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# Nocturnal Blood Pressure Variability in Patients with Obstructive Sleep Apnea Syndrome

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**Abstract**

Obstructive sleep apnea (OSA) is a common respiratory disorder associated with hypertension and cardiovascular complications. Blood pressure variability may be a sign of risk of cardiovascular events. The aim of this study was to investigate the hypothesis that severe OSA syndrome is associated with increased blood pressure variability. Based on respiratory polygraphy, 58 patients were categorized into two groups: severe OSA with apnea/hypopnea index (AHI) greater than 29 episodes per hour (mean 52.2 ± 19.0/h) and mild-to-moderate OSA with AHI between 5 and 30 episodes per hour (mean 20.2 ± 7.8/h). A 24-h noninvasive blood pressure monitoring was performed. The standard deviation of mean blood pressure was used as the indicator of blood pressure variability. In patients with severe, compared with mild-to-moderate OSA, a higher mean nocturnal systolic blood pressure (133.2 ± 17.4 mmHg *vs.* 117.7 ± 31.2 mmHg, $p < 0.05$) and diastolic blood pressure (80.9 ± 13.1 mmHg *vs.* 73.8 ± 9.2, $p < 0.01$), nocturnal systolic blood pressure variability (12.1 ± 6.0 *vs.* 7.6 ± 4.3, $p < 0.01$) and diastolic blood pressure variability (10.5 ± 6.1 *vs.* 7.3 ± 4.0 $p < 0.05$), nocturnal mean blood pressure variability (9.1 ± 4.9 mmHg *vs.* 6.8 ± 3.5 mmHg) were detected. The findings of the study point to increased nocturnal systolic and diastolic arterial blood pressure and blood pressure variability as risk factors of cardiovascular complications in patients with severe OSA.

**Keywords**

Apnea/hypopnea index • Arterial blood pressure • Arterial oxygen saturation • Hypertension • Obstructive sleep apnea • Cardiovascular risk factor • Sleep disordered breathing

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## 1 Introduction

Obstructive sleep apnea (OSA) is a common sleep disorder characterized by a collapse of upper airways in the setting of continued respiratory effort, leading to cessation of airflow, large swings in intrathoracic pressure, and arterial oxygen desaturation, often terminated by an arousal.

OSA has been independently associated with cardiovascular diseases, such as hypertension (Peppard et al. 2000), stroke (Munoz et al. 2006), myocardial ischemia (Peled et al. 1999), and arrhythmias (Mehra et al. 2006), which all increases risk for sudden cardiac death. OSA and hypertension, in turn, have common risk factors such as age, obesity, and sedentary lifestyle. OSA syndrome is found in about 50 % of patients with hypertension (Pedrosa et al. 2011) and in 70 % of patients with resistant hypertension (Florczak et al. 2013). There are some data indicating that OSA is associated with hypertension independent of age and obesity (Pankow et al. 1997). The pathogenesis of systemic arterial hypertension in the course of OSA is complex and not fully explained. The most important factor seems hypoxia observed during or immediately after apneic or hypopneic incidents underlying OSA. Sympathetic excitation, expressed by increased catecholamine level and chemoreceptor alterations, caused by intermittent hypoxia has been suggested as a hypertension promoting factor (Fung et al. 2014; Freet et al. 2013). Other pathogenic factors leading to hypertension in OSA patients include systemic inflammation and endothelial dysfunction (Chen et al. 2015).

Hypertension is the most common risk factor for cardiovascular disease and the single most important risk factor for stroke (Roger et al. 2012). Traditionally, cardiovascular risk in hypertension has been attributed to the mean blood pressure load (Taylor et al. 2015). However, inherent variability of an individual's blood pressure may also be contributory (Rothwell 2010). Systemic arterial blood pressure undergoes marked variations during day and night (Mancia 2012). Blood pressure variability (BPV) is influenced by multiple factors, including neural dysregulation due to age, diabetes, or neuropathies, vascular, humoral, and central nervous system disorders, and mental and environmental stress (Kai et al. 2014). Association between BPV and organ damage (Matsui et al. 2011), cardiovascular events (Johansson et al. 2012), stroke (Shimbo et al. 2012), and mortality (Muntner et al. 2011) have been described. However, some other studies have failed to substantiate such associations or found the BPV of lesser importance than the actual level of blood pressure (Schutte et al. 2012).

