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SCIENTIFIC INVESTIGATIONS

Polysomnographic analysis of respiratory events during sleep in young nonobese Japanese adults without clinical complaints of sleep apnea

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Study Objectives: The present study aimed to investigate the occurrence and characteristics of apnea-hypopnea events in young nonobese healthy Japanese participants.

Methods: One hundred and three young adult participants without sleep complaints (men: 56; women: 47; age: 24.5 ± 3.0 years; body mass index: 20.9 ± 1.8 kg/m^2) underwent 2-night polysomnography. Data on the 2nd night were scored according to American Academy of Sleep Medicine criteria version 2.1. The apnea-hypopnea index (AHI) was estimated. The arousal threshold was calculated in participants with AHI ≥ 5 events/h. Apnea-hypopnea events were rescored by 3 other criteria issued by the American Academy of Sleep Medicine (AASM): Chicago criteria in 1999 and recommended and alternative criteria in 2007.

Results: Participants had good sleep characterized by high sleep efficiency (93.2%). Mean AHI of AASM 2.1 recommended criteria was 4.0 ± 5.3 events/h. AHI was significantly higher in men (median [range] = 4.0[.3–35.8] events/h) than in women (1.6 [.1–18.1] events/h). The prevalence rates of AHI ≥ 5 events/h and ≥ 15 events/h were 25.2 and 3.9%, respectively. The arousal threshold was estimated as −7.7 ± 2.6 cm H_2O. AHI was lower for AASM 2007 recommended criteria (.8 [.0–18.2 events/h]) and AASM 2007 alternative (2.0 [.1–32.2] events/h) than for AASM version 2.1 recommended criteria (2.4 [.1–32.9] events/h) and AASM Chicago (4.6 [.1–35.8] events/h). The percentage of participants with AHI ≥ 5 events/h was approximately 2-fold higher with AASM Chicago (44.6%) than with AASM version 2.1 recommended criteria.

Conclusions: The present study demonstrated that 25% of young nonobese Japanese participants had subclinical obstructive sleep apnea. The presence of frequent airflow limitations may be a risk factor for the development of obstructive sleep apnea in Japanese individuals.

Keywords: sleep-related breathing disorders, polysomnography, definitions of hypopnea, normative data

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Ethnicity, diagnostic equipment, and the respiratory event definition adopted influence the prevalence of obstructive sleep apnea; however, limited polysomnographic information is currently available on respiratory characteristics during sleep in normal young Asian participants. We investigated the occurrence and characteristics of apnea-hypopnea events in young nonobese healthy Japanese participants without sleep complaints using in-lab polysomnography.

Study Impact: The present study demonstrated that 25% of young nonobese Japanese participants had subclinical obstructive sleep apnea. The analysis of respiratory events using the different rules for scoring hypopnea showed a high frequency of respiratory events with airflow limitations without desaturation or arousal in this population.

INTRODUCTION

Sleep is characterized by a compromised upper airway space due to weaker upper airway muscle tone than that during wakefulness.[1] In healthy participants, physiological airway narrowing during sleep may be balanced by the decreased respiratory demands associated with low metabolic functions.[2] However, this balance during sleep may be disturbed when physical (eg, obesity and micrognathia) and physiological (eg, hypotonia) conditions cause the repetitive occurrence of partial and/or complete airway obstruction, as observed with obstructive sleep apnea (OSA). Therefore, respiration during sleep may exhibit a continuous and divergent spectrum from normal to pathological conditions.

In adults, the prevalence of OSA increases with age, particularly after middle age.[3,4] A major factor contributing to age-related increases in the prevalence of OSA is weight gain or obesity, which exacerbates compromised upper airways during sleep. In the general population, the prevalence of OSA as apnea-hypopnea index (AHI) ≥ 5 events/h was found to vary markedly among studies (between 9 and 38%).[3] Ethnicity, diagnostic equipment, and the respiratory event definition adopted influence the prevalence of OSA.[4] The majority of studies using polysomnography (PSG) have been from Western

countries,[5–8] and no information has been obtained using PSG on the prevalence of OSA and sleep variables in Japan. Previous studies reported that Asian patients with OSA are leaner and have a smaller craniofacial structure than the white population with OSA.[9,10] Therefore, a young Asian population may be predisposed to airway narrowing during sleep. However, limited PSG information is currently available on respiratory characteristics during sleep in normal young Asian participants and the presence of subgroups with asymptomatic OSA.

Therefore, the present study aimed to investigate normal values for sleep variables and the occurrence of respiratory events in young nonobese Japanese participants without sleep complaints using in-lab PSG. To achieve this, respiratory events were assessed by 4 different scoring criteria (American Academy Sleep Medicine [AASM] Chicago [Chicago],[11] AASM2007 recommended [2007Rec] and alternative [2007Alt],[12] and AASM version 2.1 [Ver2.1])[13–14] that provide information on the different types of hypopneic respiratory events. The arousal threshold was also assessed to clarify the relationship between respiratory events and nonanatomical factors in the subgroup with respiratory events.[15–17]

