A 4-Week Home-Based Aerobic and Resistance Exercise Program During Radiation Therapy: A Pilot Randomized Clinical Trial

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Abstract During radiation therapy, cancer patients may report cancer-related fatigue (CRF), which impairs aerobic capacity, strength, muscle mass, and, ultimately, quality of life (QOL). The purpose of this pilot clinical trial was to examine the feasibility and initial efficacy of a home-based aerobic and progressive resistance exercise intervention for aerobic capacity, strength, muscle mass, CRF, and QOL. Daily steps walked (DSW), daily minutes of resistance exercise (MRE), and number of resistance exercise days (RED) were assessed to evaluate intervention adherence. Breast and prostate cancer patients (n = 38) beginning radiation therapy were randomized to undergo 4 weeks of exercise or no exercise. Participants in the exercise group demonstrated good adherence to the exercise intervention, with significantly more DSW, MRE, and RED at post intervention and 3 month follow-up than controls. Participants in the exercise intervention exhibited significantly higher QOL and significantly lower CRF post intervention and at 3-month follow-up than controls. Results of this pilot study provide positive preliminary evidence that exercise during radiation may be beneficial for cancer patients.

Cancer-related fatigue (CRF) is a multifaceted subjective and physiologic state characterized by persistent, overwhelming exhaustion and a decreased capacity for physical and mental work, which are not relieved by rest.[1] CRF is the most frequently reported side effect resulting from radiotherapeutic, surgical, chemotherapeutic, hormonal, and biological response modification treatments. Reports suggest that between 60% and 99% of patients undergoing these therapies experience CRF.[1,2] The severity of CRF, like its prevalence, depends on many factors, including the treatment regimen, assessment technique, and patient population. In general, during radiation therapy, CRF gradually increases in severity, and the proportion (78%–89%) of patients reporting increases in CRF over the course of treatment.[1,3,4] CRF peaks at the completion of radiation therapy and persists in more than 30% of patients for many months.[1,3,4]

The pathophysiology of CRF is not well understood but may result, at least in part, from physical deconditioning. Physical deconditioning refers to generalized physiologic deterioration resulting from a simple reduction in physical activity or exercise. This deconditioning occurs fairly rapidly and is often first recognized clinically by patient reports of shortness of breath, weakness, and fatigue.[5] Objective assessment reveals reduced aerobic capacity, muscle strength and muscle mass. Deconditioning, as a consequence of diminished physical activity resulting from either the cancer itself or its treatments, produces these reductions in aerobic capacity, muscle strength, and muscle mass and, ultimately, causes CRF.[5–7]

CRF portends a less-than-optimal recovery from cancer and its treatments, and it may prevent or delay the completion of treatment (eg, radiation therapy); diminish functional capacity; interfere with normal daily activities; and lead to other debilitating problems such as sleep disruption, mood disturbance, muscle weakness, and cognitive im-

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This study was supported by grants from the National Cancer Institute (1R25CA102618 and 1K07CA120025).

Manuscript submitted February 13, 2009; accepted April 15, 2009.

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J Support Oncol 2009;9:158–167

pairment. CRF interferes with the ability to pursue occupational and social activities, eventually impairing QOL.[1, 8] CRF and its associated effects on QOL are not alleviated by periods of rest, as is fatigue resulting from physical exertion.[1,8]

Although guidelines exist, a clear standard for the effective treatment of CRF is lacking.[1] Currently, clinicians tend to adopt a multimodal methodologic approach to CRF, consisting of patient education, pharmaceutical agents, etiology-specific interventions, and nonpharmacologic therapies, but a paucity of research exists to provide an evidence base for these methods.[1,8] Despite these measures, large numbers of cancer patients continue to report CRF, and, given the lack of an effective pharmacologic remedy for this problem, randomized controlled trials are needed to confirm the efficacy of promising behavioral interventions such as exercise.[1,8] The National Institutes of Health (NIH) has recently identified improved management of CRF as a priority for advancing the clinical care of cancer patients.[9]

Exercise and Cancer-Related Fatigue

Researchers have shown that physical exercise among cancer survivors during and after treatment produces improvements in CRF, aerobic capacity, emotional distress, immunologic parameters, flexibility, body composition, and QOL.[10–12] Schwartz stated that "fatigue is the most common side effect of cancer and its treatments, and it frequently goes unrecognized and untreated."[13]

To our knowledge, only four studies have specifically assessed the benefits of physical exercise among breast and prostate cancer patients receiving radiation therapy.[14–17] Three studies included women with breast cancer receiving radiation and used a home-based aerobic exercise intervention (self-paced walking) prescribed 4–5 days a week for 20–30 minutes and demonstrated improvements in CRF.[14–16] These studies among women with breast cancer are limited because they did not include a resistance training component and the walking prescription was not individually tailored.

One study among men with prostate cancer receiving radiation used a moderately intense (60%–70% of maximal heart rate; MHR) home-based aerobic exercise program (walking) performed 3 times a week for 30 minutes over 10 weeks; it resulted in no worsening of CRF among the exercising patients compared with significant increases in CRF among the nonexercising patients.[17] This study is also limited because resistance training was not a component of the exercise intervention and the walking program was not individually tailored. The results of these four studies suggest that aerobic exercise (walking) is beneficial for CRF, aerobic capacity, and QOL among breast and prostate cancer patients undergoing radiation therapy, but the role of resistance exercise and individual tailoring of exercise prescriptions remains unclear.

