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Weight Loss Intervention in Survivors of ER/PR-negative Breast Cancer

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ABSTRACT: Numerous studies have found that increased body size (weight or body mass index) is a risk factor for breast cancer development, recurrence, and death. The detrimental relationship between body size and breast cancer recurrence may be more pronounced among women with estrogen receptor (ER)/progesterone receptor (PR)-negative breast cancer. Considering the limited availability of treatments, and the association between body size and recurrence, alternative treatments are needed for ER/PR-negative breast cancer survivors, particularly overweight survivors. The objective of this pilot study was to examine the feasibility of a 12-week, multi-component meal-replacement weight loss intervention among overweight or obese ER/PR-negative breast cancer survivors; and to obtain preliminary data on changes in anthropometrics, biomarkers, and health-related quality of life (QOL). The 12-week intervention included a portion-controlled diet (including meal replacements) and a multi-component intervention (including behavioral techniques, diet modification, physical activity, and social support). The goal of the intervention was to help participants lose 5% or more of their initial weight by reducing their caloric intake and increasing their physical activity (to at least 15 minutes each day). Paired *t*-tests assessed changes in continuous measures. Body weight was measured weekly and mixed-model regression analysis assessed change in weight over time. Nineteen ER/PR-negative breast cancer survivors with a mean age of 59 years participated in the study. All but two of the participants completed the 12-week intervention. Women lost an average of 6.3 ± 4.9 kg ($P < 0.001$), equivalent to 7.5% of their baseline weight. There were significant reductions in waist circumference ($P = 0.001$), percent fat mass ($P < 0.001$), total cholesterol ($P = 0.026$), and triglycerides ($P = 0.002$); and improvements in health-related QOL ($P = 0.017$). Findings suggested that a meal-replacement weight loss approach among ER/PR-negative breast cancer survivors was feasible and was well received.

KEYWORDS: weight loss, estrogen negative breast cancer, nutrition intervention, meal replacement

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Introduction

While prognosis has improved, breast cancer remains the second most common cause of cancer-related death among US women, after lung cancer. Approximately one in eight (12%) women will develop invasive breast cancer at some time in their lives.[1] The American Cancer Society's estimates for 2014 include approximately 232,670 new cases of invasive breast cancer, 62,570 new cases of carcinoma in situ (the most invasive and earliest form of breast cancer), and approximately 40,000 breast cancer deaths.[1] Furthermore, numerous studies have provided strong evidence of statistically significant, positive correlations between body weight and either breast cancer recurrence or survival.[2–4] Several explanations may account for the relationship between body size and cancer prognosis. Insulin pathways have been suggested as one such mechanism.[5,6] Visceral fat distribution is known to increase

insulin resistance, predisposing to hyperinsulinemia, glucose intolerance, dyslipidemias, and hypertension.[7] Hyperinsulinemia raises plasma levels of the free form of insulin-like growth factor (IGF)-1, a stimulatory hormone of cancerous cell growth.[7–9] IGF-binding protein-3 (IGFBP-3) is important because it binds to IGF-1, reducing circulating free forms.

Compared to women with tumors that are estrogen receptor (ER)/progesterone receptor (PR)-positive, women lacking ER and PR expression have an estimated 1.5 to 2 fold higher risk of death.[10,11] Breast cancers that are ER/PR positive are associated with the most favorable prognosis, primarily because expression of these markers is predictive of successful response to hormonal therapy. Women diagnosed with ER/PR-negative breast cancers are not candidates for hormonal therapies, including tamoxifen and aromatase inhibitors.[1] Therefore, there is strong association between body size and cancer recurrence, and the limited availability of treatments for ER/PR-negative breast cancer emphasizes the need for alternative therapies, particularly among overweight survivors. Offering ER/PR-negative breast cancer survivors a weight loss intervention that may potentially reduce their risk of recurrence and improve their general health, lipid profiles and quality of life (QOL) are highly desirable.

