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Original article

Relationship between sleep-disordered breathing and metabolic syndrome after adjustment with cardiovascular risk factors

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ABSTRACT

Aims: It is important to identify the risk factors for metabolic syndrome (MetS) in order to prevent the development of cardio-/cerebrovascular diseases. The authors estimated the risk factors for the development of MetS with special emphasis on the severity of sleep-disordered breathing (SDB).
Methods: We conducted as a cross-sectional study in subjects undergoing intensive health examination (581 men aged 33–84 years). Diagnosis of MetS was based on the criteria of the National Cholesterol Education Program Expert Panel.
Results: The prevalence of MetS in subjects with severe SDB, which was defined as an apnea–hypopnea index (AHI) of 30 or higher, was 40.7%, which was significantly higher than that in the subjects without severe SDB (29.3%). The odds ratio (OR) (95% confidence interval [CI]) of the logarithmic-transformed AHI for MetS was 1.6 (1.1–2.4) after adjustments for age, serum uric acid, logarithmic-transformed serum C-reactive protein, smoking history, exercise history and alcohol history. When the subjects were categorized by the severity of SDB, the OR (95% CI) of severe SDB, which was the only category that showed significant association, was 2.2 (1.2–4.0).
Conclusion: A significant association was observed between severe SDB and the presence of MetS in the subjects (all male) of this study.

1. Introduction

Metabolic syndrome (MetS) is a well-known risk factor for the development of cardiovascular diseases (CVD) [1,2], independent of other factors such as smoking, psychological stress and drinking [1]. In addition, sleep-disordered breathing (SDB) has been reported to be closely associated with the risk of CVD in subjects with MetS [3,4].

The prevalence of moderate-severe SDB, which is defined as an apnea–hypopnea index (AHI) of 15 or higher, is 49.7% in men [4]. We have previously reported the existence of a significant association of an increased AHI with the risk of hypertension, diabetes, MetS and depression, with the strongest association found for MetS [4]. As information on the effect of SDB on the risk of CVD is limited [5], further studies are required to confirm the causal association.

To clarify the relationship between SDB and MetS, we carried out this cross-sectional study with special reference to the severity of SDB as assessed by determination of the AHI. SDB is considered as a risk factor for the components of MetS, and herein, we provide an overview of a trial of interventions for SDB.

2. Subjects and methods

2.1. Study populations

A total of 581 male subjects aged 33 to 84 years who attended an intensive health checkup program from June in 2012 to June in 2015 were enrolled in this study. Subjects who were receiving treatment for coronary heart disease, cerebrovascular disease, hypertension, diabetes mellitus and/or dyslipidemia were included. At baseline, all the participants underwent measurements of the anthropometric, biochemical and physiological parameters. Informed consent was obtained from each of the participants. The study was conducted with the approval of the Institutional Review

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Board of Ota Memorial Hospital, Gunma Prefecture, Japan (April 27, 2015).

2.2. Health examination data

Venous blood samples were collected in the morning after the subjects had fasted overnight. The serum levels of triglycerides (TGs), high-density lipoprotein cholesterol (HDLC) and fasting blood glucose were determined (AU2700, Olympus Co. Ltd., Japan). High-sensitive C-reactive protein (CRP) level was also determined. The blood pressure was measured three times in all the participants (Nippon COLIN BP-103i II, Japan), and the mean values of the three measurements were adopted for the analysis. Waist circumference was measured midway between the iliac crest and the 12th rib, around the level of the umbilicus.

2.3. Definitions of lifestyle-related variables and MetS

Self-reported Information on the lifestyles was collected. The smoking habit was categorized as "current smoking" or "no smoking". The drinking habit was categorized as "daily drinking" or "no daily drinking" (including "no drinking"). Physical activity was categorized as presence of habitual exercise (exercise ≥2 times per week for more than one year) or absence of the exercise habit.

In accordance with the criteria of the US National Cholesterol Education Program Adult Treatment Panel III [6], MetS was diagnosed when 3 or more of the following criteria were fulfilled: fasting blood glucose ≥100 mg/dL (5.6 mmol/L) or receiving treatment for diabetes mellitus, blood pressure ≥130/85 mmHg (either value) or receiving antihypertensive drug treatment, serum TGs ≥ 150 mg/dL (1.7 mmol/L), serum HDLC < 40 mg/dL (1.0 mmol/L), or receiving treatment for dyslipidemia, and waist circumference ≥85 cm [7].