The purpose of this pilot clinical trial was to conduct an initial test of the feasibility and efficacy of a 4-week, tailored, home-based aerobic (walking) and progressive resistance (therapeutic bands) exercise intervention among breast and prostate cancer patients for improving resistance exercise days (RED), CRF, aerobic capacity, strength, muscle mass, and QOL. Adherence to and compliance with the exercise intervention program and the level of exercise contamination in the control condition were also examined.

Methods

SUBJECTS

Women with breast cancer and men with prostate cancer beginning standard radiation therapy were recruited for this study between August 2004 and December 2006 by physician and nurse referrals to study staff at the University of Rochester James P. Wilmot Cancer Center. Breast and prostate cancer patients were collectively recruited for this feasibility study because the radiation therapy dose is similar in the current study design. After expressing an initial interest in the investigation, each potential participant met with the study coordinator, was screened for inclusion criteria using a brief eligibility checklist, and learned about the details of the study.

Patients participating in the study met the following eligibility criteria: (1) a primary diagnosis of breast or prostate cancer; (2) no distant metastases; (3) no recurrent disease; (4) no contraindications prohibiting participation in a low-to-moderate intensity walking or resistance exercise program or physical fitness testing, as assessed by patients' radiation oncologist (or physician designee); (5) completion of enrollment and baseline assessments before the end of the first calendar week of radiation treatments; (6) at least 30 scheduled radiation treatments (6 weeks); and (7) sedentary lifestyle (no regular exercise or fewer than two exercise sessions per week). The Human Subjects Review Board approved the study prior to patient consent and enrollment.

DESIGN AND PROCEDURES

This study was a two-arm, pilot, randomized, controlled, clinical trial. All patients underwent a series of baseline assessments over 7 days, including completion of an on-study form; clinical record form; self-report questionnaires (ie, Brief Fatigue Inventory [BFI]; Functional Assessment of Chronic Illness Therapy–Fatigue [FACIT–F]); a daily diary; pedometer assessment; a 6-minute walk test; a handgrip dynamometry test; and a bioelectrical impedance test. After completing all baseline assessments, patients were stratified by diagnosis (breast or prostate cancer) and, subsequently, randomized, using a randomization scheme with blocks of four, to the control condition consisting of radiation therapy alone or the intervention condition consisting of radiation therapy plus an individually tailored home-based, progressive walking and therapeutic resistance band exercise program.

Patients randomized to the control group were instructed not to begin any new formal physical exercise program (eg, joining a gym or a walking group), and they did not keep the pedometer during the study intervention period to avoid exercise contamination. Patients in both the control and intervention groups completed daily diaries and were monitored by study staff during the following four calendar weeks while

receiving radiation alone or radiation plus exercise. All patients underwent the same series of assessments completed at baseline, after completing the 4-week monitoring/intervention period during the sixth week of radiation (post intervention) and again 3 months later (3-month follow-up).

This pilot study was not fully blinded; however, the condition allocation was concealed from the patient and coordinators until after the completion of the baseline assessments. A clinical research coordinator obtained patient consent and collected all the self-report assessments (eg, BFI) while a second coordinator with a Master's in Exercise Science performed the objective tests (eg, 6-minute walk, handgrip dynamometer) and explained the home-based exercise program to participants. The study statistician and data managers remained blinded at all times.

HOME-BASED AEROBIC (WALKING) AND PROGRESSIVE RESISTANCE (THERAPEUTIC BANDS) EXERCISE INTERVENTION

The home-based aerobic and progressive resistance exercise program was designed by a certified exercise scientist from the American College of Sports Medicine (ACSM) and adhered to the ACSM guidelines for exercise testing and prescription.[18] The exercise intervention was designed to be delivered easily and quickly to cancer patients in a busy radiation oncology clinic at the beginning of radiation therapy and to be implemented concurrently by patients during the course of receiving radiation therapy. The intervention was provided to the patient via a single, 45-minute, instructional session with the study coordinator, a Master's-trained exercise physiologist, and a prepackaged individual "exercise kit." The kit contained all of the written instructions and materials necessary for the patient to complete the home-based walking and resistance band exercise intervention, including written instructional materials, a pedometer, and therapeutic resistance bands. The aerobic and resistance components of the home-based exercise program followed the guidelines below.

The first component was an individually tailored walking prescription intended to provide moderately intense aerobic exercise (60%–70% of heart rate reserve, 3–5 exercise rating of perceived exertion on the ACSM revised rating scale—a visual analog scale ranging from 0 = no exertion at all to 10 = very, very strong: maximal exertion) 7 days a week for the entire 4-week exercise intervention time period. A pedometer was given to all patients in both study arms during the baseline assessment period. Using the pedometer, patients were instructed to record the number of steps they walked daily for one full week. Using the baseline average number of steps walked daily, patients in the home-based exercise intervention arm were instructed to increase their total steps walked each day by 5% to 20% each week while maintaining a moderate intensity during the 4-week intervention. Patients were encouraged to reach the ACSM-suggested 10,000 steps a day if possible. As an instructional, tailoring, and motivational tool at the start of the exercise intervention, a table including the average number of steps they walked at baseline, as well as the number of steps that would represent increases of 5%, 10%, 15%, and 20% over this baseline number for each of the 4 weeks of the intervention period, was given to patients in the exercise group.

The second component of the exercise program, an individually tailored therapeutic resistance band exercise prescription, was designed to provide low to moderately intense progressive resistance exercise (3–5 exercise rating of perceived exertion on the ACSM revised rating scale) 7 days a week for the entire 4-week period to maintain muscle strength in the upper body. This portion of the exercise prescription was designed to focus on the upper body because the walking component focused on the lower body. Patients were given a set of three color-coded therapeutic resistance bands, representing low and moderate levels of resistance. The study coordinator thoroughly explained the proper use of the resistance bands and the appropriate mechanics for safely performing the resistance exercises.