Weight loss interventions that feature a portion-controlled, energy-restricted diet, and include liquid meal-replacement beverages, have been shown to safely and effectively produce significant, sustainable weight loss, im-prove weight-related risk factors of disease, and produce greater weight loss when compared to groups randomized to reduced calorie traditional diets.[12–16] Specifically, meal-replacement strategies have been associated with improvements in cardiometabolic risk factors, such as reductions in waist circumference, body fat mass, systolic and diastolic blood pressure, and total cholesterol,[14] and improvements in physical functioning, general health and vitality.[15] They promote portion control, are well tolerated, provide nutritional adequacy, are convenient and easy to prepare, and enhance dietary structure that may help reduce the temptation of choosing high-calorie foods for the meals replaced.[15,17,18] These findings may explain the success of such strategies during weight loss and weight loss maintenance.[13,19]

A variety of meal-replacement products exist; however, soy-based products may provide additional health benefits. Soy protein, a common ingredient in meal replacements, is naturally low in calories. Soy-based meal replacements have been shown to be a safe and an effective aid in reducing weight, body fat, and insulin, lipid, leptin, hemoglobin A1c, and C-reactive protein concentrations.[20–25] In addition, researchers have reported that soy protein, which is rich in naturally occurring isoflavones, may attenuate the increase in fat deposition and prevent loss of lean tissue and bone during weight loss.[24,26,27] Both the American Institute for Cancer Research's (AICR's) Foods that 2012 American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Survivors, written by a panel of experts, concluded that current research finds no harmful effects to breast cancer survivors from eating soy.[28,29] These guidelines do not recommend taking soy supplements because they contain much higher isoflavone concentrations than naturally found in food, have not been as rigorously tested, and may have other potent effects on body tissues.

A recent study evaluated soy consumption in the diets of 9,514 breast cancer survivors who were participating in three studies of dietary intake and other lifestyle factors after breast cancer.[30] Two of the studies were from the US and one was from China. Women from both the US and China who consumed 10 mg/day or more of soy had a 25% lower risk of breast cancer recurrence. These protective associations were slightly stronger in women with ER-negative tumors. In women with ER-positive tumors, the associations also seemed protective for women regardless of whether they were taking tamoxifen. These studies, which vary in ethnic composition and type and level of soy consumption, provide important evidence that clinicians no longer need to advise against soy consumption for women who have been diagnosed with breast cancer. Recently, an in vitro model was used to investigate the effect of commercially available soy milk on the inhibition of inflammation.[31] Hydrolysates from the soy milk inhibited the production of nitric oxide, interleukin-1β, and tumor necrosis factors (TNF)-α. In summary, including soy-based meal replacements as part of an evidence-based dietary prescription for ER/PR-negative breast cancer survivors has the potential to reduce body weight, inflammation, and risk for cancer recurrence.

Although studies have reported favorable effects on weight loss and metabolic risk factors using soy-based meal replacements, and despite the known complexities of ER/PR-negative breast cancer, no one has used this intervention among these survivors. Hence, the aim of this pilot study was to investigate the feasibility of a 12-week, multi-component meal-replacement weight loss intervention among ER/PR-negative breast cancer survivors. Additionally, we aimed to obtain preliminary data on the impact of the intervention on body weight, waist circumference, body composition, biomarkers [total cholesterol, high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), triglycerides, glucose, insulin and IGFBP-3], and health-related QOL.

Materials and Methods

Study overview. A 12-week feasibility pilot study was conducted to apply known effective strategies for weight loss promotion to ER/PR-negative breast cancer survivors. The intervention was an open-label, single-arm intervention and included a portion-controlled diet (including meal replacements), a multi-component intervention (including behavioral techniques, diet modification, physical activity, and social support), and ongoing regular contact with study assistants throughout the study period. The goal of the intervention was to help participants lose 5% or more of

their pre-intervention weight by reducing their caloric intake and increasing their physical activity (to at least 15 minutes each day).

