ONLINE EXCLUSIVE

Hot Flashes and Related Outcomes in Breast Cancer Survivors and Matched Comparison Women

Janet S. Carpenter, PhD, RN, David H. Johnson, MD, Lois J. Wagner, MSN, RN, and Michael A. Andrykowski, PhD

Purpose/Objectives: To compare the hot flash symptom experience and related outcomes between breast cancer survivors and healthy women.

Design: Descriptive, cross-sectional, comparative study.

Setting: Southeastern university medical center.

Sample: 69 of 207 breast cancer survivors contacted via a tumor registry and 63 age-matched healthy female volunteers. Survivors were a mean of 57 years and a mean of 39 months postdiagnosis.

Methods: Mailed survey included a demographic, disease, and treatment information form; a gynecologic history form; a two-day, prospective, hot flash diary; a detailed hot flash questionnaire; mood and affect scales; and the Hot Flash-Related Daily Interference Scale.

Main Research Variables: Hot flashes, mood, affect, interference with daily activities, and overall quality of life.

Findings: Breast cancer survivors had hot flashes that were significantly more frequent, severe, distressing, and of greater duration. Breast cancer survivors were less likely to be using hormone replacement and more likely to have tried nonhormonal prescription interventions in the past, but reported significantly less effectiveness from hot flash treatments. Breast cancer survivors with severe hot flashes reported significantly greater mood disturbance; higher negative affect; more interference with daily activities, including sleep, concentration, and sexuality; and poorer overall quality of life in comparison to breast cancer survivors with no hot flashes to mild hot flashes. Hot flash quality and triggers were not significantly different between groups. No clear temporal pattern of hot flashes emerged.

Conclusions: Hot flashes are a significant problem for breast cancer survivors, even for those who are naturally postmenopausal (i.e., did not undergo menopause as a result of surgery or the effects of chemotherapy). Hot flashes remained fairly stable over time and did not diminish in frequency, severity, or associated distress.

Implications for Nursing: The findings guide the assessment of the uniqueness of the problem of hot flashes experienced by breast cancer survivors and help define outcomes to address in clinical practice or include in future hot flash intervention research.

Key Points . . .

- Women with breast cancer may be predisposed to hot flashes as a result of chemotherapy, tamoxifen use, potential disruptions in circadian rhythms of hormones and body temperature, and contraindications against the use of hormone replacement therapy.
- Breast cancer survivors had hot flashes that were significantly more frequent, distressing, and of greater duration than healthy women of the same age. Naturally postmenopausal breast cancer survivors reported a more severe symptom pattern than naturally menopausal healthy women.
- No clear temporal pattern of hot flashes was noted in either group.
- Breast cancer survivors with severe hot flashes reported more problems in other areas of functioning, including mood, affect, daily activities, and quality of life.

Hot flashes are sudden episodes of flushing, sweating, and a sensation of heat often preceded or followed by chills (Kronenberg, 1994). Although hot flashes rapidly are becoming recognized as a frequent, severe, and bothersome

Janet S. Carpenter, PhD, RN, is an assistant professor in the School of Nursing, David H. Johnson, MD, is a professor in the School of Medicine, and Lois J. Wagner, MSN, RN, is a doctoral student in the School of Nursing, all at Vanderbilt University in Nashville, TN. Michael A. Andrykowski, PhD, is a professor in the Department of Behavioral Science at the University of Kentucky in Lexington. *(Submitted July 2001. Accepted for publication November 12, 2001.) This research was supported by the 1998–2000 ONS Foundation/Sigma Theta Tau International Research Grant, the Vanderbilt University School of Nursing Joint Center for Nursing Research, and the Vanderbilt-Ingram Cancer Center.*

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symptom among breast cancer survivors (Carpenter, 2000; Carpenter et al., 1998), a detailed study of hot flashes in breast cancer survivors with comparison to healthy women has not been published previously. Because several unique factors predispose breast cancer survivors to hot flashes, existing data describing hot flashes in healthy women (Kronenberg, 1990, 1994) may not generalize to breast cancer survivors. These predisposing factors include ovarian disruption caused by chemotherapy and subsequent early and artificial menopause (Carpenter et al., 1998; Reichman & Green, 1994), side effects of the antiestrogen tamoxifen and the selective estrogen receptor modulator raloxifene (Carpenter et al., 1998; Love, 1989; Love, Cameron, Connell, & Levanthal, 1991; Pasacreta & McCorkle, 1998), potential disruptions in circadian rhythms of hormones (Bartsch et al., 1989; Mormont & Levi, 1997) and body temperature (Carpenter, Gautam, Andrykowski, & Freedman, 2001), and contraindications to the use of hormone replacement therapy (HRT) because of concerns about stimulating cancer recurrence (Brzezinski, 1995; Runowicz, 1996). These factors may act singly or in combination to alter hot flashes in breast cancer survivors when compared to healthy women. Although the exact physiology of hot flashes is unknown, several of these factors are associated with estrogen withdrawal, which has been implicated as a trigger of hot flashes. Thus, data previously and exclusively gathered among healthy women may not reflect the hot flash experience of breast cancer survivors.

