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Menopausal symptoms among breast cancer patients 6 months after cancer diagnosis: a report from the Shanghai Breast Cancer Survival Study (SBCSS)

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Abstract

Objective—To estimate the prevalence of menopausal symptoms in relation to treatment modalities in Asian women treated for breast cancer.

Design—A population-based cohort of 5,023 Chinese women aged 20–75 years with primary stage 0–III breast cancer was identified from a population-based tumor-registry and enrolled in the study approximately 6 months after diagnosis. Patients were asked about the occurrence of specific menopausal symptoms. Associations between these symptoms and breast cancer treatments were evaluated by stratified, multivariate logistic regression.

Results—67.2% of premenopausal women and 46.3% of postmenopausal women with a recent breast cancer experienced at least one menopausal symptom, namely hot flashes, night sweats and/or vaginal dryness. Symptom prevalence among postmenopausal women decreased progressively with age at diagnosis (63.3% for women 51–55, 51.5% for women 56–60, and 34.4% for women >65 years [$P<0.01$]). Overall, the highest prevalence of most symptoms occurred in women aged 46–55 years ($P<0.01$). Chemotherapy was positively associated with the occurrence of any symptom and with each individual symptom, mainly in premenopausal women [adjusted odds ratios (OR_{adj}) range of 2.2–3.3 (all P -values <0.05)]. Tamoxifen use and immunotherapy were associated with having any symptom and with each individual symptom, regardless of menopausal status (OR_{adj} range: 1.5–1.8 and 1.3–1.5, respectively; $P<0.05$ for all). Women treated before menopause were at particularly high risk of experiencing ≥ 2 symptoms after chemotherapy ($OR=1.77$, 95% CI 1.54–4.98, $P_{interaction}=0.05$).

Conclusions—Menopausal symptoms are prevalent among Chinese women recently treated for primary breast cancer. These symptoms are associated with age and menopausal status at the time of diagnosis, as well as with the type of treatment received.

Keywords

Menopausal symptoms; Breast cancer; Chemotherapy; Immunotherapy; Tamoxifen; Radiotherapy; Age; Menopause; BMI; Chronic disease; QOL; Chinese women

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Introduction

During the menopausal transition, women commonly experience a variety of symptoms that affect their quality of life and may require medical treatment,^{1,2} such as hormone replacement therapy (HRT).^{3,4} Menopausal symptoms may also be precipitated by cancer treatments.^{5–7} Numerous studies have shown that Caucasian women with breast cancer frequently experience severe menopausal symptoms after receiving treatment, particularly chemotherapy and tamoxifen.^{8–10} Among postmenopausal breast cancer patients, hot flashes were observed in 46–65%, night sweats in 36%, and vaginal dryness in 48%.^{11,12} A similarly high prevalence of menopausal symptoms^{9,13} has been reported in women who were premenopausal at the time of breast cancer diagnosis and treatment, and these symptoms are likely to reflect overall reproductive health.^{14–16}

The prevalence of menopausal symptoms varies by geographic region and by ethnicity of population.¹⁷ Few studies have examined menopausal symptoms among Asian women. The Study of Women's Health Across the Nation (SWAN) found that Chinese and Japanese women reported significantly fewer menopausal symptoms than Caucasian women.¹⁸ In the Pan-Asia Menopause (PAM) study, the prevalence of menopausal symptoms varied substantially across ethnic groups. Asian women were more likely to experience body aches or joint aches and pains (76–93%) and less likely to complain of hot flashes or vasomotor symptoms than their Western counterparts.¹⁹

Limited data are available regarding menopausal symptoms in Asian women who received treatment for primary breast cancer. In this study, we examined the prevalence of menopausal symptoms in a large, population-based prospective study of breast cancer survival conducted among urban Chinese women and evaluated the relationship between these symptoms and recent cancer treatments. We focused on the most common symptoms, namely hot flashes, night sweats and vaginal dryness, and evaluated the demographic, lifestyle, and medical correlates of these symptoms.

Methods

Study population

The Shanghai Breast Cancer Survival Study (SBCSS) is a large, population-based, longitudinal study of women who were diagnosed with primary breast cancer between the ages of 25 and 70 years in Shanghai, China. Incident breast cancer cases were identified between April 2002 and December 2006 from the population-based Shanghai Cancer Registry. Cancer diagnoses were confirmed by medical record review; detailed methods have been published elsewhere.²⁰ Briefly, 6,303 patients were identified who met the study inclusion criteria: 1) a first diagnosis of primary breast cancer; 2) permanent resident of Shanghai; and 3) alive at study recruitment. Of eligible women, 757 (12%) refused to participate, 258 (4.1%) were visiting other cities, 83 (1.3%) could not be contacted, and 159 (2.5%) were excluded for miscellaneous reasons such as health or communication problems that prevented them from participating in the initial survey at 6 months post-diagnosis. A total of 5,046 cases participated in the study and provided written, informed consent (80.1% participation). In this analysis, 23 women who had stage IV cancer at the time of the survey were excluded, leaving a total of 5,023 patients. The institutional review boards of all participating institutions approved the study protocol.

