Menopause: The Journal of The North American Menopause Society
Vol. 27, No. 5, pp. 000-000
DOI: 10.1097/GME.0000000000001507

ORIGINAL STUDY

Changes in hot flash experiences and related factors in women with breast cancer

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Abstract

Objective: Taiwanese women are younger than women in western countries when diagnosed with breast cancer, and many of them are still menstruating. One of many distressing side effects reported by premenopausal women treated for breast cancer are hot flashes (HFs). The purposes of this study were to identify: (1) the trajectories of hot flash (HF) occurrence, frequency, and interference and (2) potential factors associated with HF changes.

Methods: Peri- or premenopausal women newly diagnosed with breast cancer scheduled to receive chemotherapy and hormonal therapy were enrolled. HF frequency, HF interference, and other symptoms were measured six times from prechemotherapy to 24 months after chemotherapy. Data were analyzed using hierarchical linear modeling.

Results: A total of 90 women were eligible for the study. The prechemotherapy occurrence rate of HFs was 7.9%, but rapidly increased to 42.5% immediately after chemotherapy. The change curve of HF frequency and interference appeared quadratic, increasing first and slightly decreasing later. At any time point, increased body mass index (BMI) was associated with both higher HF frequency ($P = 0.020$) and HF interference ($P = 0.002$), whereas anxiety ($P < 0.001$) and loss of sexual desire ($P = 0.038$) were associated with higher HF interference. Six months after completing chemotherapy, premenopausal women reported significantly higher HF frequency than perimenopausal women ($P = 0.041$).

Conclusion: A significant proportion of pre- and perimenopausal women experienced HFs after receiving breast cancer treatment. Our findings on HF trajectories can educate patients newly diagnosed with breast cancer. Special attention should be paid to those with increased body mass index changes and those still regularly menstruating.

Key Words: Breast cancer – Chemotherapy – Hormonal therapy – Hot flashes.

Women with early-stage breast cancer receive a standard treatment of adjuvant chemotherapy to prevent recurrence and prolong survival.[1] In Taiwan, around 63% of stage I and II breast cancer patients receive chemotherapy.[2] The most commonly used chemotherapy drugs include anthracyclines, taxanes, 5-fluorouracil, cyclophosphamide, and carboplatin. These drugs, often used in combination, can destroy patients' follicular cells[3] causing premature menopause among young women.

The age at which women are diagnosed with breast cancer in Taiwan is younger than that in Western countries. The percentage of young patients (ie, younger than 50 years) newly diagnosed with breast cancer was 52.2% in Taiwan,[2] but this percentage was only 19% in the United States[4] and 19% in the United Kingdom.[5] Furthermore, 75% of premenopausal Taiwanese women with breast cancer were found to experience chemotherapy-induced amenorrhea, and 80% of them reported that their period did not come back 2 years after diagnosis (Li CY. Menstruational change and climacteric symptoms in women with breast cancer receiving chemotherapy [unpublished master's thesis]; 2010).

One of the distressing menopausal symptoms reported by premenopausal women treated for breast cancer is hot flashes (HFs).[6,7] HFs may cause sleep disorders[8,9] and diminished quality of life.[9,10] Clinicians are, however, unlikely to provide information to young breast cancer patients about potential menopause after chemotherapy.[11] Furthermore, 85% of women (29-65 years old) treated within the previous 5 years

Received October 16, 2019; revised and accepted December 2, 2019.
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Abstract previously presented at the International Psycho-Oncology Society conference held October 29 - November 2, 2018 in Hong Kong.
Funding/support: This study was funded by the Ministry of Science and Technology, Taiwan (Grant number: 101-2314-B-182-078-MY3).
Financial disclosure/conflicts of interest: None reported.
Supplemental digital content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's Website (www.menopause.org).
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for breast cancer had HFs, but only 23% of them received treatment for HFs.[10] The main reason for neglecting this problem may be that oncology clinicians, including physicians and nurses, lack knowledge about the HF experience.

