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Obstructive Sleep Apnea Risk and Subclinical Atherosclerosis in South Asians Living in the United States

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Abstract

Objectives: We examined the association between high risk of obstructive sleep apnea (OSA) and subclinical atherosclerosis among South Asians in the United States.

Design: A secondary analysis of cross-sectional data.

Setting/Participants: A community-based cohort of 906 men and women participating in the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study.

Measurements: The Berlin Questionnaire was used to screen for OSA risk. Coronary artery calcium (CAC), common carotid artery intima media thickness (IMT) and internal carotid artery IMT were used as measures of subclinical atherosclerosis.

Results: The majority of participants (59%) with high OSA risk had a CAC scores >0 compared to only 41% of participants with low OSA risk ($p<.001$). The high OSA risk group was older ($p=.005$), male ($p=.04$), had higher BMI ($p<.001$) and had greater common carotid artery IMT (0.96±0.27 mm) and internal carotid artery IMT (1.33±0.42 mm) measurements. Snoring, sleep disordered breathing, and high OSA risk were associated with subclinical atherosclerosis. However, only high OSA risk remained significant in multivariable models that after controlling

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for demographic and clinical factors that included hypertension, obesity, diabetes and dyslipidemia.

Conclusions: High OSA risk, which includes overlapping comorbidities of hypertension and obesity, was not associated with time living in the US, but was associated with subclinical atherosclerosis markers. These cardiovascular disease risk factors should include evaluation of the spectrum of sleep disordered breathing among all adults, including South Asian men and women.

Keywords

sleep disordered breathing; daytime sleepiness; coronary artery calcium; carotid intima media thickness; hypertension; obesity

INTRODUCTION

Obstructive sleep apnea (OSA) is a common condition seen in 5–15% of the adult population in developed countries[1] and has been associated with increased cardiovascular and cerebrovascular morbidity.[2,3] OSA is characterized by sleep disordered breathing (SDB), with snoring that reflects frequent and repetitive partial or complete closure of the pharynx, apneic events causing arterial oxygen desaturation, sympathetic activation and frequent micro-arousals from sleep. Because of resulting hypertension (HTN) and endothelial pathology from apneic episodes, OSA is a risk factor for cardiovascular disease, myocardial infarction and mortality.[4,5]

We recently reported that risk of OSA was high (24%) among South Asian adults in the United States.[6] South Asians (individuals of Indian, Pakistani, Bangladeshi, Nepali, and Sri Lankan origin) are also known to have a high prevalence of cardiovascular disease.[7,8] Raleigh, Kiri and Balarajan[9] reported that South Asians were more likely to die prematurely from cardiovascular disease, with a mortality rate 40% higher than white Europeans. Yet there is limited research on atherosclerosis and its association with OSA in South Asians

OSA is thought to contribute to the pathogenesis of cardiovascular disease and increased risk of cardiovascular morbidity and mortality.[10] Considering the high rate of cardiovascular disease and high rate of OSA reported in South Asians, the purpose of this analysis was to describe the association between subclinical atherosclerosis and risk of OSA in a cohort of South Asian men and women in the United States (US). We hypothesized that even after controlling for salient demographic and clinical characteristics, high risk of OSA would be associated with subclinical atherosclerosis.

PARTICIPANTS AND METHODS

This was a secondary analysis of baseline clinical examination data from the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study. Participants were enrolled between 2010 and 2013; the prevalence of type 2 diabetes, OSA, and subclinical atherosclerosis been reported elsewhere.[6,11,12]

The sample included 906 South Asian men and women from the San Francisco Bay Area and from the greater Chicago metropolitan area. The institutional review boards at

Northwestern University and University of California, San Francisco approved the study protocol. All participants provided written informed consent in the language of their choice. To be eligible, participants were: 1) of South Asian ancestry, defined as at least three grandparents born in either India, Pakistan, Bangladesh, Nepal, or Sri Lanka; 2) 40–84 years of age; and 3) able to speak and/or read English, Hindi, or Urdu. Potential participants were excluded if there was: 1) physician-diagnosed myocardial infarction, stroke or transient ischemic attacks, angina, heart failure, use of nitroglycerin, or history of any cardiovascular procedures such as angioplasty, valve replacement, pacemaker/defibrillator, 2) current atrial fibrillation, 3) active cancer treatment, 4) impaired cognitive ability, 5) life expectancy < 5 years, 6) out of study region within 5 years of enrolling, 7) living in a nursing home or on wait list; and 8) weight > 136 kg due to computerized tomography (CT) scanner limitation.

