Flow oscillations on the flow-volume loop: Clinical and physiological implications

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In 1981, Sanders et al [1] described the "saw-tooth" sign, a sequence of rapid oscillations of the flow-volume loop tracing, as an aid for the detection of sleep apnea in awake patients. Such flow oscillations had been recognised before - in fact ever since the flow-volume loop came into clinical practice at the beginning of the sixties - but generally were discarded as a noisy disturbance, created in the measuring instruments or in the subject's airway and blurring the signal contained in the flow-volume loop [2-5]. To illustrate this, in Miller and Hyatt's important paper [4] on the usefulness of flow-volume loops in the evaluation of obstructing lesions of the larynx and trachea it can be literally read that the flow plateaux characteristic of upper airway obstruction "... often contained noise or rapid oscillations because of marked flow turbulence..." and that the figures shown in the article "... show smooth contours for simplicity of display." Smoothing of flow-volume loops has been the preferred approach to display flow-volume loops, not only to meet the need of both manufacturers and users of pulmonary function equipment to get rid of the noisy disturbances, but also to minimize the possible contributions of oscillations to the variability of derived forced expiratory flow rates [3, 6]. Some oscillations seen on flow-volume loops may indeed be nothing else but noise. However, recent evidence indicates that flow oscillations in some instances, may signal the presence of a functional or structural disorder, usually located in the upper airways. In this paper we will try to collect the evidence that should change our view on flow oscillations, an example of how noise may become signal.

Definition

Flow oscillations are defined as a reproducible sequence of alternating decelerations and accelerations of flow, creating a "saw-tooth" pattern superimposed on the general contour of the flow-volume loop produced by the awake subject (fig. 1). Flow oscillations can occur on any portion of the inspiratory and/or expiratory parts of the flow-volume loop, whether obtained during forced or tidal breathing.

Contrary to the definition of "saw-toothing" by Sanders et al [1], our definition remains descriptive, purposefully avoiding quantitative characteristics such as the amplitude and periodicity (frequency) of individual oscillations, or the number of oscillations in one sequence. The reason for this is that flow-volume loops are volume- and not time-based recordings, so that oscillation frequency cannot directly be quantified from them. In order to do so, simultaneously obtained flow-time recordings (fig 2, right panel) or volume integrations of the flow-volume loop are required, but these are not always available in routine pulmonary function testing. The number of oscillations in one sequence may vary with the duration of the breathing manoeuvre. In our experience, tidal as well as forced inspiration is shorter than expiration in normal subjects as well as in patients with various pathologic conditions, with the exception of fixed or variable extrathoracic upper airway obstruction [4]. Therefore an expiratory sequence is likely to contain more oscillatory cycles than an inspiratory sequence. A minimum of 3 oscillations, as proposed by Sanders et al. [1] should however be
The amplitude of flow oscillations may to a major extent be modified by the damping characteristics of the different measuring and recording devices used in different pulmonary function laboratories: underdamped components may overestimate oscillation amplitude, while overdamped system components (such as some flow measuring devices and even some so-called “fast-response” x-y recorders) may underestimate oscillation amplitude.

Clinical correlations

In most papers reporting flow oscillations, a clinical substrate usually has been found to underly flow oscillations (table 1). The “saw-tooth” sign, initially reported by Sanders et al [1] in patients with the obstructive sleep apnoea syndrome (OSAS), was shown to correspond to rapid fluttering of redundant pharyngeal tissue visible at endoscopy. This finding has been amply confirmed since, by a number of authors [10-16] (table 2). In various of these papers, “saw-toothing”, although not very sensitive, was considered highly specific for the OSAS, merely because its incidence in the OSAS was compared to that in normal control subjects. However, the high specificity of flow oscillations for the OSAS could not be confirmed when comparing OSA patients to control subjects, mostly snorers, referred for excessive somnolence but not having the OSAS [15]. This was further substantiated in a large retrospective survey of 2800 flow-volume loops, revealing flow oscillations in 40 cases, an incidence of 1.4% [17]. Of these 40 cases, only 9 (22.5%) had the OSAS, while in a large part of the remaining 31 cases, rather than the OSAS, another structural or functional disorder of the upper airway or its surrounding musculature was present. More particularly, 8 patients had a structural upper airway lesion, 8 had a neurological disorder potentially involving the upper airway muscles, 10 were labelled COPD because of chronic respiratory symptoms and 5 had miscellaneous disorders. Three of the 10 COPD patients were later shown to have concomitant or sole upper airway dysfunction characterized by abnormally lax and

![Flow-volume loop](image)

Fig 2. - Flow-volume loop (left) and flow-time tracing (right) during tidal breathing in a patient with Parkinson's disease, showing flow oscillations occurring at a frequency of 5 Hz. Volume (V) along the X-axis (each mark is 0.5 l) and expiratory (Ve) and inspiratory (Vi) flow along the Y-axis (each mark is 0.5 l/s). (Reprinted, by permission of the New England Journal of Medicine, [51]).

