Comparison of Polysomnographic and Clinical Presentations and Predictors for Cardiovascular-Related Diseases between Non-Obese and Obese Obstructive Sleep Apnea among Asians

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Introduction: Unlike Caucasians, many Asians with obstructive sleep apnea (OSA) are non-obese but are affected by the disease due to predisposing craniofacial structure. Therefore, non-obese and obese OSA may represent different disease entities. The associated risk factors for developing cardiovascular-related diseases, consequently, may be considered separately for the two types of OSA.

Method: We reviewed polysomnographic studies performed in adults (aged ≥ 18 years) diagnosed with OSA (respiratory disturbance index [RDI] ≥ 5). We divided the patients into obese (body mass index [BMI] ≥ 25) and non-obese (BMI < 25) groups. We aimed to determine the differences between these two groups in terms of clinical presentations, polysomnographic findings, and association with cardiovascular-related diseases including hypertension, diabetes mellitus, coronary artery disease, and/or cerebrovascular disease.

Results: Among 194 patients with OSA (RDI ≥ 5), 63.4% were non-obese and 36.6% were obese. Compared with obese OSA patients, non-obese OSA patients were noted to have smaller neck size, less prevalence of hypertension, and less history of frequent nocturia (> 3 -4/week), with equal prevalence of excessive daytime sleepiness. Overall, non-obese OSA patients were noted to have milder disease indicated by lower

total, supine, and non-supine, NREM RDI and higher mean and nadir oxygen saturations. In the non-obese group, only total obstructive apnea index (OAI) was noted to be a predictor for developing any of the cardiovascular-related diseases after controlling for age, sex, and RDI (odds ratio = 9.7). However, in the obese OSA group, frequent snoring ($> 50\%$ of total sleep time), low sleep efficiency ($\leq 90\%$), and low mean oxygen saturation ($< 95\%$) were noted to be significant predictors of cardiovascular-related diseases (odds ratios = 12.3, 4.2, and 5.2, respectively).

Conclusion: Among Asians, most OSA patients were not obese. Compared to obese OSA patients, non-obese OSA patients were noted to have less prevalence of hypertension and less history of nocturia. They were also noted to have overall milder OSA. Only OAI was noted to be a significant predictor for cardiovascular-related disease in the non-obese OSA group.

Keywords: Obstructive sleep apnea, obesity

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Majority of obstructive sleep apnea among Asians are not obese (BMI < 25) and believed to have predisposing craniofacial structure. Differences between obese and non-obese obstructive sleep apnea groups are investigated in this current study.

Study Impact: Obese and non-obese obstructive sleep apnea among Asians appeared to have some different clinical and polysomnographic entities as well as risk factors for cardiovascular-related diseases development.

ering the risk factors for developing cardiovascular-related diseases in the patient, the two types of OSA may present different risk factors.

Obstructive sleep apnea (OSA) is characterized by repetitive episodes of complete (apnea) or partial (hypopnea) upper airway obstruction occurring during sleep. These events often result in reduction in blood oxygen saturation and are usually terminated by brief arousals from sleep.¹ Prior study has shown that obesity is one of the important risk factors for developing OSA.² A recent study from a bariatric surgery clinic in which patients had a median BMI of 41.9 showed that 79% of these patients had at least a moderate degree of obstructive sleep apnea.³ However, unlike Caucasians, many Asians with OSA are not obese. Predisposing craniofacial structure most likely contributes to developing OSA among non-obese Asians.⁴ We believe that obese and non-obese OSA may represent different disease entities. Thus, when consid-

METHODS

This is a retrospective study referencing the data of patients aged ≥ 18 years who were referred to a sleep laboratory at the Excellence Center for Sleep Disorders, King Chulalongkorn Memorial Hospital for suspected OSA from January 1, 2010, to June 30, 2010. All polysomnographies conducted in the sleep laboratory were using standard EEG including frontal leads (F1, F2), central leads (C3, C4), occipital leads (O1, O2), and reference leads at mastoids (M1, M2); electromyography, and electrooculography. Oxygen saturation (SpO_2) was measured with a finger probe. Air flow was measured by 2 methods: nasal pressure transducer and oral-nasal thermocouple. The thoracic and abdominal respiratory movements were monitored by respiratory inductance plethysmography. The body position was measured by a position sensor, which was attached to the anterior chest wall on the thoracic belt. The sensor differentiated 5 positions, including supine and non-supine position (right, left, prone, and upright position). Sleep stages were scored in 30-sec epochs according to the standard criteria from the AASM Manual for the Scoring of Sleep and Associated Events.⁵ Apnea was defined using oral-nasal thermocouple excursion, and hypopnea was defined using nasal pressure transducer excursion. Apnea, hypopnea, and respiratory effort-related arousals (RERAs) were scored using the standard criteria from the AASM manual.⁵ The alternative rule was used to define hypopnea.⁵ The number of apneas, hypopneas, and RERAs per hour of NREM and REM and total sleep time (TST) were calculated and reported as NREM RDI, REM RDI, and total RDI, respectively. The number of each type of respiratory events per hour of total sleep time were defined including obstructive apnea events, central apnea events, mixed apnea events, and hypopnea event as total OAI, total CAI, total MAI, and total HI, respectively. Parameters of oxygenation included in the study were absolute minimum SpO_2 during sleep and mean oxygen saturation during sleep. Arousals/h of TST, arousals/h of during NREM, and arousals/h during REM sleep were reported as total arousal index, NREM arousal index, and REM arousal index, respectively. Sleep efficiency was defined as a ratio of TST over the total recording time in percentage. Time spent in NREM1, NREM2, NREM3, and REM was calculated as percentage of the TST. Periodic limb movement index (PLMI) was calculated using standard criteria.⁵ Demographic and comorbidity data of the patients included age (years), gender, BMI, and neck size (cm).