Data specifically assessing hot flashes in breast cancer survivors are limited to only a handful of published studies (Carpenter et al., 1998; Carpenter & Andrykowski, 1999; Couzi, Helzlsouer, & Fetting, 1995; Finck, Barton, Loprinzi, Quella, & Sloan, 1998). Hot flashes have been found to affect 65% of breast cancer survivors (Carpenter et al., 1998; Couzi et al.) and have been described as both severe and distressing (Carpenter et al., 1998; Carpenter & Andrykowski; Couzi et al.; Finck et al.). These studies are limited further in that they only have included qualitative data from a small sample of women with breast cancer (Finck et al.); assessed hot flash frequency, severity, or distress without providing additional descriptive data (Carpenter et al., 1998; Carpenter & Andrykowski; Couzi et al.); or did not include any comparison groups (Carpenter et al., 1998; Carpenter & Andrykowski; Couzi et al.; Finck et al.). For example, potential differences in the quality and temporal pattern of hot flashes between breast cancer survivors and healthy women have not been studied previously. In addition, the majority of published reports focus on evaluating hot flash treatment options and typically limit description and measurement of outcomes to hot flash frequency counts and severity or distress ratings (Barton et al., 1998; Goldberg et al., 1994; Loprinzi et al., 1994, 1998; Quella et al., 1998). Thus, data describing the problematic nature of hot flashes generally are limited in these intervention studies. In addition, outcomes other than hot flashes, such as mood, affect, daily activities, and overall quality of life (QOL) are not assessed routinely. A need exists to better understand the impact of hot flashes on such outcomes to determine which, if any, might be appropriate to address in clinical practice and include in future hot flash intervention studies.

The purposes of this study were to obtain a detailed, multidimensional assessment of hot flashes in breast cancer survivors and compare the experience of hot flashes in breast cancer survivors to age-matched healthy women. Detailed data were gathered, including hot flash frequency, severity, bother (distress), duration, quality, aggravating factors, alleviating factors, temporal pattern, and impact on mood, affect, daily activities, and overall QOL.

Conceptual Framework

The University of California, San Francisco (UCSF) model of symptom management (Dodd, Miaskowski, & Paul, 2001; UCSF School of Nursing Symptom Management Faculty Group, 1994) guided this study. The UCSF model depicts three interrelated dimensions: symptom experience, symptom outcomes, and symptom management strategies. The symptom experience includes an individual's perception and evaluation of internal cues as a symptom (i.e., feeling suddenly hot and flushed is perceived as a hot flash; ratings of severity and distress). Symptom outcomes include other aspects of the individual and her life that may be affected by a symptom, including QOL and emotional and functional status. Symptom management strategies include various components of interventions, such as dose and route. This model considers the thorough assessment of a given symptom within the context of related outcomes as necessary for choosing, implementing, and evaluating appropriate symptom management interventions. Thus, the investigators sought to describe the hot flash symptom experience (frequency, severity, bother or distress, duration, quality, aggravating factors, alleviating factors, and temporal pattern) and potentially related symptom outcomes (mood, affect, interference with daily activities, and overall QOL) to better address symptom management needs.

Methods

Design

A cross-sectional, descriptive, comparative study was used to address the study purposes.

Participants

Inclusion criteria for breast cancer survivors were (a) first time diagnosis of breast cancer (i.e., had not experienced recurrence), (b) no other history of cancer, (c) disease free at the time of study participation, (d) at least three months postcompletion of surgery, radiation, or chemotherapy, and (e) less than or equal to six years postdiagnosis. The latter criteria reflected the availability of women in the cancer registry. Inclusion criteria for healthy women were (a) no history of cancer, (b) naturally pre-, peri-, or postmenopausal (i.e., intact uterus and ovaries), and (c) age matched to a breast cancer survivor within two years. In addition, all women were over age 18 and able to speak, read, and write English.

Procedures

Following Institutional Review Board approval, eligible breast cancer survivors were identified through a university-based medical center tumor registry located in the southeastern United States. A list of potentially eligible women was released to their physicians, who then sent a letter introducing the principal investigator and describing the purpose and nature of the study. The purpose of the study as stated in the letter was "to learn about hot flashes in breast cancer survivors

and how they compare to hot flashes experienced by women without cancer." To avoid response bias (i.e., only women with hot flashes agreeing to participate), the letter also stated the following in bold typeface: "We are interested in receiving information from you even if you do not have hot flashes." The letter included a consent form for women to sign and return to the principal investigator indicating their interest. Those who did not return a signed consent received a second mailing six weeks later.

Study materials were mailed to all breast cancer survivors who returned signed consent forms. Instructions for completing the materials were detailed in a cover letter. Women were asked to return their completed study materials in a postage-paid envelope provided. Women who did not return completed questionnaires received a telephone call about two to four weeks following the mailing to assess their interest in participating. Women who completed and returned study materials received a thank you letter and $5 for their participation. Study staff reviewed medical records of all breast cancer survivor participants to obtain accurate information about cancer diagnosis and treatment. Permission to abstract medical records was included in the consent.

Recruitment of healthy women began about three months after the initial invitation letter was sent to the breast cancer survivors. This time allowed for a large enough pool of breast cancer survivors to be accrued so that age matching of healthy women could be accomplished. Comparison women were recruited via word-of-mouth and newspaper advertisements. Advertisements asked interested women to phone a research project office. Women who called the office were screened to determine eligibility. If eligible, they were mailed a packet of study materials, including a consent form, to sign and return along with their completed questionnaires. Healthy women nonresponders were contacted in the same manner as breast cancer survivor nonresponders.

Measures

Seven measures were included in the mailed study packets.

Demographic and disease and treatment information: A form was used to assess demographic information, including birth date, race, education, marital status, employment status, and household income. Women also were asked to record their height and weight, which was used to calculate body mass index. Routine information regarding date of diagnosis, stage of disease, and types and dates of cancer treatments was obtained from medical records.