Data collection

Information on demographic factors, personal and first-degree family history of cancer, other chronic diseases, reproductive factors, lifestyle, diet, use of complementary and alternative

medicine, and quality of life (QOL) was collected through in-person interviews conducted by trained staff using a structured questionnaire. Two previously-validated, generic quality of life instruments, the Medical Outcome Study of Quality of Life (MOSQOL-74) and the Short-Form Health Survey (SF-36) were used in the study to assess the health related QOL among breast cancer survivors. The first 2,232 patients were administered the MOSQOL-74, and the remaining 2,814 patients were administered the SF-36.²¹ During the interviews, anthropometric measurements were taken, including height, weight, waist circumference, and hip circumference. Body-mass index (BMI) and waist-to-hip ratio (WHR) were calculated from these measurements. Clinical and pathology information was collected, including the stage of disease at the time of breast cancer diagnosis, hormone receptor status (tumor estrogen receptor [ER] and progesterone receptor [PR] expression), and primary treatments (surgery/mastectomy, radiation therapy, chemotherapy, immunotherapy, and/or hormonal therapy such as tamoxifen). Medical charts were reviewed to verify clinical and treatment information. Commonly used chemotherapeutic drugs included cytoxan, adriamycin and 5-fluorouracil, taxotere, epirubicin-adriamycin (epi-ADM) and navelbine, and immunotherapy (interferon, interleukin, and thymosin).

Detailed information was collected on menopausal symptoms by asking: "Have you ever experienced any of the following menopausal symptoms since having breast cancer, such as hot flashes, night sweats, or vaginal dryness?" Those who answered 'Yes' to one of these symptoms were considered patients with 'any menopausal symptom'. Participants were also asked for dates of onset/end and, if applicable, resolution of each symptom. Almost all women reported having menopausal symptoms since having breast cancer and that they continued to experience menopausal symptoms at 6 months after breast cancer diagnosis and treatment. Women who answered 'Yes' to having symptoms were asked about treatments or methods used regularly (3 times per week constantly since having breast cancer) to alleviate these symptoms. We plan to evaluate and publish an analysis of the treatment information in the future.

Statistical analysis

The sociodemographic, lifestyle, and clinical factors of women with and without menopausal symptoms were compared using the Cochran-Mantel-Haenszel Statistics (CMH) or Analysis of Variance (ANOVA) with adjustment for age at diagnosis (categories). Unconditional logistic regression was used to derive odds ratios (ORs) and 95% confidence intervals (CIs) to measure the association between menopausal symptoms with various cancer treatment modalities with adjustment for potential confounders. Factors included in the model were age at breast cancer diagnosis (continuous), education, number of live births (0, 1, or ≥ 2), current marital status (married/living with partner vs. single/widowed or divorced/separated), WHR (quartiles), menopausal status (pre- and post-), history of chronic disease (yes/no), perceived quality of life (poor, average, or good), stage of disease (tumor-node-metastasis [TNM] classification 0-I, II and III), hormone receptor status of the tumor (ER+/PR+, ER-/PR-, ER-/PR+ or ER+/PR-, or unknown), and treatment for breast cancer (mastectomy, radiotherapy, chemotherapy, immunotherapy, and/or tamoxifen use). Menopausal status was defined as "cessation of menstruation for 12 months or longer, excluding lapses due to pregnancy and breastfeeding"²² All statistical tests were based on two-tailed probability and a significance alpha (α) level of <0.05 . Breast cancer cases were also grouped into three categories based on the number of menopausal symptoms that women experienced: those without any symptoms and those with 1, or ≥ 2 symptoms. Polychotomous logistical regression analysis was applied to evaluate the association of number of menopausal symptoms with cancer treatments using women without any symptoms as the reference.

To evaluate the association of breast cancer treatments with specific menopausal symptoms in the context of the endogenous estrogenic environment, we conducted stratified analyses by menopausal status (pre- vs. post-) and body-mass index (BMI, normal vs. overweight/obese) using the universal definition of obesity ($\geq 25.0 \text{ kg/m}^2$).²³ We also conducted analyses stratified by self-reported history of chronic disease (coronary heart diseases, stroke, hypertension, diabetes mellitus, bronchitis, asthma, gastritis, and hepatitis; yes/no) and overall perceived QOL (poor vs. average vs. good). Tests for interaction were performed using the log-likelihood test. All statistical analyses were performed using SAS software, version 9.1 (SAS Institute, Cary, NC).

