

ENVIRONMENTAL DETERMINANTS

Adiposity, Adipokines, and Exhaled Nitric Oxide in Healthy Adults Without Asthma

SANG-HEON KIM, M.D., TAE HYUNG KIM, M.D., JI SEON LEE, M.D., TAI YEON KOO, M.D.,
CHANG BEOM LEE, M.D., HO JOO YOON, M.D., DONG HO SHIN, M.D., SUNG SOO PARK, M.D., AND
JANG WON SOHN, M.D.*

Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Republic of Korea.

Background. Epidemiological studies have shown that obesity/adiposity is closely associated with asthma in terms of development, severity, and control of asthma. However, effects of obesity/adiposity on airway inflammation are not well known in subjects without asthma. We assessed whether fractional exhaled nitric oxide (FeNO), a marker of eosinophilic airway inflammation, was associated with obesity/adiposity in nonasthmatic healthy adults. **Methods.** We measured FeNO and serum levels of adipose-derived hormones and adipokines in 117 adult subjects without a previous diagnosis of asthma or current asthmatic symptoms. Associations between FeNO and measures of obesity/adiposity [body mass index (BMI), body fat mass, and body fat percentages] were examined by correlation analyses and uni- and multivariate linear regression analyses. **Results.** FeNO was not significantly associated with BMI, body fat mass, or body fat percentage by a multivariate linear regression model, adjusting for age, gender, chronic rhinitis, atopy, and lung function. No significant association of FeNO with serum levels of leptin, adiponectin, tumor necrosis factor (TNF)- α , or interleukin (IL)-6 was observed. **Conclusions.** These findings suggest that in healthy subjects without asthma, obesity/adiposity has no significant effect on eosinophilic airway inflammation and that hormones and systemic inflammation derived from adipose tissue do not affect eosinophilic airway inflammation.

Keywords adipokines, adipose-derived hormones, adiposity, airway inflammation, body mass index, exhaled nitric oxide

INTRODUCTION

Both obesity/adiposity and asthma are serious public health problems and the prevalence of both is on the rise. Epidemiological studies have found a close relationship between obesity and asthma; obesity increases the risk of incident asthma (1). In established asthma, obesity is related to severe asthma and poor control of asthma (2). The relationship between obesity and asthma has been explained by several possible mechanisms, including the effects of obesity on lung mechanics, impact of obesity on airway inflammation, aggravation of asthma by obesity-related morbidities, and common etiologies underlying both obesity and asthma (3). Obesity is now understood as a kind of inflammatory disorder and includes low-grade systemic inflammation. Adipose-derived hormones, such as leptin and adiponectin, and adipokines, such as tumor necrosis factor (TNF)- α and interleukin (IL)-6, secreted from adipose tissue, have been suggested to affect airway inflammation (4). Based on this background, numerous clinical and experimental studies have explored the link between obesity and airway inflammation. However, the results have so far been conflicting.

Fractional exhaled nitric oxide (FeNO) reflects eosinophilic airway inflammation, and measurements of FeNO have proven useful in the diagnosis and

management of asthma (5). An earlier study in a small population of healthy nonsmoking adults found that body mass index (BMI), a measure of obesity, was positively associated with FeNO (6, 7). This relationship between BMI and FeNO was not found in healthy children or adolescents, when FeNO was adjusted for age (8, 9).

In patients with asthma, the association between obesity and airway inflammation seems quite different from that in healthy subjects without asthma. Obese subjects showed significantly lower levels of FeNO compared to nonobese subjects (10) and BMI was negatively associated with FeNO in adults with asthma (11–13). In addition to FeNO, sputum cell counts, another marker for airway inflammation, showed no significant association with BMI in either patients with asthma or nonasthmatic subjects (14). Thus, any impact of obesity on airway inflammation and FeNO remains unclear. The incoherent results on the associations between airway inflammation and FeNO in both healthy and asthmatic subjects can be partially caused by incomplete consideration of the affecting factors for FeNO in the analyses.

