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Poor Asthma Control in Obese Children May Be Overestimated Because of Enhanced Perception of Dyspnea

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Abstract

BACKGROUND—Although studies in adults have shown a non-T_H2 obese asthma phenotype, whether a similar phenotype exists in children is unclear.

OBJECTIVE—We hypothesized that asthmatic children with obesity, defined as a body mass index above the 95th percentile for age and sex, would have poorer asthma control as well as decreased quality of life, increased health care utilization, and decreased pulmonary function measures as a function of increased T_H1 versus T_H2 polarization.

METHODS—This study involved a *post hoc* analysis of cross-sectional data from 269 children 6 to 17 years of age enrolled in the National Heart, Lung, and Blood Institute Severe Asthma Research Program. Children answered questionnaires and underwent spirometry, plethysmography, exhaled nitric oxide determination, and venipuncture for T_H1/T_H2 cytokine determination. Asthma control was defined according to national asthma treatment guidelines that are based on prespecified thresholds for lung function and symptom frequency.

RESULTS—Fifty-eight children (22%) were overweight and 67 (25%) were obese. Obese children did not have poorer asthma control but were more likely to report nonspecific symptoms such as dyspnea and nocturnal awakenings. Obese children did have decreased asthma-related quality of life and increased health care utilization, but this was not associated with airflow limitation. Instead, obese children had decreased functional residual capacity. A unique pattern of T_H1 or T_H2 polarization was not observed.

CONCLUSIONS—Poor asthma control in obese children with asthma may be overestimated because of enhanced perception of nonspecific symptoms such as dyspnea that results from altered mechanical properties of the chest wall. Careful assessment of physiologic as well as symptom-based measures is needed in the evaluation of obese children with respiratory symptoms.

Keywords

Airflow limitation; Asthma; Children; Cytokines; Functional residual capacity; Inflammation; Obesity; Spirometry

Despite advances in asthma treatment over the past decade, asthma remains poorly controlled in many children; thus, the overall burden of asthma continues to be high.¹ The prevalence of asthma in children is also steadily rising and is now at the highest recorded level,² in parallel with the growing “obesity epidemic.”³ Although the concomitant increase in asthma and obesity has led to speculations about mechanistic linkages between the 2 disorders,^{4–6} the casual nature of the obesity/asthma relation remains uncertain. Indeed, obesity is associated with altered mechanical properties of the respiratory system^{7,8} which may result in increased chest symptoms and dyspnea independent of asthma.^{9,10} However, although it is clear that asthma can be misdiagnosed in obese persons if physiologic testing is not performed,^{11–13} a growing body of literature also supports the role of obesity in the modulation of asthma severity and control,¹⁴ perhaps through augmentation of the underlying inflammatory state.¹⁵

In adults, the case for a unique obese asthma “phenotype” has been made in large studies in which asthma was confirmed by bronchodilator reversibility testing and/or airway hyperresponsiveness testing. For example, 2 independent cluster analyses of heterogeneous samples of asthmatic adults each identified a group of older, obese women with late-onset asthma with a significant degree of symptoms despite increased asthma medication requirements.^{16,17} Subsequent studies have also shown airway neutrophilia¹⁸ and diminished responses to glucocorticoids^{19–22} within this group and suggest that the obese asthma “phenotype” may only be present in adults without T_H2-mediated eosinophilia.^{23,24} In keeping with this notion, a recent cluster analysis of children with confirmed asthma failed to identify an association between obesity and the resulting phenotypic clusters, which were all associated with some degree of allergic sensitization.²⁵ However, other reports have noted relations among obesity, symptoms, and clinical outcomes in selected subpopulations of asthmatic children,^{26,27} although these findings have not been consistently replicated.^{28,29}

Thus, although studies suggest that obesity may be an important determinant of asthma in adults, the degree to which obesity contributes to asthma control in children remains unclear. Furthermore, a major limitation of existing research is the focus on self-reported asthma and associated outcomes. Because studies that use objective measures of asthma have been few and limited in children, we sought to integrate clinical, physiologic, and inflammatory assessments within a highly characterized sample of children with physician-diagnosed and confirmed asthma across a wide spectrum of adiposity. We hypothesized that asthmatic children with obesity, defined as a body mass index (BMI) greater than the 95th percentile for age and sex, would have poorer asthma control as well as decreased quality of life, increased health care utilization, and decreased pulmonary function measures as a function of increased T_H1 versus T_H2 polarization.

