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SCIENTIFIC INVESTIGATIONS

Race, Sex, Age, and Regional Differences in the Association of Obstructive Sleep Apnea With Atrial Fibrillation: Reasons for Geographic and Racial Differences in Stroke Study

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Study Objectives: To examine the cross-sectional association between obstructive sleep apnea (OSA) risk and atrial fibrillation (AF) in the REasons for Geographic And Racial Differences in Stroke (REGARDS), a cohort of black and white adults.

Methods: Using REGARDS data from subjects recruited between 2003–2007, we assessed 20,351 participants for OSA status. High OSA risk was determined if the participant met at least two criteria from the Berlin Sleep Questionnaire (persistent snoring, frequent sleepiness, high blood pressure, or obesity). AF was defined as a self-reported history of a previous physician diagnosis or presence of AF on electrocardiogram. Logistic regression was used to determine odds ratio and 95% confidence interval for the association between OSA status and AF with subgroup analysis to examine effect modification by age, race, sex, and geographical region.

Results: The prevalence of AF was 7% (n = 1,079/14,992) and 9% (n = 482/5,359) in participants at low and high risk of OSA, respectively ($P < .0001$). Persons at high risk of OSA had greater prevalence of diabetes and stroke history, and were more likely to be obese and taking sleep medications. In a multivariable analysis adjusted for demographics, cardiovascular risk factors, and potential confounders, high risk for OSA was associated with an increased odds of AF compared to low risk for OSA (odds ratio = 1.27, 95% confidence interval = 1.13, 1.44). This association differed significantly only by race (P for interaction = .0003). For blacks, there was a significant 58% increase in odds of AF in participants at high risk versus low risk of OSA, compared to a nonsignificant 12% increase in odds in whites. We were limited by self-reported variables, inability to adjust for obesity, and the cross-sectional nature of our study.

Conclusions: High risk of OSA is associated with prevalent AF among blacks but not whites.

Commentary: A commentary on this article appears in this issue on page 1459.

Keywords: atrial fibrillation, obstructive sleep apnea, racial differences, REGARDS

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Obstructive sleep apnea (OSA) is prevalent among 32% to 49% of patients with atrial fibrillation (AF) and has been associated with increased cardiovascular risk including several AF risk factors; this association may differ by race, sex, age, and region. We explored the association between AF and OSA risk in the REGARDS cohort and assessed whether this association differed by race, sex, age, or region.

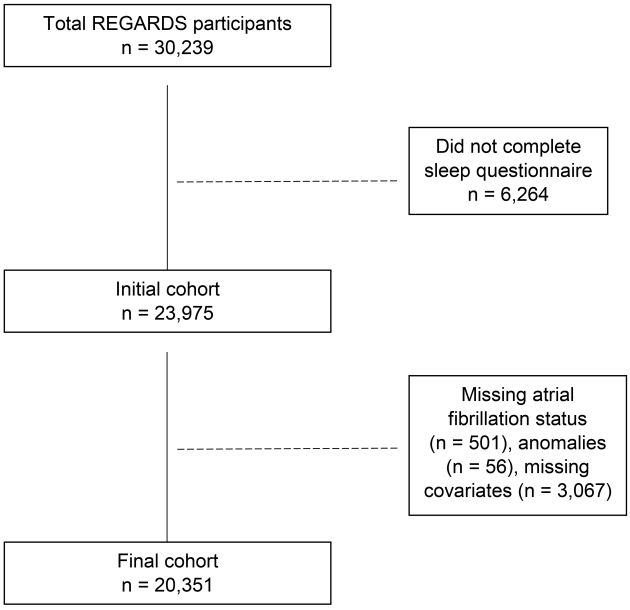
Study Impact: Individuals at high risk for OSA have increased prevalence of AF and after multivariable adjustment this association remained significant in blacks but not in whites. This study showed that this association did not differ by sex, region, or age as previously presumed; understanding this association will be key to reducing the burden of AF.