BMI has been widely used as an index of obesity because BMI correlates with morbidity risk and BMI measurements are inexpensive and easy to conduct (15). However, it has some limitations in representing body fat content (16). Subjects with high body fat and low muscle mass can be misclassified as normal when using a BMI classification. For other markers of obesity/adiposity, we also measured body fat mass and body fat percentage using whole-body bioelectrical impedance analysis, which can be performed easily and quickly (17).

*Corresponding author: Jang Won Sohn, Department of Internal Medicine, Hanyang University Guri Hospital, Hanyang University College of Medicine, Gyomun-dong 249-1, Guri-si, Gyeonggi-do 471-701, Republic of Korea; Tel: +82-31-560-2224; Fax: +82-31-553-0392; E-mail: jwsohn@hanyang.ac.kr

In this study, we hypothesized that obesity/adiposity would be associated with eosinophilic airway inflammation, as determined by FeNO, in healthy adults without asthma. We examined whether FeNO was associated with measures of obesity/adiposity (BMI, body fat mass, body fat percentage) with a multivariate linear regression analysis of FeNO by adjusting the factors affecting FeNO levels. Furthermore, we assessed whether FeNO was related with adipose-derived hormones (leptin, adiponectin) and markers of chronic systemic inflammation from adipose tissue (TNF- α , IL-6).

METHODS

Study Design and Subjects

Healthy adult subjects aged 20–68 years were recruited from employees at Hanyang University Guri Hospital, Guri, Korea, during their routine health examination in July 2008. This study was approved by the institutional review board. After obtaining informed consent, individuals were evaluated for their respiratory and nasal symptoms related to asthma and rhinitis and any previous diagnosis of asthma by physicians, and any recent respiratory infection and smoking status using a questionnaire. Spirometry was performed in all subjects to measure forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV₁). Exclusion criteria were the following: current or former smokers; respiratory symptoms, such as dyspnea and wheezing, in the past 12 months; physician-diagnosed asthma; respiratory infection in the last 3 weeks; chronic pulmonary disease; taking medicine(s) known to affect the levels of FeNO, the skin-prick test, or plasma adipokines; <0.7 in the FEV₁/FVC ratio or <80% predicted FEV₁; and abnormal chest radiographs. Among 160 recruited subjects, 43 were excluded based on these criteria and 117 subjects were enrolled. To determine atopic status, we performed skin-prick tests for ten common aeroallergens using a commercial kit (Allergopharma, Reinbek, Germany): house dust mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*), *Tyrophagus putrescentiae*, grass pollen mixture (velvet grass, orchard grass, rye grass, timothy grass, Kentucky blue grass, meadow grass), mugwort, ragweed, cat, dog, using *Alternaria* sp., and *Aspergillus* sp. We used histamine (1 mg/ml) as positive control and normal saline as negative control. A wheal of 3 mm or more was considered positive and atopy was defined as one or more positive responses to these allergens.

BMI, Body Fat Mass, and Body Fat Percentage

BMI (in kg/m²) was calculated from the measured height and weight. Obesity was defined as BMI $\geq$ 25 kg/m² (18). We measured body fat mass and body fat percentage using a body composition analyzer (In Body J20, Biospace Co. Ltd., Seoul, Korea).

Measurement of FeNO

NO measurements were performed before spirometry. Levels of FeNO were measured using a NO analyzer (Sievers NOA280i; GE Analytical Instruments, Boulder, CO, USA) according to ATS/ERS recommendations (19). Briefly, FeNO levels were assessed online during a single slow breath against a resistance of at least 10 cm H₂O. The expiratory flow rate was set at 50 ml/s. Exhalations were repeated up to eight times to obtain three acceptable values of FeNO that were within 10% of each other. The mean of the three acceptable values was determined as the level of FeNO.

