

## CLINICAL SCIENCE

## INFLUENCE OF THE AGEING PROCESS ON THE RESISTIVE AND REACTIVE PROPERTIES OF THE RESPIRATORY SYSTEM

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**INTRODUCTION:** In an increasingly old society, the study of the respiratory system changes and new techniques dedicated to older patients are of interest in physiologic studies as well as in the diagnosis of respiratory diseases.

**OBJECTIVES:** (1) To investigate the impact of ageing on the resistive and reactive properties of the respiratory system, and (2) to compare the easiness of accomplishment of spirometry and forced oscillation for assessing lung function.

**METHODS:** We conducted a cross-sectional study in which forced oscillation was used to investigate respiratory system resistive and reactive properties, while spirometry was used as a reference test to evaluate 80 normal subjects aged between 20 and 86 years. A questionnaire was used to evaluate the easiness of accomplishment of spirometry and forced oscillation.

**RESULTS:** There was a significant increase in the respiratory system resonance frequency ( $p < 0.003$ ) and a reduction in the mean reactance ( $p < 0.004$ ) with increasing age. Respiratory system resistance and dynamic compliance were not related to the ageing process. The easiness of accomplishment of forced oscillation measurements was greater than that of spirometry. This result was particularly relevant in subjects over 70 years old ( $p < 0.05$ ).

**CONCLUSIONS:** Respiratory system resistance and dynamic compliance are not modified with ageing. On the other hand, respiratory system homogeneity decreases during the ageing process. Forced oscillation is easy to perform and provides information complementary to spirometry. This technique may be a promising alternative and/or complement to other conventional exams used to evaluate older people who are unable to adequately perform spirometric tests.

**KEYWORDS:** Age; Respiratory mechanics; Forced oscillation technique; Elderly.

## INTRODUCTION

The respiratory system undergoes considerable physiologic changes with ageing.<sup>1,2</sup> Late or missed diagnoses of respiratory problems can increase morbidity and mortality rates, also resulting in unnecessary or inadequate therapeutic approaches.<sup>3-5</sup> Older patients and health professionals frequently attribute respiratory symptoms

to senescence, given the less obvious symptomatology along with the difficulty in establishing normal patterns in these patients.<sup>6</sup> Therefore, a deep understanding of the functional modifications that are part of the ageing process is indispensable for the appropriate handling of respiratory pathologies in older patients and may contribute to a better distinction between normal and pathological states.<sup>7</sup>

Spirometric tests provide an objective means to verify ventilatory dysfunction and to estimate its severity in respiratory disorders. Although they are useful for diagnosis and prognosis, spirometric test results are strongly dependent on the cooperation of the patient. Older people may be unable to adequately perform spirometric tests, because of reduced cooperation, mood alterations, fatigue, or cognitive impairment.<sup>8-10</sup> In a recent editorial, it was pointed

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out that it is necessary to seek alternatives for those who are unable to perform these exams.<sup>4</sup> This statement follows a general agreement in the literature that it is necessary to develop new accurate and noninvasive tests of lung function.<sup>11,12</sup>

The Forced Oscillation Technique (FOT) is based on the application of low amplitude pressure oscillations to the respiratory system. Measurement of the applied pressure and the resultant flow allows estimation of the respiratory impedance, which describes the simultaneous effects of resistance, inertance and compliance in the obstruction to respiratory flow.<sup>13,14</sup> This technique has great potential as an alternative examination in the absence of conditions for adequate spirometry examination.<sup>13,14</sup> Another important advantage, particularly in pathophysiological research, is that FOT can provide information about the mechanical characteristics of the respiratory system that are complementary to spirometry.<sup>13-17</sup> Given these characteristics, several research groups have been using this technique in pathophysiological research.<sup>14</sup> In theory, FOT provides a simple and non-invasive method to yield highly relevant information about respiratory mechanics and the effects of the ageing process. Although this technique has been successfully applied in older patients to assess lung function,<sup>18</sup> determine reference values<sup>8</sup> and diagnose obstructive lung disease,<sup>9,10</sup> there are few studies in the literature concerning the use of FOT to evaluate the effect of increasing age on respiratory mechanics.<sup>19</sup>

In this context, the purpose of the present study was twofold: (1) to investigate the impact of the ageing process on the resistive and reactive properties of the respiratory system and (2) to compare the easiness of accomplishment of spirometry and FOT measurements for assessing lung function in groups with increasing age.

