Vascular Endothelial Function and Self-reported Sleep

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Abstract: *Background:* The authors investigated the relationship between self-reported sleep characteristics and brachial artery flow-mediated dilation (FMD) in a community-based population. Previous studies document that sleep apnea may be related to endothelial dysfunction but disagree whether subjective reports of sleep may also reflect such associations. *Methods:* In 684 subjects (32% male) aged between 37 and 60 years enrolled in the Emory-Georgia Tech Predictive Health Institute study, the authors measured reported sleep characteristics using the Epworth Sleepiness Scale and the Pittsburgh Sleep Quality Index (PSQI) along with cardiovascular risk factors. Endothelial function was assessed using brachial artery FMD. Multivariate analysis of covariance was used to adjust for various cardiovascular risk factors including age, race, gender, smoking, hypertension, diabetes and body mass index. *Results:* Lower brachial artery FMD values were correlated with higher Epworth Sleepiness Scale scores ($P = 0.0275$), even after adjustment for risk factors ($P = 0.03$). Total PSQI score was unrelated to brachial artery FMD. However, lower sleep quality (PSQI component 1) was associated with lower brachial artery FMD (multivariate $P = 0.038$), and participants who coughed or snored during sleep also had lower brachial artery FMD (6.24% ± 3.42%) compared with those who did not (6.92% ± 4.30%) ($P = 0.056$). This difference remained significant after adjustment for risk factors ($P = 0.03$). *Conclusions:* In a community-based population, our analysis indicates a significant association between sleepiness and snoring assessed by questionnaires and endothelial function. Simple subjective reports about individuals' sleep may be highly revealing indicators of endothelial function impairment and thus important indicators of cardiovascular disease risk.

Key Indexing Terms: Flow-mediated dilation; Survey-based sleep assessment; Proxy sleep apnea symptoms. **[Am J Med Sci 2014;347 (6):425–428.]**

Abnormal endothelial function has been associated with sleep apnea using biochemical markers such as vascular endothelial growth factor,[1] declines in nitric oxide bioavailability,[2] monocyte activation[3] and with radiologic or dynamic vascular measures such as coronary artery calcification,[4] carotid intima-media thickness[5] and flow-mediated vasodiliation.[6] Some of these alterations may even be reversible with nasal continuous positive airway pressure therapy.[1,2,7] Far more equivocal are associations between endothelial function and subjective reports of sleep duration or other aspects such as snoring or low sleep quality. For example, although laboratory-based studies of experimental sleep deprivation may increase adhesion molecules and E-selectin[8] or result in elevated blood pressures,[9] whether such relationships are also reflected in subjects' verbal reports about their own short duration of sleep remain far more dubious. Low reported sleep quality in a large population-based sample[10] was reported to be unrelated to altered flow-mediated dilation (FMD) and short reported sleep durations were unrelated to levels of endothelial progenitor cells,[11] but other studies suggest that reported (or actigraphically assessed) short sleep durations may be associated with increased carotid intima-media thickness[12,13] or coronary artery calcification.[14] In this study, we examined self-reported sleep-related symptoms in a community-based nonclinical population with commonly used standardized scales and related these results to brachial artery FMD—long recognized to be the gold standard of abnormal endothelial dysfunction.[15]

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METHODS

Study Sample

The sample was derived from the "Predictive Health Institute: The Center for Health Discovery and Well Being," which consists of participating Emory University and Georgia Tech University employees (mean age = 48 ± 11 years, 68% female and 71% white). History of diabetes and hypertension were defined with the use of antidiabetic and antihypertensive medications, respectively. History of smoking, obtained using standardized questionnaires, was defined as current or never/former (no cigarettes within the past 30 days). Height and weight were measured. Blood pressure was monitored with an automatic blood pressure monitor. The study was approved by the Emory University and Georgia Tech University Institutional Review Committees. Informed consent was obtained from all participants.

Measurement of Reported Sleep Characteristics

Participants enrolled in the study completed 2 questionnaires collecting data related to their sleep: the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS). The PSQI is a self-administered validated 19-item scale that assesses overall sleep quality and a wide range of sleep-related symptoms experienced during the previous 1 month.[16] The 19 items of the PSQI yield 7 component scores that reflect the frequency of sleep problems. The sum of the 7 components yields a global score that ranges from 0 to 21, with higher scores indicating poorer sleep quality. We used total PSQI scores, the 7 component scores and selected item analysis of specific sleep disturbance complaints as done previously.[17] These items included self-reports of cough/snore, sleep durations and reports of getting up at night to use the restroom—all symptoms that have been associated with sleep apnea.

