Total Resistance and Reactance in Patients with Respiratory Complaints with and without Airways Obstruction

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A comparison was made of the frequency dependence of total respiratory resistance, (Rrs), and reactance (Xrs), determined by a forced oscillation technique in 442 healthy subjects and in 126 patients with respiratory complaints, with or without slight airways obstruction. The comparison was performed by means of a discriminant analysis. The latter demonstrated that the Rrs and Xrs data, measured between 5 and 24 Hz, of patients differ from those of healthy subjects primarily by a decrease of Rrs with frequency associated with more negative Xrs (and thus with an increase in resonant frequency). This probably also applies to patients with more advanced airways obstruction. The addition of the FEV1 values to the analysis provides only a small amount of independent information. The forced oscillation technique thus appears to be a sensitive tool to separate healthy subjects (smokers and nonsmokers) from patients with respiratory complaints associated or not with a reduced FEV1.

Several investigators suggested that the frequency dependence of total resistance, and the resonant frequency of the respiratory system, measured by the forced oscillation technique, might be sensitive indicators of early airways obstruction.

So far, little is known about the extent with which resistance, (Rrs), and reactance (Xrs), vs frequency (f), curves may deviate from the average "normal" course observed in healthy subjects. It has been shown that the values of Rrs and Xrs in normal individuals depend on weight, height, age, and smoking habits. However, taking into account these influences reduces only slightly the scatter of the data. Besides, it is difficult to evaluate by eye the importance of distortions of the shape of the Rrs and Xrs-f curves. These difficulties may be overcome by performing a discriminant analysis on the Rrs and Xrs-f functions, comparing a sample of healthy subjects with one of the patients. This technique is used in the present study to investigate which features of the Rrs and Xrs-f functions are characteristic for patients with complaints of shortness of breath and/or cough and sputum, associated or not with airways obstruction.

**METHOD AND MATERIAL**

**Technique**

The technique has been described in detail in another publication. The seated subject supports his cheeks with his hands and breathes quietly via a screen pneumotachograph through a low impedance side tube; a bias flow reduces the CO2 build-up at the mouth. Simultaneously, a pseudo-random noise pressure signal, containing all harmonics of 2 Hz to 24 Hz with a peak-to-peak amplitude smaller than 0.2 kPa, is applied at the mouth by means of a loudspeaker. Mouth pressure and airflow, recorded by two identical differential transducers (Validyne MP 45) (±0.2 kPa) are fed into a Fourier analyzer. The latter performs an ensemble averaging over a time interval of 15 seconds (s), to average out the disturbing signals produced by the subject's breathing, and calculates the impedance of the respiratory system at 2, 4, 6 . . . 24 Hz. That impedance is partitioned into a real and an imaginary part. The real part, or resistance, Rrs, is the equivalent of a total resistance in a resistance-inductance-capacitance (R-L-C) circuit. The imaginary part or reactance, Xrs, depends on the elastic and inertial properties of the system: at lower frequencies, the reactance is negative because it is influenced mainly by the capacity of the system. At higher frequencies, the inertial properties dominate Xrs: the latter is then positive. The frequency at which Xrs equals zero is called the resonant frequency: in a R-L-C circuit, the influences of capacitance and inductance on Xrs cancel out at the resonant frequency.

The accuracy of the computations is evaluated at each frequency by means of a coherence function. The latter indicates the amount of noise generated by the subject's spontaneous breathing present in the measured signals. Only these Rrs and Xrs values with coherence functions exceeding or equal to 0.95 (1.00 meaning a complete absence of noise or linealities) were retained. In patients with increased respiratory impedance, the forced oscillatory flow is reduced. Accordingly, the signal to noise ratio is less favorable at the frequencies containing a significant amount of respiratory signal: in many patients, the coherence function of measurements between 2 and 6 Hz turned out to be lower than 0.95. Therefore, only the data between 8 and 24 Hz were used in the main part of the study. No correction was applied for the shunt characteristics of the cheeks. Though the latter may affect the shape of the Rrs-f and Xrs-f curves differently in healthy subjects and in patients, and thus influence the results of the computations, the validity of the discriminant analysis is not impaired. It is only in the interpretation of the factors distinguishing healthy subjects from patients that the influence of the cheeks should be taken into account.

