Detection of Wheezing During Maximal Forced Exhalation in Patients With Obstructed Airways*

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Study objectives: Wheezing is a common clinical finding in patients with asthma and COPD during episodes of severe airway obstruction, and can also be heard in normal subjects during forced expiratory maneuvers; however, the properties of wheezing are difficult to perceive and quantify during auscultation. We therefore developed and evaluated a new technique for recording and analyzing wheezing during forced expiratory maneuvers in a group of patients with obstructed airways (asthma, COPD) and a control group of healthy subjects.

Material and methods: Sixteen patients with asthma (9 men and 7 women), 6 patients with COPD (6 men), and 15 healthy subjects (7 men and 8 women) were enrolled. The patients had moderate-to-severe obstruction (FEV₁ of 40 to 53% predicted). A contact sensor on the trachea was used to record sound during forced expiratory maneuvers. Wheeze detection was carried out by a modified algorithm in a frequency-time space after applying the fast Fourier transform.

Results: More wheezes were recorded in patients with obstructed airways than in control subjects: asthma patients, 8.4 ± 6.4 wheezes; COPD patients, 10.4 ± 6.1 wheezes; and control subjects, 2.9 ± 2.0 wheezes (mean ± SD). The mean frequency of all detected wheezes was higher in control subjects than in patients with obstructed airways (asthma patients, 560.9 ± 140.8 Hz; COPD patients, 669.4 ± 250.1 Hz; and control subjects, 750.7 ± 175.7 Hz). The total number of wheezes after terbutaline inhalation changed more in patients with obstructed airways than in control subjects.

Conclusions: The new method that we describe for studying airway behavior during forced expiratory maneuvers is able to identify and analyze wheeze segments generated in patients with obstructed airways, as evidenced by the greater number of wheezes detected in the patient group, the main finding of this study. This method clearly and objectively identifies the presence of obstructive disease.

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Key words: asthma; COPD; monitoring; signal processing; wheezing

Abbreviation: ANOVA = analysis of variance

Wheeze are continuous adventitious lung sounds that can be heard in patients with several diseases, including asthma and COPD. Wheezes are common occurrences during acute episodes of airway obstruction but can also be heard in normal subjects during forced expiratory maneuvers. Most wheezes are represented as spectrum peaks with frequencies < 2 KHz and mean frequencies between 200 Hz and 800 Hz, and probably occur when airflow in large, central airways exceeds a critical velocity. Wheezing can appear “monophonic,” denoting a single note, or “polyphonic,” but these properties are difficult to perceive and quantify during auscultation. Such differences in wheezing characteristics during forced exhalation have therefore not been studied in depth, given the need for new systems able to analyze sounds objectively.

As forced expiratory wheezes are a consequence of flow limitation, we hypothesized that wheeze characteristics are probably different for normal subjects and patients with obstructive airway disease. To test this hypothesis, we developed and evaluated an objective technique for recording and analyzing wheezes during forced expiratory maneuvers, com-

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paring results from patients with airway obstruction (asthma or COPD) to those from healthy subjects.

**Materials and Methods**

Sixteen nonsmoking patients (9 men and 7 women; mean [SD] age, 53.6 [16.3] years) with persistent but clinically stable moderate-to-severe asthma† (at least 1 month without an acute attack) for the ≥15 years, and 6 patients with COPD (6 men; age, 58.8 [4.9] years) were enrolled. All were ex-smokers from our hospital-based outpatient clinic. Fifteen healthy nonsmoking subjects (7 men and 8 women; age, 46.0 [12.5] years) made up the control group. None had any other disease. The patients were being treated with inhaled corticosteroids and sustained-action bronchodilators, but had not received inhaled β-agonists for at least 12 h before the test.

Maximal exhalation maneuvers were performed using a spirometer (PFT; Horizon; Manchester, OH) on all patients and normal subjects at baseline and 20 min after the inhalation of 1 mg of terbutaline (two puffs of 500 µg each) [Turbuhaler; Astra Draco AB; Lund, Sweden] according to the criteria of the American Thoracic Society.‡ Wheezing was detected by auscultation in all patients and 11 control subjects during FVC maneuvers.

