-treat exercise adherence data reported for the 48 women who were randomized to the 12-month trial. We calculated means and standard deviations (SDs) of aerobic exercise min/wk and % of supervised strength training sessions attended overall. We also stratified by demographic and medical characteristics, dividing continuous variables into dichotomous categories split on median values. In univariate analyses we used t-tests for dichotomous categories and an F-test for multi-level categories to generate p-values for mean differences in the outcome of interest. We then used generalized linear models, adjusting means for covariates previously significant at a p<0.1 level, to generate adjusted means for univariate modifiers of adherence. We used SAS 9.3 (Cary, NC) in all analyses.

Results

Participant Characteristics

The average age of study participants was 62 years (Table 1). The majority of participants were white (87%) and diagnosed with Stage I breast cancer (59%). Average time between diagnosis and enrollment was 2.5 years, and average time on AI therapy was 1.9 (SD 1.9) years. Women had an average BMI of 30.0 kg/m², and a worst pain severity score of 5.7 (SD 1.9) as reported on the BPI. Study follow-up was high, with 58 of 61 exercisers (95%) completing 6-month follow-up visits, and 45 of 48 exercisers (94%) completing 12-month follow-up visits.

Exercise Adherence

Women randomized to exercise reported an average 115 min/wk and 119 min/wk aerobic exercise at 6- and 12-months, respectively (Table 2). Approximately 50% of women reported 120 min/wk (80% of aerobic exercise goal) at both 6 and 12 months post-randomization and over 30% of women reached the goal of 150 min/wk. Participants attended an average of 72% and 70% of strength training sessions at 6- and 12-months, respectively.

There were five women in the exercise intervention who reported $0 \, \text{min/wk}$ of aerobic exercise and attended $0 \, \text{strength}$ training sessions; yet their results of $0 \, \text{min/wk}$ of aerobic exercise and 0% participation in strength training were included in the exercise adherence results described above. These non-adherers were between 43-61 years old, had an average BMI of $36.6 \, \text{kg/m}^2$, and had been taking AIs for an average of $1.1 \, \text{years}$. Two of the women who did not exercise had stage I breast cancer, two had stage II breast cancer and the third had a stage III tumor.

Cardiorespiratory Fitness (VO₂max)

At baseline, mean VO_2 max was 23.4 ml/kg/min (SD 5.3); at follow-up, the mean VO_2 max increased to 24.6 ml/kg/min (SD 5.9), for a 5.1% increase (Table 2).

Factors Associated with Exercise Adherence

In unadjusted analyses, we observed higher mean min/wk of aerobic exercise measured at 6-and 12-months among women who were more educated, and had a higher baseline VO_2 max and BMI $<30~kg/m^2$. At 6-months we found higher aerobic exercise levels among women who had been taking an AI for 1.9~years (Table 3). Participation in supervised strength training sessions was higher among women who were older, more educated, had a BMI $<30~kg/m^2$, reported higher baseline physical activity levels, had been on an AI for 1.9~years, received radiation therapy (only significant for 6 month exercise adherence), and among women who were not married (only significant for 12 month exercise adherence). Disease stage, adjuvant treatment, and AI-associated arthralgia assessed by the BPI were not associated with exercise adherence. We also looked at change in BPI and adherence and found no significant associations for predicting aerobic or strength training at either time point.

We further adjusted mean exercise levels for those factors that were significant at a p<0.1 level in unadjusted analyses (Table 4). In aerobic exercise models we thus included age, race, education, VO_2max , BMI and years on AIs. Fully adjusted models showed that participants with a higher baseline VO_2max performed more aerobic exercise at 6 months, and more educated and women with a BMI < 30 kg/m^2 performed more aerobic exercise at 12 months. Only VO_2max was statistically significant at a more stringent p<0.05 level in the fully adjusted models. For supervised strength training attendance we included age, education, BMI, years on AIs, baseline physical activity and marital status in models. At 12 months, age 62 years was associated with better attendance at supervised exercise training sessions; higher educational level also suggested better attendance, although was not statistically significant at a p<0.05 threshold.

Discussion

Among physically inactive breast cancer survivors with aromatase inhibitor-associated arthralgias, women randomized to exercise performed 119 (SD 78) min/wk of aerobic exercise and attended 70% of strength training sessions. Although all women had AI-associated arthralgia at baseline, this arthralgia, as measured by worst pain score on the BPI, did not influence exercise adherence. From baseline to end of study, VO₂max increased by an average 5.1%. These findings demonstrate that approximately 120 min/wk of aerobic exercise and twice-weekly strength training is feasible among this population of sedentary breast cancer survivors with AI-induced arthralgia.

