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Endothelial function in postmenopausal women with nighttime systolic hypertension

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Abstract

Objective—Hypertension becomes more prevalent in women during their postmenopausal years. Nighttime systolic blood pressure (SBP) is especially predictive of adverse cardiac events and the relationship between rising nighttime SBP and cardiovascular risk increases more rapidly in women compared to men. The reasons for the prognostic significance of nighttime SBP are not completely known, but may involve vascular endothelial dysfunction. The purpose of this study was to examine the relationship of nighttime SBP and endothelial function, assessed by brachial artery flow-mediated dilation (FMD) and to determine whether postmenopausal women with nighttime hypertension (SBP≥120 mm Hg) evidenced greater endothelial dysfunction compared to women with normal nighttime SBP.

Methods—One-hundred postmenopausal women (mean age: 65.8 ± 7.5 years, body mass index: 28.3 ± 4.7 kg/m^2, hypertension: 47%, coronary artery disease: 51%, mean clinic BP 137 ± 17/67 ± 11 mm Hg, 34 with nighttime hypertension) underwent 24-hour ambulatory BP monitoring, actigraphy, and brachial artery FMD assessments.

Results—Multivariate regression models showed that higher nighttime SBP and larger baseline artery diameter were inversely related to FMD. Nighttime SBP and baseline artery diameter accounted for 23% of the variance in FMD. After adjusting for baseline artery diameter, women with nighttime hypertension had lower FMD than women with normal nighttime SBP (2.95% ±0.65 vs 5.52%±0.46, p = .002).

Conclusions—In postmenopausal women, nighttime hypertension was associated with reduced endothelial function. Research examining the therapeutic benefits of treating nighttime hypertension on endothelial function and future cardiovascular risk in postmenopausal women is warranted.

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Keywords

nighttime BP; endothelial function; flow-mediated dilation; nighttime hypertension; postmenopausal women

Cardiovascular morbidity increases with age but on average women are 10 years older than men when they develop cardiovascular disease.[1] Consequently, the majority of cardiovascular events in women occur during their postmenopausal years. Cardiovascular risk is multifactorial but estrogen decline may also contribute to greater cardiovascular disease among postmenopausal women. Postmenopausal women have reduced endothelial function compared to premenopausal women[2,3] and estrogen supplementation has been found to improve endothelial function in some postmenopausal women.[4] These findings suggest that estrogen withdrawal associated with menopause may, in part, adversely affect vascular function. The menopausal transition is also associated with an increasing prevalence of hypertension becoming equivalent to and then surpassing that of men after 65 years of age.[1] Postmenopausal women with hypertension have reduced endothelial function in comparison to postmenopausal women with normotension.[5] Taken together these findings suggest that menopause and hypertension negatively affect endothelial function.

Unlike menopause hypertension is a major modifiable cardiovascular risk factor. Among all blood pressure (BP) parameters, nighttime systolic blood pressure (SBP) is the most predictive of adverse cardiovascular events in both hypertensive cohorts and general populations.[6-9]

Interestingly, as nighttime SBP levels rise, the relationship between BP and cardiovascular risk increases more rapidly in women than men.[10,11]

The reasons for the prognostic significance of nighttime SBP are not completely known, but may involve impaired endothelial function. Functional changes to the endothelium are considered to emerge early in the atherosclerotic disease process.[12] Endothelial function can be assessed noninvasively via ultrasound measurement of brachial artery vasodilator responses to hyperemic blood flow (flow-mediated dilation; FMD).[13] Endothelial dysfunction, quantified as reduced FMD, is a predictor of cardiovascular events in general populations,[14,15] cardiac and hypertensive patients,[16,17] and postmenopausal women.[18]

Although higher office BP,[19-22] home BP,[19] 24-hour ambulatory BP (ABP),[23,24] and BP nondipping,[25,26] are associated with greater endothelial dysfunction less is known regarding the relationship between nocturnal hypertension and endothelial function. There is some evidence of an inverse association between FMD and nighttime SBP in patients with hypertension or coronary heart disease.[27,28] However, these previous studies included few women and no studies evaluated the relationship between nighttime SBP and FMD in postmenopausal women. Given that postmenopausal women are at higher risk of cardiovascular disease and the relationship between nighttime SBP and cardiovascular risk increases more drastically for woman than men the objectives of this study were: (1) to evaluate whether nighttime SBP was associated with endothelial function (FMD) and; (2) to evaluate the hypothesis that endothelial function in postmenopausal women with nighttime

hypertension (nighttime SBP≥120mm Hg) is impaired relative to postmenopausal women with normal nighttime SBP (<120mm Hg).

