Influence of Sleep Apnea on 24-Hour Blood Pressure*

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**Objective:** To study the influence of obstructive sleep apnea (OSA) on 24-h BP.

**Setting:** Sleep laboratory of the Medical Department, Neukölln Hospital, Berlin, Germany.

**Methods:** In 93 subjects, noninvasive 24-h BP monitoring was performed with BP recordings made at 15-min intervals. Apnea severity was evaluated by means of a portable device that allows calculation of an oxygen desaturation index (ODI). A normal 24-h BP profile (dipping) was defined by a night/day BP ratio of 0.9.

**Results:** ODI was related to systolic and diastolic daytime (p<0.001) and nighttime BP (p<0.001) as well as systolic and diastolic BP night/day ratios (p<0.001). Multiple regression analysis showed that age and ODI were independently related to daytime BP. When subjects were grouped according to apnea severity, daytime BP increased as ODI increased: 127/80±10/11 mm Hg in habitual snorers (ODI 0 to 5), 135/87±15/9 mm Hg in mild OSA (ODI 6 to 30), and 140/90±13/10 mm Hg in severe OSA (ODI >30) (p values <0.05 for comparisons of OSA groups with habitual snorers). Compared to subjects with mild OSA or habitual snorers, BP night/day ratios were greater in patients with severe OSA (p values <0.05). Accordingly, hypertension and nondipping increased as ODI increased.

**Conclusion:** OSA is associated with hypertension independent of the confounding factors of age and obesity. Nondipping is related to apnea severity. These alterations might contribute to the increased mortality in patients with severe OSA. (CHEST 1997; 112:1253-58)

**Key words:** ambulatory BP monitoring; hypertension; obesity; obstructive sleep apnea; snoring

**Abbreviations:** BMI=body mass index; ODI=oxygen desaturation index; OSA=obstructive sleep apnea; PSG=polysonomography

Several epidemiologic studies have shown that the prevalence of arterial hypertension is elevated in snorers.1-3 Snoring is a frequent symptom of obstructive sleep apnea (OSA).4 Since the association between hypertension and OSA is well known,5-8 a direct relationship between snoring alone and hypertension has been questioned.9 Accordingly, the increased prevalence of arterial hypertension in snorers might reflect an increased proportion of OSA. However, patients with OSA and snoring are often overweight, a condition that is also known to be associated with arterial hypertension. The controversial question as to whether OSA constitutes an independent risk factor in the development of high BP is the subject of much debate in the literature.9-14 Most studies addressing this problem have so far been based on occasional BP measurements or on invasive measurements of BP in small populations. Using noninvasive 24-h BP monitoring, it is now possible to examine large populations. With this method, the question of a disturbance of circadian BP rhythm may also be addressed; the presence of a disturbed circadian BP profile might be a further risk factor with regard to cardiovascular sequelae.13-17 It has been shown that OSA carries an increased risk of cardiovascular disease18 and an increased mortality.19,20 The few published studies on 24-h BP profiles in patients with OSA report elevated BP during wakefulness and sleep21 and disturbances of the circadian BP rhythm—namely an absence of or a reduced drop in nocturnal BP.22-25 However, studies so far were performed on either a limited number of patients22-25 or on selected patient groups with either mild21 or severe OSA.26

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Thus, the aim of our study was to measure 24-h BP in a large, unselected sample of 238 snorers who were investigated for OSA in our sleep laboratory over a period of 19 months. This study aimed to detect the influence of OSA on 24-h BP profile, independent of obesity and age.

