

Association Between Body Mass Index and Moderate-to-Severe Vasomotor Symptoms in Thai Postmenopausal Women

Kitirat Techatraisak, M.D., Ph.D.* , Nattamon Jiwornlerk, M.D.**

*Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, **Division of Obstetrics and Gynaecology, Charoen Krung Pracha Rak Hospital, Bang Ko Lam, Bangkok 10120, Thailand.

ABSTRACT

Objective: Body mass index (BMI) has been controversially reported to be positively, inversely, or not associated with vasomotor symptoms (VMS) in postmenopausal women. This study analysed the association between BMI and moderate-to-severe VMS in Thai population.

Methods: A cross-sectional study was conducted among 178 Thai postmenopausal women aged 30-60 years. They were categorized into two groups by BMI. The two groups (normal BMI $<25.0 \text{ kg/m}^2$ and high BMI $\geq 25.0 \text{ kg/m}^2$) were compared. Modified menopausal rating scale (MRS) was used to assess the severity of VMS. The association between BMI, types and duration of menopause, and VMS were analyzed by chi-square test and *t*-test analysis. Multiple logistic regression analysis was used to evaluate the associations between BMI, other variables, and severity of VMS.

Results: Each group comprised 89 consecutive postmenopausal women. The percentage of women with moderate-to-severe VMS was significantly higher in the normal BMI group than in the high BMI group (60.9% vs 39.1%, respectively; $p=0.007$). The association between normal BMI and moderate-to-severe VMS was statistically significant after adjustment for other confounding variables that included age, medical illness, duration or type of menopause and current medications (adjusted odd ratios [OR]: 2.378; 95% confidence interval [CI]: 1.273, 4.447).

Conclusion: Interestingly, Thai postmenopausal women with a normal BMI experience a higher rate of moderate-to-severe VMS than those with a high BMI. The finding indicates that BMI is a risk factor for VMS among Thai postmenopausal women. Healthcare providers should focus on normal BMI Thai postmenopausal women when assessing for and treating VMS.

Keywords: BMI; VMS; postmenopausal women; Thai (Siriraj Med J 2019; 71: 370-376)

INTRODUCTION

Menopause is recognized after 12 months' absence of menstruation. The typical age range for onset of menopause is 47 to 50 years.¹ Menopausal symptoms such as vasomotor symptoms (VMS: hot flushes and

night sweats), sleeplessness, urinary frequency, vaginal dryness, anxiety and depression, adversely affect quality of life.^{2,3} In general, VMS persists for six months to two years, but they may last for more than 10 years.⁴⁻⁶ The frequency and severity of VMS are different in each

Corresponding author: Kitirat Techatraisak

E-mail: kitirat.tec@mahidol.ac.th

Received 2 November 2018 Revised 1 July 2019 Accepted 5 August 2019

ORCID ID: <http://orcid.org/0000-0001-8449-9379>

<http://dx.doi.org/10.33192/Smj.2019.56>

woman. The prevalence of VMS varies widely across populations and ethnicities. Approximately 40-70% of postmenopausal women experience VMS.⁷

VMS affects quality of life by causing insomnia, depression, anxiety and fatigue. There are many methods for treating VMS such as lifestyle modifications, taking vitamin supplements, and/or using herbs.^{4,6-8} Hormonal therapies (e.g., estrogen and tibolone) and non-hormonal therapies (e.g., clonidine, gabapentin, and some serotonin and serotonin–norepinephrine reuptake inhibitors), are also used for treating VMS. However, the easiest and most widely available treatment method is change in lifestyle. Women with moderate-to-severe VMS are indicated for hormonal therapy.⁹

The pathophysiology of VMS is not well understood. The first hypothesis is that a central event that is initiated in the hypothalamus drives an increase in core body temperature, metabolic rate and skin temperature. Another hypothesis is that estrogen withdrawal or deficiency causes VMS. This hypothesis is supported by the effectiveness of estrogen therapy for relieving VMS.⁹ The physical and financial burdens of VMS are considerable. If practitioners know the risk factors for VMS, they can advise postmenopausal women regarding the behaviors to avoid or adopt in order to relieve the symptoms of VMS, and reduce the probability of developing VMS. Lower BMI was reported to be a risk factor for VMS.^{10,11} The large SWAN cross-sectional study found BMI to be positively correlated with self-reported hot flashes and/or night sweats.¹² One recent study reported that obese women have a more symptomatic menopausal transition compared to normal weight women.¹³ However, some previous studies did not find association between BMI and VMS among postmenopausal women.¹⁴⁻¹⁶

If we could identify postmenopausal women at high risk for VMS, we could develop appropriate preventive strategies including lifestyle modifications and surveillance in postmenopausal women. Accordingly, the aim of this study was to investigate the association between BMI (normal vs. overweight) and moderate-to-severe VMS in Thai postmenopausal women.

