ORIGINAL ARTICLE

Screening method for severe sleep-disordered breathing in hypertensive patients without daytime sleepiness

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Summary The high prevalence of sleep-disordered breathing (SDB) in hypertensive patients has been well studied. However, regular screening of SDB in these patients is not performed routinely as the diagnostic procedures are both time-consuming and labour-intensive. Overnight portable device screening is useful, but is sometimes not acceptable for asymptomatic SDB patients. We evaluated the usefulness of daytime 30-min recording with a portable recording device during pulse wave velocity (PWV) measurement sessions as a screening method for detection of asymptomatic SDB in hypertensive patients. Eighty-one hypertensive patients underwent 30-min daytime screening session using a Type III portable recording device during PWV measurement. Each screening session was followed by full overnight Level I polysomnography (PSG). The screening session included recordings of airflow (mouth—nose), chest movement, oximetry, and electrocardiography. The correlation coefficient between respiratory disturbance index (RDI) by screening session and apnea—hypopnea index (AHI) by PSG was 0.64. Using AHI ≥ 30 as diagnostic of severe SDB, 47 of 80 patients had the disorder based on PSG results. Using an RDI cut-off value of 22, the sensitivity and specificity for detection of severe SDB were

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86.1% and 64.5%, respectively. Daytime 30-min recording with a portable device for apnea detection during PWV recording is useful for screening of asymptomatic severe SDB in hypertensive patients.

Introduction

Sleep-disordered breathing (SDB) is commonly observed in patients with cardiovascular problems, especially in hypertensive patients [1]. A diagnosis of obstructive sleep apnea syndrome (OSA) is made in SDB patients with subjective symptoms including excessive daytime sleepiness. Overnight full polysomnography (PSG) is performed in such symptomatic patients to measure multiple biological parameters during sleep, and when applicable, nasal continuous positive airway pressure (nCPAP) may be prescribed. However, for a number of reasons identification and diagnosis of SDB are not routinely performed in patients with cardiovascular problems. First, standard treatment for asymptomatic SDB has yet to be established [2]. Although nCPAP treatment is effective to decrease the blood pressure in symptomatic OSA patients, it has been reported to be ineffective for asymptomatic SDB patients [3]. Second, the standard PSG, the diagnostic method for SDB/OSA, is both time-consuming and labour-intensive and requires overnight hospitalization. Due to the lack of apparent benefit, many asymptomatic patients are reluctant to undergo time-consuming PSG. Moreover, the number of institutions that perform PSG on a regular basis is limited. Recently, numerous portable recording systems have been developed for OSA screening. These systems utilize small devices with limited recording channels, and the examination does not require hospitalization but one overnight home recording [4–7]. However, screening of SDB in hypertensive patients is still difficult even utilizing such portable devices. Hypertensive patients are usually asymptomatic, and the overnight examination is still unacceptable for many patients.

On the other hand, many studies have indicated a high incidence of cardiovascular problems in SDB patients [8]. Untreated OSA patients are known to have high mortality rates [9]. The mortality in asymptomatic SDB patients has not yet been clarified, because available data for severity of SDB are largely from sleep laboratories where the patients are symptomatic. Although the standard treatment has not yet been established, severity evaluation of SDB in patients with cardiovascular problems is necessary for risk stratification. Simple methods for screening and evaluating SDB in hypertensive patients are urgently needed for their routine management. Based on the observation of frequent snoring and apnea during the 30-min sessions for pulse wave velocity (PWV) measurement reported by technicians, we propose a new method for screening of SDB. For the new screening method, we measured airflow and oxygen saturation in hypertensive patients during a 30-min rest period in a quiet room during the day. PWV measurements are commonly performed for hypertensive patients, and they will likely readily accept the additional simultaneous measurements. In the present study, we evaluated the validity of the new screening method to detect SDB and an appropriate cut-off level was suggested.

Methods

Patients receiving care for primary hypertension from the Cardiology Department of Teikyo-University Hospital were eligible for screening measurement. Patients undergoing pulse wave velocity (PWV) recording between 1 September 2004 and 30 December 2006 were asked for permission to perform the simultaneous apnea screening measurements described in the next section. Informed consent was obtained from all patients prior to enrolling in the study in accordance with the instructions of the institutional ethical committee. Each patient completed the Epworth Sleepiness Scale (ESS) to assess and quantify daytime sleepiness.

