

## Obstructive Sleep Apnea-hypopnea Syndrome Patients with Overweight and Hypertension in a Japanese Workplace

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**Abstract: Obstructive Sleep Apnea-hypopnea Syndrome Patients with Overweight and Hypertension in a Japanese Workplace: Ken OKABAYASHI, et al. JR East Health Promotion Center, East Japan Railway Company**—The objective of this study was to determine the relationship between obstructive sleep apnea-hypopnea syndrome (OSAHS) and overweight combined with hypertension and to examine whether OSAHS in conjunction with overweight and hypertension is associated with daytime sleepiness. In a Japanese workplace of 28,636 employees, 368 men (19–62 yr old), who were anxious regarding their OSAHS symptoms, underwent home pulse oximetry. Of these, 153 men subsequently underwent all-night polysomnography (PSG), and OSAHS was diagnosed in 149. We next classified these 149 men into the following groups: A [Overweight (–)/Hypertension (–), n=41], B [Overweight (–)/Hypertension (+), n=15], C [Overweight (+)/Hypertension (–), n=46], and D [Overweight (+)/Hypertension (+), n=47]. The Epworth Sleepiness Scale (ESS) was used to evaluate daytime sleepiness and the apnea-hypopnea index (AHI) was used to evaluate the severity of OSAHS. The averages of the ESS score and the AHI were compared in each group. Both the average ESS scores and the percentage of ESS scores  $\geq 11$  were not significantly different among the groups. The average AHI of group D was the highest among all of the groups and that of group C was significantly higher than those of groups A and B. In all the groups, the OSAHS patients with overweight

and hypertension in this study had the highest AHI. The level of daytime sleepiness evaluated by the ESS in this study was almost the same in the OSAHS patients regardless of the degree of overweight or hypertension. These observations suggest that it is necessary to positively recommend PSG to men who are suspected of having OSAHS with overweight and hypertension, even if they do not have daytime sleepiness.

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**Key words:** Epworth Sleepiness Scale (ESS), Home pulse oximetry, Hypertension, Overweight, Polysomnography, Sleep apnea

Accumulating evidence has suggested that obstructive sleep apnea-hypopnea syndrome (OSAHS) is not only a phenomenon of the cessation of breathing during sleep but also the cause of sleepiness during the day and various other physical disorders<sup>1–3</sup>. Moreover, neurocognitive sequelae, such as daytime sleepiness and impaired executive function, are important factors implicated in motor vehicle accidents and probably contribute to the loss of work-related productivity<sup>4</sup>. The true prevalence of OSAHS in Japan has not been established. A community-based study of sleep apnea in middle-aged Chinese men (30–60 yr old) residing in Hong Kong used full polysomnography (PSG) and demonstrated an estimated 4.1% prevalence of OSAHS<sup>5</sup>. Most population-based studies that have estimated the sex-specific prevalence indicate a greater risk of OSAHS in men than in women<sup>6</sup>. Thus, OSAHS is common in adult males and remains an important public health problem. However, many people with OSAHS remain undiagnosed and untreated because the symptoms of OSAHS, such as snoring and cessation of breathing, are not necessarily

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recognized.

While screening for OSAHS, it is necessary to look for various objective symptoms such as overweight and hypertension rather than rely on subjective symptoms. Overweight and obesity are known to be risk factors for the development of OSAHS<sup>7-9</sup>. Several studies have demonstrated that OSAHS is related to the development of hypertension<sup>10-15</sup>. However, to our knowledge, few epidemiological studies have examined the relationship between OSAHS and overweight combined with hypertension. We have initiated an OSAHS awareness program in a Japanese workplace from the viewpoint of preventing traffic and labor accidents and with respect to health promotion and preventive medicine. The purpose of this study was to determine the relationship between OSAHS and overweight combined with hypertension and to examine whether OSAHS in conjunction with overweight and hypertension is associated with daytime sleepiness in a Japanese workplace.

## Materials and Methods

### *Subjects and measurements*

The study population comprised 28,636 employees (male, 26,111; female, 2,525) in a workplace in Japan. In March 2003, we produced pamphlets and an educational video on OSAHS and distributed these to each section in the workplace. The participants watched the video and read the pamphlets. In these pamphlets and the video, persons with symptoms such as snoring or cessation of breathing when sleeping as identified by family members, and who experienced drowsiness during the daytime, were particularly encouraged to undergo home pulse oximetry. In this study, 368 male subjects (19–62 yr old), who were anxious regarding their OSAHS symptoms, were recruited from a workplace in Japan and underwent home pulse oximetry once over a 2-yr period (April 2003–March 2005). Since there were only 4 female subjects with similar symptoms, females were excluded from this study.

