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HOT FLASHES AND BLOOD PRESSURE IN MIDLIFE WOMEN

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Abstract

Objectives—Recent epidemiological studies suggest that hot flashes may have a detrimental impact on the cardiovascular system. The purpose of this study was to examine the associations between hot flashes and blood pressure among women aged 45 to 54 years who had never used hormone therapy.

Study Design—Data were analyzed from 603 women who participated in the Midlife Health Study, a cross-sectional study conducted in the Baltimore Metropolitan region.

Main Outcome Measures—All participants came to the clinic where systolic and diastolic blood pressure was measured, height and weight were assessed, and a questionnaire was administered that ascertained detailed data on history of hot flashes and participant demographics and health habits.

Results—The data showed that 56.9% of the participants reported ever experiencing hot flashes. In the age-adjusted analyses, both systolic and diastolic blood pressures were significantly and positively associated with hot flashes. However, the estimates were markedly attenuated and not statistically significant after adjustment for age, race, smoking status, current alcohol use, body mass index, and use of an anti-hypertensive agent or a cholesterol-lowering medication. Similar results were observed for moderate or severe hot flashes, hot flashes experienced for one or more years, and hot flashes experienced within the previous 30 days.

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CONTRIBUTORS AND THEIR ROLES

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The authors have no competing interests to declare.

ETHICAL APPROVAL

The work includes human subjects, which all provided informed consent. Further, the work was approved by the Institutional Review Boards at the University of Illinois and Johns Hopkins University.

Conclusions—These findings indicate that hot flashes are not significantly associated with blood pressure during midlife.

Keywords

Blood pressure; cardiovascular disease risk; hot flashes; midlife; menopause

1. INTRODUCTION

Hot flashes are commonly reported by women during the menopausal transition [1]. Numerous studies have reported that hot flashes are associated with a decrease in quality of life; this is thought to reflect the fact that hot flashes can cause physical discomfort as well as disturbed sleep, fatigue, irritability, and depression [1–3].

In addition to being associated with a decrease in quality of life, recent studies suggest that hot flashes may have a detrimental impact physiologically on the cardiovascular system. In a publication from the Study of Women's Health Across the Nation (SWAN) Heart Study, Thurston et al [4] showed that, compared to their counterparts, women with hot flashes had significantly reduced flow-mediated dilation and greater aortic calcification, indicating increased subclinical cardiovascular disease. Similarly, data from the Eindhoven Perimenopausal Osteoporosis Study (EPOS), a large screening program established in the Netherlands to assess determinants of low bone mineral density in perimenopausal women, showed that women with complaints of hot flashes had significantly higher mean cholesterol levels, body mass index (BMI), and diastolic blood pressure measurements compared to asymptomatic women [5]. However, several other recent publications suggest no difference in cardiovascular health [6,7] or even better cardiovascular function [8] among women with hot flashes compared to those without hot flashes.

The results of several more clinically-based studies support the recently reported positive findings of an association between hot flashes and cardiovascular disease, although the relationship between the short-term cardiovascular effects of hot flashes shown in the clinical studies and any long-term effects, such as those described in the SWAN and EPOS studies, is unknown. Gerber et al [9] showed that, compared with women who did not report hot flashes, mean awake and sleep systolic blood pressures, measured using an ambulatory blood pressure monitor for 24 consecutive hours, were significantly higher among women who reported experiencing hot flashes. These findings are consistent with those reported by James et al [10], which showed that mean systolic blood pressure, similarly measured using an ambulatory blood pressure monitor, was higher at work and during sleep among women who experienced hot flashes during the study period compared to women who were asymptomatic. Other clinic-based laboratory studies have shown no difference in mean blood pressure between women with and without hot flashes [11,12], or, in contrast to the studies described above, decreases in blood pressure during the experiencing of a hot flash [13,14]. The reasons for these contrasting results are not well understood, and, as stated above, it is not known whether these short-term blood pressure effects of hot flashes translate into long-term cardiovascular disease.