The HF experience has been correlated with several factors. For example, HFs were more likely in women with breast cancer who gained weight after diagnosis,[12,13] were premenopausal before breast cancer treatment,[14] had fewer pregnancies before diagnosis,[9] had a higher education level,[9] did not exercise regularly before diagnosis,[15] and had depression[16] and/or anxiety.[17]

The above-mentioned studies often used a cross-sectional design to explore HF prevalence rate[8,14,18] or factors related to HF severity,[9,12,16] a design that cannot capture the dynamic nature of HF-symptom experience over time. During the long process of cancer treatment, patients' symptoms may be relieved when treatment ends or deteriorate as the disease progresses. The snapshot approach used in cross-sectional studies often results in different HF prevalence or severity, depending on the timing of data collection, which may not help in understanding the real trajectory of the HF symptom experience. Therefore, this study was undertaken to identify: (1) HF trajectories in terms of prevalence, frequency, and interference and (2) potential factors associated with HF change.

METHODS

Study design

For this longitudinal prospective study, data were collected from prechemotherapy to 24 months after the end of chemotherapy. Demographic and clinical data were collected at baseline (prechemotherapy). HF frequency, HF interference, symptoms (anxiety, depression, and loss of interest in sex), and body mass index (BMI) were measured six times: prechemotherapy, end of chemotherapy (around 5 months after prechemotherapy), then every 6 months for 4 times (around 11, 17, 23, 29 months after prechemotherapy).

Participants

Women who were treated for breast cancer at Chang Gung Memorial Hospital, Linkou branch were invited to participate in this study if they met the following inclusion criteria: (1) 18 years or older, (2) newly diagnosed with breast cancer and planned to receive chemotherapy and hormonal therapy, peri- or premenopausal at diagnosis, and (3) able to read Chinese or speak Mandarin or Taiwanese.

This study was approved by the Institutional Review Board (100-4427B) of Chang Gung Memorial Hospital. Written informed consent was obtained from each participant.

Measures

Hot flash experience

HF frequency was measured by the author-developed hot flash diary (HFD), in which patients were asked to record every episode of daytime HF they were aware of and nighttime HFs they could remember when they woke up the next morning. The sum of daytime and nighttime HF frequency was used to represent the overall HF frequency for each day. The HFD was completed for 3 consecutive days before each follow-up time point and the mean HF frequency over 3 days was used.

The degree of HF interference with daily activities and overall quality of life was measured by the Hot Flash-Related Daily Interference Scale (HFRDIS).[19] The 10-item HFRDIS has 9 items measuring interference with daily functions (work, social activities, leisure activities, sleep, mood, concentration, relations with others, sexuality, enjoyment of life) and one item measuring interference with quality of life. Each item is rated on a 0 (does not interfere) to 10 (completely interferes) scale. Higher scores on the HFRDIS indicate higher levels of HF interference. Cronbach alpha was 0.96 in the current sample.

Covariates included anxiety, depression, loss of interest in sex, BMI change, demographic factors, and clinical factors.

Anxiety, depression, and loss of interest in sex were measured by Greene Climacteric Scale (GCS).[20] The GCS measures menopause symptoms on four subscales, but only the 11-item psychological subscale and 1-item sex problem subscale were used in this study. On the GCS psychological subscale, six items assess the severity of anxiety symptoms and five items assess the severity of depressive symptoms. Only one item assesses the severity of loss of interest in sex. Each item (symptom) is rated from 0 (not at all) to 3 (very much) regarding the degree to which it bothers the participant. Total scores range from 0 to 18 for anxiety, 0 to 15 for depression and 0 to 3 for loss of interest in sex. The Chinese version GCS was reported to have a content validity index of 0.98 and a Cronbach alpha of 0.93.[21]

BMI was computed by dividing the participant' weight in kilograms by the squared height in meters. BMI change was defined as the difference between current BMI and last measured BMI. A positive value of BMI change indicates an increase in BMI, whereas a negative value indicates a decrease in BMI. The BMI change at baseline was set at zero.

Demographic factors included age at diagnosis, menstrual status, education level, marital status, religious affiliation, living status, childbirth experience, work status before illness, household income, and exercise habit before illness. Clinical factors were comorbidity, cancer stage, and treatment received (including information regarding surgery, chemotherapy, radiation therapy, and hormonal therapy). All demographic information was collected at baseline, whereas the complete treatment information was collected at 12 months after hormonal therapy.