Results

The characteristics of breast cancer cases at 6 months post-diagnosis in relation to reported menopausal symptoms are presented in Table 1. The median time since diagnosis was 6.4 months. A total of 56.0% of women reported one or more menopausal symptoms during the first 6 months after diagnosis. The median age of cancer patients at diagnosis was 51.1 years. The mean age was lower among women experiencing any menopausal symptoms (51.7 ± 8.5 years) than among those who did not experience any menopausal symptoms (55.7 ± 1.4 years). Women with and without menopausal symptoms had similar educational attainment, income, exercise participation, and did not differ significantly regarding smoking or alcohol consumption habits. Compared with women who did not experience any menopausal symptoms, women with symptoms were more likely to be premenopausal or to have one child ($P < 0.01$ for both) and to report poor quality of life or a history of chronic disease ($P < 0.01$ for both). They were also more likely to have received immunotherapy or tamoxifen for breast cancer treatment ($P < 0.01$ for both) and to have hormone receptor-positive tumors ($P = 0.01$) than asymptomatic women. The prevalence of HRT use was low among women in this study and did not differ according to the presence or absence of menopausal symptoms.

The numbers and prevalences of each individual menopausal symptom are presented in Table 2 by age and menopausal status of women at breast cancer diagnosis. Premenopausal women were more likely to be symptomatic than postmenopausal women (67.2% vs. 46.3%, respectively). The highest prevalence of reporting any menopausal symptom was in women 46–55 years of age ($\approx 70\%$) and decreased to 34% in women > 65 years of age ($P < 0.01$). The highest prevalence of reporting any symptom occurred in premenopausal women older than 45 years (71–75%) and in the youngest group of postmenopausal women (60–63%). The prevalence of each individual menopausal symptom in our population was as follows: 2,218 (44%) for hot flashes, 1,777 (35%) for night sweats, and 460 (9%) for vaginal dryness. Premenopausal women were more likely than postmenopausal women to experience hot flashes (55% vs. 34%) or night sweats (43% vs. 28%); $P < 0.05$ for all. Reporting of individual symptoms also varied across age groups. Hot flashes, night sweats, and vaginal dryness were more prevalent in women 46–55 years of age than in other age groups of women, regardless of menopausal status ($P < 0.01$ for all, except for vaginal dryness among premenopausal women (Table 2).

Multivariate logistic regression analyses controlling for age at diagnosis, education, number of live births, marital status, perceived quality of life status, a history of chronic disease, menopausal status, and clinical characteristics showed that chemotherapy, immunotherapy, and tamoxifen were each positively and independently associated with menopausal symptoms. The associations between these treatments and each individual menopausal symptom, such as hot flashes and night sweats, were statistically significant (Table 3). Radiation treatment was not significantly associated with menopausal symptoms in this population. Stratified analyses showed that chemotherapy-related menopausal symptoms were confined to women who were premenopausal at the time of breast cancer diagnosis. These women reported an increased

likelihood of reporting any and individual menopausal symptoms following chemotherapy. Adjusted odds ratios (OR_{adj}) for the association of chemotherapy with each individual menopausal symptom in this subgroup were 2.23 (95% CI: 1.35–3.67) for hot flashes, 2.55 (95% CI: 1.47–4.40) for night sweats, and 3.32 (95% CI: 1.12–9.83) for vaginal dryness. In contrast, chemotherapy-treated women who were postmenopausal at cancer diagnosis did not experience a significant increase in any of these symptoms (Table 3).

The risk of experiencing of any menopausal symptom increased with tamoxifen use among all women ($OR_{adj}=1.63$, 95% CI: 1.42–1.87), while the types of symptoms reported in pre- and postmenopausal women did not differ appreciably. Premenopausal women treated with tamoxifen reported near 1.8-fold increase in hot flashes and night sweats (OR_{adj} 1.78; 95% CI: 1.44–2.21 and 1.79; 95% CI: 1.43–2.24, respectively). Vaginal dryness was also modestly increased after tamoxifen therapy, but these associations did not reach statistical significance ($OR_{adj}=1.25$; 95% CI: 0.88–1.78). Among women who were postmenopausal at the time of breast cancer diagnosis, the prevalence of reporting any menopausal symptom and each individual menopausal symptom increased significantly with tamoxifen use, with adjusted ORs ranged from 1.5 to 1.8 ($P<0.05$ for all, Table 3). We also examined the association across BMI groups (<25.0 vs. ≥ 25.0) and found no differences. However, the risk of experiencing each individual menopausal symptom with tamoxifen use was higher among younger women (age at diagnosis <50 years) with BMI ≥ 25.0 (data not shown). Immunotherapy in both pre- and postmenopausal women with breast cancer was associated with an increased risk of each individual menopausal symptom (OR_{adj} range: 1.3–1.5; $P<0.05$ for any and each individual symptoms in premenopausal women, and OR_{adj} range: 1.3–1.8, $P<0.05$ for any and each individual symptoms in postmenopausal women).