Information regarding cardiovascular-related diseases was obtained from a pretest questionnaire, which all the patients were required to fill out prior to undergoing polysomnographic study. The pretest questionnaire consisted of self-administered “yes” or “no” questions. The patients were asked if they had any cardiovascular-related diseases, including hypertension (HTN), diabetes (DM), coronary artery disease (CAD), or cerebrovascular disease (CVA). Other medical conditions included were congestive heart failure, hyperthyroidism, hypothyroidism, anemia, asthma, cancer, renal disease, iron deficiency, and depression. Using the Epworth Sleepiness Scale (ESS), which was recently validated to Thai language,⁶ the measurement of each patient’s sleepiness was obtained from pretest questionnaire. Additionally, patient reports of snoring intensity (mild, moderate, or severe) were obtained from this pretest questionnaire. The patients

were also asked about their history of witnessed apnea, habitual snoring, morning headache, nocturia, and morning dry throat.

Patient data collected in the study included technician observation of snoring frequency and intensity. Snoring frequency was divided into 3 categories ($< 20\%$, 20% to 50% , and $> 50\%$ of TST). The snoring intensity was also divided into 3 severity levels (low [can only be heard when getting close to the patient], moderate [can be heard when opening the door], and severe [can be heard through the closed door]).

Our exclusion criteria were: (1) $\text{RDI} < 5$, (2) CPAP study, and (3) missing data.

Dividing the patients into obese ($\text{BMI} \geq 25$) and non-obese ($\text{BMI} < 25$), we aimed to determine the differences between these 2 groups in terms of clinical presentation, polysomnographic findings, and predictors for developing cardiovascular-related diseases including HTN, DM, CAD, and/or CVA.

Our primary aim was to determine the difference between obese and non-obese OSA subjects in terms of:

1. Baseline characteristics: age, sex, and neck size.
2. Clinical presentation: history of witnessed apnea, habitual snoring, morning headache, nocturia, dry throat (> 3 -4/week), daytime sleepiness ($\text{ESS} \geq 10$), and associated comorbidities (CAD, CHF, DM, HTN, CVA, depression).
3. Polysomnographic findings: total RDI, total OAI, total CAI, total HI, total MAI, REM RDI, NREM RDI, mean oxygen saturation, nadir oxygen saturation, sleep latency, REM latency, sleep efficiency, total arousal index, REM arousal index, NREM arousal index, supine sleep time (min), supine REM time (min), supine NREM (min), %NREM1, %NREM2, %NREM3, %REM, supine RDI, non-supine RDI, snoring frequency and intensity, and total PLMI.

Our secondary aim was to determine the association of cardiovascular-related diseases (CAD, CHF, DM, HTN, CVA) with obese and non-obese OSA.

Statistical Analysis

The comparison of the baseline characteristics, clinical presentations, and polysomnographic findings between obese and non-obese OSA subject were statistically analyzed. If the data were observed to have normal distribution, the continuous data were evaluated by Student *t*-test. If the data did not have normal distribution, a nonparametric method (Mann-Whitney U test) was used for evaluation. The nominal data were evaluated by χ^2 test. To identify the association with cardiovascular-related diseases, the data were then evaluated by multivariate regression analysis by stepwise logistic regression analysis. All statistical analysis was performed using statistical software (SPSS for Windows, version 17.0). Our study was approved by the institutional review board, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

RESULTS

A total of 221 studies of patients ≥ 18 years were reviewed in our laboratory from Jan 1, 2010, to June 30, 2010. We excluded 8 CPAP studies and 19 studies with incomplete questionnaires (missing information on comorbidities). A total of 194 patient records were analyzed. Among these 194 patients with OSA

Table 1—Baseline clinical characteristics, comorbid diseases, and clinical presentations in obese and non-obese OSA subjects