METHODS

Participants

One hundred and ten young adult volunteers (age: 24.5 ± 3.0 years) were recruited via flyers posted at Osaka University and introductions by participants. They were undergraduate and graduate students in Osaka University and other universities and university staff in Osaka University. Applications were allowed if there were no concerns and dissatisfaction with sleep, no history of medical diseases, not taking medications, and ability to stay at the sleep laboratory for 2 nights. Prior to sleep recording, participants completed self-administrated questionnaires on sleep habits and qualities (Japanese version of the Epworth Sleepiness Scale, the Pittsburgh Sleep Quality Index) and health-related assessments. They also filled out an itemized list containing sleep-related issues, caffeine and alcohol consumption, smoking, and medications. On the day of PSG, participants were interviewed for sleep habits and sleep-related issues to confirm the absence of the following, which were exclusion criteria: the presence of any signs or symptoms related to sleep issues and disorders, such as snoring, respiratory pauses, severe day-time sleepiness, insomnia symptoms (eg, difficulty falling asleep and frequent awakening), sleep paralysis, nightmares, nocturnal behavior, and an irregular lifestyle (ie, part-time job at night and day and night reversal). Trained dentists (AT, SH, and TK) performed a regular oral examination to confirm that participants had at least 28 teeth without malocclusion or craniofacial deformities, such as progenia, prognathism, crowded dentitions, and open bites. Written informed consent was obtained from all participants for participation in sleep recordings in the present study. None of the participants had regular bedpartners. Seven of the initial 110 volunteers screened for the study were excluded for the following reasons: 4 drop outs after the first night and 3 due to sensor issues. Therefore, data from 103 participants (56 men and 47 women, age: 24.5 ± 3.0 years, body mass index [BMI]: 20.9 ± 1.8 kg/m^2) were ultimately analyzed. The study protocol was approved by the Ethics Committees of the Graduate School and School of Dentistry, Osaka University and Osaka University Dental Hospital.

Polysomnography

Participants underwent PSG on 2 consecutive nights in the sleep research laboratory at the Osaka University Graduate School of Dentistry. The sleep laboratory had a sound-attenuated and furnished bedroom. Technicians and/or researchers attended the recording in a separate monitoring room. During the night, participants were permitted to use the restroom with electrodes and sensors still attached if they made a request to the attending technician. Participants went to bed between 10:30 and 11:00 PM and woke up between 6:30 and 7:00 AM. The first night was used for habituation to the sleep laboratory environment.

According to AASM Manual Version 2.1 (Ver2.1,[13,14] the PSG montage included electroencephalography (F3-M2, F4-M1, C3-M2, C4-M1, O1-M2, and O2-M1); electro-oculography (E1-M2 and E2-M1); electromyography of submental muscles (ChinZ, Chin1, and Chin2) and the anterior tibial muscle; electrocardiography; and oronasal thermistor and nasal pressures for airflow, chest, and abdomen respiratory movements; and oxygen measured by pulse oximetry (Spo_2). Signals were recorded by commercial software using Embla N7000 (Natus Medical Incorporated, Pleasanton, CA) at a sampling rate of 200 Hz with .3- to 70-Hz filters for electroencephalography and electro-oculography and higher than 10 Hz for electromyography. Data obtained on the 2nd night were analyzed in the present study.

Scoring respiratory events

To examine the sleep architecture, PSG data were initially scored according to AASM Scoring Manual Version 2.1. To assess AHI, respiratory events were scored using currently recommended criteria published in 2014 (AASM Version 2.1 [Ver2.1]).[13,14] Apnea events were scored as a decrease in the peak signal excursion by ≥ 90% of the pre-event baseline with a duration of ≥ 10 seconds using an oronasal thermistor. Hypopnea events were defined by peak signal excursions with a decrease in nasal pressure by ≥ 30% of the pre-event baseline with a duration of ≥ 10 seconds in association with the presence of ≥ 3% oxygen desaturation from the pre-event baseline or the occurrence of an arousal (AASM Version 2.1 recommended criteria [2.1Rec]). PSG data were scored by one of the authors, S.N., who is a Registered Polysomnographic Technologist.

To assess the characteristics of respiratory events in the study population, hypopnea events were additionally scored according to the following 3 previously published scoring criteria. Adopted from the AASM manual for the scoring of sleep and associated events,[12] hypopnea events were defined as ≥ 30% reduction in nasal pressure signal excursions from the baseline with ≥ 4% desaturation from the pre-event baseline (2007Rec). The alternative definition in the AASM2007 was also used: ≥ 50% reduction in nasal pressure signal excursions in association with ≥ 3% desaturation or arousal (2007Alt). The criteria published by the AASM Task Force 1999[11] were used to score hypopnea events (Chicago); hypopnea events were defined as either ≥ 50% airflow reduction from the baseline or a

Table 1—Participant characteristics.

