Obesity Is a Risk Factor for Dyspnea but Not for Airflow Obstruction

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Background: Previous research suggests that obesity is an important risk factor for asthma. However, since obesity can cause dyspnea through mechanisms other than airflow obstruction, diagnostic misclassification of asthma could partially account for this association.

Objective: To determine whether there is a relationship between obesity and airflow obstruction.

Methods: A total of 16,171 participants (17 years or older) from the Third National Health and Nutrition Examination Survey (NHANES III) were divided into 5 quintiles based on their body mass index (BMI) to determine the association between BMI quintile and risk of self-reported asthma, bronchodilator use, exercise performance, and airflow obstruction. Significant airflow obstruction was defined as a ratio less than 80% the predicted value of forced expiratory volume in 1 second to forced vital capacity adjusted for age, sex, and race.

Results: The highest BMI quintile (ie, the most obese participants) had the greatest risk of self-reported asthma (odds ratio [OR], 1.50; 95% confidence interval [CI], 1.24-1.81), bronchodilator use (OR, 1.94; 95% CI, 1.38-2.72), and dyspnea with exertion (OR, 2.66; 95% CI, 2.35-3.00). Paradoxically, the highest BMI quintile had the lowest risk for significant airflow obstruction (P = .001).

Conclusions: This study demonstrates that while obesity is a risk factor for self-reported asthma, obese participants are at a lower risk for (objective) airflow obstruction. Many more obese than nonobese participants were using bronchodilators despite a lack of objective evidence for airflow obstruction. These data suggest that mechanisms other than airflow obstruction are responsible for dyspnea genesis in obesity and that asthma might be overdiagnosed in the obese population.

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THE PREVALENCe of obstructive airway disease (OAD) is rising rapidly in the United States and elsewhere. Between 1980 and 1994, the prevalence of asthma and related disorders increased by 75% for all ages; while the age-adjusted death rate increased by 71%. During the same period, body weight and obesity have increased at similar rates, suggesting a possible link between obesity and OAD in the community.

Recently, several cross-sectional and prospective longitudinal studies have experientially supported the concept that obesity is an important risk factor for OAD. Findings from the Nurse’s Health Study, for instance, suggest that a 25-kg weight increment is associated with a 2.5-fold increase in the risk for asthma compared with no significant weight gain. Weight reduction, on the other hand, leads to significant improvement in asthma symptoms.

While it is increasingly evident that obesity leads to increased symptoms of dyspnea and wheezing, it is not certain whether airflow obstruction is directly responsible for these symptoms in obese and overweight populations. Aside from airflow obstruction, obesity also adversely affects respiratory mechanics, decreases respiratory muscle function and lung volumes, and increases the work and energy cost of breathing, which independently or in combination could also cause asthmalike symptoms. Thus, self-reports of asthma in the obese might not be reliable. Spirometric data are needed to establish a direct link between obesity and airflow obstruction. From a clinical perspective, an accurate diagnosis of OAD is important because symptoms related to other mechanisms have different therapeutic and prognostic implications for these patients.

We used data from the Third National Health and Nutrition Examination Survey (NHANES III) to determine whether obesity is an important risk factor for OAD (using spirometric information), self-reported asthma, and use of bronchodilators. Specifically, we wanted to test the hypothesis that obesity is associated

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METHODS

DATA SOURCE AND STUDY PARTICIPANTS

The NHANES III used a stratified multistage probability sample for the US population and was conducted between 1988 and 1994 by the National Center for Health Statistics of the Centers for Disease Control and Prevention.13 Once chosen, study participants were asked to complete a questionnaire and a comprehensive physical examination, which included spirometric measurements either in the household or at a specially equipped mobile examination center. The data were then collated and entered into a database. The full sampling methods and the survey protocols have been described elsewhere.14 From the larger data set of approximately 40,000 Americans, we included only participants 17 years or older who had valid body mass index (BMI) information (BMI is calculated by dividing the subject’s weight in kilograms by the square of height in meters). For the participants chosen for this report (n = 16,692), we abstracted the following information from the NHANES III database: age, sex, race, BMI, self-reports of asthma, smoking status, forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), FEV₁/FVC ratio, emergency/physician visits, hospitalizations, exercise capacity (walking and jogging), and use of bronchodilators.

EXPOSURE AND OUTCOMES VARIABLES

We divided the study participants into 5 equal categories according to their BMI status: (1) <22.1; (2) 22.1-24.8; (3) >24.8-27.3; (4) >27.3-31.0; and (5) >31.0; (Table 1). The outcome variables of interest were divided into 3 large categories: (1) lung function, (2) self-reported asthma (including drug use), and (3) exercise performance.

