Published in final edited form as:

Explore (NY). 2014 ; 10(4): 241–247. doi:10.1016/j.explore.2014.04.003.

Hot Flashes Severity, Complementary and Alternative Medicine Use, and Self-Rated Health in Women with Breast Cancer

Kavita D. Chandwani, MD, MPH, DrPH^{1, #}, Charles E. Heckler, PhD, MS¹, Supriya G. Mohile, MD, MS¹, Karen M. Mustian, PhD, MPH¹, Michelle Janelins, PhD¹, Luke J. Peppone, PhD, MPH¹, Peter Bushunow, MD², Patrick J. Flynn, MD³, and Gary R. Morrow, PhD, MS¹

¹Department of Radiation Oncology, University of Rochester Medical Center, Rochester, NY

²Rochester General Hospital, Rochester, NY

³Metro-Minnesota CCOP, Minneapolis, MN

Abstract

Context—Hot flashes (HF) are a common distressing symptom in women with breast cancer (BC). Current pharmacologic options are moderately effective and are associated with bothersome side effects. Complementary and alternative medicine is commonly used by cancer patients. However, information on the association of hot flashes severity with such use and self-rated health is lacking.

Objective—To examine the hot flashes severity in women with breast cancer and its association with complementary and alternative medicine use and self-rated health (SRH).

Design—Longitudinal multicenter study to assess information needs of cancer outpatients.

Participants—Patients with a diagnosis of breast cancer who were scheduled to undergo chemotherapy and/or radiotherapy.

Outcome Measures—Hot flashes severity (0 = not present and 10 = as bad as you can imagine), use of complementary and alternative medicine (yes/no), and self-rating of health (SRH) status post-treatment and six-months thereafter (1–5, higher score = better SRH).

Results—The majority of women with HF (mean age = 54.4 years) were Caucasian and married, with higher education, and 93% had received surgical treatment for BC. At the end of treatment, 79% women reported experiencing HF [mean severity = 5.87, standard deviation (SD) = 2.9]; significantly more severe HF were reported by younger women with poor SRH, better performance status, and those reporting doing spiritual practices. At follow-up, 73% had HF (mean severity = 4.86, SD = 3.0), and more severe HF were reported by younger women with poor self-rated health who had undergone chemotherapy plus radiotherapy, used vitamins, and did not exercise.

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[#]Correspondence to: Saunders Research Building, 265 Crittenden Blvd, CU 420658, Rochester, NY 4642
kavita_chandwani@urmc.rochester.edu.

Presented in part at the Annual meetings of Society of Behavioral Medicine, April 2012, New Orleans, LA; American Society of Preventive Oncology, March 2012, Washington, DC; and International Research Congress on Complementary and Integrative Medicine and Health, May 2012, Portland, OR.

Conclusions—A high percentage of women experienced hot flashes at the end of treatment and at six-month follow-up. A significant association of hot flashes severity with spiritual practice, increased vitamin use, and reduced exercise emphasize the need for future studies to confirm the results. This can facilitate safe use of complementary and alternative medicine and favorable outcomes while managing cancer-related hot flashes.

Keywords

Breast cancer; hot flashes; complementary and alternative medicine; self-rated health

Introduction

Hot flashes (HF) are one of the most common symptoms related to chemotherapy or hormonal treatment in women with breast cancer (BC). About 64–85% of women with a history of breast cancer report HF, and these are correlated with less education, young age at diagnosis, high body mass index, and the use of tamoxifen and aromatase inhibitors.^{1–3} About 59% of women with a history of breast cancer have described HF as severe.¹ Cancer-related HF are more severe than those during natural menopause and interfere with life routines affecting quality of life.^{1,4}

Currently available pharmacologic agents for the treatment of HF from cancer-related and non-cancer-related etiologies are only moderately effective and are associated with unpleasant side effects.⁵ Hormonal treatment is effective in controlling HF; however, hormone replacement therapy is contraindicated in women with breast cancer.⁶ Several non-pharmacologic treatments including Complementary and Alternative Medicine (CAM) modalities are commonly used by cancer patients; however, their efficacy is uncertain. These include biologically based practices (herbs and diets), mind–body medicine (prayer, meditation, and yoga), energy healing (Reiki and therapeutic touch), manipulative and body-based practices (chiropractic care and massage), and whole medical systems (such as traditional Chinese medicine and Ayurveda).⁷ Some techniques such as prayer, spirituality, diet, and exercise are included in the list of CAM therapies as defined by National Center for CAM (NCCAM) and are recommended as a part of usual care; however, quite often, they are not considered as CAM therapies.

