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Impact of menopausal symptoms on quality of life (QOL) within six months of systemic breast cancer treatment: Results from the Shanghai Breast Cancer Survival Study (SBCSS)

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Abstract

Menopausal symptoms (MPS) after breast cancer treatment are associated with reduced health-related quality of life (QOL) among Caucasian women. Little is known about whether MPS similarly impact QOL in Asian women with breast cancer. QOL was assessed by using the Generic Quality of Life Inventory (MOSQOL-74) or Short Form-36 Health Survey (SF-36) in 4,976 Chinese participants of the Shanghai Breast Cancer Survival Study who were treated for incident, non-metastatic breast cancer within the six months before the study interview. Relationships between MPS and QOL were assessed by multiple linear regression, controlling for potential confounders. 71.4% of study participants experienced MPS, including hot flashes, night sweats, vaginal dryness, depressed mood, and/or dry skin. Women with MPS reported lower overall QOL than women without MPS [mean scores 61.0 vs. 64.0, respectively (MOSQOL-74) and 54.9 vs. 66.9, respectively (SF-36); $P < 0.01$]. Adjusted mean differences (β) in overall QOL in the presence and absence of MPS were -3.1 (95% CI $-3.8, -2.4$) with the MOSQOL-74 and -12.3 (95% CI $-13.8, -10.9$) with the SF-36. Women with any MPS had lower scores for the MOSQOL-74 physical and psychological domains and for the SF-36 social and emotional subscales than those without MPS ($P < 0.05$ for all). Having a higher number of MPS predicted poorer QOL in all domains measured regardless instrument used ($P_{\text{trend}} < 0.01$ for all). Our study indicates that in Chinese women with recently-treated breast cancer, MPS adversely impacts QOL. Actively soliciting and treating MPS in these women should significantly improve their QOL.

Keywords

Breast cancer; Quality of life; Menopausal symptoms; MOSQOL74; SF36; Systemic treatment; China

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INTRODUCTION

Breast cancer is the second most prevalent cancer in women worldwide and its prevalence is expected to rise (1). The growing numbers of women undergoing breast cancer treatment and surviving this disease underscore the need for more effective prediction and management of treatment complications, which significantly impact their quality of life and productivity (2, 3).

During the course of natural menopause, women commonly experience vasomotor (hot flashes and night sweats), psychological (anxiety, negative emotion and depression) and atrophic (vaginal dryness and dry/itchy skin) symptoms (4,5). The adverse effect of these menopausal symptoms (MPS) on health-related quality of life is well known (QOL) (4,6), and many women seek medical treatment, particularly hormone replacement therapy, for these symptoms (7,8). In breast cancer patients, MPS are prematurely induced or compounded by the ovarian failure that often results from systemic treatment (9,10), including chemotherapy, radiation, tamoxifen and immunotherapy (11–14).

Numerous studies have investigated the association between cancer treatment and QOL among women with breast cancer (2). However, few studies have examined the relationship between MPS and QOL in women recently treated for breast cancer. The most commonly studied symptoms are hot flashes and psychological distress, such as anxiety and depression, and results have been mixed (15–17). MPS appear to be the most common determinants of QOL in breast cancer survivors and may influence women's treatment decisions (11–13,18). These findings, however, are based on studies conducted among primarily Caucasian women residing in Western countries (2). Similar studies investigating the association between MPS and QOL in Asian breast cancer patients are lacking, and Asian women are generally underrepresented in breast cancer studies. The aim of the present study, therefore, was to examine the relationship between menopausal symptoms and quality of life patterns reported by newly diagnosed patients who had undergone initial systemic treatment for breast cancer in urban China.

PATIENTS AND 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 at approximately 6 months post-diagnosis from the Shanghai Cancer Registry. The study was conducted in two-phases between April 2002 and July 2004 (Phase I) and between August 2004 and December 2006 (Phase II). Detailed study methods have been published elsewhere (19). Briefly, 6,303 patients were identified, who met the following study inclusion criteria: 1) first diagnosis of primary breast cancer; 2) permanent resident of Shanghai; and 3) alive at study recruitment. Of eligible women, 757 (12%) refused participation, 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 women (80.1%) participated in this study, and all subjects provided written, informed consent. A total of 4,976 patients were included in the present analysis after the additional exclusion of 70 women who had recurrent or stage IV cancer at the time of the interview. Most patients had completed primary cancer treatment (99% for surgery and 97% for radiation therapy) and were receiving adjuvant therapy (chemotherapy, immunotherapy and tamoxifen). The institutional review boards of all participating institutions approved the study protocol.

Data collection

Information on demographic features, personal and first-degree family history of any cancer, other chronic diseases, reproductive factors, lifestyle, diet, and the use of complementary and alternative medicines were collected through in-person interviews conducted by trained staff using a structured questionnaire. Menopausal status was defined as the cessation of menstruation for 12 months or longer, excluding lapses due to pregnancy or breastfeeding. History of chronic disease before breast cancer diagnosis was collected and quantified using the Charlson co-morbidity score (20) and the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) (21). After completing the interview, anthropometric measurements including height, weight, waist circumference, and hip circumference were taken. Body-mass index (BMI) and waist-to-hip ratio (WHR) were calculated from these measurements. Clinical and pathology information, 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 (mastectomy, radiation therapy, chemotherapy, immunotherapy, and/or hormonal therapy (tamoxifen) was collected. Medical charts were reviewed to verify clinical and treatment information. Commonly used chemotherapeutic drugs included cyclophosphamide, adriamycin and 5-fluorouracil, taxotere, epirubicin-adriamycin, and navelbine, and immunotherapy (interferon, interleukin and thymosin).

Women were queried about the presence of menopausal symptoms including hot flashes, night sweats, depressed mood, vaginal dryness, and dry skin or skin dryness/itching since diagnosis and during adjuvant treatment for breast cancer. Participants were also asked for dates of onset/end and, if applicable, resolution of each symptom.

