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SCIENTIFIC INVESTIGATIONS

The differences between daytime and nighttime heart rate variability may usefully predict the apnea-hypopnea index in patients with obstructive sleep apnea

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Study Objectives: The association between daytime/nighttime heart rate variability (HRV) and the apnea-hypopnea index (AHI) remains unclear. We sought a relationship between AHI and the daytime-to-nighttime HRV ratio as measured by 24-hour Holter monitoring in patients with obstructive sleep apnea.

Methods: We prospectively enrolled 66 patients who visited our sleep clinic complaining of habitual snoring or sleep apnea. All underwent 24-hour Holter monitoring (to measure HRV) combined with full-night polysomnography. Sixty-two met our enrollment criteria. We evaluated the associations between HRV frequency domains and the polysomnography indices. We also considered medical histories and anthropometric data.

Results: The nighttime very-low-frequency (VLF), low-frequency (LF), and high-frequency HRVs were significantly higher than the daytime values. On correlation analysis, the day/night VLF ($r = .550$, $P < .001$), LF ($r = .556$, $P < .001$), and high-frequency ($r = .303$, $P = .017$) HRVs were significantly related to the AHI. Of the day/night HRV ratios, the VLF (P for trend = .003) and LF (P for trend = .013) ratios decreased significantly by obstructive sleep apnea severity. Multivariable analysis showed that the day/night VLF ($\beta = 16.387$, $P < .001$) and day/night LF ($\beta = 25.248$, $P < .001$) were independently (and significantly) associated with the AHI.

Conclusions: Twenty-four-hour Holter monitoring may usefully predict AHI. The day/night VLF and day/night LF ratios tended to decrease by obstructive sleep apnea severity and were independently associated with the AHI.

Keywords: heart rate variability, 24-hour Holter monitoring, obstructive sleep apnea, polysomnography

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Currently, the association between apnea-hypopnea index and nocturnal heart rate variability (HRV) has been presented. However, there is a gap in how to interpret nocturnal HRV without a reference point. This study was performed to find a simple and accurate method to estimate apnea-hypopnea index using day/night HRV measured by 24-hour Holter monitoring.

Study Impact: The day/night very-low-frequency and day/night low-frequency ratios that are measured by 24-hour Holter monitoring could be considered in future obstructive sleep apnea diagnostic criteria, because they are more accurate way to use HRV to approximate obstructive sleep apnea severity as opposed to nighttime HRV alone.

INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by repeated upper airway collapse that disrupts sleep and commonly causes intermittent hypoxia.[1] If left untreated, OSA may trigger cardiovascular events such as coronary artery disease, arrhythmia, and stroke.[2] Undiagnosed or untreated OSA is frequently associated with daytime sleepiness and impaired social functioning.[3] It is a prevalent disease; the incidence of OSA (defined as an apnea-hypopnea index [AHI] ≥ 5 events/h) in men and women and females is 22% and 17%, respectively.[4]

Currently, in-laboratory polysomnography (PSG) is the recommended gold standard test for OSA[5]; however, PSG is inconvenient in that it requires a large space, specialized equipment, and trained testers. In addition, the "first night effect" caused by the unfamiliar environment is a major limitation.[6] Heart rate variability (HRV) can be measured via single-lead electrocardiography (ECG) using the quantitative variations between normal-to-normal heartbeats. It can be calculated by extracting and processing the R-R interval from the ECG recording of patients, and this simple noninvasive test evaluates cardiac autonomic activity.[7] In patients with OSA, the AHI correlates with the nighttime HRV.[8] The efficacy of OSA treatments such as continuous positive airway pressure, mandibular advancement devices, and sleep surgery, can be evaluated by comparing the nocturnal HRVs before and after treatment.[9–11] However, the relationship between AHI and HRV is difficult to quantify, presumably because HRV varies individually by age, sex, and the extent of physical activity.[12] Recently, it was reported that the daytime-to-nighttime cardiac autonomic activity ratio differed in patients with OSA compared to a normal population.[13] We hypothesized that patients with more severe

OSA would have larger changes in cardiac autonomic modulation during sleep compared with during daytime, regardless of baseline cardiac autonomic activity. The aim of this study is to evaluate the AHI by comparing the difference between daytime and nighttime HRV as measured via 24-h Holter monitoring in patients with OSA.

