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Faye Routledge, *Emory University*
[Sandra B Dunbar](#), *Emory University*
[Melinda K Higgins](#), *Emory University*
[Ann E Rogers](#), *Emory University*
Christine Feeley, *University of Pittsburgh*
[Octavian Cosmin Ioachimescu](#), *Emory University*
Kristina Euwer, *University of Pittsburgh*
[Danny Eapen](#), *Emory University*
[Arshed Ali Quyyumi](#), *Emory University*

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Insomnia Symptoms are Associated with Abnormal Endothelial Function

Faye S. Routledge, PhD, RN¹, Sandra B. Dunbar, PhD, RN¹, Melinda Higgins, PhD¹, Ann E. Rogers, PhD, RN¹, Christine Feeley, PhD, RN², Octavian Ioachimescu, PhD, MD³, Kristina Euwer, MD^{4,5}, Danny Eapen, MD⁵, and Arshed Quyyumi, MD⁵

¹Emory University, Nell Hodgson Woodruff School of Nursing, Atlanta, GA

²University of Pittsburg, School of Nursing Medical Center, Pittsburg, PA

³Atlanta Veterans Affairs Medical Center and Emory University, Division of Pulmonary, Allergy, Critical Care and Sleep Medicine, Atlanta, GA

⁴University of Pittsburg Medical Center, Pittsburg, PA

⁵Emory University, School of Medicine, Atlanta, GA

Abstract

Background—Insomnia is a prevalent sleep disorder and it has been increasingly associated with cardiovascular morbidity and mortality. The reasons for this relationship are not completely understood but may involve endothelial dysfunction. In this study, we hypothesized that insomnia symptoms would be associated with reduced endothelial function.

Methods—Working adults [n=496, 67.5% female, 78.6% white, mean age: 48.7±10.8 years, body mass index (BMI): 28.2±6.7 kg/m², diabetes: 5.8%, hypertension: 20.0%, hyperlipidemia: 17.9%, heart disease: 2.6%] enrolled in the Emory-Georgia Tech Predictive Health Institute study completed baseline demographic, clinical, depression (Beck Depression Inventory II; BDI-II), anxiety (General Anxiety Disorder-7; GAD-7) sleep (Pittsburg Sleep Quality Index, PSQI) and non-invasive endothelial function (brachial artery flow-mediated dilation; FMD) measures. Insomnia symptoms were defined as subjective sleep latency of ≥ 30 minutes, nighttime or early morning awakenings and/or sleep medication use occurring ≥ 3 times per week in the past month.

Results—Insomnia symptoms were reported by 39.5% of participants. Multivariable regression models showed that insomnia symptoms, age, baseline artery diameter and dyslipidemia were inversely related to FMD. After adjusting for age, baseline artery diameter, and dyslipidemia participants reporting insomnia symptoms had lower FMD than participants reporting better sleep (adjusted FMD means= 6.13%±0.28 vs 6.83%±0.26, *p*=.035).

Conclusion—In this study insomnia symptoms were associated with reduced FMD. Research examining the therapeutic benefits of treating insomnia on endothelial function and future cardiovascular risk is warranted.

Keywords

Insomnia; Sleep; Vasodilation; Endothelium-Dependent Vasodilation; Cardiovascular Disease; Sleep Latency; Awakenings

INTRODUCTION

Insomnia is a sleep disorder characterized by subjective reports of difficulties initiating sleep, maintaining sleep during the night, and/or awakening earlier than desired, combined with daytime distress or impairment.¹ Based on epidemiological studies, insomnia is estimated to affect 6-48% of the general population with approximately 6% of people reaching the diagnostic threshold for insomnia disorder and another 30-48% reporting insomnia symptoms.² In a prospective cross-sectional study of 3282 adults 18-65 years of age the overall prevalence of insomnia was 21.4% but was significantly higher for people with medical disorders compared to those without medical disorders (26.3% vs 14.8%, $p < 0.001$). Specifically, heart disease and hypertension were associated with an adjusted odds of insomnia of 1.6 and 1.5, respectively.³