Measurement of Serum Levels of Adipokines and Inflammatory Cytokines

Fasting venous blood samples were collected from the subjects in the morning after an overnight fast. Serum was isolated after centrifuging the blood and was stored at -70°C for later analyses. Serum levels of leptin, adiponectin, TNF- α , and IL-6 were measured using multiplex assay kits based on Luminex xMAP technology (Linco Research, St. Charles, MO, USA).

Statistical Analyses

Data are expressed as geometric means $\pm$ SD unless otherwise indicated. Because FeNO levels were not normally distributed, analyses of FeNO were performed with log-transformed values. Characteristics of the groups were compared using the chi-square test for categorical variables and the Student's *t*-test for continuous variables. Associations between FeNO levels and BMI, body fat mass, body fat percentage, and serum levels of hormones and adipokines were determined by Pearson's correlation and simple linear regression analyses. Multivariate linear regression analysis of FeNO was performed with independent variables including age, gender, chronic rhinitis, atopy, and BMI (or body fat mass or body fat percentage) in separate models. These variables were selected based on *a priori* decisions. Statistical analyses were performed using SPSS (version 17.0, SPSS Inc., Chicago, IL, USA). *P* values < .05 were deemed to indicate statistical significance.

RESULTS

Characteristics of the Study Population

The characteristics of the 117 subjects enrolled in this study are presented in Table 1. The subjects' mean age was 36.4 $\pm$ 10.0 years and 42 (35.9%) were males. Mean BMI was 23.3 $\pm$ 3.4 kg/m² and 31 (26.5%) subjects were obese (BMI $\geq$ 25 kg/m²). FeNO values ranged from 8.6 to 89.6 ppb with a median value of 26.8 ppb (interquartile range 16.7).

Association of FeNO with BMI, Body Fat Mass, and Body Fat Percentage

BMI was positively correlated with FeNO in the whole study population ($r = 0.267$, $p = .004$; Figure 1A) and

TABLE 1.—Clinical characteristics of the subjects.

Characteristics	Subjects (<i>n</i> = 117)
Age, years	36.4 ± 10.0
Males, <i>n</i> (%)	42 (35.9)
Height, cm	163.6 ± 7.7
Weight, kg	62.6 ± 12.0
BMI, kg/m ²	23.3 ± 3.4
Obese (BMI ≥ 25.0), <i>n</i> (%)	31 (26.5)
Body fat mass, kg	17.2 ± 6.1
Body fat percentage, %	27.4 ± 7.0
Chronic rhinitis, <i>n</i> (%)	61 (51.2)
Atopy, <i>n</i> (%)	51 (43.6)
FVC, % predicted	101.8 ± 12.2
FEV ₁ , % predicted	100.1 ± 12.4
FeNO, ppb, median (interquartile range)	26.8 (16.7)

Data are shown as the means ± standard deviation, if not otherwise mentioned.

showed a significant relationship with FeNO in a univariate linear regression analysis [coefficient, 0.036; 95% confidence interval (CI) 0.012–0.060; *p* = .004]. When

we performed a multivariate linear regression analysis of FeNO by adjusting the factors affecting FeNO levels, BMI was not significantly associated with FeNO levels (coefficient, 0.016; 95% CI –0.020–0.042; *p* = .228; Table 2). However, age (coefficient, 0.012; 95% CI 0.002–0.022; *p* = .021) and male sex (coefficient, 0.229; 95% CI 0.007–0.450; *p* = .043) showed significant associations with FeNO levels in the multivariate linear regression analysis.

BMI was positively correlated with body fat mass (*r* = 0.742, *p* < .001) and body fat percentage (*r* = 0.366, *p* < .001). Figure 1B illustrates no correlation of body fat mass with FeNO in healthy subjects without asthma (*r* = 0.037, *p* = .691). In a multivariate linear regression analysis, no significant relationship was observed between body fat mass and FeNO (coefficient, 0.003; 95% CI –0.010 to 0.015; *p* = .700). As shown in Figure 1C, there was no correlation between body fat percentage and FeNO (*r* = –0.175, *p* = .062). In addition, body fat percentage also showed no significant association

