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Weight gain prior to entry into a weight-loss intervention study among overweight and obese breast cancer survivors

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Abstract

Purpose—Changes in cancer therapy, in addition to changes in obesity prevalence, suggest the need for a current assessment of weight gain patterns following breast cancer diagnosis. The aim of this study was to evaluate factors associated with weight gain among breast cancer survivors prior to enrolling into a behavioral weight loss intervention.

Methods—Anthropometric measures and data on weight-related factors were collected at baseline on 665 breast cancer survivors. Postdiagnosis weight gain was determined between entry into the trial and previous diagnosis up to 5 years. Multivariate logistic regression analyses were used to evaluate the association between weight gain and influencing factors.

Results—The mean weight gain was 4.5 % body weight (standard deviation=10.6); 44 % of women experienced ≥5 % body weight gain. The risk of weight gain was inversely associated with age (adjusted odds ratio (OR_{adj})=0.97, 95 % confidence interval (95 % CI) 0.95–0.99), Hispanic ethnicity (OR_{adj}=0.30, 95 % CI 0.13–0.68), and overweight (OR_{adj}= 0.11, 95 % CI 0.05–0.23) or obese (OR_{adj}=0.03, 95 % CI 0.02–0.07) status at diagnosis and positively associated with time elapsed since diagnosis (OR_{adj}=1.19/year, 95 % CI 1.04–1.36). Women prescribed aromatase inhibitors were 46 % less likely to gain weight compared to women prescribed selective estrogen-receptor modulators (OR_{adj}=0.54, 95 % CI 0.31–0.93). The risk of weight gain was positively associated with smoking at diagnosis (OR_{adj}=2.69, 95 % CI 1.12–6.49) although this was attributable to women who subsequently quit smoking.

Conclusions—Postdiagnosis weight gain is common and complex and influenced by age, ethnicity, weight, smoking status, time elapsed since diagnosis, and endocrine-modulating therapy.

Implications for cancer survivors—Weight gain continues to be a concern following a diagnosis of breast cancer. Factors influencing this weight gain include age, ethnicity, weight, smoking status, time elapsed since diagnosis, and endocrine-modulating therapy. Effective weight management strategies are needed for this population of women.

Keywords

Breast cancer survivors; Weight gain; Women

Introduction

Obesity contributes to worse prognosis among women diagnosed with either pre- or postmenopausal breast cancer [1]. A 33 % higher risk for overall mortality, as well as breast cancer specific mortality among women who are obese at the time of diagnosis as compared to normal weight women has been reported in a meta-analysis of 43 studies [1]. Weight gain following breast cancer diagnosis also appears to contribute to worse prognosis, although this finding has not been consistently demonstrated [2–6]. Weight gain after a breast cancer diagnosis has also been shown to be associated with increased hot flashes [7, 8], pain [9], and poorer health-related quality of life [10].

Most breast cancer survivors are overweight or obese at diagnosis in part due to excess adiposity being a risk factor for postmenopausal breast cancer [11], as well as the high prevalence of overweight and obesity in the USA [12]. To compound this problem, breast cancer survivors often experience additional weight gain following diagnosis, partly related to the effects of their cancer treatments [13].

Previous studies have evaluated predictors of weight gain following breast cancer diagnosis [14–16], but ongoing changes to cancer therapy, as well as secular changes in the prevalence of overweight and obesity warrant further evaluation of the weight gain patterns following a diagnosis of breast cancer. The objective of this study was to evaluate the factors associated with weight gain among a self-selected cohort of breast cancer survivors prior to enrolling into the Exercise and Nutrition to Enhance Good Health for You (ENERGY) trial, a multicenter, randomized controlled trial of a behavioral weight loss intervention.