Participants and recruitment. ER/PR-negative breast cancer survivors were identified by nurses and physicians at both Wake Forest University School of Medicine Comprehensive Cancer Center Breast Clinic and Derrick L. Davis Forsyth Regional Cancer Center in Winston-Salem, North Carolina. Participants were 21 years or older who were previously diagnosed with stage I, II, or III ER/PR-negative breast cancer, but were free from cancer as of their last clinical visit. Additionally, the patients were six months post cancer treatment, had a body mass index (BMI) $\geq$ 25 kg/m^2, had no history of soy allergies, and were willing to sign protocol-specific informed consent. Women were excluded from participation if they were unable or unwilling to give informed consent, were receiving treatment for ER/PR-negative breast cancer, were using medications for weight loss at the time, were pregnant or planning a pregnancy, had definite plans to move out of the local geographic area within the study period, had uncontrolled high blood pressure, diabetes mellitus (type 1 or 2), hyperthyroidism, or hypothyroidism, or were diagnosed with other medical, psychiatric, or behavioral conditions that in the judgment of the Principal Investigator may interfere with study participation or the ability to follow the intervention protocol. Ethical approval for this study was obtained through the Institutional Review Boards at both institutions, and all women signed informed consent documents.

Intervention description. The 12-week study intervention relied principally on cognitive behavioral therapy (CBT) to help participants modify their eating and activity habits, to set realistic goals, and to cope with other challenges. According to a systematic review of literature related to behavior change strategies used in nutrition counseling, the Academy of Nutrition and Dietetics concluded that strong evidence supports the use of CBT in facilitating the modification of targeted dietary intake behaviors, weight, and cardiovascular and diabetes risk factors.[32]

Individual and group sessions. Participants attended weekly sessions—one individual and three group sessions each month. During individual sessions, participants were provided with more personal attention and an opportunity to tailor treatment to their specific needs and preferences, while group sessions provided social support, and focused on shared experiences and problem solving. Participants were asked to complete homework assignments each week which involved modifying an aspect of their eating, physical activity, or thinking habits. Dietary intake and physical activity self-monitoring were accomplished through the use of diet and activity logs, and participants were encouraged to discuss their progress in the weekly sessions. Individual and group meetings were held at the General Clinical Research Center (GCRC).

Group activities included discussion of barriers to weight loss that participants encountered during the prior week, taste-testing low-fat recipes, and identifying and preparing low-calorie foods. Participants were encouraged to discuss adherence problems during individual and group meetings in order to elicit support and assistance from the Project Manager, GCRC nutritionist, and other group members.

Weight loss. Participants were encouraged to lose weight at a safe rate (approximately 1–2 pounds per week) and not to lose so much weight that their BMI dropped below 21 kg/m^2 (considered "normal" BMI). Caloric restriction was the primary method to achieve weight loss, and calorie goals were established based on the Harris–Benedict equation. Participants were encouraged to aim for a weight loss of 5% of their baseline weight. Healthy meal plans were determined during the participants' individual sessions with a GCRC bionutritionist. Participants consumed 1–2 meal replacements each day, which reduced participant burden for recording daily dietary intake. Participants were encouraged to be physically active as weight loss without concomitant physical activity has been shown to result in the loss of lean body mass. Furthermore, unsupervised physical activity has been shown to be effective in weight loss and risk factor modification.[33,34] The primary type of physical activity recommended was brisk walking; however, participants were also encouraged to perform other aerobic activities. Participants used pedometers to record minutes of physical activity and steps per day in their activity logs. As participants were exercising without study supervision, they were initially encouraged to be physically active for at least 15 minutes, 6 days every week, lower than national recommendations (90 minutes/week) as a cautionary measure. During weekly meetings, participants were counseled to safely increase minutes of physical activity as they felt that they could and as they became more fit.

Meal replacement. Almased® (Almased® USA, Inc., St. Petersburg, FL), the meal-replacement product used in this study, is composed of soy, honey, and yogurt, and has a low glycemic index and low glycemic load. Almased is commercially available and contains naturally occurring levels of isoflavones, thus the product falls within the category of a food supplement which is classified as a generally regarded as safe (GRAS) item.[26] The powder was used to replace 1–2 meals each day (based on participant baseline weight) and participants were also instructed to eat healthy meals (lunch/dinner) to achieve a specified calorie level. Individual monthly sessions with the GCRC bionutritionists provided an opportunity to modify these diet options to the participant's preference. To encourage retention, participants were given a one week supply of meal replacements weekly at either the individual or group meetings.