Taking into account that OSA is accompanied by autonomic cardiovascular dysregulation which may be related to the frequency of obstructive apneic and hypopneic episodes and to increased sympathetic excitation, we hypothesized that BPV could be associated with the severity of OSA. In the present study we addresses this issue by examining BPV in the patients with mild-to-moderate and severe OSA during a 24-h period.

## 2 Methods

The study was approved by the Bioethics Committee of the Medical University in Wroclaw, Poland and was conducted according to the principles set in the Declaration of Helsinki for Human Research. Fifty eight patients, with newly diagnosed OSA syndrome, of the mean age of 54.3 ± 10.3 years and the mean body mass index (BMI) of 37.8 ± 6.7 kg/m$^2$ were enrolled into the study. Thirty one (53 %) of the patients were on antihypertensive treatment. Based on the severity of OSA, patients were categorized into two groups: severe OSA with AHI ≥30/h (35 men, 5 women) and mild-to-moderate OSA with AHI between 5 and 30/h (4 men, 14 women). All patients underwent in-hospital, nocturnal polygraphic examination at the Department of Pulmonology and Lung Cancer of Medical University in Wroclaw. The following parameters were recorded during sleep: thoracic and abdominal respiratory

movements, oro-nasal airflow, and arterial oxygen saturation ($SaO_2$) with finger pulsoximetry. Abnormal respiratory events: apneas, hypopneas, and episodes of desaturations were evaluated according to the standard criteria of the American Academy of Sleep Medicine Task Force (Berry et al. 2012). The following parameters were calculated: apnea/hypopnea index (AHI) – mean number of apneic and hypopneic episodes per hour of sleep, oxygen desaturation index (ODI) – mean number of arterial oxygen desaturations per hour of sleep, and the mean of the minimal values of $SaO_2$ at the end of apneic and hypopneic episodes.

During the day following the polygraphic examination, arterial blood (BP) pressure was monitored noninvasively, using the oscillometric method, along with pulse rate. Readings were obtained every 30 min during diurnal (6:00 a.m. to 10:00 p.m.) and every 60 min during nocturnal (10:00 p.m. to 6:00 a.m.). The BP data were calculated as means of total systolic (TSBP) and total diastolic blood pressure (TDBP) collected over the 24-h period, and separately as diurnal mean BP (DMBP), diurnal systolic (DSBP), diurnal diastolic BP (DDBP) and nocturnal mean BP (NMBP), nocturnal systolic (NSBP), nocturnal diastolic BP (NDBP). Based on the mean standard deviations (SD) of the data above listed, BP variability was calculated: total systolic BP variability (TSBPV), total diastolic BP variability (TDBPV), diurnal systolic BP variability (DSBPV), diurnal diastolic BP variability (DDBPV), nocturnal systolic BP variability (NSBPV), nocturnal diastolic BP variability (NDBPV), total mean BP variability (TMBPV), diurnal mean BP variability (DMBPV), and nocturnal mean BP variability (NMBPV). The thresholds for increases in blood pressure were taken as those set by the European Society of Hypertension/European Society of Cardiology 2013 criteria (Kjeldsen et al. 2013). Nocturnal BP changes were classified as follows: deep fall if a drop was greater than 10 % of the diurnal baseline, mild fall if a drop was between 0 and 10 % off the diurnal baseline level, and a rise if BP went over the diurnal baseline.

Data were presented as means ± SD. Distribution of variables was tested with the Shapiro-Wilk test. Inter-group data with normal distribution were statistically compared with a *t*-test, and those with skewed distribution were compared with the Mann-Whitney *U* test. Relationship between variables was estimated with the Spearman correlation coefficient. Significance of differences was considered at $p < 0.05$. Statistical analysis was performed using Statistica 6.0 software (StatSoft, Tulsa, OK).

## 3 Results

There were no significant differences in the anthropometric characteristics of patients with severe and milder OSA. The main OSA characteristics such as AHI, ODI, and $SaO_2$ dips during breathless episodes were clearly intensified in the group of patients with severe OSA compared with those in milder OSA. However, due to a large scatter of individual data, the man values did not differ statistically between the two groups (Table 1).

