




ORIGINAL RESEARCH

Association of Night-to-Night Adherence of Continuous Positive Airway Pressure With Day-to-Day Morning Home Blood Pressure and Its Seasonal Variation in Obstructive Sleep Apnea

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BACKGROUND: The aim of this study was to investigate the association between night-to-night adherence to continuous positive airway pressure (CPAP) therapy and both home blood pressure (BP) level on the following day and seasonal variation in home BP in patients with obstructive sleep apnea.

METHODS AND RESULTS: We analyzed 105 participants who had been diagnosed with obstructive sleep apnea (average apnea-hypopnea index, 49.7±18.4 per hour) and who were already receiving CPAP therapy. Home BP (twice every morning and evening) and CPAP adherence data were automatically transmitted to a server for 1 year. A mixed-effects model for repeated measures analysis was used to examine associations of night-to-night good CPAP adherence with day-to-day home BP within the same patient after adjusting for covariates. The average number of days in which patients achieved both CPAP adherence and morning or evening home BP measurement was 206.6±122.7 days (21 487 readings) and 191.2±126.3 days (20 170 readings), respectively. Good CPAP adherence (>4 hours per night of use) was achieved on the evening or morning before home BP measurements (86.8% and 86.9%, respectively). After adjustment for confounders, good CPAP adherence was negatively associated with morning home systolic BP (β , -0.663; $P=0.004$) and diastolic BP (β , -0.829; $P<0.001$). Morning home systolic BP in winter in the individuals with good CPAP adherence was significantly lower than that in individuals without such adherence ($P<0.05$). These associations were not found in evening home BP.

CONCLUSIONS: Good adherence to CPAP therapy was negatively associated with morning home BP on the following day in patients with obstructive sleep apnea. The association was remarkable in the winter season.

Key Words: adherence ■ continuous positive airway pressure ■ home blood pressure monitoring ■ obstructive sleep apnea

The strong linkage between obstructive sleep apnea (OSA) and hypertension has been well acknowledged in both cross-sectional and longitudinal studies,^{1,2} and OSA has been recognized as one of the causes of secondary hypertension.^{3–5} Continuous positive airway pressure (CPAP) therapy has been recommended as the first-choice treatment

for severe OSA. Several previous studies have reported that CPAP therapy reduces blood pressure (BP) in patients with OSA and hypertension, but this effect is partly dependent on adherence to CPAP use.^{6–8}

Recent international guidelines recommend the use of home BP monitoring (HBPM) for the management of

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CLINICAL PERSPECTIVE

What Is New?

- In 105 participants who had been diagnosed with obstructive sleep apnea and who were already receiving continuous positive airway pressure therapy, good adherence to continuous positive airway pressure therapy was negatively associated with morning home blood pressure on the following day; the association was remarkable in the winter season.
- The current study shows that night-to-night good adherence to continuous positive airway pressure therapy (>4 hours per night) is negatively associated with home blood pressure on the following morning, but not to evening home blood pressure in patients with obstructive sleep apnea.
- The individuals with good adherence to continuous positive airway pressure therapy showed a negative association in seasonal variation of morning home blood pressure compared with those without.

What Are the Clinical Implications?

- The results of the present study suggest that good adherence to continuous positive airway pressure therapy is negatively associated with morning home blood pressure, and thereby contributes to the prevention of cardiovascular events throughout the year in patients with obstructive sleep apnea.

Nonstandard Abbreviations and Acronyms

DBP	diastolic blood pressure
HBPM	home blood pressure monitoring
SBP	systolic blood pressure
SDB	sleep disordered breathing

hypertension,^{3–5} because HBPM, especially home BP readings in the morning period, has greater predictive power for cardiovascular events compared with office BP.^{9,10} Hence, the identification of factors that are determinant of morning BP is clinically important for the control of morning BP, and thereby for a reduction of cardiovascular events. OSA has been considered to be an important factor affecting morning hypertension.^{11,12} Although chronically poor CPAP adherence is already known to worsen BP control, clinical evidence for daily home BP control related to nightly CPAP adherence is lacking. To the best of our knowledge, there has been no study about the daily association between CPAP

adherence and morning BP over a long-term follow-up period. Moreover, previous studies have demonstrated a significant seasonal variation in home BP, with higher home BP in winter than summer.^{13,14} However, this association was observed only for morning home BP and not for evening home BP.¹⁵ Therefore, we further hypothesized that night-to-night adherence to CPAP use may affect the seasonal variation in morning home BP.

The aim of this study was thus to investigate whether night-to-night adherence to CPAP is associated with home BP on the successive days during long-term follow-up or the seasonal variation in home BP in patients with OSA.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Patients

We enrolled study participants who were diagnosed with OSA according to the American Academy of Sleep Medicine guidelines,¹⁶ namely, all participants had an apnea-hypopnea index of ≥ 20 on overnight polysomnography or that of ≥ 40 on polygraphy. We performed CPAP therapy according to the recommendations of the Japanese health insurance system. The details of the OSA diagnosis and CPAP therapy are given in Data S1. The participants were recruited from 4 institutes. The institutional review board of Jichi Medical University approved the study. All participants provided written informed consent. Demographic information was collected by physicians at each participating institute. Diagnosed hypertension, dyslipidemia, and diabetes were defined as a self-reported physician's diagnosis of each disease or current use of correspondent medication. Body mass index (BMI) was calculated from measured weight and height. The adherence to pharmacotherapy at baseline was evaluated by a Morisky score.¹⁷ Office BP measurements were obtained at local medical centers using any validated cuff oscillometric device. All participants included in this study used a SLEEPMATE9 or SLEEPMATE10 CPAP device (TEIJIN, Tokyo, Japan). CPAP titration was exclusively performed by using these CPAP devices, which provide an autotitrating function, or partly by using these devices and also conventional polysomnography, depending on the individual institute. These CPAP devices record daily CPAP usage data and automatically transmit the data to a server. CPAP adherence was measured using the internal clocks in the CPAP devices. Good CPAP adherence was defined as >4 hours per night according to a previous study.¹⁸ According to the guidelines of the

health insurance system in Japan, all participants performing CPAP therapy were required to visit the clinic or hospital once within 3 months to receive education on OSA and its treatment by their physician, in addition to updating their antihypertensive drug information.

