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SHORT COMMUNICATION

Characterization of obstructive sleep apnea in patients with insomnia across gender and age

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Abstract
Objectives A large number of clinical observational studies have suggested that women patients with obstructive sleep apnea (OSA) have a higher presence of insomnia symptoms compared to men with OSA. There is no study that has examined the effect of age and gender on the relationship between OSA and chronic insomnia in a large number of patients with insomnia.
Methods We collected data on 860 patients with chronic insomnia and included both sexes and a wide range of ages (mean age 43.0±12.1 (range 18–81) years, 409 men). All participants underwent overnight polysomnography (PSG) in a sleep medicine center.
Results The prevalence of OSA based on three different apnea-hypopnea index (AHI) categories (events/h >5, >15, and >30) were 42.5, 21.8, and 8.3 % in men and 19.1, 6.2, and 1.8 % in women, respectively. Across age ranges of <35, 35~<45, 45~<55, and ≥55 years, the prevalence of OSA was remarkably greater in men than in women up to 55 years of age, but not in subjects with ages ≥55 years. AHI was a significant risk factor for hypertension; the odds ratio of hypertension in patients with high AHI (>30) compared to patients in the lowest AHI category (<5) was 3.68 (95 % confidence interval [CI], 1.47–9.21), after adjusting for all other factors.
Conclusion Similar to the gender differences reported in general population studies, men had a much greater OSA prevalence than women prior to 55 years of age, but not at ages greater than 55 years.

Keywords Sleep apnea · Insomnia · Prevalence · Hypertension

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Introduction

The co-occurrence of obstructive sleep apnea and insomnia was identified as early as 1973 [1]. Through clinical investigations screening for the symptoms of insomnia in patients with obstructive sleep apnea (OSA), Krakow et al. reported that over 50 % of patients with OSA had clinically significant insomnia symptoms [2]. As reviewed by Luyster et al. [3], recent papers have reported that the prevalence of this type of comorbidity is substantial. A recent study suggested that comorbidity of insomnia in OSA patients even might be a particular phenotype [4]. Investigations of insomnia symptoms among OSA patients suggest that the prevalence of concurrent insomnia and OSA are higher in the elderly than in the middle-aged populations, and that women have a greater presence of insomnia symptoms than do men [2, 5, 6].

Unfortunately, investigations that screened for OSA in patients with insomnia have mainly been carried out in elderly patients, and do not include a full range of adult ages. Early studies using overnight polysomnography (PSG) in patients with insomnia have reported that insomnia patients may suffer from OSA to a degree similar to controls [7, 8]. More recent studies have reported that as many as 50–75 % of elderly

insomnia patients may suffer from OSA [9]. To our knowledge, there have been no studies that have examined the effect of age and gender on the relationship between OSA and chronic insomnia in a large group of middle-aged insomnia patients. To examine this relationship, we carried out a PSG study in a large number of patients with chronic insomnia.

Furthermore, it is not known whether sleep parameters differ between insomnia patients without OSA and with different levels of OSA severity. Sleep in OSA patients without insomnia symptoms and its relationship with OSA severity, and sleep in patients with insomnia alone without OSA were recently reported by our group [10, 11]. Therefore, another aim of this work was to characterize sleep measures in insomnia patients without OSA and with different levels of OSA severity.

Methods

Participants were 860 patients with chronic insomnia and included both genders and a wide range of ages (mean age 43.0 ±12.1 (range 18–81) years, 409 male). Participants were patients referred to the Sleep Medicine Center of the West China Hospital with the chief complaint of chronic insomnia. Participants met the diagnostic criteria for primary insomnia in symptoms, severity, and exclusion according to the DSM-IV, with the additional criterion of a duration of illness greater than 6 months [12]. We did not use the ICSD-2 diagnosis [13] because many patients with insomnia might be identified as having paradoxical insomnia based on PSG examination [11]. In fact, the diagnosis of paradoxical insomnia is poorly supported in clinical research [14]. Based on self-reports, the participants either rarely or never took hypnotics. A history of present illness was collected, and the history of hypertension, diabetes, coronary disease, and the use of hypnotics, alcohol, cigarette, and caffeine was obtained. On the morning after the overnight PSG recording, a self-report sleep estimate was assessed by a brief morning questionnaire (e.g., how long (min) did you sleep?).