Assessment of quality of life (QOL)

Two previously-validated, generic quality of life instruments, the Medical Outcome Study of Quality of Life Inventory (MOSQOL-74) and the Short-Form Health Survey (SF-36) were used in the study to assess the health related QOL among breast cancer patients at 6 months post-diagnosis. The first 2,200 patients were administered the MOSQOL-74; the remaining 2,776 patients were administered the SF-36.

Based on WHO Quality of Life-BREF (WHOQOL-BREF) (22), the MOSQOL-74 instrument for Chinese populations was developed by assessing its reliability, validity, and sensitivity in both healthy samples and breast cancer patients in China (3,23). This questionnaire comprises a total of 74 items that can be grouped into four domains and 20 facets, which include perceived health status and overall QOL status. The domains are: 1) physical well-being, which includes sleep and energy level, pain and physical discomfort, eating functioning, sexual functioning, sensory function, and activities of daily living; 2) psychological well-being, which includes psychological distress, negative feelings, positive feelings, cognitive functioning, body/self-image; 3) social well-being, which includes social support, interpersonal relationships, work and study capacity, recreational and leisure activities, marriage and family; and 4) material well-being, which includes housing situation, community services, living environment, and financial situation. Participants' responses were converted to a score from 0 to 100 for each domain and facet; higher summed scores reflected better QOL.

The SF-36 instrument is used internationally (24), and the Chinese version was developed (25,26) and evaluated for reliability, validity, and sensitivity in both healthy persons and cancer patients in China (27–29). The survey is composed of 16 questions with 36 items in eight health subscales: health-related physical functioning, physical role functioning, bodily pain, social functioning, general mental health, emotional role functioning, and general health perceptions. These subscales are summarized by a physical health scale and a mental health scale. Each

subscale and summary scale have a value, ranging from 0 to 100, where 0 corresponds to the worst score and 100 to the best score for health status (30). In this analysis, we did not include the sexual health facet that is part of the MOSQOL-74 instrument, since about 94% patients (total of 2,200) reported no sexual activity during the 2–4 weeks before the interview.

Statistical methods

For data analysis, the presence and absence of any symptom, each individual symptom, and the total number of experienced MPS were the main explanatory variables, while quality of life (domains/facets for MOS QOL-74, scales/subscales for SF-36 and overall QOL for both instruments) were the dependent variables. Differences in social demographics, lifestyle factors, and clinical characteristics of patients with and without any MPS were compared using the one-way analysis of variance (ANOVA) procedure or the Wald chi-square test with adjustment for age at diagnosis. Multivariate linear regression models were used to compute regression coefficients (β) and associated 95% confidence intervals as estimates of the mean difference of quality of life scores associated with the presence of absence of any symptoms, or each individual symptom, or the total number of MPS (0, 1, 2 or ≥ 3 symptoms), adjusting for potential confounding variables. The following potentially confounding variables were included in all regression models: age at breast cancer diagnosis (continuous), education, current marital status (married/living with partner vs. single/widowed or divorced/separated), WHR (continuous), menopausal status (pre- and post-), history of chronic disease or Charlson co-morbidity score ($=0$ / >0), hormone receptor status of the tumor (ER+/PR+, ER-/PR-, ER-/PR+ or ER+/PR-, or unknown), treatment for breast cancer (chemotherapy, immunotherapy, and/or tamoxifen use) and other menopausal symptoms, excluding the same variables. Tests for trend were performed by entering the categorical variables as continuous parameters in the model. Women without any symptoms were used as the reference group throughout the analyses. Statistical tests were based on a two-tailed probability with a significance level of 0.05. All statistical analyses were performed using SAS.9.1 (SAS Institute, Cary, NC).

RESULTS

Demographic and clinical characteristics of all study participants at 6 months post-diagnosis and stratified by presence of MPS are presented in Table 1. The median time since diagnosis was 6.4 months. A total of 71.4 % of women reported experiencing one or more MPS during the first 6 months after cancer treatment. The mean age at cancer diagnosis was 53.4 (± 10 SD) years. The mean age was lower among women reporting any MPS (52.5 ± 9.3 years) than among those who did not (55.9 ± 11.3 years), $P < 0.01$. Compared to women without MPS, women with symptoms were more likely to be premenopausal ($P < 0.01$), to have a slightly higher WHR ($P = 0.06$), and to have a history of chronic disease (Charlson co-morbidity score > 0 : 39.1% and 44.9%, respectively; $P \leq 0.01$). The prevalence of HRT use was low among women in this study and did not differ according to the presence or absence of MPS. Approximately 95% of patients underwent mastectomy, and the frequencies of other systemic treatments in the study population were as follows: chemotherapy (91.1%), radiation therapy (31.8%), immunotherapy (14.7%), and tamoxifen use (52.1%). Women reporting any MPS were also more likely to have received immunotherapy or tamoxifen ($P < 0.01$ for both) and to have hormone receptor-positive (ER+/PR+) tumors ($P = 0.01$) than those without symptoms. Women with and without MPS did not differ significantly with regard to tumor stage. Overall, the demographic and clinical characteristics of subjects in both phases of the SBCSS were very similar (data not shown).

The comparison of mean (SD) QOL scores and the mean differences (β) of QOL scores in both the MOSQOL-74 and SF-36 instruments between cases without and with any menopausal symptoms are shown in Table 2. The mean overall QOL scores and most of the domain- and

facet-specific scores assessed by the MOSQOL-74 instrument were significantly lower among cases reporting any MPS compared with cases not reporting any MPS. There were significant differences in scores for the physical and psychological domains and several facets, including sleep/rest and energy, pain and discomfort, negative feelings, and positive feelings between cases with and without any symptoms ($P < 0.05$ for all). The smallest difference in scores was observed in the material domain and facets compared with other domains and facets. The adjusted mean difference (β) for the association was -4.6 (95% CI $-5.7, -3.6$) for the physical domain, -4.8 (95% CI $-5.8, -3.9$) for the psychological domain, -1.6 (95% CI $-2.4, -0.8$) for the social domain, -1.3 (95% CI $-2.3, -0.2$) for the material domain, and -3.1 (95% CI $-3.8, -2.4$) for overall QOL ($P < 0.05$ for all), respectively.

