

Spirometric values in elderly asthmatic patients are not influenced by obesity

R. C. Agondi, C. Bisaccioni, M. V. Aun, M. R. Ribeiro, J. Kalil and P. Giavina-Bianchi

Clinical Immunology and Allergy Division, University of São Paulo, São Paulo, Brazil

Clinical & Experimental Allergy

Summary

Background Studies have suggested that asthma in obese individuals differs from the classic asthma phenotype, presenting as a disease that is more difficult to control.

Objective The objective of the present study was to determine whether obesity, age or a combination of the two are associated with worse spirometry parameters in patients with asthma.

Methods This was an observational cross-sectional study involving patients over 18 years of age who had been diagnosed with asthma (allergic or nonallergic). We evaluated the results of their spirometric tests. The patients were classified in accordance with two criteria: body mass index (BMI) and age. Based on their BMIs, the patients were divided into three groups: normal weight, overweight and obese. Patients were also separated into two categories by age: 18–59 years of age; and ≥ 60 years of age.

Results We evaluated 451 patients with asthma and their spirometry tests. In the present study, the pulmonary function parameters were negatively correlated with BMI and age ($P < 0.05$). We found that there was a statistically significant correlation between spirometric values and BMI among patients 18–59 years of age ($P < 0.001$), however, among patients over 60, we did not observe this negative association.

Conclusions and Clinical Relevance The spirometric values decreased significantly in proportion to the increase of BMI and age in patients with asthma, especially among young adults. There was no negative correlation between BMI and FEV₁ in the group ≥ 60 years of age, suggesting that perhaps the time of disease is a major factor in the loss of lung function than weight gain in the elderly.

Submitted 19 August 2011; revised 11 November 2011; accepted 14 December 2011

Correspondence:

Rosana Câmara Agondi, R. Bagé 100 ap.152, Zip Code: 04212-140, São Paulo, SP, Brazil.

E-mail: ragondi@gmail.com

Cite this as: R. C. Agondi, C. Bisaccioni, M. V. Aun, M. R. Ribeiro, J. Kalil and P. Giavina-Bianchi, *Clinical & Experimental Allergy*, 2012 (42) 1183–1189.

Introduction

The world-wide prevalence of asthma is high, as is that of obesity, and many studies suggest that the two conditions are correlated [1–4]. There is epidemiological evidence that obesity is a risk factor for developing asthma, and the association between obesity and asthma might be mediated by common genetic, environmental and psychosocial factors [2–4]. According to a meta-analysis conducted in 2007, the incidence of asthma can be as much as 50% higher in individuals who are overweight or obese than in those of normal weight [5].

Both obesity and asthma have an enormous impact on public health and their prevalence is on the rise. It is estimated that 45% of adults in Brazil and 65% of adults in the USA are overweight or obese, and asthma affects approximately 10% of individuals worldwide

[6–9]. In addition, the prevalence of overweight tends to increase with age, and this increase is accelerated after the age of 45 years [9]. Although the exact nature of the correlation between asthma and obesity has yet to be fully clarified, some epidemiological data suggest that obesity can precede asthma and can increase its severity, as well as decrease the effectiveness of the drugs that are commonly used in asthma treatment [6, 10, 11].

In asthma, patients who are obese, weight loss can lead to clinical and physiological improvement in relation to the symptoms of asthma [1, 12]. Certain factors complicate the diagnosis of asthma in obese individuals [3]. Even in individuals without asthma, obesity has numerous consequences for respiratory physiology, including decreased lung compliance (caused by reduced lung volume and chest wall restriction).

Obesity also increases airway resistance, increases oxygen consumption during respiratory effort, causes respiratory muscle dysfunction and creates an imbalance in the ventilation/perfusion ratio. Forced expiratory volume in one-second (FEV_1), forced vital capacity (FVC) and, especially, expiratory reserve volume (ERV) are reduced [6, 13]. In addition, obesity contributes to comorbidities, such as gastroesophageal reflux disease and sleep apnoea, both of which can mimic asthma or can coexist with it and make it difficult to control [5].

It has been speculated that the association between asthma and obesity is attributable in part to the effect that excess weight has on respiratory physiology, as well as to the increased production of inflammatory mediators seen in obese individuals. Although obesity and impaired pulmonary function both correlate positively with age, body mass index (BMI) has been shown to have an age-independent effect on pulmonary function [9, 12].

