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Could Obstructive Sleep Apnea Syndrome be a Component of Metabolic Syndrome?

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Aim: Obstructive sleep apnea syndrome (OSAS) is a prevalent disorder and is associated with increased cardiovascular morbidity and mortality. OSAS is independently related to the cardiovascular risk factors that comprise metabolic syndrome, atherosclerosis, acute coronary syndrome, and sudden death. The prevalence of metabolic syndrome is 30%-40% in the Turkish population. However, there are no data about the prevalence of metabolic syndrome (MS) in Turkish patients with OSAS. The aim of this study was to determine the prevalence of MS in Turkish patients with OSAS and MS-related cardiovascular diseases.

Materials and Methods: The medical records of patients who were admitted to our Sleep Disorders Center were evaluated retrospectively. OSAS was diagnosed by polysomnography (apnea-hypopnea index (AHI) ≥ 5). MS was diagnosed according to Adult Treatment Panel III. Individuals in whom AHI < 15 were recruited as group 1 and those in whom AHI ≥15 as group 2.

Results: We studied 277 patients with OSAS (206 men and 71 women, aged 52.8 ± 9.8 years). The prevalence of MS in patients with OSAS was 39.71% (110 patients). This prevalence is higher than that in the Turkish population. The prevalence of MS in groups 1 and 2 was 25.5% and 74.5%, respectively (P < 0.005). Rates of MS were higher in patients with AHI ≥ 15 than in those with AHI < 15. In addition, the prevalence of hypertension, arrhythmia, atherosclerotic heart disease, and stroke in patients with and without MS was 73.5% and 26% (P = 0.00), 10.2% and 8.5% (P = 0.41), 42.5% and 18.3% (P = 0.00), and 3% and 0.06% (P = 0.23), respectively.

Conclusions: The prevalence of MS is high in OSAS patients. In addition, the prevalence of MS is significantly high in patients with moderate-severe OSAS.

Key Words: Obstructive sleep apnea syndrome, metabolic syndrome, cardiovascular disease

Obstrüktif Uyku Apne Sendromu Metabolik Sendromun Bir Komponenti Olabilir mi?

Amaç: Obstrüktif uyku apne sendromu (OSAS), kardiyovasküler morbidite ve mortalitenin belirgin artış gösterdiği; metabolik sendrom (MS), ateroskleroz, akut koroner sendrom ve ani ölüm ile seyreden sistemik hastalıkların birbirine eklendiği, genel populasyonda yaygın görülen bir hastalıktır. Türk popülasyonunda MS sıklığı % 30 – 40 olarak bulunmuştur. Ancak OSAS'lı hastalarda MS sıklığı bilinmemektedir. Bu çalışmada amaç; uyku bozuklukları merkezimize başvuran ve polisomnografik inceleme ile OSAS tanısı alan hastalarda MS ve MS ile ilişkili kardiyovasküler hastalıkların görülme sıklığını belirlemektedir.

Yöntem ve Gereç: Çalışmada Uyku Bozuklukları Merkezimize başvuran hastaların kayıtları retrospektif olarak incelendi. Tüm gece boyunca uygulanan polisomnografi (PSG) verilerine göre OSAS tanısı (Apne-Hipopne İndeksi=AHİ > 5) ve Adult Treatment Panel III kriterlerine göre MS tanısı alan hastalar kayıt edildi. Hastalar orta-ağır (AHİ < 15) ve hafif (AHİ ≥ 15) olmak üzere grup 1 ve grup 2 olarak ayrıldı. Her iki grup arasındaki MS oranı karşılaştırıldı, ayrıca hastaların demografik özellikleri kayıt edildi.

Bulgular: Çalışmaya OSAS tanısı olan toplam 277 hasta alındı. Bu hastaların 206' sı erkek, 71'i kadın ve yaş ortalamaları 52,8 ± 9,8 yıl idi. OSAS'lı hastalarda MS sıklığı % 39,71 (110 hasta) olarak saptandı. Grup 1'de MS sıklığı % 25,5 ve grup 2'de % 74,5 (P < 0.005) olarak bulundu. Ayrıca kardiyovasküler hastalıklar açısından incelendiğinde MS olan ve olmayan gruplarda hipertansiyon, aritmi, aterosklerotik kalp hastalığı ve inme sıklığı karşılaştırıldığında sırasıyla % 73,5 - % 26 (P = 0,00), % 10,2-% 8,5 (P = 0,41), % 42,5 - % 18,3 (P = 0,00) ve % 3 - % 0,06 (P = 0,23) olarak bulundu.