An important limitation of the published literature in both the population- and clinic-based studies assessing hot flashes and cardiovascular disease is the lack of a detailed history of hot flashes collected from participants. The published studies have used a single general question about hot flashes history ("Have you ever had hot flashes?") [6] or queries regarding the hot flash experience during a short time interval prior to the completion of the questionnaire [4, 5,7,9,10]. Understanding the relationship between a woman's entire history of midlife hot flashes, including severity, frequency, and duration, and cardiovascular health could have important implications in terms of the treatment of these common midlife symptoms. Thus, to

expand on the published literature, we examined blood pressure, a known cardiovascular risk factor, in relation to the midlife hot flash experience, assessed using a detailed survey that included information on the severity, frequency and duration of hot flashes. Towards this aim, data were analyzed from women participating in the Midlife Health Study, a large study of women aged 45 to 54 years living in the Baltimore metropolitan area. None of the participants had ever taken hormone therapy.

2. MATERIALS AND METHODS

2.1 Study sample

The Midlife Health Study is a large cross-sectional study of hot flashes and health among midlife women that was conducted during 2000 to 2004 among residents of the Baltimore metropolitan region. Detailed methods of this study have been published elsewhere [15,16]. All participants gave written informed consent according to procedures approved by the University of Maryland School of Medicine, University of Illinois, and Johns Hopkins University Institutional Review Boards.

Briefly, names and addresses of women aged 45 to 54 residing in Maryland were obtained from a commercial data clearinghouse (AccuData America; Fort Myers, Florida). Recruitment letters for the study were mailed to all names on this list, sent initially to women residing in zip codes nearest to the clinic and then in concentric circles to women residing farther from the site. Women who received mailings and 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. The Midlife Health Study was a single site study.

During this initial call, the clinic staff determined whether the potential participant met the eligibility criteria. Women were eligible for study participation if they were between 45 and 54 years of age and had an intact uterus and ovaries. In addition, to ensure that women enrolled in the study were not post-menopausal, women were eligible only if they reported having at least 3 menstrual periods in the last 12 months. Women were excluded if they were pregnant, were taking hormone replacement therapy or hormonal contraception, or had a history of cancer of the reproductive organs. If the clinic staff determined that the potential participant met the eligibility criteria, a clinic visit was scheduled.

At the clinic visit, women completed a 26-page, single-sided survey which ascertained data on demographic characteristics, reproductive history and menstrual cycle characteristics, hormonal contraceptive use, menopausal symptoms (including hot flashes), hormone replacement therapy use, medical and family history, and health behaviors (smoking, alcohol use, vitamin use, eating habits). In addition, the staff recorded any medications that the participant was taking on a regular basis. A blood sample was donated, and blood pressure, height, and weight were measured by the study staff, as described below. In total, 639 women completed the required clinic visit.

2.2 Hot flashes

A detailed hot flash history was obtained through a series of questions that asked for information on the following: whether the woman had ever experienced midlife hot flashes; the age when hot flashes first occurred; the severity of hot flashes; the frequency of the hot flashes; and whether the woman had experienced hot flashes within the last 30 days. Severity of hot flashes was determined using the question “*How would you describe the majority of your hot flashes?*” In response to this question, participants were asked to select one of the following possible responses: “mild (sensation of heat without sweating),” “moderate (sensation of heat with sweating),” and “severe (sensation of heat with sweating that disrupts

your usual activity.” Frequency of hot flashes was determined using the question “*Generally, how often do you experience hot flashes?*” with choices of “every hour,” “every 2–5 hours,” “every 6–11 hours,” “every 12–23 hours,” “1–2 days per week,” “3–4 days per week,” “5–6 days per week,” “2–3 days per month,” “1 day per month,” “less than 1 day per month,” “never,” and “don’t know.” Based on the distribution of the data, outcomes examined were the experiencing of any hot flashes (yes/no), moderate or severe hot flashes (yes/no), at least daily hot flashes (yes/no), hot flashes experienced for one or more years (yes/no), and hot flashes experienced during the last 30 days (yes/no).

