Accelerated lung aging in patients with morbid obesity*
Envelhecimento pulmonar acelerado em pacientes com obesidade mórbida

Saulo Maia D’Ávila Melo, Valdinaldo Aragão de Melo, Enaldo Vieira de Melo, Raimundo Sotero de Menezes Filho, Vinicius Leite de Castro, Matheus Santana Paes Barreto

Abstract

Objective: To determine the lung age of patients with morbid obesity and to compare it with the chronological age of these patients, emphasizing the premature damage that morbid obesity does to the lungs. Methods: An open, prospective cross-sectional study comprising 112 individuals: 78 patients with morbid obesity (study group); and 34 non-obese individuals with normal pulmonary function results (control group). All of the patients underwent spirometry for the determination of lung age. The lung age and the chronological age of the individuals in each group were compared in isolation and between the two groups. Results: The difference between lung age and chronological age in the group with morbid obesity was significant (p < 0.0001; 95% CI: 6.6-11.9 years), the mean difference being 9.1 ± 11.8 years. The difference between the study group and the control group in terms of lung age was significant (p < 0.0002; 95% CI: 7.5-16.9 years), the mean difference being 12.2 ± 2.4 years. Lung age correlated positively with chronological age and body mass index (BMI), whereas it correlated negatively with the spirometric variables (p < 0.0001 for all). Multiple linear regression analysis identified BMI and chronological age (p < 0.0001) as significant predictors of lung age. Conclusions: Lung age is increased in patients with morbid obesity, suggesting premature damage and accelerated lung aging, as evidenced by the discrepancy between chronological age and lung age. The determination of lung age might become a new tool for understanding pulmonary function results, for patients as well as for health professionals, in relation to obesity control.

Keywords: Spirometry; Obesity, morbid; Respiratory function tests.

Resumo

Objetivo: Determinar a idade pulmonar de pacientes com obesidade mórbida e compará-la com a idade cronológica desses pacientes, ressaltando o dano precoce da obesidade mórbida sobre os pulmões. Métodos: Estudo transversal, prospectivo e aberto que envolveu 112 indivíduos: 78 pacientes com obesidade mórbida (grupo de estudo) e 34 indivíduos não obesos e com função pulmonar normal (grupo controle). Todos os pacientes realizaram espirometria para a determinação da idade pulmonar. A idade pulmonar e a idade cronológica dos indivíduos em cada grupo foram comparadas isoladamente e entre os grupos. Resultados: A diferença entre a idade pulmonar e a idade cronológica no grupo com obesidade mórbida foi significativa (p < 0.0001; IC95%: 6.6-11.9 anos), com uma diferença média de 9.1 ± 11.8 anos. A diferença da idade pulmonar entre o grupo de estudo e o grupo controle foi significativa (p < 0.0002; IC95%: 7.5-16.9 anos), com uma diferença média de 12.2 ± 2.4 anos. A idade pulmonar demonstrou uma correlação positiva com a idade cronológica e o índice de massa corpórea (IMC) e uma correlação negativa com as variáveis espirométricas (p < 0.0001 para todos). A análise de regressão linear múltipla identificou as variáveis IMC e idade cronológica (p < 0.0001) como fatores preditivos significativos da idade pulmonar. Conclusões: A idade pulmonar está aumentada em pacientes com obesidade mórbida, sugerindo dano precoce e envelhecimento pulmonar acelerado, como evidenciado pela discrepância entre a idade cronológica e idade pulmonar. A determinação da idade pulmonar pode se tornar uma nova ferramenta na compreensão dos resultados da função pulmonar para pacientes e profissionais da saúde em relação ao controle da obesidade.

Descritores: Espirometria; Obesidade mórbida; Testes de função respiratória.