INTRODUCTION

Atrial fibrillation (AF) is the most common chronic cardiac arrhythmia in adults and is associated with significant morbidity and mortality,[1,2] Epidemiological studies have consistently found an increased prevalence of AF with age,[1,3] less prevalence among blacks,[4] and greater age-adjusted prevalence in European and North American men than women.[5] No regional differences in the prevalence of AF between the stroke belt and other regions in the United States have been observed.[6] Prevalence of AF is expected to increase from 2.3 million Americans currently to 5.6 million Americans by the year 2050 and thereby will require more health care utilization irrespective of sex or race.[1,7]

Obstructive sleep apnea (OSA), or the periodic collapse of the upper airway during sleep, is a common but underdiagnosed

Figure 1—Exclusion cascade.



sleep disorder; 13% of men and 6% of women have moderate to severe sleep.[8] In a recent meta-analysis, OSA was shown to be more prevalent and severe in blacks than whites, as measured by the respiratory disturbance index, the apnea-hypopnea index, and the oxygen desaturation index of 4%.[9] Furthermore, OSA is associated with increased cardiovascular risk and several AF risk factors including heart failure (HF), diabetes, coronary heart disease (CHD), myocardial infarction, and hypertension.[10] Overall OSA prevalence with AF is 32% to 49%.[11] In the Sleep Heart Health Study (SHHS), 4.8% of patients with OSA had AF versus 0.9% without OSA.[12]

There is also an increased risk of AF in patients with untreated OSA, and the 12-month recurrence of AF in patients after cardioversion is greatest (82%) among those with untreated OSA, compared to 53% without OSA and 42% for those with OSA managed with continuous positive airway pressure.[13] Several studies have previously assessed OSA as a predictor of AF in special populations including patients who have undergone cardiac surgery, ablation, electrical cardioversion, coronary artery bypass patients, or those with underlying congestive heart failure.[14–16] Risk factors such as age, race, and sex are common for OSA and AF. Previous investigations have shown an independent association between OSA and AF. In SHHS, a prospective community-based cohort (7% black patients), central sleep apnea but not OSA was associated with incident AF after adjustment for cardiovascular risk factors.[17] In the cross-sectional analysis of outcomes of sleep disorders in older men, increased severity of sleep-disordered breathing (SDB) was associated with increased odds of AF, and in the unadjusted analysis OSA severity was associated with AF.[18] However, the quality of the published data was limited because some studies examined only specific patient populations,[12,19] and in a case-control study the association of sleep apnea with AF could not be verified.[20,21]

The REasons for Geographic And Racial Differences in Stroke (REGARDS) study, a large, biracial, and national cohort, provides a unique opportunity to study this association and offers the advantage of examining race-specific associations. Therefore, we examined the cross-sectional association between OSA risk and AF in the REGARDS study, and evaluated whether differences exist by race, age, or sex. Given the REGARDS cohorts' unique geographical distribution, we also explored whether geographical regional disparities altered this association. It is well known that geographical disparities in cardiovascular disease exist,[22] but no data exist on the OSA and AF interplay.

METHODS

Study Population and Design

The REGARDS study is an ongoing nationwide large, biracial (blacks and whites) prospective cohort study of adults age 45 years or older. The aim of the study is to assess factors that increase risk of vascular events with emphasis on racial and regional disparities. Details of the study have been published previously.[23] Between 2003–2007, the study recruited 30,239 participants through postal mailing and telephone calls. The study oversampled blacks and individuals residing in the stroke belt (North Carolina, South Carolina, Georgia, Alabama, Mississippi, Tennessee, Arkansas, and Louisiana). Demographic information and medical history were obtained at baseline by a trained interviewer using a computer-assisted telephone interview (CATI) system. Additional information was obtained 3 to 4 weeks later during an in-home visit, including blood pressure (BP) measurements, electrocardiogram (ECG) recording, recording of information on medications, and collection of blood and urine samples. Participants are followed by CATI every 6 months to obtain information on potential stroke hospitalizations and change in cognitive function.

Between September 2008–2010, a series of sleep questions were added to the 6-month follow-up phone calls such that all active participants were asked questions about sleep, including OSA risk. The sleep assessment included the Berlin Sleep Questionnaire (BSQ),[24] sleep medication use, and previous sleep apnea diagnosis and treatment.

