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Effect of Obesity on Asthma Phenotype is Dependent upon Asthma Severity

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Abstract

Background—We recently reported that obese and non-obese patients with asthma have similar airflow limitation and bronchodilator responsiveness, but obese patients have more symptoms overall. There is limited information on the effect of obesity on asthmatics of varying severity measured by objective physiological parameters. Understanding how obesity affects asthmatics of differing severity can provide insights into the pathogenesis of asthma in the obese and a rationale for the therapeutic approach to such patients.

Methods—Participants with asthma from two American Lung Association-Asthma Clinical Research Center studies were grouped by tertiles of airflow obstruction (FEV_1% predicted, FEV_1/FVC) and methacholine reactivity ($PC_{20}FEV_1$). Within each tertile we examined the independent effect of body mass index (BMI), divided into normal weight, overweight and obese categories, on lung function, airway reactivity and symptoms.

Results—Overall, both FEV_1 and FVC decreased and symptoms worsened with increasing BMI; airway reactivity was unchanged. When stratified by the degree of airflow obstruction, higher BMI was not associated with greater airway reactivity to methacholine. Higher BMI was associated with more asthma symptoms only in the least obstructed FEV_1/FVC tertile. When stratified by degree of airway reactivity, BMI was inversely associated with FVC in all $PC_{20}FEV_1$ tertiles. BMI was directly associated with asthma symptoms only in those with the least airway reactivity.

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Conclusions—Obesity does not influence airway reactivity in patients with asthma and it is associated with more symptoms only in those with less severe disease.

INTRODUCTION

As people in the United States and other western countries grow increasingly obese [1,2], it is important to understand the effects of obesity on common diseases. Although cited as a risk factor for asthma prevalence and severity [3–8], obesity remains incompletely understood as an asthma modifier, especially with regard to its effect on airway reactivity.

A number of mechanisms have been proposed to explain the association between obesity and asthma severity, including the influence of adipokines on airway reactivity and immune responses in the lung [9], the presence of co-morbid diagnoses such as sleep-disordered breathing [10,11] and gastroesophageal reflux disease (GERD) [12–14], and the mechanical effects of obesity. For example, Skloot and colleagues indicated that a mechanical effect of obesity is breathing at low lung volumes [15], which may impair the ability of inspiration to stretch airway smooth muscle, leading to increased airway responsiveness [16].

We recently reported that obese and non-obese patients with asthma have similar airflow limitation and bronchodilator responsiveness, but obese patients reported more symptoms, sleep disturbance, and GERD [17]. Obese subjects also had higher blood levels of the inflammatory proteins interleukin (IL)-6 and c-reactive protein and exhibited an altered response to theophylline [17].

Airflow obstruction and airway reactivity reflect objective physiological measurements of asthma severity [18–20]. We designed a study to explore the impact of obesity on asthmatics of differing physiological severity to understand if obesity has a consistent relationship in all asthmatics, which would merit a uniform approach to all obese asthmatics, or if obesity could be relatively more significant in asthmatics of differing severity. We did this by comparing normal weight, overweight, and obese asthmatics, stratified by either airflow obstruction or airway reactivity. Our primary hypothesis was that when “matched” for the degree of airflow obstruction, obese asthmatics would have increased airway reactivity and more respiratory symptoms than non-obese asthmatics.

MATERIALS AND METHODS

Study Population

All participants in two American Lung Association Asthma Clinical Research Center (ALA-ACRC) studies, The Leukotriene Modifier or Corticosteroid or Corticosteroid-Salmeterol Trial (LOCCS) [21] and Study of Acid Reflux and Asthma (SARA) trial [22], were included for analysis if they met the following criteria: age ≥18 years, a body mass index (BMI) ≥ 20 kg/m^2, acceptable spirometry, available asthma control scores by the Juniper Asthma Control Questionnaire (ACQ) [23], and a methacholine challenge test at study entry.