Measures

Risk of OSA was assessed with self-report responses on the Berlin Questionnaire. Three non-invasive measures were used to assess subclinical atherosclerosis: coronary artery calcification, and carotid artery intima media thickness of both the internal carotid artery, and the distal common carotid artery. Demographic data were obtained by bilingual data collectors from a detailed sociodemographic questionnaire that included self-report items on age, sex, smoking status, physical activity,[13] alcohol intake, years in the US, history of HTN and use of antihypertensive medication, and use of lipid lowering medication (statins). Clinical measures included height (m) and weight (kg) to calculate body mass index (BMI) using the formula kg/m^2, waist circumference (cm), systolic and diastolic blood pressure (mmHg), fasting blood sample for a lipid panel to classify them as normal, borderline, or having high-risk dyslipidemia (as described elsewhere).[12] Participants were classified normal glucose tolerance, prediabetes, or diabetes based on a 2-hour glucose tolerance test and American Diabetes Association criteria.[14]

Risk of OSA: the Berlin Questionnaire (BQ)—The Berlin Questionnaire (BQ) was developed at the 1966 Berlin Conference on Sleep in Primary Care to screen for SDB and risk of OSA.[15] The BQ had 86% sensitivity and 95% specificity for detecting OSA in a patient sample from north India.[17] There are ten questions that yield three categories. Category 1 addresses symptoms of sleep disordered breathing (SDB) and consists of an initial question about snoring (yes, no, or don't know). If the response is yes, there are four follow-up questions on snoring frequency and severity. Category 1 is scored positive for SDB if the participant is symptomatic more than 3–4 times a week with at least two of the four follow-up questions. BQ Category 2 has three items about excessive daytime sleepiness (EDS) and is scored positive for EDS if the participant is symptomatic 3–4 times a week on at least two of the three questions. Category 3 has a question on history of HTN and a question on obesity (BMI ≥ 30 kg/m^2) and a "yes" response to either question is positive for comorbidities. Because the World Health Organization (WHO)[16] defines obesity in the South Asian population as >27.5 kg/m^2, this value was also used for determining a positive score for Category 3.

Regardless of the response in Category 1 about snoring and symptoms of SDB, a high risk of OSA on the BQ is identified by any two of the three categories being positive. To

specifically address each component of OSA risk, we also examined the three BQ categories separately for their unique contribution to each of the non-invasive markers of subclinical atherosclerosis.

Coronary Artery Calcium (CAC)—Coronary artery calcium (CAC) is a noninvasive measure of subclinical atherosclerosis[18] and is highly predictive of coronary artery disease.[19] CAC was assessed with coronary CT using a cardiac gated electron beam computed tomography scanner. The San Francisco site used Phillips 16D scanner or Toshiba MSD Aquilion 64; the Chicago site used Siemens Sensation Cardiac 64 Scanner (Siemens Medical Solutions, Malvern PA). Participants were examined in the supine position with both arms stretched above the head. A four-sample calibration phantom was placed under the thorax. A scout image was done to determine the level of the carina, and the first scan had a total of 46 images in 3 mm slice thickness. Exposures were set at kV 140 and mAs 50 for participants weighing ≤100 kg and at mAs 63 for participants weighing >100 kg. Reconstruction was done in the 35 cm field of view. All scans were sent to the CT reading center and read with Rephot Imaging Software according to protocol described elsewhere.[20]

A majority of participants (58%, n=517) had CAC scores of 0, but 42% had a score ranging from 2 to 4,794. A CAC score of 0 was considered normal and CAC >0 was considered evidence of atherosclerotic plaque development. For clinical relevance, CAC scores were categorized as 0, 1–99, 100–399, and 400 or higher. For multivariable analysis, log transformations were used to meet the assumptions for linear regression.

Carotid Artery Intima Media Thickness (IMT)—Intima media thickness (IMT) of the carotid artery is a marker for early atherosclerosis.[21] Carotid IMT can be measured non-invasively using ultrasonography of the combined thickness of the innermost layers of the arterial wall (tunica intimal and media). According to some clinical trials, IMT >0.8 mm characterizes carotid atherosclerosis.[22–24] High resolution B-mode ultrasonography was conducted to measure IMT of the right and left internal and common carotid arteries. The San Francisco site used an 8MHz linear array transducer with General Electric Vivid 7 ultrasound (General Electric, Fairfield, Connecticut) and the Chicago site used the Acuson Sequoia C256 (Siemens, Germany) to perform carotid ultrasound recordings.