Gynecologic and reproductive history form: This questionnaire was designed to obtain information regarding menopausal status, date of last menstrual period, and dates of any hysterectomy or oophorectomy. This form included questions adapted from the Massachusetts Women's Health study that were designed to assess menopausal status using the following definitions: premenopausal—regular menstrual cycles during the last three months, perimenopausal—3–11 months of amenorrhea or increased menstrual irregularity if still cycling, and postmenopausal—12 or more months of amenorrhea. Women were classified as chemically menopausal if their last menstrual period occurred during the months chemotherapy treatments were received or occurred less than or equal to three months after the last chemotherapy treatment (Avis, Brambilla, McKinlay, & Vass, 1994; Brambilla, McKinlay, & Johannes, 1994).

Hot flash questionnaire: The hot flash questionnaire was designed to provide detailed information about current hot flashes. Questions were modeled on previous work by Kronenberg (1994) and assessed hot flash severity, bother, quality, aggravating factors, alleviating factors, and temporal pattern. Current overall severity and bother (distress) were rated using two separate 0 (not at all) to 10 (extremely) numeric rating scales. Current hot flash quality was assessed using a list of 19 separate descriptors. Women were asked to check all phrases that coincided with feelings they encountered during a hot flash. Additional items also asked women to describe whether and where they perspired during hot flashes. Aggravating factors were assessed using a list of seven potential hot flash triggers; women were asked to check all items they felt triggered their hot flashes. Alleviating factors were presented as a list of five behaviors that women might perform or use to relieve their hot flashes, and 10 potential hot flash treatment strategies, including HRT, prescription medications, vitamins, herbs, diet, exercise, behavioral methods (e.g., relaxation), acupuncture, massage, and "other," were listed. Women indicated whether they currently were using each treatment (yes or no) and whether they had tried each treatment in the past (yes or no with no time frame specified). In addition, women were asked to rate the overall level of effectiveness of any current treatment strategies using a 0 (not at all effective) to 10 (extremely effective) numeric rating scale. The temporal pattern of hot flashes was assessed by asking women to indicate the time of day and season of the year hot flashes were most frequent, severe, and bothersome. In addition, women were asked whether their hot flashes had increased, decreased, or stayed the same in frequency, severity, bother, and duration during the prior six months. Responses were intended to be analyzed as individual items rather than as a summed score. Thus, Cronbach's alpha coefficient was not assessed. Given the changing nature of hot flashes, test-retest reliability also was not assessed, as it was expected to be low. The questionnaire was pilot-tested with five participants to assess whether questions were understandable and contained appropriate descriptors.

Hot flash diary: The hot flash diary allowed for a detailed, prospective assessment of hot flashes occurring over a 48-hour period. Women were asked to record the date and time of each hot flash, rate the severity using a 0 (not at all) to 10 (extremely) numeric rating scale, and record the duration in minutes. Women were asked to complete the diaries around the same time they completed the hot flash questionnaire. Pre- and perimenopausal women were not instructed to complete the diaries at a particular time of their menstrual cycle. Hot flash frequencies were calculated as the number of hot flashes recorded per day. Mean severity ratings were calculated by summing individual severity ratings and dividing the sum by the number of hot flashes experienced. Mean duration ratings were calculated similarly. Frequency counts and mean severity and duration ratings were calculated separately for days one and two. This type of diary methodology has been used previously (Carpenter, Andrykowski, Freedman, & Munn, 1999; Barton et al., 1998; Goldberg et al., 1994) and is considered the gold standard for assessing hot flash frequency and severity when objective sternal skin conductance monitoring is not feasible (Carpenter et al., 1999).

Profile of Mood States-Short Form (POMS-SF): The POMS-SF is a measure of current (i.e., during the past two

weeks) mood disturbance consisting of 37 items (Shacham, 1983) from the original 65-item POMS (McNair, Lorr, & Droppelman, 1981). A total mood disturbance score (TMD) is computed, as are scores for six subscales (depression, tension, anger, confusion, vigor, and fatigue). Among patients with cancer, the POMS-SF possesses reliability and validity equal to that of the full-length POMS (Curran, Andrykowski, & Studts, 1995). In this study, Cronbach's alphas were greater than 0.80 for each of the six subscales and equal to 0.94 for TMD.

Positive and Negative Affect Scale (PANAS): The PANAS is a 20-item, adjective list of feelings and emotions that yields subscale scores for positive and negative affect (Watson, Clark, & Tellegen, 1998). Participants respond to each item from 1 (very slightly or not at all) to 5 (extremely) to indicate how they have been feeling during the past week. The PANAS has been used in prior research to assess the relationship between negative affect and symptom reporting in patients with cancer (Koller et al., 1996). In this study, Cronbach's alpha coefficient was 0.90 for positive affect and 0.89 for negative affect.

Hot Flash-Related Daily Interference Scale (HFRDIS): The HFRDIS is a 10-item scale measuring the degree to which hot flashes interfere with nine daily activities. The tenth item measures the degree that hot flashes interfere with overall QOL. The HFRDIS was modeled on the Brief Pain Inventory (Daut, Cleeland, & Flanery, 1983) and the Fatigue Symptom Inventory (Hann, Winter, & Jacobsen, 1999), both of which invite respondents to rate the degree to which pain or fatigue interferes with various daily activities and overall enjoyment or QOL. The HFRDIS was developed to include daily life activities specific to the impact of hot flashes. Psychometric analysis supports validity and reliability of the HFRDIS for use with breast cancer survivors and healthy women with a Cronbach's alpha of 0.96, strong correlations with other hot flash variables, and demonstrated sensitivity to change over time (Carpenter, 2001). Participants rate the degree hot flashes have interfered with each of these items during the previous week using a 0 (do not interfere) to 10 (completely interfere) scale. A total score is computed by summing items. Higher scores indicate higher interference by hot flashes and, thus, greater impact on QOL. Women without hot flashes are asked to mark 0 for each item.

