Total respiratory resistance and reactance in ankylosing spondylitis and kyphoscoliosis

J.A. van Noord*, M. Cauberghs, K.P. Van de Woestijne, M. Demedts

ABSTRACT: Ankylosing spondylitis and kyphoscoliosis both alter the function of the lung by modifying the mechanical properties of the thoracic cage. The purpose of the present study was to assess the changes in total respiratory resistance (Rrs) and reactance (Xrs) in these patients and to compare these data with conventional pulmonary function tests.

In 16 patients with ankylosing spondylitis and seven with kyphoscoliosis we measured lung volumes, maximal flows, diffusing capacity, airway resistance, lung compliance and Rrs and Xrs between 2-26 Hz by means of the forced oscillation technique (FOT).

In the patients with ankylosing spondylitis mean total lung capacity was 83% predicted (range 60-105%). Mean values of Rrs were normal; there was a small decrease in Xrs at the lowest frequency. In the patients with kyphoscoliosis mean total lung capacity (TLC) was 41% predicted for arm span (range 26-75%). Mean Rrs was elevated with a negative frequency dependence, and mean Xrs was decreased.

The observed differences in Rrs and Xrs between the two groups of patients are related to differences in severity of the restriction. There is evidence that the changes in Rrs and Xrs in both groups are mainly attributable to an increase in chest wall resistance and a decrease in chest wall compliance, while in the patients with kyphoscoliosis an increase in airway resistance and a decrease in lung compliance also intervenes.


Keywords: Ankylosing spondylitis; forced oscillation technique; kyphoscoliosis; respiratory impedance.

Received: April 2, 1990; accepted after revision April 17, 1991.

This study was supported by a grant from the “Nederlands Astma Fonds” and the “Fonds voor Geneeskundig Wetenschappelijk Onderzoek”.

The clinical disorders of ankylosing spondylitis and kyphoscoliosis, like strapping of the rib cage in healthy subjects, affect the movements of the thoracic cage and modify the mechanical properties of lungs and chest wall [1, 2]. In clinical practice, measurements of chest wall recoil are seldom performed, as it is very difficult to obtain reliable data in untrained subjects. The forced oscillation technique (FOT) is a potential tool to investigate disorders of the chest wall, as it provides information on the mechanical behaviour of airways, lungs and chest wall. The method is simple to perform, rapid, non-invasive and demands only passive cooperation of the patient. It allows evaluation of total respiratory impedance over a wide range of frequencies and provides values of its two components, i.e. total respiratory resistance (Rrs), which is the sum of airway, lung tissue and chest wall resistance, and of total respiratory reactance (Xrs), which is a function of the elastic and inertial properties of the respiratory system [3, 4].

In healthy adult subjects, Rrs does not vary or increases only slightly with frequency (positive frequency dependence) in the range of commonly investigated frequencies, 2–30 Hz; Xrs increases markedly with frequency: its value is negative below 10–12 Hz (the resonant frequency), and positive at higher frequencies [4–6]. In pathological conditions of lungs and airways Rrs is generally increased with negative frequency dependence (i.e. lower values at higher frequencies); Xrs is reduced at all frequencies [6–10]. In a previous study [11], we found that strapping of the rib cage in healthy subjects caused similar changes in Rrs and Xrs: increase of Rrs at low oscillatory frequencies, resulting in a negative frequency dependence, and a decrease of Xrs with a shift of the resonant frequency to higher values. By partitioning the impedance of lungs and chest wall by means of an oesophageal balloon, we demonstrated that the changes of Rrs and Xrs were mainly the result of the altered mechanics of the chest wall.

To our knowledge, no report exists about the influence of ankylosing spondylitis and kyphoscoliosis on Rrs and Xrs, measured with the forced oscillation technique. The purpose of the present study was to measure Rrs and Xrs at various frequencies in these patients, to compare the data obtained with routine lung function tests and to evaluate the implications of the method for clinical use.
Patients and methods

Patients

Sixteen patients, 2 females and 14 males, with ankylosing spondylitis, and 7 patients, 5 females and 2 males, with kyphoscoliosis were selected for the study. The diagnosis of ankylosing spondylitis was made according to the classical New York criteria [12]. Patients with a history or clinical evidence of chronic obstructive lung disease or other complicating pulmonary disorders were excluded, and the ratio forced expiratory volume in one second/vital capacity had to be more than 70%.