Patients were instructed to begin with an individually determined number of sets (1 set = 8–15 repetitions) for each of the 11 exercises (ie, bicep curl, tricep extension, overhead press, rows, chest press, internal and external rotation, lateral and front raises, horizontal adduction, and abduction) at a low to moderately challenging level up to 7 days a week. Patients were instructed to perform these resistance band exercises as many as 7 days a week because the resistance level and number of sets and repetitions were minimal and focused on maintaining strength in a clinical population of cancer patients receiving radiation treatments, not on increasing strength, as would be expected with vigorous resistance training programs. Patients were instructed to increase the intensity by changing the band color or shortening the initial length of the band for increased resistance. Patients were instructed to progressively increase from their individual baseline sets and repetitions to a maximum of 4 sets of 15 repetitions for each exercise daily over the course of the 4-week intervention at an optimally challenging rate.

All walking and progressive resistance exercises were performed off-site from the University of Rochester Cancer Center in a home-based patient-selected environment.

Measures

QUESTIONNAIRES

On-study and clinical record forms. Demographic information obtained included age, gender, race, partnered status, job status, and educational background. Relevant medical information included height, weight, body mass index (BMI), and cancer treatment history.

BFI. CRF was assessed using the BFI, which is a nine-item, patient-report instrument with established reliability and validity commonly used in studies of CRF.[19] The BFI allows for the rapid assessment of fatigue in cancer patients and identifies those patients with severe fatigue. The reliability and validity of the BFI were demonstrated in a study of 305 cancer patients and 290 community-dwelling adults. An internal consistency coefficient (Cronbach's alpha) of 0.96 was demonstrated when

the BFI was administered to 305 patients with cancer.[19]

FACIT–F. CRF and QOL were assessed using the 28-item FACIT–F, developed by Cella and colleagues[20–22] specifically for cancer survivors. This well-validated measure is widely used among oncology researchers and yields a total QOL score. Each item is anchored by a five-point Likert scale based on how true each statement is for the individual during the previous week (0 = not at all, 4 = very much). Sample items include the following: "I am bothered by the side effects of treatment" (physical subscale), "I am satisfied with family communication about my illness" (social subscale), and "I am enjoying the things I usually do for fun" (functional subscale). Cella and colleagues also developed a 13-item subscale for the FACIT–F specifically to measure CRF.[20–22] The CRF subscale is anchored by the same five-point Likert scale as the previous subscales; sample items include "I am frustrated by being too tired to do the things I want to do" and "I need to sleep during the day."

FUNCTIONAL MEASURES

6-Minute walk test. Aerobic capacity was estimated using a 6-minute walk test protocol, which has been used extensively in clinical exercise trials to estimate aerobic capacity.[18,23] A recent systematic review concluded that this method possesses excellent measurement properties, is better tolerated, and is more reflective of activities of daily living than any other walk test in use.[23] Participants were given a short warm-up and then asked to walk for a total of 6 minutes and to cover as much distance as possible. The 6-minute walk was followed by a short cool-down period. This walk test was conducted in a designated walking area in the University of Rochester Medical Center. Upon completion of the test, the total distance walked was recorded and used to estimate aerobic capacity. The coefficient of variation for the 6-minute walk test ranged from 0.24 to 0.25 for the current study.

Handgrip dynamometry. Strength was evaluated using a handgrip dynamometer to assess the maximal voluntary grip strength.[18] The elbow joint angle was held constant at 180°. Trials were performed in an alternating bilateral sequence for a total of six attempts (three with each arm), and a rest period of 30 seconds was required between each trial to standardize the test procedures. An average of the data from the three trials for the involved arm (on the side of the surgery) was used for analysis, except in patients with bilateral mastectomies, from whom data from the right side (also the dominant arm in both cases) were consistently used. Although not a direct measure of overall body strength, this measure was chosen because handgrip dynamometry is correlated with overall body strength as measured by other gold standard methods (eg, repetition maximum testing), and this measure is easily implemented in a busy radiation oncology clinical environment.[18] The coefficient of variation for the handgrip dynamometer test ranged from 0.29 to 0.32 for the current study.

Bioelectrical impedance. Muscle mass was calculated using bioelectrical impedance analysis (BIA, Quantum-II Desktop with a real-time resolution of 0.1 ohm).[18] BIA is a noninvasive, easy-to-administer, and safe method of assessing body composition in a fitness environment. BIA involves passing a small electrical current through the body and evaluating the conductivity. The resistance to flow is inversely related to fat-free mass and total body water.

Patients were instructed to prepare for the BIA by fasting for 4 hours, abstaining from physical activity for 12 hours, abstaining from alcohol and diuretics (unless prescribed) for 48 hours, being well hydrated (water only), and voiding prior to assessment. Participants were instructed to lie down on a flat surface in a prone position for approximately 5 minutes prior to the test to ensure a resting metabolic state. Electrodes were attached to the right hand (distal end of the third and fourth metacarpals and distal end of the ulna and radius) and the right foot (distal end of the third and fourth metatarsals and distal end of the tibia and fibula). Prediction of lean body mass from BIA is as reliable as skin-fold measurements and hydrostatic weighing.[18] Although not a direct measure of lean body mass, this measure was chosen because BIA is portable and easily implemented in a busy radiation oncology clinical environment.[18] Muscle mass was calculated from the resistance measured.[24] The coefficient of variation for the bioelectrical impedance analysis ranged from 0.16 to 0.17 for the current study.