Sex, Men:Women	56:47	Men: 56	Women: 47	*P*
Age years	24.5 ± 2.9	24.6 ± 2.1	24.5 ± 3.2	
Height (cm)	166.6 ± 8.3	172.7 ± 5.9	159.5 ± 4.6	.40
Weight (kg)	58.2 ± 8.5	63.3 ± 7.3	51.6 ± 4.7	< .01*
BMI (kg/m^2)	20.9 ± 1.8	21.3 ± 1.7	20.3 ± 1.5	<.01*
Overweight (BMI > 25 kg/m^2)	2	1	1	.90[a]
Smokers	13	10	3	.08[a]
JESS	9.5 ± 4.2	9.8 ± 4.3	9.1 ± 4.1	.50
TST (min)	437.0 ± 42.2	440.0 ± 49.4	433.2 ± 31.8	.06
Sleep efficiency (%)	93.2 ± 6.5	92.8 ± 7.6	93.8 ± 5.0	.41
Sleep latency (min)	7.4 ± 12.8	7.0 ± 13.7	7.9 ± 11.8	.17
REM latency (min)	99.2 ± 42.4	94.1 ± 40.7	103.0 ± 44.3	.44
Sleep stage proportion, % of TST				
N1	11.6 ± 5.2	13.1 ± 5.5	9.7 ± 3.8	.01*
N2	46.5 ± 7.0	46.4 ± 7.6	46.6 ± 6.2	.93
N3	22.8 ± 6.4	21.4 ± 6.5	24.6 ± 6.1	.02*
R	19.1 ± 4.0	19.1 ± 4.2	19.1 ± 3.9	.93
ArI (times/h)	14.3 ± 5.8	15.6 ± 6.1	12.7 ± 5.0	.01*
PLMI (events/h)	1.3 ± 3.0	1.2 ± 2.5	1.4 ± 3.6	.83
3%ODI	2.7 ± 4.1	3.9 ± 5.1	1.4 ± 1.8	<.01*
AHI (2.1Rec) (events/h)	4.0 ± 5.3	5.7 ± 6.5	2.2 ± 2.2	<.01*
NREM AHI (events/h)	3.2 ± 4.8	4.5 ± 60	1.5 ± 1.5	<.01*
REM AHI (events/h)	8.2 ± 10.1	10.1 ± 10.7	8.1 ± 7.8	<.01*
HI (2.1Rec) (events/h)	3.1 ± 4.0	6.5 ± 19.0	1.4 ± 1.5	<.01*
NREM HI (events/h)	2.3 ± 3.7	3.4 ± 4.5	.9 ± 1.0	<.01*
REM HI (events/h)	6.1 ± 7.1	7.7 ± 7.6	3.6 ± 4.6	<.01*

Values are presented as means ± standard deviation.*Mann-Whitney *U* test between men and women. [a]Chi-squared test. AASM = American Academy of Sleep Medicine, AHI = apnea-hypopnea index, ArI = arousal index, BMI = body mass index, HI = hypopnea index, JESS = Japanese version of the Epworth Sleepiness Scale, NREM = non-rapid eye movement, ODI = oxygen desaturation index, PLMI = periodic limb movements in the sleep index, 2.1Rec = AASM version 2.1 recommended criteria, REM = rapid eye movement, TST = total sleep time.

marked reduction in the airflow amplitude, not reaching the aforementioned criterion, but associated with either oxygen desaturation of ≥ 3% or arousal (Chicago).

Respiratory arousal threshold

The respiratory arousal threshold (ArTH) was calculated in a subsample with AHI more than 5 events/h based on 2.1Rec. ArTH was estimated using AHI scored by 2.1Rec, according to a recently validated score derived from standard PSG variables.[16,17] Specifically, a low ArTH was defined as a score of 2 or more on the following 3-point scale: (AHI < 30 events/h sleep) + (nadir Spo_2 > 82.5%) + (fraction of hypopnea > 58.3%). This approach shows high sensitivity (80%) and specificity (88%) for detecting patients with OSA with a low ArTH.[16] We also estimated the ArTH values of each participant using the following multiple linear regression model described by Edwards and colleagues[16,17]: arousal threshold = −65.391 + (.0636 × age) + (3.692 × sex [where men = 1, women = 0]) − (.0314 × BMI) − (.108 × AHI) + (.533 × nadir Spo_2) + (.0906 × % hypopnea).

Statistical analysis

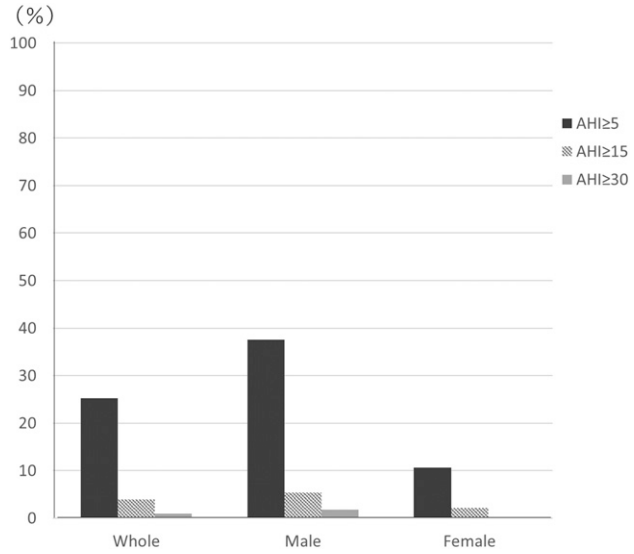
PSG variables scored by 2.1Rec and ArTH data are presented as means ± standard deviation. Data on AHI scored by the 4 scoring criteria are presented as median (range). In 2-group comparisons, nonparametric statistics (the Mann-Whitney *U* test) were applied. The Friedman test followed by the post hoc Wilcoxon test was used to compare AHI among the 4 scoring criteria. Univariate comparisons between groups were performed using the chi-squared test. McNemar tests were used to compare the percentage of patients with AHI of more than 5 or 15 events/h for the 4 scoring criteria. The level of significance was defined as $P < .05$. All analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan.[18]