Inclusion and exclusion criteria for LOCCS [21] and SARA [22] have been previously reported. Briefly, LOCCS included subjects with physician-diagnosed asthma, pre-bronchodilator FEV_1 ≥ 60% predicted, beta-agonist reversibility (defined as 12% or greater reversibility

using up to 4 puffs of albuterol) or airway hyperreactivity by methacholine challenge (defined as the provocative concentration of methacholine producing a 20% fall in FEV_1), and ACQ score of 1.5 or greater if not on daily controller medication. Subjects were excluded if they were current smokers, had greater than a 20 pack-year tobacco history, or were using chronic or current oral steroid therapy. The SARA trial included subjects with physician-diagnosed asthma, pre-bronchodilator $FEV_1 \geq 50\%$ predicted, beta-agonist reversibility or a positive methacholine challenge test, at least 8 weeks of stable use of an inhaled corticosteroid, and poor asthma control (defined by either an ACQ score ≥ 1.5 or two or more episodes of asthma symptoms in the past year, each requiring unscheduled medical care). Participants were excluded if they were current smokers, had at least a 10 pack-year smoking history, or reported GERD symptoms or previous anti-reflux or peptic ulcer surgery.

Data Collection

Variables measured in the two ACRC studies included age, sex, race, height, weight, spirometry at randomization including forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and FEV_1/FVC measured before and after inhalation of 180 μg of albuterol [24], methacholine airway reactivity, expressed as the methacholine concentration causing a 20% reduction in FEV_1 ($PC_{20}FEV_1$) [25] at study entry, ACQ score (measured on a scale of 0 to 6, with lower scores indicating better control of symptoms) [23], presence or absence of GERD and rhinitis by subject self-report, and subject-reported use of inhaled corticosteroids and montelukast (a positive response was defined as usage at least twice weekly). The lung function results are pre-bronchodilator values unless specifically noted.

Data and Statistical Analysis

Subjects were stratified by tertiles of severity of airflow obstruction (FEV_1 % predicted in one analysis and FEV_1/FVC in a second analysis) and airway reactivity to methacholine ($PC_{20}FEV_1$). Within each lung function or airway reactivity tertile we examined the effect of BMI by normal weight (20–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (≥30 kg/m^2) categories. We took this approach rather than dividing the weight categories into tertiles because using the normal, overweight and obese categories is more meaningful clinically. We examined the mean value (with SD) of several measurements in each of these BMI groups and we also assessed the relationship between the measurements and obesity by using simple linear regression with the calculated BMI for each subject as the independent variable. Regressions adjusted for self-reported gastroesophageal reflux, rhinitis, and controller medication use were also examined, but were not significantly different from unadjusted regressions and therefore are not reported. For analyses involving methacholine $PC_{20}FEV_1$, we also assessed the data for relationships with BMI using non-parametric methods (Spearman correlation coefficients), but these were similarly negative and we report the linear regression values for consistency.

Because of the substantial heterogeneity of asthma presentation, we hypothesized *a priori* that there are distinct subgroups in asthma (e.g., obese versus non-obese) and that there is an interaction between weight and lung function or airway reactivity. We did not base our subgroups on an examination of the data or the detection of significant interaction, but rather

constructed our subgroups and divisions based on our *a priori* hypotheses. All data analyses were performed with SAS software, version 9.1 (SAS Institute, Cary, NC).

RESULTS

Two hundred and twenty-six participants were included in this study, including 64 from the LOCCS trial and 162 from the SARA trial. Bronchodilator response data were available for 104 (47 from LOCCS and 57 from SARA). All other data were complete for all participants.

As shown in Table 1, more females and blacks were in the obese category compared to the other weight categories. Increasing BMI was associated with lower FEV_1 and FVC ($p < 0.01$ for both), but unchanged FEV_1/FVC, $PC_{20}FEV_1$ and bronchodilator responsiveness. Increasing BMI was also associated with higher symptom scores ($p < 0.01$) and more GERD ($p < 0.05$), but not more rhinitis or use of inhaled corticosteroids or montelukast.