Although the direction of causality between insomnia and cardiovascular (CV) risk is unknown studies have linked insomnia symptoms to a risk of future CV morbidity and mortality. A meta-analysis of 13 prospective cohort studies including 122, 501 healthy subjects at baseline found that people experiencing insomnia symptoms had a 45% increased risk of cardiovascular disease (CVD; defined as myocardial infarction, stroke or heart disease) and CV mortality compared to people without sleep complaints.⁴ Another recent meta-analysis of 17 cohort studies with a 1 year follow-up in 311, 260 adults initially free of CVD found that insomnia was associated with an increased risk of individual types of CVD including myocardial infarction (relative risk; RR 1.41), coronary heart disease (RR 1.28), and stroke (RR 1.55) after adjusting for established CV risk factors.⁵

Flow-mediated dilatation (FMD) is a commonly used noninvasive measure of endothelial function. Endothelial (dys)function is quantified as the amount of brachial artery dilation to a hyperemic blood flow stimulus.⁶ Disruption of endothelial function characterizes the early stages of the atherosclerosis disease process⁷ therefore, FMD is considered to be a surrogate marker of preclinical CVD. Prognostic studies have demonstrated that FMD is inversely associated with long-term CV events in healthy subjects and populations with variable levels of CV risk.⁸

Although there is growing evidence supporting the relationship between insomnia and CV health, the reasons for this relationship are unclear. Lower FMD has been observed in sleep apnea populations,⁹ people reporting poorer overall sleep quality,¹⁰ and experimental sleep restriction in healthy subjects.¹¹ Less is known about the relationship between insomnia symptoms and endothelial function with only one study of healthy adults finding lower FMD in women, but not men, reporting frequent early morning awakenings.¹² Endothelial dysfunction may be a mechanism by which insomnia affects CV health. The aim of this cross-sectional, secondary analysis of the Emory-Georgia Tech Predictive Health Initiative cohort study was to compare endothelial function in a community sample of working adults

(n=496) with and without symptoms of insomnia. We hypothesized that insomnia symptoms would be associated with reduced endothelial function.

METHODS

This study is a secondary analysis of the Emory-Georgia Tech Predictive Health Initiative, a large observational cohort study. The methodology has been reported previously.^{13,14} In brief, the cohort was recruited largely (~ 90%) from a random sample of university and healthcare employees and lesser (~ 10%) from self or healthcare provider referral.¹³ Participants were eligible for enrollment if they were: 18 years of age without a previous 12 month history of non-accident related hospitalization, Axis 1 psychosocial disorder, medication adjustment for treatment of a chronic condition (except for changes to antihypertensives or antidiabetics), substance or alcohol abuse, current malignant neoplasm, uncontrolled or poorly controlled chronic condition, acute illness within 2 weeks of the baseline visit, inability to participate in study assessments or inability to give informed consent.^{13,14} The study involved two baseline assessments (2-4 weeks apart), a 6 month assessment and 4 annual assessments. At each time point multiple psychosocial, physical and biomarker assessments were completed as previously described.^{13,14}

In this study only baseline data were used. A total of 653 adults (18-82 years) completed the baseline visits. Participants were also excluded if they did not have baseline FMD data (n=35), had a sleep apnea diagnosis (n=8) or reported symptoms of sleep apnea (i.e. frequent snoring, apnea and/or excessive daytime sleepiness; n=114) resulting in a sample of 496 (19-82 years). The study was approved by the Emory University Institutional Review Committee. Written informed consent was obtained from all participants.

Variables and Measures

The baseline assessment consisted of 2 study visits 2-4 weeks apart. Demographics, anthropometrics, blood draw and FMD assessments were completed at the first in-office baseline visit. The Pittsburgh Sleep Quality Index (PSQI), Beck Depression Inventory-II (BDI-II) and Generalized Anxiety Disorder 7-item (GAD-7) scale and Epworth Sleepiness Scale (ESS), were completed via web-portal at the participants' homes in between the 2 baseline visits.

Sleep Groups—Three items (sleep latency of ≥ 30 minutes; nighttime or early morning awakenings; sleep medication use) from the PSQI, a 19-item self-report and 5-item bed partner/roommate self-report scale used to evaluate general sleep quality over the past month,¹⁵ were used to categorize participants into the insomnia symptoms group or better sleepers group.