Home BP Measurement

Self-measured home BP values were obtained according to the current guidelines.⁵ The participants measured their BP twice every morning and twice every evening, with the measurements taken in a seated position in both the morning (within 1 hour of waking and before taking antihypertensive medication) and evening (before going to bed) for 1 consecutive year. The averages of morning and evening BP per 1 day were calculated separately. Data of HBPM in all participants were collected during June 2016 and March 2018. Home BP and heart rate were measured using an HEM-7252G-HP automatic device (Omron Healthcare, Kyoto, Japan).¹⁹ All data of home BP and pulse rate were automatically transmitted to the server (<https://www2.med-link.jp/ht/pro/index.php>).

Statistical Analysis

A total of 110 patients with OSA undergoing CPAP therapy initially consented to participate in this study. Two of them later withdrew consent, and 3 other participants lacked sufficient HBPM data. Therefore, our final sample comprised 105 participants. Of these 105 participants, 1 participant failed to perform HBPM in the morning, and therefore the analysis related to morning home BP was performed in only 104 participants. Categorical variables and mean (SD) for continuous variables were used to describe the study population. Each of the morning and evening home BP measurements was matched with the duration of CPAP use taken the previous night during 1 year from the start of home BP measurement. A mixed-effects model for repeated measures analysis was used to examine associations of night-to-night good CPAP adherence with day-to-day home BP within each patient at the inter- and intraindividual level after adjusting for age, sex, BMI, drinking, smoking, prevalent diabetes and cardiovascular disease (CVD), and the use of an antihypertensive drug. We also performed stratified analysis according to these covariates. Moreover, to examine the monthly association of good night-to-night CPAP adherence with day-to-day home BP within the same person, we used a mixed-effects model of repeated measures analysis that included CPAP adherence, time points (month), and the interaction between CPAP adherence and time points as fixed effects, and age, sex, BMI, drinking, smoking, prevalent diabetes and CVD, and the use of an antihypertensive drug as covariates. We conducted an additional sensitivity

analysis using a previous study's definition of good CPAP adherence as >3 hours per night.²⁰ A 2-sided *P* value <0.05 was accepted as significant. All statistical analyses were performed with SAS version 9.4 software (SAS Institute, Cary, NC).

RESULTS

Baseline characteristics of the 105 participants and the groups of lower and higher CPAP adherence using the median value of the percentage (77.7%) of good CPAP adherence during study period are shown in Table 1. When confirming the diagnosis for OSAS, the average apnea-hypopnea index was 49.7±18.4 per hour. The average duration of CPAP use before the study was 40.9 months (range, 0.5–178.3 months). The average number of days with morning and evening home BP measurement per patient was 206.6±122.7 days and 191.2±126.3 days, respectively. In total, 21 487 readings for morning home BP and 20 170 readings for evening home BP were analyzed for night-to-night CPAP adherence. There were no significant differences in baseline characteristics between the group with lower and higher CPAP adherence except for age and morning pulse rate. Figure 1 shows the distribution of the hours of CPAP use per night in each individual during the study. The prevalence of good CPAP adherence was 86.8% (18 661/21 487) and 86.9% (17 530/20 170) in the morning home BP and evening home BP matched with the duration of CPAP use taken the previous night, respectively. The mean morning and evening home systolic BP (SBP)/diastolic BP (DBP) values were 131.8±13.3/82.6±10.1 mm Hg and 127.1±16.0/77.0±9.8 mm Hg, respectively.

Table 2 shows the association between good CPAP adherence and home BP. Good CPAP adherence was negatively associated with morning home SBP (β , -0.670; *P*=0.004), and this association remained after adjustment for covariates (β , -0.663; *P*=0.004). When we also stratified the individuals according to demographics (<65 years old versus ≥65 years old; women or men; <25 versus ≥25 kg/m² in BMI; and the absence versus presence of smoking, drinking, diabetes, CVD, and the use of an antihypertensive drug), adjusted multiple linear regression analysis showed that good CPAP adherence was negatively associated with morning home SBP in individuals ≥65 years old, men, and those with BMI ≥25 kg/m², diabetes, CVD, or the use of an antihypertensive drug. In the subgroup analysis, this association was larger in participants with BMIs ≥25 kg/m².

Similar findings were observed in the association between good CPAP adherence and morning home DBP (Table 3). On the other hand, there was no significant association between good CPAP adherence and evening home SBP or DBP (Tables S1 and S2).

