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Apnea-hypopnea Index is Correlated with Pulse Rate in Patients with Sleep-related Breathing Disorder without Hypertension, Cardiovascular Disease, or Diabetes Mellitus

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Objective: This study aimed to compare the mean pulse rate (PR) and mean blood pressure (BP) between patients with obstructive sleep apnea (OSA) and those with simple snoring (SS) during a 24-hour period, and to investigate the correlation between apnea-hypopnea index (AHI), PR, and BP in sleep-related breathing disorder (SRBD) patients with and without hypertension, diabetes mellitus (DM), and cardiovascular diseases (CVDs).
Methods: Ninety SRBD patients underwent full-night polysomnography, and ambulatory BP and PR were monitored for 24 hours. Participants were classified into OSA (AHI $\geq$ 5) and control (SS) (AHI $<$ 5) groups, and BP and PR were compared. Participants were also divided into groups with and without hypertension, CVDs, or DM to analyze the correlation between AHI, BP, and PR in each group.
Results: Mean PRs during the daytime period and during the whole 24-hour period in the OSA group were significantly higher than those in the SS group after controlling for potential confounders. No significant difference was observed in mean BP between the groups. Partial correlation analysis after controlling for confounders showed significant correlation between AHI and PR during daytime and the 24-hour period in participants without hypertension, DM, or CVDs, but not in participants with these conditions.
Conclusion: The significant differences and correlations only in PR (not in BP) found in this study suggest that PR could be an early marker for SRBD in individuals without comorbidities, and that an increased sympathetic tone could be responsible for future occurrence of CVD.

KEY WORDS: Apnea-hypopnea index; Obstructive sleep apnea; Sleep-related breathing disorders; Polysomnography; Pulse rate; 24-hour ambulatory blood pressure test.

INTRODUCTION

Obstructive sleep apnea (OSA) is a sleep disorder that decreases the quality of life and productivity of individuals and increases the risk of medical complications including hypertension, cardiovascular disorders (CVDs), and diabetes mellitus (DM) [1]. Although Koreans have a relatively lower prevalence of obesity compared with Western populations, 27% of males and 16% of females in an epidemiological study met the OSA criteria (apnea-hypopnea index [AHI] $\geq$ 5) [2].

OSA causes increased pulse rate (PR) and blood pressure (BP). PR and arterial BP are continuously changing hemodynamic phenomena that are influenced by several factors such as an individual's physical and emotional condition as well as environmental circumstances [3]. Therefore, BP and PR measured at the physician's office

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might not represent an individual's actual BP and PR [3]. Hence, BP and PR measurements with 24-hour ambulatory BP (ABP) monitoring have been widely used during the last three decades [3], the data of which are readily available, and 24-hour monitoring may be superior to office measurements in terms of prognostic value in the population [4,5]. In addition, in OSA patients, it is important to measure not only daytime BP and PR, but also BP and PR during the sleeping period at night as abnormalities in nocturnal BP and PR are reported to reflect enhanced sympathetic activation and the development of hypertension in OSA [6,7]. The monitoring of nocturnal PR is safe, widely available, and could be used to better understand sympathetic activity in OSA [6]. Thus, 24-hour ABP monitoring has an advantage in this respect. The monitors are programmed to record readings at desired intervals (usually every 15 to 60 minutes) throughout the day and night [8].

A large number of 24-hour BP studies using ABP for OSA patients have been performed. In a study conducted in 38 OSA patients, a stepwise multiple regression analysis showed that minimal arterial oxygen saturation and total sleep time significantly affected diastolic and mean BP values during a 24-hour period [9]. In a study conducted in 93 subjects with suspected sleep-related breathing disorder (SRBD) 24-hour ABP and oxygen desaturation were examined using portable devices, and concluded that oxygen desaturation index was associated with BP after adjusting for the confounding factors of age and obesity [10]. In another study using 24-hour ABP and overnight recordings of PR and arterial oxygen saturation, OSA patients reported increased ambulatory diastolic BP during the day and night and increased systolic BP at night compared with the control group [11]. Children with sleep apnea syndrome also showed increased levels of diastolic and mean BP when compared with a primary snoring group of children aged 8 to 12 years [12].

