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An Aerobic Weight-Loaded Pilot Exercise Intervention for Breast Cancer Survivors: Bone Remodeling and Body Composition Outcomes

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Abstract

Objective—Weight gain and bone loss are commonly reported in breast cancer survivors. The purpose of this pilot study is to assess feasibility and explore the effect of an aerobic weight-loaded exercise intervention on bone remodeling, weight, and body composition.

Design—A one-group pre-posttest design was used to test a 16–24-week supervised walking exercise intervention among women within 2 years of menopause. Through Weeks 1–4, time and weight were progressively increased. By Week 5 and through the end of the intervention, a waist belt was loaded with 5 lb and participants spent 45 min on the treadmill 3 times/week. Bone remodeling was measured by serum biomarkers (N-terminal propeptides of type I collagen [NTX] and serum osteocalcin). Dual-energy absorptiometry scans assessed body composition. Data were collected at baseline and 16 and 24 weeks.

Results—The majority of the 26 participants were married, well educated, and employed, with a mean age of 51.3 years ($SD = 6.2$). The high adherence ($M = 88.2\%$, $SD = 6.8$) demonstrated feasiblity. There were no significant changes in serum osteocalcin ($p = .67$), serum NTX ($p = .31$), lean muscle mass ($p = .08$), or percent fat mass for the group as a whole ($p = .14$), but fat mass increased for women on adjuvant endocrine therapy ($p = .04$). The women maintained their weight.

Conclusions—This novel exercise intervention for breast cancer survivors was feasible, and women otherwise at high risk for weight gain and bone loss maintained their weight and bone mass.

Keywords

breast cancer; exercise; bone loss; body composition; cancer survivors

Women with a history of breast cancer represent 40% of the 5.6 million female cancer survivors in the United States. In 2007, there was an estimated 178,480 new cases of invasive breast cancer and 62,030 cases of in situ breast cancer (Jemal et al., 2007). With advances in detection and treatment, the number of women who will enjoy long-term survival after breast cancer will substantially increase. Unfortunately, persistent and late effects of cancer treatment influence the quality of life of the survivors and may contribute to morbidity and mortality (Institute of Medicine [IOM], 2006). Cancer survivors are at risk

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not only for recurrence, but also for cardiovascular disease, diabetes, functional decline, and osteoporosis (Demark-Wahnefried, Pinto, & Gritz, 2006).

Weight gain during and after breast cancer treatment is common (Irwin et al., 2005; McInnes and Knobf, 2001) and has been associated with an increased risk of recurrence and lower rate of survival (Kroenke, Chen, Rosner, & Holmes, 2005). Body composition changes in women who have received chemotherapy for breast cancer include an increase in body fat and a decrease in lean muscle mass (Demark-Wahnefried et al., 2001; Ingram & Brown, 2004; Irwin et al., 2005). Treatment with Tamoxifen has been associated with increases in body fat (Ali, Al-Ghorabie, Evans, El-Sharkawt, & Hancock, 1998). Gaining weight in midlife and becoming over-weight or obese are associated with a high metabolic risk profile for cardiovascular disease, especially in younger women with induced menopause (Astma, Bartelink, Grobbee, & vander Schouw, 2006), as well as with an increased risk for diabetes (Eyre et al., 2004). Breast cancer survivors, in particular, have an increased risk for comorbid illness due to weight gain during and after treatment, changes in body composition, decreased physical functioning, and bone loss.

Adjuvant therapy for breast cancer is associated with premature-induced menopause in up to 40% of women younger than 40 years of age and 50–100% of women more than 40 years of age (Goodwin, Ennis, Pritchard, Trudeau, & Hood, 1999). Young midlife women with cancer-treatment-induced premature menopause are at high risk for bone loss, leading to osteopenia, osteoporosis, and fractures (Chen et al., 2005; Shapiro, Manola, & Leboff, 2001). Post-menopausal breast cancer survivors on aromatase inhibitors and premenopausal women who receive luteinizing hormone-releasing hormone (LHRH) or gonadotropin-releasing hormone (GnRH) analogues for gonadal quiescence or as adjuvant therapy in clinical trials have lower bone mineral density and a high predicted risk of developing osteopenia and osteoporosis (Eastell et al., 2006). Tamoxifen therapy is associated with preservation of bone mass in postmenopausal women, but the protective effect dissipates over time. In contrast, bone loss is reported in premenopausal women who take Tamoxifen (Vehmanen, Elomaa, Blomqvist, & Saarto, 2006). Low bone mass is the major risk factor for osteoporotic fractures, which are associated with acute and chronic pain, decreased functional ability, height loss, and increased mortality.