Respiratory sounds were recorded using a contact microphone (PPG sensor; Technion University; Haifa, Israel) with a flat response between 50 Hz and 1,800 Hz and a resonance frequency of 2,600 Hz. The microphone was attached directly to the patient’s skin at the trachea at the level of the cricoid cartilage, using an elastic band.§ At the same time, the air flow from a pneumotachograph (Screenmate; Jaeger; Höchberg, Germany) was recorded in the mouth. The sound signal was amplified and filtered using a pass-band filter between 80 Hz and 2,000 Hz by a Desktop computer with a sampling frequency of 2,600 Hz. The microphone was attached directly to the skin at the trachea at the level of the cricoid cartilage, using an elastic band.§ At the same time, the air flow from a pneumotachograph (Screenmate; Jaeger; Höchberg, Germany) was recorded in the mouth. The sound signal was amplified and filtered using a pass-band filter between 80 Hz and 2,000 Hz by means of a filtering system (Butterworth KH 39168; Krohn-Hite Corporation; Avon, MA). The sound and flow signals were processed through a desktop computer with a sampling frequency of 5,000 Hz. Analysis was on the average of three forced expirations, each after a prior deep inspiration.

Wheezing detection was carried out by a modification of the algorithm proposed by Shahtai-Musih et al. The algorithm detected the airflow between 1.2 L/s and 0.2 L/s during expiratory maneuvers, and analyzed sound signal segments of 128 points (25 ms). Power spectrum density was computed using a fast Fourier transform with a Hanning window. The mean power in the spectrum was calculated and subtracted from each spectral point. Next, the spectral points were normalized by the variance of the spectrum. We evaluated peaks of > 3.5 variances, with the highest possible score being seven. The scoring criteria were as follows: (1) the peak was at least 2.5-fold greater than the mean of the absolute values of the preceding three points; (2) the peak was at least 2.5-fold greater than the mean of the absolute values of the following three points; (3) the peak was greater by at least 2 variances than its immediately preceding point; (4) the peak was greater by at least 2 variances than its immediately following point; (5) the peak was greater by at least 3.5 variances than its next-to-immediately preceding point; (6) the peak was at least 3.5-fold greater than its next-to-immediately following point; (7) the sum of the differences between the peak and its two preceding and two following points was > 15 variances; and (8) a score was lowered by one point if one of the next-to-immediately neighboring points was higher than the immediately neighboring point on the same side of the peak. We considered the peak to be a wheeze if the score was > 3, the peak was at least 0.2-fold greater than the maximum peak, and its frequency was > 100 Hz.

The next step consisted of applying a wheeze-grouping algorithm that detected peaks located in a time-frequency space. The grouping algorithm was as follows: (1) proximal peaks were located in one segment; (2) peak proximity was checked for frequency (< 50 Hz for one segment and < 65 Hz for the second segment); (3) the peak with maximal proximity and amplitude that verifies one and two points was added to the wheeze; and (4) wheezes lasting < 80 ms were not accepted.

The following parameters were computed: (1) mean frequency (hertz) of all detected wheezes, (2) number of wheezes, (3) percentage of time with monophonic wheezes, (4) percentage of time with polyphonic wheezes, (5) percentage of time without wheezes, and (6) absolute change in number of wheezes after bronchodilator dosing. Analysis of variance (ANOVA) for unpaired samples was applied to compare the wheeze parameters of patients with asthma and normal subjects with statistical significance at p < 0.05. ANOVA was followed by Scheffé post-hoc test.

**Results**

Table 1 shows the anthropometric and spirometric parameters for the 16 patients with asthma, 6 patients with COPD, and 15 control subjects. The control subjects were younger than the patients, but the differences were not significant. The asthma

<table>
<thead>
<tr>
<th>Table 1—Anthropometric and Spirometric Parameters of Patients With Asthma and COPD and Control Subjects*</th>
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<tbody>
<tr>
<td>Variables</td>
</tr>
<tr>
<td>------------</td>
</tr>
<tr>
<td>Male/female gender, No.</td>
</tr>
<tr>
<td>Age, yr</td>
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<tr>
<td>Weight, kg</td>
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<tr>
<td>Height, cm</td>
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<td>FVC, L</td>
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<tr>
<td>% predicted</td>
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<td>FEV1, L</td>
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<tr>
<td>% predicted</td>
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<tr>
<td>FEV1/FVC, %</td>
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<tr>
<td>FVC, %†</td>
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<td>FEV1, %†</td>
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*Data are presented as mean (SD) unless otherwise indicated.
† Response to bronchodilator.
patients and COPD patients had moderate-to-severe obstruction (FEV₁ of 40 to 53% predicted). Figure 1 is the time-frequency spectrogram of a patient with asthma, showing activity lines consistent with wheezes over time. An airflow level between 1.2 L/s and 0.2 L/s is represented by a superimposed thin line.

