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The effect of high evening blood pressure on obstructive sleep apnea–related morning blood pressure elevation: does sex modify this interaction effect?

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Abstract

Purpose Obstructive sleep apnea (OSA) can lead to increased morning blood pressure (BP). We hypothesized that high evening BP may aggravate OSA-related morning BP elevation. Additionally, this interactional effect may be modified by sex.

Methods This retrospective, cross-sectional study included newly diagnosed OSA patients with an apnea-hypopnea index (AHI) ≥ 5 per hour on a full-night polysomnography. An analysis of covariance (ANCOVA) was used to determine whether severe OSA (AHI ≥ 30) was associated with higher morning BP than mild-to-moderate OSA (5 ≤ AHI < 30) and whether there was an interaction between apnea severity and evening BP on morning BP. To identify the sex effects, analyses were performed separately in each sex group.

Results A total of 1445 patients with an average age of 51.9 years (SD 11.7) (male 77.9% vs. female 22.1%; high evening BP group 22.4% vs. normal evening BP group 59.6%) were included in the study. Based on the ANCOVA, patients with severe OSA had significantly higher morning systolic BP (SBP) ($p = 0.003$), diastolic BP (DBP) ($p < 0.001$), and mean BP (MBP) ($p < 0.001$) than the mild-to-moderate group in male subjects. A significant interaction between apnea severity and evening BP was identified on morning DBP and MBP in male subjects. However, there were no differences in morning BP between severe and mild-to-moderate OSA groups in female subjects.

Conclusions In male subjects, severe OSA contributed to higher morning BP than mild-to-moderate OSA. OSA-associated morning BP elevation was more prominent in the high evening BP group than in the normal BP group. Such relations were not found in female subjects.

Keywords Obstructive sleep apnea · Blood pressure · Hypertension · Sex · Diastolic blood pressure · Morning blood pressure

Introduction

Obstructive sleep apnea (OSA) is a common disease that is characterized by the repeated collapse of the upper airway during sleep, which leads to transient asphyxia [1]. Recurrent sleep apnea increases nocturnal blood pressure (BP) during the sleep period, and OSA patients are likely to have a non-dipper/riser pattern [2], which consequently may lead to increased morning BP and has been well documented in previous studies [3–5]. Furthermore, more than 70% of resistant hypertension patients also have OSA [6]. The epidemiological data suggest that there is a bidirectional relationship between OSA and hypertension, where many patients with OSA also present a high prevalence of hypertension [6, 7].

OSA-related BP elevation may be multifactorial in origin and may depend on systemic inflammation, oxidative stress, endogenous vasoactive factors, endothelial dysfunction, increased sympathetic activation, and metabolic dysregulation [8, 9]. There is mounting evidence of interaction effects between OSA and hypertension on BP-elevating pathophysiology such as blood levels of aldosterone, inflammatory markers, the progression of atherosclerosis, and adverse cardiovascular effects [10–13]. Therefore, it is speculated that

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individuals with underlying hypertension may have an additive effect on the OSA-associated BP elevation and there may be increased adverse effects in hypertensive-OSA patients when compared with normotensive OSA or non-OSA hypertensive subjects. However, research on this subject is limited. White et al. [14] found that hypertensive-OSA patients had increased nocturnal hypertension, while normotensive OSA patients were not likely to be susceptible to the BP-elevating effects of OSA. Walia et al. [15] reported that the severity of underlying hypertension affected the relationship between OSA and BP elevation. Especially, interactional effect of high evening BP may be more critical because of their non-dipper/riser BP pattern of patients with OSA. It may be important to control evening BP with evening administration of antihypertensive drugs in patients with OSA although previous data were conflicting about the effect of administering the medication at night [16, 17].

