Obstructive Sleep Apnea Syndrome in Morbid Obesity*

Effects of Intragastric Balloon

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Study objectives: In obese patients, obstructive sleep apnea syndrome (OSAS) is attributed to a reduction in pharyngeal cross-sectional area due to peripharyngeal fat deposition. The effect of weight loss on the size of the upper airways of obese subjects is still unknown. We analyzed the pharyngeal cross-sectional area before and after weight loss in morbidly obese patients with OSAS.

Design, setting, and subjects: A group of 17 middle-aged, morbidly obese men was evaluated by anthropometry and cardiorespiratory sleep studies before and after weight loss obtained by insertion of an intragastric balloon. The pharyngeal cross-sectional area was measured by acoustic pharyngometry.

Results: The mean (± SD) body mass index was 55.8 ± 9.9 kg/m² at baseline and 48.6 ± 11.2 kg/m² at the time of balloon removal (6 months after insertion) [p < 0.001]. At baseline, patients had visceral obesity, large necks, and severe OSAS. Weight loss was associated with a significant mean reduction of waist circumference (156.4 ± 17.6 vs 136.7 ± 18.4 cm, respectively; p < 0.001), sagittal abdominal diameter (37.8 ± 3.0 vs 32.3 ± 4.0 cm, respectively; p < 0.001), and neck circumference (51.1 ± 3.7 vs 47.9 ± 4.3 cm, respectively; p < 0.001). Moreover, weight loss induced a nearly complete resolution of OSAS (apnea-hypopnea index, 52.1 ± 14.9 vs 14.0 ± 12.4 events/h, respectively; p < 0.001). At baseline, obese patients had significantly lower pharyngeal cross-sectional areas compared to a group of 20 nonobese male control subjects, both in the upright and supine position, at different levels of the pharynx. In obese patients, the weight loss induced by the positioning of the intragastric balloon was associated with an increase in the size of the upper airway passage. After weight loss, both the mean pharyngeal cross-sectional area and the area at glottis level were still lower in obese subjects than in nonobese subjects; however, the pharyngeal cross-sectional area at the oropharyngeal junction was similar in the two groups.

Conclusions: Morbidly obese men with OSAS have a reduced pharyngeal cross-sectional area. A weight reduction of about 15% of baseline body weight may substantially increase the pharyngeal cross-sectional area and substantially improve the severity of OSAS in morbidly obese subjects with sleep apnea.

Key words: obesity; obstructive sleep apnea syndrome; weight loss

Abbreviations: AHI = apnea-hypopnea index; BMI = body mass index; ESS = Epworth sleepiness scale; NMR = nuclear magnetic resonance; OSAS = obstructive sleep apnea syndrome; SpO₂ = pulse oximetric saturation

Obesity is the most important reversible risk factor for obstructive sleep apnea syndrome (OSAS),¹ with an estimated 40% prevalence of OSAS among patients with morbid obesity.² Visceral fat accumulation³ and large neck circumference⁴ are predictive risk factors for OSAS in obese patients. The high prevalence of OSAS among obese patients has been attributed to a mass loading of the upper airway by adipose tissue.⁵ In fact, obese patients with OSAS have been shown to have increased fat deposition adjacent to the upper airway⁶,⁷ and reduced pharyngeal cross-sectional area⁸ when compared to control subjects.

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In morbidly obese patients who have been treated with bariatric surgery, weight loss was associated with an improvement in daytime symptoms of OSAS and a reduction of apneic episodes during sleep. However, the effect of weight loss on the upper airway size of obese subjects is still largely unknown. In this study, we analyzed upper airway size before and after weight loss in a group of morbidly obese men with OSAS.

**Materials and Methods**

**Experimental Design**

A total of 18 middle-aged (age range, 26 to 62 years), non-smoking, morbidly obese men with documented OSAS were recruited into the study. Patients were treated with the temporary insertion of an intragastric balloon in preparation for later laparoscopic adjustable gastric-banding surgery. According to established criteria, patients with a body mass index (BMI) of > 40 kg/m² are eligible for surgery. Prior to laparoscopic gastric-banding surgery in patients with a BMI > 50 kg/m² (ie, severe visceral obesity) or extremely high anesthesiologic risk, an intragastric balloon was used temporarily to achieve sufficient weight loss that was able to reduce the anesthesiologic risk and the risk of conversion to open surgery. All patients gave their written informed consent to the experimental and clinical procedures, and were evaluated just before the placement of the intragastric balloon and immediately after its removal. None of the patients had shown weight changes of > 3 kg during the 3 months before the baseline evaluation. Patients were evaluated with anthropometry, spirometry, pulse oximetry, cardiorespiratory sleep study, and acoustic pharyngometry.