For QOL assessed by the SF-36 instrument (Table 2), differences in scores between groups with and without MPS were observed for social role functioning (mean score 61.9 for women with any symptom and 75.0 for those without symptoms; $P < 0.01$), emotional role functioning (mean scores were 59.8 and 83.4 for women with and without symptoms, respectively; $P < 0.01$), and bodily pain (66.3 for women with and 75.5 for women without symptoms, respectively; $P < 0.01$). Similarly, lower QOL scores in relation to having any MPS were observed for all subscales of QOL using the SF-36 instrument, particularly for the mental health scale ($\beta = -15.0$, 95% CI $-16.7, -13.2$) including social role functioning, general mental health, and emotional role functioning ($P < 0.01$ for all) and the physical health scale ($\beta = -8.6$, 95% CI $-9.9, -7.3$). The perceived health and QOL and overall QOL scores using both instruments were much lower among cases that experienced any MPS compared to those without any symptoms ($P < 0.05$ for both).

Inverse associations were also observed between different domains/facets and scales/subscales of QOL and each individual MPS (Table 3). The strongest associations were observed between depressed mood and all domains and facets of the MOSQOL-74 instrument, particularly for the psychological and physical domains ($\beta = -9.5$; 95% CI $-10.5, -8.5$ and $\beta = -6.7$; 95% CI $-7.8, -5.6$, respectively) and their corresponding facets, including negative and positive feelings, psychological distress, sleep/rest and energy, and pain and discomfort (β range: $-14.0, -8.5$; $P < 0.05$ for all). Moreover, most domain-specific and facet-specific QOL scores were slightly lower among women who experienced night sweats, vaginal dryness, or skin dryness. The adjusted mean differences (β) in overall QOL scores were -1.3 (95% CI $-2.1, -0.5$) for night sweats and -2.1 (95% CI $-3.0, -1.1$) for skin dryness/itching. Hot flashes were significantly but weakly associated with negative feelings in the psychological domain only ($\beta = -1.4$ (95% CI $-2.7, -0.1$)). No other QOL measures were associated with hot flashes.

We also estimated the mean differences for QOL scores between cases with and without specific symptoms using the SF-36 instrument (Table 3). Consistent with the MOSQOL-74 instrument, overall QOL, total, and subscale QOL scores measured by the SF-36 were inversely associated with depressed mood, vaginal dryness, night sweats, and dry skin. Breast cancer patients experiencing depressed mood reported the poorest QOL in all subscales, particularly in emotional role functioning ($\beta = -38.0$, 95% CI $-40.9, -35.0$), general mental health ($\beta = -26.3$, 95% CI $-27.8, -24.7$), and social role functioning ($\beta = -18.3$, 95% CI $-20.6, -15.9$). Patients with depressed mood were more likely to have lower scores for the mental health scale and for the physical health scale ($\beta = -20.3$, 95% CI $-21.6, -19.0$ and $\beta = -8.0$, 95% CI $-9.0, -6.9$, respectively). In general, there was a significant inverse association between the presence of night sweats and different subscales of role functioning, except for emotional role functioning (β range: $-1.8, -6.6$, $P < 0.05$ for all). Similarly, dry skin was inversely associated with all subscales of QOL (β range: $-2.1, 5.4$; $P < 0.05$ for all, except for the social subscale). Similar mean difference for overall QOL scores in patients with night sweats or skin dryness/itching were observed ($\beta = -4.0$, 95% CI $-4.1, -0.1$ or -4.3 , 95% CI $-5.8, -2.8$, respectively). Vaginal dryness was associated with both physical and mental scales and overall QOL ($P < 0.05$).

for all), but not with the health subscales, except for vitality. On the whole, hot flashes were not associated with overall QOL or specific role functioning, except for bodily pain ($\beta = -2.8$; 95% CI $-4.7, -0.9$). In addition, we carried out the same analyses stratified by menopausal (pre- vs. postmenopausal) and chronic disease status (Charlson co-morbidity score; 0 vs. >0). These factors did not appreciably modify the association of MPS with QOL, particularly for night sweats, depressed mood, and skin dryness (data not shown).

We further evaluated the association between specific domains/facets and scales/subscales of QOL and number (0, 1, 2, ≥ 3) of MPS among breast cancer patients (Table 4). In general, a decrease in QOL scores was associated with an increasing number of MPS reported. The poorest QOL scores were found among women who experienced ≥ 3 MPS compared to women without any MPS, and adjusted mean differences (β) for the association of QOL scores using the MOSQOL-74 instrument were -5.8 (95% CI: $-6.8, -4.8$) for overall QOL, -8.1 (95% CI: $-9.5, -6.7$) for the physical domain, -8.6 (95% CI: $-9.9, -7.3$) for the psychological domain, -3.0 (95% CI: $-4.1, -1.9$) for the social domain, and -3.3 (95% CI: $-4.7, -1.8$) for the material domain ($P_{\text{trend}} < 0.01$ for all). For the SF-36 instrument (Table 4), there was a significant inverse association between overall QOL and number of symptoms reported ($\beta = -8.3$ for one symptom, -11.7 for 2 symptoms and -17.9 for ≥ 3 symptoms; $P_{\text{trend}} < 0.01$). The strongest indicators for poorest QOL were the social, general mental health, and emotional subscales for ≥ 3 symptoms ($\beta = -19.4, -25.7$, and -35.5 , respectively; $P_{\text{trend}} < 0.01$). These results did not differ by menopausal status or Charlson co-morbidity score (data not shown).