2.4. Portable monitoring system for the diagnosis of SDB

A portable recording system for detecting sleep apnea (SAS-2100, NIHONKOHDEN CO. Ltd., Tokyo) was used and the AHI was defined as the number of apneas and hypopneas per hour of sleep. Hypopnea was defined according to a previous report [8], and participants were classified as not having SDB (AHI < 5), or having mild (AHI of 5–14.9), moderate (AHI of 15–30), or severe (AHI ≥ 30) SDB [9].

This apparatus used recorded physiological parameters such as airflow (nasal pressure transducer) and SpO2+ heart rate (probe tape placed on the finger). A trained technician placed the cannulas in the nostrils, and the oximeters on a finger.

Apnea events were defined as airflow cessation for ≥10 s, and hypopnea was defined as a decrease by >50% from the baseline of the amplitude of the nasal cannula recording during sleep or a clear amplitude reduction of the nasal cannula recording during sleep (<50%) associated with an oxygen desaturation of >3%. The hypopnea events were also required to last for 10 s or longer. AHI was calculated using the total recording time as the denominator.

2.5. Statistical analysis

The subjects were classified into four groups based on the severity of SDB, as described above. The analysis was carried out with the SPSS 21 software package (SPSS Japan, Tokyo). Logistic regression analysis was mainly used for the multivariate analysis, and a two-tailed p-value of <0.05 was considered as denoting significance.

3. Results

The mean age (one standard deviation) of the subjects was 53.3 (10.4) years. The prevalence of intake of specific medications, MetS-related variables and severe SDB are shown in Table 1. The prevalence of MetS was 30.9%, and the prevalences of mild, moderate and severe SDB were 35.6%, 20.7% and 14.1%, respectively. The prevalences of MetS in the subjects with and without severe SDB were 40.7% and 29.3%, respectively.

The geometric means of the serum C-reactive protein (CRP) and AHI were compared between the patients with and without MetS and according to the presence/absence of each component of MetS (Table 2). Except for the blood pressure and serum HDLC, a positive status of each of the variables was associated with a significantly higher geometric mean of the AHI than a negative status of the same variable. In the case of blood pressure, the geometric mean of the serum CRP was significantly higher in the patients with hypertension than in those without hypertension.

The odds ratios (ORs) (95% confidence intervals [CIs]) of the logarithmic-transformed serum CRP and AHI for MetS were 1.2 (0.79–1.9) and 1.6 (1.1–2.4), respectively, after adjustments for several other risk factors for CVD (Table 3). When the AHI was categorized into four grades of severity of SDB, the adjusted ORs (95% CIs) of mild, moderate and severe SDB for MetS were 1.5 (0.95–2.5), 1.7 (0.98–2.9) and 2.2 (1.2–4.0), respectively (Table 4).

Finally, the association between components of the MetS and severe SDB (n = 81) were evaluated with adjustments for several conventional factors. The OR (95% CI) of waist circumference ≥85 cm, which was the only factor showing significant association, for severe SDB was 18.2 (5.6–59.0).

4. Discussion

In this study, SDB was found to be significantly associated with the presence of MetS, especially severe SDB, consistent with recent study [4]. The prevalence of moderate to severe SDB in the men was 34.7%, which is higher than the prevalence reported for men in the US [10] and lower than the prevalence reported for men in Switzerland [4]. As the study was only a cross-sectional study, the causal association could not be established. In addition, the significant association between the presence of MetS and age, habitual exercise, smoking history, log-transformed values of the serum CRP and serum uric acid in our previous cross-sectional

Table 1
The prevalences of intake of medication for DM, hypertension and/or dyslipidemia, and that of metabolic syndrome, its components, and SDB (classified by the severity).

Variables	576 men (%)
DM treatment	6.9
HT treatment	22.7
DL treatment	11.5
MetS	30.9
Component of MetS	
WC	61.1
Glucose	38.9
Blood pressure	37.3
TG	39.6
HDLC	16.7
SDB	
Mild	35.6
Moderate	20.7
Severe	14.1

DM, diabetes mellitus; HT, hypertension; DL, dyslipidemia; MetS, metabolic syndrome; WC, waist circumference; TG, triglyceride; HDLC, high-density lipoprotein cholesterol; SDB, sleep disordered breathing; AHI, apnea–hypopnea index. Mild, moderate and severe SDB were defined as AHI of 5–14.9, 15–29.9 and 30–, respectively.