

OBESITY

Airway Responsiveness Measured by Forced Oscillation Technique in Severely Obese Patients, before and after Bariatric Surgery

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Background. The influence of obesity on airway responsiveness remains controversial. **Objective.** This study was designed to investigate airway responsiveness, airway inflammation, and the influence of sleep apnea syndrome (SAS), in severely obese subjects, before and after bariatric surgery. **Methods.** A total of 120 non-asthmatic obese patients were referred consecutively for pre-bariatric surgery evaluation. Lung function, airway responsiveness to methacholine, exhaled nitric oxide measurement, and sleep studies were performed. Airway hyperresponsiveness (AHR) was defined as a 50% or greater increase in respiratory resistance measured using the forced oscillation technique in response to a methacholine dose ≤ 2000 μ g. Forced expiratory volume in 1 second (FEV₁) was measured after the last methacholine dose. Airway responsiveness was reevaluated after weight loss in patients with a pre-surgery AHR. **Results.** AHR was found in 16 patients. The percent FEV₁ decrease or percent respiratory resistance increase in response to methacholine was related to baseline expiratory airflow (forced expiratory flow at 50%) ($r = 0.26$, $p < .006$ and $r = 0.315$, $p = .0005$, respectively) but not to body mass index (BMI) or exhaled nitric oxide. Both airway responsiveness parameters were significantly related to forced expiratory flow at 25–75%/forced vital capacity, a measure of airway size relative to lung size ($r = 0.27$, $p < .005$ and $r = 0.25$, $p < .007$, respectively). Sleep apnea was not significantly associated with AHR or airway inflammation. About 11 patients with AHR were reevaluated 18 months to 2 years after surgery, with no change in AHR associated with weight loss. **Conclusion.** Airway responsiveness is not related to BMI or to SAS. AHR in severely obese patients might be related to distal airway obstruction or low relative airway size.

Keywords airway hyperresponsiveness, distal airway obstruction, exhaled nitric oxide measurement, low relative airway size, severe obesity

INTRODUCTION

The prevalence of both obesity and asthma has increased worldwide in recent years, and obesity has been implicated as a risk factor for asthma and as a predisposing factor for airway hyperresponsiveness (AHR) (1–3). Although several studies found associations between asthma symptoms and obesity, whether obesity exacerbates asthma or is linked to AHR remains unclear (1, 2, 4–6). Lung function studies in obese patients showed that higher body mass index (BMI) values were associated with smaller lung volumes and higher respiratory resistance (Rrs) that added to the breathing load, possibly contributing to produce respiratory symptoms (7). However, there is little evidence that obesity is associated with objective markers for asthma such as AHR or airway inflammation.

The objective of this study was to further investigate the association between morbid obesity and AHR in healthy, non-asthmatic patients scheduled for bariatric surgery, and to determine whether reductions in body

weight after bariatric surgery were associated with improvements in airway responsiveness. In addition, because asthma and sleep-disordered breathing share common risk factors such as obesity and airway inflammation (8), sleep studies and exhaled nitric oxide measurements were performed in all patients.

METHODS AND MATERIALS

Patient Selection

Inclusion criteria were morbid obesity and scheduled bariatric surgery. Exclusion criteria were history of asthma, airway obstruction due to chronic obstructive pulmonary disease and defined as a ratio of forced expiratory volume in 1 second (FEV₁) over forced vital capacity (FVC) lower than 70%, history of upper respiratory tract disorders, previous evaluation or treatment for sleep apnea syndrome (SAS), and BMI lower than 40 kg/m².

Overall 135 consecutive patients (114 females and 21 males) scheduled for bariatric surgery at the Henri Mondor Teaching Hospital, Créteil, France, prospectively underwent lung function testing for preoperative assessment. All these patients had morbid obesity defined as a BMI ≥ 40 kg/m² (9). We excluded 15 patients with a known history of asthma. None of the remaining patients had any of the other exclusion criteria. Therefore, 120

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patients (106 females and 14 males) were included in the study. In addition, pulmonary function, including methacholine challenge test, was reevaluated at distance of bariatric surgery in patients with a pre-surgery AHR.