**Materials and Methods**

**Patients**

From September 1991 until March 1993, 238 patients were referred to our institution for suspected sleep-disordered breathing. The main complaint in the group of the habitual snorers (see below) was the noise that disturbed the spouse. The patients with OSA mainly reported about irregular loud snoring with apneas observed by the spouse and about excessive daytime sleepiness. Patients were assigned to a waiting list according to the date of referral and every alternate patient on the list was asked to participate in a research protocol on sleep-disordered breathing and BP. Ten patients were receiving antihypertensive medication. Any patient who was taking antihypertensive medication was asked to discontinue treatment 3 days prior to the clinical visit, if this was clinically safe and after consultation with the patient’s personal physician. No patient was receiving sedatives or muscle relaxants. There were no shift workers in our population. From 119 subjects (9 women) thus selected for the study, 13 subjects were excluded (12 because of continued intake of antihypertensive medication, 1 because of presence of untreated hypothyroidism). Another 13 subjects had to be excluded owing to failure of BP and/or sleep-monitoring equipment. The mean age and body mass index (BMI) of these 26 patients were not significantly different from those of the total sample. Thus, the data for 93 subjects (8 women) were analyzed.

**Measurements**

**Blood Pressure:** On the first day after hospital admission, noninvasive 24-h BP monitoring was performed on all patients (using the SL 90207 recorder; SpaceLabs GmbH; Kaarst, Germany). Two BP cuffs of different size in relation to the upper arm circumference were selected: a smaller one appropriate to 24- to 32-cm arm circumference and a larger one appropriate to 32- to 42-cm arm circumference. Systolic and diastolic arterial BP was determined by the oscillometric method, with one measurement made every 15 min during the 24-h period. The daytime period was defined as the interval between 6 AM and 10 PM and the nighttime period as between 10 PM and 6 AM. Before the BP measurements began, three manually released test measurements were done, which were then compared with a simultaneous measurement using a sphygmomanometer on the other arm. If the difference was >5 mm Hg, the arm cuff’s fit was corrected, and further test measurements were carried out. For the evaluation of the 24-h BP profile, an average of 77 (range, 48 to 96) single measurements was analyzed.

**Sleep Studies:** Patients took part in the usual clinic activities and were allowed to move freely in the hospital area during the daytime period. After 10 PM, bed rest was requested. During their first night of the stay in hospital, an evaluation of sleep-disordered breathing was performed using a portable recording device (MESAM 4; Madius, Gundelfingen, Germany). This device allows recording of heart rate, body position, breathing sounds, and arterial oxygen saturation (pulse oximetry) and gives an oxygen desaturation index (ODI) with a specificity and sensitivity >90% compared to polysomnography (PSG).

**Other Measurements:** BMI was calculated by dividing body weight (in kilograms) by the square of height (in meters). Subjects were classified into nonobese (BMI <27 kg/m²) and obese (BMI ≥27 kg/m²). A limit of 45 years was used to divide the population into a younger (<45 years) and older (≥45 years) group.

**Analysis**

Statistical analysis was performed to evaluate the relationship among daytime BP, nighttime BP and the BP night/day ratio, sleep apnea severity (ODI), obesity (BMI), and age. The ODI obtained with the portable monitoring device was used to define the severity of OSA. A lower limit of ODI of five events per hour was considered to differentiate between habitual snorers and subjects with OSA. A ODI of >30/h was regarded as indicating more severe OSA. Our cases were thus divided into three groups: group A, 20 subjects with an ODI of 0 to 5/h (habitual snorers); group B, 35 subjects with an ODI of 6 to 30/h (mild OSA); and group C, 38 subjects with an ODI ≥30/h (moderate to severe OSA). To define hypertension, we used a lower limit of 140/90 mm Hg daytime BP obtained with 24-h BP measurements—as in a recently published proposal. This approach was chosen to avoid the possible problem of the white coat effect occurring in the clinical setting. A minimum drop of 10% systolic and diastolic mean BP at night was regarded as characteristic of a normal 24-h BP profile (dipping). Accordingly, a BP night/day ratio >0.9 was used to characterize patients as nondippers.

Data were analyzed using statistical software (Statgraphics; STSC; Rockville, Md) for descriptive statistics, analysis of variance, multiple regression analysis, and correlation analysis. To determine significant differences between groups, Student’s t test was used. A p value <0.05 was considered to be significant.

