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A randomized-controlled trial comparing supervised aerobic training to resistance training followed by unsupervised exercise on physical functioning in older breast cancer survivors

Kerri M. Winters-Stone, PhD^{1,2,*}, Britta Torgimson-Ojerio, PhD, RN⁴, Nathan Dieckmann, PhD¹, Sydnee Stoyles¹, Zahi Mitri, MD², Shih-Wen Luoh, MD^{2,3}

¹School of Nursing, Oregon Health & Science University, Portland, OR

²Knight Cancer Institute, Oregon Health & Science University, Portland, OR

³Portland Veterans Affairs Health Care System, Portland, OR

⁴The Center for Health Research, Kaiser Permanente Northwest, Portland, OR

Abstract

Introduction: This study compared the relative efficacy of aerobic training to resistance training on physical functioning in older breast cancer survivors and determined whether benefits could be maintained by transitioning to unsupervised home-based training.

Materials and Methods: Early-stage, post-treatment, older (≥ 65 years) breast cancer survivors (n=114; mean age 72 years) were randomized to 12 months of supervised aerobic (n=37), resistance (n=39) or stretching (active control; n=38) training followed by 6 months of unsupervised home-based training. Outcomes included aerobic capacity by 6-minute walk distance (6MWD; m), maximal upper and lower body strength (1-repetition maximum; kg); physical function by short physical performance battery (SPPB), SF-36 and Late Life Function and Disability Instruments.

Results: Over 12-months of supervised exercise, all groups improved in muscle strength and SPPB scores, but resistance trained women also improved 6MWD. Improvements in upper and lower body strength in the resistance group were significantly greater than those in the stretching control (+2.5 kg vs. +1.8 kg; p=0.05) and aerobic groups (+8.3 kg vs +2.7 kg; p=0.047), respectively, with trends for greater improvements in 6MWD (+57.9m vs. +22.5m; p=0.057) and

*Corresponding author at: Oregon Health & Science University Mailcode: KCRB-CPC 3455 SW US Veteran's Hospital Rd Portland, OR 97239, wintersk@ohsu.edu.

AUTHOR CONTRIBUTIONS

Study concept and design (KWS, SWL); Study oversight (KWS, BT); Data analysis (ND, SS); Data interpretation and dissemination (KWS, BT, ND, ZM, SWL)

CONFLICT OF INTEREST

The authors have no conflicts to declare

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self-report physical function (+4.8 vs. -4.4; 0.066) in resistance trained women versus controls. Compared to values at 12 months, there were no changes during unsupervised training in any measure within or between groups, except for self-reported advanced lower extremity function which improved in the resistance group and fell in the aerobic group (+1.3 vs. -3.1; $p=0.043$).

Discussion: Supervised exercise can improve strength and physical functioning among older breast cancer survivors. Resistance training may lead to better improvements compared to aerobic or flexibility training, whether in a supervised or unsupervised setting.

Keywords

physical activity; exercise; neoplasm; physical fitness; gerontology; ADLs; neoplasm

Introduction

Older women (65 years+) constitute the largest group of breast cancer survivors in the U.S.^{1,2} By 2040 the proportion of cancer survivors who are older will rise to 73% and most will survive for 5 years or longer.³ Cancer treatment may accelerate aging, which could hasten the trajectory toward dependence and disability among older women.⁴ Older cancer survivors are more likely to report difficulty with daily activities requiring endurance, strength, and mobility than their older peers without cancer.^{5,6} Poor physical functioning could impact overall survival as persistent declines in physical functioning following a breast cancer diagnosis predicts shorter survival time in older women.⁷

Despite these projections, studies of older women cancer survivors comprise only a small proportion of research, especially exercise research, on reducing symptoms, maintaining function, and improving quality of life.^{8,9} Reissued in 2018, the DHHS Physical Activity Guidelines (PAG) for Americans recommend that all adults, regardless of age, aim for 150 minutes of moderate intensity aerobic exercise and 2–3 sessions of resistance exercise every week.¹⁰ Older women cancer survivors report falling short of recommended aerobic activity levels and virtually none participate in resistance training.¹¹ Recently updated exercise guidelines for cancer survivors from an American College of Sports Medicine (ACSM) roundtable recommend lower levels of exercise (i.e., 30 minutes of moderate-intensity exercise 3 times per week) than those in the PAG may be sufficient to improve cancer-related health outcomes, including physical functioning. However, due to the lack of trials in older survivors and of trials that directly compared two or more training modalities, the ACSM recommendations could not include age-specific guidelines for older survivors nor recommend an optimum training modality for specific outcomes. While the ACSM guidelines also suggest that supervised exercise may lead to greater improvements in outcomes and be safer for higher risk populations than unsupervised training, these recommendations were not empirically derived from studies including both supervised and unsupervised training periods.