An overnight PSG recording was performed using standard techniques according to the 2007 version of the American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events. Overnight PSG consisted of continuous recordings from six electroencephalographic leads (F3-A2, F4-C1, C3-A2, C4-A1, O1-A2, O2-A1, international 10–20 system), two electrooculographic leads (ROCA1, LOC-A2), four electromyography leads (two submental and bilateral tibialis anterior), thermistors for nasal and oral airflow, strain gauges for thoracic and abdominal excursion, finger pulse oximetry, and electrocardiography. Thirty-second epochs were analyzed and sleep stages were scored according to the criteria of the AASM Manual. An apnea was defined as more than 90 % reduction in airflow for at least 10 s, hypopnea as 50 % or more reduction of airflow for at least 10 s associated with 3 % or more reduction in oxygen saturation. Sleep data were collected and manually scored via the Alice 5 Diagnostic Sleep System (Philips Respironics, Bend, USA).

This study was approved by the Research Ethics Board of the West China Hospital of Sichuan University.

Results

In all participants, the prevalence of OSA based on three different apnea-hypopnea index (AHI) categories (events/h >5, >15, and >30) were 42.5, 21.8, and 8.3 % in men and 19.1, 6.2, and 1.8 % in women, respectively. Further, as shown in Fig. 1, across ages of <35 (n=189, 92 male), 35~<45 (n=327, 148 male), 45~<55 (n=187, 84 male), and ≥55 (n=157, 85 male) years, the prevalence of OSA was remarkably greater in men than in women in the three different age groups below 55 years of age according to all three different AHI levels, but not in the group aged ≥55 years. In men, the highest prevalence of moderate and severe OSA (AHI >15 and >30) occurred in the 45~<55-year-old age group, whereas in women the highest prevalence was observed in the ≥55-year-old age group for all three different AHI levels. The prevalence of severe OSA in men dropped remarkably in the ≥55-year-old age group compared to that in the 45~<55-year-old age group.

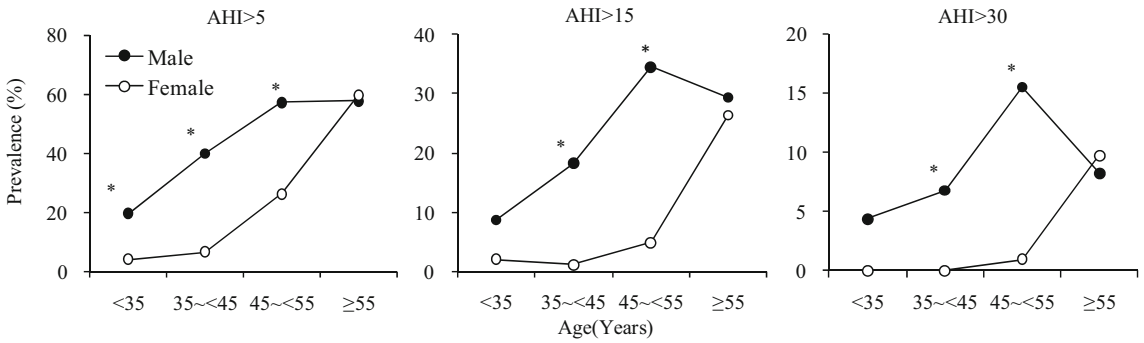

Fig. 1 OSA prevalence in male and female patients across four age groups for three different levels of AHI (AHI>5, >15, and >30) used for OSA diagnosis (*asterisk* indicates significant differences (p<0.001) between male and female patients within age conducted by the partition of chi-square test)

Table 1 Clinical and polysomnographic characteristics for groups with AHI <5, 5~<15, 15~<30, ≥30 (different letters indicate significant differences across the groups of AHI <5, 5~<15, 15~<30, ≥30, as assessed by post hoc Tukey's tests)