Insomnia symptoms group: Participants were included in the insomnia symptoms group if they reported experiencing a sleep latency of ≥ 30 minutes; nighttime or early morning awakenings and/or sleep medication (prescription or over-the-counter) use ≥ 3 times per week in the past month.

Better sleepers group: Participants were included in the better sleepers group if they experienced a sleep latency of ≤ 30 minutes; nighttime or early morning awakenings and/or sleep medication (prescription or over-the-counter) use not during the past month, < 1 once a week or 1-2 times per week in the past month.

Depressive Symptoms—Depressive symptom severity was measured with the 21-item self-reported BDI-II. Items were rated from 0 to 3 and summed with higher scores suggesting higher levels of depressive symptom severity.¹⁶

Anxiety—Generalized anxiety disorder severity was measured using the self-reported GAD-7 scale. Each item was rated from 0 to 3 and then summed with higher scores representing greater generalized anxiety disorder symptom severity.¹⁷

Sleepiness—Daytime sleepiness was measured with the ESS, an 8-item self-reported scale assessing general level of daytime sleepiness.¹⁸ Participants rated from 0-3 their propensity to fall asleep during sleep-inducing situations with higher scores indicating greater daytime sleepiness.

Brachial Artery Flow-Mediated Dilatation—Prior to the FMD assessment, participants abstained from smoking for 30 minutes, eating and drinking (except for water) for 6 hours, consuming supplements containing herbal stimulants, caffeine or calcium for 6 hours and exercising heavily for 24 hours. Participants were instructed to continue taking prescribed medication the day of their visit.

FMD was measured using an Acuson 10-mHz linear-array transducer and an Acuson Aspen ultrasound system (Acuson, Mountain View, CA) and following established methodology.¹⁹ Briefly, under standardized conditions participants were imaged after resting quietly and supine for at least 10 minutes. Longitudinal B-mode ultrasound images of the right brachial artery, 2 to 10 cm above the antecubital crease, and at end-diastole were obtained under baseline conditions (at rest) and during hyperemia —induced by a 5-minute right forearm BP cuff inflation to 200 mm Hg and rapid deflation of the forearm BP cuff. Hyperemic arterial diameters were obtained at 1 minute after rapid deflation of the forearm BP cuff in response to increased blood flow following cuff deflation. Images were digitized online, and arterial diameters were measured with customized software (Medial Imaging Applications, Inc.) by an ultrasound technician unaware of participants sleep group status. FMD was defined as the percent increase in arterial diameter from baseline.²⁰ Brachial artery diameter percent change may result in bias towards greater vasodilation in smaller arteries¹⁹ therefore, baseline arterial diameter was used as a covariate in multivariate analyses. In an evaluation of 11 participants who underwent this laboratory FMD protocol twice over an average of 8 days, repeat FMD values demonstrated acceptable variability (a mean difference of $1.26 \pm 0.76\%$, $r = .75$). The FMD mean difference between two readings of the same 11 measurements was $0.82 \pm 0.48\%$, $r = .97$.²⁰ FMD measurements were read by two ultrasound technicians experienced in FMD assessment.

Demographics, Anthropometrics and Laboratory Analysis—Standardized questionnaires were used to assess demographics, medical history and medications (self-

report). Height and weight were measured by a trained research assistant and body mass index (BMI, weight/height², in kg/m²) was calculated. Framingham risk score (FRS) was calculated using the risk calculator (<https://www.framinghamheartstudy.org/risk-functions/cardiovascular-disease/10-year-risk.php>). BP was measured using the LifeSource TM-2655 oscillometric BP monitor. Blood was drawn by a research nurse following 6-hour fast and analyzed in a clinical laboratory using the spectrophotometry method for total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride and glucose levels, and the nephelometric method for high-sensitivity C-reactive protein (hsCRP).

Statistical Analysis

Normality statistics, histograms, boxplots and normal probability plots were examined to assess normality. Triglycerides underwent log transformation for normality. Glucose, BDI-II, GAD-7 and ESS variables remained non-normally distributed following transformations therefore non-parametric testing was used. Group characteristics were compared using the Student's t-test, Wilcoxon two-sample tests and chi-square tests. Data is presented as means (\pm standard deviation, SD), medians (25th-75th interquartile ranges) or percentages, respectively. Pearson and Spearman correlations were used to assess bivariate associations with FMD.