DISCUSSION

Vasomotor, psychological, and atrophic symptoms, namely hot flashes, night sweats, depressed mood, vaginal dryness, and dry skin/itching, are common symptoms of natural menopause frequently reported by women who undergo systemic treatment for breast cancer (9,15). These symptoms are often quite severe (9,15) and may affect patients' QOL and influence their treatment decisions (14,31). In this large, population-based prospective study of Chinese women, we found strong evidence that occurrence of MPS was significantly related to the QOL of cancer patients 6-months after diagnosis and treatment. Our findings are in general agreement with findings from studies of Caucasian populations (2).

Our results are compatible with previous findings that breast cancer patients who experience MPS have much lower QOL scores in physical and social domains, and differences were more apparent for sleep/rest and low energy, pain and discomfort, and negative or positive feelings, as measured by the MOSQOL-74 (32,33), and for social and emotional functioning, as measured by the SF-36 (34–36). The prevalence of depressed mood was common in our population and was the strongest indicator of limitations in various other subscales of the SF-36 as reported previously (37,38). Other studies have indicated that high prevalence of co-morbidity (19,39,40), younger age (40–42), premature menopause induced by systemic cancer treatment (10,43), and mastectomy (44,45) are related to depressed mood, and consequently may influence QOL. In our study, the differences in the association of QOL with MPS persisted after adjustment for these factors. However, the mechanisms underlying the psychological and QOL changes related to MPS remain unknown.

Contrary to most other studies, hot flashes play a minor role in the QOL of our population (15–17). This discrepancy may be due to differences in the social, cultural, ethnic, lifestyle, and clinical characteristics of the study populations (5,11). Finally, as has been reported previously, QOL in our study population deteriorated significantly in all domains and facets of the MOSQOL-74 and all scales and subscales of the SF-36 among women who experienced several MPS compared to those who did not or those who experienced fewer MPS (15,16).

It is important to acknowledge some limitations of this study. Over-reporting of the types of MPS is possible, since women suffering from more symptoms may also have been more likely to respond to questions about MPS. However, all women responded to these questions, making significant bias of this sort less likely. In addition, data on MPS were subjective and relied on self-reports; hence, misreporting of symptoms could have occurred. The short duration between diagnosis or cancer treatment and the interview should have minimized recall bias, since our study subjects would have been more likely to accurately recall MPS and treatments received. Furthermore, such misclassification would most likely be random. We were unable to examine the sexual functioning aspect of QOL in relation to MPS, because most patients were sexually inactive during the two weeks to one month before the interview, although the majority reported living with their husband or partner.

To our knowledge, this is the first population-based study to investigate relationships between MPS and QOL in women treated for primary breast cancer in China, where lifestyle, diet-related risk factors, and prevalence of HRT use are significantly different from those in Western populations. Selection and recall bias were also 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 on socioeconomic factors, lifestyle factors, chronic disease history, and clinical characteristics allowed for analyses to be adjusted for these potential confounding factors. Finally, the use of both the MOSQOL-74 and SF-36 instruments allowed us to investigate the impact of MPS on all aspects of QOL.

In summary, in this large population-based study, we found that the QOL of breast cancer patients varied by the type and number of MPS. Depressed mood was the strongest predictor of poor QOL, while hot flashes were the weakest, using both the MOSQOL-74 and SF-36 measurements. Our data indicate information on the importance of ancillary mental health care and other multidisciplinary supportive measures in the management of all breast cancer patients, particularly in China. Actively soliciting information on such symptoms and promoting interventions to treat them promises to improve QOL among women who undergo life-changing treatment for breast cancer and who are becoming long-term breast cancer survivors.

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Table 1

Age-adjusted[†] demographic and clinical characteristics of breast cancer patients at 6 months post-cancer diagnosis by presence of menopausal symptom[‡], SBCSS

Characteristics	All patients n= 4,976	Patients without symptoms n=1,422 (28.6%)	Patients with any symptom n=3,554 (71.4%)	P value [*]
Demographic and lifestyle characteristics	(mean, %)	(mean, %)	(mean, %)	
Age at diagnosis, y	53.4 ± 10.0	55.9 ± 11.3	52.5 ± 9.3	<0.01
Current marital status				
Married/living with partner	4,414 (87.9)	86.8	88.7	0.03
Other	608 (12.1)	13.1	11.4	
Education				
<High school	2,299 (46.2)	45.6	46.3	0.38
High school	1,874 (37.7)	36.8	37.9	
>High school	802 (16.1)	17.6	15.8	
Household income, ¥/month				
<700	2,847 (57.3)	57.9	56.9	0.24
<2000	1,528 (30.7)	29.4	31.4	
≥2000	598 (12.0)	12.7	11.7	
Menopause status				
Premenopausal	2,440 (49.0)	44.7	50.3	<0.01
Postmenopausal :	2,536 (51.0)	55.3	49.7	
Age at menopause	49.1 ± 4.3	44.1	44.0	0.47
HRT use	171 (3.4)	3.5	3.7	0.41
Body mass index, BMI	24.1 ± 3.4	23.7	23.9	0.17
Waist to hip ratio, WHR	0.834 ± 0.05	0.829	0.824	0.06
Exercised regularly	3,226 (64.8)	64.5	65.2	0.55
Vitamin supplement use	1,346 (27.0)	25.2	27.7	0.09
Charlson comorbidity score >0	2,155 (43.3)	39.0	44.9	<0.01
Ever smoked cigarettes regularly	127 (2.5)	2.3	2.5	0.95
Ever drank alcohol regularly	151 (3.0)	2.1	3.2	0.08
Clinical characteristics				
Treatment				
Mastectomy	4,712 (94.7)	94.0	94.8	0.46
Radiotherapy	1,581 (31.8)	31.0	32.1	0.43
Chemotherapy	4,533 (91.1)	90.6	91.3	0.48
Immunotherapy	732 (14.7)	11.9	15.7	0.001
Tamoxifen use	2,595 (52.1)	47.0	54.0	<0.01
Stage, TNM (%) [§]				
0-I	1,834 (36.9)	35.6	37.2	0.54
II	2,469 (49.6)	51.3	49.2	