The subjects volunteered to undergo home pulse oximetry as a screening test for OSAHS. Next, the use of a pulse oximeter was explained to these subjects. They answered several questions regarding their OSAHS symptoms, including those scored by the Epworth Sleepiness Scale (ESS)<sup>16</sup>; underwent physical examinations, including the measurement of height, weight, systolic blood pressure (SBP), and diastolic blood pressure (DBP); and also underwent an oropharyngeal examination. The ESS is a questionnaire on daytime sleepiness. It consists of 8 questions each allocated a score from 0 to 3 according to the subjects daytime sleepiness; an excessive daytime sleepiness is defined as an ESS score  $\geq 11$ . Blood pressure was measured twice in the left arm during the daytime using a manual mercury sphygmomanometer. The measurements were taken by

a physician or nurse after the subjects had rested for  $\geq 5$  min in a seated position in a quiet area. Subsequently, the means of 2 separate SBP and DBP measurements were calculated in order to derive the blood pressure values that are reported in this study. The subjects underwent pulse oximetry at home during their sleep. A PULSOX-3Si (Minolta Co. Ltd., Japan) pulse oximeter was used for this purpose. The internal memory of this device stored the values of blood oxygen saturation by performing a moving average for the last 5 s and updated the data every second. This sampling time was sufficiently short to avoid underestimating oxygen desaturation. The data thus obtained were fed into a personal computer and used to calculate the desaturation cycles per hour as an oxygen desaturation index (ODI).

The study protocol was approved by the Ethics Committee of the JR East Health Promotion Center and informed consent was obtained from all subjects prior to the commencement of this study.

### *Polysomnography*

Based on the results of the home pulse oximetry, we judged that the subjects with a 2% ODI  $\geq 5$  dips/h were those suspected of suffering from OSAHS. The subjects with a 2% ODI  $\geq 5$  dips/h were advised to undergo all-night PSG for a detailed examination of OSAHS. The reason for selecting a 2% ODI instead of either a 3% or 4% ODI was to avoid, as far as possible, overlooking apneas that were not accompanied by oxygen desaturation. Those subjects with a 2% ODI  $< 5$  dips/h, who were anxious regarding their OSAHS symptoms, were advised to undergo PSG.

PSG was performed at a sleep unit in the JR Tokyo General Hospital between 8 p.m. and 6 a.m. by using a Sleep-Watcher-P (Teijin Co. Ltd., Japan) as a digital PSG system. Oronasal airflow measured by a thermister sensor, 4 channels of electroencephalogram, bilateral electro-oculogram, submental electromyography, electrocardiogram, movements of the chest and abdominal walls, arterial oxygen saturation, and snoring sounds were all recorded. Among the subjects undergoing PSG, OSAHS was diagnosed in those with an apnea-hypopnea index (AHI)  $\geq 5$  per hour, but was ruled out in those with an AHI  $< 5$  per hour. Apnea was defined as the complete cessation of airflow lasting more than 10 s, and hypopnea as a 50% visual reduction in airflow associated with a decrease of 3% or more in the arterial oxygen saturation of hemoglobin lasting more than 10 s. The AHI was defined as the number of apneas and hypopneas per hour of sleep.

### *Classification by a combination of overweight and hypertension*

After establishing the baseline PSG, subjects in whom OSAHS was diagnosed were classified into group A

**Table 1.** Baseline characteristics of the 368 subjects classified on the basis of a 2% ODI

Pulse oximetry		Subjects (number)	Age (yr)	BMI (kg/m <sup>2</sup> )	SBP (mmHg)	DBP (mmHg)	ESS (score)	ESS score $\geq 11$ (number)	(%)
	Total	55	43.0 $\pm$ 1.5	23.5 $\pm$ 0.4	127 $\pm$ 1.6	79.4 $\pm$ 1.4	8.0 $\pm$ 0.6	18	32.7
2% ODI (dips/h)	<5								
	PSG (+)	2	39.5 $\pm$ 9.5	23.3 $\pm$ 3.6	128 $\pm$ 0.5	80.0 $\pm$ 5.0	8.5 $\pm$ 1.5	0	0
	PSG (-)	53	43.2 $\pm$ 1.5	23.5 $\pm$ 0.4	127 $\pm$ 1.7	79.3 $\pm$ 1.4	8.0 $\pm$ 0.6	18	32.7
	Total	313	46.2 $\pm$ 0.5	26.2 $\pm$ 0.2	132 $\pm$ 1.0	83.6 $\pm$ 0.7	8.3 $\pm$ 0.2	90	28.8
	$\geq 5$								
	PSG (+)	151	46.0 $\pm$ 0.7	26.7 $\pm$ 0.4	133 $\pm$ 1.6	84.0 $\pm$ 1.1	8.7 $\pm$ 0.4	49	32.5
	PSG (-)	162	46.5 $\pm$ 0.7	25.8 $\pm$ 0.3	131 $\pm$ 1.4	83.3 $\pm$ 0.9	8.0 $\pm$ 0.3	41	25.3
	Total	368	45.7 $\pm$ 0.5	25.8 $\pm$ 0.2	131 $\pm$ 0.9	83.0 $\pm$ 0.6	8.3 $\pm$ 0.2	108	29.3

ODI, oxygen desaturation index; PSG, polysomnography; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ESS, Epworth sleepiness scale. Age, BMI, SBP, DBP and ESS are represented as mean  $\pm$  SEM.

