

Palpitations and Co-Occurring Menopausal Symptoms in Women Prior to Breast Cancer Surgery

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OBJECTIVES: To determine the occurrence rate of palpitations in women prior to breast cancer surgery and evaluate for differences in demographic and clinical characteristics and menopausal symptoms in patients with and without palpitations.

SAMPLE & SETTING: Presurgery data on palpitations and menopausal symptoms from 398 patients who underwent breast cancer surgery were analyzed.

METHODS & VARIABLES: The Menopausal Symptoms Scale was used to evaluate the occurrence, severity, and distress of 46 symptoms, including palpitations. Parametric and nonparametric tests were used to evaluate for differences between patients with and without palpitations.

RESULTS: Women with palpitations had lower annual income, lower functional status, higher comorbidity burden, and higher rates of back pain than women without palpitations. Women with palpitations had twice the number of menopausal symptoms and had higher occurrence rates for 39 of the 45 menopausal symptoms. They reported significantly higher severity scores for difficulty concentrating, dizziness, swollen hands/feet, and wake during the night, and higher distress scores for anxiety, hot flashes, swollen hands/feet, and wake during the night.

IMPLICATIONS FOR NURSING: Clinicians should perform routine assessments of palpitations and make appropriate referrals to a cardiologist.

KEYWORDS breast cancer; palpitations; menopausal symptoms; breast-conserving surgery; mastectomy
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Breast cancer is the most common cancer in women (Siegel et al., 2021). Almost all patients with stages I, II, and III breast cancer and about half of patients with stage IV breast cancer will undergo surgery for breast cancer (DeSantis et al., 2019). Although menopausal symptoms are common in these patients and are associated with a lower quality of life (QOL) (Carpenter & Andrykowski, 1999; Carpenter et al., 2002; Gupta et al., 2006), most research has focused on vasomotor symptoms (e.g., hot flashes, night sweats). Emerging evidence suggests that palpitations are another common menopausal symptom (Carpenter & Andrykowski, 1999; Carpenter et al., 2002; Gupta et al., 2006). Palpitations may be experienced as missed, skipped, irregular, or exaggerated heartbeats or the sensation that one's heart is racing or pounding (Cho, 2006; Sievert & Obermeyer, 2012).

Understanding palpitations is important for several reasons. First, palpitations are reported by 42% and 54% of peri- and postmenopausal healthy women, respectively (Carpenter, Sheng, et al., 2021). Second, in healthy peri- and postmenopausal women, the occurrence of palpitations is associated with worse depressive symptoms and worse sleep disturbance, as well as higher levels of perceived stress and poorer QOL (Carpenter, Tisdale, et al., 2021). Third, patients with palpitations have higher rates of healthcare utilization and life-threatening arrhythmias. In the general population, regardless of gender, palpitations account for 16% of primary care visits and are the second leading reason for cardiologist visits (Raviele et al., 2011). Of note, palpitations that affect sleep and work (Thavendiranathan et al., 2009) and occur more frequently (Clementy et al., 2018) are more likely to be associated with serious, life-threatening arrhythmias.

Little is known about the occurrence, severity, and distress related to palpitations in women

with breast cancer. Of the two studies that evaluated palpitations in these women (Choo et al., 2019; Kyvernitis et al., 2014), both included only patients receiving oral endocrine treatment. In one study (Choo et al., 2019), the prevalence of palpitations was 16.6% among those taking tamoxifen and 21.3% among those taking aromatase inhibitors. In the second study (Kyvernitis et al., 2014), palpitation rates were 47.8% after one year and 44% after two years of oral endocrine therapy. In addition, women who reported palpitations trended toward lower adherence with oral endocrine therapy ($p = 0.089$). Because neither study reported the prevalence of palpitations before endocrine treatment, the occurrence rate for this symptom prior to breast cancer surgery is not known.

Neither Choo et al. (2019) nor Kyvernitis et al. (2014) reported associations between palpitations, demographic and clinical characteristics, and other menopausal symptoms. In healthy women, race and ethnicity, higher body mass index (BMI), lower education levels, poorer sleep, presence of vasomotor symptoms, and greater anxiety were associated with higher occurrence and severity of palpitations (Carpenter et al., 2022). To improve the care of patients with breast cancer, a detailed examination of these associations is warranted. Therefore, the purpose of this study was to evaluate women who did and did not report palpitations prior to breast cancer surgery for differences in demographic and clinical characteristics, as well as occurrence, severity, and distress related to 45 menopausal symptoms.

Methods

This study is part of a larger descriptive, longitudinal study evaluating neuropathic pain and lymphedema in women who underwent breast cancer surgery (Kyranou et al., 2013; Van Onselen et al., 2013). The theoretical framework for the entire study was the theory of symptom management (Humphreys et al., 2014). The symptom experience dimension of this theory served as the focal point for this analysis.

From 2004 to 2008, a convenience sample of patients was recruited from breast cancer centers in a comprehensive cancer center, two public hospitals, and four community practices. Criteria for eligibility were as follows: being an adult woman aged 18 years or older who was undergoing unilateral breast cancer surgery; being able to read, write, and understand English; having consented to participate; and having provided written informed consent. Patients were excluded who were scheduled for

bilateral breast surgery or had distant metastases when diagnosed.

