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A Menopause Strategies–Finding Lasting Answers for Symptoms and Health (MsFLASH) Investigation of Self-Reported Menopausal Palpitation Distress

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Abstract

Background: Study to describe the degree of menopausal palpitation distress and its demographic, clinical, symptom, and quality-of-life (QOL) correlates. Analysis of existing, baseline, data from peri- and postmenopausal women, 42 to 62 years of age, who participated in the Menopause Strategies–Finding Lasting Answers for Symptoms and Health (MsFLASH) clinical trials testing interventions for vasomotor symptoms ($n = 759$). Up to 46.8% of menopausal women report having palpitations, yet the symptom is relatively understudied. Little is known about palpitation distress or its correlates.

Materials and Methods: Degree of distress from ''heart racing or pounding'' was self-reported over the past two weeks as ''not at all,'' ''a little bit,'' ''moderately,'' ''quite a bit,'' or ''extremely.'' Other measures included self-report forms, clinic-verified body mass index (BMI), vasomotor symptom diaries, and validated symptom and QOL tools.

Results: The percentage who reported palpitation distress was 19.6%, 25.2%, and 33.5% in the three trials or 25.0% overall. In multivariate analysis, the odds of reporting palpitation distress was lower in past smokers (odds ratio [OR] = 0.59 [95% confidence interval (CI) 0.38–0.90]) and current smokers (OR = 0.48 [0.27–0.87]) relative to never-smokers and lower with every 5 kg/m^2 higher BMI (OR = 0.82 [0.69–0.98]).The odds of reporting palpitation distress was higher with every five point more severe insomnia (OR = 1.28 [1.05–1.54]), five point worse depressive symptoms (OR = 1.47 [1.11–1.95]), five point worse perceived stress (OR = 1.19 [1.01–1.39]), and one point worse menopausal QOL (OR = 1.29 [1.06–1.57]).

Conclusions: Menopausal palpitation distress is common and associated with demographic, clinical, symptom, and QOL factors. Findings can be used for screening in clinical practice and to justify additional research on this understudied symptom.

Keywords: menopausal symptom, postmenopause, perimenopause, palpitations

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Introduction

COMPARED WITH THE abundance and breadth of research on menopausal vasomotor symptoms and sleep, there is a relative scarcity of research on menopausal palpitations. Menopausal palpitations are described as loud, racing, or skipped heart beats, flip-flops, fluttering, or pounding that occurs with or without dizziness and/or lightheadness.[1,2] Based on symptom checklists, four studies provide palpitation prevalence rates based on self-reported presence of the symptom (yes, no) in the past two to four weeks[1,3–5] Prevalence rates by sample were: 18.6% of 12,425 American women,[5] 28.7% of 300 Spanish women,[1] 28.8% of 293 American women,[1] 34.1% of 299 Moroccan women,[1] 38.0% of 81 Brazilian women,[3] 46.8% of 243 Brazilian women,[4] and 46.9% of 301 Lebanese women.[1] Given that every woman around the world who reaches mid-life will experience menopause, these prevalence rates indicate that millions of women could be experiencing menopausal palpitations.

Little is known about distress associated with menopausal palpitations. Although symptom distress is a commonly assessed concept, only one study has assessed the degree of discomfort associated with palpitations (no, slight, moderate, severe).[6] The study, done in Austria, included 88 naturally postmenopausal women and 142 surgically postmenopausal women. Palpitation distress was significantly higher in the latter group (55.7% no, 6.6% slight, 19.7% moderate, 18.0% severe) compared with the former group (57.0% no, 16.2% slight, 19.7% moderate, 7.1% severe).[6] Additional studies of palpitation distress in American women could lead to a broader understanding of the symptom.

Little is known about demographic, clinical, or quality-of-life (QOL) correlates of palpitations or palpitation distress. Some evidence suggests that demographic and clinical variables, sleep, and QOL are related to palpitations.[3,5–7] Higher prevalence of palpitations was significantly associated with lower income, difficulty paying for basics, being Hispanic, higher parity, past or current smoking, being perimenopausal, and lower physical activity.[5] Higher prevalence of palpitations and greater palpitation discomfort was associated with being surgically versus naturally menopausal.[5,6] Higher odds of reporting palpitations was seen with sleep disturbances. Swedish women with poor sleep were 2.5 times more likely and those with nightmares at least once per week were 2.0 times more likely to report palpitations.[7] Higher prevalence of palpitations was also associated with significantly lower physical ($p < 0.01$) but not mental QOL among Brazilian women.[3] However, no studies were identified that comprehensively evaluated demographic, clinical, symptom, and QOL correlates of palpitations or palpitation distress in menopausal women.

