Oscillatory Mechanics of the Respiratory System in Neuromuscular Disease*

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Respiratory impedance measurements by means of the technique of forced oscillations together with spirometry and measurements of maximal mouth pressures were performed in 27 patients with a variety of neuromuscular disorders to assess the value of adding respiratory impedance measurements in the evaluation of lung function and the influence of neuromuscular disease. Using the technique of forced oscillations, impedance measurements are easily performed in physically disabled persons, since they require little active cooperation and no forced respiratory maneuvers. Normal respiratory impedance characteristics were found, although resistance values were somewhat higher than those found in normal subjects, signifying the absence of airflow limitation. Spirometric values were markedly reduced, as were maximal mouth pressures. No significant correlations were found between the forced expiratory volumes in 1 s (FEV,) and the impedance data. A strong curvilinear relationship was observed between PEmax and the RV/TLC ratio and a strong correlation existed between FEV, and PEmax. It is concluded from our study that forced oscillometry is a useful tool for the assessment or exclusion of airflow obstruction in patients with neuromuscular disorders when plethysmography is difficult to perform and forced expiratory flow-volume data reflect muscle weakness rather than airflow limitation. (Chest 1992; 102:1752-57)

In patients with neuromuscular disorders, respiratory impairment is often an early sign of progressive disease.1-3 It is therefore important to evaluate lung function in patients with neuromuscular disorders during the course of the disease. Generally, lung function measurements in these patients reflect respiratory muscle strength2-6 and little information on the mechanical characteristics of the respiratory system can be obtained. Thus, concomitant airflow obstruction can remain unnoticed. The use of maximum expiratory flow volume (MEFV) curves to detect airflow obstruction in patients with muscular weakness can be hampered by several limitations. In general, the MEFV curve is partitioned into an effort-dependent and an effort-independent part,6 based on the presence of an equal pressure point. The occurrence of an equal pressure point requires the generation of a critical pleural pressure. It can be hypothesized that a pleural pressure build-up high enough to generate an equal pressure point is impaired in severe neuromuscular weakness. In that case, flow-volume data reflect the expiratory driving pressure rather than airflow resistance-derived airflow limitation over a larger part of the expired volume.

Furthermore, the elastic recoil pressure largely determining maximum expiratory flow in the effort-independent phase of the MEFV curve is thought to be reduced in neuromuscular weakness.5 A similar phenomenon is observed in normal subjects in rib cage strapping.7 With the use of the body plethysmograph, airway resistance can be measured, but this procedure requires complex equipment and is time consuming. Furthermore, patients with neuromuscular disorders may be immobile and unable to sit in a body plethysmograph without support and to undergo measurements while panting.

The technique of forced oscillations8 may be of particular value in the evaluation of respiratory mechanics in patients with neuromuscular disorders. The measurements can be performed in patients in a wheelchair. No forced respiratory maneuvers are necessary for the measurements, since these are performed during spontaneous quiet breathing, and no active cooperation is required from the patient. Using modern computer techniques, forced oscillations with various frequencies can now be applied simultaneously and the analysis of pressures and flows at these frequencies is possible using fast Fourier techniques.

The aim of the present study was to analyze the oscillatory mechanical characteristics of the respiratory system using forced oscillations and to compare

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these findings with spirometric and maximal mouth pressure measurements in patients with neuromuscular disorders.

**Materials and Methods**

*Patient Selection*

We studied 27 patients with various neuromuscular diseases. A summary of the patient characteristics is presented in Table 1. All patients were suffering from advanced stages of neuromuscular disease and were referred to the Department of Pulmonary Diseases with the purpose of screening for long-term mechanical ventilatory support. Two of the patients were current smokers (patients 5 and 9), one was an ex-smoker (patient 20, 30 pack-years), and all others were life-long nonsmokers. All patients denied symptoms of asthma, more specifically episodic breathlessness with perceptible wheezing, and none of the patients used any form of bronchodilating medication. As is evident from Table 1, the majority of the patients had some degree of kyphoscoliosis and in five patients a surgical correction for kyphoscoliosis by means of spondylodesis had been performed at an earlier stage of the disease.