2.3 Blood pressure

Systolic and diastolic blood pressure was measured in a standardized manner using a mercury manometer and a WelchAllyn adult one-tube durable one-piece blood pressure cuff (arm circumference range: 25.3 centimeters to 34.3 centimeters). A larger cuff was available if needed. Two blood pressure measurements per participant were taken by a trained research assistant, of which there were two for the study, before other study procedures, including the blood draw. The blood pressure measurements were taken with the participant seated in an upright position with her legs uncrossed and only after she was seated for at least 15 minutes. The same arm was used for all readings for all patients. The averages for systolic and diastolic blood pressures were recorded. Hypertension was defined as a systolic blood pressure of 140 mmHg or greater and/or a diastolic blood pressure of 90 mmHg or greater and/or the use of at least one antihypertensive drug.

2.4 Confounders

Data on a number of potential confounders were collected as part of the questionnaire. Race was self-reported and categorized as white, black, and other. Smoking status at the time of enrollment was determined using the questions “*Have you ever smoked cigarettes?*” and “*Do you still smoke cigarettes?*” Based on the participant’s responses to these questions, she was categorized as a current, former, or never smoker. Alcohol use was assessed using participant responses to the questions “*In the last 12 months, have you had at least 12 drinks of any kind of alcoholic beverage?*” and “*In any one year have you had a least 12 drinks of any kind of alcoholic beverage?*” Women who answered ‘yes’ to the first question were categorized as current drinkers, while those who answered ‘no’ to both questions were categorized as never drinkers. Women who answered ‘no’ to the first question and ‘yes’ to the second question were considered former drinkers. As there were a small percentage of never drinkers overall (5.1%), former and never drinkers were combined for the analyses of the alcohol variable.

BMI was obtained using height and weight of the participant measured at the clinic visit. To obtain weight data, the participant was weighed without shoes in street clothing to the nearest 0.05 lb, rounding down, on a calibrated Detecto Portable Digital Fitness Scale (Webb City, Missouri). Her height was measured without shoes to the nearest 0.5 in, rounding down, with a Seca stadiometer (Hanover, Maryland). BMI was calculated using the National Institutes of Health on-line BMI calculator [17]. Usual physical activity was categorized as inactive/light and moderate/heavy using participant responses to questions regarding usual physical activity performed at work, home, and leisure during the last 12 months. For each area (work, home, and leisure), a participant was asked to think about the things she usually did during the last 12 months and to describe the kind of physical activity she performed. Possible responses were: inactive, light, moderate, and heavy. Detailed definitions of these responses were provided for the participant on the questionnaire (for example, heavy physical activity was defined as performing vigorous activity on a regular basis, including jogging, singles tennis, paddleball, high intensity aerobics; or engaging in heavy activities such as carrying weights, strenuous farm work or gardening). A score was assigned to each response such that inactive equaled 1 and heavy equaled 4. For women who were employed, home, leisure, and work physical activity

scores were added; for women who were not employed, the total score equaled the home score plus the leisure score plus the average of the home and leisure score. A woman who had a physical activity score of 7 or less was categorized as inactive or having light overall physical activity; a woman who had a physical activity score of 8 or greater was categorized as having moderate/heavy overall physical activity.

2.5 Data analysis

Because hormone therapy has been shown to be associated with cardiovascular disease, women who reported past hormone therapy use were excluded from this analysis (29 women with hot flashes and 7 women without hot flashes). Characteristics of women who reported ever experiencing hot flashes and never experiencing hot flashes were compared using Student's t-tests for continuous variables (all were normally distributed) and chi-square tests for categorical variables. Linear regression analysis was used to examine the associations between the hot flash variables and the continuous dependent variables systolic blood pressure and diastolic blood pressure. For these analyses, the regression coefficients and 95% confidence intervals (CI) are reported. Logistic regression analysis was used to examine the associations between the hot flash variables and the dichotomous dependent variable hypertension. Odds ratios (OR) and 95% CI are presented for the logistic regression analyses.