The technician located the bifurcation of the carotid artery, distinguished the internal from external carotid artery, and identified maximal wall thickening in the carotid bulb or internal carotid artery. IMT was measured in 12 pre-defined segments (6 per side) including one transverse scan sequence of the common carotid through the bulb and five longitudinal images taken at both the right and left side carotid arteries. These digitalized data were batched and mailed to the Wake Forest University reading center to measure wall thickness. IMT measurements for this analysis were from the distal common carotid artery and internal carotid artery.

Data Analysis

Frequencies (n) and percentages (%) were used to describe categorical data. Chi-square (X^2) analyses were used to test associations between CAC score categories (0 to 3), and each of the three BQ risk categories. Means and standard deviations (SD) were used to describe the

sample. However, transformations were necessary to meet statistical assumptions: CAC scores were normalized with a log transformation, common carotid artery IMT measurements were normally distributed, and internal carotid artery IMT measurements were normalized with square root transformation. Independent sample *t*-tests or one-way ANOVA *F* tests were used to evaluate differences between OSA risk category groups and subclinical atherosclerosis measures.

To determine the contribution of OSA risk to each of the subclinical atherosclerosis outcomes, three linear multiple regression models were performed. The variance in each of the three noninvasive measures of subclinical atherosclerosis due to the overall BQ risk of OSA using BMI ≥30 k/m^2 was assessed after controlling for all demographic and clinical variables. For sensitivity analysis with each model, overall BQ OSA risk was then replaced with either OSA risk using >27.5 k/m^2 criterion, or with the three individual BQ risk categories entered simultaneously. Demographic variables included age, sex, geographic study site, years in the US, family income, and education. Clinical variables included self-reported smoking history, alcohol amount past week and physical activity estimated in metabolic equivalent task-minutes (MET-mins) per week categorized as sedentary (<500 METS-mins/wk) or active (≥500 METs-mins/wk), and taking antihypertensive or lipid lowering medication (statin). Other clinical measures included systolic blood pressure, diastolic blood pressure, waist circumference, BMI, diabetes, and dyslipidemia. High risk dyslipidemia was defined as total cholesterol ≥240 mg/dL, LDL ≥160 mg/dL, HDL <40 mg/dL, or use of a statin medication. SPSS (version 23) was used for all analyses and statistical significance was set at $p \leq .05$.

RESULTS

The mean age of participants enrolled in the original MASALA study was 55±9 years, 54% were men and 98% were South Asian immigrants who had lived in the US for a mean 27±11 years. Only 4% of the participants (11 men and 28 women) requested a consent form and clinical examination in Urdu or Hindi. In this sample, 24% were categorized as high risk for OSA on the BQ. As seen in Table 1, participants with high OSA risk were more likely older with higher BMI and waist circumference. They also had higher systolic and diastolic blood pressure, more likely took blood pressure medication, and more likely reported a diagnosis of HTN. Men and current or former smokers were more likely to be at high OSA risk than women or nonsmokers. Persons with diabetes were significantly (p <.001) more prevalent in the high OSA risk group (35%) than low OSA risk group (23%). Dyslipidemia was more prevalent in the high OSA risk group (53%) than low OSA risk group (48%), but the difference did not reach statistical significance (p=.06). There was no association between OSA risk group and alcohol use, study site, or years in the US.

The high OSA risk group had significantly higher CAC scores and greater IMT values than the low OSA risk group. The four categories of CAC scores did not differ by study site ($X^2_{[3]}$=6.8, p=.083); the Chicago site had 46% with CAC scores >0 and the San Francisco site had 40% with CAC scores >0 ($X^2_{[1]}$=3.8, p=.062).

Both BQ high OSA risk and low OSA risk groups had average IMT measurements above 0.8 mm and there were significant differences (t >8.0, p <.001) by study site. The Chicago sample averaged common and internal carotid artery IMT measurements of 0.81±0.22 mm and 1.03±0.19 mm, respectively. The San Francisco sample had higher average measurements of 0.93±0.23 mm and 1.13±0.17 mm, respectively.

Risk of Obstructive Sleep Apnea (OSA) and Subclinical Atherosclerosis

Of the 906 participants enrolled in the study, 898 had CAC measurements. As seen in Table 1, significantly more participants with CAC scores >0 were at high risk for OSA (59%) compared to participants with CAC=0 (41%) (p <.001). Among participants with BMI >27.5 kg/m^2 the prevalence of OSA was similar: 44% of participants with CAC=0 and 56% of participants with CAC >0 had high risk of OSA (p < .001; data not shown).