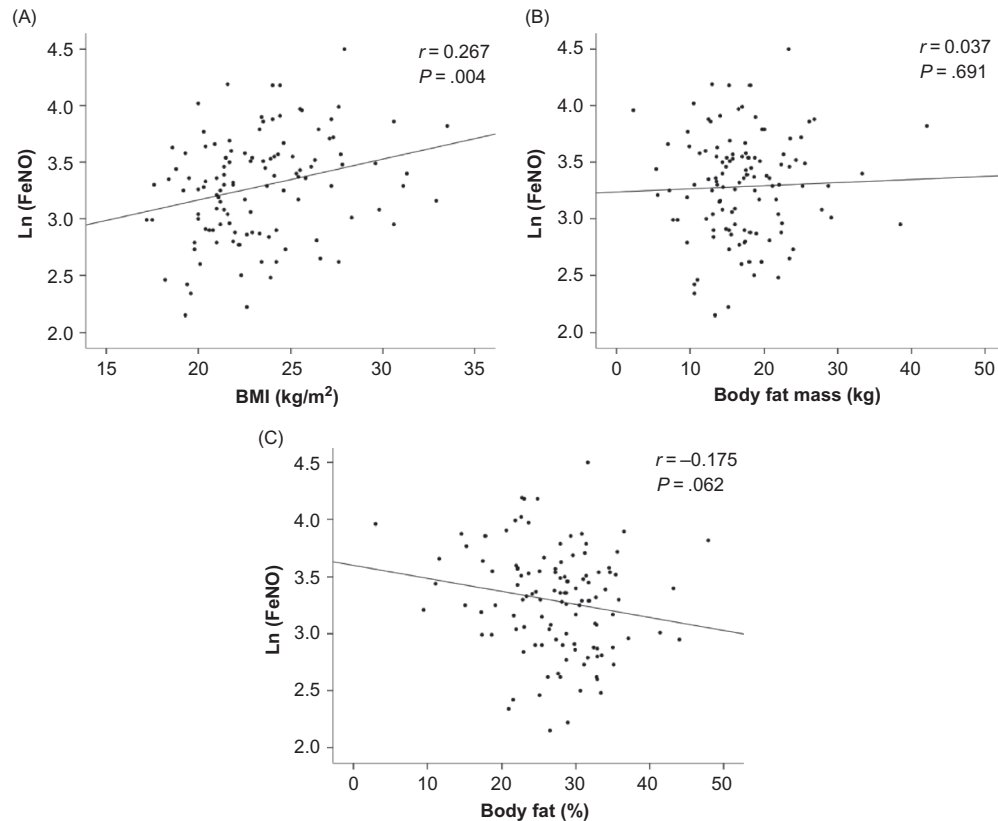


FIGURE 1.—Association of FeNO with indices of obesity/adiposity in healthy adults. (A) Correlation between BMI and FeNO; (B) correlation between body fat mass and FeNO; and (C) correlation between body fat percentage and FeNO.

TABLE 2.—Linear regression analysis for log-transformed exhaled nitric oxide.

Variables	Univariate analysis		Multivariate analysis	
	Coefficient (95% CI)	<i>p</i> -Value	Coefficient (95% CI)	<i>p</i> -Value
BMI	0.036 (0.012 – 0.060)	.004	0.016 (–0.020 to 0.042)	.228
Body fat mass	0.003 (–0.011 to 0.017)	.691	0.003 (–0.010 to 0.015)	.700
Body fat percentage	–0.011 (–0.023 to 0.001)	.062	–0.001 (–0.014 to 0.011)	.821

Note. Multivariate linear regression analysis adjusted for age, gender, chronic rhinitis, atopy, and BMI (or body fat mass or body fat percentage) using separate models.

