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Effect of CPAP on brachial-ankle pulse wave velocity in patients with OSAHS: An open-labelled study ☆

Yoshihiro Kitahara, Noboru Hattori*, Akihito Yokoyama, Masamitsu Nakajima, Nobuoki Kohno

Department of Molecular and Internal Medicine, Division of Clinical Medical Science, Graduate School of Biochemical Sciences, Hiroshima University, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-8551, Japan

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Summary Pulse wave velocity (PWV) is a good indicator of arterial stiffness and an important predictor of cardiovascular events. Recent studies have revealed that PWV increases in patients with obstructive sleep apnea–hypopnea syndrome (OSAHS) and it also correlates with its severity. However, the therapeutic effect of continuous positive airway pressure (CPAP) on PWV remains undetermined. To clarify this point, we started CPAP treatment on 17 OSAHS patients. Brachial-ankle PWV was measured before starting CPAP, and at 2 months and 4 months after the start of CPAP. Before the CPAP treatment, mean brachial-ankle PWV of the patients was 15.6 ± 0.6 m/s, and mean Epworth sleepiness scale (ESS) score was 8.6 ± 1.0. Brachial-ankle PWV was found to positively correlate with heart rate, systolic and diastolic blood pressures, mean blood pressure, and arousal index. During the study period, the CPAP treatment did not have a significant effect on heart rate, blood pressures and serum total cholesterol levels. However, it significantly improved ESS score at 4 months after the start of CPAP ($P = 0.001$), while it effectively decreased brachial-ankle PWV at 2 months and at 4 months after the start of CPAP ($P = 0.010$ and $P = 0.027$, respectively). The CPAP treatment was shown to decrease brachial-ankle PWV without affecting blood pressures in OSAHS patients. Although the precise

Abbreviations: AHI, apnea–hypopnea index; BMI, body mass index; CPAP, continuous positive airway pressure; ESS, Epworth sleepiness scale; OSAHS, obstructive sleep apnea–hypopnea syndrome; PWV, pulse wave velocity; SpO_2, percutaneous arterial saturation.

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*Corresponding author. Tel.: 81 82 257 5196; fax: 81 82 255 7360.
E-mail address: nhattori@hiroshima-u.ac.jp (N. Hattori).

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mechanism for this effect is unclear, our finding suggests a close relationship between OSAHS and arterial stiffness, while also reemphasizing the clinical importance of CPAP treatment.

Introduction

Obstructive sleep apnea–hypopnea syndrome (OSAHS) is a condition characterized by repeated episodes of partial or complete obstruction of the upper airway during sleep, thus resulting in hypoxemia, arousal, and fragmentation of sleep.[1,2] Individuals with OSAHS have a higher prevalence of cardiovascular disorders such as hypertension,[3,4] ischemic heart disease,[5,6] stroke,[7] and arrhythmia.[8,9] Strong evidence has identified OSAHS to be an independent risk factor for increased cardiovascular mortality.[10] Recent epidemiological studies have revealed that treatment with continuous positive airway pressure (CPAP) decreases blood pressure,[11] reduces the risk of cardiovascular events,[12] and improves cardiovascular mortality in patients with OSAHS.[13] These findings demonstrate a strong causative link between OSAHS and cardiovascular morbidity and mortality, and CPAP treatment can reduce both of them.

Over the past few years, arterial stiffness has been widely investigated because it may predict cardiovascular events beyond the classic risk factors such as blood pressure.[14,15] In fact, arterial stiffness increases with advancing age[16] and other cardiovascular risk factors including a sedentary lifestyle,[16] and hypercholesterolemia.[17] Among a number of parameters, arterial pulse wave velocity (PWV) has emerged as a good indicator of arterial stiffness.[14] PWV has been demonstrated as an important predictor of cardiovascular events in hypertensive patients.[18] A reduction in PWV has been obtained in hypertensive patients who received antihypertensive treatment.[19] Of particular interest, recent studies have revealed that PWV increases in OSAHS patients and also correlates with apnea–hypopnea index (AHI) which is a measure of the severity of OSAHS.[20–22] These findings suggest a strong link between arterial stiffness assessed by PWV and OSAHS. We, therefore, investigated whether CPAP treatment has any effect on arterial stiffness in patients with OSAHS. We performed brachial-ankle PWV measurements on patients with moderate to severe OSAHS, and then compared brachial-ankle PWV recorded during successful CPAP treatment with that before the treatment.