There is sound evidence to recommend exercise as a healthy lifestyle behavioral intervention to reduce the risk of persistent symptoms and late effects of cancer treatment (IOM, 2006; McNeely et al., 2006). After cancer treatment, many women view the initiation of healthy lifestyle behaviors as a means to cope with the experience, gain some control over their lives, and reduce their risks for cancer recurrence and other health conditions (Knobf, 2002; Lauver, Connolly-Nelson, & Vang, 2007). Exercise interventions with cancer patients have resulted in improved cardiovascular fitness, quality of life, psychological adjustment, physical functioning, physical strength, aerobic capacity, and muscle strength and a decrease in fatigue, depression, anxiety, and sleep disturbance (Knols, Aaronson, Uebelhart, Franson & Aufdemkampe, 2005; Schmitz, Holtzman et al., 2005). Very few studies, however, have addressed body composition outcomes (Ingram, Courneya, & Kingston, 2006; Schmitz, Ahmed, Hannan, & Yee, 2005). Furthermore, we could find only one published study that targeted bone mass as a primary outcome utilizing a home-based exercise intervention in breast cancer survivors with osteopenia (Waltman et al., 2003).

Aerobic exercise improves endurance and overall well-being in midlife women and has been shown to stabilize or prevent weight gain in healthy women (Donnelly, Jacobsen, Heelan, Seip, & Smith, 2000) and cancer survivors (Schmitz, Ahmed et al., 2005). Exercise is also recognized as an important intervention to help preserve bone mass, particularly for the early postmenopausal woman without osteopenia or osteoporosis (North American

Menopause Society, 2006). However, while aerobic exercise activities improve physical and psychological well-being for midlife women, exercise as a strategy to ameliorate bone loss in postmenopausal women requires an increased osteogenic stimulus (Bemben & Fetters, 2000; Lanyon, 1996). The results of exercise trials with weight loading in healthy postmenopausal women support the hypothesis that the skeleton responds to dynamic forces, leading to preservation or increases in bone mass in women (Bemben & Fetters, 2000; Kelly, Kelly, & Tran, 2001). These types of interventions also help build and preserve muscle mass and strength and control weight. Thus, we designed an aerobic weight-loaded exercise intervention trial to evaluate the feasibility and effects of an aerobic weight-loaded exercise intervention on body composition and bone mass in midlife breast cancer survivors with early menopause (natural or induced).

Methods

We conducted a study with a one-group pre-posttest design to determine the feasibility and explore the effects of a 16–24-week aerobic weight-loaded exercise intervention on bone mass, weight, and body composition. Eligible participants were women diagnosed with Stage I or Stage II breast cancer who had completed adjuvant chemotherapy and/or radiation therapy within the past 3 years and were premenopausal or perimenopausal at diagnosis and either perimenopausal (irregular menses with amenorrhea of 2 months or more between menses in the past year; Taffe & Dennerstein, 2002) or postmenopausal (no menses for 12 months or more) at study entry. In addition, women needed to be physically able to participate in the exercise program, as determined by their physician, speak and understand English, be able to complete questionnaires, and give informed consent to participate in the study. Exclusion criteria included concurrent major health problems, specifically aortic stenosis, episodes of syncope, history of thrombolic events, tachyarrhythmias, anemia (hematocrit < 25), hypertension (>140/90 resting), uncontrolled asthma (i.e., frequent asthma attacks), or a history of shortness of breath with activity; any resistive or vigorous regular exercise program three or more times per week in the past year; or current treatment with estrogen-replacement therapy. Inclusion and exclusion criteria were verified by the participants’ physicians. Women were recruited through oncology practices, flyers, and local newspapers. The study was approved by the Human Subjects Research Review Committee, and all participants signed written informed consent.

