Impact of Obesity on Asthma Severity in Symptomatic Adults

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A. Study Purpose and Rationale

Asthma and obesity are both highly prevalent diseases in the adult community to which Columbia University Medical Center provides health care. Approximately 5% of adults in Washington Heights and Inwood carry a diagnosis of asthma, and more than 1 in 5 adults in this neighborhood are obese[1]. Prior research efforts have demonstrated multiple relationships between these two diseases. Adolescent males and young adult women initially being diagnosed with asthma are more likely to be obese[2]. Obese adults with asthma appear to have lower lung function than their non-obese counterparts, and obese adults with respiratory symptoms are more likely to be misdiagnosed with asthma[3]. Asthma symptoms, such as wheezing, are more frequent in both obese adolescents and adults[4,5]. However, it has also been shown that the impact of obesity on both symptomatic and objective measures of disease severity appears to be less in adults[6]. Peak expiratory flow, an objective marker of lung function and asthma severity, has been shown to be reduced in individuals with a higher body mass index (BMI)[7]. Peak flow measurement is also known to be more variable in asthmatics[8], but this variability may not be any more increased in individuals with an elevated BMI[9].

The patient's perception of disease can be measured through a variety of questionnaires that have been validated in both adults and children[10,11]. Both perception of symptoms and lung volume measures were shown to be similar for obese and non-obese adults after a standardized airway insult in the form of a methacholine challenge[12]. However, the effect of obesity on perception of asthma outside of this controlled medical environment is more interesting. The perception of the severity of asthma symptoms in children was shown to be both magnified in obese children and less accurate when compared to more objective measures[13]. The data is lacking for similar studies in the adult asthmatic population.

The purpose of this study will be to evaluate the objective severity of asthma in an adult patient population with significant symptomatic burden, and evaluate for any significant difference between obese and non-obese individuals. The results of such a

study should increase our knowledge about the impact of obesity on the patient's experience of disease and potentially effect clinical management.

B. Study Design and Statistical Analysis

This study will recruit asthmatic adult patients who report their symptoms to be inadequately controlled as defined by a score of <20 on the Asthma Control Test. They will be assigned to one of two groups, either "obese" or "non-obese" as defined by whether their calculated body mass index (BMI) is ≥30 or <30 respectively. The average percent predicted peak flow for the study participants in each group will be calculated and used for statistical analysis in an unpaired T-test. For the purposes of our study, a statistically significant difference between the obese and non-obese groups will be defined as $P<0.05$.

In order to ensure that the study is adequately powered (80%), the number of subjects required for enrollment in each study group was estimated as 26. This was determined by using the unpaired T-test sample size formula:

$$n \text{ (in each group)} = 1 + 16 \text{ (standard deviation / effect)}^2$$

While limited data was available to assess the true standard deviation of percent predicted peak flow in the study population, using the investigators' clinical judgment, it was estimated that the vast majority (~95%) of subjects would have a percent predicted peak flow ranging from 30% to 80%. From this range, it can be estimated that the standard deviation is 12.5%. The change in percent predicted peak flow that was deemed to be clinically relevant (the effect) was determined to be 10%. To ensure adequate enrollment, the goal enrollment for each arm was set as 30 patients.

Given that the standard deviation used for this calculation was estimated based on the investigators' clinical judgment, the initial data obtained from the first 5 subjects enrolled in each study arm will be analyzed by a neutral third-party statistician to calculate the standard deviation of the study population based on early data collection. If this standard deviation significantly differs from that previously estimated, the number of subjects required for adequate power may need to be modified.

C. Study Procedure

Once an asthmatic patient is recruited for the study and deemed to be eligible after the administration of the Asthma Control Test questionnaire and receiving a score of <20, they will have their height and weight measured in the outpatient clinic. This data will be used to calculate the patient's body mass index, and determine whether they are to be assigned to the obese or non-obese study group.

During this initial clinic visit, the subject will be given a peak flow meter to take home and trained on appropriate PEF measurement technique. The patient will then record his/her PEF as measured from the best of three attempts upon waking 1, 8, 15, and 22 days after the clinic visit. This measurement should not place the subjects at any risk or discomfort. The investigators will obtain these recorded PEF values via a phone call placed by a member of the investigative team. These PEF values will be converted to the percent of predicted peak flow for an individual of that gender, age, and height by dividing by the value obtained using the formulas from Knudson et al[14]:

Estimated PEF in Adult Men: ((Height (in) * 5.48) + 1.58) – (Age (yr) * 0.041)) * 60
Estimated PEF in Adult Women: ((Height (in) * 3.72) + 2.24) – (Age (yr) * 0.03)) * 60

The average percent predicted PEF will be calculated for use in statistical analysis as described in section B. These repeated PEF measurements will likely be above standard clinical practice for the study participants, but provide no additional risk to the patients.

Each subject's participation in the study will last less than 1 month. The study will continue recruitment until an adequate number of subjects are enrolled to satisfy power requirements.