**Intragastric Balloon**

An intragastric balloon system (BioEnterics Intragastric Balloon; INAMED Health; Santa Barbara, CA) was used. The intragastric balloon system that was used is an insufflatable smooth elastic silicone balloon that can be filled with 500 to 700 mL saline solution. Both the placement and the removal of the device were endoscopically performed under anesthesia. After placement of the intragastric balloon system, patients were instructed to follow a modified liquid diet for 2 weeks. Thereafter, they graduated to a solid diet, with a list of rules specifically developed for patients using this system. Both diets were designed to provide 24-h energy intake of 2.5 MJ (40% proteins, 25% fats, and 35% carbohydrates). The removal of the balloon was performed 6 months after its placement.

**Anthropometry**

All anthropometric measurements were performed with the subjects wearing light clothes without shoes. Waist circumference was measured according to an established reference method. Sagittal abdominal diameter, a further index of visceral fat accumulation, was determined at the highest point of the abdominal surface with the subject in the supine position and during normal breathing by means of a specifically made instrument. Neck circumference, which is a prognostic index of OSAS, was determined at the level of the cricothyroid membrane.

**Pulmonary Function Evaluation**

Pulmonary function tests were performed by a Fleisch thermostatic pneumotachograph connected to a microcomputer system (Biomedin; Padova, Italy). All tests were performed according to the standard criteria. FVC and FEV₁ were measured, and the FEV₁/FVC ratio was calculated. Reference values are those of Viljanen et al. Pulse oximetric saturation (SpO₂) was measured (model 8500A pulse oximeter; Nonin; Plymouth, MN) with the patient in both the upright and supine positions.

**Sleep Study**

All patients underwent a cardiorespiratory sleep study, which included assessment of the following signals: air flow (with mouth and nose thermistors); thoracic and abdominal movements (with strain gauges); snoring (with a microphone); pulse rate; and oximetry (with a finger probe) [Poly-Mesam device; MAP; Martinsried, Germany]. Abnormal respiratory events were defined as follows: obstructive apnea, cessation of airflow for a minimum of 10 s with continued thoracoabdominal wall movement; central apnea, cessation of airflow and thoracoabdominal wall movements for a minimum of 10 s; mixed apnea, cessation of airflow and thoracoabdominal wall movements for at least the duration of one respiratory cycle; followed by a return of respiratory efforts but the continued absence of airflow, with the duration of the event being a minimum of 10 s; and hypopnea, a minimum 50% reduction in the amplitude of the airflow signal or both thoracic and abdominal efforts for at least 10 s. We did not include desaturation as a criterion for scoring apneas or hypopneas. The number of episodes of apnea plus hypopnea per hour of sleep was referred as the apnea-hypopnea index (AHI).

**Daytime Symptoms of OSAS**

The Epworth sleepiness scale (ESS) was used to assess all patients and was implemented by trained interviewers. The ESS is an eight-item questionnaire that is designed to evaluate the patient’s likelihood of falling asleep in common situations. Scores range from 0 (least sleepy) to 24 (most sleepy).

**Acoustic Pharyngometry**

Upper airway size was evaluated by acoustic pharyngometry (EccoVision Acoustic Pharyngometer; SensorMedics; Pembroke, MA). The pharyngometer uses acoustic technology to evaluate the cross-sectional area of the upper airway, from the oral cavity to the hypopharynx. The technique is based on the analysis of sound waves that are launched from a loudspeaker and travel along the wave tube into the subject’s airways, where they are reflected. The incident waves and the reflected waves are recorded by a microphone located at the opening of the mouth. From the difference in the two signals, changes in the area of the airways are inferred as a function of distance from the recording microphone. Therefore, a graphic representation of the variations of pharyngeal cross-sectional area (in square centimeters) through the length of the pharynx (in centimeters) was obtained. Along this curve, different pharyngeal anatomic structures can be identified, and the cross-sectional area of the pharynx can be measured at several anatomic levels. According to the method described by Martin et al., the pharyngeal cross-sectional area at the level of the oropharyngeal junction, the pharyngeal cross-sectional area at the level of the glottis, and the mean pharyngeal cross-sectional area in the tract between the oropharyngeal junction and the glottis were measured in this study. The mean of four consecutive measurements was used. Pharyngeal cross-sectional areas were measured during quiet tidal breathing through the oral cavity, with the patient in both the upright and supine positions. Data were obtained and analyzed by a single trained investigator.
**Statistical Analysis**

All data were expressed as the mean ± SD. The Wilcoxon rank sum test was used to compare values obtained before and after weight loss in obese patients. Differences between obese patients and control subjects were analyzed by the Mann-Whitney U test. The relationships among numeric variables were studied by univariate and multivariate regression analyses. Statistical analysis was performed with a statistical software package (SPSS, version 10.0; SPSS; Chicago, IL).

