

sensitized subjects. Allergists thus need to be aware of such potential allergens to which patients may be exposed in routine medical procedures.

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Obesity and airway inflammation in asthma

To the Editor:

The concurrent increase in the prevalence of obesity and asthma leads to the interest in potential mechanisms linking these 2 epidemics.¹ Obesity has been recently suggested as a proinflammatory state,² but the links with airway inflammation are still scarce. Our study aimed to investigate the association between overweight or obesity assessed by the body mass index (BMI) and asthma airway inflammation assessed by exhaled nitric oxide (F_{ENO}), a simple, quick, noninvasive, and highly reproducible surrogate marker of airway inflammation that could enhance diagnosis and management of asthma.

After informed consent, 297 nonsmoking patients, age 15 to 73 years, with a medical diagnosis of asthma were recruited from an asthma and allergy outpatient clinic at University Central Hospital in Porto. The study protocol included F_{ENO} measurement using the online technique with the NIOX system (Aerocrine, Stockholm, Sweden)³; FEV₁ determination using PIKO-1 (Ferraris Respiratory, Hertford, United Kingdom)⁴; and body weight and height anthropometric measurements using a mechanical balance with stadiometer (Seca model 700; Seca, Hamburg, Germany) followed by BMI determination (weight/height²). The World Health Organization BMI Classification was used to define underweight (<18.5 kg/m²), normal weight (18.5-24.9 kg/m²), overweight (25.0-29.9 kg/m²), and obesity (≥30.0 kg/m²).⁵ Atopy, defined by skin prick test to common aeroallergens, and inhaled corticosteroid

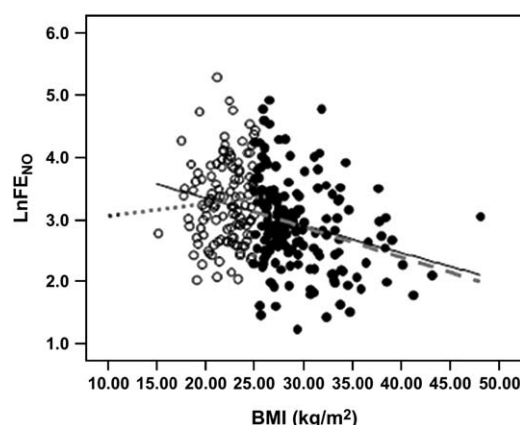


FIG 1. Association between BMI (kg/m²) and F_{ENO} (ppb) in patients with asthma. (...) Normal/underweight regression line ($R^2 = 0.004$); (—) overweight/obese regression line ($R^2 = 0.074$); (---) all patients regression line ($R^2 = 0.094$). (○) Normal/underweight patients with asthma; (●) overweight/obese patients with asthma. LnF_{ENO}, F_{ENO} logarithmically transformed.

use were registered. The data analysis was performed by using the statistical package SPSS, 12.0 version (SPSS Inc, Chicago, Ill). F_{ENO} was logarithmically transformed to attain normal distribution. Spearman correlation, linear regression, and general linear model were fitted to estimate the association between BMI and F_{ENO} and the effect after adjusting for age, FEV₁, sex, atopy, and inhaled corticosteroid use. A .05 level of significance and 95% CIs were considered.