We excluded participants who did not complete the sleep questionnaire (n = 6,264), were missing AF status (n = 501), had data anomalies (n = 56), or had missing covariates (n = 3,067). The remaining 20,351 participants were included in the analysis (**Figure 1**).

Obstructive Sleep Apnea

OSA status was determined by the BSQ,[24] which was part of the sleep assessment (2008–2010). BSQ uses three symptom categories of risk for OSA including: (1) snoring (5 items), (2) daytime sleepiness (3 items), and (3) high blood pressure (BP) and body mass index (BMI) (2 items). BMI was calculated from measured height and weight from the baseline in-home visit. Hypertension (high BP) was defined as systolic BP (SBP) ≥ 140 mmHg or diastolic BP (DBP) ≥ 90 mmHg or self-reported use of antihypertensive medications obtained using the CATI system. Participants were placed into two categories based on their response: high risk for OSA diagnosis and low

risk for OSA diagnosis per standard protocol.[24,25] Participants were considered high risk for OSA if they met criteria in two of the three symptom categories, that is, ≥ 2 affirmative responses in symptom category 1, ≥ 2 in category 2, and ≥ 1 in category 3 (or a BMI ≥ 30 kg/m^2). Participants were considered low risk for OSA if they met criteria in none or only one of the symptom categories. BSQ is a widely used tool in screening for OSA, and its validity may vary in different populations. BSQ in a population-based setting has been shown to have a high negative predictive value (96.3%) and good sensitivity (76.9%) in ruling out OSA and has moderate sensitivity (58.8%) and moderately high negative predictive value (82.9%) in predicting apnea-hypopnea index ≥ 15 (moderate OSA).[26–28]

Atrial Fibrillation

The presence of AF was determined by ECG evidence obtained during the in-home visit or self-reported history of a physician diagnosis of AF during the initial telephone survey (2003–2007). Self-reported history of AF was assessed by a positive response to the question: "Has a physician or a health professional ever told you that you had atrial fibrillation?"[29] The ECGs were read at a central reading center by trained ECG technicians who were blinded to all other participant data (Epidemiological Cardiology Research Center, Wake Forest School of Medicine, Winston-Salem, North Carolina, United States). A 7-lead ECG recording acquired by applying the standard 4 limb electrodes and a midsternal electrode was done on the first 8,459 REGARDS study participants; the remaining participants underwent standard 12-lead ECG recording. The ability to detect AF is not affected whether a participant underwent a 7-lead or 12-lead ECG.[30,31]

Covariates

Demographic characteristics and socioeconomic factors included self-reported age, race (black or white), sex, income (less than $20,000, $20,000–$34,000, $35,000–$74,000, $75,000 and higher, refused), education (less than high school, high school graduate, some college, college graduate and above), geographic region (stroke belt, stroke buckle, non-belt or buckle[23]), alcohol habits, and smoking status. Alcohol use was classified as heavy (> 2 drinks/d for men and > 1 drink/d for women), moderate (1 to 2 drinks/d for men and 1 drink/d for women), and none.[32] Smoking was categorized into never, past (at least 100 cigarettes during a patient's lifetime), and current. Pulse pressure was calculated as the difference between SBP and DBP. History of stroke/transient ischemic attack (TIA) was considered affirmative if participants reported a history of physician verified stroke, or ministroke or TIA during the telephone interview.[33] Other medical conditions consisted of CHD (self-reported history of myocardial infarction, coronary artery bypass grafting, coronary angioplasty or stenting, or evidence of myocardial infarction on the baseline ECG), left ventricular hypertrophy [LVH] (Sokolow–Lyon Criteria[34]), and diabetes (fasting glucose level ≥ 126 mg/dL, nonfasting glucose ≥ 200 mg/dL, or a history of taking diabetes medications). We assessed digoxin use at baseline as proxy for HF similar to other REGARDS publications. Current clinical indications for use of digoxin include HF and AF, and digoxin use has 28% sensitivity and 99% specificity in diagnosing HF.[35] Physiological markers included albumin:creatinine ratio (> 30 mg/g was considered as renal dysfunction[36]), levels of total cholesterol, high-density lipoprotein cholesterol, and high-sensitivity C-reactive protein. Sleeping pill usage was self-reported and measured with the questions, "How many days/nights in the last month have you used prescription sleeping pills?" and "How many days/nights in the last month have you used non-prescription, or over the counter sleeping pills?" Sleep medication use was then categorized as any (prescription or over the counter) versus none.

