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Menopausal-related Symptoms in Women One Year After Breast Cancer Surgery

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Abstract

Context—Approximately 60% to 100% of women with breast cancer experience at least one menopausal-related symptom. Little is known about associations between menopausal status and symptoms in women 12 months after breast cancer surgery.

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Objective—Purpose of this study was to evaluate for differences in occurrence, severity, and distress of symptoms between pre- and post-menopausal women 12 months after breast cancer surgery.

Methods—Women with breast cancer (n=327) completed the Menopausal Symptoms Scale, that evaluated the occurrence, severity, and distress of 46 common menopausal-related symptoms. Regression analyses were used to evaluate for between group differences in the seven symptoms that occurred in 30% of the sample (i.e., hot flashes, night sweats, depression, daytime sweats, joint pain or stiffness, wake during the night, numbness or tingling).

Results—Of the 327 breast cancer patients who completed the 12-month assessment, 35.2% were premenopausal and 64.8% were postmenopausal prior to surgery. In the conditional models, when significant interactions were found, the differences in symptom occurrence rates between pre- and postmenopausal patients depended on their age.

Conclusions—Regardless of menopausal status, women reported relatively high occurrence rates for several menopausal symptoms. Associations between symptom occurrence rates and menopausal status depended on the patient's age.

Implications for Practice—During the development of a survivorship care plan, clinicians need assess symptom burden within the context of a woman's menopausal status and salient demographic and clinical characteristics. This approach will assist with the prescription of more effective interventions.

Keywords

symptoms; premenopausal; postmenopausal; breast cancer; surgery

INTRODUCTION

Between 65% and 100% of women with breast cancer experience at least one treatment-induced, menopausal-related symptom.^{1,2} These symptoms include: sleep disturbance, musculoskeletal pain, mood changes, vasomotor symptoms, sexual dysfunction, vaginal dryness and atrophy, cognitive impairment, headaches, weight gain, and fatigue.^{3,4} These menopausal-related symptoms are some of the most common and distressing side effects of breast cancer treatment.^{2,5} Moreover, because of abrupt changes in sex steroid hormones, these symptoms are often more frequent and severe than those experienced during a natural menopausal transition.⁶ For premenopausal women, this unexpected exacerbation of symptoms can have a negative impact on their quality of life (QOL).^{6,7}

The occurrence, severity, and distress from these menopausal-related symptoms vary based on a woman's menopausal status,^{8–10} age,^{4,11} type of cancer treatment (i.e., chemotherapy (CTX), endocrine therapy (ET));^{12,13} and time since completion of treatment; as well as demographic, health and illness, and psychosocial factors.¹² For example, following breast cancer treatment, compared to postmenopausal patients, women who were premenopausal at diagnosis reported more severe vasomotor symptoms,¹⁴ sexual dysfunction,¹⁵ and sleep disturbances.¹⁴ In addition, in another study,¹⁶ the highest menopausal-related symptom burden was reported in the first six months after the completion of primary treatment.

While, the impact of menopausal-related symptoms is well documented,^{1,2,5,12,17-19} little is known about differences in the occurrence, severity, and distress of these symptoms between premenopausal and postmenopausal women one year after breast cancer surgery. The majority of these studies compared differences in the symptom experience of older versus younger women;^{4,11,20} younger women who did or did not experience treatment-induced menopause;^{1,2,10} and/or specific types of treatment (i.e., CTX, tamoxifen, aromatase inhibitors (AIs)).^{12,13,21-24} Moreover, the majority of these studies evaluated a single symptom; a single dimension of the symptom experience; included women several years after a breast cancer diagnosis; and/or did not evaluate the impact of menopausal status on differences in patients' symptom experiences. (for reviews see^{1, 3, 10}) In fact, to our knowledge, only five studies reported on differences in menopausal-related symptoms between pre- and postmenopausal women after primary breast cancer treatment.^{8,9,14,15,25}

These five studies evaluated for associations between pre-diagnosis menopausal status and symptom occurrence^{8,9,25} or severity^{14,15} in women who had received adjuvant CTX and/or ET. Two longitudinal studies evaluated symptom severity before and immediately after CTX.^{28,29} Three cross-sectional studies evaluated menopausal symptom occurrence six months²¹ to several years^{7,27} after diagnosis. Compared to postmenopausal patients, premenopausal women reported higher occurrence rates of hot flashes, night sweats,^{8,9,25} vaginal dryness, and libido reduction.⁸ In one study,⁸ while two-thirds of the menopausal-related symptoms were reported as severe by premenopausal women, differences in severity scores between pre- and postmenopausal women were not evaluated.

Findings from these five studies provide preliminary evidence of differences in the occurrence^{8,9,25} and severity^{14,15} of menopausal-related symptoms based on pre-diagnosis menopausal status. However, a number of limitations warrant consideration. These studies evaluated only a single symptom¹⁴ and/or one dimension of the symptom experience.^{8,9,14,15,25} Two studies did not include relevant covariates such as body mass index (BMI) in their analysis.^{8,25} In two studies, the assessments were done either several years after the cancer diagnosis²⁵ or the time since diagnosis was not reported.⁸ In addition, in two studies,^{14,15} the sample sizes of premenopausal women were relatively small. If differences were found in the symptom experience of pre- versus postmenopausal women after surgery, this information could be used to guide symptom management interventions.

Given the paucity of research on the association between menopausal status prior to surgery and menopausal-related symptoms after primary breast cancer treatment, the purpose of this study was to evaluate for differences in multiple dimensions of the symptom experience (i.e., occurrence, severity, distress) between pre- and postmenopausal women one year after breast cancer surgery. We hypothesized that both groups of women would report the co-occurrence of multiple menopausal-related symptoms. In addition, we hypothesized that compared to postmenopausal women, women who were premenopausal at diagnosis would report higher occurrence rates of and severity and distress ratings for vasomotor symptoms (i.e., hot flashes, night sweats, daytime sweats).

METHODS

The methods for the larger descriptive, longitudinal study that evaluated neuropathic pain and lymphedema in women who underwent breast cancer surgery are described in detail elsewhere.^{26–30} In brief, women were recruited from seven Breast Cancer Centers in Northern California. Women were eligible if they: were 18 years of age; were scheduled for unilateral breast cancer surgery; were able to read, write, and understand English; agreed to participate; and provided written informed consent. Patients were excluded if they had bilateral breast surgery and/or had distant metastases at the time of diagnosis.

Instruments

Patients completed a demographic questionnaire, the Karnofsky Performance Status (KPS) scale,³¹ and the Self-Administered Comorbidity Questionnaire (SCQ).³² Menopausal status was determined by the patient's response (yes/no) at the time of study enrollment to the question "Have you gone through menopause yet (stopped having your menstrual cycle)?".

The Menopausal Symptoms Scale (MSS), that was modified from the Seattle Women's Health Study questionnaire,³³ was used to evaluate the occurrence, severity, and distress of 46 menopausal-related symptoms. Women were asked to indicate whether they experienced each symptom during the past week (i.e., symptom occurrence). If they experienced the symptom, they were asked to rate its severity and distress. Symptom severity was rated on a 0 ('none') to 10 ('intolerable') numeric rating scale (NRS). Symptom distress was rated on a 0 ('not at all distressing') to 10 ('very distressing') NRS. The MSS has well established validity and reliability.³⁴

Study Procedures

The study was approved by the Committee on Human Research at the University of California, San Francisco and by the Institutional Review Boards at each of the study sites. A clinician explained the study, determined the woman's willingness to participate, and introduced her to the research nurse. All patients provided written informed consent. Women completed the enrollment questionnaire an average of four days prior to surgery. For the current study, data from the KPS, SCQ, and MSS that were obtained one year after surgery were analyzed. Medical records were reviewed for disease and treatment information.

