Cross-cultural comparison of the sleep-disordered breathing prevalence among Americans and Japanese

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Running head: SDB Prevalence in the US and Japan

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Abstract

To compare the sleep-disordered breathing prevalence among Hispanic and white Americans and Japanese, we performed a one-night sleep study with a single channel airflow monitor on 211 Hispanics and 246 whites from the Minnesota Field Center of the Multi-Ethnic Study of Atherosclerosis (MESA), and 978 Japanese from three community-based cohorts of the Circulatory Risk in Communities Study (CIRCS) in Japan.

The respiratory disturbance index and sleep-disordered breathing, defined as respiratory disturbance index \geq 15 disturbances/hr, were estimated. The sleep-disordered breathing prevalence was higher in men (34.2%) than women (14.8%), and higher among Hispanics (36.5%) and whites (33.3%) than among Japanese (18.4%), corresponding to differences in body mass index. Within body mass index strata, the race difference in sleep-disordered breathing was attenuated. This was also true when we adjusted for body mass index instead of stratification. The strong association between body mass index and sleep-disordered breathing was similar in Japanese and Americans.

The sleep-disordered breathing prevalence was lower among Japanese than the Americans. However, the association of body mass index with sleep-disordered breathing was strong, and similar among the race/ethnic groups studied. The majority of the race/ethnic difference in sleep-disordered breathing prevalence was explained by a difference in body

mass index distribution. (200 words/200 limits)

Key words: cross-sectional study, epidemiology, prevalence, sleep apnea

Introduction

Sleep-disordered breathing (SDB) is a condition of repetitive episodes of decreased or arrested respiratory airflow during sleep. In the United States, approximately 1 in 5 adults has at least mild obstructive sleep apnea (OSA), a major category of SDB, and 1 in 15 adults has OSA of moderate or worse severity [1]. More than 85% of people with OSA who might benefit from treatment remain undiagnosed [1]. However, these prevalence estimates are confined to whites since data in other race/ethnicities are scarce. Furthermore, lifestyle may also affect the prevalence of SDB, but data on cross-cultural differences in etiology of SDB are scant.

A paradox has been suggested for Asians: compared with whites, Asians are less obese but may have an equivalent or even greater prevalence or severity of SDB [2, 3]. It is hypothesized that this is due to a different craniofacial profile compared with whites [3, 4]. However, this hypothesis is highly speculative because available prevalence data from Asia derive largely from hospital-based studies. The prevalence of SDB among Asians in community settings has been rarely reported [5-7] due to the difficulty in carrying out a full polysomnogram test in such settings. In these contexts, we sought to compare the prevalence of SDB among community-based populations of Hispanics and whites in the United States, and Japanese living in Japan, using a portable sleep monitoring device. Specifically, we focused on the impact of body mass index (BMI), the most important risk factor for SDB, on race-specific prevalence of SDB. Our *a priori* hypotheses were that (1) the prevalence of SDB is higher among Hispanics and whites than among Japanese corresponding to higher BMIs, but that (2) Japanese are more influenced by elevated BMI than Americans, so that the BMI-SDB association is stronger, among Japanese than the Americans.

