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ORIGINAL ARTICLE

Relationship between sleep apnea syndrome and sleep blood pressure in patients without hypertension

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Polysomnography

Summary
Background and purpose: Ambulatory blood pressure monitoring (ABPM) provides an accurate assessment of blood pressure (BP) and shows non-dipper BP pattern in many sleep apnea syndrome (SAS) patients with hypertension (HTN); however, little information is available on the relationship between the severity of SAS and circadian BP changes in SAS patients without HTN. This study investigated whether SAS patients without HTN would have different BP courses in the severity of SAS.
Methods and subjects: Seventy-four consecutive outpatients without HTN [systolic BP (BPs) at clinic <140 mmHg and/or diastolic BP (BPd) at clinic <90 mmHg], who received no antihypertensives, underwent overnight polysomnography (PSG) and ABPM. The apnea—hypopnea index (AHI) was calculated from the PSG results; patients were stratified into the following 4 groups based on their AHI: non-SAS, mild-, moderate-, or severe-SAS.
Results: The diurnal BPs and BPd showed no differences in the severity of SAS; however, the sleep BPs, lowest BPs, and pre-awake BPs were significantly higher in the severe-SAS group than the non-SAS group ($p = 0.02$, $p = 0.04$, and $p = 0.006$, respectively). The sleep BPd and pre-awake BPd were significantly higher in the severe-SAS than the non-SAS ($p = 0.01$ and $p = 0.0003$, respectively) and mild-SAS ($p = 0.01$ and $p = 0.008$, respectively) groups.
Conclusions: The results of this study suggested that SAS affected nocturnal BP elevation even in SAS patients without HTN. The diurnal BP showed no difference in the severity of SAS; however, the severe-SAS group revealed significant nocturnal BP elevation.

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Introduction

Sleep apnea syndrome (SAS) is widely accepted as one of the risk factors for cardiovascular events, such as atherosclerosis and ischemic heart disease [1,2]. The 7th Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7) has defined SAS as a treatable cause of secondary hypertension (HTN) [3]. Hypoxemia plays a crucial role in sympathetic nerve system activation in SAS patients, which is related to nocturnal HTN including secondary HTN and non-dipper blood pressure (BP) pattern, and triggers cardiovascular events [4]. Our previous studies reported the influence of sleep disordered breathing (SDB) on the acute onset time of dyspnea and chest pain in patients with congestive heart failure [5] and acute coronary syndrome [6]. Currently, 24-h ambulatory blood pressure monitoring (ABPM) provides accurate BP assessment during sleep. Many studies have investigated HTN in SAS patients; however, no study has been conducted on SAS patients without HTN to evaluate the influence of SAS on circadian BP changes, especially on nocturnal BP changes. Here, we investigated whether SAS patients without HTN would have BP elevation during sleep as the SAS severity increased.

Subjects and methods

This study was conducted on 74 consecutive SAS outpatients (63 males and 11 females) without HTN who presented to the St. Marianna University School of Medicine Hospital between April 2006 and August 2008. HTN was defined as laboratory-measured systolic BP (BPs) $\geq$ 140 mmHg and/or diastolic BP (BPd) $\geq$ 90 mmHg and/or the use of antihypertensives. Blood samples were collected at the first examination for the measurements of the serum concentrations of total cholesterol, triglyceride (TG), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, fasting plasma glucose (FPG), the percentage of glycosylated hemoglobin (HbA1c), and creatinine. Diabetes mellitus was defined as FPG $\geq$ 126 mg/dl or patients who were under diabetes mellitus treatment. Hyperlipidemia was defined as total cholesterol $\geq$ 220 mg/dl and/or TG $\geq$ 150 mg/dl and/or patients who received hypolipidemic agents. Obese patients were defined as body mass index (BMI) $\geq$ 30 kg/m^2. Patients with respiratory disease, renal disease, aged <15 years, and those who refused to undergo ABPM were excluded from this study. Patients treated with antihypertensives due to cardiac or renal disease were also excluded.

