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Relationship between sleep-disordered breathing and central systolic blood pressure in a community-based population: the Toon Health Study

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Abstract

Sleep-disordered breathing (SDB) is linked with brachial blood pressure. Although central systolic blood pressure (cSBP) is a better predictor of cardiovascular diseases than is brachial blood pressure, the association between SDB and cSBP is not fully understood. This cross-sectional study included 1484 participants without cardiovascular diseases who were enrolled in the Toon Health Study between 2009 and 2012. The respiratory disturbance index (RDI) was estimated with a one-night sleep test using an airflow monitor. Participants were grouped into three categories according to RDI level: mild (<10 events/h), moderate (10 to <20 events/h), and severe (≥20 events/h). The cSBP was measured using a noninvasive automated tonometer. Multivariable-adjusted cSBP means for the mild, moderate, and severe RDI categories were, respectively, 116.0, 118.0, and 120.7 mm Hg (p for trend = 0.02) for men and 111.8, 113.7, and 111.7 mm Hg (p for trend = 0.59) for women. The association for men was no longer significant after adjusting for BMI. When stratified by BMI (<22 or ≥22 kg/m^2), the RDI was associated with cSBP among men with BMI ≥ 22 kg/m^2, and this association was of borderline significance. Augmentation index, pulse pressure amplification, and brachial blood pressure were not significantly associated with the RDI. Higher RDI values were associated with increased multivariable-adjusted cSBP means among men. This association was more evident among those with BMI ≥ 22 kg/m^2. In conclusion, we found that the RDI was associated with cSBP among men, and this association was independent of confounding variables among individuals above the ideal weight.

Keywords central systolic blood pressure · respiratory disturbance index · sleep-disordered breathing

Introduction

Blood pressure is commonly measured using a cuff sphygmomanometer in clinical settings, and elevated brachial blood pressure is known to be the major risk factor for cardiovascular events [1]. In contrast, central systolic blood pressure (cSBP) is the blood pressure in the aorta and has unique properties that differ from those of brachial

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blood pressure. cSBP is determined by a variety of elements, such as arterial stiffness, pulse wave velocity, and pressure wave reflection, in addition to cardiac output and peripheral vascular resistance [2]. Furthermore, cSBP is reported to be a better predictor of future cardiovascular disease than is brachial blood pressure [3–7].

Sleep-disordered breathing (SDB) is a condition of repetitive episodes of apnea and hypopnea during sleep [8], with an estimated prevalence between 10 and 17% [9]. Epidemiological evidence shows that those with SDB have a higher risk of developing hypertension and other cardiovascular risk factors [10–12].

To date, the association between SDB and cSBP is not fully understood. A study of 57 subjects with suspected obstructive sleep apnea (OSA) found that the respiratory disturbance index (RDI) did not significantly correlate with cSBP [13]. Continuous positive airway pressure (CPAP) has been shown to reduce cSBP in OSA patients [14, 15], while another study found that treatment with CPAP was ineffective in improving cSBP [16]. However, the subjects in these studies were limited to OSA patients. Furthermore, we conducted stratification analyses by sex and body mass index (BMI) to control these confounding variables, since male sex and obesity are well-known risk factors for OSA [9, 17].

Thus, this study examined the associations of SDB with cSBP, augmentation index (AIx), and pulse pressure amplification (PP amplification) in a community-dwelling population in Japan using the RDI measured with a single-channel airflow monitor.

Methods

Study subjects

This cross-sectional study was conducted using baseline data from the Toon Health Study, an epidemiological study held in Toon City, Ehime Prefecture, Japan. From 2009 to 2012, a total of 2032 participants aged 30–79 years were enrolled in the study [18, 19]. Individuals with missing information regarding the RDI ($n = 54$), cSBP ($n = 4$), PP amplification ($n = 23$), or hours of sleep ($n = 4$) were excluded. Moreover, we excluded those who were taking medication for hypertension ($n = 444$), ischemic heart disease (including angina pectoris and coronary heart disease, $n = 36$), and/or stroke ($n = 16$) to minimize the effect of antihypertensive drug therapy on the association. Ultimately, 485 men and 999 women were included in the analysis. The Institutional Review Board of Ehime University Graduate School of Medicine and the Ethics Committee of Juntendo University approved the study protocol. Informed consent was obtained from each study participant.