The effect of sex on the development of hypertension in OSA has also not been entirely elucidated [8]. Several studies have looked into the role of sex in OSA-associated BP elevation, but their results were inconsistent, possibly due to differing methodologies [3–5, 18–22]. Previous research has found that males were vulnerable to OSA-associated BP elevation [3, 4, 19, 22]. In contrast, other studies have indicated that female OSA patients have a higher prevalence of hypertension [18]. Population-based studies, however, have not revealed any differential effect of sex on OSA-associated hypertension [20, 21]. Additionally, little research has investigated the effect of sex on the interaction between underlying hypertension and OSA in morning BP.

Therefore, we investigated the potential interaction of high evening BP on the effect of OSA on morning BP, and the role of sex on this interactional effect.

Methods

Patients and clinical data

In this cross-sectional study, we retrospectively examined subjects who visited a sleep laboratory for evaluation of suspected OSA between 2009 and 2015. Patients were eligible for the trial if they were older than 18 years of age and if they had a new diagnosis of OSA with an apnea-hypopnea index (AHI) ≥ 5 per hour with a full-night polysomnography (PSG). Subjects were excluded if polysomnographic and clinical data were insufficient. Patient information including age, sex, body mass index (BMI) calculated as the weight in kilograms divided by the square of the height in meters, and Epworth sleepiness score (ESS), as well as history of hypertension, antihypertensive agent use, periodic limb movement index (PLMI), periodic limb movement arousal index (PLMAI), arousal index, diabetes mellitus (DM), and smoking was collected. Subjects were classified as mild-to-moderate OSA ($5 \leq AHI < 30$) and severe OSA ($AHI \geq 30$) according to AHI per hour.

BP was measured on the right arm before sleep onset and after sleep offset, using a standard mercury sphygmomanometer. During all measurements, patients were supine and awake, with all PSG monitoring equipment attached. Prior to the measurement of evening BP, patients remained supine for at least 15 to 20 min. Morning BP was measured in the bed after patients awakened. Based on BP measured before sleep onset, participants were divided into a high evening BP group and a normal evening BP group. Previously, Walia et al. defined elevated BP as BP ≥ 130/80 mmHg including high normal BP in consideration of the association with cardiovascular risk [15]. But we followed the European Society of Hypertension/European Society of Cardiology guidelines published in 2013 [23] and the Eighth Joint National Committee (JNC 8) guidelines [24] for the management of hypertension; subjects with systolic BP (SBP) ≥ 140 mmHg and/or diastolic BP (DBP) ≥ 90 mmHg [4, 25] were classified as having high BP. Mean BP (MBP) was calculated as follows: $DBP + 1/3(SBP - DBP)$ [26]. The study was reviewed and approved by the institutional review board of Asan Medical Center. All of the participants provided written informed consent to participate in the study.

Sleep studies

OSA was diagnosed using standard PSG procedures. Sleep and associated events were scored according to the guidelines of the American Academy of Sleep Medicine (AASM) [27]. Apnea was defined as a 90% drop in the peak thermal sensor excursion from the baseline value for at least 10 s. Hypopnea was defined as a 30% drop in nasal pressure signal excursion from the baseline value for 10 s accompanied by a 4% reduction in O_2 saturation from the pre-event baseline. AHI was defined as the average number of episodes of apnea and hypopnea per hour. Objective OSA severity was evaluated using AHI and minimal arterial oxygen saturation. Arousals were scored according to AASM scoring guideline [27], and arousal index was defined as the number of arousals per hour of sleep. Periodic limb movements (PLMs) were identified by the pattern of limb movement according to AASM scoring manual (more than 4 limb movements and an interval of 5–90 s) [27]. The PLMI is the number of PLMs per hour of sleep, and PLMAI is the number of PLM arousals per hour of sleep.