For each regression analyses, two models were examined. The first model adjusted for only participant age. The second model adjusted for age, race, smoking status, current alcohol drinking, BMI, use of a cholesterol-lowering medication, and use of an anti-hypertensive medication; these variables were identified in the bivariate analyses as potential confounders due to their association with the experiencing of hot flashes. A third model was built additionally adjusting for estradiol levels, which were measured in the donated blood sample; however, the estimates did not change from the fully-adjusted model, and, therefore, the results of this third model are not presented.

Analyses were first conducted for all participants and subsequently for only women who were not taking an anti-hypertensive medication (i.e. untreated). Stratified analyses were also conducted by age (<50 versus ≥ 50 years), race (white versus black), smoking status (ever versus never), and BMI (<25 kg/m² versus ≥ 25 kg/m²). Within these strata, estimates were similar to the results generated for all participants, although the confidence intervals were wider due to smaller numbers. Thus, the stratified results are not presented.

P-values < 0.05 were considered statistically significant. All statistical analyses were performed using SAS 9.1 (SAS Institute, Inc.).

3. RESULTS

In the study sample, 56.9% of the participants reported ever experiencing hot flashes (Table 1). Compared to women who reported no hot flashes, women experiencing hot flashes were significantly older and had a higher mean BMI. Further, women reporting hot flashes were significantly more likely to be of black race and to be current smokers than women reporting no hot flashes. Mean systolic and diastolic blood pressures were significantly different by hot flash status in the entire study sample; the mean systolic blood pressure was also significantly different by hot flash status when the analysis was limited to women who were not taking anti-hypertensive medications. In addition, a significantly greater percentage of women who reported ever experiencing hot flashes were categorized as hypertensive or reported taking a cholesterol-lowering medication or an anti-hypertensive agent compared to women who reported never experiencing hot flashes. Other variables such as physical exercise, education, household income and marital status were not significantly associated with hot flashes.

In the age-adjusted analysis, both systolic and diastolic blood pressure were significantly and positively associated with any hot flashes (Table 2; $\beta = 2.98$ for systolic blood pressure and $\beta = 1.73$ for diastolic blood pressure). Similar associations were observed for moderate or severe hot flashes, hot flashes experienced for one or more years, and hot flashes experienced within the previous 30 days, with the strongest associations observed between systolic and diastolic blood pressure and hot flashes experienced in the previous 30 days (Table 3; $\beta = 4.72$ for systolic blood pressure and $\beta = 2.95$ for diastolic blood pressure). However, after adjustment for confounders, all of the associations were markedly attenuated and not statistically significant. Results were essentially the same among the group not taking antihypertensive medications (untreated), although the majority of the β coefficients were not statistically significant even in the age-adjusted only models.

Women reporting any hot flashes, moderate to severe hot flashes, hot flashes for one or more years or hot flashes within the previous 30 days were at significantly increased odds of having hypertension compared to their counterparts after adjustment for age. However, only the OR for moderate or severe hot flashes remained statistically significant after adjustment for confounders (OR 1.91, 95% CI 1.14, 3.19).