Results for FEV_1 and FEV_1/FVC tertiles

To evaluate the association between BMI and airway reactivity, symptoms, and medication use, subjects in the three BMI categories were stratified into tertiles of FEV_1 % predicted and tertiles of FEV_1/FVC. Within each FEV_1 tertile, $PC_{20}FEV_1$ and bronchodilator response did not change with increasing BMI (table 2). There was a non-significant trend toward more symptoms (as measured by ACQ) with increasing BMI in FEV_1 tertile 3 (least obstructed group). These findings were unchanged when GERD and rhinitis prevalence and medication use were included in the model. As expected, BMI decreased as FEV_1 increased.

When airflow obstruction was categorized by FEV_1/FVC tertiles (table 3), we found similar results. Symptoms were unaffected by BMI in subjects with the most airflow obstruction. In contrast, symptoms increased with increasing BMI in tertile 2 ($p=0.039$) and tertile 3 ($p=.032$). These findings were unchanged when GERD and rhinitis prevalence and medication use were included in the model. As seen with FEV_1, BMI decreased as FEV_1/FVC increased.

Results for $PC_{20}FEV_1$ tertiles

To evaluate the association between BMI and airflow obstruction, asthma symptoms, and medication use, subjects in the three BMI categories were stratified into $PC_{20}FEV_1$ tertiles. FVC decreased as BMI increased within each tertile of airway reactivity (table 4). In the most reactive group (tertile 1), greater BMI was not associated with FEV_1, but it was associated with increased FEV_1/FVC ($p = .015$). In those with less airway reactivity (tertiles 2 and 3), both FEV_1 and FVC decreased with increasing BMI, while FEV_1/FVC was unchanged. The results were not influenced by adjusting for GERD and rhinitis prevalence and medication use.

An association between BMI and symptoms was seen only in those with the least airway reactivity (tertile 3) – higher BMI was associated with higher ACQ ($p = 0.03$). This association was not affected by adjusting for GERD and rhinitis prevalence and medication use. In contrast to what was seen with the FEV_1 and FEV_1/FVC groups, BMI did not differ between $PC_{20}FEV_1$ tertile groups.

DISCUSSION

By isolating for airflow obstruction or airway reactivity in our analyses, we were able to study the independent effects of obesity on asthma phenotype. Our decision to stratify patients by asthma severity was based on an *a priori* hypothesis that a) the effect of obesity on symptoms and physiology would differ in patients with differing asthma severity and b) for a given degree of airflow obstruction, obese asthmatics would have increased airway reactivity compared with non-obese asthmatics. We reasoned that if there is a different relationship between obesity and asthma symptoms and physiology that is dependent upon severity of physiologic parameters (in our case, FEV_1, FEV_1/FVC, and $PC_{20}FEV_1$), a global interaction analysis between BMI and those physiologic parameters might have been negative. Contrary to our hypothesis, we found that in patients with mild to moderate asthma, obesity does not influence bronchial reactivity to methacholine, nor bronchodilator response to beta agonist. On the other hand, we confirmed the association between obesity and reduced FVC and FEV_1, as well as an association between obesity and symptom severity, though only among those with the least airway reactivity to methacholine or minimal airflow obstruction. With more severe airflow obstruction and airway reactivity, one might infer that asthma itself is the driving force behind respiratory symptoms, and the influence of BMI is less perceptible.

How can we explain these results in light of what we know about the physiology of asthma and obesity and given the wealth of data supporting an association between poor asthma control and obesity [3–8,26–28]? Nicolacakis and colleagues recently analyzed the physiologic effects of asthma and obesity both independently and in combination in 210 adults [29]. They found that these two distinct insults are additive, not synergistic. Therefore, when asthma is mild, respiratory symptoms may be mostly due to obesity. When asthma is more severe, as reflected by greater airflow obstruction and airway reactivity, the relative contribution of obesity to symptoms is less.