Statistical Analysis

We compared baseline characteristics between those with low risk versus high risk for OSA. Categorical variables were reported as percentages and frequencies, continuous variables as mean ± standard deviation. Logistic regression was used to test the association between OSA categories and baseline AF. We computed odds ratio (OR) and 95% confidence interval (CI). A sequential adjusted logistic regression was performed as follows: model 0 unadjusted model, model 1 adjusted for pulse pressure. Pulse pressure has been associated with new-onset AF independent of other measures of arterial pressure and other previously recognized AF risk factors and therefore was included in model 1.[37,38] Model 2 included model 1 covariates with the addition of age, sex, race, region, and socioeconomic status (income category and education level); model 3 included model 2 with the addition of all previous medical conditions (eg, diabetes, CHD, HF, LVH, stroke); model 4 included model 3 as well as physiological markers and health behaviors (albumin:creatinine ratio, total cholesterol, high-density lipoprotein, C-reactive protein, smoking, alcohol use, and prescribed and over-the-counter sleep medications [frequency]). Additionally, a test for interaction and stratified analysis was performed to examine effect modification by race, sex, age (younger than 75 years and 75 years or older; based on the cutoff used by the AF risk stratification CHADS(2) score [congestive heart failure, hypertension, age 75 years or older, diabetes, prior stroke/transient ischemic attack][39]), and region. Evidence of effect modification was demonstrated by a value of $P < .10$ for the interaction term. We conducted a sensitivity analysis looking into the association of OSA and AF with different methods of AF ascertainment: self-reported AF, ECG reported AF, and AF detected by self-reports and ECG reports. SAS, version 9.4 (SAS, Cary, North Carolina, United States), was used for all the analyses.

RESULTS

Of the 20,351 participants included in the analysis 14,992 (73.7%) were at low risk for OSA and 5,359 (26.3%) were at high risk for OSA. Baseline characteristics of study participants categorized by OSA risk are shown in **Table 1**. Of those at low risk for OSA, AF was present in 1,077/14,992 (7.2%) and of those at high risk for OSA, AF was present in 482/5,359 (9%). Similar AF prevalence using only self-reported AF was reported in low- (1,023/14,992; 6.8%) and high-risk (467/5,359; 8.7%) OSA participants (**Table S1** in the supplemental material).

Table 1—Baseline characteristics of REGARDS patients by OSA risk (n = 20,351).