Prevalence and odds ratios for number of menopausal symptoms (0, 1, and/or ≥ 2) after specific breast cancer treatment modalities are presented in Table 4. Overall, premenopausal patients were more likely to experience ≥ 2 symptoms than postmenopausal women (37.1% vs. 20.6%). Radiation therapy was not associated with the number of menopausal symptoms experienced, regardless of menopausal status. Women reported an increased frequency of ≥ 2 symptoms after chemotherapy treatment ($OR_{adj}=1.48$, 95% CI: 1.10–1.98 in all women). However, this association was significant only among premenopausal women ($OR_{adj}=1.75$, 95% CI 1.00–3.05 for one symptom and $OR_{adj}=1.77$, 95% CI: 1.54–4.98 for ≥ 2 symptoms, $P_{interaction}=0.05$). Both immunotherapy and tamoxifen use were associated with an increased risk of experiencing ≥ 2 menopausal symptoms in all women ($OR_{adj}=1.47$ and 1.74, respectively), and the risk of developing one symptom with tamoxifen use was slightly higher among premenopausal women ($OR_{adj}=1.74$, 95% CI: 1.36–2.23) than among postmenopausal women ($OR_{adj}=1.39$, 95% CI: 1.11–1.73), however the difference was not significant across the subgroups ($P_{interaction}=0.87$).

Furthermore we examined the association between number of menopausal symptoms and breast cancer adjuvant treatment in the stratified analyses by body-mass index (BMI) <25.0 vs. ≥ 25.0 (normal or overweight/obese), history of chronic diseases (yes vs. no) and perceived quality of life (poor, average vs. good QOL). Approximately 35% of patients in the study population were overweight or obese, and this group was more likely to experience ≥ 2 menopausal symptoms than normal-weight women (30.2% vs. 25.7%, $P<0.01$). Overweight/obese women had an increased risk of experiencing menopausal symptoms with use of chemotherapy compared with normal-weight women ($OR_{adj}=1.92$, 95% CI: 1.22–3.03 vs. 1.03, 95% CI: 0.88–1.44 for one symptom). Similarly, the association between tamoxifen use and experiencing several symptoms was stronger among overweight/obese women than normal-weight women ($OR_{adj}=2.1$ vs. 1.6 for ≥ 2 symptoms). In contrast, use of immunotherapy was significantly and positively associated with experiencing menopausal symptoms among normal-weight women but the association was weak in overweight/obese

women. Overall, interaction tests between menopausal symptoms and all treatments and across BMI categories were statistically non-significant (data not shown).

In analyses stratified by history of chronic, the prevalence of experiencing menopausal symptoms did not differ significantly between breast cancer patients with and without a history of chronic diseases (56.3 % vs. 55.4%). Although the risk of developing ≥ 2 symptoms with chemotherapy was higher among women without a history of chronic disease ($OR_{adj} = 2.84$, 95% CI: 1.13–7.14) than those with ($OR_{adj} = 1.37$, 95% CI: 1.00–1.88), the difference was not statistically significant ($P_{interaction} = 0.29$). On the other hand, the positive association between tamoxifen use and occurrence of ≥ 2 menopausal symptoms was stronger among women with a history of chronic disease than among women without ($OR_{adj} = 1.95$, 95% CI 1.61–2.36 vs. $OR_{adj} = 1.31$, 95% CI 0.94–1.83). Again, the test of interaction was not statistically significant, ($P_{interaction} > 0.05$).

Women who reported poor QOL were more likely than those reporting average or good QOL to report any menopausal symptom (59.4%, 56.5 % or 52.6%, respectively; $P = 0.03$) or ≥ 2 symptoms (29.3% vs 24.1% vs. $P = 0.005$). The odds ratio of experiencing ≥ 2 menopausal symptoms with tamoxifen use varied across categories of QOL ($OR_{adj} = 2.14$, 95% CI 1.19–3.96 for poor, $OR_{adj} = 1.83$, 95% CI 1.51–2.21 for average QOL and $OR_{adj} = 1.17$, 95% CI 0.78–1.75 for good QOL, respectively, $P_{interaction} = 0.06$). The associations between chemotherapy and immunotherapy with number of menopausal symptoms did not differ by QOL category (data not shown).