Many studies have demonstrated that obesity leads to a systemic inflammatory state. Adipocytes can release proinflammatory hormones, which might increase the prevalence and severity of asthma in the obese population [11, 14]. Therefore, BMI is a variable that should be taken into consideration in patients with asthma [7]. Studies have suggested that asthma in obese individuals differs from the classic asthma phenotype, presenting as a disease that is not only more difficult to control but also one that does not respond as well to inhaled corticosteroids [11, 15].

The objective of the present study was to determine whether obesity, age or a combination of the two are associated with worse spirometry parameters in patients with asthma, particularly FEV_1 , which is one of the criteria for classification of asthma severity and its control [2].

Methods

Sample

This was an observational and cross-sectional study involving patients over 18 years of age who had been diagnosed with asthma (allergic or nonallergic). Patients were recruited from the Asthma Outpatient Clinic of the Department of Clinical Immunology and Allergy of São Paulo University, located in the city of São Paulo, Brazil. All patients were under clinical treatment and out-of-attack of asthma. Patients with persistent asthma were using inhaled corticosteroids and those with intermittent asthma, were using nasal steroids daily.

We evaluated the results of spirometric tests conducted between February of 2009 and December of 2009. All patients met the criteria for a diagnosis of asthma as set forth in the Global Initiative for Asthma guidelines [2]. All of them were over 18 years of age,

with technically adequate spirometry. Patients with other lung diseases were excluded.

Patients were classified in accordance with two criteria: BMI and age. Based on their BMIs, the patients were divided into three groups: normal weight (BMI: 18–24.9 kg/m²); overweight (BMI: 25–29.9 kg/m²); and obese (BMI: ≥ 30 kg/m²). Waist–hip ratio (i.e. the waist circumference divided by the hip circumference) was suggested as an additional measure of body fat distribution. BMI has traditionally been the chosen indicator by which to measure body size and composition, and to diagnose underweight and overweight [16]. Although alternative measures that reflect abdominal adiposity, such as waist circumference, waist–hip ratio and waist–height ratio, have been suggested as being superior to BMI in predicting cardiovascular disease risk, we have chosen BMI because it is an index used frequently in studies of change in lung function and obesity [17]. Index measuring manoeuvres which are more practical and reliable than the values of the formula are presented and to be checked before each spirometry. Patients were also separated into two categories by age: 18–59 years of age; and ≥ 60 years of age.

Spirometry

All spirometric tests were performed between 7:00 and 9:00 am, by the same technician, with a Koko spirometer (PDS Instrumentation, Louisville, CO, USA), which provides flow-volume curves and volume-time curves. Bronchodilator treatment was discontinued 12 h before the test, whereas other medications were not. The tests measured FVC, flow-volume curves and volume-time curves. The spirometric tests provided values for FEV_1 and FVC, from which the FEV_1 /FVC ratio was calculated.

The techniques used for performing spirometry and interpreting the results were those recommended by the 2005 American Thoracic Society consensus and the 2005 European Respiratory Society consensus [18, 19]. However, the reference values used were those established in the Brazilian Spirometry Guidelines set forth at the Second Brazilian Consensus on Spirometry in 2002 [20]. The tests were repeated 15 min after the inhalation of 400 µg of albuterol via a metered-dose inhaler with a spacer.

Bronchodilator response was defined as an increase (over baseline) of at least 12% and 200 mL in FEV_1 or FVC. The FEV_1 values were categorized based on the percentage of the predicted value ($FEV_1\%$): normal (≥ 80); mild defect (60–79); moderate defect (41–59); and severe defect (≤ 40).

Statistical analysis

To compare the groups with regard to BMI, age and spirometric values ($FEV_1\%$ and FVC%), we used one

way analysis of variance (ANOVA) and the multiple comparison procedures (Student–Newman–Keuls method). We used Pearson's chi-square test to compare categorical data, which are expressed as absolute frequency (n) and relative frequency (%) of FEV₁ and FVC values. The level of significance was set at $P < 0.05$.

Results

We evaluated 451 patients and 451 corresponding sets of spirometry results. Patient ages ranged from 18 to 86 years (mean age: 49.2 ± 15.7 years), and 351 (78%) of them were women. Of the 451 patients evaluated, 153 (33.9%) were classified as normal weight, 153 (33.9%) as overweight and 145 (32.2%) as obese. Of the 145 obese patients, 123 (84.8%) were female patients. Mean age was higher in the obese group than that in the overweight and normal-weight groups (51.6 years vs. 50.4 years and 45.8 years). Table 1 shows the mean BMI, demographic characteristics and spirometric data for each group.

