Analysis of Inspiratory Flow Shapes in Patients With Partial Upper-Airway Obstruction During Sleep*

Tero Aittokallio, MSc; Tarja Saarensranta, MD; Päivi Polo-Kantola, MD, PhD; Olli Nevalainen, MSc, PhD; and Olli Polo, MD, PhD

Study objective: To study the spectrum of inspiratory flow signal shapes in patients with partial upper airway obstruction during sleep.

Design: We identified seven different inspiratory flow shapes and determined their frequencies in two groups of patients (10 postmenopausal women and 19 men after surgical treatment for sleep apnea) and in 9 control subjects.

Setting: Sleep research unit, Department of Physiology, University of Turku, Finland.

Measurements and results: Nasal flow was recorded with nasal prongs. The shape analyses were performed with an automated attribute grammar recognizer. The inspiratory flow-shape distributions differed significantly between patients and control subjects. The flow shapes were also different between postmenopausal women and men after uvulopalatopharyngoplasty.

Conclusions: The differences in the inspiratory flow-shape distributions between the control subjects and the two patient groups suggest that the upper airways behave differently in the three study groups. Automated inspiratory flow-shape analysis seems to be a promising tool to distinguish patient groups with different upper airway function to be treated with different treatment alternatives. The physiologic correlates of each flow-shape class remain to be elucidated.

(CHEST 2001; 119:37–44)

Key words: flow limitation; menopause; obstructive sleep apnea syndrome; pattern recognition; snoring; uvulopalatopharyngoplasty

Abbreviations: AI = apnea index; BMI = body mass index; CPAP = continuous positive airway pressure; FI = flattening index; HSD = honest significant difference; OSAS = obstructive sleep apnea syndrome; REM = rapid eye movement; UPPP = uvulopalatopharyngoplasty

The sleep state is characterized by decreased muscle tone of postural muscles. In all individuals, decreased muscle tone in the upper airway during sleep leads to increased upper airway resistance and relative hypoventilation, which is normally counteracted by increasing respiratory activity of the diaphragm and by recruitment of the upper airway dilatory muscles during inspiration (phasic activity). Nonsnorers compensate the decreased tone effect already at a relatively low respiratory drive, whereas heavy snorers may need to maintain markedly increased respiratory drive to overcome the increased upper airway resistance and severe obstructive hypoventilation during sleep. In patients with obstructive sleep apnea syndrome (OSAS), the upper airways fail to maintain upper airway patency during sleep. The upper airway does not open until arousal restores the postural muscle tone.

Conventionally, the severity of the OSAS is defined in terms of the apnea/hypopnea index, which is based on monitoring variations in respiratory efforts with thoracoabdominal strain gauges and semiquantitative changes in the airflow with orobuccal thermistors. Measurement of the esophageal pressure is regarded as the reference method for monitoring increased respiratory effort during partial upper airway obstruction. Only a few methods are available to monitor the behavior of the collapsible part of the upper airway during sleep. The critical pressure1 and the upper airway closing pressure2 are measures of

*From the Turku Centre for Computer Science (Mr. Aittokallio); the Department of Mathematical Sciences (Dr. Nevalainen), University of Turku; the Department of Pulmonary Diseases and Clinical Allergology (Dr. Saarensranta), Turku University Central Hospital; the Department of Obstetrics and Gynecology (Dr. Polo-Kantola), Turku University Central Hospital; and Department of Physiology (Dr. Polo), University of Turku, Turku, Finland.

Manuscript received February 16, 2000; revision accepted July 10, 2000.

Correspondence to: Tero Aittokallio, MSc, Turku Centre for Computer Science, Lemminkäinenkatu 14 A, 20520 Turku, Finland; e-mail: tero.aittokallio@cs.utu.fi
the upper airway collapsibility in static conditions, where the upper airway blocks the airflow completely. Monitoring the phasic activity of the upper airway dilator muscles with an electromyogram provides information about the drive but not their effect on the flow kinetics.