Data Analysis

Demographic, disease, and treatment data were analyzed using frequencies and descriptive statistics. Potential differences between women responding to the survey and those not responding to the survey were assessed using chi-square tests or t-tests. Group differences in hot flashes and other outcome variables also were assessed using chi-square tests or t-tests. Correlations were assessed using Pearson correlation coefficients.

Results

Participants

A total of 226 eligible women were identified through the cancer registry and sent a letter of invitation for the study between January and March 1999. Of these 226 women, 2 were deceased and 17 had moved with no forwarding address. Of the 207 women who received the mailing, 95 returned a signed consent form indicating their willingness to participate (46%). The remaining 112 women (54%) did not respond to either invitation to participate. Completed packets were received from 71 of the 95 consenting women (75% of consenting breast cancer survivors; 34% of women who received the mailing). However, upon reviewing completed packets, the investigators found two women to be ineligible. Therefore, the final number of eligible breast cancer survivor responders was 69, representing 73% of the consenting women and 33% of the 207 women contacted. To ensure that a representative sample was gathered despite the lower than anticipated response rate, the investigators compared the 69 breast cancer survivor responders to the 112 breast cancer survivors who did not respond to either invitation to participate on the only variables available for comparison. No group differences were found for age at breast cancer diagnosis ($p = 0.64$) or year of diagnosis ($p = 0.65$). Thus, the breast cancer survivor sample appeared representative of the larger registry population. Comparisons on stage at diagnosis and treatment were not feasible because of the lack of registry information for 24% of the nonresponders. A total of 83 packets were mailed to interested healthy women. Completed materials were returned by 63 healthy women (76%).

Participants were primarily Caucasian, postmenopausal, middle-aged, of moderate educational level, and with mixed incomes (see Table 1). Breast cancer survivors were a mean of slightly more than three years postdiagnosis and treatment. Stage at diagnosis was 0–I (59%), IIA–IIB (38%), and IIIA (3%). Breast cancer treatments received included surgery (28%), surgery plus radiation therapy (25%), surgery plus chemotherapy (29%), and surgery, radiation, and chemotherapy (19%). In addition, 50% of breast cancer survivors were using tamoxifen at the time of the survey.

Breast cancer survivors and healthy women groups were not significantly different in age, race, employment status, income, education, or body mass index, but significantly more breast cancer survivors were married (see Table 1). Marital status was not related significantly to any of the primary outcome variables and, therefore, was not included as a covariate in any of the subsequent analyses. As expected, groups differed in menopausal status, with 79% of breast cancer survivors being postmenopausal as compared to only 57% of age-matched healthy women. In addition, given inclusion and exclusion criteria, all healthy women were naturally menopausal, whereas breast cancer survivors were naturally, surgically, or chemically postmenopausal.

Detailed Assessment of Hot Flashes in Breast Cancer Survivors With Comparison to Healthy Women

Frequency, severity, bother, and duration: Using hot flash questionnaire data, overall severity and bother ratings were strongly correlated among breast cancer survivors ($r = 0.81$, $p < 0.001$) and healthy women ($r = 0.90$, $p < 0.001$). Significantly higher hot flash severity and bother were noted among breast cancer survivors in comparison to healthy women (see Table 2). Mean breast cancer survivors' severity and bother ratings were about three times that of healthy women. Using frequency distributions, 73% of healthy women provided overall severity and bother ratings of 0, whereas 48% of breast cancer survivors provided severity ratings greater than or equal to 5, and 46% of breast cancer

Table 1. Sample Characteristics

Characteristic	Breast Cancer Survivors (n = 69)	Healthy Women (n = 63)	χ^2	p
Race			2.67	0.10
Caucasian	94%	86%		
Other	6%	14%		
Marital status			9.69	0.02
Single	10%	21%		
Partner/spouse	78%	57%		
Widowed	3%	14%		
Other	9%	8%		
Employment			2.31	0.32
Full-time	41%	48%		
Part-time	6%	11%		
Other	53%	41%		
Menopausal status			37.88	0.001
Naturally pre-menopausal	6%	19%		
Naturally peri-menopausal	15%	24%		
Naturally post-menopausal	33%	57%		
Surgically post-menopausal	30%	–		
Chemically post-menopausal	15%	–		
Household income			6.09	0.53
≤ $20,000	17%	17%		
$20,001–$40,000	15%	25%		
$40,001–$60,000	22%	16%		
> $60,000	28%	29%		
Do not care to respond	18%	13%		

Characteristic	$\bar{x}$	SD	$\bar{x}$	SD	t	p
Age at interview	57.23	11.00	55.69	17.41	0.61	0.54
Years of education	14.13	2.96	14.87	3.39	–1.32	0.19
Body mass index	27.13	5.00	27.03	6.86	0.09	0.93
Age at diagnosis	53.96	11.20	–	–	–	–
Months post-diagnosis	39.25	21.62	–	–	–	–
Months postsurgery	38.69	21.83	–	–	–	–
Months post-treatment	35.88	21.45	–	–	–	–

survivors provided bother ratings greater than or equal to 5. Diary data supported hot flash questionnaire data. Using diaries, significantly more breast cancer survivors reported daily hot flashes (65%) in comparison to healthy women (16%) ($p < 0.001$). Breast cancer survivors also reported significantly more frequent and severe hot flashes with greater duration on diary days one and two in comparison to healthy women.