About 38% of adults in the USA reported using some form of CAM when asked about its use “in the last 12 months.”⁸ Although most CAM use was reported for conditions like backache and neck or joint pain,⁹ its use is on the increase among cancer patients in different phases of their cancer experience, with studies reporting prevalence of use ranging from 7% to 80%.^{10–15} One study reported 86% women used CAM soon after the diagnosis of breast cancer.¹⁶ CAM modalities commonly used by cancer patients are mind–body medicine, herbs, manipulative practices, and energy medicine.¹⁷ A study from our group found 91% of the cancer patients used at least one CAM technique during treatment, most commonly used being prayer, relaxation, and exercise.¹⁸ Prevalence of CAM use by women with natural menopause to manage their menopausal symptoms is about 22%.¹⁹ However, association between CAM use and HF severity in cancer has not been studied.¹⁹

Cancer patients using CAM are more likely to have symptoms that are associated with reduced quality of life, such as anxiety, depression, and sleep disturbances, compared to those without cancer²⁰. Research has shown that symptoms like pain, fatigue, shortness of breath, feelings of depression, and physical discomfort experienced in cancer are associated with poor self-rated health (SRH).²¹ Small reduction in SRH with increasing age has been observed in non-menopausal women and those undergoing natural menopausal transition.²² However, the association of cancer-related HF severity with SRH at the end of treatment and follow-up has not been studied. The objective of this study was to examine the severity of HF in women with breast cancer and their association with CAM use and with SRH at the end of treatment and at six-month follow-up. We hypothesized that women with self-reported use of CAM therapies will be experiencing more severe HF and will have lower self-rated health.

Methods

This article is based on a secondary analysis of data involving women with BC who participated in a multicenter longitudinal study of cancer outpatients conducted through the University of Rochester Cancer Center-Community Clinical Oncology Program Research Base. The purpose of the original study was to determine the information needs of cancer patients during and after treatment.¹⁸

Patients with a diagnosis of cancer, 18 years or older, having a life expectancy of 10 months, who were scheduled to undergo chemotherapy or radiotherapy were included in the study; those who were taking tamoxifen alone were excluded from the study. After consenting to participate in the study, patients answered self-administered questionnaires at four time points: baseline, pre-treatment, two weeks after completion of treatment (RX), and six months following it (FU). The questions related to their demographic and medical information, SRH, symptom inventory, and their cancer-related concerns. Information on their use of CAM and other resources was obtained at RX and FU. An earlier publication has reported on the use of CAM among all the participants.¹⁸ This study was approved by the Human Subjects Review Board at the University of Rochester and the local Institutional Review Boards at the participating Community Clinical Oncology Groups.

Measures

The outcomes of interest for this article included the following—Demographic data and information related to cancer diagnosis and treatment were obtained through the questionnaires. Karnofsky performance score (KPS) was abstracted from the patients' medical records.

HF severity: A question relating to HF was one of the 13 items from the MD Anderson Symptom Inventory²³ used in this study. Women with breast cancer rated their HF at RX responding to a question about HF: "Please rate how severe the following symptoms were during your treatment." They were asked "Your hot flashes at their worst," with response indicated on a scale of 0 (*not present*) to 10 (*as bad as you can imagine*). Similar question was asked about hot flashes "during the past five days" at FU on a 0–10 scale. Severity

score of zero meant an absence of HF and those reporting a severity of 1–10 were included in further analysis.

CAM use: Question asked at RX and at FU regarding CAM use was as follows: “Since your cancer diagnosis, have you used any of the following complementary or alternative therapies?” Women responded (*yes/no*) to the question reporting on their use of 13 CAM therapies (exercise, prayer, relaxation, chiropractic, massage, imagery, spirituality, diet, herbs, vitamins, group therapy, hypnosis, and acupuncture). It must be noted that very often exercise, spirituality, diet, herbs, vitamins, and group therapy are not considered a part of CAM therapies (although they are a part of the CAM list of NCCAM).