All subjects were healthy, with no cardiac or major metabolic disorders. They had no persistent cough or other respiratory symptoms, nasal polyposis, acute nasosinusitis, allergic disease, gastroesophageal reflux, or diurnal or nocturnal symptoms suggesting SAS (e.g., daytime sleepiness or fatigue or breathing pauses during sleep).

Informed consent was obtained before study inclusion from all patients. The study was approved by local ethical review boards.

Lung Function Tests

Spirometry and lung volume measurements were performed. Flow-volume curves were obtained using a spirometer (SensorMedics Corporation, Yorba Linda, CA, USA). Three technically acceptable measurements were obtained for each test, according to international guidelines (10). The values were expressed as percentages of predicted values (10).

Forced Oscillation Technique. Respiratory impedance was determined using the standard forced oscillation technique (Oscilink, Datalink-MSR, Rungis, France) as described elsewhere (11, 12) and according to recommendations (13).

The patient was equipped with a mouthpiece and a nose clip and was comfortably seated with the head in the neutral position and the cheeks held firmly. A pseudorandom noise signal mixing integer frequencies between 4 and 32 Hz was generated by a loudspeaker and superimposed on the spontaneous breathing of the patient. Auto- and cross-spectra of mouth flow and pressure were averaged over a 16 seconds period to yield a mean estimate of impedance (Z_{rs}) and coherence function (γ^2) for each frequency component. A measurement period was considered acceptable if γ^2 was greater than 0.9 for more than 80% of the frequency components. The real component of Z_{rs} (R_{rs}), related to the resistive properties of the respiratory system, was subjected to linear regression analysis over the 4–16 Hz frequency range to obtain the intercept (R_0 , resistance extrapolated to 0 Hz). At least three acceptable 16 seconds measurement periods were averaged to yield the final value of these parameters. Specific respiratory resistance (sR_{rs}) (i.e., the product of resistance by functional residual capacity, FRC), which is the conventional way of taking into account the volume dependence of R_{rs} , was also determined.

Methacholine Challenge Test. All study patients underwent methacholine challenge testing performed using a nebulization dosimeter (Mediprom FDC88, Paris, France) that sequentially delivered four increasing doses of methacholine (100, 500, 1000, and 2000 μ g). The R_{rs} was measured using the forced oscillation technique at baseline, after inhalation of diluent, and after each inhalation of methacholine. R_{rs} measurements were

performed 2 minutes after each inhalation to ensure that the deep inhalations during methacholine challenge testing had no major effect on the measurement results. The provocation test was terminated when R_{rs} increased by 50% with any concentration or when the maximum methacholine dose was administered, whichever occurred first, as previously reported (13, 14). In addition, as AHR is commonly defined by provocative dose of methacholine equal to or less than 2000 μ g causing a 20% decrease of FEV_1 , flow-volume curves were obtained at baseline and after the last methacholine dose. After challenge testing, the patient was given an inhaled dose of beta-adrenoceptor agonist (two 100 μ g puffs), and R_{rs} and FEV_1 were measured 15 minutes later. If the FEV_1 and R_{rs} values were different from the baseline values, an additional beta-adrenoceptor agonist dose was given and measurements performed 15 minutes later. At the end of the test, all patients had normal R_{rs} values and $FEV_1 \geq 90\%$ of the baseline FEV_1 value.

Exhaled Nitric Oxide (NO). Fractional exhaled NO concentration was measured before basal spirometry and methacholine challenge testing. Maximum conducting airway flux of NO (J'_{awNO}) and alveolar NO concentration ($CalvNO$) were calculated using a chemiluminescent analyzer (ENDONO 8000, SERES, Aix en Provence, France) after obtaining several exhaled NO values at different expiratory flow rates, using the previously described linear approach (12). In each patient, values were obtained for at least four expiratory flow rates, in the 50–250 mL/s range. The criteria used for each exhaled NO measurement were those recommended in international guidelines (15). We used a validity criterion for this linear approach, as previously described (16).