Three successive measurements, each lasting 15 s, are performed in every subject. The vital capacity (slowly expired), VC, and FEV1 are measured by means of conventional spirometry. The highest value of three maneuvers is retained.
Table 1—Characteristics of the Investigated Subjects

<table>
<thead>
<tr>
<th>Samples</th>
<th>N</th>
<th>Mean (yrs)</th>
<th>Range</th>
<th>Height (cm) Mean ± 1 SD</th>
<th>FEV₁ (l) Mean ± 1 SD</th>
<th>Percent Expected ± 1 SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>442</td>
<td>29.4</td>
<td>15-57</td>
<td>176.1 ± 6.1</td>
<td>4.36 ± 0.57</td>
<td>101.4 ± 10.8</td>
</tr>
<tr>
<td>B</td>
<td>83</td>
<td>28.0</td>
<td>16-57</td>
<td>173.6 ± 6.8</td>
<td>4.02 ± 0.71</td>
<td>98.8 ± 14.5</td>
</tr>
<tr>
<td>C</td>
<td>43</td>
<td>35.6</td>
<td>18-57</td>
<td>173.5 ± 7.3</td>
<td>2.77 ± 0.60</td>
<td>67.6 ± 8.4</td>
</tr>
<tr>
<td>D</td>
<td>26</td>
<td>45.8</td>
<td>22-57</td>
<td>171.2 ± 6.8</td>
<td>1.25 ± 0.47</td>
<td>33.9 ± 10.7</td>
</tr>
</tbody>
</table>

**Investigated Subjects**

The group of healthy subjects (sample A) consists of 442 male subjects, 15 to 57 years old, free of complaints and with normal results on clinical examination. In all subjects, VC and FEV₁ were within normal limits (80 percent or more of expected). Since a previous study demonstrated only minimal differences in Rrs and Xrs values among smokers and nonsmokers in this group, the smoking habits were not taken into account.

Three groups of patients were considered. All were males, aged between 16 and 57 (Table 1). The first group (sample B) consists of 83 men with complaints of recurring wheezing (and/or dyspnea) (73 subjects) or cough and expectorations (10 subjects), or both (39 subjects). The dyspnea was generally episodic, elicited by exposition to certain substances, exercise, or following respiratory infections. A hyperventilation syndrome was not accepted as a criterion. Skin hypersensitivity and positive RAST tests, investigated in 71 subjects, were present in 53. Vital capacity and FEV, were within normal limits. The second group (sample C) is made up by 43 subjects, suffering from chronic obstructive pulmonary disease (COPD) or asthma, with a moderate reduction of FEV₁ (50 percent to 77 percent of expected). Finally, 26 subjects with severe COPD (FEV₁ less than 50 percent of expected) (sample D) were investigated.

**Statistical Analysis of the Data**

In every subject, i, calculations were made of the mean value and the average of the first four derivatives of Rrs and Xrs vs frequency, between 8 and 24 Hz, following the technique described in a previous paper. These data were compared with the corresponding normal values, determined as a function of the subject’s height, weight, and age. The individual differences, D, between observed and predicted means and successive derivatives of Rrs and Xrs (Rrs, Rrs¹, Rrs², Xrs, Xrs¹, Xrs²) were used for a discriminant analysis. The latter combines the D, values in a linear equation:

\[ y_i = \alpha D_1(Rrs) + \beta D_2(Rrs^2) + \ldots \]  (I)

the weighing coefficients \( \alpha, \beta \ldots \) being calculated by a method which achieves an optimal discrimination between the individual \( y_i \) scores of patients as compared with those of healthy subjects. The mean of the scores in the sample of healthy subjects (sample A) is zero: indeed, this sample has been used as a reference to calculate the prediction equations (thus, the average of their D, values should be zero). A negative discriminant score \( y_i \) is observed in patients: when a given \( y_i \) value is less than 1.645 times the standard deviation of the \( y_i \) values found in sample A (5 percent lower percentile), it is considered as abnormal.

**Results**

**Total Respiratory Resistance (Rrs) and Reactance (Xrs) vs Frequency (f) Curves**

The mean course of Rrs and Xrs vs f in the investigated samples are shown in Figures 1 and 2.

**Discriminant Analysis**

To investigate which factor best separates healthy subjects from patients with minor complaints with or without slight reductions of FEV₁ (samples B and C), first an analysis was performed on sample A (healthy subjects) and the combined samples B and C. Among the investigated ten factors (mean Rrs and Xrs, first four derivatives of Rrs and Xrs), only five turned up to be significant (Rrs, Rrs¹, Rrs², Xrs, Xrs²). The other five were omitted. As shown in Table 2, the total discriminative power is made up mainly by Rrs² and Xrs: together they account for 84 percent of the difference between patients and healthy subjects.

