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Predictors of Obstructive Sleep Apnea Risk among Blacks with Metabolic Syndrome

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Abstract

Introduction: Identification of risk factors for obstructive sleep apnea (OSA) is important to enable comprehensive intervention to reduce OSA-related cardiovascular disease (CVD). The metabolic syndrome outcome study (MetSO) provides a unique opportunity to address these factors. This study investigated risk of OSA among blacks with metabolic syndrome.

Methods: The present study utilized data from MetSO, an NIH-funded cohort study of blacks with metabolic syndrome. A total of 1,035 patients provided data for the analysis. These included sociodemographic factors, health risks, and medical history. Physician-diagnosed conditions were obtained using an electronic medical record system (Allscripts, Sunrise Enterprise). Patients were diagnosed with metabolic syndrome using criteria articulated in the joint interim statement for harmonizing the metabolic syndrome. Patients with a score ≥6 on the Apnea Risk Evaluation System (ARES) questionnaire were considered at risk for OSA. Obesity is defined by body mass index (BMI ≥ 30 kg/m^2)

Results: Of the 1,035 patients screened in the MetSO cohort, 48.9% were at high risk for OSA. Using multivariate-adjusted logistic regression analysis, we observed that obesity was the strongest predictor of OSA risk (OR=1.59, 95%CI=1.24-2.04, p<0.0001). This finding remained significant even after adjustment for known covariates including blood pressure, low-density lipoprotein, high-density lipoprotein, and glucose levels (OR=1.44, 95%CI=1.11-1.86, p<0.001).

Conclusion: Blacks in the MetSO cohort are at greater OSA risk, relative to the adult population in developed countries. Consistent with previous observations, obesity proved the strongest independent predictor of OSA risk among blacks with metabolic syndrome.

Keywords: Obstructive sleep apnea; Metabolic syndrome; Obesity; Blacks

Introduction

Obstructive sleep apnea (OSA) is characterized by recurring sleep disruptions, intermittent hypercapnia and hypoxia, resulting in increased sympathetic nerve activity, oxidative stress and hemodynamic changes [1,2]. Oxidative stress has been shown to reduce vasodilatation and increase platelet adhesion, leading to metabolic dysfunction, systemic inflammation, and hypercoagulation [3]. OSA has also been associated with obesity, insulin resistance and metabolic syndrome [4,5], which is characterized by a constellation of cardio-metabolic risk factors (i.e., obesity, hypertension hyperlipidemia and diabetes), that are associated with adverse cardiovascular outcomes [6,7]. The term Syndrome Z has been coined to explain the combination of interrelated diseases in recent sleep literature [8]. Syndrome Z includes metabolic syndrome features of increased waist circumference, hypertension, diabetes, dyslipidemia, the incorporation of sleep apnea [8].

Despite evidence that OSA is associated with metabolic syndrome as well as its components [9], little is known about OSA risk among blacks with a diagnosis of metabolic syndrome, although previous studies have suggested that they are generally at higher risk for OSA [10]. Understanding the mechanisms underlying the higher prevalence of OSA among blacks with associated cardio-metabolic risk factors is important in elucidating the relationship between OSA and metabolic syndrome. Thus, we sought to (1) assess OSA risk among blacks with metabolic syndrome and (2) explore cardio-metabolic predictors of OSA risk in this vulnerable population.

Methods

Data was collected as part of the metabolic syndrome outcome study (MetSO) an on-going study of blacks with metabolic syndrome in Brooklyn, New York. A total of 1,035 patients provided data for the analysis. These included sociodemographic factors, health risks, and medical history. Physician-diagnosed conditions were obtained using an electronic medical record system (Allscripts, Sunrise Enterprise). Patients were diagnosed with metabolic syndrome using the National Heart, Lung and Blood Institute and the American Heart Association guidelines [11]. According to these guidelines, metabolic syndrome is diagnosed when a patient has at least three of the following five conditions: fasting glucose ≥ 100mg/dl or receiving treatment for hyperglycemia, blood pressure ≥ 130/ 85 mm Hg or receiving drug therapy for hypertension, triglycerides ≥ 150 mg/dl or receiving drug treatment for hypertriglyceridemia, HDL-C < 40 mg/dl in men or < 50 mg/dl in women or receiving drug therapy for HDL-C and a waist circumference ≥ 102 cm (40 in) in men or ≥ 88 cm (35 in) in women.