Polysomnography

SAS was determined based on the results of full polysomnography (PSG) using SLEEP WATHCER® (Compumedics, Abbotsford VIC, Australia) or Polymate® (Miyuki Giken Co., Ltd., Tokyo, Japan). PSG included an electroencephalogram (EEG), electro-oculogram, chin electromyogram, and electrocardiogram. Four-channel EEG electrodes were attached to the right and left sides at the top and back of the head. A nasal cannula was placed at the nostril to measure the respiratory airflow using a disposable airflow sensor, and a strain gauge sensor monitored respiratory movements of the chest and abdominal walls. Arterial oxygen saturation (SpO_2) was continuously measured using a pulse oxymeter. Technicians analyzed the sleep states according to the manual [7]. Apnea was defined as a continuous cessation of breathing airflow for 10 s, or more per hour of sleep; hypopnea was defined as a reduction in breathing airflow of 50% or more of a normal breath with a SpO_2 desaturation $\geq$3% or an EEG arousal response. The apnea—hypopnea index (AHI) was calculated as the total number of episodes of apnea and hypopnea per hour of sleep based on the PSG results. Low-oxygen exposure was defined as SpO_2 < 90% and the rate of SpO_2 < 90%. The 3% oxygen desaturation index (ODI; the number of desaturation episodes per hour of sleep) and 4% ODI were calculated. The sleep states were classified into non-rapid eye movement (NREM) sleep, rapid eye movement (REM) sleep, or stage W based on the results of EEG, chin electromyogram, and the presence or absence of rapid eye movement. Moreover, NREM sleep was classified into the following 4 stages: Stage 1, Stage 2, Stage 3, and Stage 4. A micro-arousal was defined as an abrupt shift in EEG frequency (3 $\leq$ micro-arousal < 15 s), which was not counted as stage W; the arousal index was used to evaluate patients' sleep states. The percentages of REM (REM %), Stage 1 (Stage 1%), Stage 2 (Stage 2%), Stage 3 (Stage 3%) and Stage 4 (Stage 4%) in the total sleep time were calculated and evaluated. Patients with AHI $\geq$5/h were defined as having SAS. The severity of SAS was classified as follows according to AHI: non-SAS (AHI < 5, n = 11), mild (5 $\leq$ AHI < 15, n = 20), moderate (15 $\leq$ AHI < 30, n = 22), and severe (30 $\leq$ AHI, n = 21).

BP measurement at the clinic

BP was measured twice using a mercury sphygmomanometer with stethoscope in the sitting position after at least 5 min rest at our outpatient facility between 09:00 and 17:00. The 13-cm width tourniquet was wrapped around the upper arm, which was kept at the same height of the heart, and a stethoscope was placed over the upper arm artery.

24-h ABPM

Noninvasive ABPM was performed for 24 h using a FM-800® (Fukuda Denshi Ltd., Tokyo, Japan) at 30-min intervals [8]. ABPM and PSG were performed on two different days. BP was measured by the oscilloscopic method with an automated BP cuff or by the Korotkoff method. The ABPM data were analyzed based on the method described by Kario et al. [9] and the following BPs and BPd were measured: sleep BP, the average BP during sleep at night; awake BP, the average BP during the rest of the day; evening BP, the average BP 1.5 h before sleep; morning BP, the average BP 1.5 h immediately after awakening; the lowest BP, the average BP of 3 readings centered on the lowest reading during sleep; pre-awake BP, the average BP 1.5 h just before awakening (Fig. 1).

Statistical analysis

The data are expressed as means $\pm$ standard deviation. Differences between groups were determined by the analysis