The mean values of TSBP, TDBP, DSBP, and DDBP were similar in both groups of OSA patients. However, NSBP and NDBP were significantly higher in the severe OSA than those in the milder OSA patients (Table 2). The mean nocturnal falls in systolic and diastolic BP were between 0 and 10 % off the diurnal baseline levels in the severe OSA. These BP falls were greater than 10 % in the milder OSA.

Blood pressure variability, assessed from the magnitude of the standard deviation of the mean value, was significantly greater for the mean, systolic, and diastolic blood pressure during nighttime in the severe OSA than those in the milder OSA patients (Table 3). Positive linear correlations were found between AHI, on the one side, and NSBPV ($r = 0.57$, $p < 0.05$), TDBPV ($r = 0.58$, $p < 0.05$), and DDBPV ($r = 0.70$, $p < 0.05$), on the other side.

**Table 1** Anthropometric and polygraphic features of obstructive sleep apnea (OSA) patients

| | Severe OSA (n = 40) | Mild-to-moderate OSA (n = 18) | |
|---|---|---|---|
| Age (yr) | 53.9 ± 10.1 | 57.2 ± 12.3 | ns |
| Weight (kg) | 112.1 ± 17.8 | 110.0 ± 26.5 | ns |
| BMI (kg/m$^2$) | 38.3 ± 6.2 | 35.6 ± 5.7 | ns |
| AHI (per h) | 52.2 ± 19.2 | 20.2 ± 7.8 | ns |
| ODI (per hour) | 52.7 ± 18.1 | 22.3 ± 9.3 | ns |
| $SaO_2$ at the end of sleep apneas/hypopneas (%) | 83.7 ± 4.9 | 88.9 ± 3.2 | ns |

Data are means ± SD. *BMI* body mass index, *AHI* apnea/hypopnea index, *ODI* oxygen desaturation index, *ns* nonsignificant

**Table 2** Diurnal, nocturnal, and day blood pressure changes in severe and milder forms of obstructive sleep apnea (OSA)

| | Severe OSA | Mild-to-moderate OSA | p |
|---|---|---|---|
| TSBP | 137.0 ± 14.0 | 133.1 ± 1.9 | ns |
| TDBP | 86. 8 ± 11.5 | 83. 3 ± 10.3 | ns |
| DSBP | 136.6 ± 13.8 | 135.3 ± 13.7 | ns |
| DDBP | 87.8 ± 10.5 | 85. 3 ± 11.6 | ns |
| NSBP | 133.3 ± 17.4 | 117. 7 ± 31.2 | <0.01 |
| NDBP | 80.9 ± 13.2 | 73. 8 ± 9.2 | <0.05 |

All data are presented as mmHg and are means ± SD. *TSBP* total (over the 24-h period) systolic blood pressure, *TDBP* total diastolic blood pressure, *DSBP* diurnal systolic blood pressure, *DDBP* diurnal diastolic blood pressure, *NSBP* nocturnal systolic blood pressure, *NDBP* nocturnal diastolic blood pressure, *ns* nonsignificant

## 4 Discussion

The major finding of the present study is that nocturnal blood pressure variability was significantly greater in patients suffering from severe OSA, with the AHI over 29 episodes per hour of sleep, than that in milder forms of OSA. The potentially confounding factors such as age, weight, or BMI were similar in both groups of patients and thus may be excluded as the underlying reason of blood pressure variability, acting via increased sympathetic drive (Charkoudian and Rabbits 2009). There are a number of methods to assess blood pressure variability, such as based on the coefficient of variation, weighted standard deviation (mean of diurnal and nocturnal standard deviation values of blood pressure measurements weighted for the number of hours covered by these two periods during ambulatory monitoring), average real variability, or the difference between maximum and minimum blood pressure levels. In the present study we assessed blood pressure variability on the basis of the standard deviation of the mean values of the amplitude of blood pressure measured. This method is regarded as a good index of apnea-related blood pressure elevations (Planès et al. 2002). Our finding of increased nocturnal blood pressure variability in severe OSA is, generally, in line with that of Steinhorst et al. (2014), although those authors investigated clearly hypertensive OSA patients. Planès et al. (2002) have also shown that systemic hypertension is associated with increased short-term blood pressure variability during sleep in OSA patients.