Methods

Vital capacity (VC), total lung capacity (TLC), functional residual capacity (FRC), residual volume (RV), and forced expiratory volume in one second (FEV₁) were obtained by standard methods of spirometry and multi-breath helium equilibration. Peak expiratory flow (PEF) and maximal flow at 50% of the forced vital capacity (MEF₅₀) were obtained from MEFV curves recorded at the mouth with a Lilly-type pneumotachograph and integrator. Highest values of three manoeuvres were retained. Diffusing capacity of the lung for carbon monoxide (DLco) was determined with the single-breath method; breath-holding time was calculated after Jones and Meade [13] and alveolar volume (VA) was determined as the sum of the inspired volume and RV, measured separately with the multi-breath helium equilibration technique. Results were related to the reference values of the European Community of Coal and Steel (ECCS) [14]. Because a flexion deformity in ankylosing spondylitis sometimes, and in kyphoscoliosis systematically, reduces the height of the patient, results were related to predicted values for height before the onset of the disease in the patients with ankylosing spondylitis and to predicted value for arm span in the patients with kyphoscoliosis.

Airway resistance (Raw) and specific airway conductance (sGaw) were measured in a constant-volume plethysmograph (Jaeger body test) at a respiratory rate of about 0.5 Hz. The slope of the mouth flow-box pressure loop was determined by connecting the points of 0.5 l/s above and below the zero flow line and midway between the ascending and descending limbs of the loop. The means of three measurements, expressed in absolute values, are reported. Static transpulmonary pressure-volume curves were determined during apnoea's from volume, obtained by integration of the flow signal at the mouth, and oesophageal pressure (oesophageal balloon: length 10 cm, perimeter 5 cm, containing 0.5 ml of air, positioned at 40 cm from the nares). The static expiratory compliance was calculated as the mean slope (of three curves) between FRC and FRC +0.5 l. For maximal inspiratory transpulmonary pressure the highest values of three manoeuvres were selected. Values of elastic lung recoil were related to the reference values of Yernault et al. [15].

Rrs and Xrs were determined by means of a forced oscillation technique described in detail previously [3, 4]. Briefly, a pseudorandom noise signal, containing the harmonics of 2 Hz up to 26 Hz (2, 4, 6, ..., 26 Hz) is applied at the mouth. The harmonics have a flat amplitude spectrum and appear in random order. The signal is repeated every 0.5 s; its total peak-to-peak amplitude is less than 0.2 kPa at the mouth. Pressure and flow signals, recorded by two identical differential transducers Validyne MP45 (±0.2 kPa) are digitized at a frequency of 128 Hz and split up into time blocks of 4 s. Four successive blocks are recorded and submitted without preliminary filtering to a fast Fourier transform, yielding the frequency content of pressure and flow for each of the investigated frequencies. From the auto- and crosspower spectra, averaged over the four time blocks, a resistance (Rrs) and reactance value (Xrs) of the respiratory system and a coherence function are computed. Only Rrs and Xrs values with a coherence function equal to or exceeding 0.95 were retained, resulting in the elimination of the 2 Hz values in most subjects. The measurements were repeated at least thrice; the mean of three satisfactory measurements is given. To describe the Rrs and Xrs vs frequency (f) relationships, the mean of Rrs and Xrs (Rrs and Xrs), and the average values of the first and second derivatives of Rrs and Xrs with respect to frequency (respectively, Rrs', Xrs', Rrs'', Xrs'') were calculated from 6-26 Hz according to a method described previously [5]. The first and second derivatives represent, respectively, the slope and the curvature of the Rrs-f and Xrs-f relationships. Measured values of Rrs and Xrs were compared to the reference values of Landser et al. [5].

Correlation coefficients between the various lung function measurements were computed.