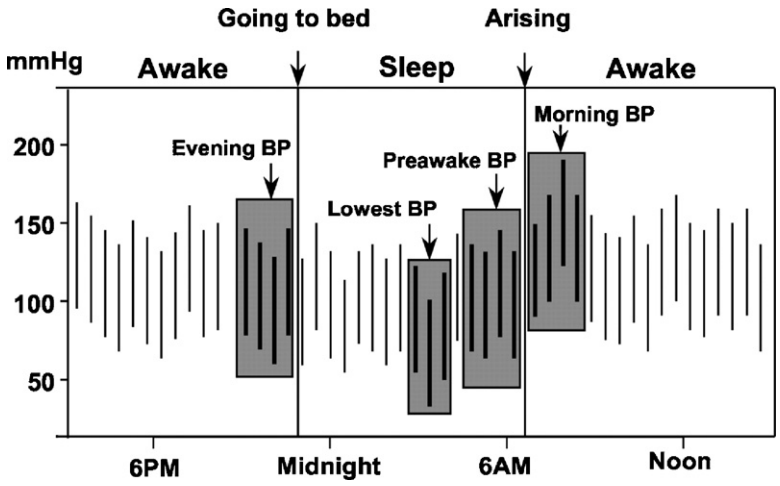

Figure 1 The time zone of blood pressure (BP). The ambulatory blood pressure monitoring (ABPM) data were analyzed based on the method described by Kario et al. [9]: sleep BP, the average BP during sleep at night; awake BP, the average BP during the rest of the day; evening BP, the average BP 1.5 h before sleep; morning BP, the average BP 1.5 h immediately after awakening; the lowest BP, the average BP of 3 readings centered on the lowest reading during sleep; and pre-awake BP, the average BP 1.5 h just before awakening.

of variance and the Scheffé correction was used for multiple comparisons. Analysis of covariance (ANCOVA) was also used for the evaluation of the variables. Correlations among the groups were examined using the single regression analysis. The level of statistical significance was established at $p < 0.05$.

Ethics

This study was performed in accordance with the ethical principles set forth in the Declaration of Helsinki. The study protocol was approved by the St. Marianna University School of Medicine Institutional Committee on Human Research (No. 1142). Written informed consent was obtained from all of the patients prior to their enrollment.

Results

Baseline characteristics

Table 1 shows the baseline characteristics in each group. The body weight and BMI showed significant differences among the 4 groups ($p = 0.002$ and $p = 0.008$, respectively); whereas, the age and height showed no significant differences. In the study population, 4 patients (5%) had diabetes mellitus, 36 (49%) had hyperlipidemia, and only 6 patients (8%)

Table 1 Baseline characteristics.

	All	Non-SAS	Mild-SAS	Moderate-SAS	Severe-SAS	*p* value
Number of patients	74	11	20	22	21	
Sex (M/F)	63/11	6/5	18/2	19/3	20/1	
Age (year)	45.5 ± 14.5	38.7 ± 15.3	43.7 ± 14.5	49.0 ± 13.9	47.3 ± 14.4	0.23
Height (cm)	168.8 ± 7.4	165.5 ± 9.0	169.3 ± 7.5	168.5 ± 6.9	170.4 ± 6.7	0.24
Weight (kg)	71.4 ± 12.2	62.7 ± 10.2	72.2 ± 12.2	68.9 ± 9.3	77.8 ± 13.0	0.002
BMI (kg/m^2)	25.0 ± 3.7	23.0 ± 3.9	25.1 ± 3.5	24.2 ± 3.0	26.7 ± 4.0	0.008
Diabetes mellitus (%)	4 (5)	0 (0)	1 (5)	1 (5)	2 (10)	0.73
Hyperlipidemia (%)	36 (49)	2 (18)	9 (45)	13 (59)	12 (57)	0.13
Obesity (%)	6 (8)	1 (9)	1 (5)	1 (5)	3 (14)	0.95
Total cholesterol (mg/dl)	194.0 ± 31.8	191.0 ± 29.0	191.2 ± 25.9	200.8 ± 31.8	191.8 ± 38.1	0.75
HDL cholesterol (mg/dl)	49.9 ± 13.6	63.0 ± 16.6	48.6 ± 13.2	46.9 ± 11.4	47.1 ± 10.5	0.004
LDL cholesterol (mg/dl)	110.3 ± 36.5	111.3 ± 29.0	105.3 ± 36.9	114.7 ± 46.8	109.9 ± 28.6	0.24
TG (mg/dl)	145.6 ± 96.7	83.5 ± 45.7	158.7 ± 113.2	138.9 ± 66.5	193.1 ± 13.5	0.08
FPG (mg/dl)	105.6 ± 19.1	97.7 ± 11.8	110.2 ± 15.9	105.0 ± 19.9	106.0 ± 23.3	0.40
HbA1c (%)	5.1 ± 0.4	4.9 ± 0.3	5.2 ± 0.5	5.1 ± 0.4	5.2 ± 0.3	0.11
Creatinine (mg/dl)	0.9 ± 0.2	0.8 ± 0.2	0.9 ± 0.2	0.8 ± 0.1	0.9 ± 0.1	0.52