Characteristics	All patients n= 4,976	Patients without symptoms n=1,422 (28.6%)	Patients with any symptom n=3,554 (71.4%)	P value*
III	446 (9.0)	9.1	8.9	
Unknown	227 (4.5)	4.0	4.7	
Hormone receptor status (%)				
ER+/PR+	2,498 (50.2)	46.7	51.1	0.01
PR≥/PR≥	1,414 (28.4)	31.7	27.4	
Mixed	968 (19.5)	19.0	19.8	
Unknown	96 (1.9)	2.6	1.7	

[†] Adjusted for age at breast cancer diagnosis

[‡] Includes hot flashes, night sweats, vaginal dryness, depressed mood, and skin dryness/itchiness

* Derived from GLM procedure for continuous and CMH statistics for categorical variables, respectively.

Table 2

The crude mean and adjusted mean differences in QOL scores for breast cancer patients at 6 months post-diagnosis by presence of any menopausal symptom (n=4,976)

QOL categories	Crude scores of QOL (mean $\pm$ SD)		
	Patients without symptoms	Patients with any symptom	β (95% CI) [†]
MOSQOL-74 (domains/facets), n=2,200	n=818	n=1,382	
Physical domain	64.3 $\pm$ 12.2	60.6 $\pm$ 11.7	-4.6 (-5.7, -3.6)*
Sleep/rest and energy	59.9 $\pm$ 16.6	55.0 $\pm$ 16.6	-5.5 (-7.0, -4.0)
Pain and discomfort	67.3 $\pm$ 18.0	61.2 $\pm$ 17.5	-6.7 (-8.3, -5.2)*
Eating ability	66.1 $\pm$ 14.4	64.0 $\pm$ 14.6	-2.8 (-4.1, -1.5)*
Capability of daily living	64.1 $\pm$ 12.8	62.1 $\pm$ 12.0	-3.5 (-4.5, -2.5)*
Psychological domain	70.9 $\pm$ 9.7	66.4 $\pm$ 11.2	-4.8 (-5.8, -3.9)*
Psychological distress	78.8 $\pm$ 12.5	74.4 $\pm$ 14.2	-4.5 (-5.8, -3.3)*
Negative feelings	75.0 $\pm$ 12.0	68.9 $\pm$ 14.8	-6.3 (-7.5, -5.0)*
Positive feelings	70.9 $\pm$ 15.9	64.8 $\pm$ 18.0	-6.5 (-8.0, -4.9)*
Cognitive functioning	65.3 $\pm$ 14.1	62.7 $\pm$ 14.3	-3.4 (-4.6, -2.2)*
Bodily image and appearance	64.3 $\pm$ 11.9	61.3 $\pm$ 12.0	-3.4 (-4.5, -2.4)*
Social domain	65.2 $\pm$ 9.5	64.0 $\pm$ 9.3	-1.6 (-2.4, -0.8)*
Social support	67.0 $\pm$ 17.7	66.4 $\pm$ 17.9	-1.7 (-3.2, -0.1)*
Interpersonal relationship	76.9 $\pm$ 11.9	76.4 $\pm$ 11.8	-1.1 (-2.1, 0.0)*
Work capacity	54.9 $\pm$ 12.2	53.3 $\pm$ 12.6	-2.1 (-3.2, -1.0)*
Recreational and leisure activities	58.9 $\pm$ 11.7	57.8 $\pm$ 11.6	-1.1 (-2.1, 0.0)*
Family relationships	68.1 $\pm$ 14.2	66.3 $\pm$ 14.3	-2.3 (-3.5, -1.0)*
Material domain	55.2 $\pm$ 12.4	53.0 $\pm$ 12.2	-1.3 (-2.3, -0.2)*
Home environment	67.0 $\pm$ 18.8	64.7 $\pm$ 18.8	-1.0 (-2.6, 0.6)
Participation in community activities	45.5 $\pm$ 17.3	43.8 $\pm$ 17.2	-2.4 (-3.9, -0.9)*
Neighborhood environment	56.6 $\pm$ 17.6	54.9 $\pm$ 17.7	-1.2 (-2.8, 0.4)
Financial recourses	51.8 $\pm$ 19.2	48.8 $\pm$ 19.2	-0.5 (-2.2, 1.1)
Overall QOL	64.0 $\pm$ 8.2	61.0 $\pm$ 8.3	-3.1 (-3.8, -2.4)*
Perceived health and QOL	57.8 $\pm$ 13.6	54.9 $\pm$ 13.2	-3.3 (-4.5, -2.2)*
SF-36 (scales/scales), n=2,776	n=604	n=2,172	
Physical functioning	80.8 $\pm$ 13.8	79.1 $\pm$ 14.5	-2.5 (-3.8, -1.3)*
Physical role functioning	25.9 $\pm$ 36.7	14.2 $\pm$ 28.0	-11.8 (-14.5, -9.1)*
Bodily pain	75.5 $\pm$ 23.0	66.3 $\pm$ 23.3	-9.4 (-11.5, -7.3)*
Social role functioning	75.0 $\pm$ 30.2	61.9 $\pm$ 32.3	-14.0 (-16.9, -11.1)*
General mental health	78.3 $\pm$ 17.0	60.2 $\pm$ 24.2	-18.1 (-20.2, -16.0)*