Discussion

In this study, we found that Chinese women treated for primary breast cancer had a high prevalence of menopausal symptom similar to results reported from studies conducted in Western countries with largely Caucasian populations.^{6,11,24} Similar to other studies, the occurrence of menopausal symptoms was not affected by education, income, or lifestyle factors, including smoking, alcohol use, or physical activity.⁶ The median age of natural menopause was ≈ 49 years in this population.²⁵ We found that peri-menopausal women and women who had recently undergone menopause had the highest prevalence of menopausal symptoms. We also found that, in general, premenopausal women had a higher prevalence of menopausal symptoms than postmenopausal women.^{26,27}

Hot flashes were the most common symptom experienced by our patients, with a prevalence of 44.2% for all women, 55.0% for premenopausal women, and 33.7 % for postmenopausal women. This rate was lower compared to the $\geq 65\%$ prevalence rate found among breast cancer patients 40–65 years of age in Caucasian women.^{6,11,12} We also found that the prevalence of specific menopausal symptoms varied across age groups and menopausal status. The lowest prevalence of hot flashes (26%) occurred among women ≤ 40 years of age, mainly among premenopausal cancer cases, which was much lower compared to the same group of Caucasian women (46%)¹³. The highest occurrence of hot flashes or night sweats was observed among women aged 46 to 55 years, which is consistent with a previous report by Ganz et al., where hot flashes and night sweats were highest among breast cancer patients 45–51 years of age compared to younger patients.¹⁵ In general, hot flashes, night sweats, and vaginal dryness were higher in the oldest group of premenopausal women (46–55 years) and in the younger groups of postmenopausal women (< 55 years); these symptoms decreased with age in the latter case.

In our study, breast cancer patients were at increased risk of experiencing any and each individual menopausal symptom with the use of adjuvant therapy (chemotherapy or tamoxifen), consistent with the results of clinical trials,^{28,29} case-control studies,^{9,30} and cross-sectional^{6,31,32} studies in women who received treatment for primary breast cancer in

Western countries. The association between chemotherapy and menopausal symptoms (any and each individual symptom) was more pronounced among premenopausal compared with postmenopausal women,³³ reflecting the premature ovarian failure induced by chemotherapy in premenopausal women.^{26,34}

The biological mechanism underlying vasomotor symptoms such as hot flashes and night sweats is still unclear. However, vasomotor symptoms have been correlated with the acute decline in estrogen levels in the body^{35,36} that occurs as a result of natural menopause or the reduced ovarian reserve induced by chemotherapy or adjuvant tamoxifen therapy, which, in turn, leads to early onset of menopause in premenopausal women.^{26,37} We speculate that because women 45–55 years of age (i.e., those closer to biological menopause) experience dramatic changes in their ovarian function due to the reduction in primordial ovarian follicles, they are more susceptible to ovarian suppression or estrogen deficiency when they undergo adjuvant treatments and are thus more likely to experience menopausal symptoms than other age groups of women.

In this study, both pre- and post- menopausal breast cancer patients who received tamoxifen experienced one or more menopausal symptoms than patients who had not received tamoxifen. These findings are in agreement with reports from the NSABP P-1 trial²⁸ and the Wisconsin Tamoxifen Trial,³⁸ in which tamoxifen recipients experienced a higher prevalence of night sweats, hot flashes, and genitourinary symptoms than the placebo group. The use of tamoxifen was associated with an increased risk of vaginal dryness among postmenopausal women but not premenopausal women in our study.

Carpenter et al. reported severe hot flashes with tamoxifen use among younger women with a higher BMI, which is consistent with the findings of our study.³⁹ The occurrence of multiple symptoms (≥ 2) was much higher among breast cancer patients who were tamoxifen users, in particular among postmenopausal women, overweight/obese women, women with a history of chronic disease, and self-perceived poor QOL. Some studies have reported associations between weight gain and physiological distress with use of adjuvant therapy, namely chemotherapy⁴⁰ or tamoxifen^{10,41} among breast cancer patients, although others have not found such an association.²⁶ In addition, Kenne et al. reported that co-morbidity has an effect on the occurrence of distress and health-related quality of life⁴² and survivorship⁴³ in breast cancer patients. Consistent with the findings of previous studies^{5,6,39}, self-reported total QOL score was strongly associated with reporting of menopausal symptoms in this study and modified the association of adjuvant treatments and tamoxifen use with menopausal symptoms. Detailed analyses on menopausal symptoms and various domains of QOL among breast cancer patients are on going and results will be published in the future.

In our observation, women who had immunotherapy were more likely to experience menopausal symptoms, regardless of menopausal status, obesity, the existence of co-morbidity, or QOL categories. We found no previous reports on immunotherapy and menopausal symptoms. We cannot exclude the possibility that the adverse associations we found are due to chance, given the multiple comparisons involved, particularly considering that relatively few women were involved in this analysis (15%). More studies on the effects of immunotherapy on menopausal symptoms are needed.