Methods

Study population

We included Hispanic and white participants of the Minnesota field center of the Multi-Ethnic Study of Atherosclerosis (MESA) and Japanese participants of the Akita-Osaka study and the Kyowa study, which constitute the Circulatory Risk in Community Study (CIRCS). In 2000-2002, MESA recruited and assessed cardiovascular risk factors of 6,814 men and women aged 45 to 84 years, who were free of clinically apparent cardiovascular disease at that time, and who lived in 6 US communities, including St Paul, Minnesota [8]. They were followed by clinic visits every two years. In 2007, we recruited the MESA participants of the Minnesota Field Center, who participated in the 4th MESA follow-up examination (Exam 4: 2005-2007), who were aged 50-74, were living in the Saint Paul metro area, and whose race/ethnicity was Hispanic or white. The participants underwent a one-night sleep study with a single channel airflow monitor. Of 720 eligible participants, 464 provided an informed consent and underwent the sleep study, and 457 completed the study successfully. The CIRCS is a dynamic community cohort of Japanese, consisting of 5 communities in Japan: Ikawa and Ishizawa in Akita; Yao in Osaka; Noichi in Kochi; and Kyowa in Ibaraki [9]. Annual cardiovascular checkups were provided by the local governments. All residents aged 30 or over in each community were eligible to participate. In 2006-2008 visits, we asked participants in checkups at Ikawa, Yao and Kyowa to undergo the sleep study, with the same methods and devices as for MESA. Of 6,233 people aged 50-79 who participated in the checkups, 978 randomly selected participants provided an informed consent and completed the study successfully. Since approximately 60% of the CIRCS participants were women (which is the case for most Japanese community health surveys), we settled on an annual recruiting plan to oversample male participants to be comparable with MESA (see Supplementary Table 3). Informed consent was obtained as approved by the

local institutional review committees for MESA, and those at the University of Tsukuba, Osaka University and Osaka Medical Center for Health Science and Promotion for CIRCS.

Measurement

We used a single channel airflow monitor SOMNIE (NGK Spark Plug Co. Ltd, Nagoya, Japan) to estimate the respiratory disturbance index (RDI). Details about this device are published elsewhere[10]. Briefly, the SOMNIE detects nasal and oral breathing through a sensor of polyvinylidene fluoride film, converts the airflow signals into digital data at a sampling frequency of 10 Hz, and stores the data for 24 hr until downloaded. The RDI was automatically derived from the spectral analysis of the amplitude of air flow waves using Flow.exe software (Institute of Sleep Health Promotion, Tokyo, Japan) [11]. Since the data were automatically processed, no interscorer variability exists in this study. We used examination (device recording) time instead of sleep time as the denominator for the calculation of the RDI, because the exclusion of subjective awake time on the sleep log from the recording time had proved to be useless in a validation study of this portable monitor [10]. Although the RDI is underestimated by this method, this did not affect the RDI values very much in the previous studies [10], partly due to the fact that awake RDI is significantly

higher in SDB subjects than non-SDB subjects [11]. Repeatability (r =0.92 between two night tests) and validity (sensitivity =89% and specificity =96% to detect apnea/hypopnea index (AHI) \geq 30/hr using a polysomnogram as the gold standard) of RDI values derived from this device were fairly good [10], although the RDI values from this device tended to be higher than apnea/hypopnea index values from a full polysomnogram test (our RDI values of 15.0, 11.2, 10.4, and 7.1 can be translated to AHIs of 12.5, 9.0, 8.2, and 5.2, respectively). SDB was defined as an RDI of \geq 15 disturbances/hour.

Well-trained study staff explained and demonstrated to participants how to do the sleep study, and they performed the following measurement in the home (MESA) or at the health checkup site (CIRCS). Height was measured in stocking feet, and weight was measured with light clothing. BMI was calculated as weight (kg) divided by square of height (m). Smoking status, drinking status, and amount of usual alcohol consumption (g/day) were derived from a questionnaire.

Statistical analysis

In total, 211 Hispanics and 246 whites from MESA and 978 Japanese from CIRCS were included in the study. Differences in baseline characteristics among the race/ethnic groups

were calculated using analyses of covariance, chi-square or Kruskal-Wallis rank tests. Odds ratios (OR) and 95% confidence intervals (CI) of SDB in relation to race, age and BMI groups were calculated using logistic regression models. Covariates included age (except for analysis stratified by age), race (except for analyses stratified by race), BMI (except for analysis stratified by BMI), daily alcohol consumption (continuous) and smoking status (3 categories: current, ex-, or non-smokers). Interaction of BMI with race/ethnicity in relation to SDB was tested in the logistic regression models using a cross-product term with BMI (continuous) and race/ethnicity (dichotomous). We used SAS version 9.1.3 Service Pack 4 (SAS Institute Inc., Cary, NC, USA) for the analyses. All probability values for statistical tests were two-tailed and values of p<0.05 were regarded as statistically significant.