QOL categories	Crude scores of QOL (mean $\pm$ SD)		
	Patients without symptoms	Patients with any symptom	β (95% CI) [†]
Vitality	54.0 $\pm$ 20.4	43.4 $\pm$ 19.4	-11.1 (-12.8, -9.3) *
Emotional role functioning	83.4 $\pm$ 33.8	59.8 $\pm$ 44.9	-23.4 (-27.3, -19.5) *
General health perceptions	61.9 $\pm$ 17.1	54.4 $\pm$ 18.6	-8.2 (-9.9, -6.6) *
Physical health	59.6 $\pm$ 15.9	51.5 $\pm$ 14.3	-8.6 (-9.9, -7.3) *
Mental health	70.5 $\pm$ 15.6	55.9 $\pm$ 19.9	-15.0 (-16.7, -13.2) *
Overall QOL	66.9 $\pm$ 15.1	54.9 $\pm$ 16.6	-12.3 (-13.8, -10.9) *

[†] Obtained from multivariate linear regression model adjusted for age, education, marital status, WHR (continuous), menopausal status, Charlton co-morbidity score (0/>0), ER/PR status and cancer treatment (immune and tamoxifen)

* P value <0.05

Note: β (regression coefficient) is the adjusted mean difference in QOL score by presence of menopausal symptoms. Reference group in all analyses was the group of women reporting no menopausal symptoms (n=818 in the MOSQOL-74 and n=604 in the SF-36, respectively).

Note: Facets for sexual activity were excluded, since 93.8% of patients reported no sexual activity in the 2–4 weeks before the interview.

Table 3

Adjusted mean differences $\ddagger$ in QOL scores by specific menopausal symptoms among breast cancer patients at 6 months post-diagnosis (n=4,976)

QOL categories	Hot flashes/flushes (44.2%) β (95% CI)	Night sweats (35.3%) β (95% CI)	Vaginal dryness (9.1%) β (95% CI)	Depressed mood (40.8%) β (95% CI)	Skin dryness/itching (18.6%) β (95% CI)
MOSQOL-74 (n=2,200)	n=917	n=793	n=169	n=583	n=360
<i>Physical domain</i>					
Sleep/rest and energy	-0.4 (-1.5, 0.7)	-2.6 (-3.7, -1.5)*	-1.7 (-3.6, 0.1)	-6.7 (-7.8, -5.6)*	-3.3 (-4.6, -1.9)*
Pain and discomfort	-0.6 (-2.2, 0.9)	-3.2 (-4.8, -1.6)*	-2.4 (-5.1, 0.2)	-8.8 (-10.4, -7.3)*	-3.3 (-5.2, -1.4)*
Eating ability	-1.1 (-2.7, 0.6)	-2.8 (-4.5, -1.1)*	-3.7 (-6.5, -0.9)*	-8.5 (-10.2, -6.8)*	-5.5 (-7.5, -3.5)*
Capability of daily living	0.4 (-0.9, 1.8)	-1.9 (-3.3, -0.5)*	0.4 (-1.9, 2.7)	-5.0 (-6.4, -3.6)*	-1.9 (-3.5, -0.2)*
	-0.4 (-1.5, 0.7)	-2.3 (-3.5, -1.2)	-1.1 (-3.0, 0.7)	-4.5 (-5.6, -3.4)*	-2.5 (-3.8, -1.1)*
<i>Psychological domain</i>					
Psychological distress	-0.1 (-1.1, 0.9)	-0.9 (-1.9, 0.1)	-1.2 (-2.8, 0.5)	-9.5 (-10.5, -8.5)*	-2.5 (-3.7, -1.3)*
Negative feelings	0.0 (-1.3, 1.3)	-0.4 (-1.7, 0.9)	-1.3 (-3.5, 0.8)	-10.3 (-11.5, -9.0)*	-2.2 (-3.8, -0.6)*
Positive feelings	-1.4 (-2.7, -0.1)*	-1.6 (-2.9, -0.2)*	-2.9 (-5.1, -0.7)*	-12.0 (-13.2, -10.7)*	-3.2 (-4.8, -1.6)*
Cognitive functioning	1.4 (-0.2, 3.0)	-1.1 (-2.8, 0.5)	-1.9 (-4.6, 0.9)	-14.1 (-15.7, -12.4)*	-3.6 (-5.6, -1.6)*
Bodily image and appearance	-0.2 (-1.6, 1.1)	-0.7 (-2.0, 0.7)	-0.2 (-2.4, 2.0)	-5.5 (-6.8, -4.1)*	-2.5 (-4.1, -0.9)*
	-0.1 (-1.2, 1.0)	-0.6 (-1.8, 0.5)	0.5 (-1.3, 2.4)	-5.7 (-6.9, -4.6)*	-1.2 (-2.5, 0.2)
<i>Social domain</i>					
Social support	0.0 (-0.8, 0.9)	-0.5 (-1.4, 0.4)	1.6 (0.2, 3.1)*	-3.2 (-4.1, -2.3)*	-1.4 (-2.5, -0.4)*
Interpersonal relationship	-0.7 (-2.4, 1.0)	1.6 (-0.1, 3.3)	2.2 (-0.6, 5.0)	-3.7 (-5.4, -2.0)*	-0.8 (-2.8, 1.3)
Work capacity	-0.5 (-1.6, 0.6)	-0.5 (-1.6, 0.6)	2.0 (0.1, 3.8)*	-1.7 (-2.9, -0.6)*	-1.2 (-2.6, 0.1)
Recreational and leisure activities	1.0 (-0.1, 2.2)	-1.1 (-2.2, 0.1)	1.3 (-0.6, 3.2)	-3.3 (-4.5, -2.1)*	-2.2 (-3.7, -0.8)*
Family relationship	-0.0 (-1.1, 1.1)	-0.8 (-1.9, 0.4)	0.0 (-1.9, 1.8)	-2.8 (-4.0, -1.7)*	-0.8 (-2.2, 0.5)
	0.4 (-1.0, 1.7)	-1.7 (-3.1, -0.3)*	2.8 (0.5, 5.0)*	-4.4 (-5.8, -3.0)*	-2.1 (-3.8, -0.5)*
<i>Material domain</i>					
Home environment	-0.8 (-1.9, 0.3)	-1.6 (-2.8, -0.5)*	-0.2 (-2.1, 1.7)	-2.0 (-3.2, -0.9)*	-1.3 (-2.7, 0.1)
Participation in community activities	-0.3 (-2.0, 1.5)	-2.0 (-3.7, -0.2)*	0.2 (-2.7, 3.2)	-0.8 (-2.6, 1.1)	-1.1 (-3.2, 1.0)
Neighborhood environment	-1.5 (-3.1, 0.1)	-1.6 (-3.3, 0.0)*	0.0 (-2.8, 2.7)	-2.9 (-4.6, -1.2)*	0.1 (-1.9, 2.1)
Financial resources	-1.3 (-3.0, 0.4)	-2.3 (-4.0, -0.6)*	-0.2 (-3.0, 2.6)	-1.9 (-3.7, -0.2)*	-1.7 (-3.8, 0.3)
Overall QOL	-0.2 (-1.9, 1.6)	-0.5 (-2.2, 1.3)	-0.7 (-3.6, 2.2)	-2.5 (-4.3, -0.7)*	-2.4 (-4.5, -0.3)*
	-0.3 (-1.0, 0.5)	-1.3 (-2.1, -0.5)*	-0.3 (-1.6, 1.0)	-5.5 (-6.3, -4.8)*	-2.1 (-3.0, -1.1)*