ADHERENCE AND COMPLIANCE

Adherence to and compliance with daily steps walked (DSW), daily minutes of resistance exercise (MRE), and RED were assessed in both groups to determine the level of exercise each patient achieved during the study assessment periods. The level of exercise is determined by four specific components: frequency (numbers of times per week; DSW, RED), duration/volume (length of time/volume of the exercise bout; DSW, MRE), mode (type of exercise), and intensity (difficulty level of the effort put forth to perform the exercise; ACSM rating of perceived exertion scale[18]).

Daily diary. Adherence to and compliance with DSW, MRE, and RED were assessed using a self-report daily diary. The frequency of exercise was determined by summing the total numbers of days each week that a patient reported doing any exercise (ie, DSW, RED). The duration was determined by patients recording the DSW from a pedometer and the MRE. The mode was determined by having the patients record aerobic and resistance exercise. The intensity was assessed by having patients record a rating of perceived exertion for the exercise sessions.[18]

Pedometer. Adherence to and compliance with the prescribed walking program were also assessed by pedometers. Study patients reset the pedometer to zero steps each morning and put the pedometer on every morning upon waking and removed it before bed each night. Patients recorded the DSW in a daily diary each night before going to bed.

DATA ANALYSIS

Data analyses were conducted using SPSS software. Unless otherwise stated, all statistical tests were performed at

Table 1

Demographic and Treatment-Related Characteristics of the Exercise and Control (No-Exercise) Groups

CHARACTERISTIC	EXERCISE GROUP (n = 19)		CONTROL GROUP (n = 19)		STUDY SAMPLE (n = 38)	
Gender (diagnosis)						
Male (prostate cancer)	6 (32%)		5 (26%)		11 (29%)	
Female (breast cancer)	13 (68%)		14 (74%)		27 (71%)	
Race						
White	16 (84%)		18 (95%)		34 (90%)	
Asian	2 (11%)		0 (0%)		2 (5%)	
Black	1 (5%)		1 (5%)		2 (5%)	
Currently employed	17 (90%)		12 (63%)		29 (76%)	
Marital status						
Married	14 (74%)		9 (47%)		23 (61%)	
Divorced	2 (11%)		5 (26%)		7 (19%)	
Single	2 (11%)		2 (11%)		4 (10%)	
Widowed	1 (5%)		3 (16%)		4 (10%)	
Partial college education or greater	16 (84%)		12 (63%)		28 (74%)	
Previous surgery	16 (84%)		16 (84%)		32 (84%)	
Previous chemotherapy	9 (47%)		10 (53%)		19 (50%)	
Current hormone therapy	1 (5%)		2 (10%)		3 (8%)	
CHARACTERISTIC	MEAN ± SD	RANGE	MEAN ± SD	RANGE	MEAN ± SD	RANGE
Karnofsky performance status	96.3 ± 6.8	60–100	93.7 ± 10.1	80–100	95.0 ± 8.6	60–100
Age, yr	56.6 ± 13.7	36–82	63.3 ± 9.4	48–78	60.0 ± 12.1	36–82
Height, ft	64.7 ± 3.6	59–72	65.0 ± 3.5	60–72	64.8 ± 3.5	59–72
Weight, lb	173.7 ± 46.8	109–256	188.3 ± 43.9	130–264	181.0 ± 45.4	109–264
Body mass index, kg/m^2	28.7 ± 5.4	21–39	31.3 ± 6.8	20–42	30.0 ± 6.2	20–42
Total radiation dose, Gy	66.6 ± 13.1	50–101	61.7 ± 7.9	49–75	64.1 ± 11.0	49–101
Weekly work hours	32.8 ± 12.4	10–57	23.7 ± 12.3	0–45	28.8 ± 13.0	0–57

SD = standard deviation

the two-tailed 5% level of significance. The data were coded and cleaned by independent data managers using Teleforms scanned into an Access database, and then a different data manager visually audited the data. Data were analyzed on an "intent-to-treat" basis, with patients being analyzed in the group to which they were assigned. The assumptions underlying all statistical analyses were thoroughly checked. No outliers or influential data were detected; thus, analyses included all of the fully evaluable patients. The reasons for missing data and the causes and pattern of the missing data were examined. Very few data were missing, and no imputations were necessary for the current pilot study analyses. Two participants withdrew from the study immediately after they consented and did not provide any data; therefore, no data from these two participants were used in the analyses.

The main statistical purpose was to determine the means and standard deviations for the dependant variables to calculate the sample size for a future phase III clinical trial. Analyses consisted of calculating descriptive statistics, frequency distributions, means, mean change scores (ie, baseline assessment subtracted from the post-intervention assessment, baseline subtracted from the follow-up assessment, and post intervention subtracted from follow-up assessment), and standard deviations for the dependent variables in the two study arms. Baseline characteristics of the two groups were compared using two-sample t-tests for the continuous variables and chi-square tests for the categorical variables. Analyses of covariance (ANCOVA), with baseline as the covariate and an interaction term, were used to examine the difference in means between the exercise group and the no-exercise control group on DSW, MRE, RED, CRF, strength, muscle mass, and QOL.

Results

PARTICIPANTS

A total of 120 patients were initially screened, and 82 were potentially eligible. After physician or nurse referral, study coordinators approached 61 patients; 40 were eligible and agreed to participate. The remaining 21 patients were not enrolled because they were ineligible due to maintaining a regular exercise program or because they declined to participate. A total of 40 patients agreed to participate in the study and were enrolled; of the 40 patients accrued, 2 patients (5%)—one from each arm—did not complete any of the study materials and were not included in the analysis. The analyses presented are based on 38 fully evaluable patients.