At the time of consent, women were asked what days and times were best for them for performing the exercise intervention and what fitness center location was most convenient. Using the concept of social support to promote adherence, 2-hr blocks of time were provided 4 days a week. A weekend morning session was later added for make-ups for weather cancellations and missed days.

Measurement and Data Collection

Primary outcome measures for the study included serum biomarkers for bone re-modeling, weight, and body composition, and data were collected at baseline and at 16 and 24 weeks. Serum biomarkers included N-terminal propeptides of type I collagen as a marker for bone resorption and osteocalcin as a marker for bone formation. The Osteomark NTX serum kit is an enzyme-linked immunosorbant assay that provides a quantitative measure of cross-linked *N*-telopeptides of type I collagen (NTX) in serum as an indicator of bone resorption (Osteomark, 1999). For this study, the intra-assay CV was 4.6% and the interassay CV was 6.9%. Serum osteocalcin samples were analyzed via human osteocalcin radioimmunoassay (Gundberg, Looker, Niemen, & Calvo, 2002) and in this study, the intra-assay variation was 7.2% and interassay variation 3.8%. Sensitivity of serum osteocalcin has been previously reported as 0.5 ng/ml (Kemmler et al., 2004).

Standard venipuncture was used to obtain two redtop tubes of serum, which were spun down immediately. The supernatant was frozen at −70°C or below for storage and kept in the Clinical Research Center Core Laboratory storage freezer. Weight was recorded in pounds, with participants wearing light clothing and no shoes on a balance beam scale at the General Research Unit. Whole-body dual-energy X-ray absorptiometry (DEXA) scans (Hologic QDR 4500), which use a three-component model to assess lean body mass, fat and bone, were used in this study to determine lean body mass and body fat. A spine phantom was scanned daily to detect any drift in machine precision.

Heart rate was recorded by the on-site interventionist on a standardized intervention log before the intervention, every 5 min during the exercise session and after cool down. Women on beta blockers used the Borg scale for perceived level of exertion (Borg, 1982). Adherence was calculated as the percentage of scheduled sessions completed.

Procedures

The intervention was a supervised progressive walking exercise on a treadmill performed three times per week with a weight belt and backpack. Participants were assigned to one of three fitness centers in the local community. The sites for weight loading were the thoracic vertebrae (backpack) and the hip (waist belt). The aerobic walking occurred on treadmills, with the speed determined by a trained research assistant to be congruent with the intervention protocol. Each session throughout the intervention included a 5-min warm-up period and a 5-min cool down. Target heart rates were calculated for each woman individually, adjusting for age. All women wore a heart rate monitor watch, and those on beta-blockers used the Borg scale for perceived level of exertion (Borg, 1982).

Weighted vests have been used instead of free weights or machines to provide optimal loading of the hips and allow for distribution around the torso (Going et al., 2003; Snow, Shaw, Winters, &Witzke, 2000). For this study, weight belts with slots for 0.5 and 1 lb weights were used. Weights were initially placed in slots corresponding to the sides of the hips and then equally distributed around the belt as weight progressed from 1 to 5 lb. In Week 1, women were coached on the proper use of the treadmill, how to monitor their heart rate, use of the weight belts and backpacks with 1 lb weights, and the walking intervention (Figure 1). They also completed three bouts of treadmill walking of 10–20 min duration with the 1-lb weights. In Week 2, there were three 20-min exercise periods with 1–3-lb belt and back-pack weights to achieve maximal heart rate of 50–60%. In Weeks 3–4, exercise periods consisted of three 30-min bouts with 3–5 lb belt and backpack weights to achieve maximal heart rate of 60–65%. In Weeks 5–16, there were three 45-min walking bouts using 5-lb belt and backpack weights to achieve maximal heart rate of 75%.