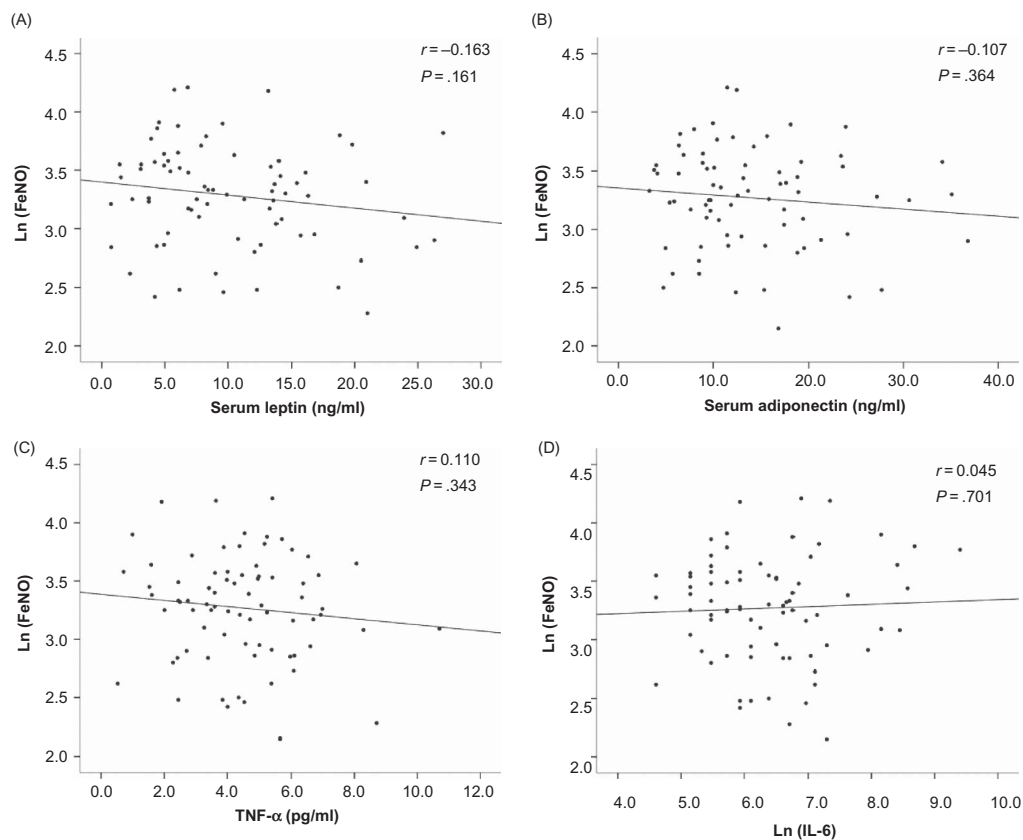


FIGURE 2.—Association of FeNO with serum levels of adipose-derived hormones and adipokines in healthy adults. (A) Correlation between serum leptin levels and FeNO; (B) correlation between serum adiponectin levels and FeNO; (C) correlation between serum TNF- α levels and FeNO; and (D) correlation between serum IL-6 levels and FeNO.

with FeNO in a multivariate linear regression analysis (coefficient, -0.001 ; 95% CI -0.014 to 0.011 ; $p = .821$).

Association of FeNO with Serum Levels of Adipose Derived Hormones and Adipokines

Serum levels of leptin did not correlate with FeNO ($r = -0.163$, $p = .161$; Figure 2A). No significant association was observed between serum adiponectin levels and FeNO ($r = -0.107$, $p = .364$; Figure 2B). FeNO was not related to serum levels of TNF- α ($r = -0.110$, $p = .343$) or IL-6 ($r = 0.045$, $p = .701$; Figure 2C,D).

DISCUSSION

We found no significant association of FeNO with BMI, body fat mass, and body fat percentage in healthy, non-smoking adults without asthma in multivariate linear regression analyses. Serum levels of adipose-derived hormones (leptin, adiponectin) and adipokines (TNF- α , IL-6) did not correlate with FeNO. These results confirm that obesity and adiposity do not have any great impact on eosinophilic inflammation of airway or FeNO in healthy adults without asthma.

