Airflow Limitation in Morbidly Obese, Nonsmoking Men

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Study Objective: To determine the effect of obesity on pulmonary function.

Design: Case-control study, using nonobese, age- and weight-matched nonsmokers.

Setting: Metabolic and obesity clinics of two major teaching hospitals.

Patients: One hundred and three obese, lifelong nonsmokers without cardiopulmonary disease.

Controls: One hundred and ninety healthy, nonobese nonsmokers recruited from among hospital personnel.

Measurements and Main Results: Complete pulmonary function measurements in all patients and controls. These measurements included maximum expiratory flow-volume curve, lung volumes and airway resistance using body plethysmograph, single-breath diffusing capacity for carbon monoxide, and total lung capacity using the helium dilution technique. Obese persons were found to have lower functional residual capacity, expiratory reserve volume, and total lung capacity by helium dilution than nonobese controls. In addition, residual volume and diffusing capacity were higher in the obese group. Finally, we found that obese men, but not women, had reduced maximum expiratory flow rates at 50% and 75% of exhaled vital capacity.

Conclusion: Obesity may contribute independently of smoking habits to chronic airflow limitation in men.

Annals of Internal Medicine. 1990;**112**:828-832.

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Recent vital statistics (1) indicate that approximately 34 million American adults from 20 to 75 years of age are overweight and that the prevalence of obesity in the general population is increasing, particularly among men between 25 and 55 years of age. Between 1979 and 1985, the prevalence of chronic obstructive pulmonary disease in the United States increased considerably (2). It is well established that obesity alone, without associated disease, alters respiratory function in humans; by altering chest-wall mechanics, it leads to restrictive respiratory impairment (3-9). It is important to identify pulmonary function abnormalities associated with obesity, because obese persons might be at greater risk for development of further respiratory impairment when exposed to other factors associated with increased respiratory morbidity, such as cigarette smoking and respiratory infections (10).

The most characteristic pulmonary function abnormalities in obese persons are decreased functional residual capacity (FRC) and expiratory reserve volume (ERV), which appear to be due to splinting of the diaphragm during tidal breathing (3-9). Previous studies (5-7, 11-16) suggested that the lungs are normal in obese persons; however, the effects of obesity on airway caliber, as inferred from physiologic measurements of airway function, are not clear. Douglas and Chong (17) found decreased dynamic lung compliance in 9 obese subjects with low lung volumes, suggesting peripheral airway narrowing. Crapo and colleagues (13) showed, however, that the average forced expiratory flow rate at midexpiration in 103 morbidly obese women and 11 morbidly obese men having bariatric surgery was 100% of predicted, implying normal airway size. These investigators did not indicate, however, whether smokers and patients with underlying systemic or pulmonary disorders were excluded from their study. Emirgil and Sobol (18) studied 4 obese subjects without hypoventilation and found decreased maximal midexpiratory flow and borderline-low specific airway conductance in 3. Ray and colleagues (11) studied 43 obese nonsmokers and found that the forced expiratory volume exhaled in 1 second (FEV_1) to forced vital capacity (FVC) ratio (FEV_1/FVC) fell within the 95% confidence intervals (CI) for the predicted values. However, they neither reported maximal expiratory flow rate measurements, despite the fact that spirometry was done in every subject, nor measured airway resistance in their subjects.

These conflicting reports on airway function in obesity illustrate some of the problems associated with the studies. These problems include small sample size; use of predicted values rather than values from a nonobese, age- and height-matched control group; predominance of women; incomplete pulmonary function testing; and inclusion of smokers and subjects with underlying systemic or pulmonary disorders. Because obesity and

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chronic obstructive pulmonary disease are becoming more prevalent in the United States and because of conflicting reports on pulmonary function in obesity, we studied the effects of obesity on airway function in a large group of nonsmoking, obese men and women who had no evidence of underlying cardiorespiratory or endocrine disorders, and we compared the results with pulmonary function measurements from nonsmoking, age- and height-matched, nonobese controls.

Methods

Selection of Subjects

We studied 293 subjects who were divided into obese and nonobese groups. The obese subjects had body mass indexes of 30 or more kg/m^2 body surface area (19). One hundred and three obese persons (79 women and 24 men) were chosen from 954 consecutive obese subjects referred to St. Michael's and the Toronto Hospital's metabolic clinic. They fulfilled the following selection criteria: no history of cigarette smoking; no clinical or laboratory evidence of endocrine disorders; and no cardiorespiratory abnormalities, including sleep-disordered breathing and hypercapnia. The latter was ascertained on the basis of clinical history and determination of arterial blood gases. A postero-anterior chest radiograph and a 12-lead electrocardiogram were obtained for each subject and were interpreted as normal. All 103 subjects were diagnosed as having obesity without any concomitant or associated medical illness.

