The Relationship Between Esophageal Pressure and Apnea Hypopnea Index in Obstructive Sleep Apnea-Hypopnea Syndrome


*Department of Clinical Neuroscience, Psychiatry, Osaka University Graduate School of Medicine, Osaka, Japan

Severity of negative esophageal pressure (Pes) and apnea hypopnea index (AHI) were investigated in 34 patients with obstructive sleep apnea-hypopnea syndrome (OSAHS). The OSAHS patients were diagnostically classified as having obstructive sleep apnea syndrome (OSAS) or upper airway resistance syndrome (UARS). Diagnosis of OSAS was based on an AHI of more than 5, and that of UARS on an AHI of less than 5, EEG arousals which were associated with apnea, hypopnea and/or respiratory effort occurring more than 10 times per hour, and daytime sleepiness. Negative Pes was represented by the greatest peak (NPes Max) and the number of increased (more than 13.5 cmH₂O) episodes per hour (NPesI13.5). There was no significant correlation between the AHI and Pes indices, but NPes Max and NPesI13.5 showed significant correlation (p<0.01). NPes Max and NPesI13.5 showed no significant differences among the severe OSAS (AHI>50; 8 cases), moderate OSAS (50>AHI>15; 10 cases), mild OSAS (15>AHI>5; 9 cases) and UARS (7 cases) groups. We conclude that AHI does not reflect the severity of the increase in negative Pes, which is an important aspect of the pathophysiology of OSAHS. Assessment of OSAHS based on AHI alone may therefore underestimate the risk of increased negative Pes in cases with reduced AHI.

CURRENT CLAIM: AHI does not reflect the severity of increased negative intrathoracic pressure in OSAHS including UARS.

Obstructive sleep apnea syndrome (OSAS) is characterized by repetitive episodes of upper airway obstruction that occur during sleep (American Sleep Disorders Association, 1990). A complete or partial obstruction manifests itself as an apnea or a hypopnea. As hypopneas lead to the same clinical consequences as apneas lead, the apnea hypopnea index (AHI) is widely used as a diagnostic criterion and for the assessment of the severity of OSAS (American Academy of Sleep Medicine Task Force, 1999).

Recently, it has been recognized that electroencephalographic arousals (EEG arousals) can be caused by respiratory efforts against upper airway resistance even in the absence of an apnea or hypopnea, and that these could lead to daytime sleepiness (upper airway resistance syndrome; UARS) (Guilleminault et al., 1993, Exar and Collop, 1999). The EEG arousals accompanying non-apneic respiratory efforts are commonly observed in mild cases of OSAS, and there is evidence that these arousals exacerbate daytime sleepiness (Mikami et al., 1999; Fietze et al., 1999). The American Academy of Sleep Medicine (AASM) Task Force proposed that these EEG arousals be defined as respiratory effort-related arousals (RERA) and recommended the use of the term "obstructive sleep apnea-hypopnea syndrome (OSAHS)" which includes UARS (AASM Task Force, 1999).

In the pathophysiology of OSAS, increases in negative intrathoracic pressure caused by respiratory efforts against complete or partial upper airway obstruction during an apnea or hypopnea are considered to be very important (Redline and Strohl, 1998). Negative intrathoracic pressure encourages venous return to the right ventricle, increases afterload on the left ventricle, causes ventricular hypertrophy (Berman et al., 1991; Salejee et al., 1993), and results in congestive heart failure. Moreover, a significant drop in blood pressure, which is called pulsus paradoxus (Shiomi et al., 1991, 1993), can be caused by a drop of the intrathoracic pressure which is then followed by a significant overshoot accompanied with arousal response. These fluctuations in blood pressure are considered to play a role in the pathogenesis of hypertension (Morgan et al., 1998), and are likely to be harmful to the blood vessels and may raise the mortality of OSAS. These hypotheses seem to be applicable to the patients with UARS because they present increased intrathoracic pressure and frequent arousals, although the patients have few apneas, hypopneas and desaturations. In spite of its importance in pathophysiology, esophageal pressure (Pes) measurement, which has generally been considered to be an accurate method for the detection and quantification of respiratory efforts and intrathoracic pressure, is not so easily included in routine polysomnography (PSG).
As the severity of OSAS is usually assessed in terms of the AHI, UARS is easily overlooked. Furthermore, the relationship between the AHI and the variables associated with an increase in negative Pes has not yet been clarified, so certain important questions remain unanswered. For example, does a higher AHI for OSAHS indicate a severe increase in the negative Pes? From the viewpoint of negative intrathoracic pressure, do patients with UARS have a lower risk of complications than those with OSAS?