Measures

Baseline and post-intervention assessments. Participants completed an assessment visit before and after the

12-week intervention. All assessment visits took place at the GCRC. The participants were asked to fast for 12 hours prior to each assessment visit. After participants were determined eligible, a baseline assessment visit was scheduled. During the baseline assessment, final eligibility was confirmed and participants signed written, informed consent and Health Insurance Portability and Accountability Act (HIPAA) documents, as well as completing demographics and medical questionnaires. Blood pressure, height, weight, and percentage of body fat were measured, and a fasting blood sample was collected to measure cholesterol (total, HDL-c, LDL-c and triglycerides), glucose, insulin, and IGFBP-3. The Functional Assessment of Cancer Therapy-Breast (FACT-B) health-related QOL survey was completed and a snack was provided to each participant following the venipuncture. At the end of this visit, the first individual diet counseling session was scheduled with the GCRC bionutritionist. In addition to the measures assessed at baseline (biomarkers, anthropometrics, and FACT-B), an individual counseling session with the GCRC bionutritionist was held during the post-intervention assessment visit.

Study adherence. Recruitment success and study adherence (using both adherence to the meal replacement and completion of diet and activity logs) were assessed. Participants were considered successful in their adherence to the dietary intervention if they consumed at least 80% of the meal replacements as prescribed by the protocol, and consumed within 110% of their prescribed daily calorie goal. Also, participants were considered successful in adherence to their physical activity goal if they met or exceeded the activity goals at least 80% of the time. Finally, the percentage of participants who completed the study was calculated as a measure of overall study adherence.

Anthropometrics. Participant's height, weight, waist circumference, and body fat percentage [via Bioelectrical Impedance Analysis (BIA)] were measured in the GCRC. Height was measured (without shoes) to the nearest 0.1 cm, and weight was measured to the nearest 0.1 kg. Waist circumference was measured in triplicate, using a non-stretchable measuring tape, to the nearest 0.1 cm at the level of the iliac crest.

Serum biomarkers. A fasting blood sample was collected from participants at baseline and post-intervention. Total cholesterol, HDL-c, LDL-c, and triglyceride, glucose, insulin, and insulin-like growth factor-binding protein-3 (IGFBP-3) concentrations were measured.

Health-related QOL. Participant's health-related QOL was assessed at baseline and post-intervention using the FACT-B, which consists of the FACT-G and an additional breast concerns subscale. The FACT-G is a multidimensional QOL instrument developed for use with cancer patients.[35] This scale assesses a participant's physical, social/family, emotional, and functional well-being. The Fact-B is scored by adding the four individual scores of the FACT-G and the additional breast cancer concerns subscale. These measures have established reliability and validity, and extensive information on their psychometric properties is available.[36]

Demographic and medical characteristics. Marital status, date of birth, racial/ethnicity, occupation, highest educational attainment, and prescription drug use were collected. Participants were instructed to bring all medications (including over the counter) to the study visits.

Statistical considerations. This study was designed to estimate the proportion of patients who completed the intervention, one of the primary measures of feasibility. We planned to recruit 25 participants, which would allow us to estimate retention to within ±20%. Descriptive statistics such as means, standard deviations, frequencies, and percentages are calculated for pre-treatment participant characteristics and the outcome measures assessed pre- and post-intervention. Exact binomial confidence intervals are calculated for the estimated proportions, and approximate confidence intervals are calculated for means, differences in means, and differences in proportions. Paired *t*-tests are used to assess the significance of changes over time in the continuous outcomes that were measured pre- and post-intervention. Weight was measured approximately weekly over the course of the study, and mixed effects models are used to assess the significance of the weight changes over time. Least squares means are obtained from the fitted models.

Results

Twenty-two ER/PR-negative breast cancer survivors were identified by nurses and physicians to participate in the study. Three declined, leaving 19 participants. Descriptive characteristics for these women are summarized in Table 1. The majority of participants were White, married, employed full-time, and had at least some college. Just under half had an

Table 1. Participant demographic characteristics.

