Preventing sarcopenic obesity among breast cancer patients who receive adjuvant chemotherapy: results of a feasibility study

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Abstract

Purpose—Weight gain is a common side effect of adjuvant chemotherapy for breast cancer—a side effect that decreases quality of life and also may decrease both disease-free and overall survival. This weight gain also is unique, since patients lose lean body mass while they gain weight. These body composition changes become apparent within six months of diagnosis.

Methods—We explored whether a clinic-based exercise program, which promoted a specialized program of strength training, aerobic activity and a healthful (≤20% fat; fruit, vegetable and calcium-rich) diet could prevent body composition change among Stage I/II premenopausal breast cancer patients who would receive adjuvant chemotherapy. Dual energy x-ray absorptiometry was used to assess body composition at both baseline and at six-month follow-up. Data from patients participating in the intervention (N=9) were compared to data from historic patient controls (N=36).

Results—Mean changes (SE) in body weight and composition at 6 month follow-up were as follows among historic patient controls and intervention participants, respectively: body weight +2.2(.4) kg vs. −2.0(1.3) kg (p=.02); % body fat +1.8(1.6)% vs. −1.3(1.2)% (p=.002); lean body mass −0.3(.01) kg vs. +0.1(1.5) kg (p=.80); and fat mass +2.0(.3) kg vs. −1.2(1.5) kg (p=.04).

Conclusion—Data from this pilot study suggest that exercise/diet interventions may yield promise in preventing adverse chemotherapy-induced weight and body composition changes among young women who receive adjuvant chemotherapy for breast cancer, and that further study is needed. Since over half of the women approached for this intervention study refused on the basis of time and travel requirements, interventions that utilize home-based approaches may be necessary to reach greater numbers and a greater diversity of patients.

Keywords
breast neoplasms; exercise; body composition; body weight
experience is unique, since it occurs either in the absence of gains in lean tissue or in the 
presence of lean tissue losses (7–12).

This pattern of weight gain, i.e., gain in weight without concomitant gain in lean tissue, is 
termed sarcopenic obesity (13). Acute sarcopenic obesity is uncommon, and is typically 
associated with the chronic use of corticosteroids, hypopituitarism, specific neuromuscular 
diseases, hypogonadism, and prolonged physical inactivity or bed rest (13). Gradual sarcopenic 
obesity is noted with aging and menopause (14).

Physical activity, especially resistance training, represents the cornerstone of prevention and 
treatment for sarcopenic obesity (13). To date, physical activity interventions directed toward 
brust cancer patients have largely concentrated on aerobic exercise, with findings suggesting 
that it reduces nausea (15) and fatigue (16), and improves quality of life (17–19). Reductions 
in percent body fat (measured via skinfold measure derived formulas) also were reported with 
an aerobic exercise intervention by Winningham et al. (20). However, few interventions have 
incorporated resistance training into protocols that target breast cancer patients, and to date 
there have been no reports that have assessed the benefit of resistance training during active 
treatment for breast cancer. Resistance training exercises, especially those directed toward the 
lower body may be particularly useful in preventing deleterious body composition change, 
since past research that assessed body composition change among breast cancer patients using 
dual energy x-ray absorptiometry (DXA) found greater losses of lean tissue in the lower body 
(11,12). Thus, exercise programs that combine elements of both aerobic and resistance training 
exercise for breast cancer patients may have even greater and far-reaching benefit than that of 
either modality alone.

We explored whether a clinic-based program, that promoted a targeted program of strength 
training to the lower extremities and aerobic exercise is feasible and could prevent adverse 
body composition changes (specifically gains in body fat and losses in lean body mass) among 
Stage I/II premenopausal breast cancer patients who would receive adjuvant chemotherapy. 
The program also promoted a healthful diet characterized by high consumption of vegetables 
and fruit (≥ 5 daily servings), and calcium-rich, low fat foods (≤20% of energy from dietary 
fat and an intake of ≥1,200 mg of calcium/day).