Methods

Design and study population

The ENERGY trial is a multi-center randomized controlled trial designed to evaluate the effect of a group-based cognitive-behavioral weight loss program on intentional weight loss and quality of life measures among early stage breast cancer survivors. Details of the design and recruitment of the trial have been published previously [17]. Briefly, 693 women with stage I (≥1 cm), II, or III breast cancer who had been diagnosed 6 months to 5 years prior to study entry and had completed all their initial breast cancer treatment excluding endocrine-modulating therapy, who were ≥21 years of age, and had a body mass index (BMI) of 25 to 45 kg/m^2 were recruited between the fall of 2010 and spring of 2012. Women were recruited from four sites (University of Alabama at Birmingham; University of California, San Diego; University of Colorado Denver; Washington University in St. Louis). Following the baseline study visit, participants were randomized to either a group-based cognitive behavioral weight loss intervention or to a less intensive intervention control group. This trial was approved by the institutional review boards of all collaborating sites, and written informed consent was obtained from all participants.

The current analysis is based on cross-sectional and retrospective data collected by clinic measurements and self-reports at baseline. Subsequent to the baseline publication [17], there was one postrandomization exclusion for a sample of 692 women. Of the 692 women enrolled in the ENERGY trial, 27 women were excluded from this analysis due to missing data on weights at breast cancer diagnosis, mastectomy, endocrine-modulating therapy, Hispanic ethnicity, or smoking status at diagnosis. The analytical sample for this report was therefore 665 breast cancer survivors.

Data collection

At the baseline visit of the ENERGY trial, questionnaires were used to collect self-reported information about education, race, Hispanic ethnicity, smoking status (including the quit date if applicable), menopausal status (including last menstrual period if applicable), and weight at diagnosis. Staff reviewed all questionnaires for completeness. Medical record

review was conducted by trained staff to obtain information on breast cancer diagnosis, treatment including surgery and chemotherapy, and endocrine-modulating therapy. Aromatase inhibitors (AIs) included anastrozole, exemestane, and letrozole whereas selective estrogen-receptor modulators (SERMs) included tamoxifen and raloxifene.

According to study protocol, anthropometric measures of height and weight were conducted following a ≥6-hour fast by trained staff at the baseline visit. Height was measured and rounded to the nearest 0.5 in. by having the participant stand fully erect in stocking or bare feet using a wall-mounted stadiometer and a Frankfort horizontal plane. Weight was measured to the nearest 0.5 lb using a calibrated scale by having the participant empty any heavy objects and/or change from their pockets and without shoes.

Analytical methods

The outcome measure for this study is the percentage weight change between breast cancer diagnosis and entry into the ENERGY trial. This measure was calculated by subtracting the participant's measured weight at ENERGY baseline from the participant's self-reported weight at diagnosis divided by participant's self-reported weight at diagnosis and then multiplying by 100 %. The outcome measure of percentage weight change was then dichotomized into <5 % body weight gain versus ≥5 % body weight gain. This cut point was chosen since modest weight loss of ≥5 % body weight has been recommended to improve health outcomes among overweight and obese individuals [18–20] as well as this cut point has been used previously to evaluate the effect of weight change among breast cancer survivors [3, 4, 21, 22]. To further determine the effect of this particular cut point, weight gain was also analyzed and dichotomized as <10 % body weight gain versus ≥10 % body weight gain as well as a continuous weight change variable.

Bivariate analyses were conducted to evaluate the association between ≥5 % weight gain and demographic, breast cancer treatments, and other potential risk factors. Two-sample *t* tests were used to evaluate continuous variables whereas chi-squared analyses were used for categorical variables. All factors with *p* values <0.20 by bivariate analyses (except for menopausal status at diagnosis) were included in a multivariate unconditional logistic regression model to evaluate the independent association between the two categories of weight gain and other potential risk factors. Since menopausal status and age at diagnosis were highly correlated (Spearman 0.73, $p<0.01$), only age was included in those models. Adjusted odds ratios (OR_{adj}) and 95 % confidence intervals (95 % CI) were reported. The final model adjusted for age at diagnosis, education, Hispanic ethnicity, smoking at diagnosis, BMI at diagnosis, years elapsed since diagnosis, mastectomy, chemotherapy, endocrine-modulating therapy, and oophorectomy. The receiver operating characteristic (ROC) curve as a measure of the C-statistic was used to discriminate among participants. Analyses were also conducted with the outcome variable of ≥10 % weight gain, and linear regression analysis was used to evaluate the association between weight change as a continuous variable adjusted for the variables listed above. Quitting smoking is a risk factor for gaining weight [23–26]; however, we only had 14 women who quit smoking within this time period of which 11 gained weight. Given the small number of women, we were unable to adjust for this factor in the analysis; however, a sensitivity analysis was conducted with