For all these reasons, we prefer to regard flow oscillations in descriptive terms as a configurational flow-volume loop pattern, easily recognisable by visual inspection. If quantitative characteristics are required, they might be obtained from time-based flow recordings. Based on these, the frequency of flow oscillations observed in awake subjects in our laboratory widely varies between 4 and 60 Hz. Higher oscillation frequencies have been recorded in other laboratories, but only in conditions accompanied by audible sound generation such as snoring in sleeping subjects (40-90 Hz) [7] or forced expiratory wheezes (up to 2.7 kHz) [8, 9].

Although the recent introduction of computers for the acquisition and the recording of flow-volume loops has facilitated the calculation of forced in- and expiratory flow rates, it should be realized that most flow-volume loops digitally generated do not have sufficient flow or volume resolution. As a result, computer-steered flow-volume loop recordings may underestimate the frequency content and flow-oscillations may go unrecognized. Real-time x-y records obtained on x-y recorders or storage oscilloscopes therefore should remain the preferred way of graphically displaying flow-volume loops.
unstable upper airway structures [18]. In these COPD patients flow oscillations led to detection of an upper airway disorder which, in the presence of concomitant peripheral airflow limitation, often goes undetected [19, 20].

Table 1. - Clinical conditions associated with flow oscillations.

<table>
<thead>
<tr>
<th>Clinical Conditions</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstructive sleep apnea syndrome (OSAS)</td>
<td>[10-16]</td>
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<tr>
<td>Snorers without the OSAS</td>
<td>[15]</td>
</tr>
<tr>
<td>Upper airway stenosis (structural lesions)</td>
<td>[17]</td>
</tr>
<tr>
<td>Upper airway dysfunction</td>
<td>[18]</td>
</tr>
<tr>
<td>Extrapyramidal disorders</td>
<td>[22-27]</td>
</tr>
<tr>
<td>Neuromuscular disorders (with bulbar involvement)</td>
<td>[24]</td>
</tr>
<tr>
<td>Burn injury of upper airway</td>
<td>[22, 23]</td>
</tr>
<tr>
<td>Leewenhock's disease</td>
<td>[38]</td>
</tr>
<tr>
<td>Herpes Zoster of abdominal muscles</td>
<td>[39]</td>
</tr>
</tbody>
</table>

Table 2. - Flow oscillation in obstructive sleep apnoea syndrome.

<table>
<thead>
<tr>
<th>Source (reference)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanders, 1981 JAMA</td>
<td>85</td>
<td>100</td>
</tr>
<tr>
<td>Haponik, 1981 ARRD*</td>
<td>55</td>
<td>92</td>
</tr>
<tr>
<td>Chaidary, 1982 ARRD</td>
<td>56</td>
<td>100</td>
</tr>
<tr>
<td>Tamemien, 1983 ARRD</td>
<td>68</td>
<td>57</td>
</tr>
<tr>
<td>Riley 1983 SLEEP*</td>
<td>50</td>
<td>80</td>
</tr>
<tr>
<td>Shore 1984 THORAX**</td>
<td>41</td>
<td>92</td>
</tr>
<tr>
<td>Krieger 1985 CHEST</td>
<td>61</td>
<td>54</td>
</tr>
</tbody>
</table>

Legend: *, saw-toothed and increased FEF_{50}/FIF_{50} combined; **, supine flow-volume loop.

Pathogenetic mechanisms of flow oscillations

Since flow is the result of a driving pressure acting across a flow resistance, flow oscillations can on theoretical grounds be predicted to result from rapid intermittent changes in either driving pressure or airway resistance (table 3).

Rapid intermittent changes in airway resistance can result from several mechanisms. They can be due to excessive turbulence and the Bernoulli effect created past a structural narrowing of the upper airway, i.e. the "noise" referred to by Miller and Hyatt [4], or to airway instability. Airway instability may result from altered intrinsic mechanical properties of the airway wall or from loss of the stabilizing and airway patency promoting function of the striated musculature surrounding the upper airway [28-32]. As an example, besides reduced maximal expiratory flow rates, flow oscillations were noticed after instillation of proteolytic enzymes in canine tracheas, which resulted in increased compliance of central airways [33]. Similarly, the incidence of abnormal flow-volume loop contours suggestive of upper airway dysfunction, such as flow plateaus with or without flow oscillations, is significantly higher in neuromuscular disorders affecting the bulbar (upper airway) musculature than in neuromuscular disorders without bulbar muscle involvement [24]. In all these instances, flow oscillations probably represent airway walls flutter and flow turbulence leading to small high-frequency (more than 20 Hz) flow transients exceeding the maximal flow-volume loop envelope.