The purpose of our study was to directly compare supervised aerobic and resistance exercise to each other and to an active control group on physical functioning in older women breast cancer survivors. We felt a head-to-head trial comparing single modalities in older survivors was warranted first, since adding a combined aerobic + resistance training group creates

confounding across groups with regard to delivered dose of aerobic and resistance training. We also included a transition period to unsupervised exercise to determine whether or not benefits could be maintained when exercising at home. We hypothesized that supervised aerobic and resistance training would significantly improve physical functioning compared to a control condition and that improvements from aerobic and resistance training would be equivalent and maintained with unsupervised exercise. In a separate publication we reported the effects of supervised training on biomarkers associated with breast cancer recurrence.¹²

METHODS

Study Design and Setting

The study was a single-blind, randomized controlled trial comparing three parallel groups with an allocation ratio of 1:1:1 to the following progressive low-moderate intensity exercise programs: 1) aerobic (AET), 2) resistance (RET) or 3) flexibility (FLEX; active control) training. Training was supervised for 12 months, then unsupervised for another 6 months. Outcomes were measured at baseline, 3, 6, 12 and 18 months by trained technicians blinded to group assignment. The primary outcome was physical function, measured objectively and by self-report. Secondary outcomes of physical fitness were included to assess fidelity of each training modality. A statistician used a computer-generated random numbers table to allocate participant ID numbers to intervention groups. Randomization was stratified by current use of anti-estrogen therapy (yes/no) in order to reduce potential confounding that could occur due to associated symptoms which might differentially affect exercise tolerance (e.g, arthralgia, myalgia). Individual assignments were placed into sealed envelopes prior to enrollment and were sequentially opened by each participant after completion of baseline testing.

The study was approved by the Oregon Health & Science University (OHSU) Institutional Review Board and each participant gave written informed consent prior to baseline testing. Testing took place at OHSU, while exercise training occurred there and at two community sites in the Portland metro area.

Sample

Participants were recruited through the Oregon State Cancer Registry, physician referrals, support groups and cancer-related community events. To be eligible women had to meet the following inclusion criteria: stage I-III breast cancer; 65 years old; 2 years post-chemotherapy and/or radiation therapy, to avoid exercise limitations due to treatment-related symptoms such as fatigue; insufficiently physically active (<60 minutes / week of planned moderate-vigorous intensity aerobic and/or resistance exercise)¹³; and, physician clearance to exercise. Current anti-estrogen therapy with a selective estrogen receptor modulator or aromatase inhibitor was permitted. Enrollment was open from 2011–2014.

Supervised Exercise Training

Women participated in three supervised 60-minute (including 5-minute warm-up and cool-down periods) group classes per week led by exercise physiologists or certified fitness instructors. To maintain quality control over intervention delivery, the same set of instructors

taught across all three study exercise sites and followed a written protocol. The volume of resistance and aerobic exercise gradually and progressively increased from low to moderate intensity over the first 9 months of training to provide continuous overload and then remained steady for the last 3 months (Table 1). Low to moderate intensity exercise should provide an adequate stimulus for adaptation in older adults¹⁴ yet ensure safety in novice exercisers, but is a lower intensity than that recommended in current guidelines for cancer survivors. Thus, we included measures of aerobic capacity, muscle strength and flexibility to evaluate fidelity of training protocols. Increases in intensity were modified when a participant showed signs of limited tolerance, such as an inability to use proper form. On a weekly basis the exercise trainer verbally queried participants about adverse events related to study exercise programs. Adverse events were subsequently documented by the trainer and severity was then assigned by the project director according to institutional criteria.

AET: The aerobic exercises consisted of low-impact dance aerobic exercises designed to increase heart rate (HR) by working large muscle groups of upper and lower body. Exercises including a variety of marching exercises, side steps, knee lifts, upper arm movements, and dance movements. Over 9 months the duration of aerobic exercise progressed from 20 to 45 minutes of active training and intensity progressed from 35% to 65% of estimated heart rate reserve (HRR).¹⁵ Participants used the Borg Perceived Exertion Scale¹⁶ and HR monitors (Polar RS400; Kempe, Finland) to adjust their effort to the prescribed intensity. Data from HR monitors were downloaded weekly so that compliance to training could be subsequently calculated.

RET: Resistance exercises consisted of 5 upper body and 5 lower body exercises designed to utilize major muscle groups and employ functional movements (chair stands, lunges (front, backward, lateral), calf raises, one-arm row, chest press, front/lateral shoulder raise, and push-ups). Based on ACSM resistance training guidelines for older adults, participants completed 2–3 sets of 10–15 repetition maximum (RM) of each exercise.¹⁴ Upper body exercises were performed with body weight (e.g., pushups) or dumbbells and weight was progressively increased to maintain a 10–15 RM. The lower body exercises were performed with participants wearing a weighted vest that was gradually increased from 1% of a participant's body weight up to 10%, or as tolerated.

FLEX: The active control group performed supervised stretching and relaxation exercise. Stretching exercises targeted the whole body and followed the ACSM recommendations for static stretching, where 2–3 repetitions of each stretch were held to the point of tension for 15–60 seconds.¹⁵ Stretches were performed in either a seated or lying position to provide a contrast to the weight-bearing aerobic and resistance training groups. Relaxation techniques (guided imagery, progressive neuromuscular relaxation, focused breathing) were included during the last 10 minutes of each session.

Unsupervised Training

After the first 12-months of the study, supervised exercise classes ended and participants were encouraged to follow a DVD-based version of their program, 3x/week. The exercise

DVD was provided at no cost and was led by their same in-class exercise instructors using exercises consistent with those in supervised sessions. Participants were provided some equipment for home training (i.e., weight vest, resistance bands, HR monitors, stretching straps). Adherence, as well as any exercise-related AEs, were tracked on calendars mailed back monthly to the research team or collected by phone.