these 14 women removed. Statistical analyses were based on two-sided statistical tests with an alpha-level of 0.05. Analyses were conducted using Stata/IC version 11 (Stata Statistical Software: Release 11, StataCorp LP, College Station, TX).

Results

Among 665 early stage breast cancer survivors who enrolled in the weight loss trial, the mean age was 53.5 years (standard deviation (SD)=9.5) with the majority being postmenopausal at breast cancer diagnosis (57.1 %), White (84.5 %), non-Hispanic (93.4 %) women with at least a college degree (60.1 %) who never smoked (65.6 %) (Table 1). In this cohort, 166 (25.0 %) women gained ≥10 % of their body weight, 126 (19.0 %) women gained between 5.0 % up to 10.0 % of their body weight, 268 (40.3 %) women maintained their weight with less than 5 % change, and 105 women (15.8 %) lost >5 % body weight up to 5 years following their breast cancer diagnosis. The mean weight gain was 4.5 % body weight (SD=10.8). Fifteen percent of the women were at normal BMI (<25 m/kg^2) at breast cancer diagnosis but subsequently gained weight over a mean period of 2.7 years postdiagnosis. Women who experienced ≥5 % weight gain were more likely to be younger, premenopausal, non-Hispanic, smokers, and had a normal BMI upon diagnosis. In the ENERGY trial, there were 30 % diagnosed with stage I (≥1 cm), 52 % with stage II, and 18 % with stage III. The majority of women had received a mastectomy (52.5 %), chemotherapy (77.6 %), and radiation (73.7 %) and also received endocrine-modulating therapy (75.6 %). Women who had ≥5 % gained weight were less likely to have had a mastectomy or use a selective estrogen-receptor modulator (SERM) but more likely to have had an oophorectomy.

The factors that were independently associated with ≥5 % gained weight included younger age at diagnosis (OR_{adj}= 0.97/year, 95 % CI 0.95–s0.99), non-Hispanic ethnicity (OR_{adj}=0.30, 95 % CI 0.13–0.68), being a smoker at the time of diagnosis (OR_{adj}=2.69, 95 % CI 1.12–6.49), and time elapsed since diagnosis (OR_{adj}=1.19/year, 95 % CI 1.04–1.36) (Fig. 1). When the women who quit smoking were removed from the analysis, the association between being a smoker at diagnosis and weight gain was no longer significant (OR_{adj}=1.92, 95 % CI 0.64–5.75). After adjustment, women with a higher BMI at diagnosis were less likely to gain weight as compared to normal weight women; overweight (OR_{adj}= 0.11, 95 % CI 0.05–0.23) and obese (OR_{adj}=0.03, 95 % CI 0.02–0.07). Women on AI alone were 46 % less likely to gain ≥ 5 % as compared to those who were prescribed a SERM after adjustment for covariates (OR_{adj}=0.54, 95 % CI 0.31–0.93). In addition, the greater the amount of time elapsed since diagnosis, the greater the gain in weight such that for each year postdiagnosis the odds of weight gain increased by 19 %. When the analysis was conducted with ≥10 % weight gain versus <10 % gain, comparable estimates were observed although only age, years since diagnosis, and BMI at diagnosis remained significant while adjusting for the same covariates (data not shown). Furthermore, age, Hispanic ethnicity, current smoking, years since diagnosis, and BMI at diagnosis remained significant in the linear regression analysis with change in body weight as the outcome variable (data not shown).