METHODS

Subjects

This study was approved by the Ethics Committee of Kangwon National University Hospital (IRB no. A-2019-10-003) and adhered to all tenets of the Helsinki Declaration. From January 2020 to February 2021, we prospectively enrolled 70 patients according to following inclusion criteria: 1) adult patients (age ≥ 18 years); 2) patients who visited our sleep clinic complaining of habitual snoring or sleep apnea combined with other symptoms, such as unintentional sleep episodes during wakefulness, daytime sleepiness, unrefreshing sleep, and/or fatigue. Among them, we excluded 4 patients as following exclusion criteria that were related to significant changes in PSG and HRV results according to history taking: 1) patients who had been treated for OSA via any modality, 2) patients who habitually used a sedative and a hypnotic, and 3) patients with a pathology related to significant HRV changes (histories of myocardial infarction or diabetic neuropathy). We obtained written informed consent from the 66 patients who satisfied the inclusion and exclusion criteria. PSG and 24-h Holter monitoring were performed contemporaneously. Before examination, all participants were told to avoid beverages containing caffeine, excessive exercise, and alcohol consumption on the study day. All ECG data were interpreted by C.K.J., who is a cardiologist. We also excluded patients who met the following criteria: 1) atrial fibrillation, 2) low-quality data (artifacts > 20% of total PSG sleep time or > 10% on Holter monitoring), 3) total sleep time < 5 h, 4) being awake for more than 30 min from midnight to 5 AM, and 5) any other sleep disorder (ie, insomnia, narcolepsy, or periodic leg movement during sleep). Finally, 62 patients were evaluated. Anthropometric data and medical histories were recorded.

Attended in-laboratory full-night PSG

All patients underwent PSG during 24-h Holter monitoring. PSG was performed using a commercially available recording system (EmblaTM N7000; Embla, Reykjavik, Iceland). The standard electrodes and sensors, which were recommended according to the American Academy of Sleep Medicine Manual, were used to detect bio-signals from 11 PM to 7 AM under the supervision of a skilled technician. All sleep parameters were manually interpreted by a technician according to the standard criteria of the 2017 American Academy of Sleep Medicine Manual (v2.4) for the Scoring of Sleep and Associated Events and were reviewed by certified physicians.[14] The AHI was the total number of apneas and hypopneas per hour of sleep. The participants with AHI < 5 events/h were considered as simple snoring group. OSA severity was defined as follows: mild, 5 ≤ AHI < 15 events/h; moderate, 15 ≤ AHI ≤ 30 events/h; and severe, AHI > 30 events/h.

Heart rate variability

HRV data were acquired via 24-h Holter monitoring (MARS; GE Healthcare, Chicago, IL) and analyzed by the frequency domains. The Fast Fourier Transform (a nonparametric method of spectral estimation) was used to convert single-lead ECG signals to power spectral densities. According to default method of the program, the cubic spline-interpolated R-R interval function was sampled at 1,024 samples/300 s or 3.413 samples/s. R-R interval ratios < 0.80 or > 1.20 and R-R intervals < 150 ms or > 5,000 ms were excluded prior to HRV analysis. The power spectrum includes a very-low-frequency (VLF) component (0.0033–0.04 Hz), a low-frequency (LF) component (0.04–0.15 Hz), and a high-frequency (HF) component (0.15–0.4 Hz). We used 5-hour ECG recordings to evaluate the nighttime HRV because participants commonly were in a sleep state from 00:00 to 05:00. A 5-hour HRV was also used for the daytime analysis corresponding to the nighttime. HRV parameters were expressed in 3 forms: daytime (12:00∼17:00), nighttime (00:00∼05:00), and as the day/night ratio.

Statistical analysis

Descriptive statistics are presented as percentages (categorical variables) or means ± standard deviations (normally distributed continuous variables). Pearson correlation coefficients were used to assess the relationships between HRV indices and PSG parameters. Any linear trend across the day/night HRV was regarded as a continuous variable. We used the lowest category (simple snoring) as the reference. Multiple linear regression analyses were performed to identify significant predictors of AHI; we evaluated parameters that had biological and statistical plausibility with P values < .2 on univariate analyses. We used 4 regression models to delete multicollinearity between VLF and LF. Model 1 included age; sex; the body mass index, hypertension, hyperlipidemia, and smoking status; and the day/night VLF ratio. Model 2 was identical, except that the day/night LF ratio replaced the day/night VLF ratio. In Models 3 and 4, night VLF and night LF were used instead of day/night VLF, respectively. All analyses were performed using SPSS version 18.0 software (IBM Corp, Armonk, NY), and a P value < .05 was considered statistically significant.