Although only 33% of women met the U.S. Physical Activity Guidelines of 150 minutes of moderate-intensity aerobic activity weekly, our observed levels of weekly aerobic exercise and strength training attendance were similar to previously observed exercise trials in breast cancer survivors [9, 17, 20]. The increase in activity levels that we observed have still been

associated with significant health benefits [23]. Previous studies have also reported BMI [17], baseline physical activity [17], and aerobic fitness [9] as predictors of exercise adherence, similar to our univariate, or unadjusted findings. However, our finding that at 12 months post-randomization only older age predicted strength training adherence in multivariate adjusted analyses suggests that physical activity interventions may need to be adapted to meet the needs of younger breast cancer survivors.

Previous studies have shown a worse CVD risk profile among breast cancer patients compared to healthy controls [15] and CVD is a leading cause of death among breast cancer survivors. At baseline in HOPE, the average VO₂max among participants was 23.4 ml/kg/min, indicating relatively low-normal fitness levels. Our observed average 1.2 ml/kg/min improvement in VO₂max is encouraging in regard to improving survival in this group of inactive breast cancer survivors, as it has been reported that a 1 ml/kg/min improvement in VO₂max is associated with a 12% lower mortality risk [19].

Strengths of our study include the population-based recruitment strategy, detailed measurement of physical activity and adherence, gold standard assessment of VO_2 max, the yearlong study duration, and a focus on women experiencing arthralgias due to AI use. Study limitations include that our participants were predominantly non-Hispanic white and highly educated, limiting generalizability of study results to other populations.

Our study builds on previous literature supporting exercise as feasible in breast cancer survivors, and uniquely supports the feasibility of an exercise program in breast cancer survivors with aromatase inhibitor-induced arthralgia, a population who might suffer additional barriers to exercise and additional cardiovascular disease risk. Furthermore, our findings help identify predictors of exercise adherence, which could inform future exercise trials using personalized intervention strategies. Our findings thus should encourage referral of breast cancer survivors to community-based exercise programs. Community-based exercise programs are becoming increasingly available, such as the LIVESTRONG® at the YMCA program, which offers free exercise programs to cancer survivors at various YMCAs across the United States.

In summary, as new breast cancer therapies are developed and breast cancer survivorship rates improve, physical activity behaviors and cardiovascular health will be increasingly important to maintain health among this population. As we transition into the era of "personalized medicine" in oncology, it will be critical to identify exercise prescriptions that are suitable for the clinical and treatment characteristics of patient subgroups. Our findings of good exercise adherence among women with AI-induced arthralgia will inform and encourage future effective, targeted exercise plans among breast cancer survivors.

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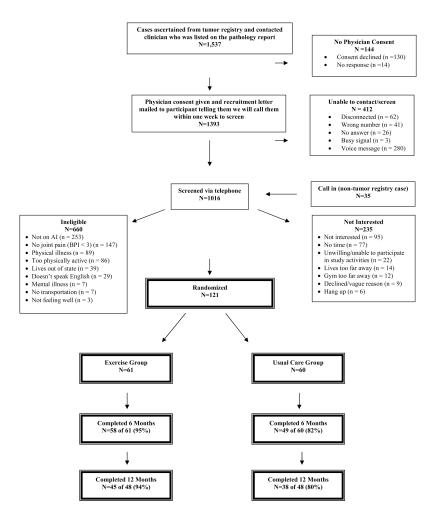


Figure 1. Flow of participants through the HOPE Study

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Table 1
Baseline characteristics of women randomized to the exercise intervention in the HOPE