Statistical analysis

Demographic characteristics, clinical characteristics, and study variables were summarized by descriptive statistics (mean, standard deviation, number, frequency). HF frequency was calculated by taking the mean of 3 day's episodes of HFs recorded in participants' HFDs. The trajectories of HF frequency, HF interference, and their associated factors were identified using multilevel analysis. In this analysis, individual changes in HF frequency/interference were modeled in level I and between-individual factors (eg, age) that influenced individual changes were modeled in Level II. To examine the relative size of within-individual variance and between-individual variance, we first specified an unconditional null model. To determine whether the between-individual variation was sufficient for two-level analysis (ie, intraclass correlation coefficient >0.138), we calculated the intraclass correlation coefficient. To determine the overall change patterns using deviance statistics, we then compared different time models (linear vs quadratic) in months. Once the overall time model was set, potential level I factors (time-varying variables such as anxiety, depression, loss of interest in sex, and BMI change) and level II factors (time-invariant factors such as age, menstrual status before chemotherapy, and other demographic and clinical factors) were explored by adding them separately into the time model to test their effect on the intercept and time parameters. Only parameters with significant error variances were screened for potential covariates. Significant covariates were then built into a multivariate model with time centered at 6 months after completing chemotherapy. Nonsignificant predictors were removed from the model one by one based on P values. The predictors kept in the final model were all significant at $P < 0.05$. The sample size of this study was determined based on findings from Mass and Hox's simulation study in which they reported that the size of second level less than 50 would lead to biased estimates of second-level standard errors.[22] And if the variance of error terms was the main concern, the size of second-level should be at least 100.[23] Therefore, the sample size was set to be 100. Data were analyzed using SPSS version 22 and HLM 6.03.

RESULTS

Sample characteristics

Of the 127 participants who met the inclusion criteria, 37 were excluded from analysis because they did not receive hormonal therapy ($n = 27$) or chemotherapy ($n = 9$) due to treatment change or they have metastatic disease ($n = 1$). Data were available for 90 women at baseline (prechemotherapy), 84 at the end of chemotherapy, 79, 76, 79, and 78 at 6, 12, 18, and 24 months after completing chemotherapy, respectively. The 90 women had a mean age of 43.86 years and menarche age of 13.06 years. Most of them (87.8%) were still regularly menstruating (premenopausal), whereas 11 (12.2%) had irregular menstruation (perimenopausal). Most of the women were married (78.9%), had childbirth experience (83.3%), had stage I or II disease (85.5%), and had received breast cancer surgery (100%). Their number of chemotherapy cycles ranged from 6 to 9. More than half (64.4%) had received radiation therapy, and most participants (98.9%) had received 5 years of tamoxifen. Other demographic and clinical characteristics are in Table 1.

TABLE 1. *Participants' demographic and disease/treatment characteristics, N = 90*

Characteristic	n (%)	Mean (SD)	Range
Age, y		43.86 (5.22)	31-56
Menarche age, y		13.06 (1.37)	10-18
Menstrual status (baseline)			
Premenopausal (regular)	79 (87.8)		
Perimenopausal (irregular)	11 (12.2)		
Marital status			
Single	13 (14.4)		
Married	71 (78.9)		
Divorced/separated/widowed	6 (6.7)		
Childbirth experience			
No	15 (16.7)		
Yes	75 (83.3)		
Breastfeeding experience ($n = 75$)			
No	32 (42.7)		
Yes	43 (57.3)		
Education level			
Elementary	2 (2.2)		
Junior	11 (12.1)		
Senior	40 (44.4)		
College	12 (12.2)		
University	19 (21.1)		
Graduate	7 (7.8)		
Religious affiliation			
None	30 (33.3)		
Buddhism	45 (50)		
Other	15 (16.6)		
Live alone			
No	83 (92.2)		
Yes	7 (7.8)		
Employed before illness			
No	11 (12.2)		
Yes	79 (87.8)		
Family economic source			
Self	28 (31.1)		
Spouse	49 (54.4)		
Parents	2 (2.2)		
Other	11 (12.1)		
Monthly family income (NTD)			
None	3 (3.3)		
10,000-30,000	16 (17.8)		
30,001-50,000	18 (20)		
50,001-80,000	23 (25.6)		
80,001-100,000	12 (13.3)		
100,001-150,000	14 (15.6)		
Refused to answer	4 (4.4)		
Exercise habit before diagnosis			
No	56 (62.2)		
Yes	34 (37.8)		
Histories			
No	56 (62.2)		
Yes	34 (37.8)		
Tumor location			
Left	40 (44.4)		
Right	46 (51.1)		
Bilateral	4 (4.4)		
Number of lymph nodes involved		1.65 (2.31)	0-10
Chest/skin invasion			
No	89 (98.9)		
Yes	1 (1.1)		
Invasion to supra/subclavian lymph nodes			
No	90 (100)		
Yes	0 (0)		
Distant organ metastases			
No	90 (100)		
Yes	0 (0)		