Several mechanisms have been proposed to explain the association between respiratory symptoms and obesity in normal subjects and patients with asthma. Salome and colleagues [7,30], as well as others [31,32], suggested that obesity affects lung tissue compliance, in addition to chest wall compliance. Obesity may also reduce airway caliber [30], allowing a greater increase in resistance for a given absolute reduction in airway diameter and manifesting as increased airway reactivity. Data from healthy subjects suggested that airway reactivity is inversely correlated with BMI [33]. Others have suggested that asthma severity in obesity is affected by altered levels of adipokines and inflammatory cytokines [34,35]. However, most literature supporting an association between obesity and poor asthma control or asthma severity relies upon endpoints centered on patient perception, not physiologic measurements. These include symptom-based questionnaires [6] and subject-reported symptoms, missed work days, medication use [4], and asthma exacerbations [8]. While exacerbations might seem more specific to asthma than dyspnea, exacerbations are closely linked to dyspnea. If the effects of obesity and asthma are additive, then it may take a smaller asthma insult to push an obese patient over a respiratory symptom threshold, beyond which medical attention is sought for an “asthma exacerbation.”

This phenomenon may also explain, at least in part, the observed increase among obese subjects of developing incident asthma [26–28]. Obese patients, who are more likely to experience shortness of breath due to effects of their weight, may be more likely to receive an asthma diagnosis compared to individuals of normal weight and similar degrees of airflow obstruction or airway reactivity. Therefore, the phrase “symptomatic bronchial hyperresponsiveness” coined by Celedon and colleagues to describe what seems to correlate with obesity, may be apt [36]. Pakhale and colleagues recently reported that compared with non-obese patients carrying a diagnosis of asthma, obese individuals who made recent urgent health care visits for respiratory symptoms were more likely to have been misdiagnosis [37].

Our findings are consistent with those reported by Schachter and colleagues. In a general adult population, obesity was a risk factor for recent asthmatic wheeze and recent medication use, but not airway hyperresponsiveness [3]. Additionally, obese subjects had decreased FEV_1 and FVC, but not lower FEV_1/FVC. These data, like ours, suggest that obese subjects do not have worse obstruction or airway reactivity, but they do have more respiratory symptoms.

Our study differs from this and other studies [3,29,38–43] in a number of ways. We included data for BMI, lung function, and $PC_{20}FEV_1$, along with asthma symptoms in a well-characterized group of patients with asthma. This allowed us to compare objective measures of lung physiology with patient symptoms across BMI groups. Controlling for airway reactivity and airflow obstruction was a unique approach that allowed us to better understand the independent effects of obesity on lung function and symptoms. As a confirmation of the reliability of our data, we demonstrated the expected decrease in FVC and FEV_1 widely observed with increasing BMI. Additionally, our subjects had a wide BMI range, as well as a reasonable range of airflow obstruction.

A potential limitation of the study is failure to include an even broader population of asthmatics. Therefore, an association between BMI and either airway obstruction or airway reactivity, which may primarily exist in either very mild or severe asthma, might have been missed. However, a study involving severe asthmatics would be difficult, given the risk of methacholine challenge in such patients. One might hypothesize that very mild asthmatics would behave like non-asthmatic subjects. However, data concerning the relationship between obesity and airway hyperreactivity in otherwise healthy subjects are conflicting, with some studies supporting an association [33,40,44–47] and others not [7,39,41,48].

Another potential limitation is the retrospective nature of the study. Reliance on data from two previous trials resulted in eliminating some participants from analysis because of missing data. Also, controlling for FEV_1 and $PC_{20}FEV_1$, while dividing subjects into BMI groups, left some normal weight groups with relatively small numbers. Unfortunately, this is a limitation of multiple stratifications and small sample size within each stratum. While some of our negative findings may certainly have resulted from limited power and we may have missed small differences between groups, it is encouraging that our data are consistent with other publications. Moreover, the data in tables 2, 3, and 4 do not suggest meaningful differences between the BMI categories for reported measurements except FVC, particularly

in the tertiles of greater severity. Understanding the limits of our data, they at least suggest that obesity may have a more significant effect in those with less severe asthma.