The backpack was eliminated 12 weeks after the study was initiated, as 1 of the 4 participants with pre-existing arm lymphedema had an increase in arm circumference. Although it was unclear whether this was related to the intervention or to other lifestyle activities, it prompted an extensive consultation with experts in the field. Taking a conservative approach, a decision was made to eliminate the backpack based on concerns about the fit of the shoulder straps of the backpack, the hypothetical risk of exacerbating pre-existing lymphedema or contributing to the risk of developing lymphedema and the measurement challenges in identifying the presence of lymphedema (Armer, 2005).

Data were double entered into an Access database and imported into SAS for cleaning and analysis. Univariate statistics, including stratification by time, were performed to describe the sample and for continuous variables to evaluate the distribution. When necessary, variables were log-transformed to meet model assumptions. Repeated measures analysis of variance was carried out through mixed modeling using compound symmetry as the covariance matrix. Multiple comparisons were addressed through the least squared means function using Bonferroni and Tukey tests.

Results

Sample

Of the 33 women who consented to participate in the study, 2 never started, 3 dropped out due to injuries unrelated to the intervention (previous shoulder injury needing physical therapy, recurrent bone spur, knee injury falling on the ice), 1 dropped out due to a breast cancer recurrence, and 1, who was self employed, dropped out because she was too busy. The final sample consisted of 26 participants, the majority of whom were married, well educated, and employed, with a mean age of 51.3 years ($SD = 6.2$; Table 1). Body mass index (BMI) was calculated at baseline: 52% of women were overweight (BMI 25–29.9 kg/m^2) and 8% were obese (BMI > 30 kg/m^2). Of the 26 participants, all but the last 2 enrolled participants (due to funding limitations for continued supervision) were offered an extension of the intervention, and 19/24 (79.2%) elected to extend to 24 weeks. Sixty-five percent of participants had completed adjuvant chemotherapy, with a mean time since completion of therapy of 9.15 months. The majority of participants were on adjuvant endocrine therapy with either Tamoxifen and/or an aromatase inhibitor.

Adherence and Bone Mass

The high adherence rate ($M = 88.2\%$, $SD = 6.8$, range = 75–98%) demonstrates the feasibility of this intervention. Women reported feeling empowered and positive about doing something for themselves to stay healthy. Bone remodeling was stable, as demonstrated by the absence of significant changes in serum osteocalcin levels ($F = 0.40$, $p = .67$) or serum NTX levels ($F = 1.19$, $p = .31$; Table 2). The bone mineral density (BMD) outcome variable was exploratory, as bone density is not a sensitive marker when repeated at a 6-month interval. However, when combined with the absence of change in serum biomarkers for bone remodeling, the absence of a significant change in BMD suggests that a weight-loaded aerobic exercise intervention has the potential to maintain bone mass in women at risk for bone loss. These results are particularly notable as many women in this sample were at high risk for bone loss due to recent menopause (< 2 years), 27% were on aromatase inhibitors and 1 woman was on GnRH analog for ovarian suppression.

Weight and Body Composition

The women had no significant change in weight ($F = 0.54$, $p = .59$) over the 4–6-month intervention (Table 3). One woman, who went on a diabetic diet prescribed by her physician, lost 33 lb (197.9 lb at baseline and 164 lb at 24 weeks) and was excluded from the body composition analysis. Generally, the women maintained their body composition, as demonstrated by the absence of significant changes in lean muscle mass over time ($p = .08$) and percent fat mass for the group as a whole over time ($p = .14$). Despite the absence of change in fat mass in the group as a whole, there was an interaction effect for endocrine treatment over time ($p = .04$), and fat mass increased significantly more for women on Tamoxifen ($p = .006$) and women on an aromatase inhibitor ($p = .05$) compared to women who were not on adjuvant endocrine therapy. The mean percent fat mass for women on Tamoxifen was 38.5 at baseline and 40.2 at 24 weeks. Similarly, women on an aromatase inhibitor had a baseline percent fat mass of 36.8, which increased to 39.1 at 24 weeks. In contrast, the mean percent fat mass for women on no endocrine therapy remained relatively stable (baseline = 37.8; 24 weeks = 38.1).

