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Brachial Artery Diameter, Blood Flow and Flow-mediated Dilation in Sleep-Disordered Breathing

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Abstract

Clinic-based case-control studies linked sleep-disordered breathing (SDB) to markers of endothelial dysfunction. We attempted to validate this association in a large community-based sample, and evaluate the relation of SDB to arterial diameter and peripheral blood flow. This community-based cross-sectional observational study included 327 men and 355 women, age 42 to 83 years, from the Framingham Heart Study site of the Sleep Heart Health Study. Polysomnographically derived apnea-hypopnea index and hypoxemia index (percent sleep time with oxyhemoglobin saturation below 90%) were used to quantify the severity of SDB. Brachial artery ultrasound measurements included baseline diameter, percent flow-mediated dilation, and baseline and hyperemic flow velocity and volume. Baseline brachial artery diameter was significantly associated with both apnea-hypopnea index and hypoxemia index. The association was diminished by adjustment for body mass index, but remained significant for apnea-hypopnea index. Age-, sex-, race- and body mass index-adjusted mean diameters were 4.32, 4.33, 4.33, 4.56, 4.53 mm, respectively, for those with apnea-hypopnea index <1.5, 1.5–4.9, 5–14.9, 15–29.9, ≥30; $p=0.03$. Baseline flow measures were associated with apnea-hypopnea index but this association was non-significant after adjusting for body mass index. No significant association was observed between measures of SDB and percent flow-mediated dilation or hyperemic flow in any model. In conclusion, this study supports a moderate association of SDB and larger baseline brachial artery diameter, which may reflect SDB-induced vascular remodeling. This study does not support a link between SDB and endothelial dysfunction as measured by brachial artery flow-mediated dilation.

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Disclosures

The Authors disclosed no conflict of interest.

Keywords

Sleep Apnea; Obstructive; Endothelium; Vascular; Remodeling; Vascular; Epidemiology

INTRODUCTION

Numerous studies have shown that sleep-disordered breathing (SDB) is associated with hypertension^{1,2} and cardiovascular disease.^{3,4} SDB-related endothelial dysfunction is one proposed mechanism underlying these associations. Several, clinic-based case-control studies have shown an association between SDB and markers of endothelial dysfunction.^{5–7} Markers of endothelial function improved in SDB patients following continuous positive airway pressure (CPAP) therapy,^{8–11} and following vitamin C administration.¹² Caution must be exercised, however, in extrapolating from clinic-based observational studies that are prone to selection bias and from treatment studies without control arm.^{8,9,11} Moreover, it is uncertain whether the results of these studies are generalizable to the large number of milder cases of undiagnosed SDB in the general population.

One community-based study reported an association of the apnea-hypopnea index (AHI) with increased brachial artery (BA) diameter and impaired flow-mediated dilation (FMD) in elderly subjects (age >68), although the association between AHI and FMD was not significant after adjusting for body mass index (BMI).¹³ As increased BA diameter has been also associated with cardiovascular disease^{14,15} we further hypothesize that outward artery remodeling is another potential mechanism linking SDB and cardiovascular disease. Increased arterial blood flow and shear stress may be the stimulus for outward arterial remodeling. In the present study, we evaluate the association of SDB with baseline and reactive hyperemia measures of BA diameter and blood flow velocity in a large community-based sample of middle-aged and older individuals.

METHODS

Study Sample

The study sample is a subset of the Framingham Offspring and Omni cohort subjects who participated in the Sleep Heart Health Study (SHHS, Figure 1). The designs of the SHHS, the Framingham Offspring and Omni cohorts have been described elsewhere.^{16,17} Briefly, SHHS is a cohort of individuals 40 years or older was recruited from participants in several ongoing cohort studies of cardiovascular and pulmonary diseases in the United States. Exclusion criteria were treatment of SDB with continuous positive airway pressure or an oral device, oxygen treatment at home, or having a tracheostomy. It includes 6441 subjects who underwent polysomnography between 1995 and 1998, including 699 participants who were recruited from the Framingham Offspring cohort and 300 from the Framingham Omni cohort. The Framingham Offspring Cohort enrolled 5141 (mostly Caucasian) offspring of 1644 couples and 378 members of the original Framingham Heart Study cohort in 1971. The Omni cohort of the Framingham Heart Study was recruited from December 1995 to January 1998. The Omni cohort included residents of Framingham age 40 to 75 who identified themselves as members of a minority group (58% women; 36% African American, 40% Hispanic).