Materials and methods

Subjects, polysomnography, and CPAP treatment

The present study was conducted in the respiratory division at Hiroshima University Hospital between April 2004 and March 2005. Informed consent was obtained from each subject and the study protocol was approved by the ethics committee. Seventeen subjects (16 men and 1 woman) were enrolled. All subjects underwent standard in-laboratory polysomnography using a computerized system (Alice 4®, Respironics; Pittsburgh, PA, USA). Apnea was defined as a continuous cessation of airflow lasting at least 10 s. Hypopnea was defined as an airflow reduction of $\geqslant$50% from the baseline lasting at least 10 s, or a less significant reduction in the airflow accompanied by the presence of arousal or oxygen desaturation of $\geqslant$3%. AHI was calculated as the number of apnea and hypopnea events per hour of sleep. According to the criteria of the American Academy of Sleep Medicine,[1] we defined moderate OSAHS as $15 \leqslant \text{AHI} < 30$ and severe OSAHS as $\text{AHI} \geqslant 30$. An automated CPAP device (REMstar Auto®, Respironics), which calibrates CPAP pressures automatically,[23] was applied for all patients. Each patient visited our outpatient clinic at least once a month and was encouraged to use the CPAP device every night. At every visit to our hospital, the average usage time of CPAP and AHI per night under the CPAP treatment were calculated by the software package included with the CPAP device (Encore Pro®, Respironics).

Measurement of brachial-ankle PWV and other variables

Brachial-ankle PWV was measured in the supine position after 5 min of bed rest using an automatic pulse-wave velocimeter (Form PWV/ABI®, model BP-203RPE, Colin Medical Technology Co., Komaki, Japan).[24,25] To minimize the influence of diurnal variation, brachial-ankle PWV was measured between 10:00 and 11:00 A.M.[26] In addition, subjects were required to withhold meals, caffeine, and smoking before brachial-ankle PWV measurement

to avoid any confounding influence of these factors on arterial stiffness.[27–29] Patients who were on anti-hypertensive medication were required to take their drugs immediately after waking up. The procedure for the measurement of brachial-ankle PWV was as follows; four blood pressure cuffs were wrapped around the bilateral brachia and ankles, and two sensors were placed around the bilateral wrists. Depending on the index line printed on the pressure cuffs, we checked whether the cuff size was appropriate for each subject. A microphone was set on the left edge of the sternum at the fourth intercostal space. Pulse waves and blood pressures of brachial and tibial arteries, heart sounds, and heart rate were recorded simultaneously. Blood pressures were measured by an oscillometric method. The time lag between the wavefront of brachial waveform and that of ankle waveform was defined as the time interval between the brachial and ankle pulses (ΔT_{ba}). The path lengths from the suprasternal notch to the brachium (L_b) and to the ankle (L_a) were calculated using following equation: $L_b = 0.2195 \times$ height (cm)—2.0734, $L_a = 0.8129 \times$ height (cm)+12.328. Brachial-ankle PWV was calculated using the following equation: brachial-ankle PWV $= (L_a - L_b)/\Delta T_{ba}$ (cm/s) $= (L_a - L_b)/\Delta T_{ba}/100$ (m/s).[24,25] We measured brachial-ankle PWV at least three times, and then selected the lowest right systolic brachial blood pressure of the three measurements. Systolic and diastolic brachial blood pressures, pulse pressure, and brachial-ankle PWV were measured bilaterally, and the average of the recorded values was used for the analysis. Mean brachial blood pressure was calculated bilaterally according to formula: (systolic brachial blood pressure−diastolic brachial blood pressure)/3+diastolic brachial blood pressure, and the average value was used for the analysis. Each measurement was made before starting CPAP, and at 2 months and 4 months after the start of CPAP treatment. At the same time, daytime sleepiness was evaluated using the Epworth sleepiness scale (ESS), and serum total cholesterol levels and body weight were measured. Body mass index (BMI) was defined as the weight in kilograms divided by the square of the height in meters.

Statistical analysis

All statistical analyses were performed with the statistical program SPSS for Windows (version 11.0; SPSS; Chicago, IL, USA). The data are presented as mean ± SEM. The relationships between brachial-ankle PWV and other variables were assessed using Pearson's correlation analysis. Paired *t*-test was used to compare the variables before the CPAP treatment with those measured at 2 months and 4 months after the start of CPAP treatment. Simple linear regression analysis was performed between the magnitude in changes of brachial-ankle PWV (Δbrachial-ankle PWV) and each of those in BMI (ΔBMI), heart rate (Δheart rate), and systolic, pulse, and mean blood pressures (Δeach blood pressure). A *P*-value of less than 0.05 was considered to be statistically significant.