To find answers to such questions, we performed all-night PSG, including Pes measurements, for the diagnosis and assessment of OSAS and UARS. The results and data were then analyzed to investigate the relationship between AHI and increases in negative Pes in cases with OSAS and UARS.

**METHODS**

**Subjects**

The subjects were 34 patients with OSAHS including UARS (31 males and 3 females; mean age: 48.7±2.1 years. Mean BMI: 26.8±0.6 kg/m²).

All of the PSGs, including all-night Pes monitoring, were performed at Osaka University Hospital between February 5, 1997 and February 5, 1999. Electroencephalography (C3-A2, C4-A1, 01-A2, 02-A1), electrooculography (horizontal and vertical) and electromyography (bilateral submental and anterior tibial muscles) were performed, while oro-nasal airflow was monitored with a three-pointed thermistor, thoraco-abdominal movements with strain gauges, snoring with a piezo crystal sensor and oxygen saturation with a finger pulse oximeter. Pes swings were also monitored. For Pes measurement, a balloon catheter (TU-101U, Nihon Kohden) was placed in the lower third of the esophagus. The catheter was connected to a pressure transducer (TP-604T, Nihon Kohden), and its signal enhanced with an amplifier (AR-601G, Nihon Kohden). All measures were recorded on paper and an FM data recorder (XR-7000 and XR-7000L, TEAC). Sleep stages were scored in each 10-second epoch according to standard methods (Rechtschaffen et al., 1968).

**Definitions of Respiratory Disturbances, EEG Arousals and Pes Indices**

An apnea is defined as a cessation of airflow and a hypopnea as a more than 50% reduction in the amplitude of the airflow. These events must last at least 10 seconds. The apnea hypopnea index (AHI) is defined as the total number of apneas and hypopneas per hour of sleep.

EEG arousals which met the criteria of the American Sleep Disorders Association (1992) were scored. An EEG arousal, which is associated with an apnea, a hypopnea and/or a respiratory effort indicated by increases in negative Pes, is defined as a breathing-related arousal (B-Ar). The breathing-related arousal index (B-ArI) is defined as the number of B-Ars per hour of sleep.

The severity of the increase in negative Pes was represented by two indices, NPes Max and negative Pes of more than 13.5 cmH₂O (NPesI13.5). The nadir Pes was expressed as NPes Max (cmH₂O). The increase in negative intrathoracic pressure was defined as a drop in the Pes nadir of more than 13.5 cmH₂O, because a drop in Pes of more than 13.5 cmH₂O could cause pulsus paradoxus (Shiomi et al., 1993). The NPesI13.5 is expressed as the number of drops in Pes of more than 13.5 cmH₂O per hour of sleep.

**Data Analysis**

The correlation coefficients among AHI, NPes Max and NPesI13.5 were calculated with StatView-J 4.11 (Macintosh). The comparisons among the four groups, i.e., severe OSAS, moderate OSAS, mild OSAS and UARS, in terms of age, BMI, AHI, NPes Max and NPesI13.5, were analyzed using the Kruskal-Wallis test in conjunction with StatView-J 4.11.

**RESULTS**

The mean AHI, NPes Max and NPesI13.5 of our subjects were 30.6±4.6/hour, 30.8±1.9 cmH₂O, and 236.8±53.1/hour, respectively. Three cases in the moderate OSAS group and one case in the severe OSAS group were excluded from NPes Max measurements because their maximum values were beyond the range (40 cmH₂O) of the recorder. Mean B-ArI for the UARS group was 21.9. There was no significant correlation between AHI and Pes indices. Only NPes Max and NPesI13.5 showed significant correlation (correlation coefficient: 0.862; p<0.01) (Figure 1). The severe OSAS group included eight cases, the moderate OSAS group included ten, the mild OSAS group included nine, and the UARS group included seven. There were no significant differences in age or body mass index among the four groups. The AHI for all groups was significantly different. Neither NPes Max nor NPesI13.5 showed a significant difference among the four groups (Table 1).