Assessment of the RDI

Each participant was asked to use a single-channel airflow monitor (Somnie; NGK Spark Plug Co. Ltd, Nagoya, Japan) for one night. The thermal sensor containing a polyvinylidene fluoride film detects the airflow from both nasal and oral breathing. The device stores the airflow signal as digital data at a sampling frequency of 10 Hz [20], which can be analyzed using Flow.exe software (Institute of Sleep Health Promotion, Tokyo, Japan); the algorithm has been previously described [21]. A previous study reported that the RDI has a high agreement with the apnea hypopnea index (AHI) assessed by concurrent polysomnography (PSG) [20]. We used RDI cutoff values of 10 and 20 events/h, which were found to represent AHIs of ≥15 events/h and ≥30 events/h, respectively, as determined by full PSG [20]. Thus, participants were grouped into three categories according to RDI level: mild (<10 events/h), moderate (10 to <20 events/h), and severe (≥20 events/h).

Assessment of blood pressure

A noninvasive automated tonometer (HEM-9000AI; Omron Healthcare, Kyoto, Japan) was used to measure cSBP. Details regarding this measurement have been described elsewhere [22]. In brief, participants were asked to place their left wrist on a sensor during 5-min intervals of rest in a seated position; the radial wave form SBP was calibrated, and the absolute pressure of the late systolic peak was considered to be cSBP [22]. AIx was calculated by computing the ratio of the height of the first systolic peak to that of the late systolic peak [22]. PP amplification is the absolute value of the difference between central pulse pressure and brachial pulse pressure [23]. Brachial SBP (bSBP) and brachial diastolic blood pressure (bDBP) were measured during 5-min intervals of rest in a seated position using an automatic sphygmomanometer (BP-103iII; OMRON Colin Co, Tokyo, Japan). The mean of the two measurements was used for the analysis of brachial blood pressure. Heart rate was also measured by the autonomic sphygmomanometer, and the mean of the two measurements was used for the analysis.

Other measurements

Height and weight were measured without shoes and with light clothing. BMI was calculated as the weight (kg) divided by the square of the height (m^2). Each participant's medical history, including hypertension, ischemic heart disease, diabetes mellitus, dyslipidemia, and chronic kidney disease, was obtained by physicians. "Under treatment" was defined as participants taking medication for the disease. Trained dietitians asked the participants about their alcohol

drinking (current, former, or never-drinker) and smoking (current, former, or never-smoker) status. For the evaluation of physical activity, the metabolic equivalent of task (MET) metric was estimated using the Japan Arteriosclerosis Longitudinal Study Physical Activity Questionnaire [24]. Hours of sleep were assessed using the relevant section of the Pittsburgh Sleep Quality Index [25].

Statistical analysis

Age- and sex-adjusted means and the proportion of characteristics were calculated by analysis of covariance (ANCOVA). Age- and sex-adjusted partial correlation coefficients between cSBP and bSBP were calculated. The multivariable-adjusted means of cSBP, AIx, PP amplification, bSBP, and bDBP according to RDI categories were analyzed using ANCOVA after adjustment for potential confounding factors, such as age, sex, BMI, smoking status (current, former smoker, or never-smoker), drinking status (current, former smoker, or never-drinker), physical activities (METs h/day), hours of sleep, and medication for diabetes mellitus and dyslipidemia. The association between the RDI and blood pressure measurements (cSBP, AIx, PP amplification, bSBP, and bDBP) was also assessed as a linear trend using a multivariable regression model with the median RDI variable. Further analyses were performed with stratification by sex and by both sex and BMI (<22 or ≥ 22 kg/m^2). A BMI of 22 kg/m^2 was used as the cutoff for stratification because it is considered to be the ideal BMI with the lowest morbidity in Japan [26, 27]. The SAS statistical package version 9.4 (Statistical Analysis System Inc., Cary, NC) was used for the analysis. Probability values for statistical tests were two-tailed, and $p < 0.05$ was regarded as statistically significant.