SRH: Women's perception of their health was recorded through a single question—In general, would you say that your health is? —at baseline, RX, and FU; for this question, a scale of 1–5 was used (1 = excellent, 2 = very good, 3 = good, 4 = fair, and 5 = poor). SRH is the first question about general health in the Medical Outcomes Study 36-item short-form survey.²⁴

Data Analyses

Descriptive analyses of demographic characteristics of the sample, hot flashes severity, and use of CAM therapies were conducted. A general linear model (GLM) analysis was used to study the association of HF severity with CAM use adjusting for significant demographic and medical variables using SAS version 9.2. Variable selection was performed using PROC GLMSELECT with a stepwise selection method from the demographic variables of age (categorized: less than 55 years and 55 years or older); race (Caucasian or non-Caucasian); marital status (married or single); educational status (high school or higher education); time since diagnosis; treatment taken (chemotherapy, radiotherapy, both chemotherapy plus radiotherapy); KPS; and 13 CAM variables, namely, prayer, relaxation, exercise, chiropractor, massage, imagery, spirituality, diet, herbs, vitamins, group therapy, hypnosis, and acupuncture. SRH coding was reversed such that higher scores meant better SRH. For PROC GLMSELECT, an entry and stay *P* value of .15 was considered significant. For the association of HF severity with demographic variables, CAM therapies, or self-rated health (SRH), a *P* value of .05 or less was considered as significant. Path analysis with bootstrap confidence intervals for mediation was used to explore the mediation effect of SRH at baseline on HF at RX by spirituality at RX, and similarly for exercise and vitamin use at FU. MPLus Version 7 was used for mediation analysis.

Results

In the original study, at the end of treatment, there were 917 cancer patients, of which, 378 (41%) were women with breast cancer, and their data is reported in this article. Mean age during treatment was 54.4 years [standard deviation (SD) = 11.5, range: 31–82], with 52% of the sample below the age of 55 years (Table 1). Most women were Caucasian (94%), married (76%), and had more than high school education (65%). Mean time since diagnosis at the time of baseline was four months, and about 65% women had KPS of 100. About 92% of the women had undergone surgery at the time of entry into the study; 45% reported

having undergone chemotherapy, while 39% had undergone chemotherapy and radiotherapy.

A total of 306 women at RX and 278 women at FU responded to the question on HF severity. At RX, 243 (79%) women had HF while 203 (73%) reported having HF at FU (Table 2). Mean HF severity was 5.87 (SD = 2.9) at the end of treatment and was 4.86 (SD = 3.0) at six-month follow-up after completion of treatment, the range of severity being 1–10. About 46% women at Rx and 30% at FU reported severe HF (severity = 7–10).²⁵

Questions on the use of CAM therapies were answered by 309 women with breast cancer. The use of at least one of the 13 CAM therapies by the women is presented in Table 3. The most used CAM therapy was prayer (82%). Other highly used CAM therapies were relaxation (61%) and exercise (53%) at RX. The use of exercise increased to 65% at FU. The use of the other CAM therapies during treatment and at six-months follow-up ranged from 2% to 28%. The therapies that were used by 10% or more of the participants were considered for analysis of their association with HF severity at RX and FU.

During Treatment

General linear model (GLM) analysis showed a significant association of HF severity during treatment (RX) with age ($P < .0001$), spiritual practices ($P = .01$), SRH ($P < .03$), and KPS ($P = .04$); type of treatment was not significant ($P = .15$). Women younger than 55 years reported more severe HF than those who were 55 years or older (mean = 5.71, SD = 0.34 vs. mean = 3.94, SD = 0.31). Women who reported practicing spirituality also reported more severe HF compared to those who reported not engaging in spiritual practices (mean = 5.43, SD = 0.44 vs. mean = 4.22, SD = 0.24). Similarly, SRH was related to more severe HF, with a decrease of SRH by one being associated with an increase of 0.5 in mean HF severity. Increase in KPS by one unit was associated with a 0.04 increase in HF severity.