RESULTS

Characteristics of the study participants

Twelve women and 50 men were included, aged 44.2 ± 14.1 years. Totals of 11, 11, 17, and 23 exhibited simple snoring and mild, moderate, and severe OSA, respectively. As OSA severity increased, the AHI, the oxygen desaturation index (ODI), and total arousal tended to increase; and the lowest oxygen saturation and mean oxygen saturation tended to decrease. In terms of medical history, hypertension was associated with increasing OSA severity (**Table 1**).

Table 1—Baseline characteristics of the participants.

	Simple Snoring (n = 11)	Mild OSA (n = 11)	Moderate OSA (n = 17)	Severe OSA (n = 23)
Age, years	38.6 ± 14.2	42.3 ± 16.1	44.5 ± 9.6	47.7 ± 15.6
Female, n (%)	7 (63.6)	2 (18.2)	3 (17.6)	0 (0.0)
BMI, kg/m^2	22.6 ± 1.8	26.3 ± 3.1	27.6 ± 4.5	28.7 ± 4.2
AHI, /h	2.4 ± 1.1	9.7 ± 3.3	21.6 ± 4.0	54.7 ± 19.3
AI, /h	0.2 ± 0.1	1.1 ± 1.9	3.0 ± 2.8	26.0 ± 25.6
ODI, /h	0.6 ± 0.5	5.3 ± 3.3	13.0 ± 5.9	43.0 ± 21.7
Snoring, %	15.1 ± 11.3	33.6 ± 21.7	45.8 ± 23.7	42.5 ± 18.8
Total sleep time, min	419.4 ± 59.1	431.1 ± 38.5	444.9 ± 64.2	414.2 ± 75.9
Sleep efficiency, %	83.8 ± 11.5	88.2 ± 6.3	87.9 ± 12.7	84.6 ± 14.0
Sleep stage				
N1, %	16.1 ± 7.8	19.6 ± 8.3	17.9 ± 5.5	36.5 ± 18.8
N2, %	48.3 ± 4.6	41.0 ± 6.7	46.3 ± 8.5	33.5 ± 13.9
N3, %	12.4 ± 6.5	16.7 ± 8.4	8.9 ± 6.6	7.2 ± 7.4
REM, %	21.1 ± 5.7	21.8 ± 4.7	21.6 ± 5.1	17.3 ± 7.5
Total arousals, /h	11.6 ± 5.8	13.0 ± 3.5	16.6 ± 4.4	33.5 ± 17.9
Lowest O_2 saturation, %	92.0 ± 3.8	88.0 ± 3.3	84.1 ± 5.6	73.8 ± 18.6
Mean O_2 saturation, %	97.0 ± 1.2	96.2 ± 0.9	95.7 ± 1.6	89.7 ± 19.7
Hypertension, n (%)	0 (0.0)	1 (9.1)	3 (17.6)	14 (60.9)
Diabetes mellitus, n (%)	1 (9.1)	0 (0.0)	1 (5.9)	2 (8.7)
Hyperlipidemia, n (%)	0 (0.0)	0 (0.0)	1 (5.9)	4 (17.4)
Current smoking, n (%)	1 (9.1)	0 (0.0)	2 (11.8)	5 (21.7)

Values are means ± standard deviations. AHI = apnea-hypopnea index, AI = apnea index, BMI = body mass index, ODI = oxygen desaturation index, OSA = obstructive sleep apnea, REM = rapid eye movement, Snoring (%) = percentage of snoring time to total sleep time.