**Results**

Ninety-three (87 men) patients were investigated. Anthropometric data grouped to OSA severity are specified in Table 1. The mean ODI was 26/h (±21 SD, range 0 to 71/h). For the studied population of 93 subjects, there were significant correlations between ODI and age (r=0.31, p=0.002) and ODI and BMI (r=0.37, p<0.001). Fifty-one patients (55%) were hypertensive and 42 patients (45%) were found to be normotensive according to 24-h BP criteria.

**Daytime BP**

The severity of OSA (ODI) was positively related to systolic and diastolic daytime BP (r=0.42, p<0.001 and r=0.40, p<0.001, respectively). Significant correlations were also found between age and systolic/diastolic BP (r=0.38, p<0.001 and r=0.29, p=0.005, respectively) and between body weight (BMI) and systolic/diastolic BP (r=0.26, p=0.013 and r=0.26, p=0.011, respectively). BP was significantly higher among subjects with mild OSA and subjects with moderate to severe OSA compared with habitual snorers (Table 1). Differences in daytime BP of groups selected for age, BMI, and ODI
Table 1—Characteristics and BP Data of Subjects Grouped by Apnea Severity*

<table>
<thead>
<tr>
<th></th>
<th>Habitual Snorers (ODI 0-5)</th>
<th>Mild OSA (ODI 6-30)</th>
<th>Moderate to Severe OSA (ODI&gt;30)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No.</td>
<td>20</td>
<td>35</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Sex, female/male</td>
<td>2/18</td>
<td>3/32</td>
<td>3/35</td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>45 (8)</td>
<td>52 (10)</td>
<td>53 (7)</td>
<td>&lt;0.005†</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28 (4)</td>
<td>29 (4)</td>
<td>32 (5)</td>
<td>&lt;0.005†</td>
</tr>
<tr>
<td>BP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daytime BP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>127 (10)</td>
<td>135 (15)</td>
<td>140 (13)</td>
<td>&lt;0.005†</td>
</tr>
<tr>
<td>Diastolic</td>
<td>80 (11)</td>
<td>87 (9)</td>
<td>90 (10)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Nighttime BP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>113 (11)</td>
<td>120 (17)</td>
<td>134 (15)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Diastolic</td>
<td>69 (11)</td>
<td>75 (10)</td>
<td>84 (12)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>BP night/day quotient</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>0.89 (0.05)</td>
<td>0.88 (0.06)</td>
<td>0.96 (0.05)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Diastolic</td>
<td>0.86 (0.07)</td>
<td>0.86 (0.06)</td>
<td>0.93 (0.08)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day</td>
<td>75 (10)</td>
<td>78 (11)</td>
<td>81 (9)</td>
<td>&lt;0.05†</td>
</tr>
<tr>
<td>Night</td>
<td>63 (8)</td>
<td>66 (9)</td>
<td>69 (8)</td>
<td></td>
</tr>
<tr>
<td>ODI, events/h</td>
<td>2 (1)</td>
<td>15 (7)</td>
<td>48 (11)</td>
<td></td>
</tr>
</tbody>
</table>

*Values are mean (SD).
†Comparison between habitual snorers and those with mild OSA.
‡Comparison between habitual snorers and those with moderate to severe OSA.
§Comparison between those with mild OSA and those with moderate to severe OSA.

Figure 1. Mean daytime BP in subjects without and with obesity (BMI <27 kg/m² and ≥27 kg/m², left), younger and older subjects (age <45 and ≥45 years, center), and with different apnea severity (right): habitual snorers (ODI 0 to 5/h), mild OSA (ODI 6 to 30/h), and moderate to severe OSA (ODI >30/h). Graphs show means of systolic and diastolic BP obtained by noninvasive 24-h BP measurements. Significant differences are given for covariant analysis.

In the group of hypertensives compared to the normotensives (ODI 33±4 [SD]/h vs 16±4 [SD]/h, p<0.0001). Matching the two groups for age and BMI still revealed a significantly higher ODI in the hypertensives (p<0.0001).