Results

Patient characteristics and sleep study

Characteristics of the patients are shown in Table 1. Ages of the subjects ranged between 42 and 69 years old. Two current smokers and 8 past smokers were included. Smoking status of the current smokers did not change during the study period. Mean brachial-ankle PWV was 15.6 ± 0.6 m/s. Mean ESS score was 8.6 ± 1.0. Based on polysomnography results, moderate OSAHS was diagnosed in 7 patients and severe OSAHS in 10. Eleven hypertensive patients, who were already taking antihypertensive drugs before OSAHS was diagnosed, were included. The antihypertensive medication for these patients did not change during the study period. Because recruitment of non-OSAHS subjects

Table 1 Patient characteristics.

$n = 17$	Mean ± SEM
Age (yr)	58.6 ± 2.0
Height (cm)	166.7 ± 1.6
Body weight (kg)	70.9 ± 2.9
Body mass index (kg/m^2)	25.4 ± 0.8
Smoking status (never/past/current)	7/8/2
Total cholesterol* (mg/dl)	194.8 ± 7.6
Heart rate (beats/min)	64.7 ± 2.6
Systolic blood pressure (mmHg)	128.9 ± 3.3
Diastolic blood pressure (mmHg)	80.9 ± 2.4
Mean blood pressure (mmHg)	96.9 ± 2.6
Pulse pressure (mmHg)	48.0 ± 2.1
Brachial-ankle pulse wave velocity (m/s)	15.6 ± 0.6
Epworth sleepiness scale	8.6 ± 1.0
Apnea–hypopnea index (events/h)	38.5 ± 4.2
Arousal index (events/h)	36.3 ± 3.4
Lowest SpO2 during sleep study (%)	79.8 ± 2.9

*Note that data of total cholesterol were obtained from 13 subjects.

matched for age, sex, and hypertension profile was difficult to achieve, we were not able to compare brachial-ankle PWV of the studied OSAHS patients with that of the control subjects.

To determine whether brachial-ankle PWV was associated with other variables, we performed Pearson's correlation analysis (Fig. 1 and Table 2). Brachial-ankle PWV was found to positively correlate with arousal index (Fig. 1c; $r = 0.596$, $P = 0.012$) but not with maximal desaturation from the baseline (Fig. 1e; $r = 0.371$, $P = 0.143$), the lowest percutaneous arterial saturation (SpO_2) during sleep study (Fig. 1f; $r = -0.323$, $P = 0.206$). Brachial-ankle PWV tended to increase with an increasing ESS score (Fig. 1a; $r = 0.464$, $P = 0.061$), AHI (Fig. 1b; $r = 0.478$, $P = 0.053$), and desaturation index, the number of desaturation episodes (drop in $SpO_2 \geqslant 3\%$ from the baseline) per hour of sleep (Fig. 1d; $r = 0.419$, $P = 0.094$), but these correlations were not statistically significant. As shown in Table 2, brachial-ankle PWV was found to positively correlate with heart rate ($r = 0.510$, $P = 0.036$), systolic blood pressure ($r = 0.678$, $P = 0.003$), diastolic blood pressure ($r = 0.603$, $P = 0.010$), mean blood pressure ($r = 0.670$, $P = 0.003$), but not with BMI ($r = -0.029$, $P = 0.912$), serum total cholesterol levels ($n = 13$, $r = 0.459$, $P = 0.115$), or pulse pressure ($r = 0.366$, $P = 0.148$).

Effect of CPAP treatment

Based on the recorded data on CPAP usage and AHI, we confirmed that all patients utilized CPAP appropriately and the treatment was successful (the first 2 months: CPAP usage time, 295.2 ± 17.1 min/night, AHI, 3.9 ± 0.7 events/h; the last 2 months: CPAP usage time, 331.5 ± 20.8 min/night, AHI, 3.1 ± 0.5 events/h).