METHODS

Participants

The sample consisted of 100 postmenopausal women between 50 and 80 years of age who participated in the ENDEAVOR study at Duke University Medical Center. The methodology of ENDEAVOR was reported previously.[4] In brief, ENDEAVOR was a randomized, double-blind, crossover study to examine the acute effects of transdermal estrogen therapy (17β-estradiol 0.05 mg/d), estrogen plus progesterone therapy (17β-estradiol 0.05 mg/d+norethindrone acetate 0.14 mg/d) and placebo on cardiovascular parameters and endothelial function. All participants included in the current analysis were women randomized to a placebo transdermal patch, had 24-hour ambulatory blood pressure monitoring (ABPM) recordings with ≥15 daytime and ≥5 nighttime readings and completed FMD testing.[4] Postmenopausal status was defined by amenorrhea ≥ 12 months, and was confirmed by a reproductive hormone panel. Exclusion criteria included: use of hormone replacement therapy or selective estrogen receptor modulators within 30 days of enrollment; congestive heart failure NYHA Class > II; pacemaker dependency; uncontrolled hypertension (defined by a resting blood pressure ≥ 180/105 mm Hg); persistent atrial fibrillation or tachyarrhythmia; myocardial infarction (MI) and/or percutaneous transluminal coronary angioplasty within 30 days of enrollment; coronary artery bypass grafting within 3 months of enrollment; uncorrected valvular disease; hypertrophic or restrictive cardiomyopathy; uncorrected thyroid disease; renal or hepatic dysfunction; dementia; or body mass index (BMI) ≥ 40 kg/m^2. Participants were recruited from the Duke University cardiology clinics and by advertisements in the Piedmont region of North Carolina. The study protocol was approved by the Institutional Review Board at Duke University Medical Center. All eligible individuals provided written informed consent prior to participation in the study.

Demographic, Anthropometric and Biochemical Assessment

Data were collected on age, ethnicity, current cigarette smoking, number of years post-menopausal, previous cardiovascular disease (angina, coronary artery disease defined as ≥50% occlusion of ≥1 major coronary vessel on cardiac catheterization, myocardial infarction, peripheral vascular disease, stroke, transient ischemic attack), diabetes, and/or hypertension diagnoses, and current cardiovascular (angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, diuretics, nitrates, statins) medications by medical record review and self-report. Blood samples were collected in the morning after an overnight fast. Specimens were analyzed by Labcorp using automated enzymatic assays for total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), and triglycerides.

Clinic BP Measurement

Clinic BP was measured following a 5 minute, quiet seated rest period in a temperature controlled room. Five standard auscultatory BP readings were taken using a mercury

sphygmomanometer and stethoscope at 2 minute intervals. The average of the last 3 readings was used to represent clinic SBP and clinic diastolic (D) BP.

24-Hour Ambulatory Blood Pressure Monitoring

Participants were instrumented with the validated noninvasive oscillometric Oscar 2 ambulatory blood pressure monitor (ABPM; SunTech, Raleigh, NC)[29,30] between 11:00 AM and 1:00 PM on a weekday. SBP and DBP were measured every 20 minutes during the day and every 30 minutes during the night over a consecutive 24-hour period. Waking and sleep periods, defined by self-report, and confirmed by a wrist-watch style actigraph (ActiWatch64, Mini-Mitter Co., Inc., Sunriver, OR), were used to compute mean daytime BP and mean nighttime BP values, respectively. The actigraph was also used to provide a measure of physical activity while awake. Artifactual ABPM readings were identified by the Oscar 2 ABPM software. A minimum of 15 daytime ABPM recordings and 5 nighttime ABPM recordings were the number of measurement necessary for inclusion in the analysis. For the study sample (n=100) there was a mean of 35.6±8.2 daytime ABPM readings and 16.4±3.6 nighttime ABPM readings. Nighttime SBP was further categorized into nighttime hypertension (SBP ≥ 120mm Hg)[31] and normal nighttime BP (SBP < 120mm Hg).[32,33] A nighttime SBP threshold of ≥ 120mm Hg for nighttime hypertension has been used in previous studies.[34-37]

Assessment of Endothelial Function

FMD assessments were carried out a minimum of 4 hours after a light, fat-free, caffeine free breakfast, provided as a part of the study. Participants abstained from using vasoactive medications from 12am the night before until after the FMD assessments were completed. Adherence to these instructions was confirmed prior to testing.