Between 1998 and 2001, 3539 Offspring cohort and 405 Omni cohort participants were eligible for BA ultrasound measurements. Of these, 656 Offspring and 40 Omni cohort participants were excluded for nursing-home residence, previous mastectomy, Raynaud's disease, subject's refusal, equipment malfunction/miscellaneous, pre-digital capture or technically inadequate study. Of the remaining 3248 subjects, 741 also participated in the SHHS. Six were excluded for missing covariate data, and 53 for smoking immediately prior to the BA ultrasound resulting

in 682 participants eligible for the present investigation. BA flow velocity measures were available for 361 participants. The Boston University Medical Center Institutional Review Board approved the protocol and participants provided signed informed consent.

Brachial Artery Measurements

The methods used to measure the BA diameter, determine %FMD and obtain baseline and hyperemic BA flow velocities and derive the respective flow volumes have been previously described.^{18,19} In brief, after overnight fast, excluding water and decaffeinated beverages, a blood pressure cuff placed on the proximal forearm was inflated to the highest of 200mmHg or 50mmHg above the systolic blood pressure to interrupt the distal blood flow for 5 minutes and was then deflated. End diastolic images of the brachial artery were acquired at baseline and for 2 minutes after cuff deflation using the Toshiba SSH-140A ultrasound system and 7.5-mHz linear-array transducer. Blinded sonographers analyzed the images offline using the Brachial Analyzer software (Medical Imaging Applications). Baseline brachial artery diameter was calculated as the average diameter from all baseline images measured. Flow-mediated vasodilatation (FMD) was calculated by subtracting baseline brachial artery diameter from the brachial artery diameter at 60 seconds. The later was calculated by averaging all the measurements from images obtained between 55 and 65 seconds after cuff deflation. Relative FMD was expressed as the percent change from baseline (%FMD), calculated by dividing the FMD by the baseline brachial artery diameter and multiplying by 100. Flow was recorded at baseline and for up to 15 seconds after cuff release until flow peaked. A randomly assigned sonographer blinded to the FMD measurements and SDB status visually confirmed the timing of peak flow, inspected the raw spectral analysis and selected the appropriate beats representing peak flow. Baseline and hyperemic flow velocities were multiplied by the baseline cross sectional area to obtain the respective flow volumes. The quality-assurance procedures and reproducibility of FMD measures in the Framingham Study were also previously reported.¹⁸

Polysomnography

SHHS participants underwent in-home polysomnography using the Compumedics P-series portable monitor (Abbotsford, Victoria, Australia). The polysomnography recordings included the following channels: electroencephalogram, electrooculogram, electrocardiogram, chin electromyogram, pulse oximetry, chest and abdominal excursion, airflow (by thermocouple) and body position. The polysomnography recordings were analyzed and scored centrally at the SHHS reading center (Cleveland OH) previously published scoring guidelines and quality-assurance procedures.^{20–22} The AHI was defined as the number of apneas plus hypopneas per hour of sleep, where apnea was defined as a decrease in airflow amplitude to <25% of baseline lasting for at least 10 sec, hypopnea was defined as a decrease in airflow or chest wall movement amplitude to less than 70% of baseline lasting for at least 10 sec, with both apneas and hypopneas requiring an associated 4% oxyhemoglobin desaturation. Hypoxemia index was defined as the percent of sleep time with oxyhemoglobin saturation less than 90%.

Statistical Analysis

AHI was categorized using the common clinical thresholds of 5, 15, and 30 events/hour, with the lowest category further divided at AHI of 1.5 events/hour. Hypoxemia index (percent sleep time with oxyhemoglobin saturation below 90%) was also divided into 5 categories, using thresholds of 0.05, 0.5, 4, and 12% sleep time. Descriptive statistics are presented by AHI category. Analysis of covariance was used to evaluate the relation between BA ultrasound measurements and SDB measures, using PROC GLM in SAS 9.1.²³ The dependent variables for the main analyses were baseline BA diameter and %FMD. The dependent variables for the flow analysis were baseline and hyperemic flow velocity and respective flow volume. Models are presented with adjustment for age, race and sex (Model 1); further adjustment for BMI

(Model 2); and further adjustment for variables found in a prior analysis to predict brachial reactivity in the Framingham Heart Study, including systolic blood pressure, heart rate, use of lipid-lowering agents, and performance of a 6-minute walk test prior to BA measurements, as well as diastolic blood pressure and antihypertensive medication use (Model 3).¹⁸ Significance of overall adjusted mean difference among SDB categories was tested. Secondary analyses were performed to assess effect modification stratifying by median age and sex. Two-sided $p < 0.05$ were considered statistically significant.