Previous studies\textsuperscript{3,4} reflect the increasing interest in using nasal prongs for monitoring upper airway flow limitation on a breath-by-breath basis. The validity of this signal is demonstrated by the fact that changes in the inspiratory flow shapes have been successfully used to control the continuous positive airway pressure (CPAP) device to provide the optimal therapeutic airway pressure during sleep.\textsuperscript{5} Although much of the previous work\textsuperscript{6–9} has concentrated on demonstration of the presence or absence of flow limitation, it seems that the inspiratory flow shape could also provide information on upper airway behavior throughout the inspiratory cycle, in a similar fashion as the flow-volume loops do in the lung function test.

During inspiration, the upper airway is submitted to at least three forces that affect its patency during inspiration. These are (1) phasic activity of the dilator muscles (activation at or prior to the onset of inspiration, activity profile muscle specific), (2) negative airway pressure (maximum effect at midinspiration with peak flow), and (3) tracheal traction support\textsuperscript{10,11} (maximum effect at end-inspiration with high lung volumes). We presume that action of these different forces results in specific changes in the inspiratory flow shape and that the type and severity of upper airway dysfunction can be specified by analyzing the shape changes. Our hypothesis was that well-defined subgroups could be differentiated with inspiratory flow-shape analysis. Accordingly, we first screened the inspiratory flow shapes from all-night sleep recordings in heavy snorers and patients with sleep apnea and classified them into seven categories. We then developed an automated classifier, the necessary tool to allow flow-shape analysis in representative patient populations.\textsuperscript{12} The aim of the present study was to evaluate the usefulness of this tool by quantifying the nocturnal inspiratory flow shapes in well-defined patient populations as well as in control subjects.

### Materials and Methods

#### Subjects

Analysis of the inspiratory flow shapes is of particular interest in subjects who have relatively few episodes of obstructive sleep apnea but present with prolonged episodes of obstructive hypventilation during sleep. Therefore, we chose two well-defined patient groups in whom partial upper airway obstruction is known to occur frequently during sleep\textsuperscript{13,14} but whose upper-airway structure and function were likely to differ.\textsuperscript{15,16} These were 10 postmenopausal women (referred to as female patients) and 19 men (male patients) with OSAS treated with uvulopalatopharyngoplasty (UPPP). Significant partial upper airway obstruction during sleep had previously been demonstrated in all patients by earlier sleep studies. The nine healthy young men, who were recruited as control subjects, experienced their first sleep study during the present study protocol.

The characteristics of the three study groups are shown in Table 1. The female patients were postmenopausal, nonsmoking, generally healthy obese women who had previously volunteered for estrogen replacement therapy and sleep study, and who had demonstrated significant partial upper airway obstruction during sleep. All male patients had had UPPP for sleep apnea but presented with clinically significant residual obstruction in postoperative control. The control subjects were normal weight, nonsmoking, nonsnoring, asymptomatic men without breathing abnormalities during sleep. Two of them used inhaled corticosteroids for mild asthma. Both asthmatic subjects were asymptomatic during the study period.

Written informed consents were obtained from patients, and the control subjects gave oral informed consents. The Joint Commission on Ethics of Turku University and Turku University Central Hospital approved protocols.

#### Diagnostic Measurements

In all patients and control subjects, body movements and respiratory effort were monitored during sleep with a static-charged sensitive bed (Bio-Matt; Biorec; Helsinki, Finland).\textsuperscript{17} The all-night respiratory monitoring also included continuous arterial oxyhemoglobin saturation using a finger probe (Biox 3700; Datex-Ohmeda; Helsinki, Finland), transthoracic heart pressure of oxygen and carbon dioxide (TINA; Radiometer; Copenhagen, Denmark), and partial end-tidal carbon dioxide pressure (Normocap; Datex-Ohmeda). The airflow signal was measured with nasal prongs (Hudson RCI; Temecula, CA) connected to a pressure transducer inside a CPAP device (Sullivan Autoset; Resmed; Sydney, Australia), which was run in a diagnostic mode. Biosignals were recorded and saved on a personal computer hard disk using UniPlot software (Unesta; Turku, Finland). The female patients also underwent a standard polygraphic sleep study, including continuous recordings of EEG, electro-oculogram, chin electromyogram, and ECG.

