Change in Body Mass Index, Weight, and Hot Flashes: A Longitudinal Analysis from the Midlife Women's Health Study

Lisa Gallicchio, PhD,¹⁻³ Susan R. Miller, ScD,⁴ Judith Kiefer, MS, RN,⁴ Teresa Greene,⁴
Howard A. Zacur, MD, PhD,⁴ and Jodi A. Flaws, PhD⁵

Abstract

Background: The goals of this study were to examine the associations between body mass index (BMI), as well as BMI change and weight change, with midlife hot flashes.

Methods: Data were analyzed from an ongoing 5-year cohort study of 631 midlife women (ages 45–54 years) recruited from Baltimore, Maryland, and its surrounding counties. Height and weight were measured at clinic visits conducted annually. Questionnaires administered at each clinic visit collected detailed data on hot flashes, including the severity and frequency, and other covariates. Data were analyzed using logistic regression and generalized estimated equation models, adjusting for potential confounders.

Results: Among women enrolled in the study, 45.2% reported hot flashes and 32.0% were categorized as being obese (BMI ≥ 30 kg/m²) at baseline. At baseline, BMI was not significantly associated with ever experiencing hot flashes (BMI ≥ 30 versus < 25 kg/m²: odds ratio [OR] 0.92; 95% confidence interval [CI]: 0.58, 1.15) or any of the other hot flashes outcomes (recent, frequent, or severe). In addition, no statistically significant associations between BMI, BMI change, or weight change, and the hot flash outcomes were observed in the longitudinal models (for example, any hot flashes: BMI ≥ 30 versus < 25 kg/m²: OR 0.81; 95% CI: 0.56, 1.17).

Conclusion: BMI, BMI change, and weight change during midlife were not related to hot flashes in this study. The data suggest that other factors, such as smoking habits, are more important in determining hot flashes risk during midlife.

Introduction

HOT FLASHES ARE THE MOST PREVALENT SYMPTOM experienced by women undergoing the menopausal transition.¹ Hot flashes are described as transient periods of intense heat in the upper body, arms, and face that are often followed by flushing of the skin and profuse sweating.² Hot flashes can be extremely bothersome, affecting a woman's quality of life,³ work performance,³ mood,⁴ and sleep.^{5,6} Recent evidence also suggests that hot flashes may be associated with more severe health conditions, including cardiovascular disease.^{7,8}

Epidemiologic studies have consistently shown that obesity is a risk factor for midlife hot flashes.^{1,9-14} This observation refutes the hypothesis initially proposed by researchers—

the “thin hypothesis”—which states that women with a greater amount of body fat have more circulating estrogens than thin women because androgens are converted to estrogens in body fat, and thus they are at decreased risk for hot flashes.¹⁵ The finding that obese women are more likely to report hot flashes than thinner women is, in fact, consistent with a thermoregulatory model in which body fat acts as an insulator and inhibits heat dissipation, thus increasing the likelihood of a woman experiencing a hot flash.¹⁶

Research on the association between obesity and hot flashes has primarily been cross-sectional in nature; however, recent longitudinal studies have confirmed findings from the cross-sectional studies, showing that body mass index (BMI) is associated with hot flashes over time^{1,14} and that gains in

¹The Prevention and Research Center, The Weinberg Center for Women's Health and Medicine, Mercy Medical Center, Baltimore, Maryland.

²Department of Epidemiology and Public Health, University of Maryland, Baltimore, Baltimore, Maryland.

³Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland.

⁴Johns Hopkins University School of Medicine, Baltimore, Maryland.

⁵Department of Comparative Biosciences, University of Illinois, Urbana, Illinois.

body fat over two time points during midlife are associated with a higher likelihood of reporting menopausal symptoms.¹⁷ These associations were reported to be statistically significant even after adjustment for hormone concentrations such as estradiol and follicle-stimulating hormone¹⁷ and other potential confounders such as smoking and race.^{1,14,17}

The overall goal of this study was to examine obesity, assessed using a woman's BMI, and risk of hot flashes using data from an ongoing 5-year cohort study of 631 midlife women recruited in Baltimore, Maryland, and the surrounding counties. Height and weight were measured at a yearly clinic visit and hot flash data were collected by taking a detailed history at each time point, which was not done in the previous longitudinal studies because they were not developed specifically to look at the endpoint of hot flashes.^{1,14,17} A secondary goal of this analysis was to examine weight change over the study period and hot flashes.