METHODS

Subjects

Women with newly diagnosed, breast carcinoma were identified from the Breast Program at 
the Duke Comprehensive Cancer Center (Durham, NC) or were referred by community-based 
physicians. Given results of previous studies which suggest that weight gain is greater and 
more problematic among younger women, only premenopausal (defined as < 4 months since 
the last menstrual period and/or follicle-stimulating hormone in the premenopausal range) 
patients were screened for enrollment (1–3). Other eligibility criteria for participants were as 
follows: 1) diagnosis of Stage I or II breast cancer; 2) scheduled to receive adjuvant 
chemotherapy, but prior to the first treatment; 3) euthyroid, without taking thyroid medication; 
4) mentally competent, English speaking; 5) willingness to pursue a low fat, calcium-adequate 
diet that contained ≥ 5 daily servings of vegetables and fruits; and 6) willingness to exercise 
at least 3 days per week at the Duke Center for Living.

Patients were contacted within three weeks of surgery (mastectomy or lumpectomy) and prior 
to the initiation of adjuvant treatment. The protocol was approved by the Institutional Review 
Board at Duke University Medical Center, and signed consent was obtained from all subjects 
who agreed to participate.
Intervention

A clinic-based program was fully developed and pretested that included the following components: 1) diet counseling and written materials regarding a low fat (<20% of total kcal), calcium-adequate (1,200–2,500 mg/day), high vegetable and fruit (≥ 5 servings/day) diet; and 2) one-on-one fitness training that promoted aerobic exercise with specifically tailored resistance exercises. The physical activity component promoted exercise at least three times per week at the Duke Center for Living, a state of the art fitness facility housed on the Duke University Medical Center campus in Durham, NC.

The physical activity component included 15–60 minutes of aerobic activity three to five days per week and resistance training of the lower extremities two to three days per week on non-consecutive days.

Aerobic Exercise—Each participant performed a maximal effort exercise test on a Quinton Model Q65 treadmill (Quinton Instrument Company: Bothell, WA) to screen for heart disease and to establish a safe exercise heart rate range. Study participants were advised to perform the aerobic exercises based on the 6–20 Borg Rate of Perceived Exertion (RPE) Scale, keeping their exertion between 11–15 (“fairly light to hard”) and to keep their level of fatigue in mind when they rated their exertion (21). Participants self-selected aerobic activities based upon personal preference; the following activities were pursued: walking on a treadmill; riding a stationary bike; swimming; and participating in land-based aerobic classes.

Resistance Training Exercise—Resistance training exercises were confined to the lower trunk and legs since previous studies suggest that losses of lean body mass may be accentuated in this region (11,12), and also to avoid any risk of lymphedema that might be induced with upper body exercise in this population (22). In developing the exercises used in this intervention, exercise physiologists at the Duke Center for Living carefully studied dual energy x-ray absorptiometry (DXA) scans from a prior observational study (11), and devised exercises aimed specifically at preventing muscle losses in body regions where they had been previously noted. Cybex weight machines (LUMEX, Inc: Owatonna, MN) were utilized for seated leg presses, leg extensions, leg curls, abduction and adduction exercises. One repetition maximum was performed at baseline to assess leg strength and to establish appropriate weight loads for the resistance program. Each subject was oriented to the weight machines by an exercise physiologist and instructed to perform 10 to 15 repetitions to “volitional fatigue” in compliance with the American College of Sports Medicine Guidelines (21). The RPE scale also was used to assist each subject in self-monitoring and progression.

Self-monitoring—All participants were asked to record their level of exercise indicating what activity (ies) they performed, the time they spent doing the activity, their RPE and their heart rate. A separate log was used to record weight lifted and number of repetitions performed for each session of resistance training. Participants also were asked to keep a dietary record and to record the foods they ate, making note of the number of servings of fruits and vegetables, as well as recording and summing the number of fat grams they consumed.

Study Measures

Body Composition—Body composition was measured using the Hologic QDR2000 multiple detector fan-beam dual-energy x-ray absorptiometry (DXA) densitometer (Hologic Inc, Waltham, MA). The densitometer was calibrated daily by using an anthropomorphic phantom. Single-beam, whole-body scanning was used which required participants to lie still on the imaging table in a supine position for approximately 15 minutes. The QDR 2000 provided output of total and percentage body fat, and lean body mass. Measures were obtained at baseline and six-month time points.
Height/Weight—Heights were assessed at baseline using a wall-mounted stadiometer as outlined by Gordon et al (23). Weight was assessed at baseline and six months using a calibrated platform balance scale.