It is important to interpret our results in the context of the limitations of this study. Information bias may have led to over-reporting of the types of menopausal symptoms, because women suffering from more symptoms may have been more likely to respond to questions about menopausal symptoms. However, this bias is likely to be minimal, since all patients responded to the questions. In addition, information bias may have led to misreporting of the types of symptoms, since data on menopausal symptoms is by definition subjective and must be based

on self-reports. Recall bias must also be considered, but the short duration between disease occurrence, cancer treatment, and the interview, suggests that our study participants are likely to have accurately recalled their menopausal symptoms and treatments received, thus any misclassification is likely to have been random. Although our questionnaire includes the common menopausal symptoms reported previously, the questionnaire has not been validated in the study population. Furthermore, we did not collect information on menopausal symptoms that patients experienced prior to breast cancer diagnosis and treatment. This precluded us from evaluating differences in menopausal symptoms occurring before and after breast cancer diagnosis.

Our study has also several noticeable strengths. To our knowledge, this is the first and largest population-based study to investigate the prevalence of menopausal symptoms in relation to breast cancer treatment among Chinese women, who have very different lifestyle and dietary risk factors and a much lower prevalence of HRT use than Caucasian women or women residing in Western countries. The selection bias and recall bias were minimized in this study due to the high participation rate and the use of an interviewer-administered questionnaire. The large sample size and extensive information collected on socioeconomic, lifestyle, and clinical characteristics allowed for analyses stratified by menopausal status, BMI, history of chronic disease, and self-perceived overall QOL in several cancer treatments groups.

In summary our study, the largest to date to characterize menopausal symptoms prospectively among pre- and postmenopausal Chinese women treated for primary breast cancer, identified a high prevalence of menopausal symptoms in these women. The likelihood of menopausal symptoms varied by age and menopausal status at diagnosis and was highest among peri-menopausal women and recently postmenopausal women. Chemotherapy was associated with menopausal symptoms among premenopausal, but not postmenopausal, women with breast cancer. Tamoxifen use was related to a high prevalence of all types of symptoms in both pre- and postmenopausal women. Poor quality of life was related to a high prevalence of menopausal symptoms and modified the association of tamoxifen use with menopausal symptoms. Research on developing management and treatment strategies for menopausal symptoms among breast cancer patients is needed.

Summary points

- The prevalence of menopausal symptoms including hot flashes, night sweats, and vaginal dryness is high among Chinese women following breast cancer diagnosis and treatment.
- The likelihood of menopausal symptoms varied by age and menopausal status at diagnosis and was highest among peri-menopausal women and recently postmenopausal women.
- Chemotherapy, tamoxifen use, and immunotherapy were associated with increased prevalence of menopausal symptoms, and the association may be modified by menopausal status and overall quality of life.

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Table 1

Characteristics of breast cancer patients with and without menopausal symptoms at 6 months post-diagnosis in the Shanghai Breast Cancer Survival Study (SBCSS)

	All patients n=5,023 (%)	With any symptoms* n=2,815 (56.0%)	Without any symptoms* n=2,208 (44.0%)	P value*
Demographic characteristics				
Age at diagnosis (mean ± SD)	53.5 ± 10.0	51.7 ± 8.5	55.7 ± 11.3	<0.01
Education (%)				
Primary/below	585 (11.6)	11.1	12.2	0.38
Middle school	1,740 (34.7)	35.4	33.6	
High school or technical training	1,892 (37.7)	37.5	37.8	
College or above college	805 (16.0)	16.0	16.4	
Monthly family income, Yuan ¥, (%)				
<700.00	1,399 (27.9)	27.0	28.6	0.45
<2,000.00	3,020 (60.2)	61.0	59.6	
≥2,000.00	601 (12.0)	12.0	11.8	
Number of live births (%)				
Nulliparous	42 (0.9)	1.0	0.8	<0.01
1	3,384 (70.2)	72.2	67.2	
2	832 (17.3)	16.0	19.8	
≥3	563 (11.7)	10.8	12.2	
Marital status (%)				
Married or living with partner	4,739 (94.4)	95.4	93.5	<0.01
Unmarried/widowed/divorced/separated	284 (5.6)	4.6	6.5	
Menopausal status (%)				
Premenopausal	2,459 (48.9)	51.3	44.9	<0.01
Postmenopausal	2,564 (51.1)	48.7	55.1	
HRT use, ever/never (%)	174 (3.4)	4.1	3.3	0.11
Lifestyle factors				
Body mass index, kg/m ² (mean ± SD)	24.1 ± 3.4	23.6	23.8	0.13
Waist to hip ratio, (mean ± SD)	0.834 ± 0.05	0.828	0.825	0.18
Exercised regularly since cancer diagnosis (%)	3,245 (64.6)	64.9	64.6	0.87
Ever smoked cigarettes regularly (%)	131 (2.6)	2.5	2.3	0.61
Ever drank alcohol regularly (%)	153 (3.0)	3.3	2.5	0.11
History of chronic disease (%)	3,690 (73.5)	75.0	71.1	<0.01
Self-reported quality of life (%)				
Poor	411 (8.2)	9.2	7.3	<0.01
Average	3,673 (73.1)	73.6	72.5	
Good	937 (18.7)	17.2	20.2	
Clinical characteristics				
Treatment (%)				
Surgical treatment (mastectomy)	4,751 (94.4)	94.5	94.0	0.48
Radiotherapy	1,607 (32.0)	31.5	32.8	0.32
Chemotherapy	4,575 (91.1)	91.6	90.5	0.19
Immunotherapy	738 (14.7)	16.2	12.6	<0.01
Tamoxifen use	2,611 (52.0)	56.8	44.5	<0.01
Stage, TNM (%) [§]				
0-I	1,837 (36.6)	36.9	35.9	0.18
II	2,483 (49.4)	49.7	49.8	
III	466 (9.3)	8.5	10.1	
Unknown	237 (4.7)	4.9	4.2	
Hormone receptor status (%)				
ER+/PR+	2,509 (50.0)	52.0	46.2	<0.01
PR-/PR-	1,434 (28.5)	25.6	31.9	
Mixed	976 (19.4)	19.8	19.2	
Unknown	104 (2.1)	1.6	2.7	