The results of this study differ from those of De Winter-de Groot et al. (6), who showed a positive association between BMI and FeNO in 24 healthy adults. However, most of the subjects had normal BMIs and only a small

number of subjects were overweight or obese. Thus, the impact of obesity on FeNO could not be assessed well. A study by Kajaks et al. (7) also reported a significant positive association between BMI and FeNO in 25 healthy adults, which was significant after adjustment for age, gender, and lung function. Because the authors did not present a definition or the characteristics of healthy subjects, we cannot exclude the possibility that the positive relationship between BMI and FeNO could have been affected by other confounding factors, such as atopy, ethnicity, combined respiratory diseases, and smoking status (20). Contrary to the findings in healthy adults, no significant association was found between BMI and FeNO in healthy children (8, 9). A reason for the differing relationship between adults and children may be that obese children are less exposed to adipose-derived hormones and adipokines than obese adults (8). FeNO levels are influenced by various demographic, anthropometric, and clinical variables (19, 21). Thus, other factors affecting FeNO should be strictly controlled in evaluating any association between obesity and FeNO. A pediatric study by Santamaria et al. (8) found that the positive association between BMI and FeNO was lost after BMI was adjusted for age in healthy children.

In this study, we excluded current or former smokers, subjects with other respiratory diseases or recent infection, those who showed abnormal chest radiographs, those with decreased lung function, and those with

physician-diagnosed asthma or asthmatic symptoms in the previous 12 months. All the enrolled subjects were ethnically Korean. Thus, our study population could be relatively free from the effects of ethnicity, smoking status, respiratory diseases, and airway obstruction. Although BMI and FeNO showed a correlation and a positive association in the univariate linear regression analysis, no significant association was seen between BMI and FeNO in a multivariate linear regression analysis. After adjustment, FeNO appeared to be affected by age and gender only. Because in the study population, age was correlated with BMI and BMI was higher in males than females, the positive correlation between BMI and FeNO appears to be influenced by effects of age and gender.

Because of the limitations of BMI as a marker of obesity and adiposity, we also measured body fat mass and body fat percentage using bioelectrical impedance analysis. We found that both body fat mass and body fat percentage also showed no significant association with FeNO. These results are in agreement with those of a study of a 32-year-old young adult cohort by McLachlan et al. (22). They found that body fat percentage was associated with asthma in women, and not with FeNO in men or women. However, the association between adiposity and FeNO could not be determined in either healthy subjects or patients with asthma because the cohort included high percentages of both people with asthma and non-asthmatics. The relationship between BMI with FeNO could be different between healthy subjects and patients with asthma (7). Our results showing no association between body fat measures and FeNO suggests that adiposity is not associated with eosinophilic inflammation of airway in healthy adults without asthma. Because FeNO does not reflect noneosinophilic inflammation well, it can be speculated that obesity/adiposity could affect airway inflammation without recruitment of eosinophils into airway. However, in analyses of sputum inflammatory cells, there was no association of obesity with neutrophils and macrophages count in sputum (14).

Theories on links between obesity and other morbidities hold that systemic inflammation, spilling over into the blood from adipose tissue, can cause local inflammation in distant organs, including the airways (23). Clinical and experimental studies suggest that these processes are mediated by adipose-derived hormones and adipokines synthesized by adipose tissue (24, 25). However, the role(s) of leptin and adiponectin in the link between obesity and asthma is controversial (26, 27). In patients with asthma, no significant interaction was observed between systemic and airway inflammation, suggesting that other mechanisms may explain the relationship (28). The effect of obesity on allergic sensitization and atopy could be one of these mechanisms (29, 30). In this study, we found no association between serum leptin and adiponectin with FeNO in healthy adults. Serum levels of TNF- α and IL-6 also did not correlate with FeNO. These findings confirm the absence of a direct effect of adipose-derived hormones or adipokines on airway inflammation in healthy adults.