Statistical Analysis

Data were analyzed using SPSS Version 23 (IBM, Armonk, NY). Descriptive statistics and frequency distributions were generated on sample characteristics and symptom occurrence rates, severity scores, and distress scores. Using their self-reported status, women were categorized into the premenopausal and postmenopausal groups at enrollment (i.e., prior to surgery). Independent Student t-tests, Mann-Whitney U tests, Fisher Exact tests, and Chi Square analyses were used to evaluate for differences in demographic and clinical characteristics between the two menopausal groups. Characteristics that differed significantly between the menopausal groups were considered for use as potential covariates in the logistic and linear regression analyses.

As part of the evaluation of between group differences, symptom occurrence rates were generated for each symptom and mean scores for severity and distress ratings were calculated for patients who reported a symptom. Unadjusted and adjusted logistic regression analyses were used to evaluate for between group differences in symptom occurrence rates. For symptoms that occurred in $\geq 30\%$ of the total sample, unadjusted and adjusted linear regression analyses were used to evaluate for between group differences in symptom severity and distress scores. First, menopausal status was entered into the regression analysis (unadjusted model). Then, characteristics that were found to be significantly different between the two menopausal groups and identified as potential covariates were added into the model along with menopausal status (adjusted model). Finally, the interaction between age and menopausal status group was evaluated. If the age by menopausal status group interaction was statistically significant, an adjusted stratified analysis was done for premenopausal and postmenopausal women.³⁵ The stratified analyses were done because the interaction term was significant, but the sample size was too small to generate stable combined estimates. A p-value of $<.05$ was considered statistically significant.

RESULTS

Differences in demographic characteristics

Of the 327 women with breast cancer who completed the 12-month assessment, 35.2% were premenopausal and 64.8% were postmenopausal prior to surgery. Compared to postmenopausal women, premenopausal women were significantly younger, were less likely to live alone, and were more likely to be employed (Table 1).

Differences in clinical characteristics

Compared to postmenopausal women, premenopausal women had a lower SCQ score. In addition, a lower percentage of premenopausal women reported high blood pressure, diabetes, ulcer, osteoarthritis, a prior hysterectomy, a prior oophorectomy, were on HRT prior to surgery, and had external beam radiation therapy (RT) during the prior 12 months. A higher percentage of premenopausal women had a mastectomy versus conservation surgery, had breast reconstruction during the prior 12 months, received adjuvant CTX during the prior 12 months, and had undergone genetic testing for BRCA1 and BRCA2 (Table 1).

Differences in symptom occurrence rates and total number of symptoms

Occurrence rates for the 46 symptoms on the MSS and for the top ten occurring symptoms are listed in the Supplementary Table 1 and in Table 2, respectively. No differences were found in the total number of symptoms reported by premenopausal versus postmenopausal women. The five symptoms with the highest occurrence rates in premenopausal women were: wake during the night, hot flashes, fatigue or tiredness, difficulty falling asleep, and night sweats. While wake during the night, fatigue or tiredness and hot flashes, were among the 5 most common symptoms in the postmenopausal group, they reported two different symptoms (i.e., joint pain or stiffness and waking too early).

Unadjusted and adjusted analyses of symptoms with higher occurrence rates in premenopausal women—As shown in Table 3, in the unadjusted models,

premenopausal patients reported higher occurrence rates for eating more than usual, skin breakout/acne, hostility, weight gain, irritability, and lost sexual interest. In the multivariate analyses, after adjusting for nine covariates, no differences in these symptoms' occurrence rates were found between the two menopausal groups.

Unadjusted and adjusted analyses of symptoms with higher occurrence rates in postmenopausal women—In the unadjusted and adjusted analyses, none of the symptom occurrence rates were significantly higher in the postmenopausal group.

Differences in occurrence rates for symptoms with interaction effects—As shown in Table 4, in the unadjusted models, premenopausal women reported higher occurrence rates for hot flashes, night sweats, depression, and daytime sweats. Postmenopausal women reported higher occurrence rates for joint pain or stiffness.

In the adjusted models that evaluated seven symptoms for which significant interactions were found between age and menopausal status (i.e., hot flashes, night sweats, depression, daytime sweats, joint pain or stiffness, wake during the night, numbness or tingling), the differences in symptom occurrence rates between pre- and post-menopausal women depended on their age. In the premenopausal group, as age increased, women were significantly more likely to report depression and joint pain or stiffness. In the postmenopausal group, as age increased, women were significantly less likely to report hot flashes, night sweats, depression, daytime sweats, wake during the night, and numbness or tingling.

Differences in symptom severity scores

The severity scores for the 46 as well as for the ten symptoms with the highest mean severity scores are listed in the Supplementary Table 1 and in Table 2, respectively. For premenopausal women, the five symptoms with the highest severity scores were: cramps, diarrhea, lost sexual interest, fatigue or tiredness, and mood swings. While lost sexual interest and cramps were among the five most severe symptoms in the postmenopausal group, they reported three different symptoms (i.e., abdominal bloating, vaginal dryness, hot flashes).

Unadjusted and adjusted analyses of symptoms with higher severity scores in premenopausal women—As shown in Table 5, in the unadjusted models for symptoms that occurred in >30.0% of the sample, premenopausal women reported higher symptom severity scores for impatience and irritability. In the adjusted analysis, premenopausal women reported higher symptom severity scores for fatigue.

Unadjusted and adjusted analyses of symptoms with higher severity scores in postmenopausal women—In the unadjusted and adjusted analyses, none of the severity scores were significantly higher in the postmenopausal group.

Differences in symptom distress scores

The distress scores for the 46 symptoms, as well as for the ten symptoms with the highest mean distress scores, are listed in the Supplementary Table 1 and in Table 2, respectively. For premenopausal women, the five symptoms with the highest distress scores were: weight gain, diarrhea, swollen hands/feet, hostility, and tearful/crying spells. While weight gain was one of the five most distressing symptoms in the postmenopausal women, they reported four different symptoms (i.e., lost sexual interest, cramps, abdominal bloating, eating more than usual).

Unadjusted and adjusted analyses of symptoms with higher distress scores in premenopausal women—As shown in Table 5, in the unadjusted analyses for symptoms that occurred in >30% of the sample, premenopausal women reported higher distress scores for impatience. In the adjusted analyses, none of the distress scores were significantly higher in premenopausal women.

Unadjusted and adjusted analyses of symptoms with higher distress scores in postmenopausal women—In the unadjusted and adjusted analyses, none of the symptom distress scores were significantly higher in the postmenopausal women.

DISCUSSION

This study is the first to describe associations between preoperative menopausal status and symptom occurrence, severity, and distress in women one year after breast cancer surgery. Consistent with previous studies,^{1,2,4,36} our first hypothesis was supported. All women, regardless of menopausal status, reported an average of 11 co-occurring symptoms (range of 0 to 38). Our second a priori hypothesis was only partially supported. After accounting for multiple demographic, clinical, and treatment characteristics, the relationship between menopausal status and the occurrence rates for vasomotor symptoms was dependent on women's age. In terms of severity, fatigue was the only symptom that was more severe in premenopausal women. Of note, no differences in symptom distress ratings were found between the menopausal groups.