PR is an important and sensitive variable that predicts sequelae such as heart disease and mortality. In data from the first National Health and Nutrition Examination Survey Epidemiologic Follow-up study, risk of death from all causes, CVDs, and non-CVDs was elevated in white men with elevated PR independent of any other risk factors. Risk of death from all causes and CVDs was elevated in black women and men with elevated PR [13]. In a study involving a large French population, increased resting PR represented an independent predictor of non-cardiovascular mortality in both men and women and of cardiovascular mortality in men, independent of age and hypertension [14]. In 4,682 untreated patients with isolated systolic hypertension, heart rate greater than 79 beats per minute was a significant predictor of all-cause mortality [15]. An increase in PR and change in PR variability is also a common and important phenomenon in OSA [16,17]. A PR increase following apnea termination is due to increased sympathetic activity related to arousal and hypoxemia [18,19]. In a previous study, mean PR and heart rate over a period of 24 hours during wakefulness and sleep correlated significantly with AHI and the lowest peripheral oxygen saturation in patients with OSA [20,21]. However, in another study, there was no significant difference in PR and BP between the no-to-mild OSA group and the moderate-to-severe OSA group classified according to the respiratory disturbance index [22]. Thus, the findings on the relationship between OSA and PR have been inconsistent. Therefore, the change of PR in OSA is an interesting research topic since OSA is a risk factor for cardiac complications.

Despite previous studies on the association between OSA, PR, and BP, there is little research on the relationship between the severity of OSA, PR, and ABP during a 24-hour period in Koreans with low body mass index (BMI). In addition, studies examining whether there is a difference in PR and BP between OSA and simple snoring (SS) groups in Koreans are lacking. Many studies have evaluated sleep apnea and AHI using portable devices that measure oxygen saturation rather than a Level 1 polysomnography (PSG) test. In addition, little is known about the correlation between AHI and PR in Korean SRBD patients with and without CVDs and DM.

The aim of this study was to compare the mean PR and mean BP between the OSA group and the SS group during a 24-hour period and to investigate the correlation between AHI, PR, and BP in SRBD patients with and without hypertension, DM, and CVDs. Our hypotheses were that 1) there would be differences in PR and BP between the OSA and SS groups; 2) the correlation between AHI, PR and BP would be significant; and 3) this correlation may differ depending on the presence or absence of hypertension, DM, and CVDs.

METHODS

Participants

Polysomnography was performed on 285 consecutive participants. Since this study was a secondary study of the prediction study of OSA in Koreans with suspected OSA [23], of the 285 people who underwent polysomnography, 114 participants additionally agreed to ABP monitoring. Of these, 7 withdrew from the study, and 17 were excluded from the analysis as they had less than 70% of 24-hour ABP data. Finally, 90 participants (age range: 18−65 years) were included in the analysis of this study. The participants were recruited from the sleep clinic of Gil Medical Center and Daegu Catholic University Medical Center from June 2011 to February 2016. All participants were habitual snorers reported by an observer and Koreans who met the Breathing-related sleep disorder diagnostic criteria including frequent snoring, daytime sleepiness, choking during sleep, and witnessed apnea during sleep according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (text revision) [24].

Patients' medical conditions including hypertension, CVDs (history of ischemic heart disease including myocardial infarction, angina pectoris, and cerebral vascular disease), and DM were identified through detailed questions. Participants with severe and acute medical and surgical comorbidities or major psychiatric disorders were excluded from the study. Participants who had previously been diagnosed with OSA, treated with uvulopalatopharyngoplasty, or clinically suspected of having another major sleep disorder were also excluded. We obtained written informed consent from all participants. The study was approved by the Institutional Review Boards of Gil Medical Center (GIRBA2764-2012) and Daegu Catholic University Medical Center (CR-11-063). Our study was performed in accordance with the Declaration of Helsinki regarding the ethical principles for medical research involving human subjects.

PSG and 24-hour Ambulatory BP and PR Monitoring

All participants underwent laboratory-monitored nocturnal PSG. Standard PSG recordings were made in accordance with the American Academy of Sleep Medicine (AASM) recommendations [25]. PSG examination used six electroencephalography leads (F3, F4, C3, C4, O1, and O2), two electrooculogram channels, three electromyography channels, and one electrocardiography channel. The COMET and Beehive-7 systems (Grass-Telefactor Corp., West Warwick, RI, USA) were used to acquire the PSG data and to record results. The PSG results were scored based on the AASM criteria included in the manual [25]. The presence of apnea and hypopnea during sleep was determined according to recommended rules in the AASM manual. OSA was defined as AHI $\geq$ 5 per hour, and SS (control group) was defined as AHI $<$ 5 per hour and identified by audio signal peaks (recorded by a microphone) corresponding to snoring, as confirmed via PSG by the attendant technical staff.