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**Table 1—Characteristics of the Three Study Groups**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Characteristics</th>
<th>Age, yr</th>
<th>BMI, kg/m(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control subjects</td>
<td>9 young healthy men</td>
<td>26.0 ± 2.9</td>
<td>22.7 ± 3.0</td>
</tr>
<tr>
<td>Male patients</td>
<td>19 men with OSAS and treated with UPPP</td>
<td>49.9 ± 8.0</td>
<td>27.5 ± 3.8</td>
</tr>
<tr>
<td>Female patients</td>
<td>10 postmenopausal women with partial upper airway obstruction</td>
<td>60.1 ± 4.9</td>
<td>30.8 ± 3.7</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD.*

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Clinical Investigations
The apnea index (AI) and flattening index (FI) were automatically determined using the Sullivan AutoSet device. FI is calculated by the AutoSet software to determine the degree of flow limitation and the need to adjust nasal CPAP. The exact formula has not been made public by the manufacturer, but a low FI corresponds to more severe flow limitation. Value 0.15 is the critical threshold value of FI, below which flow limitation becomes significant. In the diagnostic mode with nasal prongs, the percentage of time with FI < 0.15 was used as an indicator of the severity of flow limitation. Episodes of arterial oxyhemoglobin desaturation of four percentage units or more were determined by UniPlot software. The diagnostic indexes of the subjects are shown in Table 2.

**Flow Signal Measurements**

Inspiratory flow signals were evaluated on a breath-by-breath basis with the attribute grammar recognizer. The pressure signal from the nasal prongs was digitized at a sampling frequency of 250 Hz and with amplitude resolution of 12 bits throughout the sleep study. Since the essential parts of the flow signal have relatively low frequency, the high-frequency fluctuations were considered as noise and were removed using a low-pass filter with a 2.5-Hz cutoff frequency. Each inspiratory flow shape was then extracted from the filtered signal using a prespecified baseline level and area threshold value. After that, the flow shape was partitioned into segments of successive points for which the approximation of the first derivative preserves the same sign. Each segment was encoded to a primitive, which describes either an increasing, decreasing or flat signal part. The recognition of the flow shape was performed by testing the membership of the string of primitives in the attribute grammars constructed for the shape classes. The attributed finite state automata were used in the parsing phase in which the flow shape was classified into one of the seven classes shown in Figure 1. At the same time as the method classifies the flow shape, it measures also certain parameters of the current respiratory cycle, eg. the maximum slope of the initial part of inspiratory flow signal (first segment) and the area of the inspiratory signal. Mouth breathing was identified by observing prolonged episodes of absent nasal airflow. We defined that the subject was breathing through the mouth if the latency from the last expiration to the next inspiration was > 90 s.

The algorithm reported the recording time, the length of the mouth breathing phases, and the number of respiratory cycles. Inspiratory area and slope values of each subject were calculated as means from the shapes during the recording. The flow-shape indexes of the classes 1 to 7 were calculated as the number of the shapes of each class per hour of recording.

**Statistical Analysis**

One-way analysis of variance was used to assess the differences among the three subject populations with respect to the inspiratory area and slope values, as well as to the flow-shape indexes. If statistically significant differences were observed, further analysis was done using Tukey’s honest significant difference (HSD) procedure for post hoc multiple comparisons. In all tests, the error risk p < 0.05 was considered significant. Statistical analyses were performed with SPSS 8.0 for Windows software (SPSS; Chicago, IL).

**RESULTS**

**Validation**

The group characteristics measured from the airflow signal are shown in Table 3. The total number of respiratory cycles analyzed was 207,389 during 276 h of recording. In control subjects and female patients, the frequency of analyzed inspirations equaled the normal respiratory rate of about 14 cycles/min. Since the male patients had more apnea episodes than others (Table 2), the frequency of analyzed inspirations per hour was lower. The subjects did not report any major disturbances of sleep during the study night, and the quality of the recorded signals was good. The proportion of mouth breathing was negligible in all study groups.