Of the 906 enrolled participants, 904 had common carotid artery IMT measurements and 903 had internal carotid artery IMT measurements. Both IMT measurements were greater among participants with higher risk for OSA compared to participants at low risk for OSA (Table 1). Because the BQ includes Category 3 risk factors of HTN and obesity that are already established risk factors for heart disease, each BQ category was examined individually for associations with the three noninvasive measures of subclinical atherosclerosis.

Symptoms of Sleep Disordered Breathing (BQ Category 1) and Subclinical Atherosclerosis

In Category 1, 492 (55%) participants responded that they snored, 269 (30%) responded that they did not snore, and 137 (15%) did not know if they snored. Of the 492 who responded that they snored, 75% (n=371) met the duration and severity criteria to be categorized as positive for symptoms of SDB (BQ Category 1).

As seen in Table 2, CAC groups differed significantly in rates of snoring and SDB (p<.001). Almost half of the participants (48%) with CAC scores >0 reported snoring and 51% had SDB. In comparison, most participants (64%) with CAC scores =0 reported no snoring or not knowing if they snored.

There was also a significant difference in mean common carotid artery IMT measurements between the snoring groups. Participants who snored had greater common carotid artery IMT measurements compared to participants who did not snore or did not know if they snored (Table 2). Furthermore, the significant difference in IMT remained, and the mean difference was even larger when comparing the group categorized as positive for SDB to the group categorized as not having SDB (t=3.8, p<.001).

When internal carotid artery IMT measurements were compared by snoring groups, however, there was no difference between snorers and non-snorers (p=.358). When internal carotid artery IMT measurements for the positive SDB group were compared to the non-snoring group, the mean difference did approach significance (p=.056) (see Table 2).

Daytime Sleepiness (BQ Category 2) and Subclinical Atherosclerosis

Only 12% (n=110) of participants were positive for excessive daytime sleepiness (EDS) in BQ Category 2. As seen in Table 2, there was no significant difference in rates of self-reported EDS for participants who had CAC scores >0 compared to participants with CAC scores =0. There were also no significant mean differences in either the common carotid artery IMT or internal carotid artery IMT measurements between participants with and without EDS.

Hypertension (HTN) and Obesity (BQ Category 3) and Subclinical Atherosclerosis

As expected, over half (59%) of the participants with a CAC score >0 were positive for BQ Category 3 (Table 2) comorbidities of HTN and obesity (BM1≥30 kg/m^2). The common carotid artery and internal carotid artery IMT measurements were also significantly higher in participants with HTN and obesity compared to participants without HTN or obesity. The differences were similarly significant, but less pronounced, when BQ Category 3 obesity was defined as BMI >27.5 kg/m^2 (data not shown).

Multivariable Analysis

To account for the variance in each of the three non-invasive measures of subclinical atherosclerosis, 15 demographic and clinical variables were entered as independent variables in linear multiple regression models. After accounting for these variables, BQ OSA risk (low or high) was entered to determine whether any additional variance due to OSA risk was significant. The models were also tested by replacing BQ OSA risk with each BQ category.

In the first model with CAC score [log transformed] as the dependent variable, 6 of the 15 demographic and clinical variables were significant: older age, male sex, longer time in the US, higher BMI, dyslipidemia, and prediabetes or diabetes. This model accounted for 38% of the variance in CAC scores (R^2=.384; $F_{[16,843]}$=32.2, p<.001). Study site, education, income, waist circumference, physical activity, diastolic and systolic pressure, smoking, and alcohol consumption were not significant in the model. While controlling for the 15 demographic and clinical variables, BQ risk of OSA was entered and accounted for an additional 0.3% of the variance (t=2.16, p=.031). Table 3 presents the full model with 16 variables, including BQ OSA risk. In the sensitivity model replacing BQ high risk with the three BQ individual categories of SDB, EDS and comorbidities as independent predictors, no individual BQ category made a significant contribution. Replacing BMI >30 kg/m^2 with BMI >27.5 kg/m^2 was also not significant (t=1.63, p=.103).