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Characteristic Mean (SD) or N (%) Age (years) 62.0 (7.0) Time since diagnosis (years) 2.7 (3.1) Time on AIs (years) 1.9 (1.9) Ethnicity 1.9 (1.9) Non-Hispanic White 53 (86.9%) African American 6 (9.8%) Asian/Pacific Islander 1 (1.6%) Other 1 (1.6%) Cancer Stage 5tage 0 Stage II 36 (59.0%) Stage III 6 (9.8%) Type of surgery Lumpectomy or partial mastectomy Lumpectomy or partial mastectomy 43 (70.5%) Radical Mastectomy 1 (1.6%) Simple Mastectomy 9 (14.8%) Double radical mastectomy 1 (1.6%) Simple radical mastectomy 7 (11.5%) Treatment None 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise <td< th=""><th></th><th></th></td<>		
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Asian/Pacific Islander 1 (1.6%) Other 1 (1.6%) Cancer Stage 1 (1.6%) Stage I 36 (59.0%) Stage II 18 (29.5%) Stage III 6 (9.8%) Type of surgery Lumpectomy or partial mastectomy 43 (70.5%) Radical Mastectomy 1 (1.6%) Simple Mastectomy 9 (14.8%) Double radical mastectomy 7 (11.5%) Treatment None 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Non-Hispanic White	53 (86.9%)
Other 1 (1.6%) Cancer Stage 1 (1.6%) Stage I 36 (59.0%) Stage II 18 (29.5%) Stage III 6 (9.8%) Type of surgery 43 (70.5%) Radical Mastectomy 1 (1.6%) Simple Mastectomy 9 (14.8%) Double radical mastectomy 1 (1.6%) Simple radical mastectomy 7 (11.5%) Treatment None 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	African American	6 (9.8%)
Cancer Stage 36 (59.0%) Stage I 36 (59.0%) Stage II 18 (29.5%) Stage III 6 (9.8%) Type of surgery 43 (70.5%) Radical Mastectomy 1 (1.6%) Simple Mastectomy 9 (14.8%) Double radical mastectomy 1 (1.6%) Simple radical mastectomy 7 (11.5%) Treatment 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Asian/Pacific Islander	1 (1.6%)
Stage 0 1 (1.6%) Stage I 36 (59.0%) Stage III 18 (29.5%) Stage III 6 (9.8%) Type of surgery 43 (70.5%) Lumpectomy or partial mastectomy 43 (70.5%) Radical Mastectomy 1 (1.6%) Simple Mastectomy 9 (14.8%) Double radical mastectomy 7 (11.5%) Treatment None 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Other	1 (1.6%)
Stage I 36 (59.0%) Stage II 18 (29.5%) Stage III 6 (9.8%) Type of surgery 43 (70.5%) Lumpectomy or partial mastectomy 43 (70.5%) Radical Mastectomy 9 (14.8%) Double mastectomy 1 (1.6%) Simple mastectomy 7 (11.5%) Treatment 7 (11.5%) None 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Cancer Stage	
Stage III 18 (29.5%) Stage III 6 (9.8%) Type of surgery 43 (70.5%) Radical Mastectomy 1 (1.6%) Simple Mastectomy 9 (14.8%) Double radical mastectomy 1 (1.6%) Simple radical mastectomy 7 (11.5%) Treatment 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Stage 0	1 (1.6%)
Stage III 6 (9.8%) Type of surgery Lumpectomy or partial mastectomy 43 (70.5%) Radical Mastectomy 1 (1.6%) Simple Mastectomy 9 (14.8%) Double radical mastectomy 7 (11.5%) Treatment None 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Stage I	36 (59.0%)
Type of surgery 43 (70.5%) Radical Mastectomy 1 (1.6%) Simple Mastectomy 9 (14.8%) Double radical mastectomy 1 (1.6%) Simple radical mastectomy 7 (11.5%) Treatment 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Stage II	18 (29.5%)
Lumpectomy or partial mastectomy 43 (70.5%) Radical Mastectomy 1 (1.6%) Simple Mastectomy 9 (14.8%) Double radical mastectomy 1 (1.6%) Simple radical mastectomy 7 (11.5%) Treatment 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Stage III	6 (9.8%)
Radical Mastectomy 1 (1.6%) Simple Mastectomy 9 (14.8%) Double radical mastectomy 1 (1.6%) Simple radical mastectomy 7 (11.5%) Treatment 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Type of surgery	
Simple Mastectomy 9 (14.8%) Double radical mastectomy 1 (1.6%) Simple radical mastectomy 7 (11.5%) Treatment 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Lumpectomy or partial mastectomy	43 (70.5%)
Double radical mastectomy 1 (1.6%) Simple radical mastectomy 7 (11.5%) Treatment 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Radical Mastectomy	1 (1.6%)
Simple radical mastectomy 7 (11.5%) Treatment 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Simple Mastectomy	9 (14.8%)
Treatment None 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Double radical mastectomy	1 (1.6%)
None 7 (11.5%) Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Simple radical mastectomy	7 (11.5%)
Radiation only 22 (36.1%) Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Treatment	
Chemotherapy only 4 (6.6%) Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	None	7 (11.5%)
Radiation and chemotherapy 28 (45.9%) Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Radiation only	22 (36.1%)
Weight (kg) 78.4 (18.0) BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Chemotherapy only	4 (6.6%)
BMI (kg/m²) 30.0 (6.8) Mean min/week of exercise 55.1 (92.9)	Radiation and chemotherapy	28 (45.9%)
Mean min/week of exercise 55.1 (92.9)	Weight (kg)	78.4 (18.0)
,	BMI (kg/m ²)	30.0 (6.8)
Worst pain severity reported on BPI 5.7 (1.9)	Mean min/week of exercise	55.1 (92.9)
	Worst pain severity reported on BPI	5.7 (1.9)