We first intended to see whether the association of brachial-ankle PWV with other variables changed at 2 months and 4 months after the start of CPAP (Table 2). Systolic blood pressure, mean blood pressure, and pulse pressure were significantly correlated with brachial-ankle PWV at both 2 and 4 months after the start of CPAP. The data obtained from 13 patients showed that serum total cholesterol levels also significantly correlated with brachial-ankle PWV at both 2 and 4 months after

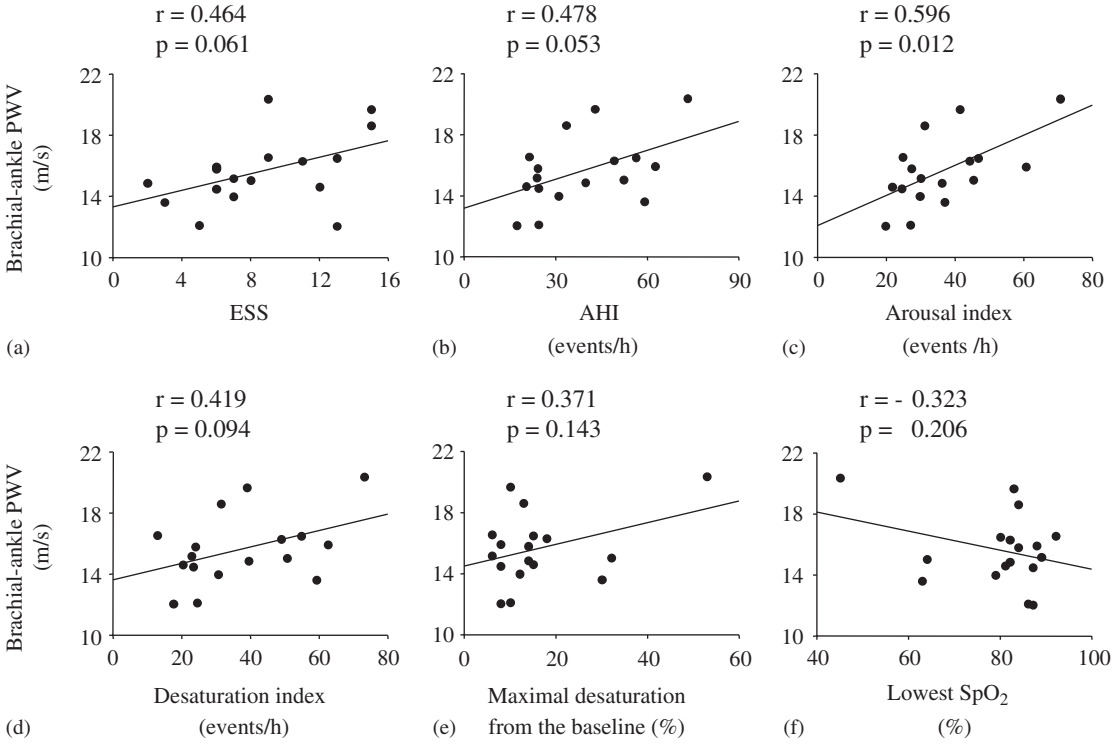

Fig. 1 Relationships between brachial-ankle pulse wave velocity (PWV) and Epworth sleepiness scale (ESS) score and sleep data. Brachial-ankle PWV was found to positively correlate with arousal index (c; $r = 0.596$, $P = 0.012$), but not with maximal desaturation from the baseline (e; $r = 0.371$, $P = 0.143$) and the lowest percutaneous arterial saturation (SpO_2) during sleep study (f; $r = -0.323$, $P = 0.206$). Brachial-ankle PWV tended to increase with an increasing ESS score (Fig. 1a; $r = 0.464$, $P = 0.061$), apnea–hypopnea index (AHI) (b; $r = 0.478$, $P = 0.053$), and desaturation index (d; $r = 0.419$, $P = 0.094$), but these correlations were not statistically significant.

Table 2 Correlation between brachial-ankle PMV and other variables before, and at 2 months, and 4 months after the start of CPAP.

	Correlation between brachial-ankle PWW		
	Mean ± SEM	*r*	*P*
Body mass index (kg/m^2)			
Baseline	25.4 ± 0.8	−0.029	0.912
2 months after	25.5 ± 0.8	−0.041	0.876
4 months after	25.7 ± 0.8	−0.235	0.364
Total cholesterol (mg/dl, n = 13)			
Baseline	194.8 ± 7.6	0.459	0.115
2 months after	192.2 ± 6.4	0.565	0.044†
4 months after	199.2 ± 9.8	0.74	0.004†
Heart rate (beats/min)			
Baseline	64.7 ± 2.6	0.51	0.036†
2 months after	63.8 ± 2.6	0.528	0.029†
4 months after	64.2 ± 2.8	0.305	0.234
Systolic blood pressure (mmHg)			
Baseline	128.9 ± 3.3	0.678	0.003†
2 months after	127.6 ± 4.1	0.683	0.003†
4 months after	132.6 ± 3.6	0.706	0.002†
Diastolic blood pressure (mmHg)			
Baseline	80.9 ± 2.4	0.603	0.010†
2 months after	79.6 ± 2.4	0.514	0.035†
4 months after	80.9 ± 2.6	0.459	0.064
Mean blood pressure (mmHg)			
Baseline	96.9 ± 2.6	0.67	0.003†
2 months after	95.6 ± 2.9	0.616	0.008†
4 months after	98.1 ± 2.7	0.607	0.010†
Pulse pressure (mmHg)			
Baseline	48.0 ± 2.1	0.366	0.148
2 months after	47.9 ± 2.4	0.631	0.007†
4 months after	51.8 ± 2.6	0.537	0.026†