Results

Table 1 shows the characteristics of the study population according to RDI categories. The prevalence rates of mild to moderate SDB and severe SDB were 32.1% and 16.7%, respectively. Compared to those with a lower RDI category, participants with a higher RDI category tended to be men, be older, have a higher BMI, and have a higher heart rate. The scatter plots displaying the relationship between cSBP and the RDI as well as between bSBP and the RDI are shown in supplemental figure 1. Age- and sex-adjusted partial correlations of the RDI with cSBP were statistically significant ($r = 0.06$, $p < 0.01$), but those with bSBP were not ($r = 0.04$, $p = 0.10$). We also confirmed the correlation between cSBP and bSBP, and the correlation was statistically significant ($r = 0.80$, $p < 0.01$)

Table 1 Characteristics of the study population according to RDI categories

	RDI, events/h			p for trend
	<10	10 to <20	20≤	
N (%)	758 (51.1)	478 (32.1)	248 (16.7)	
Men, n (%)	170 (22.4)	155 (32.4)	160 (64.5)	<0.01
Age	52.2	57.1	60.3	<0.01
BMI, kg/m^2	22.4	23.0	23.4	<0.01
Current drinker, %	52.0	50.9	56.9	0.31
Current smoker, %	10.8	8.8	7.3	0.10
Diabetes (under treatment), %	2.0	1.5	1.5	0.61
Dyslipidemia (under treatment), %	9.4	7.0	9.0	0.65
CKD (under treatment), %	0.1	0.1	0.1	0.30
Heart rate, bpm	67.1	67.3	69.7	<0.01
Physical activity, METs h/day	36.1	35.8	35.3	0.03
Hours of sleep, h	6.5	6.6	6.5	0.95
cSBP, mm Hg	113.3	115.1	115.8	0.04
AIx, %	86.4	87.2	87.1	0.40
PP amplification, mm Hg	31.0	29.8	30.1	0.19
bSBP, mm Hg	121.8	122.8	124.1	0.09
bDBP, mm Hg	73.7	74.9	76.0	<0.01

Adjusted for age and sex

RDI respiratory disturbance index, *BMI* body mass index, *CKD* chronic kidney disease, *bpm* beats per minute, *METs* metabolic equivalent of tasks, *cSBP* central systolic blood pressure, *AIx* augmentation index, *PP amplification* pulse pressure amplification, *bSBP* brachial systolic blood pressure, *bDBP* brachial diastolic blood pressure

Table 2 shows the age-adjusted and multivariable-adjusted cSBP, AIx, PP amplification, and bSBP/bDBP means according to RDI categories. We found significant positive associations between the RDI and cSBP as well as between the RDI and bDBP in the age- and sex-adjusted model for all participants. After stratification by sex, the association remained statically significant in men but not in women. In men, the association remained significant even after adjusting for potential confounding factors: the multivariable-adjusted mean values of cSBP for the mild, moderate, and severe RDI categories were, respectively, 116.0, 118.0, and 120.7 mm Hg (p for trend = 0.02). However, those associations with the RDI were attenuated and no longer significant when further adjusted for BMI (p for trend = 0.25). None of the other measurements of blood pressure was significantly associated with the RDI. The multivariable-adjusted means of AIx for the