Endothelial function assessments of the brachial artery were performed as previously described.[4] Longitudinal B-mode images of the brachial artery, in the region 4 to 6 cm proximal to the antecubital fossa, were recorded by the same sonographer and stored digitally using a 7-11 MHz linear-array transducer and Aspen ultrasound system (Acuson, Mountain View, CA). For the FMD assessment, images were captured after 10 minutes of supine rest and during the first 120 seconds of reactive hyperemia, achieved by inflation of a pneumatic occlusion cuff, located around the forearm, to supra-systolic pressure (~200 mm Hg) for 5 minutes. End-diastolic images were stored and arterial diameters measured as the distance between the proximal and distal arterial wall intima-media interfaces using PC-based software (Brachial Analyzer -Version 5.0, Medical Imaging Applications LLC, Iowa City, Iowa). Peak FMD response was assessed from 10-120 seconds post-deflation of the cuff, with peak arterial diameter quantified using polynomial curve fitting.

FMD was initially expressed as percent increase in arterial diameter (maximum arterial diameter - baseline arterial diameter / baseline arterial diameter×100%), which is the index that has been adopted most widely.[38] Given that the percent change index may result in bias towards greater vasodilation in smaller arteries,[38,39] baseline arterial diameter was used as a covariate in multivariate analyses.

All FMD studies were conducted in our research facility, using the same Acuson Aspen ultrasound machine, were obtained by the same research sonographer, and were analyzed and quantified by the same observer (AS) who was blinded to the identity of the image source. In an unpublished evaluation of 20 healthy men and women who underwent our FMD assessment protocol on two consecutive days, repeat FMD values showed a correlation of r=0.81, p<.001, a mean difference of 0.64 ± 2.67%.

Statistical Analysis

Normality statistics (skew, kurtosis, Kolmogorov-Smirnov), histograms, boxplots and normal probability plots were examined to assess normality. Results are presented as means with standard deviations (SD) for continuous variables and counts with percentages (%) for categorical variables. Student's t-tests, Wilcoxon two-sample tests (HDL, triglycerides) and chi-square tests were used for the comparison of characteristics of study participants with nighttime hypertension and normal nighttime SBP. Simple correlations between participant characteristics and FMD responses were described using Pearson's r correlations for continuous variables and Spearman's r correlations for categorical variables.

The SBP parameters (daytime, nighttime, 24-hour and clinic) were found to correlate with FMD. When all 4 SBP parameters were entered into a regression model predicting FMD the variance inflation factors were greater than 2 indicating the presence of multicollinearity, as expected. Given the related nature of these SBP variables, in model 1 the stepwise variable selection method (p<.05 for variable entry, p>.10 for removal) was initially used to assess the relationship between SBP parameter and FMD. The only variable retained in model 1 was mean nighttime SBP. Therefore, the purpose of model 2 was to examine the relationship between mean nighttime SBP and FMD after considering baseline artery diameter and participant characteristics (age, BMI, race/ethnicity, smoking, daytime physical activity, diabetes, high cholesterol, cardiovascular disease, total cholesterol, HDL cholesterol, cardiovascular medications and BP medications) using the stepwise variable selection method (p<.05 for variable entry, p>.10 for removal). As a follow-up to model 2, analysis of covariance (ANCOVA) was used in comparing FMD means between the nighttime hypertension and normal nighttime SBP groups to adjust for the covariance of baseline artery diameter associated with FMD in the regression analysis. Statistical analyses were conducted using the SAS 9.3 system (SAS Institute, Cary, NC) with significance set at p=.05.

RESULTS

Table 1 summarizes the demographic and clinical characteristics of the 100 postmenopausal women who comprised the study sample. Women with nighttime hypertension were older, had lower HDL cholesterol, greater clinic SBP, mean daytime BPs, mean nighttime BPs, 24-hour ambulatory BPs, diabetes, hypertension and reduced FMD.