**Table 2.** Baseline characteristics of the 153 subjects who underwent all-night PSG

PSG		Subjects (number)	Age (yr)	BMI (kg/m <sup>2</sup> )	SBP (mmHg)	DBP (mmHg)	ESS (score)	ESS score $\geq 11$ (number)	(%)
AHI	<5	4	33.5 $\pm$ 7.2	25.6 $\pm$ 1.4	125 $\pm$ 11	83.5 $\pm$ 7.0	9.3 $\pm$ 2.5	2	50.0
(per hour)	$\geq 5$	149	46.2 $\pm$ 0.7	26.7 $\pm$ 0.4	133 $\pm$ 1.6	83.9 $\pm$ 1.1	8.7 $\pm$ 0.4	47	31.5

PSG, polysomnography; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ESS, Epworth sleepiness scale; AHI, apnea hypopnea index. Age, BMI, SBP, DBP and ESS are represented as mean  $\pm$  SEM.

[Overweight (-)/Hypertension (-)], group B [Overweight (-)/Hypertension (+)], group C [Overweight (+)/Hypertension (-)], and group D [Overweight (+)/Hypertension (+)]. Overweight (+) was defined as a body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup> and Overweight (-) as a BMI  $< 25$  kg/m<sup>2</sup>. Hypertension (+) was defined as an SBP  $\geq 140$  mmHg or a DBP  $\geq 90$  mmHg. The subjects for whom hypertension had previously been diagnosed at hospital and who were under treatment were also included in group B (n=9) or D (n=19). Hypertension (-) was defined as an SBP  $< 140$  mmHg and a DBP  $< 90$  mmHg.

#### Data analysis

All groups were compared with respect to the average ESS score for the evaluation of sleepiness and the average AHI. The Mann-Whitney U test was used for the comparison of these averages among the groups. An analysis of covariance was used to compare the influence of BMI on the AHI among the groups. A chi-squared test was used to compare the percentages of ESS scores  $\geq 11$  among the groups. A *p* value  $< 0.05$  was considered to be significant. Moreover, we analyzed the correlation of the AHI with the BMI of the subjects who underwent PSG. Correlations were tested by calculation of Pearson's correlation coefficient (*r*). All analyses were performed using the statistical software SPSS (version 10.0).

## Results

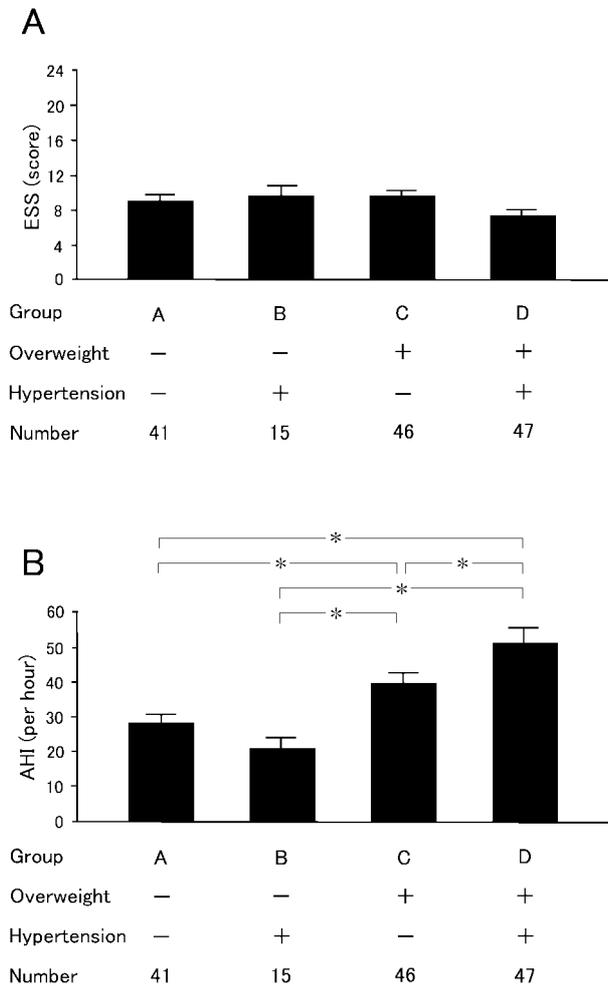
### Baseline characteristics of the subjects classified by home pulse oximetry