Figures 2 and 3 show, respectively, wheezes in a healthy subject and in a patient with asthma, found by applying the identification and grouping algorithms. The graph shows that patients with asthma had more wheezes than control subjects.

Table 2 and Figure 3 give the wheezing parameters detected in both patient groups (asthma and COPD) and control subjects. We found significant differences between patients and control subjects for the number of wheezes, the mean frequency of all detected wheezes, the percentage of polyphonic wheezes, and the absolute change in number of wheezes after bronchodilator administration. Mean wheeze frequency in hertz was higher in the control group. The relationship between the number of wheezes and FEV₁ for all subjects is shown in Figure 4 to be negative and linear (log wheeze number, 3.69 to 0.77; r = 0.77; r² = 0.59; F = 47; p < 0.0001).

**DISCUSSION**

The main finding of this study was that more wheezes were detected in patients with airway obstruction than in control subjects during forced exhalation maneuvers. Moreover, the change in the absolute number of wheezes after bronchodilator administration was greater in patients with obstructed airways.

The system we developed records wheezes generated throughout the bronchial tree and is based on principles of sound wave propagation. Intraluminal airway lesions and airway wall thickening in patients with airway obstruction produce an increase in intraluminal airflow velocity or eddy-induced wall oscillations affecting a greater number of airways during forced expiratory maneuvers, explaining why wheezing occurs at relatively low airflow in the trachea. In patients with airway obstruction, all airway generations are thickened and all layers of the wall contribute. In humans, airflow limitation develops when increasing transpulmonary pressure is no longer associated with increasing airflow at the mouth, a phenomenon that occurs at flow-limiting choke points when the local wave speed (at which a pressure wave is propagated) is equal to airflow velocity. In normal subjects, airflow limitation only occurs during forced expiration, the only time when a forced wheeze can be generated. In patients with asthma, choke point upstream displacements to smaller airways can be expected during maximal forced exhalation at different lung volumes due to increasing resistance, such that more airways contribute to limit flow and are able to flutter and

![Figure 1. Spectrogram of tracheal sound in a patient with asthma during a forced expiratory maneuver. Wheezes are represented by thick red lines along the time axis. Right: the color spectrum represents the intensity of sound spectrum and is presented in decibels (dB).](image-url)
generate wheezes. Physical characteristics of the airways determine which lower airway generation is able to vibrate, with resonance frequencies ranging from 400 Hz in the upper airway to 1,700 Hz in bronchial airways with a diameter of 3 mm. For airways of 5 mm in diameter, wheeze sound intensity is very low and airways of < 2 mm are unable to transmit sound because the energy is lost as friction heat. We therefore hypothesize that the last bronchial generation that potentially generates wheezes is probably the subsegmentary bronchi of 4 to 5 mm in diameter. The model of Weibel and Gómez\textsuperscript{14} forecasts that from 20 to 50 bronchi can begin to vibrate.

In 1994, Schreur et al\textsuperscript{15} reported findings of no
significant differences in wheezing extension between eight normal subjects and nine symptom-free patients with asthma during maximal exhalation maneuvers. In that study, peaks in the power spectrum were considered wheezes when $> 150$ Hz and at least three times higher than the baseline level. In our study, although time occupied by wheezing was not different for patients and healthy control subjects, we were nevertheless able to detect that more individual wheeze segments occurred in patients with airway obstruction using our modification of the algorithm of Shabtai-Musih et al. Thus, we were able to detect that patients with airway obstruction are producing not a single extended wheeze but rather a series of many wheezes.

Our system of objective sound analysis was also able to detect that the administration of a bronchodilator had a greater impact on the number of wheezes in patients with airway obstruction than in control subjects, and also that wheeze extension decreased more in patients with airway obstruction. Bronchodilators can make an airway begin to vibrate or counter the vibration, either of which are reflected in the absolute change in wheeze number. The severity of airway obstruction determines wheeze number, with lower values of FEV$_1$ percent predicted corresponding to a greater number of wheezes, as previously observed by Marini et al$^1$ in patients with asthma.