The mean value and standard deviation of the discriminant score \( y \) is \( 0 \pm 0.00147 \) and \( -0.00311 \pm 0.00331 \), respectively in healthy subjects and in patients. The difference between both groups is highly significant.
Table 2—Coefficients of the Factors of the Discriminant Function (Equation 1) with Statistical Significance (F Test) and Relative Contribution (Percent) to the Total Discriminative Power

<table>
<thead>
<tr>
<th>Factors</th>
<th>A vs B and C</th>
<th></th>
<th>A vs B</th>
<th></th>
<th>A vs C</th>
</tr>
</thead>
<tbody>
<tr>
<td>D Rrs</td>
<td>0.006</td>
<td>3.80t</td>
<td>-2.4</td>
<td>0.001</td>
<td>3.52t</td>
</tr>
<tr>
<td>D Rrs'</td>
<td>0.347</td>
<td>9.86t</td>
<td>40.3</td>
<td>0.053</td>
<td>4.15t</td>
</tr>
<tr>
<td>D Rrs^2</td>
<td>0.033</td>
<td>7.34t</td>
<td>1.7</td>
<td>0.054</td>
<td>2.09</td>
</tr>
<tr>
<td>D Xrs</td>
<td>0.029</td>
<td>10.75t</td>
<td>43.8</td>
<td>0.002</td>
<td>1.94</td>
</tr>
<tr>
<td>D Xrs^2</td>
<td>-0.706</td>
<td>10.37t</td>
<td>16.6</td>
<td>-0.122</td>
<td>6.55t</td>
</tr>
</tbody>
</table>

* and † Significant at the 0.05 level.

The discriminant analysis was repeated on samples B and C separately. Though their mean Rrs and Xrs vs frequency curves are quite different (Fig 1), exactly the same factors as for the combined group turned up as being statistically significant for discriminating between patients and healthy subjects (Table 2).

The y scores were computed separately in the patients of sample D, with severe airways obstruction, using the coefficients of Table 2. All subjects were rated as abnormal (Fig 3). As shown by the mean differences (Table 3), the alterations of the Rrs-f and Xrs-f curves in subjects with severe obstruction are of the same type but more pronounced than those met in patients with less obstructive disease (except for the shape factor D Xrs^2, which is less modified in sample D than C).

**Addition to FEV\textsubscript{1}, to the Discriminant Function**

To investigate whether the addition of spirographic data increases the information provided by the Rrs and Xrs-f curves, and thus allows for a better separation between healthy subjects and patients, the discriminant function was extended by adding FEV\textsubscript{1,2}, expressed as a difference in liters between observed and predicted value, as a supplementary parameter. The latter improves, indeed, the discrimination (F = 4.65, p = 0.05), though moderately. The contribution of FEV\textsubscript{1} to the discriminant function for healthy subjects and patients (samples B and C) is only 18 percent of the total, the influence of the other parameters of Table 2 being practically unchanged. The addition of FEV\textsubscript{1} thus only refines the sensitivity of the scores. Among the 67 patients of samples B and C with previously abnormal scores, only one (of sample B) returned to normal after introduction of FEV\textsubscript{1}; his FEV\textsubscript{1} was 0.7 L higher than predicted. Conversely, of the 59 considered as normal, five (of sample C) became abnormal when FEV\textsubscript{1} was added. All five demonstrated FEV\textsubscript{1} values less (by 1.4 L or more) than predicted; results of forced oscillations and of spirometry thus conflict in these cases. Among the 26 healthy subjects with abnormal score, only one returned to "normal" after addition of FEV\textsubscript{1}. Of the 416 other healthy subjects with normal discriminant scores, nine became abnormal when the FEV\textsubscript{1} was included. The previous scores of these nine fell close to the limit of normality, so that

![Graph](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21335/)
the addition of FEV₁ resulted only in a slight adjustment of the scores.