**Table 2—Diagnostic Indexes of the Three Study Groups**

<table>
<thead>
<tr>
<th>Groups</th>
<th>AI, l/h</th>
<th>FI &lt; 0.15, % of Time</th>
<th>ODI4, l/h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control subjects</td>
<td>0.7 ± 1.1</td>
<td>0.5 ± 0.5</td>
<td>0.49 ± 0.54</td>
</tr>
<tr>
<td>Male patients</td>
<td>11.9 ± 11.0</td>
<td>31.3 ± 17.7</td>
<td>5.25 ± 6.49</td>
</tr>
<tr>
<td>Female patients</td>
<td>3.5 ± 4.2</td>
<td>38.4 ± 16.7</td>
<td>1.92 ± 1.51</td>
</tr>
</tbody>
</table>
*Data are presented as mean ± SD. ODI4 = oxyhemoglobin desaturation of four percentage units or more.

**Figure 1.** Representatives of the inspiratory flow shape classes used in the present study. The shapes are normalized for duration and amplitude. Since the classes cover all variations of flow shapes, the classification is in fact a continuum of shapes.
Inspiratory Area and Slope

Figure 2 shows the mean inspiratory area and slope values in the three groups. The mean inspiratory areas were similar in all groups, but inspiration was more gently sloping in female patients than in male patients \( (p < 0.05) \) or control subjects \( (p < 0.01) \). The inspiratory slopes were similar in male patients and control subjects. Area or slope did not correlate with body mass index (BMI).

Flow Shapes

The indexes of the flow-shape classes are shown in Figure 3. All shape types were observed in each subject. In control subjects, the sinusoidal flow-shape class 1 was dominant \( (48\% \text{ of all shapes}) \), although class 4 was also frequent \( (24\%) \). The sinusoidal class 1 was the dominant shape \( (34\%) \) also in male patients. The female patients had the most uniform class distribution. In female patients, the two-peak class 2 dominated \( (28\%) \) and also the class 6 was frequent \( (20\%) \). The female patients were the only group to have a noteworthy representation of the class 3 \( (5\%) \) and class 5 \( (6\%) \), whereas in male patients the plateau flow class 7 was quite frequent \( (10\%) \).

There were significant \( (p < 0.05) \) differences among the three groups in all flow shape indexes, except for class 7. As expected, within the sinusoidal class 1, the control subjects showed significantly higher index values than did the male and female patients \( (p < 0.01; \text{Fig 3}) \). Similarly, the class 4 index was higher in control subjects than in patients \( (p < 0.05) \). In the rest of the shape indexes, differences were observed between the female group and the other two (male) groups. The female patients had higher indexes of shape classes 2 and 3 \( (p < 0.05) \) and classes 5 and 6 \( (p < 0.01) \). The index of the plateau flow-shape class 7 was similar in all the three groups. The flow-shape analysis was most powerful to distinguish between the female patients and the control subjects, since six (classes 1 to 6) of the seven indexes differed significantly.

**Discussion**

Using noninvasive nasal prongs and an automated pattern recognizer, we were able to quantify the various inspiratory flow shapes in two well-defined patient populations with predominantly partial upper airway obstruction during sleep. Significant differences in flow shapes were observed not only between patients and control subjects but also between female and male patients. Although the pathophysiologic phenomena explaining variation in inspiratory flow shapes are not yet well understood, the observed flow-shape differences suggest that although the two patient groups present with similar breathing abnormalities during sleep, the behavior of the upper airway differs.

Nasal pressure profile, measured with simple nasal prongs, provides information about possible sleep-induced flow limitation in the upper airway. Flattening of the pressure profile, in particular during the latter part of inspiration, is regarded as a marker of flow limitation.\(^6\)–\(^9\) Upper-airway flow limitation, when severe enough, may result in obstructive hypoventilation and arousal. There is not only one but

