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Exercise and dietary advice intervention for survivors of triple-negative breast cancer: effects on body fat, physical function, quality of life, and adipokine profile

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Abstract

Purpose—Regular exercise and healthy eating are routinely recommended for breast cancer survivors, and past studies show benefits in quality of life and decreased inflammation. However, this has not been testing specifically in triple-negative breast cancer survivors. Increasing physical activity and losing body fat are thought to positively affect inflammatory biomarkers that have been associated with breast cancer. Therefore, the primary purpose of this study was to determine if participation in an exercise and dietary counseling program can improve body fat, physical

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function, and quality of life in survivors of this aggressive breast cancer. Secondly, we sought to determine if participation in the program had beneficial effects on obesity-related markers of the adipokine profile.

Methods—Sixty-six survivors of triple-negative breast cancer with BMI >25 were invited to participate. Twenty-eight enrolled and 23 completed the randomized, controlled trial (13 intervention, 10 control). Moderate-intensity aerobic exercise (150 min per week, for 12 weeks) and diet counseling were compared to usual care, education only. The primary outcome of interest was weight loss (body mass, BMI, % fat), and secondary outcomes included physical function (exercise capacity), quality of life (Function After Cancer Therapy—Breast (FACT-B)), cytokines (C-reactive protein (CRP), TNF- α , IL-6), and adipokine profile (leptin, adiponectin, insulin).

Results—Participants in the program lost more body fat (2.4 % loss vs. 0.4 % gain, $p<0.05$) than the control group. The intervention group also improved quality of life (FACT-B total score +14 pts) and decreased sedentary time but did not improve peak exercise capacity. The intervention had no effect on serum cytokines and adipokines after 12 weeks in the program. However, serum leptin and adiponectin and their ratio were significantly correlated with BMI in the intervention group ($p<0.05$).

Conclusions—Exercise and dietary counseling led to loss of body fat and improved quality of life in survivors of triple-negative breast cancer. BMI was associated with favorable changes in leptin and adiponectin which may reflect a change in adiposity with intervention. Exercise and healthy eating may be equally effective in this high-risk population as in other breast cancer survivors and should be encouraged as a part of a cancer survivorship program.

Keywords

Exercise; Diet; Cytokines; Adipokines; Breast cancer; Inflammation

Introduction

Women who have been diagnosed with breast cancer are a growing population for rehabilitation professionals. Currently, there are over 3.1 million women in the USA who are breast cancer survivors [1].

In a diverse population, mortality among breast cancer patients exists and recurrence does occur even years after treatment concludes. Regular exercise and eating a healthy diet have been recommended to improve survival and prevent recurrence of breast cancer [2].

For women whose tumors are estrogen/progesterone (ER/PR) and HER2neu negative (so-called “triple-negative” breast cancer), these lifestyle changes may be especially important, as medical treatment options are limited. Specifically, being sedentary has been linked to recurrence of breast cancer [3] and obesity increases the risk of developing triple-negative breast cancer, in particular [4]. Thus, it is possible that adopting these healthy behaviors could decrease risk of recurrence, which is particularly high in the triple-negative type of breast cancer.

Physical activity and weight loss/maintenance interventions are becoming standard elements of breast cancer survivorship and have shown to have important outcomes. Recent large studies have shown improvements in fitness, quality of life, and adherence to physical activity guidelines in women who participate in trials of exercise interventions [5, 6]. Programs including caloric restriction along with exercise, in an attempt to decrease obesity in breast cancer survivors, have shown modest weight loss [7–9]. Some of these studies have found positive changes in markers of inflammation [7, 8] but not all [9], suggesting that inflammation may link obesity, sedentary lifestyle, and risk of cancer or cancer recurrence.

Obesity presents an additional clinical challenge that influences mortality for breast cancer survivors. Obesity has been shown to be associated with a 30 % high risk of mortality in all types of breast cancer, while being physically active is associated with a 30 % lower risk [2].

In studies of women with hormone-positive breast cancer, decreasing body fat, through low-fat diet and regular physical activity, has been shown to decrease levels of circulating cytokines and adipokines produced by fat [10].