Physical Function—A six-minute walk test to evaluate cardiovascular fitness was performed at baseline, three and six months on an indoor track. To assess leg strength, one repetition maximum (1RM) of a seated leg press was performed on the Cybex weight machine. This assessment was repeated at both three and six months.

Statistical Analysis

Given the exploratory nature of this investigation, an emphasis was placed on descriptive statistics. Data expressed in terms of means and standard errors (SE) were compared to those of breast cancer patients who participated in a prior observational study where body composition changes were monitored in the year following diagnosis (11). Two-tailed t-tests ($\alpha = 0.05$) were used to compare body composition data from intervention patients to those of historic patient controls; functional endpoints over time in the intervention group were explored using ANOVA with repeated measures with participants serving as their own controls.

RESULTS

A total of 22 patients were approached for this investigation, 2 (9%) of whom were disinterested in behavior change during treatment; 10 (45%) of whom could not invest the time or travel (it must be noted that the Duke Breast Program attracts women from a large catchment area which extends primarily from Virginia to South Carolina, but also attracts patients from the eastern seaboard); and 10 (45%) accepted. Of these, one patient was lost to follow-up. Of the nine women who completed the program, average adherence was “fair” for one, “good” for three, and “excellent” for five (as assessed from exercise logs, where dedicated exercise of $\geq 90$ minutes/week was considered “excellent” adherence, 60–89 minutes per week was considered “good,” and 30–59 minutes/week was considered “fair”). Self-monitoring adherence of food intake was not uniform, with only three of the nine participants submitting complete data. Due to the difficulty in interpretation of these data, no data regarding diet are presented.

Baseline characteristics of the nine patients participating in the intervention are presented in Table 1 and are compared to historic control patients who participated in the prior observational study (11). There were no significant differences between groups with regard to any of these characteristics.

Data regarding functional status over time, as assessed from 1 RM of the seated leg press and 6 minute walk tests, are plotted for all intervention participants in Figure 1. Significant improvements over time were seen for both measures ($p<.01$).

Values for total body, lean body, leg lean and fat mass, and percent body fat at baseline and six month follow-up for both the historic patient control group and the intervention group are presented in Table 2. Several significant differences were observed between groups with regard to change in body mass and composition, with intervention group participants experiencing losses in body weight, fat mass and % body fat, while historic control patients experienced increases. Despite a loss in total body mass, the intervention group experienced a modest net gain in total body lean mass and leg lean mass; this is in contrast to the small net losses in lean mass among historic control patients despite gains in total body mass. While the exercise intervention was targeted primarily at the lower extremities, losses in fat mass appeared proportional throughout the body. Mean percent loss in the absolute amount of adipose tissue was 5.5% (1.1) for the entire body versus a 4.9% (0.9) loss in the legs ($p=0.89$). Change in
body composition among intervention participants and historic patient controls are graphed in Figure 2.

