CURRENT APPROACHES TO MANAGING MENOPAUSE (I. ALEXANDER, SECTION EDITOR)



A Systematic Review of Palpitations Prevalence by Menopausal Status

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Abstract

Purpose of the Review The purpose was to systematically review evidence on the prevalence of palpitations by menopausal stage. Palpitations are a feeling of missed, irregular, or exaggerated heart beats.

Recent Findings Carefully delineated search, screening, and data extraction strategies resulted in five articles for review. Articles offered cross-sectional findings from menopausal symptom surveys from five countries between 1974 and 2011 with clinic- and community-based samples of premenopausal, perimenopausal, and postmenopausal women. Reported studies were good (n = 2) to fair (n = 3) quality with low (n = 2) to moderate (n = 3) bias. Menopausal palpitations were not the focus of any study but were assessed as a single item of heart racing, pounding, or discomfort over the past 2 weeks, month, or year. Palpitations prevalence rates by menopausal stage were 3.7 to 40.2% premenopausal, 20.1 to 40.2% perimenopausal, and 15.7 to 54.1% postmenopausal. Three of five articles showed that compared with premenopausal and postmenopausal women, palpitation prevalence was significantly higher among perimenopausal and surgically postmenopausal women.

Summary Good-quality evidence on palpitation prevalence by menopausal stage is limited but suggests that physiological changes of menopause may play a role in this symptom. Measurement varied, suggesting a need to standardize the assessment of menopausal palpitations. The review findings suggest a strong need for clinicians and researchers to collaborate to standardize documentation of menopausal palpitations across the menopause transition.

Keywords Menopause · Palpitations · Menopausal symptoms · Prevalence · Epidemiology

Introduction

About 21 million women living in the USA today and 1.1 billion women worldwide by 2025 will experience menopausal symptoms [1–5], which begin when menses become irregular or stop [1, 6]. Menopausal symptoms can last for 10 to 15 years [1, 6]. Women's symptoms vary [7] with > 75% of

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women reporting vasomotor symptoms (hot flashes, night sweats) [1] that sometimes occur with palpitations [8, 9]. Although hot flashes are a frequently researched symptom with evidence-based effective hormonal and non-hormonal treatments, less is known about perimenopausal and postmenopausal palpitations.

Palpitations are described by women as missed, irregular, or exaggerated heart beats [10•, 11]. In research, the symptom is assessed by a variety of methods including standard menopausal symptom assessment tools. As examples, on the 11-item Menopause Rating Scale, women are asked about "heart discomfort (unusual awareness of heart beat, heart skipping, heart racing, or tightness)" [12•], and on the Kupperman Index, women are asked about "palpitations" [13]. Despite the widespread use of these and other similar assessment tools, no published reviews synthesize findings on palpitations across studies of menopausal women. In particular, the lack of published information regarding the prevalence of palpitations interferes with understanding the scope of the problem at



a population level. Without that information, it is difficult to determine whether this is a menopausal symptom that warrants attention, such as electrocardiogram monitoring. To address this gap in the literature, the purpose of this review was to integrate quantitative evidence on the prevalence of palpitations by menopausal status.

Methods

This was a systematic review of studies reporting rates of palpitations by menopausal status that followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Eligibility Criteria

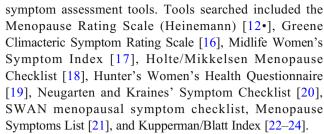
Inclusion criteria were full-length, peer-reviewed, English language articles that contained data on menopause and palpitations in human, female, adults. For the menopause criteria, articles were included if there was a description of the sample as midlife or menopausal, or data were reported on the proportion of the sample who were perimenopausal and/or postmenopausal. We compared article sample descriptions of menopausal status to the Stages of Reproductive Aging Workshop (STRAW) [14] or STRAW+10 definitions for consistency of terminology [15]. For palpitations, studies were included if (1) there were specific data related to palpitation prevalence (or similar symptom such as racing or pounding heart) and (2) the measurement item, recall period, and response options were clearly described.

The review excluded studies focusing exclusively on premenopausal women and studies of transgender or gender transitioning populations, men, and animals. We also excluded articles that were not data based including editorials, opinion papers, reviews, abstracts, and published protocols for reviews or research studies. Studies that defined their populations as "menopausal women" or "symptomatic women" without further clarification or definition of menopausal status or that did not report prevalence by menopausal stage were also excluded.

Literature Search Strategy

The search was conducted in PubMed, CINAHL, and PsycInfo on May 19, 2020. We did not search outside the medical literature (e.g., ERIC) because of the health-related focus of the review topic. We did not search SCOPUS because the review criteria excluded textbooks, published abstracts, or other non-full-length materials.