RESULTS

Ages of participants at the time of BA measurements were between 42 and 83 years. Fifty-two percent were women, 30% were ethnic minorities, 5% were current smokers but had not smoked the morning of the examination and 10% had known cardiovascular disease. The mean %FMD was 2.93% (SD 2.81%), the mean baseline BA diameter was 4.36 (SD 0.87) mm, the mean baseline flow velocity was 7.63 (SD 4.54) cm/s, the mean hyperemic flow velocity was 51.1 (SD 19.5) cm/s, similar to values previously reported from the Framingham Offspring Study.¹⁸ The median AHI was 3.1 (25th–75th percentile: 0.8–9.0) events/hour.

Polysomnography was performed a mean of 2.3 (SD 0.7) years prior to the BA ultrasound. The mean difference in BMI between the time of polysomnography and that of brachial ultrasound exam was 0.11 kg/m² and the BMI measurements at the two time points were highly correlated $r = 0.94$. The characteristics of the study sample for each AHI category are shown in Table 1.

In analyses adjusted for age, sex and race, the mean BA diameter was progressively larger with increasing AHI or hypoxemia index (Table 2, Model 1). The magnitude of this association was diminished if analyses were also adjusted for BMI, but remained statistically significant for AHI (Model 2). No further diminution in association was seen with further adjustment for systolic and diastolic blood pressure, heart rate, use of lipid-lowering and antihypertensive medications and performance of a 6-minute walk test prior to the BA measurements (Model 3, Figure 2). No apparent association was observed between either measure of SDB and % FMD in any model (Table 2). Further adjustment for shear stress by adding hyperemic flow velocity to the models examining the association between measures of SDB and %FMD did not alter the findings (data not shown).

When analyses were stratified by age, the relation of AHI to baseline BA diameter was apparent only in subjects older than the median age of 59 years, although an interaction term for AHI category by age above or below the median age was not statistically significant. No relation of AHI or hypoxemia index to %FMD was observed in either age group (Table 3). The association of BA diameter with AHI was similar in men and women and no significant association between %FMD and AHI was observed in either men or women; terms for interaction of AHI category with sex were not statistically significant for either BA diameter or % FMD ($p = 0.80$ and $p = 0.34$, respectively).

The baseline flow velocity and baseline flow volume were significantly higher in subjects with higher AHI in the model adjusted for age, race and sex (Table 4, Model-1). This association became non-significant after adjusting for BMI (Model-2). There was no significant association between the hyperemic flow velocity or volume and AHI in any model (Table 4). We found no association between either flow measure and the hypoxemia index (data not shown).

The results were very similar if analyses were repeated using a revised definition of apneas and hypopneas requiring only 3% rather than 4% oxyhemoglobin desaturation or if subjects

with 10% or more change in BMI between the polysomnography and BA ultrasound study were excluded (data not shown).

Although the mean time difference between the polysomnograms and the BA measurements was 2.3 years, there was little change in BMI between the two measurements (mean difference 0.11Kg/m², $r=0.94$). Exclusion from analysis of subjects whose BMI changed by more than 10% between the two measurements did not meaningfully alter the findings, nor did adjustment for the length of time between the polysomnogram and brachial artery measurements.

Given the sample size of 682 subjects and a significance level of $\alpha=0.05$, this study had >80% power to detect a significant association of AHI (or hypoxemia index) with %FMD in multiple linear regression models if AHI (or hypoxemia index) increased the model R-squared by 1.5%, assuming that the other covariates in the model account for R-squared of 10%.

DISCUSSION

The results of this study indicate that SDB, as quantified by the AHI using a conservative respiratory event definition that requires a 4% oxyhemoglobin desaturation, was associated with a significantly larger baseline BA diameter. After adjusting for relevant covariates, the magnitude of the association of SDB with baseline diameter is moderate; subjects with an AHI 15–29.9 and AHI ≥ 30 having an adjusted mean baseline diameter that is respectively 0.40 SD and 0.35 SD greater than those with AHI <1.5 (Model-3). Although this association was observed only in subjects age ≥ 59 years but not in younger subjects, the effect modification by age was not statistically significant. We observed no significant association between SDB and %FMD or between SDB and hyperemic flow velocity or hyperemic flow volume. Although AHI was associated with baseline flow velocity and baseline flow volume in models adjusted for age, sex and race, the association was diminished and no longer statistically significant after adjusting for BMI.