Characteristics	Non-obese OSA	Obese OSA	p value
Clinical characteristic			
Age, years	52.6 (12.1)	51.5 (12.1)	0.57
Male sex, %	80.3	72.4	0.22
Neck circumference, cm*	36.6 (3.0)	40.4 (3.5)	< 0.01
ESS $\geq$ 10, %	51.5	47.8	0.63
Comorbid disease			
Coronary artery disease, %	1.5	5.2	0.46
Congestive heart failure, %	0	0.8	0.60
Hypertension, %*	28.8	54.2	< 0.01
Cerebrovascular disease, %	3.1	0.8	0.26
Diabetes mellitus, %	10.4	15.3	0.36
Depression, %	1.6	6.8	0.12
Clinical presentation			
Nocturia (> 3-4/week), %*	54.4	71.3	0.02
Morning headache (> 3-4/week), %	13.0	18.0	0.39
Morning dry throat (> 3-4/week), %	52.9	55.0	0.79
Snoring frequency (> 3-4/week), %	82.3	87.2	0.37
Witnessed apnea (> 3-4/week), %	23.0	23.2	0.97

Values are mean (SD). *Statistically significant.

Table 2—Polysomnographic characteristics of obese and non-obese OSA patients

Polysomnographic findings	Non-obese OSA	Obese OSA	p value
NREM2/TST-%	57.3 (13.0)	55.6 (15.5)	0.45
NREM3/TST-%	12.8 (10.6)	13.8 (10.8)	0.56
REM/TST-%	15.0 (8.5)	14.6 (7.4)	0.75
Supine sleep time (min)*	258.4 (101.9)	210.3 (115.9)	< 0.01
Supine RDI*	31.5 (20.0)	43.3 (26.2)	< 0.01
REM time (min)	58.3 (36.3)	53.7 (34.0)	0.38
Total CAI	0.7 (1.9)	0.6 (1.5)	0.67

Tested by Student *t*-test; values are mean (SD). *Statistically significant.

(RDI $\geq$ 5), 63.4% were non-obese and 36.6% were obese. Compared with obese OSA patients, non-obese OSA patients had smaller neck size, less prevalence of hypertension, and less history of frequent nocturia (> 3-4/week), with equal prevalence of excessive daytime sleepiness (**Table 1**). Overall, non-obese OSA patients had milder disease, indicated by lower total, supine, and non-supine NREM RDIs, and higher mean and nadir oxygen saturations (**Tables 2 and 3**).

In the non-obese group, only total OAI was noted to be the sole predictor for developing cardiovascular-related diseases after controlling for age, sex, and RDI (odds ratio = 9.7; **Table 4**). This is in contrast to the obese OSA group, which had multiple predictors; frequent snoring (> 50% of TST), low sleep efficiency ($\leq$ 90%), and low mean oxygen saturation (< 95%) were noted to be significant predictors (odds ratios = 12.3, 4.2, and 5.2, respectively; **Table 5**).

DISCUSSION

Prior studies have shown that obese and non-obese OSA patients are not identical in many aspects. Non-obese OSA patients have generally been noted to have less severe disease, as indicated by less severe oxygen desaturation.⁷ Ling et al.

published a paper demonstrating that oxygen desaturation index (ODI) is not accurate for diagnosis of OSA in non-obese OSA and should not be used in isolation as a diagnostic test, since this group of OSA patients may not have significant oxygen desaturations.⁸ We have confirmed this finding: we found that measurements in non-obese OSA patients, when compared to obese OSA patients, were less severe not only in terms of oxygen desaturations; they were also noted to have lower RDI. However, obesity itself may have unique clinical significance. A prior study has shown that obesity, not RDI, is associated with increased levels of C-reactive protein (CRP)—the marker for cardiovascular-related diseases.⁹ We demonstrated that these two groups were had different predictors for cardiovascular-related disease after controlling for age, sex, and RDI. In the non-obese group, total OAI, not oxygen desaturation, was a significant predictor for cardiovascular-related disease. This finding can be explained by higher mean and nadir oxygen saturation in the non-obese group when compared to the obese group. In the non-obese group, only the most severe form of event (obstructive apnea) predicted occurrence of cardiovascular-related diseases. However, due to limited sample size of this study, the association between other predictors and the cardiovascular-related diseases may not be statistically expressed.