RESULTS

Sleep variables

Demographic and sleep variables for 103 participants are shown in **Table 1**. The mean BMI was 20.9 ± 1.8 kg/m^2. The mean

Figure 1—Prevalence of obstructive sleep apnea



The prevalence of an apnea-hypopnea index (AHI) ≥ 5, ≥ 15, and ≥ 30 events/h according to the recommended American Academy of Sleep Medicine Version 2.1[13] criteria in all, male, and female participants.

total sleep time was 437.0 ± 42.2 minutes with high sleep efficiency (93.2 ± 6.5%). A significant sex difference was observed for sleep variables. Men had a significantly higher percentage of N1 sleep (13.1%) and lower percentage of N3 sleep (21.4%) than women (N1: 9.7%, $P = .01$ and N3: 24.6%, $P = .02$). Arousal was more frequent in men (mean arousal index: 15.6 times/h) than in women (12.7 times/h, $P = .01$).

Respiratory events

According to 2.1Rec, mean AHI was 4.0 events/h in the study population. Mean AHI was significantly higher in men (5.7 events/h) than in women (2.2 events/h; $P = .002$). The oxygen desaturation index, calculated by the frequency of more than a 3% decrease in Spo_2, was significantly higher in men (4.0 events/h) than in women (1.4 events/h; $P = .0001$). Mean Spo_2 was significantly lower in men (96.8%) than in women (97.1%, $P = .0005$).

Figure 1 shows the percentage of participants with an AHI more than 5 events/h in young nonobese Japanese adult participants according to the 2.1Rec hypopnea criteria. Approximately one-fourth of participants (25.2%) had AHI of 5 events/h or more, and this was more frequent in men (37.5%) than in women (10.6%, chi-squared test: $P = .0018$). Furthermore, 3.9% of participants had AHI ≥ 15 events/h, and this was more frequent in men (5.4%) than in women (2.1%) ($P = .39$).

Arousal threshold

Twenty-six participants with AHI of more than 5 events/h according to 2.1Rec were used to analyze the arousal threshold (21 men and 5 women; age: 26.5 ± 4.0 years, BMI: 21.5 ± 2.2 kg/m^2) (**Table 2**). All of these participants had low ArTH (a score of 2 or more, [AHI < 30 events/h sleep], [nadir Spo_2 > 82.5%], [fraction of hypopnea > 58.3%)] and the mean estimated ArTH value was estimated to be −7.5 ± 2.6 cm H_2O (−3.0 to −12.8 cm H_2O).

Table 2—The estimated value of the respiratory arousal threshold in a subsample with AHI more than 5 events/h with 2.1Rec.

Men:Women	21:5
Age (y)	26.4 ± 3.8
Height (cm)	171.0 ± 7.2
Weight (kg)	64.6 ± 9.0
BMI (kg/m^2)	22.0 ± 2.0
AHI (2.1Rec) (events/h)	10.9 ± 7.3
Arousal threshold (cm H_2O)	-7.7 ± 2.6

Values presented as means ± standard deviation. AHI = apnea-hypopnea index, BMI = body mass index, 2.1Rec = AASM version 2.1 recommended criteria.

Comparison of AHI among scoring criteria

Table 3 shows the AHI and hypopnea index calculated by 2.1Rec, 2007Rec, 2007Alt, and Chicago. AHI significantly differed among the scoring criteria ($P < .001$, Friedman test). The median AHI was the highest with Chicago (4.6 [.1–35.8] events/h), decreased to 2.1Rec (2.4 [.1–32.9] events/h) and 2007Alt (2.0 [.1–32.2] events/h) and was the lowest with 2007Rec (.8 [0–18.2] events/h). Post hoc comparisons revealed significant differences within each set of criteria. The influence of criteria was similar regardless of sex.

Prevalence of OSA

Using Chicago, 44.6% of participants (46/103) had AHI of 5 events/h or more, while similar AHI was only observed in 8.4% (7/103) with 2007Rec. Using 2007Rec, the percentage of participants with AHI ≥ 5 events/h was significantly lower (8.4%) and that of Chicago (44.6%) was significantly higher ($P < .001$) than that of 2.1Rec (25.2%). According to the Chicago criteria, 11.6% of participants (12; 10 men, 2 women) had AHI of 15 events/h or more. Furthermore, only the Chicago definition had a significantly higher rate ($P = .02$) than 2.1Rec (**Table 4**).

DISCUSSION

To the best of our knowledge, this is the first study to assess the presence of respiratory events using full-night PSG in nonobese healthy young Japanese participants with a BMI within the normal range in Japan.[19] Mean AHI assessed by 2.1Rec was 4.0 events/h in all participants, and 25% of participants had AHI 2.1Rec ≥ 5 events/h with a low arousal threshold. With the other scoring criteria, AHI significantly differed among the 4 scoring rules: it was lower for 2007Rec and 2007Alt than for Ver2.1 and Chicago. The percentage of participants with AHI ≥ 5 events/h was the lowest with 2007Rec (only 8.4%), whereas it was the highest for Chicago (44.6%). These results suggest that

Table 3—Apnea-hypopnea indices according to hypopnea criteria.

