

EDITORIAL

Anxiety and hot flashes as predictors of mid-life palpitations: getting to the heart of the matter in the time of COVID-19

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For more than a year now, we have looked at life through the lens of COVID anxiety. Fear of infection, dire outcomes, and transmission to loved ones have been reflected in every aspect of daily living—from wiping down our groceries in the early days to the endless handwashing and mask-wearing and more recently, the ceaseless searching on multiple electronic devices for that precious first vaccination appointment, all the while coping with mind-numbing isolation, when even a simple hug takes on enormous peril. It is no wonder that upticks in telemedicine visits for hair loss, gastrointestinal symptoms, irregular periods, insomnia, and other stress-related problems are being reported in this prolonged era of uncertainty.¹

It was within this context that I read the work by Enomoto et al² who report in this issue of *Menopause* on factors associated with the prevalence and severity of self-reported palpitations in middle-aged Japanese women. Study participants were ages 40 to 59 attending a Tokyo menopause clinic between 2007 and 2020 (presumably pre-COVID). The report is significant because it is one of the few studies to specifically evaluate risk factors for palpitations—a symptom often recognized as a menopause manifestation but seldom the focus of study.³

Palpitations or “the uncomfortable awareness of a beating heart”⁴ are typically thought to be harmless in healthy individuals, caused by premature atrial/ventricular beats or stress-induced sinus tachycardia (a normal increase in heart rate). Frequently associated with panic disorder, anxiety, depression, and decreased health-related quality of life (QOL), palpitations are one of the most common problems of outpatients who present to internists and cardiologists.⁵ As defined by the American Heart Association,⁶ they can be brought on by anxiety, fright, strenuous exercise, excessive smoking, alcohol and caffeine intake, medications, and recreational drugs, and are especially prevalent in women. One cross-country survey of 1,100 mid-life community women in the United States, Spain, Morocco, and Lebanon demonstrated prevalence rates of 29% in cohorts from both the United States and Spain, 34% in Morocco, and 47% in Lebanon.⁷

Although “postmenopausal syndrome” is listed as one of the systemic causes of palpitations by the European Heart Rhythm Association,⁸ their association with menopause remains somewhat unclear, given the paucity of studies.³ Moreover, palpitations have frequently been considered a manifestation of other symptoms or conditions, rather than as a separate entity, making cross-study comparisons difficult. For example, investigators of the Hilo Women’s Health Survey study included “change in pulse” as a characteristic of hot flashes,⁹ while another group used “pounding or racing heart” as one of the four defining symptoms of anxiety:¹⁰ in a third study, sensations of heart thumping and heart racing were regarded as cardiovascular symptoms.¹¹

From the earliest report of the US-based Study of Women Across the Nation (SWAN),¹² we know that palpitations (when defined as heart pounding) were reported more commonly during the perimenopause or after surgically induced menopause, although this has not been consistently observed in other populations.¹³ Although considered generally benign, when palpitations do occur during menopause, they are not without discomfort, especially for those with frequent hot flashes. Participants of the MsFLASH study (Menopause Strategies—Finding Lasting Answers for Symptoms and Health) demonstrated an overall distress rate of 25% from any degree of “heart racing or pounding.”¹⁴ In women after hysterectomy, palpitations may be especially distressing.¹⁵

Just as with hot flashes, the prevalence of palpitations varies significantly by race/ethnicity, suggesting the importance of cultural attitudes, social salience, and lifestyle differences.^{12,16} Indeed, Asian-American women have typically demonstrated fewer and milder menopause symptoms including palpitations than most other ethnic groups,^{9,17-19} prompting one group of researchers to conclude that Asian-American midlife women may not be a high-risk group for targeting preventive health interventions for cardiovascular disease.¹¹ The lower rates of menopause symptoms have been attributed to a lower body mass index on average coupled with higher soy intake, lower smoking rates, and possible differences in hormone metabolism,³ but in the Hilo study, BMI and soy intake did not account for fewer hot flashes in Japanese Americans,⁹ again pointing to cultural context.

In the work reported here, the investigators conducted one of the first investigations to combine both self-reported assessments and biomedical measures as a way to get to

Received April 27, 2021; revised and accepted April 27, 2021.