Results

Conventional lung function tests

Mean values of the lung function tests are presented in table 1. In the patients with ankylosing spondylitis mean TLC and VC were slightly reduced, whereas mean RV and FRC were approximately normal. However, the latter values showed substantial interindividul variability above and below the predicted values. Mean values of DLco, Raw and static lung compliance were within the normal range. In the patients with kyphoscoliosis, static lung volumes were all severely reduced, RV being least affected. There was a small increase in airway resistance, however, due to the decrease in FRC, sGaw was normal; by virtue of selection the ratio FEV₁/VC was also normal. Static lung compliance and transpulmonary pressure at TLC were decreased.
Table 1. - Mean values (±so) of the pulmonary function tests in ankylosing spondylitis and kyphoscoliosis

<table>
<thead>
<tr>
<th>Test</th>
<th>Ankylosing spondylitis</th>
<th>Kyphoscoliosis</th>
</tr>
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<tbody>
<tr>
<td>Age (yrs)</td>
<td>39 ± 13</td>
<td>40 ± 7</td>
</tr>
<tr>
<td>Height/span (cm)</td>
<td>170 ± 6</td>
<td>162 ± 8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68 ± 9</td>
<td>47 ± 11</td>
</tr>
<tr>
<td>VC (% pred.)</td>
<td>79 ± 14</td>
<td>36 ± 21</td>
</tr>
<tr>
<td>RV (% pred.)</td>
<td>94 ± 21</td>
<td>51 ± 12</td>
</tr>
<tr>
<td>TLC (% pred.)</td>
<td>83 ± 13</td>
<td>41 ± 18</td>
</tr>
<tr>
<td>FRC (% pred.)</td>
<td>95 ± 22</td>
<td>42 ± 13</td>
</tr>
<tr>
<td>RV/TLC (% pred.)</td>
<td>112 ± 19</td>
<td>134 ± 28</td>
</tr>
<tr>
<td>FRC/TLC (% pred.)</td>
<td>111 ± 17</td>
<td>114 ± 23</td>
</tr>
<tr>
<td>FEV1 (% pred.)</td>
<td>79 ± 13</td>
<td>36 ± 24</td>
</tr>
<tr>
<td>FEV1/VC (%)</td>
<td>81 ± 7</td>
<td>83 ± 7</td>
</tr>
<tr>
<td>PEF (% pred.)</td>
<td>93 ± 23</td>
<td>46 ± 21</td>
</tr>
<tr>
<td>MEF50 (% pred.)</td>
<td>75 ± 14</td>
<td>47 ± 31</td>
</tr>
<tr>
<td>Tco (% pred.)</td>
<td>96 ± 17</td>
<td>68 ± 9</td>
</tr>
<tr>
<td>Kco (% pred.)</td>
<td>101 ± 20</td>
<td>119 ± 40</td>
</tr>
<tr>
<td>Raw (kPa·l·s)</td>
<td>0.12 ± 0.03</td>
<td>0.28 ± 0.14</td>
</tr>
<tr>
<td>sGaw (kPa·l·s)</td>
<td>2.45 ± 0.66</td>
<td>2.73 ± 1.01</td>
</tr>
<tr>
<td>Cst (% pred.)</td>
<td>91 ± 15</td>
<td>37 ± 19</td>
</tr>
<tr>
<td>Ptp, max (% pred.)</td>
<td>85 ± 21</td>
<td>67 ± 9</td>
</tr>
</tbody>
</table>

In ankylosing spondylitis original height at the onset of the disease, and in kyphoscoliosis arm span are given. VC: vital capacity; RV: residual volume; TLC: total lung capacity; FRC: functional residual capacity; FEV1: forced expiratory volume in one second; MEF50: maximal expiratory flow at 50% of the forced vital capacity; PEF: peak expiratory flow rate; Tco: single-breath diffusing capacity for carbon monoxide; Kco: Tco over lung volume; Raw: airway resistance; sGaw: specific airway conductance; Cst: static lung compliance; Ptp, max: transpulmonary pressure at TLC. *: because of severe restriction not available in four patients.