(Continued on next page)

The prevalence of hot flash

The baseline (prechemotherapy) HF prevalence rate was 7.9%, but escalated drastically to 42.5% at the end of

TABLE 1 *(Continued)*

Characteristic	n (%)	Mean (SD)	Range
Stage (AJCC)			
Ia	22 (24.4)		
Ib	3 (3.3)		
IIa	35 (38.9)		
IIb	17 (18.9)		
IIIa	9 (10)		
IIIb	3 (3.3)		
IIIc	1 (1.1)		
Surgery received			
No	0 (0)		
Yes	90 (100)		
Surgery method			
Partial mastectomy	41 (45.6)		
MRM	49 (54.4)		
Chemotherapy received			
No	0 (0)		
Yes	90 (100)		
Chemotherapy regimen ($n = 91$)			
CMF	29 (32.2)		
CEF	15 (16.5)		
CEF + Taxol	2 (2.2)		
CEF + Taxotere	32 (35.6)		
Other	12 (13.3)		
Number of chemotherapy cycles			
6	18 (20)		
8	43 (47.8)		
9	29 (32.2)		
Radiotherapy received			
No	32 (35.6)		
Yes	58 (64.4)		
Dose of radiotherapy ($n = 58$)			
4,000-5,000 cGy	8 (13.8)		
5,001-6,000 cGy	23 (39.6)		
>6,000 cGy	19 (32.8)		
Missing	8 (13.8)		
Hormonal therapy received			
No	0 (0)		
Yes	90 (100)		
Hormonal therapy			
Tamoxifen, 5 y	89 (98.9)		
Unknown (transferred to another hospital)	1 (1.1)		

ACJCC, American Joint Committee on Cancer; CEF, cyclophosphamide + epirubicin + 5-fluorouracil; CMF, cyclophosphamide + methotrextate + 5-fluorouracil; MRM, modified radical mastectomy; NTD, New Taiwan dollars (33 NTD-1 $US).

chemotherapy and then slightly increased to the highest rate of 46.8% six months after completing chemotherapy. The prevalence of HFs during the 24-month follow-up period ranged from 39.7% to 46.8%, which was much higher than the baseline rate (Fig. 1).

Overall changes in hot flash patterns

To determine the best change patterns in HF frequency and HF interference, we compare deviance values of three change models: null, linear, and quadratic. The quadratic model demonstrated the best fit with the smallest deviance value for both HF frequency (see Table, Supplemental Digital Content 1, http://links.lww.com/MENO/A534, which illustrates the time models for HF frequency) and HF interference (see Table, Supplemental Digital Content 2, http://links.lww.com/MENO/A534, which illustrates the time models for HF interference). The HF frequency change curve first increased and started to decrease 18 to 19 months after completing chemotherapy (Fig. 2). The HF interference change curve followed a similar pattern except that it reached its highest point 17 to 18 months after completing chemotherapy (Fig. 3).