Variables that were significantly correlated with FMD at $p < 0.1$ [age, gender, baseline artery diameter, systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), glucose, triglycerides, smoking, hypertension, antihypertensive medication, dyslipidemia, antidyplidemic medications, antiglycemic medication and insomnia] were initially explored as covariates in multivariable regression analysis. Gender and baseline artery diameter were found to be highly correlated ($\rho = -0.69$, $p < 0.001$) as expected given that women generally have smaller arteries than men. To reduce confounding between gender and baseline artery diameter, baseline artery diameter was chosen to be entered into the model because baseline artery diameter was more strongly correlated with FMD ($r = -0.410$, $p < 0.001$) than gender ($\rho = 0.130$, $p = 0.004$). Therefore, in multivariable regression model 1, the stepwise variable selection method ($p < 0.05$ for variable entry, $p > 0.10$ for removal) was initially used to assess the relationship between age, baseline artery diameter and FMD. In model 2, we examined the relationship between age, baseline artery diameter and participant clinical characteristics (SBP, DBP, HR, glucose, triglycerides, smoking, hypertension, antihypertensive medication, dyslipidemia, antidyplidemic medications, and antiglycemic medication) using the stepwise variable selection method ($p < 0.05$ for variable entry, $p > 0.10$ for removal). Given that high correlations between SBP and DBP ($r = 0.678$, $p < 0.001$) and hypertension and antihypertensive medication ($\rho = 0.596$, $p < 0.001$) were found; SBP and hypertension were chosen to be entered into the model because FMD was more strongly correlated with SBP ($r = -0.203$, $p < 0.001$) and hypertension ($\rho = -0.124$, $p = 0.006$) than DBP ($r = -0.140$, $p = 0.002$) or antihypertensive medications ($\rho = -0.078$, $p = 0.084$), respectively. In model 3, we examined the relationship between insomnia symptoms and FMD after considering age, baseline artery diameter and dyslipidemia using the stepwise variable selection method ($p < 0.05$ for variable entry, $p > 0.10$ for removal). Given the age range of the sample we also tested the interaction between age and insomnia on FMD.

As a follow-up to model 3, analysis of covariance (ANCOVA) was used in comparing FMD means between the insomnia symptoms and better sleepers after adjusting for age, baseline artery diameter and dyslipidemia associated with FMD in the regression analysis. Statistical analyses were conducted using the SAS 9.4 system (SAS Institute, Cary, NC) with significance set at $p=0.05$.

RESULTS

Participant Characteristics

The sample ($n=496$) was largely female (67.5%), white (78.6%), and well educated (Table 1). Insomnia symptoms were reported by 39.5% of participants. In univariate analysis, participants with insomnia symptoms had a higher BMI, more prevalent hypertension and hyperlipidemia, higher depressive and anxiety symptoms, a smaller absolute brachial artery diameter change and a smaller FMD response compared to the better sleepers (Table 1).

Initial Bivariate Correlational Analyses

Variables associated with FMD at $p \leq 0.1$ included age ($r=-0.176$, $p<0.001$), baseline artery diameter ($r=-0.410$, $p<0.001$), SBP ($r=-0.203$, $p<0.001$), DBP ($r=-0.140$, $p=0.002$), HR ($r=0.113$, $p=0.012$), logtriglycerides ($r=-0.123$, $p=0.007$), glucose, ($\rho=-0.136$, $p=0.003$), insomnia ($\rho=-0.081$, $p=0.072$), gender ($\rho=0.130$, $p=0.004$), hypertension ($\rho=-0.124$, $p=0.006$), dyslipidemia ($\rho=-0.178$, $p<0.001$), current smoker ($\rho=-0.133$, $p=0.003$), antihypertensives ($\rho=-0.078$, $p=0.084$), antidyslipidemics ($\rho=-0.111$, $p=0.013$), antiglycemics ($\rho=-0.081$, $p=0.070$). No other variables were associated with FMD at $p \leq 0.1$.