Statistical analysis

For comparison, Student's t test and the χ^2 test were used. Analysis of covariance (ANCOVA) was used to determine whether severe OSA raised morning BP compared with mild-to-moderate OSA and whether there was an interaction between apnea severity and evening BP on morning BP. We

selected evening BP as a modifying factor to investigate whether it may have an additive effect on OSA-associated BP elevation, and to identify the clinical significance of high evening BP in patients with OSA. The dependent variables were morning SBP, DBP, and MBP. The independent variables were OSA type (severe or mild-to-moderate) and evening BP (high or normal). Age, BMI, ESS score, current antihypertensive medication use, presence of DM, and smoking status were covariates. PLMAI was also controlled because it may be a potential risk factor for elevated morning BP [28]. To identify the sex effects, ANCOVA analyses were performed separately for females and males. The ANCOVA regression results were reported as estimated parameter values (β) to present the size of effects. Significance was set at $p < 0.05$. IBM SPSS 21.0 software (IBM Inc., Armonk, NY) was used to perform these statistical analyses.

Result

Patient characteristics

Table 1 compares the clinical characteristics between the male and female groups and high and normal evening BP groups in each sex. A total of 1445 patients (1126 males, 265 with high evening BP and 861 with normal BP; 319 females, 58 with high evening BP and 261 with normal BP) with an average age of 51.9 years (standard deviation 11.7) were included in the study. Male subjects were younger, more obese, and had higher BP, higher arousal index, and more severe OSA than female subjects. High evening BP was more prevalent in male subjects (male 265 (23.5%) vs. female 58 (18.2%), $p = 0.043$).

In male subjects, AHI was significantly higher in the high evening BP group than in the normal evening BP group ($p < 0.001$). In female subjects, AHI did not significantly differ between the high evening BP and the normal evening BP groups ($p = 0.396$). In male subjects only, ESS scores and the presence of smoking were higher in the high evening BP group than in the normal evening BP group. The presence of DM was higher in high evening BP group than in the normal evening BP group for both sexes.

Comparison of morning blood pressure between patients with severe obstructive sleep apnea and mild-to-moderate obstructive sleep apnea, and severe obstructive sleep apnea-high blood pressure interaction

In male subjects, the severe OSA group had significantly higher morning SBP ($p = 0.003$), DBP ($p < 0.001$), and MBP ($p < 0.001$) than the mild-to-moderate group based on the ANCOVA (Table 2). However, morning SBP (partial eta^2, 0.008), DBP (partial eta^2, 0.012), and MBP (partial eta^2, 0.014) had minimal partial eta^2 values accounting for about 1% of the total variance. A significant severe OSA–high evening BP interaction effect was identified on morning DBP ($p = 0.029$) and MBP ($p = 0.026$), but not morning SBP ($p = 0.081$) in male subjects (Table 2). A difference in morning DBP between severe OSA and mild-to-moderate OSA was identified in the high evening BP group ($\beta = 3.167$, $p = 0.010$), but not in the normal evening BP group ($\beta = 0.988$, $p = 0.077$) (Table 2). Differences in morning MBP between severe OSA and mild-to-moderate OSA were more than two times larger in the high evening BP group ($\beta = 3.466$, $p = 0.006$) than in the normal evening BP group ($\beta = 1.115$, $p = 0.043$) (Table 2). Figure 1 shows a severe OSA–high evening BP interaction. The interaction plot slopes between estimated marginal mean DBP/MBP of severe and mild-to-moderate OSA were steeper in the high evening BP group than in the normal evening BP group (Fig. 1 (B) and (C) in men). However, there was no difference in slope of SBP between the two BP groups in men (Fig. 1 (C) in men).

In female subjects, there were no significant differences in morning BP between OSA groups and no significant severe OSA-high evening BP interaction was identified (Table 3). A significant difference in slope between the high evening BP group and normal BP group was not detected for SBP, DBP, or MBP (Fig. 1).

Discussion

In this study, male patients with severe OSA had significantly higher morning SBP, DBP, and MBP than male patients with mild-to-moderate OSA. Although the small effect sizes (partial eta^2 values about 1%) reduced the significance, our findings are in agreement with previous studies, which suggested that OSA is associated with morning BP elevation [3–5]. Additionally, a significant severe OSA–high evening BP interaction was identified on morning DBP and MBP in male subjects. However, these effects of severe OSA group and severe OSA–high evening BP interaction on morning BP were not detected in female subjects.