Instruments

A demographic questionnaire was used to collect data on age, education, race, ethnicity, marital status, employment status, living situation, financial status, and menopausal status. Patients used the Karnofsky Performance Status Scale to rate their functional status on a scale ranging from 30 ("I feel severely disabled and need to be hospitalized") to 100 ("I feel normal; I have no complaints or symptoms"). Validity and reliability of the Karnofsky Performance Status Scale are well established (Karnofsky et al., 1948).

The Self-Administered Comorbidity Questionnaire (SCQ) was developed to measure comorbidity in clinical and health service research settings. The SCQ assesses 13 common medical conditions that have been described in simple language that can be easily understood without prior medical knowledge. Patients indicate whether they have the condition (yes or no); whether they received treatment for it (a proxy for disease severity); and whether it limits their activities (indication of functional limitations). SCQ scores range from 0 to 39, with higher scores indicating a higher comorbidity burden. Validity and reliability of the SCQ are well established, and the SCQ has been used in studies of patients with various chronic conditions (Sangha et al., 2003).

Palpitations were assessed using a single item from the Menopausal Symptoms Scale (MSS), which was modified from the Seattle Midlife Women's Health Study questionnaire (Woods et al., 1999). The MSS is a self-report measure that assesses the occurrence, severity, and distress related to common menopausal symptoms. Using the MSS, participants indicated whether they had experienced the symptom of "heart races/pounds" in the past week (occurrence). Participants who had experienced the symptom rated its severity and related distress. Symptom severity was rated on a numeric rating scale ranging from 0 (none) to 10 (intolerable). Symptom distress was rated on a numeric rating scale ranging from 0 (not at all distressing) to 10 (very distressing). This single self-report item embedded in a larger symptom questionnaire is comparable to measures used in previous studies of palpitations in women with breast cancer (Choo et al., 2019; Kyvernitis et al., 2014) and in 108 studies of healthy women (Sheng et al., 2021).

The remaining 45 menopausal symptoms were assessed using the MSS, and occurrence, severity, and distress for each of the symptoms were rated. The

TABLE 1. Differences in Demographic and Clinical Characteristics Between the No-Palpitations and Palpitations Groups at Enrollment (N = 398)

	No Palpitations (N = 338)		Palpitations (N = 60)			
Characteristic	\bar{X}	SD	\bar{X}	SD	t	p
Age (years)	55	11.7	54.5	10.7	0.3	0.768
Education (years)	15.7	2.7	15.7	2.6	0.08	0.936
Body mass index (kg/m ²)	26.5	5.8	28.5	7.7	-1.97	0.052
Karnofsky Performance Status Scale score	93.9	10	89.7	11.1	2.91	0.004
Self-Administered Comorbidity Questionnaire	4.1	2.7	5.3	3.2	-2.93	0.004
Number of breast biopsies in past year	1.5	0.8	1.5	0.8	0.39	0.698
Total number of menopause symptoms (excluding palpitations)	10.4	7.8	21.5	7.8	-10.21	< 0.001
Demographic Characteristic	n	%	n	%	Statistic	p
Annual household income (\$)					U	0.001
Less than 30,000	53	19	17	32	-	-
30,000-99,000	111	40	23	43	-	-
Greater than 100,000	112	41	13	25	-	-
Living, marital, and employment status						
Lives alone	76	23	19	32	FE	0.137
Married or partnered	140	42	25	42	FE	1
Works for pay	160	48	29	49	FE	0.888
Race and ethnicity					$\chi^2 = 3.17$	0.366
Asian or Pacific Islander	41	12	9	15	-	-
Black	32	10	8	13	-	-
Hispanic, mixed ethnic background, or other	47	14	4	7	-	-
White	216	64	39	65	-	-
Clinical Characteristic	n	%	n	%	Statistic	p
Comorbid condition						
Anemia	25	7	7	12	FE	0.299
Back pain	86	25	26	43	FE	0.008
Depression	69	20	18	30	FE	0.126
Diabetes	23	7	8	13	FE	0.111
Heart disease	10	3	5	8	FE	0.059
High blood pressure	99	29	24	40	FE	0.129
Kidney disease	3	1	-	-	FE	1
Liver disease	9	3	1	2	FE	1
Lung disease	9	3	3	5	FE	0.402
Osteoarthritis	54	16	15	25	FE	0.097
Rheumatoid arthritis	11	3	3	5	FE	0.452
Ulcer	13	4	2	3	FE	1
Menopausal status						
Has gone through menopause	210	64	38	66	FE	0.882
Receptor status						
Estrogen receptor-positive	257	76	50	83	FE	0.315
HER2/neu receptor-positive	47	15	12	23	FE	0.227

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TABLE 1. Differences in Demographic and Clinical Characteristics Between the No-Palpitations and Palpitations Groups at Enrollment (N = 398) (Continued)

Clinical Characteristic	No Palpitations (N = 338)		Palpitations (N = 60)		Statistic	p
	n	%	n	%		
Receptor status (continued)						
Progesterone receptor-positive	237	70	42	70	FE	1
Stage of disease					U	0.205
0	63	19	10	17	–	–
I	132	39	19	32	–	–
IIA and IIB	117	35	24	40	–	–
IIIA, IIIB, IIIC, and IV	26	8	7	12	–	–
Treatment history						
Received neoadjuvant chemotherapy	63	19	16	27	FE	0.162
On hormone replacement therapy prior to diagnosis of breast cancer	55	16	12	20	FE	0.453

FE—Fisher's exact test; U—Mann-Whitney U test

Note. The n values per characteristic may not add up to the total N because some participants did not answer every question.