Excess adipose tissue has been linked to higher risk of breast cancer recurrence [11–13], as well as higher all-cause mortality [14].

However, it is currently unknown if women with triple-negative breast cancer would show similar outcomes.

Body mass index, physical activity, and serum markers of inflammation and insulin resistance are linked to obesity and obesity-related cancers [15]. Biologically active adipokines (leptin and adiponectin) and serum markers of low-grade chronic inflammation, such as C-reactive protein, tumor necrosis factor alpha, and interleukin 6, are gaining recognition in breast cancer research as modifiable through increased physical activity and weight loss [16]. There are a number of biological mechanisms explaining the relationship between exercise, adiposity, adipokines, and inflammatory cytokines in breast cancer and preventive oncology [17]. Leptin increases with adiposity and has direct mitogenic actions on breast cancer cells or acts indirectly by promoting ER production and insulin resistance. In contrast, adiponectin has a strong inverse correlation with adiposity and is acknowledged to be anti-inflammatory. To date, few trials have examined the effects of physical activity on leptin and adiponectin [18]. Moreover, questions still remain whether exercise alone, or in combination with dietary intervention, is sufficient to cause favorable changes in these adipokines and inflammatory cytokines.

Many breast cancer survivors struggle with obesity (either preexisting or due to cancer treatment) and its effects on impairing physical function and quality of life [19]. Adopting a physically active lifestyle has been shown to improve functional capacity and quality of life in women with breast cancer [20–22]; however, it is currently unknown if women with triple-negative breast cancer would receive the same benefits. It is also unknown if weight loss due to this physical activity will show similar changes in important cytokines and adipokines that have been linked to recurrence in hormone-positive breast cancer, although this has been theorized [4]. Therefore, we sought to determine the impact of a supervised 12-week exercise and dietary counseling program on body fat, functional capacity, quality of

life, levels of inflammatory cytokines, and adipokine profile compared to a usual-care control group in overweight and obese survivors of triple-negative breast cancer.

Methods

Study design

This project was designed as a randomized controlled clinical trial (NCT01498536). Approval for the study was granted from the West Virginia University Institutional Review Board, and all participants signed informed consent documents prior to any data collection. A specially created program (Get Fit for the Fight®) was developed based on physical activity and healthy eating recommendations [23].

The study was powered for the primary outcome, weight loss, at 80 % to detect a 3 % weight loss ($p < 0.05$) in the intervention group, yielding a target sample size of ten participants per group. The study was designed with a 2:1 randomization scheme to allow for anticipated dropout in the intervention group, based on other similar studies [5, 24], for a planned enrollment of 20 in the intervention group and 10 in the control group. Randomization was determined a priori by the study statistician, and group assignments were placed in opaque envelopes. Group assignment was not revealed until the completion of all baseline testing.

Participants and recruitment

Women were approached during regularly scheduled visits to their oncologists by a member of the research team to describe the study and enroll participants. Inclusion criteria included the following: stage I, II, or III invasive breast cancer; >3 months after completion of active treatment; body mass index (BMI) >25; confirmed ER/PR/HER2neu-negative status (per pathology report); and age less than 80 years. Exclusion criteria included the following: significant cardiac disease, renal failure, significant symptomatic lymphedema, and physical or psychological comorbidities that would prohibit exercise testing or participation, diagnosis of diabetes mellitus, or active smoking status.

Testing procedures and questionnaires

BMI was calculated from height and weight measurements without shoes and in light clothing. Waist and hip circumferences were measured using a spring-loaded tape measure, and body fat percentage was calculated from skinfold measurement at seven body sites according to American College of Sports Medicine standards [25].

Peak exercise capacity (VO_{2peak}) was determined from a progressive treadmill walking exercise test and expired gas analysis. Briefly, participants walked at a comfortable, self-selected constant speed while the treadmill grade increased 1 % per minute to exhaustion.

Physical activity was determined from the Habitual Activity Estimation Scale (HAES), in which participants record minutes of weekday and weekend day physical activity during typical days in the past 2 weeks (corresponding to inactive, somewhat inactive, somewhat active, and very active categories). This tool, originally developed to measure physical activity in children, has also been used for a variety of chronic diseases [26].