CHARACTERISTIC	NUMBER (%)
Total	19 (100)
Age—median (range)	59 (38–72)
<50	5 (26)
50–59	6 (32)
60–69	6 (32)
70+	2 (11)
Weight (lbs)—median (range)	176.6 (151.4–309.8)
150–174.9	9 (47)
175–199.9	5 (26)
200–249.9	3 (16)
250+	2 (11)
BMI (kg/m^2)—median (range)	31.3 (26.8–47.1)
Overweight (25.0–29.9)	6 (32)
Obese (30.0–34.9)	6 (32)
Very obese (35.0+)	7 (37)

(*continued*)

Table 1. (*Continued*)

CHARACTERISTIC	NUMBER (%)
Race	
Black	5 (26)
White	14 (74)
Marital status	
Married	15 (79)
Divorced/separated	3 (16)
Widowed	1 (5)
Employment*	
Retired	6 (33)
Homemaker	1 (6)
Full-time	11 (61)
Annual income	
<$50,000	4 (21)
$50,000–$74,9999	7 (37)
$75,000–$99,999	3 (16)
$100,000+	5 (26)
Highest educational attainment	
High school graduate	3 (16)
Some college	10 (53)
College graduate	3 (16)
Beyond college	3 (16)

Note: *Missing one participant's employment status.
Abbreviation: BMI, body mass index.

annual income of at least $75,000. None of the women were tobacco users at the time of their study participation.

Feasibility. Although we stopped accrual prior to our goal of 25, recruitment was considered successful, as 86% of the women who were eligible for participation entered the study. Accrual took 12 months to complete. Of the 19 women who participated, 17 (89%; 95% CI: 67%–99%) completed the study. One woman discontinued participation after finding the taste of the meal-replacement shake intolerable, and the second participant dropped out without explanation and was lost to follow-up. Including the baseline and follow-up visits, the maximum visit attendance was 14. The average session attendance was 12 visits. Among those who completed the study, more than 90% were compliant with their dietary intervention (consumed at least 80% of the prescribed meal replacements and consumed within 110% of their prescribed calorie goal). Only 44% of the participants met their physical activity goals (met or exceeded their prescribed activity goal at least 80% of the time). Attendance at the individual meetings was excellent and only three individuals missed three or more group meetings.

Anthropometrics, body composition, and biomarkers. Changes in anthropometrics, body composition, and biomarkers are summarized in Table 2. Women lost an average of 6.3 ± 4.9 kg ($P < 0.001$), equivalent to 7.5% of their baseline weight.

Significant reductions in waist circumference [109.3 (14.2) vs 100.3 (18.7), $P = 0.001$] and percent fat mass [47.4 (4.8) vs 43.1 (7.2), $P < 0.001$] were observed from baseline to the 12-week follow-up assessment (Table 2). Significant reductions in total cholesterol ($P = 0.026$) and triglyceride ($P = 0.002$) concentrations were also observed. Slight, but not significant reductions were observed for glucose and insulin concentrations.

Health-related QOL. Figure 1 shows QOL data. A significant improvement in the FACT-B total score ($P = 0.048$) was observed from baseline to the 12-week follow-up assessment (Fig. 1). Physical ($P = 0.029$), emotional ($P = 0.013$), and functional ($P = 0.022$) well-being improved significantly, and at least 75% of the participants improved in the physical

Table 2. Change in anthropometric, body composition and biomarkers.[§,#]