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Introduction

The alarming worldwide increase in overweight and obesity has reached epidemic proportions in recent years, becoming a public health and economic problem, and its prevention has been one of the priorities of the World Health Organization (WHO). Because obesity is a systemic disease, it is associated with various comorbidities such as diabetes mellitus, arterial hypertension, coronary insufficiency, and sudden death, and it is currently one of the leading causes of morbidity and mortality in individuals of all ages and from all social classes. However, the influence of obesity on the respiratory tract often goes unnoticed and has yet to be fully investigated.

The concept of lung age, as determined by spirometry, has been used in order to motivate smoking cessation and has recently received international attention because it provides clear and understandable pulmonary function results—patients and the general public can readily understand the spirometric changes—becoming a new tool for the early identification of functional abnormalities in lung disease. Although spirometry is the most common and essential pulmonary function test used by pulmonologists for clinical evaluation, it is a complementary test that is largely unknown and little used by other health professionals.

There have been no previous studies employing the concept of lung age for the early detection of impaired pulmonary function in morbidly obese individuals. The objective of the present study was to determine the lung age of patients with morbid obesity and to compare it with the chronological age of these patients, emphasizing the premature pulmonary impairment that morbid obesity causes.

Methods

This was an open, prospective, cross-sectional analytical study, conducted between January of 2007 and July of 2009. A total of 78 patients with morbid obesity, defined as a body mass index (BMI) ≥ 40 kg/m², were selected for the study (study group). The patients included were referred to the obesity outpatient clinics of the Universidade Federal de Sergipe (UFS, Federal University of Sergipe) and the São Lucas Hospital, both located in the city of Aracaju, Brazil, for the assessment of pulmonary risk related to surgical treatment of obesity.

We selected a control group of 34 healthy individuals without respiratory symptoms and with normal pulmonary function results, in accordance with the criteria established in the Brazilian Thoracic Association Guidelines for Pulmonary Function Tests. This control group consisted of volunteers (family members and friends of the patients, or health professionals) and patients referred for clinical or outpatient surgical evaluation, all of whom had a BMI ≤ 29.9 kg/m². Therefore, the final sample consisted of 112 patients (78 patients with morbid obesity and 34 healthy controls). The control group patients were matched to the study group patients for gender, age, and height.

All of the patients were referred to and evaluated at the UFS outpatient clinic, where the clinical evaluation and the pulmonary function tests were performed by an attending pulmonologist.

Individuals with acute or chronic lung diseases were excluded from the study, as were active and former smokers, regardless of smoking history; individuals who were unable to perform the pulmonary function tests; individuals with severe or uncontrolled arterial hypertension, heart failure, chronic kidney disease, severe systemic disease, or decompensated diabetes mellitus; and individuals under 20 years of age, as determined by the original formula for calculating lung age.

Patients diagnosed with bronchospasm or with a history of bronchospasm, at any age, even in childhood, were classified as having asthma and were excluded.

All individuals in the sample underwent chest X-ray, electrocardiography, echocardiography, and laboratory tests in order to identify the exclusion criteria.

The study design was approved by the UFS Research Ethics Committee (registration no. CAAE 0050.0.107.000-07), and all patients gave written informed consent.

Individuals were classified as morbidly obese (BMI ≥ 40 kg/m²) in accordance with the recommendations of the WHO. All such individuals had unsuccessfully attempted clinical treatments for obesity at least three times.

After clinical evaluation, body weight was measured with individuals wearing light clothing and no shoes, and height was measured with an...
the selection of the independent variables, we used stepwise multiple linear regression. The dependent variable was lung age, whereas the four independent variables were chronological age, BMI, gender, and the presence of comorbidities. The assumptions of normal distribution, homogeneity, and independence of errors were satisfied in accordance with established guidelines. The level of statistical significance was set at $p < 0.05$, and all statistical tests were two-tailed.