While not validated in the breast cancer population, it was chosen as it is a short tool that minimizes recall bias and asks participants to rate “typical” weekdays and weekend days.

Quality of life was assessed with the Function After Cancer Therapy—Breast (FACT-B) questionnaire. This tool consists of four subcategories: physical well-being, social/family well-being, emotional well-being, and functional well-being, as well as a breast cancer-specific scale and total score.

Assays for serum cytokines and adipokines

Venous blood samples (15–20 mL) were drawn following an overnight fast. Blood collected was kept on ice and centrifuged within 30 min to collect the serum and then stored at -80°C until analyzed. Single-plex and multi-plex assays (Meso Scale Discovery, Gaithersburg, MD) were completed. Serum from intervention ($n=18$) and control ($n=10$) subjects was incubated on a multiplex 96-well plate-based assay that contained antibodies to IL-6 and TNF- α or a single-plex assay for C-reactive protein (CRP), leptin, adiponectin, and insulin conjugated with electrochemiluminescent labels (MSD SULFO-TAGTM). Briefly, the plex assays were run using calibration curves with diluent for human serum, with ranges of 40,000 to 1.2 pg/mL, depending on the cytokine, according to the manufacturer. Results were read with a Meso Scale Discovery Sector Imager 6000. Sample cytokine concentrations were determined with SoftMax Pro Version 4.6 software using curve fit models. Intra-assay and inter-assay coefficients of variation were 7 and 15 %, respectively. Non-specific binding was less than 0.6 % for all assays within the kit.

Intervention

Participants randomized to the intervention group then began the Get Fit for the Fight[®] program. The program consisted of supervised, moderate-intensity aerobic exercise three times per week at the exercise facility and two unsupervised sessions per week at home. Briefly, an exercise physiologist determined the initial exercise intensity based on the peak VO_2 achieved on the exercise test. Participants utilized a variety of exercise equipment (stationary bicycle, treadmill, elliptical trainer, etc.) for a total of 30 min of aerobic exercise. The goal of the program was to complete 150 min per week of moderate-intensity aerobic exercise, defined as rating of perceived exertion of 11–14 (corresponding to 60–75 % of peak heart rate achieved on the exercise test). Participants were also encouraged to perform stretching and resistance training during the supervised sessions; however, this was not required. All training was individually supervised by exercise physiologists trained in medical rehabilitation (for the supervised sessions), and participants were instructed in use of perceived exertion ratings for home exercise (typically walking). Participants completed exercise logs for both supervised and unsupervised exercises each week.

Dietary counseling consisted of two individual sessions with the study dietitian, a specialist in nutrition for cancer patients. Participants completed a 3-day diet record during baseline testing before meeting individually with the dietitian. She then reviewed the diet record and helped participants set goals for changes, such as decreasing portion sizes, substituting lower-calorie options, and increasing fruit and vegetable intake. The goal of diet counseling was to decrease dietary fat caloric intake by 200 kcal per week. Approximately 1 month

after initial counseling sessions, participants had a follow-up appointment with the dietitian to review goals and progress. Participants were asked to keep daily food logs, which were reviewed by the research staff weekly.

Participants randomized to the control group received written materials about healthy eating for cancer survivors and suggestions on ways to achieve regular physical activity. They were not instructed to avoid diet change or exercise, as it was felt that this would be unethical and contrary to best advice. However, they did not receive any specific counseling or supervision.

Data analyses

Data were analyzed using a repeated measures ANOVA (group $\times$ time) for within-group and between-group changes. BMI was considered a primary outcome of the study with physical function, quality of life, and adipokine profiles as secondary endpoints. In cases of missing posttrial blood samples in both groups, adipokine concentrations were considered unchanged from baseline values and included in the analysis (intent-to-treat approach). Serum markers were non-normally distributed; therefore, change scores between groups were analyzed using Mann-Whitney *U* test, and the results are presented as median values with interquartile ranges. Delta values were calculated and the mean change in serum markers was tested for the potential confounders of age, BMI, and exercise days using a general linear model. A two-sided Spearman's correlation coefficient was used to determine the relationship between BMI and adipokine levels. All data were analyzed using SAS JMP version 9.1 (Cary, NC). A *p* value of <0.05 was determined a priori to indicate significance.

