Original Article

Prevalence of Cardiovascular Disorders in Iranian Patients Suffering from Obstructive Sleep Apnea

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Abstract

Objectives: Obstructive sleep apnea (OSA) can lead to various cardiovascular disorders (CVD) such as hypertension. There is no documented data about this relationship among the Iranian population. The aim of this study was to obtain comprehensive information about the severity of OSA as a cause of CVD and its relationship with other important risk factors.

Materials and Methods: In this cross sectional study, we studied patients with OSA and apnea/hypopnea index of 5 or more. The data were collected from the patients' polysomnography report and medical files. Data analysis was done with SPSS version 18.

Results: The majority of patients were males (71.9%). Among the studied individuals, 26.5% showed at least one sign of CVD, and hypertension was the most common condition (74.5%). Multiple regression analysis showed that the odds ratios for one unit increase in BMI and one year increase in age were 1.13 and 1.12, respectively (P<0.001).

Conclusions: In our study, BMI and age had the strongest relationship with CVD. Thus, public health care providers should implement weight control strategies and improve diagnostic and treatment procedures for the elderly patients.

Keywords: Sleep Apnea, Obstructive; Body Mass Index; Cardiovascular Diseases; Hypertension; Aging

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INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by frequent episodes of termination of respiratory airflow caused by upper airway collapse during sleep, followed by oxyhemoglobin desaturation, persistent inspiratory attempts against the obstructed airway and arousals from sleep [1]. The inspiratory airflow can either decrease (hypopnea) or be completely absent (apnea), and an apnea that lasts 10 seconds or longer, associated with ongoing ventilatory effort, characterizes a patient with OSA. The airflow limitation episodes are usually accompanied by decrease in hemoglobin level, which are usually terminated by quick micro-arousals as a result of excessive respiratory drive caused by the continuing hypoxemia [2-3].

To establish a definite diagnosis, a complete polysomnography is required [4]. The diagnosis of OSA is confirmed when a person has an apnea/hypopnea index (AHI: number of apneas and hypopneas per hour of sleep) of more than five events per hour, associated with symptoms of excessive daytime sleepiness [5].

Although known to be a benign disease, numerous studies have shown that OSA is usually correlated with increased morbidity and mortality because of CVD such as systemic and/or pulmonary hypertension as its most common consequence, heart failure, myocardial infarction and stroke [6-9]. Oxyhemoglobin desaturation-resaturation, which is common in OSA patients,

results in free radical production, release of proinflammatory cytokines and prothrombotic mediators and endothelial dysfunction and leads to sympathetic nervous system activity and increased blood pressure, as well as impairment of cerebrovascular auto-regulation [10,11].

Continuous positive airway pressure (CPAP) has been shown to have cardio protective effects, decreasing mortality and morbidity among these patients [12-14]. Mandibular advancement devices [15] and airway surgery are other known treatment modalities for OSA [16,17].

Numerous community-based studies have examined the relationship between OSA and CVDs [10, 18-21]. Based on these studies, age, gender, smoking status, BMI, AHI, total sleep time and day sleepiness were some of the clinically important predictors of CVD outcomes in OSA patients.

We hypothesized that the AHI, currently used to determine the severity of OSA, is not by itself enough to accurately predict cardiovascular outcomes in individuals with OSA. We also hypothesized that several factors such as patients' demographic and clinical characteristics would have greater accuracy for predicting CVDs.

Based on our electronic search, there is no published data about the prevalence of CVD among the Iranian population with OSA. Our study aimed to resolve conflicting evidence on the impact of severity of OSA, gender, age, BMI, smoking status and socioeconomic status on the association between OSA and development of CVDs.

MATERIALS AND METHODS

Medical files of 385 patients (from 2009 to 2011) with definite OSA, confirmed by overnight polysomnography were selected in Noor Sleep Clinic, Tehran, Iran. Participants were eligible if they only had OSA (not other types of sleep apnea such as central or mixed sleep apnea) with AHI of equal or more than five events/hour. Demographic data were collected from patient files and included gender, age (as reported by patients), smoking status and educational status (last academic degree reported by patients).