Patients were also assessed for OSA risk using the Apnea Risk Evaluation System (ARES), individuals with an ARES score ≥ 6 were considered at risk for OSA. We used ARES to identify individuals who were at OSA risk because of its accuracy in evaluating populations with a large pretest of OSA probability. Data solicited included sociodemographics, diseases associated with OSA, the Epworth Sleepiness Scale, and frequency of breathing abnormalities. The questionnaire has a sensitivity of 0.94, specificity of 0.79 (based on a clinical cut-off of AHI > 5), positive predictive value of 0.91 and negative predictive value of 0.86 [2]. Our rationale for using the ARES questionnaire is also based on our previous experience. In the last 4 years, we have screened 1,250 black patients in primary-care settings and 150 blacks in the community with no documented refusals [2,12,13]. The institutional review boards (IRB) at SUNY Downstate Medical Center (protocol # 09-193) approved this study prior to implementation.

Statistical Analysis

Frequency and measures of central tendency were used to describe the sample. In preliminary analyses, Pearson and Spearman correlations were used to explore relationships between variables of interest. To determine the best cardio-metabolic predictor of OSA risk among blacks with metabolic syndrome, we utilized multivariate-adjusted logistic regression modeling. Covariates entered in the model were age, sex, and income. Before constructing the model, correlational analyses were performed to assess associations between hypothesized predictors (i.e., obesity defined as BMI ≥ 30 kg/m^2, hypertension, dyslipidemia, and diabetes) and the dependent variable (i.e., OSA risk). In preliminary analyses, these factors were associated with the main predictor (BMI) and the dependent variable (OSA risk).

Results

A total of 1,035 patients with metabolic syndrome provided data for this study. The average age of the sample was 62±14 years (range: 20-97 years); 71% were female and 43% reported an annual income lower than $10K. Of the sample, 93% were diagnosed with hypertension; 61%, diabetes; 72%, dyslipidemia; 90% were overweight/obese; 33% had a history of heart disease and 10% had a stroke. ARES data indicated that 48% were at high OSA risk. Descriptive characteristics of cardio-metabolic parameters are presented in Table 1.

Variable	Mean	SD
Systolic BP	134.98mm/hg	16.39 mm/hg
Diastolic BP	75.77 mm/hg	10.55 mm/hg
LDL Cholesterol	105.6 mg/dL	36.88 mg/dL
HDL Cholesterol	48.03 mg/dL	16.49 mg/dL
Triglycerides	134.98 mg/dL	73.24 mg/dL
Glucose	138.38 mg/dL	68.27 mg/dL
HbA1c	7.93%	1.63%

Note: BP= Blood Pressure; LDL= Low-density lipoprotein,
HDL = High-density lipoprotein; HbA1c= glycated hemoglobin

Table 1: Metabolic characteristics of the study participants

Using multivariate logistic regression analysis, adjusting for age sex, and income, we observed that obesity was the strongest predictor of OSA risk (OR = 1.59, 95% CI = 1.24-2.04, p < 0.0001). This finding remained significant even after adjustment for blood pressure, low-density lipoprotein, high-density lipoprotein, and glucose levels (OR = 1.44, 95 % CI = 1.11-1.86, p < 0.001). Descriptive characteristics of a t-test p-value between risk group and non-risk group obesity parameters are presented in Table 2.

Variables	OSA risk	No OSA risk	Fisher Exact Significance (*p* value)
Insulin/Glucose	48.6%	51.4%	N.S.
Dyslipidemia	48.6%	51.4%	N.S.
Elevated BP/Hypertension (>130/85)	49.2%	50.8%	N.S.
BMI Male	51.4%	48.6%	.039
BMI Female	49.6%	50.4%	.059

Insulin/Glucose=Fasting plasma glucose > 110 mg/dL; Dyslipidemia=Plasma triglycerides > 150 mg/dL, HDL cholesterol < 40 mg/dL in men and < 50 mg/dL in women; Elevated BP/Hypertension=BP medication or BP > 130/85 mm/Hg; BMI Overweight-Obese > 25

Table 2: Cross-Tab with MetS indicators of OSA risk

Discussion

Using data from the Metabolic Syndrome Outcome Study, the largest cohort of blacks with metabolic syndrome, we found that 48% of the patients were at high OSA risk, which exceeds OSA risk observed in the general US population [14]. Equally important, results of this study showed that obesity is the strongest predictor of OSA risk among blacks with a diagnosis of metabolic syndrome.