Note. Scores for the Karnofsky Performance Status Scale range from 30 ("I feel severely disabled and need to be hospitalized") to 100 ("I feel normal; I have no complaints or symptoms").

Note. Scores for the Self-Administered Comorbidity Questionnaire range from 0 to 39, with higher scores indicating a higher comorbidity burden.

total number of menopausal symptoms (excluding palpitations) was calculated by summing the number of symptoms women reported (range = 0–45). The validity and reliability of the MSS are well established (Woods et al., 2014).

Study Procedures

The study was approved by the Committee on Human Research at the University of California, San Francisco, and by the institutional review boards at each of the study sites. During scheduled pre-operative visits, clinicians explained the study and established patients' willingness to participate. Patients were then introduced to the research nurse, who determined eligibility and obtained written informed consent prior to surgery. After providing consent, patients completed the enrollment questionnaires at home an average of four days before surgery. The research nurse evaluated the questionnaires for completeness at the in-person enrollment visit. Medical records were reviewed for disease and treatment information.

Statistical Analysis

Descriptive statistics were calculated for demographic, clinical, and symptom characteristics using IBM SPSS Statistics, version 28.0. Differences in

demographic, clinical, and symptom characteristics between patients with and without palpitations were evaluated using independent sample t tests, chi-square analyses, Fisher's exact tests, and Mann-Whitney U tests. A p value of less than 0.01 was considered statistically significant.

Results

Of the 398 patients who completed the enrollment questionnaires, 15% (n = 60) had palpitations and 85% (n = 338) did not have palpitations before breast cancer surgery. Among those who reported palpitations, the mean severity score was 3.48 (SD = 2.2) and the mean distress score was 3.8 (SD = 2.66), indicating mild severity and distress. As shown in Table 1, compared to patients without palpitations, patients with palpitations had a lower annual household income, a lower functional status, a higher level of comorbidity, and were more likely to self-report a diagnosis of back pain (all p < 0.01). In addition, patients with palpitations (\bar{X} = 21.5, SD = 7.8) reported twice the number of menopausal symptoms compared with patients without palpitations (\bar{X} = 10.4, SD = 7.8; p < 0.001).

Differences in Menopausal Symptoms

As shown in Table 2, patients with palpitations reported higher occurrence rates for 39 of the 45

menopausal symptoms. For six symptoms (alcohol craving, daytime sweats, hostility, increased sexual desire, skin breakout/acne, and vaginal dryness), no significant between-group differences in occurrence rates were found. In terms of symptom severity and distress, only a limited number of symptoms exhibited between-group differences at the prespecified p value of less than 0.01. Compared with the no-palpitations group, patients with palpitations reported higher severity scores for difficulty concentrating, dizziness, swollen hands/feet, and wake during the night (all $p < 0.004$). Compared with the no-palpitations group, patients with palpitations reported higher distress scores for anxiety, hot flashes, swollen hands/feet, and wake during the night (all $p < 0.009$).

Table 3 lists the 10 menopausal symptoms with the highest occurrence rates and severity and distress scores for the two groups. Occurrence rates for the top 10 symptoms ranged from 36% to 58% and from 70% to 87% in the no-palpitations versus palpitations groups, respectively. In terms of occurrence, 8 of the 10 symptoms were the same for both groups (wake during the night, anxiety, fatigue or tiredness, difficulty concentrating, tension, nervousness, irritability, and difficulty falling asleep). The following symptoms were unique: waking too early and impatience in the no-palpitations group and forgetfulness and depression in the palpitations group.

Severity and distress patterns indicate that the symptoms that were the most common were not necessarily the ones that were the most severe or distressing. The most severe and distressing symptoms were more varied between the two groups. For severity, 6 of the top 10 symptoms were the same for both groups (loss of sexual interest, vaginal dryness, anxiety, difficulty falling asleep, wake during the night, and fatigue or tiredness). The following symptoms were unique to the no-palpitations group: backache or neckache, weight gain, night sweats, and numbness and tingling. The following symptoms were unique to the palpitations group: hot flashes, swollen hands/feet, panic feelings, and waking too early. For both groups, severity scores for the top 10 symptoms were in the moderate range.

For distress, 5 of the top 10 symptoms were the same in both groups (weight gain, difficulty falling asleep, anxiety, panic feelings, and numbness and tingling). The following symptoms were unique to the no-palpitations group: eating more than usual, backache or neckache, anger, loss of sexual interest, and night sweats. The following symptoms were unique to the palpitations group: dizziness, swollen hands/feet,

wake during the night, hostility, and hot flashes. Mean distress ratings for the top 10 symptoms were in the moderate range. Of note, for both groups, anxiety and difficulty falling asleep were among the top 10 symptoms for occurrence, severity, and distress.