**Lung Function Measurements**

Forced expiratory volume in 1 s (FEV₁) and inspiratory vital capacity (IVC) were measured using a wet spirometer (Gould Pulmonary III) with the patients in a seated position, and the highest value from three maneuvers is reported and compared with reference values. Because a flexion deformity in kyphoscoliosis systemically reduces the height of the patient, results were related to predicted arm-span in all patients. Functional residual capacity (FRC) was determined by a closed circuit helium dilution method. Residual volume (RV) was calculated as the difference between TLC and IVC. In order to rule out bronchospasm contributing to eventually existing abnormalities, reversibility was tested after the inhalation of 0.5 mg terbutaline (from a Turbuhaler). The impedance of the respiratory system was measured with the technique of forced oscillations. This technique allows the determination of the impedance of the respiratory system at various frequencies simultaneously.

Briefly, a pseudo random-noise signal containing all harmonics of 4 Hz up to 52 Hz (4, 5, 12...52 Hz) appearing with random phase shift, repeated every 0.25 s, is applied at the mouth of the seated subject, who is instructed to breathe quietly and to support the cheeks and the floor of the mouth with both hands. The impedance (Z) of the respiratory system (s) obtained from pressures and flows measured at the mouth at each of the investigated frequencies is partitioned into a real part or resistance (R) and an imaginary part or reactance (X). The reactance depends on the elastic and inertial properties of the system: at lower frequencies, the reactance is negative because at lower frequencies it is influenced mainly by the capacitance of the system. At higher frequencies, the inertial properties dominate Xₛ; the latter is then positive. The frequency at which reactance is zero is called the resonant frequency: the influence of capacitance and inductance on Xₛ cancel out at the resonant frequency. Only impedance values with a
coherence function equal to or exceeding 0.95 were retained. This function indicates the reliability of the derived values and is the equivalent in the frequency domain of the correlation coefficient used in the time domain. A more detailed description of this technique is presented elsewhere.9

Values for \( R \) at 8 Hz (\( R_{8\Omega} \)) and at 28 Hz (\( R_{28\Omega} \)), of \( X \) at 8 Hz (\( X_{8\Omega} \)), of resonant frequency \( f_0 \), and of the frequency dependence (FD) of resistance were used for the study. FD was defined as \( R_{28\Omega} \) minus \( R_{8\Omega} \) divided by 20. This value stands for the slope of the resistance versus frequency curve. Each impedance measurement lasted 8 s and the values of three measurements were averaged to be used in the study.

Maximal inspiratory and expiratory mouth pressures were obtained using the method described by Black and Hyatt.10 Pimax and Pemax were measured in triplicate. The highest (expiratory) and lowest (inspiratory) values were recorded. The values for Pimax were expressed as a positive number. In all instances, the impedance measurements preceded spirometry and the measurements of respiratory muscle strength.

Linear regressions were calculated between the findings of spirometry and maximal mouth pressures and between spirometry and the impedance parameters.

RESULTS

In all patients, the spirometric, mouth pressure, and impedance measurements could be easily performed while the patients remained seated in their wheelchairs. In Table 1, the physical characteristics and the indices of respiratory impedance, maximal mouth pressures, and ventilatory function are listed. For the total group, reduced values for IVC and FRC are found. Mean IVC as a percentage of predicted was 61.0 percent \( \pm \) 31.3 percent and mean FRC was 82.1 percent \( \pm \) 19.4 percent. The FEV1 was 60.0 percent \( \pm \) 31.2 percent of predicted. The mean baseline FEV1 was 1.94 \( \pm \) 0.97 L; after inhalation of terbutaline, mean FEV1 was 1.93 \( \pm \) 0.96 L. Residual volume (RV) averaged 108.9 \( \pm \) 32.5 percent predicted and mean RV/TLC ratio was 42.8 \( \pm \) 14.4 percent. As is shown in Table 1, muscle strength varied widely; mean Pmax was 4.27 \( \pm \) 2.24 kPa and Pemax was 3.74 \( \pm \) 2.33 kPa. The mean Pmax/Pemax ratio averaged 1.14 \( \pm \) 0.36. \( R_{ns} \) (0.380 \( \pm \) 0.136 kPa/L/s) was found to be lower than \( R_{res} \) (0.427 \( \pm \) 0.127 kPa/L/s) and thus, a positive value for the frequency dependence of resistance was found. Mean reactance at 8 Hz (\( X_{8\Omega} \)) was \(-0.058 \pm 0.070\) kPa/L/s and resonant frequency averaged 10.81 \( \pm \) 3.21 Hz.