Discussion

This study evaluated weight change patterns among breast cancer survivors who self-selected to enter a weight loss trial and thereby more likely to have a higher starting BMI on average. This study found that among the 665 breast cancer survivors, those who gained more than 5 % of their body weight over an average 2.5 years postdiagnosis, were significantly more likely to be younger, non-Hispanic White, current smokers (attributable to those who quit following diagnosis), less obese, and had a longer time since diagnosis. Additionally, breast cancer survivors who were initially prescribed AIs were less likely to gain ≥5 % body weight as compared to those prescribed SERMs.

In this cohort, the mean weight gain was 4.5 % body weight, and 44 % of women gained ≥5 % body weight postdiagnosis between 6 months to 5 years after diagnosis. Previous studies have reported that 10–48 % of breast cancer survivors gain ≥5 % over an average of 2 to 7 years postdiagnosis [3, 4, 6, 15, 21, 22, 27–32] with rates ranging from 36–46 % among US and European cohorts [3, 4, 15, 21, 22, 31, 32]. In a pooling project of 12,915 breast cancer patients with prospectively collected data from the USA and China, the mean weight gain was 34.7 and 33.7 % in the USA and 36.6 % in China [6]. In the Women's Healthy Eating and Living (WHEL) study, a dietary intervention trial without a weight loss component, 45 % of the 3,088 early-stage breast cancer survivors gained weight from 1 year before breast cancer diagnosis up to 6 years postdiagnosis [21] with similar weight gain observed in an early subset of this cohort [15]. In the Life After Cancer Epidemiology (LACE) cohort study, 36 % of 1,692 breast cancer survivors gained weight from 1 year pre-diagnosis to on average 2 years postdiagnosis [4]. Among smaller cohort studies, weight gain was noted among 46 % of French breast cancer survivors over 15 months [31] and 36 % for US breast cancer survivors over 18 months [32].

In the general population, weight gain is also commonly seen among women as they age [33, 34]. Among healthy women age 30–55 years enrolled in the Nurses' Health Study, a mean weight gain of 1.9 kg (SD=4.6) was observed over the first 4 years of follow-up and 1.6 kg (SD=4.6) over the second 4-year period [34]. In the Australian Longitudinal Study on Women's Health, an average weight gain of 2.42 kg (95 % CI 2.29–2.54) was reported among 8,071 women, age 45 to 55 years old, over 5 years [35]. In the current investigation, breast cancer survivors gained an average of 3 kg (6.5 lbs) which is similar to the 2.4 kg weight gain from the US sites of the pooling project among breast cancer survivors [6].

Even though the national obesity rates are higher in Hispanics as compared with non-Hispanic Whites, Hispanic women had a lower odds of gaining ≥5 % of body weight in the current investigation. Forty-five percent of non-Hispanic Whites gained ≥5 % of body weight as compared with only 30 % of Hispanic breast cancer survivors in our study, though these statistics should be interpreted cautiously given the small number of Hispanic women (*n*=44). In the Healthy Eating, Activity, and Lifestyle (HEAL) study of 514 women with stage 0–IIIA breast cancer, the adjusted mean weight gained experienced by 78 Hispanic women also was lower compared to 436 non-Hispanic Whites women (1.1 vs. 1.9 kg) 3 years following diagnosis [36]. In the WHEL study, no significant difference in weight gain was observed between Hispanic (*n*=154) as compared to non-Hispanic Whites (*n*= 2,625)

breast cancer survivors [21]. Within the prospective SUNSHINE study of 214 non-Hispanic Whites and 91 Hispanic breast cancer survivors, 40 % of Hispanic women and 35 % of non-Hispanic Whites women gained ≥5 % of body weight after a mean follow-up of 6 years [22].

