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# Is mandatory screening for obstructive sleep apnea with polysomnography in all severely obese patients indicated?

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## Abstract

*Purpose* The study aims to assess the risk factors for the presence and severity of obstructive sleep apnea (OSA) among severely obese patients evaluated for bariatric surgery.

Patients and methods Polysomnography recordings were performed in consecutive patients undergoing Roux-en-Y

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Present Address: G. Carneiro (⊠) Rua Leandro Dupret, 365 Vila Clementino, São Paulo CEP: 04025-011, Brazil e-mail: glauciacarneiro@uol.com.br e-mail: glauciacarneiro@hotmail.com gastric bypass from January 2004 to January 2007. Sleep apnea was noted as present or absent and graded from mild to severe according to the apnea/hypopnea index. Patient gender, age, weight, height, body mass index, neck circumference, and waist circumference were recorded. Results A total of 132 patients were included in the study group, and 85 patients had a confirmed diagnosis of OSA (64.4%). The prevalence of OSA was 55.7% in female and 77.4% in male. The prevalence of moderate or severe sleep apnea was higher in males (71.6%) than in females (31.6%). In OSA patients, body mass index (p=0.020), neck circumference (p < 0.001), and age (p = 0.003) were higher as compared with obese patients without OSA, whereas no differences were found in waist circumference between groups. After multiple regression analysis, body mass index, age, and male gender were independent predictors of sleep apnea. In the female group, age greater than 49 years was the only significant predictor of moderate or severe OSA (odds ratio 5.42 (95% confidence interval 1.61-18.1; p=0.006).

*Conclusion* Males and females with age greater than 49 years are at greatest risk for OSA. Preoperative sleep studies should be mandatory in this group of severely obese patients.

Keywords Sleep apnea · Severe obesity · Polysomnography

## Introduction

Obstructive sleep apnea (OSA) is a highly prevalent disease defined as an apnea–hypopnea index (AHI) on polysomnography (PSG)  $\geq$ 5 apneas and hypopneas per hour of sleep. It affects 9% and 24% of middle-aged men and women, respectively [1]. In severely obese individuals (body mass

index (BMI) $\geq$ 40), the prevalence rates of OSA are considerably higher, often reported in the range of 39% to 71% [2]. Despite the well-known risk factors related to OSA in the general population in morbidly obese subjects, these risks are not as clear. In addition, the spectrum of OSA severity and the influence of gender are not well documented.

Bariatric surgery is the most effective therapy available for severely obese patients. It markedly lowers body weight, reverses or ameliorates the obesity comorbidities, and improves the quality of life [3]. In addition, weight loss is associated with an improvement in daytime symptoms of OSA [4] and a reduction of apneic episodes during sleep [5].

However, perioperative risks for OSA patients are great, including complications of anesthesia and analgesia with associated prolonged periods of apnea with a high risk of respiratory arrest [6]. The preoperative and perioperative use of continuous positive airway pressure (CPAP) or bilevel positive airway pressure can reduce hypercarbia, hypoxemia, and pulmonary artery vasoconstriction, as well as prevent the anesthetic and analgesic complications [7]. Therefore, a diagnosis of OSA preoperatively would allow treatment with CPAP to reduce those risks.

The aim of the present study was to evaluate the prevalence of OSA among severely obese subjects referred for bariatric surgery. We also report the predictive factors that increase the risk and severity of OSA in this population.

### Patients and methods

We prospectively performed overnight polysomnography on 132 consecutively severely obese patients without known OSA who had been referred for a bariatric surgery evaluation at the Obesity Outpatient Clinic and Sleep Disorders Center of the Federal University of Sao Paulo from 2004 to 2007. These patients, aged from 18 to 65 years and with a body mass index between 40 and 73 kg/m<sup>2</sup>, were classified according to their AHI: normal, <5 events per hour; mild sleep apnea, 5 to 14 events per hour; moderate sleep apnea, 15 to 29 events per hour; and severe sleep apnea, 30 or more events per hour.