MATERIALS AND METHODS

This retrospective cross-sectional study, was conducted during 2012-2013 among consecutive new menopausal patients who attended the Gynecologic Endocrinology Unit, of the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand during 2008-2011. The protocol for this study was approved by the Ethic Committee of Faculty of Medicine Siriraj Hospital (Si 659/2011).

The target population included naturally, surgically and prematurely menopausal women aged 30–60 years. Women currently using of hormonal therapies or drugs that affect VMS (e.g., SSRIs, clonidine, and gabapentin) were excluded. Detailed menopausal symptoms were obtained from subject response to structured questions (modified menopausal rating scale, modified MRS). The scale was originally developed and validated over several years by a research network consisting of many institutions located in Germany during the 1990s. [Thai questionnaire Version 5.0 (validation with permission), was used for the research “Menopause-related symptoms and quality of life in peri- and postmenopausal women in Thailand: multicenter study” that was published in *Asian Biomedicine* 2017;11:207-15]. The objectives of MRS were to measure the severity of menopausal symptoms, changes before and after treatment with hormone replacement therapy, and their impact on health-related quality of life. The patients first read a menopausal symptoms list, including VMS. They then ranked the level of severity from 0-4 (no symptom, mild, moderate and severe symptoms, respectively). Scores of 0 and 1 were classified as mild symptoms, and scores of 2, 3, or 4 were classified as moderate-to-severe symptoms.^{17,18}

The sample size was calculated based on a pilot study of 20 patients who were divided into two groups: normal weight (BMI <25kg/m²) and overweight (BMI ≥25kg/m²) according to World Health Organization’s definitions.¹⁹ BMI was calculated as weight in kilograms (kg) divided by height in meter squared (m²). The results revealed that 4 of 10 patients in the normal weight group experienced moderate-to-severe VMS. In the overweight group, only 2 of 10 patients experienced moderate-to-severe VMS. The estimated sample size (type I error of 5 %, and type II error of 20%) was 81 patients in each group. The estimated sample size was increased by 10% to compensate for missing or incomplete data. Patients were consecutively recruited from 2008 until the total sample size of 89 participants per group was achieved, as shown in Fig 1.

Retrieved demographic and clinical data included age, body weight, height, medical history, health behaviors, such as smoking and alcohol use, type of menopause, current medication, hormone replacement therapy, and severity of menopausal symptoms.

Statistical analysis

The study variables were compared among groups using the SPSS 18.0 statistical package. Chi-square test and Fisher’s exact test were used for categorical data. T-test