Materials and Methods

Study sample

A cohort study of hot flashes among midlife women (45–54 years of age) was conducted among residents of the Baltimore metropolitan region, which includes Baltimore city and its surrounding counties. Recruitment for the cohort began in 2006. All participants gave written informed consent according to procedures approved by the University of Illinois and Johns Hopkins University Institutional Review Boards.

Names and addresses of women in the selected age range were obtained from a commercial mailing house that compiles names from public sources. Recruitment letters were mailed to all names on this list. Women who were interested in participating in this study, which was presented as a general "Midlife Health Study" to avoid reporting bias, were invited to call the clinic to obtain more information. During a call, the clinic staff determined whether the woman met the eligibility criteria. Women were eligible if they were between 45 and 54 years of age, had intact ovaries and uteri, and were either pre- or perimenopausal. Women were excluded if they were pregnant, had a history of cancer, or were postmenopausal. Women were also excluded if they were taking exogenous female hormones or herbal or plant substances to enable studying risk factors for hot flashes without the confounding effects of known treatments for hot flashes. Menopausal status was defined as follows: premenopausal women were those who experienced their last menstrual period within the past 3 months and reported 11 or more periods within the past year. Perimenopausal women were those who experienced: 1) their last menstrual period within the past year but not within the past 3 months or 2) their last menstrual period within the past 3 months and experienced 10 or fewer periods within the past year. Postmenopausal women were those women who had not experienced a menstrual period within the past year.

If a woman was eligible and interested in participating in the study, she was asked to make a clinic visit (the baseline visit) to a Johns Hopkins clinical site. During this baseline clinic visit, the participant completed the detailed 26-page baseline study survey, donated blood and urine samples, was weighed and measured (height), had her blood pressure measured, and received a transvaginal ultrasound to measure ovarian volume. Each participant was then asked to visit the

clinic once a week for the 3 weeks following the baseline visit so that the study staff could obtain additional blood and urine samples. Women also completed a brief questionnaire at the last of the three weekly visits following the baseline visit. These four consecutive weekly clinic visits were then repeated on a yearly basis throughout the woman's participation in the study. The first visit during each of the follow-up years was similar to the baseline visit, described above. The remaining three visits were for collection of specimens and for administration of the brief questionnaire (final weekly visit of each year only). If a woman missed a single visit or a year of visits, she was still asked to remain in the study and data from those visits were considered missing. Only data for the baseline clinic visit and the first yearly visit for each follow-up year over the woman's participation in the study were analyzed in this study.

Through February 2013, 634 women were enrolled in the study; 632 completed the baseline (year 1) clinic visit and the baseline questionnaire. As of July 2012, these 632 women had been followed for 1 to 5 years depending on their date of enrollment and whether they returned for annual follow-up visits for their years 2 through 4. A small percentage (5.5%) of the participants in the cohort dropped out after the first year of participation, and approximately 3% dropped out after each subsequent year of participation (years 2–4). Some reasons for drop out included lack of time or a medical condition. A total of three participants died during the follow-up time period. The deaths were not related to the study protocol. The decision was also made to stop follow-up of women if they reported that they were on hormone therapy ($n=17$), had an oophorectomy ($n=13$), or were diagnosed with cancer ($n=9$). Follow-up was also discontinued for women who were determined to be postmenopausal at the year four visit ($n=64$). Thus, of the 632 women enrolled in the cohort with data at their baseline (year 1) visit, 423 were being actively followed as of March 1, 2013. For this analysis, one woman was excluded because she was determined at baseline to have premature ovarian failure. Thus, the present analysis includes year 1 through year 4 data for 631 women with at least baseline data (445 had year 2 data, 330 had year 3 data, 195 had year 4 data). To note, not all 631 women included in the analysis had reached year 3 and year 4 of follow-up at the time of this analysis.

Variable definitions

On the study questionnaires, hot flashes were defined for participants as "a sudden feeling of heat in the face, neck, or upper part of the chest. Hot flashes are often accompanied by reddening or flushing of the skin followed by sweating and chills." At baseline, a detailed hot flash history was obtained through a series of questions on the survey that asked for information on the following: whether the woman had ever experienced hot flashes, the age at which she first experienced hot flashes, whether she had a hot flash in the past 30 days, the number of hot flashes in the past 30 days, the usual severity of hot flashes, and the frequency of hot flashes. On all subsequent questionnaires that the participant completed, she was asked whether she had experienced hot flashes since her last clinic visit and, if she responded yes, she was further queried regarding the number of hot flashes in the past 30 days as well as the usual severity and frequency of those hot flashes. Women who responded no to experiencing hot flashes since

their last clinic visit were prompted to skip the more detailed hot flash questions. The hot flashes questions chosen for inclusion on the questionnaires have been used to collect data on hot flashes in the Midlife Health Studies for over 10 years.