MEASURE	N*	BASELINE*	12-WEEK FOLLOW-UP*	MEAN DIFFERENCE (kg)*	MEAN % RELATIVE CHANGE*	P-VALUE
Weight	18	88.0 (18.3)	81.7 (19.6)	−6.3 (3.6)	−7.5 (4.9)	<0.001
Waist (cm)	12	109.3 (14.2)	100.3 (18.7)	−8.9 (7.1)	−8.6 (7.1)	0.001
% fat mass‡	15	47.4 (4.8)	43.1 (7.2)	−4.3 (3.6)	−9.4 (8.3)	<.001
Cholesterol (mg/dl)	17	210.4 (41.5)	191.9 (27.9)	−18.5 (31.1)	−7.5 (12.2)	0.026
LDL-c (mg/dl)	17	124.1 (35.3)	121.3 (41.3)	−2.8 (14.4)	−2.6 (10.6)	0.430
HDL-c (mg/dl)	17	53.8 (7.4)	54.1 (9.4)	0.3 (9.1)	1.4 (15.6)	0.896
Triglycerides (mg/dl)	17	162.2 (64.5)	111.5 (37.6)	−50.8 (57.4)	−25.4 (27.3)	0.002
Glucose (mg/dl)	17	97.8 (9.8)	95.2 (11.7)	−2.5 (7.2)	−2.6 (7.3)	0.168
Insulin (mg/dl)	16	17.1 (12.6)	15.9 (10.8)	−1.2 (4.0)	−5.0 (25.3)	0.255
IGFBP-3 (mg/l)	17	4.2 (1.1)	4.3 (0.8)	0.04 (1.3)	8.4 (42.0)	0.894

Notes: #Data from participants with both baseline and follow-up data. *Values are mean and standard deviation. ‡Percent body fat mass determined using bioelectrical impedance analysis.
§**Abbreviations:** LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; IGFBP-3, insulin-like growth factor binding protein-3; FACT-B, Functional Assessment of Cancer Therapy-Breast.

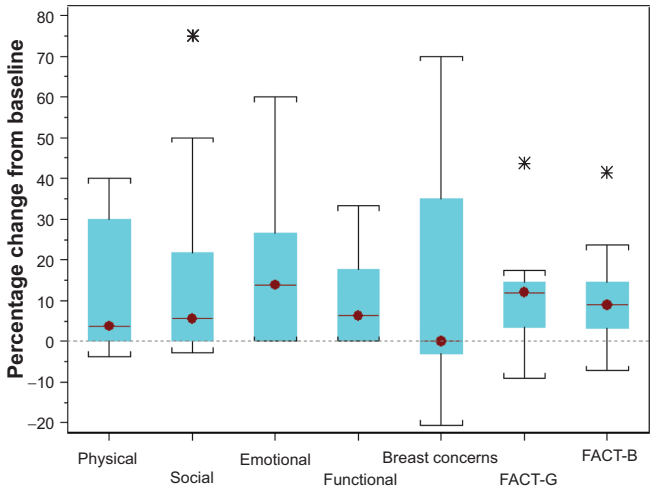

Figure 1. Changes in quality of life results.
Notes: Data is from participants with both baseline and follow-up data. Higher values indicate greater quality of life. *Asterisks represent outliers.

and social subscales. One hundred percent of the participants improved in the emotional and functional subscales.

Discussion

The results of this pilot study suggest that a multi-component meal-replacement weight loss intervention among ER/PR-negative breast cancer survivors is feasible and has beneficial impact on important health outcomes. Although recruitment to the study was slow, there was excellent adherence to the dietary intervention components as well as overall adherence. Significant reductions in weight, waist circumference, and percent fat mass and significant improvements in total cholesterol and triglyceride concentrations, and physical, emotional, and functional health-related QOL were observed.

The findings of this pilot study show promise considering comparable results of larger-scale weight loss interventions. In a recent study, Konig et al[37] showed that even over a short period of time, a meal-replacement diet produced a 12% reduction in the prevalence of the metabolic syndrome among participants. This six week lifestyle intervention, which included lifestyle education, increased physical activity, and the replacement of two meals per day with Almased was more effective in reducing metabolic risk factors, insulin and leptin, and in improving anthropometric measures than a fat-restricted, low-calorie diet. Participants randomized to the meal-replacement diet also experienced significant reductions in weight, BMI, waist circumference, and fat mass when compared to baseline measures.