Discussion

This novel exercise intervention for breast cancer survivors is feasible, and the participants, at high risk for weight gain and bone loss, had stable weight and bone mass. Our adherence rate compares favorably with other reported studies with breast cancer survivors (Schmitz, Ahmed et al., 2005). Cancer survivors appear motivated to engage in healthy lifestyle behaviors, and even previously sedentary individuals are willing to engage in physical-activity interventions following cancer treatment (Rabin, Pinto, Trunzo, Frierson, & Bucknam, 2006). Structured group exercise interventions for breast cancer survivors provide emotional and social support and enhance women's confidence in their ability to exercise to their capacity (Campbell, Mutrie, White, McGuire, & Kearney, 2004).

Weight gain is common and well documented in midlife breast cancer survivors (Irwin et al., 2005; McInnes & Knobf, 2001). Decline in physical activity during cancer treatment likely contribute to the weight gain observed in breast cancer survivors (Demark-Wahnefried et al., 1997), and increased physical activity is known to attenuate weight gain in healthy midlife women (Sternfeld, Bhat, Wang, Sharp, & Quesenberry, 2005). In this study, weight was maintained, which was a positive outcome as women with breast cancer are known to gain weight during and after cancer treatment. Exercise interventions of a similar dose intensity (30–60 min 3 times per week) have also resulted in weight maintenance (McNeely et al., 2006; Schmitz, Ahmed et al., 2005). Many breast cancer survivors are psychologically distressed by weight gain (Knobf, 2001), which can further contribute to body-image concerns. Thus, maintaining weight through increased physical activity helps to reduce physical and psychological effects of cancer treatment and to improve quality of life (Burnham & Wilcox, 2002).

With or without weight gain, women with breast cancer have been reported to experience changes in body composition, specifically increases in percent body fat and decreases in lean muscle mass (Freedman et al., 2004; Ingram et al., 2006). Body composition in this study was unchanged during the intervention except for a subset of women on adjuvant endocrine therapy. The findings of stable body composition in this study are similar to the findings from a 12-week physical activity intervention (Matthews et al., 2007) and a 16-week strength training/cardiovascular fitness intervention for women with breast cancer (Ligibel et al., 2006). However, when researchers compared outcomes of an exercise intervention group to a control group of breast cancer survivors, improvement in body composition was reported (Ingram et al., 2006; Schmitz, Ahmed, et al., 2005).

Weight gain in women on adjuvant endocrine therapy with Tamoxifen has been reported (Fallowfield et al., 2001; Fisher et al., 1996; McInnes & Knobf, 2001), but there was not a statistically significant difference between the Tamoxifen and control participants for weight gain (Fallowfield et al., 2001; Fisher et al., 1996). However, similar to our findings related to body composition changes, Ali and colleagues (1998) used dual-energy absorptiometry to assess body composition in women on Tamoxifen and reported increases in fat mass. Our data support women's complaints from clinical practice about increases in central fat associated with weight gain on Tamoxifen.

This is the first known study of a weight-loaded exercise intervention in breast cancer survivors who are at high risk for bone loss due to early menopause. Furthermore, 27% of the participants were on aromatase inhibitors, which are associated with increased risk of bone loss (Chen et al., 2005). Using serum biomarkers as indicators of skeletal health, bone remodeling was found to be stable over the course of the 4–6-month intervention. Although this is a relatively short duration to assess bone turnover, serum osteocalcin as a marker of bone formation has been reported in studies of longer durations (12–26months) (Judge et al., 2005; Kemmler et al., 2004). These studies suggest that the outcome of moderate exercise may reflect decreases in bone resorption versus increases in bone formation in the context of increased or stable bone mass as measured by bone mineral density. In our study, there was a slight but nonsignificant decrease in bone resorption. Moderate-intensity resistive exercise interventions with adequate durations (i.e., 12 months) in healthy early postmenopausal women have demonstrated the ability to preserve or increase bone mass (Kemmler et al., 2004;Wallace & Cumming, 2000), but high-intensity resistance exercise may be needed to effect change in markers of bone formation (Bemben & Fetters, 2000; Judge et al., 2005). The findings from this pilot study on bone outcomes warrant examination in a larger randomized trial of longer duration.