Finally, it is possible that the associations or effects of BMI are not homogeneous across all asthmatics. As suggested by cluster analysis studies, obesity seems to be more closely associated with a clinical phenotype characterized by late-onset, non-atopic asthma, primarily among women [49,50]. It is still possible that in a more select subset of asthmatics (with a more susceptible phenotype), obesity does in fact lead to functional airway changes. While it might have been interesting to separate atopic from non-atopic asthmatics, these data were not available to us.

Our results argue for adoption of a distinct therapeutic approach to the obese asthmatic. A careful physiological assessment, including testing for bronchodilator responsiveness and/or airway reactivity, is critical for confirming an asthma diagnosis and limiting over-diagnosis of asthma in this population. For obese asthmatics with normal pulmonary function one might consider setting a higher than usual symptom threshold for initiation of treatment. An emphasis on weight loss intervention in those with normal or mildly abnormal pulmonary function may be more effective than aggressive asthma pharmacotherapy. When prescribing systemic corticosteroids in such patients, it might be particularly important to objectively monitor pulmonary function before, during, and after therapy. If no significant difference in FEV_1, airway reactivity, or measures of hyperinflation can be documented with therapy, the clinician may be more likely to discontinue treatment, avoid stepping up therapy including the use of systemic corticosteroids, or consider another diagnosis. Alternatively, when treating an obese patient with airflow obstruction and/or airway hyperreactivity, the treatment approach should be the same as in the non-obese asthmatic.

In summary, obesity does not influence airway reactivity in asthmatics with mild-to-moderate disease and it worsens symptoms only in those with less severe disease.

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Table 1

Study population by BMI category

	All	Normal weight (BMI 20–24.9 kg/m^2)	Overweight (BMI 25–29.9 kg/m^2)	Obese (BMI ≥ 30.0 kg/m^2)	P value*
N	226	56	69	101	
BMI (kg/m^2)	30.6 ± 7.7	22.6 ± 1.4	27.3 ± 1.6	37.3 ± 6.4	
Age (years)	37.3 ± 12.5	35.3 ± 13.6	37.0 ± 13.6	38.6 ± 10.9	.058
Male (%)	29.6	32.1	37.7	22.8	.013
White (%)	61.1	67.9	63.8	55.4	.016
Black (%)	32.3	26.8	29.0	37.6	.023
Hispanic (%)	4.9	3.6	4.3	5.9	.364
Other (%)	1.8	1.8	2.9	1.0	.516
FEV_1 % predicted	89.6 ± 11.7	91.9 ± 13.4	90.0 ± 11.4	88.0 ± 10.7	.004
FVC % predicted	96.9 ± 13.1	100.6 ± 13.7	98.6 ± 12.4	93.8 ± 12.5	<.001
FEV_1/FVC	.76 ± .07	.76 ± .07	.75 ± .07	.78 ± .07	.187
$PC_{20}FEV_1$ (mg/mL)	3.03 ± 3.79	3.43 ± 4.14	2.51 ± 2.98	3.16 ± 4.06	.618
BDR (change in FEV_1 % predicted)	7.0 ± 7.9	7.6 ± 8.2	6.1 ± 8.3	7.2 ± 7.5	.458
ACQ	1.85 ± .81	1.71 ± .89	1.69 ± .70	2.03 ± .81	.007
GERD (% prevalence)	15.0	7.1	17.4	17.8	.032
Rhinitis (% prevalence)	62.4	67.9	60.9	60.4	.198
ICS use (% prevalence)	87.6	83.9	86.9	90.1	.453
Montelukast use (% prevalence)	18.6	19.6	14.5	20.8	.556

*p-value calculated from simple linear regression with BMI as the independent variable

Mean ± standard deviation
BDR = bronchodilator response to inhaled albuterol
ACQ = Juniper Asthma Control Questionnaire score
GERD = gastroesophageal reflux disease
ICS = inhaled corticosteroid