From the Columbia University School of Nursing, New York, NY
Funding/support: None reported.

Financial disclosure/conflicts of interest: None reported.

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the heart of the matter regarding risk factors. To do this, a medical record analysis was performed of demographic, lifestyle, medical, and social history data obtained from 394 women ages 40 to 59 attending a menopause clinic for the first time; in a subset of 198 women, assessments were carried out on multiple biomedical correlates: body composition, cardiovascular status, basal metabolism, physical fitness, and autonomic nervous system (ANS) activity. Self-reported palpitations were defined using a single question that measured the impact on daily life of a “rapid or irregular heartbeat” on a scale from 0 (none) to 4 (severe). The Menopausal Health Related Quality of Life (MHR-QOL) questionnaire characterized the impact of vasomotor symptoms (both hot flashes and night sweats), while anxiety and depression symptoms were measured with the Hospital Anxiety and Depression Scale (HADS).

Strengths of the study included the use of the HADS scale which does not include physical symptoms, thus avoiding overlap with the dependent variable, as well as multiple tests of cardiovascular health status including the cardio-ankle vascular index (as an indicator of atherosclerosis), ankle-brachial pressure index (for ischemia), and a 5-minute morning electrocardiogram study to detect arrhythmias and determine ANS activity. In addition, patients had to report at least moderate distress resulting from palpitations to be defined as a “yes” in the yes/no multivariate logistical regression models.

Unlike the SWAN findings³ but similar to results from MsFLASH,¹⁴ no differences in distressing palpitations were observed based on menopause status. In addition, after adjusting for confounds, only vasomotor symptoms (VMS) and anxiety scores were shown to be independently associated with moderate to severe palpitations. None of the other well-known correlates such as arrhythmia, ANS activity, caffeine intake, or alcohol consumption were significant predictors, although thyroid function was not assessed, which the authors acknowledged. Most remarkable to the investigators was the high palpitation rate (40%), compared with rates of 10% and 3% for women of Japanese identity living in the United States³ and Australia,²⁰ respectively. Although differences in recruitment characteristics were evident, (menopause clinic patients vs snowball sampling of community-based respondents), other factors such as the level of acculturation in the United States and Australian populations were likely at play.^{21,22}

To their credit the authors recognized the design weakness of using a single question to define the dependent variable as a rapid or irregular heartbeat that impacts daily life, but failed to explain why this might be a problem. There are a number of subjective cardiac sensations reported to cardiologists by US patients that have been characterized as palpitations including “heart flutter” or “beating wings,” “flip-flopping,” “skipped a beat,” “heart-sinking,” and “pounding in the neck,” but were not considered as part of the definition under study.^{5,8} To what extent these other sensations apply to the menopause experience of women either in Japan or elsewhere is not clear, given the paucity of studies on palpitations in general. Indeed, just as the Japanese language includes a

number of terms for VMS in both formal and informal conversation,²³ the same may be true for palpitations.

Although the 5-minute electrocardiogram recording provided a measure of ANS activity, the authors recognized the failure to longitudinally characterize in real time the frequency and pattern of these symptomatic palpitations using 24-hour Holter monitoring. It would have been helpful to know whether these distressing palpitations were more likely to occur during the day or at night, and in association with night sweats or other symptoms. For example, in an earlier report using the same data base, these investigators demonstrated that “chilliness” was the most common symptom among their patient cohort,²⁴ which like palpitation distress demonstrated a significant association with the HADS anxiety subscale.

In other studies of menopause-related palpitations conducted in Asia, frequency and prevalence rates have been similar²⁵ or much lower²⁶ compared with other menopause symptoms, depending on recruitment setting. In a sample of more than 20,000 Taiwanese women over age 39 who called a menopause helpline, rates of palpitations were similar (approximately 45%) but well below the 5 most common symptoms reported, and varied by age rather than menopause status.¹³ To what extent these different approaches to the assessment of menopause symptoms are measuring the same phenomenon is not clear. Having said that, the high rate of distressing burden caused by a rapid or irregular heartbeat reported here (40%) suggests that the sensitivity of the approach was sufficient to capture an important phenomenon in this patient population, setting the stage for additional research.