In this study, we observed that the presence of high evening BP modified an OSA-associated morning BP elevation in men, and that OSA-associated morning DBP/MBP elevation was more prominent in the high evening BP group than in the normal BP group. Walia et al. [15] and White et al. [14] also suggested the effect of high BP on the OSA-associated BP elevation. In the hypertensive subjects using three or more antihypertensive medications, the percentage of elevated BP (SBP ≥ 130 mmHg or DBP ≥ 80 mmHg) almost doubled in the severe OSA group (58.3%) compared with the moderate OSA group (28.6%) [15]. In contrast, there was no difference in prevalence of elevated BP (SBP ≥ 130 mmHg or DBP ≥ 80 mmHg) between moderate OSA (38.1%) and severe OSA

Table 1 Clinical characteristics of patients

	Total		Male		Female	
	Male ($n = 1126$)	Female ($n = 319$)	High evening BP ($n = 265$)	Normal evening BP ($n = 861$)	High evening BP ($n = 58$)	Normal evening BP ($n = 261$)
Age, years	50.7 ± 11.9	56.1 ± 10.0***	50.7 ± 10.4	50.7 ± 12.4	57.9 ± 11.0	55.7 ± 9.7
Body mass index, m^2/kg	26.2 ± 3.3	25.0 ± 3.9***	27.3 ± 3.8	25.9 ± 3.1***	26.2 ± 4.3	24.7 ± 3.7**
Epworth sleepiness score	9.5 ± 5.0	9.6 ± 5.3	10.1 ± 5.2	9.4 ± 4.9*	9.7 ± 5.9	9.6 ± 5.2
Smoking, *n* (%)	372 (33.0%)	6 (1.9%)***	104 (39.2%)	268 (31.1%)*	0 (0.0%)	6 (2.3%)
History of hypertension, *n* (%)	410 (36.4%)	116 (36.4%)	135 (50.9%)	275 (31.9%)***	36 (62.1%)	80 (30.7%)***
Current antihypertensive medication use, *n* (%)	285 (25.3%)	72 (22.6%)	94 (35.5%)	191 (22.2%)***	25 (43.1%)	47 (18.0%)***
Diabetes mellitus, *n* (%)	129 (11.5%)	38 (11.9%)	41 (15.5%)	88 (10.2%)*	12 (20.7%)	26 (10.0%)*
Morning SBP, mmHg	129.6 ± 12.6	127.6 ± 14.0*	140.6 ± 13.8	126.2 ± 10.1***	142.7 ± 15.1	124.3 ± 11.3***
Morning DBP, mmHg	86.2 ± 9.6	80.9 ± 9.2***	94.5 ± 9.8	83.6 ± 7.9***	88.9 ± 8.1	79.1 ± 8.4***
Morning MBP, mmHg	100.7 ± 9.9	96.4 ± 9.9***	109.9 ± 10.1	97.8 ± 7.9***	106.8 ± 8.7	94.1 ± 8.6***
Evening SBP, mmHg	127.3 ± 12.3	126.8 ± 12.8	141.6 ± 12.4	122.9 ± 8.3***	144.2 ± 11.3	122.9 ± 9.4***
Evening DBP, mmHg	82.9 ± 9.4	79.2 ± 9.3***	94.4 ± 7.4	79.4 ± 6.8***	90.2 ± 7.5	76.8 ± 7.8***
Apnea-hypopnea index, /h	34.2 ± 21.1	25.3 ± 20.2***	41.2 ± 23.4	32.1 ± 19.8***	27.4 ± 22.4	24.9 ± 19.7
Minimal arterial oxygen saturation, %	79.4 ± 8.3	82.7 ± 7.2***	78.1 ± 9.6	79.8 ± 7.8**	80.2 ± 10.1	83.2 ± 6.3*
Obstructive sleep apnea group						
Mild ($5 \leq$ AHI < 15)	225 (20.0%)	122 (38.2%)	34 (12.8%)	191 (22.2%)	20 (34.5%)	102 (39.1%)
Moderate ($15 \leq$ AHI < 30)	328 (29.1%)	114 (35.7%)	62 (23.4%)	266 (30.9%)	23 (39.7%)	91 (34.9%)
Severe (AHI ≥ 30)	573 (50.9%)	83 (26.0%)***	169 (63.8%)	404 (46.9%)***	15 (25.9%)	68 (26.1%)
Periodic limb movement index, /h	45.9 ± 118.4	47.0 ± 97.9	44.2 ± 142.5	46.5 ± 110.0	46.9 ± 87.9	47.1 ± 100.2
Periodic limb movement arousal index, /h	4.9 ± 20.5	6.7 ± 20.9	4.5 ± 20.5	5.1 ± 20.5	8.3 ± 23.7	6.3 ± 20.2
Arousal index, /h	39.0 ± 47.8	28.5 ± 15.5***	41.8 ± 18.5	36.6 ± 24.5	31.7 ± 16.8	27.9 ± 15.2