Screening session

Enrolled patients reclined on a comfortable bed for about 30 min in an ambient-quiet room prior to measurement of PWV. Brachial and ankle cuffs for PWV measurement were set during this period with the patients in the supine position. Airflow (mouth–nose), oximetry (SpO$_2$), chest movement, bronchial sound, and electrocardiogram were monitored using a type III portable recording device (FM-500; Fukuda Denshi, Tokyo, Japan) throughout the session. In accordance with the manufacturer's

instructions, the qualities of recordings were judged by airflow signal amplitude indicated on the display attached to the device. Data were analyzed with an SCM-6000 workstation (Fukuda Denshi) by semi-auto measurement and manual editing. One laboratory technician observed both the patient and the recording conditions during the session. The technician also recorded whether the patient snored for more than 10 s during the session. The snoring was confirmed by bronchial sound recording afterward. If no snoring was observed, the patients were asked whether they fell sleep during the session and their responses were recorded.

In accordance with the analysis software provided by the manufacturer of the airflow monitor, apnea and hypopnea were defined as follows. Apnea was identified when a nearly flat airflow (<10% of baseline, at which the baseline amplitude was identified during the nearest preceding period of regular breathing with stable oxygen saturation) for at least 10 s was observed. Hypopnea was identified when an airflow of approximately <70% of the baseline for at least 10 s followed by oxygen desaturation events was observed. The oxygen desaturation event was described as percentage arterial oxygen saturation (SpO_2) decrease >3% lasting more than 10 s. Apnea—hypopnea index (AHI) was defined as the number of apnea and hypopnea events per hour of sleep, and the value could not be obtained without actual sleeping time. In this screening session, we determined the respiratory disturbance index (RDI) [5]. The value was defined as the number of apnea and hypopnea events per hour of monitoring time. We recommended full PSG for all patients undergoing the screening session.

PWV measurements were performed at the end of the screening session. Bilateral brachial and ankle cuffs were used for measurement of blood pressure and pulse wave analysis (Form PWV/ABI; Colin Medical Technology, Tokyo, Japan). The systolic and diastolic blood pressures presented in this study were brachial blood pressures measured using this device.

Polysomnography

Overnight PSG was performed 4—8 weeks after the screening session at the university hospital or in an adjacent sleep laboratory. A standard examination was performed using two electroencephalogram (EEC) channels, two electrooculogram (EOG) recordings with a reference, one submental electromyogram (EMG), one electrocardiogram (ECG) lead for heart rate, and one intercostal EMG for respiratory effort. Respiration was moni-

Table 1 Patient Demographics.

|	Screening	Full PSG	p
n	289	81	
Male/female	141/148	51/30	N.S.
Age	65.7 ± 10.3	64.9 ± 9.6	N.S.
ESS	5.6 ± 3.6	6.5 ± 4.1	N.S.
BMI	25.5 ± 4.2	25.9 ± 4.3	N.S.
BP (mmHg)			
Systolic	131.3 ± 15.8	128.8 ± 15.5	N.S.
Diastolic	77.8 ± 10.6	78.1 ± 11.1	N.S

tored by recording thoracic and abdominal effort using piezoelectric sensors, and oronasal flow was determined with a thermistor. Snoring sounds were recorded using a microphone connected to an amplifier, and body position was checked by video recording. SpO_2 was detected using a finger probe oximeter. PSG paper speed was set at 10 mm/s to allow correct sleep staging. Apnea was identified by a nearly flat airflow (<10% of baseline, at which the baseline amplitude was identified during the nearest preceding period of regular breathing with stable oxygen saturation) for at least 10 s. Hypopnea was identified as airflow or thoracoabdominal excursion of approximately <70% of baseline for at least 10 s associated with either oxygen desaturation of >3% or arousal.

Evaluation of validity and determination of cut-off level

To evaluate the validity of the new screening method, its sensitivity and specificity to detect SDB with overnight PSG as the gold standard was determined at various RDI. From this, an appropriate RDI cut-off to obtain high sensitivity and acceptable specificity was proposed.