Subjects' mean (SD) age was 39 (15.1) years, 76% (n = 226) were female, 55% were atopic, and the mean (SD) percent predicted FEV₁ was 85.7 (20.5). Geometric mean (95% CI) of F_{ENO} was 30.6 (27.9-33.6) and of BMI was 26.0 (25.4-26.5). One in 5 (20%) of the patients was obese, 38% were overweight, 40% were normal, and 2% underweight. Spearman correlation and linear regression analysis showed a negative association between mean BMI and mean F_{ENO} ($r_s = -0.329$, $P < .001$; $B = -0.044$; 95% CI, -0.060 to -0.028 ; $P < .001$). A different relationship was noted between overweight or obese patients with asthma with the others. In normal weight/underweight patients with asthma, no association between BMI and F_{ENO} ($r_s = -0.061$, $P = .499$; $B = 0.019$; 95% CI, -0.039 to 0.077 ; $P = .511$) was found. In overweight or obese patients with asthma, a significant negative association with F_{ENO} ($r_s = -0.307$, $P < .001$; $B = -0.049$; 95% CI, -0.075 to -0.023 ; $P < .001$) was observed (Fig 1). By general linear model analysis, BMI maintained the negative association with F_{ENO} ($B = -0.032$, 95% CI, -0.051 to -0.014 ; $F = 11.75$, $P = .001$) after adjustment for age, FEV₁, sex, atopy, and inhaled corticosteroid use. Age was also negatively associated with F_{ENO} ($B = -0.014$; 95% CI, -0.020 to -0.008 ; $F = 18.10$, $P < .001$). In overweight or obese patients with asthma, BMI ($B = -0.047$, 95% CI, -0.077 to -0.017 ; $F = 9.38$, $P = .003$) and age ($B = -0.013$, 95% CI, -0.022 to -0.003 ; $F = 6.23$, $P = .014$) maintained a significant

negative association with FE_{NO} . In normal weight/underweight patients with asthma, only age affected FE_{NO} ($B = -0.017$, 95% CI, -0.026 to -0.008 ; $F = 13.89$, $P < .001$).

We observed a negative association between BMI and FE_{NO} in overweight or obese patients with asthma, independent from sex, atopy, lung function, or corticosteroid use. Despite the adjusting to these main confounders, we cannot exclude the hypotheses that FE_{NO} measurement could be affected by others factors that cannot have been controlled.

Several cross-sectional and case-control studies have found obesity to be associated with asthma diagnosis, respiratory symptoms, poor lung function, and increased airway hyperreactivity. Plausible links between asthma and obesity include mechanical factors, inflammatory conditions, and stress models. The increased abdominal and chest wall mass causes decreased functional residual capacity and reduced lung and tidal volumes.^{6,7} Obesity is also a state of chronic and low-grade systemic inflammation with increased levels of the proinflammatory leptin and plasminogen activator inhibitor and decreased serum levels of the protective anti-inflammatory adiponectin.³ The relation between BMI and FE_{NO} has provided conflicting evidence. In children, BMI had no association with FE_{NO} ,⁸⁻¹⁰ whereas in 24 nonobese adults without asthma, a positive association has been reported.¹¹ Recently, a case-control study described a positive association in normal weight and obese healthy adults, but no significant association was observed in the asthma group. Although BMI was correlated with serum leptin levels in both groups, FE_{NO} was not related to serum leptin levels in patients with asthma.¹²

Our findings are based on cross-sectional data, and a causal relationship cannot be inferred. Although BMI is not the gold standard to assess body composition, it correlates with total body fat content and has been the most widely used measure to assess overweight or obesity and to monitor changes in body weight. In the future, research should include more complex anthropometric measures (eg, waist-circumference, skinfold thickness, or bioelectrical impedance analysis) that assess total body mass distribution, including body fat mass measure.

In conclusion, the observed negative association between BMI and FE_{NO} in overweight or obese patients with asthma provides additional support to the hypothesized mechanical link between obesity and asthma.

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Eosinophil β_1 integrin activation state correlates with asthma activity in a blind study of inhaled corticosteroid withdrawal

To the Editor:

Eosinophilic inflammation is a characteristic feature of asthma regulated by many factors, including treatment with corticosteroids.¹ On gradual inhaled corticosteroid (ICS) reduction, there is an increase in sputum eosinophils that often precedes changes in airway caliber and loss of asthma control.^{2,3} Conversely, ICS treatment directed toward a reduction in sputum eosinophils improves asthma control and prevents exacerbations.⁴ These and other reports suggest that eosinophils in the airway are associated with diminished asthma control and increased risk for exacerbation and that eosinophil recruitment to the airway likely is a key step in the development of bronchial inflammation and exacerbation.

Eosinophil recruitment to the airway involves integrins and their ligands.⁵ $\alpha_4\beta_1$ Integrin mediates blood eosinophil adhesion to vascular cell adhesion molecule 1, preferentially induced on endothelium in response to T_H2