Findings from this study have a number of clinical implications. For example, our findings suggest that women who used HRT prior to their breast cancer diagnosis were two to three times more likely to report vasomotor symptoms even one year after stopping the medication. Therefore, previous use of HRT should be assessed as part of survivorship care. Given the large number of symptoms and dimensions evaluated, the discussion will focus primarily on significant differences in symptom dimensions found between pre- and postmenopausal women and the interaction of age and menopausal status.

Symptom Occurrence

Differences in the occurrence of symptoms with interaction effects—One of the strengths of this study is that for each of the symptoms, after controlling for clinically meaningful characteristics, the interaction between menopausal status and age was evaluated. For example, significant interactions were found between age and menopausal

status for all three vasomotor symptoms (i.e., hot flashes, night and daytime sweats). While this specific interaction was not reported previously, relative to younger and older premenopausal women, it is common for older premenopausal and younger postmenopausal women to report vasomotor symptoms.^{36,37} Similarly, in our study, as premenopausal women aged, they were 25% to 48% less likely to report vasomotor symptoms. However, contrary to previous findings,¹ as premenopausal women's age increased, they did not report higher occurrence rates for vasomotor symptoms. Our sample size may have been too small to detect the effects of age on the occurrence of hot flashes in our premenopausal women.

While the occurrence of nighttime awakenings was the most common symptom in both pre- and postmenopausal women, a significant interaction was found between menopausal status and age. While no studies evaluated for interaction effects, in previous reports, pre- and postmenopausal women differed on post-treatment occurrence rates for restless sleep¹⁰ and insomnia.⁸ Moreover, consistent with prior reports,¹⁵ none of the other covariates in the multivariate analysis predicted variations in the occurrence of wake during the night. Given the high occurrence rates of nighttime awakenings in women with and without breast cancer, the causes for this symptom warrant additional investigation so that appropriate interventions can be prescribed.¹⁵

Numbness and tingling are associated with the neurotoxic effects of CTX.³⁸ Therefore, it is not surprising that women in our study who were treated with CTX in the past 12 months were 2.5 times more likely to report this symptom. Given that numbness and tingling can be related to hormonal changes during menopause³⁹ and/or the neurotoxicity of CTX,³⁸ the etiology of these symptoms warrant evaluation in future studies.

Symptom Severity

Fatigue was the only symptom that was more severe in premenopausal women and in women with a higher level of comorbidity. Consistent with a previous report,⁴⁰ premenopausal women were more likely to report the occurrence as well as more severe fatigue after CTX and during the first three years of hormone therapy. Given that fatigue is common, moderately severe, persists over time,¹⁹ and may be associated with a higher symptom burden,⁴¹ it warrants ongoing assessment and management.

While we hypothesized that premenopausal women would report higher severity scores for vasomotor symptoms, our findings are not consistent with previous reports. In previous studies, compared to postmenopausal women with breast cancer, premenopausal women reported more severe vasomotor symptoms¹⁵ and hot flashes¹⁴ after CTX and were more likely to report severe hot flashes while taking tamoxifen.²⁵ These inconsistent findings may be related to differences in how symptoms were assessed and categorized, the timing of the assessments, and failure to control for significant covariates in the analyses.

The ranking of the five most severe symptoms differed by menopausal group. Moreover, regardless of menopausal status, the ten most severe symptoms were in the moderate severity range. In fact, for the entire sample, using a moderate cutoff score of >4.0,⁴² 13 of the 46 symptoms were in the moderate to severe range. A survivorship care plan, that

includes aggressive symptom management interventions, is warranted after surgery to prevent the escalation of symptoms during the subsequent year.

Symptom Distress

No between group differences in symptom distress scores were identified. In contrast, previous reports suggested that younger women were more bothered by menopausal symptoms than older women.^{21,43–45} For example, compared to women older than 60, younger women reported that vasomotor symptoms, vaginal symptoms, and weight problems were more bothersome.²¹ However, the influence of menopausal status was not evaluated in this study.

In our study, the analysis of severity and distress ratings included only those women who reported the occurrence of the symptom. The exclusion of women who did not experience the symptom provides a more accurate evaluation of the impact of each symptom.³ However, in most of the previous studies, the analyses included women who did not have the symptom. In addition, one of the most common instruments used to evaluate menopausal-related symptoms in breast cancer patients is the Breast Cancer Prevention Trial (BCPT) checklist.^{4,46} The BCPT assesses “bother” using a 0 “not at all” to 4 “extremely” Likert scale. While this instrument is valid and reliable,⁴⁶ the term “bother” is used interchangeably with “severity”,^{10,21} “intensity”,⁴⁷ and “distress”.⁴⁸ These differences make comparisons of severity and distress scores across studies difficult.

Similar to severity, the rankings of the five most distressing symptoms differed by menopausal status. Regardless of menopausal status, many of the ten most distressing symptoms were in the moderate range. While both menopausal groups reported approximately 11 symptoms, premenopausal women reported a higher number of distressing symptoms. This difference highlights the importance of comprehensive assessments of all symptom dimensions in women after breast cancer treatment.

Limitations

Several limitations warrant consideration. The woman’s self-report of menopausal status at diagnosis was used to create the two groups. Moreover, the inclusion of five women who were on HRT in the premenopausal group suggests that some women may have been perimenopausal. While the gold standard for determining menopausal status includes an assessment of menstrual cycle, hormonal levels, and symptoms,⁴⁹ previous studies support the validity and reliability of self-report.^{18,50} Moreover, while menopausal status was not re-evaluated at 12 months, this study’s aim was to compare pre-surgical menopausal status and women’s symptom experience at 12 months after surgery. In addition, testing for interactions between age and menopausal status accounted for variations between younger and older pre- and postmenopausal women. Some of the symptoms on the MSS (e.g., cramps) may be interpreted differently by pre- (i.e., menstrual cramps) versus post- (i.e., gastrointestinal cramps) menopausal women. Lastly, the majority of women in this study was Caucasian and well educated, which limits the generalizability of our findings.

Implications for Clinical Practice and Research

Regardless of menopausal status, at one year following surgery, our patients experienced multiple co-occurring symptoms that were in the moderate to severe range for both severity and distress. Moreover, similar to previous reports of women after breast cancer treatment,^{2,10,11} the occurrence of menopausal-related symptoms varied based on menopausal status, as well as demographic (e.g., age), clinical (e.g., level of comorbidity), and treatment (e.g., prior HRT use, receipt of adjuvant CTX in prior 12 months) characteristics. Of note, all of the differences in symptom occurrence rates depended on the interaction between age and menopausal status. Accordingly, both characteristics warrant consideration during the assessment of symptom burden. Given that these menopausal symptoms negatively impact women's well-being after primary breast cancer treatment, assessment and education prior to and during therapy may help manage expectations of symptom burden over time. Findings from this study can be used by clinicians to focus their assessments and individualize patient education and interventions.