Results

Two hundred and eighty-nine patients gave their informed consent to allow the recording for screening (141 men and 148 women). Background characteristics of the patients are summarized in the left part of Table 1. Mean ESS scale was less than 7, and the majority of the patients were free from excessive daytime sleepiness. All of the patients were taking at least one anti-hypertensive drug, and blood pressure at the time of PWV recording was within the normal limit. Fig. 1 shows an example of an apnea episode in a 71-year-old female patient. Mouth—nose airflow, chest movement, and oxygen saturation curves are shown.
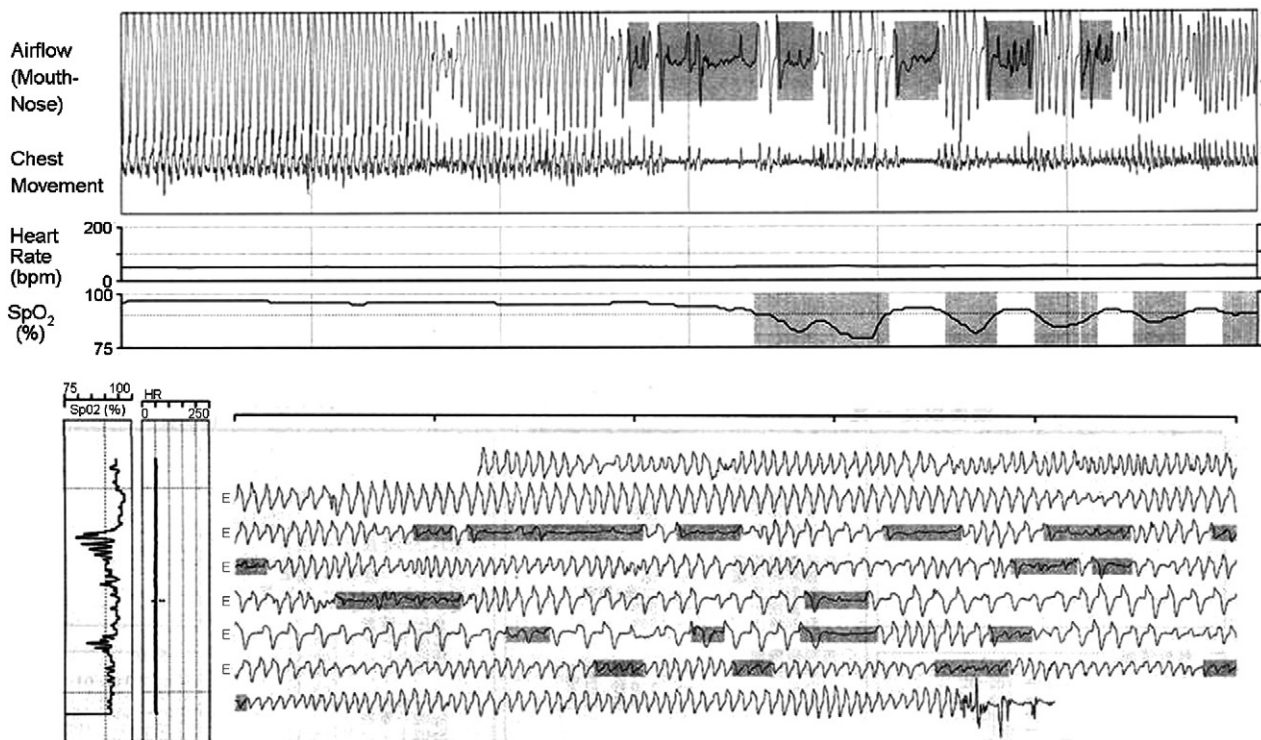
Figure 1 A representative recording of screening session in a 71-year-old female. Upper Panel: 6 min recording showing mouth—nose airflow, chest movement, heart rate, and oxygen saturation curves are shown. Gray markers denote the apnea—hypopnea events and desaturation events. Apnea episodes and subsequent desaturation (<90%) episodes were obvious. Lower Panel: entire recording showing mouth—nose airflow (right side), heart rate, and oxygen saturation curves (left side). 18 apnea—hypopnea episodes are observed.