Table 2

Exercise, Aerobic Capacity, Muscle Strength, Muscle Mass, and Quality of Life

	CONTROL GROUP (n = 19)					EXERCISE GROUP (n = 19)				
MEASUREMENT	BASELINE	POST-Tx	3-Mo FU	CHANGE 1	CHANGE 2	BASELINE	POST-Tx	3-Mo FU	CHANGE 1	CHANGE 2
Daily steps	5,544.9 ± 2,746.7	4,796.9 ± 2,613.9	5,180.8 ± 3,258.9	–572.3 ± 2,139.1	–64.4 ± 2,756.4	7,222.2 ± 2,691.3	11,200.1 ± 5,851.8	12,878.9 ± 7,570.1	3,977.6 ± 5,959.3	5,792.2 ± 7,094.6
Daily resistance, min	1.57 ± 4.73	0.00 ± 0.00	0.73 ± 3.03	–1.57 ± 4.73	–1.03 ± 6.06	1.16 ± 2.95	10.59 ± 11.37	8.00 ± 10.26	9.43 ± 11.44	6.81 ± 9.94
Days/week of resistance	0.21 ± 0.63	0.00 ± 0.00	0.12 ± 0.49	–0.21 ± 0.63	–0.12 ± 0.86	0.21 ± 0.54	3.26 ± 2.92	1.56 ± 2.50	3.05 ± 2.99	1.33 ± 2.52
Fatigue (BFI)	2.62 ± 2.14	2.44 ± 2.08	2.73 ± 2.60	–0.18 ± 1.16	0.12 ± 1.95	1.85 ± 1.87	1.60 ± 1.36	1.16 ± 0.98	–0.25 ± 1.24	–0.66 ± 1.52
Fatigue[a] (FACIT–F)	36.89 ± 11.73	35.84 ± 12.08	40.35 ± 12.24	–1.05 ± 4.84	3.88 ± 6.97	38.68 ± 11.66	41.79 ± 8.99	43.17 ± 7.74	3.11 ± 8.69	3.89 ± 7.77
Aerobic capacity, ft (6-min walk test)	1,478.21 ± 401.02	1,425.28 ± 438.27	1,600.33 ± 468.86	–28.44 ± 303.75	78.73 ± 484.12	1,894.37 ± 296.78	1,937.95 ± 261.99	2,020.59 ± 386.36	43.58 ± 227.84	133.53 ± 396.79
Muscle strength, kg (hand-grip dynamometer)	24.92 ± 7.89	24.12 ± 8.74	23.87 ± 7.79	–0.80 ± 3.86	–0.59 ± 3.30	26.02 ± 7.16	25.49 ± 7.29	26.89 ± 8.71	–0.53 ± 2.83	0.33 ± 3.75
Skeletal muscle mass, kg (bioelectric impedance)	23.56 ± 5.63	23.35 ± 5.43	23.42 ± 6.22	–0.21 ± 0.95	–0.12 ± 1.90	24.48 ± 8.78	24.54 ± 8.96	25.32 ± 8.12	0.06 ± 1.42	–0.09 ± 1.52
Quality of life (FACIT-F)	117.59 ± 29.65	116.92 ± 30.58	126.13 ± 31.81	–0.67 ± 11.51	8.55 ± 11.28	124.19 ± 25.12	130.19 ± 20.13	132.96 ± 16.41	6.00 ± 18.31	8.76 ± 16.51

Post-Tx = post-intervention; 3-Mo FU = 3-month follow-up; Change 1 = change from baseline to post-intervention; Change 2 = change from post-intervention to 3-month follow-up; BFI = Brief Fatigue Inventory; FACIT–F = Functional Assessment of Chronic Illness Therapy–Fatigue subscale

[a] A higher score on the FACIT–F Fatigue subscale denotes a lower level of cancer-related fatigue.

Participant demographic data are summarized in Table 1. There were no significant differences between the groups at baseline in gender, race, employment status, weekly work hours, marital status, education, previous surgery, previous chemotherapy, previous hormone therapy, Karnofsky performance status, age, height, weight, BMI, total radiation dose, DSW, CRF, strength, muscle mass, or QOL. As a result of the study eligibility criteria, all participants had early-stage cancer diagnoses with no distant metastases or recurrent disease. Significant differences between the groups were observed for aerobic capacity ($t = -3.636$; $P < 0.05$), with the exercise group walking further on the 6-minute walk test than the no-exercise group at baseline (Table 2). Two participants in the control group reported doing 15 minutes of resistance training 2 days during the week of baseline testing, and three individuals in the exercise group reported doing an average of 7 minutes of resistance training on 1–2 days during baseline testing.

EXERCISE ADHERENCE AND COMPLIANCE

Aerobic exercise (walking). Exercise data are summarized in Table 2. Of the 19 patients assigned to the exercise group, 15 reported increasing DSW, with a mean increase of 5,959 steps from baseline to post intervention and 7,095 steps from baseline to the 3-month follow-up. The DSW rose from an average of 7,222 (SD [standard deviation] = 2,691) at baseline to 11,200 (SD = 5,851) post intervention, and, finally, to 12,878 (SD = 7,570) at the 3-month follow-up (above the ACSM recommended 10,000 steps a day for health-related benefits). In contrast, patients assigned to the no-exercise control group reported decreasing DSW, with a mean decrease of –572 steps from baseline post intervention and –64 steps from baseline to the 3-month follow-up. The DSW for the control group declined from 5,544 steps at baseline to 4,796 steps post intervention and rose slightly to 5,180 at the 3-month follow-up (below 5,000 steps per day is considered sedentary and between 5,000 and 7,499 is very low active, according to ACSM recommendations). ANCOVA comparing the means between the two groups with baseline DSW as the covariate showed significantly more DSW post intervention and at the 3-month follow-up in the exercise group than in the control group (all P values < 0.05).