Results

A total of 66 women were invited and 28 enrolled in this study (Fig. 1). The main reason for declining participation was the requirement to travel to the training facility, as the population of patients seen at our cancer center is rural and often travels up to 3 h to attend clinic. As shown in Table 1, participants were primarily middle-aged and were enrolled, on average, 4–5 years after their initial diagnosis. Most had undergone lump-ectomy, chemotherapy, and radiation therapy. For the women who completed the intervention arm ($n=13$), attendance to the program was at least 80 % of scheduled visits.

Body weight and composition

Table 2 shows the results of body weight and body composition. Participants in both groups were predominately in the obese category, with mean BMI over 30 kg/m². Significant decreases were seen in the intervention group for body weight, BMI, and all skinfold measures except mid-axillary. Body fat was significantly decreased in the intervention group compared to the control group, with a decrease of 2.5 %, compared to a slight increase (0.4 %) in the controls. There were no significant changes in the control group from baseline to end of study.

Physical function and physical activity

Exercise time, but not peak oxygen consumption (VO_{2peak}), improved in the intervention group ($p=0.05$). The intervention group significantly decreased minutes spent in “somewhat inactive” and increased minutes in “somewhat active” categories on the weekdays from baseline to 12 weeks (both $p<0.01$). Taken together, these data indicate shifting away from physical inactivity toward increasing time spent in moderate physical activity during weekdays. There was a tendency ($p=0.08$) for the intervention group to spend more time in the somewhat active weekday category at study conclusion, while the control group tended to decrease time in the somewhat active weekday category (see Table 3).

Quality of life

Quality of life, as measured by the FACT-B, showed significant improvement in the physical well-being ($p<0.05$) and breast cancer-specific ($p<0.01$) subscales, as well as the total score ($p<0.05$) for the intervention group (Table 3). The magnitude of change in total score for the intervention group exceeded the minimally important differences (MIDs) for breast cancer-specific subscore of 2–3 points, with a change of almost 5 points, as well as the FACT-B total score MID of 7–8 points, with a change of 14 points [27].

No significant changes were seen in the control group nor between intervention and control groups.

Serum cytokines and adipokines

The intervention had no effect on serum cytokines and adipokines (Table 4). Given that 54 % ($n=13$) of women in the intervention group lost at least 1 kg or more of body weight and 30 % ($n=10$) in the control group gained more than 1 kg of body weight, we investigated the association of BMI with changes in blood adipokines. Serum leptin and adiponectin were significantly correlated to BMI in the intervention group ($r=0.6469$, $p=0.0314$ and $r=-0.7924$, $p=0.0036$), respectively) (Table 5). The correlation of BMI with serum leptin/adiponectin ratio was also significant in the intervention group ($r=0.1165$, $p=0.0137$).

Discussion

In this randomized, controlled trial, we attempted to determine if a 12-week exercise and dietary counseling program could positively alter body weight, exercise capacity, self-reported physical function, and markers of inflammation in a relatively homogeneous group of women with triple-negative breast cancer. To our knowledge, we are the first to find that these lifestyle changes decreased body fat, improved physical activity and breast cancer-specific quality of life, and improved adipokine profile in this high-risk population.

The women in our intervention group lost, on average, 3 kg of body weight and decreased body fat by 2.5 %, despite moderately good adherence to a program designed to lead to at least a 5-kg weight loss. The weight loss seen in our participants was similar to other studies of similar design, leading to little or no weight loss [8, 21, 28].

However, in a 6-month study that also included a packaged diet [29], more than 10 % of body weight loss was seen. Our study used a pragmatic approach to diet counseling in order

to encourage changes that could be maintained for many years, as opposed to the problems with long-term adherence to a packaged diet. However, based on 3-day diet records at the conclusion of the study, few participants made consistent changes in their diet. This may suggest that increasing physical activity is more acceptable to these women than making dietary changes. Similar barriers to lifestyle changes have been seen in other studies of breast cancer survivors [5, 24].