ABP was monitored using an ABP monitor (Mobil Graph, New Generation 24h ABPM Classic; IEM GmbH, Stolberg, Germany) at 30-minute intervals during the day and at 60-minute intervals during the night. This brachial BP-detection unit was validated according to standard protocol [26]. Mean 24-hour systolic and diastolic BP and PR were automatically measured by 24-hour monitoring. Daytime and nocturnal BP and PR were defined as BP and PR from 06:00 to 00:00 and from 00:00 to 06:00, respectively. The monitor was programmed for BP and PR measurements every 30 minutes from 06:00 to 00:00 and every 60 minutes from 00:00 to 06:00. Measurements were used for the analysis if more than 70% of the recordings were valid, as suggested by the European Society of Hypertension practice guidelines [27].

Statistical Analysis

We used descriptive statistics, chi-squared test, Fisher's exact test, and independent t test to calculate and compare the demographic characteristics and PSG results between the OSA group and the SS group. We also used the analysis of covariance to compare 24-hour BP and PR between the groups after controlling for age, sex, and BMI. Non-parametric ANCOVA test was performed when parametric assumptions (i.e., normality and homogeneity of variance) were not satisfied. Partial Pearson's correlation analysis was performed to determine whether there were significant correlations between AHI, PR, and BP after controlling for age, sex, and BMI. IBM SPSS software (version 25.0; IBM Corp., Armonk, NY, USA) programs were used to perform the statistical tests. Two-tailed p values $<$ 0.05 were considered statistically significant. Power calculations were performed using G*Power 3.1.4 statistical power analyses [28].

RESULTS

Demographics, Clinical Characteristics, and PSG Data

The demographic and clinical characteristics of the participants and comparison between the OSA group and the SS group are presented in Table 1. No significant differences were observed in age and sex between the groups. However, BMI was significantly greater in the OSA group ($p = 0.002$). BP and PR measured before PSG were not significantly different between the groups. The incidence of hypertension and CVDs was higher in the OSA group ($p = 0.020$), while the frequency of DM was not significantly different. Thirty-two participants (35.6%)

Table 1. Demographic and clinical characteristics of participants with OSA and SS

Variable	OSA (n = 72)	SS (n = 18)	Statistics[a]
Demographics			
Age (yr)	47.1 ± 10.0	43.5 ± 10.3	$t = -1.36$, $p = 0.177$
Sex, male	61 (84.7)	14 (77.8)	$\chi^2 = 0.35$, $p = 0.514$
Body mass index (kg/m^2)	26.9 ± 3.8	23.9 ± 2.7	$t = -3.13$, $p = 0.002$
Clinical information			
Duration of snoring, years	9.5 ± 8.2	4.7 ± 4.3	$t = 2.90$, $p = 0.006$
ESS score	7.5 ± 3.9	5.6 ± 3.3	$t = -1.95$, $p = 0.054$
Systolic blood pressure (mmHg)	130.3 ± 15.2	127.6 ± 14.0	$t = -0.69$, $p = 0.495$
Diastolic blood pressure (mmHg)	84.8 ± 10.2	81.61 ± 11.3	$t = -1.19$, $p = 0.238$
Pulse rate (beats/min)	73.0 ± 13.2	68.7 ± 7.3	$t = -1.68$, $p = 0.101$
Hypertension and CVDs	29 (40.3)	2 (11.1)	$\chi^2 = 5.43$, $p = 0.020$
Diabetes mellitus	5 (6.9)	0 (0)	$\chi^2 = 1.32$, $p = 0.579$

Data are presented as mean ± standard deviation or number (%).
OSA, obstructive sleep apnea; SS, simple snoring; ESS, Epworth sleepiness scale; CVDs, cardiovascular diseases.
[a]Independent t test, χ^2 test, or Fisher's exact test.