Factors influencing hot flash frequency and hot flash interference

The variances of individual differences in HF frequency were significant for both the intercept (μ_0) and linear slope (μ_1) ($P < 0.001$) (see Table, Supplemental Digital Content 1, http://links.lww.com/MENO/A534, which illustrates the time models for HF frequency), whereas the variance of individual differences in HF interference was only significant for the intercept (μ_0) ($P < 0.001$) (see Table, Supplemental Digital Content 2, http://links.lww.com/MENO/A534, which illustrates the time models for HF interference). To explain the above significant variance components, we explored both time-varying (level I) and time-invariant (level II) predictors. Potential time-varying predictors examined were anxiety, depression, loss of interest in sex, and BMI change. Potential time-invariant predictors screened were age, menstrual status, education level, marital status, religious affiliation, living alone or not, childbirth experience, prior working status, household income, prior exercise habit, histories, cancer stage, received radiation therapy, and chemotherapy regimen.

Univariate analysis showed that significant predictors of HF frequency were menstrual status ($P = 0.006$), loss of interest in sex ($P = 0.013$), and BMI change ($P = 0.020$). Significant predictors of HF interference were anxiety ($P < 0.001$), depression ($P < 0.001$), loss of interest in sex ($P = 0.001$), and BMI change ($P = 0.003$) (see Table, Supplemental Digital Content 3, http://links.lww.com/MENO/A534, which illustrates the univariate analysis of HFs). Significant predictors were entered into multivariate models for HF frequency and HF interference. The final multivariate model for HF frequency showed that 6 months after completing chemotherapy, premenopausal women experienced higher HF frequency than perimenopausal women ($\beta_{01} = 0.33$, $P = 0.041$). In addition, women's HF frequency fluctuated with their BMI change ($\beta_{30} = 0.16$, $P = 0.020$); a greater BMI increase was associated with higher HF frequency at any time point (Table 2). For HF interference, the final model showed that women's HF interference level fluctuated with their level of anxiety ($\beta_{30} = 1.01$, $P < 0.001$), loss of interest in sex ($\beta_{40} = 1.00$, $P = 0.038$), and BMI change ($\beta_{50} = 1.01$, $P = 0.002$); greater anxiety, more loss of interest in sex, and greater BMI increase were associated with higher HF interference at any time point (Table 3). No variables significantly predicted the change parameters (ie, slope and curvilinear coefficients) for both HF frequency and HF interference.

DISCUSSION

We found that the prevalence rate of HFs was 7.9% at prechemotherapy but rapidly increased to 42.5% after chemotherapy. During the 24-month period of follow-up, the prevalence of HFs remained high, ranging from 39.7% to

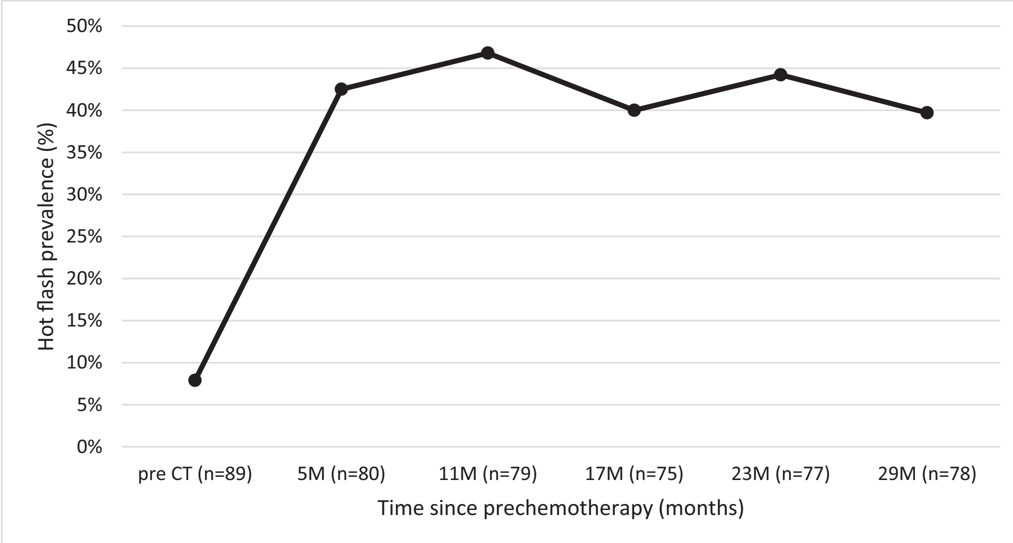

FIG. 1. Prevalence of hot flashes over time since prechemotherapy.