The intervention group saw important improvements in quality of life. These changes have been seen in other physical activity intervention studies in breast cancer populations and reinforce the need to encourage regular physical activity in breast cancer survivors [8, 29, 30].

Physical activity is well known to improve strength, functional ability, and ease of daily activity in many clinical populations. Our intervention group reported more physical activity on typical weekdays at the end of the study, as compared to the beginning, when more time was spent in sedentary behaviors. This is similar to what was seen by Ligibel et al. [20] in a large study, as well as Hayes et al. [6]. Anecdotally, many participants felt that they were empowered to continue regular exercise after the conclusion of the study as a way to feel better and resume important daily activities. We are the first to report these outcomes in women specifically with triple-negative breast cancer. Thus, physical activity should also be recommended to these women for reasons other than simply weight loss.

Although women in the intervention group experienced a significant reduction in body fat and had a significant loss of body weight, however, we found no significant reduction in central adiposity as measured by waist circumference. Central adiposity is linked to elevated levels of leptin and insulin resistance, including markers of chronic inflammation [12].

However, our intervention of diet counseling and exercise showed no effect on serum cytokines and adipokines. Rogers et al. [31] and Jones et al. [9] also failed to achieve significant changes in inflammatory cytokines, despite participation in exercise programs for breast cancer survivors. You et al. [10] showed that a similar exercise and healthy eating program in postmenopausal women without cancer led to fat loss as well as decreasing levels of inflammatory cytokines. In a larger study, George et al. [32] found that postdiagnosis diet quality in breast cancer survivors was inversely related to CRP, but no association was observed among women engaging in physical activity. Varying levels of adherence to the exercise and/or dietary interventions may explain these conflicting results.

Both leptin and adiponectin are secreted from adipose tissue, and these adipokines may play a role in energy stores and expenditure. Although our study failed to show a significant change in serum levels of adipokines between groups, it did provide evidence that circulating adipokines like leptin and adiponectin are closely linked to BMI changes in breast cancer survivors who modify their lifestyle. Previous research has supported moderate correlations between reductions in body fat and circulating leptin levels following hypocaloric diets in overweight breast cancer survivors [33].

Energy metabolism is also influenced by adiponectin which is thought to increase insulin sensitivity. In this study, we observed an inverse correlation of adiponectin to BMI in the

intervention group, indicating that as participants lost weight, their adiponectin levels improved. In the growing body of survivorship research, data suggest that obesity is associated with lower levels of adiponectin and increased breast cancer mortality [34].

Further studies are required to determine if adiponectin levels can be maintained in survivors who adopt better-quality diets and regular physical activity behaviors.

Study limitations

We were unable to fully recruit the planned number of participants in the time period allotted for this study, leading to a smaller total sample size than that for which the statistics were powered. Triple-negative breast cancer is relatively rare, and there were few women meeting inclusion criteria during the recruitment period. Of those who were approached, a large percentage declined participation due to travel, further limiting our pool. In addition, we had attrition in our intervention group, further decreasing sample size. Despite planning the intervention group to be twice the size of the control group, we did not sufficiently fill our intervention group. These factors certainly impacted our ability to detect changes in some of our outcomes and have been seen in other similar studies in breast cancer survivors [5, 24, 35]. The high levels of non-enrollment and dropout in these studies suggest that barriers to participation need to be minimized, where possible, in order to promote success in future larger scale programs.

As mentioned, we did not strictly control diet of our participants. Our program was designed to allow flexibility in dietary choices and physical activity modalities, making it more adaptable for participants and perhaps creating a program that could be expanded beyond the research setting. This likely impacted the total weight loss seen compared to other studies.

While time spent in physical activity improved, we did not see an increase in maximal exercise capacity. This may reflect primarily a submaximal training effect that did not translate to high workloads. Alternatively, many women disliked the testing apparatus (facemask) and may have ended the test prematurely. As our participants were not regular exercisers before the study, they may have had less inclination to tolerate the discomfort of maximal intensity exercise required by the treadmill test. Other studies have found that breast cancer survivors had very low peak exercise capacity [36] or have not improved their exercise capacity with a physical activity program [37].