Values are presented as mean ± standard deviation for numerical data or number (%) for nominal variables

*p value < 0.05, **p value < 0.01, ***p value < 0.001

BP, blood pressure; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *MBP*, mean blood pressure; *AHI*, apnea-hypopnea index

High evening BP was more prevalent in male subjects (males 265 (23.5%) vs. females 58 (18.2%), $p = 0.043$)

Table 2 The main effects of severe OSA group and OSA group by evening blood pressure interaction on morning blood pressure in male subjects ($n = 1126$)

	Evening BP by OSA group interaction, p value	OSA group effect					
		Evening BP group	Estimate	SE	F value	p value	Partial eta^2
Morning systolic BP	0.081	–	1.962	0.655	8.974	0.003	0.008
Morning diastolic BP	0.029	–	–	–	13.218	< 0.001	0.012
		High ($n = 265$)	3.167	1.219	–	0.010	
		Normal ($n = 861$)	0.988	0.558	–	0.077	
Morning mean BP	0.026	–	–	–	15.373	< 0.001	0.014
		High ($n = 265$)	3.466	1.239	–	0.006	
		Normal ($n = 861$)	1.115	0.549	–	0.043	

BP, blood pressure; *OSA*, obstructive sleep apnea; *SE*, standard error

Estimate = difference in BPs in the group with severe OSA minus BPs in the group with non-severe OSA

These models were adjusted by age, body mass index, Epworth sleepiness score, current antihypertensive medication use, history of diabetes mellitus, smoking status, and periodic limb movement arousal index