In the common carotid artery IMT regression model, significant demographic and clinical variables accounting for the variance in IMT included older age, male sex, and higher BMI, but not diabetes. Living longer in the US, smoking, higher systolic pressure, and dyslipidemia were also significant in this model. Other variables that were not significant included education, income, study site, physical activity, waist circumference, diastolic pressure, and alcohol consumption. After controlling for the 15 demographic and clinical variables (R^2=.310; $F_{[15,849]}$=26.4, p<.001), BQ risk of OSA was a significant addition to the model, accounting for an additional 0.7% of the variance in common carotid artery IMT (t=3.0, p=.003), and systolic pressure remained significant while BMI was no longer

significant (p=.169). This full model accounted for 32% of the variance in common carotid artery IMT (R^2=.316; $F_{[16,849]}$=25.6, p<.001). In the sensitivity analysis regression model that replaced BQ high risk with the three BQ categories, only Category 3 comorbidities with BMI ≥30 k/m^2 was significant (t=2.33, p=.020); the model with BMI >27.5 k/m^2 did not reach significance (t=1.92, p=.055). When BQ risk of OSA using BMI >27.5 k/m^2 was substituted into model, results were identical to the model with BQ risk using BMI ≥30 k/m^2. Table 4 summarizes the full model with 16 variables including BQ OSA risk.

In the internal carotid artery model, demographic and clinical variables that significantly accounted for the variance in IMT [square root transformed] included older age, male sex, living longer in the US, higher systolic pressure and lower diastolic pressure. For this dependent variable, BMI (p=.061), dyslipidemia (p=.060) and diabetes (p=.233) did not reach significance. Alcohol consumption, smoking, education, income, study site, physical activity, and waist circumference were also not significant. These 15 variables accounted for 32% of the variance in internal carotid artery IMT (R^2=.319; $F_{[15,848]}$=26.1, p<.001). When BQ OSA risk using BMI ≥30 k/m^2 was added to the model, it was not significant (t=1.86, p=.063) but BQ OSA risk using BMI >27.5 k/m^2 was significant (t=2.06, p=.040), and contributed an additional 0.3% while the other five demographic and clinical variables remained significant. As seen in Table 5, the full model with 16 variables including BQ OSA risk using BMI >27.5 k/m^2 was significant (R^2=.323; $F_{[16,848]}$=24.8, p<.001). In the sensitivity regression model that replaced BQ high risk with the three BQ categories, Category 1 SDB was not significant but Category 2 EDS (t=2.1, p=.039) and Category 3 comorbidities were significant regardless of whether BMI ≥30 k/m^2 (t=3.0, p=.003) or BMI >27.5 k/m^2 (t=2.9, p=.004) was entered.

DISCUSSION

Our hypothesis that risk of OSA would be associated with subclinical atherosclerosis in South Asian adults living in the US was supported. In bivariate associations, snoring, SDB, and OSA risk were significantly associated with all three noninvasive measures of subclinical atherosclerosis (CAC score, common carotid artery IMT, and internal carotid artery IMT). However, when demographic and clinical factors were considered in multivariable models, only BQ OSA risk contributed significant additional information about subclinical atherosclerosis, indicating that OSA risk was primarily a result of the overlapping comorbidities of BMI and HTN in BQ Category 3 rather than SDB or daytime sleepiness. It was surprising that Category 3 was significant when both BMI and systolic and diastolic pressure were already included in the models.

Our findings regarding CAC in this sample of South Asian adults support prior studies. Sorajja et al[25] reported an association between OSA and CAC, independent of co-existing factors, yet Kim et al[26] found that OSA was not associated with CAC in healthy young men once obesity was included in their model. In the Multi-Ethnic Study of Atherosclerosis (MESA) study, Kwon et al[27] found that participants who reported a diagnosis of OSA at baseline (4% of the sample), but had no baseline evidence of atherosclerosis, had more of an increase in CAC 8 years later compared to patients who did not report a baseline diagnosis of OSA.

To better understand the relationship between OSA and subclinical evidence of atherosclerosis, we examined each distinct component of OSA risk on the BQ. Snoring, more extensive SDB, and daytime sleepiness were not significant factors in accounting for the variance in CAC scores or common carotid artery IMT. The average internal carotid artery IMT measurements were above the 0.8 mm cutpoint identified for carotid atherosclerosis[22–24] in this sample of South Asians. While snoring and SDB (BQ Category 1) were not significant in the model for internal carotid artery IMT, excessive daytime sleepiness (BQ Category 2) was significant after controlling for all other variables. Of note, two of the three daytime sleepiness questions are about fatigue upon awakening or during the day, and the other question is about falling asleep while driving an automobile. Fatigue is a common symptom in cardiovascular disease, and more research is needed to better understand this relationship and why BQ EDS Category 2 was not associated with CAC or common carotid IMT measures. Measures that better distinguish fatigue from daytime sleepiness should be considered in future research to better understand how the common carotid artery and internal carotid artery IMT measures contribute to this health profile. Given the surprising significant contribution from having a lower diastolic blood pressure in the model for internal carotid artery IMT but not in the other two models, further investigation of the relationship between fatigue and diastolic blood pressure is also warranted.