SAS: sleep apnea syndrome, BMI: body mass index, HDL: high-density lipoprotein, LDL: low-density lipoprotein, TG: triglyceride, FPG: fasting plasma glucose, HbA1c: glycosylated hemoglobin.
Values are presented as the mean ± SD.

Table 2 Sleep study data.

	All	Non-SAS	Mild-SAS	Moderate-SAS	Severe-SAS	*p* value
AHI (/h)	25.3 ± 23.2	2.0 ± 1.5	9.5 ± 2.8	22.0 ± 3.8	56.1 ± 19.8	<0.001
Arousal index (/h)	23.1 ± 20.6	8.7 ± 6.9	14.6 ± 13.5	19.9 ± 10.2	41.9 ± 25.9	<0.001
3% ODI (/h)	23.4 ± 23.9	10.3 ± 23.7	10.4 ± 4.7	18.6 ± 6.7	54.9 ± 25.8	<0.001
4% ODI (/h)	18.0 ± 22.9	7.6 ± 18.8	5.6 ± 3.2	11.9 ± 5.6	48.6 ± 27.0	<0.001
REM (%)	15.0 ± 11.0	15.1 ± 9.1	17.1 ± 5.8	17.6 ± 17.3	10.3 ± 4.6	0.12
Stage 1 (%)	23.2 ± 16.3	13.5 ± 9.7	17.2 ± 9.8	23.6 ± 10.7	33.1 ± 10.7	0.002
Stage 2 (%)	47.1 ± 12.3	45.7 ± 7.5	49.8 ± 10.3	48.6 ± 11.0	43.8 ± 16.6	0.41
Stage 3 (%)	8.3 ± 5.9	13.5 ± 9.5	9.3 ± 4.1	7.2 ± 4.8	5.7 ± 4.2	0.002
Stage 4 (%)	5.5 ± 6.0	8.4 ± 5.9	6.5 ± 6.2	5.0 ± 6.9	3.4 ± 4.1	0.12

SAS: sleep apnea syndrome, AHI: apnea—hypopnea index, ODI: oxygen desaturation index, REM: rapid eye movement.
Values are presented as the mean ± SD.

were obese, which revealed no significant differences. No significant differences in the serum concentrations of total cholesterol, TG, LDL cholesterol, FPG, HbA1c, and creatinine were observed among the 4 groups. Only the serum concentration of HDL cholesterol was higher in the non-SAS group than the other 3 groups ($p = 0.004$).

Table 2 shows the sleep study data in each group. The mean AHI increased as the severity of SAS increased. The other variables, such as the arousal index, SpO_2 90%, 3% ODI, 4% ODI, Stage 1 and Stage 3, showed significant differences among the 4 groups ($p < 0.0001$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$, $p = 0.002$, and $p = 0.002$, respectively); whereas, the REM, Stage 2 and Stage 4 showed no significant differences.

In the present study, we investigated the association between the sleep BP and the AHI, arousal index, 3% ODI or 4% ODI using ANCOVA (Table 2). When the level of <5% was considered statistically significant, we found significant differences in the arousal index ($p = 0.008$), 3% ODI ($p = 0.027$), and 4% ODI ($p = 0.039$). A significant correlation was observed between the arousal index ($p = 0.021$) and 3% ODI ($p = 0.017$).