In the present study, the pulmonary function parameters were negatively correlated with BMI ($P < 0.05$) and age ($P < 0.05$), as can be seen in Fig. 1. The spirometry results were evaluated in terms of the FEV₁%. Almost half the patients (48.3%) presented with an FEV₁% ≥ 80 , and only 2.0% presented with an FEV₁% ≤ 40 (Fig. 2).

In the FEV₁% ≥ 80 group, there were more non-obese individuals than obese, representing 73.9% of the non-obese group (Table 2), with statistically significant difference ($P = 0.012$, χ^2). The highest proportion of patients with abnormal FEV₁% values was seen in the obese group, 60.7% of these patients presenting with an FEV₁% < 80 (Fig. 2).

Among the overweight patients, the pattern of distribution of FEV₁ values was similar to that observed among the normal-weight patients, although the proportion of patients presenting with a baseline FEV₁% ≥ 80 was lower (51% of overweight and 54.2% of normal-weight patients). In the obese group, only 57 individuals (39.3%) and in non-obese (normal weight plus overweight) 161 patients (52.6%) had FEV₁% ≥ 80 ($P = 0.012$), as shown in Fig. 2. Moreover, there was a loss in volume FEV₁ (L) of 17.7% when we compared the obese patients to those with normal weight

(Table 1). The decrease in the number of patients is directly proportional to the fall in FEV₁ in non-obese (normal weight plus overweight) patients, which did not occur in the obese group, where only 39.3% had FEV₁ $\geq 80\%$. In addition, groups of FEV₁ between 40% and 79% have a predominance of obese patients compared to those non-obese patients.

The FVC analysis showed that about 80% of normal or overweight patients had levels above 80%, and among obese patients 73% had FVC% ≥ 80 ($P = 0.088$, χ^2). Analysing the mean FVC% among the three groups, we found a decrease in FVC% in the obese group compared to the other two groups (Fig. 3). We found that only 27% of obese patients had FVC% < 80 , although 60.7% of the obese group had FEV₁% < 80 . There was a loss in volume of FVC of 14% in obese compared to normal-weight patients (Table 1).

The patients were also separated into two categories by age, 18–59 years of age; and ≥ 60 years of age. Table 3 shows the mean BMI and spirometric data for each group, stratified by age (18–59 years of age and ≥ 60 years of age). Of the 451 patients, 328 (72.7%) were 18–59 years of age, and 123 (27.3%) were ≥ 60 years of age.

The mean age of patients over 60 was 68.1 ± 6.6 years. In the group of patients 18–59 years of age, BMI was found to correlate positively with age and negatively with FEV₁, similar to what was observed for the sample as a whole (Figs 4a and c).

Although the FEV₁ and FVC values were lower in the group of patients ≥ 60 years of age, there was no correlation between FEV₁(%) values and BMI in this age bracket ($P < 0.746$), as shown in Fig. 4b. This figure also shows the negative correlation between FEV₁ and age only in the group of patients 18–59 years of age.

The spirometric patterns differed between the two age brackets. Figure 5 shows the FEV₁% values for the normal-weight group only, comparing the two age brackets. Within the normal-weight group, 64.6% of 18–59 years of age patients had FEV₁% ≥ 80 , whereas 75% of elderly patients (≥ 60 years of age) had FEV₁% < 80 , showing that the number of abnormal spirometry results was significantly higher among the patients ≥ 60 years of age ($P = 0.015$, χ^2). Among the overweight patients, the proportion presenting with FEV₁%

Table 1. Patients distribution according to BMI

	Age (years)	BMI (kg/m ²)	FVC (L)	FVC (%)	FEV ₁ (L)	FEV ₁ (%)	Index (FEV ₁ /FVC)	Female (%)
Normal weight	45,8 $\pm$ 17,8	22,7 $\pm$ 1,71	3,17 $\pm$ 0,98	93,0 $\pm$ 16,7	2,31 $\pm$ 0,87	81,2 $\pm$ 19,3	0,72 $\pm$ 0,1	70,8
Overweight	50,4 $\pm$ 14,6	27,3 $\pm$ 1,33	2,95 $\pm$ 0,83	91,2 $\pm$ 15,1	2,11 $\pm$ 0,67	79,9 $\pm$ 17,1	0,71 $\pm$ 0,1	77,3
Obese	51,6 $\pm$ 13,6	34,0 $\pm$ 3,73	2,71 $\pm$ 0,80	86,8 $\pm$ 15,0	1,90 $\pm$ 0,62	74,9 $\pm$ 17,7	0,70 $\pm$ 0,1	84,8

Results: mean $\pm$ SD.