Last, the interventions were designed to reduce body weight and functional well-being in breast cancer survivors. However, in order to see more beneficial effects on serum cytokines and adipokines, future interventions should be designed and sufficiently powered to produce greater reductions in central adiposity which is causally related to biomarkers of chronic inflammation and obesity-related morbidity in breast cancer survivors [14].

Conclusions

Participation in an exercise and diet counseling program led to decreased body fat, improved quality of life, and increased habitual physical activity in a group of women with triple-

negative breast cancer compared to a usual-care control group. Reductions in BMI were correlated with improvements in serum leptin and adiponectin, suggesting that there was some benefit of weight loss on adipokine profile. Future work should look at long-term effects of adopting a physically active lifestyle on breast cancer recurrence and other disease risks in these women, as an important part of cancer survivorship.

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Fig. 1.
CONSORT diagram of subject enrollment and completion

Table 1

Demographics

	Intervention	Control
Age (yrs) mean (range)	53.8 (43–65)	53.6 (36–71)
Surgery		
Lumpectomy (no.)	13	6
Mastectomy (no.)	5	4
Radiation (Y/N)	13/5	7/1 ^a
Chemotherapy (Y/N)	17/1	7/1 ^a

^aInformation about radiation and chemotherapy not available for two participants

Table 2

Measurements of body habitus and exercise performance

Measurement mean (SD)	Control			Intervention		
	Baseline (n = 10)	12 weeks (n = 10)	Change	Baseline (n = 18)	12 weeks (n = 13)	Change
Body weight (kg)	85.4 (21.4)	85.0 (21.5)	−0.4	80.2 (9.6)	77.2 (10.3)	−3.0
BMI (kg/m ²)	32.5 (7.1)	32.2 (7.1)	0.2	30.9 (3.3)	29.3 (3.4)	−1.6 [*]
Body fat (%)	35.3 (5.4)	35.7 (5.1)	0.4	33.6 (4.3)	31.2 (5.6)	−2.5 ^{**} ***
Waist (cm)	106.0 (15.6)	104.1 (16.2)	−1.9	98.0 (12.8)	94.7 (14.4)	−3.3
Hip (cm)	118.0 (17.7)	117.7 (16.8)	−0.3	112.5 (6.9)	109.9 (8.3)	−2.6
Waist/hip ratio	0.90 (0.05)	0.88 (0.06)	−0.02	0.87 (0.08)	0.86 (0.09)	−0.01
VO _{2peak} (mL/kg/min)	20.2 (5.7)	20.5 (6.3)	0.3	19.4 (4.2)	18.7 (5.7)	−0.7
Exercise time (min)	13.8 (3.6)	14.4 (4.5)	0.6	12.4 (3.6)	13.3(3.6)	0.9 [*]

BMI body mass index^{*}
p value <0.05, within-group change^{**}
p value <0.01, within-group change^{***}
p<0.05, between-group difference