Resistance exercise (therapeutic resistance bands). Post intervention, 12 patients (79%) assigned to exercise reported doing resistance training during the intervention period. These 12 patients reported an average of 17 minutes 3 days a week, with an exercise rating of perceived exertion (RPE) of 4 out of 10, indicating moderate intensity. At the 3-month follow-up, eight patients (42%) in the exercise group reported doing resistance exercise; they reported an average of 18 minutes 1.5 days a week, with four of these eight patients (21%) reporting resistance exercise 3 or more times a week at an average exercise RPE of 4 out of 10.

The mean change in daily minutes spent in resistance training from baseline to post intervention was 9.4 minutes (SD = 11.4), and the mean change in daily minutes spent in resistance training from baseline to the 3-month follow-up was 6.81 minutes (SD = 9.94) for the entire exercise group. None of the patients in the control group reported doing resistance exercise post intervention, and only one patient (5%) reported doing resistance exercise for an average of 13 minutes 3 times

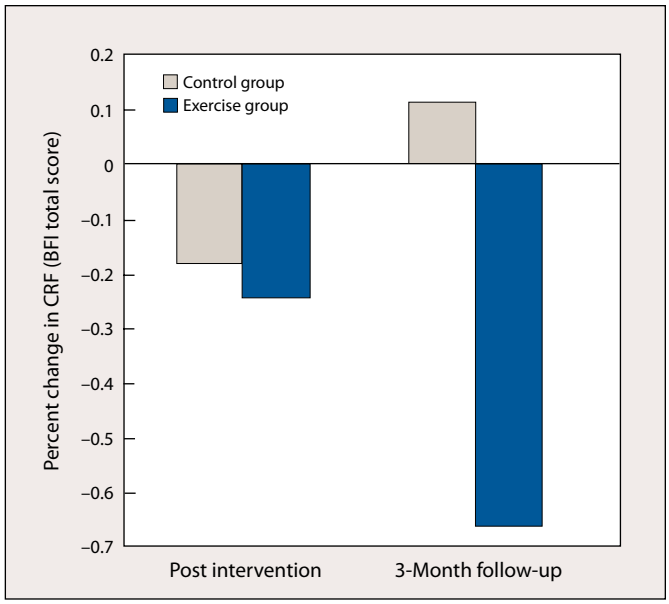

Figure 1 Change in Cancer-Related Fatigue (CRF) as Assessed by BFI from Baseline to Post Intervention and Follow-Up

BFI = Brief Fatigue Inventory

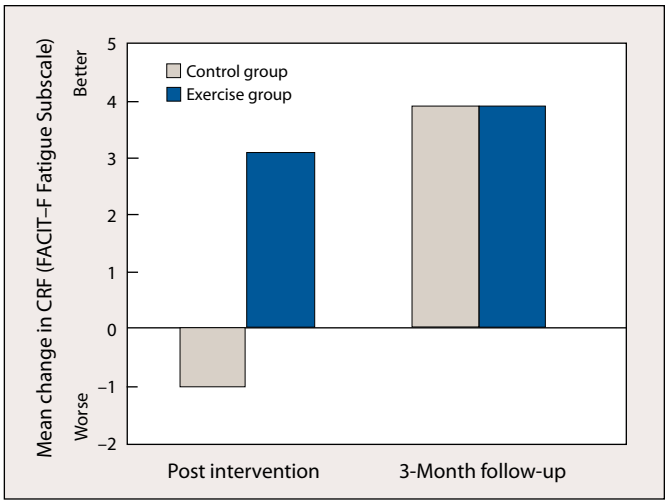

Figure 2 Change in Cancer-Related Fatigue (CRF) as Assessed by FACIT–F from Baseline to Post Intervention and Follow-Up

FACIT–F = Functional Assessment of Chronic Illness Therapy–Fatigue

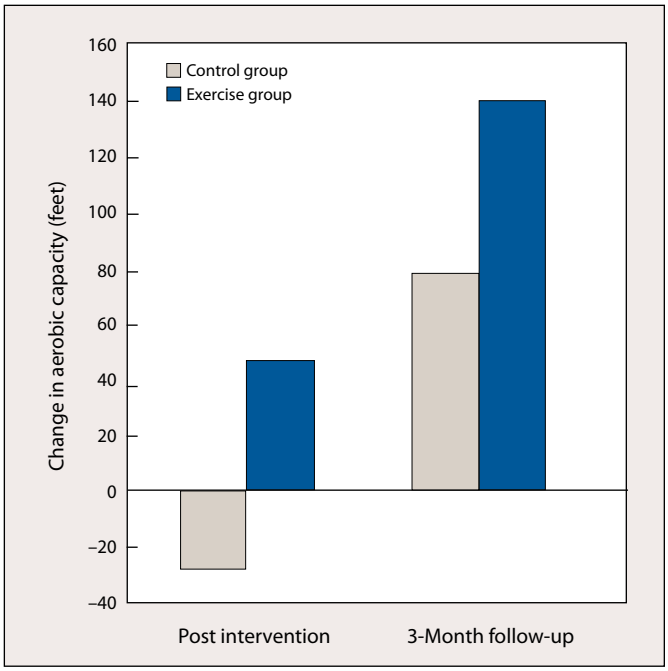

Figure 3 Change in Aerobic Capacity from Baseline to Post Intervention and Follow-Up

a week at the 3-month follow-up in the control group, indicating that "exercise contamination" in the control group was minimal. The mean change in daily minutes spent in resistance training from baseline to post-intervention was –1.6 minutes (SD = 4.73), and the mean change in daily minutes spent in resistance training from baseline to the 3-month follow-up was –1.0 minutes (SD = 6.06) for the entire control group. ANCOVA comparing the means between the two groups with baseline MRE and RED as the covariates showed significantly more MRE and RED post intervention and at the 3-month follow-up in the exercise group than in the no-exercise control group (all P values < 0.05).