Pulmonary function tests were performed based on the 1987 American Thoracic Society recommendations.15 In brief, the study personnel used either a dry rolling seal spirometer in the mobile examination center or a portable spirometer in the household to test the participants. Each study participant performed 5 to 8 forced expiratory maneuvers to meet the American Thoracic Society standards. Absolute values from these tests were recorded in the database. To adjust for height, age, sex, and race, we used published prediction equations for FEV₁ and FVC for the NHANES III population.16 We defined airflow obstruction as an FEV₁/FVC ratio of less than 80% of the predicted value adjusted for age, sex, and race.17 Mild airflow obstruction was defined as an FEV₁ that was 80% or more of the predicted value in the presence of significant airflow obstruction.18 Moderate and severe airflow obstructions were defined similarly, except the FEV₁ had to be 50% to less than 80% of the predicted value and less than 50% of the predicted value, respectively.19

A positive answer to the question “Has a doctor ever told you that you have asthma?” was used to define subjects with asthma for this study. We also included participants who answered negatively to this question but were identified as using an asthma medication (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9 CM] code 493) in any 1 of the 16 medication fields. We used the questions “During the past 12 months, how many times have you gone to a doctor’s office or a hospital emergency room for one of these episodes of wheezing or whistling?” and “How many times in the past 12 months were you hospitalized overnight or longer for these episodes of wheezing or whistling?” to determine the use of physician offices, emergency departments, and hospitals for asthma. Medication information concerning bronchodilator use was obtained by searching through the 16 medication fields in the NHANES III database.16 We determined the physical (exercise) activity of our study participants based on a series of questions: “In the past month, did you . . . walk, jog, or run?”

COVARIATES

We classified age into 6 strata (17-24; >24-44; >44-64; >64-74; >74-84; and >84 years). Race was divided into 3 categories: white, black, and other. Smoking status was divided into 3 strata: never smoker, current smoker, and ex-smoker. Sex was classified into either male or female.

STATISTICAL ANALYSES

The baseline characteristics of the study participants divided according to the 5 BMI groups (ie, quintiles) were compared using a χ² test for binary variables and analysis of variance for continuous variables. To adjust for multiple comparisons, 4 df were used in the χ² analysis and Tukey t test for continuous variables.

To control for baseline variables (age, sex, race, and smoking status), we used multiple logistic regression (for binary outcome variables) and linear regression (for continuous outcome variables). We included age, sex, and race in the test models because all of these variables are clinically important determinants of lung function, asthma diagnosis, and physical activity. To test for trends in outcome variables along the BMI quintile gradient, we used a Mantel-Haenszel χ² test for trends. All tests were 2-tailed, and P values lower than .05 were considered statistically significant. For the purposes of this study, NHANES III population weights were not used. All analyses were conducted using SAS software, version 8.1 (SAS Institute Inc, Cary, NC).

RESULTS

There were 16,692 participants in our study cohort. Of these, 7822 (46.9%) were men, 11,326 (67.9%) were white, and 4818 (28.9%) were black. The mean ± SD age of the participants was 45.8 ± 20.0 years. Most (52.9%) of the participants (n=8825) were lifetime nonsmokers, while 4246 (25.4%) were current smokers. Self-reported subjects with asthma represented 6.9% of the study population (n = 1158). Only 389 people (2.3%) were currently using bronchodilators at the time of the survey. In total, there were 1745 emergency department and office visits for wheezing during the 12 months prior to the survey date.