Sonuç: OSAS'lı hastalarda MS görülme oranı belirgin olarak fazladır. Ayrıca AHİ değerine göre gruplandırılan orta-ağır OSAS'lı hastalarda MS sıklığının daha fazla olduğu bulunmuştur.

Anahtar Sözcükler: Obstrüktif uyku apne sendromu, metabolik sendrom, kardiyovasküler hastalık

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Introduction

Obstructive sleep apnea syndrome (OSAS) is a prevalent disorder particularly among middle-aged and obese men, characterized by repeated episodes of cessation of breathing during sleep and daytime sleepiness; it affects approximately 5% of the adult population (1). Recent studies showed that OSAS is associated with increased cardiovascular and cerebrovascular morbidity and mortality, and there is growing evidence of an independent contribution of OSAS toward this (2,3). Several features of OSAS suggest that sleep apnea is a part or manifestation of metabolic syndrome (MS) (4-7). MS, also known as insulin resistance syndrome, is known as a cluster of obesity, glucose intolerance, dyslipidemia, and hypertension. Previous studies have shown that there is an independent association between OSAS and insulin resistance and several determinants of MS including hypertension and dyslipidemia independent of obesity (4-7); however, there is little information in the literature about the prevalence of MS, which is a major risk factor for early development of cardiovascular disease in OSAS patients (3,5). These studies found the prevalence of MS to be significantly high in OSAS patients compared to the general population (1,7). Furthermore, there is no previously published study about the prevalence of MS in OSAS patients in the Turkish adult population, although a recent study was conducted in children (8). The prevalence of MS is 30%-40% in the Turkish population (9). The aim of this study was to determine the prevalence of MS in Turkish patients with OSAS and MS-related cardiovascular diseases.

Materials and Methods

Patients

We enrolled 277 patients diagnosed with OSAS based on overnight polysomnography (PSG) at the Sleep Disorders Center at Gazi University School of Medicine between January 2001 and December 2005. Before the study, patients with central apnea, stroke, coronary artery disease, congestive heart failure, intrinsic pulmonary disease, and renal or liver disease were excluded. We accepted a threshold apnea-hypopnea index (AHI) ≥ 5 as diagnostic of sleep apnea.

The patients were divided into 2 groups, according to the severity of OSAS: group 1 OSAS (AHI < 15/h) and group 2 (AHI ≥ 15/h). Informed consent was obtained from all patients, the protocol was approved by the ethics committee of Gazi University School of Medicine, and the study was performed in accordance with the current revision of the Declaration of Helsinki.

Clinical and Laboratory Measurements

We measured height and weight in bare feet and light clothing in the morning. Body mass index (BMI) was defined as weight (kg)/height^2 (m). Blood pressure was measured between 8 and 11 a.m. in the supine position after 5 min rest.

All blood samples were obtained in the morning after an overnight fast. C-reactive protein, fasting glucose, total cholesterol, triglyceride, and high density lipoprotein (HDL) cholesterol were measured after an overnight fast. Low density lipoprotein (LDL) cholesterol was derived using the Friedwald formula.

Definition of MS

MS was diagnosed according to the National Cholesterol Education Program Expert Panel on Detection, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III, ATP III) criteria (10). A diagnosis of MS was made if the patient met at least 3 of the following criteria: 1) fasting plasma glucose ≥110 mg/dl, 2) blood pressure ≥ 130/85 mmHg or current use of antihypertensive drugs, 3) triglycerides ≥150 mg/dl, 4) HDL cholesterol < 40 mg/dl and 50 mg/dl in men and women, respectively. Details of waist circumference were not available in this study.

PSG

Overnight PSG was performed in all patients using a computerized system (Somnostar alpha; Sensormedics, USA) on the basis of variables described previously. Sleep parameters were determined using the criteria of Rechtschaffen and Kahles, and arousals were defined in accordance with the definitions of the American Sleep Disorders Association (11,12).