Six-Month Follow-up

At FU, the GLM model showed a significant association of HF severity with age, treatment type, exercise, vitamin use, and SRH. Women younger than 55 years were found to have more severe HF than those 55 years or older (mean = 4.42, SD = 0.34 vs. mean = 3.5, SD = 0.30; $P < .02$). Those who had undergone both chemotherapy and radiotherapy reported more severe HF (mean = 4.68, SD = 0.34) than those who had received chemotherapy (mean = 3.99, SD = 0.30) or radiotherapy alone (mean = 3.20, SD = 0.52), $P < .02$. Exercise was associated with less severe HF (mean = 3.47, SD = 0.27 vs. mean = 4.45, SD = 0.37, $P < .02$). However, vitamin users reported more severe HF than non-users (mean = 4.95, SD = 0.40 vs. mean = 2.97, SD = 0.24; $P < .0001$). A decrease in the SRH by one was associated with an increase of 0.5 in the mean HF severity ($P = .03$).

Educational and marital status was not significantly associated at either time points. No significant mediation effects of spirituality at RX, exercise at FU, or vitamin use at FU on the effect of baseline SRH on HF at RX were found.

Discussion

This study showed a high prevalence of HF (79% at treatment completion and 73% six months thereafter) in women with breast cancer which is consistent with observations in previous studies.^{1–3} Absence of menstruation has been reported in one study by about 86% of women (age: 25–56 years) with breast cancer 6–12 months after completion of chemotherapy and/or adjuvant treatment and by 55% at 33-month median follow-up.²⁶ About 65% women who are 40–65 years of age with a history of breast cancer report having HF²⁷ and another study observed that 46% of women ($n = 371$) aged 40 years or younger and with a history of BC had hot flashes.²⁸ Although the women's menopausal status in the current study was not known, 52% of the sample was younger than 55 years at the time of diagnosis. Thus, the potential magnitude of distressful experience of HF by the young breast cancer survivors proves to be a big public health concern.

The severity of HF at the end of treatment completion (5.87) and at the six-month follow-up (4.86) is close to the HF severity reported by Carpenter et al.,²⁹ in 2012, which was 5.1 and 5.12 in the breast cancer survivors and postmenopausal women without cancer, respectively. However, there was a slight difference in the mean age of the women in the current study (54.4 years) and the mean age of the two groups in the latter study (53 years in breast cancer survivors and 52 years in the postmenopausal women without cancer). Although the severity of HF in women with breast cancer was greater during treatment, the prevalence of HF at six-month follow-up continued to be high. In fact, about one-third of the women perceived their HF as severe at six-month follow-up. There are reports of younger women with cancer perceiving HF as a problem^{3,30,31}; it is noted that in the current study women younger than 55 years reported more severe HF. Moreover, those who received chemotherapy and radiotherapy had significantly more severe HF than those who received either treatment alone.

In this study, the majority of women used CAM, with prayer, relaxation, and exercise being the most frequently used. This is in agreement with the finding reported in all cancer patients in the original CCOP study.¹⁸ A wide range of the reported prevalence of CAM use can be found in literature³²: 80% patients with early breast cancer had used CAM during treatment,³³ and about 66% breast cancer survivors used CAM in the previous 12 months; most commonly used CAM treatments were relaxation or meditation, herbs, and “spiritual healing.”³⁴ This has varied with the heterogeneous samples of populations studied, study designs, types of cancers and CAM modalities, and time of study relative to cancer experience. Another such example is a prospective study of women with early breast cancer in Australia where 16.4% had consulted a CAM practitioner and 11% had used one of the CAM products (hormonal or herbal) commonly used for relief of menopausal symptoms in the previous 12 months in comparison to about 7% at the time of diagnosis.³⁵ The variety of population samples, lengths of cancer experience, non-standard questionnaires for CAM use, as well as diverse definitions of each CAM modality in previous studies makes comparison of the results a complex and challenging task.

Exercise

Exercise is linked to a range of cancer preventive and control benefits and is usually recommended to persons with cancer.^{36–39} Although previous research has shown that physical activity is reduced after cancer diagnosis,⁴⁰ in the current study, the increase in percentage of those who exercised from the end of treatment to the follow-up period could be promising. Our results also confirm previous reports of increasing exercise among women with early breast cancer within two years of diagnosis³⁵ and among breast cancer survivors.³

The results of the current study also showed that hot flashes were less severe in those who reported exercising. Increase in hot flashes severity in non-exercisers at six-month follow-up was also observed in all the participants of the original study, which included all cancer types, although this was not significant.⁴¹ However, research on the relationship between exercise and menopausal symptoms in postmenopausal women has not yielded consistent results with some reports indicating increased severity of HF in physically active women with HF^{42,43} while a recent study reported no beneficial effects of exercise intervention on menopausal symptoms in women with a history of breast cancer.⁴⁴ Whether exercise by female cancer survivors with severe HF will be beneficial and safe needs to be confirmed through further research to help make appropriate recommendations.