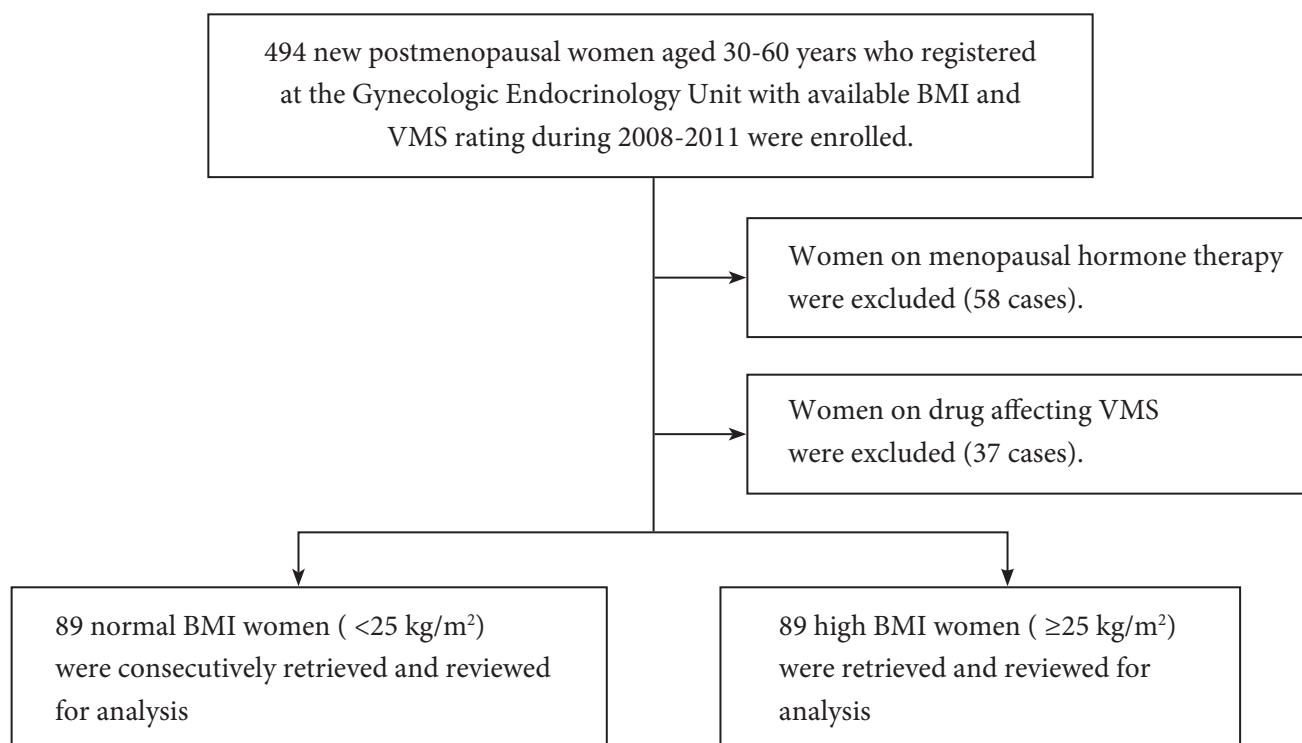


Fig 1. Flow diagram of the subject selection process.

was used for analyzing continuous data. Multiple logistic regression analysis was used to estimate the association between each of the independent variables, and for adjusting for potential confounders. The adjustments were used for independent variables, including BMI, age, medical illness, duration of menopause, type of menopause, and current medication. Significant level was defined as p -value <0.05 .

RESULTS

One hundred and seventy-eight postmenopausal women that were included in this study. Characteristics of the normal weight and overweight groups are presented in [Table 1](#). In addition, both groups of participants were non-smoking and non-alcohol drinking. The demographic and clinical characteristics were similar between groups except for age, medical illness, and antihypertensive drug use. The mean duration of menopause was not significantly different between groups. Aside from hypertensive drug use, there were no differences between groups for current medications.

The associations between BMI and severity of VMS, type of menopause, duration of menopause and other variables are shown in [Table 2](#). Postmenopausal women with BMI <25 kg/m² were significantly more likely to report moderate-to-severe VMS than higher BMI postmenopausal women ($p=0.004$). No significant

association was observed between severity of VMS and type or duration of menopause, age, medical illness, or current medication.

After adjustment for covariates using multiple logistic regression, the normal weight group was significantly associated with greater odds of reporting moderate to severe VMS as shown in [Table 3](#). Only the association between normal BMI and moderate to severe VMS remained significant after adjustment for age, medical illness, duration of menopause, type of menopause and current medication (adjusted odd ratios [OR]: 2.378; 95% confidence interval [CI]: 1.273, 4.447).

DISCUSSION

One of the most commonly studied menopausal symptoms associated with obesity is VMS. Obesity was reported to be a protective factor for VMS.^{20,21} On the contrary, the finding from this study in Thai population showed a different result. Thai postmenopausal women with a BMI <25 kg/m² were more likely to experience moderate - to - severe VMS than women with a higher BMI after adjusting for confounding variables.

The result of this study may be explained by estrone, which is a predominant form of estrogen in postmenopausal women that is produced in adipose tissue via the conversion of androstenedione. We assumed that women with lower BMI might have less adipose

TABLE 1. Characteristics of study population.

