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Risk of obstructive sleep apnea in African American patients with chronic rhinosinusitis

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ABSTRACT

Background: It is widely known that patients with chronic rhinosinusitis (CRS) commonly experience sleep disruption. Many of these patients have the associated diagnosis of obstructive sleep apnea (OSA). However, little is known about the risk factors for developing OSA in the CRS population.

Objective: To identify the risk factors for OSA in CRS to determine who should be screened for OSA among patients with CRS.

Methods: We evaluated a large cohort of patients with confirmed diagnostic criteria for CRS. Patient medical records were reviewed to identify those with OSA confirmed by overnight polysomnography. Records were further reviewed for demographic information (age, sex, race, and ethnicity), body mass index, and medical history, including the presence of nasal polyps, asthma, aspirin-exacerbated respiratory disease, allergic rhinitis, and eczema. The number of endoscopic sinus operations, duration of CRS, presence of subjective smell loss, and computed tomography Lund-Mackay score were also ascertained.

Results: A total of 916 patients with CRS were included in the study. Implementation of a multivariable regression model for identifying adjusted risk factors revealed that African American patients had a significantly higher risk for OSA than white patients, with an adjusted odds ratio of 1.98 (95% confidence interval, 1.19–3.29). Furthermore, patients with CRS without nasal polyps were at higher risk for OSA, with an odds ratio of 1.63 (95% confidence interval, 1.02–2.61) compared with patients with CRS with nasal polyps.

Conclusion: African American patients with CRS were at higher risk for OSA compared with white patients, and this patient group needs to be screened for OSA.

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Introduction

Chronic rhinosinusitis (CRS) is defined as an inflammatory disorder that involves the mucosae of the nose and paranasal sinuses.¹

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Approximately 5% to 10% of the US population has CRS, and it primarily affects middle-aged adults.^{2,3} The classification of CRS is generally delineated into 2 phenotypes: CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP).^{1,4} It is well known that patients with CRS have poor sleep quality and decreased quality of life,^{5,6} which have been attributed to a multitude of factors, including upper airway obstruction, nasal congestion, and the inflammatory disease process.^{7,8} Previous studies investigating sleep quality in CRS have found that 60% to 75% of patients with CRS experience poor sleep,^{8–11} which is considerably higher than the general population (8%–18%).¹²

Breathing cessation during sleep, also known as apnea, is the underlying mechanism of obstructive sleep apnea (OSA). OSA is a chronic sleep-related breathing disorder associated with advancing

age and increased body mass index (BMI). The prevalence of OSA is high in the US population,¹³ with marked increase during the last 2 decades.¹⁴ Peppard et al¹⁴ found that 10% to 17% of men and 3% to 10% of women aged 30 to 70 years have an apnea hypopnea index (AHI) above 15, correlating with moderate to severe OSA. Two previous studies^{5,9} found an association of OSA with CRS. In a report from the United States,⁵ physician-diagnosed OSA was reported in 15% of CRS cases. A more recent article from Taiwan⁹ reported that up to 64.7% of patients with CRS who were prospectively screened by polysomnography were diagnosed with OSA. The discrepancy between these 2 studies indicates that possibly a significant proportion of patients with CRS have sleep apnea, which is underdiagnosed and underreported. It is also possible that the prevalence of OSA is different in patients from different racial and ethnic groups. Despite these associations, no studies have evaluated the risk factors for OSA in patients with CRS. It is known that patients with OSA have increased morbidity with higher incidence of hypertension, cardiovascular disease, and depression.¹³ Independent of these comorbidities, OSA has significant health care costs, estimated to be \$65 billion to \$165 billion dollars annually.¹¹ There are also morbidities and dangers associated with fatigue commonly induced by untreated OSA; fatigue increases the risk of motor vehicle crashes by up to 7-fold and are associated with poor performance at work.¹⁵ Furthermore, individuals with OSA and AHI above 30 have a 3-fold increase in all-cause mortality compared with those without sleep disordered breathing.¹³ This points to the fact that undiagnosed and untreated OSA places patients at a significant risk and reinforces the importance of identifying at-risk groups and properly diagnosing OSA as early as possible to implement effective treatment modalities for this condition. In this study, we aimed to identify the risk factors for OSA in patients with CRS presenting to allergy or otolaryngology clinics to determine the at-risk groups that need screening for OSA among patients with CRS.

Methods

This retrospective cohort study, approved by the institutional review board of Rush University Medical Center, was performed to investigate the correlation between CRS and OSA. We reviewed the medical records of all patients in our previously reported large retrospective cohort of CRS.^{16,17} CRS was diagnosed per the American Academy of Otolaryngology–Head and Neck Surgery Chronic Rhinosinusitis Task Force criteria,¹⁸ with more than 12 weeks of continuous rhinosinusitis symptoms, along with nasal endoscopy or computed tomography demonstrating objective findings of sinusitis.