As supplementary analyses, we performed similar analyses for questionnaire-based self-reported snoring and nocturnal apnea in the whole MESA cohort attending visit 4 (n=3,257, further including African Americans, but not Chinese Americans) and in CIRCS participants (n=5,785 at 2000-2005 surveys) aged 50-74. We excluded Chinese Americans from MESA because of the small sample size (n=430) and the narrow distribution of BMI (85% of Chinese Americans were between BMI of 17.5 to 27.4 kg/m²). The proportions of 'don't know if they snore or not' were lower among Japanese (7% for men and 15% for

women) than Hispanics (21% for men and 28% for women), Blacks (24% for men and 34% for women), Whites (20% for men and 29% for women) and Chinese Americans (22% for men and 32% for women). Sex-specific scatter diagrams of RDI by age and BMI for the three ethnic groups are also presented as Supplementary figures.

Results

The age and sex distributions were similar across the race/ethnic groups (Table 1). For men, the proportion of current drinkers was larger among whites and Japanese than among Hispanics. For women, this proportion was the largest among whites, followed by Hispanics and Japanese. The proportion of current smokers was larger among Japanese men than American men, and was larger among white women than Hispanic and Japanese women. Median values of RDI were 11.2/hr among whites, 10.4/hr among Hispanics and 7.1/hr among Japanese. Prevalence of SDB was higher among Hispanics (36.5%, n=77) and whites (33.3%, n=82) than among Japanese (18.4%, n=180). Correspondingly, mean BMI was higher among Hispanics (31.5 kg/m²) and whites (29.0 kg/m²) than among Japanese (23.5 kg/m²). Median values of RDI were higher in men (10.0/hr) than in women (7.0/hr) and the

prevalence of SDB was approximately twice as high in men as women (34.2% vs 14.7%). The race/ethnic differences were similarly observed between men and women.

The association between age and prevalent SDB was weak among whites compared with Hispanics and Japanese (Table 2) for both men and women (Figure E1 in the online data supplement). On the other hand, the prevalence of SDB was similar in BMI strata across the race/ethnic groups (Table 2), although the scatter diagram of RDI and BMI showed that RDI was lower in high BMI strata among Japanese women than Hispanic and white women (Figure E2). For example, the SDB prevalence for those with BMI of 22.5-24.9 kg/m² was 17.2% among Japanese, 18.2% among whites and 20.0% for Hispanics (p for overall difference =0.95). Similarly, the SDB prevalence for BMI \geq 30.0 kg/m² was 35.3% among Japanese, 43.8% among whites and 40.0% among Hispanics (p for overall difference =0.67) (Table 2). Multivariable-adjusted ORs of SDB for those with BMI \geq 30.0 kg/m² compared with BMI of 22.5-24.9 kg/m² were also similar between the Japanese and MESA participants; 4.15 (1.86-9.25) and 3.43 (1.53-7.92), respectively. Of note, the prevalence of SDB for BMI of 30.0-32.4 kg/m², was 42.1% (n=16) for whites, 32.6% (n=14) for Hispanics, and 40.9% (n=9) for Japanese, albeit with small sample sizes. When BMI was expressed as a continuous variable, the multivariable-adjusted odds ratio per 5 kg/m² increment was 1.82

(1.39-2.38) in Japanese and 1.42 (1.17-1.72) in Hispanic and whites pooled. There was no significant interaction of BMI with race/ethnicity in relation to SDB (p=0.11).