	AHI				*p* value
	<5 (*n*=600)	5~<15 (*n*=143)	15~<30 (*n*=75)	≥30 (*n*=42)	
Age	40.2±11.4[b]	49.3±11.3[a]	50.3±11.4[a]	49.3±11.5[a]	0.001
BMI	22.2±3.2[c]	23.9±3.4[b]	25.6±3.7[a]	26.6±2.6[a]	0.001
ESS	4.0±4.7	5.0±4.5	5.4±5.5	5.1±4.8	0.001
AHI (events/h)	1.3±1.3[d]	8.8±2.8[c]	20.7±4.3[b]	49.3±17.9[a]	0.001
Self-evaluated TST (h)	4.3±2.5	4.4±2.2	4.1±2.4	4.7±2.4	0.694
PSG evaluated TST (h)	6.5±1.4	6.4±1.5	6.4±1.4	6.4±1.7	0.746
Sleep perception (%)	65.3±38.2	70.0±38.8	64.4±36.6	74.8±40.4	0.605
N1 (%)	17.0±12.1[b]	23.7±14.2[a]	27.1±14.2[a]	30.9±17.4[a]	0.001
N2 (%)	53.2±13.5	48.3±14.5	48.5±14.5	48.0±15.1	0.001
N3 (%)	12.8±8.3[a]	12.2±10.0[a,b]	9.2±7.0[b,c]	7.8±8.1[c]	0.001
REM (%)	17.1±6.8[a]	15.7±6.8[a,b]	15.2±7.3[a,b]	13.4±6.4[b]	0.001
Arousal index (events/h)	20.0±11.0[c]	21.3±10.5[c]	27.2±12.5[b]	36.3±16.2[a]	0.001

BMI body mass index, *ESS* Epworth daytime sleepiness scale, *TST* total sleep time, *REM* rapid eye movement sleep, *N1-3* non-REM sleep stage 1–3, *AHI* apnea-hypopnea index

Body mass index (BMI) increased linearly with OSA severity with the highest BMI observed in the most severe group.

In all patients, the means for PSG-determined and self-evaluated total sleep time were 6.5±1.4 h and 4.3±2.4 h, respectively. Furthermore, as shown in Table 1, there were linear increases in N1 time and brief arousal index, and decreases in N3 and rapid eye movement sleep time associated with severity of OSA. No differences were observed in PSG-determined and subjective total sleep time, and sleep perception (subjective sleep time/objective sleep time × 100 %).

Ordinal logistic regression revealed that being male, snoring, and being older and heavier were significant risk factors for OSA (Table 2). Patients with more severe OSA had a greater prevalence of hypertension compared to patients without OSA. AHI was a significant risk factor for hypertension, the odds ratio (OR) of hypertension in patients with high AHI (>30) compared to patients in the lowest AHI category (<5) was 3.68 (95 % confidence interval [CI], 1.47–9.21), after adjusting for gender, age, snoring, BMI, Epworth daytime sleepiness scale (ESS), heart disease, diabetes, alcohol, smoking, and caffeine use.

Discussion

The current study is the first to screen for OSA prevalence in a large number subjects with clinically diagnosed insomnia and to systematically examine age and gender effects. The higher prevalence of OSA in chronic insomniacs in this study compared to earlier clinical studies or general population studies may reflect increased awareness of sleep apnea-related symptoms among referring physicians and the public.

Table 2 Association of the severity of AHI (<5, 5~<15, 15~<30, ≥30) determined by ordinal logistic regression in observed insomnia patients (Model 1, adjusted for gender, age, snoring, BMI (body mass index) and ESS (Epworth Sleepiness Scale); Model 2, adjusted for gender, age, snoring, BMI, ESS, hypertension, heart disease, diabetes, alcohol, smoking, and caffeine use)