Given the various etiologies for menopausal-related symptoms, longitudinal evaluations of how symptoms change from pre- to post-treatment are warranted. These time-sensitive evaluations may identify other causal associations between menopausal status and symptom burden (e.g., pre-surgical anxiety). Moreover, studies of the inter-relationships among symptoms (i.e., symptom clusters) using multiple dimensions of the symptom experience are warranted. Increased information on menopausal symptom clusters could be used to support future studies on the common and distinct mechanisms that underlie these symptom clusters, well as interventions to manage single and multiple menopausal-related symptoms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Differences in demographic and clinical characteristics between premenopausal and postmenopausal women 12 months after breast cancer surgery

| Demographic characteristics | Premenopausal n=115 (35.2%) | Postmenopausal n=212 (64.8%) | Statistics |
|---|--------------------------------|---------------------------------|------------------|
| | Mean (SD) | Mean (SD) | |
| Age (years) | 45.2 (6.2) | 61.0 (10.4) | t=-17.21; p<.001 |
| Education (years) | 15.9 (2.4) | 15.6 (2.8) | t=1.04; p=.296 |
| | % (n) | % (n) | |
| Ethnicity | | | |
| White | 63.5 (73) | 68.9 (146) | FE; p=.328 |
| Non-white | 36.5 (42) | 31.1 (66) | |
| Lives alone (% yes) | 13.9 (16) | 28.4 (60) | FE; p=.004 |
| Married/partnered (% yes) | 35.7 (41) | 44.8 (95) | FE; p=.127 |
| Currently working for pay (% yes) | 60.5 (69) | 44.5 (94) | FE; p=.007 |
| Total annual household income | | | U; p=.150 |
| < \$10,000 to \$19,999 | 6.9 (7) | 5.4 (9) | |
| \$20,000 to \$99,000 | 47.5 (48) | 59.9 (100) | |
| \$100,000 | 45.5 (46) | 34.7 (58) | |
| Clinical characteristics | Mean (SD) | Mean (SD) | |
| Body mass index (kg/m ²) | 25.9 (5.6) | 27.1 (6.1) | t=-1.82; p=.069 |
| Karnofsky Performance Status score | 94.2 (9.8) | 93.6 (10.0) | t=0.50; p=.620 |
| Self-Administered Comorbidity Scale score | 3.1 (2.2) | 4.4 (3.4) | t=-4.02; p<.001 |
| Number of menopausal symptoms | 12.0 (8.7) | 10.3 (8.0) | t=1.83; p=.068 |
| Months since diagnosis | 13.6 (2.9) | 13.8 (2.3) | t=-0.52; p=.601 |
| | % (n) | % (n) | |
| Occurrence of comorbid conditions (% and number of women who reported each comorbid condition from the Self-Administered Comorbidity Questionnaire) | | | |
| Heart disease | 1.7 (2) | 5.7 (12) | FE; p=.150 |
| High blood pressure | 14.8 (17) | 38.7 (81) | FE; p<.001 |
| Lung disease | 1.7 (2) | 2.4 (5) | FE; p=1.000 |
| Diabetes | 1.7 (2) | 12.7 (27) | FE; p<.001 |
| Ulcer | 0.0 (0) | 5.2 (11) | FE; p=.010 |
| Kidney disease | 0.0 (0) | 0.0 (0) | FE; p=1.00 |
| Liver disease | 0.0 (0) | 1.9 (4) | FE; p=.302 |

| Demographic characteristics | Premenopausal n=115 (35.2%) | Postmenopausal n=212 (64.8%) | Statistics |
|---|--------------------------------|---------------------------------|-------------------------|
| | Mean (SD) | Mean (SD) | |
| Anemia | 5.2 (6) | 4.3 (9) | FE; p=.783 |
| Depression | 13.0 (15) | 16.5 (35) | FE; p=.427 |
| Osteoarthritis | 9.6 (11) | 22.2 (47) | FE; p=.004 |
| Back pain | 22.6 (26) | 24.1 (51) | FE; p=.787 |
| Rheumatoid arthritis | 3.5 (4) | 5.2 (11) | FE; p=.588 |
| Diagnosed with mastitis (% yes) | 13.0 (15) | 12.7 (27) | FE; p=1.000 |
| Diagnosed with fibrocystic disease (% yes) | 15.8 (18) | 23.4 (48) | FE; p=.115 |
| Exercise on a regular basis (% yes) | 77.4 (89) | 73.5 (155) | FE; p=.525 |
| Ever breast fed (% yes) | 50.4 (58) | 43.4 (92) | FE; p=.246 |
| Prior hysterectomy (% yes) | 4.3 (5) | 17.9 (38) | FE; p<.001 |
| Prior oophorectomy (% yes) | 4.3 (5) | 13.7 (29) | FE; p=.008 |
| Type of surgery | | | |
| Breast conservation | 72.2 (83) | 84.4 (179) | X ² ; p=.009 |
| Mastectomy | 27.8 (32) | 15.6 (33) | |
| Sentinel lymph node biopsy (% yes) | 86.1 (99) | 84.0 (178) | FE; p=.748 |
| Axillary lymph node dissection (% yes) | 35.1 (40) | 31.6 (67) | FE; p=.538 |
| Re-excision or mastectomy during the 12 months (% yes) | 33.9 (39) | 27.4 (58) | FE; p=.254 |
| Breast reconstruction during the 12 months (% yes) | 20.9 (24) | 9.0 (19) | FE; p=.003 |
| Received neoadjuvant chemotherapy (% yes) | 15.8 (18) | 19.8 (42) | FE; p=.454 |
| Received adjuvant chemotherapy during the 12 months (% yes) | 42.6 (49) | 28.3 (60) | FE; p=.010 |
| Received external beam radiation therapy during the 12 months (% yes) | 65.2 (75) | 76.9 (163) | FE; p=.027 |
| On hormonal therapy during the 12 months (% yes) | 65.2 (75) | 62.3 (132) | FE; p=.632 |
| On HRT prior to surgery (% yes) | 4.4 (5) | 24.6 (52) | FE; p<.001 |
| Stage of disease | | | |
| Stage 0 | 21.6 (25) | 18.0 (38) | U; p=.264 |
| Stage I | 41.4 (48) | 39.3 (83) | |
| Stage IIA and IIB | 31.9 (37) | 35.5 (75) | |
| Stage IIIA, IIIB, IIIC, and IV | 5.2 (6) | 7.1 (15) | |
| Estrogen receptor positive (% yes) | 78.3 (90) | 76.8 (162) | FE; p=.784 |
| Progesterone receptor positive (% yes) | 77.4 (89) | 67.3 (142) | FE; p=.057 |

| Demographic characteristics | Premenopausal n=115 (35.2%) | Postmenopausal n=212 (64.8%) | Statistics |
|------------------------------------|--------------------------------|---------------------------------|-------------------------------|
| | Mean (SD) | Mean (SD) | |
| HER2/neu receptor positive (% yes) | 16.5 (17) | 16.9 (32) | FE; p=1.000 |
| BRCA1 and BRCA2 genetic testing | | | X ² =10.78; p=.004 |
| Positive | 2.6 (3) | 1.0 (2) | |
| Negative | 18.4 (21) | 7.2 (15) | |
| Not done | 78.9 (90) | 91.9 (192) | |

Abbreviations: BRCA = breast cancer; FE = Fisher's Exact; HER2/neu = human epidermal growth factor receptor 2; HRT = hormone replacement therapy; kg = kilogram; m² = meters squared; SD = standard deviation; U = Mann Whitney U test