Strengths and Limitations

The strengths of this study include the use of three non-invasive measures of subclinical atherosclerosis that are known predictors of future coronary events and correlates of OSA[21,29] with prior studies showing strong associations.[30,31] Another strength is the large sample from two specific geographic regions of the US. We previously reported on the similarity of this sample to South Asian data from the 2010 US Census.[28] However, findings still do not adequately represent all South Asians living in the US.

There are also some limitations to consider with these findings. First, it was a secondary analysis of data using self-report of OSA risk on the BQ rather than more costly and invasive laboratory assessments with polysomnography to assess OSA severity or with multiple sleep onset latency tests to assess daytime sleepiness. Given the non-dipping nocturnal systolic blood pressure pattern seen in men with hypertension and OSA[32] monitoring systolic and diastolic blood pressure during the night may add to our understanding of the association between OSA and subclinical atherosclerosis. Finally, this was a cross-sectional analysis comparing measures at one time point, and it would be difficult to determine whether OSA was causally linked to subclinical atherosclerosis. The strong association between daytime sleepiness/fatigue and internal carotid IMT is interesting in that sleepiness can often be a later manifestation of SDB. However, not all participants who met criteria for excessive daytime sleepiness on the BQ also reported snoring, and this relationship needs to be replicated and studied longitudinally in future research. Because only 4% of the sample participated in their native language of Urdu or Hindi, we were not able to address potential cultural issues regarding daytime sleepiness or napping behavior.

CONCLUSIONS

In summary, high OSA risk was associated with subclinical atherosclerosis measures in this large cohort of South Asians living in the US. Because of the high prevalence of cardiovascular disease and OSA in this cohort, findings suggest that clinicians in primary care should screen for both OSA and cardiovascular disease when evaluating this vulnerable population. It may be important to treat both conditions simultaneously in order to achieve more positive outcomes.

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R. D. developed the research question, conducted the review of literature, and wrote the manuscript draft. K. L. reviewed and edited the manuscript and assisted with statistical analyses. N. K. and A. K. designed the original study, collected the original data, and reviewed and edited the manuscript.

LIST OF ABBREVIATIONS

ANOVA	Analysis of Variance
BMI	Body Mass Index
BQ	Berlin Questionnaire
CAC	Coronary Artery Calcium
CT	Computerized Tomography
EDS	Excessive Daytime Sleepiness
HTN	Hypertension
IMT	Intima Media Thickness
MASALA	Mediators of Atherosclerosis in South Asians Living in America
MESA	Multi-Ethnic Study of Atherosclerosis
MET	Metabolic Equivalent Task
OSA	Obstructive Sleep Apnea
PSQI	Pittsburgh Sleep Quality Index
SD	Standard Deviation
SDB	Sleep Disordered Breathing
US	United States
WHO	World Health Organization

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Table 1 -

Demographic and clinical comparisons of participants by low and high risk for obstructive sleep apnea (OSA) on the Berlin questionnaire.