Group differences in hot flashes also were analyzed using only the subset of women who naturally were postmenopausal (22 breast cancer survivors versus 35 healthy women). These naturally postmenopausal groups were not significantly different in age, employment status, income, education, or body mass index ($p > 0.25$). However, groups differed significantly in race and marital status ($p < 0.05$), with more breast cancer survivors being Caucasian and married. However, because neither marital status nor race was significantly related to any of the primary outcome variables, neither was included as a covariate. Table 3 presents group differences in hot flash variables among the subset of naturally postmenopausal women. With the exception of frequency on diary day two, hot flashes were significantly more frequent, severe, bothersome, and of greater duration among naturally postmenopausal breast cancer survivors in comparison to naturally postmenopausal healthy women ($p < 0.05$).

Quality: Breast cancer survivors used a mean of 5.22 phrases (SD = 2.85) to describe what they felt during a hot flash from the list of 19 phrases provided. This number was not significantly different from healthy women ($p = 0.96$). Twenty-seven percent of breast cancer survivors used 3 or fewer descriptors, 50% used 4–6 descriptors, 18% used 7–10 descriptors, and 5% used more than 10 descriptors. Percentages of breast cancer survivors endorsing each descriptor were as follows: 93% heat, 89% sweating or perspiring, 77% flushed, 46% clammy, 32% irritated or annoyed, 27% chills, 27% burning sensation, 23% anxious, 18% frustrated, 16% pressure in head, 16% embarrassed, 11% depressed, 11% change in heart rate, 9% ill or nauseous, 9% feeling of suffocation, 7% pressure in chest, 7% panicked, and 7% change in breathing rate. No responder reported feeling suicidal. These percentages were not significantly different from the healthy women group ($p > 0.12$), indicating that the quality of hot flashes was similar between groups. Additional items regarding

Table 2. Overall Group Differences in Hot Flashes

Characteristic	Breast Cancer Survivors (n = 69) $\bar{x}$	SD	Healthy Women (n = 63) $\bar{x}$	SD	t	p
Overall hot flash severity	3.84	2.96	1.35	2.63	5.11	0.001
Overall hot flash bother	3.80	3.35	1.40	2.78	4.50	0.001
Diary day 1						
Frequency[a]	2.67	3.47	0.73	2.48	3.72	0.001
Severity[b]	2.56	2.57	0.72	1.98	4.60	0.001
Duration[c]	2.67	3.65	0.99	3.87	2.57	0.011
Diary day 2						
Frequency	2.20	3.08	0.68	3.16	2.79	0.006
Severity	2.25	2.71	0.64	1.74	4.08	0.001
Duration	2.52	4.40	0.66	2.05	3.16	0.002

[a] Number of hot flashes per day

[b] Mean severity of all hot flashes experienced in a given day

[c] Mean number of minutes of each hot flash experienced in a given day

Note. Overall severity and bother were rated using 0–10 numeric rating scales.

Table 3. Group Differences in Hot Flashes Among the Subset of Naturally Postmenopausal Participants

	Breast Cancer Survivors (n = 22)		Healthy Women (n = 35)			
Characteristic	$\bar{X}$	**SD**	$\bar{X}$	**SD**	**t**	**p**
Overall hot flash severity	3.23	2.91	1.46	2.84	2.27	0.027
Overall hot flash bother	3.23	3.12	1.40	2.98	2.21	0.031
Diary day 1						
Frequency[a]	3.05	3.51	0.97	3.16	2.31	0.025
Severity[b]	2.98	2.58	0.70	2.02	3.52	0.001
Duration[c]	2.49	2.69	0.46	1.46	3.25	0.003
Diary day 2						
Frequency	2.45	3.00	1.06	4.20	1.36	0.181
Severity	2.65	2.96	0.73	1.98	2.69	0.011
Duration	2.39	2.95	0.44	1.28	2.93	0.007

[a] Number of hot flashes per day

[b] Mean severity of all hot flashes experienced in a given day

[c] Mean number of minutes of each hot flash experienced in a given day

Note. Overall severity and bother were rated using 0–10 numeric rating scales.

perspiration/sweating revealed that 51% of breast cancer survivors reported always perspiring during hot flashes, 42% reported sometimes perspiring, and 7% reported never perspiring with hot flashes. These findings also were not significantly different from healthy women ($p = 0.53$). For the breast cancer survivors who reported perspiration, 34% stated their whole upper and lower body perspired during hot flashes, 34% upper body only, 10% face only, and 22% had varied sites of perspiration.

Aggravating factors: Breast cancer survivors endorsed a mean of 2.20 aggravating factors (SD = 1.19) from a list of 7 potential hot flash triggers. This number was not significantly different from healthy women ($p = 0.58$). The majority of breast cancer survivors (71%) endorsed one to two triggers, 23% endorsed three to four triggers, and 6% endorsed five to six triggers. The percentages of breast cancer survivors endorsing each trigger were as follows: 59% no trigger (i.e., hot flashes just seem to happen), 52% stressful or emotional situations, 46% external heat sources (e.g., stove, sunshine, hot room), 23% alcoholic beverages, 18% confined spaces, 14% caffeine, and 9% other (not specified). Only stressful or emotional situations were endorsed more frequently by breast cancer survivors (52%) than healthy women (12%) as a hot flash trigger ($p < 0.01$).