QOL categories	Hot flashes/flushes (44.2%)	Night sweats (35.3%)	Vaginal dryness (9.1%)	Depressed mood (40.8%)	Skin dryness/itching (18.6%)
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Perceived health and QOL	0.0 (-1.2, 1.2)	-0.9 (-2.2, 0.4)	-0.6 (-2.8, 1.5)	-6.7 (-8.0, -5.4)*	-1.6 (-3.2, -0.1)*
SF-36 (n=2,776)	n=1,283	n=965	n=286	n=1,449	n=564
Physical functioning	0.4 (-0.7, 1.5)	-1.8 (-2.9, -0.7)*	-0.5 (-2.2, 1.1)	-2.1 (-3.1, -1.0)*	-3.9 (-5.2, -2.6)*
Physical role functioning	-0.1 (-2.5, 2.3)	-6.5 (-8.9, -4.0)*	-2.4 (-6.2, 1.3)	-11.4 (-13.6, -9.1)*	-5.0 (-7.8, -2.2)*
Bodily pain	-2.8 (-4.7, -0.9)*	-6.5 (-8.4, -4.7)*	-1.6 (-4.5, 1.2)	-7.3 (-9.0, -5.5)*	-5.4 (-7.5, -3.2)*
Social role functioning	0.3 (-2.2, 2.9)	-3.8 (-6.4, -1.2)*	-0.6 (-4.5, 3.3)	-18.3 (-20.6, -15.9)*	-2.1 (-5.1, 0.9)
General mental health	-0.5 (-2.3, 1.3)	-2.0 (-3.9, -0.2)*	-2.5 (-5.3, 0.3)	-26.3 (-27.8, -24.7)*	-4.4 (-6.6, -2.3)*
Vitality	-1.5 (-3.1, 0.0)	-4.6 (-6.2, -3.0)*	-2.4 (-4.9, -0.1)*	-10.9 (-12.3, -9.4)*	-3.5 (-5.4, -1.7)*
Emotional role functioning	0.5 (-2.9, 3.9)	-2.3 (-5.7, 1.2)	-3.5 (-8.8, 1.7)	-38.0 (-40.9, -35.0)*	-5.4 (-9.3, -1.4)*
General health perceptions	-1.1 (-2.5, 0.3)	-4.2 (-5.7, -2.8)*	-2.8 (-5.0, -0.6)*	-8.2 (-9.5, -6.8)*	-4.8 (-6.4, -3.2)*
Physical health	-1.0 (-2.2, 0.1)	-4.7 (-5.9, -3.6)*	-2.0 (-3.8, -0.2)*	-8.0 (-9.0, -6.9)*	-4.5 (-5.9, -3.2)*
Mental health	-0.5 (-2.0, 1.0)	-3.4 (-4.9, -1.9)*	-2.4 (-4.7, -0.1)*	-20.3 (-21.6, -19.0)*	-4.1 (-5.8, -2.3)*
Overall QOL	-0.6 (-1.9, 0.7)	-4.0 (-5.3, -2.7)*	-2.1 (-4.1, -0.1)*	-15.3 (-16.4, -14.1)*	-4.3 (-5.8, -2.8)*

[†] Obtained from multivariate linear regression model adjusted for age, education, marital status, WHR (continuous), menopausal status, Charlton co-morbidity score (0/>0), ER/PR status, cancer treatment (immune and tamoxifen), and other menopausal symptoms

* P value <0.05 Note: Reference group in all analyses was the group of women reporting no specific menopausal symptoms (n=818 in the MOSQOL-74 and n=604 in the SF-36, respectively).