Initial Bivariate Correlational Analyses

Variables significantly associated with FMD included baseline artery diameter (r=-.38, p<.001), clinic SBP (r=-.28, p=.005), clinic DBP (r=-.26, p=.011), mean daytime SBP (r=-.31,

p=.002), mean nighttime SBP (*r*=-.38, *p*<.001), mean daytime DBP (*r*=-.27; *p*=.006), mean nighttime DBP (*r*=-.40; *p*<.001), 24-hour ambulatory SBP (*r*=-.36, *p*<.001), 24-hour ambulatory DBP (*r*=-.33, *p*=.001), nocturnal SBP hypertension category (r_s=-.34, *p*<.001), diabetes history (r_s=-.23, p=.024), and calcium channel blocker (CCB) medication use (r_s=-.20, *p*=.043). No other variables correlated with FMD at the p=.05 level of significance.

Regression Analyses

Because of the significant bivariate relationships found between the BP parameters (all *r*'s>.48, all *p*'s <.001) the stepwise variable selection method was used to identify the BP variable (s) significantly associated with FMD. When considering all of the systolic BP parameters (daytime, nighttime, 24-hour and clinic) as expected only mean nighttime SBP was significantly associated with FMD (Table 2, model 1). Mean nighttime SBP accounted for approximately 14% of the FMD variance. In model 2 (Table 2), we considered the potential relationships between mean nighttime SBP, baseline artery diameter, participant characteristics (age, BMI, ethnicity, smoking status, daytime physical activity, diabetes, high cholesterol, cardiovascular disease, total cholesterol, HDL cholesterol, cardiovascular medications and BP medications) and FMD. Mean nighttime SBP and baseline artery diameter were significantly and inversely associated with FMD following the stepwise variable selection method for multivariate regression. Baseline artery diameter contributed to an additional 9% of the variance in FMD. No other participant characteristics were significantly associated with FMD.

FMD and Nocturnal SBP

The sample was divided into postmenopausal women with nighttime hypertension and normal nighttime SBP. ANCOVA analysis indicated that women with nighttime hypertension had lower FMD than those with normal nighttime SBP ($F(1, 97) = 10.18$, *p*=.002; FMD = 2.95%±0.65 vs 5.52%±0.46) following adjustment for baseline artery diameter (*p*<.001) .

DISCUSSION

The main finding of our study was that impaired endothelial function, as indicated by reduced brachial artery FMD, was associated with greater mean nighttime SBP and larger baseline artery diameter. Women with nighttime hypertension exhibited FMD responses that were approximately 2.5% lower than women with normal nighttime SBP. These findings are significant given that a recent meta-analysis[40] found that a 1% decrease in FMD was associated with an 8% to13% increase in the risk of future cardiovascular events. To our knowledge, this is the first study to report an inverse association between nighttime SBP and FMD in postmenopausal women. This finding is especially noteworthy because the risk of adverse cardiac events is increased in postmenopausal women and may be mediated, in part, by impaired endothelial function.

There are a limited number of studies that have examined the relationship between endothelial function and nighttime SBP in men and women. For example, Konrad and colleagues (2011)[27] reported that higher nighttime SBP was associated with reduced

endothelial function (FMD) in 49 patients (53.5±8.9 years; 20 females) with treated hypertension. In a study of 73 patients (20 females) with stable coronary artery disease nighttime SBP correlated with FMD (r=-.31, p<.01) but multivariate associations were not reported.[28] Other investigators[24] described an inverse relationship between 24-hour SBP and FMD responses, but without examining the relationship between nighttime SBP and FMD. Our study extends prior research to include postmenopausal women and may identify a group of women at higher cardiovascular risk due to poorer endothelial function.

Endothelial dysfunction has been proposed as a gauge of cardiovascular risk. [41] Meta-analyses have found impairment of brachial FMD to be predictive of future cardiovascular events with some studies indicating a stronger relationship observed among diseased populations.[40,42] Specifically in postmenopausal women, poorer endothelial function was found to be an independent predictor of cardiovascular events in 400 women with hypertension[43] and an independent predictor of cardiovascular risk beyond traditional cardiovascular risk factors in 2,264 initially asymptomatic postmenopausal women with risk factors for atherosclerosis.[18] Antihypertensive therapy has been shown to improve FMD[44] with some suggestion that aldosterone inhibition may improve endothelial function beyond its BP lowering effects in postmenopausal women.[45] The prognostic significance of improved FMD was reported by Modena and colleagues.[43] In this study, hypertensive postmenopausal women whose FMD improved following treatment of clinic BP to target (<140/90mm Hg) for 6 months had a more favorable cardiovascular prognosis compared to treated hypertensive postmenopausal women whose FMD had not improved.[43] ABPM was not within the scope of the Modena et al.[43] study, therefore the effect of treatment on nighttime SBP and FMD could not be assessed. However, the findings of our study raise the possibility that nighttime SBP could have played a partial role in accounting for the postmenopausal hypertensive women who achieved clinic BP control, but lacked improvement in FMD.