Discussion

This study is the first to evaluate the occurrence, severity, and distress related to palpitations in women prior to breast cancer surgery. In addition, associations between the occurrence of palpitations and various demographic and clinical characteristics, as well as common menopausal symptoms, were examined among these patients.

This study's 15% occurrence rate for palpitations is at the lower end of the range reported in other studies, compared with occurrence rates among healthy perimenopausal (20.7%–42%) and postmenopausal (15.7%–54.1%) women (Carpenter, Sheng, et al., 2021) and among women taking oral endocrine therapy for breast cancer (16.6%–48%) (Choo et al., 2019; Kyvernitakis et al., 2014). These inconsistent findings may be related to differences in menopausal status, use of oral endocrine therapy, and the measures used to assess for the occurrence of palpitations (e.g., wording of symptoms, response options, recall periods).

Patients with palpitations reported twice as many symptoms as patients without palpitations and had higher occurrence rates for 39 of the 45 menopausal symptoms evaluated using the MSS. These findings suggest that palpitations co-occur with a large number of menopausal symptoms in women prior to breast cancer surgery. This result is consistent with a previous study of healthy women that found that individuals who reported hot flashes and palpitations had higher levels of depressive symptoms and perceived stress and poorer QOL (Carpenter, Tisdale, et al., 2021).

Demographic Characteristics

The only demographic characteristic associated with having palpitations was lower annual income. This finding is consistent with findings from a previous population-based study of more than 12,000 women that found that the prevalence of palpitations increased in women who had greater difficulty paying for basic necessities (Gold et al., 2000). Gold et al. (2000) found that palpitations occurred in only 13.9% of the women who had no difficulty paying for basic necessities but in 33.7% of the women who reported that it was very hard to pay for basic necessities.

TABLE 2. Differences in Symptom Occurrence, Severity, and Distress Ratings Between the Patients With and Without Palpitations

Symptom	Occurrence					Severity ^b					Distress ^c				
	No P		P		p ^a	No P		P		p	No P		P		p
	n	%	n	%		\bar{X}	SD	\bar{X}	SD		\bar{X}	SD	\bar{X}	SD	
Abdominal bloating	39	12	16	27	0.004	3.7	1.9	4.2	2.2	0.406	3.6	3.1	4.7	3.6	0.278
Alcohol cravings	15	4	8	13	0.013	3.5	2.4	3.8	2.7	0.8	2.5	3.2	4	4.7	0.394
Anger	90	27	35	58	<0.001	3.8	2	3.7	2.1	0.729	4.2	2.9	4.3	2.4	0.764
Anxiety	191	57	51	85	<0.001	4.5	2.2	5.2	2.2	0.058	4.2	2.7	5.7	2.7	0.001
Backache or neckache	101	30	32	53	0.001	4.4	2.4	4.7	2.3	0.479	4.2	2.8	4.8	2.8	0.277
Constipation	59	18	22	37	0.001	3.9	2.4	3.9	2.6	0.997	3.6	3	3.8	3	0.836
Cramps	24	7	13	22	0.001	3.5	2.7	3.5	2.1	0.985	3.8	3.3	3.9	3.5	0.924
Daytime sweats	58	17	19	32	0.013	3.7	2.1	4.7	2.8	0.082	3.6	2.9	4.6	3.3	0.245
Depression (feeling sad/blue)	113	33	42	70	<0.001	3.4	2.1	4.1	2.1	0.067	3.7	2.6	4.7	3	0.046
Diarrhea	37	11	16	27	0.003	2.4	1.5	4.5	2.9	0.015	1.9	2	4	3	0.023
Difficulty concentrating	145	43	46	77	<0.001	3.2	1.9	4.3	2.3	0.001	3.2	2.3	4.2	2.9	0.015
Difficulty falling asleep	120	36	45	75	<0.001	4.4	2.7	5.4	2.3	0.041	4.4	3.1	5.3	2.8	0.093
Dizziness	20	6	10	17	0.007	2.6	1.4	4.8	2.6	0.004	2.7	1.9	5.9	3.1	0.024
Eating more than usual	30	9	19	32	<0.001	4	2.1	3.6	2	0.542	4.3	2.9	3.9	2.5	0.639
Fatigue or tiredness	181	54	52	87	<0.001	4.1	2.2	5	2.5	0.016	3.5	2.6	4.6	3.3	0.042
Forgetfulness	111	33	48	80	<0.001	2.8	1.8	3.8	2.5	0.017	3	2.4	4.1	3	0.022
General body aches	91	27	34	57	<0.001	3.6	1.9	4.6	2.7	0.06	3.5	2.8	5	3.1	0.016
Headache	64	19	33	55	<0.001	3.5	2.5	3.3	2.5	0.837	3.6	3	3.5	2.9	0.85
Hot flashes	96	28	31	52	0.001	4	2.2	5.4	2.9	0.021	3.3	2.7	5	3.3	0.009
Hostility	30	9	12	20	0.02	3.1	2	4.5	2.2	0.065	3.6	2.6	5.4	3.4	0.084
Impatience	128	38	41	68	<0.001	3.4	2	4	2.4	0.116	3.3	2.5	3.9	2.8	0.187
Increased sexual desire	16	5	7	12	0.063	4.1	2.4	3.1	1.9	0.377	2	3.1	2.2	3.9	0.919
Indigestion	27	8	19	32	<0.001	3.4	2.1	4.8	3	0.083	3.3	2.8	4.5	3.1	0.199
Irritability	123	36	43	72	<0.001	3	1.8	3.3	1.9	0.247	3	2.5	3.9	2.7	0.062