**Discussion**

In patients with manifest COPD, the Rrs and Xrs vs f curves are usually clearly altered:¹⁻⁴⁻⁹ there is a frequency dependence of Rrs and the resonant frequency is increased. In milder cases, the alterations of the Rrs and Xrs-f curves may be less pronounced and resemble the tracings sometimes met in presumably healthy subjects. Of course, one may wonder if some of the latter subjects, without complaints and with normal spiographic values, are not in an early stage of a disease, which might develop later on into COPD. Since it is impossible to answer this question on an individual basis, a comparison was made of measurements performed in a sample of symptomatic patients with and without slight airways obstruction, with those obtained in a comparable group of healthy individuals. Previously, the latter group had been submitted to a discriminant analysis⁴ to investigate whether the Rrs-f and Xrs-f curves separated smokers from nonsmokers. The observed differences were slight, possibly because it was not possible to measure Rrs below 4 Hz. Thus, it was decided not to take the smoking habits into account in the present study. This does not defeat the purpose of the analysis: even if the forced oscillation technique is not a sensitive indicator of smoking, this does not imply that the technique is unable to detect beginning obstructive lung disease, and thus, separate healthy smokers (and nonsmokers) from patients with respiratory complaints and slight airway obstruction. The presence of smokers both in the group of healthy subjects and of patients does not influence the results of the discriminant analysis. Exactly the same factors turned out to be of importance for discrimination, when the analysis was repeated after exclusion of all smokers. In order to avoid the risk for marked abnormalities to possibly mask the moderate ones, this comparison excluded patients with pronounced obstructive disease (FEV₁ less than 50 percent of expected).

The Rrs and Xrs vs f curves can be described by a number of morphologic characteristics such as overall level, slope, curvature, intersection points (eg, resonant frequency). In the present study, such aspects

Table 3—Mean and Standard Deviations of Differences Between Predicted and Observed Values (D) of Averge (Rrs, Xrs) and First and Second Derivatives of Rrs and Xrs (Rrs⁰, Rrs¹, Xrs⁰, Xrs¹) in Healthy Subjects (Sample A) and Patients (Samples B, C, and D)*

<table>
<thead>
<tr>
<th>Samples</th>
<th>D Rrs</th>
<th>kPa.L⁻¹.s</th>
<th>D Rrs⁰</th>
<th>kPa.L⁻¹.s.f⁻¹</th>
<th>D Rrs¹</th>
<th>kPa.L⁻¹.s.f²</th>
<th>D Xrs</th>
<th>kPa.L⁻¹.s</th>
<th>D Xrs⁰</th>
<th>kPa.L⁻¹.s.f⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0±0.054</td>
<td>0±0.002</td>
<td>0±0.0007</td>
<td>0±0.026</td>
<td>0±0.0007</td>
<td>0±0.0007</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>-0.009±0.058</td>
<td>-0.002±0.003</td>
<td>-0.0004±0.0012</td>
<td>-0.022±0.0038</td>
<td>0.0004±0.0017</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>0.052±0.084</td>
<td>-0.007±0.008</td>
<td>0.0005±0.0040</td>
<td>-0.096±0.069</td>
<td>0.0014±0.0027</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>0.070±0.106</td>
<td>-0.011±0.005</td>
<td>0.0011±0.0018</td>
<td>-0.239±0.130</td>
<td>0.0003±0.0028</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*By definition, the mean differences between predicted and observed values are zero in sample A.
were quantified in terms of the mean value and the first four derivatives of \( R_{rs} \) and \( X_{rs} \) with respect to frequency. This procedure allows for an accurate description of the \( R_{rs-f} \) and \( X_{rs-f} \) curves, more detailed than the usual characterization of the frequency dependence of \( R_{rs} \) (eg, by the difference of \( R_{rs} \) at a low and a high oscillating frequency) or of the \( X_{rs-f} \) curve (by the resonant frequency). An additional disadvantage of the resonant frequency is its poor reproducibility because it represents only one point of the \( X_{rs-f} \) curve; besides it cannot be defined in this study below 8 Hz or above 24 Hz.) One may combine the parameters characterizing the \( R_{rs-f} \) and \( X_{rs-f} \) curves into a single score, possibly attaching more weight to some parameters than to others, depending on their relative importance to separate healthy subjects from patients. This is the procedure followed by a discriminant analysis. The latter yields a score for each individual. These scores, \( y_i \), were distributed symmetrically among the healthy subjects. In the group of patients, the distribution of the scores was skewed and their variance was larger than in the healthy subjects. This was expected: a sample of patients is generally heterogeneous because of the varying severity of impairments among the patients. An “abnormal” subject had a score which was lower than that met in 95 percent of the healthy subjects. This threshold is arbitrary. However, if the limit were displaced towards higher scores, one would increase the prevalence of false “abnormals” among the healthy subjects, ie, reduce the specificity, and decrease simultaneously the risk of missing true patients, ie, increase the sensitivity. The reverse procedure, displacing the limit to lower scores, would increase the specificity and reduce the sensitivity. If the exact prevalence of incipient COPD in the population were known, an objective criterion based on Bayes’ theorem might be used for fixing the limit. In the present study, the threshold was selected in such a way that 6 percent of the healthy subjects and 53 percent of the patients of samples B and C) were retained as abnormal. The \( R_{rs} \) and \( X_{rs} \) vs f curves thus really part healthy subjects and patients. The same discriminant function in a separate group of 26 patients with advanced COPD (sample D) achieved a complete separation with healthy subjects. Accordingly, the use of this function may probably be extended to patients with more severe obstruction because their changes of \( R_{rs-f} \) and \( X_{rs-f} \) curves continue the trends met in incipient or moderate airways obstruction.