A questionnaire including demographic data and sleep symptoms was administered. Physical examinations and anthropometric measurements were recorded, including neck and waist circumference (in centimeters), weight (in kilograms), and height (in meters). Waist circumference was measured in supine position at the midpoint between the lateral iliac crest and the lowest rib, and neck circumference was measured at the level of the cricothyroid membrane. BMI was calculated as the weight divided by the height-squared.

Polysomnograms were recorded by the Sleep Analyser Computer (Alice 3 Diagnostics system) for obstructive sleep apnea syndrome diagnosis and severity. The following channels were included: three for electroencephalography, two for oculogram channels, two for chin and tibial electromyography, one for electrocardiography, one for airflow (nasal pressure), two for thoracic-abdominal movements (calibrated inductance plethysmography), one for tracheal sound (snoring), one for pulse oxymetry, and one for recording of body position. An experienced sleep physician scored all sleep stages [8], arousals, and respiratory events according to the American Sleep Disorders Association criteria [9, 10]. An abnormal breathing event during sleep was defined according to the common clinical criteria of either a complete cessation of airflow lasting  $\geq 10$  s (apnea) or a reduction in airflow accompanied by a decrease of  $\geq 3\%$  in oxyhemoglobin saturation or arousal (hypopnea), using a pressure nasal cannula. The average number of episodes of apnea and hypopnea per hour of sleep (i.e., the AHI) was calculated. Excessive daytime sleepiness (EDS) was assessed based on the subject's response to eight questions regarding the probability of dozing in specific situations using a four-point scale, and the Epworth sleepiness scale score was calculated [11]. A score of >10 was considered to be suggestive of EDS. The study was approved by the UNIFESP Ethics Committee, and written informed consent was obtained from all participants.

#### Statistical analysis

Normally distributed variables are expressed as means  $\pm$  SD or percentiles when appropriate. Continuous variables comparisons were performed using the unpaired Student *t* test. To assess differences between categorical variables, chi-square statistics were used. Multivariate analysis was performed to evaluate the effects of age, gender, BMI, neck circumference, and waist circumference on the risk of having OSA. *p* values <0.05 were considered significant.

## Results

Of the 132 subjects scheduled for bariatric surgery during the study period, 85 (64.4%) had sleep apnea (AHI $\geq$ 5 events per hour). Subjects with OSA had a significantly greater age and BMI compared to subjects without OSA. Waist circumference was similar between the groups, and participants did not have correlations between neck and waist circumference (*p*= 0.424). The mean AHI was 47.7 $\pm$ 3.9 events per hour, and the mean oxygen saturation was 90.9 $\pm$ 5.3% in the OSA group. Overall demographic and anthropometric characteristics of the study group are shown in Table 1.

Obese males had a greater prevalence (77.4% vs 55.7%, p=0.011) and severity of OSA than did females (AHI 66.1±34.6 vs 30.5±29.6 events per hour; p<0.001).

<b>Table 1</b> Clinical and polysom-nography characteristics of se-		OSAS		р
verely obese patients with and without sleep apnea		Yes ( <i>n</i> =85)	No ( <i>n</i> =47)	
	AHI, events/h	47.7±36.6	$1.8 \pm 1.7$	< 0.001
	Mean oxygen saturation	$90.4{\pm}6.0$	94.4±2.1	0.002
	Gender (male, %)	41 (48.2%)	12 (25.5%)	0.011
	Age, years	45.3±10.9	$38.9 \pm 12.0$	0.003
	Waist, cm	128.6±15.9	$124.1 \pm 17.8$	0.205
Data are expressed by mean $\pm$ SD; <i>n</i> (%)	BMI, kg/m <sup>2</sup>	$48.8 \pm 7.3$	45.7±6.5	0.020
	Neck, cm	44.1±5.2	$40.1 \pm 4.0$	< 0.001
<i>AHI</i> apnea-hypopnea index, <i>BMI</i> body mass index	ESE	10.8±6.3	9.7±5.3	0.461

Among males, 5.7% had mild OSA (5≥AHI<15), 11.3% had moderate OSA (15≥AHI<30), and 60.4% had severe OSA (AHI≥30). Among females, 24.1% had mild OSA  $(5 \ge AHI < 15)$ , 12.7% had moderate OSA  $(15 \ge AHI < 30)$ , and 19.0% had severe OSA (AHI≥30). In the entire group, the average age of males was significantly lower than that of the females, whereas waist circumference and neck circumference were greater for male subjects. No significant difference in BMI was observed between male and female subjects (Fig. 1; Table 2).