The baseline characteristics of all the 368 male subjects classified on the basis of a 2% ODI, including sex, age, BMI, SBP, DBP and ESS, are shown in Table 1. Among the 368 subjects, 313 exhibited a 2% ODI  $\geq 5$  dips/h. The remaining 55 subjects exhibited a 2% ODI  $< 5$  dips/h. Although 292 subjects (79.3%) were more than 40 yr of age and the remaining 76 subjects (20.7%) were less than 39 yr of age, all subjects were analyzed together as follows. In this study, 151 of the 313 subjects with a 2% ODI  $\geq 5$  dips/h and 2 of the 55 subjects with a 2% ODI  $< 5$  dips/h underwent PSG. The reason why the 2 subjects with a 2% ODI  $< 5$  dips/h underwent PSG is that cessation of breathing during sleep was noted by family members and the subjects expressed a strong desire to undergo PSG. All the 313 subjects with a 2% ODI  $\geq 5$  dips/h were advised to undergo all-night PSG; however, 162 of the 313 subjects did not undergo PSG either because of their work schedules or for economic reasons. Concerning the subjects with a 2% ODI  $\geq 5$  dips/h, the averages of BMI and the ESS score, and the percentages of the ESS score  $\geq 11$ , were not significantly different between the 151 subjects who underwent PSG and the 162 subjects who did not undergo PSG (Table 1). The respective *p*

**Table 3.** Baseline characteristics of the 149 subjects who underwent all-night PSG and in whom OSAHS was diagnosed

Group	Subjects (number)	Age (yr)	BMI (kg/m <sup>2</sup> )	SBP (mmHg)	DBP (mmHg)	ESS (score)	ESS score ≥11 (number)	ESS score ≥11 (%)	AHI (per hour)	AHI corrected for BMI (per hour)
A	41	45.6 ± 1.3	22.8 ± 0.3	120 ± 1.7	74.7 ± 1.2	8.6 ± 0.6	12	29.3	27.6 ± 3.0	37.2 ± 3.7
B	15	53.2 ± 1.4	22.9 ± 0.4	141 ± 2.7*#	88.6 ± 1.8*#	9.1 ± 1.2	5	33.3	24.7 ± 2.7	34.1 ± 5.4
C	46	45.0 ± 1.4	27.4 ± 0.4*†	123 ± 1.3	77.8 ± 0.9	9.4 ± 0.7	17	37.0	40.0 ± 3.0*†	38.0 ± 2.9
D	47	45.7 ± 1.3	30.4 ± 0.6*†#	151 ± 2.7*†#	96.4 ± 1.9*†#	7.9 ± 0.6	13	27.7	54.2 ± 3.6*†#	44.7 ± 3.5
Total	149	46.2 ± 0.7	26.7 ± 0.4	133 ± 1.6	83.9 ± 1.1	8.7 ± 0.4	47	31.5	39.5 ± 1.9	39.5 ± 1.9

Group A, Overweight (-)/Hypertension (-); Group B, Overweight (-)/Hypertension (+); Group C, Overweight (+)/Hypertension (-); Group D, Overweight (+)/Hypertension (+); PSG, polysomnography; OSAHS, obstructive sleep apnea-hypopnea syndrome; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ESS, Epworth sleepiness scale; AHI, apnea hypopnea index. Age, BMI, SBP, DBP, ESS and AHI are represented as mean ± SEM. \**p*<0.05 vs Group A, †*p*<0.05 vs Group B, #*p*<0.05 vs Group C



**Fig. 1.** (A) The effects of overweight and hypertension on the Epworth Sleepiness Scale (ESS; score). None of the groups exhibited significant differences. (B) The effects of overweight and hypertension on the apnea-hypopnea index (AHI; per hour). Group D exhibited the highest AHI average of all the groups and the average AHI of group C was higher than those of groups A and B; these observations were statistically significant (\**p*<0.05). In particular, the average AHI of group D was higher than that of group C. The number presented is the total number of patients in each group.

<5 dips/h. Thus, OSAHS was diagnosed in 149 subjects, but ruled out in the remaining subjects (n=4) with an AHI <5 per hour. Table 2 shows the baseline characteristics of these 153 subjects who were classified on the basis of the AHI.

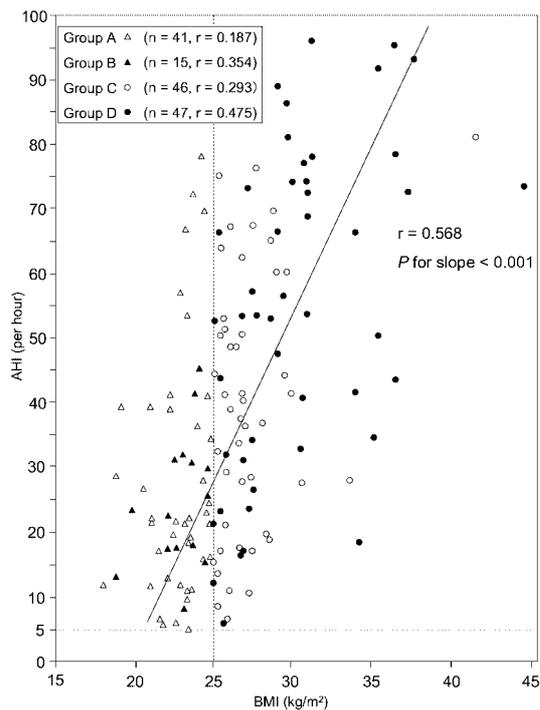
*The relationship between ESS and AHI with the combination of overweight and hypertension*