BMI, body mass index; FEV₁, Forced expiratory volume in one-second; FVC, forced vital capacity.

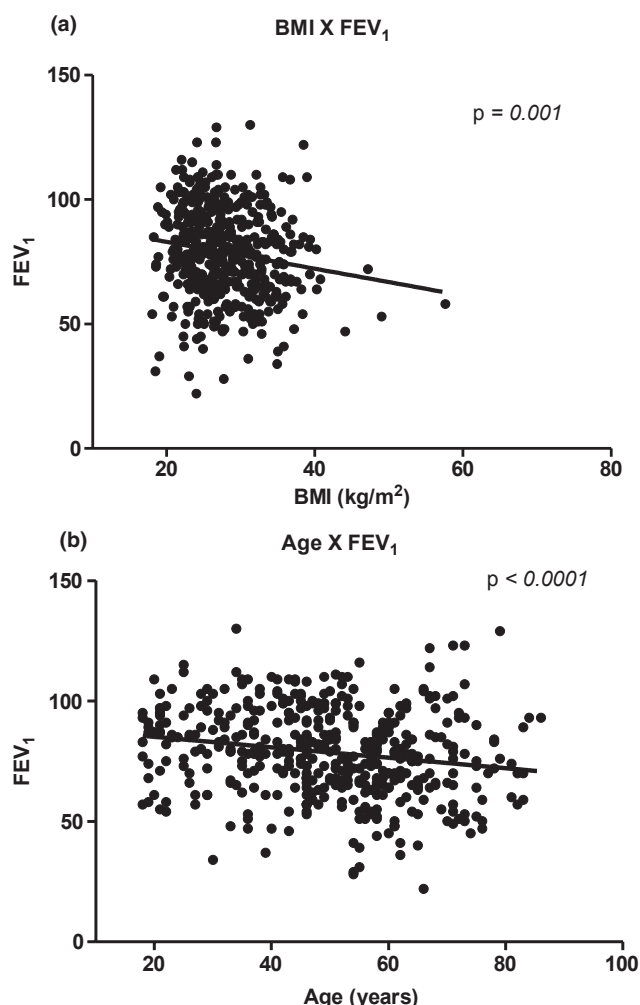


Fig. 1. Correlation between FEV₁ (%) pre-bronchodilator and BMI (kg/m²) or age (years). (a) Negative correlation between FEV₁ and BMI (Pearson correlation, $P = 0.001$); (b) negative correlation between FEV₁ and age (Pearson correlation, $P < 0.0001$).

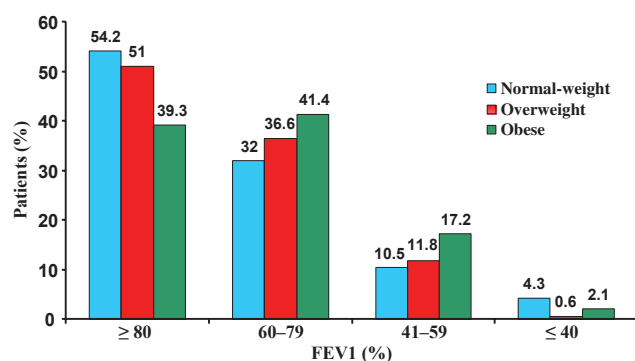


Fig. 2. FEV₁(%) pre-bronchodilator values according to BMI (kg/m²). Statistical analysis $P = 0.012$, χ^2 . FEV₁% ≥ 80 group represents 48.3% of the sample.

values between 41 and 59 was 9.6% for those 18–59 years of age and 17.9% for those ≥ 60 years of age (data not shown).

Table 2. Patients distribution according to FEV₁% and weight

FEV ₁ %	Non-obese (n/%)	Obese (n/%)
$\geq 80\%$	161/73.9	57/26.1
60–79%	105/63.5	60/36.5
41–59%	34/57.6	25/42.4
$\leq 40\%$	6/66.7	3/33.3

Non-obese: normal weight plus overweight patients.