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TABLE 2. Differences in Symptom Occurrence, Severity, and Distress Ratings Between the Patients With and Without Palpitations (Continued)

Symptom	Occurrence					Severity ^b					Distress ^c				
	No P		P		p ^a	No P		P		p	No P		P		p
	n	%	n	%		\bar{X}	SD	\bar{X}	SD		\bar{X}	SD	\bar{X}	SD	
Joint pain/stiffness	99	29	37	62	<0.001	3.8	2.1	4.8	2.8	0.052	3.2	2.6	4.8	3.4	0.018
Loss of appetite	43	13	22	37	<0.001	4	2.5	4.7	2.8	0.308	2.7	2.9	3	2.7	0.678
Loss of interest in things	42	12	25	42	<0.001	3.7	2.1	4.2	2	0.305	3.6	2.6	4.4	2.7	0.276
Loss of sexual interest	61	18	24	40	<0.001	5	2.7	5.6	3	0.391	4.2	3.2	4.5	3.7	0.814
Mood swings	77	23	33	55	<0.001	3.5	2.4	4.3	2.4	0.116	3.3	2.4	4.3	2.4	0.046
Nausea/upset stomach	35	10	18	30	<0.001	3.7	2.5	4.2	2.7	0.538	3.7	2.8	4.6	3	0.292
Nervousness	131	39	46	77	<0.001	3.7	2.2	4.3	2.5	0.17	3.4	2.4	4.4	3.1	0.049
Night sweats	79	23	28	47	<0.001	4.2	2.4	4.9	3	0.253	4	2.9	4.7	3.1	0.303
Numbness and tingling	60	18	22	37	0.002	4.2	2.4	4.9	3.3	0.375	4	2.9	5.2	3.4	0.154
Painful/tender breasts	85	25	30	50	<0.001	3.4	2.2	3.4	2.3	0.888	3.1	2.6	3.8	3	0.25
Panic feelings	68	20	33	55	<0.001	3.7	2.5	5.2	2.7	0.012	4.2	2.8	5.5	3	0.036
Shortness of breath	23	7	21	35	<0.001	3.5	2.3	3.9	2.6	0.607	3.5	3	4.3	3.1	0.375
Skin breakout/acne	33	10	10	17	0.117	3.5	2.3	3.6	2.3	0.936	3.1	2.8	4.1	3.6	0.387
Swollen hands/feet	34	10	16	27	0.001	3.1	1.7	5.3	2.4	0.001	3.1	2.3	5.7	2.7	0.002
Tearful/crying spells	100	30	36	60	<0.001	3.6	2.5	4	2.6	0.409	3.4	2.9	4.3	2.9	0.127
Tension	136	40	46	77	<0.001	3.9	2.4	4.8	2.5	0.026	3.5	2.7	4.7	3	0.018
Urinary frequency	53	16	20	33	0.003	3.6	2.1	4.3	2.6	0.3	3	2.5	3.4	3.4	0.578
Vaginal dryness	51	15	16	27	0.038	4.7	2.3	5	2.9	0.687	3.8	2.9	4.4	3.2	0.499
Wake during the night	196	58	52	87	<0.001	4.2	2.4	5.5	2.8	0.001	3.7	3	5.4	3.1	0.001
Waking too early	142	42	38	63	0.003	4	2.4	5.1	2.5	0.013	3.7	2.9	5	2.5	0.017
Weight gain	50	15	23	38	<0.001	4.2	2.6	4.7	2.8	0.534	4.9	3.3	5.5	3.8	0.485

^a Fisher's exact test^b Symptom severity scores ranged from 0 (none) to 10 (intolerable).^c Symptom distress scores ranged from 0 (not at all distressing) to 10 (very distressing).

No P—patients without palpitations; P—patients with palpitations

Note. Symptom severity and distress scores are for patients who reported the occurrence of the symptom.**Note.** P values of less than 0.01 are considered significant.

Although lower income is often associated with poorer health status (Adler & Ostrove, 1999), the relationship between income and palpitations requires additional evaluation because in another study of healthy women (Nisar et al., 2015), no association between income and palpitations was found.