46.8%. The longitudinal trajectories of both HF frequency and HF interference were identified as quadratic change patterns that best fit the data, characterized as first ascending, then descending. Six months after completing chemotherapy, premenopausal women had significantly higher HF frequency than perimenopausal women. Greater BMI increase was associated with higher HF frequency and HF interference at any time point. In addition, HF interference positively fluctuated with anxiety level over time.

The prevalence rate of HFs found in this study is similar to that reported for Asian women with breast cancer,[9,14] but much lower than that reported for women who survived breast cancer treatment in western countries.[18] The lower HF prevalence in our sample may be explained by ethnic differences. Indeed, the severity of vasomotor symptoms was higher in peri- or postmenopausal African American women than in their Chinese or Japanese counterparts.[24,25] Another possible reason for this inconsistent finding on HF prevalence is the sample composition. Many previous reports of high HF prevalence were on mixed samples of pre-, peri-, and postmenopausal women after breast cancer treatment,[8,26] whereas we recruited women who were still menstruating (ie, pre- and perimenopausal). The more important finding of the current study is that the prevalence of HFs was still relatively high 2 years after completing chemotherapy.

We found that 6 months after completing chemotherapy, the main between-individual factor contributing to the variation in HF frequency was menstrual status. The abrupt decline

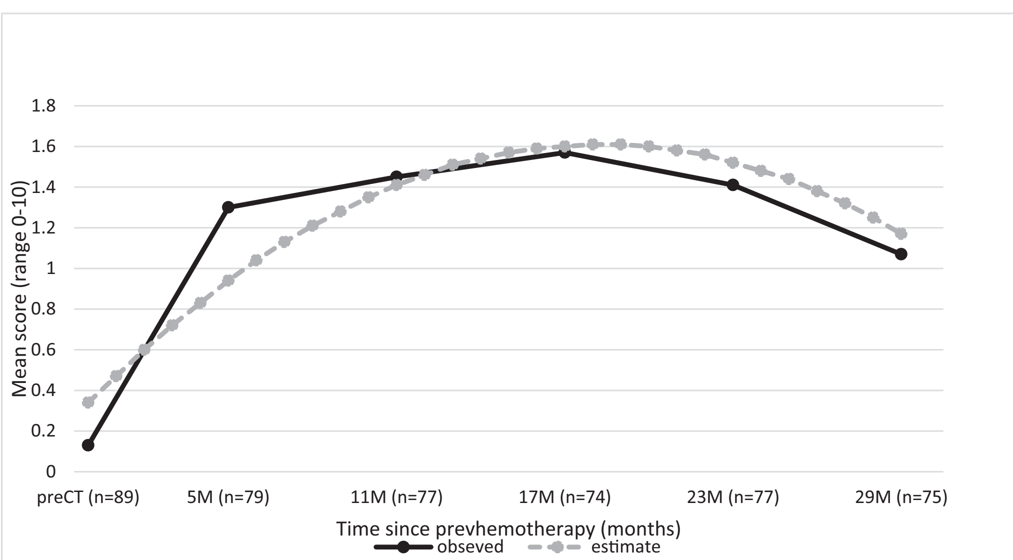

FIG. 2. Observed and estimated changes in hot flash frequency over time since prechemotherapy.