**Table 1. Mean Age, BMI, AHI, NPes Max and NPesI13.5 of the Mild OSAS, Moderate OSAS, Severe OSAS and UARS Patients**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Severe OSAS</th>
<th>Moderate OSAS</th>
<th>Mild OSAS</th>
<th>UARS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.4±7.0</td>
<td>27.2±0.8</td>
<td>26.6±1.7</td>
<td>26.0±1.8</td>
</tr>
<tr>
<td>AHI</td>
<td>71.3±3.7</td>
<td>34.4±2.8</td>
<td>12.2±0.6</td>
<td>2.2±0.6</td>
</tr>
<tr>
<td>NPes Max (cmH₂O)</td>
<td>35.6±6.5</td>
<td>31.3±2.7</td>
<td>28.4±2.6</td>
<td>28.6±2.7</td>
</tr>
<tr>
<td>NPesI13.5</td>
<td>350.5±172</td>
<td>289.6±91.4</td>
<td>104.8±31.8</td>
<td>201.1±94.2</td>
</tr>
</tbody>
</table>

BMI: Body Mass Index; AHI: Apnea Hypopnea Index; NPes Max: nadir Pes; NPesI13.5: negative Pes of more than 13.5 cmH₂O index.
In this study, the AHI did not reflect the severity of the increase in negative intrathoracic pressure. The AHI did not correlate with Pes indices, and neither the maximum value (NPes Max) nor the frequency (NPesI13.5) of the increase in negative Pes showed significant differences among severe OSAS, moderate OSAS, mild OSAS and UARS. Loube et al. (1999) compared OSAS and UARS in terms of mean Pes nadir for each 30-second epoch and reported that they were not significantly different for the two groups. These findings suggest that severity criteria based on the AHI fail to reflect one important aspect of the pathophysiology of OSAHS. The pathogenesis of OSAHS is very complicated and far from fully understood, but repeated increases in negative intrathoracic pressure have been considered to be one of the most likely candidates for the cause of cardiovascular complications in OSAHS (Berman et al., 1991; Guilleminault et al., 1996; Morgan et al., 1998; Exar and Collop, 1999). The patients with a lower AHI, even UARS patients are at the same level of risk for cardiovascular complications as patients with a higher AHI, at least from the viewpoint of increased negative intrathoracic pressure.

We defined NPesI13.5 differently from maximum value (NPes Max) because repeated episodes of increased negative Pes showed not only a progressive increase pattern but also a long-lasting pattern without apnea or hypopnea. This pattern was termed the UARS pattern (F pattern) by Mikami et al. (1998). This non-apneic, long-lasting pattern of Pes increase was often observed in both the UARS and the mild OSAS groups and resulted in increased NPesI13.5 values for the cases with a lower AHI. NPes Max and NPesI13.5 showed significant correlation in this study. This result may suggest that these two indices, which were thought to be independent, are actually closely related. Be that as it may, there is no absolute level of Pes that is known to be abnormal (AASM Task Force, 1999). Further studies are therefore needed to clarify the consequences and establish a definition of an abnormal level of increase in negative intrathoracic pressure.

Until now, AHI has been the only accepted indicator for assessing the severity of obstructive sleep disordered breathing. However, this study has shown that assessment of the severity of sleep disordered breathing requires measurements of Pes rather than of the AHI. Recently, the AASM Task Force proposed a new definition of obstructed breathing events, which was not adopted for the current study. This new definition includes any combination of obstructive apneas/hypopneas or RERA, so that the definition of OSAHS allows for the inclusion of UARS. However, it causes confusion when the severity of OSAHS is assessed in terms of these obstructed breathing events. As Pes measurements, which are indispensable for scoring RERA, are not routinely included in the standard PSG, there could be some confusion between "obstructed breathing events which do not include RERA" (=AHI) and "obstructed breathing events which
include RERA" (=AHI+RERA). Of course, RERA needs verification as an indicator of severity, and this is why we used "obstructed breathing events which do not include RERA" for the current study. This study showed the limitations of the severity assessment of OSAHS based only on AHI, and that this issue warrants further attention both in clinical and research fields.

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REFERENCES