Multivariate regression analysis showed that male gender, age greater than 36 years (2° terciles), and BMI were independent predictors of OSA (Table 3) in severely obese patients undergoing bariatric surgery. The Epworth Sleep Score does not predict the presence and severity of sleep apnea. Male gender and females with age greater than 49 years (3° terciles) showed an increase of four times and five times, respectively, the risk of developing OSA. When age, BMI, and gender were included in a second multiple logistic regression to predict the severity of OSA using only those participants with AHI $\geq$ 5 (*n*=85), male gender was the only significant predictor of OSA severity (odds ratio 13.9; p < 0.001).

## Discussion

In the present study, 132 subjects presenting for bariatric surgery were consecutively screened for OSA regardless of

Male

60.4

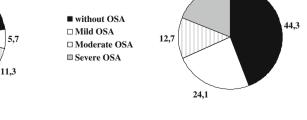
22,6

Fig. 1 Gender differences according to severity of obstructive sleep apnea

symptoms. PSG was conducted in all patients. We demonstrated that over 60% of obese individuals undergoing bariatric surgery had sleep apnea (AHI≥5 events per hour). In addition, we showed that male gender, BMI, and age were associated with the presence of OSA, but only male gender was significantly related to the severity of OSA.

Obesity is the most important reversible risk factor for OSA [12]. Approximately 70% of individuals with OSA are obese [13]. In addition, the prevalence of OSA in obese men and women is approximately 40% [14]. In severely obese subjects, the rate of OSA is 12 to 30 times higher compared with the general population [15, 16], and BMI alone is not a good predictor of the presence or absence of sleep apnea in this group of patients [17]. Bariatric surgery is the best current treatment for severe obesity, providing the only mechanism for reproducible, effective, and sustained weight loss. OSA is a common comorbidity found in patients undergoing bariatric surgery. Given this high likelihood and the association of OSA with other concerning comorbidities such as pulmonary artery hypertension, severely obese patients should be referred for further evaluation before bariatric surgery.

Unrecognized OSA can have a significant influence upon perioperative morbidity and mortality. Failed intubation can occur in as many as 5% of attempted surgeries in patients with OSA [18, 19]. Severely obese patients with a polysomnography-confirmed diagnosis of OSA were at



Female

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	Male ( <i>n</i> =53)		Female (n=79)	
	Control <i>n</i> =12; (22.6%)	OSA <i>n</i> =41; (77.4%)	Control <i>n</i> =35; (44.3%)	OSA <i>n</i> =44; (55.7%)
AHI, events/h	1.9±2.0	66.1±34.6	1.8±1.6	30.5±29.6**
Mean oxygen saturation	94.6±1.5	$90.0 \pm 4.1$	94.4±2.3	$90.9 {\pm} 7.6$
Age, years	35.6±9.7	42.1±11.5	40.1±12.6	48.2±9.4**
Waist, cm	$141.0 \pm 14.3$	137.6±15.1	118.5±15.3*	121.4±12.7**
BMI, kg/m <sup>2</sup>	45.7±3.8	48.5±7.6	45.8±7.3	$48.8 {\pm} 7.0$
Neck, cm	46.7±1.7	$48.5 \pm 3.6$	39.1±3.2*	40.8±3.5**
ESE	9.5±5.0	12.1±6.6	9.8±5.5	9.8±6.1

Table 2 Clinical and polysomnography characteristics of severely obese patients according to gender

\*p<0.05 vs control male; \*\*p<0.05 vs OSA male

significantly greater risk for postoperative hypercarbia, hypoxemia, and pulmonary artery vasoconstriction than were severely obese patients without respiratory disturbance [7, 20]. Postoperative respiratory complications can also result from pain management. Sedatives, analgesics, and anesthetics alter airway tone, and death has been reported in patients with OSA after minimal doses of sedatives and anesthetics [6, 21]. Opioids, in combination with the retention of carbon dioxide, can further blunt the ventilatory response [18]. Stellato et al. have showed that intensive preoperative evaluation and treatment of OSA decreased complications and length of hospital stay in bariatric patients [22].