CANCER-RELATED FATIGUE

The outcome variables are summarized in Table 2. Participants in the exercise condition demonstrated improvements in CRF, as assessed by the BFI, from baseline to post intervention (Cohen's d = –0.15) and continued to improve from baseline to the 3-month follow-up (Cohen's d = –0.58; Figures 1 and 2). In contrast, the control group exhibited a smaller improvement in CRF from baseline to post intervention (Cohen's d = –0.08), but CRF worsened from baseline to the 3-month follow-up (Cohen's d = 0.04). ANCOVA with baseline CRF as the covariate showed a statistical trend toward significantly lower CRF in the exercise group than in the control group post intervention (P = 0.07) and at the 3-month follow-up ($P < 0.05$).

Participants in the exercise condition also showed improvements in CRF, as assessed by the FACIT–F subscale, from baseline to post intervention (Cohen's d = 0.29) and from baseline to the 3-month follow-up (Cohen's d = 0.45). (Higher scores on the FACIT–F and positive effect sizes indicate lower levels of CRF.) In contrast, the control group reported a worsening of CRF from baseline to post intervention (Cohen's d = –0.09), but CRF improved from baseline to the 3-month follow-up (Cohen's d = 0.29). ANCOVA with baseline CRF as the covariate showed significantly lower CRF in the exercise group than in the control group post intervention and at the 3-month follow-up (all $P < 0.05$).

AEROBIC CAPACITY

The means, change scores, and standard deviations for

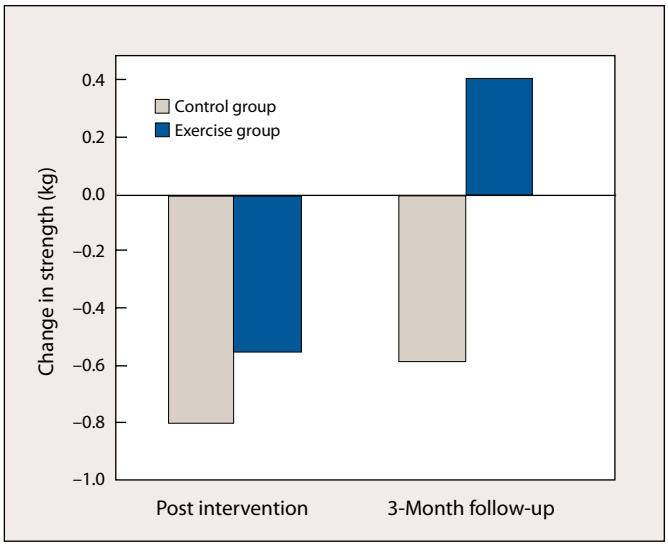

Figure 4 Change in Strength from Baseline to Post Intervention and Follow-Up

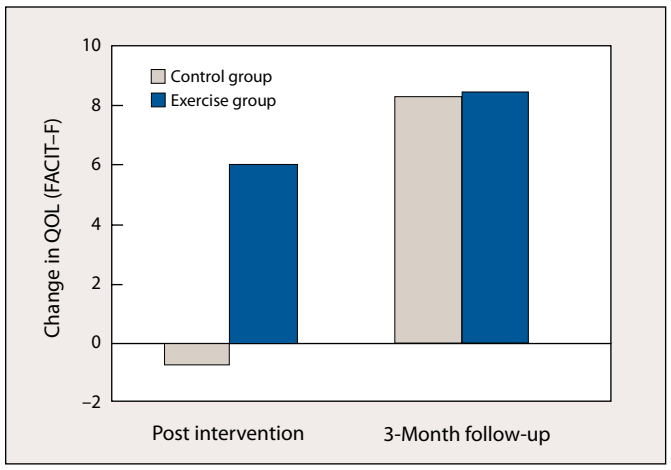

Figure 5 Change in Quality of Life (QOL) as Assessed by FACIT–F from Baseline to Post Intervention and Follow-Up

FACIT–F = Functional Assessment of Chronic Illness Therapy–Fatigue

aerobic capacity are presented in Table 2. Participants in the exercise group demonstrated small improvements in aerobic capacity from baseline to post intervention (Cohen's d = 0.16) and continued with modest improvements from baseline to the 3-month follow-up (Cohen's d = 0.37; Figure 3). In contrast, the control group exhibited a worsening of aerobic capacity from baseline to post intervention (Cohen's d = –0.13) but showed small improvements from baseline to the 3-month follow-up (Cohen's d = 0.28). ANCOVA, with baseline aerobic capacity as the covariate, revealed no statistically significant differences in aerobic capacity post intervention or at the 3-month follow-up. Although these results were not statistically significant, participants in the exercise group exhibited better aerobic capacity than participants in the control group post intervention and at the 3-month follow-up.

STRENGTH

The means, change scores, and standard deviations for strength are presented in Table 2. Participants in the exercise group demonstrated small declines in strength from baseline to post intervention (Cohen's d = –0.07) but conversely exhibited small improvements from baseline to the 3-month follow-up (Cohen's d = 0.11; Figure 4). In contrast, the control group exhibited declines in strength from baseline to post intervention (Cohen's d = –0.10), with further declines from baseline to the 3-month follow-up (Cohen's d = –0.06). ANCOVA, with baseline strength as the covariate, revealed no statistically significant differences in strength post intervention or at the 3-month follow-up. However, participants in the exercise group exhibited greater strength than participants in the control group post intervention and at the 3-month follow-up.