One hundred and ninety nonobese, healthy persons (122 women and 68 men) were recruited from among hospital personnel and matched for gender, age, and height with the obese subjects. They were lifelong nonsmokers, without respiratory symptoms or disease, and had normal postero-anterior chest radiographs.

Pulmonary Function Studies

Spirometry was done with the patient sitting with nose clips in place, using a wedge spirometer interfaced with an X-Y recorder (HP 7045B, Hewlett-Packard Corporation, Toronto, Ontario, Canada) and equipped with a 1-second timer. Three reproducible (± 5%) maximal expiratory flow-volume curves were obtained from each subject, and the curve with the greatest sum of FEV_1 and FVC was selected for analysis (20). The maximum expiratory flow rates at 50% and 75% of FVC (V_{50} and V_{25}, respectively) were also computed from this curve (Figure 1). Inspiratory capacity was measured from end-expiration during tidal breathing to the maximal volume recorded during a slow inspiratory vital capacity maneuver.

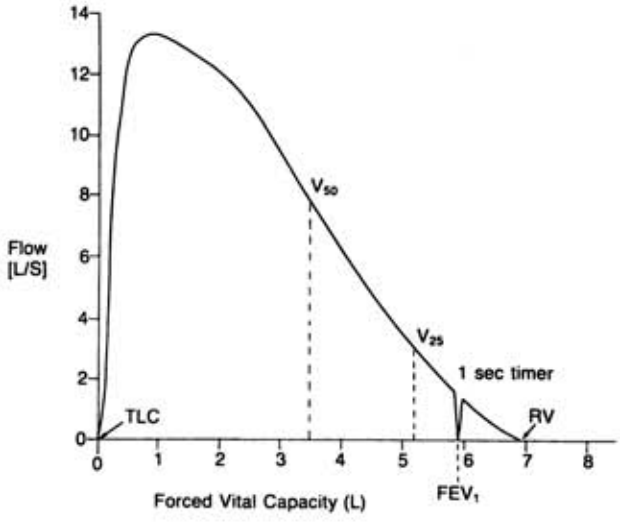

Figure 1. Typical flow-volume curve in a healthy person. TLC = total lung capacity; V_{50} = forced expiratory flow at 25% of vital capacity; RV = residual volume; and FEV_1 = forced expiratory volume in 1 second.

Table 1. *Anthropometric Data*

Variable	Men*		Women†	
	Obese	Nonobese	Obese	Nonobese
Number	24	68	79	122
Age, *y*	37 ± 11	37 ± 11	38 ± 11	38 ± 11
Height, *cm*	177 ± 7	177 ± 8	161 ± 7	162 ± 6
Weight, *kg*	147 ± 39	77 ± 9	117 ± 19	60 ± 8
Body mass index, *kg/m^2*	47 ± 3	25 ± 2	45 ± 7	23 ± 2

* The *P* value for age is 0.9684; for height, 0.7075; and for weight and body mass index, 0.0001.

† The *P* value for age is 0.6087; for height, 0.1434; and for weight and body mass index, 0.0001.

In all subjects, functional residual capacity (FRC) and airways resistance (Raw) were measured in a variable-pressure, constant-volume body plethysmograph using standard techniques (21). Specific airway conductance was calculated as an inverse of Raw normalized by FRC. Total lung capacity (TLC) was obtained by adding inspiratory capacity to FRC and was also measured by the single-breath helium dilution technique (*see* below). Residual volume (RV) was obtained by subtracting FVC from the TLC obtained by body plethysmography.

The diffusing capacity for carbon monoxide (D_{LCO}) was measured (with the patient sitting) using a commercial D_{LCO} apparatus and the single-breath technique with helium as the carrier gas and a breath-holding time of 10 seconds. The breath-holding time was calculated by the method of Ogilvie and colleagues (22). In each subject, D_{LCO} was measured at least twice, and the reported value represents an average of two reproducible (± 10%) measurements. Alveolar volume at TLC was obtained from the single-breath helium dilution measurements. No correction for the back pressure of carbon monoxide was made, because none of the patients required repeated measurements of diffusing capacity over a short period of time. Measured values of the diffusing capacity were all corrected for hemoglobin.

