Effect of Weight Reduction on Respiratory Function and Airway Reactivity in Obese Women*

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Background: Population-based studies have documented an association between obesity and an increased prevalence of asthma in women.

Methods: We prospectively studied 58 obese women with a body mass index of > 30 kg/m², 24 of whom had asthma, who were enrolled in an intensive 6-month weight loss program to determine whether loss of body mass would be correlated with improvements in bronchial reactivity, lung function, and disease-specific health status.

Results: Patients lost an average of 20 kg over the 6-month period. For every 10% relative loss of weight, the FVC improved by 92 mL (p = 0.05) and the FEV₁ improved by 73 mL (p = 0.04), however, bronchial reactivity did not significantly change with weight loss (p = 0.23). Patients who lost > 13% of their pretreatment weight experienced improvements in FEV₁ (p = 0.01), FVC (p = 0.02), and total lung capacity (p = 0.05) compared to patients in the lowest quartile who failed to lose significant amounts of weight. Neither group experienced any significant change in methacholine responsiveness (p = 0.57). Patients who completed the 6-month weight loss program experienced improvements in respiratory health status, irrespective of weight loss.

Conclusion: We concluded that weight loss can improve lung function in obese women, however, the improvements appear to be independent of changes in airway reactivity.

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Key words: asthma; obesity; pulmonary function

Abbreviations: BMI = body mass index; kcal = kilocalorie; PC₂₀ = provocative concentration of a substance causing a 20% fall in FEV₁; SGRQ = St. George Respiratory Questionnaire; TLC = total lung capacity

The prevalence of obesity has increased worldwide to reach epidemic proportions in many industrialized countries.¹ Recent cross-sectional studies have suggested that there exists a significant association between obesity and asthma in women. A Canadian population-based study² showed that the adjusted odds ratio for asthma was 1.52 in obese women compared to nonobese women. Population-based studies in the United Kingdom³ and the United States⁴,⁵ have yielded similar results, suggesting an increased prevalence of asthma among Canadian, British, and American obese women.

One controlled clinical trial⁶ randomized 38 obese asthmatic subjects to an 8-week supervised weight reduction program or to a control program. Patients in the weight-reduction group significantly improved their FEV₁ and FVC values relative to control subjects. Similarly, they improved their health status, as measured by a disease-specific quality-of-life questionnaire, relative to control subjects. However, this study did not evaluate methacholine responsiveness or other measures of airway reactivity associated with asthma. Therefore, it is unclear whether the observed improvement in lung function and respiratory health status was due to an improvement in asthma and airway reactivity per se, or due to a...
reduction in mass-loading of the respiratory system that occurs following significant weight reduction.

The overall aim of this study was to determine whether a relationship exists between changes in body weight and airway reactivity in overweight women. We studied 58 women with a body mass index (BMI) of > 30 kg/m² to determine the following: (1) whether loss of body mass improves lung function in these subjects; and (2) whether this may be correlated with improvements in bronchial reactivity.

**Materials and Methods**

**Patients**

We enrolled consecutive female subjects with a BMI > 30 kg/m² who had entered the Ottawa Hospital Weight Loss Clinic and consented to participate in the study. We enrolled an approximately equal number of patients during the summer and winter months to try to control for potential seasonal changes in bronchial responsiveness. Patients were excluded if they had been receiving oral corticosteroids on a regular basis, if they were pregnant, if they had a history of myocardial infarction or stroke within the previous 3 months, or if they had a known history of aortic aneurysm. The study was approved by the Ottawa Hospital Research Ethics Board, and all subjects signed informed consent forms.

Patients were placed on a regimen of three liquid meal replacement supplements per day, which delivered 300 kilocalories (kcal) per meal (40% of calories from protein, 30% of calories from carbohydrates, and 30% of calories from fat). Those with severe obesity (ie, initial BMI, > 35 kg/m²) were enrolled into a long program consisting of a diet of 900 kcal per day that continued for 12 weeks. Patients with less severe obesity (ie, mean initial BMI, 30 to 35 kg/m²) were enrolled into a shorter program consisting of the same diet of 900 kcal per day that continued for 6 weeks. Patients were counselled to adopt a restricted calorie diet, and follow-up of enrolled patients occurred on a weekly basis for at least 6 months.

Patients were assessed in a series of three paired study visits, as follows: before beginning the weight reduction program; at 3 months after enrolling in the weight reduction program; and at 6 months after enrolling in the weight reduction program. At the first visit, they underwent prebronchodilator and postbronchodilator spirometric testing, and measurements of plethysmographic lung volume. Measurements were performed after bronchodilator therapy had been withheld for at least 12 h and were obtained by certified pulmonary technologists according to American Thoracic Society criteria. At a second visit the same week, a standardized bronchial challenge test was performed. Increasing concentrations of inhaled methacholine were administered, and spirometry was performed after each inhalation according to published protocols. The tests were stopped once the FEV₁ had fallen 20% from baseline, or after a concentration of 32 mg/mL had been administered. All study visits were made when patients were clinically stable and were receiving their usual doses of anti-inflammatory asthma medications.