Table 2. Polysomnographic data and comparison between the OSA group and the control group

Variable	OSA (n = 72)	SS (n = 18)	Statistics	
			t test[a]	ANCOVA[b]
Sleep and wake duration				
Time in bed (min)	413.6 ± 33.2	421.9 ± 27.3	$t = 0.97$, $p = 0.333$	$F = 0.73$, $p = 0.394$
Total sleep time (min)	333.6 ± 55.3	334.4 ± 66.8	$t = 0.05$, $p = 0.960$	$F = 0.00$, $p = 0.980$
Sleep latency (min)	16.1 ± 27.8	16.4 ± 25.3	$t = 0.05$, $p = 0.964$	$F = 0.02$, $p = 0.894$
Sleep efficiency (%)	81.1 ± 12.5	79.4 ± 16.0	$t = -0.51$, $p = 0.613$	$F = 0.25$, $p = 0.616$
WASO (min)	61.5 ± 48.2	71.1 ± 66.2	$t = 0.70$, $p = 0.486$	$F = 0.67$, $p = 0.415$
REM sleep latency (min)	130.4 ± 68.1	157.1 ± 81.1	$t = 1.43$, $p = 0.156$	$F = 1.71$, $p = 0.194$
Sleep stage (%)				
N1	35.6 ± 18.7	17.8 ± 7.1	$t = -6.41$, $p < 0.001$	$F = 13.01$, $p = 0.001$
N2	47.3 ± 15.9	63.3 ± 9.5	$t = 5.50$, $p < 0.001$	$F = 15.92$, $p < 0.001$
N3	1.7 ± 4.3	3.5 ± 4.3	$t = 1.58$, $p = 0.118$	$F = 0.96$, $p = 0.329$
R	15.1 ± 7.3	15.4 ± 6.7	$t = 0.13$, $p = 0.900$	$F = 0.14$, $p = 0.706$
Respiration				
AHI, events per hour	37.5 ± 23.9	1.8 ± 1.7	$t = -12.54$, $p < 0.001$	$F = 39.22$, $p < 0.001$
Oxygen desaturation index	32.0 ± 22.9	1.3 ± 1.2	$t = -11.07$, $p < 0.001$	$F = 34.06$, $p < 0.001$
Minimum oxygen saturation (%)	76.6 ± 9.3	89.6 ± 3.0	$t = 10.02$, $p < 0.001$	$F = 32.89$, $p < 0.001$
Movement index				
PLMS	4.2 ± 12.9	2.4 ± 4.4	$t = -0.59$, $p = 0.554$	$F = 0.00$, $p = 0.997$
PLMS arousal	0.7 ± 2.2	0.7 ± 1.3	$t = -0.13$, $p = 0.899$	$F = 0.03$, $p = 0.865$

Data are presented as mean ± standard deviation.
OSA, obstructive sleep apnea; SS, simple snoring; ANCOVA, analysis of covariance; WASO, wake time after sleep onset; REM, rapid eye movement; N1, non-REM (NREM) stage 1; N2, NREM stage 2; N3, NREM stage 3; R, REM stage; AHI, apnea-hypopnea index; PLMS, periodic limb movements during sleep.
[a]Independent t test, [b]ANCOVA after controlling for age and sex.

had one or more diseases among hypertension (n = 25), CVDs (n = 9), and DM (n = 5), while 58 participants (64.4%) had no disease.

The PSG data and the comparison between the OSA group and the SS group are presented in Table 2. No significant differences were observed in total sleep time, sleep latency, sleep efficiency, and periodic limb movements during sleep index between the groups (Table 2). The OSA group showed higher AHI ($p < 0.001$), oxygen desaturation index, and percentage of N1 sleep, and lower percentage of N2 sleep and minimum oxygen saturation than the SS group.

Difference in PR and BP between the OSA and the SS Group

The mean BP and PR during the daytime period, the

Table 3. Comparison of 24-hour pulse rate and ambulatory blood pressure between the OSA group and the control group