Smoking at the time of breast cancer diagnosis was associated with a 2.7-fold increased risk for weight gain as compared to never smokers. Of the 35 women who were smokers at their breast cancer diagnosis, 40 % (*n*=14) quit smoking following their breast cancer diagnosis. The high rate of quitting may be due in part to smoking being contraindicated for reconstructive surgery [37], thereby these women would likely have been counseled to quit prior to surgery. When these women were removed from the model, the association was no longer significant. Weight gain is common following smoking cessation, with weight gains ranging from 1.5 to 3.8 kg [23–26]. The mechanism for this weight gain is not fully elucidated, but possible factors include increase in energy intake, decrease in resting metabolic rate and physical activity, and changes in lipoprotein lipase activity [38]. In the current investigation, smoking at diagnosis was significantly associated with modest weight gain of ≥5 % of body weight but not with weight gains of 10 % or more.

Breast cancer treatments and treatment-related factors have also been associated with weight gain. Chemotherapy has been associated with weight gain among breast cancer survivors in some [14–16, 21, 39, 40] but not in all studies [22, 28, 32, 41]. A significant association was not observed between chemotherapy and weight gain following a breast cancer diagnosis after adjustment for other factors. As reported previously [3, 4, 6, 15, 21, 22, 32, 39], we observed an inverse association between BMI at diagnosis and subsequent weight gain such that normal weight women were more likely to gain weight as compared to heavier women. This finding remained significant when we used either a 5 %- or 10 %-body weight cut point, or weight change as a continuous variable. The average BMI in this study is considerably higher than in other cohorts, which is expected; given the eligibility criteria included only women who were overweight or obese. In the current investigation, the average BMI at diagnosis was 30.3 kg/m^2 (SD=5.3); 27.7 kg/m^2 (SD=4.1) for those women who gained ≥5 % body weight as compared to 32.4 kg/m^2 (SD=5.3) in those who had <5 % body weight gain. Within the US sites of the pooling project, the average pre-diagnosis BMI was reported at 26.5 kg/m^2 (SD=5.4) [6]. Additionally at the time of diagnosis, 19 % of ENERGY participants reported having a BMI less than 25 kg/m^2 as compared with 30 to 60 % from other investigations [3, 4, 21, 22, 31].

In the current study, women on AI therapy had a 44 % reduced risk of gaining ≥5 % body weight as compared to those on tamoxifen therapy after adjustment for other covariates. A finding of a lower weight gain among women prescribed aromatase inhibitors as compared to tamoxifen has not been previously reported. There is considerable epidemiologic literature, recently reviewed by Vance and colleagues [13], reporting no difference in weight gain associated with tamoxifen among breast cancer treatment, but fewer data are available investigating the association between AIs (anastrozole, exemestane, and letrozole) and weight gain. Within the Arimidex (anastrozole), Tamoxifen Alone, or in Combination (ATAC) trial conducted among 9,366 postmenopausal breast cancer survivors, weight gain was similar in the three study arms with an average weight gain of 1.65 kg or 2.5 % body weight over 2 years [42]. Similarly, no significant difference in weight change was observed

in a small study (*n*= 55) conducted among postmenopausal breast cancer survivors who received exemestane following 2 years of tamoxifen as compared to those who remained on tamoxifen, although a significant reduction in fat mass and the ratio of fat mass to fat-free mass was observed among patients who also took exemestane as compared to those who remained on tamoxifen [43]. Our findings of an association between lower weight gain and AIs was limited to analyses of ≥5 % body weight. When weight change was evaluated with a cut point of ≥10 % or as a continuous variable the association was attenuated and no longer significant. The current standard of care for estrogen-receptor-positive postmenopausal breast cancers recommends adjuvant endocrine-modulating therapy with an AI whereas endocrine-modulating therapy with tamoxifen is recommended for premenopausal women [37]. However, this relationship is complex because many cancer therapies can cause premenopausal women to undergo early menopause [16, 44, 45], and both age and menopausal status are associated with weight gain [3, 4, 15, 27, 32, 36, 39]. The median age of our study cohort at diagnosis was younger than US breast cancer patients that included localized stage; 53 versus 62 years [46]. In our analysis, we adjusted for age and not menopausal status because they were highly correlated. When we used either menopausal status with age or menopausal status alone in the analysis, similar results were observed (data not shown). Given that differences may exist by the type of AI and possible differences in fat free mass, our findings of reduced ≥5 % body weight gain associated with AIs as compared to those prescribed SERMs warrants further investigation.