Table 2

BMI Categories by FEV_1 tertiles

	All	Normal weight (BMI 20–24.9 kg/m^2)	Overweight (BMI 25–29.9 kg/m^2)	Obese (BMI ≥ 30 kg/m^2)	P value*
Tertile 1 - FEV_1 77.7 ± 4.3%					
N	75	17	20	38	
BMI (kg/m^2)	31.9 ± 8.7	22.3 ± 1.6	27.4 ± 1.8	38.5 ± 7.1	
$PC_{20}FEV_1$ (mg/mL)	2.88 ± 3.94	2.63 ± 4.15	2.50 ± 2.96	3.19 ± 4.36	.625
BDR (% change in FEV_1 predicted)	13.1 8.8	13.1 ± 7.7	15.4 ± 12.8	12.2 ± 7.9	.313
ACQ	1.98 ± .79	2.10 ± .59	1.84 ± .65	2.01 ± .93	.309
Tertile 2 - FEV_1 88.2 ± 2.6%					
N	76	16	24	36	
BMI (kg/m^2)	31.1 ± 7.8	22.3 ± 1.1	27.1 ± 1.6	37.7 ± 6.0	
$PC_{20}FEV_1$ (mg/mL)	2.81 ± 3.48	3.25 ± 3.37	1.95 ± 2.45	3.18 ± 4.06	.333
BDR (% change in FEV_1 predicted)	6.41 ± 7.31	8.97 ± 11.27	5.23 ± 4.4	5.83 ± 6.65	.232
ACQ	1.91 ± .73	1.83 ± .90	1.63 ± .59	2.12 ± .69	.216
Tertile 3 - FEV_1 102.8 ± 8.2%					
N	75	23	25	27	
BMI (kg/m^2)	28.8 ± 5.9	23.0 ± 1.3	27.5 ± 1.6	34.9 ± 5.1	
$PC_{20}FEV_1$ (mg/mL)	3.41 ± 3.94	4.15 ± 4.63	3.06 ± 3.43	3.10 ± 3.79	.267
BDR (% change in FEV_1 predicted)	3.37 ± 4.66	3.58 ± 3.67	2.66 ± 4.85	3.85 ± 5.55	.944
ACQ	1.66 ± .88	1.34 ± .95	1.62 ± .83	1.95 ± .79	.058

*p-value calculated from simple linear regression with BMI as the independent variable

Mean ± standard deviation

BDR = bronchodilator response to inhaled albuterol

ACQ = Juniper Asthma Control Questionnaire score

Table 3

BMI Categories by FEV_1/FVC tertiles

	All	Normal weight (BMI 20–24.9 kg/m^2)	Overweight (BMI 25–29.9 kg/m^2)	Obese (BMI ≥ 30 kg/m^2)	P value*
Tertile 1 - FEV_1/FVC 0.688 ± .038					
N	75	21	26	28	
BMI (kg/m^2)	29.7 ± 7.5	22.6 ± 1.3	27.1 ± 1.9	37.5 ± 6.5	
$PC_{20}FEV_1$ (mg/mL)	3.11 ± 4.18	3.34 ± 4.80	2.97 ± 3.64	3.06 ± 4.30	.525
BDR (% change in FEV_1 predicted)	11.3 8.7	12.3 ± 7.3	10.5 ± 12.5	11.1 ± 7.3	.286
ACQ	1.96 ± .66	1.95 ± .89	1.92 ± .52	2.01 ± .60	.796
Tertile 2 - FEV_1/FVC 0.768 ± .017					
N	76	20	25	31	
BMI (kg/m^2)	30.5 ± 7.7	22.9 ± 1.5	27.3 ± 1.5	37.9 ± 6.4	
$PC_{20}FEV_1$ (mg/mL)	2.72 ± 3.33	2.55 ± 3.33	2.65 ± 2.94	2.86 ± 3.70	.199
BDR (% change in FEV_1 predicted)	4.69 ± 4.34	3.50 ± 2.17	5.64 ± 3.98	4.73 ± 5.59	.921
ACQ	1.71 ± .91	1.49 ± .87	1.48 ± .78	2.04 ± .96	.039
Tertile 3 - FEV_1/FVC 0.835 ± .035					
N	75	15	18	42	
BMI (kg/m^2)	31.6 ± 7.7	22.1 ± 1.2	27.7 ± 1.4	36.7 ± 6.3	
$PC_{20}FEV_1$ (mg/mL)	3.28 ± 3.83	4.75 ± 4.03	1.65 ± 1.61	3.45 ± 4.23	.175
BDR (% change in FEV_1 predicted)	5.28 ± 8.40	6.29 ± 10.96	1.86 ± 4.93	6.36 ± 8.20	.744
ACQ	1.87 ± .83	1.67 ± .88	1.63 ± .74	2.05 ± .83	.032