Findings on associations with other demographic characteristics are inconclusive, with some studies reporting no differences (Im et al., 2015; Zhang et al., 2016) and others reporting significant differences in a variety of characteristics (Gold et al., 2000; Monterrosa et al., 2008, 2009; Schnatz et al.,

TABLE 3. Rankings of the Top 10 Symptoms Based on Occurrence, Severity, and Distress in Patients With and Without Palpitations

Rank	No Palpitations (N = 338)			Palpitations (N = 60)		
	Symptom	n	%	Symptom	n	%
Symptom occurrence						
1	Wake during the night	196	58	Wake during the night	52	87
2	Anxiety	191	57	Fatigue or tiredness	52	87
3	Fatigue or tiredness	181	54	Anxiety	51	85
4	Difficulty concentrating	145	43	Forgetfulness	48	80
5	Waking too early	142	42	Difficulty concentrating	46	77
6	Tension	136	40	Tension	46	77
7	Nervousness	131	39	Nervousness	46	77
8	Impatience	128	38	Difficulty falling asleep	45	75
9	Irritability	123	36	Irritability	43	72
10	Difficulty falling asleep	120	36	Depression (sad/blue)	42	70
Rank	Symptom	\bar{X}	SD	Symptom	\bar{X}	SD
Symptom severity ^a						
1	Loss of sexual interest	5	2.7	Loss of sexual interest	5.6	3
2	Vaginal dryness	4.7	2.3	Wake during the night	5.5	2.8
3	Anxiety	4.5	2.2	Difficulty falling asleep	5.4	2.3
4	Backache or neckache	4.4	2.4	Hot flashes	5.4	2.9
5	Difficulty falling asleep	4.4	2.7	Swollen hands/feet	5.3	2.4
6	Weight gain	4.2	2.6	Panic feelings	5.2	2.7
7	Wake during the night	4.2	2.4	Anxiety	5.2	2.2
8	Night sweats	4.2	2.4	Waking too early	5.1	2.5
9	Numbness and tingling	4.2	2.4	Vaginal dryness	5	2.9
10	Fatigue or tiredness	4.1	2.2	Fatigue and tiredness	5	2.5
Symptom distress ^b						
1	Weight gain	4.9	3.3	Dizziness	5.9	3.1
2	Difficulty falling asleep	4.4	3.1	Anxiety	5.7	2.7
3	Eating more than usual	4.3	2.9	Swollen hands/feet	5.7	2.7
4	Anxiety	4.2	2.7	Panic feelings	5.5	3
5	Backache or neckache	4.2	2.8	Weight gain	5.5	3.8
6	Panic feelings	4.2	2.8	Wake during the night	5.4	3.1
7	Anger	4.2	2.9	Hostility	5.4	3.4
8	Loss of sexual interest	4.2	3.2	Difficulty falling asleep	5.3	2.8
9	Night sweats	4	2.9	Numbness and tingling	5.2	3.4
10	Numbness and tingling	4	2.9	Hot flashes	5	3.3

^aSymptom severity scores ranged from 0 (none) to 10 (intolerable).

^bSymptom distress scores ranged from 0 (not at all distressing) to 10 (very distressing).

2006). For example, in the Study of Women's Health Across the Nation, which included healthy women (Gold et al., 2000), lower levels of education and not being employed full-time were associated with higher rates of palpitations. In addition, compared with non-Hispanic White women, although Japanese and Chinese women reported a lower frequency of palpitations (Gold et al., 2000), Hispanic women reported a higher frequency of palpitations (Gold et al., 2000; Schnatz et al., 2006). In contrast, Im et al. (2015) found no ethnic or racial differences in the occurrence of palpitations. Given this study's finding regarding lower income, as well as the disparate findings related to education, employment status, and race and ethnicity, future research should recruit more diverse samples and examine the influence of a wide variety of social determinants of health on the occurrence and impact of palpitations in women prior to breast cancer surgery (McCall et al., 2020).

Clinical Characteristics

In this study, patients with palpitations reported a poorer functional status and higher comorbidity burden and were more likely to report back pain. One explanation for these associations is that all three of these characteristics interfere with physical activity. This hypothesis is supported by findings from a study of healthy women that found that higher levels of physical activity were associated with lower rates of palpitations (Gold et al., 2000). In addition, in another study of healthy women, Conde et al. (2006) found that individuals with palpitations reported lower physical component summary scores on the SF-12®. Finally, based on data from the 2005 U.S. National Health and Wellness Survey, Whiteley et al. (2013) reported that the occurrence of palpitations in healthy women was associated with greater activity impairment and lower physical component summary scores.

Associations are inconsistent for other clinical characteristics (e.g., menopausal status, BMI) in healthy women. For example, in the authors' recent review (Carpenter et al., 2022), although no associations were found in 15 studies, 14 studies reported that occurrence rates for palpitations increased with advancing menopausal stage. Similarly, in two studies, a higher BMI was associated with an increased rate of palpitations (Ishizuka et al., 2008; Liu et al., 2015), but in four other studies, no associations were found (Gold et al., 2000; Kirchengast, 1993; Saccomani et al., 2017; Tan et al., 2014).

Because previous research identified higher occurrence rates for a variety of menopausal symptoms in

KNOWLEDGE TRANSLATION

- Palpitations should be assessed and treated before breast cancer surgery.
 - Prior to surgery, women with palpitations experienced a higher occurrence of menopausal symptoms as well as higher severity and distress for several menopausal symptoms.
 - The associations between palpitations and the occurrence, severity, and distress of menopausal symptoms can be used to design appropriate interventions to improve multiple menopausal symptoms for women prior to surgery.
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patients with breast cancer following chemotherapy (Reeves et al., 2018) and hormone therapy (Choo et al., 2019; Kyvernitis et al., 2014; Reeves et al., 2018), it is surprising that no associations were found between palpitations and breast cancer stage, receipt of neoadjuvant chemotherapy, or use of hormone therapy prior to the cancer diagnosis. This lack of associations may be a result of the relatively small number of patients in the group with palpitations and the fact that patients were assessed prior to surgery. Additional research is warranted to confirm this study's findings.