**Results**

The general characteristics and the spirometry results of the two groups are shown in Table 1. There were no statistical differences between the two groups in terms of chronological age, gender, height, or ethnicity. The mean BMI was $24.6 \pm 0.6 \text{ kg/m}^2$ in the control group (range, $19.2$-$29.8 \text{ kg/m}^2$) and $47.5 \pm 0.7 \text{ kg/m}^2$ in the study group (range, $40.0$-$65.6 \text{ kg/m}^2$), the difference between the two groups being significant ($p < 0.0001$). Significant differences were found between the two groups in terms of FVC and FEV$_1$, in absolute values and in percentage of predicted. However, no significant difference was found in terms of the FEV$_1$/FVC ratio ($p = 0.63$).

Of the 78 morbidly obese patients selected, 38 (48.7%) had one or more comorbidities: 36 (46.1%) had hypertension; 17 (21.7%) had diabetes; 15 (19.2%) had symptoms...

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control group</th>
<th>Obesity group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronological age, years</td>
<td>31.2 ± 11.0</td>
<td>34.1 ± 8.5</td>
<td>0.18*</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
<td>0.28**</td>
</tr>
<tr>
<td>Female</td>
<td>19 (55.9)</td>
<td>52 (66.7)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>15 (44.1)</td>
<td>26 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Height, m</td>
<td>1.7 ± 0.1</td>
<td>1.7 ± 0.1</td>
<td>0.86*</td>
</tr>
<tr>
<td>Caucasian, n (%)</td>
<td>16 (47.1)</td>
<td>36 (46.2)</td>
<td>0.93**</td>
</tr>
<tr>
<td>BMI, kg/m$^2$</td>
<td>24.6 ± 0.6</td>
<td>47.5 ± 0.7</td>
<td>0.0001*</td>
</tr>
<tr>
<td>FVC, L</td>
<td>4.1 ± 0.8</td>
<td>3.6 ± 0.9</td>
<td>0.003*</td>
</tr>
<tr>
<td>FVC, % of predicted</td>
<td>97.7 ± 11.0</td>
<td>86.2 ± 11.0</td>
<td>0.0001*</td>
</tr>
<tr>
<td>FEV$_1$, L</td>
<td>3.4 ± 0.7</td>
<td>3.0 ± 0.7</td>
<td>0.003*</td>
</tr>
<tr>
<td>FEV$_1$, % of predicted</td>
<td>97.2 ± 9.1</td>
<td>86.8 ± 10.7</td>
<td>0.0003*</td>
</tr>
<tr>
<td>FEV$_1$/FVC, %</td>
<td>85.3 ± 6.8</td>
<td>85.9 ± 5.9</td>
<td>0.63*</td>
</tr>
</tbody>
</table>

BMI: body mass index. Values expressed as mean ± SD, except where otherwise indicated. *Student’s t-test. **Chi-square test.
Accelerated lung aging in patients with morbid obesity

Table 2 - Comparison of the two groups in terms of lung age and chronological age.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control group</th>
<th>Obesity group</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 34)</td>
<td>(n = 78)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronological age, years</td>
<td>31.2 ± 11.0</td>
<td>34.1 ± 8.5</td>
<td>0.18</td>
</tr>
<tr>
<td>Lung age, years</td>
<td>31.0 ± 10.2</td>
<td>43.2 ± 14.5</td>
<td>0.0002</td>
</tr>
<tr>
<td>Chronological age – lung age, years</td>
<td>−0.1 ± 9.8</td>
<td>9.1 ± 11.8</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

Values expressed as mean ± SD. *Student's t-test.

suggestive of sleep apnea (snoring or nocturnal suffocation, or both); and 38 (48.7%) had other comorbidities (anxiety, depression, osteoarthritis, gastroesophageal reflux disease, gastritis, dyslipidemia, hepatic steatosis, or hypothyroidism). However, the comorbidities of all of these patients were clinically controlled with diet or medications (or a combination of the two), and, therefore, the patients were considered to be candidates for the surgical treatment of obesity.