METHODS

This study involved *post hoc* analysis of cross-sectional data from children 6 to 17 years of age with physician-diagnosed asthma enrolled in the National Heart, Lung, and Blood Institute (NHLBI) Severe Asthma Research Program^{30,31} at Emory University in Atlanta, Georgia. All children had historical evidence (within the previous year) of airway hyperresponsiveness to methacholine or at least 12% reversibility in the forced expiratory volume in 1 second (FEV₁) after short-acting bronchodilator administration. Other inclusion criteria included treatment by an asthma subspecialist for at least 12 months and the ability to speak and understand English. Exclusion criteria included premature birth before 34 weeks’ gestation or other comorbid pulmonary disorders, such as immunodeficiency, vocal cord dysfunction, or aspiration disorders. Sinus disease, obstructive sleep apnea, and gastroesophageal reflux were not criteria for exclusion, provided they were medically treated and controlled for at least 12 months. This study was conducted under approval from

the Emory University Institutional Review Board. Written informed consent was obtained from the parents or legal guardians of participating children. Children 12 to 17 years of age also provided written assent, whereas children 6 to 11 years of age provided verbal assent to the study procedures.

Characterization procedures

Children were assessed during a research-only outpatient encounter that was rescheduled if the following were reported within the preceding 4 weeks: (1) upper respiratory viral symptoms such as rhinorrhea, (2) acute worsening of asthma symptoms, (3) antibiotic use, or (4) a systemic glucocorticoid “burst.” Children whose lung function was not within 10% of their baseline as determined from a review of clinical records were also rescheduled. Participating children and their caregivers completed questionnaires about asthma control over the previous 3 months and health care utilization over the preceding 12 months. Children also completed the 32-item Asthma Quality of Life Questionnaire.³² Self-reported asthma characteristics and medical history information, including asthma medications, comorbid conditions, and health care utilization were verified by a review of medical records.

Spirometry was performed in the presence of daily medications with a portable spirometer (KoKo PDS; Ferraris, Louisville, Colo). Subjects withheld short-acting bronchodilators and caffeine for at least 4 hours before the procedure. Results met criteria for reproducibility,³³ and the best of 3 forced vital capacity (FVC) maneuvers was interpreted. Population reference equations were used to calculate percentage of predicted values for FVC, FEV₁, and the mid-expiratory flow rate at 25% to 75% of vital capacity.³⁴ Spirometry was repeated after 4 inhalations of albuterol sulfate (90 µg/actuation) delivered through a valved holding chamber with a mouthpiece. Total lung capacity (TLC), residual volume (RV), airway resistance, and functional residual capacity were measured with a body plethysmograph (MedGraphics Elite Series; Medical Graphics Corporation, St. Paul, Minn).³⁵ Exhaled nitric oxide concentrations were analyzed with online methods (NIOX MINO; Aerocrine Inc, New Providence, NJ) with a fixed flow rate of 0.05 L/s and exhalation duration of 6 seconds.

Whole blood and serum were analyzed for the percentage of eosinophils and serum IgE concentrations, respectively, by a commercial laboratory (Quest Diagnostics, Tucker, Ga). Concentrations of TNFα, IFNγ, IL-4, IL-5, IL-6, IL-8, IL-10, and IL-13 were measured in the plasma with a commercial bead-based assay with a sensitivity of 0.1 to 5.7 pg/mL (Millipore, Billerica, Mass). Data were analyzed with the Bio-Rad Bio-Plex System (Bio-Rad Laboratories, Hercules, Calif) with gates of 4,335 and 10,000.

Obesity determination

Height and weight were determined with an electronic scale and wall-mounted stadiometer, respectively. BMI percentiles were determined from standardized charts from the Centers for Disease Control and Prevention, according to each child’s age and sex. Children were assigned to 1 of the following 3 groups: normal weight (BMI <85th percentile), overweight (85th to 95th percentile), or obese (≥95th percentile).

Outcome variables

The primary outcome variable was a composite variable of asthma control that was based on definitions proposed by the 2007 National Asthma Education and Prevention Program Expert Panel Report (see Table E1 in this article’s Online Repository at www.jaci-inpractice.org).³⁶ Briefly, uncontrolled asthma was defined according to prespecified thresholds for baseline FEV₁ and FEV₁/FVC and the frequency of daytime asthma symptoms, short-acting bronchodilator use, and nocturnal awakenings from asthma averaged

over the previous 12 weeks.³⁶ Secondary outcomes included quality of life, health care utilization, pulmonary function measures, and concentrations of systemic inflammatory cytokines.