	BMI <25 kg/m ² (N=89)	BMI ≥25 kg/m ² (N=89)	P-value
Age (Mean±SD, yr)	51.87 ± 5.35	53.47 ± 4.22	0.028
Type of menopause (case, %)			0.332
Natural menopause	60 (67.4%)	56 (62.9%)	
Surgical menopause	29 (32.6%)	31 (34.8%)	
Premature menopause	0 (0%)	2 (2.2%)	
Duration of menopause (Mean±SD, yr)	4.84 ± 4.63	5.34 ± 4.53	0.467
Medical illness (case, %)	24 (26.7%)	36(40.9%)	0.044
Hypertension	12 (13.3%)	23 (26.1%)	0.032
Diabetes mellitus	4 (4.4%)	7 (8%)	0.331
Dyslipidemia	10 (11.1%)	13 (14.8%)	0.467
Chronic kidney disease	1 (1.1%)	0 (0%)	1
Thyroid disease	3 (3.3%)	2 (2.3%)	1
Allergy	1 (1.1%)	1 (1.1%)	1
Gout	2 (2.2%)	0 (0%)	0.497
CA breast	2 (2.2%)	0 (0%)	0.497
Cerebrovascular disease	1 (1.1%)	0 (0%)	1
Osteoporosis	2 (2.2%)	1 (1.1%)	1
Current medications (case, %)	19 (21.1%)	27 (30.7%)	0.145
Antihypertensive drug	9 (10%)	20 (27%)	0.022
Anti-hyperglycemic drugs	3 (3.3%)	5 (5.7%)	0.494
Hypolipidaemic agents	7 (7.8%)	11 (12.5%)	0.296
Thyroid drug	2 (2.2%)	0 (0%)	0.497
Allopurinol	2 (2.2%)	0 (0%)	0.497
Tamoxifen	2 (2.2%)	0 (0%)	0.497
Bisphosphonate	1 (1.1%)	1 (1.1%)	1

tissue, so they might have lower estrone and a higher risk of developing VMS. A lower level of estrogen is also one of the possible causes of VMS. There are many reports that support the results of this study. A group of postmenopausal women was divided into two subgroups and estrogen levels were measured and compared. The results showed that the severe VMS group had lower levels of estrone, estradiol, and body weight than the other

group that never experienced VMS ($p < 0.05$).²² The result of our study supported one former study of naturally postmenopausal women that found that overweight women suffered from hot flushes and perspiration less than thinner women.¹⁰ Another later study also found the risk of VMS to be higher in heavier women. A cross-sectional study of women aged 40-60 years that were classified according to BMI (≤ 24.9 , $25.0-29.9$, or ≥ 30 kg/m²)

TABLE 2. The association between BMI, type of menopause, duration of menopause, age, medical illness, current medications and severity of VMS.

	Vasomotor symptoms		P-value
	Mild (N=91)	Moderate - to - severe (N=87)	
BMI			0.004
< 25 kg/m ²	36 (39.6%)	53 (60.9%)	
≥ 25 kg/m ²	55 (60.4%)	34 (39.1%)	
Type of menopause			0.372
Natural menopause	58 (63.7%)	58 (66.7%)	
Surgical menopause	31 (34.1%)	29 (33.3%)	
Premature menopause	2 (2.2%)	0 (0%)	
Duration of menopause (Mean±SD, yr)	5.42 ± 4.47	4.74 ± 4.69	0.326
Age (Mean±SD, yr)	52.75 ± 4.63	52.59 ± 5.35	0.829
Medical illness	33 (35.9%)	27 (31.4%)	0.528
Current medications	25 (27.2%)	21 (24.4%)	0.675

TABLE 3. Multivariable logistic regression model for moderate to severe VMS.

	Unadjusted odds ratio (95 % CI)	Adjusted odds ratio (95 % CI)	P-value
BMI			
< 25 kg/m ²	2.38 (1.307-4.359)	2.38 (1.273-4.447)	0.007
≥ 25 kg/m ²	1	1	
Type of menopause			
Natural menopause	1.033	0.868	0.7
Surgical menopause	1	1	
Premature menopause	NA	NA	
Age	0.996 (0.938-1.058)	1.024 (0.954-1.099)	0.512
Duration of menopause	0.97 (0.909-1.035)	0.973 (0.901-1.052)	0.496
Medical illness	0.818 (0.439-1.526)	0.938 (0.333-2.64)	0.904
Current medications	0.86 (0.442-1.0697)	1.033 (0.344-3.1)	0.953