The multivariable adjusted ORs of SDB were 2.82 (1.98-4.02) for Hispanics compared with Japanese and 2.52 (1.81-3.51) for whites compared with Japanese. As expected, further adjustment for BMI attenuated the association: OR =1.50 (0.98-2.31) for Hispanics and 1.62 (1.11-2.36) for whites (data not shown). Race did not greatly confound the association of BMI with SDB: in the total sample, the multivariable-adjusted OR of SDB per 5 kg/m² increment of SDB was 1.70 (1.50-1.93) before adjustment for race and 1.51 (1.29-1.77) after adjustment for race.

Similarly, the prevalences of questionnaire-based snoring and apnea outcomes (Tables E1 and E2) were similar among most race/ethnic groups within each BMI stratum. The exception was that Japanese women had the lowest prevalence of sleep apnea in almost all BMI strata.

Discussion

As hypothesized, the prevalence of SDB was lower among Japanese than in the St Paul, Minnesota MESA sample. However, contrary to our second hypothesis —that Japanese are more affected by elevated BMI than Hispanics and whites—we found the association of BMI with SDB was strong and homogeneous between the race/ethnic groups, ie, no effect modification on the multiplicative scale. Furthermore, the difference in SDB prevalence between Japanese and the MESA samples was largely explained by a difference in BMI distribution, because the adjustment for BMI eliminated the race/ethnic difference in SDB prevalence. The prevalence of SDB, in both non-obese (eg, BMI of 22.5-24.9 kg/m²) and obese (BMI≥30.0 kg/m²) strata, did not differ significantly among Hispanics, whites and Japanese. Supplemental analyses of questionnaire-based snoring and apnea agreed with these results, although women, especially Japanese women, showed generally lower prevalence of SDB in the same BMI stratum than men.

Our hypothesis was based on a previous report that male sleep apnea patients of far-east Asian male extraction (Chinese, Japanese and Korean), despite being non-obese, had greater severity of RDI than did white men; this corresponded to decreased cranial base dimensions (ie, shorter anterior cranial base and narrower cranial base fracture) [4]. However, posterior airway space and hyoid position, which were also associated with prevalent OSA among Asians in that study, were less abnormal in Asian men than white men [4]. A Japanese study reported that the cephalometric characteristics of Japanese sleep apnea patients were similar with those of white patients [12]. Craniofacial difference undoubtedly contributes to the development of SDB, but the racial/ethnic difference in the prevalence or severity of SDB seems to be difficult to explain solely by cephalometric profile. Another Japanese study showed that cephalometric profile interacted with BMI in relation to SDB; that is, craniofacial profile (based on cranial base dimensions and hyoid position) was associated with the prevalence of SDB more among men with higher BMI than those with lower BMI [13].

Although our results suggested that the prevalence of SDB strongly correlated with BMI across all race/ethnic groups, it should be noted that SDB is frequent even among non-obese people. Indeed, SDB prevalence was substantial (17-20 %) among those with a lean BMI of 22.5-24.9 kg/m² regardless of cultural settings. This means that paying attention only to typical symptoms, characterized as "Pickwickian" – often described as extremely obese, always sleepy, middle-aged men – may overlook sleep apnea in non-obese patients [14].

The present study is the first to compare the prevalence of SDB directly between Hispanics, whites and Japanese in different community-based settings using identical procedures. Usage of a portable one-channel flow-sensor device, instead of a polysomnogram, has both advantages and limitations. The reliability and validity of the device was fairly good and quite comparable with full polysomnogram tests [10]. The traditional thermal sensors have been reported to be likely to overlook hypopnea events, and the polyvinylidene fluoride film sensor we used has excellent ability to detect hypopnea [15]. This portable device afforded a simple procedure for a one-night test at the participant's own home, which might have reduced resistance to participate in the study. On the other hand, our RDI are not identical to the AHI values from a polysomnogram and we did not measure oxygen desaturation, so this should be considered when comparing our SDB prevalence values with those elsewhere. We are aware that our RDI values were overestimated compared with AHI values from polysomnography as stated in the Methods section. Moreover, the median RDI values from our study were substantiallyhigher than the AHI values of landmark studies such as the Wisconsin Sleep Cohort Study [16] and the Sleep Heart Health Study [17].

