Reference values of total respiratory resistance, determined with the "opening" interruption technique

P.H. Vooren*, B.C. van Zomeren **

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ABSTRACT: In a large epidemiological survey of lung function the subjects performed maximum expiratory flow volume (MEFV) manoeuvres. They were also interviewed by trained interviewers using a standardized questionnaire. In a random subset of the subjects the resistance of the respiratory system was measured with the "opening" Interruption technique, in which the mouth pressure before the end of the interruption period is divided by the flow shortly after the end of it. The subset contained men and women, and smokers as well as nonsmokers, 229 of whom were considered to be healthy because they had no history of complaints and a "normal" flow-volume curve. In this group mean inspiratory and expiratory resistances did not differ significantly (0.27 and 0.29 for men and 0.39 and 0.38 kPa·t·s for 0.29 for men and 0.39 and 0.38 kPa·t·s for women). The averages of in- and expiratory resistance were 0.28±0.10 kPa·t·s for men and 0.39±0.11 kPa·t·s for women. The resistance values were slightly but significantly correlated with body height, FEV and MEF50 but not with smoking habits. Due to the considerable variability the method does not permit sharp discrimination between normal and abnormal subjects. However, it appears to be useful in histamine challenge testing, to detect and monitor bronchial asthma, being not subjected to the disturbing effect of forced ins- and expirations.

Eur Respir J., 1989, 2, 966-971.

Received: April 27, 1989; accepted after revision June 22, 1989.

Patients and measurements

The data were obtained during the 1985 survey of the Vlaardingen-Vlagtwedde longitudinal lung function study [12]. All subjects were between 30 and 75 years of age. They were interviewed by trained interviewers using a slightly modified version of the Medical Research Council questionnaire. From the answers it was determined whether subjects were suffering from persistent cough or phlegm, or shortness of breath when walking with persons of the same age, wheezing of the chest, or asthmatic attacks, which are symptoms of Chronic Non Specific Lung Disease (CNSLD). People without any of these symptoms, either in the present or in the past, were assigned to the "no history" group. The questionnaire also contained questions on smoking habits. People who had stopped smoking at least one month before the study was conducted were considered to be ex-smokers.
A large group of the subjects in the study also performed maximal expiratory flow volume (MEFV) manoeuvres. Following the recommendations of the European Commission for Coal and Steel [13] we measured forced vital capacity (FVC), peak flow (PEF), maximal mid-expiratory flow (MMEF), maximum expiratory flow at 25, 50 and 75% of the forced vital capacity (MEF25, MEF50 and MEF75), and forced expiratory volume in one second (FEV1). Reference equations for MEF50 and FEV1 were used in [13], and the corresponding residual standard deviations (sd) were used to detect abnormal subjects, as characterized by a value of MEF50 or FEV1, more than 1.64 sd below the predicted value. Only persons with normal values for both MEF50 and FEV1 were considered to have a normal MEFV curve.

The measurement of respiratory resistance was performed in a random subsample from the group which had already performed the flow-volume manoeuvre. This resulted in a total of 395 measurements. Of these, 16 were discarded because the resistance measurement had been technically unsatisfactory and 5 more because the resistance values showed unacceptably high differences between inspiratory and expiratory values. Of 3 persons the height value was missing and 19 flow-volume curves were discarded for technical reasons. A total of 352 records, 198 of male and 154 of female subjects remained.

Methods

Flow volume curves

Maximum expiratory flow volume curves were obtained by trained operators. After maximum inspiration the subject (instanding position) exhaled as forcibly and as long as possible through a heated, straight and smooth PVC tube with a length of 50 cm and an internal diameter of 2.5 cm, which was connected to a Lilly-type pneumotachograph equipped with differential pressure transducer (Jaeger pneumotachoscript). The flow signal was recorded by a computer which computed the usual flow volume indices. Following the ECCS recommendations at least 3 technically satisfactory MEFV curves were recorded. The FEV1 and MEF50 values used in this paper are the largest values of these parameters occurring in those curves that had an FVC within 5% of the largest FVC.