A greater understanding of the extent of palpitation distress is important for determining their clinical relevance. The purpose of this study was to investigate menopausal palpitation distress in peri- and postmenopausal women who provided data in the Menopause Strategies–Finding Lasting Answers for Symptoms and Health (MsFLASH) national research network studies. Specific aims were to describe the degree of palpitation distress and the demographic, clinical, symptom, and QOL correlates in peri- and postmenopausal women.

Materials and Methods

Design and participants

This cross-sectional analysis was performed on existing baseline, prerandomization data from 759 peri- and postmenopausal women who participated in three randomized controlled trials of vasomotor symptom interventions conducted by the MsFLASH network. Details of the design, methods, inclusion and exclusion criteria, and main study findings for the trials are published elsewhere.[8–12] All data were collected between 2008 and 2012 from American clinical sites located in Boston, Indianapolis, Oakland, Philadelphia, and Seattle.

Details of common and trial-specific inclusion and exclusion criteria are detailed in online supplements of another publication.[13] Women were 40 to 62 years of age; peri- or postmenopausal; in good general health per self-report, vital signs, and blood tests; not using vasomotor symptom treatments; had no history of drug or alcohol abuse in the past year; and no major depressive episode in the past three months. Weekly vasomotor symptoms had to be frequent (≥28 per week in trial 01, ≥14 in trials 2 and 3) and bothersome or severe on ≥ four or more days or nights per week.

Measures

Palpitation distress was self-reported. One baseline questionnaire item asked women to report distress associated with ''heart racing or pounding'' in the past two weeks. Responses of ''not at all'' were coded as no palpitation distress. Responses of ''a little bit,'' ''moderately,'' ''quite a bit,'' and ''extremely'' were coded as ''yes'' palpitation distress.

Demographic and clinical data were self-reported and/or assessed by study staff during baseline visits. In addition to trial number and clinical site, we collected data regarding age, race, ethnicity, education, marital status, smoking and alcohol use, menopausal status, and self-reported health status. Height and weight were collected in clinic by study staff for body mass index (BMI) calculations.

Symptom and QOL data came from well-validated tools, where higher scores indicated worse symptoms or QOL. Women reported vasomotor symptom frequency, severity (0 mild to 2 severe), and bother (0 not at all to 3 a lot) twice daily in paper-based diaries. Insomnia severity over the past two weeks was reported on the 7-item Insomnia Severity Index (ISI) with item response options of 0 to 4. Scores are used to estimate the severity of insomnia as none (0–7), subthreshold (8–14), moderate (15–21), and severe (22–28).[14] Women reported depressive symptoms over the past two weeks on the 8-item Patient Health Questionnaire-8 (PHQ-8) with response options of not at all to nearly every day. Scores to estimate the severity of depressive symptoms are mild (≤5), moderate (>5 but ≤10), moderately severe (>10 but ≤15), and severe (>15 but ≤20).[15,16] Study participants reported anxiety over the past two weeks on the 7-item generalized anxiety disorder questionnaire (GAD-7) with response options of not at all to nearly every day. Scores to estimate the severity of anxiety are mild (≤5), moderate (>5 but ≤10), and severe (>10 but ≤15).[17,18] Women reported stress during the past month on the 10-item Perceived Stress Scale (PSS) using response options of never to very often.[19] Menopausal QOL was reported using the 29-item

menopause-specific quality of life (MENQOL). For each item, women indicate no or yes if they have had each problem, and if yes, rate bother from 0 not at all to 6 extremely bothered. Total MENQOL scores reflect four domains—vasomotor, psychosocial, physical, and sexual.[20]

Data analysis

This analysis included all randomized participants who provided baseline data on palpitation distress and selected demographic, clinical, symptom, and QOL correlates (smoking, BMI, ISI, PHQ-8, PSS, MENQOL total score). Because of missing data, the final sample size was 759 of the 899 women (84% in the original samples across the three trials. Women excluded for missing data did not differ from those in the analysis sample by age or trial. Of the 140 participants excluded for missing data, 105 (75%) were due to missing MENQOL. Participants missing MENQOL had higher levels of anxiety, stress, and insomnia compared with participants included in the analysis sample.