Other randomized trials have shown that participants who consumed soy-based meal replacements experienced greater weight loss and improvements in metabolic outcomes when compared to individuals in control groups.[20–22,25–27] Furthermore, participants consuming soy-based meal replacements have shown significantly improved metabolic and anthropometric outcomes when compared to their baseline values. For example, at 12 weeks, participants consuming a soy-based meal replacement lost an average of 9% initial body weight and experienced significant reductions in waist circumference, glucose, total cholesterol, LDL-c, and triglyceride concentrations.[26] Similarly, in a subsequent study, at 16 weeks, obese women who consumed a soy-based meal replacement lost approximately 8% of their baseline weight, and experienced significant reductions in waist circumference, percent body fat, Homeostatic Model Assessment (HOMA) values, glucose, total cholesterol, and LDL-c concentrations.[22]

To date, the biological plausibility responsible for the associations between body size and ER/PR-negative breast cancer are not well studied. Inflammatory markers, including adipokines, inflammatory cytokines [TNF-α, interleukin (IL)-1, IL-6], and acute-phase protein serum amyloid A (SAA) are elevated in obese individuals and have been associated with the onset and progression of breast cancer. SAA is a nonspecific acute-phase protein that is primarily produced by hepatocytes, following inflammatory stimuli. Given the inflammatory state in obesity, a recent study investigating the relationship between SAA concentrations and tumor characteristics among overweight/obese and non-obese breast cancer patients reported higher SAA concentrations in patients with ER-negative tumors than those with ER-positive.[38] Additional investigations of the clinical role of SAA should be conducted including a larger sample size and prospective study design.

This study has several strengths. The weight loss intervention included meal replacements and physical activity; both are strategies that have been recommended by the American Dietetic Association as effective tools for weight loss.[32] Physical activity was assessed using subjective and objective measures, and participants attended both individual and group sessions. Individual sessions allowed the intervention to be tailored to the individual, and group sessions provided social support. The meal replacements were well tolerated, and participant adherence to the diet and activity logs was high, as was adherence to the study overall.

This study also has limitations. This was a pilot trial with a small sample size and only 12 weeks of follow-up. The purpose of this study was to assess if we could recruit women post-treatment to participate in a weight loss intervention and if they would remain adherent to the protocol. This study did not include a treatment comparison condition or a non-treatment control condition. The limitations are specific to this being a feasibility pilot study. Although accrual took 12 months to complete, this was likely due to the less common diagnosis of ER/PR-negative (versus ER/PR-positive) patients as well as the lower survival rates. While BIA tends to underestimate fat mass and overestimate lean mass measurements, this method

is a safe alternative for assessing body composition among breast cancer survivors.[39] Finally, just over 40% of the participants met physical activity recommendations. Future studies may consider the inclusion of a structured physical activity component and providing incentives for participants to meet physical activity recommendations.

Conclusion

Our data suggest that a 12-week weight loss intervention which incorporates soy-based meal replacements and physical activity should be tested in a larger group of ER/PR-negative breast cancer survivors. We have preliminary evidence that demonstrates a reduction in participant's body weight, waist circumference, and percent fat mass; and an improvement in total cholesterol and triglyceride concentrations, as well as physical, emotional, and functional health-related QOL. A long-term study among ER/PR-negative breast cancer survivors to improve body weight and body composition and to potentially impact the risk for breast cancer recurrence is warranted. Since overweight and obesity are common risk factors for the development and recurrence of a wide array of cancers, this meal-replacement weight loss regimen may have applicability beyond ER/PR-negative breast cancer populations.

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Author Contributions

Conceived and designed the experiments: MZV. Analyzed the data: DC. Wrote the first draft of the manuscript: MZV and BJM. Contributed to the writing of the manuscript: MZV and BJM. Agree with the manuscript results and conclusions: MZV, BJM, JOH, AF, JL, SM, DC. Jointly developed the structure and arguments for the paper: MZV, BJM, JOH, AF, JL, SM. Made critical revisions and approved final version: MZV, DC, BJM. All authors reviewed and approved of the final manuscript.

DISCLOSURES AND ETHICS

This paper was subject to independent, expert peer review by a minimum of two blind peer reviewers. All editorial decisions were made by the independent academic editor. All authors have provided signed confirmation of their compliance with ethical and legal obligations including (but not limited to) use of any copyrighted material, compliance with ICMJE authorship and competing interests disclosure guidelines and, where applicable, compliance with legal and ethical guidelines on human and animal research participants.

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