**Total respiratory resistance and reactance**

Individual values of Rrs and Xrs vs frequency of all patients are shown in figures 1 and 2. In the ankylosing spondylitis patients the Rrs curves showed a certain amount of scatter, but they were nearly all within normal limits. However, the positive frequency dependence of Rrs, usually found in healthy subjects, was absent. The Xrs vs frequency curves were mostly within normal limits, except for the 4 Hz value which was decreased in a few subjects (fig. 1). In the kyphoscoliosis patients the range of the Rrs curves was very large, varying from normal to very abnormal values with relatively small negative frequency dependence (especially at higher frequencies) (fig. 2). In most patients Xrs was reduced, especially at low frequencies. Figure 3 illustrates the difference in mean impedance between the two groups. In the ankylosing spondylitis patients, mean values of Rrs, Rrs0, Rrs0.01 and Xrs were normal, but the mean values of Xrs at 6 Hz (p<0.001), of Xrs0 (p<0.01) and of Xrs0 (p<0.01) were significantly different from the predicted values [5]. In the kyphoscoliosis patients, mean Rrs was significantly increased with a clear negative frequency dependence and Xrs was decreased (p<0.001).
Fig. 3. — Mean total respiratory resistance (top) and reactance (bottom) as a function of frequency in 16 patients with ankylosing spondylitis and in 7 patients with kyphoscoliosis.

Table 2. — Correlation coefficients between total respiratory resistance, reactance and routine lung function indices in ankylosing spondylitis

<table>
<thead>
<tr>
<th></th>
<th>Rs</th>
<th>Rs0</th>
<th>Xrs</th>
</tr>
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<tbody>
<tr>
<td>VC % pred.</td>
<td>0.24</td>
<td>0.34</td>
<td>0.34</td>
</tr>
<tr>
<td>TLC % pred.</td>
<td>-0.05</td>
<td>0.50*</td>
<td>0.66**</td>
</tr>
<tr>
<td>FRC % pred.</td>
<td>-0.41</td>
<td>0.45</td>
<td>0.87**</td>
</tr>
<tr>
<td>FEV1/VC %</td>
<td>-0.64**</td>
<td>0.24</td>
<td>0.34</td>
</tr>
<tr>
<td>Raw kPa·l·s</td>
<td>0.65**</td>
<td>-0.15</td>
<td>-0.17</td>
</tr>
<tr>
<td>Cst % pred.</td>
<td>0.28</td>
<td>0</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Number of patients: 16. *: p<0.05; **: p<0.01. Rs, Rs0: mean value of respiratory resistance (Rs) and first derivative (slope) of Rs, respectively; Xrs: mean value of respiratory reactance (Xrs). For further abbreviations see legend to table 1.

Correlations between the various measurements

Tables 2 and 3 show the results of the correlation analysis, relating mean Rs and its slope and mean Xrs to the most relevant conventional lung function tests. In the ankylosing spondylitis patients, mean level of Rs turned out to be correlated with Raw and with the FEV1/VC ratio. There was a weak correlation between the mean slope of Rs and TLC. Mean level of Xrs was correlated satisfactorily with TLC and FRC. In other words, as TLC decreased, the mean slope of Rs tended to decrease (from positive to zero, or to negative) and Xrs shifted towards lower values (i.e. resonant frequency moved to higher frequencies). There was no significant correlation between VC and RV, Raw or lung compliance.

In the kyphoscoliosis patients mean slope of Rs was correlated with lung compliance, and mean level of Xrs with VC, TLC and lung compliance. There was a significant relationship between VC and RV (r=0.87, p<0.01), VC and Raw (r= -0.75, p<0.05), and VC and lung compliance (r = 0.84, p<0.05).

Discussion

In this study the patients with ankylosing spondylitis had no major functional restriction in contrast to the patients with kyphoscoliosis. Indeed, in the patients with ankylosing spondylitis mean VC was 79% predicted (lowest value was 53% predicted). Mean values of RV and FRC were about normal, but showed marked variations above and below the reference values. According to the literature, the most consistent finding in ankylosing spondylitis is the reduction in VC, which in most studies is on average 70% predicted, with a lower limit of about 50% [16-26]. The reduction in VC is limited because the diaphragmatic excursions are unimpaired and even greater than normal [24, 27]. Most authors have found an increased RV and a normal or increased FRC [18, 20-22, 24]. However, normal [16, 19] or decreased values [25] of RV have been reported. These discrepancies may be caused by difference in stage of the disease and to a large extent by differences in reference values. Indeed, whatever the reported change in RV, be it an increase [20], a decrease [25], or no change [19], it appears that the ratios RV/TLC are remarkably similar among these studies: 40, 36 and 37%, respectively.