Interruption method

The interrupter consisted of a tube with a diameter of 2 cm and a length of about 3 cm [14]. The distal end could be closed by a small valve which moved along the axis of the tube and was activated by a 7 cm lever, driven by an electromagnet. About 5 ms were required to open or close the valve.

The narrowed cross-section at the distal end of the tube functioned as a pneumotachograph when the valve was open. The pressure difference across the constriction, which was almost proportional to the squared flow rate, was fed into a microcomputer which computed the corresponding flow value. Figure 1 illustrates a manoeuvre for the determination of inspiratory resistance. During inspiration the valve was closed when a predetermined flow rate of 0.2 l s−1 was reached. Next the pressure at the proximal side of the valve - equal to mouth pressure - was measured, and the valve was opened when the pressure reached a value of 0.4 kPa. The pressure data obtained during interruption were used to estimate by extrapolation the pressure at about 16 ms after opening. Respiratory resistance, \( R_e \), was calculated as the ratio of this extrapolated pressure and the corresponding flow. In this way all resistance values were determined not at one and the same arbitrary flow, as in bodyplethysmographic and other resistance measurement methods, but at one and the same arbitrary pressure.

![Fig. 1. - Course of measurements in the opening interruption technique. Real tracings of mouth pressure and flow against time in the upper panel, schematic explanation in lower panel. The shutter is closed as soon as an inspiratory flow of 0.2 l s−1 is reached and opened when the pressure in the mouth becomes 0.4 kPa. Extrapolated mouth pressure at 16 ms after opening (after correction for resistance of the equipment) is divided by the flow measured at 16 ms after opening.](image-url)
and supported their cheeks with their fingertips. Resistance was first measured during expiration, for at least 5 consecutive breathing cycles, immediately after which followed at least 5 successive inspiratory measurements. The standard deviation of the resistance values was computed online and displayed to the operator. The objective was to obtain 5 consecutive resistance values with a coefficient of variation of at most 15%. Additional measurements were made if necessary. This could not be achieved in 16 cases. However, the material discussed here does not contain measurements with a standard deviation higher than 0.06 kPa·l⁻¹·s⁻¹. The data to be presented are the mean values of the inspiratory (Rᵢ) and expiratory (Rₑ) resistances.

During the survey, three different resistance measurement instruments were used and subjects as well as instructors were assigned at random to these instruments. To check whether there was an instrument bias, a one-way analysis of variance (ANOVA) was performed for men and women separately. Differences between the instruments were not significant and therefore the results of the three instruments were pooled.

Table 1. - Mean values for Rᵢ

<table>
<thead>
<tr>
<th></th>
<th>Normal MEFV</th>
<th>Abnormal MEFV</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>nonsmokers</td>
<td>smokers</td>
</tr>
<tr>
<td>Male NH</td>
<td>0.258</td>
<td>0.290</td>
</tr>
<tr>
<td></td>
<td>0.282</td>
<td>0.309</td>
</tr>
<tr>
<td>n</td>
<td>81</td>
<td>40</td>
</tr>
<tr>
<td>Female NH</td>
<td>0.389</td>
<td>0.394</td>
</tr>
<tr>
<td></td>
<td>0.377</td>
<td>0.392</td>
</tr>
<tr>
<td>n</td>
<td>76</td>
<td>32</td>
</tr>
<tr>
<td>Male PH</td>
<td>0.307</td>
<td>0.304</td>
</tr>
<tr>
<td></td>
<td>0.301</td>
<td>0.327</td>
</tr>
<tr>
<td>n</td>
<td>16</td>
<td>32</td>
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<tr>
<td>Female PH</td>
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<td>0.444</td>
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<td></td>
<td>0.436</td>
<td>0.470</td>
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<td>n</td>
<td>26</td>
<td>11</td>
</tr>
</tbody>
</table>

Mean values for Rᵢ in kPa·l⁻¹·s⁻¹ for the different subgroups. Rᵢ=Rᵢ during inspiration, Rₑ=Rₑ during expiration. NH: negative history for CNSLD, PH: positive history for CNSLD.