	Low Risk (n = 14,992)	High Risk (n = 5,359)	*P*
Demographics			
Age, years, mean ± SD	64.9 ± 9.2	62.5 ± 8.5	< .0001
Blacks, n (%)	5,566 (37.1)	2,071 (38.7)	.0487
Females, n (%)	8,367 (55.8)	2,853 (53.2)	.0012
Income, n (%)			.0253
Less than $20k	2,248 (15.0)	802 (15.0)	
$20k–$34k	3,531 (23.6)	1,257 (23.5)	
$35k–$74k	4,747 (31.7)	1,762 (32.9)	
$75k and above	2,692 (18.0)	989 (18.5)	
Refused	1,774 (11.8)	549 (10.2)	
Education, n (%)			.0117
Less than high school	1,513 (10.1)	554 (10.3)	
High school graduate	3,742 (25.0)	1,391 (26.0)	
Some college	3,957 (26.4)	1,484 (27.7)	
College graduate and above	5,780 (38.6)	1,930 (36.0)	
Region, n (%)			.0065
Stroke belt	5,079 (33.9)	1,926 (35.9)	
Stroke buckle	3,222 (21.5)	1,168 (21.8)	
Non belt or buckle	6,691 (44.6)	2,265 (42.3)	
Smoking, n (%)			< .0001
Never	7,261 (48.4)	2,339 (43.7)	
Past	5,829 (38.9)	2,262 (42.2)	
Currently	1,902 (12.7)	758 (14.1)	
Alcohol Use (NIAAA), n (%)			.7143
Heavy	606 (4.0)	223 (4.2)	
Moderate	5,320 (35.5)	1,870 (34.9)	
None	9,066 (60.5)	3,266 (60.9)	
Baseline Medical Conditions, n (%)			
Hypertension	7,419 (49.5)	4179 (78.0)	< .0001
History of stroke/TIA	1,132 (7.6)	518 (9.7)	< .0001
Coronary heart disease	2,172 (14.5)	1,015 (18.9)	< .0001
Left ventricular hypertrophy	1,288 (8.6)	575 (10.7)	< .0001
Heart failure	295 (2.0)	95 (1.8)	.3715
Diabetes	2,481 (16.6)	1,325 (24.7)	< .0001
Physiologic Markers			
SBP, mmHg, mean ± SD	125.8 ± 16.2	129.8 ± 15.9	< .0001
DBP, mmHg, mean ± SD	75.8 ± 9.4	78.3 ± 9.5	< .0001
PP, mmHg, mean ± SD	51.5 ± 12.9	50.0 ± 13.1	< .0001
Renal function: ACR > 30, n (%)	1,813 (12.1)	756 (14.1)	.0001
Total cholesterol, mg/dL, mean ± SD	192.9 ± 39.1	189.6 ± 39.2	< .0001
High density lipoprotein, mg/dL, mean ± SD	53.1 ± 16.4	49.0 ± 14.8	< .0001
C-reactive protein, mg/L, median ± IQR *	2.8 ± 4.7	1.9 ± 3.6	< .0001
Body Mass Index, n (%)			< .0001
Underweight (< 18.5 kg/m^2)	162 (1.1)	18 (0.3)	
Normal (18.5–24.9 kg/m^2)	4,144 (27.7)	618 (11.6)	
Overweight (25–29.9 kg/m^2)	6,140 (41.1)	1,513 (28.4)	
Obese (≥ 30 kg/m^2)	4,495 (30.1)	3,183 (59.7)	
Medications, n (%)			
Sleep medication use, any	2,783 (18.6)	1,246 (23.3)	< .0001

* = Kruskal-Wallis test used for comparison. ACR = albumin:creatinine ratio, DBP = diastolic blood pressure, IQR = interquartile range, NIAAA = National Institute on Alcohol Abuse and Alcoholism, PP = pulse pressure, SBP = systolic blood pressure, SD = standard deviation, TIA = transient ischemic stroke.

Table 2—Association of atrial fibrillation with obstructive sleep apnea.

OSA	Model 0	Model 1	Model 2	Model 3	Model 4
Low risk	Ref	Ref	Ref	Ref	Ref
High risk	1.27 (1.14, 1.43)	1.26 (1.13, 1.41)	1.34 (1.20, 1.51)	1.30 (1.15, 1.46)	1.27 (1.13, 1.44)

Values are presented as odd ratios (95% confidence intervals) for OSA categories. Model 0 is the unadjusted model. Model 1 includes pulse pressure. Model 2 is adjusted for age, sex, race, region, education, and income. Model 3 is adjusted for model 2 and stroke/transient ischemic attack, coronary heart disease, heart failure, left ventricular hypertrophy, and diabetes. Model 4 is adjusted for model 3 and albumin:creatinine ratio, total cholesterol, high density lipoprotein, C-reactive protein, smoking, alcohol use, and use of sleep medications. OSA = obstructive sleep apnea.

Table 3—Atrial fibrillation by OSA among whites versus blacks.