Table 2 Multivariable-adjusted means of cSBP according to RDI categories

	RDI, events/h			p for trend
	<10	10 to <20	20≤	
Total, N	758	478	248	
Age and sex adjusted, mm Hg	113.3	115.1	115.8	0.04
Multivariable adjusted, mm Hg[a]	113.2	115.2	115.7	0.04
Multivariable adjusted, mm Hg[b]	113.8	114.8	114.8	0.36
Men				
Age adjusted, mm Hg	116.0	118.0	120.8	0.02
Multivariable adjusted, mm Hg[a]	116.0	118.0	120.7	0.02
Multivariable adjusted, mm Hg[b]	117.0	118.3	119.4	0.25
Men BMI < 22, N	58	44	35	
Age adjusted, mm Hg	112.7	110.7	109.4	0.37
Multivariable adjusted, mm Hg[a]	112.9	110.4	109.5	0.39
Multivariable adjusted, mm Hg[b]	112.8	110.5	109.5	0.39
Men BMI ≥ 22, N	112	111	125	
Age adjusted, mm Hg	117.8	120.9	123.9	0.01
Multivariable adjusted, mm Hg[a]	117.8	121.0	123.8	0.01
Multivariable adjusted, mm Hg[b]	118.4	121.2	123.1	0.05
Women				
Age adjusted, mm Hg	111.8	113.6	111.7	0.60
Multivariable adjusted, mm Hg[a]	111.8	113.7	111.7	0.59
Multivariable adjusted, mm Hg[b]	112.1	113.2	111.3	0.99
Women BMI < 22, N	326	154	43	
Age adjusted, mm Hg	107.8	108.7	106.0	0.71
Multivariable adjusted, mm Hg[a]	107.8	108.7	105.8	0.63
Multivariable adjusted, mm Hg[b]	107.8	108.6	106.4	0.80
Women BMI ≥ 22, N	262	169	45	
Age adjusted, mm Hg	116.5	118.4	117.8	0.45
Multivariable adjusted, mm Hg[a]	116.4	118.5	117.9	0.42
Multivariable adjusted, mm Hg[b]	116.8	118.1	116.9	0.78

cSBP central systolic blood pressure, *RDI* respiratory disturbance index, *BMI* body mass index

[a]Adjusted for age, current drinking and smoking (yes/no/ex), physical activity (metabolic equivalent of tasks (METs) h/day), hours of sleep, taking medication for angina, diabetes mellitus, and dyslipidemia

[b]Adjusted for age, current drinking and smoking (yes/no/ex), physical activity (METs h/day), hours of sleep, taking medication for angina /diabetes mellitus/dyslipidemia, and BMI

mild, moderate, and severe RDI categories were, respectively, 81.0, 83.1, and 82.0% (p for trend = 0.59) in men and 88.9, 89.3, and 89.8% (p for trend = 0.44) in women. Respective multivariable-adjusted mean values of PP amplification were 34.5, 34.2, and 33.9 mm Hg (p for trend = 0.66) in men and 29.2, 27.9, and 27.9 mm Hg (p for trend = 0.11) in women. The multivariable-adjusted means of bSBP for the mild, moderate, and severe RDI categories were, respectively, 127.2, 125.2, and 127.5 mm Hg (p for trend = 0.75) in men and 120.3, 121.0, and 120.3 mm Hg (p for trend = 0.83) in women. Respective multivariable-adjusted means of bDBP were 79.1, 78.9, and 80.1 mm Hg (p for trend = 0.36) in men and 71.7, 72.6, and 72.5 mm Hg (p for trend = 0.31) in women.

When stratified by BMI (<22 or ≥22 kg/m^2), the RDI was positively associated with cSBP among men with BMI ≥ 22 kg/m^2 (Table 2). However, this association was not observed in men with BMI < 22 kg/m^2 or in women. We also conducted the stratification analyses by BMI for the association between the RDI and AIx, PP amplification, and bSBP/bDBP (Tables 3–6). None of the measurements of blood pressure was significantly associated with the RDI after stratification.

Discussion

We found that SDB was associated with cSBP after adjustment for confounding factors among male normotensive participants. This association was more evident among men with BMI ≥ 22 kg/m^2. The association between the RDI and the other blood pressure measurements (AIx, PP amplification, bSBP, and bDBP) was not statistically significant.

The relationship between SDB and cSBP has previously been investigated, but only in a small number of subjects. A previous study of 57 men with suspected OSA found that the RDI value was not significantly correlated with cSBP [13]. The findings of our study provide evidence for the association between SDB and cSBP. Furthermore, several clinical studies have examined the impact of CPAP treatment on cSBP and have reported a reduction in cSBP ranging from 4.0 to 6.7 mm Hg [14, 15, 28], suggesting the importance of the early detection and treatment of SDB. In addition, the ASCOT-CAFÉ study reported that a reduction in cSBP of 3.6 mm Hg resulted in a 25% decrease in mortality [29], further indicating the importance of early detection and treatment of SDB from a public health perspective.