Strengths and limitation of this epidemiologic study should be acknowledged. This is a large study of well-characterized breast cancer survivors in which treatment variables have been determined through medical chart abstraction. Given the ENERGY trial recruited overweight and obese breast cancer survivors for a weight loss intervention, this study cannot be generalizable to all early stage breast cancer survivors; however, it may be generalizable to breast cancer survivors who are younger and overweight or obese. It also should be noted that our observation of weight gain of ≥5 % body weight among 44 % of participants is similar to what has been observed in other investigations [3, 4, 15, 21, 22, 31, 32]. Due to weight at diagnosis being measured by self-report, there is the potential for misclassification especially among obese women who may underreport their weight [47]. To minimize this potential bias, we adjusted our models for BMI at diagnosis. The difference in mean weight was 0.77 kg (1.7 lb). Since dietary or physical activity measures at diagnosis as well as time on endocrine-modulating therapy or adherence measures were not collected, we were unable to address these factors. Also, given the small number of women who quit smoking following their breast cancer diagnosis, we could not fully explore this relationship.

In conclusion, within this study of breast cancer survivors who enrolled in a weight loss trial, weight gain of ≥5 % was reported by 44 % approximately 2.5 years after diagnosis. Gaining weight following a breast cancer diagnosis may be associated with a higher risk of recurrence and mortality [2–6] as well as cancer-related symptoms and poorer health-related quality of life [7–10]. Furthermore, being overweight or obese is associated with comorbid conditions such as diabetes, cardiovascular disease as well as other cancers [48–50]. Weight and weight gain continues to be an issue for breast cancer survivors that has implications for the patients as well as the healthcare system. Public health efforts need to focus on

developing effective approaches of weight management that can be disseminated within this growing population of women.

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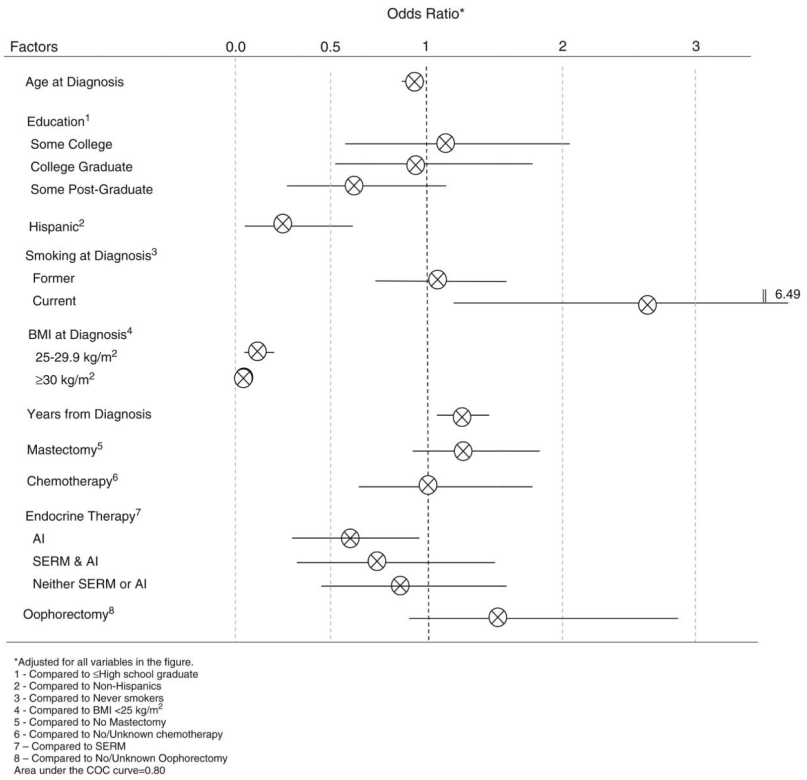