Regression Analysis

Both age and baseline artery diameter were found to be significantly associated with FMD in model 1 (Table 2). In model 2, we considered the potential relationships between age, baseline artery diameter, and clinical characteristics (SBP, HR, glucose, triglycerides, smoking, hypertension, dyslipidemia, antidyslipidemic medications, and antiglycemic medication) and FMD. Age, baseline artery diameter and dyslipidemia were significantly associated with FMD following the stepwise variable selection method for multivariable regression. In model 3, insomnia symptoms were found to be inversely associated with FMD along with age, baseline artery diameter and dyslipidemia. No other participant characteristics were significantly associated with FMD. We tested the interaction between age and insomnia in the regression model but it was not found to be significant. In comparing means, ANCOVA analysis indicated that participants with insomnia symptoms had lower FMD than those reporting better sleep ($F(1, 487) = 4.48$, $p=0.035$; adjusted mean FMD = $6.13\% \pm 0.28$ vs $6.83\% \pm 0.26$) following adjustment for baseline artery diameter ($p<0.001$), age ($p=0.012$), and dyslipidemia ($p=0.020$).

DISCUSSION

The present study indicated that participants with insomnia symptoms had reduced endothelial function compared to better sleepers. Specifically, participants with insomnia

symptoms exhibited FMD responses that were approximately 0.7% lower than better sleeping participants. These findings are significant as a 1% decrease in FMD is associated with a 13% increase in the risk of future CV events.²¹ A recent meta-analysis reported insomnia symptoms were associated with an increased risk of CV morbidity and mortality (RR 1.45, 95% CI 1.29-1.62; $p < .00001$).⁴ Given our findings, it is possible that reduced endothelial function may be contributing, in part, to this increased CV risk among people with symptoms of insomnia.

Prior studies have reported that experimental laboratory sleep deprivation reduced endothelial function in healthy men,²² poorer subjective sleep quality was related to reduced endothelial function in working adults,¹⁰ and early morning awakenings several times a week in women, but not men, was associated with reduced endothelial function in otherwise healthy adults free of CVD and antihypertensives.¹² This study extends findings by reporting an association between insomnia symptoms and FMD in people with relatively low cardiovascular risk factor burden (FRS 6.1%±5.7).

The mechanisms linking insomnia symptoms to reduced endothelial function remain poorly understood and are likely multifactorial. It has been proposed that people with insomnia have physiologic hyperarousal as evidenced by greater nighttime resting HR,^{23,24} central and sympathetic nervous system dysregulation,^{23,25-29} heightened hypothalamic-pituitary-adrenal axis activation,³⁰⁻³² and greater nighttime whole-body metabolism.³³ Other, but not all,³⁴ studies reported a relationship between insomnia symptoms and higher levels of inflammatory markers (IL-6,³⁵⁻³⁷ CRP^{37,38}) compared to good sleepers. In our study we did not find that daytime resting heart rate or CRP differed between people with symptoms of insomnia or good sleepers. Methodological differences between studies may, in part, explain discordant findings. For instance, higher HRs in insomnia were observed during sleep under controlled laboratory conditions in healthy participants²³ or in objectively defined insomnia participants.²⁴ However, similar to our study, no differences in daytime HR were found between subjects with insomnia and good sleepers.²⁴ Additionally, studies that found an association between insomnia symptoms and CRP were conducted in samples of healthy women.^{37,38} Although the participants in our study were of lower cardiovascular risk burden, approximately 33% of participants had at least 1 CV risk factor (e.g. hypertension, diabetes, dyslipidemia). This may have played a role, in part, in attenuating a potential relationship between insomnia symptoms and CRP in our study.

Psychological mechanisms may also factor into the association between insomnia and endothelial function. Insomnia and depression are closely associated with one another; in fact, insomnia is predictive of depression.³⁹ Depressive symptoms have been linked with reduced endothelial function.⁴⁰ In our study, we did find that individuals with insomnia symptoms had greater depressive and anxiety symptoms than the better sleepers. It should be noted that in this study both symptom scores were in the mild ranges and were not correlated with FMD. Additionally, the association between insomnia symptoms and endothelial function may be due, in part, to adverse health behaviors. Studies have reported associations between insomnia symptoms and greater alcohol consumption,⁴¹ less physical activity,⁴¹ reduced physical fitness,⁴² and weight gain⁴³ all of which can increase CVD risk.