DISCUSSION

Over a decade ago, Winningham et al. (20) reported body composition data from a study where 24 early stage breast cancer patients receiving adjuvant chemotherapy were randomized between a group that was instructed to pursue routine aerobic activity (exercise on a calibrated cycle ergometer with exertional levels of 60–85% maximal heart rate for 20–30 minutes, 3 times per week) versus a sedentary control group. This study had the following limitations: it utilized indirect methods to assess body composition (i.e., % body fat was derived from prediction equations that relied on skinfold measures, rather than hydrostatic weighing or whole body imaging via dual energy x-ray absorptiometry); and it focused solely on aerobic exercise. Despite these limitations, it represented a pioneering effort to prevent sarcopenic obesity accompanying breast cancer treatment – an effort that was undertaken before sarcopenic obesity was even an acknowledged entity within this population. In the Winningham et al. study, weight gain was still observed in both groups (.82 kg in the experimental group vs. 1.99 kg in the control group, p=.88), however significant differences were observed in the change in percent body fat (−0.51% in the experimental group versus +2.19% in the control group). A decade later, we now know that the weight gain that breast cancer patients experience is distinctive and occurs without concomitant gains in muscle, a pattern of weight gain termed as sarcopenic obesity. While exercise represents the cornerstone of treatment for sarcopenic obesity, resistance training exercises rather than aerobic activity are hypothesized to have a greater impact. Data from the present study suggest that this is true, since this intervention, which included both resistance training and aerobic activity components appeared effective in curtailing weight gain (a 2.0 kg loss was actually noted), and despite the loss in weight, intervention group women were observed to have a 0.1 kg gain in lean body mass. This is in direct contrast to what is observed among historic controls who experienced a mean 2.2 kg weight gain in the presence of a 0.3 kg lean tissue loss. Thus, this intervention which included both resistance training and aerobic components resulted in a −1.3% decrease in percent body fat (more than twice that observed by Winningham et al.) versus the 1.8% gain observed among historic controls (comparable to the 1.99% gain noted by Winningham et al among their controls). Given that the intervention also promoted a low fat, high vegetable and fruit diet, if indeed optimal interventions are to be developed to combat sarcopenic obesity in this patient population, a dietary component also may be necessary. Therefore, further study appears necessary to test the comparative efficacy of exercise interventions (which include both resistance training and aerobic components) and multiple factor interventions which include both exercise and diet. Such research should employ a randomized controlled design and be adequately powered – acknowledged limitations of the present study.

In addition, more study is needed to refine exercise interventions, so that they can further optimize improvement in body composition during adjuvant treatment. As previously mentioned, the exercises promoted within this intervention were devised by studying DXA scans of previous observational studies and developing exercises that specifically targeted muscle groups that were affected. We targeted lower extremity exercise based upon these considerations, fully expecting that while the focus was to increase lean body tissue in the lower extremities, any loss of body fat would be widely distributed and not confined to the exercising limbs. This expectation was born out in the analysis. While these exercises were evidence-based, an empirical approach was used to determine the dose, frequency and intensity of exercise. Given the preponderance of fatigue in this patient population, more research is needed to titrate and refine exercise, especially since these women have limited energy and thereby should be advised to apportion it in the most efficient manner.

Clin Exerc Physiol. Author manuscript; available in PMC 2006 August 30.
Additionally, there is a need to develop interventions that have the potential to overcome barriers of traditional clinic-based programs. In this pilot study, barriers of time and travel were listed as primary reasons for non-participation. With cancer patients traveling significant distances to receive their care, these barriers are not new and have been noted previously (24). Thus, the creation of distance-medicine based programs and especially home-based programs is important. By overcoming these barriers, participation rates should improve. This may be of particular importance in minority and underserved populations who may not have the resources (transportation, social support, etc.) to attend clinic-based programs that primarily attract the worried, white and well.

Given their convenience, home-based programs also may invite better compliance. A recent study by Segal et al. (25) suggests that exercise programs that target breast cancer patients are met with improved physical functioning as measured by the SF-36 quality of life instrument. In this study 123 breast cancer patients were randomized between programs that promoted supervised exercise, self-directed exercise and a control group. Participants in the self-directed exercise group were the most adherent and experienced the greatest gains in physical functioning. In the present study, gains in functional status (i.e., improved scores on the 6-minute walk test and 1RM of the seated leg press) also were observed among intervention group participants. It will be important to see if such a program can be instituted and effective in a home-based program.

**CLINICAL IMPLICATIONS**

The results of this pilot study suggest that a multifactor intervention that promotes exercise (both resistance training and aerobic activity) and a healthful diet shows promise in being able to curtail weight gain and the incidence of sarcopenic obesity among women who receive adjuvant chemotherapy for breast cancer. Further work is needed to refine interventions with regard to optimal dosing, as well as to develop interventions that assure optimal compliance and attract a diversity of patients, as well as address mechanisms underlying the program’s benefits. Until that time, breast cancer patients should be provided with support, to pursue moderate physical activity, making sure that counseling and recommendations reflect factors, such as current co-morbidity, and risk of lymphedema [which may be exacerbated by axillary node dissection and/or radiation (22)].