Table 1. Baseline Characteristics

Characteristic	Value
No. of patients	105
Age, y	61.0±13.2
Men, %	82.9
Body mass index, kg/m ²	29.6±5.5
Habitual drinking, %	30.5
Current smoking, %	14.3
Diabetes, %	27.6
Dyslipidemia, %	50.5
Atrial fibrillation, %	8.6
Prevalent cardiovascular disease, %	16.2
Antihypertensive drug use, %	81.9
Calcium antagonist, %	58.1
Angiotensin II receptor blocker, %	56.2
ACE inhibitor, %	1.9
β-Blocker, %	17.1
α-Blocker, %	11.4
Diuretics, %	24.8
Office SBP, mm Hg	138.0±17.5
Office DBP, mm Hg	81.5±12.9
Office PR, bpm	74.0±11.0
Morning SBP, mm Hg	131.8±13.3
Morning DBP, mm Hg	82.6±10.1
Morning PR, bpm	68.5±9.5
Evening SBP, mm Hg	127.1±16.0
Evening DBP, mm Hg	77.0±9.8
Evening PR, bpm	72.8±10.3
Parameters of sleep apnea	
AHI, events/h	49.6±18.4
Obstructive apnea index, events/h	28.7±18.0
Mixed apnea index, events/h	4.6±7.4
Central apnea index, events/h	2.0±3.4
Hypopnea index, events/h	20.7±15.9
Minimal SpO ₂ , %	72.4±10.4
Mean SpO ₂ , %	91.2±3.9

Data are mean±SD or percentages. ACE indicates angiotensin-converting enzyme; AHI, apnea-hypopnea index; DBP, diastolic blood pressure; PR, pulse rate; SBP, systolic blood pressure; and SpO₂, oxyhemoglobin saturation.

Of 105 participants, 21 (20%) changed their antihypertensive medication during follow-up (15.2% increased the amount of similar antihypertensive drugs or added another antihypertensive drug; 14.3% decreased the amount of similar antihypertensive drugs or decreased the number of antihypertensive drugs). After additional adjustment for the change in antihypertensive medication, the association between high CPAP adherence and morning home SBP remained (β , -0.664 ; $P=0.004$). When we further added uncontrolled office SBP at baseline (presence or absence of ≥ 140 mm Hg in office SBP) as a covariate, the result did not change

from those of the previous model (β , -0.680 [95% CI, -1.136 to -0.224]; $P=0.003$). After adding the residual apnea-hypopnea index (presence or absence of a score ≥ 5 as noted by CPAP devices) to the covariates, the association between good CPAP adherence and morning home SBP remained (β , -0.693 [95% CI, -1.149 to -0.238]; $P=0.003$). After dividing the respective nights within each patient into tertiles dependent on the total hours of daily CPAP use, we analyzed the association between the tertiles and morning home SBP. Compared with the nights with the lowest of the time of CPAP use, the nights with the second (β , 0.09 [95% CI, -0.21 to 0.39]) and third tertiles (β , 0.03 [95% CI, -0.26 to 0.33]) showed no significantly greater association with morning home SBP. In the sensitivity analysis, good CPAP adherence defined as >3 hours per night was negatively associated with morning home SBP (β , -1.146 [95% CI, -1.700 to -0.592]; $P<0.001$), and this association remained after adjustment for covariates (β , -1.137 [95% CI, -1.691 to -0.583]; $P<0.001$).

Figure 2 shows the average morning and evening home SBP measurements for each month in individuals with or without high adherence to CPAP. Average morning home SBP in December, January, February, and March in the individuals with good adherence to CPAP was significantly lower than that in those without good adherence, respectively. The largest difference in monthly morning SBP between the group with good adherence to CPAP and those without was 3.7 mm Hg in January. In the group with good adherence to CPAP, the highest and lowest morning home SBP were 129.5 mm Hg in November and 124.8 mm Hg in July, respectively, whereas the highest and lowest morning home SBP were 132.5 mm Hg in January and 124.7 mm Hg in June in those without good adherence to CPAP. There was a significant interaction between adherence to CPAP and morning home SBP throughout the 1-year study period ($P<0.001$), but not between adherence to CPAP and evening home SBP. Although there was a significant difference in evening home SBP in June between those with and without good adherence to CPAP, there was no interaction between those with and without good adherence to CPAP. For seasonal variation of morning and evening home DBP, the trend was almost identical to that for morning and evening home SBP (Figure S1).

DISCUSSION

In this study, we observed several important findings. First, when we investigated the association between night-to-night good adherence to CPAP therapy (defined as >4 hours per night of CPAP use) and morning home BP in patients with OSA over a 1-year observation period, night-to-night good adherence to CPAP therapy was attributed to a reduction in home SBP on