After stratification by BMI and sex, the association between cSBP and the RDI was of borderline significance among men with BMI ≥ 22 kg/m^2. The sex difference in the association between SDB and hypertension has been examined in several studies. A case-controlled study showed a dose-response relationship between OSA and hypertension in men but not in women [30]. A cross-sectional study of the Yale Sleep Cohort reported that obese men with OSA had higher odds of having hypertension than did obese women with OSA [31]. Possible explanations underlying this sex difference include differences in upper airway anatomy, fat distribution, and sex hormones [32]. However, other population-based studies were unable to demonstrate a sex difference in the association between SDB and hypertension [10, 11, 33]; thus, the effect of sex is not fully understood. Consistent with our results, a previous study of 1424 Japanese men reported that the relationship between SDB and elevated brachial blood pressure was

Table 3 Multivariable-adjusted means of AIx according to RDI categories

	RDI, events/h			p for trend
	<10	10 to <20	20≤	
Total, N	758	478	248	
Age and sex adjusted, %	86.4	87.2	87.1	0.40
Multivariable adjusted, %[a]	86.4	87.2	87.1	0.35
Multivariable adjusted, %[b]	86.4	87.2	87.1	0.35
Men				
Age adjusted, %	81.1	83.1	81.9	0.67
Multivariable adjusted, %[a]	81.1	83.1	81.9	0.66
Multivariable adjusted, %[b]	81.0	83.1	82.0	0.59
Men BMI < 22, N	58	44	35	
Age adjusted, %	80.4	82.3	81.5	0.69
Multivariable adjusted, %[a]	80.5	81.9	81.7	0.66
Multivariable adjusted, %[b]	80.5	81.9	81.7	0.66
Men BMI ≥ 22, N	112	111	125	
Age adjusted, %	81.4	83.5	82.0	0.89
Multivariable adjusted, %[a]	81.4	83.6	82.0	0.89
Multivariable adjusted, %[b]	81.2	83.5	82.2	0.66
Women				
Age adjusted, %	88.9	89.2	89.7	0.52
Multivariable adjusted, %[a]	88.9	89.3	89.8	0.42
Multivariable adjusted, %[b]	88.9	89.3	89.8	0.44
Women BMI < 22, N	326	154	43	
Age adjusted, %	88.1	88.0	89.2	0.68
Multivariable adjusted, %[a]	88.2	87.9	89.3	0.69
Multivariable adjusted, %[b]	88.2	87.9	89.5	0.65
Women BMI ≥ 22, N	262	169	45	
Age adjusted, %	89.9	90.5	90.3	0.65
Multivariable adjusted, %[a]	89.8	90.5	90.5	0.58
Multivariable adjusted, %[b]	89.8	90.6	90.6	0.50

AIx augmentation index, *RDI* respiratory disturbance index, *BMI* body mass index

[a]Adjusted for age, current drinking and smoking (yes/no/ex), physical activity (metabolic equivalent of tasks (METs) h/day), hours of sleep, taking medication for angina, diabetes mellitus, and dyslipidemia

[b]Adjusted for age, current drinking and smoking (yes/no/ex), physical activity (METs h/day), hours of sleep, taking medication for angina /diabetes mellitus/dyslipidemia, and BMI

Table 4 Multivariable-adjusted means of pulse pressure amplification according to RDI categories