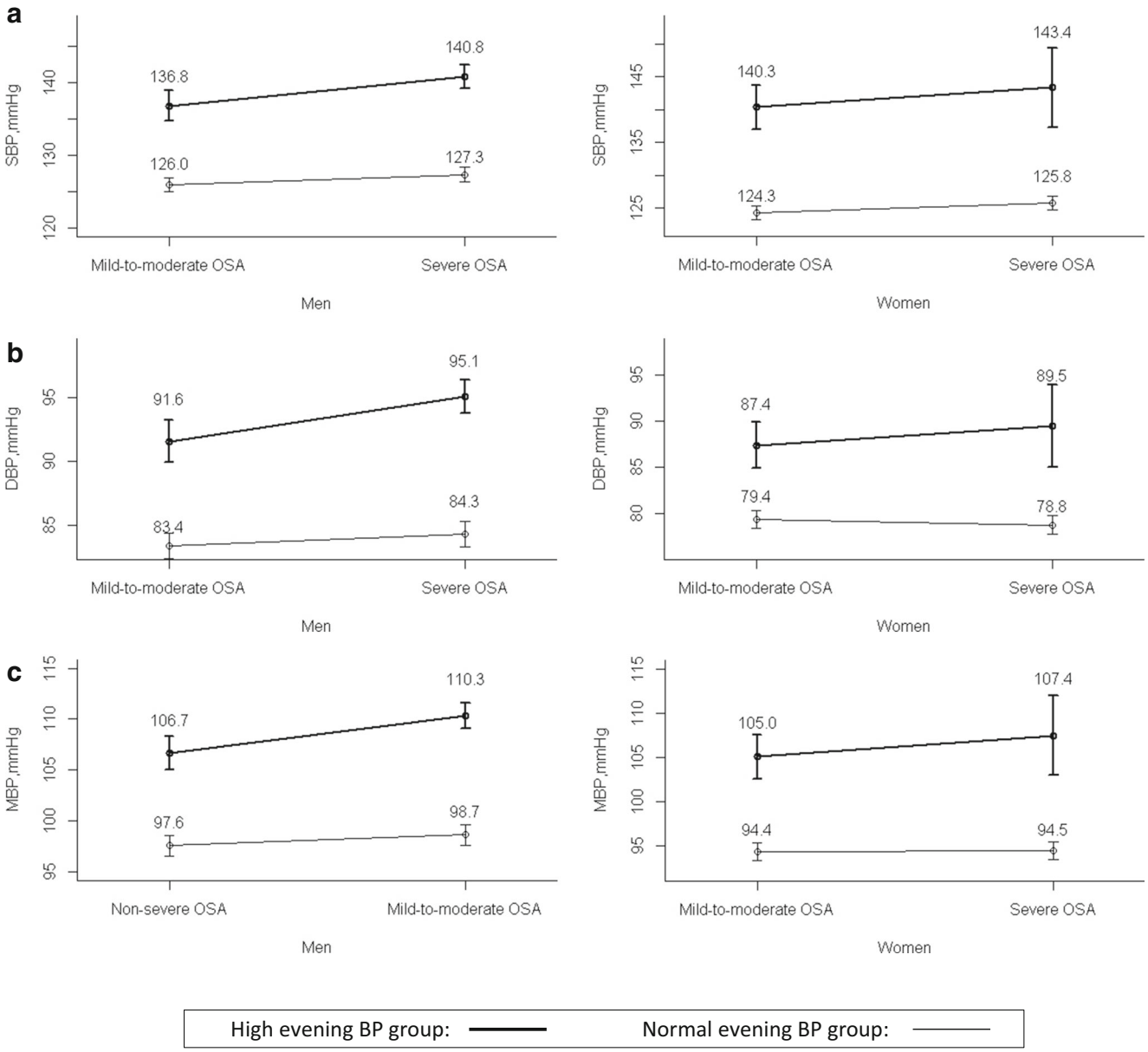

Fig. 1 Evening BP–OSA interaction on morning BP in men and women. Estimated marginal means and 95% confidence intervals of morning SBP (A), DBP (B), and MBP (C) in subjects with mild-to-moderate OSA and severe OSA. Interaction between OSA group and high evening BP was analyzed separately for men and women. Covariates included age, body mass index, Epworth sleepiness score, current antihypertensive medication use, history of diabetes mellitus, smoking status, and periodic limb movement arousal index. BP, blood pressure; OSA, obstructive sleep apnea; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure

(39.5%) in subjects not using three or more antihypertensive medications [15]. White et al. [14] found that, in hypertensive patients, OSA exacerbates the reversal of the normal circadian sodium excretion pattern by elevating the nocturnal urine sodium excretion rate; on the other hand, normotensive OSA patients did not have increased nocturnal sodium excretion. Their results suggested that normotensive OSA patients do not appear to be susceptible to the BP-elevating effect of OSA, in contrast to the hypertensive-OSA patients in whom OSA probably exacerbated their nocturnal hypertension.

The interaction effect between OSA and high BP on BP-elevating pathophysiology may be explained by several potential mechanisms including endogenous vasoactive factors, inflammatory markers, the progression of atherosclerosis, and endothelial dysfunction [9–13]. For example, endothelial-dependent vasodilatory capacity is impaired in OSA and OSA has an incremental effect on endothelial dysfunction in hypertensive patients [9]. A meta-analysis of 13 studies showed that aldosterone levels were higher in OSA patients with hypertension than in normotensive OSAS patients [29].

