Flow-Volume Curve Abnormalities and Obstructive Sleep Apnea Syndrome*

Jean Krieger, M.D.; Emmanuel Weitzenblum, M.D.; André Vandevenne, M.D.; Jean-Luc Stierle, M.D.; and Daniel Kurtz; M.D.

Recent reports have suggested that flow volume curve abnormalities may be of interest in the diagnosis of obstructive sleep apnea syndromes by showing either extrathoracic airway obstruction (ratio of expiratory flow to inspiratory flow at 50 percent of forced vital capacity [FEF50/FIF50] exceeding 1) or upper airway fluttering (indicated by a sawtooth aspect on the mid-half of the inspiratory part of the curve) or both. In our study, 57 patients referred for a suspected sleep apnea syndrome (SAS) underwent conventional spirometry, assessment of flow-volume curves, ENT examination, and polysomnography. Thirty patients had an obstructive SAS, four patients a central SAS, and 23 patients no SAS. Signs of upper airway fluttering (the sawtooth sign) were present in 61 percent of the patients with obstructive SAS and in 46 percent of the patients without obstructive SAS (central SAS or no SAS). Signs of extrathoracic upper airway obstruction (FEF50/FIF50 >1) were present in 67 percent of the patients with obstructive SAS and in 71 percent of the patients without obstructive SAS. These results suggest that upper airway abnormalities, as reflected by abnormal flow volume curves, are not always associated with obstructive SAS; they favor the hypothesis of a central component in the mechanism of upper airway occlusion during sleep.

It has been suggested recently that flow-volume curves might be of interest in the diagnosis of obstructive sleep apnea syndromes (O-SAS) by demonstrating in the awake individual the presence of abnormalities related to modifications of the extrathoracic upper airways. Two different signs have been reported as being strongly related to O-SAS. The first sign is an increase in the ratio of forced expiratory flow to forced inspiratory flow at 50 percent of vital capacity (FEF50/FIF50), this ratio being greater than one. This sign, which is considered to be related to upper airway obstruction, was present in 44 percent of 27 O-SAS patients and only in 8 percent of 25 non-O-SAS patients. The second sign is "the sawtooth sign," which consists of regular oscillations occurring at constant intervals on the forced expiratory or forced inspiratory flow-volume tracing, and is supposed to reflect fluttering of upper airway tissue; this sign was present in 85 percent of 13 O-SAS patients and in none of eight non-O-SAS subjects. When the two signs were combined, 75 percent of 16 O-SAS patients were found to have at least one abnormal sign, while none of eight non-O-SAS patients had an abnormal flow-volume curve, suggesting that flow-volume curve abnormalities could be very highly specific for O-SAS. However, more recent studies found abnormal flow-volume curves in three out of seven and in one out of five non-O-SAS patients. Thus, results of earlier studies agree on the existence of a relatively high frequency of abnormal flow-volume curves in O-SAS patients, but there is some disagreement on the specificity of these abnormalities.

The question of specificity with regard to abnormal flow-volume curves may be of some importance if one considers current hypotheses on the mechanism of airway occlusion during sleep in O-SAS patients. According to these hypotheses, airway occlusion results from an imbalance between upper airway negative pressure during inspiration and the tone of upper airway walls. The question remains open whether this imbalance is due to increased negative pressures or to decreased tone of upper airway walls. Mechanical hypotheses favor the role of an anatomic narrowing of the upper airway as being responsible for a more negative inspiratory pressure; functional hypotheses favor the role of a sleep-related decrease in upper airway muscle tone, central in origin. A high sensitivity of flow-volume curve abnormalities would suggest that upper airway abnormalities are a strict prerequisite for upper airway occlusion during sleep; a high specificity would suggest that they are sufficient in and of themselves.

Because of discrepancies in the results of earlier studies, we further investigated flow-volume curves derived from a larger series of patients.