## METHODS

This study was approved by the Ethics Committee of the Rio de Janeiro State University (UERJ) and was a cross-sectional study involving comparative analysis among different age groups with regard to chronological age and respiratory mechanics. The young volunteers and adults were students and researchers of the Rio de Janeiro State University (UERJ), while the older volunteers were participants in the courses promoted by the Rio de Janeiro State University (UERJ). The objectives of the study were explained to all individuals, and their written consent was obtained before inclusion in the study. The inclusion criteria were the absence of respiratory symptoms and hospital internment episodes in the last six months, the absence of cardiovascular co-morbidity and thoracic surgeries, and

presentation of normal clinical and radiological exams. The exclusion criteria were the presence of pneumopathy (obstructive, restrictive or mixed), cognitive deficits, institutionalization, influenza or colds for 30 days prior to the evaluation, severe postural alterations (hyperkyphosis, scoliosis), neuromuscular disease, asthma and bronchitis in childhood, and smoking or former smoking. The participants were classified into six groups according to age (A: 20-29; B: 30-39; C: 40-49; D: 50-59; E: 60-69 and F: 70 years or more).

A standard multifrequency FOT test system operating in the most commonly used frequency range<sup>14,16</sup> as previously described in detail<sup>20,21</sup>, was used to measure total respiratory resistance and reactance. Measurements were taken according to the recommendations issued by a task force of the European Respiratory Society.<sup>14</sup> Briefly, small amplitude pressure variations from 4-32 Hz generated by a loudspeaker were applied at the mouth using a mouthpiece. The pressure input was measured with a Honeywell 176 PC transducer (Honeywell Microswitch, Boston, MA, USA), and the airflow was measured with a screen pneumotachograph connected to the same type of pressure measurement system with a matched frequency response. These signals were digitized for periods of 18 s, and their fast Fourier transform was computed. Three measurements were made, and the result of the test was calculated as the mean of these measurements.

Resistive impedance data were subjected to linear regression analysis over the frequency range from 4 to 16 Hz. The resistive impedance at 0 Hz (R0) was extrapolated from this analysis. This parameter is related to the total resistance of the respiratory system, including the airways, lungs, and chest wall resistive properties, and is usually used as an index of airway obstruction.<sup>22</sup> The mean resistance (Rm), which is sensitive primarily to airway caliber<sup>13</sup> and, therefore, to airway resistance, was also calculated for this frequency range. In addition, the slope of the resistive component of the respiratory impedance (S), which is associated with respiratory system homogeneity,<sup>23</sup> was obtained. Negative values of this parameter reflect abnormal patterns of ventilation distribution in the lung.

The properties of energy accumulation were characterized by the mean reactance (Xm), a property that is also usually related to the homogeneity of the ventilation distribution in the lung<sup>24</sup>. This parameter was calculated based on the entire studied frequency range (4 to 32 Hz). The properties of energy accumulation were also characterized by both the resonance frequency (Fr), which is defined as the frequency at which the Xrs equals zero, and the respiratory system dynamic compliance (Crsdyn), which was estimated using the Xrs at 4 Hz ( $C_{rs,dyn} = -1/(2\pi f X_{rs})$ ).<sup>25</sup>

This parameter is related to the lungs and chest wall elastic properties.