Alleviating factors: When hot flashes occurred, breast cancer survivors reported doing significantly more things to alleviate their hot flashes in comparison to healthy women ($p < 0.05$). Breast cancer survivors reported fanning themselves (71%), removing clothing to cool off (64%), moving to a cooler environment (64%), doing nothing (21%), and doing other unspecified behaviors (23%). Breast cancer survivors reported using a mean of 2.04 hot flash treatments (SD = 1.66) at the time of the survey and a mean of 2.23 treatments (SD = 1.75) in the past. The mean number of treatments used currently or in the past was not significantly different from healthy women ($p > 0.50$). The use of only two types of treatments varied significantly between the groups. HRT was being used by significantly fewer breast cancer survivors at the time of the survey (4% breast cancer survivors versus 27% healthy women, $p < 0.001$) but had been used by significantly more breast cancer survivors in the past (51% breast cancer survivors versus 34% healthy women, $p < 0.05$). In addition, significantly more breast cancer survivors had tried nonhormonal prescription medications (e.g., clonidine) in the past (15% breast cancer survivors versus 3% healthy women, $p < 0.05$). Additional strategies used by breast cancer survivors at the time of the survey included exercise (57%), vitamins (56%), diet (30%), behavioral methods such as relaxation (24%), herbs (9%), massage (6%), and other (unspecified) (11%). None of the breast cancer survivors or healthy women reported using acupuncture for hot flashes. Interestingly, despite the similarity in the types and numbers of current treatments (with the exception of HRT), breast cancer survivors reported their current hot flash treatments to be significantly less effective than did healthy women. Using a 0–10 numeric rating scale, breast cancer survivors reported moderate effectiveness ($\bar{X} = 4.71$, SD = 3.30) whereas healthy women reported extreme effectiveness ($\bar{X} = 9.76$, SD = 1.55) ($p < 0.05$).

Temporal pattern: As shown in Table 4, no differences in the temporal pattern of hot flashes were noted between breast cancer survivors and healthy women ($p > 0.05$). The majority of breast cancer survivors reported no particular time of day that hot flashes were most frequent or severe, whereas nighttime was endorsed as the time of day hot flashes were most bothersome. Healthy women endorsed nighttime as the time of day hot flashes were most frequent, severe, and bothersome. The majority of breast cancer survivors and healthy women also stated that there was no particular season of the year when hot flashes were most frequent, severe, or bothersome. In addition, when asked how hot flashes had changed over the previous six months, no group differences were seen for frequency, severity, bother, or duration. The majority of women reported no changes in frequency (57% breast cancer survivors versus 59% healthy women), severity (67% breast cancer survivors versus 65% healthy women), bother (64% breast cancer survivors versus 71% healthy women), or duration (68% breast cancer survivors versus 77% healthy women). None of the differences were statistically significant.

Impact on Mood, Affect, Daily Activities, and Overall Quality of Life

Breast cancer survivors and healthy women were compared in terms of mood, affect, activity, and overall QOL (see Table 5). Using the POMS-SF, no significant group differences in mood scores were noted. However, mean scores indicated higher mood disturbance on all POMS-SF subscales among breast cancer survivors in comparison to healthy women. Using the PANAS, breast cancer survivors reported significantly higher negative affect in comparison to healthy women ($p < 0.05$). In addition, breast cancer survivors reported that hot flashes had a significantly greater interference with daily activities and overall QOL ($p < 0.01$). Four activities on the HFRDIS appeared to be particularly affected by hot flashes. Breast cancer survivors who reported daily hot flashes reported

Table 4. Temporal Pattern of Daily Hot Flashes in Breast Cancer Survivors and Healthy Women

	Breast Cancer Survivors (n = 45)			Healthy Women (n = 17)		
Occurrence	**Most Frequent**	**Most Severe**	**Most Bothersome**	**Most Frequent**	**Most Severe**	**Most Bothersome**
Time of day						
Morning	9%	2%	2%	12%	12%	6%
Afternoon	9%	2%	–	–	–	–
Evening	7%	17%	16%	6%	18%	6%
Nighttime	36%	38%	52%	47%	47%	71%
Variable	40%	41%	30%	35%	23%	18%
Season of the year						
Spring	–	–	–	6%	–	–
Summer	22%	24%	42%	18%	23%	23%
Fall	9%	2%	2%	–	–	–
Winter	–	7%	11%	–	–	–
Variable	69%	67%	44%	76%	77%	77%

moderate to severe interference (ratings of 5 or greater) with sleep (40%), concentration (33%), mood (29%), and sexuality (28%).

Mood, affect, activity, and overall QOL also were compared between 36 breast cancer survivors with none to mild hot flashes (severity less than 5) and 33 breast cancer survivors reporting moderate to severe hot flashes (severity of 5 or greater). Significant group differences were seen on the POMS-SF, PANAS, and HFRDIS, with more severe hot flashes being associated with greater mood disturbance, more negative affect, greater interference with daily activities, and poorer overall QOL (see Table 6).

Discussion

To the best of the researchers' knowledge, this study provides the most comprehensive assessment of the symptom experience of hot flashes in breast cancer survivors available in the literature. In addition, this study is the only one to include a comparison group of healthy women. The healthy women sample in this study was limited to naturally pre-, peri-, or postmenopausal women to provide a consistent baseline for comparison. The investigators were interested in comparing breast cancer survivors to other naturally postmenopausal women of the same age because the majority of menopausal survey research, and thus knowledge used in clinical practice, is limited to naturally postmenopausal women (Dennerstein et al., 1993; Koster, 1991; Kronenberg, 1990, 1994).