MUSCLE MASS

Participants in the exercise group demonstrated a maintenance of muscle mass from baseline to post intervention (Cohen's d = 0.00), with improvements from baseline to the 3-month follow-up (Cohen's d = 0.10). In contrast, the control group exhibited reductions in muscle mass from baseline to post intervention (Cohen's d = –0.04) and from baseline to the 3-month follow-up (Cohen's d = –0.02). ANCOVA, with baseline muscle mass as the covariate, revealed no statistically significant differences in muscle mass post intervention or at the 3-month follow-up. Again, as with aerobic capacity and strength, participants in the exercise group exhibited greater muscle mass than participants in the control group post intervention and at the 3-month follow-up.

QOL

Participants in the exercise group demonstrated small improvements in QOL from baseline to post intervention (Cohen's d = 0.26) and continued modest improvements from baseline to the 3-month follow-up (Cohen's d = 0.41; Figure 5). In contrast, the control group demonstrated small declines in QOL from baseline to post intervention (Cohen's d = –0.02) but then showed small improvements from baseline to the 3-month follow-up (Cohen's d = 0.28). ANCOVA, with baseline QOL as the covariate, showed significantly higher QOL in the exercise group than in the control group post intervention and at the 3-month follow-up (all $P < 0.05$).

Summary

Participants in the exercise intervention showed good adherence to and compliance with the intervention, with significantly more DSW, MRE, and RED post intervention and at the 3-month follow-up compared with the control participants. Participants in the exercise group exhibited significantly higher QOL and significantly lower CRF post intervention and at 3-month follow-up than the controls. Participants in the exercise group also demonstrated significantly higher QOL post intervention and 3 months later. Although not statistically significant, there were improvements in aerobic capacity

among participants in the exercise group post intervention and 3 months later. There was a slight decline in strength, with maintenance of muscle mass post intervention, whereas improvements in strength but not muscle mass were found at the 3-month follow-up among the exercise group. In contrast, the control group declined in DSW, MRE, RED, CRF, aerobic capacity, strength, muscle mass, and QOL post intervention. The control group also declined in DSW, MRE, RED, CRF, strength, and muscle mass, with improvements in aerobic capacity and QOL at 3 months.

Discussion

The results of this clinical trial provide preliminary support suggesting that the combination of home-based aerobic (walking) and resistance (therapeutic bands) exercise during radiation therapy is safe, easy to implement in a busy radiation oncology clinic, well adhered to by cancer patients undergoing radiation therapy, and has a positive influence on CRF and QOL in women diagnosed with breast cancer and in men diagnosed with prostate cancer. These findings support previous research by confirming the safety of and showing benefits from aerobic exercise during radiation treatments.[14–17] These data expand previous research by confirming the safety of and showing benefits from therapeutic resistance exercise during radiation treatments.

Our generally positive findings of benefit from a home-based aerobic and resistance exercise program during radiation therapy must be interpreted cautiously because of several study limitations. The small size of this pilot study is a limitation that restricts statistical power and may explain why some of the observed changes did not achieve statistical significance. The heterogeneity of the participants (women with breast cancer and men with prostate cancer) in this small sample may also explain some of the lack of statistical significance. These data are not generalizable to the larger cancer patient population (eg, children, individuals with disease at other sites, or individuals undergoing different doses of radiation therapy or different types of cancer treatments).

Additionally, participants may have been particularly receptive to exercise and/or these particular modes of exercise, creating a self-selection bias, and the results may not be applicable to those less amenable to exercise in general or these specific modes of exercise. Furthermore, BIA may not be the ideal method of measuring body composition, since hydration status can affect findings; however, this method of body composition has been used successfully in previous clinical trials with cancer patients and survivors.[6,25] Handgrip dynamometer may not be the best method for estimating strength compared with repetition maximum testing, but it has been used in previous studies and is easily implemented in a busy radiation oncology clinic.[6,25] Finally, because this study was neither fully blinded nor placebo-controlled, it is possible that the benefits reported from the intervention were due to experimenter bias, participant expectancy effects, or nonspecific treatment effects (eg, differences in patient attention or social interaction).

Despite these limitations, the results of this pilot clinical trial are positive and provide preliminary evidence that home-based aerobic and resistance exercise during the course of receiving radiation therapy is safe and may be beneficial for RED, CRF, and QOL in women diagnosed with breast cancer and in men diagnosed with prostate cancer. The importance of combining aerobic and resistance exercise for health-related benefits is well documented in healthy individuals and other chronically ill populations, and this combination of exercise modes possesses great potential as a therapeutic intervention for optimizing recovery during radiation therapy for breast and prostate cancers.

Future phase III, randomized, controlled clinical trials are needed to confirm and expand these preliminary findings regarding RED, CRF, aerobic capacity, strength, muscle mass, and QOL as well as other biopsychosocial consequences that result from radiation treatments for breast and prostate cancers. Future research also needs to compare the separate and combined effects of aerobic and resistance exercise and to determine the optimal dose of aerobic and resistance exercise needed to elicit benefits among breast and prostate cancer patients during radiation therapy to facilitate effective recovery. Finally, additional research should determine whether breast and prostate cancer patients enjoy and are more likely to adhere to home-based exercise programs than to community-based exercise programs.

Conflicts of interest: None to disclose.

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