Several prospective studies have found nighttime SBP, compared to daytime or 24-hour ABP, to be the most significant prognostic marker of cardiovascular disease morbidity and mortality. [6-9,46,47] Recently, Hermida and colleagues[48] found nighttime SBP to be the most significant predictor of cardiovascular events in over 3,300 normotensive and hypertensive patients prospectively studied for 5.6 years. This relationship remained significant following adjustment for daytime SBP, age, sex and diabetes. During follow-up, a progressive decrease in sleeping BP was the most significant predictor of event-free survival; a 5 mm Hg decrease in the mean nighttime (sleeping) SBP was associated with a 17% reduction in cardiovascular risk. These findings support decreasing nighttime BP as an approach to reducing cardiovascular disease risk.[48] Compared to the typical morning antihypertensive medication administration regimen, nighttime (bedtime) administration of ≥ 1 antihypertensive medications had a greater impact on reducing nighttime BP[49,50] and was associated with reduced cardiovascular disease risk in general hypertensive patients,[50,51] and cohorts of hypertensive patients with resistant hypertension,[52] type 2 diabetes mellitus,[53] and chronic kidney disease.[54] Therefore, one may speculate that reductions in BP at night may ameliorate cardiovascular risk, in part, via favorable changes in endothelial function.

Limitations

Because our study employed a cross-sectional design, we cannot infer that nighttime hypertension was causally related to impaired endothelial function. Also our findings are limited to postmenopausal women; we did not study premenopausal women or men. Nevertheless, study of postmenopausal women is important because postmenopausal women are at greater cardiovascular risk than premenopausal women and cardiovascular risk increases more dramatically during these years for women relative to men. Another limitation of the study was measurement of only one 24-hour ABPM session. It could be argued that additional ABPM sessions may increase the reproducibility of the BP findings. However, 24-hour monitoring is considered the standard in clinical practice and generates BP values that are likely more representative of true BP compared to clinic BP measurements. Coronary angiography (in women without CAD), overnight polysomnography and pulmonary dysfunction assessments were not included in the study design. Therefore, it is possible that the extent of atherosclerosis, sleep depth, sleep disorders and pulmonary dysfunction, as well as unrecognized confounding factors, may have contributed to individual differences in nighttime BP. Study strengths include the use of actigraphy for the objective determination of awake and asleep periods and more accurate calculation of daytime and nighttime BP means.

CONCLUSION

Nighttime SBP was associated with reduced endothelial function. Our findings raise the possibility that normalization of nighttime SBP may improve endothelial function and cardiovascular risk. Research examining the therapeutic benefits of treating nighttime hypertension on endothelial function and future cardiovascular risk in postmenopausal women is warranted.

