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Gender difference in sleep profile of severely obese patients with obstructive sleep apnea (OSA)

O. Resta[a,*], G.E. Carpagnano[a], D. Lacedonia[a], G.Di Gioia[a], T. Giliberti[a], A. Stefano[a], P. Bonfitto[b]

[a]*Department of Clinical Methodology and Medical-Surgical Technologies, Institute of Respiratory Diseases, University of Bari, School of Medicine, Policlinico, Piazza Giulio Cesare 11, Bari 70124, Italy*
[b]*Institute of Respiratory Diseases, University of Foggia, School of Medicine, Foggia, Italy*

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Summary *Objectives*: Few papers addressed the gender difference in the polisomnographic features of obstructive sleep apnea (OSA). In this paper we investigated the sleep architecture and the nocturnal respiratory pattern in a group of severely obese women with OSA compared with a group of men with OSA matched by age and weight.

Design: A cross-sectional study.

Setting: Primary-care setting.

Subjects, main outcome measures: Anthropometric parameters, respiratory function data and a full night polisomnography were evaluated in a group of 45 obese subjects, 20 females and 25 males, with a previous diagnosis of OSA.

Results: The group of the severely obese women with OSA presented greater disturbances of the sleep architecture than the group of the men does (wake time after sleep onset 92.6 ± 52.4 vs 58.2 ± 45.2 min, $P<0.05$; total wake time 104.8 ± 51.4 vs 67.8 ± 47.4, $P<0.05$; number of awakenings 15.5 ± 3.6 vs 10.2 ± 6.215, $P<0.001$; OSA that occurred almost exclusively during REM sleep (REM OSA) 35% vs 4%, $P<0.05$) and a reduced sleep efficiency (69.6 ± 15.9 vs 80.3 ± 14.0%, $P<0.05$).

Conclusions: Severely obese women with OSA, even with milder OSA, present greater disturbances of the sleep architecture with a more severe sleep disruption and more frequently REM OSA in comparison with men matched by age and weight.

Introduction

In the early reports obstructive sleep apnea (OSA) was considered particularly a disease of males. Consequently, for many years, epidemiologic studies investigating the prevalence of OSA included only men and women were not considered.[1–4] More recently it has been well recognized that OSA among women is not so rare as it was believed. In fact whereas early studies suggested that women were about 10% or less of the OSA cases, later studies suggest that women are about a third of all cases.[5–7] Moreover we demonstrated that the prevalence of sleep related breathing disordered (SRDB) in moderate and severe obesity is very high, especially among women.[8] However many aspects

*Corresponding author. Tel.: +39-08-0547-8590; fax: +39-080-559-2907.
E-mail address: o.resta@pneumol.uniba.it (O. Resta).

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of the symptoms of SRDB in women have not been adequately studied. At this regard, to our knowledge, only a previous paper studied gender difference in polysomnographic features of OSA.[9] This is an important question because OSA in women has often different clinical pictures and characteristics when compared with men. In this paper we investigated the sleep architecture and the nocturnal respiratory pattern in a group of severely obese women with OSA compared with a group of men with OSA matched by age and weight.

Method

Subjects

We evaluated a group of 45 obese subjects, 20 females and 25 males, with a previous diagnosis of OSA (AHI >10) recruited at the sleep laboratory of respiratory disease, University of Bari, School of Medicine, from September 1999 to 2002. Patients were eligible for the study if they had body mass index (BMI) $>30\,kg/m^2$, and if they spent at least 150 min of total sleep time with a REM sleep percentage of at least 5% of the sleep period time.[10]

We excluded patients with endocrinological diseases, narcolepsy, or idiopathic hypersonnia, neuromuscular diseases, psychiatric disorders, overt cardiopulmonary diseases, severe airway obstruction, anatomic maxillomandibular skeletal anomalies, heavy ear, nose or throat pathologies, or with history of benzodiazepines, narcotic or alcohol abuse at the time of the study. Patients were excluded also if they had been enrolled in a previous sleep study. No woman was pregnant. Nineteen of twenty obese women were either severely (BMI $\geqslant 32$) or morbidly (BMI >39) obese in comparison with 23 out of 25 obese males.

