Diastolic Blood Pressure Is the First to Rise in Association With Early Subclinical Obstructive Sleep Apnea: Lessons From Periodic Examination Screening

Yehonatan Sharabi, Alon Scope, Natasha Chorney, Itamar Grotto, and Yaron Dagan

Background: Obstructive sleep apnea syndrome (OSAS) is associated with long-term cardiovascular morbidity. Little is known about these relations at early stages. We conducted a case-control study in which we analyzed the clinical characteristics of young adults who underwent a periodic health examination and were screened for, and eventually found to experience, OSAS.

Methods: We identified 121 subjects newly diagnosed in a sleep study as having OSAS, and 229 matched control subjects in which screening for OSAS was negative. All had a medical interview, physical examination, and routine laboratory tests.

Results: Subjects who had OSAS had a higher body mass index (3-kg/m² difference) and a higher diastolic blood pressure (4-mm Hg difference) value, without elevation in systolic blood pressure. There was no metabolic difference (lipids profile and fasting glucose levels) between groups.


Key Words: Obstructive sleep apnea, blood pressure, screening, periodic examination.
fasting for 14 h for blood sugar level, lipid profile, and a complete blood count. Systolic and diastolic blood pressure (SBP and DBP, respectively) were taken at rest and in a sitting position using a sphygmomanometer. A complete physical examination including height (cm) and weight (kg) were performed, and a resting 12-lead electrocardiogram was obtained at that time. In addition, subjects underwent chest x-ray and spirometry. Results were recorded and computerized to establish the Young Adults Periodic Examination database.9

The questionnaire included queries adopted from the Berlin Questionnaire. The Questionnaire was an outcome of the Conference on Sleep in Primary Care, held in 1996 in Berlin, Germany.10 Questions were selected from the literature to elicit factors or behaviors that, across studies, consistently predicted the presence of sleep apnea syndromes. The questionnaire consists of questions concerning snoring, daytime sleepiness, and history of hypertension and sleepiness while driving. Questions about restless sleeping, morning headaches, fatigue, morning tiredness, and difficulties in falling asleep were also included. This questionnaire was found to be of value in identifying subjects at risk for having OSAS, showing a sensitivity of 86%, specificity of 77%, and positive predictive value of 89%.10,11 A physician who reviewed the answers of the questionnaire with the subject and validated the results and the scores, based on the patient’s responses, made the identification of patients at high risk. If the score was high, the subject was then referred for a complete sleep study.

The sleep study was performed in an experienced center and interpreted by an expert in sleep disturbances. Polysomnography included the following channels: electroencephalography × 4, electrooculography, submental electromyography, snoring, oral and nasal airflow, chest and abdominal respiration movements, body position, electrocardiography, pulse oximetry, and tibialis electromyography. The polysomnography was scored according to Rechtschaffen and Kales.12 Sleep apnea was diagnosed according to the International Classification of Sleep Disorders.13 The control group comprised apparently healthy subjects of the same age and sex, who underwent the same periodic examination and whose screening tests ruled out OSAS. All parameters, ie, medical history, physical examination, and laboratory tests were taken under the same environmental conditions and by the same medical personnel. Parameters of the study population are expressed as mean ± standard deviation. For comparison between the study group values, we used the Student t test. For comparison of result frequencies, we used the χ² test. A P value < .05 was considered significant.

### Results

Of the subjects who completed the sleep studies, we identified 121 subjects who were diagnosed as having OSAS. The control group was comprised of 229 subjects, matched by age and sex.

Table 1 depicts baseline characteristics, along with physical, hemodynamic, and metabolic parameters of the OSAS and control groups. The two groups were well matched for age and sex. They also had similar cigarette smoking and alcohol consumption rates. The data show that subjects who experience OSAS are generally more obese, as indicated by an 8.5-kg weight difference and a 3-kg/m² difference in BMI. Also, OSAS is associated with

### Table 1. Baseline characteristics of the obstructive sleep apnea syndrome group and control group

<table>
<thead>
<tr>
<th></th>
<th>OSAS Group (N = 121)</th>
<th>Control Group (N = 229)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>38.6 ± 5.5</td>
<td>38.9 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>Male/Female ratio</td>
<td>118/3</td>
<td>223/6</td>
<td>NS</td>
</tr>
<tr>
<td>Cigarettes smokers</td>
<td>30%</td>
<td>31%</td>
<td>NS</td>
</tr>
<tr>
<td>Past smokers</td>
<td>21%</td>
<td>20%</td>
<td>NS</td>
</tr>
<tr>
<td>Habitual alcohol consumers</td>
<td>5.5%</td>
<td>6.5%</td>
<td>NS</td>
</tr>
<tr>
<td>Physical parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>175 ± 6.6</td>
<td>176 ± 7</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>90.6 ± 17.7</td>
<td>82.1 ± 14.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.5 ± 5.3</td>
<td>26.5 ± 4.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>121 ± 12</td>
<td>120 ± 13</td>
<td>NS</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>81 ± 11</td>
<td>77 ± 10</td>
<td>0.04</td>
</tr>
<tr>
<td>Pulse rate at rest (beats/min)</td>
<td>76 ± 15</td>
<td>75 ± 15</td>
<td>NS</td>
</tr>
<tr>
<td>Metabolic parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>204 ± 33</td>
<td>205 ± 39</td>
<td>NS</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>45 ± 16</td>
<td>45 ± 11</td>
<td>NS</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>126 ± 29</td>
<td>128 ± 37</td>
<td>NS</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>170 ± 98</td>
<td>154 ± 109</td>
<td>NS</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>14.8 ± 1.2</td>
<td>15.0 ± 1.0</td>
<td>NS</td>
</tr>
</tbody>
</table>