Statistical Analysis

Data are expressed as mean ± 1 SD. To compare pulmonary function data from obese persons with data from nonobese persons, we set up a general linear model with two classes (obesity, gender), each having two levels (obese and nonobese, men and women). This model permitted us to study not only the effect of obesity, but also whether the effect is different in men and women. All statistical analysis was done using the SAS statistical package, release 6.03 (SAS Institute Inc., Cary, North Carolina). Statistical significance was set at $P < 0.05$.

Results

The anthropometric data on 103 obese men and women and 190 nonobese, healthy controls matched for gender, age, and height are summarized in Table 1. Tables 2, 3, and 4 summarize the results of the pulmonary function studies done in obese men and women and in nonobese controls. Pulmonary function data are reported as the measured values in all subjects. We found significant differences in pulmonary function between the obese and nonobese persons, differences that were common to both men and women. The differences include reduced FRC, TLC (measured by the single-breath helium dilution technique), ERV, FVC, and FEV_1; and increased residual volume, residual-volume-

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Table 2. *Flow-Volume Data*

Pulmonary Function Variable*	Men†		Women‡	
	Obese	Nonobese	Obese	Nonobese
FVC, *L*	5.0 ± 0.9	5.7 ± 0.9	3.5 ± 0.7	3.9 ± 0.6
FEV_1, *L*	3.9 ± 0.7	4.6 ± 0.8	2.9 ± 0.6	3.3 ± 0.5
FEV_1/FVC	0.79 ± 0.05	0.81 ± 0.06	0.84 ± 0.06	0.83 ± 0.06
V_{50}, *L/s*	4.5 ± 1.1	5.6 ± 1.4	4.0 ± 1.1	4.3 ± 1.0
V_{50}/FVC	0.91 ± 0.19	1.00 ± 0.26	1.17 ± 0.33	1.10 ± 0.26
V_{75}, *L/s*	1.7 ± 0.6	2.2 ± 0.9	1.6 ± 0.7	1.7 ± 0.6
V_{25}/FVC	0.33 ± 0.07	0.39 ± 0.14	0.45 ± 0.18	0.44 ± 0.14

* FEV_1 = forced expired volume in 1 second; FVC = forced vital capacity; V_{50} = forced expiratory flow at 50% of vital capacity; V_{75} = forced expiratory flow at 75% of vital capacity; V_{25} = forced expiratory flow at 25% of vital capacity.

† The *P* value for FVC is 0.001; for FEV_1, 0.0006; for FEV_1/FVC, 0.2008; for V_{50}, 0.001; for V_{50}/FVC, 0.1663; for V_{75}, 0.005; and for V_{25}/FVC, 0.04.

‡ The *P* value for FVC and FEV_1 is 0.0001; for FEV_1/FVC, 0.5985; for V_{50}, 0.0862; for V_{50}/FVC, 0.0809; for V_{75}, 0.0790; and for V_{25}/FVC, 0.5060.

to-total-lung-capacity ratio, airways resistance, and diffusing capacity for carbon monoxide normalized to the alveolar volume (D_{LCO}/VA) in obese persons. In addition, obese men had reduced flow rates at 50% and 75% of exhaled vital capacity.

Some of the differences between the obese and nonobese persons might be attributed to different lung volumes. For example, although airways resistance was significantly higher in the obese subjects, there was no significant difference in specific conductance between the two groups. Similarly, when the maximal expiratory flow rates were normalized for vital capacity, the difference in V_{50} between the obese and nonobese groups disappeared. However, the difference in V_{25} persisted. These abnormalities in lung volumes and maximal expiratory flow rates indicate airflow limitation in obese men and air trapping in obese women.

Correlation analysis between body mass index and the pulmonary function values listed in Tables 2, 3, and 4 showed that body mass index is a significant determinant for all of the values, except for FEV_1/FVC ratio and D_{LCO}.

Discussion

The results of our study show that obesity alone, without other disease, is associated with significant abnormalities in pulmonary function. Although obese men and women showed many similar abnormalities when compared with nonobese controls, there were some significant gender differences. Obese men had reduced forced expiratory flow rates at low lung volumes, whereas obese women did not. These findings show that nonsmoking, morbidly obese men have peripheral airway obstruction and suggest that obesity might contribute, independently of smoking habits, to chronic airflow limitation in men.