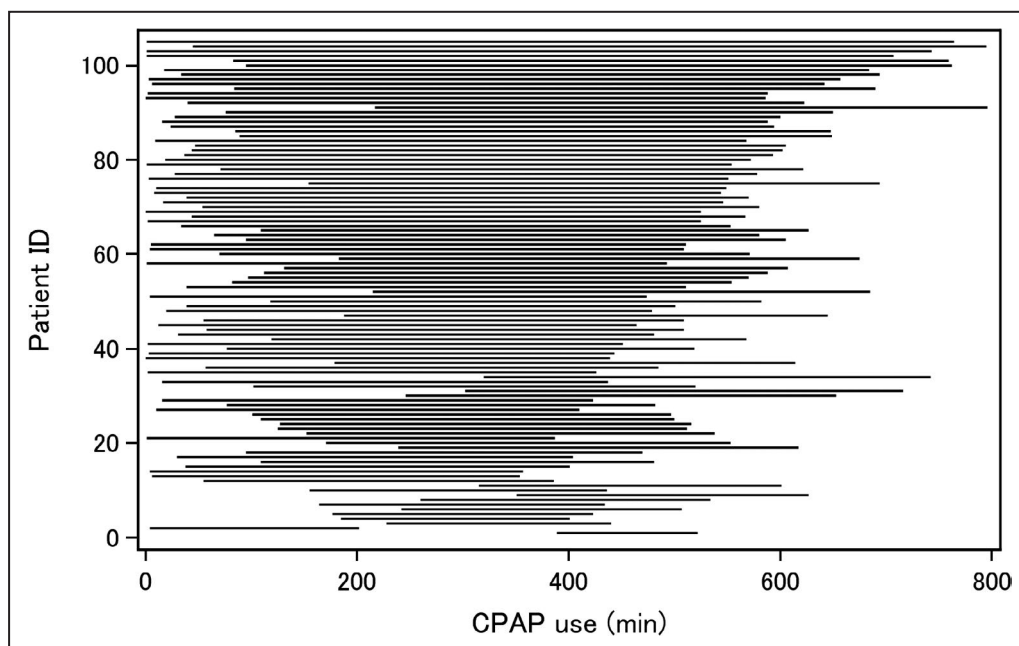


Figure 1. Distribution of the hours of continuous positive airway pressure (CPAP) use per night in each individual during study.

Model: systolic blood pressure=MM; c240; age 65 years; male sex; body mass index b25; habits: drink, current smoking; diabetes; cardiovascular disease; antHT; MM*c240. ID indicates identification.

the next morning, but not to a reduction in evening home BP. In the subgroup analysis, this association was larger in older participants, men, and participants with obesity, smoking, prevalent diabetes and CVD, or the use of antihypertensive drugs. Second, the favorable effect of good CPAP adherence on morning home SBP was more pronounced in winter than in the 3 other seasons. Our findings confirm that the amelioration of hypertension previously associated with good adherence to CPAP therapy extends to a reduction in home BP, which could lead to the prevention of CVD events.

To the best of our knowledge, this is the first study to examine the association between night-to-night adherence to CPAP therapy and changes in BP on the next day as assessed by home BP measurement. International guidelines have recommended that hypertension be managed using out-of-office BP measurement (ie, ambulatory BP monitoring and HBPM),³⁻⁵ because both ambulatory and HBPM exhibit stronger prognostic power compared with office BP. Several meta-analyses showing a beneficial effect of CPAP therapy on BP reduction have been reported.^{7,21,22} However, in those studies, the evaluation of BP was performed by office BP and/or ambulatory BP monitoring. Evidence of an association between morning home BP and the progression of target organ damage or cardiovascular events has been accumulating.^{9,10,23} The results of our study contribute the clinically relevant information that CPAP therapy is associated with

morning home BP, which in turn would help to prevent cardiovascular events. A previous study examined the association between the severity of sleep disordered breathing (SDB) assessed by pacemakers with implanted SDB monitoring and incident atrial fibrillation.²⁴ That result showed that, on a per-patient basis, the nights in the highest quartile of respiratory disturbance index were associated with a risk of incident atrial fibrillation compared with the nights with the lowest oxygen desaturation index. The present and previous study confirms that nightly severity of SDB may be a more accurate daily risk factor for CVD than SDB severity per se.

In the subgroup analysis, the reduction of morning home BP by good CPAP adherence was remarkable in the individuals with BMI ≥ 25 kg/m². Moreover, good CPAP adherence was negatively associated with morning home SBP in individuals with other cardiovascular risk factors (ie, old age, male sex, and diabetes). The population with these cardiovascular risk factors is known to have increased sympathetic nervous activity.²⁵⁻²⁷ In addition to a mechanism by which sympathetic activation causes a BP response in patients with OSA²⁸ and the linkage between sympathetic nervous activity after awakening and morning BP,^{29,30} the presence of cardiovascular risk may deteriorate morning BP, which in turn would result in a greater response to CPAP therapy. Although several studies have investigated whether CPAP therapy is beneficial for secondary prevention in patients with CVD,^{20,31,32} those

Table 2. Association Between Good Continuous Positive Airway Pressure Adherence (≥ 4 h per Night) and Morning Systolic Blood Pressure