Statistical analysis

Normally distributed data were presented as means ± standard deviation of the mean (95% confidence interval for the mean), skewed data as the median, and categorical data as the number. Statistical analyses were performed using SPSS version 11.0 (Chicago, IL, USA). Unpaired t, Mann-Whitney, and chi-square tests were used in the analyses. Significance of differences was accepted at $P < 0.05$.

Results

The demographic and clinical characteristics and laboratory values of patients with MS and without MS are shown in Table 1. The prevalence of MS was 39.7% (110/277 patients). One hundred ten (39.7%) patients presented with coexisting MS and increased BMI (73.6%), increased serum fasting blood glucose level (76.4%), and high blood pressure (92.7%) as the most frequent features in men and women. All single components were present more often in OSAS patients with MS compared to OSAS patients without MS (Table 1). OSAS patients with MS were significantly older compared to those without MS (P = 0.001). Risk factors for MS did not differ between women and men. There were no differences in drug use between OSAS patients with and without MS.

Of the 277 participants, 85 (31%) had AHI scores between 5 and 15 (group 1) and 192 (69%) had AHI scores ≥ 15 (group 2). There was a linear trend effect of association with MS as the severity of OSAS increased in terms of AHI. The prevalence of MS in groups 1 and 2 was 25.5% (29/85 patients) and 74.5% (81/192 patients), respectively (P = 0.035). Rates of MS were 3-fold higher in OSAS patients with AHI score > 15 compared to OSAS patients with AHI score < 15. Hypertension and atherosclerotic heart disease were also more prevalent in OSAS patients with MS compared to OSAS patients without MS (Table 2). A significant relationship between a higher AHI with the increase in the number of features of MS in the whole study group was also demonstrated (Figure) (P < 0.05).

Table 1. Clinical parameters in all subjects with and without metabolic syndrome.

	Patients with MS (n = 110)	Patients without MS (n = 167)	P value
Age (year)	52.88 ± 9.80	47.77 ± 10.19	0.001
Body mass index (kg/m^2)	34.27 ± 6.11	28.94 ± 4.17	0.000
Systolic blood pressure (mmHg)	145.00 ± 12.8	130.05 ± 11.5	0.006
Diastolic blood pressure (mmHg)	95.80 ± 16.50	78.07 ± 10.70	0.009
HDL-cholesterol (mg/dl)	41.62 ± 10.77	47.18 ± 10.98	0.04
Total cholesterol (mg/dl)	214.75 ± 68.40	209.00 ± 41.63	0.09
Triglyceride (mg/dl)	177.45 ± 76.13	157.11 ± 84.17	0.003
Fasting blood glucose (mg/dl)	125.36 ± 43.63	94.50 ± 8.33	0.001
Apnea hypopnea index (per hour)	39.83 ± 3.79	28.69 ± 2.22	0.005

Table 2. Cardiovascular events in OSAS patients according to the presence of metabolic syndrome (MS).

	Patients with MS (n = 110)	Patients without MS (n = 167)	P value
Hypertension (n, %)	81, 73.5%	43, 26%	0.001
Arrhythmia (n, %)	11, 10.2%	14, 8.5%	0.41
Atherosclerotic heart disease (n, %)	47, 42.5%	31, 18.3%	0.001
Stroke (n, %)	3, 3%	1, 0.06%	0.23

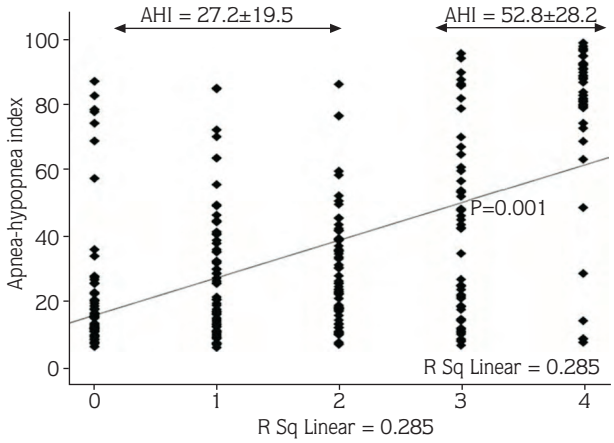

Figure. The number of components of metabolic syndrome according to apnea-hypopnea score (AHI) in patients with obstructive sleep apnea.