**Acknowledgements**

We thank Jami Norris, MS, RCEP and Gregory McElveen, MS, MBA for their input in helping to develop the exercise intervention. We also thank Cheryl Franklin-Cook for conducting the DXA scans. Furthermore, we appreciate the support of P. Kelly Marcom, M.D., Kimberly Blackwell, M.D., Heather Shaw, M.D. and Patricia Hardenbergh, M.D. who referred patients for this study. Most of all, we appreciate the effort of the women with breast cancer who agreed to participate in this effort.

**References**

Figure 1.
Values at 0, 3 and 6 months among intervention participants in the seated leg press (1RM) and the 6 minute walk test.
Figure 2.
Change in lean body mass and fat mass within six months of diagnosis among intervention participants (N=9) and historic patient controls (N=36)
Table 1

Participant Characteristics at Baseline

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention Participants (N=9)</th>
<th>Historic Patient Controls (N=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years): mean (SE)</td>
<td>42.4 (1.8)</td>
<td>41.4 (6.2)</td>
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<tr>
<td>Race: White</td>
<td>100%</td>
<td>81%</td>
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<tr>
<td>African-American</td>
<td>0%</td>
<td>19%</td>
</tr>
<tr>
<td>Native American</td>
<td>0%</td>
<td>1%</td>
</tr>
<tr>
<td>Breast Cancer Stage: I</td>
<td>22%</td>
<td>33%</td>
</tr>
<tr>
<td>II</td>
<td>67%</td>
<td>61%</td>
</tr>
<tr>
<td>III</td>
<td>11%</td>
<td>6%</td>
</tr>
<tr>
<td>BMI: mean (SE)</td>
<td>24.1 (1.4)</td>
<td>25.8 (5.1)</td>
</tr>
<tr>
<td>% Body Fat: mean (SE)</td>
<td>32.5 (2.1)</td>
<td>33.6 (8.6)</td>
</tr>
<tr>
<td>Lean Body Mass (kg): mean (SE)</td>
<td>43.1 (1.8)</td>
<td>45.4 (5.0)</td>
</tr>
</tbody>
</table>
Table 2

Body mass and composition at baseline and six month follow-up: a comparison of intervention participants and historic patient controls

<table>
<thead>
<tr>
<th>Variable [mean (SE)]</th>
<th>Intervention Participants (N=9)</th>
<th>Historic Patient Controls (N=36)</th>
<th>p-value $^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Weight (kg): Baseline</td>
<td>68.8 (4.2)</td>
<td>70.0 (1.9)</td>
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<tr>
<td>Follow-up</td>
<td>67.8 (4.7)</td>
<td>72.2 (2.1)</td>
<td></td>
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<tr>
<td>Change</td>
<td>−2.0 (1.3)</td>
<td>+2.2 (.4)</td>
<td>.02</td>
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<tr>
<td>% Body Fat: Baseline</td>
<td>32.5 (2.3)</td>
<td>33.6 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td>31.2 (2.2)</td>
<td>35.4 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>−1.3 (1.2)</td>
<td>+1.8 (1.6)</td>
<td>.002</td>
</tr>
<tr>
<td>Fat Mass (kg): Baseline</td>
<td>22.6 (2.9)</td>
<td>24.0 (1.6)</td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td>21.4 (3.1)</td>
<td>26.0 (1.9)</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>−1.2 (1.5)</td>
<td>+2.0 (.3)</td>
<td>.04</td>
</tr>
<tr>
<td>Lean Mass (kg): Baseline</td>
<td>43.1 (1.9)</td>
<td>45.4 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td>43.2 (2.2)</td>
<td>45.1 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>+0.1 (1.5)</td>
<td>−0.3 (.01)</td>
<td>.80</td>
</tr>
<tr>
<td>Leg Lean Mass: (kg) Baseline</td>
<td>14.6 (0.8)</td>
<td>14.1 (0.3)</td>
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<tr>
<td>Follow-up</td>
<td>14.7 (1.0)</td>
<td>14.0 (0.3)</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>+0.1 (0.5)</td>
<td>−0.1 (.02)</td>
<td>.81</td>
</tr>
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$^1$ t-test – two-tailed