Supplements

The percentage of women using herbal products at six-month follow-up in this study was similar to that in another study who were using herbs and hormones for menopausal symptoms.³⁵ However, in the current study, the specific herbs taken and dose were not asked, and the severity of HF was not related to the use of herbal products. Another observation in this study was the increased prevalence of vitamin use at six-month follow-up and that the vitamin users were observed to have more severe hot flashes. One study that examined the use of 21 vitamins and minerals for HF in postmenopausal women reported a decrease in HF severity, but this effect was significantly greater in the placebo group.⁴⁵ Similarly, studies of vitamin E for HF have not yielded encouraging results.^{5,46} Although high vitamin use has been reported in previous studies of cancer population, some authors have suggested possible harm from the use of antioxidants while others indicated that patients derive benefits from such use.⁴⁷ The results of this study could be indicative of more women with hot flashes consuming vitamins in expectation of a relief; however, future research should ascertain the potential effects of vitamins on HF.

Cancer patients continue to use CAM regardless of their physicians' advice, and there is a wide range of non-disclosure of antioxidant/supplement use in studies of CAM use by cancer patients to their providers.¹⁵ In one study, 61% of veterans with cancer used dietary supplements (vitamins use by 80%), but 38% did not share this information with their providers.⁴⁸ In our group's study of the original data, 57% did not disclose their CAM use.¹⁸ With the limited information sharing of such CAM use by cancer patients, more harm than benefit could be done because such CAM practices/products may be beneficial in some cases while in others this could open up numerous possible situations of unknown and untraceable drug interactions or unexplained treatment outcome anomalies. In such a

scenario, it becomes crucial for more concerted efforts to determine the efficacy of various types of CAM therapies/products during the cancer experience through future clinical trials.

Breast cancer patients use different ways to cope with their disease, and this includes spiritual practices.⁴⁹ However, one study of older cancer patients reported no differences in spirituality between CAM users and non-users, the three most common practices being exercise, herbs, and spiritual healing.⁵⁰ In a qualitative study of CAM use in cancer patients, the authors reported that patients may consider CAM use itself as a spiritual practice.⁵¹ The reason for the finding in this study of more severe HF in those who reported spiritual practices at the end of treatment and not at the follow-up is difficult to explain since the specific details of what constituted the “spiritual practices” according to the patients were not available. Additionally, “spirituality” was not defined on the survey. Prayer, which is considered a spiritual practice, was queried separately. Although, the use of prayer was high in this study population, it was not significantly associated with the HF severity.

In the current study, more severe HF were reported by those who had poorer SRH during treatment and at six-month follow-up. This is different from the observation of no significant association of SRH with menopausal symptoms or menopausal transition from two prospective studies in healthy women undergoing menopausal transition.^{22,52} However, in these studies, a different measure was used; SRH was rated relative to their peers on a 3-point scale—worse than most, about the same as others, or better than most women their age—in contrast to the 5-point scale used in the current study. CAM use in the general population is related to self-rated health.⁵³ Additionally, women after surgery for early breast cancer and reporting poor quality of life are more likely to use CAM.³³ Therefore, monitoring of SRH could be a helpful tool to identify females with a history of breast cancer and to predict their use of CAM. This can facilitate appropriate counseling and decision making, especially on the safe use of the CAM modalities with scientifically proven benefits. Another observation in this study was the association of increased HF severity with better performance status. This could not be explained given the association of poor SRH with poor physical function reported in a large cohort.⁵⁴

Although the current study made use of data drawn from a nationwide study sample, there were several limitations. Because some information such as disease stage and their use of hormones was not available, no further analyses were conducted. The menopausal status of the women was not known at entry into the study or at later time points. Thus, the analyzed sample may have included those who had developed natural menopause prior to entry into the study irrespective of the cancer treatment. Moreover, information regarding the length and other specifics of CAM use, such as the dose of exercise (e.g., mode, duration, frequency, and intensity) or type and dosage of vitamins used, was not available. Because women self-reported their CAM use from the time of their cancer diagnosis, the data are subject to recall bias. Because no data on participants' BMI was available, its association with HF and exercise could not be analyzed.