* Adjusted for age; P values were derived from the ANOVA procedure for continuous variables and CMH test for categorical variables. *Note:* Missing values (<0.2 %) were not included in percentage calculations

Abbreviations: SD, standard deviation; HRT, hormone replacement therapy; ER, estrogen receptor; PR, progesterone receptor; TNM, tumor-node-metastasis classification system.

[§] Women with stage IV disease at the time of survey were excluded

Table 2

Prevalence* of menopausal symptoms experienced by breast cancer patients by age group and menopausal status at 6 months post-diagnosis, SBCSS

Patients grouped by age and menopausal status	Any symptoms experienced n (%)	Type of symptoms experienced, %		
		Hot flashes n=2,218 (%)	Night sweats n=1,777 (%)	Vaginal dryness n=460 (%)
All cases (n=5,023)	2,815 (56.0)	44.2	35.4	9.2
≤40	76 (37.6)	25.7	23.3	4.9
41–45	356 (58.8)	46.8	38.7	10.7
46–50	913 (69.5)	58.6	45.4	10.7
51–55	673 (69.7)	58.5	44.2	10.4
56–60	308 (51.0)	38.1	28.8	11.1
61–65	167 (40.9)	28.9	24.0	7.8
>65	322 (34.4)	21.9	21.8	4.9
<i>P value</i> **	<0.01	<0.01	<0.01	<0.01
Premenopausal (n=2,459)	1,627 (67.2)	55.0	43.4	9.9
≤40	76 (37.8)	25.9	23.4	5.0
41–45	345 (59.2)	46.8	38.6	10.6
46–50	812 (70.7)	59.3	46.6	10.5
>50	394 (74.9)	66.0	49.4	9.5
<i>P value</i>	<0.01	<0.01	<0.01	0.09
Postmenopausal (n=2,564)	1,118 (46.3)	33.7	27.6	8.5
≤50	112 (59.9)	52.4	36.9	12.3
51–55	296 (63.3)	49.1	38.0	11.3
56–60	292 (51.5)	37.9	28.4	11.1
61–65	166 (40.9)	28.8	23.9	7.9
>65	322 (34.4)	21.9	21.8	4.9
<i>P value</i>	<0.01	<0.01	<0.01	<0.01

* Percentage of women with any or each individual symptom compared with women without any symptoms or without the individual symptom in each age group

** Derived from chi-square test

Table 3

Association between adjuvant treatment and menopausal symptoms among breast cancer patients at 6 months post-diagnosis, SBCSS