Statistical analyses

Data were analyzed with IBM SPSS Statistics software version 20 (SPSS Inc, Chicago, Ill). Variables such as cytokine concentrations, IgE, eosinophils, and exhaled nitric oxide that were not normally distributed were logarithmically transformed before statistical analyses. Group differences were assessed with χ^2 tests and analysis of variance, with Fisher Least Significant Difference *post hoc* tests for comparison of group means. Linear and logistic regression analyses were performed to determine the association between BMI percentile group and outcome measures. When indicated, models were adjusted for current asthma control (well controlled or not controlled), age (6–11 years or 12–17 years), and sex to minimize potential confounding on the selected outcomes of interest.^{24,26,37} Significance was defined as $\alpha < 0.05$ with the use of 2-tailed tests.

RESULTS

Of the 269 children enrolled, 46% ($n = 125$) were overweight or obese as shown in Table I. Although age and sex did not differ between groups, children who were overweight or obese were more likely to be of African American or multiracial ancestry. Obese children also had a higher frequency of obstructive sleep apnea and gastroesophageal reflux disease. However, other clinical features such as parental history of asthma, medication use, allergic sensitization, and exhaled nitric oxide concentrations did not differ between groups (Table I).

Primary outcome: asthma control

Overall, only 15% ($n = 40$) of enrolled children met criteria for “well-controlled” asthma as determined by symptoms, short-acting bronchodilator use, nocturnal awakenings, and lung function as defined by current treatment guidelines (Table II).³⁶ Of the children whose asthma was not controlled, 20% ($n = 54$) met criteria for “not well-controlled” asthma and 66% ($n = 178$) met criteria for “very poorly controlled” asthma. No associations between obesity and the composite variable of asthma control were observed, even after adjusting for the possible confounding effects of age and sex ($P > .05$ for each). Although no associations between obesity and specific asthma symptoms such as cough, chest tightness, or wheezing were noted, obese children with a BMI above the 95th percentile were more likely to report dyspnea more than twice weekly (unadjusted odds ratio [OR], 2.65; 95% CI, 1.45–4.83; $P = .002$) and nocturnal awakenings from asthma more than twice monthly (unadjusted OR, 1.89; 95% CI, 1.04–3.41; $P = .036$). The association among obesity, dyspnea, and nocturnal awakenings persisted after adjusting for current asthma control, age, and sex (dyspnea: adjusted OR, 2.65; 95% CI, 1.45–4.85; $P = .002$; nocturnal awakenings: adjusted OR, 1.94; 95% CI, 1.06–3.55; $P = .032$). Consistent with this observation, obese children with a BMI above the 95th percentile were also more likely to report that daily activities such as walking were a significant trigger of asthma symptoms (adjusted OR, 2.25; 95% CI, 1.22–4.16; $P = .010$).

Secondary outcomes

Asthma-related quality of life as measured by the Asthma Quality of Life Questionnaire score (highest possible score = 7; higher scores indicate better quality of life) was more impaired in obese children than in overweight and lean children (4.69 ± 1.21 vs 5.19 ± 1.18 vs 5.41 ± 1.22 for obese vs overweight vs lean; $P = .010$). Differences in asthma-related quality of life persisted between the groups after adjustment for current asthma control, age,

and sex (adjusted $P = .047$). Similar impairment in the obese group was also noted for the symptom, activity, emotional, and environmental domains of the instrument (Figure 1). Health care utilization over the preceding 12 months, namely emergency visits and glucocorticoid bursts, was also greater in obese children (Table III). By contrast, hospitalization for asthma did not differ between groups (Table III).

Airflow limitation, air trapping, and airway resistance were also not different between groups at baseline (Table IV) or after adjustments for current asthma control (data not shown). Post-bronchodilator spirometry also did not differ (post-bronchodilator FEV₁ percentage predicted: $103\% \pm 17\%$ vs $107\% \pm 15\%$ vs $106\% \pm 19\%$ for lean vs overweight vs obese; FEV₁ bronchodilator reversibility: $15\% \pm 17\%$ vs $19\% \pm 17\%$ vs $15\% \pm 14\%$ change from baseline; $P > .05$ for each). However, obese children had significantly lower functional residual capacity percentage predicted values compared with lean children (Table IV).