Symptoms and disease-specific quality of life were assessed using the St. George Respiratory Questionnaire (SGRQ) at baseline and every 3 months for the duration of the 6-month study. This questionnaire includes the following three domains: symptoms (ie, distress caused by specific respiratory symptoms); activity (ie, physical activities that cause or are limited by breathlessness); and impact (ie, social and psychological effects of the respiratory disease). A decrease in the score indicates an improvement in health status. A total change of −4 in the SGRQ score is considered to be clinically significant. Baseline characteristics were evaluated for all patients using measures of central tendency and dispersion. Pearson correlation coefficients were calculated to describe the relationship between weight change and unadjusted changes in FEV₁, FVC, provocative concentration of a substance causing a 20% fall in FEV₁ (PC₂₀), and SGRQ total score.

Analyses involving all 58 patients comparing relative weight change and the effect on absolute changes in lung function (ie, FEV₁, FVC, and total lung capacity [TLC]), airway reactivity (ie, PC₂₀), and quality of life (ie, SGRQ) were calculated using linear regression models. Absolute changes in FEV₁, FVC, and TLC were adjusted for age and height. Changes in airway reactivity are reported as the log₂ change in methacholine responsiveness, and were adjusted for history of asthma, atopy, and smoking status, since these patient characteristics are known to influence methacholine responsiveness. Regression coefficients were multiplied by 10 to represent a 10% relative change in weight loss.

Our previous observations of the patients who entered into the Ottawa Hospital Weight Loss Clinic program suggested that one quarter of patients fail to lose at least 10% of their pretreatment weight. Based on this observation, the study protocol stipulated that we would compare those patients in the lowest quartile of relative weight reduction to those who were in the upper three quartiles at the end of the 6-month observation period. Therefore, additional analyses were performed for the 50 patients who completed the 6 months of follow-up, dividing these patients into the lowest quartile and the upper three quartiles of relative weight change. All outcome measures are reported as average absolute changes with 95% confidence intervals.

**Results**

**Patient Characteristics**

Fifty-eight patients were enrolled in the study, and completed baseline and 3-month assessments. Eight patients withdrew from the study before completing their 6-month follow-up assessment. The mean (± SD) age of the patients was 44 ± 13 years. Twenty-four of the 58 patients (41%) had a history of physician-diagnosed asthma (Table 1), and 21 patients (36%) were receiving medication for asthma at time of enrollment. The mean BMI of the patients entering into the study was 43.1 ± 8.8 kg/m², and the mean body weight was 115 ± 26 kg. The 50 patients who completed the study lost an average of 20.0 kg over the 6-month study period (range, 0 to 35 kg), or 17.4% of their pretreatment weight.

Patients in the lowest quartile of relative weight reduction lost a mean of 8.0 ± 4.5% of their pretreatment weight (range, 0 to 12% weight loss over 6 months) compared to a mean of 17.4% of pretreatment weight in those in the upper three quartiles of relative weight loss. This difference is statistically significant (p = 0.006), suggesting that weight loss at a more rapid rate is associated with greater improvements in lung function and quality of life.
months), and patients in the upper three quartiles lost a mean of 18.8 ± 4.9% of their pretreatment weight (range, 13 to 31%). There were no significant differences at baseline between these two groups in age, smoking status, initial BMI, or the proportion of those who had atopy or asthma (Table 1).

None of the enrolled patients reported experiencing any difficulties with their asthma necessitating urgent visits to physicians or to the emergency department during the 6-month study period. Similarly, none of them reported any changes to their maintenance asthma medications during the 6-month study period.

### Changes in Lung Function

For the entire group of 58 patients, there was a significant correlation between weight loss and unadjusted changes in the FEV1 ($r = 0.29; p = 0.040$). The association between weight loss and unadjusted changes in the FVC was similar, although not quite statistically significant ($r = 0.27; p = 0.057$) [Fig 1]. However, there was no significant correlation between weight loss and changes in airway responsiveness ($r = 0.19; p = 0.203$) [Fig 2].