Conclusions

The results of this study show that a high percentage of women with breast cancer continue to experience HF of varying severity six months after the completion of chemotherapy and/or radiotherapy. Younger women had more severe hot flashes, and this was related to poor self-rated health, performance score, treatment taken, spiritual practice, exercise, and vitamin intake. Tracking the patients' self-rated health can help mark the possible use of CAM. Increasing exercise could be a positive change. Vitamins are important for overall health but are not known to offer benefit in treating cancer. Some vitamins such as vitamin D supplements are often recommended when deficient but the general role of vitamin supplementation needs to be ascertained and may have untoward side effects. With increasing use of CAM as an easily available self-care tool, it is imperative that the effects of specific CAM modalities on hot flashes be ascertained. This emphasizes the need for future trials to corroborate the results of this study so that appropriate recommendations for their use can ultimately be provided. Until then, studies of exercise and other interventions for symptom-management in cancer should consider controlling for vitamin use.

Acknowledgments

The authors acknowledge the participation of all women for sharing their information.

This work was supported by the NCI Public Health Service Grant U10 CA37420 and a supplement to the same, R25CA102618, K07CA120025 and Grant RSG-01-071-PBP from the ACS. The authors also acknowledge the informational support of Dr. Joseph Roscoe and the editorial support of Dr. Susan Rosenthal.

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Table 1
Characteristics of Women With Breast Cancer (*n* = 378)

Participant Characteristics During Treatment	Mean (SD) or %
Age (years)	54.4 (11.5)
Range	31–82
<55 years	52%
≥55 years	48%
Race	
Caucasian	
African American	94%
Hispanic	4%
Hawaiian/Pacific Islander/Asian	2%
Marital status	
Married	76.0%
Education	
Some college or higher	65%
High school or less	35%
Time since diagnosis	0.3 (2.3) years
Treatment	
Surgery	92%
Chemotherapy	45%
Radiotherapy	13%
Chemotherapy plus	
Radiotherapy	39%
None	3%
Karnofsky performance score	
91–100	65%
81–90	26%
71–80	6%
61–70	1%
≤60	2%

SD, standard deviation.

Table 2
Hot Flashes Severity at the End of Treatment and at Six-Month Follow-up

Hot Flashes Severity	End of Treatment Mean (SD) <i>n</i> = 243 (100%)	Six-Month Follow-up Mean (SD) <i>n</i> = 203 (100%)
Mild	2.46 (1.07) <i>n</i> = 81 (33.3%)	2.42 (1.11) <i>n</i> = 105 (51.7%)
Moderate	5.34 (0.48) <i>n</i> = 50 (20.6%)	5.43 (0.50) <i>n</i> = 37 (18.2%)
Severe	8.65 (1.26) <i>n</i> = 112 (46.1%)	8.74 (1.19) <i>n</i> = 61 (30.1%)

Mild = 1–4; Moderate = 5, 6; Severe = 7–10; based on MDASI user's guide.²⁵

Table 3
Use of Complementary and Alternative Medicine (CAM) by Women With Breast Cancer
(*n* = 378)

CAM Techniques	End of Treatment <i>n</i> (%)	Six-Month Follow-up <i>n</i> (%)
Prayer	255 (82.5)	228 (82.3)
Relaxation	147 (60.7)	169 (61.0)
Exercise	164 (53.1)	180 (65.0)
Imagery	64 (20.7)	45 (16.3)
Spirituality	64 (20.7)	62 (22.3)
Diet	64 (20.7)	77 (27.8)
Vitamins	59 (19.2)	71 (26.5)
Massage	45 (14.6)	63 (22.7)
Herbs	31 (10.3)	30 (10.8)
Group therapy	28 (9.1)	22 (7.9)
Chiropractor	23 (7.4)	31 (11.2)
Hypnosis	6 (1.9)	5 (1.8)
Acupuncture	6 (1.9)	9 (3.2)