Correlations between FEV1 and IVC and the various impedance parameters were not statistically significant (\( p \geq 0.05 \)).

Table 2 lists the coefficients of correlation between the results of spirometry and the maximal respiratory pressures in our patients. A strong correlation was found between FEV1 as a percentage of predicted and Pemax (\( r = 0.79, p < 0.0001 \)) and an equally strong correlation was found between the IVC (percent predicted) and Pemax. Correlations between Pemax and Pmax and total lung capacity and functional residual capacity were slightly lower, but still highly significant (\( p < 0.001 \)). A highly significant correlation was found between the RV/TLC ratio and Pemax (\( r = -0.67, p < 0.0001 \)), but as is shown in Figure 1, an even better logarithmic fit to the data was observed (\( r = 0.71, p < 0.0001 \)). Furthermore, a strong correlation was calculated between Pemax and FEV1 (\( r = 0.79, p < 0.0001 \)).

DISCUSSION

We have studied the oscillatory mechanics of the respiratory system in combination with maximal mouth pressures and spirometry in 27 patients with various neuromuscular disorders. The oscillatory mechanics were studied by means of the forced oscillations technique. The measurements require neither forced respiratory maneuvers nor active cooperation from the subject, and the data related to the mechanical properties of the respiratory system can be collected rapidly in a noninvasive way. Indeed, all measurements could be performed in the severely disabled persons in our study without difficulties, with the subjects seated in their wheelchairs.

When applying the technique of forced oscillations in these patients, it was observed that the resistance of the respiratory system increased slightly with

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Table 2 — Correlation Coefficients between Maximal Mouth Pressures and Spirometric Indices

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<td></td>
<td>( r )</td>
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<tr>
<td>IVC, %pred</td>
<td>0.79</td>
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<tr>
<td>FEV1, %pred</td>
<td>0.79</td>
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<tr>
<td>TLC, %pred</td>
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<td>FRC, %pred</td>
<td>0.34</td>
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<td>RV/TLC, %</td>
<td>0.67</td>
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* \( 0.0001 < p < 0.001 \).
† \( 0.001 < p < 0.01 \).
‡ \( p \leq 0.01 \).

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**Figure 1.** Relationship between RV/TLC and Pemax. The curve is the logarithmic fit to the data (\( r = -0.71, p < 0.0001 \)).
increasing frequency. Also, a marginally negative value for $X_n$ at 8 Hz was observed, while resonant frequency was within the normal range. Thus, in these patients with severe neuromuscular weakness, respiratory impedance vs frequency curves are similar to those found in normal subjects. Clément et al.\(^{12}\) reported that in normal subjects, the oscillatory resistance increases with increasing frequency, whereas reactance is negative only at lower frequencies and becomes positive at frequencies between 8 and 10 Hz. In patients with airflow obstruction, however, resistance is higher at lower frequencies and decreases with increasing frequencies. This phenomenon is called negative frequency dependence of resistance. In these patients, reactance remains negative up to higher frequencies, usually between 20 and 24 Hz, or sometimes as high as 38 Hz in severe COPD.\(^{13}\)

It should be kept in mind that this normal impedance vs frequency pattern observed in our study is found in the presence of moderate to severe kyphoscoliosis in the majority of our patients. This is contrary to findings reported by Van Noord et al.\(^{14}\) These investigators analyzed the respiratory impedance in patients with kyphoscoliosis and a severe restrictive lung function impairment. They found a negative frequency dependence of reactance and much higher values for resonant frequency than was found in our study. Using an electric analog of the respiratory system, including the upper airways, the intrathoracic airways (including compliance and resistance of the airway walls), lung alveoli, compressibility, and the chest wall, Van Noord et al\(^{14}\) concluded that changes in chest wall mechanics play an important role in the impedance values in kyphoscoliosis.