Table 3. - Pathogenetic mechanisms of flow oscillations

1. Intermittent changes in airway resistance
   - structural upper airway lesions
     - dynamic upper airway compression (Bernoulli phenomenon)
     - fluttering of redundant tissue
   - upper airway instability
     - altered mechanical properties of upper airway walls
     - upper airway muscle malfunction
   - phasic activity of upper airway muscles

2. Intermittent changes in driving pressure
   - phasic activity of respiratory pump muscles.

3. Artefact
   - artefact of instrumental origin
   - lack of patient cooperation (honk, cough, glottic closure)

Another mechanism underlying intermittently changing airway resistance is abnormal phasic activity of the upper airway muscles, leading to visible intermittent airway narrowing and airflow reduction. This has been clearly shown to occur in various extrapyramidal disorders, such as idiopathic Parkinson's disease, essential tremor and the Shy-Drager syndrome [25]. In 18 of 27 such patients, flow-volume loops obtained during forced as well as tidal breathing revealed flow oscillations (fig 2) occurring at a frequency of 4 to 8 Hz, which is similar to the frequency of their extremity tremor. These flow oscillations were not accompanied by synchronous pleural pressure oscillations, and hence are not due to tremor of the respiratory pump muscles - the diaphragm noticeably is spared in extrapyramidal disorders [25, 34-36] - but corresponded to upper airway muscle tremor, clearly visible at endoscopy as regular alternating abduction and adduction of glottic and supraglottic structures at a frequency of 4 to 8 Hz. Since these abnormal movements persisted during breathing, they do not represent passive fluttering of upper airway structures in the airstream but rather correspond to pha-
sic bursts of abnormal upper airway muscle activity [25].

The second major mechanism that could lead to flow oscillations consists of rapid intermittent changes in driving pressure which could be due to abnormal phasic activity of the respiratory pump muscles. This is a very rare occurrence, however, since even in Leeuwenhock's disease, characterized by rhythmic myoclonus of the diaphragm, the uvulo-palatal and laryngeal muscles [37], flow oscillations, when reported, were shown to be due to myoclonus of the upper airway rather than respiratory pump muscles [38].

The only hitherto reported instance of abnormal respiratory pump muscle activity underlying the flow oscillations consists of a patient with Herpes Zoster involving the abdominal muscles [39]. In this patient phasic bursts of abnormal abdominal muscle activity, demonstrable by electromyography, were coupled with mechanical activity producing abnormal motion of the abdominal wall (detected by inductance plethysmography) and distinct gastric and oesophageal pressure oscillations synchronous to the flow oscillations. This is in contrast to the findings in extrapyramidal disorders where oesophageal pressure oscillations were noticeably absent during the production of flow oscillations [25].

Finally, before attributing a pathological significance to the observed flow oscillations, artefactual or spurious flow oscillations, such as those created by excessive turbulence in the instrument's tubing or by lack of patient co-operation, should be excluded. Non-sustained oscillations lacking reproducibility on different days or with different instrumental set-up, are more likely to represent artefacts. Particular attention should be given to avoid either sound production ("honks", or high-frequency oscillations which usually occur around peak flow) or cough and voluntary intermittent approximation and closure of the vocal cords (low-frequency, large excursions of the flow tracing between the maximal flow-volume loop envelope and the volume axis, which usually occur at low lung volume). Figure 3) illustrates these 2 types of spurious flow oscillations voluntarily generated by the subject.

In general, flow oscillations are in most - if not all - instances the result of intermittent changes in airway resistance. In only a rare instance, phasic activity of the respiratory pump muscles may cause flow oscillations, but then synchronous oesophageal or gastric pressure oscillations, should be demonstrable. Furthermore, superimposition of flow oscillations on the general flow-volume loop contour suggests that the rapid intermittent changes in airway resistance take place in the common airway proximal to the carina or not farther out than the lobar bronchi. Indeed, even if oscillatory flow were to originate in more peripheral airways, it is likely to be damped out by non-oscillatory flow from the many other airway branches, resulting in a smooth flow-volume loop contour recorded at the mouth. Also, oscillatory flow is unlikely to occur more peripherally than the lobar bronchi where linear flow speed decreases due to an increasing cumulated cross-sectional area and the flow regime becomes progressively laminar.