†$P < 0.05$.

the start of CPAP. Heart rate and diastolic blood pressure significantly correlated with brachial-ankle PWV at 2 months after the start of CPAP.

We then analyzed the influence of CPAP on heart rate, systolic and diastolic blood pressures, mean blood pressure, pulse pressure, BMI, total cholesterol and ESS as well as brachial-ankle PWV (Figs. 2 and 3). The CPAP treatment did not have any significant effect on heart rate (Fig. 2a; $P = 0.518$ at 2 months after the start of CPAP, and $P = 0.711$ at 4 months after the start of CPAP), systolic blood pressure (Fig. 2b; $P = 0.523$ at 2 months after the start of CPAP, and $P = 0.150$ at 4 months after the start of CPAP), diastolic blood pressure (Fig. 2c; $P = 0.491$ at 2 months after the start of CPAP, and $P = 0.985$ at 4 months after the start of CPAP), mean blood pressure (Fig. 2d; $P = 0.471$ at 2 months after the start of CPAP, and $P = 0.461$ at 4 months after the start of CPAP), pulse pressure (Fig. 2e; $P = 0.968$ at 2 months after the start of CPAP, and $P = 0.057$ at 4 months after the start of CPAP) and serum total cholesterol levels (Fig. 3b; $n = 13$, $P = 0.643$ at 2 months after the start of CPAP, and $P = 0.554$ at 4 months after the start of CPAP). However, the CPAP treatment significantly improved ESS score (Fig. 3c; 5.3 ± 0.7 at 4 months after the start of CPAP, $P = 0.001$) and it effectively decreased brachial-ankle PWV (Fig. 3d; 15.0 ± 0.5 m/s at 2 months after the start of CPAP, $P = 0.010$; 14.9 ± 0.6 m/s at 4 months after the start of CPAP, $P = 0.027$). BMI significantly increased from 2 months to 4 months after the start of CPAP (Fig. 3a; 25.5 ± 0.8 kg/m^2 at 2 months after the start of CPAP and 25.7 ± 0.8 kg/m^2 at 4 months after the start of CPAP, $P = 0.036$).

Next, using simple linear regression analysis, we intended to determine whether the magnitude of changes in brachial-ankle PWV (Δbrachial-ankle PWV) was correlated with each of those in BMI, heart rate, and systolic, pulse, and mean blood