Distributions for continuous variables were verified as not requiring any transformation to address skewness. Frequencies and percentages were used to describe the presence and degree of palpitation distress across each trial and for the combined trials. Participants' demographic, clinical, symptom, and QOL characteristics were compared according to presence (yes, no) of palpitation distress with statistical differences assessed using chi-squared tests and *t*-tests. Factors that were statistically significant at $p < 0.20$ were included in a multivariate logistic regression model of palpitation distress (yes, no). In the case of highly correlated factors, for example vasomotor severity and bother or depression and anxiety, the more highly significant variable was included in multivariate modeling. The multivariate model was also adjusted for trial number and clinical site. A receiver operating characteristic curve was constructed and we report the concordance (c) statistic for the logistic regression model as a measure of how well the set of predictors discriminate between participants with and without palpitation distress. A *c*-statistic value of 0.5 indicates no discrimination ability, whereas a value of 1 indicates perfect discrimination.

Results

The presence and degree of palpitation distress in each trial and for the total sample of 759 women is shown in Table 1. The presence of any palpitation distress ranged from 19.6% to 33.5% in the three trials and averaged 25% across the combined trials. Distress from palpitations was rated ''a little bit'' by 15.7% to 25.0% in the three trials (18.6% overall), ''moderately'' by 3.6% to 6.8% (5.0% overall), and ''quite a bit'' or ''extremely'' by 0.4% to 2.3% (1.5% overall).

Tables 2 and 3 show associations among palpitation distress and demographic, clinical, symptom, and QOL correlates. Women who reported palpitation distress were more likely to have enrolled on MsFLASH trial 1 (more stringent vasomotor symptom inclusion criteria) than the other two trials ($p = 0.004$), be never smokers versus current or past smokers ($p = 0.03$), have lower BMI ($p = 0.17$), and be postmenopausal ($p = 0.19$) (Table 2). Women who reported palpitation distress reported worse vasomotor symptom bother ($p = 0.01$), insomnia ($p < 0.0001$), depressive symptoms ($p < 0.001$), anxiety ($p < 0.001$), stress ($p < 0.001$), and menopausal QOL ($p < 0.001$) (Table 3).

In the adjusted model (Table 4), the odds of reporting palpitation distress were lower in past and current smokers compared with never smokers and in women with higher BMI. Significant associations with palpitation distress were observed in women with worse insomnia, depression, perceived stress, and menopausal QOL. Five-point increases were used to interpret the model as this amount of change leads to a category change on the PHQ-8 and PSS (*e.g.*, from mild to moderate). The adjusted model had a concordance statistic of 0.75, indicating a reasonable prediction model, although not meeting the threshold for excellent ($c \geq 0.8$).

Discussion

Palpitations are an understudied symptom reported by midlife women. This is the first report to comprehensively examine palpitation distress and demographic, clinical, symptom, and QOL correlates. Percentages of women reporting palpitation distress (25% overall, 19.6%–33.5% in individual trials) were comparable to some prior studies of women reporting palpitations (18.6%–46.9%),[1,3–5] and slightly lower than a study of women reporting palpitation discomfort (43.4%).[6] In this study, palpitation distress was present if women reported any distress related to heart racing or pounding over the past two weeks. In other published studies, palpitations were marked as present if women reported palpitations in the past 2[4,5] or 4 weeks[1,3] or reported slight, moderate, or severe discomfort from palpitations.[6] Variations in reported palpitations could be due to variations in measures across studies, particularly if not all women with palpitations feel discomfort or distress related to them.

Table 1. Presence and Degree of Menopausal Palpitation Distress in the Past Two Weeks

		MsFLASH 1 (n = *176*)		*MsFLASH 2* (n = *302*)		*MsFLASH 3* (n = *281*)		*Combined trials* (n = *759*)	
Presence	*Degree*	n	%	N	%	N	%	N	%
No	Not at all	117	66.5	226	74.8	226	80.4	569	75.0
Yes	≥A little bit	59	33.5	76	25.2	55	19.6	190	25.0
Yes	A little bit	44	25.0	53	17.6	44	15.7	141	18.6
Yes	Moderately	12	6.8	16	5.3	10	3.6	38	5.0
Yes	Quite a bit	1	0.6	7	2.3	1	0.4	9	1.2
Yes	Extremely	2	1.1	0	0.0	0	0.0	2	0.3

MsFLASH, Menopause Strategies–Finding Lasting Answers for Symptoms and Health.