PSG is the gold standard for the diagnosis and assessment of treatment for OSA [23]. Because sleep apnea is absent in a small number of severely obese patients and some patients have mild OSA not requiring treatment, some authors have suggested that the use of routine screening polysomnography should be performed on all patients presenting for bariatric surgery [17]. However, this exam has some limitations. It requires qualified personnel that collect and interpret data; it is also time-consuming and costly. Several signs and symptoms have been associated with an increased prevalence of obstructive sleep apnea in the general population: snoring, morning headaches, day-time sleepiness, BMI of 35 kg/m<sup>2</sup>, neck circumference greater than 41 cm, and male sex [24]. Knowledge of risk

factors for OSA in a population of severely obese patients can provide clues as to whether a patient has OSA and can lead physicians to properly evaluate the patient with PSG [25].

Our study aimed to evaluate the prevalence of OSA in severely obese patients submitted to conventional Rouxen-Y gastric bypass surgery. We also evaluated the predictive factors that increase the risk of having OSA in the total group and according to gender. Our results confirmed the higher prevalence and severity of obstructive sleep apnea in men than in women. Moreover, the mean age of OSA in men was the lowest. In the female group, age greater than 49 years was the only predictor of OSA. In agreement with Serafini et al., we found that the Epworth Sleep Score was inadequate to identify OSA in severely obese patients [26, 27]. Because most subjects have been treated with fluoxetine as a routine medication to control depression and eating disorders, this fact could influence daytime hypersomnolence and could promote wakefulness in this population.

Obesity itself cannot explain the highest prevalence and severity of OSA in men, as both genders were BMI matched ( $48.1\pm7.5$  vs  $47.5\pm7.2$  kg/m<sup>2</sup>) in our study. This different behavior between genders might be attributed to sex differences in anatomical and functional properties of the upper airway [28, 29]. In our study, participants' waist and neck circumferences were higher in men than in

Table 3 Predictors of sleep   apnea in severely obese patients	Variable	Total group Odds ratio (95% confidence interval) p	Female Odds ratio (95% confidence interval) p
	Male	3.69 (1.54-8.83) 0.003	_
	BMI	1.07 (1.00-1.13) 0.028	1.06 (0.98–1.14) NS
	Age 1 tercil (<36 years)		
	Age 2 tercil (36-49 years)	2.78 (1.09-7.07) 0.031	3.10 (0.91–10.6) NS
Danan dant aaniahlar alaan annaa	Age 3 tercil (>49 years)	5.18 (1.83-14.6) 0.002	5.42 (1.6–18.1) 0.006

Dependent variable: sleep apnea

women. This result is consistent with findings that fat deposition in the neck and waist elevated the risk of OSA [30, 31]. However, in our study participants, we did not find correlations between neck or waist circumference with sleep apnea. Furthermore, hormone influences are also likely to have an important role in the pathogenesis of obstructive sleep apnea, as the prevalence of OSA is higher in post- than in pre-menopausal women [32]. Diminishing progesterone levels during menopause may be a cause of OSA, as progesterone is a known respiratory stimulant and upper airway dilator [33]. Previous studies have shown that female hormones can protect against OSA and male hormones can influence breathing during sleep [34, 35]. Other mechanisms proposed for the male-related higher prevalence of OSA include gender differences in pharyngeal structure and function during sleep and differences in ventilatory response during wakefulness and sleep [36, 37].

Limitations of the study are the small sample size of n= 85 subjects with OSA and the high prevalence of women in this group of patients undergoing bariatric surgery. Also, the Epworth Scale is a tool used to measure subjectively sleepiness, and subjective assessments of sleepiness are not always reliable or appropriate. Kapur et al. [38] have shown that most people with sleep-disordered breathing did not report experiencing any sleepiness from the community-based Sleep Heart Health cohort of 6,440 subjects.