Relation of obesity to systemic inflammatory cytokines

Plasma samples were available from 67 normal-weight children, 30 overweight children, and 32 obese children. Features of this subset were similar to the larger sample (see Table E2 in this article's Online Repository at www.jaci-inpractice.org). Within the group of children with well-controlled asthma (normal weight, $n = 12$; overweight, $n = 5$; obese, $n = 5$), none of the cytokines measured (TNF α , IFN γ , IL-4, IL-5, IL-6, IL-8, IL-10, IL-13) differed according to adiposity (data not shown). However, within the group of children with asthma that was not controlled, the T_H2 cytokines IL-5 and IL-13 and the anti-inflammatory cytokine IL-10 were significantly lower in obese children than in lean children (Figure 2) and remained lower after adjustment for age and sex (IL-5, $P = .024$; IL-10, $P = .008$; IL-13, $P = .05$). However, IFN γ , the ratio of IFN γ to IL-5, and the ratio of IFN γ to IL-13 were not different among groups (data not shown). Within the combined group of overweight and obese children, no associations between systemic cytokines, quality of life, lung function, or other clinical variables were observed.

DISCUSSION

In this highly characterized sample of children with physician-diagnosed and confirmed asthma, we failed to observe associations between obesity and a composite variable of asthma control as defined by current asthma treatment guidelines.³⁶ Instead, children with obesity had a high frequency of comorbid conditions and nonspecific symptoms such as dyspnea and nocturnal awakenings that were not accompanied by greater airflow limitation or airway resistance. Although asthma-related quality of life was more impaired in obese children, our finding of lower functional residual capacity coupled with increased reports of asthma symptoms triggered by activities of daily living (ie, walking or climbing stairs) implies that poor asthma control may be overestimated in this population. Indeed, children with obesity were more likely to receive multiple courses of systemic glucocorticoids but were not more likely to be hospitalized, suggesting that the symptoms in obese asthmatic children were not intrinsically more severe.²⁹

Unlike previous studies in adults that support the notion of a unique, non-T_H2 obese asthma phenotype,^{16–18} we failed to discern a distinct T_H1 or T_H2 phenotype in obese children whose asthma was not controlled with systemic cytokine analyses. This is in contrast to a previous report that showed increased IFN γ and decreased IL-4 T-helper responses to mitogen in obese versus lean children with asthma.³⁸ However, it should be noted that serum IFN γ concentrations did not differ in that report,³⁸ similar to what we have reported here. However, our findings of lower systemic concentrations of IL-5 and IL-13 accompanied by lower concentrations of the T_H1 inhibitor, IL-10, are of interest because the

majority of enrolled children (>90%) were atopic with a history of allergic rhinitis, increased systemic eosinophils, and elevated IgE and exhaled nitric oxide. Thus, although our findings do not clearly support the hypothesis that obesity in asthmatic children is associated with a unique T_H1 phenotype, additional molecular phenotyping approaches are warranted in this population. Given the heterogeneity of asthma in childhood,²⁵ obese phenotypic subgroups may exist for which this study was not sufficiently powered to detect.

The cross-sectional design of the present study ultimately does not allow us to answer the question of whether obesity plays a role in asthma development in children or whether obesity is a comorbid factor associated with symptoms. In a recent study that was restricted to adults, adults with early-onset asthma before 12 years of age had a linear increase in BMI each year after diagnosis,²⁴ perhaps because of increased glucocorticoid exposure²⁰ or decreased physical activity.^{39,40} A similar analysis that involved children with asthma also showed an increase in the prevalence of obesity between the 6- to 11- and 12- to 17-year age groups, suggesting that age may modify the obesity/asthma relation.³⁷ Interestingly, in that report, obese children in both age groups were also more sensitive to changes in peak expiratory flow than lean children.³⁷ This observation is in keeping with previous reports of altered symptom perception in obese children with asthma⁴¹ and may account for the increased health care utilization⁴² and increased use of short-acting bronchodilators and systemic glucocorticoids in this population,²⁷ as well as decreased asthma-related quality of life.⁴³