	RDI, events/h			p for trend
	<10	10 to <20	20≤	
Total, N	758	478	248	
Age and sex adjusted, mm Hg	31.0	29.8	30.1	0.19
Multivariable adjusted, mm Hg[a]	31.0	30.0	30.1	0.21
Multivariable adjusted, mm Hg[b]	31.0	30.0	30.1	0.21
Men				
Age adjusted, mm Hg	34.4	33.9	34.2	0.90
Multivariable adjusted, mm Hg[a]	34.3	34.2	34.2	0.91
Multivariable adjusted, mm Hg[b]	34.5	34.2	33.9	0.66
Men BMI < 22, N	58	44	35	
Age adjusted, mm Hg	35.3	32.5	31.2	0.09
Multivariable adjusted, mm Hg[a]	34.9	32.6	31.8	0.20
Multivariable adjusted, mm Hg[b]	34.9	32.7	31.7	0.19
Men BMI ≥ 22, N	112	111	125	
Age adjusted, mm Hg	34.0	34.5	35.1	0.46
Multivariable adjusted, mm Hg[a]	34.0	34.7	34.9	0.54
Multivariable adjusted, mm Hg[b]	34.0	34.7	34.8	0.60
Women				
Age adjusted, mm Hg	29.2	27.9	27.9	0.09
Multivariable adjusted, mm Hg[a]	29.2	27.9	27.9	0.09
Multivariable adjusted, mm Hg[b]	29.2	27.9	27.9	0.11
Women BMI < 22, N	326	154	43	
Age adjusted, mm Hg	29.3	28.0	27.6	0.17
Multivariable adjusted, mm Hg[a]	29.3	28.1	27.5	0.18
Multivariable adjusted, mm Hg[b]	29.3	28.1	27.5	0.17
Women BMI ≥ 22, N	262	169	45	
Age adjusted, mm Hg	29.1	27.8	28.0	0.32
Multivariable adjusted, mm Hg[a]	29.1	27.9	28.0	0.33
Multivariable adjusted, mm Hg[b]	29.1	27.8	27.9	0.28

RDI respiratory disturbance index, *BMI* body mass index

[a]Adjusted for age, current drinking and smoking (yes/no/ex), physical activity (metabolic equivalent of tasks (METs) h/day), hours of sleep, taking medication for angina, diabetes mellitus, and dyslipidemia

[b]Adjusted for age, current drinking and smoking (yes/no/ex), physical activity (METs hours/day), hours of sleep, taking medication for angina /diabetes mellitus/dyslipidemia, and BMI

more evident among overweight individuals [34]. The findings from this study suggested that SDB and overweight may synergistically enhance an increase in blood pressure. Thus, the finding from our study may also indicate that SDB and overweight work in synergy to raise blood pressure.

The possible mechanisms underlying the association between SDB and cSBP are as follows. Studies have indicated that OSA patients have increased sympathetic activity [35–37], reduced endothelium-dependent vascular relaxation [38], and impaired baroreflex sensitivity [39], all of which are responsible for elevating brachial blood pressure as well as cSBP.

Another important finding of our study is that SDB could be more strongly associated with cSBP than with brachial blood pressure. The exact mechanism behind this difference between cSBP and brachial blood pressure is not fully understood. OSA patients have reduced endothelium-dependent vascular relaxation, resulting in an elevation of blood pressure [38]. Vasodilation is closely linked to both cSBP and OSA, which could be a possible mechanism behind the RDI being more closely related to cSBP than to