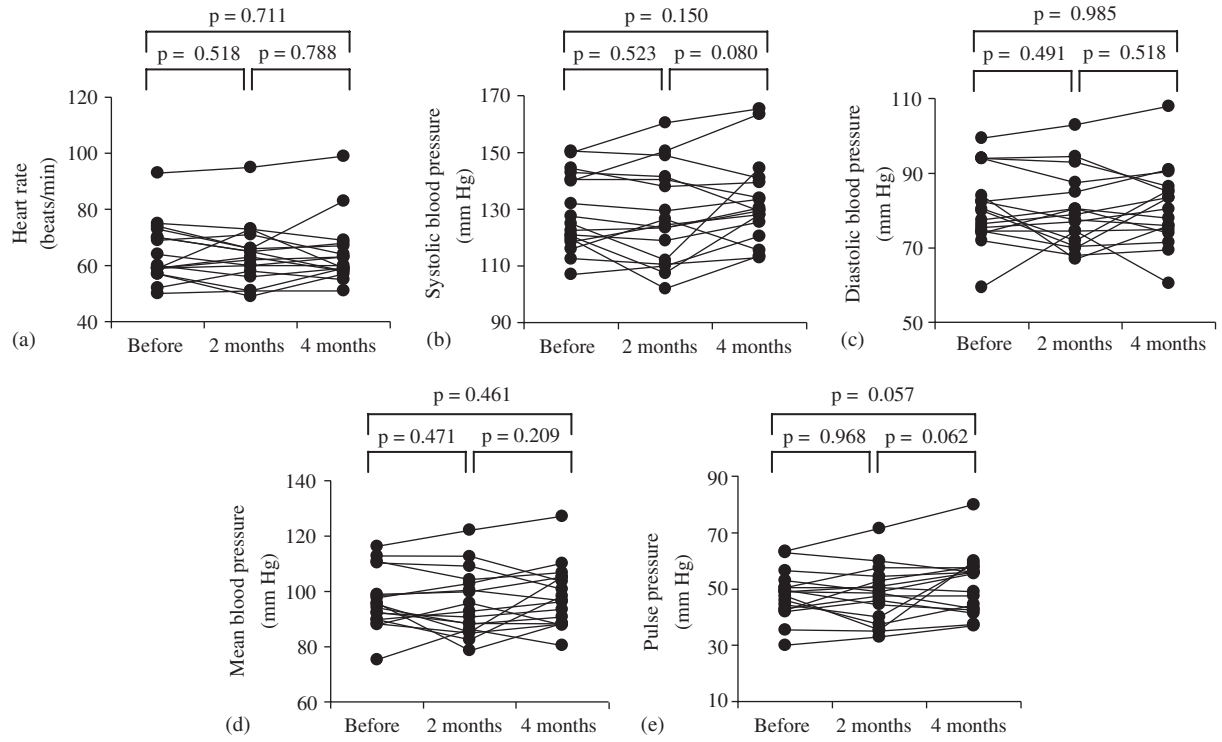

Fig. 2 Effect of continuous positive airway pressure (CPAP) treatment on heart rate (a), systolic blood pressure (b), diastolic blood pressure (c), mean blood pressure (d), and pulse pressure (e). The CPAP treatment did not have a significant effect on heart rate (a; $P = 0.518$ at 2 months after the start of CPAP, and $P = 0.711$ at 4 months after the start of CPAP), systolic blood pressure (b; $P = 0.523$ at 2 months after the start of CPAP, and $P = 0.150$ at 4 months after the start of CPAP), diastolic blood pressure (c; $P = 0.491$ at 2 months after the start of CPAP, and $P = 0.985$ at 4 months after the start of CPAP), mean blood pressure (d; $P = 0.471$ at 2 months after the start of CPAP start, and $P = 0.461$ at 4 months after the start of CPAP), pulse pressure (e; $P = 0.968$ at 2 months after the start of CPAP, and $P = 0.057$ at 4 months after the start of CPAP).

pressures, all of which have been demonstrated to affect PWV.[14,30–32] As shown in Table 3, Δbrachial-ankle PWV was found not significantly associated with each other variable.

Discussion

OSAHS is recognized as an independent risk factor for cardiovascular disorders such as hypertension,[3,4] ischemic heart disease,[5,6] stroke,[7] and arrhythmia,[8,9] and is strongly associated with cardiovascular morbidity and mortality.[10,12,13] Arterial stiffness is another cardiovascular risk factor which is believed to predict cardiovascular events better than classic risk factors such as blood pressure.[14,15] Brachial-ankle PWV is a newly introduced parameter which represents the degree of arterial stiffness with good sensitivity and reproducibility.[25] The correlation of brachial-ankle PWV with aortic PWV and carotid-femoral PWV, both of which are established indices to represent aortic stiffness and predict cardiovascular mortality, has been repeatedly demonstrated.[24,25,33]

In the present study, we found CPAP treatment to decrease brachial-ankle PWV in patients with moderate to severe OSAHS. However, serum total cholesterol levels, heart rate, systolic and diastolic blood pressures, mean blood pressure, and pulse pressure in the studied patients did not differ before and after CPAP treatment. The decrease in brachial-ankle PWV was considered to be independent of these factors which affect PWV. Previous studies have demonstrated the effects of CPAP treatment to reduce blood pressure in OSAHS patients.[11,34,35] However, some studies have failed to show any beneficial effects in the reductions of daytime blood pressure.[36,37] CPAP treatment was also shown not to affect blood pressure in normotensive OSAHS patients.[38] In addition, a recent study has shown that automated CPAP treatment does not acutely change systolic and diastolic blood pressures.[39] Considering the fact that that daytime blood pressures in the studied hypertensive patients were well controlled by optimal antihypertensive medication, the failure of the successful automated CPAP treatment to reduce blood