Menopausal Symptoms

In the authors' previous study with the same sample (Mazor, Cataldo, Lee, Dhruva, Paul, et al., 2018), differences in occurrence, severity, and distress related to menopausal symptoms were compared between pre- and postmenopausal patients prior to surgery. Consistent with this study as well as other studies (Gaudernack et al., 2021; Pozzar et al., 2021), the symptoms with the highest occurrence rates were not always the most severe or the most distressing. The remainder of this article will discuss differences in the common and distinct symptoms between the patients with and without palpitations in the context of the extant literature on healthy women and patients with breast cancer prior to surgery.

Symptom occurrence: Although the occurrence rates for the majority of the menopausal symptoms were almost double in the patients with palpitations, 8 of the 10 symptoms with the highest rates were common to both groups. Because this assessment was done prior to surgery, the high occurrence rates for anxiety, tension, nervousness, and irritability are not unexpected. This hypothesis is supported by the fact that the severity and distress scores for anxiety were in the top 10 symptoms for both groups.

Of note, in the Study of Women's Health Across the Nation (El Khoudary et al., 2019; Gold et al., 2006), anxiety in healthy women was evaluated based on a composite of four symptoms (irritability, nervousness or tension, feeling fearful for no reason at all, and heart pounding or racing) that are similar to the common symptoms reported by patients in the current study. No studies have evaluated for associations between anxiety and palpitations in women with breast cancer. However, in a study of healthy middle-aged Japanese women (Enomoto et al., 2021), higher levels of anxiety were associated with an increase in the occurrence of more severe palpitations. In another study of healthy peri- and postmenopausal women, individuals who reported distress from palpitations had higher levels of anxiety (Carpenter, Tisdale, et al., 2021).

The other four common symptoms with the highest occurrence rates were the following: difficulty falling asleep, wake during the night, fatigue or tiredness, and difficulty concentrating. Like anxiety, difficulty falling asleep was in the top 10 symptoms across all three dimensions of the symptom experience, and fatigue or tiredness was among the top 10 symptoms for occurrence and severity. Because the assessment was done an average of four days prior to surgery, it is understandable that both groups of patients would have problems with both sleep initiation and maintenance. In addition, the co-occurrence of fatigue and difficulty concentrating is common in patients with cancer, and these symptoms often occur in a cluster (Kim et al., 2008; Mazor, Cataldo, Lee, Dhruva, Cooper, et al., 2018).

In terms of differences between the palpitations groups, women without the symptom reported the occurrence of waking too early and impatience in the top 10 symptoms. In the authors' previous study with this sample (Mazor, Cataldo, Lee, Dhruva, Cooper, et al., 2018), these two symptoms were included in a psychological-cognitive-sleep symptom cluster and an irritability symptom cluster, respectively. In contrast, among patients with palpitations, 80% reported the occurrence of forgetfulness and 70% reported depression. In the general population, higher rates and severity of anxiety and depression are associated with the occurrence of palpitations (Alijaniha et al., 2016; Gale & Camm, 2016). Therefore, an assessment of the 10 symptoms with the highest rates of occurrence in relation to palpitations is warranted in women prior to breast cancer surgery.

Symptom severity: In terms of severity, although only 6 of the 10 symptoms were common between the

two groups, except for wake during the night, no differences were found in their severity ratings. For both groups, vaginal dryness and loss of sexual interest had the highest severity ratings, and all 10 symptoms were in the moderate to severe range. Although the occurrence rates for these two symptoms were similar to those reported in previous studies of healthy women (Arthur et al., 2022; Marino, 2021), these symptoms warrant preoperative screening and management because body image and hormonal changes often occur following breast cancer treatment.

Symptom distress: Only five symptoms had the highest distress ratings in both groups of patients. Similar to severity, except for anxiety, no between-group differences were found in these distress scores, and all the scores were in the moderate range. Three common distressing symptoms were weight gain, panic feelings, and numbness and tingling. Because more than 60% of the sample had gone through menopause, weight gain may be attributable to this life transition. The distress associated with panic feelings may be related to the high levels of anxiety among participants. Distress from numbness and tingling may be related to having a diagnosis of diabetes or receiving neoadjuvant chemotherapy. Further research is warranted to determine the etiologies of these symptoms and whether targeted interventions can decrease symptom-associated distress.

Symptoms Unique to the Palpitations Group

An examination of the symptoms that were unique to the palpitations group across the dimensions of the symptom experience may provide some insights. Across the three dimensions of the symptom experience, the following symptoms were unique to the palpitations group: forgetfulness (occurrence), depression (occurrence), hot flashes (severity, distress), swollen hands/feet (severity, distress), panic feelings (severity), waking too early (severity), dizziness (distress), wake during the night (distress), and hostility (distress). Because these symptoms are part of the MSS, the related literature may provide some insights into the relationships between and among these symptoms. Taken together, this study's findings suggest potential links between the occurrence of palpitations and a variety of menopausal symptoms. No studies have evaluated these potential associations in women prior to breast cancer surgery, but these associations have been reported in healthy women.