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Table 2

Differences between premenopausal and postmenopausal women in rankings of symptoms with the highest occurrence, severity, and distress ratings 12 months after breast cancer surgery

| Occurrence Rates | | | | |
|-------------------------------|---------------------------|------------|---------------------------|------------|
| Rank | Premenopausal | % of women | Postmenopausal | % of women |
| | Symptom | | Symptom | |
| 1 | Wake during the night | 61.7 | Wake during the night | 63.7 |
| 2 | Hot flashes | 58.3 | Joint pain or stiffness | 51.9 |
| 3 | Fatigue or tiredness | 54.8 | Fatigue or tiredness | 50.0 |
| 4 | Difficulty falling asleep | 44.3 | Hot flashes | 45.3 |
| 5 | Night sweats | 44.3 | Waking too early | 42.9 |
| 6 | Impatience | 43.5 | Difficulty falling asleep | 42.0 |
| 7 | Irritability | 41.7 | Backache or neckache | 35.8 |
| 8 | Waking too early | 41.7 | Impatience | 34.4 |
| 9 | Anxiety | 40.9 | Night sweats | 32.5 |
| 10 | Backache or neckache | 40.9 | Anxiety | 31.6 |
| Severity Rating [†] | | | | |
| Rank | Symptom | Mean (SD) | Symptom | Mean (SD) |
| 1 | Cramps | 5.1 (2.5) | Lost sexual interest | 6.2 (2.6) |
| 2 | Diarrhea | 5.0 (3.0) | Cramps | 4.6 (2.8) |
| 3 | Lost sexual interest | 4.7 (2.6) | Abdominal bloating | 4.6 (2.7) |
| 4 | Fatigue or tiredness | 4.7 (2.6) | Vaginal dryness | 4.6 (2.9) |
| 5 | Mood swings | 4.5 (2.8) | Hot flashes | 4.4 (2.1) |
| 6 | Hot flashes | 4.4 (2.5) | Night sweats | 4.3 (2.0) |
| 7 | Headache | 4.4 (2.6) | Joint pain or stiffness | 4.2 (2.3) |
| 8 | Backache or neckache | 4.3 (2.9) | Difficulty falling asleep | 4.2 (2.6) |
| 9 | Daytime sweats | 4.3 (2.4) | Daytime sweats | 4.2 (1.8) |
| 10 | Joint pain or stiffness | 4.3 (2.3) | Wake during the night | 4.1 (2.5) |
| Distress Rating ^{††} | | | | |
| Rank | Symptom | Mean (SD) | Symptom | Mean (SD) |
| 1 | Weight gain | 5.1 (3.3) | Lost sexual interest | 5.6 (3.4) |
| 2 | Diarrhea | 5.1 (3.8) | Cramps | 5.3 (3.3) |
| 3 | Swollen hands/feet | 4.9 (2.9) | Abdominal bloating | 4.8 (3.7) |
| 4 | Hostility | 4.8 (3.2) | Weight gain | 4.4 (3.4) |
| 5 | Tearful/crying spells | 4.5 (2.9) | Eating more than usual | 4.2 (3.1) |
| 6 | Anger | 4.5 (3.0) | Joint pain or stiffness | 4.0 (2.7) |
| 7 | Mood swings | 4.5 (3.2) | Panic feelings | 4.0 (2.3) |
| 8 | Anxiety | 4.3 (3.0) | Difficulty falling asleep | 4.0 (2.8) |
| 9 | Headache | 4.2 (3.0) | Depression | 3.9 (2.9) |

| Occurrence Rates | | | | |
|------------------|----------------------|------------|-----------------|------------|
| Rank | Premenopausal | % of women | Postmenopausal | % of women |
| | Symptom | | Symptom | |
| 10 | Nausea/upset stomach | 4.2 (3.0) | Vaginal dryness | 3.9 (2.9) |

Abbreviation: SD = standard deviation

⁺Symptom severity scores ranged from 0 (none) to 10 (intolerable).

⁺⁺Symptom distress scores ranged from 0 (not at all distressing) to 10 (very distressing).

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| SYMPTOM OCCURRENCE | | | LOGISTIC REGRESSION RESULTS | | | | | | | |
|--------------------|-------------------|----------------------------|---|------------------|------------|---------|----------------|------------|---------|--|
| Symptom | Occurrence rate % | | Covariate | Unadjusted Model | | | Adjusted Model | | | |
| | PRE (n=115) | POST (n=212) | | OR | CI | p-value | OR | CI | p-value | |
| Hostility | 16.5 | 7.1 | | | | | | | | Overall Model X ² =15.12; p=.128 |
| | | | Menopausal status * | 0.38 | 0.19, 0.79 | .009 | 0.59 | 0.23, 1.54 | .284 | |
| | | | Age (in 5 year increments) | | | | 0.77 | 0.62, 0.96 | .021 | |
| | | | Lives alone | | | | 0.96 | 0.36, 2.52 | .926 | |
| | | | Working for pay | | | | 0.85 | 0.40, 1.80 | .667 | |
| | | | SCQ score | | | | 1.09 | 0.94, 1.26 | .240 | |
| | | | Prior HRT | | | | 1.56 | 0.51, 4.75 | .433 | |
| | | | Adjuvant chemotherapy during 12 months | | | | 0.83 | 0.38, 1.82 | .637 | |
| | | | Radiation therapy during 12 months | | | | 1.54 | 0.55, 4.25 | .410 | |
| | | | Reconstruction during 12 months | | | | 1.31 | 0.36, 4.83 | .680 | |
| | | | Type of surgery: conservation (ref) vs mastectomy | | | | 1.05 | 0.31, 3.54 | .940 | |
| | | | | | | | | | | Overall Model X ² =17.02; p=.074 |
| | Weight gain | 37.1 | 24.6 | | | | | | | |
| | | | Menopausal status * | 0.57 | 0.35, 0.93 | .025 | 0.94 | 0.48, 1.83 | .846 | |
| | | | Age (in 5 year increments) | | | | 0.87 | 0.75, 1.01 | .062 | |
| | | | Lives alone | | | | 0.99 | 0.53, 1.84 | .963 | |
| | | | Working for pay | | | | 0.99 | 0.59, 1.66 | .980 | |
| | | | SCQ score | | | | 1.01 | 0.92, 1.12 | .798 | |
| | | | Prior HRT | | | | 0.64 | 0.29, 1.38 | .254 | |
| | | | Adjuvant chemotherapy during 12 months | | | | 1.38 | 0.82, 2.34 | .228 | |
| | | | Radiation therapy during 12 months | | | | 1.50 | 0.76, 2.98 | .241 | |
| | | | Reconstruction during 12 months | | | | 0.82 | 0.32, 2.09 | .680 | |
| | | | Type of surgery: conservation (ref) vs mastectomy | | | | 1.60 | 0.72, 3.6 | .251 | |
| | | | | | | | | | | Overall Model X ² =12.25; p=.269 |
| Irritability | | 41.7 | 29.7 | | | | | | | |
| | | | Menopausal status | 0.58 | 0.36, 0.94 | .027 | 0.60 | 0.32, 1.15 | .126 | |
| | | Age (in 5 year increments) | | | | 0.94 | 0.82, 1.07 | .342 | | |