This study has several limitations. First, the small size of the study population may make it impossible to detect a significant association. However, because FeNO levels are affected by many physiological and pathological variables, we tried to minimize the effects of these confounding factors. By applying strict criteria and various diagnostic tests, including spirometry, skin-prick tests, and chest radiographs, we were able to enroll 117 well-defined healthy subjects from the initially recruited 160 subjects. Second, the measurement of body fat using body impedance analysis might be inaccurate compared to the gold standard method of dual-energy X-ray absorptiometry scanning. However, body impedance analysis is inexpensive, easy to perform, and valid in epidemiological surveys (31). Third, the proportion of subjects with BMI ≥ 30 was small and no subject was severely obese (BMI ≥ 35) in the study population. The prevalence of obesity was similar to that of the general population in Korea. In Asian countries, including Korea, a definition of obesity as BMI ≥ 25 has been suggested because BMI between 25 and 30 is also associated with the obesity-related chronic diseases, such as diabetes, hypertension, and hyperlipidemia (32). Obese/overweight (BMI ≥ 25) subjects comprised 26.5% of the study population, which is comparable to the previous studies that showed positive associations in healthy subjects (6,7).

In conclusion, this study did not find significant associations between FeNO and BMI, body fat mass, or body fat percentage in healthy adults without asthma. Adipose-derived hormones and adipokines were also not correlated with FeNO levels. These findings indicate that obesity/adiposity has no great impact on eosinophilic airway inflammation in healthy subjects without asthma.

ACKNOWLEDGMENTS

This study was supported by a grant from the Korea Healthcare technology R&D project, Ministry of Health and Welfare, Republic of Korea (A040153).

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES

1. Beuther DA, Sutherland ER. Overweight, obesity, and incident asthma: a meta-analysis of prospective epidemiologic studies. *Am J Respir Crit Care Med* 2007; 175:661–666.
2. 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; 122:507–511.
3. Shore SA. Obesity and asthma: possible mechanisms. *J Allergy Clin Immunol* 2008; 121:1087–1093.
4. Sood A. Obesity adipokines and lung disease. *J Appl Physiol* 2010; 108:744–753.
5. Turner S. Exhaled nitric oxide in the diagnosis and management of asthma. *Curr Opin Allergy Clin Immunol* 2008; 8:70–76.