Relationship between the severity of SAS and BP

Table 3 shows the BPs data in each group. No differences in the awake BPs, evening BPs, and clinic BPs were observed among the 4 groups. The sleep BPs was significantly higher in the severe-SAS group than the non-SAS group ($p = 0.02$); however, no significant difference existed between the mild- and moderate- and non-SAS groups. The lowest BPs and pre-awake BPs were significantly higher in the severe-SAS

Table 3 Blood pressure study data.

Period	Blood pressure (mmHg)	Non-SAS	Mild-SAS	Moderate-SAS	Severe-SAS	*p* value
Clinic	Systole	117.2 ± 12.4	121.8 ± 15.7	125.2 ± 9.7	128.0 ± 10.1	0.09
	Diastole	70.8 ± 7.2	76.3 ± 9.4	77.0 ± 7.1	80.7 ± 8.2*	0.02
24 h	Systole	113.2 ± 8.4	116.2 ± 8.7	121.1 ± 9.7	126.3 ± 11.4*,#	0.001
	Diastole	73.8 ± 5.8	76.0 ± 6.8	78.9 ± 6.9	84.0 ± 7.4*,#	<0.001
Awake	Systole	120.2 ± 12.0	121.9 ± 9.4	126.1 ± 10.8	130.5 ± 10.9	0.27
	Diastole	78.8 ± 6.9	80.6 ± 7.7	81.9 ± 9.7	85.0 ± 8.3	0.20
Sleep	Systole	103.5 ± 10.3	107.9 ± 10.3	112.8 ± 11.8†	118.7 ± 15.1*	0.005
	Diastole	67.1 ± 8.4	69.1 ± 6.6	72.6 ± 8.6	79.5 ± 13.2*,#	0.002
Evening	Systole	118.8 ± 14.1	118.7 ± 9.1	123.5 ± 11.1	126.8 ± 14.1	0.13
	Diastole	78.4 ± 7.8	77.9 ± 8.2	80.3 ± 7.1	82.2 ± 8.4	0.31
Lowest	Systole	98.2 ± 10.9	100.9 ± 9.8	105.8 ± 10.8	110.0 ± 11.9*	0.01
	Diastole	62.5 ± 8.6	63.3 ± 7.6	68.5 ± 9.0	69.2 ± 9.1	0.047
Pre-awake	Systole	103.4 ± 10.7	110.0 ± 12.8	113.4 ± 12.5	122.4 ± 16.8*	0.003
	Diastole	66.1 ± 8.7	71.6 ± 8.5	73.3 ± 8.9	82.0 ± 8.5*,#,†	<0.001
Morning	Systole	120.4 ± 9.6	119.4 ± 10.4	126.2 ± 10.9	132.3 ± 13.8#	0.003
	Diastole	78.3 ± 7.7	78.4 ± 8.8	81.4 ± 7.6	87.6 ± 8.5*,#	0.002

SAS: sleep apnea syndrome, BPs: systolic blood pressure, BPd: diastolic blood pressure.
Values are presented as the mean ± SD.
* $p < 0.05$ vs. non-SAS group by analysis of variance with Scheffé correction.
# $p < 0.05$ vs. mild-SAS group by analysis of variance with Scheffé correction.
† $p < 0.05$ vs. moderate-SAS group by analysis of variance with Scheffé correction.

group ($p = 0.04$ and $p = 0.006$, respectively) than the non-SAS group. The morning BPs showed no significant difference between the severe-SAS and non-SAS groups ($p = 0.06$); however, the severe-SAS group revealed significantly higher morning BPs than the mild-SAS group ($p = 0.008$).

Table 3 also shows the BPd data in each group. The sleep BPd was significantly higher in the severe-SAS group than the non-SAS and mild-SAS groups ($p = 0.01$ and $p = 0.01$, respectively). The pre-awake BPd was significantly higher in the severe-SAS group than the other 3 groups (non-SAS, $p = 0.0003$; mild, $p = 0.008$; and moderate, $p = 0.03$). No significant differences in the awake BPd, evening BPd, and clinic BPd were observed in the severity of SAS.