Abbreviations: CI = Confidence Interval, NA = not applicable

investigated the relationship between lifestyle factors (e.g., BMI and smoking) and moderate-to-severe VMS. The result showed that BMI ≥ 30 kg/m² was associated with an increased risk of moderate-to-severe hot flashes when compared with BMI ≤ 24.9 kg/m² (adjusted OR: 2.1, 95% CI: 1.5-3.0) in premenopausal or perimenopausal women.⁷ This might be due to the fact that adipose tissue produces hormones (e.g., leptin, tumor necrosis factor) that inhibit ovarian steroid production. Thus, there was only a slight level of estrogen in obese women, and this led to the development of severe VMS. One other study of women aged 47–59 years demonstrated that a greater percentage of body fat was significantly associated with reporting of VMS.⁴ A possible explanation for this may be that when the body's adipose tissue volume was increased, it provided a higher level of insulation, that was followed by higher body temperature and increasing VMS. In other words, aromatization was suppressed from high body temperature.⁴ Another study of perimenopausal women aged 42–52 years examined the relationship between VMS and several factors, including hormone level measurement. The result showed that VMS was more common in women with high BMI.⁵ There was no increase in estrogen level in obese women while increasing body fat provided more insulation which would increase core body temperature and thus might increase in hot flushes, and prevent aromatization in adipose tissue. A randomized trial in women aged 40–65 years showed that perimenopausal women with a BMI ≥ 25 kg/m² were more likely to report hot flushes than women with a BMI < 25 kg/m² (OR: 2.00, 95% CI 1.28–3.12).²³ However, BMI was not associated with hot flushes in postmenopausal women. Some later studies reported similar results that obesity is associated with higher VMS prevalence during the midlife.^{24–28}

Interestingly, some studies reported no association between BMI and VMS in postmenopausal women.^{15,16} On the contrary, a cohort study of both premenopausal and postmenopausal women reported that the median duration of moderate to severe VMS was 10.2 years. That study also found that thinner women had longer duration of VMS than heavier weight women (BMI > 30 kg/m², $p = 0.003$).⁶ That group postulated that women with heavier weight have higher estradiol levels than thinner women. Another later cross-sectional study of natural menopause women aged 40–60 years in factors related to VMS reported that thin and smoking women during the premenopausal period were more likely to experience VMS than obese women ($p = 0.03$). However, from that study only BMI could not be the only factor that affected VMS.¹¹

The results of this study showed results different from many previous studies. Perception of VMS may vary among ethnicities and countries, and the structured questions used to evaluate VMS may vary among studies. The design of the study (cross-sectional vs. cohort) and subject selection (perimenopausal vs. postmenopausal) may also affect the result since VMS may be perceived mostly during the perimenopausal period.

Limitation

VMS is subjective, self-reported, and there is no standard for measuring the level of VMS in individuals. Different patients perceive different levels of VMS. In other words, an individual's perception of VMS may not be estimated as the same level between reports, which makes it difficult to compare the level of symptoms. In order to answer our questionnaire, patients had to recall their recent symptoms during their first visit to our menopause clinic.

CONCLUSION

In this study population, Thai menopausal women with a normal BMI were significantly more likely to report moderate-to-severe VMS than postmenopausal women with higher BMI. This finding supports the hypothesis that heavier Thai women may have a higher level of estrogen due to aromatization in adipose tissue. These results suggest the need for more careful screening of under or normal weight women for VMS during menopause.

ACKNOWLEDGMENTS

We would like to thank Ms. Julaporn Pooliam, statistician, for statistical analyzed and Ms. Chongdee Dangrat, scientist, for cases collected. This research was supported by a Siriraj Grant for Research and Development (grant no. R015531024).

REFERENCES

1. Delavar MA, Hajiahmadi M. Age at menopause and measuring symptoms at midlife in a community in Babol, Iran. *Menopause* 2011;18:1213–8.
2. Fallahzadeh H. Age at natural menopause in Yazd, Islamic Republic of Iran. *Menopause* 2007;14:900–4.
3. Nelson DB, Sammel MD, Patterson F, Lin H, Gracia CR, Freeman EW. Effects of reproductive history on symptoms of menopause: a brief report. *Menopause* 2011;18:1143–8.
4. Thurston RC, Sowers MR, Chang Y, Sternfeld B, Gold EB, Johnston JM, 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.
5. Gold EB, Block G, Crawford S, Lachance L, FitzGerald G, Miracle H, et al. Lifestyle and demographic factors in relation