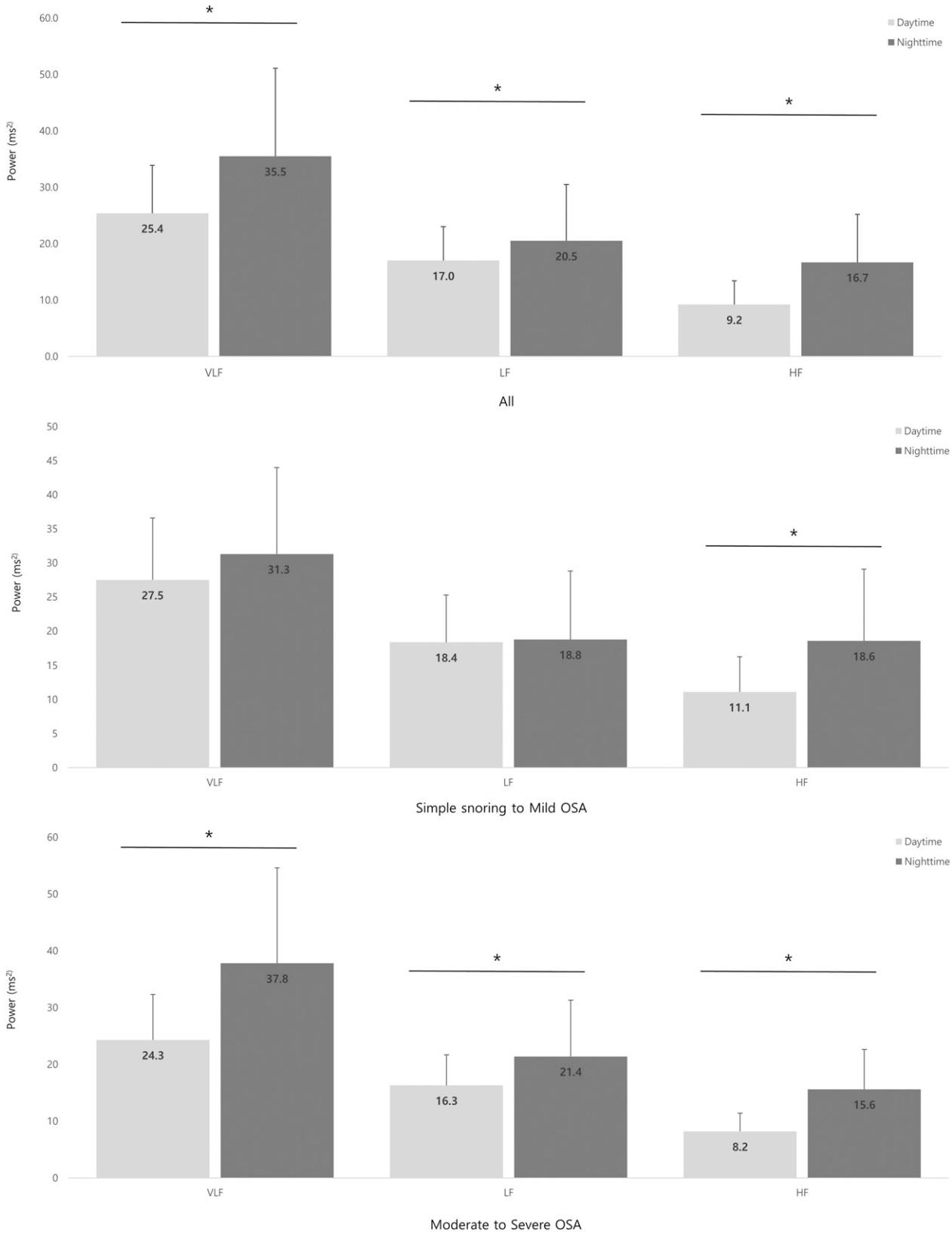
Correlation between the HRV indices and polysomnographic parameters