In terms of severity, each woman was asked to describe her hot flashes as mild (sensation of heat without sweating), moderate (sensation of heat with sweating), or severe (sensation of heat with sweating that disrupts usual activity). In terms of frequency of hot flashes, each woman was asked to describe her hot flashes as occurring: every hour, every 2–5 hours, every 6–11 hours, every 12–23 hours, 1–2 days per week, 2–4 days per week, 5–6 days per week, 2–3 days per month, 1 day per month, less than 1 day per month, or never. For analysis of the baseline data, the following hot flash variables were examined as dependent variables (outcomes): ever experienced hot flashes (yes versus no); experienced any hot flashes in the past 30 days (yes versus no); moderate or severe hot flashes (yes versus no); and weekly or daily hot flashes (yes versus no). For the longitudinal analysis, hot flash outcomes were the following: experienced any hot flashes in the past 30 days (yes versus no); moderate or severe hot flashes (yes versus no); and weekly or daily hot flashes (yes versus no).

Height and weight measured at each clinic visit were used to calculate BMI, which was categorized as less than 25 kg/m², 25–29.9 kg/m², and 30 kg/m² or greater. In this analysis, BMI and weight were analyzed in a number of ways so that the results could be compared to the findings of previously published studies on this topic (e.g., Whiteman et al.,¹⁰ Kroenke et al.,¹⁸ Van Poppel and Brown,¹⁹ Gold et al.¹). BMI change between visits was analyzed in terms of absolute change in BMI (in kg/m²) and percentage change. Categories of absolute BMI change were BMI loss, defined as a loss of more than 0.5 kg/m²; stable BMI, defined as a loss of 0.5 kg/m² or less or a gain of no more than 0.5 kg/m²; and BMI gain, defined as a gain of more than 0.5 kg/m². Categories of percentage BMI change were BMI loss, a loss of more than 1% of BMI; stable BMI, a loss of 1% of BMI or less or a gain of no more than 1% of BMI; and BMI gain, a gain of more than 1%.

Similarly, weight change between visits was analyzed in terms of absolute change in weight (in pounds) and percentage change. Categories of absolute weight change were weight loss, defined as a loss of more than 10 pounds; stable weight, defined as a loss of 10 pounds or less or a gain of no more than 10 pounds; and weight gain, defined as a gain of more than 10 pounds. Categories of percentage weight change were weight loss, a loss of more than 5% of weight; stable weight, a loss of 5% of weight or less or a gain of no more than 5% of weight; and weight gain, a gain of more than 5%. Weight change since age 18 was based on the woman's self-reported weight at 18 and calculated by subtracting weight at age 18 with measured weight at baseline. These data were categorized as less than 10 pounds, 10 to less than 30 pounds, 30 to less than 60 pounds, and 60 pounds or more.

Smoking status at each visit was categorized as current, former, and never using the questions: "Have you ever smoked cigarettes?" and "Do you still smoke cigarettes?" Current alcohol use at each visit was assessed using the question "In the last 12 months, have you had at least 12 drinks of any kind of alcohol beverage?" and was analyzed as a yes versus no variable. Data on race, marital status, and education were collected at baseline (year 1) only. In addition, information on leisure time walking habits at baseline was

collected to reflect physical activity by asking the participant the frequency with which she walks at leisure time: always, often, sometimes, seldom, and never.

Statistical analyses

Differences in baseline demographic and health habit characteristics by baseline hot flash status (ever versus never) and the baseline categorical independent variables (BMI and weight change since age 18) were examined using chi-square tests for categorical variables and Student's *t*-tests or analysis of variance (ANOVA) tests for continuous variables. To analyze the baseline data, odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using logistic regression models adjusting for potential confounders. Variables included as potential confounders in the models were those that were associated with baseline hot flash status (ever versus never) and the three category BMI variable (or the weight change since age 18 years) at $p < 0.05$. Data were collected at baseline for the following variables, which were examined as potential confounders: age, marital status, education, race, smoking status, current alcohol use, frequency of leisure time walking per day, menopausal status, and past hormone therapy use. Only age, education, smoking status, and menopausal status were included in the confounder-adjusted logistic regression models.