Table 3—Polysomnographic findings in obese and non-obese OSA patients

Polysomnographic findings	Non-obese OSA	Obese OSA	p value
Sleep onset (min)	5.50 (10.80)	9.50 (16)	0.11
REM latency (min)	103.50 (78.50)	114.50 (102.50)	0.56
Total Sleep time (min)	423.50 (59.75)	404 (56.50)	0.05
NREM1/TST (%)	9 (11.50)	10 (13)	0.68
Sleep efficiency (%)	94 (10)	92 (10)	0.79
Total arousal index	23.10 (17.95)	25.20 (20.70)	0.12
Arousal NREM index	20.40 (18.90)	23.80 (24.80)	0.13
Arousal REM index	22.30 (21.15)	20.70 (27.50)	0.64
Supine NREM time (min)	250.83 (139.20)	206.23 (153.70)	0.09
Supine REM time (min)*	29.06 (37.54)	21.81 (28.50)	0.048
Non-supine RDI*	6 (11.85)	14.30 (23.60)	0.01
RDI NREM*	17.00 (26.10)	26.40 (39.30)	0.04
RDI REM	22.70 (32.75)	31.50 (39.40)	0.09
RDI TST*	20.20 (21.35)	28.20 (37.20)	0.01
Total OAI	7.30 (13.05)	5.80 (18.70)	0.85
Total MAI	0 (0.25)	0 (0.10)	0.87
Total HI*	10.40 (11.40)	12.00 (15.60)	0.04
Mean oxygen saturation (%)*	96.00 (3)	94.00 (2)	< 0.01
Nadir oxygen saturation (%)*	85 (9.00)	80 (10.00)	< 0.01
Periodic limb movement index	4.10 (14.85)	4.20 (10.10)	0.67

Tested by Mann-Whitney U test. Median (interquartile range). *Statistically significant.

Table 4—Predictor for cardiovascular-related disease after controlling for age, sex, and RDI in non-obese group

Factor	Odds ratio	95% CI	p value
High total OAI (≥ 5 events/h)	9.7	1.2-76.6	0.03

Table 5—Predictors for cardiovascular-related disease after controlling for age, sex, and RDI in obese group

Factor	Odds ratio	95% CI	p value
Frequent snoring ($> 50\%$ of total sleep time)	12.3	1.6-100	0.02
Low sleep efficiency ($\leq 90\%$)	4.2	1.3-13.9	0.02
Low mean oxygen saturation ($< 95\%$)	5.2	1.23-22.2	0.03

We believe our finding is of interest and may be clinically applicable since Asian OSA patients are generally not obese. We found most of our OSA patients to be non-obese (63.4%) when compared to non-obese OSA incidence of 42% in the study of Young et al.¹⁰ We believe that non-obese OSA group in Asian population is unique and differs from obese OSA group found in the Western population. Future prospective studies focusing in this group of patients to identify its clinical significance and specific treatment should be encouraged.

CONCLUSION

Among Asians, most OSA patients were not obese. Compared to obese OSA patients, non-obese OSA patients were noted to have less prevalence of hypertension and less history

of nocturia. They were also noted to have overall milder OSA. Only OAI was noted to be a significant predictor for cardiovascular-related disease in the non-obese OSA group.

REFERENCES

1. American Academy of Sleep Medicine. *International classification of sleep disorders, 2nd ed: Diagnostic and coding manual*. Westchester, IL: American Academy of Sleep Medicine, 2005.
2. Young T, Skatrud J, Peppard PE. Risk factors for obstructive sleep apnea in adults. *JAMA* 2004;291:2013-6.
3. Rao A, Tey BH, Ramalingam G, et al. Obstructive sleep apnoea (OSA) patterns in bariatric surgical practice and response of OSA to weight loss after laparoscopic adjustable gastric banding (LAGB). *Ann Acad Med Singapore* 2009;38:587-7.
4. Li KK, Kushida C, Powell NB, et al. Obstructive sleep apnea syndrome: a comparison between Far-East Asian and white men. *Laryngoscope* 2000;110:1689-13.
5. Iber C, Ancoli-Israel S, Chesson A, Quan SF. *The AASM manual for the scoring of sleep and associated events: rules, terminology, and technical specifications*, 1st ed. Westchester, IL: American Academy of Sleep Medicine, 2007.
6. Banhiran W, Assanasen P, Nopmaneejumrusters C, et al. Epworth sleepiness scale in obstructive sleep disordered breathing: the reliability and validity of the Thai version. *Sleep Breath* 2010;15:571-7.
7. Peppard PE, Ward NR, Morrell MJ. The impact of obesity on oxygen desaturation during sleep-disordered breathing. *Am J Respir Crit Care Med* 2009;180:788-93.
8. Ling IT, James AL, Hillman DR. Interrelationships between body mass, oxygen desaturation, and apnea-hypopnea indices in a sleep clinic population. *Sleep* 2012;35:89-96.
9. Sharma SK, Mishra HK, Sharma H, et al. Obesity, and not obstructive sleep apnea, is responsible for increased serum hs-CRP levels in patients with sleep-disordered breathing in Delhi. *Sleep Med* 2008;9:149-56.
10. Young T, Peppard PE, Taheri S. Excess weight and sleep-disordered breathing. *J Appl Physiol* 2005;99:1592-9.

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