All indices of nighttime HRV, including the VLF, LF, and HF HRVs, were significantly higher than those of the daytime HRV. We also evaluated the difference between daytime and nighttime HRV according to severity. A simple snoring to mild OSA group represented significant difference between daytime and nighttime HRV in HF. However, a moderate to severe OSA group showed significant difference between daytime and nighttime HRVs in all indices (**Figure 1**). We found no significant correlation between the daytime HRV indices and any PSG parameter. Of the nighttime HRV indices, the VLF HRV was significantly correlated with the AHI ($r^2 = 0.478$), ODI ($r^2 = 0.514$), lowest O_2 saturation ($r^2 = -0.255$), and total arousal ($r^2 = 0.427$). The nighttime LF HRV correlated significantly with the AHI ($r^2 = 0.384$), ODI ($r^2 = 0.406$), and total arousal ($r^2 = 0.423$). However, the nighttime HF HRV was not associated with any PSG parameter. In terms of the HRV ratios (daytime to nighttime), the VLF and LF ratios correlated significantly with the AHI ($r^2 = 0.550$ and $r^2 = 0.556$ in VLF and LF, respectively), ODI ($r^2 = 0.614$ and $r^2 = 0.594$), lowest O_2 saturation ($r^2 = -0.331$ and $r^2 = -0.387$), and total arousal ($r^2 = 0.533$ and $r^2 = 0.557$). The day/night HF ratio was also significantly associated with the AHI ($r^2 = 0.303$), ODI ($r^2 = 0.295$), and lowest O_2 saturation ($r^2 = -0.304$) (**Table 2**). When the day/night HRV ratios were compared by OSA severity, the VLF (P for trend = .003) and LF (P for trend = .013) ratios significantly decreased as OSA severity increased in linear trend analysis. However, the day/night HF ratio did not trend by OSA severity (P for trend = .689) (**Table 3**).

Multivariable analyses predicting AHI

We used multiple regression to seek associations between factors significant on univariate analyses ($P < .2$) and AHI. In model 1, age, sex, body mass index, hypertension, hyperlipidemia, smoking, and day/night VLF ratio were used to covariate. Among the covariate, the body mass index ($\beta = 1.751$, $P = .009$), hypertension ($\beta = 16.004$, $P = .020$), and the day/night VLF ratio ($\beta = 16.387$, $P < .001$) were significantly associated with AHI. In model 2, age, sex, body mass index, hypertension, hyperlipidemia, smoking, and day/night LF ratio were used to covariate. The body mass index ($\beta = 1.650$, $P = .015$) and the day/night LF ratio ($\beta = 25.248$, $P < .001$) were significantly associated with AHI. The r^2 values were 0.537 and 0.522 for models 1 and 2 respectively; both models were significant (both $P < .001$). However, models of AHI using night VLF alone and night LF alone demonstrate a lesser model fit (r^2 values were 0.514 and 0.503 for models 3 and 4, respectively, both $P < .001$) than models using day/night HRV. The day/night HF ratio was not used in our models because it was not associated with OSA severity.

Figure 1—Differences between the day and night HRV indices.



All nighttime indices were significantly higher than the daytime indices. According to the severity of OSA, a simple snoring to mild OSA group represented significant difference between daytime and nighttime HRV in HF. However, a moderate-to-severe OSA group showed significant differences between daytime and nighttime HRVs in all indices. *P > .05. HF = high frequency, HRV = heart rate variability, LF = low frequency, OSA = obstructive sleep apnea, VLF = very low frequency.

Table 2—Pearson correlation analysis between HRV and PSG parameters.

	AHI	ODI	Lowest O_2 Saturation	Total Arousal
Day				
VLF	−0.122	−0.152	0.136	−0.146
LF	−0.063	−0.080	0.086	−0.026
HF	−0.215	0.193	0.223	−0.040
Night				
VLF	0.478**	0.514**	−0.255*	0.427**
LF	0.384**	0.406**	−0.247	0.423**
HF	0.020	0.027	−0.052	0.008
Day/night				
VLF	0.550**	0.614**	−0.331**	0.533**
LF	0.556**	0.594**	−0.387**	0.557**
HF	0.303*	0.295*	−0.304*	0.154

*P < .05, **P < .01. AHI = apnea-hypopnea index; BMI = body mass index, HF = high frequency, HRV = heart rate variability, LF = low frequency, ODI = oxygen desaturation index, PSG = polysomnography, VLF = very low frequency.