	AHI by 2.1Rec		AHI by 2007Rec		AHI by 2007Alt		AHI by Chicago		*P**
All	2.4 (4.3)	9.4	.8 (1.5)	3.8	2.0 (3.8)	8.1	4.6 (7.0)	15.8	< .001
Men	4.0 (5.5)	13.7	1.2 (1.8)	5.0	3.2 (5.0)	12.5	6.7 (9.5)	17.9	< .001
Women	1.6 (2.0)	4.7	.5 (1.1)	2.5	1.3 (2.1)	4.3	3.5 (5.9)	9.7	< .001

All values are shown as median events per hour (interquartile ranges) and 90th percentiles. *Friedman test. AASM = American Academy of Sleep Medicine, AHI = apnea-hypopnea index, Chicago = AASM 1999 Chicago criteria, 2007Alt = AASM 2007 alternative criteria, 2007Rec = AASM 2007 recommended criteria, 2.1Rec = AASM version 2.1 recommended criteria.

Table 4—Prevalence of obstructive sleep apnea.

OSA	2.1Rec	2007Rec	2007Alt	Chicago
AHI ≥ 5 (events/h)	25.2%[a,b]	6.8%[a]	22.3%	44.6%[b]
AHI ≥ 15 (events/h)	3.9%[c]	1.9%	2.9%	11.6%[c]

[a] and [b]P < .01, [c]P = .02, McNemar tests. AASM = American Academy of Sleep Medicine, AHI = apnea-hypopnea index, Chicago = AASM 1999 Chicago criteria, 2007Alt = AASM 2007 alternative criteria, 2007Rec = AASM 2007 recommended criteria, 2.1Rec = AASM version 2.1 recommended criteria, OSA = obstructive sleep apnea.

healthy nonobese young Japanese adults exhibit physiological signs of upper airway narrowing during sleep.

AHI and sleep variables in Japanese young adults

To date, few polysomnographic studies have been conducted to investigate the occurrence of respiratory events during sleep in young healthy participants using the current standard scoring criteria (2.1Rec) for respiratory events. Previous studies were generally performed on middle-aged participants,[9,20,21] and only a few were conducted in non-Asian countries. The standard scoring criteria for scoring respiratory events have been modified over the years.[11–14] Therefore, caution is needed when interpreting the present results and previous findings. A previous study on 100 healthy white participants reported that 20 participants younger than 30 years with a relatively high BMI (< 30 kg/m^2; 11 men and 9 women) had a median AHI of .5 events/h (.0–8.8) with a 90th percentile of 3.1 events/h.[22] In another study performed on 206 white participants from Germany, 34 young women and 39 men younger than 30 years (BMI unknown) had mean AHI of .9 and 1.7 events/h, respectively.[23] In a recent meta-analysis of routine PSG parameters worldwide, including East Asia (approximately 4% of samples), mean AHI was 1.6 events/h for participants aged between 18 and 34 years; however, studies using 2.1Rec or earlier criteria were included.[24] The present results showed that the median AHI in Japanese young adults was 2.4 events/h (.3–32.9), with a 90th percentile of 8.9 events/h or a mean of 4.0 ± 5.3 events/h when 2.1Rec was used (**Table 5**). In a study in which Type 3 monitoring was performed on 487 Japanese medical students with a similar age (24.5 years) and BMI (22.3 kg/m^2) to the participants in the present study, the respiratory event index was 5.7 ± 6.6.[25] Therefore, based on limited information, young nonobese Japanese adults have a higher AHI with larger variations than non-Asian participants. However, the present results were consistent with previous findings in terms of sex differences in sleep and respiratory variables, such as AHI: healthy young men had lower sleep quality (a higher percentage of stage N1 and higher arousal index) and higher respiratory variables (AHI, mean Spo_2, and oxygen desaturation index 3%) than women; however, sleep variables were within the normal ranges.[22–24]

The present results also demonstrated that 25.2% of healthy young adults had AHI of higher than ≥ 5 events/h, although they were nonobese (BMI: 20.9 ± 1.8 kg/m^2). More importantly, 3.9% of participants had AHI ≥ 15 events/h, a level at which OSA may be diagnosed in the absence of clinical symptoms. Limited information is currently available on the prevalence of OSA using PSG recording (Type 1 or 2) in Japan. A previous study using pulse oximetry monitoring (Type 4) in 1,313 participants reported a prevalence of 4.5% in participants aged 20–39 years and 8.5% in those aged 40–69 years.[26] Using Type 3 monitoring on 487 Japanese medical students, 29.6% were found to have respiratory event index > 5 events/h and 6.0% respiratory event index >15 events/h.[25] In a previous study using Type 4 monitoring on randomly selected Japanese community samples, the prevalence of OSA (respiratory event index > 15 events/h) also increased from 14.4% in individuals in their 50s to 26.0% in those in their 70s.[27] Another study using PSG after home sleep monitoring showed that the prevalence of OSA was 3.7% in 129 middle-aged participants.[28] In Asian countries, studies using PSG recordings for selected participants among the study population estimated the prevalence of OSA in China/Hong Kong (approximately 4–8% for more than 700 participants),[20,21] India (approximately 3.6–13.7% in 2,150 participants[29] and 12.2–26.9% in 2,505 participants),[30] Korea (4.5% in 547 men),[9] and Singapore (15.7% in 106 participants).[31] The estimated prevalence of OSA in these studies was consistent with the present results. However, caution is needed when interpreting the prevalence of OSA in Japanese and Asian populations due to the heterogeneity of study populations (eg, age, medical background, community, and presence of OSA symptoms) and methodologies (eg, instruments and scoring criteria). A potential sample bias in the