Forced oscillation exams were carried out before the spirometric tests in order to prevent changes in bronchial tone and to minimize fatigue.<sup>8,9</sup> The delay between the FOT and spirometric tests was less than thirty minutes. To perform the FOT analysis, the volunteers wore nose clips and firmly supported their cheeks and sub-mandibular tissue with their hands.<sup>14</sup> Each volunteer remained in a sitting position, keeping his or her head in a normal position and breathing at FRC through a mouthpiece. Data acquisition started 30 seconds after the beginning of the exam in order to allow the volunteer to become accustomed to the equipment. The validity of the data was measured by computing the coherence function, which evaluates the signal-to-noise ratio. This function is the equivalent in the frequency domain of the correlation coefficient used in the time domain. Only values with a coherence function of 0.9 or more were considered adequate.<sup>22,26-28</sup> Whenever the computed coherence was less than this threshold, the maneuver was considered invalid, and the exam was repeated. Whenever adequate coherence measurements could not be obtained according to these criteria, the patient was excluded from the study.<sup>26-28</sup>

Measurements of Forced Vital Capacity (FVC), Forced Expiratory Volume for the first second ( $FEV_1$ ),  $FEV_1/FVC$ , and the ratio of Forced Expiratory Flow (FEF) between 25% and 75% of FVC to FVC ( $FEF/FVC$ ) were obtained for patients in a sitting position using a closed circuit spirometer (*Vitrace VT-139; Pro-médico, Rio de Janeiro, Brazil*). These parameters are presented as raw data and percentiles of the predicted values (%). Predicted values for spirometry were obtained from Knudson et al.<sup>29</sup> and Pereira et al.<sup>30</sup> Forced expiratory maneuvers were repeated until three sequential measurements were obtained. The indices studied were those obtained from the best curve, which was selected based on the highest value of  $FEV_1$  plus FVC. Quality control of spirometry is given by the ATS criteria, with the software allowing the detection of unacceptable maneuvers.

A questionnaire was used to evaluate the easiness of accomplishment of spirometry and forced oscillation measurements. This questionnaire was administered by an interviewer, and ranged from zero, as the most difficult, to five, as the easiest exam.

Initially, the Shapiro-Wilkins test was used to evaluate the normality of the biometric data in each group. After this verification, it was found that the data followed a normal distribution; therefore, one-way ANOVA was used in the comparisons involving all of the groups, and the Tukey HSD test was used in the comparisons among adjacent classes. Analysis of the association between two variables

was initially accomplished by univariate regression among the oscilometric parameters, age and height. Height was included in the analysis because it showed a small but significant difference among the groups. Multiple linear regressions among the oscilometric parameters, age and height were also evaluated. An analysis of the effect modification or confounding of the height parameter in relation to age and oscilometric parameters was also done. The correction for height was done when the analysis found it to be an effect modification factor. These analyses were made using STATA 8.0 (Statacorp LP Texas, USA). The Chi-square test was used to compare the easiness of accomplishment attributed to FOT and spirometry.

The estimate of the sample size was based on the correlation coefficient criterion and on preliminary results<sup>31</sup> with coefficients of 0.352. This estimate was made using MedCalc 8.2 software, considering type I and type II errors of 5% and 10%, respectively. This estimate resulted in a minimum number of 80 volunteers.

## RESULTS

We initially interviewed 255 individuals. Of these, 157 were excluded because they had one or more of the exclusion criteria. The following (all volunteers) were excluded: 7 volunteers below 50 years, 14 between 50 and 59 years, 49 between 60 and 70 years and 86 above 70 years. In order to homogenize the sample, 18 other individuals were also removed. The biometric and spirometric characteristics of the 80 volunteers studied are described in Table 1. As expected, the age variation was significant among the groups ( $p < 0.001$ ). Body mass did not show significant differences, including comparisons among adjacent groups. Height, on the other hand, showed a small but significant (ANOVA,  $p < 0.001$ ) reduction with age. Comparison among the groups showed significant differences between the extreme groups, A and E. As a function of height reduction, body mass index showed a small but significant ( $p < 0.001$ ) increase.