Study (n=61)

 $\label{eq:total_continuous_problem} Table~2$ Adherence to aerobic exercise, attendance to supervised strength and aerobic training sessions and VO_2max at 6 and 12 months post-randomization in the HOPE Study

	6 months (n=61)	12 months (n=48)
· · · ·	o months (n=01)	12 months (n=40)
Aerobic exercise		
Min/wk of aerobic exercise, mean (sd)	115 (73)	119 (78)
Percent of women meeting specified cutoffs of aerobic exercise		
150 min/wk (100% of goal)	33%	33%
120 min/wk (80% of goal)	48%	48%
90 min/wk (60% of goal)	61%	71%
60 min/wk (40% of goal)	79%	79%
30 min/wk (20% of goal)	84%	81%
Strength training		
% sessions attended	72%	70%
Cardiorespiratory fitness		
VO_2 max, ml/kg/min, mean (SD) b	n/a	24.6 (5.9)
Change in VO ₂ max from baseline, ml/kg/min		1.2
Change in VO ₂ max from baseline, %		5.1%

^aAerobic exercise was calculated as min/wk from 7-day daily activity logs averaged over the trial duration.

 $^{^{}b}$ 56 women had VO₂ maximum measured at 6 months; 42 women had VO₂ maximum measured at 12 months.

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Unadjusted mean adherence levels for aerobic exercise and strength training at six and 12 months by demographics and tumor Table 3 characteristics

	Aer	Aerobic exercise, mean (SD) min/wk"	nean (SD) r				Strength	Strength training, // attenuance		
	N	6 months	p -value b	N	12 months	p -value b	9 synowy	p -value b	12 months	p -value b
Age (years)			0.152			0.081		0.066		0.017
<62.0	30	101.7 (77.4)		23	98.3 (74.4)		64.9		59.4	
62.0	31	128.6 (67.0)		25	137.3 (77.2)		78.5		7.67	
Race			0.146			0.099		0.569		0.653
White	53	120.7 (73.9)		42	125.6 (76.5)		72.6		70.7	
Other	∞	80.3 (58.7)		9	69.7 (73.0)		66.4		65.0	
Education			0.022			0.003		0.069		0.017
High school/some college	26	91.6 (77.5)		22	83.7 (75.8)		62.2		58.4	
College degree	16	111.2 (49.6)		10	117.6 (50.5)		77.0		72.3	
Graduate degree	19	151.4 (71.8)		16	167.3 (70.5)		9.08		84.4	
Chemotherapy			0.584			0.496		0.745		0.734
No	29	120.8 (68.4)		23	126.7 (66.4)		73.1		71.4	
Yes	32	110.4 (77.7)		25	111.2 (87.3)		7.07		9.89	
Disease Stage			0.938			0.736		0.810		0.503
Stage 0	-	154.0 (0.0)		-	162.0 (0.0)		0.88		87.0	
Stage I	36	117.1 (76.7)		27	127.1 (79.7)		71.2		71.9	
Stage II	18	109.3 (66.1)		16	107.2 (71.5)		74.8		70.5	
Stage III	9	116.7 (86.4)		4	96.0 (105.0)		63.8		50.3	
Radiation			0.462			909.0		0.038		0.195
No	Ξ	100.5 (98.2)		∞	130.2 (80.6)		55.6		58.0	
Yes	50	118.6 (67.0)		40	106.0 (73.8)		75.4		72.4	
Married			0.211			0.283		0.135		0.085
No	33	126.2 (68.8)		25	130.2 (80.6)		77.0		6.97	
Yes	28	102.6 (76.9)		23	106.0 (73.8)		9.59		62.4	
VO ₂ max (ml/kg/min)			0.004			0.017		0.432		0.581
<23.4	32	91.2 (58.0)		25	93.4 (64.8)		69.1		8.79	