The longitudinal data were analyzed using a generalized estimated equation model with a first-order autoregressive covariance matrix, a logit link, and a binary outcome distribution. Generalized estimated equation models take into account the nonindependence of data collected over time from the same participants. Models were adjusted for variables identified as potential confounders in the baseline analysis (age, education, smoking status, and menopausal status) as well as race, which has been shown to be associated with the hot flash experience during the menopausal transition in the published literature.²⁰ The time-dependent covariates entered into the model were age, smoking status, and menopausal status; data on education and race were those collected at baseline. Menopausal status at baseline was also examined as a potential effect modifier in all analysis prior to its inclusion into the models as a potential confounder, but it did not modify the association between obesity and hot flashes, and thus no stratified analyses are presented.

Analyses were performed with SAS, version 9.2 (SAS Institute, Inc., Cary, NC). A two-sided *p*-value of less than 0.05 was considered statistically significant.

Results

Women reporting at baseline that they had ever experienced hot flashes were more likely than those not experiencing hot flashes to be of older age, current or former smokers, and perimenopausal (Table 1). Women reporting hot flashes were significantly less likely than their counterparts to have graduated college or have had some graduate level training. The two groups did not differ significantly by marital status, race, current alcohol status, physical activity, or use of antidepressants. Among women who had ever experienced hot flashes, 72.6% reported hot flashes within the past 30 days, 63.9% reported that their hot flashes were usually moderate or severe, and 48.4% reported that they experienced hot flashes either weekly or daily.

TABLE 1. SAMPLE CHARACTERISTICS BY HOT FLASH STATUS AT BASELINE (N=631)

Characteristics	Hot flashes (n=285)		No hot flashes (n=346)		p-value
	n	%	n	%	
Age group, years					<0.0001
45–49	148	51.9	261	75.4	
50–54	137	48.1	85	24.6	
Mean (SD)	49.1 (2.4)		47.8 (2.2)		<0.0001
Marital status					0.2
Single	45	15.8	68	19.7	
Married or living with partner	196	68.8	212	61.3	
Widowed, divorced, or separated	44	15.4	63	18.2	
Education group					0.002
Less than college	41	14.4	22	6.4	
Some college or tech school	79	27.7	83	24.0	
Graduated college or tech school	78	27.4	102	29.5	
Graduate level	86	30.2	136	39.9	
Race					0.3
White	183	64.2	241	69.7	
Black	90	31.6	90	26.0	
Other	12	4.2	13	3.8	
Smoking status					0.0005
Current	38	13.3	22	6.4	
Former	117	41.1	118	34.1	
Never	129	45.3	203	58.7	
Current alcohol drinker					0.07
Yes	176	61.8	237	68.5	
No	108	37.9	107	30.9	
During leisure time I walk					0.5
Seldom or never	53	18.6	51	14.7	
Sometimes	124	43.5	157	45.4	
Always or often	107	37.5	134	38.7	
Menopausal status					<0.0001
Premenopausal	127	44.6	290	83.8	
Perimenopausal	158	55.4	56	16.2	
Use of antidepressant medication					0.3
Yes	37	13.0	36	10.4	
No	246	86.3	309	89.3	
Body mass index, kg/m ²					0.6
<25	112	39.3	141	40.8	
25–29.9	76	26.7	100	28.9	
≥30	97	34.0	105	30.3	
Mean (SD)	28.7 (7.8)		27.9 (7.2)		0.2
Change in weight from age 18, pounds					0.07
<10	44	15.4	60	17.3	
10 to <30	69	24.2	108	31.2	
30 to <60	83	29.1	94	27.2	
≥60	87	30.5	78	22.5	
Mean (SD)	44.6 (37.7)		39.3 (37.0)		0.08
Hot flashes in the past 30 days	207	72.6			
Moderate or severe hot flashes	182	63.9			
Weekly or daily hot flashes	138	48.4			

Percentages for certain variables may not add up to 100% due to missing values.
SD, standard deviation.

The distribution of women across the baseline BMI categories did not differ by baseline hot flash status (Table 1); similarly, mean baseline BMI did not differ significantly between women with and without hot flashes (hot flashes = 28.7 kg/m²; no hot flashes = 27.9 kg/m²; $p=0.2$). In addition, women with and without hot flashes at baseline did not differ in terms of distribution across change in weight from age 18 categories (Table 1) or by mean change in weight from age 18 (hot flashes = 44.6 pounds; no hot flashes = 39.3 pounds; $p=0.1$).