Statistical analysis: $P = 0.012$, χ^2 .

FEV₁, Forced expiratory volume in one-second.

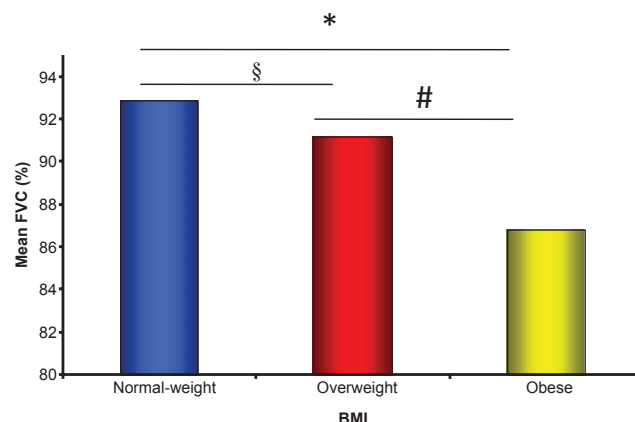


Fig. 3. Mean FVC (%) pre-bronchodilator values according to BMI (kg/m²). Statistical analysis (Student–Newman–Keuls method): * $P = 0.002$; § $P = 0.313$; # $P = 0.016$.

Discussion

In the present study, we found that there was a negative correlation between FEV₁ and BMI, and the mean FEV₁% being 17.4% lower among the obese patients than among the normal-weight patients. The proportion of female patients was higher in the obese groups than that in the other groups, as was the mean age. Our study found a high prevalence of asthmatic women (77.8%), especially those with more severe asthma (84.8%). The more severe asthma, by evaluating spirometric values such as FEV₁, was also more prevalent in the group with BMI ≥ 30 . According to WHO, obesity is more prevalent in women than in men, a ratio of 3 : 2 [16]. In addition, asthma is more prevalent and more severe in women as demonstrated in several studies [21–23]. In this study, BMI correlated positively with age and with being of the female gender. FEV₁ and FVC values were lower among asthma patients who were overweight or obese, especially among the latter, than among those of normal weight. This finding is in accordance with data in the literature [2, 13, 24].

When the spirometric values for asthma patients were evaluated by BMI and age bracket, a statistically significant correlation between spirometric values and BMI

Table 3. Spirometric values according to BMI and age group

Age group	BMI	age (mean)	BMI (kg/m ²)	FVC (L)	FVC%	FEV ₁ (L)	FEV ₁ %	FEV ₁ /FVC
<60	normal weight	37,5	22,7	3,44	96,1	2,58	84,7	0,75
	overweight	44,2	27,3	3,16	92,5	2,28	80,3	0,72
	obese	45,1	34	2,91	88,2	2,03	74,5	0,7
≥60	normal weight	69,4	22,8	2,4	84,3	1,55	71,5	0,64
	overweight	68,4	27,2	2,34	87,4	1,62	78,8	0,69
	obese	66,6	34	2,27	83,3	1,59	75,8	0,69

BMI, body mass index; FEV₁, Forced expiratory volume in one-second; FVC, forced vital capacity.