A satisfactory fit was possible in the kyphoscoliosis group when chest wall tissue resistance was increased to 0.6 kPa/L/s and chest wall compliance decreased to 0.08 L/kPa; lung compliance was 0.9 L/kPa in that calculation. This resistance of the chest wall ($R_w$) is very much higher than is found in normal subjects and in patients with COPD: the value measured by Nagels et al\(^ {15} \) was 0.054 kPa/L/s. Similar values were reported by Grimby et al\(^ {16} \) and by Sharp et al.\(^ {17} \) In normal subjects, Nagels et al\(^ {15} \) measured a value for chest wall compliance ($C_w$) of 0.45 L/kPa: the proposed value for chest wall compliance by van Noord et al\(^ {14} \) is 40 times lower, and the value for $C_w$ proposed by Nagels et al\(^ {15} \) was already lower than found in most publications. Naimark and Cherniack\(^ {18} \) measured a value of 2.45 L/kPa in the sitting position and 2.08 L/kPa in the supine position for $C_w$. This value is comparable to that found by Sharp et al.\(^ {17} \) In younger subjects, Mittman et al\(^ {19} \) measured even higher values for $C_w$ (4.75 L/kPa) and a significant decrease in $C_w$ with age (1.96 L/kPa for subjects aged 70 to 79 years). A low value for the thoracic wall capacitance was also calculated by Dubois et al\(^ {10} \) (0.18 L/kPa) and by Michaelson et al\(^ {20} \): assuming a static lung compliance of 2 L/kPa, these authors calculated an average $C_w$ of about 0.5 L/kPa. Van Noord et al\(^ {14} \) explained this discrepancy in $C_w$ values by the behavior of the chest in oscillatory mechanics as a system, consisting of two compartments coupled in parallel: the rib-cage and the abdomen-diaphragm; the rib-cage, which is stiffer, should have a shorter time-constant than the diaphragm-abdomen.

The changes in lung mechanics in clinical disorders of the chest wall, for instance kyphoscoliosis, can be simulated by chest wall strapping in normal subjects. Van Noord et al\(^ {21} \) demonstrated an increase in $R_w$ at lower oscillatory frequencies between 4 and 14 Hz, resulting in a negative frequency dependence of resistance.

$X_w$ was decreased at lower frequencies, resulting in an increase in resonant frequency from 6.3 to 10.6 Hz. By partitioning total respiratory impedance into its pulmonary and chest wall components, these authors found an increase in $R_w$ at lower frequencies, resulting in a more pronounced frequency dependence of $R_w$ and a small increase in lung tissue resistance ($R_t$), mainly at lower frequencies. However, thoracic strapping only resulted in a twofold to threefold increase in $R_w$ and a decrease in chest wall reactance to a minimal value of $-0.12$ kPa/L/s. These values are markedly different from the data calculated by the same authors in a group of patients with kyphoscoliosis.\(^ {14} \) It is noticed that the changes in the static lung volumes were higher in the patients with kyphoscoliosis.