Sleep Studies

Each patient underwent an overnight sleep study using previously described methods and equipment (11). Apnea was defined as cessation of airflow lasting 10 seconds or more and hypopnea as a 50% or greater reduction in oronasal airflow for at least 10 seconds. The apnea-hypopnea index (AHI) defined as the mean number of apneas and hypopneas per hour of sleep was calculated and used to quantify the severity of SAS. Severe SAS was defined as $AHI \geq 30$ per hour of sleep.

Statistical Analysis

All analyses were performed using a statistical software package (Statview 4; SAS Institute; Grenoble, France). Data were expressed as means $\pm$ SD. To compare patients with and without AHR, and patients with and without SAS, we used the unpaired *t*-test for continuous variables or the chi-square test for categorical variables. The chi-square test with Yates correction was used for tables with very small expected frequencies. Paired *t*-tests were used for comparisons before and after bariatric surgery.

The R_{rs} index was computed as the ratio of the difference between post-methacholine and post-diluent

values over the post-diluent value and was used to determine whether AHR was present. The FEV₁ index was defined as the ratio of the difference between post-methacholine and pre-methacholine values over the pre-methacholine value.

The methacholine dose–effect relationship was evaluated using analysis of variance (ANOVA) for repeated measures. When a significant difference was found, we compared individual means using the Scheffe test. Comparisons between groups were made using two-way ANOVA for repeated measures; when significant differences were found, individual means were compared using a modified *t*-test.

Correlations between variables were evaluated using least-square linear regression techniques.

For all comparisons, *p*-values less than .05 were considered significant.

RESULTS

Anthropometric, lung function, and sleep study data from the 120 study patients before surgery are shown in Table 1. The number of females was significantly greater than the number of males (106 vs. 14; chi-square, $p < 10^{-9}$). The BMI was not significantly different between women and men (44.6 ± 4.7 vs. 46.4 ± 5.1 , $p = .19$).

TABLE 1.—Anthropometric data, baseline lung function test results, and apnea–hypopnea index in the 120 study patients (106 females and 14 males).

	All patients (<i>n</i> = 120)
Age (years)	38.2 ± 11.1
BMI (kg/m ²)	44.8 ± 4.7
FEV ₁ (%)	96.2 ± 12.9
FVC (%)	96.1 ± 13.2
FEV ₁ /FVC (%)	85.9 ± 5.5
FEF _{25–75} (%)	95.2 ± 24.0
FEF ₅₀ (%)	98.5 ± 25.4
FEF ₂₅ (%)	81.8 ± 27.5
TLC (%)	92.3 ± 10.8
VC (%)	98.4 ± 13.3
FRC (%)	66.7 ± 14.9
RV (%)	83.1 ± 19.5
ERV (%)	45.5 ± 20.6
Rrs (cmH ₂ O.s/L)	5.1 ± 1.4
J'awNO (nL/min)	41.3 ± 31.6
CalvNO (ppb)	3.1 ± 2.6
AHI (n/h)	12.8 ± 12.7

Notes: BMI, body mass index; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; FEF_{25–75}, forced mid-expiratory flow; FEF₅₀ and FEF₂₅, forced expiratory flows at 50% and 25% of vital capacity, respectively; TLC, total lung capacity; VC, vital capacity; FRC, functional residual capacity; RV, residual volume; ERV, expiratory reserve volume; Rrs, respiratory resistance (reference value: 2.5 cmH₂O.s/L) (7, 13); J'awNO, maximum conducting airway flux of NO (reference value: 37 ± 3 nL/mn) (12, 16, 17); CalvNO, alveolar NO concentration (reference value: 5.1 ± 0.3 ppb) (12, 16, 17); AHI, apnea–hypopnea index (reference value: 10 n/h) (11, 18). The data are means ± SD and are expressed as the percentages of predicted values for FEV₁, FEV₁/VC, FEF_{25–75}, FEF₅₀, FEF₂₅, TLC, VC, FRC, RV, and ERV (10).