Table 5—Studies identifying apnea-hypopnea indices in young patients.

Study	Participants	Ethnic Group	Age (y)	BMI (kg/m^2)	Scoring Criteria	AHI (events/h)
Mitterling et al.[22]	11 men and 9 women	white	< 30	< 30	2.1Rec	.5 (.0–8.8)*
Hertenstein et al.[23]	39 men	white	< 30	unknown	2.1Rec	1.7#
	34 women					.9#
Boulos et al.[24]	meta-analysis	4% Asian	18–34	unknown	2.1Rec or earlier criteria	1.6#
Present study	56 men and 47 women	Japanese	24.5#	20.9#	2.1Rec	2.4(.3–32.9)*
						4.0#

Values are shown as medians (interquartile ranges) (*) or means (#). AHI = apnea-hypopnea index, BMI = body mass index, 2.1Rec = American Academy of Sleep Medicine 2.1 recommended criteria.

present study needs to be considered when discussing the prevalence of OSA because our study population (mainly university students) was a consecutive sample rather than a sample selected from systematic procedures (ie, random sampling from the community). Moreover, it is important to note that the above studies were performed on middle-aged populations with a higher BMI. Collectively, the significance of the present results is that more than the expected number of the population, with a male dominancy, had respiratory events that fulfill the diagnosis of OSA in young nonobese Japanese participants.

Interpretations based on the type of hypopnea

The effects of the different rules for scoring hypopnea have been recognized in comparisons of the prevalence and diagnostic outcomes of OSA.[32–36] A comparison of AHI between the different scoring criteria may represent the characteristics of respiratory events in the study population because the definitions of hypopnea events are known to differ among these 4 scoring criteria.[35,37,38] In the present study, the mean AHI of 2.1Rec (2.4 events/h) was 3-fold higher than that of 2007Rec (.8 events/h), 20% higher than that of 2007Alt (2.0 events/h), and 52% lower than that of Chicago (4.6 events/h). Therefore, the estimated prevalence of OSA (ie, AHI ≥ 5 events/h) was the lowest using 2007Rec (6.8%), the highest using Chicago (44.6%), and similar between 2.1Rec (25.2%) and 2007Alt (22.3%). Similar to the present results for young healthy participants, previous studies consistently reported that AHI assessed by 2.1Rec was significantly higher than those by 2007Rec and 2007Alt.[32,36,39,40] The higher AHI with 2.1Rec than with 2007Rec and 2007Alt is related to the inclusion of events with cardiorespiratory and cortical consequences (eg, ≥ 3% desaturation or electroencephalographyarousal) and a lower flow reduction (eg, between ≥ 50% and ≥ 30%).

In our study population, AHI assessed by Chicago was approximately 2-fold higher than that by 2.1Rec, which is in contrast to previous findings showing that AHI and the prevalence of OSA were more likely to be similar between Chicago and 2.1Rec in patients with OSA[34] and middle-aged populations.[32] The difference between Chicago and 2.1Rec represents the inclusion of a 50% flow reduction without desaturation and electroencephalography arousal.[34] Nonobese young Japanese adults, although asymptomatic for OSA, have subclinical airflow limitations without arousal or desaturation during sleep. The presence of nondesaturating breathing disturbances may represent a predisposing condition for a milder OSA phenotype, as was recently proposed.[41] Therefore, young nonobese Japanese adults have physiological signs of upper airway narrowing and may be at risk of developing OSA when the ability to maintain upper airway patency is altered in later life.

Although the lack of quantitative data on the craniofacial morphology limits its discussion in the present study, the results obtained suggest that Japanese individuals have a narrower safety margin for the maintenance of upper airway patency against weight gain. This is supported by previous findings showing the greater significance of the craniofacial morphology in the pathophysiology of OSA in Asians than in whites,[10,42,43] ie, Asian patients with OSA are less obese than whites, although AHI is similar.[10,27,29] In addition to the anatomical endotype, nonanatomical endotypes, such as low ArTHs, are other factors that need to be considered.[15,44] Participants with AHI of 5 events/h or more (2.1Rec) showed a low ArTH (-7.5 ± 2.6 cm H_2O). These values were within the range (between 0 and -15 cm H_2O) proposed as significant for the pathogenesis of OSA in nonobese patients.[45] In addition, a low ArTH was noted in approximately half of the untreated patients with OSA.[16] Therefore, the low ArTH in young Japanese participants of the present study may underlie a high AHI despite the lack of other risk factors for OSA (ie, obesity). However, the results of ArTH need to be interpreted with caution because the equation proposed for calculating ArTH may not be applicable for ethnically diverse populations. Since the role of ArTH in the pathogenesis as well as treatment of OSA may be modified by morphology, age, and ethnicity in patients with OSA,[17] further studies are needed to investigate the roles of airflow limitations and a low ArTH in the development of OSA in young nonobese Japanese individuals.