However, as demonstrated by DeTroyer et al,\(^ {2} \) thoracic strapping has a less pronounced stiffening effect on the chest at lower than at higher lung volumes. A markedly decreased lung compliance ($C_L$) was measured in the patients with kyphoscoliosis by van Noord et al.\(^ {14} \) An average decrease in $C_L$ of 40 percent was also found by DeTroyer et al\(^ {2} \) in patients with respiratory muscle weakness, suggesting changes in the elastic properties of the lung. Comparable findings of a markedly reduced $C_L$ in patients with respiratory muscle weakness were found by Gibson et al,\(^ {3} \) and these authors pointed out that these changes were similar to those seen in normal subjects in whom chest wall expansion is prevented by means of strapping. However, by relating the slope of the pressure-volume (P-V) curve to the measured TLC, DeTroyer et al\(^ {2} \) found a normal slope of the P-V curve, suggesting that in patients with long-standing respiratory muscle weakness, the largest number of the functioning alveoli retain their normal elastic properties. During submaximal neuromuscular blockade, DeTroyer and Bastenier-Geens\(^ {22} \) found that weakness of the respiratory muscles is not associated with alterations in surface
forces despite the associated low breathing volume and does not directly influence the elastic properties of the lung. Baydur recently reported an increase in the elastance of the respiratory system (Ers) of 79 percent in patients with neuromuscular disease: he also concluded that the increase in Ers was proportional to the loss of lung volume rather than to intrinsic abnormalities.

The changes in static lung volumes observed in our group of patients with neuromuscular disease are comparable with the changes observed after rib-cage strapping. Based on these data of van Noord et al., a normal respiratory impedance pattern in the measured frequency range of 8 to 28 Hz as found in our study can be expected. When the increase in the thoracic wall resistance is proportional to the decrease in chest wall compliance, the time constant of the rib cage will remain unchanged and no increase in the difference in time constants between the rib cage and the diaphragm-abdomen will be observed. Thus, frequency dependence of resistance will not be found. Slightly increased resistance values are found in our patients. Previously it has been reported that specific airway conductance is within the normal range or slightly above the normal upper limit in patients with neuromuscular disease. In the absence of time constant inhomogeneities, total respiratory resistance will be determined by airway resistance, tissue resistance, and chest wall resistance. An increase in lung tissue resistance was observed after chest wall strapping. The influence on chest wall resistance was discussed above.

Reduced maximum respiratory pressures and reduced lung volumes as measured with spirometry are a common finding in patients with neuromuscular disease, and the values for Pmax and Pemin measured with the technique described by Black and Hyatt and for the spirometric values found in our patients are in keeping with those published by others. Inspiratory muscle weakness may result in hypoventilation and expiratory weakness interferes with coughing. The ratio Pmax/Pemin represents the relative effectiveness of the inspiratory and expiratory musculature.

In normal subjects, a value of 0.5 is reported. The mean Pmax/Pemin ratio of 1.14 ± 0.36 in our patients with neuromuscular disease was much higher, indicating a more pronounced loss of expiratory muscle strength in these patients. This is consistent with the findings of others in patients with Duchenne's dystrophy and myotonic dystrophy, and myasthenia gravis. Braun et al. found that in patients with proximal myopathies, the deficit in respiratory muscle strength was evenly distributed between inspiratory and expiratory muscles.

Despite the reduced lung volumes, an increase in RV is observed, indicating inability of the impaired expiratory musculature to exhale below FRC resulting in a loss in expiratory reserve volume. A strong curvilinear correlation was calculated between RV/TLC and Pemin. A similar relationship has been described previously. From the strong correlations between spirometric and mouth pressure values found in this and earlier studies, it can be concluded that the lung volume abnormalities in patients with neuromuscular disease reflect reduced respiratory muscle strength rather than airflow obstruction.

In summary, we conclude from our study that impedance measurements of the respiratory system using the technique of forced oscillations allow the demonstration of normal relationships between resistance and reactance of the respiratory system and the frequencies of the forced oscillations indicating the absence of airflow limitation resulting from bronchus obstruction, even in the presence of impaired respiratory muscle strength, gross thoracic wall abnormalities, and reduced lung volumes. Forced oscillometry is therefore a helpful tool in the assessment of lung function and the exclusion of airflow obstruction in patients with neuromuscular disorders when body plethysmography is difficult to perform and spirometric data reflect muscle weakness rather than airflow limitation.

REFERENCES