In the present study, we took into account the influence of BMI as well as AHI on sleep BP, including lowest BP and pre-awake BP, and evaluated these using ANCOVA. The sleep BPd significantly differed from the BMI ($p = 0.003$) and the interaction between AHI and BMI ($p = 0.01$), respectively. Moreover, the interaction between AHI and BMI significantly differed from the pre-awake BPs ($p = 0.02$) and BPd ($p = 0.04$), respectively.

Discussion

SAS is an important factor for HTN management even in Japanese patients. The prevalence of SDB is reported to be 22% in the Japanese male working population [10]. In the present study, no difference in the diurnal BP was observed in the severity of SAS; however, we found higher nocturnal BP as the severity of SAS increased in the SAS patients without HTN who had normal clinic BP. The results of this study suggested that SAS affected nocturnal BP elevation even in SAS patients without HTN.

Factors affecting circadian BP changes

At baseline, significant differences in the body weight, BMI, and HDL cholesterol were observed among the 4 groups. It is considered that these factors play an important role to induce BP elevation.

Some studies reported that insulin resistance and adipose-tissue specific bioactive substances, such as leptin [11] and adiponectin [12], affected BP elevation in obese patients. In the present study, the non-SAS group had the lowest body weight and BMI, followed by the moderate-, mild-, and severe-SAS groups; however, BP in each time zone, except the morning BPs and evening BPs and BPd, tended to be elevated as the severity of SAS increased. Accordingly, we presumed that SAS, rather than body weight and BMI, affected BP elevation.

On the other hand, the non-SAS group had the highest HDL cholesterol, followed by the mild-, severe-, and moderate-SAS groups. It is well known that low HDL cholesterol is a risk factor for arteriosclerosis and coronary artery disease [13]; however, it is still uncertain whether HDL cholesterol plays a crucial role in circadian BP changes. Since our study patients were normotensive, we therefore concluded that HDL cholesterol had no direct influence on the study results.

Diabetes mellitus and insulin resistance also affect circadian BP changes. Some studies reported that BP rise was in accordance with the progression of nephropathy [14,15] and hyperinsulinemia due to insulin resistance [12,16]. Of our study population, only 4 patients (5%) had diabetes mellitus and the level of HbA1c was less than 6.5%; there was no significant difference in glycemic control among the 4 SAS groups. We thus considered that diabetes mellitus and insulin resistance had little influence on the circadian BP changes because the 4 patients had early-stage diabetic nephropathy.

In the present study, we obtained the arousal index, 3% ODI and 4% ODI and evaluated the influence of these variables on the sleep BP; however, we only found a correlation between the arousal index and 3% ODI. Accordingly, we concluded that AHI might be related to sleep BP.

The severity of SAS and the course of BP

Wright et al. [17] noted that SBD had no influence on the BP measured at the clinic 5 years later in SBD patients without HTN; however, the mean 24-h BPs, the sleep BPs, and the highest BPs during sleep significantly increased. Their study result supports our hypothesis that SAS may affect sleep BP in SAS patients without HTN. In this study, we obtained a similar result, the significant increases in the mean 24-h BPs, sleep BPs, lowest BPs, pre-awake BPs, and morning BPs as the severity of SAS increased. SAS was involved in BP elevation during sleep in SAS patients without HTN. Since we found significant differences in the body weight and BMI among the 4 groups, we evaluated the influence of BMI as well as AHI on sleep BP, lowest BP, and pre-awake BP using ANCOVA. In the SAS patients without HTN, sleep BPd became higher as the severity of SAS increased, which was attributed to BMI itself and the interaction between BMI and AHI. Moreover, SAS and obesity were considered to be associated with pre-awake BP elevation. Somers et al. [18] demonstrated that SAS patients had high sympathetic activity when awake, which might trigger transitory BP surge after the resumption of breathing due to apnea. Intermittent hypopnea due to SAS is associated with elevated sympathetic nerve activity which is sustained into the next morning [19]. O'Donnell et al. [20] investigated canine models and reported that the airway obstruction caused an increase in the mean arterial pressure, which could be accentuated by prior sleep deprivation, and that repetitive airway obstruction would cause an increase in the mean arterial pressure over time that was sustained for $\geq$2 h when normal airway patency was restored. They suggested that increased and persistent sympathetic nerve activity affected BP elevation during daytime. Even in SAS patients with normal awake BP, SAS is responsible for sympathetic nerve system activation during sleep, which results in BP changes and nocturnal HTN [8,21]. The elevated sympathetic and inhibited parasympathetic nerve activities repeat every night; the frequencies of these activities gradually increase and persist during daytime [22]. We presumed that diurnal BP elevation continuously occurred after nocturnal BP elevation in SAS patients. Moreover, BP pattern changed into non-dipper (less than 10% nocturnal BPs reduction) or riser BP (BP elevation during sleep) pattern. Cerebral, cardiac or renal disease deteriorates in patients with a non-dipper or riser BP pattern who have higher cardiovascular risks than those with dipper BP pattern [4].