In contrast, all patients with kyphoscoliosis showed a severe restrictive pattern. These observations are in line with previous reports [1, 28-30], that, depending on the angle of scoliosis, static lung volumes can reach
The difference in average pulmonary restriction between the two groups is reflected in the Rs and Xrs vs frequency curves. In the patients with ankylosing spondylitis mean values of Rs and Xrs were within normal range, except for the absence of the slightly positive frequency dependence of Rs, generally observed in healthy subjects [4, 6] and for a small decrease in Xrs at the lowest frequency with a steepening of the slope of the Xrs curve. The patients with most restriction showed, in addition, a small negative frequency dependence of Rs. As the latter patients had all values of airways resistance and lung compliance within normal limits, the changes of Rs and Xrs are likely to be related more to alterations in chest wall mechanics than in airway or pulmonary mechanics. Raw is of course an important determinant of Rs, which explains the significant correlation between both variables (table 2), but, unlike the findings in obstructive lung disease [8] Rs and Xrs were related to TLC rather than to Raw. As the mean value of Rs is virtually independent of the oscillatory frequency, one might conclude that the respiratory system behaves homogeneously and can be suitably described by a single compartment resistance-inertance-compliance (RIC) system. If so, the difference between the mean value of Rs and of Raw, i.e. 0.16 kPa·s·L, can be attributed to the resistance of the tissues, probably mainly that of the chest wall. This value is larger than the value of 0.05 kPa·s·L for chest wall resistance, measured by NAGELS et al. [4] in healthy subjects, at a frequency of 4 Hz. To our knowledge, there are no reports in the literature on the chest wall resistance in ankylosing spondylitis. From Xrs, the dynamic compliance of the respiratory system (Crs, dyn) can be calculated using the equation Xrs = l/Crs, dyn. At an oscillatory frequency of 4 Hz the mean Crs, dyn was 0.29 l·kPa⁻¹, which is less than the value of 0.61 l·kPa⁻¹ that we found in healthy subjects [11]. SHARP et al. [31], measuring chest wall and total respiratory compliance in 21 patients with ankylosing spondylitis during voluntary relaxation, found the total respiratory compliance to be decreased in most subjects and to be well correlated with VC. In the subgroup of patients with a TLC value larger than 4.5 l, as was the case in the majority of our patients, mean total respiratory compliance was 0.84 l·kPa⁻¹ and chest wall compliance was 1.44 l·kPa⁻¹, or about two-thirds of the expected value. The latter value of total compliance is larger than our calculated value, which can be explained by the mechanical inhomogeneity of the chest wall [32] and the influence of respiratory muscle activity [33], two factors which make chest wall compliance dependent of the frequency at which measurements are performed (apnoea, spontaneous breathing or forced oscillation frequency).

In the patients with kyphoscoliosis, mean Rs was considerably increased at low frequencies and Xrs was decreased. There are several factors which may contribute to these changes. Firstly, although sGaw was normal, Raw was increased because of a marked decrease in FRC. It has been demonstrated that an increase in Raw, whether central or peripheral, systematically results in a negative frequency dependence of Rs and a decrease in Xrs, due to the influence of the shunt impedance of the proximal airways [34, 35]. Secondly, the compliance of the lungs was decreased, together with a decrease in transpulmonary pressure at TLC, which is a typical feature of pulmonary restriction caused by a reduced motion of the chest wall. In diffuse interstitial lung diseases, a fall in compliance of the lungs, together with an increase in tissue resistance also causes a small increase in Rs at low frequencies and a decrease of Xrs [9]. Yet, the changes in Rs and Xrs in kyphoscoliosis are too large to be attributed to the observed small increase in Raw and decrease in lung compliance. Accordingly, it is likely that the changes in mechanical properties of the chest wall in kyphoscoliosis play an important role. Using the mid-position shift method in patients with idiopathic scoliosis, KAUFER [30] found that in the subjects with a VC of about 1 l (which is similar to the mean VC value in our group) chest wall compliances were markedly reduced: 0.04–0.5 kPa⁻¹. As VC, Raw, lung compliance and chest wall compliance are highly interrelated in this disorder [30] (table 3) correlation analysis proved not to be very useful for the interpretation of the changes in Rs and Xrs. In particular, the correlation between Raw and Rs is difficult to interpret, as, on the one hand, Raw is dependent on the degree of restriction and, on the other hand, Raw is probably not the major determinant of Rs in our patients (see below).