	No. of patients	No. of days	Unadjusted			Adjusted		
			β (95% CI)	P value	P_{int} value	β (95% CI)	P value	P_{int} value
All patients	104	206.6 \pm 122.7	-0.670 (-1.124 to -0.215)	0.004	NA	-0.663 (-1.118 to -0.208)	0.004	NA
Age								
<65 y	61	162.1 \pm 114.8	-0.345 (-0.969 to 0.280)	0.280	0.143	-0.342 (-0.967 to 0.283)	0.283	0.143
≥ 65 y	43	269.7 \pm 105.5	-1.027 (-1.690 to -0.364)	0.002		-1.023 (-1.686 to -0.360)	0.003	
Sex								
Women	18	214.0 \pm 116.2	-0.539 (-1.753 to 0.676)	0.385	0.826	-0.549 (-1.764 to 0.667)	0.376	0.827
Men	86	205.1 \pm 124.6	-0.686 (-1.177 to -0.196)	0.006		-0.683 (-1.174 to -0.193)	0.006	
BMI								
<25 kg/m ²	24	261.0 \pm 123.1	0.077 (-0.720 to 0.875)	0.849	0.044	0.077 (-0.721 to 0.874)	0.851	0.046
≥ 25 kg/m ²	80	190.3 \pm 118.5	-0.962 (-1.513 to -0.410)	<0.001		-0.955 (-1.507 to 0.404)	<0.001	
Drinking								
Yes	32	221.8 \pm 110.2	-0.097 (-0.975 to 0.781)	0.828	0.102	-0.093 (-0.971 to 0.785)	0.836	0.102
No	72	199.9 \pm 128.0	-0.921 (-1.448 to -0.394)	<0.001		-0.911 (-1.437 to -0.384)	<0.001	
Smoking								
Yes	15	97.5 \pm 86.2	-1.806 (-3.408 to -0.203)	0.027	0.129	-1.793 (-3.400 to -0.186)	0.029	0.125
No	89	225.0 \pm 118.6	-0.558 (-1.033 to -0.084)	0.021		-0.552 (-1.027 to -0.078)	0.023	
Diabetes								
Yes	29	172.4 \pm 135.1	-1.402 (-2.373 to -0.431)	0.005	0.102	-1.394 (-2.366 to -0.423)	0.005	0.104
No	75	219.8 \pm 115.8	-0.473 (-0.989 to 0.042)	0.072		-0.467 (-0.982 to 0.048)	0.076	
Prevalent cardiovascular disease								
Yes	17	248.1 \pm 110.6	-1.346 (-2.458 to -0.234)	0.018	0.144	-1.353 (-2.465 to -0.241)	0.017	0.143
No	87	198.5 \pm 123.9	-0.500 (-0.997 to -0.004)	0.048		-0.493 (-0.989 to 0.004)	0.052	
Use of an antihypertensive drug								
Yes	85	208.5 \pm 124.3	-0.862 (-1.385 to -0.339)	0.001	0.144	-0.853 (-1.377 to -0.330)	0.001	0.150
No	19	198.1 \pm 118.3	-0.075 (-0.996 to 0.845)	0.873		-0.064 (-0.985 to 0.856)	0.891	

BMI indicates body mass index; int, interaction; and NA, not applicable.

studies did not examine whether CPAP therapy is beneficial even in patients with poor adherence to CPAP therapy. In addition, those previous studies assessed CPAP adherence using the internal clock built into the CPAP device, as we did in the present study. Although this method has been widely used in clinical practice, not only the evaluation of night-to-night CPAP adherence but also home BP measurements on the next day might augment the benefit of long-term CPAP therapy, which would contribute to a prevention of CVD events.

In the meta-analysis comparing the association of CPAP treatment versus untreated controls with changes in office SBP and DBP, the reductions in office SBP and DBP were 2.5 mm Hg and 2.0 mm Hg, respectively.⁷ Compared with those results and others, the effect of CPAP adherence on home BP in this study was small. This discrepancy in outcomes may be explained by differences in study settings between our study and previous studies. These previous studies compared BP changes between groups with and

without CPAP treatment, whereas our study enrolled patients who had already been introduced to CPAP treatment to determine the daily effect of CPAP adherence on home BP. In addition, the follow-up duration was longer in our study than in previous studies. One can speculate that in populations in which CPAP has been used for a long period of time, the daily effect of CPAP adherence on BP may be small.

Several studies have demonstrated a significant seasonal variation in home BP, with values higher in winter than summer.^{13–15} One previous study on the seasonal variation in home BP among 64 536 Japanese subjects showed that the maximum winter–summer difference of home morning SBP was 6.2 mm Hg in men and 7.3 mm Hg in women.¹³ In our present study, the maximum winter–summer difference of home morning SBP among individuals without good adherence to CPAP therapy was 7.8 mm Hg (132.5 mm Hg versus 124.7 mm Hg; see Figure 2), which was marginally similar to the seasonal home SBP difference in the

Table 3. Association Between Good Continuous Positive Airway Pressure Adherence (≥ 4 h per Night) and Morning Diastolic Blood Pressure

	No. of patients	No. of days	Unadjusted			Adjusted		
			β (95% CI)	P value	P_{int} value	β (95% CI)	P value	P_{int} value
All patients	104	206.6 \pm 122.7	-0.835 (-1.129 to -0.541)	<0.001	NA	-0.829 (-1.123 to -0.535)	<0.001	NA
Age								
<65 y	61	162.1 \pm 114.8	-0.472 (-0.899 to -0.044)	0.031	0.012	-0.468 (-0.895 to -0.040)	0.032	0.011
≥ 65 y	43	269.7 \pm 105.5	-1.230 (-1.636 to -0.824)	<0.001		-1.231 (-1.637 to -0.825)	<0.001	
Sex								
Women	18	214.0 \pm 116.2	-0.650 (-1.451 to 0.152)	0.112	0.607	-0.631 (-1.433 to 0.172)	0.123	0.581
Men	86	205.1 \pm 124.6	-0.864 (-1.180 to -0.549)	<0.001		-0.862 (-1.177 to -0.546)	<0.001	
BMI								
<25 kg/m ²	24	261.0 \pm 123.1	-0.544 (-1.031 to -0.057)	0.028	0.221	-0.542 (-1.028 to -0.055)	0.029	0.227
≥ 25 kg/m ²	80	190.3 \pm 118.5	-0.951 (-1.314 to -0.588)	<0.001		-0.945 (-1.308 to -0.582)	<0.001	
Drinking								
Yes	32	221.8 \pm 110.2	-0.912 (-1.478 to -0.346)	0.002	0.758	-0.913 (-1.479 to -0.347)	0.002	0.715
No	72	199.9 \pm 128.0	-0.803 (-1.144 to -0.462)	<0.001		-0.791 (-1.132 to -0.451)	<0.001	
Smoking								
Yes	15	97.5 \pm 86.2	-1.052 (-2.142 to 0.037)	0.058	0.680	-0.982 (-2.074 to 0.111)	0.078	0.665
No	89	225.0 \pm 118.6	-0.813 (-1.119 to -0.508)	<0.001		-0.809 (-1.114 to -0.503)	<0.001	
Diabetes								
Yes	29	172.4 \pm 135.1	-0.721 (-1.375 to -0.066)	0.031	0.707	-0.706 (-1.360 to -0.051)	0.035	0.671
No	75	219.8 \pm 115.8	-0.864 (-1.193 to -0.535)	<0.001		-0.861 (-1.189 to -0.532)	<0.001	
Prevalent cardiovascular disease								
Yes	17	248.1 \pm 110.6	-0.922 (-1.614 to -0.230)	0.009	0.772	-0.926 (-1.618 to -0.234)	0.009	0.751
No	87	198.5 \pm 123.9	-0.814 (-1.139 to -0.490)	<0.001		-0.805 (-1.130 to -0.481)	<0.001	
Use of an antihypertensive drug								
Yes	85	208.5 \pm 124.3	-0.896 (-1.230 to -0.563)	<0.001	0.474	-0.890 (-1.223 to -0.557)	<0.001	0.477
No	19	198.1 \pm 118.3	-0.647 (-1.282 to -0.012)	0.046		-0.639 (-1.274 to -0.003)	0.049	