The  $VEF_1/CVF$  analysis (Table 1) revealed a discreet, although significant ( $p < 0.001$ ), decline. A more accentuated decrease was shown by  $VEF_1(L)$  ( $p < 0.001$ ) and by  $CVF(L)$  ( $p < 0.001$ ). Considering  $FEF/CVF(\%)$ , we also observed a significant decline ( $p < 0.001$ ).  $R_0$  and  $R_m$  did not change in the studied groups, while  $S$  and all of the reactive parameters showed significant variation. Figure 1 shows the changes in oscilometric parameters in the studied population. Table 2 shows the univariate analyses of these parameters in relation to age and height. Multivariate analyses showed that the contribution of age was highly significant for  $Fr$  and  $X_m$  (Table 3). The results of the confounding analysis are

**Table 1 - Biometric and spirometric characteristics of the investigated subjects**

	Group A 20-29 years (n=14)	Group B 30-39 years (n=14)	Group C 40-49 years (n=14)	Group D 50-59 years (n=13)	Group E 60-69 years (n=12)	Group F > 70 years (n=13)	ANOVA / between groups
Age (years)	24.5±2.6	35.9±2.6	42±2.0	53.5±3.1	62.9±2.4	75.3±4.4	p<0,001 / A-B-C-D-E-F-A
Body mass (kg)	66.9±10.9	62.8±10.8	70.9±12.8	67.9±11.1	62.9±7.6	63.5±9.3	p=ns / A,B,C,D,E,F,A
Height (cm)	170±10	166±8	166±9	164±10	155±6	159±8	p<0,001 / A,B,C,D-E,F-A
BMI (kg/m <sup>2</sup> )	22.9±2.2	22.6±2.4	25.6±2.5	25.0±2.4	25.9±2.4	25.1±2.5	p<0,001 / A,B-C,D,E,F-A
Male / Female	7 / 7	7 / 7	7 / 7	4 / 9	2 / 10	4 / 9	-
FEV <sub>1</sub> (L)	4.0±0.9	3.6±0.7	3.3±0.5	2.9±0.6	2.5±0.5	2.2±0.6	p<0,001 / A,B,C,D,E,F-A
FVC (L)	4.6±1.2	4.1±0.6	3.9±0.6	3.3±0.8	2.9±0.5	2.7±0.7	p<0,001 / A,B,C,D,E,F-A
FEV <sub>1</sub> /FVC (%)	87.2±5.0	86.8±5.8	84.4±4.8	89.3±5.5	86.2±5.7	79.9±3.3	p<0,001 / A,B,C,D,E,F-A
FEF/FVC (%)	104.0±25.5	105.4±28.6	100.1±25.0	137.3±46.1	115.1±28.3	78.7±13.8	p<0,001 / A,B-C-D,E-F,A
R0 (cmH <sub>2</sub> O/L/s)	2,5±0.7	2.4±0.9	2.8±0.7	3.3±1.1	3.4±1.1	2.9±1.0	ns / A,B,C,D,E,F,A
S (cmH <sub>2</sub> O/L/s <sup>2</sup> )	10.6±13.5	-2.5±20.5	-12.9±34.0	-18.4±20.3	-6.4±21.2	-5.9±37.6	p<0,009 / A,B,C,D,E,F,A
Rm (cmH <sub>2</sub> O/L/s)	2.6±0.6	2.4±0.8	2.6±0.6	3.1±1.0	3.3±1.1	2.8±0.8	ns / A,B,C,D,E,F,A
Fr (Hz)	11.1±2.6	11.7±3.3	14.8±4.3	14.5±3.6	15.8±4.4	15.6±4.9	p<0,001 / A,B-C,D,E,F-A
Xm (cmH <sub>2</sub> O/L/s)	0.56±0.33	0.46±0.31	0.09±0.34	0.16±0.56	0.05±0.37	0.06±0.59	p<0,001/ A,B-C,D,E,F-A
Crs,dyn (L/cmH <sub>2</sub> O)	0.020±0.005	0.021±0.005	0.019±0.007	0.016±0.006	0.015±0.004	0.016±0.007	p<0,002 / A,B,C,D,E,F-A

n: number of subjects; Comparisons of the five groups / comparisons between groups: dashes indicate significant difference.