Results

On the basis of sex, flow volume curve (normal or abnormal), history (CNSLD or no CNSLD) and smoking behaviour (smoker or non-smoker), the subjects were divided into 16 groups. The mean results are given in table 1. Both resistance values differed significantly (p<0.001) between men with normal and those with abnormal MEFV curves. In women the difference was significant (p<0.025) only for Rₑ. Regarding the anamnestic data, the differences between the groups with and without CNSLD were significant at the 2.5% level, except for Rᵢ in men. In general, subjects with positive history had somewhat higher resistance. Finally the differences between smokers and nonsmokers were nowhere significant.

To be on the safe side in both women and men we decided that the reference group, i.e. the group with healthy subjects who were normal with respect to respiratory resistance, should consist of asymptomatic subjects with a normal MEFV curve. We disregarded smoking behaviour. This resulted in normal groups of 121 men and 108 women. In normal men the mean Rᵢ and mean Rₑ were 0.27±0.11 and 0.29±0.10 kPa·l⁻¹·s⁻¹. For normal women these figures were 0.39±0.14 and 0.38±0.10 kPa·l⁻¹·s⁻¹ respectively. In both groups the differences between Rᵢ and Rₑ were not significant at the 10% level. Taking the average of inspiratory and expiratory resistance we found a mean Rᵢ of 0.28±0.10 kPa·l⁻¹·s⁻¹ in normal men and of 0.39±0.11 kPa·l⁻¹·s⁻¹ in normal women.

In these groups the influence of age, height, weight and overweight - as expressed in the Quetelet index - on Rᵢ and Rₑ were investigated by performing stepwise regression analysis for males and females separately. The upper part of table 2 shows which variables were entered into the equations by the stepwise procedure using a 5% significance level for entry. Although the coefficients had values which agree with common sense, i.e. slightly negative for height, and slightly positive for age and weight, the multiple correlation coefficients which are also shown in table 2 were very low. The regression of Rᵢ on age, height and weight in women produced the highest multiple correlation coefficient, 0.25. The influence of the various MEFV indices on Rᵢ and Rₑ was investigated in the same way. The lower part of table 2 shows the results of a stepwise regression of Rᵢ and Rₑ on the MEFV indices FVC, FEV₁, PEF, MEF₂₅, MEF₅₀, MEF₇₅ and MMEF.
In the “opening” interruption technique (OI), however, mouth pressure and flow are measured respectively before and after opening of the shutter. Just after opening the distribution of gas flow is essentially determined by local resistances, and little influenced by local time constants. Although an interruption of 0.15–0.30 s may be too short for complete equilibration between local alveolar pressures in patients, what is measured is probably closer to a “true negative resistance” than the values obtained by bodyplethysmography [20] or by the forced oscillation method [10]. This decreased influence of mechanical non-homogeneity may be responsible for the lower intra-individual variability of resistance with this method [6, 14].

The mean $R_w$ in our study was 0.33 kPa·l⁻¹·s⁻¹, which is substantially higher than was reported in other studies. Alinear pressure-flow relationships are unlikely to be the only cause because pressure was triggered at about 0.4 kPa, so $V$ should have been on average 1.2 l·s⁻¹. From Rohrer’s equation it follows that at that flow the average contribution of alinear resistance to $R_w$ amounts to 0.036 kPa·l⁻¹·s⁻¹, which should make resistances measured by the OI method about 0.03 kPa·l⁻¹·s⁻¹ higher than in the other studies, where alinear resistance is much smaller.

Pressure-flow relationships at the start of a respiratory movement however can be influenced by force-velocity relationships originating in the muscles [21], which means that with constant effort, the pressure exerted by the muscles falls as velocity increases, which has virtually the effect of an additional resistance.

We used the Quetelet index as an index of obesity. It did not show any relationship with $R_w$ in our study (table 2). This could mean that a large mass of tissue offers the same resistance as a small mass, or that the contribution of the resistance of thoracoabdominal tissues ($R_{th}$) to $R_w$ measured by the interruption technique is negligible. Amrein et al. [15], who found a correlation between resistance and weight, did not measure resistance including $R_{th}$, but only alinear resistance. LANDSÉR et al. [17] found a positive correlation between relative weight and total resistance including $R_{th}$. This, however, is the only indication of a positive influence of obesity on $R_w$ in the literature.
In only one of the previous studies [17] the presence of some correlation between resistance and body height was also found. The existence of such a correlation is logical because anthropometric dimensions are widely accepted as good predictors of all static lung volumes [13] and could in the same way relate to the diameters of the bronchi.