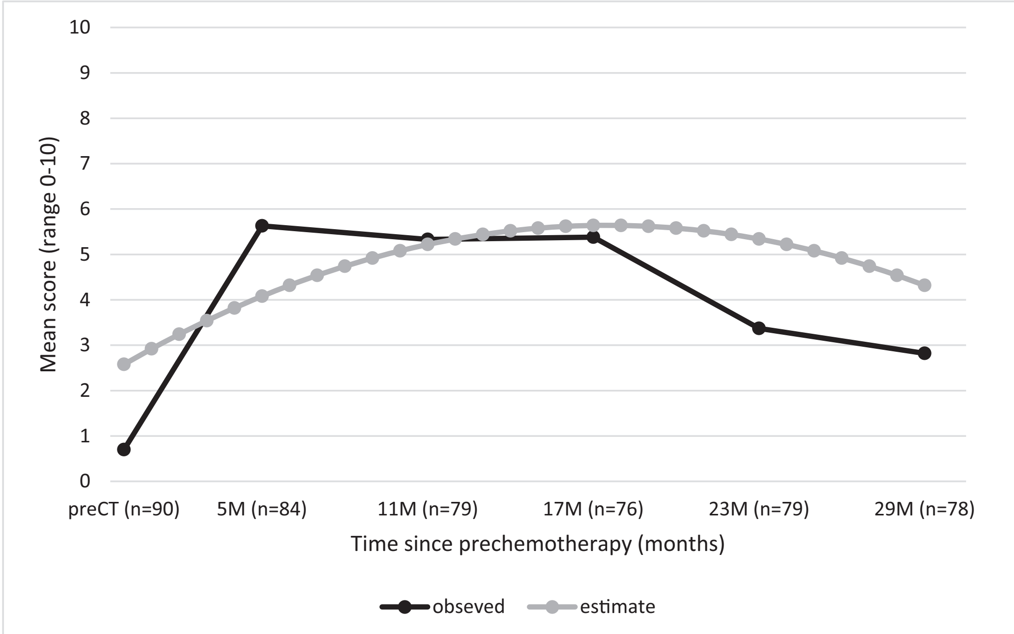

FIG. 3. Observed and estimated changes in hot flash interference over time since prechemotherapy.

of estrogen due to chemotherapy may be the cause of HFs occurring more frequently in premenopausal women than in perimenopausal women. Indeed, the abrupt decrease in estrogen after removing the ovaries and fallopian tubes (ie, bilateral salpingo-oophorectomy) results in more severe climacteric symptoms than in natural menopause.[27]

We found that higher HF frequency and HF interference at any specific time was associated with increased BMI at that time. This finding is consistent with previous reports that weight gain is associated with greater HF risk in breast cancer survivors[12] and that midlife women who gained weight had more intense menopausal symptoms,[28-30] especially vasomotor symptoms.[31,32] In a study of midlife women,[33] obesity was associated with HFs through a mechanism that may involve multiple hormones and sex hormone-binding globulin (SHBG). In that study, women with obesity had significantly lower estradiol, estrone, progesterone, and SHBG levels than

TABLE 2. *Multivariate model of hot flash total frequency (time centered at 6 months after completing chemotherapy)*

Final model			
Fixed effect	Coefficient	SE	*P*
Intercept (β_{00})	1.11	0.20	<0.001
Menstrual status (β_{01})	0.33	0.16	0.041
Time, mo, slope (β_{10})	0.06	0.02	0.001
Time, mo, square slope (β_{20})	<−0.01	<0.01	<0.001
BMI change (β_{30})	0.16	0.07	0.020

β_{00}: The mean HF frequency at 6 months after completing chemotherapy.
β_{01}: The regression coefficient of menstrual status on the intercept (ie, HF frequency at 6 months after completing chemotherapy).
β_{10}: The mean linear time effect coefficient.
β_{20}: The mean curvilinear time effect coefficient.
β_{30}: The mean regression coefficient of BMI change.
Equations for final model
Level-1 model
Y (HF total frequency) $= \pi_0 + \pi_1 \times$ (time) $+ \pi_2 \times$ (time square) $+ \pi_3 \times$ (BMI change) $+ \varepsilon$
Level-2 model
$\pi_0 = \beta_{00} + \beta_{01} \times$ (menstrual status) $+ \mu_0$
$\pi_1 = \beta_{10} + \mu_1$
$\pi_2 = \beta_{20} + \mu_2$
$\pi_3 = \beta_{30} + \mu_3$
BMI, body mass index; HF, hot flash.