Table 3

Habitual physical activity and quality-of-life outcomes

Measure mean (SD)	Control		Intervention	
	Baseline control (n = 10)	Ending control (n = 10)	Baseline intervention (n = 18)	Ending intervention (n = 13)
HAES weekday inactive	17.0 (32.2)	32.6 (43.3) *	46.4 (65.7)	26.4 (40.6)
HAES weekday somewhat inactive	273.8 (130.3)	292 (155.4)	423.8 (214.3)	367.2 (225.1) **
HAES weekday somewhat active	501.4 (181.7)	463.1 (190.4)	309.3 (147.2)	462.3 (207.7) **
HAES weekday very active	108.3 (128.6)	102.3 (148.2)	104.1 (274.6)	57.0 (63.6)
HAES weekend inactive	13.0 (28.2)	20.0 (26.8)	58.3 (105.0)	10.1 (14.4)
HAES weekend somewhat inactive	257.7 (167.7)	331.2 (168.7)	372.0 (173.9)	318.3 (183.0)
HAES weekend somewhat active	437.7 (193.7)	387.4 (187.1)	345.3 (149.4)	472.7 (199.1)
HAES weekend very active	171.6 (255.2)	105.4 (147.5)	97 (300.0)	61.2 (101.1)
FACT-B physical well-being	22.5 (5.6)	23.8 (3.1)	22.2 (4.0)	25.4 (2.5) *
FACT-B social well-being	24.2 (3.6)	24.6 (3.3)	23.1 (5.4)	24.1 (4.1)
FACT-B emotional well-being	17.7 (3.8)	18.9 (4.0)	18.0 (3.5)	20.6 (2.7) *
FACT-B functional well-being	22.7 (3.2)	23.9 (3.5)	21.5 (3.8)	23.5 (4.1)
FACT-B breast cancer-specific items	22.8 (7.8)	23.4 (5.0)	21.2 (4.5)	26.0 (5.1) **
FACT-B total	110.7 (18.5)	104.6 (30.6)	105.6 (14.5)	119.6 (14.6) *

There were no differences between groups

HAES Habitual Activity Estimation Scale (min), FACT-B Function After Cancer Therapy—Breast

*
 $p < 0.05$ **
 $p < 0.01$ for changes within group

Table 4

Blood cytokines, adipokines, and growth factors associated with 12-week outcome at baseline and after intervention with diet and exercise

Variable	Time point	Control group (n = 10) ^a	Intervention group (n = 18) ^a	P value
CRP (ng/mL)	Baseline	2.4 (0.7, 2.5)	1.3 (0.4, 11.0) ^b	0.78
	12 weeks	3.0 (0.4, 5.4)	1.3 (0.4, 7.1)	
	Change	0.4 (−1.9, 2.4)	−0.2 (−2.1, 0.8)	
IL-6 (pg/mL)	Baseline	3.1 (1.5, 8.4)	2.0 (0.7, 3.7)	0.26
	12 weeks	2.7 (1.3, 8.8)	1.6 (0.9, 3.3)	
	Change	0.3 (−0.4, 0.7)	0.02 (−0.7, 0.5)	
TNF-α (pg/mL)	Baseline	4.3 (3.8, 4.5)	3.1 (2.7, 4.8)	0.11
	12 weeks	4.3 (3.3, 4.7)	3.7 (2.9, 4.8)	
	Change	0.3 (−0.4, 0.7)	−0.3 (−0.8, 0.02)	
Adiponectin (ng/mL)	Baseline	15.4 (14.4, 23.7)	17.8 (16.8, 19.9)	0.58
	12 weeks	16.1 (14.0, 26.4)	17.5 (13.5, 25.8)	
	Change	−1.3 (−1.9, 0.03)	−0.9 (−4.7, 2.2)	
Insulin (pg/mL)	Baseline	60.4 (35.9, 95.7)	69.0 (47.1, 99.3)	0.29
	12 weeks	63.6 (41.0, 94.9)	61.0 (47.1, 103.1)	
	Change	−0.6 (−35.4, 17.8)	5.1 (−16.6, 8.6)	
Leptin (ng/mL)	Baseline	47.9 (26.3, 53.0)	39.7 (26.3, 66.1)	0.26
	12 weeks	40.5 (16.5, 69.9)	36.6 (14.7, 47.3)	
	Change	7.6 (−15.5, 12.5)	0.9 (−3.3, 20.1)	

^aMissing data in posttrial blood samples were considered unchanged from baseline values

^bData are presented as median (interquartile range)

Table 5

The correlations associated with BMI and serum levels of leptin and adiponectin

	<u>Control</u>		<u>Intervention</u>	
	<i>r</i> value	<i>P</i> value	<i>r</i> value	<i>P</i> value
BMI vs leptin	0.6415	0.0626	0.6469	0.0314*
BMI vs adiponectin	0.2599	0.4993	-0.7924	0.0036*
BMI vs leptin/adiponectin	0.1165	0.3305	0.7132	0.0137*

r value and *P* value were determined by Spearman's correlation coefficient test