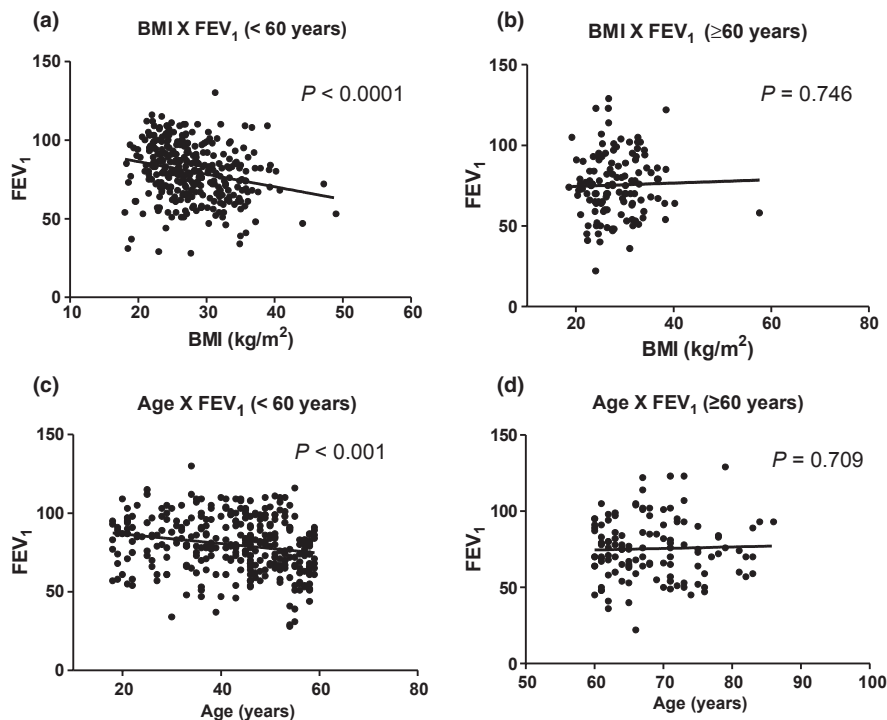


Fig. 4. Correlation between FEV₁ (%) pre-bronchodilator and BMI (kg/m²) or age (years), according to age group (< 60 years and ≥ 60 years). (a) Negative correlation between FEV₁ and BMI for patients < 60 years of age (Pearson correlation, $P < 0.0001$); (b) no correlation between FEV₁ and BMI for patients ≥ 60 years of age (Pearson correlation, $P = 0.746$); (c) negative correlation between FEV₁ and age for patients < 60 years of age (Pearson correlation, $P < 0.001$); (d) no correlation between FEV₁ and age for patients ≥ 60 years of age (Pearson correlation, $P = 0.709$).

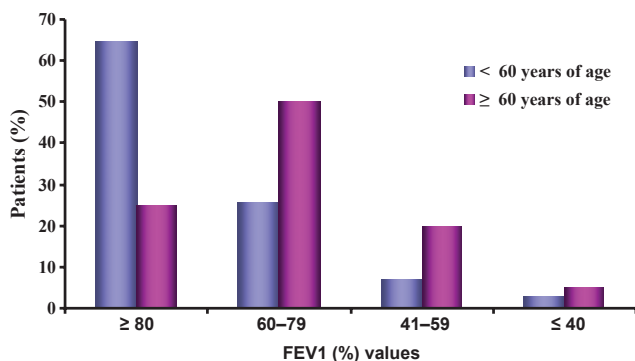


Fig. 5. FEV₁(%) pre-bronchodilator values according to age group, in patients with normal weight. Statistical analysis for comparison between < 60 years vs. ≥ 60 years of age and normal (FEV₁% ≥ 80) vs. abnormal (FEV₁% < 80) spirometric values: $P = 0.015$, χ^2 .

was found only for the patients 18–59 years of age. In this group, FEV₁% was found to be lower among the patients who were obese than among those who were not (Fig. 1a). Overall, FEV₁% was lower among the patients ≥ 60 years of age than among those 18–59 years of age. Only 25% of the normal-weight elderly patients presented with an FEV₁% ≥ 80, compared with 65% of those 18–59 years of age (Fig. 5). The negative correlation between FEV₁% and age might have a greater impact than that between FEV₁% and BMI in the group of patients ≥ 60 years of age as demonstrated in Fig. 1b.

Pulmonary function peaks in early adulthood [13]. During that phase of life, the factors affecting pulmonary function include gender and ethnicity, as

well as exposure to cigarette smoke and particulate matter. In the later stages of life, the level of pulmonary function is determined by early lung development and the level of function achieved in adulthood, as well as by the lifetime exposure to cigarette smoke, pollution and occupational contaminants. In addition, there is a decline in pulmonary function related to the ageing process itself [13].

In this study, we observed that there was loss of lung volume with increasing body weight. The FEV₁/FVC ratio remained at a similar level among the three BMI groups, suggesting that with the increase in BMI there was a decrease of FEV₁ (L) as a consequence of reduced FVC. However, when we evaluated the volume (L) drop in both age groups, we found that, in 18–59 years of age obese patients, the fall in FEV₁ was 21.3% and that in FVC was 15.4%, which suggests obstructive ventilatory defect (Table 3).

So even with the likely loss of FEV₁ as a result of FVC decline in obese patients, the decrease in FEV₁ was greater than that of FVC. Nevertheless, in elderly patients, we did not find this fall in FEV₁/FVC ratio, but these values were lower than those of patients 18–59 years of age, suggesting greater influence of disease duration. Holguin et al. recently demonstrated that increase in BMI was positively associated with asthma severity, especially in those with early asthma (<12 years of age) [25].