Table 3 The main effects of severe OSA group and OSA group by evening blood pressure interaction on morning blood pressure in female subjects ($n = 319$)

	Evening BP-by-OSA group interaction, p value	OSA group effect					
		BP group	Estimate	SE	F value	p value	Partial eta^2
Morning systolic BP	0.693	–	1.762	1.492	1.395	0.239	0.005
Morning diastolic BP	0.334	–	− 0.165	1.095	0.023	0.880	< 0.001
Morning mean BP	0.414	–	0.477	1.101	0.188	0.665	0.001

BP, blood pressure; *OSA*, obstructive sleep apnea; *SE*, standard error

Estimate = difference in BPs in the group with severe OSA minus BPs in the group with non-severe OSA

These models were adjusted by age, body mass index, Epworth sleepiness score, current antihypertensive medication use, history of diabetes mellitus, smoking status, and periodic limb movement arousal index

Pratt-Ubunama et al. also reported that the relationship between plasma aldosterone and OSA severity was modified by the presence of hypertension [12]. Drager et al. [13] found that severe OSA and hypertension were associated with arterial stiffness and heart structure abnormalities with additive effects when both conditions were present. Compared with normotensive OSA, pulse-wave velocity, left ventricular (LV) mass index, and prevalence of LV hypertrophy were significantly higher in subjects affected by both OSA and hypertension [13]. A previous study that evaluated the associations of OSA plus hypertension and prevalent cardiovascular diseases also reported that OSA may potentiate adverse cardiovascular effects in hypertensive patients but not normotensive patients [11]. The additive role of OSA and hypertension in the progression of carotid atherosclerosis and inflammatory markers was identified [10]. In aggregate, individuals with underlying physiological factors could make themselves more susceptible to hypertension; thus, there may exist an incremental effect on OSA-associated morning BP elevation.

OSA can have an influence on morning BP, which is predictive of cardiovascular risk [30]. However, OSA-associated BP elevation may dissipate by the afternoon and evening gradually [31]. Research investigating the clinical implications of evening BP in patients with OSA is rare; one study suggested that physical activity is inversely correlated with evening BP in OSA patients with high cardiovascular risk [32]. However, high BP before sleep may be critical in patients with OSA because of their nocturnal non-dipper/riser BP pattern [2] and our results demonstrating an additive effect of evening BP further support the clinical relevance of evening BP in OSA patients. Recent studies have investigated the impact of chronotherapy for hypertension in patients with OSA [16, 17]. Kasiakogias et al. [16] have suggested that evening dosing of antihypertensive drug improves nocturnal BP and dipping status in patients with OSA, but Serinel et al. [17] did not support evening dosing of antihypertensives. Given the significance of evening BP, the strict control of evening BP may be necessary in patients with OSA and evening administration of antihypertensive drugs may be appropriate despite controversy. Further investigation regarding the benefit from strict control of evening BP is needed.

In this study, the effects of severe OSA on morning BP and the interaction between severe OSA and high evening BP on morning BP were modified by sex. Among male patients, those with severe OSA had significantly higher morning SBP, DBP, and MBP than those with mild-to-moderate OSA. Additionally, a significant OSA group by high evening BP interaction was identified on morning DBP/MBP in male subjects. However, there was no interaction between OSA and high evening BP in female subjects, as severe OSA did not affect morning BP among women. There are many previous studies which investigated the sex effect in OSA-associated BP elevation, but their results were inconsistent [3–5, 18–22]. Many studies found that males were vulnerable to OSA-associated BP elevation [3, 4, 19, 22] There are also a few studies indicating female OSA patients to have a higher prevalence of hypertension [18]. Several population-based studies did not report a sex effect on OSA-associated hypertension [20, 21]. Recent studies also presented inconsistent findings. Lee and Jeoung [4] found that only male subjects had a significant association between AHI and high BP/DBP, whereas Mokros et al. [5] found that the relationship between morning DBP and AHI was found to be independent of sex. Although the human studies regarding the association between sex and OSA-associated BP elevation remain inconclusive, animal models have found differences in BP responses to OSA based on sex [33]. Sex hormones are known to play an important role in the responses and adaptations to a variety of stressors, including hypoxia [33, 34]. The adverse effects of exposure to continuous hypoxia are less dramatic in females than males in animal models [34]. In rat models, female rats subjected to intermittent hypoxic insults were less likely to develop elevated BP than their male or ovariectomized female counterparts [33]. These findings indicate that a hypertensive response to intermittent hypoxia is attenuated in females [33].