Pulse rate and blood pressure	OSA (n = 72)	SS (n = 18)	Statistics[a]
Pulse rate and blood pressure during the daytime period			
Pulse rate[b]	75.9 ± 10.0	73.0 ± 6.7	$F = 4.33$, $p = 0.040$[c]
Systolic mean BP	136.9 ± 13.3	130.9 ± 15.4	$F = 1.90$, $p = 0.172$
Diastolic mean BP	85.9 ± 9.2	82.6 ± 11.4	$F = 2.51$, $p = 0.117$
Mean arterial BP	102.7 ± 10.2	98.3 ± 12.0	$F = 2.54$, $p = 0.114$
Pulse rate and blood pressure during the nocturnal period			
Pulse rate[b]	63.0 ± 8.0	61.3 ± 6.0	$F = 1.49$, $p = 0.226$
Systolic mean BP[b]	118.4 ± 14.2	115.7 ± 14.0	$F = 0.47$, $p = 0.494$
Diastolic mean BP	74.4 ± 9.7	71.7 ± 11.6	$F = 1.02$, $p = 0.316$
Mean arterial BP[b]	88.6 ± 10.8	86.3 ± 11.9	$F = 1.28$, $p = 0.261$
Pulse rate and blood pressure during the whole 24-hour period			
Pulse rate[b]	73.1 ± 9.5	70.5 ± 5.8	$F = 3.99$, $p = 0.049$[c]
Systolic mean BP	132.9 ± 12.7	127.6 ± 14.6	$F = 1.34$, $p = 0.251$
Diastolic mean BP[b]	83.1 ± 9.7	80.2 ± 11.1	$F = 3.45$, $p = 0.066$
Mean arterial BP[b]	99.3 ± 10.6	95.8 ± 11.8	$F = 2.62$, $p = 0.109$

Data are presented as mean ± standard deviation.
OSA, obstructive sleep apnea; SS, simple snoring; BP, blood pressure.
[a]Analysis of covariance (ANCOVA) after controlling for age, sex, and body mass index. [b]Non-parametric ANCOVA test was performed when parametric assumptions (i.e., normality and homogeneity of variance) are not satisfied. [c]Significant results.

Table 4. Partial correlation analysis between AHI, mean pulse rate, and blood pressure during the 24-hour period after controlling for age, sex, and BMI

Mean pulse rate and blood pressure	Total participants (n = 90)		Participants without HTN, DM, or CVDs (n = 58)		Participants with HTN, DM, or CVDs (n = 32)	
	r[a]	p value	r[a]	p value	r[a]	p value
Pulse rate and mean blood pressure during the daytime period						
Pulse rate	0.218	0.042[c]	0.329	0.014[c]	0.099	0.609
Systolic BP	−0.153	0.157	−0.103	0.454	−0.189	0.327
Diastolic BP	−0.003	0.979	0.105	0.447	−0.149	0.441
Mean arterial BP	−0.069	0.523	0.024	0.865	−0.174	0.366
Pulse rate and mean blood pressure during the nocturnal period						
Pulse rate	0.252	0.019[c]	0.213	0.119	0.346	0.066
Systolic BP	−0.055	0.616	−0.089	0.516	0.023	0.906
Diastolic BP	0.053	0.626	0.036	0.797	0.135	0.485
Mean arterial BP	0.008	0.941	−0.020	0.887	0.093	0.631
Pulse rate and mean blood pressure during the whole 24-hour period						
Pulse rate	0.236	0.028[c]	0.349	0.009[c]	0.135	0.484
Systolic BP	−0.140	0.197	−0.100	0.469	−0.157	0.415
Diastolic BP	−0.027	0.804	0.106	0.440	−0.162	0.402
Mean arterial BP	−0.087	0.874	0.021	0.877	−0.186	0.333

AHI, apnea-hypopnea index; BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; CVDs, cardiovascular disease; BP, blood pressure.
[a]Partial correlation coefficient after controlling for age, sex, and BMI. [c]Significant results.

nocturnal period, and the whole 24-hour period, and their comparison between the OSA group and the SS group after controlling for age, sex, and BMI are presented in Table 3. PR during the daytime period (OSA: 75.9 ± 10.0, SS: 73.0 ± 6.7, $F = 4.33$, $p = 0.040$) and the whole 24-hour period (OSA: 73.1 ± 9.5, SS: 70.5 ± 5.8, $F = 3.99$, $p = 0.049$) in the OSA group was significantly higher than that in the SS group. No significant difference was observed in systolic, diastolic, and mean BP during the daytime period, the nocturnal period, and the whole 24-hour period between the groups ($p > 0.05$).

The comparison of mean BP and PR between the two groups after controlling for age, sex, BMI, and the presence of disease (i.e., hypertension, CVDs, or DM) are presented in Supplementary Table 1 (available online). Diastolic mean BP during the whole 24-hour period ($F = 4.80$, $p = 0.031$) and PR during the daytime period ($F = 4.33$, $p = 0.040$) and the whole 24-hour period ($F = 3.99$, $p = 0.049$) in the OSA group was significantly higher than that in the SS group. No significant difference was observed in the other measures between the groups ($p > 0.05$).