	Aeı	Aerobic exercise, mean (SD) min/wk ^a	nean (SD) n	M A	į,		Strength t	Strength training, % attendance	ıttendance	
	N	9 months	p -value b	N	12 months	p -value b	6 months	p -value b	12 months	p -value b
23.4	28	143.8 (79.3)		23	146.0 (82.3)		75.0		72.3	
BMI (kg/m²)			<0.001			<0.001		0.060		0.005
<30.0	33	144.8 (72.6)		25	160.1 (68.7)		78.5		81.2	
30.0	28	80.7 (57.4)		23	73.5 (60.2)		63.9		57.7	
Baseline MVPA			0.294			0.267		0.004		0.016
min/week										
<54.8	42	108.7 (72.9)		33	110.2 (70.9)		66.4		64.8	
54.8	19	130.1 (72.9)		15	137.2 (90.3)		83.7		81.3	
Diabetes			0.477			0.443		0.288		0.355
No	57	117.1 (71.2)		4	121.2 (75.8)		73.9		72.3	
Yes	4	90 (104.5)		4	89.8 (103.7)		42.3		44.3	
Depression			0.797			0.503		0.535		0.136
No	48	116.6 (68.6)		38	122.5 (72.1)		73.0		73.1	
Yes	13	110.7 (90.5)		10	103.8 (98.8)		67.4		58.0	
Worst pain reported on BPI			0.983			0.523		0.330		0.434
<5.7	30	115.6 (57.4)		25	111.6 (57.8)		75.5		73.1	
5.7	31	115.2 (86.4)		23	126.3 (96.0)		68.3		66.5	
Years on AIs			0.079			0.267		<0.001		0.009
<1.9	40	105.4 (83.3)		28	108.8 (90.7)		66.1		61.9	
1.9	21	134.5 (43.4)		20	132.3 (53.5)		82.8		81.2	
Years since diagnosis			0.527			0.999		0.199		0.541
<2.5	36	110.7 (83.5)		24	118.6 (92.2)		6.79		67.4	
2.5	25	122.0 (55.4)		24	118.6 (61.6)		77.5		72.5	

^aBaseline moderate to vigorous-intensity physical activity (MVPA) was measured by an interviewer-administered questionnaire assessing the duration, frequency and intensity of 20 recreational activities over the prior 6 months.

 $[\]frac{b}{p}$ -values for a difference in means were generated using the t-test for two categories or ANOVA for multiple categories.

Table 4 Adjusted predictors of aerobic exercise and strength training attendance levels at 6 and 12 months post-randomization a

	6 months	p-value ^b	12 months	p-value ^b
Aerobic exercise (mean min/wk)				
Age (years)		0.189		0.115
<62.0	103.4		98.6	
62.0	128.9		133.4	
Race		0.844		0.430
White	116.0		119.4	
Other	110.1		93.2	
Education		0.262		0.094
High school/some college	98.0		89.2	
College degree	116.1		122.7	
Graduate degree	136.7		145.3	
VO ₂ max (ml/kg/min)		0.033		0.331
<23.4	91.6		105.5	
23.4	143.4		132.9	
BMI (kg/m²)		0.255		0.087
<30.0	128.6		140.5	
30.0	100.9		91.4	
Years on AIs		0.402		0.974
<1.9	109.1		115.7	
1.9	126.3		116.4	
Strength Training (% attendance)				
Age (years)		0.137		0.025
<62.0	66.3		61.1	
62.0	77.1		78.1	
Education		0.213		0.089
High school/some college	64.5		61.1	
College degree	78.1		74.6	
Graduate degree	76.4		79.3	
BMI (kg/m ²)		0.240		0.134
<30.0	75.7		75.6	
30.0	67.2		63.8	
Years on AIs		0.191		0.168
<1.9	68.4		65.5	
1.9	78.3		76.2	
Baseline MVPA min/week		0.369		0.632
<54.8	69.4		68.7	
54.8	77.0		72.8	

	6 months	p-value ^b	12 months	p-value ^b
Married		0.261		0.138
No	75.5		75.2	
Yes	67.5		64.3	

 $[^]a$ Means were adjusted all variables that were significantly different at a p<0.1 level in unadjusted analyses.