Table 2. Demographic and Clinical Characteristics According to Palpitation Distress ($N=759$)

	Palpitation distress				
	Yes (n=*190*)		*No* (n=*569*)		
Characteristic	n	%	N	%	p
MsFLASH trial					0.004
1	59	31.1	117	20.6	
2	76	40.0	226	39.7	
3	55	28.9	226	39.7	
Clinical site					0.56
Philadelphia	37	19.5	117	20.6	
Boston	31	16.3	94	16.5	
Indianapolis	35	18.4	79	13.9	
Oakland	38	20.0	108	19.0	
Seattle	49	25.8	171	30.1	
Age at screening, mean (SD)	54.3	(3.8)	54.5	(3.8)	0.61
Race/ethnicity					0.47
White	116	61.1	356	62.6	
African American	57	30.0	177	31.1	
Other/unknown	17	8.9	36	6.3	
Education					0.27
≤High school/GED	15	7.9	69	12.1	
School after high school	67	35.3	193	33.9	
College graduate	108	56.8	307	54.0	
Marital status					0.51
Never married	24	12.6	71	12.5	
Divorced/separated	30	15.8	112	19.7	
Widowed	7	3.7	13	2.3	
Married/partnered	129	67.9	373	65.6	
Smoking					0.03
Never	124	65.3	310	54.5	
Past	43	22.6	175	30.8	
Current	23	12.1	84	14.8	
Alcohol use (drinks/week)					0.96
0	67	35.3	208	36.6	
>0 to <7	88	46.3	251	44.1	
≥7	33	17.4	104	18.3	
BMI (kg/m^2), mean (SD)	27.2	(4.9)	27.9	(6.1)	0.17
<25	69	36.3	193	33.9	
25 to <30	72	37.9	199	35.0	
≥30	49	25.8	177	31.1	
Menopausal status					0.19
Postmenopausal	143	75.3	423	74.3	
Perimenopausal	37	19.5	94	16.5	
Indeterminate	10	5.3	52	9.1	
Health rating					0.97
Excellent	36	18.9	103	18.1	
Very good	78	41.1	237	41.7	
≤Good	76	40.0	229	40.2	

BMI, body mass index; GED, general education degree; SD, standard deviation.

Table 3. Symptom and Quality-of-Life Characteristics According to Palpitation Distress ($N=759$)

	Palpitation distress		
	Yes *Mean (SD)*	*No* *Mean (SD)*	p
Symptoms			
Vasomotor frequency	8.5 (5.2)	8.1 (4.7)	0.31
Vasomotor severity (1–3)	2.1 (0.4)	2.0 (0.4)	0.06
Vasomotor bother (1–4)	3.1 (0.5)	3.0 (0.5)	0.01
ISI Insomnia	13.6 (5.6)	10.4 (5.5)	<0.001
PHQ-8 depression	5.0 (3.9)	3.1 (3.2)	<0.001
GAD-7 anxiety	3.8 (3.8)	2.2 (3.2)	<0.001
PSS stress	15.9 (6.7)	11.9 (6.9)	<0.001
QOL			
MENQOL total	4.3 (1.2)	3.5 (1.1)	<0.001

Higher values are worse scores on all variables.
GAD, generalized anxiety disorders; ISI, Insomnia Severity Index; MENQOL, menopause-specific quality of life; PHQ, Patient Health Questionnaire; PSS, Perceived Stress Scale.

Although the prevalence of palpitation distress was similar to the prevalence of palpitations or palpitation discomfort in other studies, the degree of palpitation distress was generally mild and lower than a study by Hartman et al.,[6] where the rates of severe discomfort (7.1% and 18.0%) were much higher than in our study (1.5%). Differences could be attributed to sample characteristics and measurements. We included a community sample of women with vasomotor

Table 4. Multivariate Associations of Demographic, Clinical, Symptom and Quality-of-Life Characteristics and Menopausal Palpitation Distress ($N=759$)

Variable	*Odds ratio [95% CI]*	P
Smoking (''Never'' as reference)		0.008
Past	0.59 [0.38–0.90]	
Current	0.48 [0.27–0.87]	
BMI, per 5 kg/m^2	0.82 [0.69–0.98]	0.03
Menopausal status (''Postmenopause'' as reference)		0.27
Perimenopausal	1.03 [0.65–1.65]	
Indeterminate	0.54 [0.25–1.16]	
Vasomotor symptom bother (per one-point)	1.28 [0.86–1.90]	0.23
ISI Insomnia (per five-point)	1.28 [1.05–1.54]	0.01
PHQ-8 depression (per five-point)	1.47 [1.11–1.95]	0.008
PSS stress (per five-point)	1.19 [1.01–1.39]	0.03
MENQOL total (per one-point)	1.29 [1.06–1.57]	0.01

c-statistic = 0.75, model adjusted for MsFLASH trial (1, 2, 3) and clinical center (Philadelphia, Boston, Indianapolis, Oakland, Seattle). Vasomotor severity not included due to high correlation with vasomotor bother. GAD-7 not included due to high correlation with PHQ-8 depression scale.
CI, confidence interval.