Detailed review of these medical records identified a group of patients with OSA confirmed by polysomnography. These patients met the criteria for OSA based on the Adult OSA Task Force of the American Academy of Sleep Medicine,¹⁹ including symptoms of daytime sleepiness, snoring, breathing interruptions in sleep, or awakenings from gasping or choking with 5 or more apnea and hypopnea respiratory events per hour of sleep or 15 or more apnea and hypopnea respiratory events per hour of sleep without symptoms.¹⁹ Two independent investigators reviewed the medical records to improve the accuracy of data. We excluded patients who had symptoms suggestive of OSA but had not had a diagnostic polysomnography to avoid confounding the data.

The REDcap database was used to record clinical and demographic data, with deidentification of health information. The race and ethnicity terms used are based on National Institutes of Health recommendations (African American, white, Asian, Native Hawaiian or Other Pacific Islander, American Indian or Alaskan Native), along with the ethnicity categories of Latino and not Latino.

Statistical Analysis

Bivariate comparisons between the groups were performed using the χ^2 test and analysis of variance. Then a multivariable logistic regression analysis was used to test the adjusted effect of covariates. The covariates are defined in eTable 1. All the covariates tested in bivariate screening were entered into the model. This approach was used to find the variables that could predict the outcome of OSA in CRS and identify the at-risk groups. Software for analyses included SAS, version 9.3 (SAS Institute Inc, Cary, North Carolina), and SPSS, version 21 (SPSS Inc, Chicago, Illinois). Statistical significance was achieved at $P \leq .05$.

Results

A total of 1028 patients from our cohort were included. After exclusion of those with possible OSA diagnosis and no documented polysomnography in the medical record, 916 patients with CRS were included in the current study. Among these patients, 100 (10.9%) had OSA diagnosed by polysomnography. The mean (SD) AHI in these OSA cases was 32.63 (28.86).

There were 211 African Americans of non-Latino ethnicity, 5 African American Latinos, 566 whites of non-Latino ethnicity, 94 whites of Latino ethnicity, 17 Asians, and 23 individuals of other races with CRS. For simplification, we refer to individuals of white race and Latino ethnicity as Latino and individuals of white race and non-Latino ethnicity as whites. We refer to individuals of African American or black race and non-Latino ethnicity as African Americans. Among these racial/ethnic groups, African Americans had a statistically significant increased risk for OSA compared with other races: 46% of the CRS and OSA group vs 20.22% of CRS without OSA groups were African Americans ($P < .001$). The mean age of OSA cases was significantly higher, and male sex was associated with higher risk of OSA ($P < .001$). The mean BMI (calculated as weight in kilograms divided by square of height in meters) of patients with CRS and OSA was 35.92, whereas the mean BMI of patients with CRS without OSA was 27.70 ($P < .001$). After adjusting for age, male sex, and BMI, which are known risk factors for OSA, African American patients still had a significantly higher odds of OSA than whites

Table 1

Demographic and Clinical Characteristics of CRS With OSA Patients Compared to CRS Without OSA Patients Calculated by Logistic Regression (Adjusted for BMI, Age, Sex, and Race)

Characteristic	Odds ratio (95% CI)
Sex	
Male	Reference
Female	0.415 (0.083–1.41)
Age	1.016 (1.001–1.03) ^a
BMI	1.160 (1.04–1.29) ^a
Race	
White (n = 566)	Reference
Black (n = 211)	1.98 (1.19–3.29) ^a
Latino (n = 94)	1.43 (0.67–3.04)
Others (n = 45)	Not tested
Nasal polyps	
CRSsNP (n = 664)	Reference
CRSsNP (n = 252)	1.63 (1.02–2.61) ^a
Asthma	0.97 (0.59–1.59)
AERD	1.35 (0.39–4.69)
Allergic rhinitis	1.23 (0.74–2.3)
Eczema	0.87 (0.539–1.25)
No. of operations	0.93 (0.76–1.13)
Duration of disease	1.017 (0.90–1.04)
Reported smell loss	1.49 (0.42–2.63)
Lund-Mackay score	0.95 (0.90–1.006)

Abbreviations: AERD, aspirin-exacerbated respiratory disease; BMI, body mass index; CI, confidence interval; CRS, chronic rhinosinusitis; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; OSA, obstructive sleep apnea.

^a $P < .05$.

(odds ratio [OR], 1.98; 95% confidence interval [CI], 1.19–3.29) (Table 1).

Among the CRS cases, 252 cases had nasal polyps and were identified as CRSwNP. OSA was significantly higher in patients with CRSsNP; 12.2% of patients with CRSsNP vs 8.5% of patients with CRSwNP had OSA ($P < .001$).