OSAS = obstructive sleep apnea syndrome; NS = nonsignificant; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

Data are either average ± SD or percentage of the study group.
a higher DBP value, without elevation in SBP. As for the metabolic aspect, neither a clinically nor a statistically significant difference was observed between the two groups. In addition, subjects underwent chest x-ray, spirometry, and baseline electrocardiography. There was no difference between OSAS and the control groups in the rate or type of abnormal findings in these examinations.

Discussion

The IDF maintains a PHEC for the purpose of disease prevention and identification. All personnel, typically between the ages of 25 to 45 years, are periodically screened. This creates a unique database representative of the health status of a relatively young Israeli population. In the previous decade, the health impact of OSAS has been increasingly recognized. This is a prevalent disease that independently increases the incidence of other cardiovascular risk factors and disease. Recognition of this morbid condition by family physicians is low. To improve detection of OSAS, we have incorporated queries, adopted from the Berlin Questionnaire, that identify subjects at risk for OSAS. In this study, we have focused on patients with newly diagnosed OSAS. The patients were identified only after screening. During the previous periodic examination 3 to 5 years earlier, screening for OSAS was negative. All patients were identified as having OSAS for the first time in the PHEC. None were previously treated. Accordingly, we can point out factors associated with relatively short duration of the disease. Our data show that only body mass index (BMI) and DBP were significantly higher among the OSAS patients compared to the matched control group.

It has been reported that OSAS correlates with the degree of obesity and weight gain. As mentioned, the average BMI in our study group was 29.5 kg/m², which was significantly higher than the control group BMI of 26.5 kg/m². Both values are in the overweight category, but the OSAS is in the upper range of overweight.

In both men and women, OSAS is independently associated with hypertension. The relationship is proportional to the severity of OSAS and is strongest in young subjects. OSAS patients in our study had significantly higher mean DBP than controls, although within the normal range ($81 \pm 77$ mm Hg). There was no significant difference in SBP values between the groups. Typically, these patients do not show night dipping of BP. In another case-control study of 24-h ambulatory BP monitoring of patients with OSAS, there was significant daytime and nocturnal increase in DBP but only a nocturnal increase in SBP. Our BP measurements were taken only at daytime, therefore not demonstrating possible nocturnal high SBP.

At night, patients experience repetitive episodic hypoxemia during sleep, with consequent sympathetic activation. The BP decreases during an apneic event, followed by an abrupt increase in the recovery period. The BP response is related to the magnitude of the postevent ventilatory overshoot, length of the event, magnitude of changes in heart rate and arterial $O_2$ saturation, and presence of arousal. It was suggested that peripheral chemoreceptor hyperactivity makes a significant contribution by causing increased sympathetic activation. Both OSAS and associated obesity that is common among OSAS patients induce sympathetic activation, which results in chronically elevated catecholamines that eventually affects the DBP. In addition, OSAS patients have impaired arterial endothelium dependent vasodilation, with blunted vasodilatory response to acetylcholine (a vasodilator that stimulates endothelial release of nitric oxide). In our study, there was no significant difference in fasting blood glucose and lipid profile between the study and control group. The mean lipid profile of the OSAS group was within normal values. The study that reported increased total cholesterol levels in sleep apnea patients evaluated older subjects.

As a PHEC, we are also concerned with recommendations of interventions that may lead to risk reduction of the long-term effects of OSAS. Management of OSAS includes weight reduction, physical activity increase, and tobacco avoidance, in addition to direct therapy such as continuous positive airway pressure and palate surgeries. To the majority of our patients, continuous positive airway pressure was recommended, in addition to lifestyle modification as well as ear–nose–throat counseling and treatment. The therapeutic strategies to treat the OSAS were shown to be beneficial for the associated hypertension. Concerning antihypertensive therapy, $\beta$-blockers were found to be the best option, which is in accordance with the sympathetic activation caused by the OSAS.

In summary, we have demonstrated that, compared to matched control subjects, individuals who experienced OSAS at a relatively early stage, were more obese, and also had higher DBP without elevation in SBP, and before other metabolic consequences. Recognizing and treating the OSAS would prevent BP elevation that seems to be affected early in the course of the disease. Our study is a retrospective case-control that aims only at identifying clinical characteristics of patients OSAS of short duration. Further longitudinal studies are required for identification of the long term effects of OSAS, as well as effects of early recognition and medical intervention.

References