The other approach in analysing impedance data is to fit a specific model of the respiratory system to the experimental data. As in kyphoscoliosis many properties of airways, lungs and chest wall are altered, resulting in a marked increase and negative frequency dependence of Rs and decrease of Xrs, this analysis requires a complex model, taking into account, in addition to elements representing airways and tissues of lungs and chest wall, the influence of the upper airway, and probably also that of intrathoracic airway wall compliance, and of gas compressibility. We fitted the 13-parameter model, described previously [9, 10], on the data, incorporating in the model the measured values of Raw, lung compliance and gas compressibility and adjusting the values of chest wall compliance and resistance in order to obtain a good fit with the measured average Rs and Xrs vs frequency curves. This was possible if chest wall resistance was increased to 0.6 kPa⁻¹ and compliance decreased to 0.08 kPa⁻¹. These figures should be regarded with caution, as approximations are highly dependent on this type of model; indeed, the latter was not validated by formal modelization techniques.

In conclusion, this study suggests that in disorders of the chest wall there is not only a decrease in chest wall compliance but also an increase in chest wall resistance. The scatter of values of Rs and Xrs in normal subjects is too large to detect the small changes in Rs and Xrs induced by ankylosing spondylitis. This result is connected with the fact that chest wall resistance only
accounts for a minor fraction of Rs [4, 36]; also, a moderate decrease in chest wall compliance, for instance by a factor of two has a limited influence on Xrs. For comparison rib cage strapping, causing a decrease in TLC of 31%, induced a reduction in Xrs resulting in a slight increase in the resonant frequency from 6.3 to 10.6 Hz [11]. De Troyer [37], imposing a similar restriction, demonstrated that this caused a reduction in chest wall compliance of more than 50%. Rs and Xrs curves, thus, lack sensitivity to detect changes in chest wall mechanics. However, when a considerable difference is present between Raw and Rs, this might suggest an increase in tissue resistance (of lungs and of chest wall). In advanced kyphoscoliosis considerable changes in Rs and Xrs are found which are the results of the combined effects of changes in mechanics of airways, lungs and chest wall. The differences in Rs and Xrs between the two disorders are probably related to the Van Noord JA, Clement J, Smeets I, Van de Woestijne KP. - Normal values of total respiratory resistance and reactance determined in ankylosing spondylitis patients with restriction similar to the ankylosing spondylitis patients also demonstrated values of Rs and Xrs within the normal range.

References

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CHEST WALL DEFORMITIES AND RESPIRATORY IMPEDANCE


Chez 16 patients atteints de spondylite ankylosante et chez 7 cyphoscoliotiques, nous avons mesuré les volumes pulmonaires, les débits maximaux, la capacité de diffusion, la résistance des voies aériennes, la compliance pulmonaire, ainsi que Rs et Xrs entre 2 et 26 Hz au moyen de la technique d’oscillation forcée (POT).

Chez les patients atteints de spondylite ankylosante, la capacité pulmonaire totale moyenne est de 83% des valeurs prédites (extrêmes: 60 à 105%). Les valeurs moyennes de Rs sont normales; il y a une légère diminution de Xrs à la fréquence la plus basse. Chez les cyphoscoliotiques, la TLC moyenne est de 41% des valeurs prédites pour l’envergure (extrêmes: 26 à 75%). La Rs moyenne est augmentée, avec une dépendance négative à l’égard de la fréquence. La Xrs moyenne est diminuée.

Les différences observées dans Rs et Xrs entre les deux groupes de patients sont en relation avec les différences de gravité du syndrome restrictif. Il apparaît que les modifications de Rs et de Xrs dans les deux groupes sont principalement attribuables à une augmentation de la résistance de la paroi thoracique et à une diminution de la compliance de cette paroi, alors que chez les patients atteints de cyphoscoliose une augmentation de la résistance des voies aériennes et une diminution de la compliance pulmonaire interviennent également.