Lung Function before Bariatric Surgery

Lung Function and Flows. Total lung capacity and vital capacity, expressed as the percentage of predicted values, were near normal. We found marked decreases in FRC and expiratory reserve volume (ERV). ERV (expressed as percentage of predicted) showed a significant negative correlation with BMI ($r = 0.275$, $p = .003$). Neither the FRC decrease nor the ERV decrease was significantly different between males and females ($p = .72$, $p = .59$).

FEV₁ and expiratory flow rates at 50%, 25%, and 25–75% of vital capacity (FEF₅₀, FEF₂₅, and FEF_{25–75}, respectively), expressed as the percentage of predicted, were near normal in all patients.

Oscillatory Parameters. Rrs was not significantly different between males and females ($p = .13$). Rrs increased significantly with BMI ($r = 0.3$, $p = .003$). sRrs was not dependent on the severity of obesity.

We found significant inverse correlations between Rrs and FEV₁ ($r = 0.26$, $p = .004$), FEF_{25–75} ($r = 0.34$, $p = .0002$), FEF₅₀ ($r = 0.27$, $p = .003$), and FEF₂₅ ($r = 0.28$, $p = .002$) expressed as the percentage of predicted. Significant inverse correlations were also found between sRrs and FEF_{25–75} ($r = 0.34$, $p = <.0002$), FEF₅₀ ($r = 0.31$, $p = .0005$), and FEF₂₅ ($r = 0.28$, $p = .002$), expressed as the percentage of predicted.

Methacholine Challenge Test. Patients showed significant dose-related increases in Rrs index (ANOVA, $p < .0001$), with significant changes after 500, 1000, and 2000 µg as compared to the 100 µg value ($p = .02$, $p < .0001$, respectively). No significant difference was noted between baseline Rrs and post-diluent Rrs.

AHR was found in 16 (13.3%) of the 120 patients, with significant dose-related increases in Rrs index (ANOVA, $p < .0001$) and a $70.9 \pm 13.0\%$ Rrs index increase at the last dose (Figure 1). All 16 patients were among the 106 women. The other 104 patients showed significant dose-related increases in Rrs index (ANOVA, $p < .0001$) without AHR; the Rrs index increase at 2000 µg was $14.5 \pm 12.0\%$.

Patients with AHR had lower, despite nonsignificantly different, FEF₂₅ and FEF₅₀ values compared to the patients without AHR (Table 2). This finding may be related to the large SD. FEF₅₀ and FEF₂₅ correlated significantly with AHR expressed as the Rrs index ($r = 0.26$, $p < .006$ and $r = 0.2$, $p < .05$, respectively) or as the FEV₁ index ($r = 0.315$, $p = .0005$ and $r = 0.21$, $p < .03$, respectively). FEF_{25–75}/FVC was significantly lower in patients with than without AHR ($p < .02$). This ratio was significantly related to the degree of methacholine airway responsiveness measured as the percentage Rrs increase ($r = 0.27$, $p < .005$) or as the percentage FEV₁ decrease ($r = 0.25$, $p < .007$).

BMI was not significantly related to the FEV₁ index or Rrs index. Neither exhaled NO nor alveolar NO concentration differed significantly between patients with and without AHR (40.8 ± 32.6 vs. 44.7 ± 24.1 and 3.1 ± 2.7 vs. 2.8 ± 1.6 , respectively).