These main findings are consistent with the results of a previous community-based study of adults age 65 and older, which also reported an association between SDB and the baseline BA diameter.¹³ In that study SDB and FMD were significantly associated in the demographics-adjusted analysis, but this association became nonsignificant after adjusting for BMI.¹³ In contrast, several clinic-based case-control studies found an association between SDB and FMD^{5–7} and intervention studies found improved FMD following treatment of SDB with CPAP,^{8–11} or following vitamin C administration.¹²

There are several potential explanations for the difference between this and prior studies. FMD measurement techniques may play a role; differences in the cuff position [above versus below the elbow] was shown to have a significant effect on FMD measurement.²⁴ Whereas in this study the cuff was placed over the proximal forearm, in two previous studies the occluding cuff was placed proximal to the elbow.^{5,8} Clinic-based case-control studies are more prone to selection bias than the community-based sample evaluated in this study. It is also possible however, that SDB in subjects with elevated AHI identified by community screening may be of lesser physiologic significance than SDB in patients with similarly elevated AHI and clinical obstructive sleep apnea syndrome. Although selection bias should not be a concern with intervention studies, three previous intervention study did not include controls.^{8,9,11} It is also possible that changes in FMD may result from SDB-independent hemodynamic effects of CPAP, which effectively reduces both preload and afterload through mechanisms independent of its effect on SDB.²⁵

Prior studies have found an association between cardiovascular disease risk factors or cardiovascular disease and increased BA diameter. In the Framingham Offspring cohort, age, male sex, and BMI were significantly associated with increasing BA diameter in stepwise

models.¹⁸ In a study of women referred for coronary angiography to evaluate chest pain, baseline BA diameter was found to be significantly associated with the presence of coronary artery disease (CAD).¹⁴ Another case-control study of male subjects found similar results.¹⁵ In post-menopausal women, increased diameter of the iliac artery and aorta have also been shown to correlate with risk factors, including weight, waist circumference, insulin levels, and lower high-density lipoprotein levels.²⁶ Although the association between arterial diameter and indices of SDB were diminished after adjustment for BMI and cardiovascular risk factors, a statistically significant association with AHI persisted.

The adjusted mean difference in baseline diameter for subjects with AHI ≥ 15 was 0.2 mm greater than those with AHI < 1.5 . This difference is half as large as the previously reported difference in mean baseline BA diameter between subjects with and without CAD.¹⁵ Furthermore, the adjusted odds ratio for prevalent CAD was reported to be 3.56 (95% CI: 1.77–7.09) in women with baseline BA diameter larger than 4.1 mm compared to women with diameter < 3.6 mm.¹⁴ Thus, the age-, sex-, race- and BMI-independent association of moderately severe SDB with baseline BA diameter is of a magnitude likely to be clinically meaningful.

The mechanisms accounting for the association between SDB and larger arterial diameter are uncertain. One important factor may be increased baseline arterial flow in certain pathological states. Shear stress relates directly to flow velocity and inversely to arterial diameter, and chronic or intermittent elevations in blood flow increase local shear stress and stimulate outward arterial remodeling, a process that continues until shear stress is restored to baseline.²⁷ We therefore examined the association between AHI and the baseline flow velocity in a secondary analysis. Although AHI was associated with increased baseline flow in the demographics-adjusted model, the relationship was not significant after adjusting for BMI. This may reflect insufficient power of the analysis, which was limited to 361 subjects. It is possible, however, that measures of awake flow velocity do not reflect the recurrent episodes of hypoxia and/or increased activity of the sympathetic nervous system that occur during sleep in subjects with SDB,^{28,29} which may lead to transient increases in peripheral blood flow and outward remodeling. Finally, SDB could have direct effects on the arterial wall that stimulate arterial remodeling. For example, elevated blood pressure and episodes of hypoxemia could induce oxidative stress and inflammation in the arterial wall,³⁰ which also have been associated with increased BA diameter³¹ and outward remodeling of coronary arteries in human subjects.³² We found that AHI was associated with the baseline BA diameter in multivariable models but, after adjusting for BMI, hypoxemia index was not. As we only included events associated with at least 4% oxyhemoglobin desaturation, our results parallel those of a study that found that the frequency of respiratory events leading to 4% desaturation, but not the time spent at saturations below 90%, was associated with increased oxidative stress.²⁹