4. DISCUSSION

The results of this study showed that women with hot flashes were at increased risk for high blood pressure compared to women who had never experienced hot flashes but that most of the increases in risk were due to the confounders that were included in the regression models (i.e. age, smoking status, current alcohol drinking, BMI, use of an anti-hypertensive medication, and use of a cholesterol-lowering medication). These findings, although in contrast to some recent studies reporting worse cardiovascular health among women with hot flashes compared to those without [4,5], are consistent with the results of studies examining hot flashes in relation to the outcome of blood pressure. For example, Gast et al [5] showed, after adjustment for confounders including smoking, education, and BMI, that experiencing hot flashes during the previous week was not significantly associated with systolic blood pressure or hypertension among all women in the EPOS study or with systolic or diastolic blood pressure among women not taking an antihypertensive medication. Further, using data collected at baseline in the Rancho Bernardo Study, a cohort of postmenopausal white women in Southern California, Svartberg et al [6] reported no differences in systolic or diastolic blood pressure among women who reported ever having hot flashes compared to those who reported never having hot flashes. Finally, in the SWAN study, mean systolic and diastolic blood pressures were not significantly different among women undergoing the menopausal transition who experienced hot flashes within the two weeks prior to the interview compared to those who did not [4].

Although studies have, in general, not shown a significant relationship between hot flashes and blood pressure, there is some mounting evidence that hot flashes are associated with worse cardiovascular health as measured using other endpoints, such as cholesterol concentrations [4,5], flow-mediated dilation, and aortic calcification [4]. The difference in the endpoints examined may be important in interpreting the overall body of evidence on the association between hot flashes and cardiovascular disease. Specifically, cholesterol levels and subclinical cardiovascular disease such as aortic calcification may reflect the effects of exposures over a longer period of time [5], while blood pressure may be modulated to a greater degree by short term influences. A suggestion of this may be shown in our data, as the strength of the hot flash-blood pressure association was strongest, almost universally, for analyses pertaining to hot flashes experienced in the last 30 days. These results are consistent with findings reported by Gerber et al [9] and James et al [10], which showed that, compared with women who did not report hot flashes, certain mean systolic blood pressures, measured using an ambulatory blood

pressure monitor, were significantly higher among women who reported experiencing hot flashes within the two weeks prior to the blood pressure measurement. Thus, when assessing the relationship between midlife hot flashes and future cardiovascular disease, measures that more directly assess subclinical cardiovascular disease than blood pressure, such as aortic calcification, may be more appropriate in determining the true long-term effect of vasomotor symptoms on cardiovascular health.

Several limitations of this study should be noted. First, as with the SWAN and EPOS study, this study was cross-sectional and, therefore, no conclusion about the temporality of any associations could be made. Second, the blood pressure measurement was based on the average of two measurements at a single clinic visit. It has been well documented that blood pressure measurements, especially taken at one time point, can be affected by individual, observer, and environmental factors, these factors include time of the day of measurement and type and amount of observer training [18]. These effects could have led to measurement error and the missing of a significant finding. In this study, we attempted to minimize these factors by having the participant be seated for at least 15 minutes with her legs uncrossed prior to their blood pressure measurement, by using the same arm for all readings for all patients using a cuff width appropriate for the woman's arm circumference, and by training the two research assistants in a similar manner. In addition, whenever possible, we also scheduled clinic visits for patients in the morning. A third limitation of the study is that we were not able to exclude women with clinically apparent cardiovascular disease, as no information on cardiovascular health other than what was presented in this manuscript was collected. The association between hot flashes and blood pressure may differ between those with and without pre-existing cardiovascular disease.

Despite these limitations, our study had several notable strengths. The major strength of this study was the detailed hot flashes history obtained from all participants, allowing for the analyses of blood pressure by severity, frequency, and length of the hot flash experience. While the hot flash history data obtained were based on survey data and not physiologic measurements, self-report of hot flashes is the most widely accepted and feasible means of collecting data on the hot flash experience in a large population-based study. Self-reported data has been used in our previously published manuscripts (examples: [15,16]) as well as by other researchers in large studies such as SWAN [4]. Additional strengths were the exclusion of current and former hormone therapy users and the collection of information on a number of important confounders, including smoking, BMI, and estradiol concentrations.

In summary, the results of our study indicate women experiencing midlife hot flashes do not have significantly higher blood pressure levels than women who do not experience midlife hot flashes. Future studies that are prospective in nature and use measures of subclinical cardiovascular disease should be conducted to better examine the relationship between hot flashes and cardiovascular disease. Detailed data on hot flashes and on cardiovascular health prior to, during, and after the menopausal transition should be collected to fully characterize the risk, if any, of cardiovascular disease associated with midlife hot flashes.