Apnea episodes and subsequent desaturation (>3%) episodes were obvious even in the short 30-min recording session. Her ESS was 4 points and she did not realize that she had fallen asleep, but examiners noted snoring. During this recording session of 30.8 min, 16 apnea—hypopnea episodes and 5 desaturation episodes were detected. Thus, RDI was calculated to be 31.0. The average value of RDI in all patients was 13.7 ± 17.4/h. One hundred and three patients (35.6%) reported subjective sleep during the session, and snoring was noted in 144 patients (49.8%). A total of 150 patients (51.9%) showed signs of sleep. ESS was ≥ 9 in 78 patients

(27.0%), and RDI was ≥ 5 in 147 patients (51.0%). The background characteristics of these patients are also shown in Table 1.

Among the hypertensive patients who underwent the screening session, 81 (28.0%) consented to undergo full overnight PSG. Seven of these subjects were excluded from the analysis—one because they did not have hypertension and 6 for whom technical problems occurred during the screening session. These patients almost exclusively had obstructive apneas, except two cases had central components more than 10% (10.8% and 15.2%). The average of central component was $1.3 \pm 2.6\%$ of total apnea
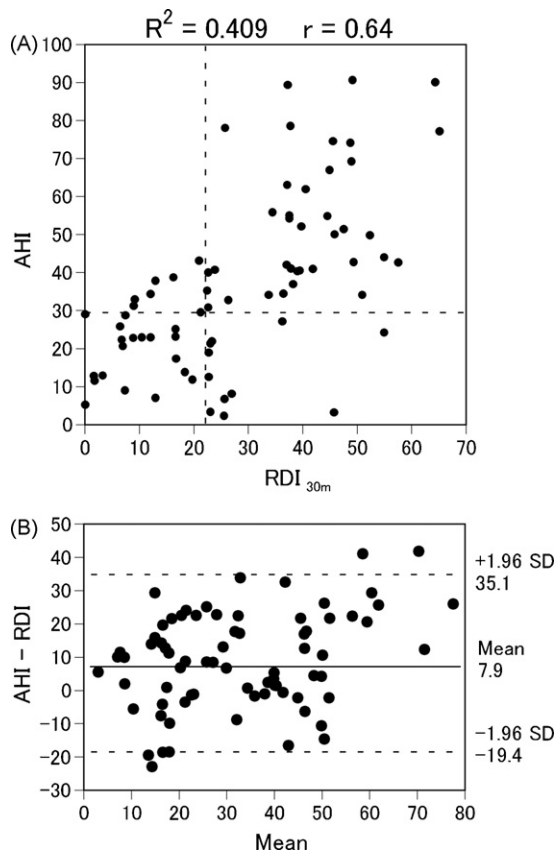
Table 2 Sensitivity and Specificity for Screening of Severe SDB.

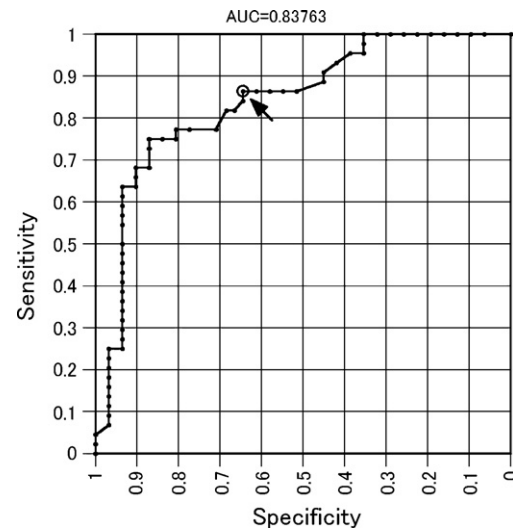| RDI Cut-off	Sensitivity% (95%CI), positive cases[a]	Specificity% (95%CI), negative cases[b]
≥ 30	72 (56—85), 31	90 (74—98), 28
≥ 25	77 (61—88), 33	81 (63—93), 25
≥ 23	79 (64—90), 34	71 (52—86), 22
≥ 22	86 (72—95), 37	65 (45—81), 20
≥ 20	88 (75—96), 38	61 (42—78), 19

[a] SDB $n = 43$ AHI ≥ 30.
[b] Non-SDB $n = 31$ AHI < 30.

Figure 2 Panel A: relationships between RDI by the new screening method and AHI by full PSG. Horizontal dashed line denotes the severe SDB level of AHI 30. Vertical dashed line denotes the proposed RDI cut off level of 22. Correlation coefficient was 0.64 ($P < 0.001$). B: Bland—Altman plot for RDI and AHI.