In conclusion, the present results demonstrated that 25.2% of nonobese young healthy Japanese adults had AHI ≥ 5 events/h and 3.9% had AHI ≥ 15 events/h, with the latter being diagnosed with OSA. The analysis of respiratory events showed a high frequency of respiratory events with airflow limitations without desaturation or arousal in this population. The presence of airflow limitations and a low ArTH may also influence current sleep quality and the future onset of OSA. Long-term polysomnographic observations in this population may clarify the

factors affecting the OSA generation mode in healthy adults with normal PSG parameters.

ABBREVIATIONS

AASM, American Academy of Sleep Medicine
AHI, apnea-hypopnea index
2007Alt, AASM 2007 alternative criteria
ArTH, arousal threshold
BMI, body mass index
Chicago, AASM 1999 Chicago criteria
OSA, obstructive sleep apnea
PSG, polysomnography
Spo2, oxygen measured by pulse oximetry
2007Rec, AASM 2007 recommended criteria
2.1Rec, AASM Version 2.1 recommended criteria
Ver2.1, AASM Version 2.1 criteria)

REFERENCES

1. Ayappa I, Rapoport DM. The upper airway in sleep: physiology of the pharynx. *Sleep Med Rev*. 2003;7(1):9–33.
2. Dempsey JA, Veasey SC, Morgan BJ, O'Donnell CP. Pathophysiology of sleep apnea. *Physiol Rev*. 2010;90(1):47–112.
3. Senaratna CV, Perret JL, Lodge CJ, et al. Prevalence of obstructive sleep apnea in the general population: A systematic review. *Sleep Med Rev*. 2017;34:70–81.
4. Franklin KA, Lindberg E. Obstructive sleep apnea is a common disorder in the population-a review on the epidemiology of sleep apnea. *J Thorac Dis*. 2015;7(8):1311–1322.
5. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med*. 1993;328(17):1230–1235.
6. Franklin KA, Sahlin C, Stenlund H, Lindberg E. Sleep apnoea is a common occurrence in females. *Eur Respir J*. 2013;41(3):610–615.
7. Durán J, Esnaola S, Rubio R, Iztueta A. 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*. 2001;163(3 Pt 1):685–689.
8. Bixler EO, Vgontzas AN, Ten Have T, Tyson K, Kales A. Effects of age on sleep apnea in men: I. Prevalence and severity. *Am J Respir Crit Care Med*. 1998;157(1):144–148.
9. Kim J, In K, Kim J, et al. Prevalence of sleep-disordered breathing in middle-aged Korean men and women. *Am J Respir Crit Care Med*. 2004;170(10):1108–1113.
10. Lee RW, Vasudavan S, Hui DS, et al. Differences in craniofacial structures and obesity in Caucasian and Chinese patients with obstructive sleep apnea. *Sleep*. 2010;33(8):1075–1080.
11. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. *Sleep*. 1999;22(5):667–689.
12. Iber C, Ancoli-Israel S, Chesson AL Jr, Quan SF; for the American Academy of Sleep Medicine. *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.
13. Berry RB, Brooks R, Gamaldo CE, et al; for the American Academy of Sleep Medicine. *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications*. Version 2.1. Darien, IL: American Academy of Sleep Medicine; 2014.
14. Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. *J Clin Sleep Med*. 2012;8(5):597–619.
15. Eckert DJ, White DP, Jordan AS, Malhotra A, Wellman A. Defining phenotypic causes of obstructive sleep apnea. Identification of novel therapeutic targets. *Am J Respir Crit Care Med*. 2013;188(8):996–1004.
16. Edwards BA, Eckert DJ, McSharry DG, et al. Clinical predictors of the respiratory arousal threshold in patients with obstructive sleep apnea. *Am J Respir Crit Care Med*. 2014;190(11):1293–1300.
17. Lee RWW, Sutherland K, Sands SA, et al. Differences in respiratory arousal threshold in Caucasian and Chinese patients with obstructive sleep apnoea. *Respirology*. 2017;22(5):1015–1021.
18. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. *Bone Marrow Transplant*. 2013;48(3):452–458.
19. Nutrition NIoHa. Health Japan 21. https://www.nibiohn.go.jp/eiken/kenkounippon21/en/eiyouchousa/kekka_shintai_chousa_nendo.html Accessed April 1, 2020.
20. Ip MS, Lam B, Lauder IJ, et al. A community study of sleep-disordered breathing in middle-aged Chinese men in Hong Kong. *Chest*. 2001;119(1):62–69.
21. Ip MS, Lam B, Tang LC, Lauder IJ, Ip TY, Lam WK. A community study of sleep-disordered breathing in middle-aged Chinese women in Hong Kong: prevalence and gender differences. *Chest*. 2004;125(1):127–134.
22. Mitterling T, Högl B, Schonwald SV, et al. Sleep and respiration in 100 healthy Caucasians–A polysomnographic study according to American Academy of Sleep Medicine Standards. *Sleep*. 2015;38(6):867–875.
23. Hertenstein E, Gabryelska A, Spiegelhalder K, et al. Reference data for polysomnography-measured and subjective sleep in healthy adults. *J Clin Sleep Med*. 2018;14(4):523–532.
24. Boulos MI, Jairam T, Kendzerska T, Im J, Mekhael A, Murray BJ. Normal polysomnography parameters in healthy adults: a systematic review and meta-analysis. *Lancet Respir Med*. 2019;7(6):533–543.
25. Nishijima T, Kizawa T, Hosokawa K, et al. Prevalence of sleep-disordered breathing in Japanese medical students based on type-3 out-of-center sleep test. *Sleep Med*. 2018;41:9–14.
26. Cui R, Tanigawa T, Sakurai S, Yamagishi K, Iso H. Relationships between sleep-disordered breathing and blood pressure and excessive daytime sleepiness among truck drivers. *Hypertens Res*. 2006;29(8):605–610.
27. Yamagishi K, Ohira T, Nakano H, et al. Cross-cultural comparison of the sleep-disordered breathing prevalence among Americans and Japanese. *Eur Respir J*. 2010;36(2):379–384.
28. Asaoka S, Namba K, Tsuiki S, Komada Y, Inoue Y. Excessive daytime sleepiness among Japanese public transportation drivers engaged in shiftwork. *J Occup Environ Med*. 2010;52(8):813–818.
29. Sharma SK, Vasudev C, Sinha S, Banga A, Pandey RM, Handa KK. Validation of the modified Berlin questionnaire to identify patients at risk for the obstructive sleep apnoea syndrome. *Indian J Med Res*. 2006;124(3):281–290.
30. Reddy EV, Kadhiravan T, Mishra HK, et al. Prevalence and risk factors of obstructive sleep apnea among middle-aged urban Indians: a community-based study. *Sleep Med*. 2009;10(8):913–918.
31. Puvanendran K, Goh KL. From snoring to sleep apnea in a Singapore population. *Sleep Res Online*. 1999;2(1):11–14.
32. Hirotsu C, Haba-Rubio J, Andries D, et al. Effect of three hypopnea scoring criteria on OSA prevalence and associated comorbidities in the general population. *J Clin Sleep Med*. 2019;15(02):183–194.
33. Mansukhani MP, Kolla BP, Wang Z, Morgenthaler TI. Effect of varying definitions of hypopnea on the diagnosis and clinical outcomes of sleep-disordered breathing: a systematic review and meta-analysis. *J Clin Sleep Med*. 2019;15(5):687–696.
34. Duce B, Milosavljevic J, Hukins C. The 2012 AASM respiratory event criteria increase the incidence of hypopneas in an adult sleep center population. *J Clin Sleep Med*. 2015;11(12):1425–1431.
35. Guilleminault C, Hagen CC, Huynh NT. Comparison of hypopnea definitions in lean patients with known obstructive sleep apnea hypopnea syndrome (OSAHS). *Sleep Breath*. 2009;13(4):341–347.