DISCUSSION

HRV noninvasively assesses cardiac autonomic modulation via single-lead electrocardiography and the variations in the times between heartbeats.[15] VLF, LF, and HF regions are evident on spectral analysis. The HF component reflects phasic vagal activity triggered by respiration. Several clinical and experimental studies, such as electrical vagal stimulation, muscarinic receptor blockade, and vagotomy were confirmed the association between HF and parasympathetic nervous system.[7] The LF component reflects sympathetic and vagal outflows.[16] The VLF component is more strongly associated with cardiovascular disease prognosis,[17] metabolic syndromes,[18] and all-cause mortality after traumatic brain injury than with the other HRV parameters.[19] Several studies have shown that the VLF is also associated with increasing chronic inflammation.[20,21]

In the time since Wolf et al[22] first reported that a reduced HRV reflected increased cardiac mortality in patients with post-myocardial infarction, many studies have sought associations between various physical conditions and HRV changes. In general, impaired autonomic function (as measured by HRV) predicts adverse outcomes in diverse clinical settings. Although, many studies reported HRV changes in patients with OSA, the results varied. In a previous study evaluating HRV in patients with moderate-to-severe OSA, the daytime LF/HF ratio and the LF normalized unit were significantly increased compared to those of controls.[23] Another (Korean) study reported that the nighttime LF/HF ratio was closely associated with the AHI.[24] The association between OSA and the VLF was first assessed in patients with OSA before and during application of a mandibular advancement device. In this study, the VLF components significantly decreased with use of a mandibular advancement device compared to baseline.[25] One study reported that the VLF increased during sleep-disordered breathing because it was modulated by the renin-angiotensin system and the parasympathetic nervous system.[26] Most studies sought associations between OSA and the HRV frequency domains, but some explored the time domains. Tsuji et al[27] emphasized the importance of changing the standard deviation of the normal-to-normal R-R interval in patients with OSA. Zhu et al[28] suggested that the normal-to-normal R-R interval optimally quantified nocturnal sympathovagal imbalance because the nighttime normal-to-normal R-R intervals were shorter in patients with OSA than in controls. The differences between the studies may be partly attributable to variations in the number of participants and the times and methods of HRV measurement. However, the

Table 3—Daytime/nighttime heart rate variability by the severity of OSA.

	Simple Snoring (n = 11)	Mild OSA (n = 11)	Moderate OSA (n = 17)	Severe OSA (n = 23)	*P* for trend
VLF day/night	0.95 ± 0.26	0.91 ± 0.26	0.75 ± 0.25	0.68 ± 0.28	.003*
LF day/night	1.03 ± 0.27	1.10 ± 0.30	0.90 ± 0.35	0.79 ± 0.28	.013*
HF day/night	0.64 ± 0.15	0.67 ± 0.21	0.57 ± 0.27	0.63 ± 0.34	.689

Values are means ± standard deviation. *P > .05. HF = high frequency, LF = low frequency, OSA = obstructive sleep apnea, VLF = very low frequency.

principal explanation may be that the appropriate HRV reference values differed by sex, age, and race.[29,30] To eliminate distortion caused by such individual differences, we compared the daytime and nighttime HRVs of the same participants. We hypothesized that patients with more severe OSA would evidence larger changes in cardiac autonomic modulation (as revealed by HRV) during sleep; this is what we found. All HRV indices significantly higher in daytime than nighttime and this phenomenon was clearer in moderate to severe OSA than simple snoring to mild OSA groups. In simple snoring to mild OSA group, only HF showed significant higher in nighttime than in daytime. Considering these, daytime-to-nighttime ratios of HF seem to have relatively less clinical implication in screening the OSA than other HRV indices. The daytime HRV exhibited no association with any PSG parameter. However, the nighttime HRV (except the HF component) did. All daytime-to-nighttime ratios (including that of HF) were significantly associated with PSG parameters; the correlation coefficients were higher than those for the nighttime HRV. Moreover, the day/night VLF and LF ratios decreased significantly by increased OSA severity (P for trend = .003 and .013, respectively). The regression models showed that the day/night VLF and LF ratios independently predicted AHI after adjusting for several confounding factors. The predictive powers were higher than nocturnal HRV alone; the variables used explained > 50% of AHI variability ($r^2 = 0.537$ and 0.522 for models 1 and 2 respectively). Compared with previous studies, which evaluated nighttime HRV and showed differences only in nighttime HRV values between OSA and non-OSA, our study may effectively screen AHI using daytime-to-nighttime ratio of HRV in patients with suspected OSA.