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**Table 3—Flow Signal Measurements of the Three Study Groups**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Analyzed Time, h†</th>
<th>No. of Breaths Analyzed, cycles</th>
<th>Respiratory Rate, cycles/min</th>
<th>Estimated Mouth Breathing, % of recording time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control subjects</td>
<td>7.3 ± 0.4</td>
<td>6,246 ± 819</td>
<td>14.4 ± 2.3</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>Male patients</td>
<td>7.6 ± 0.6</td>
<td>5,070 ± 1,492</td>
<td>11.1 ± 3.1</td>
<td>0.7 ± 2.2</td>
</tr>
<tr>
<td>Female patients</td>
<td>6.6 ± 1.4</td>
<td>5,484 ± 1,418</td>
<td>13.8 ± 1.9</td>
<td>0.7 ± 1.3</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD.
†Mouth breathing excluded.
several flow-limited (nonsinusoidal) inspiratory flow patterns, the determinants of which have not previously been studied in detail. As a preliminary approach to describe the various flow shapes and to determine their occurrence in various subgroups of patients with upper airway dysfunction, the following procedures were performed. First, after visual screening of several all-night flow shape recordings in different patient populations, seven main categories of flow shapes were identified (Fig 1). Second, an automated inspiratory flow-shape analysis method using a formal language classification system to distinguish seven variations was developed.12 The present study reports the results from the third phase, in which the performance of the flow-shape analysis was tested for the first time in a clinical setting to display differences in the upper airway function in patients and control subjects.

Interpretation of the inspiratory flow shapes is based on the assumption that the impact of the upper airway on the inspiratory flow shape is reflected as deviation from the sinusoidal shape produced by the central respiratory command. However, we do not know whether the central respiratory command remains sinusoidal through all stages of sleep. Aberration from the sinusoidal command is likely to occur at least during phasic rapid eye movement (REM) sleep. However, evidence from cats suggests that sinusoidal shape is a decent estimation of the phrenic nerve discharge pattern also during resistive loading and during hypercapnic stimulus.18

The results from the flow-shape analysis indicated that changes of the inspiratory flow shape also occur during sleep in presumably healthy control subjects. However, by including all inspirations into analysis, we were able to demonstrate differences in several individual flow-shape frequencies between the two patient groups and control subjects. This was possible even without knowledge about episodes of wakefulness or REM sleep, which are likely to be a major source of variation. Since each breath was analyzed separately and forced to fit into given shape categories, our analysis was predisposed to random errors that arise from voluntary actions, swallowing, gasping, or phasic REM events. Inclusion of random shapes could be eliminated by analyzing breaths in clusters and by including a random shape class.

Our classification of the flow shapes was based on the identification of plateaus and peaks and on the order of their appearance. Plateau may occur throughout the inspiratory flow (class 7), or only during the early (class 6), middle (class 2), or late (class 4) inspiratory phase. Certain inspiratory flow shapes are characterized by a peak at midinspiration (class 5) or several (three or more) peaks throughout the inspiratory flow (class 3). As earlier reported,12 the flow shapes form a continuum and demarcation between classes is technical rather than physiologic when using an automated system. However, the fact that peaks and plateaus may occur during the early middle or late phases of inspiration suggests that the various forces that either support the airway or promote its collapse have different action profiles.

![Figure 3](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21956/)

**Figure 3.** Indexes of each flow shape class in the three study groups (mean ± SEM). Asterisks indicate the significance (* = p < 0.05, ** = p < 0.01) in the Tukey’s HSD multiple comparisons procedure.
Failure or overaction of one force or another could result in unbalanced upper airway support and deviation of the inspiratory flow shape from the sinusoidal command. The suggested interpretations of the various flow shapes are presented in Table 4. Analysis of the inspiratory flow shapes could help in the identification of the specific upper airway dysfunction and finding the specific mode of therapy.

Table 4—Characteristics and Suggested Interpretation of the Various Inspiratory Waveforms