Because of the lack of literature identified using "palpitations" as a search term, additional pertinent studies were identified by searching for articles that used standard menopausal



The following keyword search on menopause symptom scales was conducted in PubMed, CINAHL, and PsycInfo: ("Menopause Rating Scale" OR "Greene Climacteric Symptom Rating Scale" OR "Midlife Women's Symptom Index" OR "Holte/Mikkelsen Menopause Checklist" OR "Hunter's Women's Health Questionnaire" OR "Neugarten and Kraines' Symptom Checklist" OR "SWAN menopausal symptom checklist" OR "Menopause Symptoms List" OR "Kupperman/Blatt Index" OR "Menopause Symptom Checklist" OR MENQOL). The PubMed search string for palpitations was ("Menopause" [Mesh] OR menopaus*) AND (palpitation* OR heart racing OR heart pounding OR irregular heart). The CINAHL and PsycInfo search string for palpitations was (MH "Menopause" OR menopaus*) AND (palpitation* OR heart racing OR heart pounding OR irregular heart).

The review was organized using a structured program available at Covidence.org. The program de-duplicates articles from searches, shows progress on screening and full text review, allows inter-rater reliability calculations, and allows users to create custom data extraction forms. We did not publish a separate literature search or review protocol. The review did not meet criteria for human subject research and did not require university institutional review board approval.

Screening Process

The initial search references were culled in two screening stages. The first screening stage involved independent and sequential review of titles and abstracts for possible inclusion by three authors (n = 670). Using the Covidence program, once titles and abstracts were included or excluded by two authors, they were not visible to the third person. In this way, the program ensured that each article was reviewed by two authors for possible inclusion. We followed two principles to be overly inclusive at this stage. First, we retained studies where titles or abstracts referred to menopausal or climacteric symptoms/syndrome even when palpitations were not specifically mentioned. Second, we retained studies if the abstracts listed one of the menopausal symptom assessment tools as a study measure. Where there were disagreements (8.77%), the three reviewers discussed each one and achieved consensus.

At the second screening stage, the remaining full-text articles were reviewed (n = 608). Using Covidence, each article



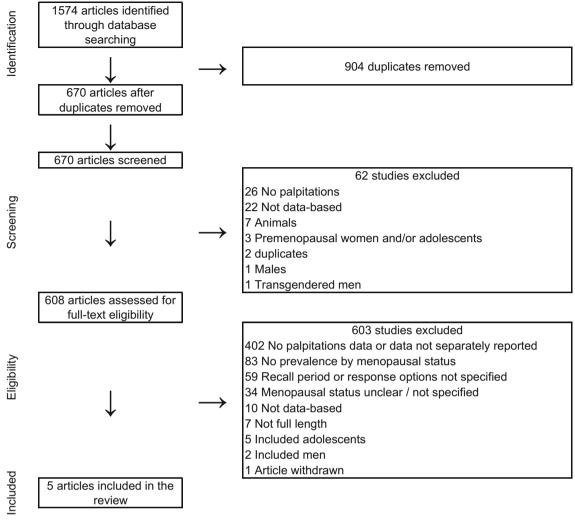


Fig. 1 Flow diagram depicting disposition of the articles. This figure depicts the disposition of articles throughout the screening stage and full-text review. The number of articles included and excluded is provided. Reasons for exclusion are also provided

was independently and sequentially read by two authors who voted on their inclusion or exclusion. Articles that did not specifically report data on palpitations were excluded. Disagreements (4.99%) were resolved through discussion and consensus.

Data Extraction Process

Our team created data abstraction forms based on the study aim. We used shared file platforms for the data extraction that allowed multiple authors to co-edit and see changes in real time. For each article, one author extracted the data and two additional authors verified accuracy. Disagreements were resolved through discussion.

The data extraction form included fields about the article metadata (title, author, year, country), study methods (design, sample details, palpitations measures), and findings (prevalence by menopausal stage). The data extraction form included field items from the Joanna Briggs Institute Checklist for

Prevalence Studies to assess study quality and bias [25]. Fields included the sampling frame, appropriateness of sampling, adequacy of the sample size, description of subjects and setting, validity of methods for identification of the condition (e.g., menopausal status), data analysis, and response rate.