| SYMPTOM OCCURRENCE | | LOGISTIC REGRESSION RESULTS | | | | | | | | | |
|---|-------------------|-----------------------------|---|------------------|------------|-------------------------------|----------------|------------|---------|------------|------|
| Symptom | Occurrence rate % | | Covariate | Unadjusted Model | | | Adjusted Model | | | | |
| | PRE (n=115) | POST (n=212) | | OR | CI | p-value | OR | CI | p-value | | |
| Lost sexual interest | 22.4 | 13.7 | Lives alone | 0.98 | 0.55, 1.75 | .939 | 0.98 | 0.55, 1.75 | .939 | | |
| | | | Working for pay | 0.93 | 0.57, 1.51 | .769 | 0.93 | 0.57, 1.51 | .769 | | |
| | | | SCQ score | 1.07 | 0.98, 1.17 | .144 | 1.07 | 0.98, 1.17 | .144 | | |
| | | | Prior HRT | 1.13 | 0.58, 2.20 | .714 | 1.13 | 0.58, 2.20 | .714 | | |
| | | | Adjuvant chemotherapy during 12 months | 0.90 | 0.54, 1.50 | .684 | 0.90 | 0.54, 1.50 | .684 | | |
| | | | Radiation therapy during 12 months | 1.63 | 0.85, 3.10 | .140 | 1.63 | 0.85, 3.10 | .140 | | |
| | | | Reconstruction during 12 months | 0.78 | 0.32, 1.91 | .588 | 0.78 | 0.32, 1.91 | .588 | | |
| | | | Type of surgery: conservation (ref) vs mastectomy | 1.85 | 0.86, 4.00 | .117 | 1.85 | 0.86, 4.00 | .117 | | |
| | | | Overall Model | | | X ² =26.27; p=.003 | | | | | |
| | | | Menopausal status* | | | 0.54 | 0.30, 0.98 | .039 | 1.18 | 0.53, 2.59 | .687 |
| Age (in 5 year increments) | | | 0.77 0.64, 0.92 .005 | | | | | | | | |
| Lives alone | | | 0.18 0.05, 0.60 .005 | | | | | | | | |
| Working for pay | | | 0.92 0.49, 1.71 .784 | | | | | | | | |
| SCQ score | | | 1.03 0.91, 1.16 .680 | | | | | | | | |
| Prior HRT | | | 1.30 0.53, 3.2 .571 | | | | | | | | |
| Adjuvant chemotherapy during 12 months | | | 0.99 0.52, 1.91 .987 | | | | | | | | |
| Radiation therapy during 12 months | | | 0.69 0.31, 1.56 .377 | | | | | | | | |
| Reconstruction during 12 months | | | 1.18 0.4, 3.51 .763 | | | | | | | | |
| Type of surgery: conservation (ref) or mastectomy | | | 0.61 0.22, 1.72 .353 | | | | | | | | |

Abbreviations: CI = confidence interval; HRT = hormone replacement therapy; OR = odds ratio; PRE = premenopausal; POST = postmenopausal; ref = reference group; SCQ = Self-administered Comorbidity Questionnaire; vs = versus

* reference group = premenopausal women

Table 4

Results of unadjusted and adjusted logistic regression analyses that evaluated for differences between premenopausal and postmenopausal women in symptom occurrence rates with interaction effects 12 months after breast cancer surgery

| LOGISTIC REGRESSION RESULTS | | | | | | | | | |
|--|---|------|------------------|------|----------------|-------------------|------------|------------|------|
| Symptom | Covariates | | Unadjusted Model | | Adjusted Model | | | | |
| | OR | CI | OR | CI | OR | CI | | | |
| Logistic Regression Results for Total Sample | | | | | | | | | |
| Hot flashes PRE = 58.3% POST = 45.3% | Overall Model X ² =59.53; p<.001 | | | | | | <.001 | | |
| | Menopausal status* | 0.56 | 0.35, 0.89 | .015 | 5681.12 | 136.43, 236576.94 | <.001 | | |
| | Age (in 5 year increments) | | | | | | 1.00, 1.92 | .050 | |
| | Lives alone | | | | | | 0.51, 1.65 | .770 | |
| | Working for pay | | | | | | 0.39, 1.07 | .089 | |
| | SCQ score | | | | | | 0.97, 1.17 | .188 | |
| | Prior HRT | | | | | | 1.10, 4.36 | .026 | |
| | Adjuvant chemotherapy during 12 months | | | | | | 0.66, 1.87 | .692 | |
| | Radiation therapy during 12 months | | | | | | 0.59, 2.10 | .739 | |
| | Reconstruction during 12 months | | | | | | 0.63, 3.68 | .352 | |
| | Type of surgery: conservation (ref) vs mastectomy | | | | | | 0.44, 2.10 | .921 | |
| | Age × menopausal status | | | | | | 0.29, 0.61 | .000 | |
| | Adjusted Regression of Hot Flashes Occurrence on Age, Stratified by Menopausal Status | | | | | | | | |
| | Premenopausal | | | | | | 1.43 | 0.99, 2.06 | .055 |
| Postmenopausal | | | | | | 0.56 | 0.46, 0.69 | <.001 | |
| Night Sweats PRE = 44.3% POST = 32.5% | Overall Model X ² =41.70; p<.001 | | | | | | <.001 | | |
| | Menopausal status* | 0.59 | 0.37, 0.94 | .026 | 1132.50 | 29.38, 43655.1 | <.001 | | |
| | Age (in 5 year increments) | | | | | | 1.30 | 0.94, 1.80 | .117 |
| | Lives alone | | | | | | 1.05 | 0.57, 1.92 | .872 |
| | Working for pay | | | | | | 0.97 | 0.59, 1.59 | .892 |
| | SCQ score | | | | | | 1.04 | 0.95, 1.15 | .397 |

| LOGISTIC REGRESSION RESULTS | | | | | | | | | | |
|--|--|------------------|------------|---------|----------------|----------------|---------|---------|---------|--|
| Symptom | Covariates | Unadjusted Model | | | Adjusted Model | | | p-value | p-value | |
| | | OR | CI | p-value | OR | CI | p-value | | | |
| Depression PRE = 34.5% POST = 24.5% | Prior HRT | | | | 2.35 | 1.18, 4.67 | | | .015 | |
| | Adjuvant chemotherapy during 12 months | | | | 1.04 | 0.62, 1.75 | | | .872 | |
| | Radiation therapy during 12 months | | | | 0.85 | 0.45, 1.62 | | | .632 | |
| | Reconstruction during 12 months | | | | 0.91 | 0.38, 2.20 | | | .837 | |
| | Type of surgery: conservation (ref) vs mastectomy | | | | 1.28 | 0.58, 2.82 | | | .536 | |
| | Age × menopausal status | | | | 0.49 | 0.34, 0.71 | | | <.001 | |
| | Adjusted Regression of Night Sweats Occurrence on Age, Stratified by Menopausal Status | | | | | | | | | |
| | Premenopausal | | | | 1.31 | 0.92, 1.88 | | | .140 | |
| | Postmenopausal | | | | 0.63 | 0.52, 0.76 | | | <.001 | |
| | Overall Model X ² =30.92; p=.001 | | | | | | | | | |
| Daytime sweats PRE = 39.7% POST = 26.9% | Menopausal status* | 0.60 | 0.37, 0.99 | .047 | 338.93 | 6.92, 16611.16 | | | .003 | |
| | Age (in 5 year increments) | | | | 1.41 | 0.98, 2.02 | | | .061 | |
| | Lives alone | | | | 0.89 | 0.47, 1.71 | | | .733 | |
| | Working for pay | | | | 1.02 | 0.60, 1.73 | | | .937 | |
| | SCQ score | | | | 1.18 | 1.07, 1.30 | | | .001 | |
| | Prior HRT | | | | 0.83 | 0.39, 1.76 | | | .620 | |
| | Adjuvant chemotherapy during 12 months | | | | 1.04 | 0.60, 1.79 | | | .889 | |
| | Radiation therapy during 12 months | | | | 0.82 | 0.42, 1.61 | | | .571 | |
| | Reconstruction during 12 months | | | | 1.19 | 0.47, 2.98 | | | .717 | |
| | Type of surgery: conservation (ref) vs mastectomy | | | | 1.16 | 0.51, 2.64 | | | .725 | |
| Age × menopausal status | | | | 0.54 | 0.36, 0.80 | | | .002 | | |
| Adjusted Regression of Depression Occurrence on Age, Stratified by Menopausal Status | | | | | | | | | | |
| Premenopausal | | | | 1.50 | 1.00, 2.25 | | | .048 | | |
| Postmenopausal | | | | 0.77 | 0.64, 0.92 | | | .003 | | |
| Overall Model X ² =34.535; p=.011 | | | | | | | | | | |
| Menopausal status* | 0.53 | 0.33, 0.87 | .011 | 137.20 | 3.53, 5329.31 | | | .008 | | |