Three modes for smoking status were considered: never-smoker, ever-smoker and ex-smoker. BMI (weight in kilograms divided by the square of height in meters) and AHI (events per hour) were derived from the polysomnography reports. Several questions were designed in a questionnaire to detect CVDs such as presence of CVD, type of CVD and medications used. If there was any controversy in the answers, the patients were questioned about their disease status to clarify their health/disease state.

Data analysis was done using SPSS version 18. STATA and binomial exact pathway were used to calculate the prevalence of CVD. The mean and standard deviations (SD) were reported for the numerical variables. Categorical variables were presented as percentages. For analysis, patients were divided into two groups of with CVD and without CVD. The data were analyzed using single regression analysis followed by multiple regression analysis (by backward method) to identify variables that were independently associated with CVD. P-value <0.05 was considered statistically significant.

RESULTS

The majority of patients were males (71.9%). Among the studied individuals, 26.5% showed at least one sign/symptom of CVD and hypertension was the most commonly reported sign (74.5%). Descriptive data are presented in Table1.

Of patients, 17.9% had hypertension, 2.6% had coronary artery disease, 0.5% had arrhythmia and 0.3% had stroke; 2.3% of the patients had both hypertension and coronary artery disease, 0.3% had both hypertension and history of myocardial infarction and 0.3% had both hypertension and history of stroke; 0.8% of patients had myocardial infarction and one of them had hypertension as well.

Table 1: Demographic characteristics and polysomnographic data of patients in CVD positive and CVD negative groups (values are presented as mean±SD)

Variable	CVD+ (n=102)	CVD– (n=283)
AHI (events/hour)	49.93±30.22	36.86±39.54
Age (year)	56.20±9.55	44.8±10.10
BMI (Kg/m^2)	31.78±5.64	29.03±4.76
Smokers	9(8.8%)	42(14.60%)
Gender (male)	62(60.8%)	215(76%)
University Education	58(52.3%)	170(60%)

This study examined six factors associated with CVD. Table 2 shows the results of simple regression analysis. All variables had a significant association with CVD, except for smoking status (P=0.77). We only selected variables with P-values less than 0.20 in simple regression analysis and entered them into the multiple logistic regression model. Multiple logistic regression analysis showed that the odds ratios for one grade increase in BMI and one year increase in age were 1.13 and 1.12, respectively (P<0.001). In presence of these variables, severity of apnea, gender and level of education (as a socioeconomic index) had no significant correlation with CVD (P=0.36, P=0.83 and P=0.79, respectively).

DISCUSSION

This study provided information on the association between OSA and CVDs. In our OSA population, 26.5% showed at least one sign/ symptom of CVD, with hypertension being the most common sign (74.5%). While AHI was found to predict CVD in simple regression analysis, no significant association was found in multiple model adjusted for potential confounders. Multiple regression analysis showed that aging and obesity were significant predictors of the occurrence of CVD in OSA patients.

Our results were in agreement with those of previous studies. Lavie and Lavie [22] in a case-control study on seventy of OSA showed that severity of OSA affected biochemical markers associated with CVDs only in severe stage and not mild or moderate stage of OSA. Shahar et al, [23] in a cross sectional study also showed modest to moderate effects of sleep disordered breathing on various manifestations of CVDs within a range of AHI values that were considered normal or only mildly upraised. Kendzerska et al, [21] in a decade-long cohort study showed that OSA-related factors other than AHI were important predictors of composite cardiovascular outcome. Our findings were in agreement with the afore-mentioned studies indicating that OSA-related factors other than AHI (BMI and aging) are important predictors of CVDs. We also found that BMI had almost the strongest impact on CVDs. The mean of BMI in CVD+ group was calculated to be approximately 32 kg/m2, which put them in obese group of BMI classification. In parallel with our study, Dacal Quintas et al, [24] found that the prevalence of OSA in normal weight patients was lower than that in overweight and obese patients. Seetho et al, [25] reported that patients with OSA and severe obesity had increased arterial stiffness, which would possibly affect cardiovascular risk independently of metabolic abnormalities. Carlson et al, [26] showed that age, sleep apnea and obesity represented both independent and additive risk factors for development of systemic hypertension. Similarly, Lenfant [27] described the correlation among obesity, hypertension and OSA as a triangular relationship; OSA and