In conclusion, our current study suggests that all severely obese men and severely obese women with age greater than 49 years should be evaluated for OSA. Anthropometric obesity measurements (BMI, waist and neck circumference) and the Epworth Scale alone are unreliable in predicting OSA in this group of severely obese patients. Furthermore, in clinical practice, it is desirable to detect other predictive variables for OSA in morbidly obese subjects. Therefore, further studies addressing variables such as OSA questionnaires, physical examination of upper airways, pulmonary function tests, and measurements of visceral fat should be evaluated to discriminate between OSA and non-OSA in this population.

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#### References

 Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S (1993) The occurrence of sleep-disordered breathing among middle age adults. N Engl J Med 328:1230–1235

- Valencia-Flores M, Orea A, Castaño VA, Resendiz M, Rosales M, Rebollar V, Santiago V, Gallegos J, Campos RM, González J, Oseguera J, García-Ramos G, Bliwise DL (2000) Prevalence of sleep apnea and electrocardiographic disturbances in morbidly obese patients. Obes Res 8:262–269
- Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K, Schoelles K (2004) Bariatric surgery—a systematic review and meta-analysis. JAMA 292:1724–1737
- Richman RM, Elliott LM, Burns CM, Bearpark HM, Steinbeck KS, Caterson ID (1994) The prevalence of obstructive sleep apnoea in an obese female population. Int J Obes Relat Metab Disord 18:173–177
- Resta O, Foschino-Barbaro MP, Legari G, Talamo S, Bonfitto P, Palumbo A, Minenna A, Giorgino R, De Pergola G (2001) Sleeprelated breathing disorders, loud snoring and excessive daytime sleepiness in obese subjects. Int J Obes Relat Metab Disord 25:669–675
- Bell R, Rosenbaum S (2005) Postoperative considerations for patients with obesity and sleep apnea. Anesthesiol Clin N Am 23:493–500
- American Society of Anesthesiologists Task Force on Management of the Difficult Airway (2003) Practice guidelines for management of the difficult airway: an updated report. Anesthesiology 98:1269–1277
- Rechtschaffen A, Kales A (1968) A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Brain Information Service/Brain Research Institute UCLA, Los Angeles
- Anonymous (1992) EEG arousals: scoring rules and examples. A preliminary report from the sleep disorders atlas task force of the American Sleep Disorders Association. Sleep 15:173–184
- 10. Anonymous (1999) Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The report of an American Academy of Sleep Medicine Task Force. Sleep 22:667–689
- Johns MW (1991) A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep 14:540–545
- 12. Young T, Shahar E, Nieto FJ, Redline S, Newman AB, Gottlieb DJ, Walsleben JA, Finn L, Enright P, Samet JM, Sleep Heart Health Study Research Group (2002) Predictors of sleep-disordered breathing in community-dwelling adults: the sleep heart health study. Arch Intern Med 162:893–900
- Malhotra A, White DP (2002) Obstructive sleep apnoea. Lancet 360:237–245
- Vgontzas AN, Tan TL, Bixler EO, Martin LF, Shubert D, Kales A (1994) Sleep apnea and sleep disruption in obese patients. Arch Intern Med 154:1705–1711
- Daltro C, Gregorio PB, Alves E, Abreu M, Bomfim D, Chicourel MH, Araújo L, Cotrim HP (2007) Prevalence and severity of sleep apnea in a group of morbidly obese patients. Obes Surg 17:809– 814
- Frey WC, Pilcher J (2003) Obstructive sleep-related breathing disorders in patients evaluated for bariatric surgery. Obes Surg 13:676–683
- 17. O'Keeffe T, Patterson EJ (2004) Evidence supporting routine polysomnography before bariatric surgery. Obes Surg 14:23–26
- Benumof JL (2004) Obesity, sleep apnea, the airway, and anesthesia. Curr Opin Anaesthesiol 17:21–30
- Siyam MA, Benhamou D (2002) Difficult endotracheal intubation in patients with sleep apnea syndrome. Anesth Analg 95:1098–1102
- 20. Ahmad S, Nagle A, McCarthy RJ, Fitzgerald PC, Sullivan JT, Prystowsky J (2008) Postoperative hypoxemia in morbidly obese patients with and without obstructive sleep apnea undergoing laparoscopic bariatric surgery. Anesth Analg 107:138–143
- 21. Gross JB (2006) Practice guidelines for the perioperative management of patients with obstructive sleep apnea: a report

by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Anesthesiology 104:1081–1093