Several tests, such as closing volume, frequency dependence of compliance, and volume of isoflow, are presently thought to be useful for diagnosis of peripheral airways obstruction. In our study, we selected the maximum expiratory flow-volume curve, currently the commonest pulmonary function test for evaluating peripheral airway function, for several reasons. The test is well standardized, reproducible in each person, routinely done in pulmonary function laboratories, and has been shown to have a good pathologic-physiologic-clinical correlation. The test's major disadvantage is that its results are highly variable among healthy nonsmokers, making it difficult to establish a range of normal values. This high intersubject variability of maximal expiratory flow rates is reflected by the relatively high SDs of these values in our study groups. However, this issue is of only minor concern, as we are comparing two groups (obese and control) in whom the same measurements were done rather than comparing data obtained in the obese group only with predicted normal values. Consequently, reduced maximal expiratory flow rates at low lung volume in the obese group relative to the control group indicates peripheral airways obstruction in obese men.

Obesity might impair pulmonary function via several mechanisms. It adversely affects chest-wall mechanics (8), reduces FRC and ERV (3-9, 11-16), and causes a decrease in total respiratory compliance due to deposition of subcutaneous adipose tissue (4, 9). Respiratory muscle function might also be impaired in obesity by the mechanical disadvantage induced by changes in chest-wall configuration, fat deposition, and increased energy expenditure to expand the lungs (9, 23).

Few clinical investigations (3-9, 11-16, 24) have examined airway function in obesity, and the findings have been conflicting, suggesting normal or decreased airway caliber. The reasons for this controversy are not clear, but methodologic limitations in earlier studies might have contributed to it. None of the studies examining the effects of obesity on airway function included an age- and height-matched control group and, therefore, pulmonary function data were reported as percents of predicted. However, the prediction equations for reference spirometric values reported by Crapo and colleagues (25) did not include weight as a predictor, because weight did not add to the regressions

Table 3. *Lung Volume Data*

Pulmonary Function Variable*	Men†		Women‡	
	Obese	Nonobese	Obese	Nonobese
TLC by body box, *L*	7.3 ± 1.3	7.6 ± 1.0	5.3 ± 0.9	5.6 ± 0.8
TLC by helium dilution, *L*	6.7 ± 1.2	7.7 ± 1.1	4.9 ± 0.8	5.7 ± 0.8
RV, *L*	2.3 ± 0.9	1.9 ± 0.4	1.9 ± 0.5	1.6 ± 0.4
FRC, *L*	2.9 ± 0.9	3.7 ± 0.7	2.4 ± 0.5	2.9 ± 0.5
ERV, *L*	0.6 ± 0.4	1.8 ± 0.6	0.5 ± 0.3	1.3 ± 0.4
RV/TLC by body box	0.31 ± 0.08	0.25 ± 0.05	0.35 ± 0.08	0.29 ± 0.06

* TLC = total lung capacity; RV = residual volume; FRC = functional residual capacity; and ERV = expiratory reserve volume.

† The *P* value for TLC by body box is 0.1744; for TLC by helium dilution, 0.0015; for RV, 0.0092; for FRC, 0.0007; for ERV, 0.0001; and for RV/TLC, 0.003.

‡ The *P* value for TLC by body box is 0.0644 and for all other variables is 0.0001.

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Table 4. *Airway Resistance and Diffusing Capacity*

Pulmonary Function Variable	Men*		Women†	
	Obese	Nonobese	Obese	Nonobese
Airway resistance, *mm Hg · s/L*	2.0 ± 1.1	1.1 ± 0.4	1.9 ± 0.7	1.5 ± 0.4
Specific conductance, $(s \cdot mm\ Hg)^{-1}$	0.22 ± 0.11	0.26 ± 0.08	0.26 ± 0.10	0.26 ± 0.07
Diffusing capacity, *mL/(min · mm Hg)*	39.0 ± 7.2	37.6 ± 5.8	27.4 ± 5.1	26.8 ± 4.1
*K*co, $(min \cdot mm\ Hg)^{-1}$‡	5.8 ± 1.1	4.9 ± 0.6	5.6 ± 0.8	4.7 ± 0.6

* The *P* value for airway resistance is 0.0001; for specific conductance, 0.0787; for diffusing capacity, 0.3750; and for *K*co, 0.0001.
† The *P* value for airway resistance is 0.0001; for specific conductance, 0.7773; for diffusing capacity, 0.3879; and for *K*co, 0.0001.
‡ *K*co = diffusing capacity divided by the volume of gas in which a single breath of carbon monoxide is diluted.

made with age and height alone. Further, these equations were obtained from a healthy, nonobese reference population so that the contribution of obesity, as an independent variable, to pulmonary function could not be tested.