Discussion

The salient findings of this study are as follows: (i) the prevalence of MS is high in patients with OSAS, (ii) the prevalence and components of MS including high blood pressure, high fasting blood glucose level, hypertriglyceridemia, and low HDL-cholesterol level increase while the severity of OSAS increases determined by AHI, (iii) OSAS patients with MS are more likely to have a history of cardiovascular disease compared to OSAS patients without MS, (iv) analysis of the MS components shows that hypertension is the primary variable associated with a diagnosis of OSAS. To the best of our knowledge, this is the first study to investigate the prevalence of MS in Turkish patients with OSAS.

The increasing recognition and acceptance of a link between OSAS and MS, mediated through obesity, high blood pressure, and insulin resistance, prompts the question of whether OSAS is a component of OSAS or a contributory factor for the development of MS. Previous studies showed that patients with OSAS had 3- to 5-fold higher risk of having MS and the prevalence of MS was 50%-85% in patients with OSAS (13-16). Moreover, mortality is 3.3 times higher in OSAS patients younger than 70 years old (17). The increase in mortality is due to the higher rate of cardiovascular disease and accidents.

It was reported in previous studies that OSAS is independently associated with a number of cardiovascular and metabolic risk factors, such as hypertension, dyslipidemia, insulin resistance, and impaired glucose tolerance. However, it is unknown whether OSAS occurs as part of the fundamental pathophysiology of MS, or whether OSAS, via repetitive nocturnal hypoxemia, systemic inflammation, and other mechanisms, promotes the components of MS (18).

In the present study, OSAS patients with MS had higher degrees of sleep-disordered breathing such as high AHI, low desaturation index, and minimum oxygen saturation (Table 1). In addition, these patients had more frequent cardiovascular comorbidity (i.e. hypertension, arrhythmia, and atherosclerotic heart disease) than patients without MS. Nevertheless, patients with MS had significantly higher blood pressures, fasting glucose, and triglyceride concentration, and reduced HDL cholesterol, which are all components of MS (Table 1).

It is well known that respiratory disturbance responses may increase blood pressure during apneic events and studies reported that OSAS is an independent risk factor for the development of hypertension (2). Hence, it is possible that OSAS directly increases MS incidence in these patients. In our study, the prevalence of hypertension was significantly high in OSAS patients with MS compared to OSAS patients without MS. There was also a positive association between the severity of OSAS and the presence of the components of MS, especially hypertension.

Recent investigations have shown that OSAS is independently associated with insulin resistance, glucose intolerance, and increased incidence of type 2 diabetes mellitus (19,20). These studies concluded that patients with OSAS have higher blood pressure, higher fasting insulin level, increased insulin resistance, lower levels of HDL-cholesterol, and an increased incidence of MS compared to patients without OSAS. Moreover, OSAS patients had a higher BMI than patients without OSAS, which raises the possibility that obesity rather than OSAS is a primary determinant of MS (19,20). Interestingly, in our study group OSAS patients with MS had a significantly higher BMI as compared with OSAS patients without MS. Thus obesity plays a pivotal role in the link between OSAS and MS. Despite the confounding effect of obesity, many recent studies have shown that there is an independent association between OSAS and other parameters of the MS, such as hypertension and insulin resistance (4,6).

Cardiovascular disease is the leading cause of death all over the world and multiple risk factors are identified as contributors, namely dyslipidemia, obesity, hypertension, and glucose intolerance, which are also components of MS. Many studies have reported that the presence of MS is independently associated with an increased incidence of all cardiovascular diseases (21,22). Hu et al. summarized 11 studies comprising more than 11,000 subjects and found that the hazard ratio for cardiovascular mortality was 2.26 for men and 2.78 for women in subjects with MS compared to subjects without MS (23). In our study we also found the prevalence of cardiovascular disease high in OSAS patients with MS compared to OSAS patients without MS.

Our study has several limitations. The data were collected retrospectively rather than prospectively. However, we reviewed the records of consecutive patients in the sleep laboratory and so there was no selection bias. We did not have access to measurements of waist circumference. Hence, the prevalence of MS might be higher than we found in this study.

In conclusion, OSAS might be a component of MS or an independent risk factor for development of MS and the prevalence of MS is high in OSAS patients. Accordingly, it seems reasonable for clinicians to include assessment of MS in the evaluation of patients with OSAS. Further studies are warranted to elucidate the pathogenesis of OSAS on development of MS and the effect of treatment of OSAS on MS.

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