**RESULTS**

The intragastric balloon was successfully positioned in all patients. However, in one patient the balloon was removed a few days after placement because of gastric intolerance. Therefore, a total of 17 patients successfully completed the 6-month treatment protocol with the intragastric balloon. No significant complications were observed.

The clinical characteristics of the 17 morbidly obese patients before insertion of the intragastric balloon and after its removal are reported in Table 1. At baseline, all subjects were morbidly obese patients (BMI range, 46.0 to 82.0 kg/m²) with a substantial amount of visceral fat accumulation, as evidenced by the high values of the waist circumference and the sagittal abdominal diameter. Pulmonary function testing revealed restrictive ventilatory impairment with further significant reductions in oxygen saturation in the clinostatic position (p < 0.001). The AHI was > 20 events/h in all patients, and > 50 events/h in 13 of 17 patients (76.5%).

The intragastric balloon produced a highly significant mean weight loss of 24.1 ± 14.5 kg (range, 3.5 to 50.0 kg), corresponding to a mean reduction of 14.5 ± 8.9% (range, 2.4 to 29.7%) from baseline body weight. However, the BMI of the patients still remained in the morbid obesity category after the procedure (Table 1). Weight loss was accompanied by a significant reduction of all the anthropometric indexes, including neck circumference. Pulmonary function improved significantly, as did both standing and lying Po2. Finally, weight loss was associated with clinically significant improvements of both sleep-disordered breathing and the diurnal symptoms of OSAS (Table 1). The relationships among anthropometric changes and improvements in pulmonary function, Po2, AHI, and ESS scores are reported in Table 2.

The improvement in the severity of OSAS was also analyzed categorically, by evaluating how many patients were treated successfully by the intragastric balloon. We defined success as a reduction in AHI of at least 50% with a reduction of the AHI to < 20 events/h.22 According to these criteria, 10 of 17 patients (58.8%) achieved success. The mean percentage weight loss after treatment with the intragastric balloon was higher in the responders than in the nonresponders (19.7 ± 7.6 vs 6.9 ± 3.3%, respectively; p < 0.001). The lowest percentage weight loss that was associated with success was 8.8%, and the highest percentage weight loss associated with failure was 12.2%.

Pharyngeal cross-sectional areas evaluated by the acoustic reflection technique in the 17 morbidly obese patients before insertion of the intragastric balloon and after its removal are reported in Figure 1. The pharyngeal measurements of a group of 20 middle-aged nonobese (BMI range, 19.7 to 29.6 kg/m²) men who were previously studied at our institution were also reported for comparison. At baseline, there were significant

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<th>Table 1—Clinical Characteristics of 17 Morbidly Obese Patients Before and After Treatment With the Intragastric Balloon*</th>
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<td>Obstructive apneas, No.</td>
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<td>Hypopnea, No.</td>
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<td>AHI, events/h</td>
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*Values given as mean ± SD.  
†p < 0.001 (Wilcoxon rank sum test).  
‡p < 0.01 (Wilcoxon rank sum test).