The subjects (n=149) in whom OSAHS was diagnosed were classified into groups A, B, C and D according to their BMI, SBP and DBP values. The baseline characteristics of these subjects are shown in Table 3. The average BMI of group D was significantly higher than that of group C. The range of the ESS among all groups was between 7.9 and 9.4. Although these ESS scores were relatively high, the average ESS score was not significantly different among all groups (Fig. 1A). Furthermore, the percentage of the ESS score ≥11 was also not significantly different among these groups (Table 3). Group D exhibited the highest AHI average among all the groups and the average AHI of group C was higher than those of groups A and B; these observations were statistically significant (*p*<0.05) (Fig. 1B). In particular, the average AHI of group D was higher than that of group

values were 0.063, 0.130 and 0.163.

*Subjects who underwent all-night PSG*

OSAHS was diagnosed in 147 of the 151 subjects with a 2% ODI ≥5 dips/h, and in the 2 subjects with a 2% ODI



**Fig. 2.** The correlation of body mass index (BMI; kg/m<sup>2</sup>) with apnea-hypopnea index (AHI; per hour) obtained by polysomnography. The BMI and AHI were observed to be significantly correlated. The study subjects were 149 men in whom OSAHS was diagnosed.  $\triangle$ ; Group A (n=41, r=0.187),  $\blacktriangle$ ; Group B (n=15, r=0.354),  $\circ$ ; Group C (n=46, r=0.293),  $\bullet$ ; Group D (n=47, r=0.475).

C. However, the average AHI corrected for BMI was not significantly different among all the groups (Table 3).

A plot of BMI against AHI for those subjects (n=149) in whom OSAHS was diagnosed is shown in Fig. 2. The BMI and AHI were observed to be significantly correlated ( $r=0.568$ ,  $p$  for slope  $<0.001$ ) without the consideration of hypertension.

## Discussion

The present study has demonstrated the relationship between OSAHS and overweight combined with hypertension. It is noteworthy that the level of daytime sleepiness evaluated by the ESS in this study was virtually the same in all the OSAHS patients regardless of the degree of overweight or hypertension.

The National Institutes of Health (NIH) and World Health Organization (WHO) guidelines<sup>17</sup> define obesity as a BMI  $\geq 30$  kg/m<sup>2</sup>, and overweight as a BMI  $\geq 25$  kg/m<sup>2</sup>. OSAHS is an increasingly common disorder that is strongly related to overweight and obesity<sup>4, 8</sup>; therefore, overweight and obesity are major risk factors for

OSAHS<sup>18</sup>. This study demonstrated that the average AHI of the groups with BMI  $\geq 25$  kg/m<sup>2</sup> (groups C and D) was higher than that of the groups with BMI  $< 25$  kg/m<sup>2</sup> (groups A and B). The exact underlying mechanisms that render the overweight or obese at risk of OSAHS are still unclear<sup>17</sup>; however, it may be related to airway narrowing as a result of excessive soft tissue in the neck and around the uvula<sup>19, 20</sup>. In several other case-control studies<sup>21, 22</sup>, weight loss in OSAHS patients led to a significant decrease in the frequency of apnea. Further, it has been demonstrated that weight loss is associated with a decrease in upper airway collapsibility in OSAHS<sup>22</sup>.

To our knowledge, there is no clinical evidence suggesting that hypertension causes OSAHS in humans. On the contrary, epidemiological and animal experimental studies have strongly supported the possibility that OSAHS could be one of the important factors contributing to hypertension<sup>11, 13, 23, 24</sup>. These studies have used various study designs; however, most of them had large samples populations, and all the studies have attempted to strictly account for confounding factors such as BMI and sex. Moreover, the Joint National Commission on Hypertension lists OSAHS first among treatable causes of hypertension<sup>25</sup>. OSAHS causes the daytime elevation of blood pressure apparently due to multifactorial mechanisms. OSAHS also causes acute nocturnal surges in blood pressure in response to chemoreflex-mediated hypoxic stimulation of sympathetic activity with a resultant increase in peripheral vascular resistance<sup>26</sup> and circulating catecholamine levels associated with sympathetic nerve activity<sup>27</sup>. Further, it enhances vasoconstrictor sensitivity partly due to vascular remodeling by the nocturnal blood pressure surges<sup>28</sup>. Moreover, the effective treatment of OSAHS with continuous positive airway pressure (CPAP) leads to a significant decrease in both nocturnal and diurnal blood pressure<sup>29-31</sup>. The uniformity of these positive results has led some researchers to conclude that OSAHS is an important risk factor for hypertension that is independent of excess weight and other potential confounding factors and should be considered as a cause of secondary hypertension<sup>9, 25, 32</sup>.