Measures

Participant Characteristics—Demographic and clinical characteristics were obtained by self-report. Women also self-reported chronic medical conditions by the Charlson Comorbidity Index,¹⁷ physical activity (kcal/week) by the Community Health Activity Model Program for Seniors (CHAMPS) physical activity questionnaire,¹⁸ which was also used to monitor for changes in physical activity across the intervention period.

Primary Outcomes: Physical Functioning—*Objective physical function* was assessed by the Physical Performance Battery (SPPB) using the standard protocol.¹⁹ The SPPB consists of 3 timed performance tests: 5 repeated chair stands, standing balance, and usual gait speed over 4 meters. Each test is scored 0 (unable) to 4 and then scores are summed. Higher scores indicate better physical function and low scores on the SPPB (< 9) predict disability, hospitalization, nursing home admission, and mortality.^{19–22} Improvements of 1 point indicate substantial meaningful change.²³ We also reported times for the chair stand (sec) and 4m walk (m/sec) separately. As mentioned below, we also considered 6MWD as an objective measure of physical functioning.

Self-report physical function was determined from both the SF-36 physical function subscale and the Late-Life Function and Disability Instrument (LLFDI). Both the SF-36 physical function subscale and LLFDI are valid and reliable instruments, though only the LLFDI contains separate subscales of basic and advanced lower extremity function and upper extremity function.^{24–26} For both instruments, scales are scored 0–100, with higher scores indicating better function. Minimally clinically important differences (MCID) in older adults for LLFDI lower extremity, advanced lower extremity and upper extremity function are 3, 4, and 4 points, respectively.²⁷

Secondary Outcomes of Intervention Fidelity: Physical Fitness—*Submaximal aerobic capacity* was measured with a valid and reliable field measure of distance (m) walked on a treadmill at a pace that can be held for six minutes (6MWD).²⁸ 6MWD predicts mortality and morbidity in older adults and clinical populations^{29–32} and a change in walk distance of 54m represents a clinically significant change in functional status among older adults,³³ and individuals with chronic lung disease.³⁴

Maximal muscle strength of the upper and lower body was evaluated by a 1-repetition maximum leg press and chest press (1-RM; kg) where the maximum weight that can be pressed once is determined. We followed standard protocols³⁵ that we have used in our prior studies.^{36, 37}

Flexibility, or range of motion, in the upper and lower extremities was measured by the back scratch and chair sit-and-reach tests conducted according to standard protocols³⁸ and

recorded as distance (cm) between fingertips of both hands and between fingertips and toes, respectively.

Statistical Analysis

Standard descriptive statistics of frequency, central tendency, and dispersion were used to describe the sample. Standard ANOVAs and chi-square tests of proportion were used to compare baseline values across groups. Study aims were tested using piecewise linear mixed-effects regression models with a break point at 12 months for all outcome measures implemented using the nlme package in R.³⁹ This strategy allowed estimation of mean baseline values and slopes representing within group changes over both the supervised (0–12 months) and unsupervised (12–18 months) periods using one model for each outcome. Group x time interaction terms for both time periods assessed differences in changes over time between groups. Fidelity measures were only assessed from 0–12 months and were tested with standard non-piecewise models. Age, baseline BMI, and Charlson comorbidity index were included as covariates to account for any influence of these variables on exercise tolerance and adaptations. The mixed-effects approach accounts for the correlation between measurements from the same individual without the requirement of complete data as needed for methods like repeated measures ANOVA.⁴⁰ Using piecewise models ensured that parameter estimates at 12 months were consistent between the intervention and follow-up periods. P-values for the main outcomes were presented as unadjusted and then adjusted using the Benjamini-Hochberg (BH) method under the assumption that the main outcome models have positive dependency.^{41,42} Fidelity measures were also adjusted using BH as a separate hypothesis family. Calculations were performed using the formula provided by Benjamini, Heller, and Yekutieli⁴³ in R's `p.adjust` function. Both the original, unadjusted p-values and the BH adjusted p-values were reported as suggested by White, van der Ende, and Nichols.⁴⁴

A priori power analyses were conducted assuming a mixed between-within ANOVA model with $\alpha=.05$ and $\text{power}=.80$. The effect of interest was the group x time (0–12 month) interaction on the primary outcomes of physical function. A priori power analyses estimated a final sample size of $n=33$ participants per group to detect a 5-point group x time difference in self-report physical function between experimental and control groups.⁴⁵ Based on prior trials in older adults this sample size was more than sufficient to also detect a 1.5 second difference in chair stand time, an objective measure of physical functioning, between groups.⁴⁶ To protect against ~20% attrition we aimed to randomize 38 women per group.

RESULTS

Sample

Of 533 women who contacted the study team about the trial, 114 women (21%) were eligible and enrolled in the trial. The majority of refusals (69%) were related to inconvenience (time and travel), while the main reason for ineligibility was being too active (65%). Women were randomized to AET ($n=37$), RET ($n=39$) or FLEX ($n=38$) groups. On average, participants were 72 years of age, inactive, overweight/obese based on BMI and had an additional comorbidity other than cancer (Table 2). Thirty-five women (31% of the

sample) had SPPB scores 9 at baseline, 39% had a history of falls in the year prior to enrollment, but as a whole the sample reported functioning independently. There were no differences in baseline characteristics across study groups.