| LOGISTIC REGRESSION RESULTS | | | | | | | | |
|--|--|------------------|------------|---------|----------------|----------------|------------|------|
| Symptom | Covariates | Unadjusted Model | | | Adjusted Model | | | |
| | | OR | CI | p-value | OR | CI | p-value | |
| Joint pain or stiffness PRE = 40.0% POST = 51.9% | Age (in 5 year increments) | | | | 1.30 | 0.93, 1.83 | .121 | |
| | Lives alone | | | | 0.78 | 0.42, 1.47 | .446 | |
| | Working for pay | | | | 0.91 | 0.54, 1.51 | .705 | |
| | SCQ score | | | | 1.08 | 0.98, 1.19 | .122 | |
| | Prior HRT | | | | 2.92 | 1.46, 5.83 | .002 | |
| | Adjuvant chemotherapy during 12 months | | | | 0.98 | 0.57, 1.66 | .931 | |
| | Radiation therapy during 12 months | | | | 1.21 | 0.61, 2.39 | .581 | |
| | Reconstruction during 12 months | | | | 0.62 | 0.24, 1.56 | .308 | |
| | Type of surgery: conservation (ref) vs mastectomy | | | | 2.18 | 0.97, 4.93 | .060 | |
| | Age × menopausal status | | | | 0.57 | 0.39, 0.83 | .004 | |
| | Adjusted Regression of Daytime Sweats Occurrence on Age, Stratified by Menopausal Status | | | | | | | |
| | | Premenopausal | | | | 1.27 | 0.89, 1.81 | .190 |
| | | Postmenopausal | | | | 0.74 | 0.63, 0.89 | .001 |
| | Overall Model X ² =23.66; p=.014 | | | | | | | |
| | Menopausal status* | 1.62 | 1.02, 2.57 | .043 | 387.32 | 6.64, 22601.80 | .004 | |
| | Age (in 5 year increments) | | | | 1.88 | 1.26, 2.79 | .002 | |
| | Lives alone | | | | 0.97 | 0.56, 1.68 | .906 | |
| | Working for pay | | | | 0.89 | 0.55, 1.42 | .614 | |
| | SCQ score | | | | 1.07 | 0.98, 1.17 | .133 | |
| | Prior HRT | | | | 1.00 | 0.54, 1.86 | .993 | |
| | Adjuvant chemotherapy during 12 months | | | | 1.40 | 0.85, 2.32 | .188 | |
| | Radiation therapy during 12 months | | | | 0.63 | 0.34, 1.17 | .145 | |
| | Reconstruction during 12 months | | | | 1.31 | 0.54, 3.16 | .551 | |
| | Type of surgery: conservation (ref) vs mastectomy | | | | 0.61 | 0.28, 1.31 | .206 | |
| | Age × menopausal status | | | | 0.54 | 0.36, 0.83 | .004 | |
| Adjusted Regression of Joint Pain Occurrence on Age, Stratified by Menopausal Status | | | | | | | | |

| LOGISTIC REGRESSION RESULTS | | | | | | | |
|--|---|------------------|------------|---------|--|---------------|---------|
| Symptom | Covariates | Unadjusted Model | | | Adjusted Model | | |
| | | OR | CI | p-value | OR | CI | p-value |
| Wake during the night PRE = 61.7% POST = 63.7% | Premenopausal | | | | 2.07 | 1.33, 3.23 | .001 |
| | Postmenopausal | | | | 1.00 | 0.86, 1.15 | .947 |
| | | | | | Overall Model X ² =23.12; p=.017 | | |
| | Menopausal status * | 1.08 | 0.67, 1.73 | .764 | 1.49.89 | 4.59, 4893.95 | .005 |
| | Age (in 5 year increments) | | | | 1.25 | 0.91, 1.72 | .170 |
| | Lives alone | | | | 0.92 | 0.52, 1.63 | .779 |
| | Working for pay | | | | 0.64 | 0.39, 1.05 | .079 |
| | SCQ score | | | | 1.10 | 1.00, 1.21 | .058 |
| | Prior HRT | | | | 1.29 | 0.67, 2.48 | .447 |
| | Adjuvant chemotherapy during 12 months | | | | 0.90 | 0.53, 1.51 | .678 |
| | Radiation therapy during 12 months | | | | 1.06 | 0.57, 1.97 | .855 |
| | Reconstruction during 12 months | | | | 2.53 | 0.99, 6.47 | .052 |
| | Type of surgery: conservation (ref) vs mastectomy | | | | 0.70 | 0.32, 1.54 | .380 |
| | Age × menopausal status | | | | 0.62 | 0.44, 0.88 | .008 |
| | Adjusted Regression of Wake During the Night Occurrence on Age, Stratified by Menopausal Status | | | | | | |
| | Premenopausal | | | | 1.29 | 0.92, 1.80 | .142 |
| | Postmenopausal | | | | 0.76 | 0.64, 0.90 | .001 |
| | | | | | Overall Model X ² =29.37; p=.002 | | |
| Numbness or tingling PRE = 27.8% POST = 29.7% | Menopausal status * | 1.12 | 0.67, 1.86 | .673 | 174.64 | 3.33, 9171.79 | .011 |
| | Age (in 5 year increments) | | | | 1.29 | 0.89, 1.87 | .185 |
| | Lives alone | | | | 1.52 | 0.83, 2.79 | .174 |
| | Working for pay | | | | 0.74 | 0.44, 1.24 | .253 |
| | SCQ score | | | | 1.08 | 0.98, 1.18 | .143 |
| | Prior HRT | | | | 1.05 | 0.52, 2.12 | .900 |
| | Adjuvant chemotherapy during 12 months | | | | 2.47 | 1.45, 4.20 | .001 |
| | Radiation therapy during 12 months | | | | 0.82 | 0.42, 1.60 | .562 |

| LOGISTIC REGRESSION RESULTS | | | | | | | |
|-----------------------------|--|------------------|----|---------|----------------|------------|---------|
| Symptom | Covariates | Unadjusted Model | | | Adjusted Model | | |
| | | OR | CI | p-value | OR | CI | p-value |
| | Reconstruction during 12 months | | | | 1.06 | 0.42, 2.67 | .905 |
| | Type of surgery: conservation (ref) vs mastectomy | | | | 1.16 | 0.52, 2.60 | .710 |
| | Age × menopausal status | | | | 0.62 | 0.41, 0.92 | .019 |
| | Adjusted Regression of Numbness or Tingling Occurrence on Age, Stratified by Menopausal Status | | | | | | |
| | Premenopausal | | | | 1.32 | 0.88, 1.98 | .176 |
| | Postmenopausal | | | | 0.79 | 0.66, 0.93 | .006 |