Overall, the study findings suggest that hot flashes are a significant symptom management problem in women following treatment for breast cancer. In comparison to naturally menopausal healthy women of the same age, breast cancer survivors experienced hot flashes that were significantly more frequent, severe, bothersome, and of greater duration. Group differences could not be attributed to differences in menopausal status alone because they also occurred when comparing the subset of naturally postmenopausal breast cancer survivors and healthy women, all with intact uterus and ovaries. Although women undergoing artificially induced menopause have been noted previously to be more symptomatic than those undergoing a natural menopause (Kronenberg, 1990, 1994), differences between naturally postmenopausal breast cancer survivors and naturally postmenopausal healthy women have not been reported previously. Our data suggest that the natural menopausal experience of breast cancer survivors is significantly different than the natural menopausal experience of healthy women, presumably because of the effects of chemotherapy and tamoxifen and inability to take HRT. Thus, healthcare providers in clinical practice must assess all breast cancer survivors, not just those experiencing a chemotherapy-induced menopause. These results support the assertion that breast cancer survivors represent a unique population whose hot flash experience differs from an age-matched group of healthy women

Table 5. Group Differences in Mood, Affect, Daily Activities, and Overall Quality of Life

	Breast Cancer Survivors (n = 69)		Healthy Women (n = 63)			
Characteristic	$\bar{x}$	**SD**	$\bar{x}$	**SD**	**t**	**p**
Profile of Mood States-Short Form						
Tension/anxiety	6.21	5.61	5.15	4.59	1.16	0.25
Anger/hostility	4.57	5.36	4.20	4.55	0.41	0.68
Fatigue/inertia	7.79	5.58	6.43	5.62	1.36	0.18
Depression/dejection	5.60	6.88	4.00	5.54	1.44	0.15
Vigor/activity	12.28	5.46	13.43	5.49	–1.18	0.24
Confusion/bewilderment	4.34	3.93	3.10	3.35	1.89	0.06
Total mood disturbance	39.78	26.10	33.21	22.39	1.46	0.15
Positive and Negative Affect Scale						
Positive affect	32.28	8.60	34.73	6.95	–1.76	0.08
Negative affect	18.41	8.22	15.53	5.65	2.35	0.02
Hot Flash-Related Daily Interference Scale						
Activity items	2.07	2.53	0.51	1.56	4.35	0.001
Overall quality-of-life item	1.58	2.31	0.46	1.69	3.22	0.002

Table 6. Differences in Mood, Affect, Daily Activities, and Overall Quality of Life by Hot Flash Severity Among Breast Cancer Survivors

Instrument	None to Mildly Severe[a] (n = 36) $\bar{x}$	SD	Moderate to Severe[b] (n = 33) $\bar{x}$	SD	t	p
Profile of Mood States-Short Form						
Tension/anxiety	4.03	3.16	8.68	6.71	–3.57	0.001
Anger/hostility	2.77	3.55	6.82	6.37	–3.01	0.004
Fatigue/inertia	5.74	4.83	10.03	5.54	–3.83	0.001
Depression/dejection	2.63	3.39	9.07	8.25	–4.00	0.001
Vigor/activity	13.20	4.60	11.20	6.22	–1.49	0.142
Confusion/bewilderment	3.11	2.90	5.77	4.52	–2.86	0.006
Total mood disturbance	29.09	16.46	54.76	29.83	–3.90	0.001
Positive and Negative Affect Scale						
Positive affect	33.83	6.87	30.41	10.12	1.55	0.129
Negative affect	14.77	4.22	22.27	9.62	–4.12	0.001
Hot Flash-Related Daily Interference Scale						
Activity items	0.53	1.19	3.64	2.47	–6.56	0.001
Overall quality-of-life item	0.44	1.13	2.73	2.60	–4.65	0.001

[a] None to mildly severe hot flashes are those women with overall severity ratings < 5.

[b] Moderate to severe hot flashes are those women with overall severity ratings ≥ 5.

undergoing a natural menopause. Although hot flashes in healthy women typically are considered a "natural" part of the normal aging process (Matthews, 1992), the data suggest that hot flashes are an "unnatural" symptom in need of intervention among breast cancer survivors.

Data suggesting that 65% of breast cancer survivors experience hot flashes, with the majority of women reporting the symptom as severe, are consistent with previous work (Carpenter et al., 1998; Couzi et al., 1995). In a survey of 190 women with breast cancer ages 40–65, 65% reported experiencing hot flashes during the prior month (Couzi et al.). Severity ratings from those reporting hot flashes were 29% mild, 37% moderate, and 34% severe. In another survey, 65% of 114 postmenopausal women with breast cancer ages 36–83 reported experiencing hot flashes during the previous two weeks (Carpenter et al., 1998). Severity ratings for those reporting hot flashes were 23% moderately severe, 28% quite severe, and 31% extremely severe. These findings suggest that clinicians should question all breast cancer survivors regarding hot flashes, as the majority of survivors will experience this symptom following diagnosis.

Frequency, severity, bother, and duration ratings of hot flashes are of particular importance given the additional results regarding use of hot flash treatments. In terms of current hot flash treatments, breast cancer survivors and healthy women endorsed using similar types and numbers of treatment strategies, with the exception of HRT. As expected, HRT was used by significantly more healthy women than breast cancer survivors.

The finding that 4% of breast cancer survivors were using HRT is consistent with previous reports that less than 5% of breast cancer survivors take HRT following diagnosis (Swain, Santen, Burger, & Pritchard, 1999). Interestingly, breast cancer survivors rated the overall effectiveness of their treatment strategies to be about half as effective as did the healthy women. Thus, these findings suggest that currently available nonhormonal hot flash treatments may be ineffective, underutilized, or not acceptable to breast cancer survivors. In particular, although five times as many breast cancer survivors reported using nonhormonal prescription medications (e.g., clonidine) in the past compared to healthy women, few breast cancer survivors were using these medications at the time of the survey despite frequent, severe, and bothersome hot flashes. This finding implies that although women may have tried these medications in the past, they may have discontinued the medications for reasons such as failure to obtain relief, cost, or side effects. Although many prescription medications are effective in reducing hot flashes, they can be associated with significant side effects (Goldberg et al., 1994; Quella et al., 1998). Further research is needed to understand why these options may not be acceptable to breast cancer survivors. In addition, exercise, vitamins, and diet were cited as the three treatments used most commonly by breast cancer survivors despite a lack of empirical evidence supporting their effectiveness (Barton et al., 1998; Carpenter, 2000; Ivarsson, Spetz, & Hammar, 1998; Mayer & Linscott, 1995; Miller, 1992). These findings support the importance of thoroughly assessing the types of strategies women are using to alleviate their hot flashes and effectively guiding breast cancer survivors toward additional interventions when previous strategies have proven ineffective.