Other study limitations warrant discussion. First, although the participants were from community-dwelling general populations, bias related to self-selection is possible. That is, people with sleep problems may have been likely to participate in this study. However, this issue applies to every sleep study, and again, the present study may be less affected by this than studies using the more burdensome polysomnogram. Indeed, baseline characteristics did not differ greatly between participants and non-participants in both MESA and CIRCS, although participants were somewhat younger than non-participants in CIRCS (Table E3 in the online data supplement). Second, since the distribution of BMI was quite different between Japanese and Americans, we pooled BMI ≥30 kg/m² into one stratum, which may leave residual confounding by BMI in that stratum. However, the prevalence of SDB did not differ greatly across race/ethnicities in the stratum of 30.0-32.5 kg/m², so this may not greatly affect the results. Third, although we observed a large difference in SDB prevalence between men and women, we could not conduct sex-specific analyses due to small sample sizes. However, the patterns were similar when examined sex-specifically (Figure E1 and E2) and by the supplementary sex-specific analyses of self-reported snoring and nocturnal apnea. Last, this is a cross-sectional study, so we cannot prove the association of BMI with SDB is causal.

In conclusion, the prevalence of SDB was lower in a Japanese population-based cohort than in the St Paul, Minnesota MESA sample. However, the strong association of BMI with SDB was similar between the ethnic groups studied, and most of the difference in SDB prevalence between these Japanese and Americans was explained by a difference in BMI distributions.

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Appendix

CIRCS Study Collaborators

The Circulatory Risk in Communities Study (CIRCS) is a collaborative study managed by the Osaka Medical Center for Health Science and Promotion, University of Tsukuba, Osaka University and Ehime University. The CIRCS investigators who contributed to this study are as follows: Masamitsu Konishi, Yoshinori Ishikawa, Masakazu Nakamura MD, Akihiko Kitamura, Masahiko Kiyama, Takeo Okada, Kenji Maeda, Masatoshi Ido, Masakazu Nakamura PhD, Kazuyo Kamei, Takashi Shimamoto, Minoru Iida and Yoshio Komachi, Osaka Medical Center for Health Science and Promotion, Osaka; Shinichi Sato, Chiba Prefectural Institute of Public Health, Chiba; Kazumasa Yamagishi, Kyoko Kirii, Mitsumasa Umesawa, ChoyLye Chei, Kimiko Yokota and Minako Tabata, University of Tsukuba, Tsukuba; Hiroyasu Iso, Tetsuya Ohira, Hironori Imano, Renzhe Cui and Satoyo Ikehara, Osaka University, Suita; Takeshi Tanigawa, Isao Saito, Katsutoshi Okada and Susumu Sakurai, Ehime University, Toon; Masayuki Yao, Ranryoen Hospital, Ibaraki; and Ai Ikeda and Hiroyuki Noda, Harvard School of Public Health, Boston, MA.

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	Number		N. 1 - 707			22v	Current	Current
	examined	Age (yr)	Male (%)	KUJ (/hr)*	SUB (%)	BMII (kg/m ⁻)	drinker (%)	smoker (%)
Total								
Hispanic	211	61.8	48	10.4	36.5	31.5	40	6
White	246	62.0	44	11.2	33.3	29.0	99	17
Japanese	978	63.0	46	7.1	18.4	23.5	44	16
p for overall difference	erence	0.02	0.70	<0.001	<0.001	<0.001	<0.001	0.03
Men								
Hispanic	101	61.6	I	14.1	47.5	30.8	45	12
White	108	62.1	I	15.1	50.9	28.9	71	18
Japanese	446	63.5	I	8.3	27.1	23.8	75	30
p for overall difference	erence	0.01	I	<0.001	<0.001	<0.001	<0.001	<0.001
Women								
Hispanic	110	62.0	I	9.5	26.4	32.2	36	9
White	138	61.9	I	9.3	19.6	29.0	62	17
Japanese	532	62.5	ı	5.8	11.1	23.4	19	4
n for overall difference	erence	0.60	I	<0.001	<0.001	<0.001	<0.001	<0.001

*median values †SDB defined by RDI ≥15/hr.