- 22. Stellato T, Hallowell P, Crouse C (2004) Two-day length of stay following open Roux-En-Y gastric bypass: is it feasible, safe and reasonable? Obes Surg 14:27–34
- 23. Gami AS, Caples SM, Somers VK (2003) Obesity and obstructive sleep apnea. Endocrinol Metab Clin North Am 32:869–894
- 24. Strollo PJ Jr, Rogers RM (1996) Obstructive sleep apnea. N Engl J Med 334:99–104
- Charuzi I, Lavie P, Peiser J, Peled R (1992) Bariatric surgery in morbidly obese sleep-apnea patients: short- and long-term followup. Am J Clin Nutr 55:5948–5968
- Serafini FM, MacDowell Anderson W, Rosemurgy AS, Strait T, Murr MM (2001) Clinical predictors of sleep apnea in patients undergoing bariatric surgery. Obes Surg 11:28–31
- 27. Rasheid S, Banasiak M, Gallagher SF, Lipska A, Kaba S, Ventimiglia D, Anderson WM, Murr MM (2003) Gastric bypass is an effective treatment for obstructive sleep apnea in patients with clinically significant obesity. Obes Surg 13:58–61
- 28. Punjab Jordan AS, McEvoy RD, Edwards JK, Schory K, Yang CK, Catcheside PG, Fogel RB, Malhotra A, White DP (2004) The influence of gender and upper airway resistance on the ventilatory response to arousal in obstructive sleep apnoea in humans. J Physiol 558(Pt 3):993–1004
- Jordan AS, McEvoy RD (2003) Gender differences in sleep apnea: epidemiology, clinical presentation and pathogenic mechanisms. Sleep Med Rev 7:377–389
- Millman RP, Carlisle CC, McGarvey ST, Eveloff SE, Levinson PD (1995) Body fat distribution and sleep apnea severity in women. Chest 107:362–366

- Dancey DR, Hanly PJ, Soong C, Lee B, Shepard J Jr, Hoffstein V (2003) Gender differences in sleep apnea: the role of neck circumference. Chest 123:1544–1550
- 32. Resta O, Caratozzolo G, Pannacciulli N, Stefàno A, Giliberti T, Carpagnano GE, De Pergola G (2003) Gender, age and menopause effects on the prevalence and the characteristics of obstructive sleep apnea in obesity. Eur J Clin Investig 33:1084– 1089
- 33. Young T, Rabago D, Zgierska A, Austin D, Laurel F (2003) Objective and subjective sleep quality in premenopausal, perimenopausal, and postmenopausal women in the Wisconsin Sleep Cohort Study. Sleep 26:667–672
- 34. Schneider BK, Pickett CK, Zwillich CW, Weil JV, McDermott MT, Santen RJ, Varano LA, White DP (1986) Influence of testosterone on breathing during sleep. J Appl Physiol 61:618– 623
- 35. Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Rein J, Vela-Bueno A, Kales A (2001) Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med 163:608–613
- 36. Kunitomo F, Kimura H, Tatsumi K, Kuriyama T, Watanabe S, Honda Y (1988) Sex differences in awake ventilatory drive and abnormal breathing during sleep in eucapnic obesity. Chest 93:968–976
- 37. Zhou XS, Shahabuddin S, Zahn BR, Babcock MA, Badr MS (2000) Effect of gender on the development of hypocapnic apnea/hypopnea during NREM sleep. J Appl Physiol 89:192– 199
- Kapur VK, Baldwin CM, Resnick HE, Gottlieb DJ, Nieto FJ (2005) Sleepiness in patients with moderate to severe sleepdisordered breathing. Sleep 28:472–477