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<th>Table 2—Simple Linear Correlation Coefficients Between the Changes in Anthropometric Parameters After Intragastric Balloon Insertion and the Changes of Pulmonary Function, Po2, AHI, and ESS Score*</th>
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<td><strong>Variables</strong></td>
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<td>ΔESS score</td>
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*Values given as r values. SAD = sagittal abdominal diameter.  
†p < 0.05.  
‡p < 0.01.
differences between nonobese and obese subjects in mean BMI (24.9 ± 2.8 vs 55.8 ± 9.9 kg/m², respectively; p < 0.001), waist circumference (89.9 ± 6.8 vs 156.4 ± 17.66 cm, respectively; p < 0.001), sagittal abdominal diameter (21.9 ± 1.9 vs 37.8 ± 3.0 cm, respectively; p < 0.001) and neck circumference (39.3 ± 2.4 vs 51.1 ± 3.7 cm, respectively; p < 0.001). Both in the upright and supine position, and along all of the pharynx, obese patients had significantly smaller pharyngeal cross-sectional areas than nonobese subjects (Fig 1). Both in nonobese subjects and in morbidly obese patients, lying in the supine position produced a significant mean reduction of the pharyngeal cross-sectional area at the level of the oropharyngeal junction (nonobese subjects, 1.82 ± 0.60 vs 1.43 ± 0.42 cm², respectively [p < 0.01]; morbidly obese patients, 1.42 ± 0.32 vs 1.20 ± 0.31 cm², respectively [p < 0.01]), and a significant mean reduction of the mean pharyngeal cross-sectional area (nonobese subjects, 2.65 ± 0.55 vs 2.38 ± 0.39 cm², respectively [p < 0.05]; morbidly obese patients, 2.05 ± 0.44 vs 1.70 ± 0.18 cm², respectively [p < 0.01]). The pharyngeal area at the level of the glottis was not significantly affected by supine position (nonobese subjects, 1.90 ± 0.59 vs 2.02 ± 0.52 cm², respectively; morbidly obese patients, 1.51 ± 0.49 vs 1.54 ± 0.23 cm², respectively). The percentage reduction in the mean pharyngeal area produced by lying in the supine position was similar in nonobese and obese subjects (6.9 ± 22.9% vs 14.8 ± 15.6%, respectively). In nonobese subjects, the mean pharyngeal cross-sectional area measured with the subject in the upright position was negatively related to BMI (r = −0.49, p < 0.05), sagittal abdominal diameter (r = −0.45, p < 0.05), and neck circumference (r = −0.66, p < 0.01). When these three variables were entered as independent variables in a multiple regression model, only sagittal abdominal diameter retained an independent relationship with upright mean pharyngeal cross-sectional area. No significant relationships between pharyngeal size and anthropometry were found in obese patients.

In morbidly obese patients, the weight loss produced by insertion of the intragastric balloon was associated with an increase in size of the pharyngeal cross-sectional area (Fig 1). Both orthostatic and clinostatic cross-sectional areas at the level of the oropharyngeal junction and the orostatic mean pharyngeal cross-sectional area significantly increased after weight loss. After weight loss, morbidly obese patients still had significantly lower values than nonobese subjects for the mean size of pharyngeal cross-sectional area (orthostatic cross-sectional area, 2.19 ± 0.37 vs 2.65 ± 0.55 cm², respectively [p < 0.01]; clinostatic cross-sectional area, 1.78 ± 0.32 vs 2.38 ± 0.39 cm², respectively [p < 0.001]).
and for the size of the pharyngeal cross-sectional area at the glottis level (orthostatic cross-sectional area, 1.63 ± 0.39 vs 1.99 ± 0.59 cm², respectively \[ p < 0.05 \]; clinostatic cross-sectional area, 1.62 ± 0.22 vs 2.02 ± 0.52 cm², respectively \[ p < 0.01 \]). However, no significant differences were found in the pharyngeal cross-sectional area at the oropharyngeal junction between the obese patients after weight loss and the nonobese control subjects (orthostatic cross-sectional area, 1.71 ± 0.61 vs 1.82 ± 0.60 cm², respectively; clinostatic cross-sectional area, 1.34 ± 0.43 vs 1.43 ± 0.42 cm², respectively). The increase in the cross-sectional area of the pharynx at the oropharyngeal junction level in the upright position was significantly related to the level of weight loss \( r = 0.547; p < 0.05 \) and to the reduction of waist circumference \( r = 0.473; p < 0.05 \), sagittal abdominal diameter \( r = 0.664; p < 0.01 \), and neck circumference \( r = 0.506; p < 0.05 \). However, the reduction of sagittal abdominal diameter was found to be the only variable that was significantly related to an increase in the upright pharyngeal cross-sectional area at the oropharyngeal junction in multivariate regression analysis.

**Discussion**

In this study, we evaluated the effects of relatively moderate weight loss on the pharyngeal dimensions of a well-selected group of middle-aged men with morbid visceral obesity and severe OSAS. The main finding of the study was that the pharyngeal cross-sectional area of these subjects, which was severely reduced at baseline, increased after weight loss. This improvement of pharyngeal patency was associated with a significant reduction of both the number of apneic episodes during sleep and the daytime symptoms of OSAS.