Results

Figure 1 shows the disposition of the articles at screening and review levels. At the title/abstract stage, 62 of the 670 articles (9.25%) were deemed irrelevant and excluded. The main reasons were no palpitation information in the title or abstract, not data based (e.g., reviews, protocols, case studies), and animal studies. This resulted in 608 articles for full text review. At full-text review, 603 articles were excluded with the three most common reasons being no palpitations data reported, reported palpitations prevalence but not in relation to menopausal status, or unspecified measurement recall periods and/



able 1 Description of the articles included in the review

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Article, country	Article, country Age M (SD), range	Sample menol	Sample menopausal status $\%$ (n)		Sample Total N	Sample Total N Sample description	Quality, bias
		Pre	Peri	Post			
(26) USA	40–55	35% (4511)	35% (4511) Early 29% (3556), Late 5% (613)	Natural 14% (1758), Surgical 16% (1988)	12,425	SWAN community based, multi-ethnic survey of women in 7 USA geographic areas	Good, low
(27) UK	45–54	Pre/Peri 58% (368)	(368)	42% (270)	638	Women living in or near London, UK	Fair, moderate
(28) Nigeria	48.1 (5.9), 40–60	49% (580)	10% (119)	41% (490)	1189	Native Nigerian women living	Good, low
(30) Malaysia	50.8 (6.3), 40–65	23% (82)	40% (141)	37% (133)	356	Multi-ethnic study of women living	Fair, moderate
(29) Bangladesh	54.5 (5.7), 40–70	24% (122)	42% (216)	33% (171)	509	Women living in or near Kushtia, Bangladesh; Unclear if multi-ethnic	Fair, moderate

All studies were cross-sectional designs

SD standard deviation, SWAN Study of Women Across the Nation, USA United States of America, UK United Kingdom

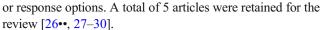


Table 1 contains descriptions of the articles. All contained findings from cross-sectional menopausal symptom surveys published between 1974 and 2010. Countries included Bangladesh, Malaysia, Nigeria, the UK, and the USA. Three samples were community based, and two did not specify whether samples which were recruited from health centers represented the community. Sample age ranges varied, and all articles included premenopausal, perimenopausal, and postmenopausal women. Total sample sizes ranged from 356 to 12,425 women.

Two studies were good quality and low bias (see Table 1). Gold et al. contained lack of clarity on the number of women eligible and approached [26••]. Olaolorun et al. lacked clarity on whether the full item from a standardized questionnaire was used [28]. Three studies were fair quality and moderate bias (see Table 1). McKinlay included a subset of the original study, a long recall period of 1 year for surveys, and lack of clarity on standardization of measurement procedures [27]. Rahman's 2010 and 2011 articles were fair quality with moderate bias due to lack of clarity on representativeness of the target population, lack of information on response rates and attrition, and lack of clarity on whether the full item from a standardized questionnaire was used [29, 30].

Table 2 shows the measurement tool name, item, recall period, and response options. All studies used single items to assess palpitations as present [26••, 27–29, 31], and one additionally assessed severity [28]. Translation and linguistic validation were not mentioned in one article [26••]. Three studies used the Menopause Rating Scale or a modified version of it though none of these articles referenced the full item stem [28–30]. Recall periods included 2 weeks [26••], a month [28–30], and a year [27].

Table 2 also shows prevalence by menopausal status. Overall prevalence rates were reported but are not useful for understanding palpitations as a menopause transition-varying symptom. Rates for premenopausal women varied 10-fold from 3.7% (Malaysia) [30] to 40.2% [27]. Prevalence rates for perimenopausal women varied 2-fold from 20.1% (USA early perimenopausal) or 20.7% (USA late perimenopausal) [26••] to 42.0% (Nigeria) [28]. Rates for postmenopausal women varied from 15.7% (Bangladesh) [29] to 54.1% (UK) [27]. Across all articles, palpitation prevalence rates in perimenopausal women tended to be higher than premenopausal and/or postmenopausal women. Statistical tests of differences in palpitation prevalence by menopausal status reported in the articles confirmed that observation. In three of five articles, compared with premenopausal and postmenopausal women, palpitation prevalence was significantly higher among perimenopausal and/or surgically postmenopausal women [26••, 29, 30].