Table 2: Results of simple logistic regression analysis

Variable	Odds ratio (OR)	P-value
AHI (events/hour)	1.01	<0.001
Age (year)	1.12	<0.001
BMI (Kg/m^2)	1.11	<0.001
Smokers	1.08	0.77
Gender (male)	0.49	0.004
University education	0.86	0.047

obesity have an interactive relation and both of them have increasing effect on incidence of hypertension. Our study showed that aging was another signi-ficant factor to explain the presence of CVD among OSA patients. This result was in agree-ment with that of previous studies in OSA population. Pływaczewski et al, [28] showed that the frequency of cardiovascular complications occurring in OSA population increased with age. Diseases of cardiovascular system were most often diagnosed among subjects older than 60 years. Gottlieb et al, [20] and Punjabi et al, [19] also found similar results. Evidence has been inconsistent on the effect of gender on the association between OSA and cardiovascular events [29]. In our study, women with OSA were more susceptible to develop CVD than men. Drummond et al, [30] and Quintana-Gallego et al, [31] found that women with OSA had hypertension more frequently than men. Faulx et al, [32] found that AHI was inversely associated with flow-mediated dilation and peak blood flow in women. In contrast, no relationship between AHI and flow-mediated dilation was found in men. These results raise the possibility that women with sleep-disordered breathing are more vulnerable to related CVDs than men. On the other hand, Mohsenin et al, [33] showed that markedly obese men with OSA may have a nearly two-fold greater risk for hypertension than women. Gaines et al, [34] showed that although women have naturally higher levels of inflam-matory and metabolic markers than men, men with sleep apnea appear to have a more severe inflammatory profile compared to women. It is important to consider the role of BMI in this study and its conclusion: male sex is more susceptible for developing CVD only "at the highest quartile of BMI".

In a case-control study by Lavie and Lavie [22], a comparison was made between smoker and non-smoker patients with OSA and they showed a significant interaction effect between smoking and severity of apnea on ceruloplasmin and high-density lipoprotein (HDL) levels. Smokers with severe sleep apnea had the highest level of ceruloplasmin and the lowest level of HDL. They concluded that smoking and sleep apnea had a synergistic effect on some of the biochemical cardiovascular risk markers. Patients with severe sleep apnea who smoked were at a greater risk for developing CVDs than smokers with mild-moderate sleep apnea and patients who did not smoke. In our study, no significant correlation was observed between smoking and CVDs (P=0.77). One probable reason may be that most ex-smokers stopped smoking before doing the sleep test according to the doctor's advice. Some studies categorized ex-smokers in the non-smoker group [35-36]. Some others categorized them in the current smoker group [23,37]. We analyzed both conditions and no significant correlation was observed in the results.

Based on the electronic search, the current study is the first to provide comprehensive information about the role of severity of OSA as a cause of CVD and its relationship with other important risk factors in an Iranian population. Data were consistently derived and the same polysomno-graphic scoring criteria were used over time. We included patients with a wide range of OSA severity and a relatively large number of females. Our findings are based on patients referred to a single center, which may reduce the generaliz-ability of our findings. Validation of our results in other patient populations is recommended.

CONCLUSION

Our study showed that AHI was significantly associated with CVD in simple regression analysis; however, this association was not significant after controlling for other predictors. Other OSA-related predictors, such as BMI and age were significantly and independently correla-ted with increased risk of CVDs, respectively.

In presence of these variables, other phenotypic and socioeconomic factors like severity of apnea, gender and level of education had no significant

correlation with CVDs. Thus, health care providers should implement BMI control strategies and improve the quality of care for the elderly patients.

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