Perhaps the most intriguing finding is the separate and independent associations of anxiety and VMS with distressing palpitations. In some ways this is not surprising, as anxiety or psychologic distress has long been considered a risk factor for menopause symptoms.²⁷⁻²⁹ Moreover, others have reported the co-occurrence of anxiety and VMS as part of symptom clusters of varying degrees and patterns in US studies,³⁰ but a clear articulation of how anxiety interacts as a precursor or consequence of VMS (or both) remains elusive. In the MsFLASH study,¹⁴ the presence of palpitation distress varied significantly according to insomnia, depression, stress, and QOL. As most of the prior work involved mostly White, non-Asian samples, the relevance of these findings is uncertain.

Although the sample was small and more rigorous studies are warranted, this finding is not trivial, as the work reported here adds to the growing evidence that distressing palpitations together with VMS and anxiety represent a constellation of symptoms that may forecast adverse cardiovascular health. There is now a burgeoning body of evidence that associates VMS with risk factors for coronary heart disease, surrogate markers for coronary heart disease, and clinical events.³¹ Just this year, the analysis of more than 22 years of annual data from the SWAN cohort study of midlife women demonstrated that frequent or persistent menopausal vasomotor symptoms were associated with a 50% to 77% increased risk of future cardiovascular disease events, including both fatal and non-fatal events.³²

Although the investigators acknowledged that a temporal link could not be assumed in this cross-sectional study, they speculated that the potent central nervous system vasodilator calcitonin gene-related peptide might trigger the induction of both hot flashes and palpitations, but were less clear about how anxiety might be involved. Given the lack of a relationship between palpitations and any measure of ANS activity, they concluded that anxiety may influence subjective palpitations more directly. Recently, a plausible pathologic pathway involving the buildup of oxidative stress and inflammation has been proposed to explain how anxiety might serve as an independent trigger for abnormal arrhythmias leading to atrial fibrillation.³³ At the same time, a Swedish study of anxiety-related palpitations in healthy mid-life women showed that the use of a smart watch that provides instant electrocardiogram feedback about the nature of the symptoms could reduce palpitations, depression, and HADS anxiety scores and improve quality of life.³⁴

In the current study, it might have been helpful to have measured the level of anxiety sensitivity (AS), a promising vulnerability trait shown to be related to mental health and functional impairment. AS is a measure of the “fear of arousal-related sensations arising from beliefs that the sensations have adverse consequences such as death, insanity, or social rejection.”³⁵ According to experts in the field,³⁶ individuals with elevated AS might fear sweating in public based on the risk of humiliation or interpret palpitations as a sign of a heart attack. In a menopause study from Brazil, researchers speculated that the higher AS scores observed in women with greater VMS burden were due to a learned association between hot flashes and a loss of control over their onset, resulting in an “extremely harmful social impact.”³⁷ A similar mechanism has been proposed to explain the strong association between hot flashes and somatic anxiety, but not emotional anxiety, that was demonstrated in the longitudinal study from the 14-year follow-up phase of the Penn Ovarian Aging Study.²⁷ In a study of menopause symptoms, the level of somatosensory amplification, a related construct to AS, was similar in breast cancer survivors and healthy volunteers, and significantly correlated with hot flash interference, and mood and sleep disturbance in both groups.³⁸

No doubt the investigators of this report could not possibly have predicted the growing relevance of their work as a baseline for future comparison studies given the repercussions of the pandemic on emotional, physical, and social well-being. Already, a growing body of literature is defining the substantial impacts of COVID stress on human health.³⁹ Women have especially been hit hard and are experiencing greater COVID-related distress.⁴⁰ In a meta-analysis of 43 studies, female sex was a predominant risk factor for the more than 3-fold higher-than-normal prevalence rate for anxiety disorder in the general population during the pandemic (25% vs 7% pre-COVID).⁴¹ Reasons for this sex difference included a greater likelihood for women to have a primary caregiver role and disruptions in daily routines, higher levels of worry about finances, the welfare of friends and family,

deterioration of family ties during quarantine, and becoming infected, and be at risk of becoming depressed. Concurrently, rates of domestic violence are spiking.⁴² Recently, results from an online survey sponsored by a commercial menopause blog⁴³ revealed that among 1,000 respondents, menopause symptoms have been impacted by COVID-related stress. Of the most troubling 13 symptoms, the top ones were mood (84%), night sweats (83%), and sleeplessness (75%), while hot flashes were #8 (63%). Additionally, 70% of respondents reported putting off preventative health appointments including visits for mammograms and Pap tests in the past year as a result of the pandemic. For female healthcare providers, the statistics are even more dire, with experts calling the expected surge in posttraumatic stress disorder and suicide as the second tsunami of the SARS-Cov-2 pandemic.⁴⁴

