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Lung Sound Analysis for Continuous Evaluation of Airflow Obstruction in Asthma*

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We developed a system for monitoring airflow obstruction noninvasively, based on the principle that the proportion of the breath cycle occupied by wheezing (Tw/Ttot) in any one subject corresponds to the severity of airways obstruction. Lung sounds were recorded continuously from the chest wall. Fifty 250 ms sound segments were randomly chosen from five-minute periods and analyzed for the presence or absence of wheezes. The proportion with wheezes was used as an estimate of Tw/Ttot (Est Tw/Ttot). For 12 wheezy patients, there was a good correlation between the Est Tw/Ttot and the forced expiratory volume in one second ($r=0.893$, $p<0.001$). The system was used to evaluate nocturnal asthma. Five subjects were studied over eight nights. It was found that there was more wheezing from 4:00 to 4:30 AM than from midnight to 12:30 AM ($p<0.05$). This technique may prove useful in continuous, noninvasive monitoring of wheezy patients.

The severity of airflow obstruction in a patient with asthma varies considerably, either spontaneously or as a result of treatment. This variation occurs over hours or even minutes, and is a defining characteristic.[1] Nocturnal asthma is well recognized clinically, and the timing of sudden deaths and of ventilatory arrests in asthmatic patients emphasize the importance of nocturnal increases in severity.[2] Adrenal cortical function, ventilatory response to CO_2, catecholamine levels in the blood, and vagal tone follow circadian cycles which each tend to make asthma worse at night.[3] Circadian rhythms, of which these are examples, should be distinguished from sleep stage related changes in breathing, which have been shown to influence breathing patterns and arterial blood gas partial pressures in patients with chronic bronchitis and emphysema.[4]

Asthmatic patients have been studied by waking them at intervals during the night and having them make a forced expiration, measuring, for example, their peak flow rate.[5] Among patients with chronic airflow obstruction, blue bloaters and pink puffers have been compared by measuring esophageal pressure changes, rib cage and abdominal movements, arterial oxygen saturation or partial pressure, without arousing the patient.[6]

Airflow obstruction in patients with asthma is often associated with wheezing, and we have recently shown, for individual patients, a relationship between the degree of obstruction and the fraction of the respiratory cycle during which wheezing is present.[7] A system has been developed which allows continuous assessment of changes in airflow obstruction by measurement of changes in sounds recorded from the chest wall and analyzed by computer. This allows monitoring for prolonged periods of time without disturbing the patient, for example by waking him; and without requiring some form of test such as a forced expiratory maneuver, which depends on effort and coordination, possibly difficult for a patient wakened during the night.

Methods

The first part of this study was designed to select the method of measuring lung sounds which would provide the best indicator of airflow obstruction. Patients seen in the Pulmonary Division of the University of Cincinnati were asked to participate if they had significant response to bronchodilator drugs documented by pulmonary function tests within the previous four weeks, and were wheezing at the time of the study. Those who agreed signed a written consent form approved by the Human Research Committee. Patients were seated in a quiet room with a contact microphone (Hewlett Packard) strapped to their chest. The microphone was attached to a portable cassette tape recorder. The patient was asked to breathe normally and was left unobserved for 30 minutes.

At the beginning and end of each session, the patient performed forced expiratory maneuvers into a seven-liter water seal spirometer attached to a dedicated microcomputer. Two or three forced maneuvers were performed, and the best forced expiratory volume in one second (FEV_1) was noted. Analysis of the recorded sounds was directed at testing several methods for estimating wheezing, and comparing the values obtained with the airflow obstruction measured by pulmonary function tests.

Some patients, chosen by availability, were asked to return to the laboratory at night, and once again, a contact microphone was attached to their chest wall. A stretch vest with impedance plethysmograph bands and an ear oximeter were used to measure ventilation and oxygen saturation. The signals from the microphone, the Respitrace sum, chest wall, and abdomen signals, and the oxygen saturation were recorded on a multichannel tape recorder.

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Table 1—*Results of Pulmonary Function Tests Obtained Within Four Weeks of Study*

Subject	Age	Before Bronchodilators FEV_1, L	After Bronchodilators FEV_1, L
1	42	1.20	1.58
2	50	1.00	1.36
3	23	.81	1.08
4	62	1.58	1.92
5	52	.90	1.25
6	40	.80	1.19
7	22	.97	1.32
8	52	.83	1.02
9	49	.77	1.21
10	50	1.11	1.50
11	55	1.20	1.50
12	31	1.41	1.80

Table 2—*Accuracy of Estimated Tw/Ttot Using Analysis of Variance: Effect of Varying the Number of Samples*

No. Samples	Intersubject Variation (F ratio)	Intrasubject Variation (F ratio)
5	7.27	1
25	10.76*	0.38
50	39.37†	1.28
75	90.13†	.23

*$p<0.05$
†$p<0.001$

The patient was studied through the night, from 11 PM to 6 AM. Standard polysomnographic recordings were used for sleep staging.[8] Pulmonary function tests were performed at the beginning and end of the sleep study.