Limitations

The observational design of the present study does not allow firm conclusions regarding underlying mechanisms or the direction of association, although vascular dysfunction is not known to play a role in the pathogenesis of SDB. The study sample included an ambulatory cohort of middle-aged and older adults, and it is possible that a relation between SDB and FMD may have been more evident in younger individuals. We were unable to withhold vasoactive medications from the study participants due to the observational nature of the study. However, a previous study found that the administration of non-nitrate vasoactive medications does not acutely influence the BA diameter or FMD,³³ another found no independent association between chronic intake of vasoactive medications and FMD.¹⁸ Similarly, we were unable to administer nitroglycerine to our participants; hence, endothelium-independent vasodilation was not tested. Although the mean time difference between the polysomnograms and the BA

measurements was 2.3 years, the stability of the AHI was previously demonstrated over a 5 years interval in the SHHS cohort.³⁴ The magnitude of changes in AHI over that interval were strongly related to changes in BMI. The shorter time interval and stability of BMI between the polysomnogram and brachial artery measurements in this study suggest even greater stability in AHI between measurements. Moreover, the results were not substantively influenced by adjustment for the length of time between the two measurements. Thus, the change in SDB status over 2.3 years interval was unlikely to have caused substantial misclassification. Finally, despite adjusting for variables found to be significantly associated with BA diameter and FMD in the Framingham Study, confounding by unmeasured variables cannot be excluded. Balancing these limitations are several strengths, including the moderately sized, ethnically diverse sample drawn from a well-defined community-based cohort and the rigorously standardized and centrally analyzed BA ultrasound measurements and polysomnography that were obtained following strict protocols and explicit quality control measures.

In summary, we observed an association between SDB and larger BA diameter, but no relation between SDB and FMD. Whereas the latter finding differs from prior smaller studies and might relate to our study design and participant characteristics, it argues against an important association of SDB with conduit artery endothelial function in a community-based population. On the other hand, the observation that SDB correlates with arterial diameter may have important clinical implications for cardiovascular disease, as recent studies suggest that BA structure, including diameter and wall thickness, predict CAD and future cardiovascular events.^{14,15,35,36}

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Figure 1.
Study sample description

Figure 2. Adjusted* mean baseline brachial artery diameter by Apnea-Hypopnea category

*Adjusting for: Age, sex, race, BMI, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, heart rate, 6-minute walk test before brachial ultrasound, lipid lowering therapy. This work was performed at Boston University School of Medicine and at the NHLBI's Framingham Heart Study.

Table 1

Characteristics of the study sample by AHI category.*

	AHI					p-value
	< 1.5	1.5–4.9	5–14.9	15–29.9	≥30	
	n=232	n=178	n=172	n=69	n=31	(trend)
Age, years	56 (8)	61 (10)	60 (9)	63 (8)	62 (9)	<0.0001
Women, %	69	52	39	32	26	<0.0001
Race, %:						
White	60	75	75	72.5	84	0.001
Black	12	8	6	14.5	2	
Hispanic	19	12	15	10	13	
Asian	9	5	4	3	1	
BMI, kg/m ²	26.1 (4.5)	28.2 (4.2)	30.1 (5.4)	31.4 (5.7)	32.7 (5.6)	<0.0001
Systolic blood pressure, mm Hg	122 (17)	127 (17)	127 (17)	133 (19)	129 (15)	<0.0001
Diastolic blood pressure, mmHg	74 (9)	74 (9)	75 (10)	78 (10)	77 (9)	0.002
Heart rate, beat per minute	62 (10)	63 (11)	64 (10)	65 (11)	65 (9)	0.003
Total/HDL cholesterol ratio	3.8 (1.2)	4.3 (1.6)	4.5 (1.3)	4.6 (1.2)	4.8 (1.4)	<0.0001
Diabetes [†] , %	6	13	15	26	19	<0.0001
Current smoking, [§] %	5	3	3	6	10	0.61
Prevalent cardiovascular disease, %	8	12	9	11	13	0.31
Hypertension [‡] , %	29	42	45	59	65	<0.001
Hypertension medications, %	23	29	31	40	52	<0.001
Lipid-lowering medications, %	12	19	20	26	32	0.003
Hormone replacement therapy, % women	34	29	27	23	25	0.14

	AHI				p-value
	< 1.5	1.5–4.9	5–14.9	15–29.9	≥30
	n=232	n=178	n=172	n=69	n=31
Walked before test, %	24	35	28	23	26
					1.0

Abbreviations: BMI = body mass index, AHI = apnea-hypopnea index, HDL = high-density lipoprotein, CVD = cardiovascular disease.