It is easy to understand how the discussed mechanisms can lead to flow oscillations during tidal breathing and forced inspiration. During forced expiration, however, the general understanding is that maximal flow is, at least in the second half of the manoeuvre (the so-called effort-independent part), determined by a complex interaction between elastic lung recoil, airway geometry (the frictional resistance of upstream peripheral airways) and dynamic airway transmural pressure area characteristics (or airway compliance) at choke points where flow speed approximates wave speed [2, 40-46]. Events downstream from the flow-limiting choke points do not appear to influence maximal expiratory flow. However, flow oscillations have been positively identified during this effort-independent portion of forced expiration. This, then, must indicate that the changes in airway resistance and caliber occurring in the upper airway downstream from choke points are of such a magnitude as to interfere with the normal flow limiting mechanisms. Choke points can then be regarded
to jump back and forth between, on the one hand, the upper airway site where the structural or functional disorder resides, and on the other hand, its more peripheral location appropriate for the lung volume prevailing at that time. Similar mechanisms have been proposed to explain the highly reproducible plateau-knee configuration or concave bump which has been noticed to occur following peak flow in some normal subjects [47]. These knees, or sudden flow decelerations comparable to the downstroke of a flow oscillation, were attributed to sudden, more peripheral relocations of airway choke points [47]. Furthermore, the location and motion of airway choke points during forced expiration were found to be altered by small changes in local airway stresses such as those induced by changes in body posture [48] or neck position [49].

Functional implications of flow oscillations

Flow oscillations related to the presence of an upper airway disorder are often accompanied by physiologic evidence of upper airway obstruction (UAO). The latter can be inferred from an excessive response to breathing of a low-density gas mixture, such as heliox (20% oxygen in helium) [20], or from an increase in the following indices: the ratio of the forced expired volume in 1 s (FEV₁) to the forced expired volume in 0.5 s (FEV₅/FEV₁), the ratio of the FEV₁ to the peak expiratory flow (FEV₁/PEF), the ratio of the forced mid-expiratory to the forced mid-inspiratory flow (FEF₁₋₅/FEF₅₋₂) or the peak inspiratory flow (PIF) [50].

Thus, in a retrospective review of 2800 flow-volume loops, physiologic evidence of UAO was present in 14 (35%) of the 40 instances with flow oscillations, including 4 of 8 patients with a structural upper airway lesion and 10 of 32 patients without such a lesion [17]. Similarly, of 27 patients with an extrapyramidal disorder, physiologic evidence of UAO was present in 10 (37%) patients, 9 of whom presented flow oscillations on their flow-volume loops [25]. In burn victims, flow-volume loop abnormalities including flow oscillations and physiologic evidence of UAO were shown to correlate with structural upper airway changes observed during nasopharyngoscopy and were shown to be useful in the early assessment of patients at risk for UAO and the eventual need for endotracheal intubation [22, 23].

The detection of flow oscillations on flow-volume loop should instigate additional examinations directed at the upper airway in the search for a structural or functional abnormality with or without physiologic evidence of UAO. The observation of flow oscillations in a structural upper airway lesion without physiologic evidence of UAO suggests that flow oscillations are more sensitive to structural upper airway lesions than the conventional spirometric criteria of UAO. Probably, then, the structural lesion is not severe enough to narrow the airway lumen down to a diameter of less than 8 mm, the critical dimension below which spirometric evidence of UAO appears [4], but is severe enough to create excessive turbulence or a Bernouilli effect on the airway walls downstream from the lesion, resulting in flow oscillations.

If a structural lesion cannot be found, a functional disorder of the upper airway, due to altered mechanical properties of its walls or to malfunction of the upper airway muscles, that in normal conditions stabilize and maintain patency of the upper airway, should be suspected.

Such a functional disorder may or may not be accompanied by physiologic evidence of UAO, but in the latter event the presence of flow oscillations should be regarded as a sensitive sign, premonitory for an ongoing upper airway disorder, not yet of consequence but eventually leading to significant UAO.

Conclusion

With proper attention given to the instrumental setup and to the correct execution and acquisition of the flow-volume loop test, flow oscillations represent a readily identifiable sign with potentially valuable diagnostic implications. Although a possible mechanism underlying the flow oscillations may be rapidly intermittent phasic activity of the respiratory pump muscles, in most instances flow oscillations represent rapid intermittent changes in airway resistance and calibre, due to a structural or functional upper airway disorder. The detection of flow oscillations on flow-volume loops should thus instigate extensive investigations primarily directed at the upper airway and its surrounding musculature. In recent years, the importance of the functional integrity of the upper airway, including its surrounding musculature, has been much emphasized. This "organ" regulates the flow of air to and from the lungs in a way integrated with the remainder of the respiratory system. Its function is often difficult to assess, and, if not specifically looked for, malfunction may go undetected. Attention to the flow-volume loop configuration may help to assess the functional status of the upper airway. Abnormal contours, such as flow oscillations, appear to be sensitive premonitory markers of ongoing disorders with potentially serious consequences. Simple visual inspection of the flow-volume loop contour should become an integral part of pulmonary function testing.

Acknowledgements: The authors thank Mrs. Carmen Datanway and her staff of the Desmond N Sicker Pulmonary Function Laboratory of the Royal Victoria Hospital, McGill University, Montreal, Canada. The authors also thank Mrs. Hilda De Backer for expert secretarial assistance.

References