We did not find significant differences between $R_s$ and $R_{se}$ in the reference groups, neither did most other authors mention such a difference. The relatively great difference between the mean $R_s$ of men and women could be based on the most obvious difference between male and female airways: the dimensions of the glottis [23].

Further, we did not see any significant influence of smoking on resistance. This is in agreement with the conclusion of other authors [16, 17] that the influence of smoking is smallest among all influences. The lung function index which is most influenced by smoking is the slope of phase III of the nitrogen washout curve [24]. This index, however, is to a large extent connected to peripheral airway disturbance. On the other hand, pure frictional resistance is mainly determined by the dimensions of the central airways [25]. This could suggest that $R_{se}$, as measured by OI, concerns almost exclusively (i.e. for 80%, c.f. [25]) the central airways, while smoking affects the resistance of the peripheral airways.

In the group of "normal" subjects, i.e. subjects with negative history and a normal MEFV curve, variability in resistance was very large. This was also reported by some of the authors shown in table 3. Apparently in this adult population respiratory- and airway-resistance, in contrast to spirometric parameters, have no direct relation with anthropometric dimensions.

Among the "abnormal" subjects scatter is also large, and there is considerable overlap between both groups. For sharp discrimination between subjects with normal and abnormal ventilatory function the OI technique does not seem to be the right choice. The method however turned out to be useful in histamine challenge testing, to detect and monitor bronchial asthma [11]. In this field it is thought to be equivalent to methods using $FEV_1$, but the results are much less dependent on the cooperation of the patient, and the technique itself is much less laborious than methods based on $R_{se}$ or $FEV_1$.

Acknowledgements: The authors wish to express their gratitude to the leaders of the field survey, R van der Lende and Ph H Quanjér. They also gratefully acknowledge useful comments contributed by J Dijkman, P J Sterk, K H van der Plas and one of the referees.

References
NORMAL RESPIRATORY RESISTANCE MEASURED BY THE "OPENING" INTERRUPTOR


Valeurs de référence de la résistance respiratoire totale, déterminées avec la technique d'interruption "ouverte". P. Vooren, B. van Zomeren.

RÉSUMÉ: Au cours d’une enquête épidémiologique importante de la fonction pulmonaire, des sujets ont exécuté des manœuvres de débit volume expiratoire maximum. Ils ont également été interviewés par des interrogateurs entraînés utilisant un questionnaire standardisé. Chez une fraction de sujets déterminée au hasard, la résistance du système respiratoire a été mesurée par la technique d'interruption "ouverte" dans laquelle la pression à la bouche avant la fin de la période d'interruption est divisée par le débit peu après la fin de celle-ci. L'échantillon contenant hommes et femmes, fumeurs aussi bien que non fumeurs; il comportait 229 sujets considérés comme bien portants sur la base de l'absence de plaintes à l'anamnèse et sur la base d'une courbe débit volume normale. Dans ce groupe, les résistances moyennes inspiratoires et expiratoires ne sont pas significativement différentes (0.27 et 0.29 pour les hommes, et 0.39 et 0.38 kPa·l·s pour les femmes). Les moyennes des résistances inspiratoires et expiratoires furent de 0.28±0.10 kPa·l·s pour les hommes et de 0.39±0.11 kPa·l·s pour les femmes. Les valeurs de résistance s'avèrent légèrement mais significativement en corrélation avec le poids corporel, le VEMS et le débit expiratoire maximum 50, mais non avec les habitudes tabagiques. En raison d'une variabilité considérable, la méthode ne permet pas de discrimination étroite entre les sujets normaux et anormaux. Toutefois, elle apparaît utile pour les tests de provocation à l'histamine et pour déceler et suivre l'asthme bronchique, car elle n'est pas sujette aux effets perturbateurs des inspirations et des expirations forcées. Eur Respir J., 1989, 2, 966-971.