The main limitations of our study were the uncontrolled case-control design and the use of only a cardiorespiratory sleep study instead of a complete polysomnographic recording. Moreover, in order to repeatedly measure the pharyngeal area noninvasively, we used an acoustic-reflection technique. Ultrasound pharyngometry was first described in the 1980s,\(^{19,20}\) and it was subsequently applied to the study of upper airways in patients with OSAS.\(^{21,23,24}\) Normal reference values for the acoustic pharyngeal dimensions have been reported in both men and women.\(^{25}\) The acoustic reflection technique has good reproducibility,\(^{25}\) and we tried to further improve it by using a single well-trained examiner and repeating the measurements four times in each subject. In our hands, intrasubject variability was < 5%. As a control group, we used an age-matched group of men of normal weight. While it would be interesting to compare our patients with middle-aged men who had similar levels of morbid obesity and visceral fat accumulation but did not have OSAS, we suspect it would be impossible to recruit a sufficient number of patients with such clinical characteristics.

Decreased pharyngeal patency was considered to be the most important pathogenetic mechanism leading to OSAS in obese patients. Our findings confirmed the small pharyngeal cross-sectional areas previously described\(^{26,27}\) by CT scan in obese patients with OSAS. The reduction of pharyngeal size in obese patients with OSAS has been attributed to a mass loading effect that is produced by fat deposited around the upper airways. By using nuclear magnetic resonance (NMR), Horner et al\(^{6}\) demonstrated that patients with OSAS had a larger accumulation of adipose tissue adjacent to the pharynx than did control subjects. Peripharyngeal fat pads were mainly located close to the posterolateral wall of the palatopharynx, which is a known site of dynamic occlusion of the upper airways during sleep.\(^{6}\) Finally, the size of the NMR-determined pharyngeal cross-sectional area was found to be inversely related to the number of apneic episodes during sleep,\(^{5}\) and neck circumference was an established risk factor for OSAS.\(^{4}\)

Whatever the mechanism of pharyngeal narrowing in obese patients with OSAS, our finding of simultaneous improvement of the size of pharyngeal cross-sectional areas and AHI with weight loss further supports the pathogenetic role of a reduced upper airway size in the determination of OSAS in patients with visceral obesity. Shelton et al\(^{5}\) demonstrated a simultaneous reduction in AHI and NMR-determined peripharyngeal adipose tissue accumulation in two obese patients who were losing weight. In our study, the improvement in the size of pharyngeal cross-sectional areas observed with weight loss was significantly related to the reduction of neck circumference, further supporting the role played by fat deposition in the neck. On the other hand, we also found a relationship between the changes in upper airway dimensions and the reduction of the sagittal abdominal diameter, which is our best index of abdominal visceral fat accumulation.\(^{13}\) It is probable that intraabdominal fat accumulation and fat deposition around the pharynx (two different faces of visceral obesity) coexist in our patients. In a previous study with CT scanning, we demonstrated a close correlation between the visceral adipose tissue area at the abdominal and thoracic levels in both men and women.\(^{28}\) A significant correlation between the size of visceral adipose tissue areas and cephalometric pharyngeal dimensions has been found by Shinohara et al\(^{4}\) in obese men and women.

It is noteworthy that in our study a nearly complete resolution of OSAS was observed after only a moderate reduction of body weight, and despite the fact that patients still remained morbidly obese. A good short-term response of OSAS to moderate weight loss has
been previously reported.⁸ We would suggest that such a rapid response could be ascribed to improved patency of the upper airways, and to the simultaneous mobilization of fat at the visceral and neck levels. In a previous study, using total-body multislice NMR, we demonstrated a preferential mobilization of abdominal visceral fat with respect to total and regional subcutaneous fat in the first phase of weight loss.⁹ Therefore, it is possible that the improvement of OSAS observed in our study may be due to the better responsiveness of visceral fat than of subcutaneous fat to caloric restriction. However, such an hypothesis needs to be proven directly.

In conclusion, we have demonstrated that moderate weight loss was able to produce a short-term improvement in OSAS in morbidly obese patients, most likely through a sizable modification of upper airway size and patency. As is well-known by anesthesiologists, morbidly obese patients with OSAS present a formidable challenge throughout the perioperative period. Life-threatening problems can arise with respect to tracheal intubation, tracheal extubation, and the provision of satisfactory postoperative analgesia.³⁰ Our findings therefore seem to support the importance of moderate weight loss prior to bariatric surgery in patients with morbid visceral obesity.

References