Retention, Adherence and Compliance

Participant retention over the 12-month supervised intervention was 77% while retention during unsupervised exercise averaged 91% (Fig 1). The majority of women dropped out for health-related reasons and dropouts did not differ across groups. Compared to women who remained in the study, dropouts had a significantly higher BMI and were further from diagnosis at enrollment. Adherence (number of sessions completed, expressed as a % of sessions prescribed) to supervised training averaged $72\% \pm 24\%$ over 12 months and dropped to $43\% \pm 40\%$ during the six months of unsupervised training (Fig 2), but was similar across groups. Compliance to the prescribed intensity of lower and upper body resistance training was tracked by vest weight and push-up RM and to aerobic training by the % of the prescribed target HRR reached during training, sampled every three months. For RET, the median final %BW in weight vests was 10% and the median RM for pushups was 12. For AET, the median % of target HRR reached was 97%. Three women in RET and 1 woman in FLEX could not fully comply with the prescribed program due to pre-existing orthopedic limitations that restricted movement and were provided alternative exercises within each modality. No AEs were reported from participation in either study program.

Supervised Training

When examining within group changes over one year of supervised exercise, improvements occurred in the following outcomes (Table 3 and 5): physical function (SPPB) in all groups, aerobic capacity (6MWD) in RET and AET, muscle strength (1-RM bench press) in all groups, lower body flexibility (chair sit-and-reach) in RET and FLEX. For physical functioning (Table 3), only RET achieved improvements in SPPB score and 6MWD that corresponded to clinically meaningful change. Self-report physical function improving more in AET or RET compared to FLEX using the SF-36 subscale (both, $p=0.066$) and RET improved lower extremity function more than FLEX using the LLFDI ($p=0.064$). For fidelity outcomes (Table 5), upper body muscle strength increased more in RET (+2.5 kg) versus FLEX (+1.1 kg; $p=0.048$), lower body muscle strength increased more in RET versus AET (8.2 kg vs 2.7 kg, respectively, $p=0.037$), while aerobic capacity increased more in RET (+57.3m) compared to FLEX (+20.4m; $p=0.048$). After BH adjustment, though, differences were no longer significant.

Unsupervised Training (Table 4)

Women in RET reported increases in advanced lower extremity function over 6 months of unsupervised training at home, which differed from declines in AET ($p=0.043$), but not from FLEX ($p=0.22$), who did not change; however, significance was lost after applying a BH adjustment. There were no other significant within or between group differences in rates of change during unsupervised training, suggesting that most outcomes remained steady over time across all groups.

DISCUSSION

Our trial is the first exercise intervention specific to older (65+ years) breast cancer survivors using supervised exercise, directly comparing two recommended exercise modalities, and including both supervised and unsupervised settings. The lack of program modification, good compliance to prescribed training protocols, and absence of study-related injuries suggest that low-moderate intensity resistance, aerobic, or stretching exercise is safe and feasible in older women with breast cancer. Across modalities, supervised training improved several objective measures of physical fitness and function, though resistance training produced the most gains in muscle strength and aerobic capacity. Both aerobic and resistance training led to modest self-reported increases in physical functioning. After transitioning to unsupervised exercise at home for another six months most outcomes remained unchanged, except that advanced lower body physical functioning slightly improved with resistance training at home.

Our findings are consistent with the most recent ACSM exercise recommendations for cancer survivors, which suggest that lower amounts of exercise than recommended in the PAG for all adults is enough to improve many cancer-related health outcomes.⁴⁷ New recommendations suggest that 30 minutes of moderate-vigorous intensity aerobic and/or resistance exercise performed 2–3 times per week for at least 12 weeks is sufficient to improve self-report physical functioning in most cancer survivors. However, age-specific recommendations were not made due to an insufficient number of trials in older survivors. Our findings suggest that the new recommendations might extend to older women with breast cancer, though more studies are needed to refine an exact prescription. Flexibility exercise was not included in the ACSM guidelines for cancer survivors due to heterogeneity of studies for this modality, but meta-analyses of yoga interventions that include stretching in cancer survivors,⁴⁸ and some controlled trials of flexibility training in older adults without cancer⁴⁹ suggest that this modality can improve mobility and range of motion, both of which contribute to physical functioning. Only women who did aerobic or resistance exercise reported improvements in self-report physical function that differed from declines in controls, though improvements did not reach those considered as clinically relevant raising a question of whether changes were enough to be meaningful to women. Aerobic and resistance training also improved 6MWD which is correlated with self-report physical function in older women.⁵⁰

While we found benefits from any of the three types of exercise, resistance exercise improved more outcomes than aerobic or flexibility exercise, including upper and lower body muscle strength, aerobic capacity, and self-report lower-extremity function. Only improvements in SPPB scores in the resistance training group reached the level for meaningful change, though the absence of significant group differences means that we cannot imply resistance exercise is superior than other modalities at improving SPPB scores.²³ Likewise, the resistance group was also the only study arm to achieve a clinically meaningful improvement in 6MWD. Muscle strength and mass have been positively associated with 6MWD in older adults³³, while trials of healthy older adults⁴⁹ or those in cardiac rehabilitation⁵¹ show that resistance training can improve 6MWD. Collectively, these improvements from RET could translate to a longer delay in disability⁵² in turn

reducing the excess morbidity and mortality associated with cancer treatment. Contrary to our expectations, aerobic training did not improve 6MWD more than RET nor by a clinically meaningful amount. Perhaps the prescribed dose of aerobic exercise and/or the achieved frequency of training were insufficient to change this outcome.