Baseline BMI and weight change from 18 years of age were not significantly associated with any of the baseline hot flashes outcomes in either unadjusted (data not shown) or confounder-adjusted models (Table 2). In addition, no statistically significant associations between BMI, BMI change, or weight change, and the hot flashes outcomes were observed in either the unadjusted or adjusted longitudinal models (Table 3). Other variables that were consistently associated with the risk of the hot flash outcomes in the adjusted

TABLE 2. ASSOCIATIONS OF BODY MASS INDEX AND WEIGHT CHANGE FROM AGE 18 WITH HOT FLASH OUTCOMES AT BASELINE

	OR (95% CI) ^a			
	<i>Ever had hot flashes</i>	<i>Hot flashes in past 30 days</i>	<i>Weekly or daily hot flashes</i>	<i>Moderate or severe hot flashes</i>
Body mass index, kg/m ²				
<25	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
25–29.9	0.73 (0.58, 1.15)	0.82 (0.49, 1.37)	1.05 (0.57, 1.93)	0.83 (0.49, 1.40)
≥30	0.92 (0.53, 1.25)	0.96 (0.59, 1.56)	0.81 (0.44, 1.48)	0.97 (0.59, 1.60)
Body mass index, kg/m ² (continuous)	0.99 (0.97, 1.02)	0.99 (0.97, 1.02)	0.98 (0.94, 1.01)	1.01 (0.98, 1.03)
Weight change from age 18 years, pounds				
<10	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
10 to <30	0.99 (0.57, 1.72)	0.80 (0.42, 1.50)	0.74 (0.34, 1.59)	0.86 (0.45, 1.64)
30 to <60	1.13 (0.65, 1.97)	0.99 (0.53, 1.87)	0.98 (0.46, 2.10)	0.90 (0.47, 1.74)
≥60	1.13 (0.64, 1.99)	0.97 (0.51, 1.83)	0.62 (0.28, 1.37)	1.05 (0.55, 2.01)

^aAdjusted for age (≥50 years, <50 years); smoking status (current, former, never); menopausal status (premenopausal, perimenopausal); education (college graduate versus high school only or some college).

OR, odds ratio; 95% CI, 95% confidence interval.

longitudinal models were smoking, race, and menopausal status (data not shown). Specifically, current smokers, black women, and peri- and postmenopausal women were at increased risk of any, more severe, and more frequent hot flashes compared to their counterparts (never smokers, white women, and premenopausal women).

Discussion

Findings from this study suggest that higher BMI does not increase a woman's risk of midlife hot flashes. These results are

at odds with several published studies that have shown that BMI and body fat are positively associated with the occurrence of hot flashes among women undergoing the menopausal transition.^{9,12,17,21–25} However, our results are similar to some published studies suggesting that BMI is not associated with hot flashes or that it is inversely associated with hot flashes among postmenopausal, or older, women.^{10,26–28} The reasons for the discrepant findings on BMI and hot flashes are unclear. Our sample is similar to those of studies reporting a positive association in that all of the women in our study were pre- or perimenopausal at baseline and less than 16%

TABLE 3. UNADJUSTED AND ADJUSTED ODDS RATIOS (OR [95% CI]) FOR THE ASSOCIATIONS OF BODY MASS INDEX AND OTHER COVARIATES WITH HOT FLASH OUTCOMES OVER TIME