But for Asian-American and Pacific Islander (AAPI) women, the second tsunami is already here. Among the most tragic repercussions has been the rise in anti-Asian hate crimes, blatant racism, and social media attacks in response to COVID-19.⁴⁵ According to the *Stop AAPI Hate* coalition,⁴⁶ nearly 3,800 incidents were reported in the first year of the pandemic by respondents over age 45, with 70% of cases targeted against women. They are considered just the tip of the iceberg, given the finding from the Pew Research Center that 3 in 10 Asian Americans (31%) report having experienced racial slurs or racist jokes since the beginning of the pandemic and 26% have feared that someone might threaten or physically attack them.⁴⁷ Just as clinicians and researchers rolled up their sleeves and set about confronting the worst disaster in a lifetime, the same level of collective energy and dedicated commitment is needed to address the systemic racism that permeates society and help blunt the impact of these traumas and microaggressions on current and future health.⁴⁸ To their credit, individual clinicians and counselors are developing thoughtful practice recommendations to combat anti-Asian sentiment in healthcare and counselling strategies to heal race-based trauma.^{49,50}

In sum, this work adds to the evidence that we can no longer assume that Asian women, regardless of country, are at low risk for disabling mid-life symptoms. Compounded by the multiple stressors of living through the pandemic as part of a targeted minority group, the menopause symptom experience for AAPI women may be especially challenging. Now more than ever there is an urgent need for culturally competent care delivered through a wider lens that embraces evidenced-based, culturally relevant interventions, psychosocial support services, and risk assessments for mental health.

REFERENCES

1. Pattani A. Sleepless nights, hair loss, cracked teeth, shingles: pandemic stress taking a toll Kaiser Health News Nov 6, 2020, *Chicago Sun Times*. Available at: www.chicago.suntimes.com/well/2020/11/6/21548072. Accessed April 23, 2021.
2. Enomoto H, Terauchi M, Odai T, et al. Independent association of palpitation with vasomotor symptoms and anxiety in middle-aged women. *Menopause* 2021;28:741-747.
3. Carpenter JS, Sheng Y, Elomba CD, et al. A systematic review of palpitations prevalence by menopausal status. *Curr Obstet Gynecol Rep* 2021;10:7-13.