Most investigators have included smokers and patients with associated systemic diseases, including lung disease; others have studied only a small number of subjects, the majority of them women (3-9, 11-16). Kollias and colleagues (26) did spirometry in 8 obese college men and 12 age-matched controls and found that FEV_1/FVC ratios and maximal expiratory flow rates were similar in the two groups. However, the obese men were taller than the control subjects (182.6 ± 4.9 cm and 173.4 ± 6.2 cm, respectively), implying that FEV_1/FVC ratios and maximal expiratory flow rates were, in fact, lower in the obese group. Crapo and colleagues (13) studied the effects of obesity on maximal expiratory flow-volume curve in 103 women and 11 men and found no abnormalities. Similarly, Thomas and colleagues (24) prospectively measured respiratory function in 28 women and 1 man having bariatric surgery and found that FEV_1/FVC ratios and peak expiratory flows were within the normal predicted range. However, the predominance of women in these studies might have skewed the conclusions, because our data clearly show that nonsmoking, obese women had maximal expiratory flow rates similar to those measured in nonobese controls, whereas nonsmoking, obese men had evidence of airway narrowing, as manifested by significantly decreased maximal expiratory flow rates.

We studied airway function in a large group of obese, nonsmoking men and women and compared the results with similar measurements obtained in age- and height-matched control groups. The obese subjects were recruited from persons referred to the metabolic clinic of two large university-affiliated hospitals for evaluation of morbid obesity. The preponderance of young subjects and the large number of women in our study reflect, therefore, the bias of referrals to the metabolic clinic and might not necessarily be representative of the entire, healthy, obese population. However, our aim was not to conduct a cross-sectional study on the effects of obesity on airway function in the general population; rather, it was to infer airway size in a limited and well defined group of persons with morbid obesity. Our finding of reduced FRC and ERV and increased *D*Lco/VA in nonsmoking, obese men and women in comparison with nonsmoking, nonobese controls is consistent with previous reports (3-9, 11-16, 27, 28). Reduced FRC and ERV suggest restricted excursions of the diaphragm and chest wall during tidal breathing. High *D*Lco/VA suggests increased pulmonary blood volume.

Unlike some investigators (11-16, 26), we found that nonsmoking, obese men had evidence of peripheral airway obstruction. Although obese men and women both had air trapping (elevated RV with increased RV to TLC ratio), only the obese men had maximum expiratory flow rates that were significantly lower than those of the nonobese controls. This finding indicates the presence of peripheral airways obstruction, particularly as the specific conductance was normal. This novel and potentially important finding was not noted in previous studies, because their subjects were mostly obese women.

Obesity is expected to increase maximal expiratory flow rates because of increased elastic recoil of the lung (29). Our failure to show such an increase and our finding that maximal expiratory flow rates were, in fact, reduced constitute strong evidence that obesity contributes to peripheral airway narrowing in nonsmoking men. Although obese women did not exhibit similar reduction in maximal expiratory flow rates as obese men, it does not necessarily exclude the possibility that such an effect exists but has not been shown in our limited population sample.

The mechanism or mechanisms underlying the decreased peripheral airway size seen in nonsmoking, morbidly obese men in our study are unknown. It is thought that pulmonary blood volume is increased in obese persons; such an increase might lead to congestion of bronchial vessels in the airway submucosa, thickening of the airway wall, and decrease in airway caliber (30). In addition, the altered lipid metabolism found in obesity might instigate and amplify these effects (10). Gonen and colleagues (31) showed that very-low-density lipoproteins trigger the release of histamine, a potent mediator of vascular permeability and smooth muscle contraction in the airway, from human basophils. If these are the underlying mechanisms, it would be implied that gender influences airway size, because we found similar airway dimensions in obese and nonobese women, but not in men. Whatever the mechanism or mechanisms, the decreased peripheral airway dimensions found in nonsmoking, morbidly obese men in the our study may have important implications for respiratory morbidity; obesity may predispose men to chronic airflow limitation or to rapid deterioration in airway function when exposed to other factors that contribute to airway narrowing, such as cigarette smoking

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and respiratory infections. Long-term, prospective follow-up of morbidly obese men is needed to test this hypothesis.

In conclusion, we found that morbid obesity is associated with significant pulmonary function abnormalities in nonsmoking men and women. Obese men had evidence of peripheral airways obstruction, as manifested by air trapping, increased airways resistance, and reduced maximum expiratory flow rates. Obese women also had evidence of air trapping and increased airways resistance, although their maximum expiratory flow rates were not significantly different from those measured in nonobese women. These findings suggest that morbid obesity might contribute, independently of smoking habits, to chronic airflow limitation in men.

Acknowledgments: The authors thank Drs. A. Angel and H.P. Higgins for their help in patient referral and the staff of St. Michael's pulmonary function laboratories and the Tri-Hospital Respiratory Service for their technical assistance.

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