Nocturnal BP

Compared to daytime BP, there was an even stronger correlation between OSA severity (ODI) and systolic/diastolic nocturnal BP (r=0.58, p<0.001 in the group of hypertensives compared to the normotensives (ODI 33±4 [SD]/h vs 16±4 [SD]/h, p<0.0001). Matching the two groups for age and BMI still revealed a significantly higher ODI in the hypertensives (p<0.0001).

Figure 2. Prevalence (percentage of total number in each group) of hypertension and nondipping in different subgroups according to apnea severity. Hypertension was defined as a mean daytime BP ≥140/90 mm Hg, obtained by noninvasive 24-h BP measurement. Nondippers were defined by a <10% decline of nighttime (10 PM to 6 AM) systolic and diastolic BP compared to daytime (6 AM to 10 PM) BP.
and \( r=0.55, p<0.001 \), respectively. Again, positive correlations were also found between age and systolic/diastolic BP \( (r=0.43, p<0.001 \) and \( r=0.32, p=0.002 \), respectively) and between BMI and systolic/diastolic BP \( (r=0.25, p=0.014 \) and \( r=0.25, p=0.016 \), respectively). BP was significantly higher among subjects with mild OSA or subjects with moderate to severe OSA compared with habitual snorers (Table 1).

**BP Night/Day Quotient**

Significant positive correlations were found between ODI and systolic/diastolic BP night/day ratios \( (r=0.55, p<0.001 \) and \( r=0.50, p<0.001 \), respectively). Age was weakly related to systolic/diastolic BP night/day ratios \( (r=0.31, p=0.003 \) and \( r=0.23, p=0.029 \), respectively), while there was no significant positive correlation of BMI and BP night/day ratios. Figure 3 shows the group differences between BP night/day quotients: systolic and diastolic BP night/day ratios were higher in subjects with moderate to severe OSA compared to those with mild OSA and habitual snorers. No significant differences were observed between older and younger subjects and between groups of different BMIs. However, the percentage of nondippers was higher in those with moderate to severe OSA compared with mild OSA and habitual snorers (Fig 2).

**Multiple Regression Analysis**

Multiple regression analysis controlling for age and BMI showed that apnea severity (ODI) was independently related to systolic and diastolic daytime BP and to systolic and diastolic night/day quotient (Table 2). The model including all three variables, however, explained only 24% of systolic daytime BP and 18% of diastolic BP, but 30% of systolic and 23% of diastolic BP night/day quotient. To evaluate the relationship between BP and apnea severity while controlling for age and BMI also, partial correlation analysis was performed. This procedure identified significant independent relationships between ODI and systolic daytime BP \( (r=0.27, p<0.001 \) and between ODI and diastolic daytime BP \( (r=0.26, p<0.001 \) after linear relationships with the two other variables (age and BMI) were removed.

**Discussion**

This study presents two main findings: (1) BP is related to apnea severity, independent of the confounding factors of obesity and age; and (2) with increasing apnea severity, the physiologic nocturnal BP decline is reduced.

Our data thus confirm and extend results of earlier investigations that have found an astonishingly high comorbidity of OSA and hypertension.1,6,13,17,33 Sleep apnea activity, BMI, and age all contributed to BP. A recent investigation using casual BP measurement has shown similar results.34 With 24-h BP monitoring, we were able to obtain more reproducible values because the so-called “white coat effect” of casual BP measurement was avoided.31 While the prevalence of hypertension in the group of habitual snorers roughly corresponded to that seen in the general population,11 hypertension was twice as prevalent in subjects with mild OSA and three times as prevalent in those with moderate to severe OSA. The strength of our study lies in the fact that we used 24-h BP monitoring in a large number of subjects with a wide spectrum of sleep-related breathing disorders, ranging from habitual snoring to severe sleep apnea. Former studies have been performed either on a much smaller number of subjects,22,24,25 or on selected subjects with either mild OSA,31 or relatively severe disease.26