Interestingly, the quality, aggravating factors, and temporal pattern of hot flashes did not differ between groups. Both breast cancer survivors and healthy women reported a similar experience in terms of the number of sensations endorsed as occurring during a hot flash and the associated perspiration, the number and types of factors aggravating hot flashes, and changes in hot flashes regarding time of day, season of the year, and occurrence over the last six months. Data presented in this study can be used to educate breast cancer survivors regarding what to expect in terms of the hot flash symptom experience.

Several items supported the unpredictable nature of hot flashes. Over half of the breast cancer survivor group stated that hot flashes "just seem to happen" with no triggering event. With the exception of hot flashes being most bothersome at night, a majority of breast cancer survivors reported no particular time of day or season of the year when hot flashes were most problematic. Time of day data support previous research results. When 21 breast cancer survivors were monitored using objective hot flash measurement methods, hot flashes did not peak in frequency at any particular time of day among breast cancer survivors and instead occurred fairly regularly throughout a 24-hour period (Carpenter et al., 2001). Again, these data can be used to educate breast cancer survivors so that they may anticipate the unpredictable nature of hot flashes.

Although previous research using other measures of QOL showed only a marginally negative association with hot flashes (Carpenter et al., 1998), results from this study clearly

suggest hot flashes have a negative impact on mood, affect, daily activities, and overall QOL. Findings concerning concentration are consistent with research showing decreased cerebral blood flow during hot flashes in healthy women (Greene, 2000). Additional research is needed to describe the types of cognitive changes that women with hot flashes may experience. In addition, findings concerning negative affect are consistent with previous research. In a study of 60 surgical patients with cancer, somatic symptoms were correlated significantly with negative affect using a German translation of the PANAS ($r = 0.65$, $p < 0.01$) (Koller et al., 1996). Individuals with higher negative affect (e.g., anger, depression) were more introspective, apprehensive, negativistic, and vigilant and, thus, may be more likely to attend to and report physical symptoms (Watson & Pennebaker, 1989). Alternatively, unrelieved physical symptoms, such as hot flashes, may result in more frustration and negative affect. In either case, findings suggest that women with unrelieved hot flashes suffer negative psychosocial consequences, and interventions that alleviate hot flashes also may improve mood; affect; daily activities, including sleep, concentration, and sexuality; and overall QOL. Thus, incorporating these outcomes in future studies will be important. In addition, assessing hot flashes in women who present in clinical practice with mood disturbances or problems with sleep, concentration, or sexuality is important because alleviating hot flashes may help to improve these other outcomes.

Findings from this study should be considered in light of limitations. First, although the investigators attempted to sample the population of breast cancer survivors identified within their cancer registry, the response rate (33%) was low. However, responders appeared representative of the larger pool of breast cancer survivors in terms of age at diagnosis and year of diagnosis. Second, healthy women were recruited from the community-at-large and, thus, do not represent a true case-control population. Therefore, these results should be generalized with caution. A third limitation was the use of self-report data only. Although objective measurement of hot flashes has been shown to be valid and reliable (Carpenter et al., 2001, 1999; Freedman, 1989), this method was not feasible to use in this study given the number of women enrolled and the limited resources. Because previous research has shown that breast cancer survivors subjectively tend to underestimate hot flash frequency when compared to objective assessment methods (Carpenter et al., 1999), hot flash frequency data reported in this study may underestimate the number of hot flashes experienced each day by breast cancer survivors.

The use of self-reported menopausal status should not be viewed as a limitation of this research. Although serum follicle-stimulating hormone (FSH) levels with or without estradiol frequently are used as a clinical indicator of menopause, data suggest that these measures may not be reliable among healthy women (Burger, 1994; Stellato, Crawford, McKinlay, & Longcope, 1998) or breast cancer survivors (Kostoglou-Athanassiou et al., 1995). FSH does not reliably distinguish among pre-, peri-, or postmenopausal healthy women (Burger; Stellato et al.), and FSH significantly is increased with tamoxifen use (Kostoglou-Athanassiou et al.). In addition, estradiol levels were 239% higher after two years of tamoxifen therapy in comparison to pretamoxifen baseline levels ($p < 0.05$) (Lum, Woltering, Fletcher, & Pommier, 1997). Thus, because FSH, with or without estradiol, is not likely to be a reliable indicator of menopausal status among breast cancer survivors, the use of self-reported menopausal status is reasonable. Furthermore, definitions of pre-, peri-, and postmenopausal used in this study are being used in large-scale epidemiologic research (Avis et al., 1994; Brambilla et al., 1994).

In summary, this report has provided a detailed description of hot flashes in breast cancer survivors with comparison to healthy women. Hot flashes appeared to be significantly more problematic in breast cancer survivors in comparison to healthy women of the same age. In addition, hot flashes appeared to be associated with disruptions in mood; affect; daily activities, including sleep, concentration, and sexuality; and overall QOL. Findings support the need for a comprehensive assessment of the hot flash experience and additional intervention research to alleviate this symptom.

Author Contact: Janet S. Carpenter, PhD, RN, can be reached at janet.s.carpenter@vanderbilt.edu, with copy to editor at rose_mary@earthlink.net.

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- ➤ National Alliance of Breast Cancer Organizations
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- ➤ Living Beyond Breast Cancer
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