BMI indicates body mass index; int, interaction; and NA, not applicable.

previous study. In contrast, the individuals with good adherence to CPAP therapy showed less seasonal home BP variation. We previously reported that morning home BP is higher in winter, and this increase may lead to a higher incidence of cardiovascular events in winter compared with the other 3 seasons.¹⁵ In addition, a previous study about the association between seasonal variation in home BP and cardiovascular events demonstrated that a small increase in morning home BP (0–4.8 mm Hg in SBP, 0–2.4 mm Hg in DBP) from summer to winter was associated with better cardiovascular outcome compared with a larger increase between the 2 seasons (≥ 9.1 mm Hg in SBP, ≥ 4.5 mm Hg in DBP) in 2787 treated patients with hypertension.³³ The results of the present study also suggest that good adherence to CPAP therapy would reduce the incidence of cardiovascular events throughout the year in patients with OSA. The reason the effect of CPAP adherence on morning SBP differs according to season may be partly explained by the results of a previous study. That study reported that the

apnea-hypopnea index was recorded more frequently in the winter season than in other seasons in patients with a suspected sleep disorder.³⁴ The authors speculated that the seasonal change in the severity of SDB is caused by winter-related fat redistribution, use of medication, fluid displacement to the neck, and/or air pollution. Another possible explanation for seasonal change in the severity of SDB may be seasonal changes in serum 25-hydroxyvitamin D levels,³⁵ which are lower in the winter season.³⁶ Low 25-hydroxyvitamin D is associated with reduced musculoskeletal function.³⁷ Because impaired upper airway muscle tone has an important role in OSA, low 25-hydroxyvitamin D may increase the risk of worse OSA.³⁵ Thus, the pathogenesis of increased risk for OSA in the winter season may be complex.

Strengths and Limitations

The strengths of the present study include its use of the same, validated home BP device, with BP data

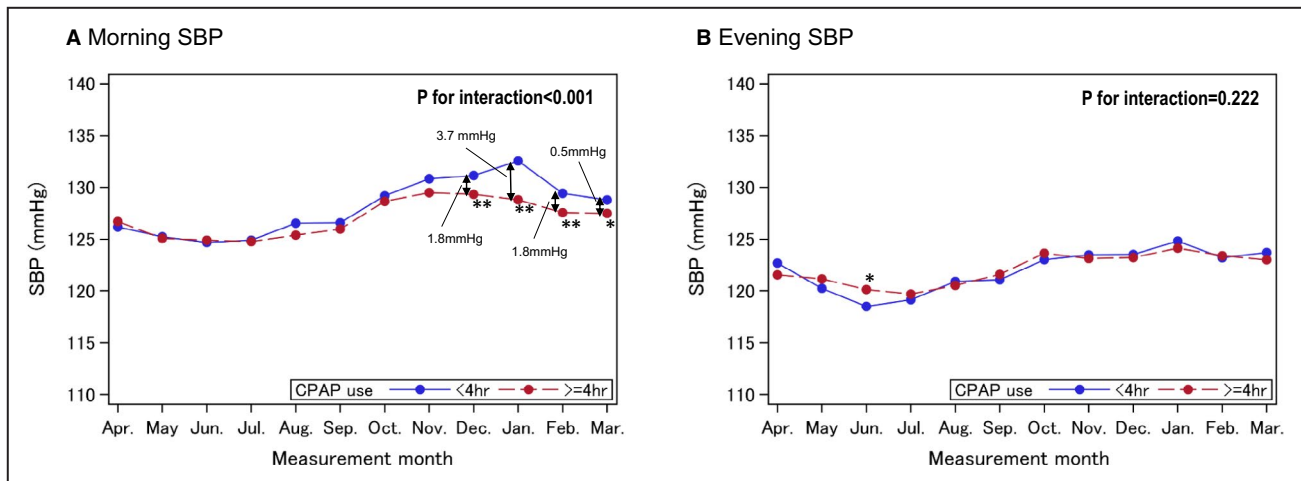


Figure 2. Monthly means of (A) home morning and (B) home evening systolic blood pressure (SBP).