There is no doubt that PSG is the gold standard for OSA diagnosis, but PSG is elaborate and associated with a first night effect.[5,6] Efforts have been made to develop accurate but simpler tests. In recent years, several studies have screened for OSA using (principally) nocturnal HRV.[31–33] However, as mentioned above, it is difficult to compare the results because the HRV reference values varied. Thus, we compared individual daytime and nighttime HRV values; this is a strength of our work. Moreover, PSG was performed during 24-h Holter monitoring. We found that the day/night HRV indices, including the day/night VLF and day/night LF ratios, correlated significantly with the AHI; Holter monitoring can be used to screen for OSA. It may be possible to use the day/night HRV ratios to predict AHI; more studies are required.

Our study had several limitations. First, all patients voluntarily visited our outpatient clinic; selection bias is thus possible. We did not include controls who did not snore and lacked sleep apnea. However, it was found that the differences of daytime and nighttime HRV values were smaller in patients with simple snoring compared to patients with OSA. Second, OSA severity was unevenly distributed; there was a high proportion of patients with moderate-to-severe OSA. Additional studies with more participants are thus needed. Third, in this study, we did not evaluate the normalized HRV indices (eg, LF normalizing unit, HF normalizing unit) because we planned to find a method to evaluate AHI using day/night HRV. The further study of the association between normalized HRV and AHI is essential because normalized HRVs are easier to interpret in the context of an individual participant, as well as between participants.

In conclusion, 24-h Holter monitoring usefully predicted AHI. The day/night HRV ratio decreased significantly by OSA severity and the day/night VLF and LF ratios were independently associated with AHI. Therefore, it may be possible to predict AHI and screen for OSA using the daytime to nighttime HRV ratios.

ABBREVIATIONS

AHI, apnea-hypopnea index
ECG, electrocardiography
HF, high-frequency
HRV, heart rate variability
LF, low-frequency
ODI, oxygen desaturation index
OSA, obstructive sleep apnea
PSG, polysomnography
VLF, very-low-frequency

REFERENCES

1. Veasey SC, Rosen IM. Obstructive sleep apnea in adults. *N Engl J Med.* 2019; 380(15):1442–1449.
2. Hopps E, Caimi G. Obstructive sleep apnea syndrome: links between pathophysiology and cardiovascular complications. *Clin Invest Med.* 2015;38(6): E362–E370.
3. Gibson GJ. Obstructive sleep apnoea syndrome: underestimated and undertreated. *Br Med Bull.* 2005;72(1):49–65.
4. Franklin KA, Lindberg E. Obstructive sleep apnea is a common disorder in the population—a review on the epidemiology of sleep apnea. *J Thorac Dis.* 2015; 7(8):1311–1322.
5. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: an American Academy of Sleep Medicine Clinical Practice Guideline. *J Clin Sleep Med.* 2017;13(3): 479–504.
6. Byun JH, Kim KT, Moon HJ, Motamedi GK, Cho YW. The first night effect during polysomnography, and patients' estimates of sleep quality. *Psychiatry Res.* 2019; 274:27–29.
7. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. *Circulation.* 1996;93(5):1043–1065.
8. Gong X, Huang L, Liu X, et al. Correlation analysis between polysomnography diagnostic indices and heart rate variability parameters among patients with obstructive sleep apnea hypopnea syndrome. *PLoS One.* 2016;11(6): e0156628.
9. Kim JW, Kwon SO, Lee WH. Nocturnal heart rate variability may be useful for determining the efficacy of mandibular advancement devices for obstructive sleep apnea. *Sci Rep.* 2020;10(1):1030.
10. Kufoy E, Palma JA, Lopez J, et al. Changes in the heart rate variability in patients with obstructive sleep apnea and its response to acute CPAP treatment. *PLoS One.* 2012;7(3): e33769.
11. Lee WH, Kwon SO, Kim JW. Effectiveness of sleep surgery versus a mandibular advancement device for obstructive sleep apnea in terms of nocturnal cardiac autonomic activity. *Sleep Breath.* 2020;24(4):1695–1703.
12. Nunan D, Sandercock GR, Brodie DA. A quantitative systematic review of normal values for short-term heart rate variability in healthy adults. *Pacing Clin Electrophysiol.* 2010;33(11):1407–1417.
13. Salsone M, Vescio B, Quattrone A, et al. Cardiac parasympathetic index identifies subjects with adult obstructive sleep apnea: A simultaneous polysomnographic-heart rate variability study. *PLoS One.* 2018;13(3): e0193879.