For every 10% relative loss of pretreatment weight, the FVC (adjusted for age and height)

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### Table 1—Baseline Characteristics of the Patients*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All Patients Enrolled (n = 58)</th>
<th>LQ (n = 12)</th>
<th>UTQ (n = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>44.3 ± 12.5</td>
<td>47.2 ± 15.0</td>
<td>44.5 ± 11.3</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>5 (9)</td>
<td>2 (16)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>23 (40)</td>
<td>3 (25)</td>
<td>19 (50)</td>
</tr>
<tr>
<td>Never smoked</td>
<td>30 (52)</td>
<td>7 (58)</td>
<td>18 (47)</td>
</tr>
<tr>
<td>Mean initial BMI, kg/m²</td>
<td>43.1 ± 8.8</td>
<td>39.8 ± 8.8</td>
<td>43.7 ± 8.0</td>
</tr>
<tr>
<td>Mean initial weight, kg</td>
<td>115.3 ± 26.3</td>
<td>107.5 ± 29.8</td>
<td>116.8 ± 24.7</td>
</tr>
<tr>
<td>History of asthma</td>
<td>24 (41)</td>
<td>6 (50)</td>
<td>16 (42)</td>
</tr>
<tr>
<td>Asthma medication use</td>
<td>21 (36)</td>
<td>6 (50)</td>
<td>12 (32)</td>
</tr>
<tr>
<td>History of atopy</td>
<td>24 (41)</td>
<td>5 (42)</td>
<td>14 (38)</td>
</tr>
</tbody>
</table>

*Values given as mean ± SD or No. (%). LQ = lowest quartile of relative weight loss after 6 mo; UTQ = upper three quartiles of relative weight loss after 6 mo.

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**Figure 1.** Correlation between relative weight loss and changes in lung function.
improved by 92 mL (p = 0.05) and the FEV₁ (adjusted for age and height) improved by 73 mL (p = 0.04). The effect of weight loss on the change in methacholine responsiveness was not significant. For every 10% relative loss of weight the log₂ change in PC₂₀ (adjusted for asthma, atopy, and smoking status) improved by 0.53, which is equal to half a doubling dilution of methacholine (p = 0.23). Adjusting the change in PC₂₀ for changes in lung volume (ie, TLC) did not influence the result (improvement in PC₂₀, 0.27; p = 0.58).

A subgroup analysis of the 24 patients who had asthma did not show any improvement in PC₂₀ with weight loss. In these patients, for every 10% relative loss of weight the log₂ change in PC₂₀ improved by only 0.19 (ie, one fifth of a doubling dilution; p = 0.66).

Fifty patients completed the entire 6-month follow-up, and they were divided into quartiles of relative weight loss. Patients in the upper three quartiles who lost ≥ 13% of their relative body weight demonstrated a significant 6-month improvement in FEV₁ relative to those in the lowest quartile who lost < 13% of their initial body weight. The mean absolute change in log₂ methacholine responsiveness was 0.18 ± 1.99 (ie, a positive change by one fifth of a doubling dilution) in those who lost weight compared to −0.23 ± 1.19 (ie, negative change by one fifth of a doubling dilution) in those who did not lose weight (p = 0.57 for the comparison between the two groups) [Table 2].

### Changes in Health Status

Patients enrolled in the weight loss program experienced a significant improvement in their disease-specific quality of life, as measured by the SGRQ instrument. The largest changes seen were in the activity domain of the SGRQ, but all domains im-

<table>
<thead>
<tr>
<th>Variables</th>
<th>LQ</th>
<th>UTQ</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative weight loss</td>
<td>8.0% ± 4.5%</td>
<td>18.8% ± 4.9%</td>
<td>0.01</td>
</tr>
<tr>
<td>FEV₁, L</td>
<td>−0.01 ± 0.15</td>
<td>0.14 ± 0.17</td>
<td>0.01</td>
</tr>
<tr>
<td>FVC, L</td>
<td>0.04 ± 0.22</td>
<td>0.21 ± 0.22</td>
<td>0.02</td>
</tr>
<tr>
<td>TLC, L</td>
<td>−0.10 ± 0.56</td>
<td>0.21 ± 0.43</td>
<td>0.05</td>
</tr>
<tr>
<td>log₂ PC₂₀</td>
<td>−0.23 ± 1.19</td>
<td>0.18 ± 1.99</td>
<td>0.57</td>
</tr>
<tr>
<td>SGRQ total score, U</td>
<td>−11.8 ± 13.1</td>
<td>−8.7 ± 10.5</td>
<td>0.42</td>
</tr>
</tbody>
</table>

*Values given as mean ± SD, unless otherwise indicated. See Table 1 for abbreviations not used in the text.*
proved significantly (Fig 3). There was no correlation seen between relative weight change and change in the total SGRQ score over 6 months ($r = -0.12$; $p = 0.44$). Patients in the lowest quartile of relative weight reduction experienced similar 6-month improvements in total SGRQ score (change in total SGRQ score, $-11.8 \pm 13.1$ U) compared to patients in the upper three quartiles who lost more weight (change in total SGRQ score, $-8.7 \pm 10.5$ U; $p = 0.42$) [Table 2].