Figure 3 Receiver operating characteristic (ROC) curve for severe SDB screening at various RDI cut-off levels. The arrow denotes the suggested RDI cut-off level. See text and Table 2 for detail.

Discussion

As patients with cardiovascular problems have been shown to have a high prevalence of SDB [2], many physicians and cardiologists have recognized SDB and sleep apnea syndrome as major problems that promote various complications [10,11]. Although the high prevalence of SDB was reported in western countries, a similar high incidence is also observed in Japan [12,13]. Data regarding the cardiovascular risk of SDB are most convincing for hypertension [1,14]. Nonetheless, routine evaluation of SDB is not common in hypertensive patients. In the present study, we proposed a simple screening method for SDB in hypertensive patients, and evaluated its validity. The plots in Fig. 2 show a significant correlation between RDI and AHI values. Although the Bland—Altman plots showed that there was a tendency to underestimate AHI by the screening method, the performance of our screening methods were satisfactory with a high degree of sensitivity of about 86%, while maintaining moderate specificity of 65%. Another advantage of this method was that the asymptomatic patients showed good acceptance of the full PSG after actual recording of their own apnea episodes.

We used a type III portable recording device under attended conditions in this study, which was a rather heavily equipped method for SDB screening. However, the recordings can be obtained during a daytime outpatient hospital visit, and the time span for recording was limited to about 30 min. The total session could be completed in about

episodes. The characteristics of the patients who underwent PSG are summarized on the right hand side of Table 1. The RDI value in these patients was 23.9 ± 16.7%, and the value was significantly higher than that of patients who did not undergo PSG (9.2 ± 15.9%; $P < 0.01$). Fig. 2 illustrates the relationships between RDI by the new screening method and AHI by full PSG. Panel A in Fig. 2 shows that the correlation coefficient was 0.64 ($P < 0.001$). Panel B shows a Bland—Altman plot of the two parameters. The estimated mean difference was 7.9 and the S.D. was 13.9. Sensitivity and specificity for detection of severe SDB (AHI ≥ 30) at various RDI levels were estimated, and are summarized in Fig. 3 (ROC curve) and Table 2. With regard to the most appropriate combination of sensitivity and specificity, an RDI cut-off value of 22 was suggested, where sensitivity and specificity were 86.1% and 64.5%, respectively. With this cut-off value, the positive and negative predictive values were calculated as 77.1% and 76.9%, respectively.

45—60 min including preparations, which was much simpler than ordinal SDB screening with overnight recording. In a review [5] of overnight recordings, the sensitivity and specificity of the screening method with portable devices were reported to be 60—100% and 20—100%, respectively, although the values were variable depending on the device and recording situation. We consider the sensitivity of our method acceptable compared to previous reports. We do not propose use of this screening method as a replacement for full PSG. The value of PSG for evaluation of SDB patients is well established, and the necessity of PSG should be further evaluated by large-scale clinical trials. The goal of the present study was to effectively detect asymptomatic hypertensive patients with a high possibility of severe SDB, and provide suitable treatment options for these patients.

The study design described here had some limitations. Although we performed screening sessions with unselected hypertensive patients, not all patients accepted the full PSG. This may have caused some bias in case selection for PSG. The sensitivity and specificity presented in this study were those for 81 of 289 hypertensive patients. The patient demographics of all cases and in the cases that accepted the full PSG were similar with the exception of the ESS score (Table 1); ESS scores in patients who accepted the PSG study tended to be higher than that of the total patient population, although the difference was not statistically significant. These observations may contribute to the high incidence of severe SDB in the patients who consented to the full PSG study. If it had been possible to perform the full PSG study in all patients, it may have resulted in higher specificity of the screening methods by including subjects without severe SDB. However, the PSG study was not performed without the screening session. Detection of 47 patients with severe SDB in the total of 298 hypertensive patients (15.8%) would have an impact on daily clinical treatment. Thus, we concluded that daytime 30-min recording with a portable device for apnea detection during PWV recording is useful for asymptomatic severe SDB screening in hypertensive patients.