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Table 2. Race	e/ethnicity	/-specific	c prevalence	and odds ra	ttios of s	leep disord	Table 2. Race/ethnicity-specific prevalence and odds ratios of sleep disordered breathing in relation to age and body mass index, Minnesota	tion to age z	and body	mass ind	lex, Minnesota
MESA (Hispanics and whites) and CIRC	anics and	whites) :	and CIRCS	S (Japanese).							
	ME	MESA Hispanic		ME	MESA White	ite	All MESA¶			Japanese	
I	Number	RDI*	SDB	Number	RDI*	SDB	Odds ratio	Number	RDI*	SDB	Odds ratio
Stratified by age group (yr) [†]	age group	(yr)†									
50-54	42	8.4	21.4%	48	11.2	37.5%	1.0 (Reference)	06	4.6	14.4%	1.0 (Reference)
55-59	43	11.2	41.9%	58	10.4	34.5%	1.30 (0.69-2.47)	219	5.5	13.2%	1.06 (0.51-2.22)
60-64	49	9.6	30.6%	46	10.9	26.1%	0.81 (0.41-1.59)	248	7.1	17.3%	1.52 (0.75-3.07)
62-69	40	10.9	45.0%	42	13.5	35.7%	1.66 (0.85-3.24)	248	7.8	20.2%	1.67 (0.83-3.34)
70-74	37	13.2	46.0%	52	11.4	32.7%	1.43 (0.74-2.77)	173	9.8	26.0%	2.28 (1.11-4.65)
Stratified by body mass index (kg/m ²)‡	body mas	s index (l	kg/m ²)‡								
<20.0	1	ı	ı	9	·			112	5.6	11.6%	0.68 (0.34-1.35)
20.0-22.4	2			21	9.2	33.3%	3.27 (0.97-11.0)	263	6.5	14.5%	0.87 (0.54-1.38)
22.5-24.9	15	5.2	20.0%	33	8.0	18.2%	1.0 (Reference)	326	6.4	17.2%	1.0 (Reference)
25.0-27.4	31	11.2	35.5%	40	9.0	25.0%	1.56 (0.62-3.95)	191	8.3	26.2%	1.64 (1.04-2.56)
27.5-29.9	42	10.5	35.7%	50	10.6	30.0%	1.79 (0.74-4.37)	52	8.5	21.2%	1.33 (0.63-2.82)
≥30.0	120	10.9	40.0%	96	13.2	43.8%	3.49 (1.53-7.92)	34	12.3	35.3%	4.15 (1.86-9.25)
(30.0-32.4)	43	9.8	32.6%	38	11.6	42.1%	2.35 (0.95-5.83)	22	13.8	40.9%	5.04 (1.96-13.0)
(32.5-34.9)	33	10.3	36.4%	24	19.9	62.5%	4.69 (1.81-12.2)	8		ı	ı
(≥35.0)	44	14.9	50.0%	34	11.8	32.4%	4.32 (1.72-10.8)	4	•	ı	ı
* median values	ues										

† Odds ratios were adjusted for sex, amount of daily alcohol consumption, smoking status and body mass index. Further adjustment for race was done for MESA. Persons with missing alcohol or smoking status (n=6) were eliminated. ‡ Odds ratios were adjusted for age, sex , amount of daily alcohol consumption and smoking status. Further adjustment for race was done for

MESA. Persons with missing alcohol or smoking status (n=6) were eliminated.

Whites and Hispanics pooled