	<i>Any hot flashes</i>		<i>Moderate or severe hot flashes</i>		<i>Weekly or daily hot flashes</i>	
	<i>Unadjusted</i>	<i>Covariate-adjusted^a</i>	<i>Unadjusted</i>	<i>Covariate-adjusted^a</i>	<i>Unadjusted</i>	<i>Covariate-adjusted^a</i>
Body mass index, kg/m ²						
<25	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
25–29.9	0.98 (0.73, 1.32)	0.73 (0.58, 1.11)	1.10 (0.80, 1.50)	0.92 (0.66, 1.28)	1.32 (0.91, 1.93)	1.19 (0.79, 1.78)
≥30	1.19 (0.88, 1.61)	0.81 (0.56, 1.17)	1.31 (0.94, 1.84)	0.95 (0.65, 1.38)	1.38 (0.96, 1.98)	0.94 (0.62, 1.43)
BMI change, ^b kg/m ²						
Stable	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Loss, >0.5	1.07 (0.79, 1.36)	0.95 (0.70, 1.28)	1.07 (0.79, 1.47)	0.99 (0.70, 1.40)	0.89 (0.57, 1.38)	0.77 (0.48, 1.24)
Gain, >0.5	1.00 (0.79, 1.26)	0.86 (0.66, 1.12)	1.07 (0.80, 1.44)	0.98 (0.71, 1.37)	1.06 (0.74, 1.51)	0.92 (0.62, 1.36)
BMI change, ^b %						
Stable	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Loss, >1%	1.11 (0.85, 1.46)	1.06 (0.78, 1.44)	0.91 (0.65, 1.28)	0.88 (0.61, 1.28)	1.00 (0.62, 1.63)	0.94 (0.55, 1.57)
Gain, >1%	1.09 (0.84, 1.42)	1.01 (0.75, 1.35)	0.99 (0.73, 1.34)	0.97 (0.69, 1.36)	1.05 (0.67, 1.65)	0.93 (0.57, 1.54)
Weight change, ^b pounds						
Stable	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Loss, >10 pounds	0.86 (0.61, 1.20)	0.79 (0.52, 1.22)	0.76 (0.50, 1.14)	0.72 (0.46, 1.14)	0.68 (0.32, 1.47)	0.66 (0.30, 1.45)
Gain, >10 pounds	0.92 (0.59, 1.46)	0.78 (0.46, 1.30)	1.37 (0.84, 2.24)	1.22 (0.71, 2.07)	1.04 (0.50, 2.17)	0.88 (0.42, 1.81)
Weight change, ^b %						
Stable	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Loss, >5%	1.06 (0.73, 1.54)	1.04 (0.67, 1.61)	0.87 (0.55, 1.37)	0.85 (0.52, 1.38)	0.59 (0.30, 1.15)	0.58 (0.30, 1.14)
Gain, >5%	1.11 (0.79, 1.57)	0.98 (0.65, 1.47)	1.14 (0.74, 1.76)	0.97 (0.61, 1.55)	1.12 (0.64, 1.94)	0.97 (0.56, 1.69)

^aAdjusted for age (≥50 years, <50 years); smoking status (current, former, never); education (college graduate versus high school only or some college); race (white, non-white); menopausal status (premenopausal, perimenopausal, postmenopausal).

^bIncludes only those women with data for two or more time points.

BMI, body mass index.

were postmenopausal at their last study visit. However, it is possible that the perimenopausal women in our cohort study were later in perimenopause than women in other similar studies of midlife women. While our study obtained information on whether the participants were premenopausal, perimenopausal, or postmenopausal, it is not possible to know from our data how early the participants were in each stage and how this compares with other studies. Thus, we can only speculate that reported differences in the association between BMI and hot flashes among studies are due to differences in where participants were in each stage of the menopausal transition. This speculation is supported by the recent work of Thurston et al.,¹⁴ which showed that associations between adipokines, adiposity, and hot flashes varied by menopausal stage, with hot flashes being associated with an adverse adipokine profile early, but not late, in the menopausal transition.

The results of this study also showed that neither BMI change nor weight change during the menopausal transition were significantly associated with the risk of hot flashes. It should be noted that there was, overall and unexpectedly, little weight or BMI change over the study period among the study sample. In previous studies, weight gain has been noted in women undergoing the menopausal transition.^{29–31} For example, Sternfeld et al.³² showed that, among women aged 40–55 years of age participating in the Study of Women's Health Across the Nation (SWAN), the mean change in weight over a 3-year study period was approximately 4.5 pounds (an average of a 3% increase); in contrast, we found a mean change of 0.4 pounds from baseline to year 3 (an average of a 0% increase). Thus, the lack of variability across time may have resulted in an inability to observe statistically significant associations between larger weight or BMI losses and gains and the hot flash outcomes. Nonetheless, our findings pertaining to BMI and weight change and hot flashes is in contrast with the results published by Van Poppel and Brown,¹⁹ which showed that among midlife women who participated in the Australian Longitudinal Study on Women's Health, weight gain, defined as an increase in weight of 5 kg or more over a 3-year time period, was associated with a statistically significant increase in the frequency of vasomotor symptoms. In addition, using data from the Women's Health Initiative, Kroenke et al.¹⁸ reported women who gained greater than 5 pounds from baseline to year 1 had higher odds of vasomotor symptoms at year 1 compared to those who maintained weight. Alternatively, weight loss was associated with an elimination of vasomotor symptoms over the same time period as well as a reduction in severity.