**MATERIALS AND METHODS**

Fifty-seven patients referred to our sleep disorder center because of excessive daytime somnolence, abnormal sleep behavior or unexplained alveolar hypoventilation or pulmonary hypertension...
underwent conventional spirometry and the registration of flow-volume curves as part of a set of routine investigations for sleep disorders. These routine investigations included the following: a clinical interview and examination, pulmonary function tests, an ENT examination, a multiple sleep latency test, and an all-night polygraphic sleep recording.

The polygraphic sleep recording included EEG, EOG, and EMG of chin muscles. Respiration during sleep was analyzed by means of a Fleisch No. 2 pneumotachograph (Godart Statham) attached to a soft silicone nasobuccal mask (Bird 3434), and by means of two separate thoracic and abdominal strain gauges. Oxygen saturation measured by ear oximeter was also recorded. Hypopneas were defined as a drop of tidal volume below 50 percent of its quiet wakefulness value without a major change in respiratory frequency; central apnea as a complete cessation of airflow, as well as thoracoabdominal movements; obstructive apnea as a cessation of airflow while thoracic and/or abdominal movements persisted; and mixed apnea as a succession of central and obstructive apneas. A patient was diagnosed as having SAS when he had an apnea index (number of apneas per hour of sleep) higher than five. The SAS patients were divided into central (C-SAS) and obstructive (O-SAS) groups according to the predominant type of sleep apnea.

Conventional spirometry was performed with a 10L closed circuit spiropgraph. Static lung volumes were measured by the closed helium dilution method. Reference values for vital capacity, FEV₁, and static lung volumes are those of the European Community for Coal and Steel. The forced inspiratory volume for one second (FIV) was measured in all cases.

Forced inspiratory and expiratory flows were measured with a pneumotachograph, exhibiting a good linearity for the flows ranging between 0.1 and 15.0 Ls⁻¹. Flow-volume curves were registered on an X-Y recorder. Three reproducible flow-volume loops were required and the highest values for the forced expiratory flow at 50 percent (FEF50) of the forced vital capacity (FVC) and for the forced inspiratory flow at 50 percent (FIF50) of the FVC were utilized. A ratio of FEF50/FIF50 > 1 was considered to be indicative of extrathoracic airway obstruction. The "sawtooth" aspect of the inspiratory and/or expiratory part of the flow-volume curve was defined according to Sanders et al as three or more consecutive peaks and troughs of no greater than 300 ml during the middle half of the vital capacity.

The investigations were performed and interpreted without prior knowledge of the final diagnosis for each patient. In accordance to the results of the polygraphic sleep recordings, the patients were divided into three groups: a group of 30 subjects with obstructive sleep apnea syndrome, a group of four patients with central sleep apnea syndrome, and a group of 23 patients without sleep apnea syndrome (Table 1). The duration of polygraphic recordings and the duration of sleep were similar in these three groups (Table 1); however, the nonapneic patients slept better than the apneic patients, in that they had less light slow wave sleep (p < 0.01) and more deep slow wave sleep (p < 0.01; Table 1). The mean sleep latency on the daytime sleep latency test was not different between these three groups; the decrease for the nonapneic patients is probably due to the presence of narcoleptic patients among them. In order to compare the flow volume curves in patients with and without upper airway obstruction during sleep, the non-sleep apneic patients and the central apneic patients were pooled; this resulted in a group of 27 subjects without obstructive sleep apnea, which was compared to the group of 30 patients with obstructive sleep apnea syndrome. The two groups had similar ages, sex distributions, height-weight ratios (Table 2), and pulmonary function test values (Table 3). The O-SAS group contained a higher percentage (93 percent) of snorers than the non-O-SAS group (70 percent; p < 0.05; Table 2). In addition, the quality of snoring was different between the two groups. The O-SAS patients were mostly heavy snorers, whereas the non-O-SAS patients were mostly occasional snorers. The ENT abnormalities were observed with a similar frequency in both groups (Table 2). These abnormalities were always of minor importance, including nasal septum deviations, hypertrophied tonsils, lung uvalae in contact with the epiglottis and/or macroglottis. When O-SAS was diagnosed by the polygraphic sleep recording, a surgical correction of these abnormalities was proposed whenever possible.