 Table 2
 Measurement of menopausal palpitations and results

Article	Article Measurement				Prevalence			Group	
	Description	Item	Recall period	Response options	Translations	Pre	Peri	Post	differences
(26)	Symptom checklist via computer-assisted telephone interviews or in person	Heart pounding or 2 racing	2 weeks	weeks Yes, no	Not specified	14.7%	20.1% (early), 20.7% (late)	19.5% all 23.7% surg post	Compared with pre: Surg meno OR = 1.43 [1.22, 1.68]; late peri OR = 1.29 [1.20, 1.64]; early peri OR = 1.19 [1.05, 1.35]; post NS
(27)	(27) Self-reported questionnaires	Palpitations	1 year	Absent, present	Not applicable	31.3%-40.2% 38.3%	38.3%	37.9%–54.1% (early) 24.0%–38.7% (late)	NS
(28)	Menopause Rating Scale	Heart discomfort	4 weeks	weeks 0 no sx to 4	Translated, back translated, pretested	28.1%	42.0%		Not analyzed
(30)	Menopause Rating Scale modified Heart discomfort / 1 for interview nahitation	Heart discomfort /		month Absent,	Translated, back translated, prefested	3.7%	28.4%	16.5%	Peri > pre and post $(p < .05)$
(29)	Menopause Rating Scale modified, Heart discomfort interview	, Heart discomfort	1 month	month Absent, present	Translated, back translated, pretested	11.4%	25.9%	15.7%	Peri > pre and post $(p < .05)$

 NS not significant, Sig diff significantly different, Sx symptom, OR odds ratio



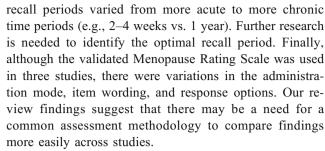
Discussion

To the best of our knowledge, this is the first review to focus on the prevalence of menopausal palpitations. This review was a first step in understanding palpitations in perimenopausal and postmenopausal women in order to determine whether this symptom requires addition follow-up, such as electrocardiogram monitoring to assess whether menopausal palpitations are associated with clinically important arrhythmias or electrocardiogram changes. This review suggests that palpitations are prevalent at a rate indicating that they warrant further attention from clinicians and researchers.

There are several important findings that will be relevant to researchers and/or clinicians. First, there are a limited number of studies overall (n = 5) and a smaller number of good-quality studies (n = 2) providing evidence on the prevalence of palpitations by menopausal stage around the world. The lack of evidence is particularly noteworthy in comparison with other well-studied menopausal symptoms, like vasomotor symptoms (e.g., hot flashes and night sweats) which result in search yields of over 17,000 articles. The few articles that were available for this review indicate that palpitations may affect nearly one of every five or more perimenopausal and/or postmenopausal women. Although differences across studies in measurement recall periods make it difficult to directly compare findings by country, palpitations were prevalent in women living in 5 different countries representing 4 continents.

Second, the higher prevalence of palpitations among perimenopausal and surgically postmenopausal women suggests that physiological changes of menopause may play a role in the development or presence of palpitations. Dennerstein et al. showed that certain menopausal symptoms were triggered by rapidly declining estrogen rather than absolute estrogen levels per se [6]. In that study, a sharper slope of change in estrogen over the menopause transition was linked to symptoms, explaining some of the intra-individual differences in menopausal symptom experiences that have been widely documented. However, the symptom assessment in that study included only four symptoms: hot flashes, night sweats, vaginal dryness, and trouble sleeping. Palpitations were not assessed but may also be related to slope of estrogen change since studies showed prevalence vary by menopausal stage.

Third, this review suggests a need to standardize the assessment of menopausal palpitations. Having clinical practitioners and menopausal women contribute their thoughts on what phrases would be best to capture the symptom could generate relevant items for future psychometric testing by researchers. In the articles reviewed, items assessing the feeling of palpitations (heart pounding or racing) may invoke different responses than the item heart discomfort, which could evoke angina-like symptoms. Standardizing recall periods would also be helpful. It is difficult to compare findings across articles where



There were several strengths and some limitations to this review. In terms of strengths, this review provides a first-time summary of prevalence of palpitations by menopausal stage. The search terms and processes for searching, screening, reviewing, and abstracting were systematically and rigorously conducted. During the screening phase, we erred on being overly inclusive so as not to eliminate potentially relevant articles. Limitations include the fact that the search was limited to English language articles. It is possible that relevant studies published in other languages were omitted. In addition, the articles resulting from the search were limited in number and most had methodological limitations as reflected in the quality and bias ratings.

Conclusions

In conclusion, this review suggests that menopausal palpitations affect at least one in five perimenopausal and postmenopausal women, suggesting that the symptom is worthy of attention in clinical practice and research. To advance the field, it will be important to standardize how this symptom is assessed in relation to menopausal status. Use of similar phrases, recall periods, and response options will help generate more standardized data across practice and research settings to facilitate evidence synthesis and comparisons across studies and populations.

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Compliance with Ethical Standards

Conflict of Interest Dr. Carpenter reports personal fees from RoundGlass Inc., personal fees from Astellas Pharma Inc., personal fees from Kappa Sante, personal fees from Sojournix, and other from QUE oncology. Mr. Elomba, Ms. Alwine, and Drs. Sheng, Yu, Chen, and Tisdale have nothing to disclose.



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