**DISCUSSION**

Obesity can have a significant effect on normal lung physiology. In 1960, Naimark and Cherniak demonstrated that obesity is associated with reduced chest wall compliance. The reduction in chest wall compliance that is seen in obesity is reflected by a reduction in functional residual capacity, expiratory reserve volume, and vital capacity, and in patients with severe obesity, by a reduction in the TLC as well. The reduced chest wall compliance represents a substantial elastic load on inspiratory muscles and causes an increased work of breathing. Thus, it is not surprising that obese patients complain of more dyspnea on exertion than patients without obesity. Conceivably, patients who are obese and dyspneic also may be more likely to receive a diagnosis of asthma.

Several large cross-sectional studies have clearly demonstrated a positive association between obesity and an increased prevalence of asthma in women. There are several possible theories that can explain the nature of the observed association linking obesity and asthma. One possibility is that diagnostic bias in these epidemiologic studies may have created an artifactual association. The effect of mass-loading the chest by adipose tissue causes dyspnea and may increase the probability of asthma being incorrectly diagnosed. Similarly, response bias may have affected these studies, so that their increased sense of dyspnea might have led obese patients to have incorrectly reported that they had asthma.

Another possibility is that confounding factors associated with both obesity and asthma, such as diet or sedentary lifestyle, could have accounted for the observed relationship. Against this hypothesis is evidence from a previous population-based study that demonstrated that leisure-time energy expenditure was not lower in asthmatic patients compared to nonasthmatic patients. Finally, the potential for a causal relationship exists, such that obesity may cause asthma in women through a yet-to-be-determined mechanism.

Increased airways reactivity is a defining characteristic of active asthma. We sought to find evidence for a causal relationship by objectively measuring changes in asthma severity, which were
reflected by changes in airway reactivity, during weight loss. The results of our study suggest that lung function improves in obese women who lose a significant amount of weight and does not improve in those who fail to lose weight. However, our study did not show any significant effect of weight loss on airway reactivity, suggesting that improvements in lung function occur due to a reduction in mass-loading on the respiratory system, rather than improvements in asthma per se.

One cannot exclude a very small effect on airway reactivity that may be detectable in large population-based studies but are not large enough to cause clinically significant differences that are detectable in a patient-based study. However, the results of our study are consistent with those of a population-based study by Schacter et al. These authors studied 1,971 Australian adults in a cross-sectional study, and found that obesity was a significant risk factor for asthma, wheeze, and asthma medication use, but not for airway hyperresponsiveness, atopy, or airflow obstruction. The authors concluded that although subjects with severe obesity reported more symptoms consistent with asthma, their levels of atopy, airway hyperresponsiveness, and airway obstruction did not support the suggestion of a higher prevalence of asthma in this group.

One controlled clinical trial randomized 38 obese asthmatic subjects to a supervised weight reduction program or to a control program. Patients in the weight-reduction group significantly improved their disease-specific health status, as measured by the SGRQ, relative to control subjects who did not go through the weight-reduction program. The results of our study also suggest that patients who go through a weight-loss program experience significant improvements in disease-specific health status, as measured by the SGRQ (Fig 3). Surprisingly, in our study improvements in health status were consistent across the entire cohort of patients, and these improvements did not correlate with the amount of weight lost. This suggests that all patients in our weight reduction program improved their quality of life, regardless of relative weight changes, presumably because the program includes an exercise component (which could improve the activity subscale of the SGRQ) and a counseling/support component (which could improve emotional well-being).

One of the potential limitations of our study is that we did not include a group of obese patients who were not going through the weight-reduction program as control subjects. Rather, we chose to compare those patients in the lower quartile of the cohort who lost the least amount of weight to those in the upper three quartiles who lost more weight. In this fashion, we were able to eliminate referral biases or selection biases that come with selecting a different population for the control arm of the study. Similarly, by ensuring that the control subjects came from the cohort, we were able to ensure that the diet, counseling, and exercise prescriptions were the same for all patients in the study, and, thus, we were able to better control for the possible confounding effects of diet, counseling, and exercise on asthma.

A second potential limitation is that not all patients enrolled in this study had a history of physician-diagnosed asthma. Perhaps only patients with preexisting asthma can be expected to improve their airway responsiveness with weight loss. However, a subgroup analysis of the 24 patients who had asthma did not show any improvement in PC_{20} with weight loss, and in these patients for every 10% relative loss of weight the log 2 change in PC_{20} improved by only 0.19 (i.e., one fifth of a doubling dilution), which is less than the 0.53 improvement seen for the group as a whole. We conclude that weight loss can improve lung function in obese women, however, these improvements appear to be independent of significant changes in airway reactivity.

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