In our study, a significant severe OSA–high evening BP interaction was identified on morning DBP and MBP, but not on SBP. Systolic and diastolic hypertension may have

different pathological mechanisms. DBP elevation is usually considered to result from increased peripheral resistance [35], while a rise in SBP is predominantly related to increased resistance in conductance vessels [36]. Furthermore, SBP is largely due to age-related arterial stiffening, whereas DBP may be associated with increased sympathetic tone [4, 5, 37]. Several studies have investigated OSA-associated BP changes in SBP and/or DBP [4, 5, 22, 38, 39]. Cho et al. noted that the OSA was associated with sleep-trough morning SBP increases [38]. However, many earlier studies indicated that OSA patients have an association with DBP elevation [4, 5, 22, 39]. A recent study of 1370 male patients with OSA suggests that a rise in DBP, but not SBP, is independently associated with the exacerbation of AHI and arousal [22]. Wu et al. also found that repetitive arousals during sleep alter sympathovagal modulation significantly, which can lead to elevation of DBP without significant change in SBP [39]. The severe OSA–high evening BP interaction with DBP but not SBP in our study may be partially explained by differing pathological mechanism between SBP and DBP, and the effect of OSA on DBP. Future studies to investigate the effect of baseline hypertension on OSA-associated BP elevation, specifically SBP and DBP elevation, are needed.

There are several limitations in this study. First, medical record data did not include information on variables such as AHI during REM (rapid eye movement) sleep. OSA during REM sleep may be a predictor for elevated morning BP; recent research suggested that OSA during REM sleep contributed to hypertension [40]. It would be particularly interesting to investigate the effect of OSA during REM sleep in each sex group as OSA in REM sleep is more prevalent in female subjects [41]. Second, BP measurements, which were performed by polysomnographic technicians, were only measured once per timepoint. There is a consensus that the mean of repeated measurements is more accurate than single measurements [42, 43]. However, there have been several reports regarding the utility of single BP measurement [44, 45] and the large sample in this study might considerably attenuate the variability of BP measurement. Third, the lack of information whether the patients who were prescribed antihypertensive medication actually took it on the day or evening of the PSG was another limitation of the study especially when the single BP measurement was made. This was because BP rises if regular BP medication is not taken, simply reflecting the effect of not taking the medication and not necessarily OSA severity. Forth, the discrepancy between male and female on morning BP increase might be due to a small number of female patients in the cohort; as there were only 319 women and 4 times as many men. In female subjects, there were no significant differences in morning BP between severe OSA and mild-to-moderate OSA group contrary to male subjects. However, there might be the possibility of no effects due to lacking power with small sample size among women. Observed difference between two OSA groups in female might be clinically significant; however, it might not reject the null hypothesis indicating no association between apnea severity and morning BP (p value > 0.05). However, given that the mean BP differences between the severe and mild-to-moderate OSA in females were smaller than in males, the non-significant findings in female subjects might be due to the absence of meaningful difference rather than the small sample size. Lastly, all participants are Korean in this study so caution is needed when generalizing the results of our current study in different populations.

Conclusion

In male patients, severe OSA rather than mild-to-moderate affected morning BP elevation. A significant interaction between apnea severity and evening BP was identified on morning DBP, but not SBP. OSA-associated morning BP elevation was more prominent in the high evening BP group than in the normal BP group. However, in female patients, no significant differences in morning BP values between the two OSA groups were observed. Further studies addressing potential mechanisms to explain the differences in susceptibility to OSA-related BP elevations are needed.

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Compliance with ethical standards

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

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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