- to vasomotor symptoms: baseline results from the Study of Women's Health Across the Nation. *Am J Epidemiol* 2004;159: 1189-99.
6. Freeman EW, Sammel MD, Lin H, Liu Z, Gracia CR. Duration of menopausal hot flushes and associated risk factors. *Obstet Gynecol* 2011;117:1095-104.
 7. Whiteman MK, Staropoli CA, Langenberg PW, McCarter RJ, Kjerulff KH, Flaws JA. Smoking, body mass, and hot flashes in midlife women. *Obstet Gynecol* 2003;101:264-72.
 8. Borelli F, Earnst E. Black cohosh (*Cimicifuga racemosa*) for menopausal symptoms: a systematic review of its efficacy. *Pharmacol Res* 2008;58:8-14.
 9. Berek JS, Novak E. Berek & Novak's gynecology. 14th ed. Philadelphia, Penn.: Lippincott Williams & Wilkins; 2007.
 10. Campagnoli C, Morra G, Belforte P, Belforte L, Prelato Tousijn L. Climacteric symptoms according to body weight in women of different socio-economic groups. *Maturitas* 1981;3:279-87.
 11. Schwingl PJ, Hulka BS, Harlow SD. Risk factors for menopausal hot flashes. *Obstet Gynecol* 1994;84:29-34.
 12. Gold EB, Sternfeld B, Kelsey JL, Brown C, Mouton C, Reame N, et al. Relation of demographic and lifestyle factors to symptoms in a multi-racial/ethnic population of women 40-50 years of age. *Am J Epidemiol* 2000;17:718-26.
 13. Fernandez-Alonso AM, Caudros JL, Cherdraui P, Mendoza M, Caudros AM, Perez-Lopez FE. Obesity is related to increased menopausal symptoms among Spanish women. *Menopause Int* 2010;16:105-10.
 14. Whiteman MK, Staropoli CA, Langenberg P, McCarter RJ, Kjerulff KH, Flawa JA. Smoking, body mass, and hot flashes in midlife women. *Obstet Gynecol* 2003;101:264-72.
 15. Sabia S, Fournier A, Mesrine S, Boutron-Ruault MC, Clavel-Chapelon F. Risk factors for onset of menopausal symptoms: results from a large cohort study. *Maturitas* 2008;60:108-21.
 16. Thurston RC, Santoro N, Matthews KA. Adiposity and hot flashes in midlife women: a modifying role of age. *J Clin Endocrinol Metab* 2011;96:E1588-E1595.
 17. Heinemann LA, DoMinh T, Strelow F, Gerbsch S, Schnitker J, Schneider HP. The Menopause Rating Scale (MRS) as outcome measure for hormone treatment? A validation study. *Health Qual Life Outcomes* 2004;2:67.
 18. Dinger J, Zimmermann T, Heinemann LA, Stoeck D. Quality of life and hormone use: new validation results of MRS scale. *Health Qual Life Outcomes* 2006;4:32.
 19. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;363(9403):157-63.
 20. Randolph JF Jr, Sheng H, Sowers MR, Crandall C, Crawford S, Gold EB, et al. Change in follicular-stimulating hormone and estradiol across the menopausal transition.: Effect of age at the final menstrual period. *J Clin Endocrinol Metab* 2011;96: 746-54.
 21. Freeman EW, Sammel MD, Lin H, Gracia CR. Obesity and reproductive hormone levels in the transition to menopause. *Menopause* 2010;17:718-26.
 22. Erlik Y, Meldrum DR, Judd HL. Estrogen levels in postmenopausal women with hot flashes. *Obstet Gynecol* 1982;59:403-7.
 23. Hyde Riley E, Inui TS, Kleinman K, Connelly MT. Differential association of modifiable health behaviors with hot flashes in perimenopausal and postmenopausal women. *J Gen Intern Med* 2004;19:740-6.
 24. Galicchio L, Visvanathan K, Miller SR, Babus J, Lewis LM, Zacur H, et al. Body mass, estrogen levels, and hot flashes in midlife women. *Am J Obstet Gynecol* 2005;193:1353-60.
 25. Kumari M, Stafford M, Marmot M. The menopausal transition was associated in a prospective study with decreased health functioning in women who report menopausal symptoms. *J Clin Epidemiol* 2005;58:719-27.
 26. Gold EB, Colvin A, Avis N, Boomerger J, Greendale GA, Powell L, 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;96:1226-35.
 27. Thurston RC, Sowers MR, Sutton-Tyrrell K, Everson-Rose SA, Lewis TT, Edmundowicz D, et al. Abdominal obesity and hot flashes among midlife women. *Menopause* 2008;15:429-34.
 28. Thurston RC, Chang Y, Mancuso P, Matthews KA. Adipokines, adiposity, and vasomotor symptoms during the menopause transition: findings from the Study of Women's Health Across the Nation. *Fertil Steril* 2013;100:793-800.