The sensitivity (percentage of patients with positive tests among those actually having the disease) and the specificity (percentage of patients with negative tests among those not having the disease) were calculated for each sign: the sign of extrathoracic airway obstruction (FEF50/FIF50 > 1) and the sawtooth sign.

The three groups were compared by means of a two-tailed, one-way analysis of variance. The two groups were compared by means of either a Student's t-test (quantitative parameters) or a Chi-square test (qualitative parameters). In addition, the relationship between the FEF50/FIF50 ratio and other parameters was analyzed either by means of a Pearson's correlation test (quantitative parameters) or a Chi-square test (qualitative parameters).

**RESULTS**

A representative example of a flow-volume curve

### Table 2—Biometric Data of Two Groups of Patients (Means ± SEM)

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex (%)</th>
<th>Snoring</th>
<th>Upper Airway Abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>O-SAS</td>
<td>53 ± 2</td>
<td>29 M</td>
<td>41 ± 5</td>
</tr>
<tr>
<td>n = 30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>non-O-SAS</td>
<td>51 ± 2</td>
<td>23 M</td>
<td>33 ± 5</td>
</tr>
<tr>
<td>n = 27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ns</td>
<td>ns</td>
<td>p &lt; 0.05</td>
<td>ns</td>
</tr>
</tbody>
</table>

**Obstructive Sleep Apnea Syndrome (Krieger et al)**
with an increased FEF50/FIF50 ratio and a sawtooth sign is given in Figure 1.

The values of the FEF50/FIF50 ratios were not different between the two groups, nor were the percentage for the sawtooth sign or for the extrathoracic airway obstruction sign (FEF50/FIF50 >1) different between the two groups (Table 4).

The sensitivity of the FEF50/FIF50 ratio was 67 percent; its specificity 29 percent. The sensitivity of the sawtooth sign was 61 percent; its specificity 54 percent. When the two signs (FEF50/FIF50 ratio and sawtooth sign) were considered jointly, the combined sensitivity (percentage of O-SAS patients having either FEF50/FIF50 >1 or a sawtooth sign) was 86 percent, but the specificity (percentage of non-O-SAS patients having none of the two signs) dropped to 13 percent.

Since a decrease in forced expiratory flow could have altered the values for the FEF50/FIF50 ratio these data were recomputed after excluding the 15 patients with a FEV/FVC ratio lower than 0.65 (five from the O-SAS group; ten from the non-O-SAS group). In the remaining patients, the sensitivity and specificity were 82 percent and 15 percent for the FEF50/FIF50 ratio, 70 percent and 53 percent for the sawtooth sign, and 91 percent and 6 percent for the two signs combined.

The FEF50/FIF50 ratio correlated positively with the FEV/FVC ratio (r = 0.53, p < 0.001) and correlated negatively with age (r = 0.48, p < 0.001), but did not correlate with the apnea index or the height-weight ratio. Furthermore, the frequency of FEF50/FIF50 ratios greater than 1 was higher in patients with ENT abnormalities (69 percent) than in patients without ENT abnormalities (39 percent; p < 0.05); however, it was not significantly different among subjects with and without the sawtooth sign, nor among snorers and nonsnorers.

The frequency of the sawtooth sign was not significantly different among snorers and nonsnorers, patients with and without ENT abnormalities, patients with and without signs of upper airway obstruction and patients with low (<40) and high (>40) apnea indices. There were no differences in the ages and in the height-weight ratios between patients with and without the sawtooth sign.

These investigations were repeated in three patients: in two after correction of ENT abnormalities (nasal septum deviation in one case, hypertrophied tonsils in the other) and in one after substantial weight loss (height-weight ratio decreasing from +41 to +23 percent). In these three patients, the polysomnographic data were unchanged, showing the persistence of O-SAS. Two of these three patients had a sawtooth sign which persisted in both cases; they all had an earlier FEF50/FIF50 ratio greater than 1, which decreased, but remained greater than 1 (from 1.5 to 1.3 after nasal septum correction; from 1.8 to 1.5 after tonsillectomy; from 2.1 to 1.5 after weight loss).