According to the discriminant analysis, the \( R_{rs} \) and \( X_{rs} \) vs f curves in patients are characterized mainly by a decrease of \( R_{rs} \) with frequency and an overall decrease of \( X_{rs} \) (resulting in an increase in resonant frequency if the shape of the \( X_{rs-f} \) curve is not modified). These are, in fact, the features considered as typical for obstructive lung disease. They can be simulated by Mead’s model of the lungs. The latter consists of an alveolar compartment with a peripheral airway in parallel with the airways compliance. In this model, an increase in the peripheral airway resistance results in a frequency-dependence of resistance and an increase in resonant frequency, similar to those met in the patients with airways obstruction. Both features are influenced also by the shunt characteristics of the cheeks. The latter were not corrected for in the present study. Accordingly, one should not use the present data to try to partition \( R_{rs} \) and to estimate the increase in peripheral resistance in our patients. The discriminant analysis also indicates that these two characteristics have to be present simultaneously (at least between 8 and 24 Hz) to achieve an optimal separation between healthy subjects and patients. This suggests that an isolated frequency dependence of \( R_{rs} \), without simultaneous increase in resonant frequency, or vice versa, should not be considered as an abnormal finding, at least in the investigated patients. A third factor improving the discrimination is a more linear course of the \( X_{rs-f} \) relationship in patients. This feature is reproduced also in Mead’s model in the presence of an increased resistance of the peripheral airways. Two more terms, the average value and the second derivative of \( R_{rs} \), contribute significantly to the discriminant function (Table 2). Their contribution is small, however, and no appreciable information would be lost in this study if they were neglected. (An isolated increase of \( R_{rs} \) without frequency dependence of \( R_{rs} \) may be found following induced bronchoconstriction, probably because of a uniform narrowing of the central airways.) These conclusions are only valid for the range of investigated frequencies. Indeed, in patients with reduced \( FEV_1 \) (samples C and D), the \( R_{rs} \) values increase markedly at lower frequencies. An extension of the discriminant analysis towards lower frequencies might thus modify substantially the importance of the various discriminant factors. To check this point, the analysis was reiterated on the 68 patients (samples B and C) in whom data were available from 4 Hz on (Fig 4). Though the reduction of the number of subjects resulted in an appreciable loss of sensitivity in the statistical tests, the share of the first derivative of \( R_{rs} \) in the discriminant power increased to 84 percent, whereas that of the average value of \( X_{rs} \) decreased to 6 percent. This means, if these findings may be generalized, that the frequency dependence of \( R_{rs} \) between 4 and 8 Hz characterizes almost entirely patients with COPD, no independent information being provided by the decrease of the average value of \( X_{rs} \) (ie, the increase in resonant frequency). Study of a larger sample of patients is necessary to confirm this conclusion.

The addition of the \( FEV_1 \) to the results of the forced oscillation technique does not greatly improve the
separation between healthy subjects and patients. This applies also to the comparison between group A and patients of group C: indeed, the amount of independent information provided by the FEV₁, not contained in the Rrs and Xrs-f curves, is small. Thus, the Rrs-f and Xrs-f curves allow a separation between healthy people and patients as efficiently as the FEV₁, even when the latter is reduced and has been used as a group selection criterion (as in sample C). In five patients (out of 126), however, the Rrs and Xrs-f curves were normal whereas the FEV₁ was reduced by more than 20 percent. These patients happen to have hyperreactive airways: they develop a marked bronchoconstriction following hyperventilation or exercise. It is possible that the FEV₁ maneuver itself induced bronchoconstriction, resulting in a decrease of FEV₁, whereas the oscillations were systematically applied prior to any forced respiratory maneuver.

In conclusion, the discriminant analysis shows that the features of the Rrs-f and Xrs-f curves characterizing patients with respiratory complaints with or without reduction of the FEV₁, value are the frequency dependence of Rrs and more negative Xrs values. A third factor, a more linear course of the Xrs-f relationship, adds to the separation between healthy subjects and patients. These alterations of the Rrs and Xrs-f curves can be simulated, in Mead's model of the lung, by an appropriate increase in the resistance of the peripheral airways.

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