* All values are percent or mean (SD)

[†] Diabetes defined as a fasting blood sugar ≥ 126mg/dl or on treatment.

[‡] HTN defined as a present if the average of 2 measured clinic visit seated systolic BP ≥140 seated diastolic BP ≥90 or if the person was on hypertension medications.

[§] Excluding subjects who smoked the morning of the brachial artery ultrasound testing

Table 2

Adjusted mean (SE) baseline brachial artery diameter and percent flow-mediated dilatation by category of sleep-disordered breathing.

	N	Model 1 (Age, race, sex)	Model 2 (Age, race, sex, BMI)	Model 3 (All covariates [*])
AHI[†]				
≥30	31	4.67 (0.11)	4.53 (0.11)	4.50 (0.11)
15–29.9	69	4.66 (0.07)	4.56 (0.07)	4.55 (0.07)
5–14.9	172	4.38 (0.05)	4.33 (0.05)	4.33 (0.04)
1.5–4.9	178	4.32 (0.04)	4.33 (0.04)	4.34 (0.04)
<1.5	232	4.24 (0.04)	4.32 (0.04)	4.32 (0.04)
Baseline Brachial Artery Diameter (mm)				
p-value [‡]		<0.0001	0.03	0.048
Hypoxemia index[§]				
≥12	33	4.59 (0.10)	4.44 (0.10)	4.37 (0.11)
4–11.9	47	4.48 (0.09)	4.33 (0.09)	4.32 (0.09)
0.5–0.399	150	4.49 (0.05)	4.42 (0.05)	4.43 (0.05)
0.05–0.49	167	4.37 (0.05)	4.37 (0.05)	4.37 (0.04)
<0.05	285	4.24 (0.04)	4.31 (0.04)	4.32 (0.04)
p-value [‡]		0.0002	0.48	0.53
AHI[†]				
≥30	31	3.17 (0.49)	3.36 (0.50)	3.40 (0.49)
15–29.9	69	2.36 (0.33)	2.50 (0.34)	2.62 (0.33)
5–14.9	172	2.90 (0.21)	2.98 (0.21)	2.94 (0.20)
1.5–4.9	178	2.94 (0.20)	2.93 (0.20)	2.95 (0.20)
<1.5	232	3.08 (0.19)	2.97 (0.20)	2.95 (0.19)
% Flow Mediated Dilatation				
p-value [‡]		0.45	0.63	0.75
Hypoxemia index[§]				

	N	Model 1 (Age, race, sex)	Model 2 (Age, race, sex, BMI)	Model 3 (All covariates*)
≥12	33	2.88 (0.48)	3.09 (0.49)	3.33 (0.48)
4–11.9	47	3.21 (0.40)	3.41 (0.41)	3.37 (0.40)
0.5–0.399	150	2.62 (0.23)	2.71 (0.23)	2.73 (0.22)
0.05–0.49	167	2.91 (0.21)	2.91 (0.21)	2.90 (0.20)
<0.05	285	3.07 (0.17)	2.96 (0.17)	2.94 (0.17)
p-value ‡		0.56	0.64	0.58

* Covariates: Age, sex, race, BMI, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, heart rate, 6-minute walk test before brachial ultrasound, lipid lowering therapy.

‡ Apnea-hypopnea index

‡ p-value obtained from analysis of covariance testing equal adjusted means

§ Percent sleep time spent with oxygen saturation <90%

Relation of baseline brachial artery diameter and percent flow-mediated dilatation to the apnea-hypopnea index stratified by median age and by sex adjusting for all covariates*.