Other authors have shown a correlation between pulmonary function and BMI [13]. A cross-sectional study conducted in 2006 employed plethysmography to evaluate the effects of BMI on the lung volumes of 373 patients with asthma [24]. It was shown that the lung volumes, principally functional residual capacity (FRC) and ERV, correlated negatively with BMI. On average, every 1 kg/m² increase in the BMI resulted in a 0.5% decrease in vital capacity, total lung capacity and residual volume. The authors found that, BMI correlated most significantly with FRC and ERV [24].

Obesity also increases airway responsiveness in otherwise healthy humans [26]. Various cross-sectional and longitudinal studies have demonstrated age-related changes in body composition. As age advances, individuals tend to become more obese, with an increase in the amount of visceral fat and a decrease in skeletal muscle mass [27–29].

Pulmonary function also decreases with age [30]. The physiological ageing of the respiratory system is associated with changes in chest wall and lung compliance, as well as with air trapping, increased FRC and increased respiratory effort [30]. Expiratory flow rates also decrease with age. Respiratory muscle function is impaired as a result of geometric changes in the chest wall and depends on nutritional status, peripheral muscle mass and the cardiac index [30]. Therefore, body

composition and body fat distribution are associated with reduced pulmonary function in elderly individuals [27]. These age-related changes are clinically relevant because reduced pulmonary function is associated with an increase in the mortality rate. In elderly individuals, there is a central pattern of fat distribution, which is negatively correlated with pulmonary function [27]. This pattern of fat distribution might be related to changes in pulmonary function through various mechanisms, such as the mechanical effect that excess fat has on the diaphragm (hindering its descent to the abdominal cavity) and on the chest wall (resulting in changes in lung compliance, respiratory effort and lung elastic recoil). Since total adiposity and visceral fat tend to increase with age, these changes contribute to the decline in pulmonary function observed in elderly individuals. It is particularly important to consider weight loss treatment in to improve pulmonary function in obese individuals [28].

One study demonstrated that obese patients with asthma benefit from weight loss, which results in increased pulmonary volumes and improved respiratory mechanics [31]. Weight loss not only reduces airway obstruction and the variability in peak expiratory flow, but also improves asthma symptoms [31]. There is less evidence that weight loss can improve bronchial hyperreactivity [5, 12].

Our results indicate that FEV₁ and FVC decrease significantly in proportion to increases in BMI and age. We found that there was a statistically significant correlation between spirometric values and BMI among patients 18–59 years of age. The group of patients ≥ 60 years of age had smaller lung volumes than the other group. However, there was not a negative correlation between BMI and FEV₁ in this age group, suggesting that perhaps the time of disease is a major factor in the loss of lung function than weight gain in the elderly.

Conclusions

The spirometric values decreased significantly in proportion to the increase of BMI and age in patients with asthma. These results are repeated only in the group < 60 years of age. This negative association was not observed in the elderly group. These results suggest that lower spirometric values observed in older patients, without correlation with obesity, may be a consequence of disease duration.

Acknowledgements

We would like to thank Serafim Fidalgo and Mauricio G Freitas, for their technical assistance. All authors declare no conflicts of interest.