Table 5 Multivariable-adjusted means of bSBP according to RDI categories

	RDI, events/h			*p* for trend
	<10	10 to <20	20≤	
Total, *N*	758	478	248	
Age and sex adjusted, mm Hg	121.8	122.8	124.1	0.09
Multivariable adjusted, mm Hg[a]	121.8	122.9	124.1	0.09
Multivariable adjusted, mm Hg[b]	122.4	122.4	122.9	0.74
Men				
Age adjusted, mm Hg	125.9	124.9	129.1	0.07
Multivariable adjusted, mm Hg[a]	126.0	124.9	129.1	0.07
Multivariable adjusted, mm Hg[b]	127.2	125.2	127.5	0.75
Men BMI < 22, *N*	58	44	35	
Age adjusted, mm Hg	121.1	115.5	117.3	0.29
Multivariable adjusted, mm Hg[a]	121.3	115.4	117.2	0.26
Multivariable adjusted, mm Hg[b]	121.3	115.5	117.2	0.26
Men BMI ≥ 22, *N*	112	111	125	
Age adjusted, mm Hg	128.6	128.6	132.3	0.07
Multivariable adjusted, mm Hg[a]	128.7	128.5	132.3	0.08
Multivariable adjusted, mm Hg[b]	129.4	128.8	131.4	0.30
Women				
Age adjusted, mm Hg	119.9	121.6	120.9	0.38
Multivariable adjusted, mm Hg[a]	119.9	121.7	120.7	0.38
Multivariable adjusted, mm Hg[b]	120.3	121.0	120.3	0.83
Women BMI < 22, *N*	326	154	43	
Age adjusted, mm Hg	115.8	115.5	113.5	0.43
Multivariable adjusted, mm Hg[a]	115.7	115.6	113.3	0.40
Multivariable adjusted, mm Hg[b]	115.7	115.5	114.0	0.55
Women BMI ≥ 22, *N*	262	169	45	
Age adjusted, mm Hg	124.7	127.5	128.5	0.12
Multivariable adjusted, mm Hg[a]	124.5	127.8	128.4	0.10
Multivariable adjusted, mm Hg[b]	125.1	127.2	126.9	0.40

bSBP brachial systolic blood pressure, *RDI* respiratory disturbance index, *BMI* body mass index

[a]Adjusted for age, current drinking and smoking (yes/no/ex), physical activity (metabolic equivalent of tasks (METs) h/day), hours of sleep, taking medication for angina, diabetes mellitus, and dyslipidemia

[b]Adjusted for age, current drinking and smoking (yes/no/ex), physical activity (METs h/day), hours of sleep, taking medication for angina /diabetes mellitus/dyslipidemia, and BMI

Table 6 Multivariable-adjusted means of bDBP according to RDI categories

	RDI, events/h			*p* for trend
	<10	10 to <20	20≤	
Total, *N*	758	478	248	
Age and sex adjusted, mm Hg	73.7	74.9	76.0	< 0.01
Multivariable adjusted, mm Hg[a]	73.7	74.9	75.9	< 0.01
Multivariable adjusted, mm Hg[b]	74.1	74.7	75.3	0.13
Men				
Age adjusted, mm Hg	78.2	78.8	81.2	0.01
Multivariable adjusted, mm Hg[a]	78.3	78.7	81.2	0.02
Multivariable adjusted, mm Hg[b]	79.1	78.9	80.1	0.36
Men BMI < 22, *N*	58	44	35	
Age adjusted, mm Hg	75.1	72.5	73.5	0.53
Multivariable adjusted, mm Hg[a]	75.4	72.3	73.1	0.33
Multivariable adjusted, mm Hg[b]	75.4	72.3	73.1	0.33
Men BMI ≥ 22, *N*	112	111	125	
Age adjusted, mm Hg	79.9	81.1	83.3	0.02
Multivariable adjusted, mm Hg[a]	80.0	81.0	83.4	0.02
Multivariable adjusted, mm Hg[b]	80.4	81.3	82.8	0.12
Women				
Age adjusted, mm Hg	71.5	72.9	72.9	0.09
Multivariable adjusted, mm Hg[a]	71.5	73.0	72.8	0.10
Multivariable adjusted, mm Hg[b]	71.7	72.6	72.5	0.31
Women BMI < 22, *N*	326	154	43	
Age adjusted, mm Hg	69.3	69.6	68.2	0.66
Multivariable adjusted, mm Hg[a]	69.3	69.5	68.0	0.56
Multivariable adjusted, mm Hg[b]	69.3	69.5	68.4	0.70
Women BMI ≥ 22, *N*	262	169	45	
Age adjusted, mm Hg	74.1	76.1	77.8	0.01
Multivariable adjusted, mm Hg[a]	74.0	76.4	77.6	0.01
Multivariable adjusted, mm Hg[b]	74.3	76.1	76.9	0.07

bDBS brachial diastolic blood pressure, *RDI* respiratory disturbance index, *BMI* body mass index