14. Berry RB, Brooks R, Gamaldo C, et al. AASM Scoring Manual Updates for 2017 (Version 2.4). *J Clin Sleep Med.* 2017 May 15;13(5):665–666.
15. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. *Eur Heart J.* 1996;17(3):354–381.
16. Lombardi F, Stein PK. Origin of heart rate variability and turbulence: an appraisal of autonomic modulation of cardiovascular function. *Front Physiol.* 2011;2:95.
17. Guzzetti S, La Rovere MT, Pinna GD, et al. Different spectral components of 24 h heart rate variability are related to different modes of death in chronic heart failure. *Eur Heart J.* 2005;26(4):357–362.
18. Assoumou HG, Pichot V, Barthelemy JC, et al. Metabolic syndrome and short-term and long-term heart rate variability in elderly free of clinical cardiovascular disease: the PROOF study. *Rejuvenation Res.* 2010;13(6):653–663.
19. Ryan ML, Ogilvie MP, Pereira BM, et al. Heart rate variability is an independent predictor of morbidity and mortality in hemodynamically stable trauma patients. *J Trauma.* 2011;70(6):1371–1380.
20. Lampert R, Bremner JD, Su S, et al. Decreased heart rate variability is associated with higher levels of inflammation in middle-aged men. *Am Heart J.* 2008;156(4): 759.e1–759.e7.
21. Stein PK, Barzilay JI, Chaves PH, et al. Higher levels of inflammation factors and greater insulin resistance are independently associated with higher heart rate and lower heart rate variability in normoglycemic older individuals: the Cardiovascular Health Study. *J Am Geriatr Soc.* 2008;56(2):315–321.
22. Wolf MM, Varigos GA, Hunt D, Sloman JG. Sinus arrhythmia in acute myocardial infarction. *Med J Aust.* 1978;2(2):52–53.
23. Narkiewicz K, Montano N, Cogliati C, van de Borne PJ, Dyken ME, Somers VK. Altered cardiovascular variability in obstructive sleep apnea. *Circulation.* 1998;98(11):1071–1077.
24. Park DH, Shin CJ, Hong SC, et al. Correlation between the severity of obstructive sleep apnea and heart rate variability indices. *J Korean Med Sci.* 2008;23(2):226–231.
25. Shiomi T, Guilleminault C, Sasanabe R, Hirota I, Maekawa M, Kobayashi T. Augmented very low frequency component of heart rate variability during obstructive sleep apnea. *Sleep.* 1996;19(5):370–377.
26. Stein PK, Pu Y. Heart rate variability, sleep and sleep disorders. *Sleep Med Rev.* 2012;16(1):47–66.
27. Tsuji H, Venditti FJ Jr, Manders ES, et al. Reduced heart rate variability and mortality risk in an elderly cohort. The Framingham Heart Study. *Circulation.* 1994; 90(2):878–883.
28. Zhu K, Chemla D, Roisman G, et al. Overnight heart rate variability in patients with obstructive sleep apnoea: a time and frequency domain study. *Clin Exp Pharmacol Physiol.* 2012;39(11):901–908.
29. Hall MH, Middleton K, Thayer JF, et al. Racial differences in heart rate variability during sleep in women: the study of women across the nation sleep study. *Psychosom Med.* 2013;75(8):783–790.
30. Sammito S, Böckelmann I. Reference values for time- and frequency-domain heart rate variability measures. *Heart Rhythm.* 2016;13(6):1309–1316.
31. Chang KM. Portable obstructive sleep apnea screening system using overnight ECG and a PDA-based wireless transmission system. *Telemed J E Health.* 2009; 15(4):353–361.
32. Parrino L, Ferrillo F, Smerieri A, et al. Is insomnia a neurophysiological disorder? The role of sleep EEG microstructure. *Brain Res Bull.* 2004;63(5):377–383.
33. Roche F, Duverney D, Court-Fortune I, et al. Cardiac interbeat interval increment for the identification of obstructive sleep apnea. *Pacing Clin Electrophysiol.* 2002; 25(8):1192–1199.

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