Significant at * $P < 0.05$, ** $P < 0.01$ vs poor adherence to continuous positive airway pressure (CPAP) therapy (<4 hours per night) after adjustment by age, sex, body mass index, drinking, smoking, diabetes, prevalent cardiovascular disease, and use of an antihypertensive drug.

automatically transmitted to a server, in all participants. This is the first study about the association between in-ternight variability of adherence to CPAP and the home BP level on the following morning.

There are several limitations in this study. First, the number of participants was small. In particular, the small number of subjects limits the statistical power and the feasibility of subgroup analysis. However, the number of home BP readings was over 20 000. Second, risk factors related to BP were assessed at baseline, and changes in these risk factors over time were not taken into account, except for the change in antihypertensive drugs. Third, detailed information about other residual confounding risk factors, which may have influenced home BP, was not available. Fourth, these results may not be generalizable to other settings, particularly for patients with uncontrolled or resistant hypertension.

Perspectives

Good night-to-night adherence to CPAP therapy was associated with a reduction in morning home BP in patients with OSA. In addition, the individuals with good CPAP adherence exhibited a reduction in seasonal variation of morning home BP compared with those without good adherence. Further studies will be needed to determine whether the results of this study would be relevant to the prevention of CVD events.

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SUPPLEMENTAL MATERIAL

Data S1.

Supplemental Methods

Overnight polysomnography was performed over the course of the hospitalization of participants using standard techniques and criteria for scoring sleep stages and arousal.³⁸ The following biological variables were continuously monitored overnight: nasal airflow, snoring sounds, thoracic and abdominal respiratory effort signals, electrocardiography, oxygen saturation via pulse oximetry and electroencephalography. All recordings were analyzed for sleep disorder breathing parameters according to the American Academy of Sleep Medicine criteria.¹⁶ Apnea was defined as an absence of airflow for more than 10 s, and hypopnea was defined as a 30% reduction in monitored airflow accompanied by a 3% oxygen desaturation.¹⁶ The apnea–hypopnea index (AHI) was defined as the number of apneas and hypopneas per hour of sleep. Standard definitions for obstructive sleep apnea and central sleep apnea were made based on the presence or absence of rib cage and abdominal excursions with an absence of airflow.³⁹

Polygraphy was performed using a validated home sleep apnea device that recorded nasal airflow, snoring sounds, thoracic and abdominal respiratory effort signals, electrocardiography, oxygen saturation via pulse oximetry and body position. Sleep studies were scored according to the guidelines. Sleep onset and offset were identified based on the patient's diary. The definition of apnea, hypopnea and AHI were made in a similar manner as the diagnosis of polysomnography. Obstructive sleep apnea was diagnosed as $AHI \geq 15$ during polysomnography or polygraphy, which apnea event was with predominantly (>50%) obstructive events.⁴⁰ All arousals and respiratory events were manually scored by experienced sleep technicians blinded to information regarding subjects.

Table S1. Association between good CPAP adherence (≥ 4 h per night) and evening systolic blood pressure

			Unadjusted			Adjusted		
	No. of patients	No. of days	β	P value	P_{int}	β (95% CI)	P value	P_{int}
All patients	105	192.1 \pm 126.3	0.240 (-0.262 to 0.743)	0.349	NA	0.248 (-0.255 to 0.750)	0.335	NA
Age								
<65 years	62	146.9 \pm 115.1	0.216 (-0.469 to 0.900)	0.537	0.911	0.222 (-0.462 to 0.907)	0.525	0.936
≥ 65 years	43	257.2 \pm 113.6	0.273 (-0.464 to 1.009)	0.468		0.262 (-0.475 to 0.999)	0.486	
Sex								
Women	18	211.6 \pm 122.5	-0.137 (-1.492 to 1.218)	0.843	0.548	-0.158 (-1.513 to 1.198)	0.820	0.555
Men	87	188.1 \pm 127.4	0.305 (-0.236 to 0.847)	0.269		0.309 (-0.232 to 0.850)	0.263	
BMI								
<25kg/m ²	24	243.7 \pm 133.3	1.065 (0.211 to 1.918)	0.015	0.046	1.061 (0.207 to 1.915)	0.015	0.048
≥ 25 kg/m ²	81	176.8 \pm 120.9	-0.077 (-0.692 to 0.539)	0.807		-0.070 (-0.686 to 0.545)	0.823	
Drinking								
Yes	32	174.7 \pm 118.4	0.928 (-0.219 to 2.075)	0.113	0.109	0.938 (-0.211 to 2.087)	0.109	0.108
No	73	199.7 \pm 129.7	0.004 (-0.542 to 0.550)	0.989		0.011 (-0.535 to 0.557)	0.969	
Smoking								
Yes	15	94.2 \pm 68.1	-0.075 (-1.600 to 1.449)	0.923	0.665	-0.079 (-1.605 to 1.448)	0.920	0.662
No	90	208.4 \pm 126.6	0.283 (-0.249 to 0.816)	0.297		0.287 (-0.246 to 0.819)	0.291	
Diabetes								
Yes	29	154.3 \pm 129.7	-0.184 (-1.274 to 0.906)	0.741	0.379	-0.174 (-1.264 to 0.917)	0.755	0.398
No	76	206.5 \pm 122.9	0.359 (-0.208 to 0.926)	0.215		0.362 (-0.205 to 0.929)	0.211	
Prevalent cardiovascular disease								
Yes	17	222.5 \pm 127.3	0.695 (-0.510 to 1.900)	0.258	0.382	0.683 (-0.522 to 1.887)	0.266	0.378
No	88	186.2 \pm 126.0	0.130 (-0.423 to 0.682)	0.646		0.137 (-0.416 to 0.689)	0.628	
Use of an antihypertensive drug								
Yes	86	197.8 \pm 126.7	0.260 (-0.327 to 0.846)	0.385	0.898	0.267 (-0.320 to 0.854)	0.372	0.895
No	19	166.3 \pm 124.6	0.187 (-0.751 to 1.124)	0.697		0.198 (-0.740 to 1.136)	0.679	