	Model 1		Model 2	
	OR (95 % CI)	*P*	OR (95 % CI)	*P*
Male	2.86 (2.01–4.07)	0.0001	2.57 (1.72–3.86)	0.0001
Female	1.00		1.00	
Age ≥55	5.24 (2.94–9.35)	0.0001	5.86 (3.10–11.06)	0.0001
Age 45~<55	3.74 (2.10–6.67)	0.0001	4.41 (2.40–8.11)	0.0001
Age 35~<45	1.23 (0.70–2.16)	0.482	1.43 (0.79–2.60)	0.235
Age <35	1.00		1.00	
Snoring	5.34 (3.63–7.87)	0.0001	4.91 (3.30–7.31)	0.0001
No snoring	1.00		1.00	
BMI ≥28	4.22 (2.52–7.05)	0.0001	3.67 (2.14–6.30)	0.0001
BMI 24~<28	2.50 (1.73–3.63)	0.0001	2.34 (1.59–3.43)	0.0001
BMI <24	1.00		1.00	
ESS ≥16	1.44 (0.57–3.63)	0.434	1.54 (0.57–4.14)	0.392
ESS11 ~<16	0.95 (0.55–1.63)	0.858	1.01 (0.58–1.75)	0.973
ESS <10	1.00		1.00	
Hypertension	–	–	1.63 (1.02–2.62)	0.043
Heart disease	–	–	1.37 (0.59–3.23)	0.465
Diabetes	–	–	0.86 (0.34–2.17)	0.753

In this study, we confirmed that being male, snoring, and being older and heavier are all significant risk factors for OSA. Also, patients with more severe OSA had a higher prevalence of hypertension, compared to OSA patients reported in many clinical and general population studies [15–18]. Furthermore, there were remarkable gender differences in OSA prevalence across ages.

First, we found that male patients with insomnia had remarkably greater OSA prevalence than female patients with insomnia at ages younger than 55 years. This is consistent with the findings from general population studies that have shown that sleep apnea in women is low premenopausally whereas it increases significantly after menopause [8]. Based on a review including a large number of studies that screened insomnia symptoms in OSA patients, Ye et al. suggested that female OSA patients have higher presence of insomnia symptoms compared to men with OSA [2, 5, 6]. In the present study that screened for OSA among patients with insomnia, we found that men had much greater OSA prevalence than women, a finding similar to the gender differences reported in studies of the general population [8].

Second, severe OSA was more prevalent in middle-aged men and older women. This is consistent with previous findings that although AHI increases with age, the most severe apnea based on clinical criteria is more prevalent in middle-aged men and postmenopausal women [8, 17, 19]. From a clinical stand point, middle-aged men and older women with the complaint of insomnia and risk factors for OSA, i.e., snoring, obesity, and hypertension, should be screened for OSA. In addition, because commonly used benzodiazepine and non-benzodiazepine sleeping aids may aggravate OSA [20], prescribing sleeping aids in insomnia patients with risk factors for OSA may be associated with adverse effects.

The prevalence of severe OSA dropped from 15.5 % in middle-aged men to 8.2 % in elderly men (nearly twofold decrease), whereas it increased from 1 % in middle-aged women to 9.7 % in elderly women (ninefold increase). The observed opposite direction of the change of prevalence of severe OSA from middle-aged to elderly men and women may be associated with age-related changes in sex hormones. Specifically, the decline of testosterone levels in men, a hormone that has been implicated in the pathology of sleep apnea, and the corresponding decline of estrogen/progesterone in women, hormones that have been considered as protective of sleep apnea, may explain this gender/age-related differences [21, 22].

In addition, there was a remarkable reduction in self-evaluated sleep time compared to PSG-determined sleep, a finding consistent with previous findings in patients with chronic insomnia [11]. Comparisons of sleep among groups with different AHI levels suggest that, in insomnia patients, increased AHI is associated with worse sleep quality. This is reflected in increased N1 time, brief arousal index, and decreased N3 time, which are similar to those observed in typical OSA patients [10]. However, no differences in PSG-determined total sleep time were observed across the groups with different AHI levels. In a previous study of OSA patients without the symptoms of insomnia, we [10] found that severe OSA patients had 1.0–1.3 h more total sleep time than did individuals with less severe OSA or no OSA. This suggests that OSA patients without the symptoms of insomnia, particularly severe OSA patients, have the capacity of increasing overnight sleep amount and even objective daytime sleeping [23] in response to worse sleep quality produced by OSA events. In contrast, insomnia patients with severe OSA have poor sleep quality similar to that of OSA patients without insomnia, but do not have the capacity to compensate for it. Therefore, compared to OSA patients without the symptoms of insomnia, insomnia patients with OSA are characterized by (1) a considerable reduction in sleep perception and (2) a lack of compensatory mechanisms to enable responses to worse sleep quality produced by OSA events.

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