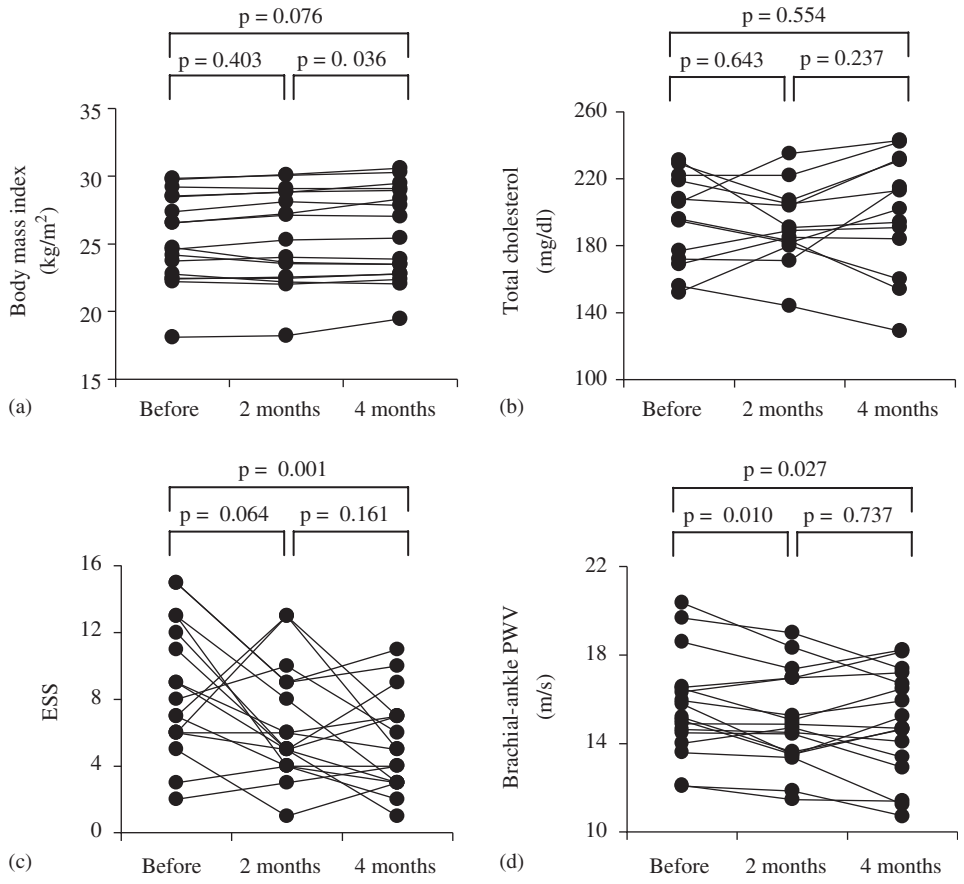

Fig. 3 Effect of continuous positive airway pressure (CPAP) treatment on body mass index (BMI) (a), serum total cholesterol levels (b), Epworth sleepiness scale (ESS) score (c), and brachial-ankle pulse wave velocity (PWV) (d). BMI significantly increased from 2 months to 4 months after the start of CPAP (a; $25.5 \pm 0.8\,kg/m^2$ at 2 months after the start of CPAP start and $25.7 \pm 0.8\,kg/m^2$ after 4 months after the start of CPAP, $P = 0.036$). Serum total cholesterol levels did not change before and after CPAP treatment (b; $n = 13$, $P = 0.643$ at 2 months after the start of CPAP, and $P = 0.554$ at 4 months after the start of CPAP). However, the CPAP treatment significantly improved ESS score (c; 5.3 ± 0.7 at 4 months after the start of CPAP, $P = 0.001$) and it effectively decreased brachial-ankle PWV as shown (d; $15.0 \pm 0.5\,m/s$ at 2 months after the start of CPAP, $P = 0.010$; $14.9 \pm 0.6\,m/s$ at 4 months after the start of CPAP, $P = 0.027$).

Table 3 Simple linear regression analysis on the magnitude of changes in brachial-ankle PWV (Δ brachial-ankle PWV) versus each of those in other variables (Δ each variable).

Δ variable	β	P	R^2
Baseline to 2 months			
Δ body mass index	0.230	0.375	0.053
Δ heart rate 0.314	0.219	0.099	
Δ systolic blood pressure	0.248	0.338	0.061
Δ mean blood pressure	0.152	0.560	0.023
Δ pulse pressure	0.242	0.350	0.058
2 months to 4 months			
Δ body mass index	−0.007	0.978	<0.001
Δ heart rate	0.229	0.377	0.052
Δ systolic blood pressure	0.431	0.084	0.186
Δ mean blood pressure	0.423	0.091	0.179
Δ pulse pressure	0.265	0.304	0.070

β = standardized regression coefficient.

pressure is considered to be consistent with these previous observations.