D. Study Drugs

N/A

E. Medical Device

N/A

F. Study Questionnaires

The Asthma Control Test questionnaire will be administered to subjects to determine their study eligibility at the initial clinic visit. This questionnaire has been shown to have internal consistency and external validity for the assessment of asthma severity[11]. This questionnaire asks 5 questions requiring the subject to answer appropriately for their experiences of the last 4 weeks. These questions include:

-In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school, or at home?

-During the past 4 weeks, how often have you had shortness of breath?

-During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain), wake you up at night or earlier than usual in the morning?

-During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication?

-How would you rate your asthma control during the past 4 weeks?

The responses to each question are scored from 1 to 5, with a maximum total score of 25 indicating total absence of symptoms. A copy of this questionnaire is being submitted concurrently.

G. Study Subjects

Study subjects must be at least 18 years of age and will be selected for inclusion by having received a prior clinical diagnosis of asthma. They also must have inadequately controlled asthma as defined by a score on the Asthma Control Test of <20 points after administration of this questionnaire.

Patients will be excluded from the study if they do not meet the above criteria or they have been previously diagnosed or are suspected of having an additional diagnosis potentially contributing to the asthma symptoms being assessed. These exclusionary

diagnoses include, but are not limited to, chronic obstructive pulmonary disease, interstitial lung disease, lung cancer, and/or congestive heart failure.

H. Recruitment of Subjects

Subjects will be identified for potential enrollment in the study by a combination of advertisement with flyers and direct identification by their health care providers. Flyers requesting participation from asthmatic patients with contact information for the study will be posted in public areas in the primary care clinics affiliated with Columbia University Medical Center. The screening process can then be completed over the phone. Information about this study and copies of the Asthma Control Test questionnaire will also be circulated to providers in these primary care clinics, as well as the asthma clinics affiliated with the medical center. Patients with known asthma and who report having symptoms can then be screened for study eligibility by their own providers, at which point they would be put in touch with the investigative team.

I. Confidentiality of Study Data

All subjects recruited for the study would receive a unique identification number. All data obtained will be kept confidential in accordance with institution policies. All personal identifier information will be kept in a secure location accessible only to the investigators.

J. Potential Conflict of Interest

There are no potential conflicts of interest to disclose for the study investigators or Columbia University Medical Center for this study protocol.

K. Location of the Study

The study is based at Columbia University Medical Center and its affiliated outpatient sites. Initial data collection will occur at these sites, and study subjects will collect PEF data in their own homes, which involves no risk.

L. Potential Risks

The study subjects may find the experience of using a peak flow meter mildly uncomfortable as it may induce a temporary sensation of shortness of breath, but has no significant adverse effect on the patient.

M. Potential Benefits

This study can potentially increase understanding about the relationship of asthma and obesity, with the potential for future effects on treatment of disease. The subjects are unlikely to personally benefit from involvement in this study.

N. Alternative Therapies

N/A

O. Compensation to Subjects

The subject will receive a peak flow meter at the time of enrollment which they may keep as part of this study. They will receive no other financial compensation.

P. Costs to Subjects

Subjects will incur the cost of traveling to and from their initial clinic visit. However, this enrollment visit will often occur simultaneously with an already scheduled appointment as part of the subject's regular medical care.

Q. Minors as Research Subjects

No minors will be participating in this study.

R. Radiation or Radioactive Substances

N/A

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Appendix:

Asthma Control Test™

This survey was designed to help you describe your asthma and how your asthma affects how you feel and what you are able to do. To complete it, please mark an ☒ in the one box that best describes your answer.

1. **In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?**

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐1	☐2	☐3	☐4	☐5

2. **During the past 4 weeks, how often have you had shortness of breath?**

More than once a day	Once a day	3 to 6 times a week	Once or twice a week	Not at all
☐1	☐2	☐3	☐4	☐5

3. **During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?**

4 or more nights a week	2 to 3 nights a week	Once a week	Once or Twice	Not at all
☐1	☐2	☐3	☐4	☐5

4. **During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as Albuterol, Ventolin®, Proventil®, Maxair® or Primatene Mist®)?**

3 or more times per day	1 or 2 times per day	2 or 3 times per week	Once a week or less	Not at all
☐1	☐2	☐3	☐4	☐5

5. **How would you rate your asthma control during the past 4 weeks?**

Not Controlled at all	Poorly Controlled	Somewhat Controlled	Well Controlled	Completely Controlled
☐1	☐2	☐3	☐4	☐5

To score the ACT

Each response to the 5 ACT questions has a point value from a 1 to 5 as shown on the form. To score the ACT, add up the point values for each response to all five questions.

If your total point value is 19 or below, your asthma may not be well-controlled. Be sure to talk to your healthcare professional about your asthma score.

Take this survey to your healthcare professional and talk about your asthma treatment plan.