Fig. 1.
Factors independently associated with 5 % weight gain

Table 1

Prevalence of ≥5 % weight gain by demographic and risk factor characteristics among ENERGY trial participants

Characteristic	Overall	<5 % weight gain	≥5 % weight gain	*p* value
N	665	373	292	
Age at diagnosis, mean (SD)	53.5 (9.5)	55.3 (9.4)	51.1 (9.5)	<0.01
Site, *n* (%)				
San Diego	215 (32.3)	124 (57.7)	91 (42.3)	0.81
Denver	177 (26.6)	101 (57.1)	76 (42.9)	
Birmingham	107 (16.1)	60 (56.1)	47 (43.9)	
St Louis	166 (25.0)	88 (53.0)	78 (47.0)	
Education				
≥High school graduate	94 (14.4)	56 (59.6)	38 (40.4)	0.14
Some college	171 (25.7)	90 (52.6)	81 (47.4)	
College graduate	185 (27.8)	95 (51.4)	90 (48.7)	
Some postgraduate	219 (32.3)	132 (61.4)	83 (38.6)	
Hispanic				
No	621 (93.4)	342 (55.1)	279 (44.9)	0.05
Yes	44 (6.6)	31 (70.5)	13 (29.6)	
Race				
White	562 (84.5)	311 (55.3)	251 (44.7)	0.61
Black	68 (10.2)	40 (58.8)	28 (41.2)	
Other	35 (5.3)	22 (5.9)	13 (37.1)	
Smoking status at diagnosis				
Never	436 (65.6)	244 (56.0)	192 (44.0)	<0.01
Former	194 (29.2)	118 (60.8)	76 (39.2)	
Smoker	35 (5.3)	11 (31.4)	24 (68.6)	
Menopausal status at diagnosis				
Premenopausal	199 (29.9)	89 (44.7)	110 (55.3)	<0.01
Perimenopausal	86 (12.9)	47 (54.7)	39 (45.4)	
Postmenopausal	380 (57.1)	237 (62.4)	143 (37.6)	
Years since diagnosis, mean (SD)	2.65 (1.4)	2.5 (1.4)	2.9 (1.4)	<0.01
BMI at diagnosis, kg/m^2				
<25	99 (14.9)	10 (10.1)	89 (89.9)	<0.01
25<30	276 (41.5)	141 (51.1)	135 (48.9)	
≥30	290 (43.6)	222 (76.6)	68 (23.5)	
Height, inches, mean (SD)	64.6 (2.5)	64.5 (2.6)	64.7 (2.3)	0.29
Stage				
I (≥1 cm)	200 (30.1)	119 (59.5)	81 (40.5)	0.46
II	344 (51.7)	190 (55.2)	154 (44.8)	
III	121 (18.2)	64 (52.9)	57 (47.1)	
Mastectomy				

Characteristic	Overall	<5 % weight gain	≥5 % weight gain	*p* value
Yes	349 (52.5)	210 (60.2)	139 (39.8)	0.03
No	316 (47.5)	163 (51.6)	153 (48.4)	
Chemotherapy				
No/unknown	149 (22.4)	91 (61.1)	58 (38.9)	0.16
Yes	516 (77.6)	282 (54.7)	234 (45.4)	
Radiation				
No/unknown	175 (26.3)	93 (53.1)	82 (46.9)	0.36
Yes	490 (73.7)	280 (57.1)	210 (42.9)	
Endocrine-modulating therapy				
SERM	144 (21.7)	63 (45.8)	81 (56.3)	<0.01
AI	269 (40.5)	178 (66.2)	91 (33.8)	
Both SERM and AI	89 (13.4)	42 (47.2)	47 (52.8)	
Neither SERM or AI	163 (24.5)	90 (55.2)	73 (44.8)	
Ooporectomy				
No/unknown	602 (90.5)	349 (58.0)	253 (42.0)	<0.01
Yes	63 (9.5)	24 (38.1)	39 (61.9)	