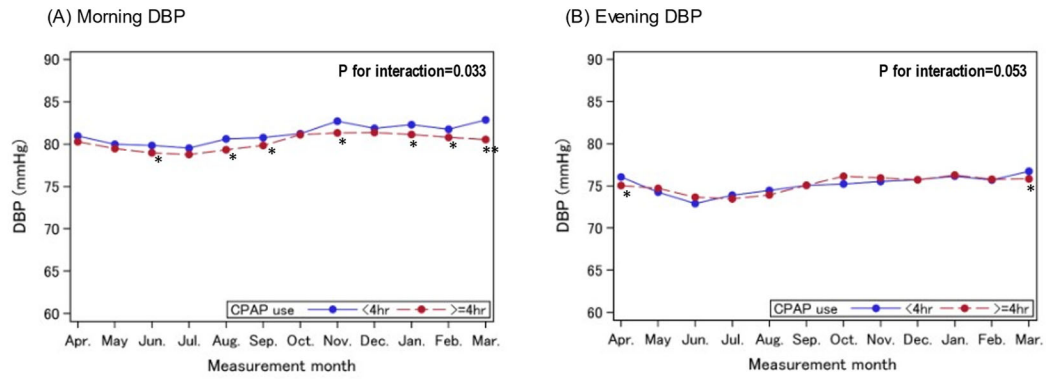
BMI indicates body mass index; CI, confidence interval; CPAP, continuous positive airway pressure; NA, not applicable.

Table S2. Association between good CPAP adherence (≥ 4 h per night) and evening diastolic blood pressure

			Unadjusted			Adjusted		
	No. of patients	No. of days	β	P value	P_{int}	β	P value	P_{int}
All patients	105	192.1 \pm 126.3	0.066 (-0.267 to 0.400)	0.696	NA	0.072 (-0.262 to 0.405)	0.674	NA
Age								
<65 years	62	146.9 \pm 115.1	-0.043 (-0.544 to 0.457)	0.865	0.481	-0.038 (-0.539 to 0.463)	0.882	0.501
≥ 65 years	43	257.2 \pm 113.6	0.198 (-0.246 to 0.643)	0.382		0.187 (-0.258 to 0.631)	0.411	
Sex								
Women	18	211.6 \pm 122.5	-0.352 (-1.242 to 0.539)	0.439	0.311	-0.351 (-1.243 to 0.541)	0.440	0.336
Men	87	188.1 \pm 127.4	0.137 (-0.222 to 0.497)	0.454		0.138 (-0.221 to 0.497)	0.451	
BMI								
<25kg/m ²	24	243.7 \pm 133.3	0.663 (0.146 to 1.180)	0.012	0.028	0.661 (0.144 to 1.178)	0.012	0.029
≥ 25 kg/m ²	81	176.8 \pm 120.9	-0.166 (-0.584 to 0.252)	0.435		-0.162 (-0.580 to 0.256)	0.448	
Drinking								
Yes	32	174.7 \pm 118.4	0.610 (-0.163 to 1.383)	0.122	0.054	0.581 (-0.191 to 1.354)	0.140	0.063
No	73	199.7 \pm 129.7	-0.123 (-0.481 to 0.236)	0.502		-0.112 (-0.470 to 0.246)	0.540	
Smoking								
Yes	15	94.2 \pm 68.1	0.149 (-0.921 to 1.219)	0.785	0.864	0.187 (-0.887 to 1.260)	0.733	0.877
No	90	208.4 \pm 126.6	0.060 (-0.291 to 0.411)	0.737		0.062 (-0.289 to 0.413)	0.728	
Diabetes								
Yes	29	154.3 \pm 129.7	-0.354 (-1.114 to 0.416)	0.361	0.219	-0.324 (-1.084 to 0.436)	0.404	0.244
No	76	206.5 \pm 122.9	0.174 (-0.195 to 0.544)	0.355		0.175 (-0.195 to 0.544)	0.355	
Prevalent cardiovascular disease								
Yes	17	222.5 \pm 127.3	0.490 (-0.233 to 1.214)	0.184	0.220	0.486 (-0.237 to 1.209)	0.188	0.219
No	88	186.2 \pm 126.0	-0.037 (-0.412 to 0.337)	0.845		-0.031 (-0.406 to 0.343)	0.869	
Use of antihypertensive drug								
Yes	86	197.8 \pm 126.7	0.229 (-0.155 to 0.613)	0.242	0.092	0.231 (-0.152 to 0.615)	0.237	0.097
No	19	166.3 \pm 124.6	-0.438 (-1.109 to 0.234)	0.201		-0.432 (-1.104 to 0.239)	0.207	

BMI indicates body mass index; CI, confidence interval; CPAP, continuous positive airway pressure; NA, not applicable.

Figure S1. Monthly means of (A) home morning and (B) home evening diastolic blood pressure (DBP)



Significantly different at * $P < 0.05$, ** $P < 0.01$ vs. poor adherence to CPAP therapy (<4 h/per night) after adjustment by age, sex, body mass index, drinking, smoking, diabetes, prevalent cardiovascular disease and use of an antihypertensive drug.