**Table 2 - Univariate regressions for respiratory impedance variables with age and height**

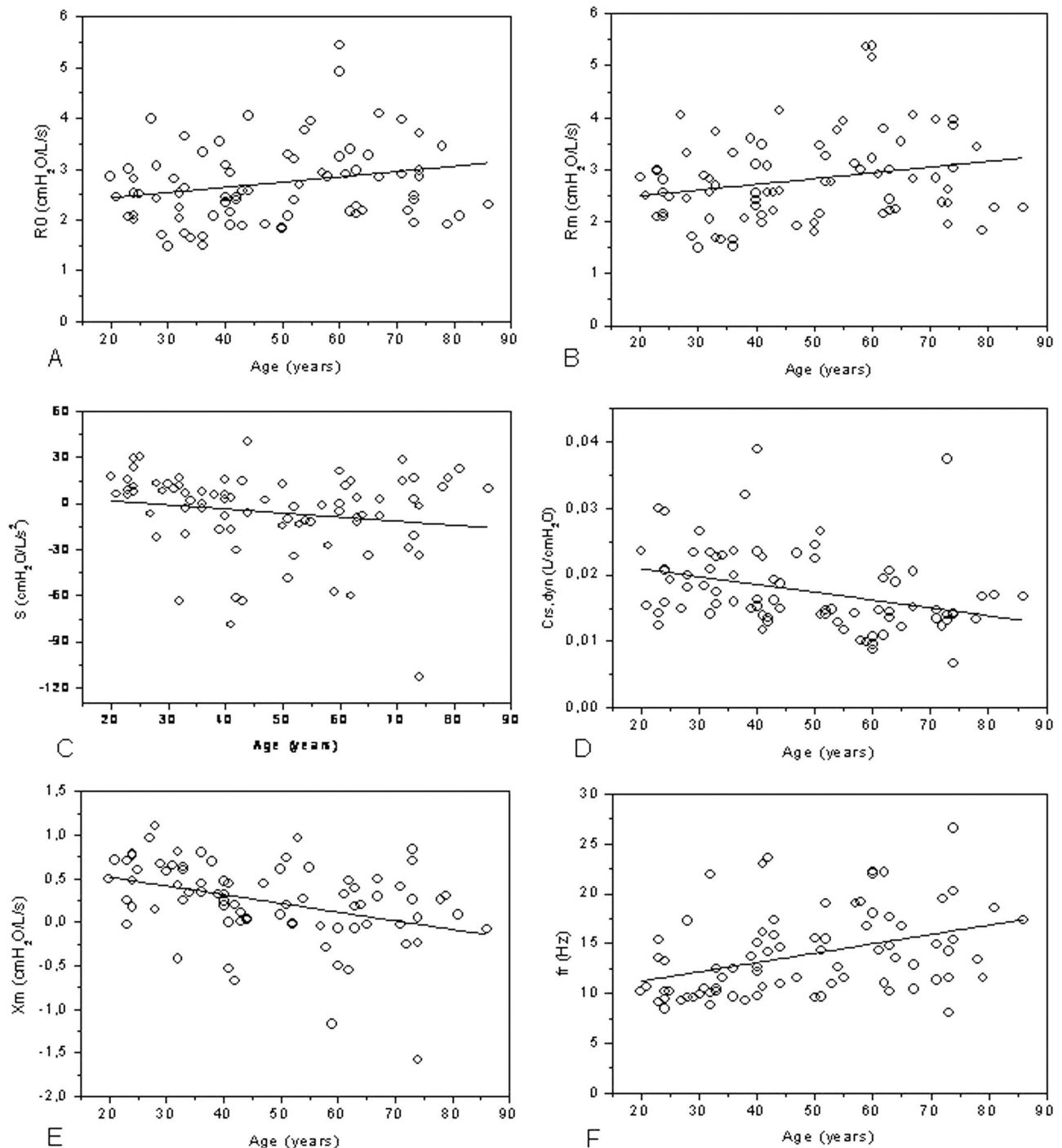
	Variable	Coefficient	CI 95%	r <sup>2</sup>	p
Age	R <sub>0</sub>	0.0138	0.001-0.025	0.0641	0.023
	S	-0.2645	-0.600-0.071	0.0305	0.1211
	R <sub>m</sub>	0.011	0.0005-0.021	0.0536	0.0388
	Fr	0.093	0.044-0.143	0.1542	0.0003
	X <sub>m</sub>	-0.010	-0.015- -0.004	0.1469	0.0004
	Crs,dyn	-0.0001	-0.0001- -0.00004	0.1163	0.002
Height	R <sub>0</sub>	-3.99	-6.041- -1.938	0.1612	0.0002
	S	22.10	-39.81-84.023	0.0064	0.4794
	R <sub>m</sub>	-3.72	-5.489- -1.966	0.1854	0.0001
	Fr	-10.003	-19.53- -0.470	0.0530	0.04
	X <sub>m</sub>	1.123	0.077- 2.169	0.0553	0.0357
	Crs,dyn	0.034	0.022-0.046	0.3064	0.0001