Current ACSM guidelines suggest that supervised exercise may yield greater benefits than unsupervised training and may be safer in higher risk populations, such as older adults. However, most older cancer survivors prefer to exercise at home.⁵³ We designed our study to first deliver exercise in a supervised setting where safety and efficacy could be maximized, but then transition women to home-based training so women could maintain benefits long term. To reduce confounding, we did not add a behavioral support intervention during the transition from supervised to unsupervised training. Retention and adherence across supervised training was good for a yearlong facility-based scheduled program in older adults, but adherence dropped considerably when women transitioned to home-based training. Though older survivors cite a preference for home-based training, women may have lost motivation to train as often due to the loss of social support and instructor attention. The lower frequency of training, though, seemed sufficient to maintain benefits gained from supervised exercise - a pattern consistent with recommendations for the maintenance phase of exercise training where exercise volume can be less than that needed to produce initial adaptations.¹⁵ On the other hand, if women continued to train more often they may have continued to improve. Future studies should consider implementing behavioral strategies to sustain exercise adherence to home-based training or possibly online delivery of exercise which has evolved since the COVID-19 pandemic.

Strengths of our study included the direct comparison of aerobic to resistance training, inclusion of both objective and self-report measures of physical functioning, and the inclusion of both supervised and unsupervised settings. We also included women with comorbidities and physical limitations as long as they did not contraindicate exercise to ensure our sample was representative of older breast cancer survivors. One-third of our sample had low SPPB scores, which could further explain why even lower intensity exercise, such as stretching, improved this outcome. Our study also had notable limitations. Though we have used a stretching control group in previous studies focused on bone outcomes^{37, 54, 55}, this group may not have been an appropriate control group for a study focused on physical functioning. Since exercise is currently recommended for all cancer survivors, we felt it was unethical to withhold exercise altogether – a tradeoff all controlled exercise trials must struggle with. In studies of older adults without cancer, flexibility exercise can improve mobility and physical activity.^{49, 56} Thus, we may be underestimating the full benefit of aerobic or resistance exercise, possibly even stretching exercise, in older breast cancer survivors. While our trial was appropriately powered, those estimates were derived from samples in older adults without cancer. Several of our outcomes nearly reached significance and trends were consistent between subjective and objective measures. However, after statistical adjustment for multiple testing significance was lost thus, it is possible we were underpowered and needed a large sample to account for variability in effort and responsiveness across older breast cancer survivors. It is also possible, though, that adaptations took longer to occur given our lower starting intensity, as evidenced by improvements in functioning that emerged at 18 months. Though we prescribed exercise

cautiously in this first study in older women, their high tolerance to training suggests that future trials might progress intensity more quickly or start at a higher level. Additional limitations include an inability to generalize our findings to older breast cancer survivors living far from an academic health center nor to those who are not white or non-Hispanic, and modest attrition over the 18-month study. Attrition was mostly due to health-related reasons that prevented women from resuming supervised exercise, thus future studies should consider whether alternate conditions could be implemented when participants have a health setback.

Older women, with and without cancer, are the most inactive and overweight segment of the U.S. population.^{57, 58} In older adults, inactivity is associated with reduced endurance and weakness and decreased physical functioning,^{59–62} a pattern that may have more dire implications in breast cancer survivors than in the general population. These limitations may begin a downward spiral of even less activity, loss of independence, and life-threatening falls and fractures.^{63–66} Our study showed that breast cancer survivors over the age of 65 can safely participate in supervised and unsupervised low-moderate intensity exercise and that any of the recommended modalities may have benefits, but efforts to boost and sustain adherence to long-term exercise need to be studied. Engaging older women in resistance training may lead to the broadest array and degree of benefits and future efforts should be directed at implementation strategies in practice, both at the clinic and community level.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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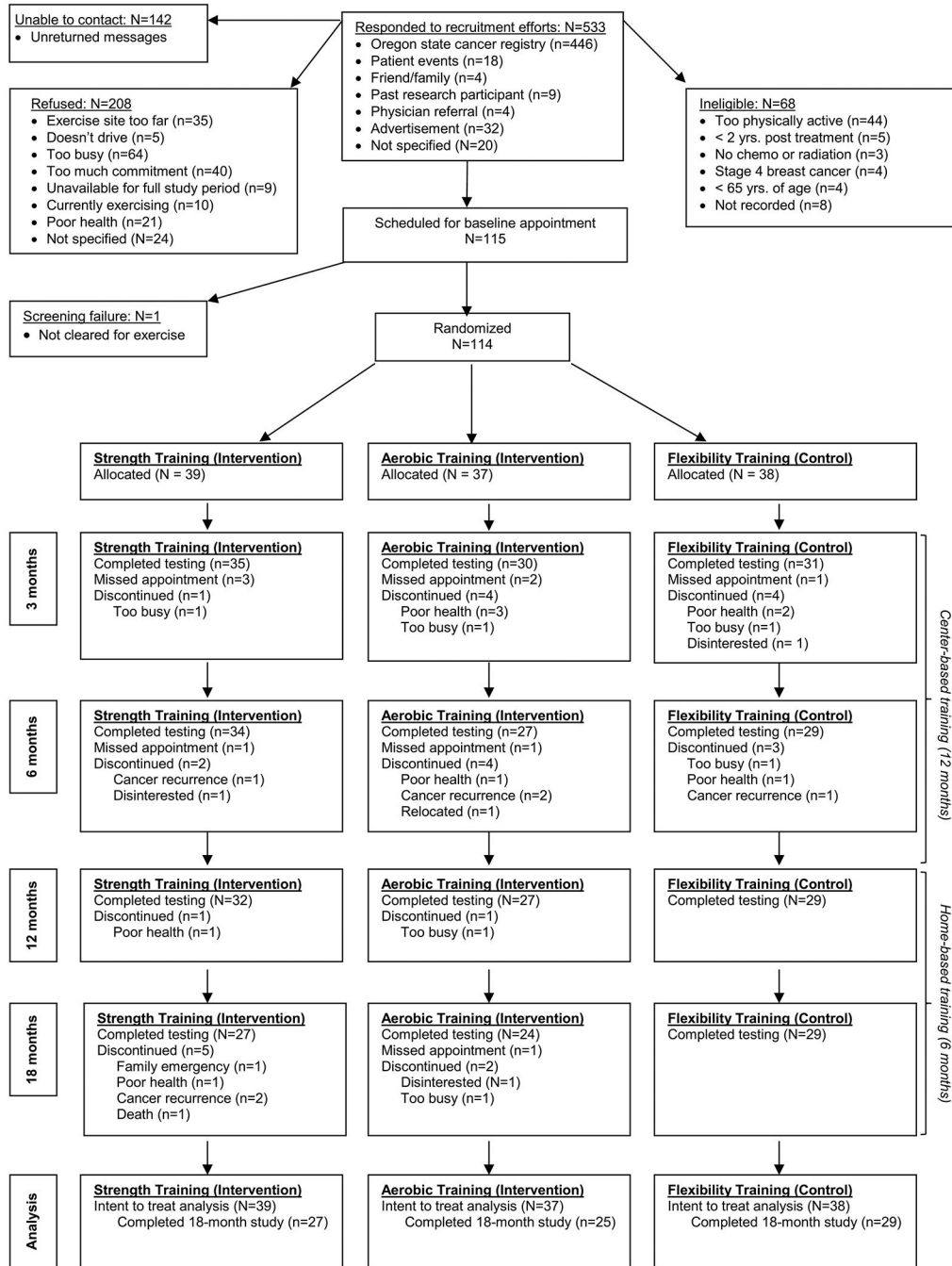