The recorded sound signal was subsequently analyzed. Several methods for sampling and for wheeze detection were investigated. Five minutes of sound was chosen as the time period to be analyzed. Two hundred and fifty millisecond segments of the sound signal were analyzed using the Fast Fourier Transform (FFT).[7] The sound signal was digitized at 2,048 samples per second, and a FFT was performed on 250 ms segments using a spectrum analyzer. The frequency spectrum was stored in a controlling computer for later analysis. Random segments were selected from each five-minute period.

Each spectrum was analyzed for the presence or absence of a peak at a frequency between 150 and 1,000 Hz. The number of spectrums with peaks divided by the total number of spectrums analyzed over the five-minute period was an estimate of the duration of wheezing present during the five minutes (Est Tw/Ttot).

The linear correlation coefficient between Est Tw/Ttot and FEV_1 was determined using the least squares technique. The F-test for simple effects was applied to determine the variation within subjects and between subjects. Comparisons between groups were tested for significance, using the Mann-Whitney U-test. A p value of less than 0.05 was considered significant.[9]

Table 3—*Accuracy of Estimated Tw/Ttot: Effect of Varying the Minimum Peak Height*

Peak Height Compared to Baseline	Correlation Est Tw/Ttot vs FEV_1	Intersubject Variation (F Ratio)
2 times	.898*	43.3*
3 times	.893*	55.0*
5 times	.767*	28.1†
8 times	.641†	14.5‡

*$p<0.001$
†$p<0.005$
‡$p<0.01$

Results

Twelve subjects were studied. All were wheezing at the time of study and all had moderate-to-severe airways obstruction with an FEV_1 between 720 ml and 1,500 ml. Table 1 shows the FEV_1 on pulmonary function tests done before and after bronchodilators, performed within four weeks of the lung sound recording.

Five five-minute periods of observation were studied in each patient. To determine the most efficient number of samples to be randomly chosen, we compared 5, 25, 50, and 75 samples per five-minute period. As shown in Table 2, the ratio for intersubject variation was significantly greater when 50 segments were analyzed rather than five segments. The addition of 25 more segments did not appear to add any additional information. We chose to analyze 50 segments per five-minute period.

Comparing sounds with corresponding spectrums, we found that an audible wheeze was associated with a peak with a narrow frequency band and a frequency between 150 and 1,000 Hz as noted previously.[7] Figure one shows two segments of the sound signal, one with and one without a peak. The FFT of the sound signal associated with a wheeze always had a peak similar to that seen on the left in Figure 1.

The minimum peak height to be considered as a wheeze was studied. Table 3 compares Est Tw/Ttot with FEV_1, using different criteria for peak height.

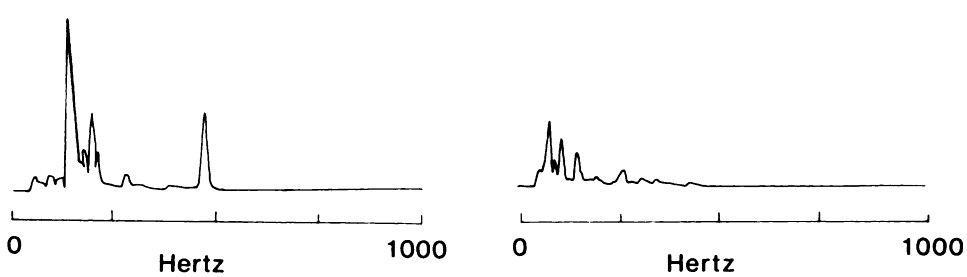

FIGURE 1. Frequency spectrum of 250 ms of sound signal. Left panel reveals a sharp peak at 490 Hz corresponding to an audible wheeze. Right panel has no significant frequency peaks above 150 Hz.

Table 4—*Estimated Tw/Ttot for Patients*

FEV_1, L	Estimated Tw/Ttot (%) For Each Five Minute Segment				
1.20	20	24	18	26	30
1.20	18	22	30	36	24
1.00	22	36	28	54	32
1.50	4	2	4	4	6
1.36	8	6	4	10	4
.80	56	36	50	48	48
.97	42	42	32	50	32
1.30	18	10	10	4	6
.72	66	60	66	74	72
.85	46	42	40	44	42
1.20	20	22	18	26	16
1.29	32	28	20	18	24

Among patients, a significant correlation was found between the FEV_1 and the percentage of segments with peaks three or more times baseline (Est Tw/Ttot) as shown in Figure 2 ($r = .89$, $p<0.001$). Table 4 shows the estimated Tw/Ttot for each subject for all five five-minute segments. All peak heights shown were associated with a significant correlation with FEV_1, but the use of three times baseline as the minimal peak value was associated with the highest F ratio on analysis of variance comparing intersubject vs intrasubject variation.