4. Brugada P, Gursoy S, Brugada J, Andrie E. Investigation of palpitations. *Lancet* 1993;341:1254-1258.
5. Zimetbaum P, Josephson ME. Evaluation of patients with palpitations. *N Engl J Med* 1998;338:1369-1373.
6. American Heart Association. Prevention and Treatment of Arrhythmia. Available at: www.heart.org. Accessed April 20, 2021.
7. Sievert LL, Obermeyer CM. Symptom clusters at midlife: a four-country comparison of checklist and qualitative responses. *Menopause* 2012;19:133-144.
8. Raviele A, Giada F, Bergfeldt L, Blanc JJ, et al. Management of patients with palpitations: a position paper from the European Heart Rhythm Association. *Europace* 2011;13:920-934.
9. Sievert LL, Morrison L, Brown DE, et al. Vasomotor symptoms among Japanese-American and European-American women living in Hilo, Hawaii. *Menopause* 2007;14:261-269.
10. Thurston RC, Sowers MF, Chang Y, et al. Adiposity and reporting of vasomotor symptoms among midlife women: the Study of Women's Health Across the Nation. *Am J Epidemiol* 2008;167:78-85.
11. Im EO, Ham OK, Chee E, Chee W. Racial/ethnic differences in cardiovascular symptoms in four major racial/ethnic groups of midlife women: a secondary analysis. *Women Health* 2015; 55: 525-547.
12. Gold EB, Sternfeld B, Kelsey JL, et al. Relation of demographic and lifestyle factors to symptoms in a multiracial/ethnic population of women 400-55 years of age. *Am J Epidemiol* 2000;152:463-473.
13. Lee PS, Lee CL. Prevalence of symptoms and associated factors across menopause status in Taiwanese women. *Menopause* 2021;28:182-188.
14. Carpenter JS, Tisdale JE, Chen CX, et al. A menopause strategies—finding lasting answers for symptoms and health (MsFLASH) investigation of self-reported menopausal palpitation distress. *J Womens Health (Larchmt)* 2012;30:533-538.
15. Hartmann BW, Kirchengast S, Albrecht A, Metka M, Huber JC. Hysterectomy increases the symptomatology of postmenopausal syndrome. *Gynecol Endocrinol* 1995;9:247-252.
16. Im EO, Kim J, Chee E, Chee W. The relationships between psychological symptoms and cardiovascular symptoms experienced during menopausal transition: racial/ethnic differences. *Menopause* 2016;23:396-402.
17. Gold EB, Colvin A, Avis N, et al. Longitudinal analysis of the association between vasomotor symptoms and race/ethnicity across the menopausal transition: study of women's health across the nation. *Am J Public Health* 2006;96:1226-1235.
18. Reed SD, Lampe JW, Qub C, et al. Self-reported menopausal symptoms in a racially diverse population and soy food consumption. *Maturitas* 2012;75:152-158.
19. Im E-O, Lee B, Chee W, et al. Menopausal symptoms among four major ethnic groups in the United States. *West J Nurs Res* 2010;32:540-565.
20. Anderson D, Yoshizawa T, Gollschewski S, et al. Menopause in Australia and Japan: effects of country of residence on menopausal status and menopausal symptoms. *Climacteric* 2004;7:165-174.
21. Im EO, Meleis AI, Lee KA. Symptom experience during menopausal transition: low income Korean immigrant women. *Women Health* 1999;29:53-67.
22. Melby MK, Lock M, Kaufert P. Culture and symptom reporting at menopause. *Hum Reprod Update* 2005;11:495-512.
23. Reame NK. Learning more about the Japanese hot flash. *Menopause* 2009;16:846-847.
24. Terauchi M, Terauchi T, Odai A, et al. Chilliness in Japanese middle-aged women is associated with anxiety and low n-3 fatty acid intake. *Climacteric* 2020;23:178-183.
25. Ishizuka B, Kudo Y, Tango T. Cross-sectional community survey of menopause symptoms among Japanese women. *Maturitas* 2008;61:260-267.
26. Asama T, Matsuzaki H, Fukushima S, Tatefuji T, Hashimoto K, Takeda T. Royal jelly supplementation improves menopausal symptoms such as backache, low back pain, and anxiety in postmenopausal Japanese women. *Evid Based Complement Alternat Med* 2018; 2018:4868412.
27. Freeman EW, Sammel M. Anxiety as a risk factor for menopausal hot flashes: evidence from the Penn Ovarian Aging cohort. *Menopause* 2016;23:942-949.
28. Sood R, Kuhle CL, Kapoor E, et al. Association of mindfulness and stress with menopausal symptoms in midlife women. *Climacteric* 2019;22:377-382.