described in Table 4. The effect of height in the comparison between ageing and the parameters of forced oscillation was only significant for Crs,dyn.

Figure 2 shows the results of the comparative analysis between the easiness of accomplishment of FOT and spirometry measurements. We included 75 volunteers in this study. Among all age groups, the FOT measurements were considered easier than spirometric tests. In groups A, C, D and F, the observed differences were significant (p<0.05).

## DISCUSSION

In the present study, older subjects presented a small significantly lower height (Table 1). Previous studies have emphasized that respiratory system resistance increases with height.<sup>14,19</sup> Thus, the small height reduction among the groups could introduce small reductions in the resistive properties of the studied groups. Table 4 shows that height represented a



**Figure 1** - Changes in oscillometric parameters R0 (A), Rm (B), S (C), Crs,dyn (D), Xm (E) e Fr (F) in the studied population. R0: intercept resistance; Rm: mean resistance between 4-16Hz; S: slope of the resistive component of the impedance; Crs,dyn: dynamic compliance of the respiratory system; Xm: mean reactance between 4-32 Hz; Fr: resonance frequency

confounding variable for the analysis of resistive parameters. The small increase observed in BMI was related to the height reduction in the more advanced age groups. The results of the present study are consistent with the progressive decrease in spirometric parameters with age reported previously.<sup>30,32</sup>

Non-significant relationships were observed among the

resistive parameters and the ageing process, both before (Table 3) and after correcting for the height effect (Table 4). On the other hand, R0 and Rm were significantly associated with height (Table 3). These observations are consistent with the results of previous studies in which it was shown that the influence of height on resistive parameters was

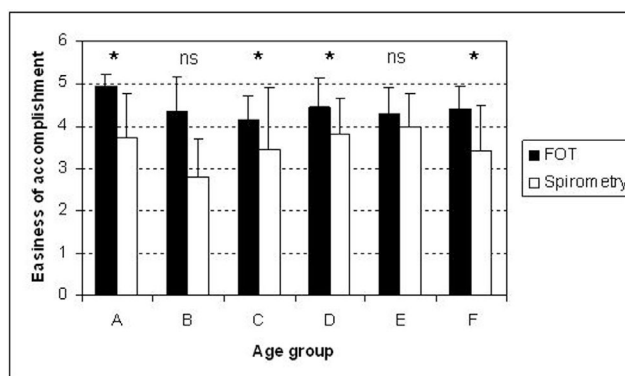
**Table 3** - Multiple linear regressions associated with age and height parameters. SE: Standard error. CI 95%: 95% confidence interval; r2: coefficient of determination; n=80