The ESS measures daytime sleepiness. A summary score is derived from the likelihood of falling asleep during the daytime in 8 different situations,[18] which the subject rates on a scale of 0–3 how likely they would be to doze off or fall

TABLE 1. Demographic characteristics for the entire study cohort, subjects who report coughing or snoring during sleep and those who did not

	All participants, n = 684	Denies cough/snore, n = 477	Reports cough/snore, n = 207	*P*
Age, yr	48 ± 11	48 ± 11	51 ± 9	0.002
Male gender (%)	219 (32.0)	169 (31.3)	46 (36.2)	0.2927
Whites (%)	483 (70.6)	392 (58.8)	80 (12.0)	0.0242
Blacks (%)	162 (23.7)	115 (17.2)	43 (6.45)	0.0242
Asians (%)	35 (5.1)	29 (4.35)	4 (0.6)	0.0242
Hypertension (%)	88 (12.9)	58 (8.7)	29 (4.4)	<0.001
Diabetes (%)	12 (1.8)	7 (1.15)	4 (0.6)	0.2348
Tobacco use	37 (5.4)	25 (3.9)	12 (1.9)	0.0477
BMI	28 ± 6.5	27 ± 6	31 ± 7	<0.0001
ESS	6.7 ± 4.1	6.3 ± 4.0	8.0 ± 4.4	<0.0001
FMD, %	6.8 ± 4.2	6.9 ± 4.3	6.2 ± 3.4	0.0557

BMI, body mass index; ESS, Epworth Sleepiness Score; FMD, flow-mediated dilation.

asleep. Scores range from 0 to 24, with higher scores indicating greater daytime sleepiness.

Assessment of Endothelial Function

The assessment of endothelial function in this study was done through FMD. Endothelium-dependent brachial artery FMD was determined as previously described.[19,20] Briefly, ultrasound images were obtained at baseline under standardized conditions and ≈60 seconds after induction of reactive hyperemia by a 5-minute cuff occlusion of the forearm. After a 15-minute period to reestablish baseline conditions, endothelium-independent dilation of the brachial artery was assessed from images obtained before and 3–5 minutes after administration of 0.4 mg of sublingual nitroglycerin. Images were digitized online, and arterial diameters were measured with customized software (Medical Imaging Applications, Inc) by individuals blinded to the clinical and laboratory status of the subjects. FMD and endothelium-independent vasodilation were expressed as the percentage increase in diameter from baseline.

Statistical Methods

Study variables were described as the mean ± standard deviation (unless otherwise specified) for continuous variables or as counts or proportions for categorical variables. Age, body mass index (BMI) and FMD were treated as continuous variables. Smoking, gender and medication use (antihypertensive drugs and glucose-lowering agents) were categorical variables. Continuous variables were tested for normality with the Kolmogorov-Smirnov criterion. Skewed variables were log transformed and tested again for normality before any parametric analysis.

Univariate correlations between brachial artery FMD and measured sleep parameters were performed with Pearson's correlation. Multivariate linear regression models were constructed to determine the relationships between sleep and vascular function parameters before and after adjustment for age, race, gender, smoking, hypertension (defined by medication use), diabetes (defined by medication use) and BMI. Group differences were evaluated by Student's *t* tests or 1-way analysis of covariance. Statistical significance was based on 2-tailed tests,

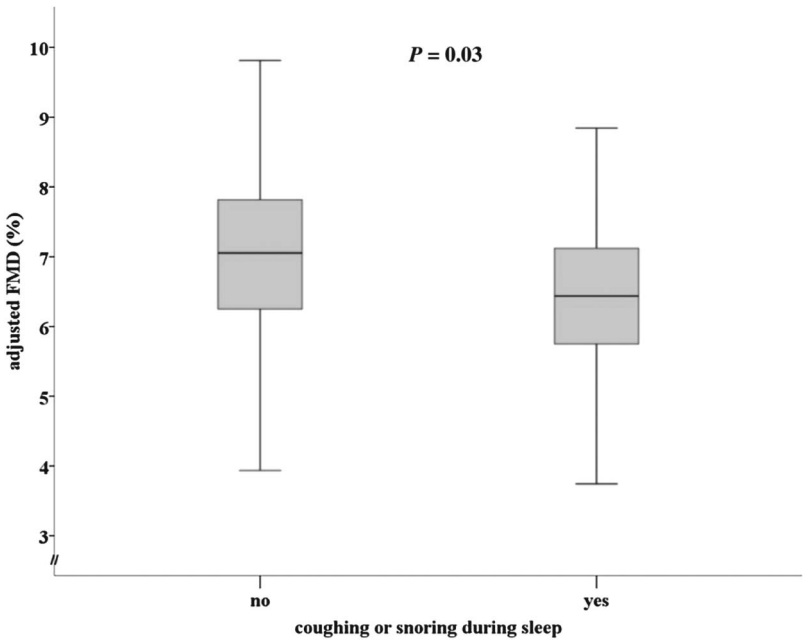

FIGURE 1. Difference in multivariate-adjusted FMD by report of coughing and/or snoring during sleep. FMD, flow-mediated dilation.