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Table 1

Characteristics of women with and without hot flashes

	Ever had Hot flashes		Never had hot flashes		p-value
Sample size	343		260		
Age, years, mean (SD)	48.9	(2.3)	48.0	(2.4)	<0.0001
Race, n (%)					
White	282	(82.2)	223	(85.8)	0.008
Black	58	(16.9)	28	(10.8)	
Other	2	(0.6)	8	(3.1)	
Marital status, n (%)					0.7
Single	43	(12.5)	35	(13.5)	
Married	227	(66.2)	178	(68.4)	
Other	72	(21.0)	47	(18.1)	
Education, n (%)					0.3
Less than college	59	(17.2)	34	(13.1)	
Some college/technical school	97	(28.3)	66	(25.4)	
College/technical school graduate	80	(23.3)	69	(26.5)	
Graduate level schooling	107	(31.2)	91	(35.0)	
Household income, n (%)					0.8
Less than \$50,000	95	(27.7)	69	(26.5)	
\$50,000 to \$99,999	142	(41.4)	117	(45.0)	
\$100,000 or more	101	(29.4)	74	(28.5)	
BMI, kg/m ² , mean (SD)	28.7	(7.2)	26.8	(6.5)	0.0008
Physical activity, n (%)					0.4
Inactive/light	199	(58.0)	160	(61.5)	
Moderate/heavy	144	(42.0)	100	(38.5)	
Systolic blood pressure, mmHg, mean (SD)	117.6	(16.1)	114.3	(15.4)	0.01
Diastolic blood pressure, mmHg, mean (SD)	74.7	(10.2)	72.9	(9.8)	0.03
Systolic blood pressure, mmHg, untreated, mean (SD)	115.5	(15.1)	113.0	(14.3)	0.04

	Ever had Hot flashes	Never had hot flashes	p-value
Diastolic blood pressure, mmHg, untreated, mean (SD)	73.6	72.4	0.2
Hypertension, n (%) ^a	90	39	0.0009
Anti-hypertensive medication, n (%)	56	19	0.0009
Cholesterol medication, n (%)	22	6	0.02
Smoking status, n (%)			
Never	166	152	0.02
Former	138	92	
Current	38	16	
Current alcohol use, n (%)	214	183	0.04
Moderate/severe hot flashes, n (%)	213		
Daily hot flashes, n (%)	74		
Hot flashes ≥ 1 year, n (%)	220		
Hot flashes in the last 30 days, n (%)	228		

SD = standard deviation

^a defined as a systolic blood pressure of 140 mmHg or greater and/or a diastolic blood pressure of 90 mmHg or greater and/or the use of at least one anti-hypertensive medication

Table 2

The associations between any hot flashes, moderate or severe hot flashes, and daily hot flashes with blood pressure outcomes