Sample Characteristics	Low OSA Risk (BMI <30 kg/m^2) *n*=693 mean ± *SD* or %	High OSA Risk (BMI ≥30 kg/m^2) *n*=213 mean ± *SD* or %	Statistic, *p* value
Age (years)	54.8 ± 9.47	56.9 ± 8.94	*t*, *p* = .005
Sex (% males)	50%	65%	X^2, *p*=.044
Living in the US (years)	27 ± 10.9	27 ± 10.8	*t*, *p* = NS
Study site: UCSF (*n*=496)	55%	56%	X^2, *p* = NS
NW (*n*=410)	45%	44%	
BMI (kg/m^2)	25 ± 3.3	29 ± 5.8	*t*, *p* < .001
Waist circumference (cm)	91 ± 9.1	99 ± 11.7	*t*, *p* < .001
Systolic BP (mmHg)	123 ± 15	129 ± 99	*t*, *p* < .001
Diastolic BP (mmHg)	73 ± 10	76 ± 10	*t*, *p* < .001
Smoke(d) cigarettes (% yes)	16%	22%	X^2, *p*=.044
Alcohol drink 1+/week (% yes)	32%	37%	X^2, *p* = NS
Physical activity (% sedentary <500 MET-min/week) (*n*=295)	32%	35%	*t*, *p* = *NS*
Hypertension (≥ 140/90 mmHg) or take antihypertensive	31%	72%	X^2, *p* <.001
Dyslipidemia or take statin (*n*=444)	48%	53%	X^2, *p*=.06
Glucose tolerance			X^2, *p*<.001
Normal (*n*=375)	45%	32%	
Pre-diabetes (*n*=295)	32%	33%	
Type 2 diabetes (*n*=229)	23%	35%	
Coronary artery calcium (CAC)			X^2, *p*<.001
CAC = 0 (*n*=517)	63%	41%	
CAC = 1–99 (*n*=206)	21%	30%	
CAC = 100–399 (*n*=109)	9%	20%	
CAC = 400+ (*n*= 66)	7%	9%	
Common carotid IMT(mm) (*n*=904)	0.85 ± 0.21	0.96 ± 0.27	*t*, *p* < .001
Internal carotid IMT (mm) (*n*=903)	1.17 ± 0.42	1.33 ± 0.42	*t*, *p* < .001

NOTE: BMI = body mass index; CAC = coronary artery calcium score; IMT = intima media thickness; NS = not significant with *p* > .10; NW = Northwestern; *SD* = standard deviation

Table 2.

Comparison of Berlin questionnaire categories by subclinical arteriosclerosis measures.

Berlin Questionnaire Categories		Coronary artery calcium score >0[a] (*n*=898) *n* (%)	Common carotid artery IMT (mm)[b] (*n*=904) mean ± *SD*	Internal carotid artery IMT (mm)[c] (*n*=903) mean ± *SD*
Category 1-Sleep Disordered Breathing				
Not Snore/Does Not Know	(*n*=406)	145 (36%)	0.85 ± 0.21	1.19 ± 0.46
Snores	(*n*=492)	236 (48%)	0.90 ± 0.24	1.22 ± 0.44
If snores, has SDB	(*n*=371)	189 (50%)[a]	0.91 ± 0.24[a]	1.24 ± 0.44[a]
Category 2-Daytime Sleepiness				
No	(*n*=788)	337 (43%)	0.88 ± 0.23	1.21 ± 0.45
Yes	(*n*=110)	44 (40%)	0.88 ± 0.23	1.24 ± 0.47
Category 3-Comorbidities				
(if hypertensive and BMI ≥30 kg/m^2)				
No	(*n*=547)	173 (32%)	0.83 ±0.19	1.12 ± 0.34
Yes	(*n*=351)	208 (59%)[a]	0.95 ± 0.26[b]	1.36 ± 0.55[c]
(if hypertensive and BMI >27.5 kg/m^2)				
No	(*n*=646)	241 (37%)	0.83 ± 0.20	1.11 ± 0.34
Yes	(*n*=252)	140 (56%)[a]	0.93 ± 0.25[b]	1.31 ± 0.52[c]

NOTE: IMT = intima media thickness; *SD* = standard deviation

[a]Significant group differences in CAC >0 scores comparing SDB (n=371) vs. no SDB (n=527): (X^2 = 18.8, p < .001) and comparing yes vs. no (X^2 >24.0, p < .001).

[b]Raw values presented; significant group differences in common carotid artery IMT comparing yes (n=375) vs no (n=529): t >5.0, p < .001.

[c]Raw values presented; significant group differences in internal carotid artery IMT comparing yes (n=375) vs no (n=528): (square root transformed) t >4.0, p < .001.

Table 3.

Multiple linear regression results for variance in coronary artery calcium scores.