Table 2 shows the mean chronological age and the mean lung age in each group, as well as the means of the differences between lung age and chronological age in each group and between the two groups. The mean chronological age was 31.2 ± 11.0 years in the control group and 34.1 ± 8.5 years in the obesity group, a difference that was not significant (p = 0.18). The mean lung age in the control group and in the obesity group was, respectively, 31.0 ± 10.2 years and 43.2 ± 14.5 years, representing a significant difference (p ≤ 0.0002). The difference between the two groups in terms of mean lung age was 12.2 ± 2.4 years (95% CI: 7.5–16.9 years).

When we analyzed mean lung age and mean chronological age in each group in isolation, we found that, in the control group, there was no statistically significant difference between mean lung age (31.0 ± 10.2 years) and mean chronological age (31.2 ± 11.0 years), the difference between these means being −0.1 ± 9.8 years (p = 0.93). However, in the obesity group, there was a significant difference between mean lung age (43.2 ± 14.5 years) and mean chronological age (31.2 ± 11.0 years), the difference between these means being 9.1 ± 11.8 years (p < 0.0001; 95% CI: 6.6–11.9 years; Table 2).

When we analyzed the differences between mean lung age and mean chronological age between the groups (control group vs. obesity group: −0.1 ± 9.8 years vs. 9.1 ± 11.8 years), we found a significant difference of 9.4 ± 2.1 years (p < 0.0005; 95% CI: 5.0–13.5 years; Table 2).

Lung age correlated positively with chronological age and BMI, whereas it correlated negatively with the spirometric variables in absolute values and in percentage of predicted, with statistical significance (p < 0.0001; Table 3).

Multiple linear regression analysis allowed the identification of BMI and chronological age as significant predictors of lung age—β = 0.471; t(109) = 5.466; p < 0.0001 and β = 0.758; t(109) = 6.903; p < 0.0001, respectively. In the final model adjusted for chronological age, BMI, gender, and comorbidities (hypertension, diabetes, and symptoms suggestive of obstructive sleep apnea syndrome—snoring and suffocation), only chronological age and BMI retained statistical significance and remained in the model (Table 4). This model was highly significant—F(2.109) = 47.72; p < 0.0001; R² = 0.454—and explained 45.4% of the variation in lung age.

The estimated variation in lung age showed an increase of 0.390 years (4.7 months) for each unit increase in BMI, assuming a constant chronological age.

Discussion

In the present study, we sought to investigate, by using the concept of lung age,
In most obese individuals, pulmonary function is affected by a mechanical effect on the respiratory tract and by metabolic effects of the adipose tissue. Intraperitoneal fat deposition raises the diaphragm, reducing FVC and TLC to values still within the normal range. Values of FEV\textsubscript{1} are affected by values of FVC, an effect that, in our study, explains the increase in lung age in the individuals with morbid obesity but with a preserved FEV\textsubscript{1}/FVC ratio. There is an inverse relationship between BMI and FEV\textsubscript{1}, with a modest effect on pulmonary function in individuals with a BMI $\geq 40$ kg/m\textsuperscript{2}. The mean predicted FEV\textsubscript{1} in healthy individuals is approximately 95\% of the actual FEV\textsubscript{1}, whereas the mean predicted FEV\textsubscript{1} in our control group was 97.2 ± 9.1\% of the actual FEV\textsubscript{1}, which could explain the fact that lung age was greater than chronological age in some healthy, non-obese individuals in our control group.

Because FEV\textsubscript{1} is an independent determinant of mortality and a major risk factor for sudden death, cancer, and cardiovascular disease, it is generally accepted as a sensitive and specific measure for clinically significant lung diseases, being part of the lung age calculation formula, which has lately been used for the early diagnosis of pathophysiological alterations caused not only by smoking but also by chronic lung diseases such as COPD, asthma, lung cancer, and interstitial diseases. Even before the onset of respiratory symptoms, greater emphasis should be placed on the use of the concept of lung age in individuals with morbid obesity.