**DISCUSSION**

The sawtooth sign was first described by Sanders et al in patients with obstructive sleep apnea syndrome (O-SAS). These authors related it to fluttering of upper airway tissue during either inspiration or expiration. They found it to be highly sensitive (85 percent) and

| Table 3—Spirometric Data of Two Groups of Patients (Means ± SEM) |
|-----------------|-------------|-----------|-------------|-------------|-------------|-------------|
|                | FVC (ml)    | FVC/Predicted | RV (ml)    | RV/TLC     | FEV1 (ml)  | FEV1/FVC    |
| O-SAS          | 3619 ± 175  | 0.97 ± 0.04  | 1863 ± 123 | 0.34 ± 0.02| 2625 ± 145 | 0.72 ± 0.02 |
| n = 30         | ns          | ns          | ns         | ns         | ns         | ns          |
| non-O-SAS      | 3628 ± 181  | 0.94 ± 0.04  | 2005 ± 137 | 0.35 ± 0.02| 2475 ± 194 | 0.68 ± 0.03 |
| n = 27         | ns          | ns          | ns         | ns         | ns         | ns          |

**Figure 1.** A representative example of an abnormal flow-volume curve, showing a "sawtooth" aspect on the inspiratory and expiratory limb of the curve, and a flattening of the inspiratory part of the curve with an increase in the FEF50/FIF50 ratio (here = 1.7). V1 is inspiratory flow; Ve, expiratory flow; and V, volume.

| Table 4—Results of Flow-Volume Curves in Two Groups of Patients |
|------------------------|------------------------|------------------------|
|                         | Sign of Extrathoracic Airway Obstruction (FEF50/FIF50 >1) | Sawtooth Sign |
|                         | (Mean ± SEM)           |                         |
| O-SAS                   | 1.27 ± 0.13            | 65%                     | 61%                     |
| n = 30                  |                         |                         |
| non-O-SAS               | 1.39 ± 0.14            | 71%                     | 46%                     |
| n = 27                  |                         |                         |

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specific (100 percent) for O-SAS. However, the presence of this sign has been reported in non-O-SAS patients.\textsuperscript{12}

A FEF50/FIF50 ratio greater than 1 is considered as a sign of extrathoracic airway obstruction\textsuperscript{13} due to dynamically variable airway narrowing resulting in a preferential limitation of inspiratory flow. This sign is both sensitive (80 percent) and specific (96 percent) of extrathoracic upper airway obstruction.\textsuperscript{11} Recently, Haponik et al\textsuperscript{1} suggested that it might be of interest for the diagnosis of O-SAS because of its 55 percent sensitivity and 92 percent specificity.

Chaudhary et al\textsuperscript{3} studied the predictive value of the combination of the two signs and found a 75 percent sensitivity and a 100 percent specificity. However, for this combination, Tammelin et al\textsuperscript{4} found a 68 percent sensitivity and only 57 percent specificity, while Riley et al\textsuperscript{5} a 50 percent sensitivity and 80 percent specificity.

Our results are in agreement with the relatively good sensitivity of flow volume curve abnormalities for the diagnosis of O-SAS (67 percent for the FEF50/FIF50 ratio; 61 percent for the sawtooth sign; 86 percent for the combination of the two signs), but show a low specificity of these signs (29 percent, 38 percent, and 13 percent, respectively).