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Table 1

Demographic and clinical characteristics of study sample

	Postmenopausal Women (n=100)	Normal Nighttime BP (n=66)	Nighttime Hypertension (n=34)	*p*
Age (years)	65.8±7.5	64.1±7.3	68.9±6.8	.002
Weight (kgs)	73.2±12.4	72.4±12.0	74.7±13.2	.390
Height (m)	1.61±0.06	1.61±0.06	1.60±0.06	.632
BMI (kg/m^2)	28.3±4.7	27.9±4.4	29.0±5.0	.264
Years Menopausal	18.4±9.7	17.0±9.9	21.0±8.8	.056
Ethnicity (% White)	75.0	75.8	73.5	.807
Smoking Status				.444[a]
Nonsmoker	88.6	90.8	84.4	
< ½ Pack/Day	5.2	3.1	9.4	
½ -1 Pack/Day	6.2	6.2	6.2	
Sqrt Daytime Physical Activity (units)	397.8±86.0	409.6±84.0	375.6±86.4	.062
Blood Pressure:				
Clinic SBP (mmHg)	137±17	133±17	144±14	.002
Clinic DBP (mmHg)	67±11	66±11	69±11	.258
Mean Daytime SBP (mmHg)	122±12	118±9	132±10	<.001
Mean Daytime DBP (mmHg)	64±8	63±8	67±8	.048
Mean Nighttime SBP (mmHg)	114±13	106±8	127±6	<.001
Mean Nighttime DBP (mmHg)	57±7	55±7	62±6	<.001
24-hour SBP (mmHg)	119±11	114±8	130±7	<.001
24-hour DBP (mmHg)	62±7	60±7	65±7	.004
Previous Cardiovascular Diagnoses:				
Angina	27.0	25.8	29.4	.697
CAD	51.0	45.4	61.8	.122
Diabetes	7.1	1.5	17.6	.006[a]
Hyperlipidemia	56.0	51.5	64.7	.208
Hypertension	47.0	37.9	64.7	.011
MI	15.0	16.7	11.8	.516
PVD	2.0	3.0	0.0	.547[a]
Stroke	1.0	0.0	2.9	.340[a]
Current Cardiovascular Medications:				
ACE	33.0	34.8	29.4	.584
ARB	9.0	4.6	17.6	.058[a]
Beta Blocker	46.0	43.9	50.0	.565
CCB	13.0	9.1	20.6	.105
Diuretic	24.0	21.2	29.4	.363
Statin	42.0	39.4	47.1	.462

	Postmenopausal Women (n=100)	Normal Nighttime BP (n=66)	Nighttime Hypertension (n=34)	*p*
Nitrates	6.0	7.6	2.9	.661[a]
Cholesterol and Triglycerides:				
Total Cholesterol (mg/dL)	216.7±43.5	218.4±46.9	213.7±36.7	.614
HDL Cholesterol (mg/dL)	53.0 (45.0-71.0)	55.0 (49.0-71.0)	47.0 (43.0-67.0)	.046
LDL Cholesterol (mg/dL)	126.7±34.4	126.9±36.0	126.3±31.6	.939
Triglycerides (mg/dL)	145.0 (97.0-200.0)	135.0 (97.0-188.0)	170.5 (99.0-227.0)	.180
Brachial Artery Endothelial Function:				
FMD (%)	4.6±4.2	5.7±4.1	2.6±3.7	<.001
Baseline Artery Diameter (mm)	3.7±0.8	3.6±0.7	3.9±0.8	.051

Normal nighttime SBP= mean nighttime SBP <120mm Hg ; Nighttime hypertension = mean nighttime SBP ≥120mm Hg

ACE = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BMI= body mass index; BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; DBP = diastolic blood pressure; FMD = flow-mediated dilation; MI = myocardial infarction; PVD = peripheral vascular disease; SBP = systolic blood pressure; SQRT= square root; TIA = transient ischemic attack.

[a] fisher's exact test.

Table 2

Predictors of nighttime brachial artery flow-mediated dilation (FMD) in postmenopausal women.

	b	*β*	*P* value	95% CI for *B*	
				Lower	Upper
Model 1: adjusted R^2 =.14					
Mean Nighttime SBP (mm Hg)	−0.13	−0.38	<.001	−0.19	−0.07
Model 2 adjusted R^2 = .23					
Mean Nighttime SBP (mm Hg)	−0.10	−0.41	<.001	−0.16	−0.04
Baseline Artery Diameter (mm)	−1.77	−0.32	<.001	−2.78	−0.76

Abbreviations: *b* = non-standardized (parameter estimate) regression coefficient; *β* = standardized regression coefficient; CI = confidence interval; SBP = systolic blood pressure. Stepwise variable selection (p<.05 for variable entry, p>.10 for removal) was used within each model.

Variables considered for model 1: mean daytime SBP, mean nighttime SBP, 24-hour SBP, clinic SBP.

Variables considered for model 2: mean nighttime SBP, baseline artery diameter, age, BMI, ethnicity, smoking status (0, non-smoker; 1, < ½ pack per day; 2, ½ to 1 pack per day), daytime physical activity, diabetes (0, no; 1, yes), high cholesterol (0, no; 1, yes), cardiovascular disease (0, no history of coronary artery disease, myocardial infarction, peripheral vascular disease, stroke; 1 history of ≥ coronary artery disease, myocardial infarction, peripheral vascular disease, stroke), total cholesterol, HDL cholesterol, cardiovascular medications (0, no; 1, yes) and blood pressure medications (0, no; 1, yes).