The presence of comorbidities in the individuals with morbid obesity was determined by multiple regression analysis, which revealed that only BMI and chronological age had a significant impact on lung age, demonstrating the influence of BMI on premature pulmonary impairment.

### Table 4 - Multiple linear regression analysis for lung age in years (dependent variable) and independent predictors.$^a$

<table>
<thead>
<tr>
<th>Variable</th>
<th>$\beta$</th>
<th>SE of $\beta$</th>
<th>95% CI</th>
<th>Student’s t-test</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>-4.751</td>
<td>4.677</td>
<td>-14.02-4.51</td>
<td>0.312</td>
<td>0.31</td>
</tr>
<tr>
<td>Chronological age</td>
<td>0.758</td>
<td>0.492</td>
<td>0.540-0.976</td>
<td>6.903</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td>BMI</td>
<td>0.471</td>
<td>0.086</td>
<td>0.300-0.642</td>
<td>5.466</td>
<td>$&lt;0.0001$</td>
</tr>
</tbody>
</table>

BMI: body mass index. $^a$F(2.109) = 47.72; $p < 0.0001$; $R^2 = 0.454$—values adjusted for chronological age, BMI, gender, and comorbidities.
The relationship between BMI and lung age was reported in a retrospective study(1) of patients divided into quartiles by BMI (≤ 21.55 kg/m²; 21.56-23.28 kg/m²; 23.29-25.22 kg/m²; and ≥ 25.23 kg/m²). As can be seen, most of the patients in that study were not considered obese as defined by the WHO criteria. In addition, a BMI ≤ 21.55 kg/m² (control group) is rare in real life, and, for the fourth group (≥ 25.23 kg/m²), which presented a significant difference when compared to the first group, the variation in BMI and the mean BMI were not reported.

Although spirometry is a basic and indispensable test in the assessment and follow-up of the vast majority of patients with lung disease, it is not always available and its use is not common in primary care, even in developed countries. One explanation is the lack of knowledge and understanding of spirometry results among patients and general practitioners.(10)

The concept of lung age was introduced in 1985 by Morris & Temple,(6) who assessed the pulmonary function of 988 healthy male and female nonsmokers, aged 20-84 years (chronological age), by spirometry. Their results revealed a similarity between lung age and chronological age. Linear regression analysis revealed that FEV₁, was the best spirometric variable to be used in the formula for calculating lung age.(6) Initial studies of lung age were used for demonstrating significant differences between lung age and chronological age in smokers, and, currently, lung age is being used for encouraging smoking cessation and for detecting, in a timely manner, pulmonary function abnormalities in patients with chronic lung diseases.(6-10)

The concept of lung age, when used in conjunction with the classic spirometry report (restrictive, obstructive, or mixed ventilatory defect), becomes a new alternative for understanding the damage that obesity does to the lungs, providing an easy, safe, rapid, and low-cost interpretation of the results, because spirometry results, when expressed to quantify the degree of pulmonary function impairment in the classic way, might not be understood by patients and by health professionals who deal with the treatment of obesity.

However, when the estimated lung age is dissimilar to the chronological age, it is possible to inform obese patients of the premature pulmonary impairment identified and to advise them such impairment can be prevented or controlled by a reduction in body weight.(21) However, caution should be exercised to avoid the possibility that these patients will interpret the concept of lung age as life expectancy, and the patients should be warned only of the danger of a premature loss of pulmonary function.

Because the present study was cross-sectional, it has certain limitations due to the lack of a view over time, which calls for further studies evaluating the psychological strength of the concept of lung age as a warning sign and an additional incentive for obese patients to adhere to treatment. In addition, future studies should evaluate the predicted formulas for calculating lung age in terms of their validity for use in the Brazilian population.

In conclusion, lung age is increased in patients with morbid obesity, suggesting premature pulmonary impairment and accelerated lung aging, as expressed by the discrepancy between chronological age and lung age. The concept of lung age can become a new tool for understanding pulmonary function results, for patients as well as for health professionals, in relation to obesity control.

References


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