The relationship between overweight and hypertension is complex and probably represents an interaction of several factors; however, the interaction has been strongly supported by the epidemiologic data<sup>33-35</sup>. As discussed above, considered individually, overweight and OSAHS are very strongly associated with hypertension. Furthermore, in this study, we observed that overweight and OSAHS coexist and that overweight may be conducive to OSAHS. Various putative pathophysiological mechanisms are involved in the interaction between overweight, OSAHS, and hypertension<sup>17</sup>. These mechanisms are as follows:

persistently increased sympathetic activity, a reduction of renal function, hyperleptinemia, insulin resistance, an activated renin-angiotensin system, chronic oxidative stress, systemic inflammation, endothelial dysfunction, and impaired baroreflex. The association of these mechanisms with OSAHS is thought to be complex. Although the associations found in observational studies suggest a casual relationship between OSAHS and elevated blood pressure, the potential for remediating hypertension by treating OSAHS is unclear. This particular study demonstrates that patients with severe OSAHS may have a higher probability of hypertension and that this would respond poorly to pharmacotherapy<sup>36</sup>. Paradoxically, severe hypertension can be caused by severe OSAHS. In this study, the average AHI of group D was significantly higher than that of group C. Because the average BMI of group D was statistically the highest of all the groups, it is natural that being overweight affects the severity of both OSAHS and hypertension and that OSAHS affects the severity of hypertension. Further, because the average AHI corrected for BMI was not significantly different among all groups (Table 3), hypertension did not affect the severity of OSAHS. Although subjects with overweight and hypertension may have severe OSAHS or at least be highly prone to OSAHS, the severity of overweight or obesity is a major factor for the development of severe OSAHS. As overweight and obesity are known to be risks factors for hypertension, the hypertension observed in group D may be caused by overweight or obesity. This point is consistent with the present data indicating that the BMI and AHI were significantly correlated (Fig. 2).

Excessive daytime sleepiness is a cardinal feature of OSAHS and several studies have demonstrated an improvement in daytime sleepiness after the treatment of OSAHS<sup>37, 38</sup>. Sleep fragmentation due to repeated arousals from apneas and hypopneas is thought to be the cause of excessive sleepiness in patients with OSAHS<sup>9</sup>. Because asymptomatic individuals are less likely to be evaluated for the presence of OSAHS than those who complain of sleepiness, patients presenting for evaluation and treatment of OSAHS may not be representative of the subjects with an elevated AHI in the general population. However, despite the strong association of the AHI with self-reported sleepiness, the majority of subjects for whom OSAHS was diagnosed did not report excessive sleepiness<sup>9, 39, 40</sup>. The observed variation in the resultant sleepiness was not explained; however, the perception and reporting of daytime sleepiness appear to vary greatly among individuals<sup>4</sup>. The ESS is widely used as a valid measure to evaluate the degree of daytime sleepiness<sup>41-43</sup>. In this study, the OSAHS patients with overweight and hypertension did not necessarily have the highest ESS score. However, this result needs careful consideration as the ESS is thought of as a valid measure

of daytime sleepiness. Therefore, the necessity of explaining the factors underlying the individual differences in susceptibility to daytime sleepiness has been suggested<sup>9</sup>.

The present study has 3 limitations. First, we did not include a large community-based sample population. Instead we recruited only subjects from a Japanese workplace who were anxious regarding their OSAHS symptoms. This might have resulted in the elevation of the average BMI or ESS scores. Second, pulse oximetry inherently underestimates apnea during sleep compared with full PSG, particularly in a non-obese population<sup>24</sup>, and overestimates apnea by picking up artifacts caused by body movements and vasoconstriction<sup>44</sup>. The reasons for the lower sensitivity of pulse oximetry among lean subjects have been considered to include the functional reserve of lung volume sufficient to maintain normal blood oxygen levels and the difficulty in detecting hypopneic events that do not cause oxygen desaturation<sup>24</sup>. In fact, in this study, 2 subjects with a 2% ODI <5 dips/h were diagnosed as having OSAHS by PSG. Third, the passage of screening in this study was not uniform. Consequently, 162 of the 313 subjects with a 2% ODI >5 dips/h did not undergo PSG. Because of this we could not prove the validity of home pulse oximetry for the screening test of OSAHS.