	Model 0	Model 1	Model 2	Model 3	Model 4
Whites (n = 12,714)					
OSA					
Low risk	Ref	Ref	Ref	Ref	Ref
High risk	1.11 (0.96, 1.28)	1.09 (0.95, 1.26)	1.18 (1.02, 1.36)	1.14 (0.98, 1.33)	1.12 (0.96, 1.31)
Blacks (n = 7,637)					
OSA					
Low risk	Ref	Ref	Ref	Ref	Ref
High risk	1.69 (1.40, 2.03)	1.68 (1.39, 2.03)	1.70 (1.41, 2.06)	1.61 (1.33, 1.97)	1.58 (1.30, 1.93)

Values are presented as odd ratios (95% confidence intervals). *P* value for interaction .0003. Model 0 is the unadjusted model. Model 1 includes pulse pressure. Model 2 is adjusted for age, sex, race, region, education, and income. Model 3 is adjusted for model 2 and stroke/transient ischemic attack, coronary heart disease, heart failure, left ventricular hypertrophy, and diabetes. Model 4 is adjusted for model 3 and albumin:creatinine ratio, total cholesterol, high density lipoprotein, C-reactive protein, smoking, alcohol use, and use of sleep medications. OSA = obstructive sleep apnea.

Participants at high versus low risk for OSA had greater prevalence of CHD, LVH, diabetes, and history of stroke/TIA; they were also more likely to be obese and were more likely to use over-the-counter/prescription sleep medications.

In the main unadjusted model, compared to those at low risk of OSA, those at high risk of OSA had increased odds of AF (OR = 1.27, 95% CI = 1.14, 1.43). After adjustment for demographics, cardiovascular risk factors, physiological markers, and other potential confounders, high risk for OSA remained significantly associated with a 27% increased odds of AF compared to low risk for OSA (OR = 1.27, 95% CI = 1.13–1.44) (**Table 2**). When self-report was considered as method of AF ascertainment, odds of AF for high risk compared to low-risk OSA remained fairly similar to that observed using self-report or ECG reported (OR = 1.28, 95% CI = 1.13–1.44) (**Table S2** in the supplemental material). The association between OSA risk and AF did not differ by age (*P* for interaction = .61, sex (*P* for interaction = .47), or geographic region (*P* for interaction = .48) (**Tables S3–S5** in the supplemental material). However, the association between OSA risk and AF differed significantly by race (*P* for interaction = .0003) (**Table 3**). For blacks, high risk for OSA remained significantly associated with AF in the fully adjusted model (OR = 1.58, 95% CI = 1.30–1.93). This association was not observed in whites (OR = 1.12, 95% CI = 0.96–1.31).

DISCUSSION

In this large diverse cohort, we found that high risk of OSA was associated with an increased prevalence of AF and this did not vary by age, sex, or geographical region. However, the association between AF and OSA risk differed significantly by race. For blacks, there was a significant 58% increase in odds of AF in high-risk OSA versus low- risk OSA, compared to a nonsignificant 12% increase in odds in whites after adjusting for sociodemographic factors, medical conditions and physiological markers.

Previous studies have mostly focused on the frequency of OSA in patients with AF; however, few studies have assessed the frequency of AF in OSA. Moreover, several studies assessed specific subgroup populations focusing on postsurgical events.[13–15,19,40] REGARDS provided a unique opportunity to assess this association in a large national cohort of blacks and whites where high-risk OSA was associated with a 27% increased prevalence of AF after multivariable adjustment. The prevalence of AF is age specific; 3.6% among those age 66–69 years and 16.3% among those age 85–89 years.[41] In our study, AF was prevalent in 9% of high-risk OSA participants, and our cohort consisted of younger individuals with mean age of 64.3 ± 9.1 and had higher rates of AF for both high and low risk of OSA (**Table 1**). This may indicate that AF is more common than we expected in individuals age 60–70 years. However, we found no difference in the association between OSA risk and AF when comparing patients younger than 75 years and those age 75 years and older (**Table S3**).

We speculate that using self-reported AF might provide sufficient information on the OSA-AF association as does ascertainment of AF using self-reported or ECG reported AF (**Table S1** and **Table S2**); this might be especially useful in cases where ECG data are unavailable. Similarly, in the REGARDS study, self-reported AF was found to be a strong

predictor of incident stroke and could be used interchangeably or in combination with ECG-reported AF.[29] We had a relatively small number of participants with AF in high-risk and low-risk OSA using ECG reports alone or using both ECG and self-reports; thus, we are unable to make any conclusions about differences between these two methods of AF ascertainment.