	Coefficient	SE	CI 95%	p	r <sup>2</sup>
<b>R<sub>0</sub></b>					0.1684
Age	0.005	0.006	-0.007-0.017	0.419	
Height	-3.577	1.151	-5.869-1.285	0.003	
Constant	8.464	2.037	4.407-12.52	0.000	
<b>S</b>					0.0305
Age	-0.262	0.189	-0.639-0.115	0.17	
Height	1.039	34.46	-67.59-69.66	0.976	
Constant	5.300	61.00	-116.1-126.7	0.931	
<b>R<sub>m</sub></b>					0.1875
Age	0.002	0.005	-0.008-0.013	0.655	
Height	-3.532	0.991	-5.506- -1.558	0.001	
Constant	8.466	1.754	4.972-11.96	0.000	
<b>Fr</b>					0.1582
Age	0.086	0.027	0.030-0.141	0.003	
Height	-3.062	5.064	-13.14-7.022	0.547	
Constant	14.72	8.965	-3.124-32.57	0.105	
<b>X<sub>m</sub></b>					0.1523
Age	-0.009	0.003	-0.015- -0.002	0.004	
Height	0.391	0.558	-0.720-1.503	0.486	
Constant	0.035	0.988	-1.932-2.003	0.971	
<b>Crs.dyn</b>					0.3180
Age	-0.00004	0.00003	-0.0001-0.0003	0.256	
Height	0.031	0.006	0.018-0.044	0.001	
Constant	-0.031	0.011	-0.054- -0.008	0.008	

**Table 4** - Effect of height in the relationship between ageing and forced oscillations parameters. \* Adjusted for height

	Confounding	Effect modification	p*
R0	0.394	-	0.379
S	0.532	-	0.117
Rm	0.411	-	0.433
Fr	0.131	-	0.043
Xm	0.588	-	0.033
Crs.dyn	-	0.0003	-

superior to that of weight and age, which were considered insignificant.<sup>9,33</sup> Plethysmographic studies indicated that the alterations in airway resistance due to the ageing process were not significant<sup>34,35</sup> and that airway resistance was similar in younger and older subjects.<sup>1,36,37</sup> In agreement with the results described in Figure 1, a comparative study between younger and older volunteers found that the resistance at 6 Hz was similar.<sup>34</sup> Lãndsér et al.<sup>19</sup> studied individuals without complaints of respiratory problems and



**Figure 2** - Comparative analysis between the easiness of accomplishment of FOT and spirometry measurements. Ns = non-significant; \* = p<0.05

with a normal clinical exam who were between 15 and 57 years old and observed a very small influence of age on the total respiratory system resistance. This is in agreement with our present work. The tendency of the total respiratory system resistance to decline that was reported in that study, however, was not observed in our present work. Figure 1 (C)

shows that S displayed a discrete decline. Both univariate and multivariate regressions showed a non-significant relationship between ageing and height.

Although the influence of height on respiratory mechanics is widely recognized in the literature, there are no studies investigating the effects of height on the reactive properties of the respiratory system. The results of the present study show that height can be considered a confounding factor for all of the reactive parameters, except in the analysis of Crs,dyn, which was a modifier variable of the age effect (Table 4). A first visual analysis of Crs,dyn indicated reduced compliance with ageing (Figure 2A). A more detailed analysis, however, showed that the effect of height on this variable was very important (Table 2), while the age effect was not statistically significant (Table 3). These results are apparently inconsistent with previous reports, which found that there was a decrease in lung elasticity with age.<sup>37</sup> Analysis of the dynamic lung compliance of older patients in spontaneous ventilation using esophageal pressure revealed values that were significantly higher in comparison with younger individuals.<sup>38</sup> These results are also in apparent disagreement with those presented in Figure 2A. It is important to emphasize that the alterations in Crs,dyn are recognized to be complex and are not limited to the mentioned lung modifications. The compliance of the thoracic wall decreases with ageing due to intercostal cartilage calcification, kyphosis and articular alterations.<sup>1,39</sup> Therefore, this reduction would theoretically reduce Crs,dyn and explain, at least in part, the tendency observed in the present study (Figure 2A).