Table 4

Adjusted mean differences[†] of QOL scores by number of menopausal symptoms among patients at 6 months post-diagnosis (n=4,976)

QOL categories	Number of menopausal symptoms			P for trend
	1 β (95% CI)	2 β (95% CI)	≥3 β (95% CI)	
MOSQOL-74 (n=2,200)	n=510	n=476	n=396	
<i>Physical domain</i>				
Sleep/rest and energy	-2.3 (-3.6, -1.0)	-4.5 (-5.8, -3.2)	-8.1 (-9.5, -6.7)	<0.01
Pain and discomfort	-2.3 (-4.2, -0.5)	-5.5 (-7.4, -3.6)	-10.1 (-12.1, -8.1)	<0.01
Eating ability	-3.5 (-5.4, -1.6)	-6.6 (-8.5, -4.6)	-11.6 (-13.8, -9.5)	<0.01
Capability of daily living	-1.3 (-2.9, 0.3)	-2.8 (-4.4, -1.1)	-5.0 (-6.8, -3.2)	<0.01
	-2.1 (-3.4, -0.8)	-3.2 (-4.6, -1.9)	-5.8 (-7.2, -4.4)	<0.01
<i>Psychological domain</i>				
Psychological distress	-3.0 (-4.1, -1.8)	-3.9 (-5.1, -2.7)	-8.6 (-9.9, -7.3)	<0.01
Negative feelings	-2.5 (-4.0, -1.0)	-3.6 (-5.2, -2.1)	-8.6 (-10.2, -6.9)	<0.01
Positive feelings	-2.9 (-4.5, -1.4)	-5.5 (-7.1, -3.9)	-11.9 (-13.6, -10.3)	<0.01
Cognitive functioning	-4.1 (-6.0, -2.2)	-5.0 (-6.9, -3.0)	-11.8 (-13.9, -9.7)	<0.01
Bodily image and appearance	-2.5 (-4.1, -1.0)	-2.7 (-4.3, -1.1)	-5.5 (-7.2, -3.8)	<0.01
	-2.7 (-4.1, -1.4)	-2.7 (-4.1, -1.3)	-5.3 (-6.8, -3.9)	<0.01
<i>Social domain</i>				
Social support	-1.2 (-2.2, -0.2)	-1.1 (-2.1, 0.0)	-3.0 (-4.1, -1.9)	<0.01
Interpersonal relationship	-1.9 (-3.9, 0.0)	-0.9 (-2.9, 1.1)	-2.2 (-4.4, -0.1)	0.07
Work capacity	-0.7 (-2.0, 0.6)	-0.6 (-1.9, 0.7)	-2.2 (-3.6, -0.8)	<0.01
Recreational and leisure activities	-1.6 (-3.0, -0.2)	-1.7 (-3.1, -0.3)	-3.3 (-4.8, -1.8)	<0.01
Family relationship	-0.4 (-1.7, 0.9)	-0.2 (-1.6, 1.1)	-3.0 (-4.5, -1.6)	<0.01
	-1.3 (-2.9, 0.3)	-1.9 (-3.5, -0.3)	-4.2 (-5.9, -2.4)	<0.01
<i>Material domain</i>				
Home environment	-0.3 (-1.7, 1.0)	-0.8 (-2.2, 0.6)	-3.3 (-4.7, -1.8)	<0.01
Participation in community activities	-0.8 (-2.8, 1.3)	-0.1 (-2.3, 1.3)	-2.4 (-4.6, -0.1)	0.10
Neighborhood environment	-1.2 (-3.1, 0.7)	-2.5 (-4.4, -0.5)	-4.1 (-6.2, -2.0)	<0.01
Financial resources	-0.1 (-2.0, 1.9)	-0.3 (-2.3, 1.7)	-3.9 (-6.0, -1.7)	<0.01
	0.8 (-1.3, 2.8)	-0.2 (-2.3, 1.9)	-2.7 (-5.0, -0.5)	0.04
Overall QOL	-1.7 (-2.6, -0.8)	-2.6 (-3.5, -1.7)	-5.8 (-6.8, -4.8)	<0.01
Perceived health and QOL	-1.8 (-3.3, -0.4)	-2.9 (-4.4, -1.4)	-6.0 (-7.7, -4.4)	<0.01
SF-36 (n=2,776)	n=794	n=651	n=727	

QOL categories	Number of menopausal symptoms			P for trend
	1	2	≥3	
	β (95% CI)	β (95% CI)	β (95% CI)	
Physical functioning	-1.4 (-2.8, 0.1)	-2.5 (-4.0, -0.9)	-4.1 (-5.6, -2.5)	<0.01
Physical role functioning	-8.4 (-11.6, -5.3)	-10.6 (-13.9, -7.3)	-17.2 (-20.5, -13.9)	<0.01
Bodily pain	-5.6 (-8.1, -3.2)	-9.5 (-12.1, -7.0)	-14.0 (-16.6, -11.5)	<0.01
Social role functioning	-10.8 (-14.1, -7.4)	-12.6 (-16.2, -9.1)	-19.4 (-22.9, -15.9)	<0.01
General mental health	-12.3 (-14.7, -9.9)	-17.8 (-20.3, 15.3)	-25.7 (-28.2, -23.3)	<0.01
Vitality	-7.6 (-9.7, -5.6)	-11.0 (-13.1, -8.8)	-15.5 (-17.6, -13.3)	<0.01
Emotional role functioning	-15.6 (-20.0, -11.1)	-21.2 (-25.9, -16.5)	-35.5 (-40.1, -30.8)	<0.01
General health perceptions	-4.9 (-6.7, -3.0)	-8.7 (-10.7, -6.8)	-12.0 (-14.0, -10.1)	<0.01
Physical health	-5.6 (-7.1, -4.1)	-8.5 (-10.0, -6.9)	-12.6 (-14.1, -11.0)	<0.01
Mental health	-10.2 (-12.2, -8.3)	-14.3 (-16.3, -12.2)	-21.6 (-23.6, -19.6)	<0.01
Overall QOL	-8.3 (-10.0, -6.7)	-11.7 (-13.5, -10.0)	-17.9 (-19.6, -16.2)	<0.01

[†] Obtained from multivariate linear regression model adjusted for age, education, marital status, WHR (continuous), menopausal status, Charlton co-morbidity score (0>0), ER/PR status, and cancer treatment (immune and tamoxifen)

Note: Reference group in all analyses was the group of women reporting no menopausal symptoms (n=818 in the MOSQOL-74 and n=604 in the SF-36, respectively).