symptoms and assessed their distress. Hartman et al.,[6] included a clinical sample, the majority of whom were surgically postmenopausal, with and without vasomotor symptoms and assessed their discomfort. In our study, women may have had palpitations but not have been distressed by them. In addition, MsFLASH trials 1 and 3 excluded women taking SSRIs and SNRIs and this could have contributed to lower palpitation distress as there are observed association among depression, vasomotor symptoms, stress, and insomnia.[21,22] Future research could include assessments of multiple dimensions of palpitations, including occurrence, frequency, severity, distress, and temporal pattern to better understand this understudied symptom.

Findings add to knowledge regarding demographic, clinical, symptom, and QOL correlates of palpitation distress. Similar to other studies of prevalence of palpitations,[3,7] we found that the presence of palpitation distress was associated with worse insomnia (poor sleep[7]) and physical symptoms (poorer physical QOL[3]). Although we did not specifically investigate surgically induced menopause as was done in two studies,[5,6] we did not find that menopausal status (peri, post) was associated with palpitation distress. Additionally, this is the first study to indicate that the presence of palpitation distress varied significantly according to insomnia, depression, stress, and overall menopausal QOL. One other study found no association between mental component QOL and palpitations.[3] Although being in trial 1 (with more stringent vasomotor symptom inclusion criteria) and vasomotor symptom distress were associated with palpitation distress, these associations were no longer significant in the adjusted model. Future research could explore associations or clustering among palpitations and other menopausal symptoms and determine if palpitations predict, co-occur, or result from other symptoms, insomnia, depression, stress, and overall menopausal QOL.

The somewhat counterintuitive findings regarding smoking and BMI could be explained by a number of factors. Smoking and high BMI are known risk factors of cardiovascular comorbidities, and thus, might have been expected to be associated with palpitation distress. However, it is important to remember that our outcome was self-reported distress and not electrocardiogram-verified arrhythmias or frequency of palpitations. In prior research, past smoking, but not BMI, was associated with reporting palpitations in the past two weeks.[5] Palpitation distress was not assessed in that study. In addition, it is possible that nonsmokers and thinner women are more attentive or attuned to their bodies and health, and thus, more distressed by the presence of palpitations. Finally, the associations between lower BMI and palpitations could be attributed to other factors that were not measures in this study such as undiagnosed hyperthyroidism or use of diet pills or other stimulants.

Study findings should be considered in the context of some study limitations. This was an analysis of existing data from studies of women who were symptomatic with vasomotor symptoms. Findings should be replicated in samples of women who do and do not report vasomotor symptoms to better describe palpitations. In addition, we relied on a single question to evaluate palpitation distress. Finally, correlates of palpitation distress identified in this article may differ from correlates of other dimensions of palpitations, such as prevalence, frequency, or temporal pattern indicating that additional research on this topic is needed.

Study findings have applicability to clinical practice and research. For clinical practice, it is well established that responding to symptom distress is important to patients' quality of life. Health care professionals should consider assessing whether peri- or postmenopausal women report palpitations and their degree of associated distress. Cognitive interventions (*e.g.*, cognitive reframing, cognitive behavioral therapy) to reduce symptom distress could then be considered. For research, we recommend conducting longitudinal research to more thoroughly assess daily variability, frequency, distress, temporal pattern, and associated factors. It will be important to tease out whether palpitations and/or palpitation distress occur as a sensation related to increased stroke volume in response to vasodilation that occurs with hot flashes and/or if they occur independently of hot flashes and/or in nonflashing women. In addition, studying and identifying any potential underlying electrocardiographic abnormalities associated with self-reported palpitations and/or palpitation distress will be important in future research.

Conclusion

Analysis of data from well-characterized symptomatic peri- and postmenopausal women quantitates the presence and degree of palpitation distress as well as associated demographic, clinical, symptom, and quality-of-life factors. Palpitation distress was a common symptom in peri- and postmenopausal women. The odds of menopausal palpitation distress were reduced in women with lower BMI, and increased in association with worse insomnia, depression, perceived stress, and menopausal quality of life.

Disclaimer

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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