This study does have limitations, which include the cross-sectional design and reliance on self-reported outcomes, as opposed to electronic diaries or other prospective monitoring tools. Although the sample size was smaller than that of other epidemiologic studies, the comprehensive phenotypic characterization of enrolled subjects did permit analysis of symptoms as well as physiologic and biological features within the same subjects. However, the lack of a matched, nonasthmatic obese control group is a limitation, particularly for the interpretation of the pulmonary function data. Furthermore, we were unable to assess airway inflammation directly; thus, it is unclear whether our findings in the plasma correlate with airway cellularity or other inflammatory features. The subset of children who underwent cytokine assessment is also relatively small, so the potential for selection bias remains. We also relied on BMI percentiles, although these may not accurately assess adiposity in children, given the varying proportions of lean and fat body mass that occur throughout the normal process of growth and development. Thus, it is unclear how our results would differ if dual-energy x-ray absorptiometric scans had been used. However, in a recent study of inner-city asthmatic children in whom adiposity was assessed by both BMI percentile and dual-energy x-ray absorptiometric scanning, the 2 methods were highly correlated and yielded similar results for the primary outcomes of interest.²⁶

In conclusion, our findings suggest that poor asthma control in obese children may be overestimated by practicing physicians, possibly because of enhanced perception of nonspecific symptoms such as dyspnea that results from altered mechanical properties of the chest wall. However, it is recognized that the specific physiologic measures used here may not reflect the status of the peripheral airways, so other techniques such as impulse oscillometry, nitrogen washout, and computed tomography may be helpful in future studies. Regardless, these results argue for careful evaluation of physiologic as well as symptom-based measures when initiating and evaluating asthma therapy in obese children. Weight loss interventions may ultimately be necessary to improve asthma-related quality of life and associated symptoms in this population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations used

BMI	Body mass index
FEV₁	Forced expiratory volume in 1 second
FVC	Forced vital capacity
RV	Residual volume
TLC	Total lung capacity

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What is already known about this topic?

Although an obese, non-T_H2 asthmatic “phenotype” has been described in adults, it is unclear whether a similar phenotype exists in children. The causal nature of obesity and asthma symptoms in children is also unclear.

What does this article add to our knowledge?

Obese asthmatic children experience more nonspecific respiratory symptoms such as dyspnea that are associated with increased health care utilization and decreased quality of life in the absence of a distinct T_H1 or T_H2 polarization.

How does this study impact current management guidelines?

Careful assessment of physiologic as well as symptom-based measures is important in the evaluation of obese children with respiratory symptoms to minimize overtreatment.

FIGURE 1.

Asthma Quality of Life Questionnaire (AQLQ) domain scores for symptoms (A), activity (B), emotions (C), and the environment (D), lean (BMI <85%), overweight (BMI 85%–95%), and obese (BMI >95%) asthmatic children. Well controlled: lean, $n = 15$; overweight, $n = 7$; obese, $n = 5$. Not controlled: lean, $n = 55$; overweight, $n = 28$; obese, $n = 39$. * $P < .05$. Comparisons between asthma control groups are not shown.

FIGURE 2.

Plasma cytokine concentrations of IL-5 (A), IL-10 (B), and IL-13 (C) for lean (BMI <85%), overweight (BMI 85–95%), and obese (BMI >95%) children with asthma. Well controlled: lean, n = 10; overweight, n = 6; obese, n = 6. Not controlled: lean, n = 51; overweight, n = 24; obese, n = 26. * $P < .05$. Comparisons between asthma control groups are not shown.