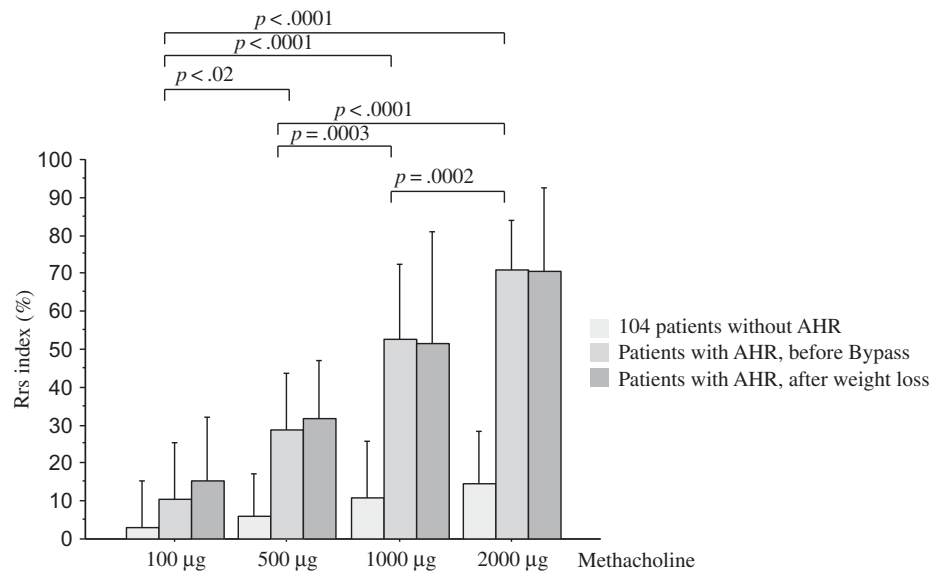


FIGURE 1.—Respiratory resistance (Rrs) index in response to inhalation of increasing methacholine doses in patients with severe obesity, before and after bariatric surgery. Rrs index was computed as the ratio of the difference between post-bronchoconstrictor and pre-diluent values over the pre-diluent value. ANOVA for repeated measures demonstrated significant dose-related increases in Rrs index ($p < .0001$) in 104 patients without AHR, with significant increases after 500, 1000, and 2000 μg as compared to the first dose ($p < .02$, $p < .0001$), significant increases after 1000 and 2000 μg as compared to 500 μg ($p = .0002$, $p < .0001$), and significant increase after 2000 μg as compared to 1000 μg ($p = .002$). ANOVA for repeated measures demonstrated significant dose-related increases in Rrs index ($p < .0001$) in 16 patients with AHR with significant increases between doses. No significant difference in airway responsiveness was reported before and after weight loss, regardless of the dose.

Lung Function after Bariatric Surgery

Among the 16 patients with AHR, 11 were reevaluated 18 months to 2 years after surgery. Three patients

TABLE 2.—Anthropometric data, lung function results, and apnea-hypopnea index in patients with and without airway hyperresponsiveness.

	$\Delta\text{Rrs} < 50\%$ (n = 104)	$\Delta\text{Rrs} \geq 50\%$ (n = 16)	P-values
Sex (M/F)	14/90	0/16	NS
Age (years)	39.2 ± 11.2	33.6 ± 8.9	.06
Smoking history, pack year	9 ± 3	8 ± 3	.68
BMI (kg/m^2)	45.1 ± 4.8	43.2 ± 4.7	.15
FEV ₁ (%)	96.6 ± 12.8	94.3 ± 13.9	.52
FVC (%)	96.3 ± 13.1	97.2 ± 10.9	.65
FEV ₁ /FVC (%)	86.2 ± 5.4	84.1 ± 5.8	.16
FEF ₂₅₋₇₅ (%)	96.7 ± 23.7	85.5 ± 25.6	.09
FEF ₅₀ (%)	100.1 ± 25.2	88.2 ± 25.3	.09
FEF ₂₅ (%)	82.7 ± 28.3	75.3 ± 24.6	.32
FEF ₂₅₋₇₅ /FVC	1.09 ± 0.29	0.89 ± 0.25	<.02
TLC (%)	91.9 ± 11.0	95.1 ± 9.8	.28
VC (%)	98.3 ± 13.7	100.1 ± 10.4	.62
FRC (%)	66.7 ± 14.7	68.4 ± 16.7	.67
RV (%)	82.9 ± 19.7	84.7 ± 20.5	.75
ERV (%)	45.2 ± 20.8	49.6 ± 19.2	.44
Rrs ($\text{cmH}_2\text{O}\cdot\text{s}/\text{L}$)	5.0 ± 1.5	5.3 ± 0.9	.49
J'awNO (nL/min)	40.8 ± 32.6	44.7 ± 24.1	.70
CalvNO (ppb)	3.1 ± 2.7	2.8 ± 1.6	.72
AHI (n/h)	13.6 ± 12.8	7.3 ± 7.2	.20