Table 3

AHI [†]	N		BAD [‡] (mm)		%FMD §	
	Age<59	Age≥59	Age<59	Age≥59	Age<59	Age≥59
≥30	11	20	4.11 (0.18)	4.77 (0.13)	4.83 (0.94)	2.28 (0.51)
15–29.9	21	48	4.26 (0.13)	4.73 (0.09)	3.10 (0.70)	2.14 (0.33)
5–14.9	77	95	4.20 (0.07)	4.47 (0.06)	3.42 (0.36)	2.43 (0.23)
1.5–4.9	82	96	4.23 (0.06)	4.44 (0.06)	3.50 (0.33)	2.34 (0.23)
<1.5	147	85	4.21 (0.05)	4.42 (0.07)	3.64 (0.27)	2.27 (0.25)
p-value [¶]			0.95	0.009	0.59	0.96
	Women	Men	Women	Men	Women	Men
≥30	8	23	3.98 (0.21)	5.07 (0.13)	3.41 (1.01)	3.09 (0.53)
15–29.9	22	47	4.03 (0.12)	5.15 (0.09)	2.52 (0.61)	2.54 (0.37)
5–14.9	67	105	3.69 (0.07)	4.99 (0.06)	3.23 (0.35)	2.67 (0.24)
1.5–4.9	95	83	3.79 (0.06)	4.95 (0.07)	3.27 (0.29)	2.60 (0.28)
<1.5	163	69	3.76 (0.05)	4.90 (0.08)	3.22 (0.23)	2.58 (0.32)
p-value [¶]			0.13	0.31	0.84	0.93

* Covariates: Age, sex, race, BMI, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, heart rate, 6-minute walk test before brachial ultrasound, lipid lowering therapy.

† Apnea-hypopnea index

‡ Baseline brachial artery diameter

§ Percent flow-mediated dilatation

¶ p-value obtained from analysis of covariance testing equal adjusted means

Table 4
Adjusted mean (SE) BA baseline and hyperemic flow velocity and volume by category of sleep-disordered breathing

	AHI*	N [†]	Model 1 (Age, race, sex)	Model 2 (Age, race, sex, BMI)	Model 3 (All covariates [‡])
	≥30	10	8.97 (1.41)	8.27 (1.42)	7.70 (1.40)
	15–29.9	34	9.33 (0.78)	8.85 (0.79)	8.56 (0.78)
Baseline Flow Velocity (cm/s)	5–14.9	84	7.72 (0.49)	7.48 (0.49)	7.44 (0.48)
	1.5–4.9	92	7.98 (0.46)	7.92 (0.46)	7.85 (0.44)
	<1.5	141	6.85 (0.39)	7.19 (0.40)	7.37 (0.40)
	p-value [§]		0.049	0.42	0.70
	≥30	10	49.0 (5.6)	51.5 (5.6)	49.9 (5.4)
	15–29.9	34	48.8 (3.1)	50.4 (3.1)	52.1 (3.0)
Hyperemic Flow Velocity (cm/s)	5–14.9	84	50.8 (1.9)	51.6 (1.9)	51.1 (1.9)
	1.5–4.9	92	51.0 (1.8)	51.2 (1.8)	52.0 (1.7)
	<1.5	141	52.0 (1.5)	51.0 (1.6)	50.3 (1.5)
	p-value [§]		0.91	1.0	0.95
	≥30	10	1.56 (0.25)	1.32 (0.25)	1.22 (0.24)
	15–29.9	34	1.58 (0.14)	1.42 (0.14)	1.39 (0.13)
Baseline Flow Volume (mL/s)	5–14.9	84	1.16 (0.09)	1.08 (0.09)	1.07 (0.08)
	1.5–4.9	92	1.23 (0.08)	1.21 (0.08)	1.20 (0.08)
	<1.5	141	0.99 (0.07)	1.10 (0.07)	1.13 (0.07)
	p-value [§]		0.002	0.19	0.31
	≥30	10	7.51 (0.96)	7.09 (0.97)	6.80 (0.95)
	15–29.9	34	7.96 (0.53)	7.68 (0.54)	8.00 (0.53)
Hyperemic Flow Volume (mL/s)	5–14.9	84	7.52 (0.33)	7.38 (0.34)	7.30 (0.33)
	1.5–4.9	92	7.33 (0.31)	7.30 (0.31)	7.36 (0.30)
	<1.5	141	6.95 (0.26)	7.15 (0.27)	7.10 (0.27)
	p-value [§]		0.48	0.93	0.63

* Apnea-hypopnea index

[†] Total number of subjects was 361 for the flow analysis. (see methods section)

[‡] Covariates: Age, sex, race, BMI, Systolic blood pressure, diastolic blood pressure, antihypertensive medication use, heart rate, 6-minute walk test before assessment of brachial ultrasound lipid lowering therapy.

[§] p-value obtained from analysis of covariance testing equal adjusted means