Abbreviations: CI = confidence interval; HRT = hormone replacement therapy; OR = odds ratio; PRE = premenopausal; POST = postmenopausal; ref = reference group; SCQ = Self-administered Comorbidity Questionnaire; vs = versus

* reference group = premenopausal women

Table 5

Results of unadjusted and adjusted linear regression analyses that evaluated for differences in symptom severity and distress scores between premenopausal and postmenopausal women 12 months after surgery

| SYMPTOM | | LINEAR REGRESSION RESULTS | | | | | | | |
|-------------------------|------------------------------------|---------------------------|--|-------|--------------|----------------|-------|--------------|---------|
| Symptom | Severity Score (0–10) Mean (SD) | Covariate | Unadjusted Model | | | Adjusted Model | | | |
| | Premen | | Postmen | B | CI | p-value | B | CI | p-value |
| SYMPTOM SEVERITY | | | | | | | | | |
| Fatigue | 4.7 (2.6) | 3.8 (2.4) | Overall Model F=2.11; R ² =.12; p=.027 | | | | | | |
| | | | Menopausal status * | -0.73 | -1.51, 0.06 | .071 | -1.00 | -1.98, -0.01 | .048 |
| | | | Age (in 5 year increments) | | | | -0.15 | -0.36, 0.06 | .163 |
| | | | Lives alone | | | | 0.36 | -0.55, 1.27 | .437 |
| | | | Working for pay | | | | -0.58 | -1.35, 0.19 | .140 |
| | | | SCQ score | | | | 0.19 | 0.05, 0.34 | .008 |
| | | | Prior HRT | | | | 0.29 | -0.74, 1.31 | .580 |
| | | | Any adjuvant chemotherapy in past 12 months | | | | 0.40 | -0.42, 1.23 | .336 |
| | | | Any adjuvant radiation therapy in past 12 months | | | | 0.50 | -0.43, 1.44 | .290 |
| | | | Any breast reconstructions months in past 12 months | | | | -0.24 | -1.58, 1.11 | .729 |
| | | | Type of surgery: lumpectomy (ref) vs mastectomy | | | | -0.30 | -1.47, 0.88 | .616 |
| Impatience | 3.8 (2.3) | 2.7 (1.8) | Overall Model F=2.22; R ² =.17; p=.022 | | | | | | |
| | | | Menopausal status * | -1.15 | -1.88, -0.42 | .002 | -0.89 | -1.80, 0.02 | .055 |
| | | | Age (in 5 year increments) | | | | -0.12 | -0.30, 0.07 | .227 |
| | | | Lives alone | | | | -0.31 | -1.20, 0.58 | .486 |
| | | | Working for pay | | | | -0.18 | -0.92, 0.56 | .639 |
| | | | SCQ score | | | | 0.14 | -0.01, 0.29 | .061 |
| | | | Prior HRT | | | | -0.12 | -1.16, 0.92 | .816 |
| | | | Any adjuvant chemotherapy in past 12 months | | | | 0.66 | -0.11, 1.43 | .091 |
| | | | Any adjuvant radiation therapy in past 12 months | | | | 0.20 | -0.74, 1.14 | .678 |
| | | | Any breast reconstructions months in past 12 months | | | | 0.66 | -0.63, 1.95 | .313 |

| SYMPTOM | | LINEAR REGRESSION RESULTS | | | | | | | | | |
|---------------------------------|---------------------------------|---------------------------|--|-------|--------------|----------------|-------|--------------|---------|-------------|------|
| | | Covariate | Unadjusted Model | | | Adjusted Model | | | | | |
| Severity Score (0-10) Mean (SD) | Premen | | Postmen | B | CI | p-value | B | CI | p-value | | |
| Irritability | 3.8 (2.4) | 2.9 (1.9) | Type of surgery: lumpectomy (ref) vs mastectomy | | | | | | -0.76 | -1.90, 0.39 | .194 |
| | | | Overall Model F=3.81; R ² =.28; p<.001 | | | | | | | | |
| | | | Menopausal status* | -1.10 | -1.91, -0.30 | .008 | -0.56 | -1.46, 0.34 | .219 | | |
| | | | Age (in 5 year increments) | | | | -0.32 | -0.52, -0.12 | .002 | | |
| | | | Lives alone | | | | 0.11 | -0.81, 1.03 | .814 | | |
| | | | Working for pay | | | | -0.31 | -1.09, 0.47 | .428 | | |
| | | | SCQ score | | | | 0.29 | 0.14, 0.45 | <.001 | | |
| | | | Prior HRT | | | | -0.08 | -1.17, 1.01 | .888 | | |
| | | | Any adjuvant chemotherapy in past 12 months | | | | 0.66 | -0.17, 1.48 | .119 | | |
| | | | Any adjuvant radiation therapy in past 12 months | | | | 0.26 | -0.70, 1.22 | .596 | | |
| | | | Any breast reconstructions months in past 12 months | | | | 0.86 | -0.45, 2.17 | .194 | | |
| | | | Type of surgery: lumpectomy (ref) vs mastectomy | | | | -0.32 | -1.4, 0.75 | .551 | | |
| | | | SYMPTOM DISTRESS | | | | | | | | |
| Symptom | Distress Score (0-10) Mean (SD) | | Unadjusted Model | | | Adjusted Model | | | | | |
| | PRE | POST | B | CI | p-value | B | CI | p-value | | | |
| Impatience | 3.9 (2.9) | 2.6 (2.0) | Type of surgery: lumpectomy (ref) vs mastectomy | | | | | | -0.69 | -1.79, 0.41 | .217 |
| | | | Overall Model F=2.01; R ² =.15; p=.039 | | | | | | | | |
| | | | Menopausal status* | -1.29 | -2.17, -0.40 | .005 | -0.18 | -0.42, 0.05 | .131 | | |
| | | | Age (in 5 year increments) | | | | -0.59 | -1.68, 0.50 | .283 | | |
| | | | Lives alone | | | | -0.28 | -1.18, 0.61 | .532 | | |
| | | | Working for pay | | | | 0.14 | -0.04, 0.32 | .134 | | |
| | | | SCQ score | | | | -0.60 | -1.87, 0.68 | .354 | | |
| | | | Prior HRT | | | | 0.53 | -0.41, 1.46 | .266 | | |
| | | | Any adjuvant chemotherapy in past 12 months | | | | -0.09 | -1.25, 1.08 | .884 | | |
| | | | Any adjuvant radiation therapy in past 12 months | | | | 0.65 | -0.92, 2.22 | .413 | | |
| | | | Any breast reconstructions months in past 12 months | | | | | | | | |

| SYMPTOM | | LINEAR REGRESSION RESULTS | | | | | | | |
|---------|------------------------------------|---------------------------|---|---|---------|-------|----------------|---------|--|
| Symptom | Severity Score (0–10) Mean (SD) | Covariate | | Unadjusted Model | | | Adjusted Model | | |
| | Premen | Postmen | B | CI | p-value | B | CI | p-value | |
| | | | | Type of surgery: lumpectomy (ref) vs mastectomy | | | | | |
| | | | | | | -0.65 | -2.05, 0.75 | .36 0 | |

Abbreviations: B = Beta coefficient; CI = confidence interval; HRT = hormone replacement therapy; Premen = premenopausal; Postmen = postmenopausal; ref = reference group; SCQ = Self-administered Comorbidity Questionnaire; vs = versus

* reference group = premenopausal women