Others have reported an association between OSA and AF and this interplay differed in some cases by OSA severity. A study following 121 consecutive patients from time of coronary artery bypass grafting surgery until hospital discharge found a higher risk of AF in patients with OSA, assessed by polysomnography (PSG), compared to those without OSA (OR = 2.8; 95% CI = 1.2, 6.8).[14] Another analysis of 566 participants from the SHHS found that among individuals with SDB, odds of AF was 4 times greater than in participants without SDB as verified by PSG (OR = 4.02, 95% CI = 1.03, 15.74) after adjusting for age, sex, BMI, and prevalent CHD, and there was no dose-response relationship between risk of AF with severe to very severe SDB.[12] In a recent study, among patients being investigated for suspected OSA by manually estimating sleep index from respiratory recordings, AF was common (13/170 = 7.6%) and the prevalence increased with OSA severity; however, all subjects with OSA were men.[42] In our study, we relied on the BSQ to determine OSA risk and we found that individuals at high risk of OSA compared to those at low risk had greater prevalence of AF. This association was lower than observed in the SHHS (OR = 4.02, 95% CI = 1.03, 15.74)[12] and this may be due to differences in cohort characteristics, study design, and method of measurement of OSA risk. The relationship between OSA and AF could be explained by several pathological mechanisms, such as oxidative stress, inflammation, sympathetic activation, atrial remodeling, intrathoracic pressure shifts, apnea-induced hypoxia, sympathovagal imbalance, and intrathoracic pressure shift, but discussing these mechanisms are beyond the scope of the current analyses.[43]

Despite OSA being a significant public health burden, it remains poorly diagnosed especially in blacks.[44,45] Racial differences have been observed in the association between OSA and cardiovascular disease.[46] However, most studies have been conducted in predominantly non-black populations, therefore limiting the generalizability of these findings.[46] The Jackson Heart Study, a study of black participants only, found a high prevalence of sleep symptoms, risk of OSA, and sleep burden, and these differed by sex.[47] Sleep symptoms (ie, snoring, stop breathing in sleep, fall asleep during the day) were associated with obesity, stress, and poor perceived health. The Multi-Ethnic Study of Atherosclerosis, or MESA < is a multisite prospective cohort study that included white, black, Hispanic, and Chinese patients aged 45–84 from six United States communities. MESA using PSG found that blacks had higher odds of sleep apnea even after adjustment for age, sex, and study site (OR = 1.78, 95% CI = 1.20, 2.63).[48] Risk factors for AF are race (black), OSA, obesity, and metabolic syndrome.[49] A previous analysis in the REGARDS study found that the association of smoking and AF differed by race, with smoking being associated with AF only in blacks. There was no differential association of AF with other risk factors, such as sex, diabetes, dyslipidemia, or income among races. However, population-attributable fractions of hypertension, obesity, and smoking were higher in blacks than whites.[50] In the Southern Community Cohort Study, hypertension and diabetes were significantly associated with AF in whites and not blacks. However, age, male sex, obesity, and CHD were similarly associated with AF between races.[51] Race is a common risk factor for OSA and AF, and race also modifies the association between AF and other predictors and outcomes. Because in our study we also found a differential association of OSA with AF by race, further studies to understand these racial disparities are warranted.

For OSA, black race also serves as a risk factor for the development of OSA both in adults and children even after adjustment for confounders.[44,52,53] The community-based SHHS, however, did not find a difference in OSA prevalence by race after adjusting for age, sex, and BMI, but this study included only 5% black participants.[54]

In the community-based study in Olmsted County, Minnesota, OSA and its severity predicted 5-year incidence of AF (hazard ratio = 2.18, 95% CI = 1.54, 3.54) and a decrease in nocturnal oxygen was predictive of AF only in those younger than 65 years; however, race was not included in the analysis.[55] In MESA, physician-diagnosed sleep apnea (based on a self-administered sleep history questionnaire) was associated with AF incidence in the multivariable analysis (hazard ratio = 1.76, 95% CI = 1.03, 3.02). However, unlike our study no significant interaction between racial/ethnic groups was observed.[56] Given the contradictory data and limited longitudinal studies that include adequate representation of races, further longitudinal studies are needed to examine the temporal association of AF with OSA. Current AF and OSA guidelines do not differentiate between races as far as screening, management, or treatment and there are no specific recommendations for AF screening in patients with OSA and vice versa.[57,58] Further studies examining the benefit of screening for AF in patients with OSA and patients with OSA and AF in a large diverse cohort would be beneficial.