In conclusion, the OSAHS patients with overweight and hypertension in this study had a higher AHI than those with only overweight, with only hypertension, or with neither overweight nor hypertension. The level of daytime sleepiness evaluated by the ESS in this study was virtually the same in all OSAHS patients regardless of the degree of overweight or hypertension. Based on these observations, it is suggested that it is necessary to positively recommend PSG to men who are suspected of having OSAHS with overweight and hypertension even if they do not suffer from daytime sleepiness.

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## References

- 1) He J, Kryger MH, Zorick FJ, Conway W and Roth T: Mortality and apnea index in obstructive sleep apnea. Experience in 385 male patients. *Chest* 94, 9-14 (1988)
- 2) Yamashiro Y and Kryger MH: Why should sleep apnea be diagnosed and treated? *Clin Pulm Med* 1, 250-259 (1994)
- 3) Smith R, Ronald J, Delaive K, Walld R, Manfreda J and Kryger MH: What are obstructive sleep apnea patients being treated for prior to this diagnosis? *Chest*

- 121, 164–172 (2002)
- 4) Caples SM, Gami AS and Somers VK: Obstructive sleep apnea. *Ann Intern Med* 142, 187–197 (2005)
  - 5) Ip MS, Lam B, Launder IJ, Tsang KW, Chung KF, Mok YW and Lam WK: A community study of sleep-disordered breathing in middle-aged Chinese men in Hong Kong. *Chest* 119, 62–69 (2001)
  - 6) Strohl KP and Redline S: Recognition of obstructive sleep apnea. *Am J Respir Crit Care Med* 154, 279–289 (1996)
  - 7) Vgontzas AN, Tan TL, Bixler EO, Martin LF, Shubert D and Kales A: Sleep apnea and sleep disruption in obese patients. *Arch Intern Med* 154, 1705–1711 (1994)
  - 8) Peppard PE, Young T, Palta M, Dempsey J and Skatrud J: Longitudinal study of moderate weight change and sleep-disordered breathing. *JAMA* 284, 3015–3021 (2000)
  - 9) Young T, Peppard PE and Gottlieb DJ: Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med* 165, 1217–1239 (2002)
  - 10) Young T, Peppard P, Palta M, Hla KM, Finn L, Morgan B and Skatrud J: Population-based study of sleep-disordered breathing as a risk factor for hypertension. *Arch Intern Med* 157, 1746–1752 (1997)
  - 11) Nieto FJ, Young TB, Lind BK, Shahar E, Samet JM, Redline S, D'Agostino RB, Newman AB, Lebowitz MD and Pickering TG: Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. *Sleep Heart Health Study. JAMA* 283, 1829–1836 (2000)
  - 12) Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Leiby BE, Vela-Bueno A and Kales A: Association of hypertension and sleep-disordered breathing. *Arch Intern Med* 160, 2289–2295 (2000)
  - 13) Peppard PE, Young T, Palta M and Skatrud J: Prospective study of the association between sleep-disordered breathing and hypertension. *N Engl J Med* 342, 1378–1384 (2000)
  - 14) Durán J, Esnaola S, Rubio R and Iztueta Á: Obstructive sleep apnea-hypopnea and related clinical features in a population-based sample of subjects aged 30 to 70 yr. *Am J Respir Crit Care Med* 163, 685–689 (2001)
  - 15) Hu FB, Willett WC, Colditz GA, Ascherio A, Speizer FE, Rosner B, Hennekens CH and Stampfer MJ: Prospective study of snoring and risk of hypertension in women. *Am J Epidemiol* 150, 806–816 (1999)
  - 16) Johns MW: A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 14, 540–545 (1991)
  - 17) Wolk R, Shamsuzzaman AS and Somers VK: Obesity, sleep apnea, and hypertension. *Hypertension* 42, 1067–1074 (2003)
  - 18) Pack AI: Obstructive sleep apnea. *Adv Intern Med* 39, 517–567 (1994)
  - 19) Davies RJ, Ali NJ and Stradling JR: Neck circumference and other clinical features in the diagnosis of the obstructive sleep apnoea syndrome. *Thorax* 47, 101–105 (1992)
  - 20) Sériés F, Chakir J and Boivin D: Influence of weight and sleep apnea status on immunologic and structural features of the uvula. *Am J Respir Crit Care Med* 170, 1114–1119 (2004)
  - 21) Smith PL, Gold AR, Meyers DA, Haponik EF and Bleecker ER: Weight loss in mildly to moderately obese patients with obstructive sleep apnea. *Ann Intern Med* 103, 850–855 (1985)
  - 22) Schwartz AR, Gold AR, Schubert N, Stryzak A, Wise RA, Permutt S and Smith PL: Effect of weight loss on upper airway collapsibility in obstructive sleep apnea. *Am Rev Respir Dis* 144, 494–498 (1991)
  - 23) Brooks D, Horner RL, Kozar LF, Render-Teixeira CL and Phillipson EA: Obstructive sleep apnea as a cause of systemic hypertension. Evidence from a canine model. *J Clin Invest* 99, 106–109 (1997)
  - 24) Tanigawa T, Tachibana N, Yamagishi K, Muraki I, Kudo M, Ohira T, Kitamura A, Sato S, Shimamoto T and Iso H: Relationship between sleep-disordered breathing and blood pressure levels in community-based samples of Japanese men. *Hypertens Res* 27, 479–484 (2004)
  - 25) Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr and Roccella EJ: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 289, 2560–2572 (2003)
  - 26) Somers VK, Dyken ME, Clary MP and Abboud FM: Sympathetic neural mechanisms in obstructive sleep apnea. *J Clin Invest* 96, 1897–1904 (1995)
  - 27) Carlson JT, Hender J, Elam M, Ejnell H, Sellgren J and Wallin BG: Augmented resting sympathetic activity in awake patients with obstructive sleep apnea. *Chest* 103, 1763–1768 (1993)
  - 28) Kraiczki H, Hender J, Peker Y and Carlson J: Increased vasoconstrictor sensitivity in obstructive sleep apnea. *J Appl Physiol* 89, 493–498 (2000)
  - 29) Faccenda JF, Mackay TW, Boon NA and Douglas NJ: Randomized placebo-controlled trial of continuous positive airway pressure on blood pressure in the sleep apnea-hypopnea syndrome. *Am J Respir Crit Care Med* 163, 344–348 (2001)
  - 30) Pepperell JC, Ramdassingh-Dow S, Crosthwaite N, Mullins R, Jenkinson C, Stradling JR and Davies RJ: Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised parallel trial. *Lancet* 359, 204–210 (2002)
  - 31) Becker HF, Jerrentrup A, Ploch T, Grote L, Penzel T, Sullivan CE and Peter JH: Effect of nasal continuous positive airway pressure treatment on blood pressure in patients with obstructive sleep apnea. *Circulation* 107, 68–73 (2003)
  - 32) Pankow W, Lies A and Lohmann FW: Sleep-disordered breathing and hypertension. *N Eng J Med* 343, 966 (2000)
  - 33) Kannel WB, Brand N, Skinner JJ Jr, Dawber TR and McNamara PM: The relation of adiposity to blood pressure and development of hypertension. *The*