It is possible that it is the change in body composition that is more important in the development of midlife vasomotor symptoms than BMI or weight. Thurston et al.¹⁷ showed that midlife women (mean of age 52 years at baseline) participating in SWAN who gained body fat over 3 years had a statistically significant 24% increase in odds of any reported hot flashes compared to women whose body fat was stable over the same period of time. Authors of the Thurston et al.¹⁷ study suggest that it may be the acquisition of body fat that is more important than actual body fat and that fat gains may present a particular thermoregulatory challenge that may trigger more dramatic thermoregulatory compensation actions. Additional research in this area is needed to better understand the mechanisms behind the association between weight or body fat gain and midlife hot flashes.

A limitation of the present study is that data on body composition were not collected. Percentage of body fat and gains or losses over the menopausal transition may be more important in terms of experiencing hot flashes symptoms than BMI, especially if the thermoregulatory model explains previous findings regarding the positive association between BMI and hot flashes. If body fat is more important, it is possible that in the present study sample, BMI did not accurately reflect body composition, and therefore no associations between BMI and hot flashes were observed. A second limitation is that data on hot flashes were self-reported; however, research has shown self-report of hot flashes to be a valid measure of the hot flash experience.³³ Finally, there were few women that were of races other than black and white; therefore, the results of this study may not be generalizable to women of other races undergoing the menopausal transition.

There are several notable strengths of the present study that should be mentioned. First, the present study was designed specifically to look at BMI and hot flashes, and detailed data on hot flashes, including frequency and severity, at each study visit were collected and used in the analysis. In contrast, many of the previous studies have based their hot flash outcome on only one question; for example, in SWAN, women were asked the number of hot flashes experienced in the preceding 2 weeks and data were analyzed based on whether women reported or did not report hot flashes or the frequency at which hot flashes were experienced over those 2 weeks.^{1,17} Second, this study is one of the few to examine BMI and weight in relation to hot flashes longitudinally, assessing associations over the menopausal transition.^{1,17,19} This is important in making statements about the temporality of the relationship between BMI, weight change, and experiencing of hot flashes. Finally, data on known risk factors for hot flashes, such as cigarette smoking, race, and alcohol drinking habits, were collected in this study and used in the analysis. It should be noted that, similar to previously published studies on this topic,^{10,34} current cigarette smoking was strongly associated with hot flashes (data not shown), indicating that the data are internally valid. Inclusion of these hot flash risk factor variables in the analysis is important because they may confound the associations examined in this study.

Conclusions

The results of this study suggest that BMI, BMI change, and weight change during midlife are not related to hot flashes. The data suggest that other factors, such as smoking habits, are more important in determining hot flashes risk during midlife.

Acknowledgments

This study was supported by the National Institute on Aging (RO1 AG18400).

Author Disclosure Statement

No competing financial interests exist.

References

1. 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.