TABLE I

Features of the sample

	Normal weight (BMI <85th percentile) [n = 144]	Overweight (BMI 85th–95th percentile) [n = 58]	Obese (BMI >95th percentile) [n = 67]
Age (y), median (IQR)	12 (9–15)	12 (9–15)	13 (10–15)
Asthma duration (y), median (IQR)	9 (5–14)	9 (6–12)	10 (7–13)
Male,	79 (55)	34 (59)	38 (57)
Non-White, no. (%)	87 (60)	45 (78) [†]	49 (73) [*]
Parent with asthma, no. (%)	75 (52)	30 (52)	38 (57)
Medical history			
Allergic rhinitis, no. (%)	127 (88)	53 (91)	62 (93)
Atopic dermatitis, no. (%)	70 (49)	33 (57)	41 (61)
Chronic sinusitis, no. (%)	57 (40)	24 (41)	35 (52)
Pneumonia, no. (%)	70 (49)	32 (55)	42 (63)
Gastroesophageal reflux, no. (%)	37 (26)	13 (22)	28 (42) ^{*†}
Obstructive sleep apnea, no. (%)	2 (1)	1 (2)	8 (12) ^{*†}
Tobacco smoke exposure, no. (%)	31 (22)	13 (22)	13 (19)
Daily asthma medications			
Montelukast, no. (%)	106 (74)	45 (78)	52 (78)
ICS (without LABA), no. (%)	34 (24)	12 (21)	17 (25)
ICS (with LABA), no. (%)	91 (63)	41 (71)	44 (66)
Omalizumab, no. (%)	6 (4)	1 (2)	4 (6)
Systemic glucocorticoids, no. (%)	17 (12)	2 (3)	7 (10)
Daily ICS dose (µg fluticasone equivalent), median (IQR)	500 (200–1000)	500 (220–1000)	500 (220–1000)
Serum IgE (kU/L), median (IQR) [‡]	124 (57–412)	331 (37–1055)	404 (81–907)
Blood eosinophils (%), median (IQR) [‡]	4 (2–8)	5 (2–9)	5 (3–10)
Exhaled nitric oxide (ppb), median (IQR) [‡]	18 (9–45)	30 (10–56)	32 (12–52)

ICS, Inhaled corticosteroid; IQR, interquartile range; LABA, long-acting β agonist.

^{*} $P < .05$ versus normal weight.

[†] $P < .05$ versus overweight.

[‡] Data were logarithmically transformed before statistical analysis.

TABLE II

Primary outcome (composite) measure of asthma control, derived from the 2007 National Asthma Education and Prevention Program Expert Panel Report³⁶

Components of control	Normal weight (BMI < 85th percentile) [n = 144]	Overweight (BMI 85th–95th percentile) [n = 58]	Obese (BMI >95th percentile) [n = 67]
Well-controlled asthma	25 (17)	9 (16)	6 (9)
Not well-controlled asthma	29 (20)	11 (19)	12 (18)
Very poorly controlled asthma	88 (61)	38 (66)	49 (73)

The level of control was based on the most severe impairment category. Data represent the frequency (%)

TABLE III

Health care utilization during the preceding 12 months

	Normal weight (BMI <85th percentile) [n = 144]	Overweight (BMI 85th–95th percentile) [n = 58]	Obese (BMI >95th percentile) [n = 67]
Emergency department visits			
1 time	22 (15)	13 (22)	7 (10)
2–4 times	35 (24)	17 (77) ^{*†}	19 (28)
>4 times	28 (19)	11 (19)	24 (36) ^{*‡}
Systemic glucocorticoids			
1–2 bursts	45 (31)	18 (62) ^{*†}	25 (37)
3 bursts	49 (34)	17 (29)	33 (49) ^{*‡}
Hospitalization	42 (29)	19 (33)	27 (40)

Data are shown as frequency (%).

^{*}*P* < .05 versus normal weight.[†]*P* < .05 versus obese.[‡]*P* < .05 versus overweight.

TABLE IV

Baseline lung function variables

	Normal weight (BMI <85th percentile) [n = 144]	Overweight (BMI 85th–95th percentile) [n = 58]	Obese (BMI >95th percentile) [n = 67]
Airflow limitation indices			
FVC	99 (89–103)	115 (97–119)	119 (101–135)
FEV ₁	89 (76–100)	83 (69–111)	105 (94–123)
FEV ₁ /FVC [*]	0.80 (0.73–0.86)	0.76 (0.60–0.80)	0.83 (0.75–0.86)
FEF _{25–75}	78 (43–100)	54 (28–93)	87 (73–95)
Air-trapping indices [†]			
RV	106 (81–135)	71 (51–138)	82 (63–122)
TLC	96 (93–106)	94 (89–106)	103 (88–108)
RV/TLC [*]	0.25 (0.18–0.29)	0.18 (0.12–0.27)	0.19 (0.15–0.25)
Airway resistance [†]	146 (121–162)	143 (127–206)	149 (146–188)
Functional residual capacity [†]	100 (90–113)	95 (79–107)	90 (71–106) [‡]

FEF_{25–75}, Mid-expiratory flow rate at 25% to 75% of vital capacity.

Data are shown as the median (interquartile range) and are expressed as percentage of predicted values, except where otherwise stated.

^{*}Data are shown as the actual ratio.

[†]Normal weight, n = 67; overweight, n = 21; obese, n = 24.

[‡]P < .05 versus normal weight.