The results of this study indicated firstly the relationship between the severity of SAS and BPd pattern; and secondly, a similar result in BPs to our previous study which did not investigate BPd [8]. Wright et al. [17] demonstrated that SDB influenced a significant increase in sleep BPd in SDB patients without HTN. This study's results also support the findings of Wright et al. that SAS could affect sleep BPd in SAS patients without HTN. To date, there is no consensus on the clinical and prognostic meaning of BPd elevation; sleep BPd has not been fully evaluated. We believe that intervention treatment for BPd as well as BPs possibly prevents the onset of cardiovascular diseases.

Recently, the importance of nocturnal BP changes has been recognized. The normal nocturnal decrease in BP averages 10—20% below daytime levels [3,23], because inhibited sympathetic nerve activity reduces BP during sleep [24]. In contrast, many SAS patients have non-dipper BP or riser BP pattern because they have an attenuated or absent fall in nocturnal BP. Therefore, nocturnal BP change is more useful to predict cardiovascular events than BP measured at clinic or home and awake BP [25]. We consider that SAS contributes to the occurrence of nocturnal HTN. Obstructive SAS (OSAS) patients have a significantly increased risk of sudden death from cardiac causes during sleep and a marked nocturnal peak in sudden death [26]. Ohkubo et al. [23] reported that the mortality risk was highest in inverted dippers, followed by non-dippers. Many OSAS patients have non-dipper or riser BP pattern and show BP surge in the early morning [27]. Accordingly, appropriate treatment for SAS patients without HTN may well prevent not only nocturnal and morning BP elevation but also future HTN and cardiovascular events. One study has suggested that SAS in patients without HTN affects sleep that occupies one-third of the human life span, which will lead to dysautonomia, increased renin—angiotensin—aldosterone system activity, BP changes, and nocturnal BP elevation [28]. It is also reported that arterial stiffness, which is evaluated by the pulse wave velocity and left ventricular function, significantly increases as the severity of SAS increases [29]; however, these mechanisms have not been fully elucidated.

SAS may therefore be associated with future HTN and nocturnal BP elevation which triggers organ disorders and cardiovascular events.

Study limitations

Since many SAS patients had high BP, it was quite difficult to find SAS patients with normal BP, especially non-SAS patients with normal BP. A further study with a larger population should be required. The adequacy of BP measured at the clinic, which identified the patients with or without HTN, was valid because all patients had the mean awake BPs < 140 mmHg and BPd < 90 mmHg. Since there is no consensus on the definition of nocturnal BP elevation and abnormal BP reduction during sleep based on ABPM, it is still a matter of debate which is more clinically important, sleep BP or abnormal BP reduction during sleep. It is vital to conduct a further study to accumulate data. In HTN patients, nocturnal BP elevation, such as non-dipper BP, is considered as a trigger of cardiovascular events; however, no study has yet investigated whether nocturnal BP elevation is associated with the onset of cardiovascular events and BP elevation during daytime. Further investigations regarding these points are thus called for.

Conclusions

This study demonstrated the relationship between the severity of SAS and circadian BP changes using PSG and ABPM, which suggested that SAS affected nocturnal BP elevation even in SAS patients without HTN. In the present study, we found no difference in the diurnal BP in the severity of SAS; however, the nocturnal BP was significantly elevated in the severe-SAS group.

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