- Framingham study. *Ann Intern Med* 67, 48–59 (1967)
- 34) Garrison RJ, Kannel WB, Stokes J 3rd and Castelli WP: Incidence and precursors of hypertension in young adults: the Framingham Offspring Study. *Prev Med* 16, 235–251 (1987)
- 35) Jones DW, Kim JS, Andrew ME, Kim SJ and Hong YP: Body mass index and blood pressure in Korean men and women: the Korean National Blood Pressure Survey. *J Hypertens* 12, 1433–1437 (1994)
- 36) Lavie P and Hoffstein V: Sleep apnea syndrome: a possible contributing factor to resistant. *Sleep* 24, 721–725 (2001)
- 37) Ballester E, Badia JR, Hernandez L, Carrasco E, de Pablo J, Fornas C, Rodriguez-Roisin R and Montserrat JM: Evidence of the effectiveness of continuous positive airway pressure in the treatment of sleep apnea/hypopnea syndrome. *Am J Respir Crit Care Med* 159, 495–501 (1999)
- 38) Engleman HM, Kingshott RN, Wraith PK, Mackay TW, Deary IJ and Douglas NJ: Randomized placebo-controlled crossover trial of continuous positive airway pressure for mild sleep Apnea/Hypopnea syndrome. *Am J Respir Crit Care Med* 159, 461–467 (1999)
- 39) Gottlieb DJ, Whitney CW, Bonekat WH, Iber C, James GD, Lebowitz M, Nieto FJ and Rosenberg CE: Relation of sleepiness to respiratory disturbance index: the Sleep Heart Health Study. *Am J Respir Crit Care Med* 159, 502–507 (1999)
- 40) American Sleep Disorders Association Atlas Task Force: EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. *Sleep* 15, 173–184 (1992)
- 41) Banno K, Al Sabbagh A, Delaive K, Higami S and Kryger MH: Experience in using split-day studies for suspected obstructive sleep apnea syndrome. *Respir Med* 99, 1334–1339 (2005)
- 42) Goldstein IB, Ancoli-Israel S and Shapiro D: Relationship between daytime sleepiness and blood pressure in healthy older adults. *Am J Hypertens* 17, 787–792 (2004)
- 43) Melendres MC, Lutz JM, Rubin ED and Marcus CL: Daytime sleepiness and hyperactivity in children with suspected sleep-disordered breathing. *Pediatrics* 114, 768–775 (2004)
- 44) Netzer N, Eliasson AH, Netzer C and Kristo DA: Overnight pulse oxymetry for sleep-disordered breathing in adults: a review. *Chest* 120, 625–633 (2001)