The mortality rate in moderate to severe sleep apnea syndrome is known to be high [9,10,15], and nCPAP has already been shown to have beneficial effects on long-term prognosis [16]. However, all these lines of evidence were provided by surveys performed in sleep laboratories and the patients were therefore symptomatic. Excessive daytime sleepiness has been proposed as a cause of hypertension in patients with sleep apnea syndrome [1], because it may stimulate sympathetic activity and the rennin—angiotensin—aldosterone system. Therefore, nCPAP effectively reduced the blood pressure in symptomatic OSA patients with hypertension [17]. However, nCPAP did not improve the blood pressure or subjective symptoms after 1 month in asymptomatic SDB patients [3]. A large multi-center study is currently underway to examine the outcomes after 6 months of therapy [2] to confirm the usefulness of nCPAP in asymptomatic SDB patients with hypertension. It will be necessary to await the results to determine whether we can apply nCPAP to hypertensive patients with asymptomatic SDB. An interesting finding regarding the problem in the present study was that more than half of our patients slept during the very short screening session despite their lack of daytime sleepiness. Although subjective sleepiness assessed by ESS score was almost absent in our patients, the results suggested many hypertensive patients were unaware of their own sleepiness. In the patients undergoing full PSG, 47 cases (58%) had severe SDB (AHI >30). Although the ESS scores in these patients were not high as shown in Table 1, we could not determine whether these patients were truly asymptomatic. The effectiveness and compliance of nCPAP therapy in these patients should be examined in future studies.

Acknowledgment

References

[1] Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Leiby BE, Vela-Bueno A, et al. Association of hypertension and sleep-disordered breathing. Arch Intern Med 2000;160: 2289—95.

[2] Pack AI. Advances in sleep-disordered breathing. Am J Respir Crit Care Med 2006;173:7—15.

[3] Barbe F, Mayoralas LR, Duran J, Masa JF, Maimo A, Montserrat JM, et al. Treatment with continuous positive airway pressure is not effective in patients with sleep apnea but no daytime sleepiness. a randomized, controlled trial. Ann Intern Med 2001;134:1015—23.

[4] Ficker JH, Wiest GH, Wilpert J, Fuchs FS, Hahn EG. Evaluation of a portable recording device (Somnocheck) for use in patients with suspected obstructive sleep apnoea. Respiration 2001;68:307—12.

[5] Flemons WW, Littner MR, Rowley JA, Gay P, Anderson WM, Hudgel DW, et al. Home diagnosis of sleep apnea: a systematic review of the literature. An evidence review cosponsored by the American Academy of Sleep Medicine, the American College of Chest Physicians, and the American Thoracic Society. Chest 2003;124:1543—79.

[6] Man GC, Kang BV. Validation of a portable sleep apnea monitoring device. Chest 1995;108:388—93.

[7] Williams AJ, Yu G, Santiago S, Stein M. Screening for sleep apnea using pulse oximetry and a clinical score. Chest 1991;100:631—5.

[8] Baguet JP, Narkiewicz K, Mallion JM. Update on hypertension management: obstructive sleep apnea and hypertension. J Hypertens 2006;24:205—8.

[9] He J, Kryger MH, Zorick FJ, Conway W, Roth T. Mortality and apnea index in obstructive sleep apnea. Experience in 385 male patients. Chest 1988;94:9—14.

[10] Caples SM, Gami AS, Somers VK. Obstructive sleep apnea. Ann Intern Med 2005;142:187—97.

[11] Takama N, Kurabayashi M. Possibility of close relationship between sleep disorder breathing and acute coronary syndrome. J Cardiol 2007;49:171—7.

[12] Tanigawa T, Horie S, Sakurai S, Iso H. Screening for sleep-disordered breathing at workplaces. Ind Health 2005;43:53—7.

[13] Hida W, Shindoh C, Okabe S, Miki H, Kikuchi Y, Taguchi O, et al. Prevalence of sleep apnea syndrome in Japanese industrial workers using a home sleep monitor. Sleep 1993;16(8 Suppl.):S126—7.

[14] Javier Nieto F, Young TB, Lind BK, Shahar E, Samet JM, Redline S, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. JAMA 2000;283: 1829—36.

[15] Teramoto S, Ohga E, Ouchi Y. Obstructive sleep apnoea. Lancet 1999;354:1213—4.

[16] Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea—hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet 2005;365:1046—53.

[17] Becker HF, Jerrentrup A, Ploch T, Grote L, Penzel T, Sullivan CE, et al. Effect of nasal continuous positive airway pressure treatment on blood pressure in patients with obstructive sleep apnea. Circulation 2003;107:68—73.