Mean reactance became more negative with age ( $p < 0.004$ , Table 3), and about 14% of this change could be explained by the age increase ( $R^2 = 0.14$ , Table 2). More negative values of  $X_m$  are associated with reductions in respiratory system homogeneity.<sup>24</sup> Thus, analysis of the results described in Figure 2B lends additional support to the hypothesis that the respiratory system has increasing non-homogeneity with age.<sup>40,41</sup> Height can be considered a confounding factor with a non-significant effect on the relationship between  $X_m$  and age (Table 4). Consequently, the significant alterations seen in this parameter may be attributable to the ageing process (Table 3).

The increase in resonance frequency is associated with impairment in air distribution in the lungs<sup>14,15,21,26-28</sup>. This parameter showed a significant correlation with the ageing process both before (Table 3) and after correcting for the height effect (Table 4). On the other hand, this parameter did not show any significant association with height (Table 4). These results are in agreement with the study conducted by Guo et al.<sup>9</sup> concerning the diagnosis of obstructive lung disease in older patients.

There are few studies in the literature concerning the evaluation of the easiness of accomplishment of FOT and spirometric measurements.<sup>10,18</sup> Carvalhaes-Neto and collaborators<sup>18</sup> investigated the feasibility of spirometry or FOT for assessing lung function in the elderly in institutionalized patients with various degrees of cognitive function impairment. The results indicated that FOT measurement seems a more useful tool than spirometry for assessing lung function in elderly patients whenever cognitive function is impaired. The study conducted by Janssens and co-workers<sup>10</sup> have shown that FOT measurements has a higher feasibility rate than spirometry in elderly subjects hospitalized in an acute-care geriatric hospital, even in the presence of cognitive impairment. The results of the present study are in agreement with that obtained in the two cited studies and with previous suggestions in the literature,<sup>8,9</sup> indicating that FOT is easier to do than spirometry (Figure 2). These results also provide additional support to the recent suggestion of Allen<sup>4</sup> that FOT may be an alternative for evaluations in frail and impaired elderly people. FOT measurements were easier in four of the six studied groups, and even in the groups B and E, where the differences were not significant, there was a tendency for FOT exams to be easier.

The limitations of the present study included a reduced number of males in groups D, E and F. This can be explained, at least in part, by men seeking out health services less often than females. Another important factor was the high prevalence of tobacco consumption and ex-smokers among males. As the sample sizes in these groups are relatively small, we made no attempt to correct these results for gender. Moreover, previous studies in healthy adults aged, on average, 26-58 yrs, have shown that the influence of gender is low, with height being by far the most significantly predictive anthropometric variable.<sup>8</sup> Beydon et al.<sup>42</sup> pointed out that no gender difference was observed in most of the studies designed to obtain normal values in healthy children ranging from the preschool age up to adolescence.

In conclusion, this study has shown that the respiratory system resistance and dynamic compliance do not change with increasing age. On the other hand, changes in  $X_m$  and  $F_r$  showed that the respiratory system becomes progressively more non-homogeneous with age. The easiness of accomplishment of FOT measurements is greater than that of spirometry, particularly in subjects over 70 years old, indicating that FOT may be a promising alternative and/or complement to other conventional exams used to clinically evaluate older patients. Wider application of this technique among older people would probably contribute toward reducing the number of undiagnosed cases of respiratory

diseases and allow appropriate therapy in order to improve the quality of life and reduce mortality.

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