Figure 1.
CONSORT diagram.

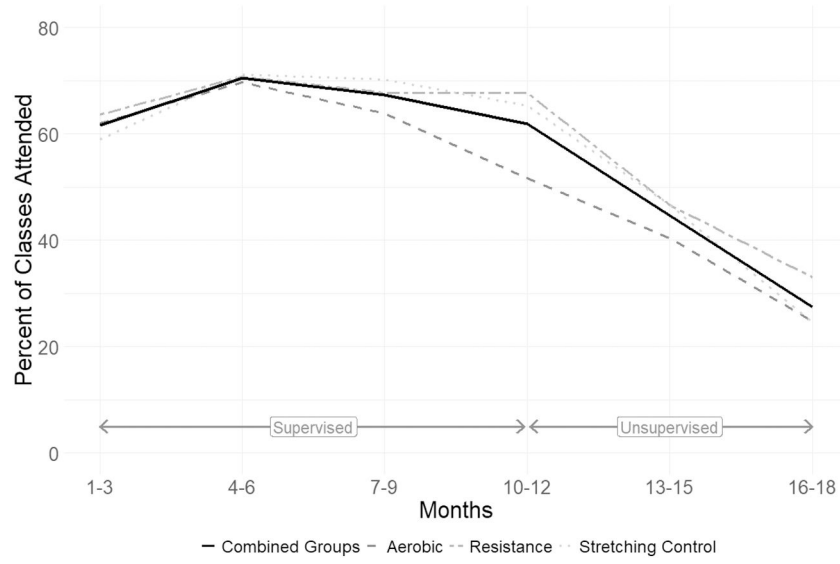


Figure 2. Session attendance by study group and combined for all groups across supervised and unsupervised phases of training.

Table 1.

Progression of resistance and aerobic training over 12 months

Month	Resistance Exercise						Aerobic Exercise	
	Lower Body			Upper Body			Intensity (%HRR)	Duration (minutes)
	Intensity	Sets	Reps	Intensity	Sets	Reps		
1	0–1% BW	1–3	14–15	14–15 RM	1–3	14–15	35–40%	20–35
2	2–3% BW	1–3	14–15	14–15 RM	1–3	14–15	40–45%	25–30
3	4–5% BW	1–3	12–13	12–13 RM	1–3	12–13	45–50%	30–35
4–6	6–8% BW	1–3	11–13	11–13 RM	1–3	11–13	50–55%	35–40
7–9	8–10% BW	1–3	10–12	10–12 RM	1–3	10–12	55–65%	40–45
10–12	10% BW	1–3	10	10 RM	1–3	10	65%	45

BW: Body Weight; RM: Repetition Maximum; HRR: Heart Rate Reserve

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Table 2.

Demographic and clinical characteristics of the full sample and by study arm.