2. Kronenberg F, Downey JA. Thermoregulatory physiology of menopausal hot flashes: a review. *Can J Physiol Pharmacol* 1987;65:1312–1324.
3. Williams RE, Levine KB, Kalilani L, Lewis J, Clark RV. Menopause-specific questionnaire assessment in US population-based study shows negative impact on health-related quality of life. *Maturitas* 2009;62:153–159.
4. Gibson CJ, Thurston RC, Bromberger JT, Kamarck T, Matthews KA. Negative affect and vasomotor symptoms in the Study of Women's Health Across the Nation Daily Hormone Study. *Menopause* 2011;18:1270–1277.
5. Xu H, Thurston RC, Matthews KA, et al. Are hot flashes associated with sleep disturbance during midlife? Results from the STRIDE cohort study. *Maturitas* 2012;71:34–38.
6. Thurston RC, Santoro N, Matthews KA. Are vasomotor symptoms associated with sleep characteristics among symptomatic midlife women? Comparisons of self-report and objective measures. *Menopause* 2012;19:742–748.
7. Thurston RC, Sutton-Tyrrell K, Everson-Rose SA, Hess R, Powell LH, Matthews KA. Hot flashes and carotid intima media thickness among midlife women. *Menopause* 2011;18:352–358.
8. Ozkaya E, Cakir E, Kara F, et al. Impact of hot flashes and night sweats on carotid intima-media thickness and bone mineral density among postmenopausal women. *Int J Gynaecol Obstet* 2011;113:235–238.
9. Gallicchio L, Visvanathan K, Miller SR, et al. Body mass, estrogen levels, and hot flashes in midlife women. *Am J Obstet Gynecol* 2005;193:1353–1360.
10. Whiteman MK, Staropoli CA, Langenberg P, McCarter RJ, Kjerulff KH, Flaws JA. Smoking, body mass, and hot flashes in midlife women. *Obstet Gynecol* 2003;101:264–272.
11. Thurston RC, Sowers MR, Sutton-Tyrrell K, et al. Abdominal adiposity and hot flashes among midlife women. *Menopause* 2008;15:429–434.
12. Thurston RC, Sowers MR, 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.
13. Li C, Samsioe G, Borgfeldt C, Lidfeldt J, Agardh CD, Nerbland C. Menopause-related symptoms: what are the background factors? A prospective population-based cohort study of Swedish women (The Women's Health in Lund Area study). *Am J Obstet Gynecol* 2003;189:1646–1653.
14. 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.
15. Erlik Y, Meldrum DR, Judd HL. Estrogen levels in postmenopausal women with hot flashes. *Obstet Gynecol* 1982;59:403–407.
16. Freedman RR. Physiology of hot flashes. *Am J Hum Biol* 2001;13:453–464.
17. Thurston RC, Sowers MR, Sternfeld B, et al. Gains in body fat and vasomotor symptom reporting over the menopausal transition: the study of women's health across the nation. *Am J Epidemiol* 2009;170:766–774.
18. Kroenke CH, Caan BJ, Stefanick ML, et al. Effects of a dietary intervention and weight change on vasomotor symptoms in the Women's Health Initiative. *Menopause* 2012;19:980–988.
19. Van Poppel MN, Brown WJ. "It's my hormones, doctor"—does physical activity help with menopausal symptoms? *Menopause* 2008;15:78–85.
20. Miller SR, Gallicchio LM, Lewis LM, et al. Association between race and hot flashes in midlife women. *Maturitas* 2006;54:260–269.
21. Ho SC, Gaen CS, Bing YY, Yee CS, Sham A. Factors associated with menopausal symptom reporting in Chinese midlife women. *Maturitas* 2003;44:149–156.
22. Freeman EW, Sammel MD, Grisso JA, Battistini M, Garcia-España B, Hollander L. Hot flashes in the late reproductive years: risk factors for African American and Caucasian women. *J Womens Health Gend Based Med* 2001;10:67–76.
23. Gold EB, Block G, Crawford S, 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;159:1189–1199.
24. 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;58:719–727.
25. Ford K, Sowers M, Crutchfield M, Wilson A, Jannausch M. A longitudinal study of the predictors of prevalence and severity of symptoms commonly associated with menopause. *Menopause* 2005;12:308–317.
26. den Tonkelaar I, Seidell JC, van Noord PAH. Obesity and fat distribution in relation to hot flashes in Dutch women from the DOM-project. *Maturitas* 1996;23:301–305.
27. 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.
28. 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;60:108–121.
29. Sternfeld B, Wang H, Quesenberry CP Jr, et al. Physical activity and changes in weight and waist circumference in midlife women: findings from the Study of Women's Health Across the Nation. *Am J Epidemiol* 2004;160:912–922.
30. Wing RR, Matthews KA, Kuller LH, Meilahn EN, Plantinga PL. Weight gain at the time of menopause. *Arch Intern Med* 1991;151:97–102.
31. Guthrie JR, Dennerstein L, Dudley EC. Weight gain and the menopause: a 5-year prospective study. *Climacteric* 1999;2:205–211.
32. Sternfeld B, Quesenberry CP Jr, Husson G. Habitual physical activity and menopausal symptoms: a case-control study. *J Womens Health* 1999;8:115–123.
33. Miller HG, Li RM. Measuring hot flashes: summary of a National Institutes of Health workshop. *Mayo Clin Proc* 2004;79:777–781.
34. Gallicchio L, Miller SR, Visvanathan K, et al. Cigarette smoking, estrogen levels, and hot flashes in midlife women. *Maturitas* 2006;53:133–143.

Address correspondence to:
Jodi A. Flaws, PhD

Department of Comparative Biosciences
University of Illinois
2001 S. Lincoln Avenue
Urbana, IL 61802

E-mail: jflaws@illinois.edu