Notes: BMI, body mass index; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; FEF₂₅₋₇₅, forced mid-expiratory flow; FEF₅₀ and FEF₂₅, forced expiratory flows at 50% and 25% of vital capacity, respectively; FEF₂₅₋₇₅/FVC, ratio between FEF₂₅₋₇₅ and FVC; TLC, total lung capacity; VC, vital capacity; FRC, functional residual capacity; RV, residual volume; ERV, expiratory reserve volume; Rrs, respiratory resistance; J'awNO, maximum conducting airway flux of NO; CalvNO, alveolar NO concentration; AHI, apnea-hypopnea index. The data are means $\pm$ SD and are expressed as the percentages of predicted values for FEV₁, FEV₁/FVC, FEF₂₅₋₇₅, FEF₅₀, FEF₂₅, TLC, VC, FRC, RV, and ERV (10).

withdrew from the study, moving to another area, and two patients renounced to surgery. The mean BMI was 27.4 ± 6.1 , significantly lower than the pre-surgery value ($p < .0001$).

Lung Function, Flows, and Oscillatory Parameters. Lung volumes increased after weight loss and, as expected, we found significant increases in FRC and ERV, volumes being near normal in all patients when expressed as the percentage of predicted values (97.0 ± 20.6 and 89.7 ± 26.9 , $p = .03$ and $p = .0035$, respectively). On the contrary, no significant changes in expiratory flows were observed, and the FEF₂₅₋₇₅/FVC values were similar (0.89 ± 0.25 vs. 0.84 ± 0.23). The Rrs was significantly lower after weight loss (5.3 ± 0.9 vs. 4.1 ± 0.9 , $p = .045$).

Methacholine Challenge Test. All 11 patients with AHR before surgery showed a similar AHR after weight loss, with significant dose-related increases in Rrs index (ANOVA, $p < .0001$), significant changes between doses, and a $70.4 \pm 22.3\%$ Rrs index increase after the last dose. No significant difference was noted between pre-surgery and post-surgery Rrs indexes (Figure 1).

Sleep Variables

AHI increased significantly with BMI ($p < .02$, $r = 0.251$), and was significantly higher in males as compared to females (34.9 ± 34.7 vs. 9.9 ± 9.7 , $p < .0001$). Males were significantly more likely than females to have SAS defined as AHI ≥ 10 (78.6% vs. 35.8%, chi-squared test, $p = .0022$), and severe SAS, defined as AHI ≥ 30 , was found in 12 patients, 6 men (42.9%) and 6 women (5.7%). Patients with SAS were significantly older than patients without SAS (43.1 ± 10.6 vs. 35.0 ± 10.4 , $p < .0001$).

No significant relationship was found between AHI and presence of AHR ($r = 0.064$, $p = .48$). Neither exhaled NO nor alveolar NO concentration was significantly different between patients with and without SAS.

DISCUSSION

The prevalence of asthma varies across countries. In France, the 2006 ESPS Survey (19) indicated a lifetime prevalence of asthma of 10.2%. Similarly, 11.1% (15/135) of the obese patients referred to us for evaluation before bariatric surgery had known asthma. Among the 120 patients without previously diagnosed asthma, 13.3% had AHR defined as a 50% or greater Rrs increase compared to the post-diluent value. The prevalence of AHR in our severely obese patients was quite similar from that in the general population (20). Nonspecific AHR is commonly defined as a 20% FEV₁ decrease versus baseline in response to a methacholine dose no greater than 2000 μ g. Forced expiratory maneuvers require active cooperation from the patient and may modify the bronchomotor tone, whereas the forced oscillation technique has neither of these disadvantages. In keeping with earlier studies (14, 21), a 50% increase in Rrs index was the adequate cut-off value corresponding to a 20% decrease in FEV₁ in terms of sensitivity.