Baseline characteristics of the study population, stratified according to BMI quintile groups, are given in Table
**Table 1. Baseline Characteristics of Study Participants According to Body Mass Index Quintiles**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q5</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index, kg/m²</td>
<td>≤22.1</td>
<td>&gt;22.1-24.8</td>
<td>≥24.8-27.3</td>
<td>≥27.3-31.0</td>
<td>&gt;31.0</td>
<td>. . .</td>
</tr>
<tr>
<td>No. of participants</td>
<td>3374</td>
<td>3324</td>
<td>3367</td>
<td>3289</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD age, y</td>
<td>40.5 ± 21.6</td>
<td>44.0 ± 20.4</td>
<td>48.3 ± 20.1</td>
<td>49.6 ± 19.0</td>
<td>46.7 ± 17.2</td>
<td>.001</td>
</tr>
<tr>
<td>Men</td>
<td>1379 (40.9)</td>
<td>1780 (52.1)</td>
<td>1775 (54.6)</td>
<td>1716 (51.9)</td>
<td>1172 (35.6)</td>
<td>.001</td>
</tr>
<tr>
<td>White</td>
<td>2253 (66.8)</td>
<td>2375 (69.4)</td>
<td>2337 (72.1)</td>
<td>2335 (69.4)</td>
<td>2026 (61.8)</td>
<td>.001</td>
</tr>
<tr>
<td>Black</td>
<td>983 (29.1)</td>
<td>914 (26.7)</td>
<td>809 (25.0)</td>
<td>942 (28.0)</td>
<td>1170 (35.6)</td>
<td>.001</td>
</tr>
<tr>
<td>Other race</td>
<td>137 (4.1)</td>
<td>130 (3.8)</td>
<td>93 (2.9)</td>
<td>90 (2.7)</td>
<td>93 (2.8)</td>
<td>.001</td>
</tr>
<tr>
<td>Current smokers</td>
<td>1105 (32.8)</td>
<td>937 (27.4)</td>
<td>778 (24.0)</td>
<td>759 (22.5)</td>
<td>667 (20.3)</td>
<td>.001</td>
</tr>
<tr>
<td>Nonsmokers</td>
<td>1809 (53.6)</td>
<td>1798 (52.6)</td>
<td>1654 (51.0)</td>
<td>1740 (51.7)</td>
<td>1824 (55.5)</td>
<td>.33</td>
</tr>
<tr>
<td>Asthma</td>
<td>214 (6.6)</td>
<td>217 (6.4)</td>
<td>179 (5.5)</td>
<td>238 (7.0)</td>
<td>310 (9.2)</td>
<td>.001</td>
</tr>
<tr>
<td>Bronchodilator use</td>
<td>72 (2.1)</td>
<td>64 (1.9)</td>
<td>65 (2.0)</td>
<td>78 (2.3)</td>
<td>110 (3.3)</td>
<td>.001</td>
</tr>
<tr>
<td>Inhaled or intranasal corticosteroid use</td>
<td>22 (0.7)</td>
<td>23 (0.7)</td>
<td>23 (0.7)</td>
<td>27 (0.8)</td>
<td>37 (1.1)</td>
<td>.03</td>
</tr>
<tr>
<td>Systemic corticosteroid use</td>
<td>42 (1.2)</td>
<td>35 (1.0)</td>
<td>26 (0.8)</td>
<td>34 (1.0)</td>
<td>43 (1.3)</td>
<td>.86</td>
</tr>
<tr>
<td>Dyspnea walking up a hill</td>
<td>636 (18.9)</td>
<td>607 (17.8)</td>
<td>712 (22.0)</td>
<td>939 (28.0)</td>
<td>1196 (36.5)</td>
<td>.001</td>
</tr>
<tr>
<td>Walked ≥1 mile (1.6 km) in last month</td>
<td>1591 (47.3)</td>
<td>1640 (48.0)</td>
<td>1493 (46.1)</td>
<td>1549 (46.1)</td>
<td>1328 (40.4)</td>
<td>.001</td>
</tr>
<tr>
<td>Jogged or ran in last month</td>
<td>611 (18.1)</td>
<td>553 (16.2)</td>
<td>438 (13.5)</td>
<td>334 (9.9)</td>
<td>207 (6.3)</td>
<td>.001</td>
</tr>
</tbody>
</table>

*Unless otherwise indicated, data are number (percentage) of subjects in body mass index quintile.
†P values denote trends across the body mass index quintile groups.

**Table 2. Association Between Body Mass Index and Self-reports of Asthma and Exercise Limitations**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Body Mass Index, kg/m²</th>
<th>P Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤22.1</td>
<td>&gt;22.1-24.8</td>
</tr>
<tr>
<td>Asthma</td>
<td>0.90 (0.74-1.11)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Bronchodilator use in last month</td>
<td>0.84 (0.56-1.22)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Walked ≥1 mile (1.6 km) in last month</td>
<td>1.01 (0.92-1.12)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Dyspnea walking up a hill</td>
<td>0.97 (0.85-1.10)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Jogged or ran in the last month</td>
<td>1.13 (0.99-1.31)</td>
<td>1.0 (ref)</td>
</tr>
</tbody>
</table>

*Unless otherwise indicated, data are relative odds ratio (95% confidence interval) and have been adjusted for age (as a categorical variable), race, sex, smoking status, forced expiratory volume in 1 second (percentage of predicted), and forced vital capacity (percentage of predicted). Ref indicates reference.

1. Those in the lowest BMI quintile (Q1) were the youngest (P = .001). More women were likely to be in the highest BMI quintile (Q5) than in the other BMI categories. Blacks were more likely to be in Q5. There were more current smokers and self-reported subjects with asthma in Q1 than in any other BMI group. Participants in Q5 were more restricted in their ability to exercise. Compared with subjects in other BMI groups, those in Q5 were less likely to walk a mile or more, jog, or run within the month prior to the survey. The FEV₁ and FVC (both as a percentage of the predicted value) were similar between Q1 and Q5 (P > .05) but lower than in the Q2, Q3, and Q4 groups.