Partial Correlation Analysis between AHI, PR, and BP

Results of partial correlation analysis after controlling for age, sex, and BMI between AHI, BP, and PR are presented in Table 4, and the scatterplots are shown in Figure 1. Significant correlations were observed between AHI and PR during the daytime period ($r = 0.218$, $p = 0.042$, Fig. 1A), nocturnal period ($r = 0.252$, $p = 0.019$, Fig. 1B), and the whole 24-hour period ($r = 0.236$, $p = 0.028$, Fig. 1C) in all participants. In participants without hypertension, DM, or CVDs, the correlation between AHI and PR during the daytime period ($r = 0.329$, $p = 0.014$, Fig. 1D) and the whole 24-hour period ($r = 0.349$, $p = 0.009$, Fig. 1F) was statistically significant. However, in participants with hypertension, DM, or CVDs, no significant correlation was observed between AHI and PR during any period (Fig. 1G-I). The post-hoc power was 0.730 in the correlation analysis between AHI and PR during the whole 24-hour period in total participants.

There was no significant correlation between AHI and BP during any of the periods in all participants and in participants with and without hypertension, DM, or CVDs.

DISCUSSION

The major findings of the present study include a significant difference in PR during the daytime period and the whole 24-hour period between the OSA group and the SS group, and a significant correlation between the severity of SRBD and PR in participants without comorbidities, including CVDs, hypertension, and DM. There was significant correlation between the severity of SRBD and PR in all participants and in participants without CVDs and DM. However, there was no significant correlation between the severity of SRBD and PR in participants with these diseases.

Sympathetic overactivity is involved in the pathogenesis of CVDs including hypertension [29]. Hence, it could be postulated that increased sympathetic tone resulting from SRBD is, at least in part, the underlying pathophysiology for developing overt CVD. Resting PR is a non-invasive physiological indicator that reflects the activity of the autonomic nervous system. Several studies have suggested that resting PR is an independent risk factor of all-cause mortality in patients with hypertension. Patients with CVDs as well as individuals in the general population with a resting heart rate > 80 beats per minute have a significantly increased risk of all-cause mortality [14,15,30-34]. Thus, along with the results from this study, it follows that PR might serve as an early marker for SRBD in patients without overt CVD, hypertension, or DM, although this should be further examined and replicated in large-scale studies given the small sample size in this study. On the contrary, the correlation between heart rate and AHI was not remarkable in patients with comorbidities, presumably due to the usage of PR-lowering medications in these patients. In addition, autonomic dysfunction is prevalent in diabetic patients, resulting in possible blunting of PR variability. These findings suggest that PR might not be a robust marker for SRBD in patients with CVDs, hypertension, or DM.

There was a significant difference in mean PR between the OSA group and the SS group after controlling for age, sex, and BMI. In OSA patients, hypoxemia occurs due to apnea or hypopnea, which in turn causes decreased myocardial oxygen delivery and activation of the sympathetic nervous system [35]. This results in promotion of endothelial cell dysfunction and eventual vasoconstriction [36]. Arousal and waking during the sleep period could also re-