Among previous studies investigating whether AHR was increased by obesity, some found a positive association between AHR and higher BMI values (1, 2), whereas others found no association (4–6, 22). As our findings do not provide any evidence for a relation of AHR to obesity, we speculated that methacholine hyperresponsiveness could be attributed to differences in distal airflows or in airway size. According to this hypothesis, distal airflows, despite not significantly different, were lower in patients with AHR compared to the patients without AHR (Table 2), and this difference was not ascribable to differences in BMI or smoking history. The presence of AHR showed significant inverse relationships with FEF₂₅ and FEF₅₀, expressed as the percent of predicted. Furthermore, we found that FEF_{25–75}/FVC, a measure of airway size relative to lung size, was significantly lower in patients with AHR than in patients without AHR (Table 2), and was significantly associated with the degree of methacholine airway responsiveness as assessed by the Rrs index or by the FEV₁ index. Among the 16 patients with AHR, those with the lowest FEF_{25–75}/FVC values had the greatest degrees of airway reactivity ($p = .0043$, $r = 0.691$). At last, no significant change in FEF_{25–75}/FVC was reported after weight loss. In several studies FEF_{25–75}/FVC showed a significant inverse relationship with the presence of AHR to methacholine (23–25) in children and adults. However, this relationship had not been studied previously in obese patients before and after weight loss.

Other factors, such as airway inflammation, may contribute to AHR in obese patients. Thus, studies in

obese patients have found elevated circulating levels of proinflammatory cytokines, which may predispose to AHR (26). However, exhaled NO was not significantly higher in our patients with AHR when compared to those without AHR. Neither did we find any association between airway inflammation, as assessed by J'awNO, and BMI, in keeping with earlier data (27).

All patients with AHR in our study were women, as previously reported (28, 29). However, the association between AHR and sex was not found to be significant, may be due to the small number of patients with AHR ($n = 16$). In addition, no significant differences were observed in the exhaled NO data between males and females. J'awNO was higher in males than in females (56.2 ± 33.4 vs. 39.1 ± 30.0 , $p = .08$), in accordance with the gender-related differences in adult exhaled NO levels reported by Taylor et al. (30).

Obesity is a major risk factor for SAS. As expected, we found a significant relationship between AHI and BMI. The American Academy of Sleep Medicine defines obstructive SAS as AHI ≥ 5 with excessive daytime sleepiness. As our patients did not have daytime sleepiness (Epworth Sleepiness Scale lower than 11), we used AHI ≥ 10 to define SAS and AHI ≥ 30 to define severe SAS, as previously described (11). Using an AHI cut-off of 10, we found SAS in 49 patients, in accordance with a previous report of SAS in approximately 40% of obese individuals (31). As expected, SAS was significantly more common in men than in women, and age showed a significant positive relationship with AHI. Airway methacholine responsiveness was not significantly higher in patients with SAS. To further analyze potential links between obesity, AHR, and sleep apnea, we looked for an increase in exhaled NO in patients with SAS, as previously reported (8, 32). We found no relationship between J'awNO and AHI, and neither did J'awNO differ between patients with and without SAS.

In conclusion, we found no evidence that higher BMI values were associated with greater airway responsiveness to methacholine or with higher exhaled NO taken as a marker for airway inflammation. Neither did we find any association of SAS with AHR or airway inflammation. Our results suggest that the AHR observed in some severely obese patients may be ascribable to distal airway narrowing, perhaps related in part to distal airway obstruction and in part to a decrease in relative airway size, as assessed based on FEF_{25–75}/FVC, which has been shown to be a significant determinant of methacholine airway responsiveness.

DECLARATION OF INTEREST

The authors have reported that no significant conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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