The present study also unraveled some distortions in the day profile of arterial blood pressure in severe OSA consisting of the lack of a physiological decrease in blood pressure at night. Four categories of nocturnal blood pressure changes are considered: extreme dippers (a fall in blood pressure of more than 20 % compared with diurnal level), dippers (a fall greater than 10 % but less than 20 %), non-dippers (a fall less than 10 %), and reverse dippers, i.e., risers (blood pressure increases at night). Non-dipping pattern in the 24-h blood pressure monitoring has been largely described in patients with OSA syndrome (Loredo et al. 2001; Suzuki et al. 1996); the finding attributable to autonomic dysfunction. In addition, we also found that nocturnal systolic and diastolic blood pressure were higher in patients with severe OSA (AHI ≥30 episodes per hour) compared with those present in milder forms of OSA. Changes in the circadian rhythm of blood

**Table 3** Blood pressure variability (BPV) assessed from the magnitude of standard deviation of the mean value in patients with severe and mild-to-moderate OSA syndrome

| | Severe OSA | Mild-to-moderate OSA | p |
|---|---|---|---|
| TSBPV | 14.8 ± 3.7 | 16.1 ± 5.5 | ns |
| TDBPV | 12.2 ± 3.3 | 12.3 ± 3.8 | ns |
| TMBPV | 11.8 ± 2.8 | 12.8 ± 4.0 | ns |
| DSBPV | 13.9 ± 4.2 | 15.5 ± 5.7 | ns |
| DDBPV | 11.0 ± 3.7 | 11.2 ± 4.0 | ns |
| DMBPV | 10.9 ± 3.1 | 3.1 ± 4.5 | ns |
| NSBPV | 12.1 ± 6.0 | 7.6 ± 4.3 | <0.01 |
| NDBPV | 10.5 ± 6.1 | 7.3 ± 4.0 | <0.05 |
| NMBPV | 9.1 ± 4.9 | 6.8 ± 3.5 | <0.05 |

All data are presented as mmHg and are means ± SD. *TSBPV* total (over the 24-h period) systolic blood pressure variability, *TDBPV* total diastolic blood pressure variability, *DSBPV* diurnal systolic blood pressure variability, *DDBPV* diurnal diastolic blood pressure variability, *NSBPV* nocturnal systolic blood pressure variability, *NDBPV* nocturnal diastolic blood pressure variability, *TMBPV* total mean blood pressure variability, *DMBPV* diurnal mean blood pressure variability, *NMBPV* nocturnal mean blood pressure variability, *ns* nonsignificant

pressure have been described by Noda et al. (1993) who show that the severity of OSA has an impact on nocturnal blood pressure elevation. Lavie et al. (1993) have also shown that blood pressure during sleep significantly correlates with the apnea/hypopnea index.

The observed changes in blood pressure variability, impaired 24-h blood pressure profile and a greater nocturnal blood pressure, in patients with severe OSA give rise to cardiovascular complications. The lack of nocturnal dipping in blood pressure has been related to more pronounced target organ damage (Verdecchia et al. 1993) and increased risk of cardiovascular events (Parati and Valentini 2006). Moreover, findings of the International Database of Ambulatory Blood Pressure in Relation to Cardiovascular Outcome (IDACO) have revealed that the night-to-day blood pressure ratio predicts both cardiovascular and non-cardiovascular mortality (Boggia et al. 2007). Sympathetic neural activity is increased in both OSA, even during the awake state, and hypertension. Sympathetic activation in patients with hypertension is associated with increases in cardiovascular risk and in end-organ damage (Mancia et al. 1999). The present study has some practical applications. The measurement of blood pressure performed once daily, or even several times a day, is clearly insufficient to determine the presence of nocturnal hypertension, the effectiveness of antihypertensive treatment, and the cardiovascular risk in OSA patients. In addition, assessment of blood pressure variability, based on the 24-h monitoring, enables to determine cardiovascular risk independently of the absolute values of blood pressure. The findings of the study indicate that in patients with severe OSA there are two important risk factors of cardiovascular complications occurring during sleep, i.e., increased nocturnal systolic and diastolic blood pressure as well as increased nocturnal blood pressure variability.

**Conflicts of Interest** The authors declare no conflicts of interest in relation to this article.

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