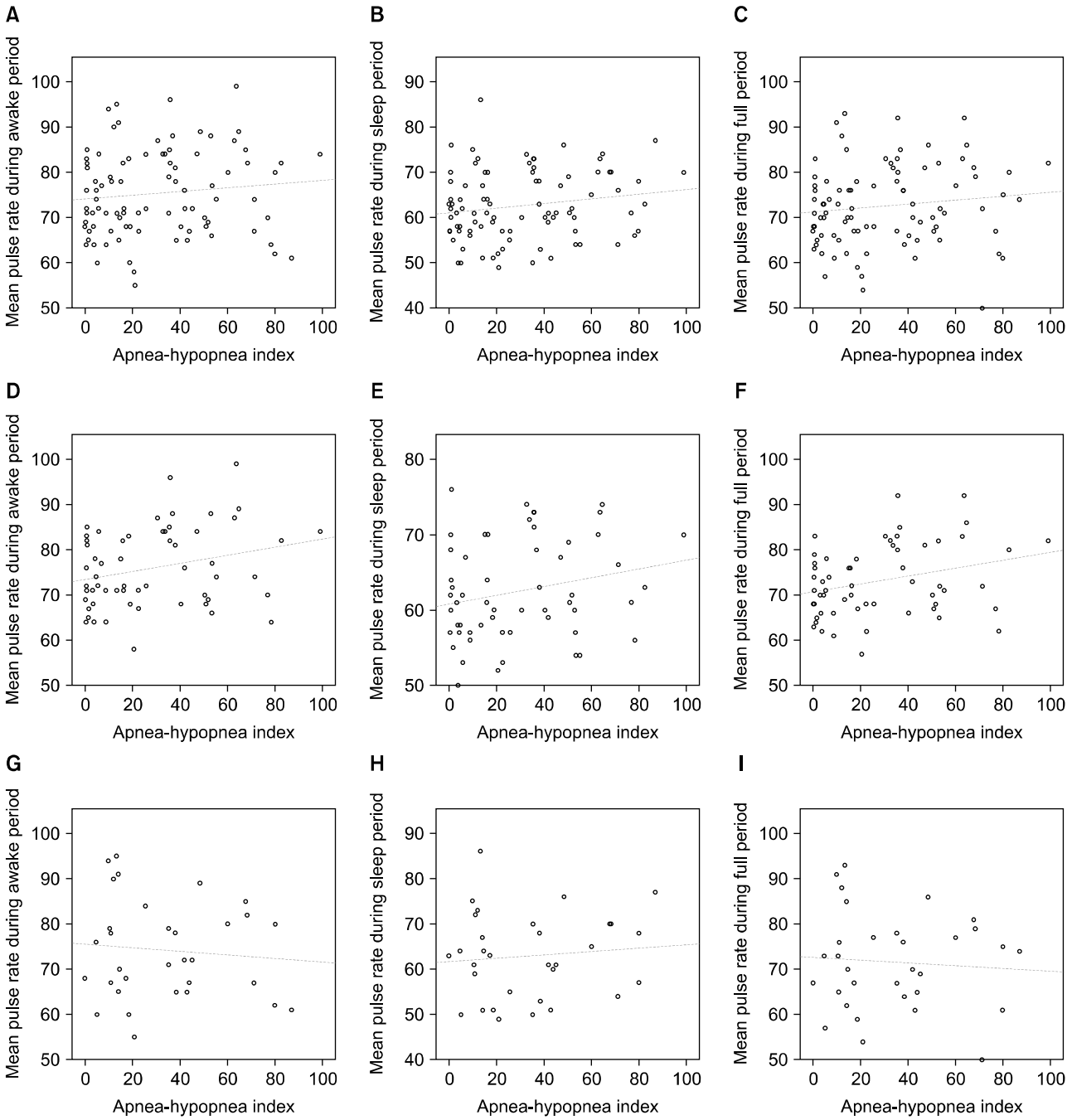

Fig. 1. Correlation between apnea-hypopnea index (AHI) and mean pulse rate according to different time periods and patient groups. (A) Correlation between AHI and mean pulse rate during the daytime period in all participants (partial correlation coefficient $r = 0.218$, $p = 0.042$). (B) Correlation between AHI and mean pulse rate during the nocturnal period in all participants (partial correlation coefficient $r = 0.252$, $p = 0.019$). (C) Correlation between AHI and mean pulse rate during the whole 24-hour period in all participants (partial correlation coefficient $r = 0.236$, $p = 0.028$). (D) Correlation between AHI and mean pulse rate during the daytime period in participants without cardiovascular diseases and/or diabetes mellitus (partial correlation coefficient $r = 0.329$, $p = 0.014$). (E) Correlation between AHI and mean pulse rate during the nocturnal period in participants without cardiovascular diseases and/or diabetes mellitus (partial correlation coefficient $r = 0.213$, $p = 0.119$). (F) Correlation between AHI and mean pulse rate during the whole 24-hour period in participants without cardiovascular diseases and/or diabetes mellitus (partial correlation coefficient $r = 0.349$, $p = 0.009$). (G) Correlation between AHI and mean pulse rate during the daytime period in participants with cardiovascular diseases and/or diabetes mellitus (partial correlation coefficient $r = 0.099$, $p = 0.609$). (H) Correlation between AHI and mean pulse rate during the nocturnal period in participants with cardiovascular diseases and/or diabetes mellitus (partial correlation coefficient $r = 0.346$, $p = 0.066$). (I) Correlation between AHI and mean pulse rate during the whole 24-hour period in participants with cardiovascular diseases and/or diabetes mellitus (partial correlation coefficient $r = 0.135$, $p = 0.484$).