TABLE 3. *Multivariate model of hot flash interference (time centered at 6 months after completing chemotherapy)*

Final model			
Fixed effect	Coefficient	SE	*P*
Intercept (β_{00})	2.53	0.91	0.007
Time, mo, slope (β_{10})	0.16	0.04	0.001
Time (time) square slope (β_{20})	−0.02	<0.01	0.001
Anxiety (β_{30})	1.01	0.21	<0.001
Loss of interest in sex (β_{40})	1.00	0.48	0.038
BMI change (β_{50})	1.01	0.31	0.002

β_{00}: The mean HF interference at 6 months after completing chemotherapy.
β_{10}: The linear time effect coefficient.
β_{20}: The quadratic time effect coefficient.
β_{30}: The regression coefficient of anxiety.
β_{40}: The regression coefficient of loss of interest in sex.
β_{50}: The regression coefficient of BMI change.
Equations for final model
Level-1 model
Y (HF interference) $= \pi_0 + \pi_1 \times$ (time) $+ \pi_2 \times$ (time square) $+ \pi_3 \times$ (anxiety) $+ \pi_4 \times$ (loss of interest in sex) $+ \pi_5 \times$ (BMI change) $+ \varepsilon$
Level-2 model
$\pi_0 = \beta_{00} + \mu_0$
$\pi_1 = \beta_{10} + \mu_1$
$\pi_2 = \beta_{20} + \mu_2$
$\pi_3 = \beta_{30}$
$\pi_4 = \beta_{40}$
$\pi_5 = \beta_{50}$
BMI, body mass index; HF, hot flash.

normal-weight women, and the association between obesity and HFs disappeared after adjusting for estrogens and progesterone, and/or SHBG.

In addition to the association of BMI change with HF interference at any given time, anxiety level was also associated with HF interference. Our finding supports a previous report that higher anxiety level was associated with higher HF occurrence in midlife women, even after controlling for the effect of covariates.[34] More recently, anxiety in women with breast cancer significantly predicted their subsequent self-reported HFs.[35] This association may be mediated by neurotransmitters. For example, anxiety has been correlated with increased norepinephrine[7,36] and reduced serotonin.[37-39] Increased norepinephrine causes vasoconstriction and consequently increases core body temperature,[40] whereas lower serotonin initiates a feedback mechanism by increasing 5-HT2A receptor sensitivity in the hypothalamus, resulting in increased body temperature.[41-43]

Loss of interest in sex was found to be positively associated with HF interference and this finding supports a previous report that sexual desire was significantly decreased in healthy midlife women during menopausal transition or early postmenopause.[44] The association between loss of interest in sex and HFs was not a surprising finding because both were considered as symptoms of menopause. Reduced estrogen may be the common cause for decreased sexual desire and HFs. Some estrogen receptors have been found in human vaginal epithelium and stroma[45,46] indicating that reduced estrogen may also cause a decrease in vaginal elasticity and lubrication.

This study has several limitations. First, menopausal status was assessed only by self-report and only at baseline. We did not follow changes of menopausal status across the time points. Since some women may regain ovarian function after chemotherapy, future study should take change of menopausal status into consideration when identifying the factors associated with HFs. Second, anxiety and depression were assessed using the subscales of the GCS which do not have known cut-off points to identify for clinical diagnosis. In addition, sleep problem was embedded in the anxiety subscale and not independently assessed. Sexual problem was only assessed with one item of the GCS. Choosing more reliable and valid instruments to assess each clustered symptom may be considered in future studies. Third, the final sample size of this study is relatively small especially for analysis of random effects. Some important risk factors may have been missed due to the small sample size. The findings of this study were preliminary and should be validated in future studies with a larger sample size.

CONCLUSION

HFs are a significant problem for patients with breast cancer after receiving cancer treatment. Clinicians should actively assess this problem. Our findings on HF trajectories may inform education of patients with breast cancer in terms of the change course of HF symptoms. Professionals may target their attention to patients who are still regularly menstruating (ie, their premenopausal status). Weight control and stress management programs may be beneficial to breast cancer survivors in dealing with their HFs caused by cancer treatment.

Acknowledgements: The authors would like to thank the staff of the Linkou Chang Gung Memorial Hospital and Chang Gung University. The authors also thank all the patients who participated in this study.

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