Our results, however, should be interpreted with caution. Several baseline characteristics were self-reported (eg, smoking, sleep medications pills); thus, they may be subject to recall bias and misclassification. We were unable to report the class and dosages of sleep medications. Because we relied only on BSQ and not on PSG data to determine OSA risk, the association between OSA and AF might have been attenuated. Relying on BSQ to assess OSA risk might have introduced false-positive results, which could have influenced our analyses. We were unable to identify the degree of hypoxemia or identify central SDB; therefore, we only identified participants as having high or low risk OSA. Also, BSQ has low specificity and modest to high sensitivity in identifying OSA in the general population and in patients with cardiovascular or cerebrovascular disease,[59–61] and this may affect the generalizability of our results. Using digoxin usage as the basis of diagnosing HF is also a limitation of the study. Obesity is an independent risk factor for AF and increases OSA risk.[62,63] However, we were unable to adjust for BMI in the model because BMI was used to determine OSA risk. We were unable to test whether BMI modifies the association between OSA risk and AF because

BMI was part of OSA risk determination. We have included stratified models based on BMI ≥ 30 kg/m^2 and BMI < 30 kg/m^2 in **Table S6** in the supplemental material. Because BMI was used to calculate OSA risk, the stratified models of BMI are not directly comparable. We found that among participants with low BMI (< 30 kg/m^2), OSA risk (participants reporting snoring and daytime sleepiness) is significantly greater than having no symptoms and this association remained significant even after adjusting for demographic and clinical characteristics. In high BMI strata (BMI ≥ 30 kg/m^2), OSA risk, whether participants had snoring or daytime sleepiness, compared to having no factors was not significant. Furthermore, because AF was established at baseline from participant self-report or ECG ascertainment, we likely missed some cases of paroxysmal AF and misclassification of AF could occur, which could skew our risk estimates. Also, incident cases of AF that could have occurred between the baseline visit and the sleep apnea module administration, and/or misclassified AF could have underestimated the prevalence of AF. Additionally, we were limited by the cross-sectional nature of the analysis, so we were not able to establish the temporal relationship between OSA risk and AF. There was some time discrepancy, as data on covariates were collected before BSQ was administered. However, in the setting of the large and diverse REGARDS cohort and with most covariates measured, we were able to explore the association of AF with OSA, which we believe is the significant contribution of this analysis. Longitudinal analyses, using REGARDS data, could be used to expand on the association between OSA and AF, once these data are available.

In conclusion, we have shown with the REGARDS cohort that OSA risk is associated with prevalent AF and persons at high risk of OSA have a 27% increased prevalence of AF compared to low risk after adjustment. This association varies by race, with blacks having a stronger association. Further research and longitudinal studies are needed to determine whether OSA can be a predictor of incident AF, and the potential for race interaction.

ABBREVIATIONS

AF, atrial fibrillation
BMI, body mass index
BP, blood pressure
BSQ, Berlin Sleep Questionnaire
CATI, computer-assisted telephone interview
CHD, coronary heart disease
CI, confidence interval
DBP, diastolic blood pressure
ECG, electrocardiography
HF, heart failure
LVH, left ventricular hypertrophy
MESA, Multi-Ethnic Study of Atherosclerosis
OR, odds ratio
OSA, obstructive sleep apnea
PSG, polysomnography
REGARDS, REasons for Geographic And Racial Differences in Stroke
SBP, systolic blood pressure
SSCS, Southern Community Cohort Study
SDB, sleep-disordered breathing
SHHS, Sleep Heart Health Study

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