*p-value calculated from simple linear regression with BMI as the independent variable

Mean ± standard deviation

BDR = bronchodilator response to inhaled albuterol

ACQ = Juniper Asthma Control Questionnaire score

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Table 4

BMI Categories by $PC_{20}FEV_1$ tertiles

	All	Normal weight (BMI 20–24.9 kg/m^2)	Overweight (BMI 25–29.9 kg/m^2)	Obese (BMI ≥ 30 kg/m^2)	P value*
Tertile 1 - $PC_{20}FEV_1$ 0.29 ± 0.17 mg/ml					
N	75	16	23	36	
BMI	31.0 ± 22.6	22.6 ± 1.5	27.5 ± 1.6	36.9 ± 5.6	
FEV_1 % predicted	86.9 ± 11.2	86.8 ± 12.6	86.7 ± 10.4	87.1 ± 11.4	.612
FVC % predicted	96.3 ± 13.2	101.0 ± 13.6	96.4 ± 13.3	94.0 ± 12.64	.034
FEV_1/FVC	.75 ± .07	.71 ± .06	.75 ± .07	.77 ± .06	.015
ACQ	1.99 ± .78	2.01 ± 1.01	1.69 ± 0.58	2.18 ± 0.74	.401
Tertile 2 - $PC_{20}FEV_1$ 1.49 ± 0.64 mg/ml					
N	75	19	25	31	
BMI	30.7 ± 8.5	22.6 ± 1.6	27.2 ± 1.7	38.4 ± 7.6	
FEV_1% predicted	90.8 ± 11.6	92.8 ± 12.2	91.9 ± 11.6	88.7 ± 11.2	.044
FVC % predicted	98.6 ± 14.2	101.8 ± 14.1	101.1 ± 12.5	94.6 ± 15.0	.045
FEV_1/FVC	.77 ± .07	.77 ± .07	.75 ± .05	.78 ± .08	.958
ACQ	1.82 ± .86	1.61 ± .80	1.78 ± .81	1.97 ± .93	.134
Tertile 3 - $PC_{20}FEV_1$ 7.26 ± 3.82 mg/ml					
N	76	21	21	34	
BMI	30.2 ± 7.3	22.6 ± 1.2	27.3 ± 1.6	36.6 ± 5.9	
FEV_1% predicted	90.9 ± 11.9	94.9 ± 14.4	91.2 ± 11.8	88.3 ± 9.7	.028
FVC % predicted	96.0 ± 11.8	99.3 ± 14.1	97.9 ± 11.3	92.7 ± 9.9	.012
FEV_1/FVC	.77 ± .06	.78 ± .06	.76 ± .07	.78 ± .06	.922
ACQ	1.74 ± .78	1.58 ± .85	1.58 ± .70	1.94 ± .75	.030

*p-value calculated from simple linear regression with BMI as the independent variable

Mean ± standard deviation

BDR = bronchodilator response to inhaled albuterol

ACQ = Juniper Asthma Control Questionnaire score