The mean (SD) AHIs in patients with OSA from different racial/ethnic groups were similar (26.4 [26.4], 28.8 [32.2], and 34.9 [27.2] in white, African American, and Latinos, respectively; $P = .34$). The mean (SD) AHIs were similar between patients with CRSsNP (27.8 [25.7]) and CRSwNP (30.3 [31.02]) ($P = .78$).

The association of multiple comorbid conditions and related factors with OSA was analyzed. These factors included asthma, aspirin-exacerbated respiratory disease (AERD), allergic rhinitis, and eczema. The other group of variables studied included the symptoms and severity of CRS, including number of sinus operations, subjective smell loss, Lund-Mackay score (LMS), and duration of CRS. We performed logistic regression analysis to test whether these variables confer increased risk of OSA after adjusting for demographic factors (age, sex, and race) and BMI. Data analysis revealed that patients with these comorbid diseases were not at statistically significant increased risk for OSA (Table 1). Among CRS-related factors, except nasal polyps, none were statistically significant in their association with OSA (Table 1).

Next we applied a stepwise multivariable regression model with all the above variables (including demographic, comorbidities, and CRS-related factors) in one model to test the associations of these variables with OSA when correcting for intervariable effects. This was because some of these variables, such as asthma and nasal polyps, are independently associated with each other and could potentially influence the results. In this model, after adjusting for variables, the risk of OSA remained significantly associated with African American race and absence of nasal polyps.

Discussion

We found that African American patients with CRS have a significantly higher odds of OSA compared with whites. We previously found that the phenotype of CRS is different and more severe in African Americans.¹⁶ African American patients with CRS have a higher CRS severity index on computed tomography (LMS) and increased smell loss than white patients with CRS.¹⁶ In our current study, no association was found between OSA and higher LMS. Therefore, the increased OSA rate is not explained by increased severity of CRS in these patients. Although CRS and OSA are comorbid conditions, at this point it is difficult to assess whether there is a relationship between the 2 conditions. Kao et al²⁰ followed up patients with OSA for 5 years and concluded that both males and females with OSA had higher risk of developing subsequent CRS. Tan et al²¹ also found that patients with CRS had increased premorbid prevalence of OSA. These findings do not prove causation but support the complex association of CRS and OSA and call for further studies. Another study²² found that African American children and adolescents are at higher risk for OSA compared with whites, which has been attributed to lifestyle and obesity. However, a large population-based study²³ in adult patients found no increased risk of OSA in African Americans after adjusting for other demographic factors and BMI. Our cohort includes adults with CRS, with the mean age older than 50 years. It is noteworthy that the observed association between African American race and OSA in the current CRS cohort was not explained by BMI, sex, or age. Therefore, our finding of the significant increased risk of OSA in African Americans adults might be specific to CRS and may be related to genetic elements and/or environmental factors. Genetic studies have found evidence of inherited molecular alterations associated with OSA specific to African Americans.^{24,25}

Future studies are needed to investigate whether the increased risk of OSA in the setting of CRS is linked to any of these genetic alterations. Furthermore, other lifestyle risk factors for OSA, such as smoking,^{26,27} which is also a major risk factor for CRS²⁸ and is more commonly practiced and sustained into adulthood among African Americans,²⁹ might be playing a role in this increased risk. The burden of sleep symptoms and risk of hypertension in the setting of OSA is higher among African Americans compared with other races.²² The current finding of increased risk of OSA in African Americans along with the evidence of the higher burden of OSA in this racial group²² further reinforces the importance of screening for this major comorbidity among African American patients with CRS and calls for in-depth studies to evaluate the underlying cause of these observations in African Americans with CRS.

Our results indicate that patients with CRSsNP are at significantly increased risk for OSA. This association remained significant in the multivariable model after adjusting for multiple demographic and disease-specific risk factors. The risk of OSA is associated with upper airway crowding in the general population. Therefore, the association between patients with OSA and CRSsNP seems counterintuitive to the idea that nasal or airway crowding by nasal polyps should worsen symptoms. However, this finding is consistent with a previous report that found a lower rate of nasal polyps in CRS cases with comorbid OSA (20%) than CRS cases without OSA (35%) ($P = .01$).⁵ In addition, OSA was not associated with the LMS (which is a radiographic indicator of CRS severity), the number of previous operations for CRS, or the report of smell loss. This finding suggests that the severity of CRS or degree of nasal obstruction is not the main risk factor for OSA in CRS patients but rather certain underlying factors making patients with CRSsNP more prone to OSA. Multiple investigations have attempted to delineate the differences between CRSwNP and CRSsNP. A previous study³⁰ suggested an association between T_H2 polarization causing increased interleukin 5 and eosinophilia in CRSwNP and a trend toward more T_H1 polarization in CRSsNP. Interestingly, a previous study³¹ of children with OSA found that those with moderate-severe OSA have a significantly higher percentage of T_H1 cells ($CD3^+CD4^+$ interferon γ^+) and higher T_H1/T_H2 ratios in peripheral blood compared with children with mild OSA and healthy controls. This finding suggests an association between OSA and T_H1 polarization, which could be the link to CRSsNP. However, this finding needs to be investigated in adult patients to be related to the present findings in adult CRSsNP and OSA.