The presence of a sawtooth sign was not related to age, height-weight ratio, snoring, ENT abnormalities, or increased FEF50/FIF50 ratio. The value of the FEF50/FIF50 ratio was correlated to the value of FEV/FVC ratio, showing that the FEF50/FIF50 ratio is highly dependent on expiratory flow. However, when patients with expiratory flow limitation (ie, with an FEV/FVC ratio lower than 65 percent) were withdrawn from the study, the specificity of the FEF50/FIF50 ratio for O-SAS was worse than for the whole group (15 percent). The dependence of the FEF50/FIF50 ratio on the expiratory flow might explain the negative correlation we observed between the FEF50/FIF50 ratio and age, since the expiratory flow is known to decrease with increasing age.\textsuperscript{13}

On the other hand, a FEF50/FIF50 ratio greater than 1 was related to the presence of upper airway abnormalities. These abnormalities, including nasal septum deviation, hypertrophied tonsils, long uvulae and/or macroglossia, were of minor importance and had never by themselves been a motive for medical consultation; however, they could have been a source of a dynamically variable upper airway narrowing, resulting in a more decreased inspiratory than expiratory flow.\textsuperscript{9}

Thus, in our patients, the sawtooth sign was not related to any of the parameters we analyzed; the FEF50/FIF50 ratio was dependent on the expiratory flow (and thus may be decreased in COPD patients and in older subjects irrespective of the presence of upper airway abnormalities) and on the presence of upper airway abnormalities, as previously shown.\textsuperscript{14} However, we found an equal frequency of upper airway abnormalities in non-O-SAS and in O-SAS patients.

The differences in specificity of abnormal flow-volume curves between the various above-mentioned studies and ours may be due to differences in control groups. Our control group was by no means composed of normal subjects; the patients were referred because of daytime somnolence, abnormal sleep behavior, or unexplained alveolar hypoventilation or pulmonary hypertension. The group was made up of 70 percent snorers, 44 percent obese patients (height-weight ratio greater than +30 percent) and 57 percent ENT abnormalities; their mean age was 51. By contrast, in the study by Sanders et al\textsuperscript{6} control subjects were mostly normal volunteers; in Chaudhary et al's study,\textsuperscript{3} and in Riley et al's,\textsuperscript{4} the control group was not defined; in Haponik et al's study,\textsuperscript{1} as in ours, control subjects were hypersomnolent patients; however, they were younger (mean age 38), less obese (mean height weight ratio +16 percent), and included fewer snorers (30 percent); no upper airway examination was performed.

Our data suggest that, when compared to a similar group of subjects, flow-volume curve abnormalities do not allow for the differentiation of O-SAS patients from non-O-SAS patients. Strict adherence to the definition of sleep apnea syndrome as five apneas per hour of sleep may have introduced an artificial separation between our patients since less than five apneas per hour of sleep does not necessarily mean normal breathing during sleep; indeed, the limit of five apneas per hour of sleep is arbitrary. It has been emphasized that there was a continuum from normal unobstructed breathing during sleep to overt obstructive sleep apnea syndromes, including occasional snorers, usual snorers, and subjects with a limited number of obstructive sleep apneas.\textsuperscript{14-15} Our results clearly show that flow-volume curves do not allow for separating clusters within this continuum. In other words, flow-volume curve abnormalities are not related to the degree of upper airway dysfunction during sleep; abnormal curves seem to be mainly related to awake upper airway abnormalities which are not specific for O-SAS.

These results are in agreement with current hypotheses on the mechanisms of upper airway occlusion during sleep in O-SAS.\textsuperscript{16-19} According to these hypotheses, two factors, either separately or in conjunction, may result in upper airway occlusion: a narrowing of the upper airways resulting in a more negative upper airway pressure during inspiration, and/or a sleep-related defect in upper airway dilatory muscle activity during inspiration. The O-SAS patients without flow-volume curve abnormalities could correspond to those patients in whom the upper airway occlusion mechanism during sleep is mainly of central origin. The non-
O-SAS patients with abnormal flow-volume curves could correspond to subjects in whom upper airways abnormalities are compensated by an increased dilatory muscle activity during sleep. Thus, discrepancies in published results concerning flow-volume curves could reflect the heterogeneity of the mechanism of upper airway obstruction during sleep in O-SAS patients.

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