Characteristic	Full Sample (n = 114)		RET (n = 39)	AET(n = 37)	FLEX (n = 38)
	Mean (SD) or % of sample	Range	Mean (SD) or % of sample	Mean (SD) or % of sample	Mean (SD) or % of sample
Age (yrs)	70.9(5.1)	64–87	70.6 (5.4)	71.1 (4.6)	70.9 (5.4)
White/Caucasian	97%		100%	100%	95%
Non-Hispanic	100%		100%	100%	100%
Charlson Comorbidity Index ^A	2.0 (1.7)	0–8	1.9 (1.7)	1.8 (1.3)	2.4 (1.9)
BMI (kg/m ²)	29.2 (5.9)	17.4–51.8	27.5 (4.6)	29.9 (7.1)	30.2 (5.4)
Time since diagnosis (months)	87.1 (45.7)	22–233	84.1 (45.9)	87.1 (472)	90.4 (44.9)
Stage					
Stage 0 (%)	12%		8%	17%	14%
Stage I (%)	47%		55%	49%	41%
Stage II (%)	30%		26%	31%	35%
Stage III (%)	8%		11%	3%	11%
Received chemotherapy (%)	46%		46%	41%	50%
Received radiation therapy (%)	84%		87%	84%	84%
Currently on hormone treatment (%) ^B	68%		69%	75%	64%
Energy expenditure - all exercise (kcal/day) ^C	327 (246)	0–1604	289.6(192.4)	349.6(285.5)	344.0(255.7)
Energy expenditure - moderate intensity exercise (kcal/day) ^C	135(166)	0–896	131.2(128.3)	154.6(198.4)	117.8(116.8)
Self-report disability ^D	81.9(14.9)	38.6–100	82.1 (15.0)	81.6(14.0)	82.0(15.3)
Self-report fall history (1 + falls in past year)	39%		41%	37%	38%

RET: Resistance Exercise Training group; AET: Aerobic Exercise Training group; FLEX: Flexibility control group

^A Charlson Comorbidity index includes non-metastatic cancer if treatment was within 5 years and/or metastatic cancer.^B Includes selective estrogen receptor modulator (SERM) and aromatase inhibitor (AI) use^C Self-reported using the Community Health Activity Model Program for Seniors (CHAMPS) physical activity survey.^D Self-reported disability subscale from the Late Life Function and Disability Instrument (scale 0–100) where higher scores indicate greater ability to perform daily activities independently

Table 3.

Baseline physical functioning and within group change over supervised exercise (0–12 months) presented as point estimate with 95% confidence intervals and p-values for group by time interactions.

Outcome ^A	RET (n=39)		AET (n=37)		FLEX (n=38)		p-value for interactions ^B		
	Estimate	(95% CI)	Estimate	(95% CI)	Estimate	(95% CI)	AET vs. FLEX	RET vs. FLEX	AET vs. RET
Chair Stand (sec)									
Baseline	13.1	(11.9, 14.3)	12.4	(11.2, 13.6)	13.1	(11.8, 14.3)			
Within group change (0–12 mos.)	–2.3	(–3.2, –1.4)	–1.2	(–2.3, –0.2)	–2.1	(–3.1, –1.1)	0.235/0.658	0.799/0.866	0.235/0.658
Walk Speed (m/s)									
Baseline	1.02	(0.98, 1.07)	1.06	(1.01, 1.11)	1.04	(0.99, 1.09)			
Within group change (0–12 mos.)	0.04	(0.00, 0.08)	0.04	(–0.01, 0.08)	0.06	(0.01, 0.10)	0.526/0.736	0.525/0.736	0.976/0.978
SPPB Sum ^C									
Baseline	10.3	(9.8, 10.7)	10.5	(10.0, 11.0)	10.3	(9.8, 10.8)			
Within group change (0–12 mos.)	1.0	(0.6, 1.4)	0.6	(0.1, 1.1)	0.8	(0.3, 1.2)	0.602/0.745	0.471/0.736	0.211/0.658
SF-36 Physical Function ^D									
Baseline	74.0	(68.0, 79.9)	75.8	(69.7, 81.9)	76.4	(70.3, 82.5)			
Within group change (0–12 mos.)	4.8	(–2.0, 11.7)	5.3	(–2.1, 12.6)	–4.4	(–11.6, 2.7)	0.066/0.554	0.066/0.554	0.144/0.658
LLFDI Upper Extremity Function ^E									
Baseline	82.9	(79.3, 86.6)	81.5	(77.8, 85.3)	82.7	(78.9, 86.4)			
Within group change (0–12 mos.)	–0.4	(–3.5, 2.8)	1.2	(–2.2, 4.6)	1.2	(–2.0, 4.5)	0.978/0.978	0.490/0.736	0.519/0.736
LLFDI Lower Extremity Function ^E									
Baseline	81.8	(77.7, 86.0)	83.5	(79.3, 87.7)	82.5	(78.3, 86.7)			
Within group change (0–12 mos.)	1.0	(–2.2, 4.2)	0.0	(–3.5, 3.5)	–3.4	(–6.7, 0.0)	0.170/0.658	0.064/0.554	0.685/0.799
LLFDI Advance Lower Extremity Function ^E									
Baseline	59.4	(55.1, 63.7)	60.4	(56.0, 64.8)	61.5	(57.1, 65.9)			

Outcome ^A	RET (n=39)		AET (n=37)		FLEX (n=38)		p-value for interactions ^B		
	Estimate	(95% CI)	Estimate	(95% CI)	Estimate	(95% CI)	AET vs. FLEX	RET vs. FLEX	AET vs. RET
Within group change (0–12 mos.)	–0.3	(–3.1, –3.1)	2.0	(–1.1, 5.1)	–1.2	(–4.2, 1.8)	0.155/0.58	0.670/0.799	0.296/0.736

RET: Resistance Exercise Training group; AET: Aerobic Exercise Training group; FLEX: Flexibility control group

^A All models controlled for age, baseline body mass index, and Charlson Comorbidity Index.