Symptom management, health promotion, and risk reduction are integral to cancer nursing practice, especially for patients who are transitioning to survivorship. The IOM report (2006) highlights the critical importance of intervention for persistent treatment effects, minimizing the risk of late effects, and enhancing quality of life for survivors. Breast cancer diagnosis and treatment are associated with psychological and physical symptom distress, which gradually improve over time. However, persistent and late effects of cancer therapy, such as weight gain, changes in body composition, and bone loss place women at higher risk for the development of comorbid conditions and may influence survival outcomes. Over the past decade, a significant body of evidence has established the physical and psychological benefits of exercise in breast cancer survivors, and specifically interventions to reduce the risks associated with weight gain and negative changes in body composition. The data from this pilot study further identify the potential benefit of a weight-loaded exercise intervention on reducing the risks associated with cancer treatment. Breast cancer survivors are interested in health promotion, not only related to reducing their risk of cancer recurrence but also to reduce risks of other health conditions, such as osteoporosis (Knobf, 2002; Lauver, et al., 2007).

Limitations

This pilot study was designed to assess feasibility and generate preliminary data on study outcomes. Small sample size is an inherent limitation of pilot studies. The other major limitation of this study was the one-group pre-posttest nonrandomized design. The limitation of lack of a control group is particularly relevant in exercise studies that assess bone and body composition. In larger randomized trials, it is common that the intervention group remains stable or slightly improves whereas the control group loses bone mass and has negative changes in body composition (e.g., increased fat mass, loss of lean muscle mass). The lack of a control group in this study prevents us from drawing any definitive conclusions about the findings of stability of bone and body composition in our sample. The participants were White, well educated, and middle class by reported income, which may influence the adherence rate observed. Also, data on calcium and vitamin D intake, which are important components of bone health in post-menopausal women, were not collected. Despite the need for caution related to the study limitations, the data are encouraging and support further investigation in a larger randomized control trial.

Conclusion

In summary, we established that the design of the aerobic weight-loaded exercise intervention was acceptable, implementation at fitness centers in the local community was feasible, and women had high adherence. Additionally, women did not gain weight or lose bone mass and they maintained body composition throughout the 4–6-month intervention period. Furthermore, women felt supported and empowered and reported improved physical and emotional functioning (Knobf et al., 2006).

The end of cancer treatment has been described as a "teachable moment" and one that should be used by providers to promote healthy lifestyle behaviors to minimize late effects of cancer treatment and possibly influence survival (Demark-Wahnefried, Aziz, Rowland, & Pinto, 2005, p. 5827). Yet there is much we still do not know about the role and outcomes of exercise in cancer (Demark-Wahnefried et al., 2006). To minimize the treatment effects in breast cancer survivors, specifically to address weight gain, negative changes in body composition, decline in physical activity, menopause and bone loss, future exercise intervention research needs to consider duration (>12 months), types of resistance, inclusion of ground and reaction forces (for osteogenic stimulus), and behavioral components to foster adherence and sustainability (Kemmler et al., 2004). The initial benefits reported for exercise on physical, psychological, social, and quality of life outcomes in cancer survivors need to be linked to the type, duration, and timing of interventions, and longitudinal research is needed to address the potential impact on survival outcomes for a broad spectrum of cancer survivors (Demark-Wahnefried et al., 2006).

In addition, supervised structured interventions are costly in money, time, and personnel. Exploration of self-directed, supported, or supervised versus some "best mixture" of approaches warrants investigation. Similarly, the dose of the intervention needs to be determined and linked specifically to outcomes of interest. For breast cancer survivors, determination of the type and dose of exercise needs to be made in the context of the target outcomes that are associated with risk for the development of chronic illness (e.g., weight gain, negative changes in body composition, bone loss). General nutrition and physical activity guidelines are recommended for cancer survivors (Doyle et al., 2006). Additional research is indicated, however, to identify the optimal type and duration of diet and exercise to promote better health outcomes in cancer survivors, especially those at higher risk for late effects of treatment or other chronic illness.