29. Arnot M, Emmott EH, Mace R. The relationship between social support, stressful events, and menopause symptoms. *PLoS One* 2021;16: e0245444.
30. Woods NF, Hohensee C, Carpenter JS, et al. Symptom clusters among MsFLASH clinical trial participants. *Menopause* 2016;23:158-165.
31. Stuenkel CA. Is it WISE to link vasomotor symptoms with cardiovascular disease? *Menopause* 2017;24:121-123.
32. Thurston RC, Aslanidou HE, Vlachos CA, et al. Menopausal vasomotor symptoms and risk of incident cardiovascular disease events in SWAN. *J Am Heart Assoc* 2021;10:e017416.
33. Severino P, Mariani MV, Maraone A, et al. Triggers for atrial fibrillation: the role of anxiety. *Cardiol Res Pract* 2019; 2019:Article ID 1208505, 5 pages.
34. Carlöf C, Schenck-Gustafsson K, Jensen-Urstad M, Insulander P. Instant electrocardiogram feedback with a new digital technique reduces symptoms caused by palpitations and increases health-related quality of life (the RedHeart study). *Eur J Cardiovasc Nurs* 2021;zvaa031.
35. Taylor S, Zvolensky MJ, Cox BJ, et al. Robust dimensions of anxiety sensitivity: development and initial validation of the Anxiety Sensitivity Index-3. *Psychol Assess* 2007;19:176-188.
36. Olatunji BO, Wolitzky-Taylor KB. Anxiety sensitivity and the anxiety disorders: a meta-analytic review and synthesis. *Psychol Bull* 2009;135:974-999.
37. Jaeger MB, Mina' CS, Alves S, Schuh GJ, Wender MC, Manfro GG. Negative affect symptoms, anxiety sensitivity, and vasomotor symptoms during perimenopause. *Braz J Psychiatry* 2020;S1516-44462020 005033202.
38. Carpenter JS, Igega CM, Otte JL, Burns DS, Yu M, Wu J. Somatosensory amplification and menopausal symptoms in breast cancer survivors and midlife women. *Maturitas* 2013;78:51-55.
39. Flannagan EW, Beyl RA, Fearnbach SN, et al. The impact of COVID-19 stay-at-home orders on health behaviors in adults. *Obesity* 2021;29:438-445.
40. Liu N, Zhang F, Wei C, et al. Prevalence and predictors of PTSS during Covid-19 outbreak: gender differences matter. *Psych Res* 2020;287: 112921.
41. Santabárbara J, Lasheras I, Lipnicki DM, et al. Prevalence of anxiety in the COVID-19 pandemic: an updated meta-analysis of community-based studies. *Prog Neuropsychopharmacol Biol Psychiatry* 2020;109: 110207.
42. Elisabeth R, Amin A, Gupta J, García-Moreno C. Violence against women during COVID-19 pandemic restrictions. *BMJ* 2020;369:m1712.
43. Available at: [https://health.gennev.com/hubfs/GENNEV_Menopause_Report2020_Final%20\(1\).pdf](https://health.gennev.com/hubfs/GENNEV_Menopause_Report2020_Final%20(1).pdf). Accessed April 23, 2021.
44. Duteil F, Mondillon L, Navel V. PTSD as the second tsunami of the SARS-Cov-2 pandemic. *Psychol Med* 2020;1-2; Online ahead of print.
45. Nguyen TT, Criss S, Dwivedi P, et al. Exploring U.S. shifts in anti-Asian sentiment with the emergence of COVID-19. *Int J Environ Res Public Health* 2020;17:7032.
46. Jeung R, Yellow Horse R, Popovic T, Lim, R. Stop AAPI Hate National Report 3/19/20-2/28/21 Available at: <https://securervercdn.net/104.238.69.231/a1w.90d.myftpupload.com/wp-content/uploads/2021/03/210312-Stop-AAPI-Hate-National-Report.pdf>. Accessed April 21, 2021.
47. Pew Research Center, July 2020, Many Black and Asian Americans Say They Have Experienced Discrimination Amid the COVID-19 Outbreak. Available at: https://www.pewsocialtrends.org/wp-content/uploads/sites/3/2020/07/PSDT_07.01.20_racism.COVID_Full.Report.pdf Accessed April 23, 2021.
48. Lee S, Waters SF. Asians and Asian Americans' experiences of racial discrimination during the COVID-19 pandemic: Impacts on health outcomes and the buffering role of social support. *Stigma Health* 2021;6:70-78.
49. Lee JH. Combating anti-Asian sentiment — a practical guide for clinicians. *New Eng J Med* 2021. Available at: <https://www.nejm.org/doi/pdf/10.1056/NEJMp2102656?articleTools=true>. Accessed April 23, 2021.
50. Litam SDA. Take your Kung-Fu back to Wuhan': counseling Asians, Asian Americans, and Pacific Islanders with race-based trauma related to COVID-19. *The Professional Counselor™* 2020;10:144-156.