Five subjects underwent eight sleep studies. None showed significant desaturation during the night. No patient had apnea. Figure 3 shows the sleep stages and wheezing of one patient. The percentage of wheezing (Est Tw/Ttot) for every five-minute period from 11 PM to 6 AM is shown. There are several time intervals during the night when there was little wheezing and other times with a large amount of wheezing.

Previous studies have compared airflow obstruction at midnight and at 4 AM.[3] The Est Tw/Ttot from midnight to 12:30 AM was compared with that from 4:00 to 4:30 AM for the eight sleep studies (Fig 4). More wheezing, and therefore more obstruction, was found between 4:00 and 4:30 AM ($p<0.05$).

Discussion

Monitoring of asthma patients for bronchoconstriction has often relied on the use of pulmonary function tests such as the PEFR.[2,5,10] Noninvasive attempts to measure respiratory obstruction have included the use of ear oximetry.[11] Although oximetry is a useful method, it is insensitive except when severe abnormalities are present.[12] It is therefore of limited value in moderate asthma. In the present study, no patient had significant desaturation while asleep.

Martin et al[13] have documented the number of wheezing episodes, night and day, in hospitalized asthmatic patients. They found increased wheezing at night, using wheezing as a measure of airflow obstruction.

We have previously noted that wheeze duration (as a proportion of the respiratory cycle duration: Tw/Ttot) and frequency of the sound signal were associated with the degree of bronchospasm, but wheeze sound intensity was not.[7] We have developed a computer algorithm to establish whether wheezes were or were not present during random samples of the breath cycle, and thus, to estimate the percentage of time in which wheezing occurs. This study demonstrates the correlation between this estimated Tw/Ttot and the level of airways obstruction observed.

Random segments of sound signal were studied to assure that there was no bias towards any portion of the respiratory cycle. A computer program was used to analyze each segment of the sound signal and deter-

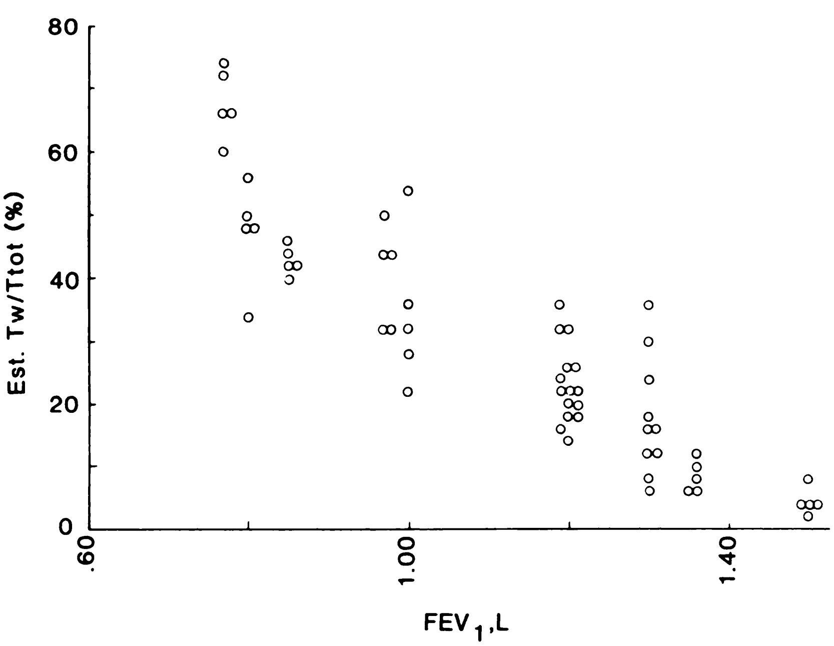

FIGURE 2. Comparison of FEV_1 to the estimated Tw/Ttot ($r=0.89$, $p<0.001$).