<table>
<thead>
<tr>
<th>Classes</th>
<th>Description</th>
<th>Interpretation</th>
<th>Flow Limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sinusoidal form</td>
<td>Normal inspiration</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>Two peaks during inspiration</td>
<td>Upper-airway reopening after a partial collapse</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>Three or more (tiny) peaks</td>
<td>Soft-tissue vibration during inspiration</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>Peak during initial phase followed by a plateau</td>
<td>Initial opening indicates effective phasic upper airway dilation</td>
<td>Yes/no</td>
</tr>
<tr>
<td>5</td>
<td>Peak at midinspiration with plateau on both sides</td>
<td>Significance uncertain; intensive phasic muscle activity at midinspiration (?)</td>
<td>Yes</td>
</tr>
<tr>
<td>6</td>
<td>Peak during late phase preceded by a plateau</td>
<td>Marked tracheal traction support during lung inflation</td>
<td>Yes</td>
</tr>
<tr>
<td>7</td>
<td>Plateau throughout the inspiration</td>
<td>Collapse of noncompliant upper airway</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Figure 4. Examples of nasal pressure profiles during 1 min of recording.
The sinusoidal shape (class 1) was common in each group, but also the other classes were represented (Fig 3). Although the sinusoidal class was dominating in the control group, it represented only one half of all the flow shapes. It is interesting that the class 4 index was also significantly higher in control subjects than in the other two groups. Our experience from treating sleep apnea patients is that while the nasal CPAP treatment (applied at a therapeutic level) increases the frequency of the sinusoidal shape and decreased the other nonsinusoidal ones, it increased the frequency of the class 4 as well. Whether this is a CPAP technical issue or whether it reflects the central respiratory command remains to be clarified. However, it seems that although the class 4 shape includes the conventional flow-limiting shape, similar shapes do also occur without flow limitation in our control subjects. More detailed analysis of the class 4 shape in control subjects and patients is needed to differentiate the flow-limiting shape from the nonlimiting one.

While classes 1 and 4 were characteristic for the control subjects, classes 2, 3, 5, and 6 were more frequent in the female patients than in the other groups. One might deduce that the subjects in the female group are often able to dilate the upper airway toward the end of inspiration and succeed in finishing inspiration withwell-contoured flow shape (classes 2 and 6). This observation is in line with the finding that postmenopausal women initiate their inspiration with significantly lower inspiratory slopes (Fig 2). It is possible that low progesterone levels in postmenopausal women are responsible for these changes.16,20

Figure 4 shows representative nasal pressure profiles from each study group. Control subject 1 demonstrates the most “normal” of all control subjects, with 62% of sinusoidal flow shapes and 19% of class 4 (see Fig 5 for the flow-shape indexes). Unlike other control subjects, the two asthmatic subjects had more shapes in class 2 than in class 1. The male patients were a more heterogeneous group, with breathing abnormalities ranging from partial upper-airway obstruction to episodes of sleep apnea (subject 2). In subject 2, the high proportion of the sinusoidal shapes (56%; Fig 5) was related to low frequency of inspirations (5.3 cycles/min) and frequent episodes of apnea (AI of 34.5/h). Subject 2 demonstrates that the flow-shape analysis is not informative in patients with severe sleep apnea. In patients with severe sleep apnea, sinusoidal inspiratory flow shapes are common because most of them appear during repetitive arousals (Fig 4). To differentiate flow-shape profiles in patients with sleep apnea and normal control subjects, we chose to use flow-shape indexes that indicate the number of particular shapes per hour of recording rather than simple percentage of all breaths encountered. Patients with frequent episodes of sleep apnea may have about normal percentages but abnormal indexes, since they have a reduced number of breaths per hour. Subject 3 is a representative female patient

![Graph showing flow shape indexes](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21956/ on 06/25/2017)
with predominantly partial upper airway obstruction (Fig 4). Shape classes 2 and 6 dominate (27% and 35%, respectively; Fig 5), and severe flow limitation is also demonstrated with high FI of 32.

Although we found significant differences in the inspiratory flow shapes in the three groups, the physiologic meanings of these differences remain difficult to interpret at this stage. Further studies are needed to evaluate the impact of age, BMI, scarring after UPPP, gender, and sex hormones on one hand, and the role of upper airway dysfunction per se on the other. However, the flow-shape analysis is a promising tool for evaluation of upper airway function and understanding the "gray zone" of nonapneic breathing disturbances during sleep.21 In the future, with increasing knowledge on the physiologic correlates of the various flow shapes, the classification of the flow shapes can be simplified and the inspiratory flow-shape recognizer can be sensitized to detect risk behavior of the upper airway. Simple setup combined with advanced signal processing can make the inspiratory flow-shape analysis one of the most sensitive methods to evaluate upper airway function during partial upper airway obstruction.

REFERENCES