Consistent with the general population, our adjusted results indicate that elevated BMI confers increased risk for OSA.^{32,33} Our crude analyses revealed an association between OSA and male sex, which was not significant in the multivariable model after adjusting for other variables. A previous study³² found that the rate of OSA increased significantly in women after menopause and is close to rates seen in men at higher ages. The mean age in our CRS series is older than 50 years, which could be the reason for the lack of association of female sex with decreased OSA risk in our series after adjusting for other factors, including age.

After controlling for demographic factors, patients with CRS and OSA do not have increased risk of comorbid diseases, such as asthma, allergic rhinitis, eczema, or AERD. The link between CRSwNP and asthma is well established,^{17,34} and it is known that the presence of nasal polyps is associated with presence and higher severity of asthma.³⁵ Likewise, AERD comprises the triad of asthma, aspirin hypersensitivity, and nasal polyposis and, by definition, is only seen in CRSwNP cases. Patients with CRSwNP have higher total symptom score and experience smell loss.²⁵ One can suspect that the lack of association of OSA with asthma, AERD, or LMS is because, in our study, most patients with CRS and OSA had CRSsNP. However, the fact that none of these variables were associated with OSA in the multivariable model after adjusting for the effect of other

variables, including nasal polyps, indicates a true lack of association.

This study was performed in a Midwest urban setting in a tertiary center, and some of the findings might be limited to similar populations. Furthermore, the retrospective nature of the study, which is the major limitation of this report, can result in under-reporting of the OSA rate in CRS. We excluded patients who had symptoms suggestive of OSA but did not have formal polysomnography analyses to avoid confounding the data and our goal to find risk factors for true OSA. By excluding these patients, we possibly eliminated some patients with OSA. Therefore, our study cannot provide the true prevalence of OSA in CRS, and it is likely that the actual prevalence of OSA in our cohort is higher than 10.9%, which was the case in another series from the United States⁵ and a series from Taiwan.⁹

Among the patients studied in our cohort, most were African American, white non-Latinos, or white Latinos. We did not have sufficient cases in the other groups, including Asian Americans, and therefore not enough power to draw any conclusion on these other racial/ethnic groups. Jiang et al⁹ note a 64.7% incidence of OSA in their series from Taiwan, which was significantly higher than the rate in a US series,⁵ suggesting a possible role of race. Future prospective studies would be beneficial to determine the prevalence of OSA within the CRS population. In addition, future studies assessing for causality and ideal treatment regimens in this patient population are needed.

This study indicates that among patients with CRS, African American patients and patients with CRSsNP are at greater risk for OSA and suggests that they should be screened for this major comorbidity. The association of OSA with CRSsNP reinforces the idea that CRSwNP and CRSsNP stem from varying molecular pathways with a pathogenesis driven by the microscopic milieu and complexity of various inflammatory markers.

Supplementary Data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.anai.2017.03.009>.

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Supplementary Data

eTable 1

Definitions of the Variables Used in the Study

Variable	Definition used in the study	Variable type	Response
Nasal polyp	Presence of nasal polyp documented in the anterior rhinoscopy, complete nasal endoscopy, or sinus CT	Binary	Yes/no
Asthma	Physician's diagnosis of asthma documented in the medical record	Binary	Yes/no
AERD	Physician's diagnosis of AERD based on presence of asthma, CRSwNP, and a documented history of a respiratory reaction to COX-1 inhibitor	Binary	Yes/no
Allergic rhinitis	Positive skin prick test result or elevated specific IgE level to aeroallergens documented in the medical record (a standard panel of 28 allergens, including local trees, grasses, weeds and mold, dust mites, cat, dog, cockroach, and mouse)	Binary	Positive ≥ 1 or more aeroallergens/negative to all aeroallergens
Eczema	Physician's diagnosis of atopic dermatitis	Binary	Yes/no
No. of operations	Documented No. of functional endoscopic sinus operations in the history	Continuous	No. of operations
Duration of disease	Documented duration of CRS disease by reviewing all the visits the patient had at Rush	Continuous	Years of disease
Smell loss	Patient's report of smell loss, documented in the history or review of systems	Binary	Yes/no
Lund-Mackay score	Based on review and scoring of CT images by a trained researcher	Continuous	Score

Abbreviations: AERD, aspirin-exacerbated respiratory disease; CT, computed tomography; COX, cyclo-oxygenase; CRS, chronic rhinosinusitis; CRSwNP, chronic rhinosinusitis with nasal polyps; OSA, obstructive sleep apnea.