The prevalence of self-reported asthma increased along the BMI quintile gradient such that the highest odds for asthma were observed in Q5 (Table 2). There was also a striking increase in the use of bronchodilators along the same BMI quintile gradient. Indeed, the relative increase in bronchodilator use was greater (odds ratio [OR], 1.94 comparing Q5 with Q2) than it was for the increase in the prevalence of self-reported asthma (OR, 1.50 comparing Q5 with Q2). Obese participants also experienced more exercise limitation than nonobese participants. For example, those in Q5 were 2.66 times more likely to experience dyspnea when walking up a hill than matched participants in Q1. Table 3 summarizes the relationship between BMI and lung function. The highest prevalence of airflow obstruction was observed in Q1, and the lowest, in Q5. Obese...
participants were less likely to have mild, moderate, and severe airflow obstruction than nonobese participants despite the increased use of bronchodilators and self-reported diagnosis of asthma.

The graphed relationship between BMI quintiles and FEV₁, FVC, and body mass index (BMI; calculated as the weight in kilograms divided by the square of height in meters) in a subgroup of participants who were lifetime nonsmokers and did not have self-reported asthma.

lower lung function. The risk for significant airflow obstruction (ie, FEV₁/FVC ratio of <80% of predicted value) was lower in Q5 than in the other BMI groups. Adjustments for age, sex, race, and smoking status made little difference to the overall findings (Figure 2). Paradoxically, however, Q5 participants were more likely to use bronchodilators (Table 1). Even in participants without evidence for airflow obstruction, bronchodilators were used more frequently in the Q5 group (Figure 3).

Using population-based data from the NHANES III questionnaire, we found that the point prevalence of self-reported asthma was higher in obese than in nonobese participants. Use of bronchodilators was likewise highest among the obese. Paradoxically, however, there was a lower prevalence of significant airflow obstruction in the high than in the low BMI quintiles. Indeed, the highest BMI quintile had the lowest risk of airflow obstruction of any severity (Figure 2).

One possible reason for the increased prevalence of asthma diagnosis among the obese might be related to the increased complaints of dyspnea and exercise limitations in this group. In our study, the obese individuals were over 2.5 times more likely to complain of dyspnea walking up a hill than participants with normal body weight. The overweight individuals were also far less likely to walk or jog than the lean participants. These symptoms may explain why the obese are more likely to be treated with bronchodilators despite an absence of objective evidence for airflow obstruction (Figure 3). Such treatment has important clinical and therapeutic implications because there is a paucity of data supporting the use of bronchodilators for dyspnea unrelated to OAD. Indeed, the overuse of bronchodilators might even be harmful for patients and lead to excess morbidity.
The mechanisms of dyspnea in obesity remain controversial. Obesity has been shown to adversely affect respiratory mechanics and gas exchange, decrease respiratory muscle function and lung volumes, and increase the work of breathing.\(^{12,13}\) The well-known decrease in expiratory lung volume in obesity has the potential to cause expiratory flow limitation despite normal airflow function.\(^{19}\) Flow limitation at rest or during exercise is a cause for ventilatory constraint, which could mimic the symptoms observed in patients with OAD who are flow limited owing to decreased maximal flow.\(^{20}\) Moreover, obesity can also increase the risk for aspiration pneumonia,\(^{21}\) obstructive sleep apnea,\(^ {22}\) and cardiac syndromes,\(^ {23}\) all of which are known risk factors for dyspnea genesis.

Several limitations of the study should be mentioned. First, due to the cross-sectional design of the survey, based on our data, there is some ambiguity regarding the direction of the described relationships. For instance, it is possible that the increased use of bronchodilators caused obesity rather than obesity causing the increased use of bronchodilators. This, however, seems unlikely since bronchodilators have not been previously implicated in obesity. Further, there is a possibility that obese participants had greater total exposure to systemic corticosteroids than the nonobese participants, which may have contributed to their weight gain. This database did not contain such information; thus, we cannot confidently rule out this possibility. However, it was reassuring to note that systemic corticosteroid use was no prospective follow-up of these participants.

Second, as with all observational studies, there is a possibility that some unmeasured variable might have confounded our results. However, we carefully controlled for the most important covariates such as age, sex, and race, making this possibility less likely. Third, since there was no prospective follow-up of these participants, the effect of increased diagnosis of asthma (in the absence of objective evidence for airflow obstruction) on patient outcomes and health service utilization remains unknown. Finally, airflow obstruction in subjects with asthma may vary with time and can be normalized by bronchodilator treatment; the absence of spirometric values before and after bronchodilator use is an important limitation of our study.

In summary, this study demonstrates that obesity is associated with increased use of bronchodilators and increased diagnosis of asthma in the community. However, the prevalence of significant airflow obstruction is lower in the obese than in the nonobese groups. This suggests that OAD might be overdiagnosed in the obese and overweight population, leading to the overuse of bronchodilators. Population-based prospective studies are needed to confirm these early findings and to better determine the role of obesity on the diagnosis and treatment of patients with asthma in the community.

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REFERENCES