While we could not determine how many of at-risk patients would actually receive an OSA diagnosis, we are guided by available data showing that among patients with metabolic syndrome referred for OSA assessment, 50.1% received a diagnosis [15]. We surmise that this might even be greater among blacks with metabolic syndrome. In other patient care settings where primary care is sought, like the Emergency Department (ED), we found a dearth of literature describing any patients with metabolic syndrome being referred for OSA screening. Available literature suggests that ED patients who do not regularly see a primary-care provider or have no primary-care provider are particularly at risk for undiagnosed OSA. Emergency physicians can play an important role in recognizing patients at risk for OSA, referring them for further diagnostic work-up, and offering recommendations from the ED [16]. Indeed, in one of our studies conducted among blacks referred from primary-care clinics for lab-based sleep assessment, 91% received an OSA diagnosis [17]. In all, these data suggest blacks with metabolic syndrome and who are at risk for OSA should be aggressively referred for OSA assessment and treatment, given evidence that OSA treatment reduces negative CVD outcomes associated with metabolic syndrome.[14] Evidence has indicated that OSA treatment with continuous airway pressure for 5.8 hours or longer is associated with reductions in diastolic and systolic blood pressures, resulting in a decrease of hypertension by suppressing sympathetic activity [18]. Data from a similar study, the Heart Biomarker Evaluation in Apnea Treatment (HeartBeat), also yielded similar findings. Investigators of that study, assessing effects of CPAP verses supplemental oxygen therapy in reducing CVD risk among high-risk patients with OSA, showed a decrease in mean arterial blood pressure and C-reactive protein with CPAP [19].

The finding that obesity was the strongest predictor of OSA risk is consistent with previous research, although this represents a unique cohort of black patients. Available data suggest that individuals experiencing a 10% gain in weight had a six-fold increased odds of developing OSA [20,21]. Furthermore, for every 6 kg/m^2 increase in BMI, risk of developing OSA increases fourfold [22]. Thus, obesity, whether assessed through BMI or waist circumference, may indeed be the common factor that is associated with increased risk of OSA and metabolic syndrome. We should also note that emerging clinical evidence reveals metabolic syndrome itself may have unique effects on the development of OSA, and that sleep apnea may be a manifestation of metabolic syndrome [23-25].

The impetus for investigating associations between obesity and OSA among blacks with metabolic syndrome was supported by evidence that obesity is more prevalent among blacks compared with any other ethnic group in the United States [26]. Data from the Cleveland family study, a cohort of 277 African-Americans participants representing 59 different lines of ancestry in a genome scan linkage suggested a genetic link in the comorbidity of obesity and OSA among blacks [27]. Specifically, linkage analysis revealed that the heritability of BMI and AHI (apnea-hypopnea index used to diagnose OSA) was 54% and 34%, respectively. When viewed in the context of the studies referenced above, our study highlights the need for sustained effort to focus on black patients, who are often at a clinical disadvantage due to lack of representation in clinical studies, undiagnosed OSA, lack of patient awareness and knowledge of the implications of obesity [28]. A better understanding of the factors underlying relationships between obesity and OSA among blacks may have important public health implications regarding CVD risk-reduction interventions for this underserved population.

Conclusion

The finding that 48% of the patients were at high OSA risk is important, suggesting that OSA risk is greater among blacks with metabolic syndrome. It is of interest to assess whether similar observations would be made in a population of healthy individuals.

Limitations

An important limitation of the study relates to the unavailability of a diagnosis of OSA. Such information would have permitted the determination of the magnitude of associations of OSA with metabolic parameters such as insulin resistance [6]. This may also help elucidate relationships of dysglycemia and OSA.

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