The mean ± SD frequency of wheezes for all our subjects (660 ± 189 Hz) was similar to those reported previously for both normal subjects (658 ± 184 Hz)$^{16}$ and patients with asthma (669 ± 100 Hz). However, the mean frequency we detected for control subjects was significantly higher than the frequency for patients, attributable to the fact that we placed microphones near the trachea, whereas previous researchers recorded at the level of the thorax, where high-frequency sounds are attenuated. The decision to record at the trachea was made mainly for convenience, based on the assumption that sounds at that or any other point should reflect sound generated by the system as a whole. Our finding of higher frequencies in control subjects suggests that the generation and/or transmission of wheezes are modified by morphologic changes in the airways and parenchyma of patients with asthma and COPD. We observed no significant differences between COPD patients and asthmatics, although the mean for patients with COPD, at 669.4 ± 250 Hz, was midway between that of asthmatics and control subjects with an approximate difference of 100 Hz between each group. Study of a larger sample might give significant differences. There was no difference in mean frequency after inhalation of the bronchodilator (Table 2). Polyphonic wheezes were also seen to be more numerous in patients with COPD, a finding that is consistent with the greater number of wheeze segments and with wheezes probably originating in different generations. Intraluminal and structural airflow lesions in patients with COPD make airflow limitation or eddy-induced wall oscillations extend to more airways during forced expiratory maneuvers; as a consequence, polyphonic wheezes are understandably more frequent.$^1$

### Table 2—Number, Duration, and Frequency of Tracheal Sounds During Forced Expiratory Maneuvers

<table>
<thead>
<tr>
<th>Variables</th>
<th>Controls Subjects</th>
<th>COPD Group</th>
<th>Asthma Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheeze, No.</td>
<td>2.9 ± 2.0 $^\dagger$</td>
<td>10.4 ± 6.1 $^\dagger$</td>
<td>8.4 ± 6.4 $^\dagger$</td>
</tr>
<tr>
<td>Change in Absolute No. of wheezes</td>
<td>0.5 ± 0.6 $^\dagger$</td>
<td>4.7 ± 5.3 $^\dagger$</td>
<td>2.8 ± 2.2</td>
</tr>
<tr>
<td>Time Without wheezes, %</td>
<td>44.7 ± 40.4</td>
<td>13.7 ± 39.7</td>
<td>22.1 ± 22.7</td>
</tr>
<tr>
<td>Time occupied by monophonic wheezes, %</td>
<td>35.7 ± 29.4</td>
<td>32.6 ± 19.0</td>
<td>55.9 ± 17.7</td>
</tr>
<tr>
<td>Time occupied by polyphonic wheezes, %</td>
<td>15.6 ± 18.3 $^\dagger$</td>
<td>53.6 ± 25.3 $^\dagger$</td>
<td>21.9 ± 15.3 $^\dagger$</td>
</tr>
<tr>
<td>Mean frequency prebronchodilator, Hz</td>
<td>750.9 ± 175.7 $^\dagger$</td>
<td>669.4 ± 250.1 $\ddagger$</td>
<td>560.9 ± 140.8 $\ddagger$</td>
</tr>
<tr>
<td>Mean frequency postbronchodilator, Hz</td>
<td>701.6 ± 170.1</td>
<td>620.6 ± 208.9</td>
<td>538.4 ± 160.5</td>
</tr>
</tbody>
</table>

*Values are mean ± SD of three spirometric maneuvers.

$^\dagger$ Significant for all groups (ANOVA, p < 0.01; F = 6.34).

$^\ddagger$ Significant between control subjects and COPD patients, and between control subjects and asthma patients (Scheffé post hoc test, p < 0.02).
In conclusion, the method that we describe for studying airway behavior during forced expiratory maneuvers is able to identify and analyze wheeze segments generated in patients with obstructed airways, as evidenced by the greater number of wheezes detected in the patient group, which is the main finding of this study. The method also revealed that the mean frequency (hertz) of wheezes is higher in healthy individuals and that the total number of wheezes after bronchodilator inhalation changes more in patients with airway obstruction than in control subjects. The technique is likely to be useful whenever objective analysis is needed in both clinical practice and research.

ACKNOWLEDGMENT: We thank Mary Ellen Kerans and Gary Shivel for language revision, and Sandra Alonso for secretarial assistance.

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Figure 4. The relation between obstruction level (FEV1%) and number of wheezes detected during a forced maneuver was linear for all subjects.