We demonstrated brachial-ankle PWV to be significantly correlated with systolic blood pressure, mean blood pressure, and pulse pressure at both 2 and 4 months after the start of CPAP, thus suggesting that these blood pressures were still major associated factors of brachial-ankle PWV even after the CPAP treatment decreased it.[14] However, we also found that the magnitudes of changes in brachial-ankle PWV from the baseline to 2 months and from 2 to 4 months after the start of CPAP did not correlate with each of those in systolic, pulse, and mean blood pressures. In addition, the magnitude of changes in brachial-ankle PWV was found not significantly associated with that in BMI nor heart rate. These observations support our conclusion that CPAP treatment decreased brachial-ankle PWV independently of the

changes in these variables including blood pressures, all of which have been reported to affect PWV.[14,30–32]

The mechanism by which CPAP treatment decreased brachial-ankle PWV in OSAHS patients was not determined in the present study. A number of factors may be involved in this process. Repetitive apnea–hypopnea events during sleep are reported to induce sympathetic nerve activity,[36,40] an impaired artery endothelial function,[41,42] reduced nitric oxide derivatives,[43] increased systemic inflammation,[44] and elevated plasma endothelin-1 levels,[45] all of which are associated with the regulation of vascular tone and elasticity. Among them, endothelin-1 is thought to be important because it is reported to regulate PWV in vivo.[46] Of particular interest, CPAP treatment is shown to blunt all of these changes in less than 1 month.[40,41,43–45] We showed in the present study that CPAP treatment decreased brachial-ankle PWV as soon as 2 months after its start. Given that this result was thereafter consistently observed, the CPAP treatment may thus have rapidly normalized some or all factors listed above, thereby causing a decrease in brachial-ankle PWV demonstrated in OSAHS patients. Particularly, among these possibilities, we speculate that a reduction in the sympathetic nerve activity by CPAP treatment is the most likely explanation for the decrease in brachial-ankle PWV in OSAHS patients. PWV is a reflection of both a central elastic component and a peripheral muscular component. Compared with carotid-femoral PWV, brachial-ankle PWV is affected more strongly by the peripheral muscular component, and in comparison to aortic stiffness, the stiffness of the muscular arteries is more strongly regulated by the sympathetic nerve system. In fact, a recent study has demonstrated brachial-ankle PWV to be closely associated with the sympathetic nerve activity in young Japanese men.[47] This finding also supports our speculation raised above.

The present study was carried out at a general outpatient clinic. Mainly for ethical reasons, we were not able to randomize OSAHS patients into a group to be treated with sham CPAP. In addition, because the recruitment of non-OSAHS subjects matched for age and hypertensive profile was difficult to achieve, we were not able to evaluate whether brachial-ankle PWV increased in OSAHS patients in comparison to control subjects, and the independent role played by OSAHS in increasing brachial-ankle PWV could not be determined. To minimize the confounding influences on PWV such as diurnal variation, meals and coffee intake, and smoking, brachial-ankle PWV was measured in the fasted and smoking-free state between 10:00 to 11:00 A.M.[26] Although we showed that successful CPAP treatment decreased brachial-ankle PWV without affecting blood pressures, further studies with adequately control for confounders by including a matched control group or a sham CPAP group are warranted to provide more convincing evidence.

PWV has been demonstrated to have a close association with all-cause mortality and cardiovascular mortality in patients with hypertension, type 2 diabetes, and end-stage renal disease.[18,48,49] For example, in patients with end-stage renal disease, aortic PWV $>$ 9.4 m/s was an independent predictor of all-cause and cardiovascular mortality. In this population, relative risk of all-cause mortality was 1.39 (95% confidence interval [CI], 1.19–1.62) for each PWV increase of 1 m/s.[48] In patients with type 2 diabetes, aortic PWV independently predicted all cause and cardiovascular mortality for each 1 m/s increase (hazard ratio, 1.08; 95% CI, 1.03–1.14).[49] If these findings are applicable to the OSAHS patients in the present study, then the effect of CPAP treatment to decrease brachial-ankle PWV should have clinical significance in reducing all-cause and cardiovascular mortality.

In conclusion, we have shown that CPAP treatment substantially decreases brachial-ankle PWV in OSAHS patients without reducing blood pressures in a non-randomized and uncontrolled study. To our knowledge, this is the first report to demonstrate an association between PWV and CPAP treatment in OSAHS patients. The precise mechanism for this CPAP effect is unclear; however, this finding suggests a close relationship between OSAHS and arterial stiffness, while also reemphasizing the clinical importance of CPAP treatment.

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