Our study is limited by using a portable monitor (MESAM) to measure apnea severity instead of performing full PSG. However, the portable monitor we used is a well-validated tool of measuring sleep-disordered breathing that correlates extremely well with the PSG results. Because for our study we found it most important to include a large number of patients, we had to use a simple recording device because of limited capacity of our sleep laboratory to perform PSG. We think that the large number of patients we were able to measure outweighs this disadvantage by far. Our results might have been affected by the short washout time for antihypertensive medication (3 days) that we had to use in order
to avoid a longer period in which the patient’s BP was not monitored. The prevalence of hypertension could thus have been underestimated, indicating that comorbidity of OSA and hypertension might even be higher than suggested by our data. A clear limitation of most previous studies, including our own, is that they were performed in a selected population of patients from a sleep laboratory. In line with our findings, however, a recent cross-sectional study using 24-h BP measurement has confirmed an independent association of sleep apnea and hypertension.21

Because there is considerable evidence now that 24-h BP monitoring is superior to occasional BP measurement in predicting cardiovascular morbidity,30 our results may contribute to explaining the increased morbidity and mortality in OSA.18,19 Evidence has also been presented that a reduced drop of nocturnal BP (nondipping) is associated with stroke16 and left ventricular hypertrophy15 independent of daytime BP. In this respect, our finding of a high percentage of nondippers in moderate to severe apnea is of special importance.

We found a clear tendency toward a reduced nocturnal BP drop with increasing apnea severity. Previous publications on 24-h BP profile in OSA subjects have produced conflicting data. Two studies are in concordance with our results, demonstrating a reduced nocturnal BP drop when subjects were compared with nonapneic individuals.22,24 In two further studies, the 24-h BP profile was not as severely disturbed as our data have suggested.21,26 By investigating subjects with less severe sleep apnea, Hla and coworkers21 might have missed nondippers, because, as our data indicate, nondipping is mainly found in subjects with moderate to severe OSA. However, in the second investigation cited,26 OSA was even more severe than in our sample. One possible explanation for the discrepant results might be different daytime activities of the examined patients, since the daytime BP values in our study are considerably lower. Our patients were hospitalized during the BP measurement, although they were told to be physically active during the daytime. The patients of the above-mentioned study were investigated outside the hospital and were presumably more active. Physical activity certainly has an important, although only modulating, influence on the 24-hour BP profile.35 Our finding of a disturbed 24-hour BP profile in subjects with moderate to severe OSA seems to be valid despite the BP recordings being made in hospital, as similar changes were not seen in habitual snorers (ie, ODI ≤5), who were studied under the same conditions.

While the pathogenesis of sustained elevation of daytime BP in sleep apnea patients is poorly understood,36 a close association of apneic events and cyclic BP elevations during sleep has been observed since the early days of sleep apnea research.37 Mechanical effects on the cardiac output induced by obstructive apnea, hypoxic vasoconstriction, and arousal-related sympathoadrenergic activation have been hypothesized as being equally responsible.36 Strong evidence that sleep apnea may be an etiologic factor in hypertension comes from studies that show a decline in daytime BP38 and 24-h BP,39-41 once OSA is effectively treated.

In conclusion, our data suggest that in addition to the already well-established risk factors, OSA is independently associated with increased BP. The likelihood that the normal physiologic nocturnal BP decline is prevented also increases. This may contribute to the increased mortality in sleep apnea, because attenuated nocturnal dipping is an independent risk factor for cardiovascular morbidity.

### ADDENDUM

After submission, a study on the influence of sleep apnea on circadian BP was published: Suzuki M, Guilleminault C, Otsuka K, et al. Blood pressure, ‘dipping’ and ‘non-dipping’ in obstructive sleep apnea syndrome patients. Sleep 1996; 19:382-87. The finding of an increased prevalence of nondipping of nocturnal BP in OSA patients is in agreement with results of the present investigation.
REFERENCES


13 Stradling JR, Crosby JH. Relation between systemic hypertension and sleep hypoxemia or snoring: analysis in 745 men drawn from general practice. BMJ 1990; 300:75-80


40 Suzuki M, Otsuka K, Guilleminault C. Long-term nasal continuous positive airway pressure administration can normalize hypertension in obstructive sleep apnea patients. Sleep 1993; 16:545-49