36. Dean DA, Wang R, Jacobs DR, et al. A systematic assessment of the association of polysomnographic indices with blood pressure: the Multi-Ethnic Study of Atherosclerosis (MESA). *Sleep*. 2015;38(4):587–596.
37. Grigg-Damberger MM. The AASM scoring manual: a critical appraisal. *Curr Opin Pulm Med*. 2009;15(6):540–549.
38. Grigg-Damberger MM. The AASM Scoring Manual four years later. *J Clin Sleep Med*. 2012;8(3):323–332.
39. Punjabi NM. The epidemiology of adult obstructive sleep apnea. *Proc Am Thorac Soc*. 2008;5(2):136–143.
40. BaHammam AS, Obeidat A, Barataman K, Bahammam SA, Olaish AH, Sharif MM. A comparison between the AASM 2012 and 2007 definitions for detecting hypopnea. *Sleep Breath*. 2014;18(4):767–773.
41. Koch H, Schneider LD, Finn LA, et al. Breathing disturbances without hypoxia are associated with objective sleepiness in sleep apnea. *Sleep*. 2017;40(11):1–10.
42. Liu Y, Lowe AA, Zeng X, Fu M, Fleetham JA. Cephalometric comparisons between Chinese and Caucasian patients with obstructive sleep apnea. *Am J Orthod Dentofacial Orthop*. 2000;117(4):479–485.
43. Wong ML, Sandham A, Ang PK, Wong DC, Tan WC, Huggare J. Craniofacial morphology, head posture, and nasal respiratory resistance in obstructive sleep apnoea: an inter-ethnic comparison. *Eur J Orthod*. 2005;27(1):91–97.
44. Edwards BA, Redline S, Sands SA, Owens RL. More than the sum of the respiratory events: personalized medicine approaches for obstructive sleep apnea. *Am J Respir Crit Care Med*. 2019;200(6):691–703.
45. Gray EL, McKenzie DK, Eckert DJ. Obstructive sleep apnea without obesity is common and difficult to treat: evidence for a distinct pathophysiological phenotype. *J Clin Sleep Med*. 2017;13(1):81–88.

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