CV risk reducing behaviors include maintaining an ideal body weight, increasing physical activity, reducing sodium, total and saturated fat, increasing fruits and vegetables, alcohol in moderation and smoking cessation.⁴⁴ There is increasing evidence that insomnia symptoms contribute to the development of HTN and CVD.^{4,5,45,46} Insomnia is not identified or included in current CV prevention guidelines. The American Academy of Sleep Medicine recommends cognitive behavioral therapy for insomnia (CBT-I) as a first-line, non-pharmacologic treatment for insomnia.⁴⁷ Studies have demonstrated sustained sleep improvements following CBT-I treatment⁴⁸ as well as patient preference for CBT-I compared to pharmacotherapy.⁴⁹ Insomnia is a common sleep disorder in adults but is frequently overlooked by healthcare professionals.² Nurses are ideally positioned to assess insomnia symptoms in patients and given its prevalence; insomnia may be an important target for reducing overall CVD risk.

Limitations

Our findings should be interpreted within the methodological limitations of the study. Participants were categorized as having insomnia symptoms or good sleep based on self-report. Self-reported questionnaires are prone to recall bias but are frequently used in the insomnia literature⁵⁰ and in studies reporting a relationship between insomnia symptoms and cardiovascular outcomes.^{45,46} Second, although we excluded participants with sleep apnea symptoms, polysomnography was not completed and cannot be certain that all individuals with sleep apnea were excluded. Third, the sample demographics of predominantly white, well educated, working women limit generalizability of the study findings. Finally, our current analysis is cross sectional, limiting our ability to draw any causal inferences between insomnia and endothelial function.

Conclusion

In summary, in a community sample of relatively low-risk factor burden participants, insomnia symptoms were associated with reduced endothelial function. Future studies should examine the longitudinal relationship between endothelial function and insomnia symptoms. Additionally, intervention trials are needed to evaluate if improving insomnia symptoms might improve endothelial function and ultimately CV outcomes.

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What is new?

- Insomnia symptoms were associated with lower FMD.
- It is possible that impaired endothelial function may be contributing, in part, to the increased cardiovascular risk among individuals with symptoms of insomnia.
- Insomnia may be an important target for reducing overall CVD risk.

Table 1

Group Characteristics

Variable	Overall (n=496)	Insomnia Symptoms (n=196)	Better Sleepers (n=300)	P
Age (years)	48.7±10.8	49.8±10.5	48.0±10.9	.073
BMI (kg/m ²)	28.2±6.7	29.0±7.6	27.7±6.0	.040
Gender (female, %)	67.5%	70.4%	65.7%	.270
Race/Ethnicity				.803
African American	21.4%	21.9%	21.0%	
White	78.6%	78.1%	79.0%	
Education				.371
High School or less (<13yrs)	1.6%	2.6%	1.0%	
Undergraduate (13-16yrs)	39.5%	40.3%	39.0%	
>Undergraduate (17+yrs)	58.9%	57.1%	60.0%	
Current Smoker	5.4%	7.1%	4.3%	.178
Past Medical History				
Diabetes	5.8%	7.1%	5.0%	.320
Hypertension	20.0%	26.0%	16.0%	.006
Hyperlipidemia	17.9%	23.0%	14.7%	.019
Heart Disease	2.6%	3.6%	2.0%	.284
Anxiety/Depression	23.2%	24.5%	22.3%	.578
Current Medication				
Antiglycemic	2.02%	3.1%	1.3%	.204
Antihypertensive	11.9%	13.3%	11.0%	.446
Antihyperlipidemic	6.0%	7.6%	5.0%	.226
Antidepressant	6.0%	6.6%	5.7%	.659
SBP (mmHg)	122±16	123±16	121±17	.151
DBP (mmHg)	76±11	77±10	76±12	.441
HR (bpm)	68.6±10.0	69.4±10.4	68.1±9.6	.159
Glucose (mg/dL)	87.0 (82.0- 93.0)	88.0 (82.0-94.0)	87.0 (82.0- 92.0)	.348
Total Cholesterol (mg/dL)	195.9±35.6	198.0±36.9	194.5±34.7	.298
LDL (mg/dL)	111.3±31.2	113.1±33.1	110.2±30.0	.319
HDL (mg/dL)	64.0±18.3	64.1±19.0	63.9±17.8	.933
Triglycerides (mg/dL)	87.0 (65.0- 121.0)	90.0 (65.0- 129.0)	84.0 (65.0- 115.5)	.402
hs-CRP (mg/L)	0.16 (0.10- 0.35)	0.17 (0.10-0.38)	0.15 (0.10- 0.33)	.384
FRS (%)	<u>6.1±5.7</u>	<u>6.6±5.8</u>	<u>5.8±5.6</u>	<u>.144</u>
BDI-II	4.0 (1.0-8.0)	5.0 (2.0-10.0)	3.0 (1.0-6.0)	<.001
GAD-7	3.0 (1.0-5.0)	4.0 (1.0-7.0)	2.0 (0-4.0)	<.001
ESS	5.0 (3.0-7.0)	5.0 (3.0-7.0)	5.0 (3.0-7.0)	.862