6. De Winter-de Groot KM, Van der Ent CK, Prins I, Tersmette JM, Uiterwaal CS. Exhaled nitric oxide: the missing link between asthma and obesity? *J Allergy Clin Immunol* 2005; 115:419–420.
7. Kazaks A, Uriu-Adams JY, Stern JS, Albertson TE. No significant relationship between exhaled nitric oxide and body mass index in people with asthma. *J Allergy Clin Immunol* 2005; 116:929–930.
8. Santamaria F, Montella S, De Stefano S, Sperli F, Barbarano F, Valerio G. Relationship between exhaled nitric oxide and body mass index in children and adolescents. *J Allergy Clin Immunol* 2005; 116:1164–1165.
9. Kovesi T, Kulka R, Dales R. Exhaled nitric oxide concentration is affected by age, height, and race in healthy 9- to 12-year-old children. *Chest* 2008; 133:169–175.
10. Maniscalco M, de Laurentiis G, Zedda A, Faraone S, Giardiello C, Cristiano S, et al. Exhaled nitric oxide in severe obesity: effect of weight loss. *Respir Physiol Neurobiol* 2007; 156:370–373.
11. Barros R, Moreira A, Fonseca J, Moreira P, Fernandes L, de Oliveira JF, et al. Obesity and airway inflammation in asthma. *J Allergy Clin Immunol* 2006; 117:1501–1502.
12. Komakula S, Khatri S, Mermis J, Savill S, Haque S, Rojas M, et al. Body mass index is associated with reduced exhaled nitric oxide and higher exhaled 8-isoprostanes in asthmatics. *Respir Res* 2007; 8:32.
13. van Veen IH, Ten Brinke A, Sterk PJ, Rabe KF, Bel EH. Airway inflammation in obese and nonobese patients with difficult-to-treat asthma. *Allergy* 2008; 63:570–574.
14. Todd DC, Armstrong S, D'Silva L, Allen CJ, Hargreave FE, Parameswaran K. Effect of obesity on airway inflammation: a cross-sectional analysis of body mass index and sputum cell counts. *Clin Exp Allergy* 2007; 37:1049–1054.
15. Daniels SR. The use of BMI in the clinical setting. *Pediatrics* 2009; 124(Suppl. 1):S35–S41.
16. Gallagher D, Visser M, Sepulveda D, Pierson RN, Harris T, Heymsfield SB. How useful is body mass index for comparison of body fatness across age, sex, and ethnic groups? *Am J Epidemiol* 1996; 143:228–239.
17. Houtkooper LB, Lohman TG, Going SB, Howell WH. Why bioelectrical impedance analysis should be used for estimating adiposity. *Am J Clin Nutr* 1996; 64:436S–448S.
18. WHO Western Pacific Region IASO and IOTF. The Asia-Pacific Perspective: Redefining Obesity and Its Treatment 2000 Health Communications Australia Pty. Ltd. Sydney, Australia, 2000.
19. ATS/ERS. Recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide, 2005. *Am J Respir Crit Care Med* 2005; 171:912–930.
20. Travers J, Marsh S, Aldington S, Williams M, Shirtcliffe P, Pritchard A, et al. Reference ranges for exhaled nitric oxide derived from a random community survey of adults. *Am J Respir Crit Care Med* 2007; 176:238–242.
21. Olin AC, Bake B, Toren K. Fraction of exhaled nitric oxide at 50 ml/s: reference values for adult lifelong never-smokers. *Chest* 2007; 131:1852–1856.
22. McLachlan CR, Poulton R, Car G, Cowan J, Filsell S, Greene JM, et al. Adiposity, asthma, and airway inflammation. *J Allergy Clin Immunol* 2007; 119:634–639.
23. Weisberg SP, McCann D, Desai M, Rosenbaum M, Leibel RL, Ferrante AW Jr.. Obesity is associated with macrophage accumulation in adipose tissue. *J Clin Invest* 2003; 112:1796–1808.
24. Shore SA, Schwartzman IN, Mellema MS, Flynt L, Imrich A, Johnston RA. Effect of leptin on allergic airway responses in mice. *J Allergy Clin Immunol* 2005; 115:103–109.
25. Shore SA, Terry RD, Flynt L, Xu A, Hug C. Adiponectin attenuates allergen-induced airway inflammation and hyperresponsiveness in mice. *J Allergy Clin Immunol* 2006; 118:389–395.
26. Sood A, Ford ES, Camargo CA Jr.. Association between leptin and asthma in adults. *Thorax* 2006; 61:300–305.
27. Fantuzzi G. Adiponectin and inflammation: consensus and controversy. *J Allergy Clin Immunol* 2008; 121:326–330.
28. Sutherland TJ, Cowan JO, Young S, Goulding A, Grant AM, Williamson A, et al. The association between obesity and asthma: interactions between systemic and airway inflammation. *Am J Respir Crit Care Med* 2008; 178:469–475.
29. Huang SL, Shiao G, Chou P. Association between body mass index and allergy in teenage girls in Taiwan. *Clin Exp Allergy* 1999; 29:323–329.
30. Ouyang F, Kumar R, Pongracic J, Story RE, Liu X, Wang B, et al. Serum lipid levels, and allergic sensitization in Chinese men and women. *J Allergy Clin Immunol* 2009; 123:940–948.
31. Roubenoff R. Applications of bioelectrical impedance analysis for body composition to epidemiologic studies. *Am J Clin Nutr* 1996; 64:459S–462S.
32. Kanazawa M, Yoshiike N, Osaka T, Numba Y, Zimmet P, Inoue S. Criteria and classification of obesity in Japan and Asia-Oceania. *Asia Pac J Clin Nutr* 2002; 11(Suppl 8):S732–S737.

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