sult in increased BP and PR through sympathetic activation, which in turn can result in systemic vascular resistance and cardiovascular damage [37]. In a previous study involving 90 patients with clinically suspected sleep apnea who underwent overnight PSG and 24-hour Holter echocardiography, mean PR during the 24-hour period was significantly higher in the severe OSA group than in the mild and the moderate OSA groups [20]. However, there was no significant difference between the SS group and the mild OSA group [20]. Moreover, mean PR during the 24-hour period, which included wakefulness and sleep in all participants, correlated with AHI [20]. In another study, PR was not significantly different between the no-to-mild OSA group and the moderate-to-severe OSA group, but the coefficient of variance (variability) in PR was significantly different between the groups [22]. In the aforementioned study, no relationship between AHI, BP, and BP variability was attributed to calcium channel blockers administered to the participants [22]. In the present study, only PR (but not BP) showed a significant correlation with severity of SRBD in the correlation analysis of all participants. Severity of OSA in our study was correlated with an increase in PR during the day as well as during the night. This could be attributed to sympathetic activation by OSA. In participants without hypertension, CVDs, or DM, the correlation coefficients between PR and AHI were higher than in all participants, and the correlation was not significant in participants with CVDs and DM. It is possible that patients with CVDs might have already been taking PR-modulating (and/or BP-lowering) medications. Hence, the increase in PR (and/or BP) may presumably have been blunted [22]. DM patients may have a blunted BP and PR response due to abnormalities of the autonomic function [38].

Although it is known that OSA can cause heart disease, it is difficult to predict CVDs by monitoring BP, as OSA and SS patients without comorbidities such as CVDs and DM do not have overt hypertension. If our results (the significant relationship of OSA with only PR, not BP) are replicated in future longitudinal studies, PR may be an early and more sensitive marker for assessing cardiac effects in SRBD patients without hypertension, CVDs, and DM. SRBD patients without comorbidities do not have objective parameters for assessment during the clinical course since their BP and other clinical measures are considered to be essentially normal. This study has several limitations. It included a small number of participants and, due to the nature of OSA, there was a significant difference in BMI between the OSA and SS groups. Significant BMI differences and other important clinical variables (age and sex) were adjusted for in the statistical analyses. Furthermore, we acknowledge that Holter monitoring could measure PR more accurately than ABP monitoring. Therefore, future studies using Holter monitoring are warranted. In our study, BP did not differ significantly between the OSA group and the SS group. OSA and SS are two conditions within the spectrum of SRBD. This may explain the non-significant difference in BP between the groups. In addition, the possibility of a type II error due to the small sample size of the SS group cannot be excluded. Therefore, to explain this association more clearly, a larger sample size and a healthy control group without snoring symptoms will be needed in future studies. It would be ideal to conduct a longitudinal study on OSA patients who did not start cardiovascular drugs, including anti-hypertensive drugs, but there would be practical difficulties and ethical issues in carrying this out in a naturalistic research setting.

The main results of this study include a significant difference in PR between the OSA group and the SS group, and a significant correlation between the severity of SRBD and PR in all participants as well as in participants without CVDs and DM. The present study found that PR was a more sensitive predictor for severity of SRBD than BP and a candidate marker for cardiac effects in OSA patients without CVDs and DM. Future studies on the relationship among AHI, PR, and 24-hour BP in healthy controls, SS patients, and OSA patients without CVDs and DM using larger samples are needed for more accurate research results.

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■ **Conflicts of Interest**

No potential conflict of interest relevant to this article was reported.

■ **Author Contributions**

Conceptualization: Seung-Gul Kang, Jeonggeun Moon. Data curation: Seung-Heon Shin, Ji-Eun Kim, Jae Kean Ryu, Seung-Gul Kang. Formal analysis: Jeonggeun Moon, Jae Hyoung Park, Kwang-Pil Ko, Seung-Gul Kang. Funding acquisition: Seung-Gul Kang. Investigation: Jeonggeun Moon, Jae Hyoung Park, Seo-Eun Cho, Seung-Gul Kang. Methodology: Jeonggeun Moon, Jae Hyoung Park, Kwang-Pil Ko, Seung-Gul Kang. Resources: Jeonggeun Moon, Seung-Gul Kang. Supervision: Seung-Gul Kang.

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