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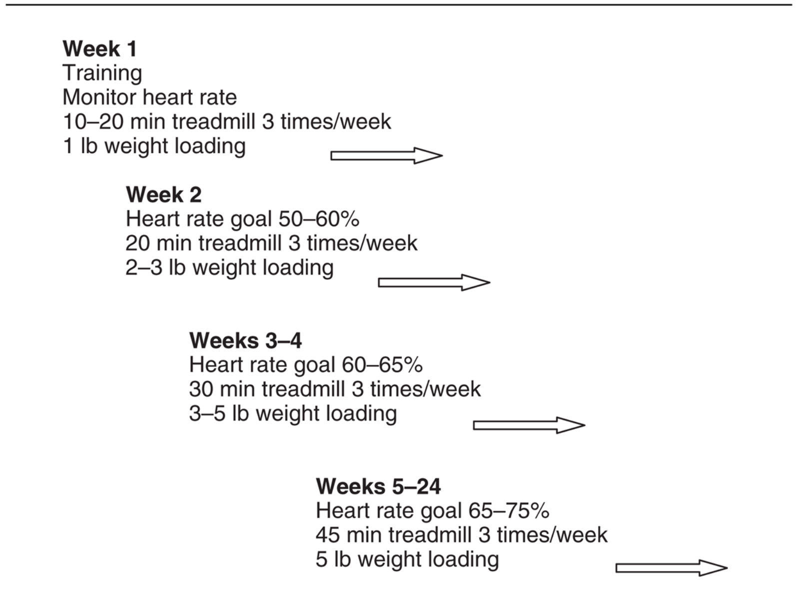

Figure 1.
Progressive training and intervention schedule.

Table 1

Demographic and Treatment Characteristics of the Sample (*N* = 26)

Participant Characteristics	***N***	**%**
Ethnicity		
Caucasian	26	100
Marital status		
Married	20	77.0
Divorced/separated	3	11.5
Single	3	11.5
Educational level		
High school graduate	2	8.0
Some college	6	23.0
College graduate	10	38.0
Graduate school	8	31.0
Employment status		
Full time	15	58.0
Part time	8	30.0
Retired/not employed	3	12.0
Household income		
< 40,000	2	8.0
40,000–79,999	5	19.5
> 80,000	15	57.5
Missing data	4	15.0
Primary/local treatment		
Mastectomy	3	11.5
Mastectomy with reconstruction	8	30.5
Breast conservation/radiation	15	58.0
Adjuvant chemotherapy		
AC	5	19
CAF/FEC	7	27
AC-T	5	19
None	9	35
Adjuvant endocrine therapy		
Tamoxifen	9	35
Aromatase inhibitor	7	27
None	10	38

NOTE: AC = doxorubicin, cyclophosphamide; AC-T = doxorubi-cin, cyclophosphamide, paclitaxel; CAF = cyclophosphamide, doxorubicin, flourouracil; FEC = cyclophosphamide, epirubicin, fluorouracil.

Table 2

Bone Mass Outcomes: Changes Over Time

	Baseline (*N* = 26) ***M* (*SD*)**	**16 Weeks (*N* = 25)** ***M* (*SD*)**	**24 Weeks (*N* = 19)** ***M* (*SD*)**	F^a	P^a
Serum biomarkers					
Osteocalcin	9.15 (4.54)	8.85 (3.99)	8.70 (4.28)	0.40	.67
NTX	18.54 (5.9)	18.01 (5.43)	17.56 (4.72)	1.19	.31
Bone mineral density	1.14 (0.08)	1.13 (0.08)	1.12 (0.07)	0.67	.52

[a]Repeated measures analysis using compound symmetry to examine time effect on outcome levels.

Table 3

Weight and Body Composition Changes Over Time

	Baseline (*N* = 25) *M* (*SD*)	**16 Weeks (*N* = 25) *M* (*SD*)**	**24 Weeks (*N* = 19) *M* (*SD*)**	***F*[a]**	***P*[a]**
Body composition					
Lean muscle mass (g)	41157 (4942)	41048 (4316)	40143 (4131)	2.84	.08
Fat mass (%)	37.38 (5.23)	37.90 (5.10)	38.05 (5.69)	1.59	.14
Weight (lb)	155.5 (21.5)	155.9 (19.0)	153.5 (19.7)	0.54	.59

[a]Repeated measures analysis using compound symmetry to examine time effect on outcome levels.