References

- Sutherland ER, Lehman EB, Teodorescu M, Wechsler ME. Body mass index and phenotype in subjects with mild-to-moderate persistent asthma. *J Allergy Clin Immunol* 2009; 123:1328–34.
- Global Initiative for Asthma – GINA [Internet]. [cited 2010 December 18] Available from: www.ginasthma.org.
- Clerisme-Beaty E, Rand CS. The effect of obesity on asthma incidence: moving past the epidemiologic evidence. *J Allergy Clin Immunol* 2009; 123:96–7.
- Camargo CA Jr, Weiss ST, Zhang S, Willett WC, Speizer FE. Prospective study of body mass index, weight change, and risk of adult-onset asthma in women. *Arch Intern Med* 1999; 159:2582–8.
- Beuther DA, Sutherland ER. Overweight, obesity, and incident asthma: a meta-analysis of prospective epidemiologic studies. *Am J Respir Crit Care Med* 2007; 175:661–6.
- Delgado J, Barranco P, Quirce S. Obesity and asthma. *J Investig Allergol Clin Immunol* 2008; 18:420–5.
- Stirbulov R, Bernd LAG, Solé D. IV Diretrizes Brasileiras para o Manejo da Asma. *Rev Bras Alerg Immunopatol* 2006; 29:222–45.
- Monteiro CA, Conde WL, Popkin BM. Income-specific trends in obesity in Brazil: 1975–2003. *Am J Public Health* 2007; 97:1808–12.
- Ministério da Saúde. Portal da saúde. [Internet]. [cited 2010 June 06] Available from: www.saude.gov.br.
- Ford ES. The epidemiology of obesity and asthma. *J Allergy Clin Immunol* 2005; 115:897–909.
- Lessard A, Turcotte H, Cormier Y, Boulet L-P. Obesity and asthma. A specific phenotype? *Chest* 2008; 134:317–23.
- Bottai M, Pistelli F, Di Pede F, Carrozzi L, Baldacci S, Matteelli G *et al.* Longitudinal changes of body mass index, spirometry and diffusion in a general population. *Eur Respir J* 2002; 20:665–73.
- Thyagarajan B, Jacobs DR Jr, Apostol GG, Smith LJ, Jensen RL, Crapo RO *et al.* Longitudinal association of body mass index with lung function: the CARDIA Study. *Respir Res* 2008; 9, 31 (pages 1–10).
- Beuther DA, Weiss ST, Sutherland ER. Obesity and asthma. *Am J Respir Crit Care Med* 2006; 174:112–9.
- Mosen DM, Schatz M, Magid DJ, Camargo CA Jr. The relationship between obesity and asthma severity and control in adults. *J Allergy Clin Immunol* 2008; 122:507–11.
- World Health Organization. www.who.int/mediacentre/factsheets/fs311/en. Updated in March 2011. Accessed in October 13th, 2011.
- Dalton M, Cameron AJ, Zimmet PZ *et al.* Waist circumference, waist-hip ratio and body mass index and their correlation with cardiovascular disease risk factors in Australian adults. *J Intern Med* 2003; 254:555–63.
- Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A *et al.* Standardization of spirometry. *Eur Respir J* 2005; 26:319–38.
- Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R *et al.* Interpretative strategies for lung function tests. *Eur Respir J* 2005; 26:948–68.
- Sociedade Brasileira de Pneumologia e Tisiologia. Diretrizes para testes de função pulmonar. *J Pneumol* 2002; 28:1–221.
- Trawick DR, Holm C, Wirth J. Influence of gender on rates of hospitalization, hospital course and hypercapnea in high risk patients admitted for asthma: a 10-year retrospective study at Yale-New Haven Hospital. *Chest* 2001; 119:115–9.
- Chena Y, Stewart P, Johansen H, McRae L, Taylor G. Sex difference in hospitalization due to asthma in relation to age. *J Clin Epidemiol* 2003; 56:180–7.
- Subbarao P, Mandhane PJ, Sears MR. Asthma: epidemiology, etiology and risk factors. *CMAJ* 2009; 9:181–90.
- Jones RL, Nzekwu M-UM. The effects of body mass index on lung volumes. *Chest* 2006; 130:827–33.
- Holguin F, Bleecker ER, Busse WW *et al.* Obesity and asthma: an association modified by age of asthma onset. *J Allergy Clin Immunol* 2011; 127:1486–93.
- Torchio R, Gobbi A, Gulotta C, Dellacà R, Tinivella M, Hyatt RE *et al.* Mechanical effects of obesity on airway responsiveness in otherwise healthy humans. *J Appl Physiol* 2009; 107:408–16.
- Santana H, Zoico E, Turcato E, Tosoni P, Bissoli L, Olivieri M, *et al.* Relation between body composition, fat distribution, and lung function in elderly men. *Am J Clin Nutr* 2001; 73:827–31.
- Villareal DT, Apovian CM, Kushner RF, Klein S. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. *Am J Clin Nutr* 2005; 82:923–34.
- Fantin F, Di Francesco V, Fontana G, Zivelonghi A, Bissoli L, Zoico E, *et al.* Longitudinal body composition changes in old men and women: interrelationships with worsening disability. *J Gerontol* 2007; 62A:1375–81.
- Janssens JP, Pache JC, Nicod LP. Physiological changes in respiratory function associated with ageing. *Eur Respir J* 1999; 13:197–205.
- Hakala K, Stenius-Aarniala B, Sovijärvi A. Effects of weight loss on peak flow variability, airways obstruction, and lung volumes in obese patients with asthma. *Chest* 2000; 118:1315–21.