	Moderate/severe		
	Any hot flashes	hot flashes	Daily Hot Flashes
Systolic blood pressure (mmHg), β (95% CI)			
Age-adjusted model	2.98 (0.39, 5.58) ^a	3.23 (0.34, 6.12) ^a	2.30 (−1.83, 6.43)
Age- and confounder-adjusted model ^b	0.63 (−1.69, 2.94)	0.87 (−1.71, 3.45)	1.52 (−2.11, 5.16)
r ² of age-and confounder-adjusted model ^b	0.27	0.27	0.26
Diastolic blood pressure (mmHg), β (95% CI)			
Age-adjusted model	1.73 (0.07, 3.38) ^a	1.87 (0.02, 3.72) ^a	2.62 (−0.02, 5.26)
Age- and confounder-adjusted model ^b	0.55 (−0.99, 2.10)	0.76 (−0.97, 2.49)	2.24 (−0.19, 4.68)
r ² of age-and confounder-adjusted model ^b	0.20	0.20	0.19
Systolic blood pressure (mmHg), untreated, β (95% CI)			
Age-adjusted model	2.33 (−0.25, 4.91)	1.98 (−0.93, 4.89)	1.78 (−2.31, 5.88)
Age- and confounder-adjusted model ^c	1.34 (−1.03, 3.70)	1.62 (−1.04, 4.28)	1.93 (−1.83, 5.69)
r ² of age-and confounder-adjusted model ^c	0.21	0.21	0.19
Diastolic blood pressure (mmHg), untreated, β (95% CI)			
Age-adjusted model	1.13 (−0.56, 2.83)	1.01 (−0.91, 2.93)	1.97 (−0.73, 4.68)
Age- and confounder-adjusted model ^c	0.60 (−1.00, 2.21)	0.82 (−0.99, 2.62)	2.07 (−0.48, 4.61)
r ² of age-and confounder-adjusted model ^c	0.16	0.16	0.15
Hypertension, OR (95% CI)			
Age-adjusted model	1.85 (1.21, 2.82) ^a	2.10 (1.33, 3.32) ^a	1.33 (0.69, 2.58)
Age- and confounder-adjusted model ^c	1.51 (0.94, 2.43)	1.86 (1.11, 3.13) ^a	1.31 (0.63, 2.72)

95% CI = 95% confidence interval; BMI = body mass index; OR = odds ratio

^a p<0.05

^b confounders in model: race, smoking status, current alcohol drinking, BMI, use of anti-hypertensive medication, use of cholesterol-lowering medication

^c confounders in model: race, smoking status, current alcohol drinking, BMI, use of cholesterol-lowering medication

Table 3

The associations between hot flashes experienced for one year or more and hot flashes experienced in the previous 30 days with blood pressure outcomes

	Hot Flashes ≥ 1 Year	Previous 30 Days
Systolic blood pressure (mmHg), β (95% CI)		
Age-adjusted model	3.44 (0.55, 6.33) ^a	4.72 (1.85, 7.58) ^a
Age- and confounder-adjusted model ^b	0.24 (−2.34, 2.81)	1.60 (−1.00, 4.20)
r ² of age-and confounder-adjusted model ^b	0.27	0.27
Diastolic blood pressure (mmHg), β (95% CI)		
Age-adjusted model	1.76 (−0.09, 3.60)	2.95 (1.12, 4.77) ^a
Age- and confounder-adjusted model ^b	0.15 (−1.57, 1.87)	1.42 (−0.32, 3.15)
r ² of age-and confounder-adjusted model ^b	0.20	0.20
Systolic blood pressure (mmHg), untreated, β (95% CI)		
Age-adjusted model	2.35 (−0.55, 5.24)	3.73 (0.84, 6.62) ^a
Age- and confounder-adjusted model ^c	0.99 (−1.66, 3.64)	2.28 (−0.41, 4.96)
r ² of age-and confounder-adjusted model ^c	0.21	0.21
Diastolic blood pressure (mmHg), untreated, β (95% CI)		
Age-adjusted model	0.92 (−0.98, 2.84)	2.31 (0.41, 4.21) ^a
Age- and confounder-adjusted model ^c	0.19 (−1.60, 1.99)	1.51 (−0.30, 3.32)
r ² of age-and confounder-adjusted model ^c	0.16	0.17
Hypertension, OR (95% CI)		
Age-adjusted model	1.95 (1.23, 3.08) ^a	2.07 (1.31, 3.25) ^a
Age- and confounder-adjusted model ^c	1.48 (0.88, 2.48)	1.56 (0.93, 2.61)

95% CI = 95% confidence interval; BMI = body mass index; OR = odds ratio

^a p<0.05

^b confounders in model: race, smoking status, current alcohol drinking, BMI

^c confounders in model: race, smoking status, current alcohol drinking, BMI, use of cholesterol-lowering medication