For example, in a study of 1,900 healthy perimenopausal Chinese women, palpitations, difficulty concentrating, nervous tension, trouble sleeping,

and feeling blue, were grouped in a psychological symptom cluster (Ho et al., 1999). In another study of symptom clusters in healthy midlife women from the United States, Spain, Lebanon, and Morocco that included an evaluation of palpitations, the clustering of the symptoms varied by country (Sievert et al., 2007). In the U.S. sample, palpitations did not load on any of the three clusters. In the Spanish sample, the symptom of palpitations loaded on an emotional cluster that included anxiety, depression, nervousness/impatience, and headaches. In the Lebanese sample, the symptom of palpitations was included in the cardiac and general symptoms cluster (chest pain/pressure, dizziness, joint pains, gastrointestinal symptoms). In the Moroccan sample, palpitations were included in the first factor, which contained 11 symptoms (chest pressure/pain, shortness of breath, sleep disturbance, numbness, joint pains, anxiety, depression, nervousness/impatience, difficulty concentrating, and memory loss). The authors attributed the differences in menopausal symptoms associations and clusters to cross-cultural variations. Additional research is warranted on the identification of menopausal symptom clusters in women with breast cancer who do and do not report the occurrence of palpitations. The identification of inter-relationships between and among these symptoms using analytic techniques such as network analysis may provide useful information on the underlying mechanisms for palpitations and associated symptoms (Papachristou et al., 2019).

A relationship between palpitations and hot flashes has not been described in women with breast cancer. Although in one study no association was found (Carpenter, Tisdale, et al., 2021), in a study of healthy middle-aged Japanese women, a higher vasomotor symptom severity score (hot flashes and night sweats) was associated with an increased risk of reporting palpitations (Enomoto et al., 2021). Additional research is warranted to confirm this association. In a systematic review of the effects of treatments for menopausal symptoms on palpitations (Sheng et al., 2022), reductions in the occurrence and severity of palpitations were reported with some pharmacologic and nonpharmacologic treatments for hot flashes.

In this study's sample, the associations between palpitations, swollen hands/feet, and dizziness may indicate underlying cardiovascular problems. Heart disease was self-reported by only 8% of the patients in the palpitations group, but high blood pressure was reported by 40%. Of note, in a study of 127 patients (of whom 74% were women) who reported palpitations or

dizziness, 65% had electrocardiographically verified arrhythmias and 29% had clinically relevant arrhythmias (Hoefman et al., 2007). Given the recent trend in the co-occurrence of cancer and cardiovascular disease (Essa & Lip, 2021), the authors' findings suggest that patients with breast cancer who have palpitations and other associated symptoms warrant an evaluation for cardiovascular disease.

Limitations

Several limitations warrant consideration. Although used in previous studies of women with breast cancer (Choo et al., 2019; Kyvernitis et al., 2014) and in 108 studies of healthy women (Sheng et al., 2021), only a single item was used to assess palpitations. Future studies should use a more detailed characterization of this symptom. Although patients with breast cancer undergo adjuvant treatments, because of the study's cross-sectional design, temporal and causal relationships cannot be determined and warrant careful evaluation. Because the majority of the participants were White and well educated, this study's findings may not generalize to more diverse samples. Although menopausal status was self-reported using a single question, it may be less of a concern. In previous studies, more than 75% of patients were postmenopausal at the time of their cancer diagnosis (Carpenter et al., 2002; Carpenter, Tisdale, et al., 2021). However, future studies should evaluate for differences in palpitations in women with breast cancer in relationship to the Stages of Reproductive Aging Workshop criteria (Harlow et al., 2012) and cause of menopause (natural, surgically induced, chemically induced).

Implications for Practice and Research and Conclusion

This study's findings suggest that a significant number of women experience palpitations that co-occur with a large number of menopausal symptoms prior to breast cancer surgery. Although causes of palpitations are most often benign and related to anxiety (Gale & Camm, 2016), palpitations can sometimes be related to a heart rhythm abnormality. Because of associations between palpitations and dizziness and swollen hands/feet as well as the increased co-occurrence of cardiovascular disease in patients with cancer (Essa & Lip, 2021), additional research is warranted to confirm the authors' findings and determine the effect of palpitations on patients' ability to function and QOL. Of equal importance, research is needed on the underlying mechanisms for palpitations with and without co-occurring

menopausal symptoms. In addition to other menopausal symptoms, clinicians need to assess for the occurrence of palpitations; determine their potential etiologies and clinical importance; and initiate appropriate referrals to cardiology and supportive care services. Consultation with cardiologists may identify treatable causes of palpitations. Referral to psychological support services may assist patients in reducing anxiety and stress associated with the diagnosis of breast cancer and its subsequent treatments. Because of the high occurrence rates for the top eight symptoms common to both groups, in the perioperative period, patients with breast cancer may benefit from interventions to decrease anxiety-related symptoms and sleep disturbance.

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