^B Original unadjusted p-values are provided followed by Bejamini-Hochberg adjusted p-values.

^C Short Physical Performance Battery

^D SF-36 Physical Function = physical function subscale from the MOS 36-Item Short Form Health Survey

^E Subscales from the Late Life Function and Disability Instrument (LLFDI)

Table 4.

Within group changes during unsupervised exercise (months 12–18) presented as point estimate with 95% confidence intervals and p-values for group by time interactions.

Outcome ^A	RET (n=39)		AET (n=37)		FLEX (n=38)		p-value for interactions ^B		
	Estimate	(95% CI)	Estimate	(95% CI)	Estimate	(95% CI)	AET vs. FLEX	RET vs. FLEX	AET vs. RET
Chair Stand (sec)	0.0	(-0.9, 0.9)	0.2	(-0.8, 1.1)	-0.2	(-1.2, 0.7)	0.549/0.744	0.707/0.803	0.804/0.866
Walk Speed (m/s)	0.04	(0.00, 0.08)	0.01	(-0.04, 0.05)	-0.02	(-0.06, 0.02)	0.424/0.736	0.057/0.554	0.306/0.736
SPPB Sum ^C	-0.3	(0.6, 0.1)	-0.1	(-0.5, 0.3)	0.2	(-0.2, 0.6)	0.404/0.736	0.098/0.658	0.451/0.736
SF-36 Physical Function ^D	-1.9	(-8.6, 4.8)	-2.9	(-10.0, 4.1)	1.8	(-4.8, 8.3)	0.343/0.736	0.444/0.736	0.840/0.882
LLFDI Upper Extremity Function ^E	-2.1	(-5.6, 1.3)	-3.5	(-7.1, 0.1)	0.0	(-3.4, 3.4)	0.177/0.658	0.389/0.736	0.603/0.745
LLFDI Lower Extremity Function ^E	-1.0	(-4.4, 2.3)	0.9	(-2.6, 4.5)	2.3	(-1.0, 5.6)	0.573/0.745	0.161/0.658	0.430/0.736
LLFDI Advance Extremity Function ^E	1.3	(-1.6, 4.2)	-3.1	(-6.2, -0.5)	-1.3	(-4.1, 1.6)	0.381/0.736	0.222/0.658	0.043/0.554 ^E

RET: Resistance Exercise Training group; AET: Aerobic Exercise Training group; FLEX: Flexibility control group

^A All models controlled for age, baseline body mass index, and Charlson Comorbidity Index.

^B Original unadjusted p-values are provided followed by Bejamini-Hochberg adjusted p-values.

^C Short Physical Performance Battery

^D SF-36 Physical Function = physical function subscale from the MOS 36-Item Short Form Health Survey

^E Subscales from the Late Life Function and Disability Instrument (LLFDI)

Table 5.

Physical fitness measures of program fidelity including baseline and within group change over supervised exercise (0–12 months) using point estimate with 95% confidence intervals and p-values for group by time interactions.

Measure ^A	RET (n=39)		AET (n=37)		FLEX (n=38)		p-value ^B		
	Estimate	(95% CI)	Estimate	(95% CI)	Estimate	(95% CI)	AET vs. FLEX	RET vs. FLEX	AET vs. RET
1 RM Bench Press (kg)									
Baseline	21.0	(19.4, 22.5)	21.9	(20.3, 23.5)	22.3	(20.7, 23.9)			
Change from 0 - 12 months	2.5	(1.6, 3.5)	1.7	(0.6, 2.8)	1.1	(0.0, 2.1)	0.396/0.580	0.048/0.192	0.288/0.533
1 RM Leg Press (kg)									
Baseline	65.1	(59.7, 70.5)	66.7	(61.2, 72.3)	69.9	(64.4, 75.5)			
Change from 0 - 12 months	8.2	(4.8, 11.7)	2.7	(-1.2, 6.5)	5.4	(1.7, 9.15)	0.311/0.533	0.280/0.533	0.037/0.192
6 Minute Walk (m)									
Baseline	475.3	(441.2, 509.4)	501.7	(467.1, 536.3)	483.1	(448.5, 517.7)			
Change from 0 - 12 months	57.3	(32.1, 82.5)	31.1	(4.0, 58.2)	20.4	(-5.7, 46.5)	0.580/0.696	0.048/0.192	0.167/0.501
Chair Sit and Reach (cm) ^C									
Baseline	-1.7	(-5.4, 2.1)	-0.2	(-4.1, 3.6)	-1.9	(-5.7, 2.0)			
Change from 0 - 12 months	3.2	(0.9, 5.5)	1.9	(-0.6, 4.4)	2.5	(0.1, 4.9)	0.738/0.738	0.679/0.738	0.435/0.580

RET: Resistance Exercise Training group; AET: Aerobic Exercise Training group; FLEX: Flexibility control group

^A All models controlled for age, baseline body mass index, and Charlson Comorbidity Index.

^B Original unadjusted p-values are provided followed by Bejamini-Hochberg adjusted p-values.

^C Negative values for chair sit and reach indicate distance between fingers and toes during reach whereas positive values indicate degree of overlap between fingers and toes. Values moving from negative to positive indicate increased range of motion