Type of symptoms	Experienced symptoms n (%) [*]	Radiotherapy n=1,607 (%) ^{**}		Chemotherapy n=4,575 (%)		Immunotherapy n=738 (%)		Tamoxifen n=2,611 (%)	
		OR (95% CI)		OR (95% CI)		OR (95% CI)		OR (95% CI)	
All cases[†]	5,023	(32.0)		(91.1)		(14.7)		(52.0)	
None	2,208 (44.0)	1.00		1.00		1.00		1.00	
Any symptom	2,815 (56.0)	0.94 (0.81–1.08)		1.37 (1.09–1.72)		1.28 (1.08–1.53)		1.63 (1.42–1.87)	
Hot flashes	2,218 (50.1)	0.97 (0.83–1.13)		1.41 (1.09–1.81)		1.36 (1.13–1.63)		1.79 (1.55–2.08)	
Night sweats	1,777 (44.6)	0.99 (0.84–1.16)		1.56 (1.19–2.04)		1.30 (1.07–1.58)		1.60 (1.37–1.87)	
Vaginal dryness	460 (17.2)	0.73 (0.56–0.95)		1.18 (0.77–1.80)		1.55 (1.16–2.05)		1.46 (1.14–1.86)	
Premenopausal cases	2,459 (48.9)	(39.8)		(96.5)		(15.3)		(53.5)	
None	832 (33.8)	1.00		1.00		1.00		1.00	
Any symptom	1,627 (66.2)	0.95 (0.78–1.17)		2.20 (1.37–3.54)		1.26 (0.97–1.62)		1.75 (1.42–2.15)	
Hot flashes	1,353 (61.9)	0.97 (0.77–1.18)		2.23 (1.35–3.67)		1.29 (0.99–1.69)		1.78 (1.44–2.21)	
Night sweats	1,068 (56.2)	0.95 (0.76–1.19)		2.55 (1.47–4.40)		1.37 (1.04–1.81)		1.79 (1.43–2.24)	
Vaginal dryness	243 (22.6)	0.68 (0.47–0.97)		3.32 (1.12–9.83)		1.46 (0.98–2.21)		1.25 (0.88–1.78)	
Postmenopausal cases	2,564 (51.1)	(24.5)		(85.9)		(14.1)		(50.6)	
None	1,376 (53.7)	1.00		1.00		1.00		1.00	
Any symptom	1,118 (46.3)	0.86 (0.70–1.07)		0.95 (0.73–1.24)		1.35 (1.06–1.72)		1.54 (1.28–1.86)	
Hot flashes	865 (38.6)	0.91 (0.72–1.24)		0.92 (0.68–1.25)		1.49 (1.14–1.93)		1.82 (1.47–2.24)	
Night sweats	709 (34.0)	0.98 (0.77–1.25)		0.99 (0.72–1.36)		1.29 (0.97–1.71)		1.46 (1.19–1.82)	
Vaginal dryness	217 (13.6)	0.67 (0.44–1.01)		0.61 (0.37–1.02)		1.80 (1.19–2.70)		1.65 (1.16–2.36)	

* Percentage of women with any or each individual symptom compared with women without any symptoms

** Adjusted for age at cancer diagnosis, education, number of live births, current marital status, history of chronic disease, WHR (quartiles), self-reported quality of life, TNM stage (0–II vs. III), ER/PR status, and other treatments (mastectomy, chemotherapy, radiotherapy, immunotherapy, or tamoxifen use: Y/N)

[†] Additionally adjusted for menopausal status

Note: Reference group in all analyses was the “none” category of women reporting no menopausal symptoms

Abbreviations: OR, odds ratio; CI, confidence interval

Association between number of menopausal symptoms of menopause and adjuvant treatment among breast cancer patients at 6 months post-diagnosis, SBCSS

Number of symptoms experienced	n (%)	Radiotherapy n=1,607 (%)	Chemotherapy n=4,575 (%)	Immunotherapy n=738 (%)	Tamoxifen n=2,611 (%)
		OR (95% CI)*	OR (95% CI)	OR (95% CI)	OR (95% CI)
All cases [†]	5,023	(32.0)	(91.1)	(14.7)	(52.0)
0	2,208 (44.0)	1.00	1.00	1.00	1.00
1	1,376 (27.4)	0.92 (0.78–1.50)	1.29 (0.99–1.69)	1.12 (0.91–1.37)	1.53 (1.30–1.80)
≥2	1,439 (28.6)	0.95 (0.80–1.12)	1.48 (1.10–1.98)	1.47 (1.10–1.98)	1.74 (1.47–2.05)
Premenopausal cases	2,459 (48.9)	(39.8)	(96.5)	(15.3)	(53.5)
0	832 (33.8)	1.00	1.00	1.00	1.00
1	716 (29.1)	1.03 (0.81–1.31)	1.75 (1.00–3.05)	1.08 (0.80–1.46)	1.74 (1.36–2.23)
≥2	911 (37.1)	0.89 (0.70–1.12)	1.77 (1.54–4.98)	1.41 (1.06–1.86)	1.76 (1.40–2.24)
Postmenopausal cases	2,564 (51.1)	(24.5)	(85.9)	(14.1)	(50.6)
0	1,376 (53.7)	1.00	1.00	1.00	1.00
1	660 (25.7)	0.78 (0.61–1.00)	1.02 (0.75–1.39)	1.18 (0.89–1.57)	1.39 (1.11–1.73)
≥2	528 (20.6)	0.98 (0.75–1.29)	0.86 (0.60–1.23)	1.57 (1.17–2.12)	1.79 (1.39–2.30)
P _{interaction}		0.29	0.05	0.84	0.87

* Polytomous Logistic Regression: Adjusted for age at cancer diagnosis, education, number of live births, current marital status, history of chronic disease (Y/N), WHR (quartiles), self-reported quality of life, TNM stage (0-II vs. III), ER/PR status, and other treatments (mastectomy, chemotherapy, radiotherapy, immunotherapy, or tamoxifen use; Y/N)

† Additionally adjusted for menopausal status