[a]Adjusted for age, current drinking and smoking (yes/no/ex), physical activity (metabolic equivalent of tasks (METs) h/day), hours of sleep, taking medication for angina, diabetes mellitus, and dyslipidemia

[b]Adjusted for age, current drinking and smoking (yes/no/ex), physical activity (METs hours/day), hours of sleep, taking medication for angina /diabetes mellitus/dyslipidemia, and BMI

bSBP in our present study. In addition, findings from previous studies have demonstrated the significance of cSBP compared to brachial blood pressure in the assessment of future cardiovascular diseases. For example, cSBP, but not brachial blood pressure, was strongly associated with cardiac and vascular remodeling and was an independent predictor of future cardiovascular events [3]. Furthermore, vascular hypertrophy, extent of atherosclerosis [5], and severity of coronary disease [40] were also associated with cSBP but not with measurements of brachial blood pressure. Taken together with findings from previous studies reporting a significant association between SDB and cardiovascular disease [41–43], we can infer that SDB increases the risk of future cardiovascular disease through the elevation of cSBP.

In this study, both PP amplification and AIx were not significantly associated with the RDI. The reasons for this result are not clear. However, this finding may be related to the fact that the participants in this study were relatively elderly. Aging is known to be a key determinant of PP amplification and AIx. PP amplification decreases as a person becomes older and as atherosclerosis progresses [44, 45]. In contrast, AIx increases with age and progression of atherosclerosis [45]. Although participants with cardiovascular disease are excluded from the analysis, atherosclerosis is presumably progressing in the participants because of their age. In addition, AIx and heart rate are known to have inverse linear relationships [46]. Increased sympathetic activity among SDB patients will increase heart rate, and as a result, AIx and PP amplification are presumably reduced.

The strength of our study is that we were able to examine the associations between the RDI and cSBP among a relatively large population composed of individuals who are leaner than most individuals in the Western population. While previous studies conducted in Western countries consist largely of obese populations, our sample had a broad range of BMI values, thus enabling us to observe a population with low BMI as well, which has not been thoroughly explored.

There are some limitations to this study. First, we observed a positive association between the severity of the RDI and cSBP among men over the ideal weight (BMI > 22), but the association was borderline and did not reach statistical significance. OSA patients are characterized by being obese [9, 17] and having several cardiovascular risk factors [17]. In this study, we excluded some major cardiovascular risk factors, including hypertension, ischemic heart disease, and stroke, to avoid reverse causality. Therefore, the number of men over the ideal weight was not sufficient. Second, we did not specify the types of antihypertensive medication when asking participants of their medical history. The different types of blood-pressure-lowering drugs could have substantially different effects on central aortic pressures [29]. We excluded participants taking medication for hypertension, stroke, and ischemic heart disease to minimize the effect of antihypertensive drug therapy on the association. However, individuals who are potentially using antihypertensive medication could still remain in the analysis, since other cardiovascular diseases, such as heart failure, require treatment by antihypertensive agents. Nevertheless, the number of these participants is expected to be low; thus, its impact on the outcome is minimal. Third, this is a cross-sectional study; thus, we cannot determine a causal relationship. However, research has shown that CPAP reduces cSBP among OSA patients [14, 15], implying a causal relationship between SDB and cSBP. Fourth, airflow monitoring was only conducted once; thus, there is a possibility of underestimating SDB severity due to measurement errors. However, such measurement errors would result in the misclassification of participants into incorrect RDI categories, thus weakening the association between SDB and cSBP. Fifth, the airflow monitor used in our study cannot separate OSA from central sleep apnea (CSA). However, CSA is far less prevalent than OSA. According to a population-based study that included 5804 community-dwelling adults, the prevalence of CSA was 0.9%, while the prevalence of OSA was 47.6% [47]. In addition, hypertension is more common among individuals with OSA than among those with CSA [48].

In conclusion, we found that the RDI was associated with cSBP among men, and this association was independent of confounding variables among individuals above the ideal weight. Our findings suggest that public health strategies for SDB could contribute to the prevention of cardiovascular events by controlling the elevation of cSBP among men.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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