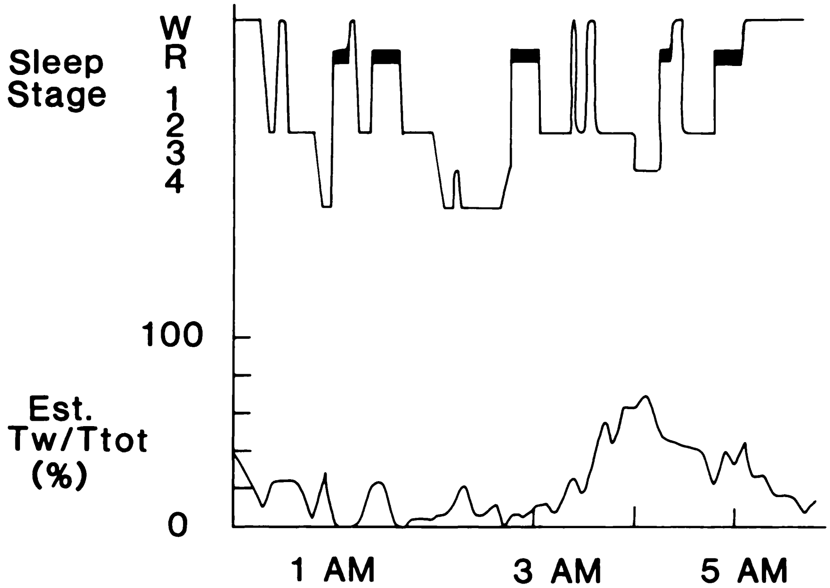

FIGURE 3. One subject studied through night. Study began at midnight. Lower panel is estimated Tw/Ttot. Upper panel shows corresponding sleep stage (W is awake; R, REM sleep; 1-4, sleep stages 1 to 4).

mine whether a peak was present. However, analysis of sound signals must include other sounds recorded, such as those associated with body movement, speech, and external noises in the room. These noises could contain tones which could lead to mistaking a peak on sound signal analysis as a wheeze. Table 3 shows the results of varying the minimal peak associated with a wheeze. Using the most sensitive value may lead to noise being accepted as wheezing, and thus, an Est Tw/Ttot which would be inappropriately high. The fact that a relationship is seen between the FEV_1 and the Est Tw/Ttot at the highest sensitivity is not surprising, since Forgacs et al[14] have noted a correlation between noisy breathing heard at the mouth and obstructive airways disease. On the other hand, if we are too discriminating, we may reject peaks which do represent wheezes. This appears to occur when peaks are counted as wheezes only when nine or more times the baseline. Accepting as wheezes peaks which were three or more times baseline led to a good correlation with FEV_1, as well as the one most sensitive to intersubject variation.

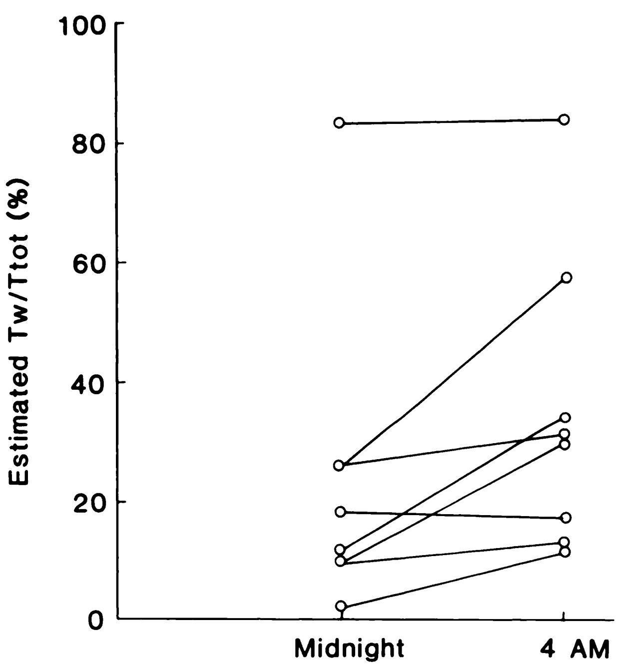

FIGURE 4. Est Tw/Ttot for Midnight to 12:30 AM vs 4:00 AM to 4:30 AM ($p<0.05$).

Wheezing depends on flow-rate and volume, and the five-minute sample contains breaths which vary in both of these respects. However, over a five-minute time period, this appears to even out. Different sets of 50 samples from a five-minute time period provide similar estimates of Tw/Ttot. Over 30 minutes, there was no significant change in the Est Tw/Ttot for different five-minute periods if the FEV_1 remained the same.

Asthma has been shown to follow a circadian pattern in some patients, with the worst obstruction occurring at around 4 AM.[3] Several possibilities have been suggested as a cause, including a rise in serum histamine levels with a fall in serum cortisol and epinephrine level.[15]

Our studies are consistent and confirm the worsening of asthma at 4 AM. This worsening of bronchospasm was demonstrated without awakening the patient, and therefore, could not be attributed to poor patient compliance in performing a test such as the PEFR.

In summary, we report a method of externally monitoring wheezes. Analysis of the lung sounds for the amount of wheezing in the breath cycle correlated with the FEV_1. In the asthmatic patient, more wheezing was noted between 4:00 and 4:30 AM than earlier in the evening.

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