Variable	Overall (n=496)	Insomnia Symptoms (n=196)	Better Sleepers (n=300)	P
Brachial Artery Diameter (mm)	3.27±0.63	3.23±0.61	3.29±0.64	.333
Absolute Artery Diameter	0.21±0.11	0.20±0.10	0.22±0.11	.027
FMD (%)	6.9±4.0	6.5±3.6	7.2±4.2	.041

BDI-II= Beck Depression Inventory II; BMI= body mass index in kilograms per square meters; CRP- C-reactive protein; DBP= diastolic blood pressure; ESS= Epworth Sleepiness Scale; FMD = brachial artery flow-mediated dilation; FRS=Framingham Risk Score; GAD-7= Generalized Anxiety Disorder 7 item assessment; HDL= high density lipoprotein; HR= heart in beats per minute; LDL= low density lipoprotein; SBP= systolic blood pressure.

Median (inter-quartile range) reported for not normally distributed variables

Table 2

Predictors of brachial artery flow-mediated dilation (FMD).

	<i>B</i>	β	95% CI for <i>B</i>		<i>p</i> value
			Lower	Upper	
Model 1: adjusted R²=.178					
Baseline artery diameter (mm)	-2.45	-0.39	-2.96	-1.94	<.001
Age (years)	-0.04	-0.13	-0.08	-0.02	.001
Model 2 adjusted R²=.188					
Baseline artery diameter (mm)	-2.40	-0.38	-2.90	-1.89	<.001
Age (years)	-0.04	-0.11	-0.07	-0.01	.008
Dyslipidemia (No=0, Yes=1)	-1.10	-0.11	-1.94	-0.25	.011
Model 3 adjusted R²=.193					
Baseline artery diameter (mm)	-2.43	-0.39	-2.94	-1.93	<.001
Age (years)	-0.04	-0.11	-0.07	-0.01	.012
Dyslipidemia (No=0, Yes=1)	-1.00	-0.10	-1.85	-0.16	.020
Insomnia (No=0, Yes=1)	-0.70	-0.09	-1.35	-0.05	.035

Abbreviations: *B* = non-standardized (parameter estimate) regression coefficient; β =standardized regression coefficient; CI = confidence interval.

Stepwise variable selection ($p < .05$ for variable entry, $p > .10$ for removal) was used within each model.

Variables considered for model 1: Age, baseline artery diameter.

Variables considered for model 2: Age, baseline artery diameter, systolic blood pressure, heart rate, triglycerides, glucose, hypertension (No=0, Yes=1), dyslipidemia (No=0, Yes=1), antidyslipidemia medications (No=0, Yes=1), antihyperglycemic medications (No=0, Yes=1), current smoker (No=0, Yes=1).

Variables considered for model 3: Age, baseline artery diameter, systolic blood pressure, heart rate, triglycerides, glucose, hypertension (No=0, Yes=1), dyslipidemia (No=0, Yes=1), antidyslipidemia medications (No=0, Yes=1), antihyperglycemic medications (No=0, Yes=1), current smoker (No=0, Yes=1), insomnia (No=0, Yes=1).