Model Variables	Unstandardized Coefficients		Standardized Coefficients	*t*	*p*
	B	**SE**	**Beta**		
(Constant)	−3.97	1.15		−3.46	.001
Age, years	.095	.010	.367	9.51	< .001
Sex (male=0; female=1)	−1.40	.177	−.289	−7.88	<.001
Living in US (years)	−.034	.138	−.007	−0.25	.804
Body mass index (kg/m^2)	.022	.007	.098	2.98	.003
Site(NW=1; UCSF=2)	.315	.225	.042	1.40	.161
College (no=0; yes=1)	−.120	.069	−.056	−1.73	.084
Income	.049	.028	.081	1.75	.080
Waist circumference (cm)	−.014	.011	−.059	−1.22	.225
Active (yes=1; sedentary=0)	−.168	.147	−.033	−1.14	.254
Systolic pressure (mmHg)	.007	.006	.045	1.14	.257
Diastolic pressure (mmHg)	−.010	.010	−.038	−0.98	.330
Smoking (no=0; yes=1)	.090	.150	.018	0.60	.547
Alcohol (no=0; yes=1)	−.152	.154	−.030	−0.99	.324
Glucose tolerance (normal=1, pre=2, diabetes=3)	.354	.091	.118	3.91	< .001
Dyslipidemia (no=1; borderline=2; high risk=3)	.292	.096	.089	3.03	.003
BQ high OSA risk BMI ≥30 (no=0; yes=1)	.367	.170	.064	2.16	.031

NOTE: Dependent variable: coronary artery calcium (CAC) score (log transformed); $R^2 = .384$; $F_{[16,843]} = 32.2$, $p < .001$

Table 4.

Multiple linear regression results for variance in common carotid artery IMT.

Model Variables	Unstandardized Coefficients		Standardized Coefficients	*t*	*p*
	B	**SE**	**Beta**		
(Constant)	−.145	.114		−1.26	.207
Age (years)	.010	.001	.396	9.85	< .001
Sex (male=0; female=1)	−.038	.018	−.083	−2.17	.031
Living in US (years)	.126	.014	.270	9.12	< .001
Body mass index (kg/m^2)	−.001	.001	−.031	−0.91	.364
Site(NW=1; UCSF=2)	−.042	.022	−.059	−1.89	.059
College (no=0; yes=1)	.011	.007	.053	1.60	.111
Income	.004	.003	.067	1.38	.169
Waist circumference (cm)	.000	.001	.003	.06	.954
Active (yes=1; sedentary=0)	−.017	.015	−.035	−1.17	.243
Systolic pressure (mmHg)	.002	.001	.104	2.53	.011
Diastolic pressure (mmHg)	.000	.001	−.011	−0.28	.782
Smoking (no=0; yes=1)	.035	.015	.073	2.35	.019
Alcohol (no=0; yes=1)	.018	.015	.036	1.15	.250
Glucose tolerance (normal=1, pre=2, diabetes=3)	−.002	.009	−.008	−0.24	.810
Dyslipidemia (no=1; borderline=2; high risk=3)	.022	.010	.069	2.27	.023
BQ high OSA risk BMI ≥30 (no=0; yes=1)	.051	.017	.094	3.01	.003

NOTE: Dependent variable: common carotid artery IMT, mm; R^2 = .329; $F_{[16,849]}$ = 25.6, p <.001

Table 5.

Multiple linear regression results for variance in internal carotid artery IMT.

Model Variables	Unstandardized Coefficients		Standardized Coefficients	*t*	*p*
	B	**SE**	**Beta**		
(Constant)	.344	.091		3.77	< .001
Age (years)	.007	.001	.349	8.65	< .001
Sex (male=0; female=1)	−.043	.014	−.116	−3.02	.003
Living in US (years)	.107	.011	.289	9.72	< .001
Body mass index (kg/m^2)	.000	.001	−.002	−0.06	.951
Site(NW=1; UCSF=2)	−.008	.018	−.015	−0.47	.639
College (no=0; yes=1)	.000	.006	.003	0.08	.938
Income	.003	.002	.067	1.36	.173
Waist circumference (cm)	.001	.001	.042	0.82	.415
Active (yes=1; sedentary=0)	.004	.012	.009	0.30	.762
Systolic pressure (mmHg)	.001	.000	.124	3.01	.003
Diastolic pressure (mmHg)	−.002	.001	−.108	−2.65	.008
Smoking (no=0; yes=1)	.011	.012	.028	0.89	.373
Alcohol (no=0; yes=1)	−.006	.012	−.014	−0.46	.645
Glucose tolerance (normal=1, pre=2, diabetes=3)	.009	.007	.038	1.19	.233
Dyslipidemia (no=1; borderline=2; high risk=3)	.015	.008	.058	1.90	.058
BQ high OSA risk BMI ≥27.5 (no=0; yes=1)	.027	.013	.065	2.06	.040

NOTE: Dependent variable: internal carotid artery IMT, mm (square root transformed); $R^2 = .323$; $F_{[16,848]} = 24.8$, $p < .001$