Height and weight were measured in the evening of the study and BMI was calculated (kg/m^2).

Neck circumference was measured at the level of the cricotyroid membrane.

The Epworth sleepiness scale (ESS) was used to evaluate the sleep propensity.[11]

The study was approved by the local ethical committee and all the subjects gave their informed consent to the study.

Protocol of polysomnography

Overnight polysomnography was performed in all patients, after a night of adaptation in hospital. The polysomnography included a two channel electroencephalogram (EEG) (C3–A2, C4-A1), electro-oculogram (EOG) and submental and leg electromyograms (EMGs). The ECG and heart rate were assessed with standard limb leads. Airflow was monitored using thermoresistors placed at the nose and at the mouth. Respiratory efforts were assessed with an inductive plethysmography using transducers placed around the chest and the abdomen. All night long recordings of arterial oxygen saturation were obtained with a finger pulse oximetry. Snoring sound was recorded with a microphone attached to the neck. Body position was assessed continuously using a closed circuit television and a body position sensor. Transcutaneous CO_2 was measured with a Radiometer apparatus (Radiometer TL100 Copenhagen, Denmark).

All variables were recorded using a 19-channel polysomnograph (Compumedic, AUSTRALIA).

Data analysis of polysimnography

The analysis of conventional sleep parameters was based on the standard guidelines using 30 s epochs [12] and was performed manually.

The following sleep parameters were scored:

Sleep architecture

Sleep latency (SL): the time between lights out and the first period of stage 2; Total sleep time (TST): the time from sleep onset to the end of final sleep epoch minus time awake; Wake time after sleep onset (WASO): wake time not including sleep latency; Total wake time (TWT: SL + WASO); Sleep efficiency (SE): the ratio between the TST and the time spent in bed (TB); Duration (%) of stage 1(SI), stage 2(S2), stage 3(S3), stage 4(S4), non-REM sleep (S1 + S2 + S3 + S4); Total duration and % of REM sleep; REM latency (REML).

In addition we scored the arousal index (AI), defined as the number of arousals (rapid increase in EEG frequency lasting >3 s and <15 s and characterized by alpha activity, eye movements and an EMG activation) per hour of sleep and calculated for TST; number of awakenings (AWI) defined as the number of awakenings (an electroencephalogram arousal lasting more than 15 s) calculated for TST.

Sleep related disordered breathing (SRDB)

An obstructive apnea was defined as the absence of airflow lasting more than 10 s in presence of continued respiratory efforts. A central apnea was defined as the absence of airflow lasting more than 10 s due to loss of respiratory efforts. A mixed apnea was defined as an initial central apnea

followed by an obstructive apnea. A hypopnea was defined as a reduction of the amplitude of respiratory efforts between 10% and 50% of the baseline level during sleep and lasting more than 10 sec and associated with >3% decrease of oxygen saturation or with a final arousal.[9] The AHI was defined as the number of apneas and hypopneas per hour of sleep: we calculated separately the AHI during TST (AHI/TST), during REM sleep (AHI REM), during non-REM sleep (AHI/NON REM), in supine position (AHI/SUP) and in non supine position (AHI/NON SUP). We calculated the mean duration of the apnea/hypopnea events (MDA), the mean desaturation during sleep (MDS) and the percentage of total sleep time spent with oxyhaemoglobine saturation <90% (TST $SaO_{2<90\%}$).

Finally we defined as hypoventilation a period of persistent (>2 min) reduction of 2/3 of abdominal ribcage excursions, associated with a persistent oxygen desaturation of 10% explained by no apnea or hypopnea event and associated with no arousal and with a mean increase of transcutaneous CO_2 >7 mmHg.[13,14] Subjects who had this respiratory pattern for almost 15% of TST were diagnosed as patients with nocturnal hypoventilation (NHP).[8]

OSA type

According to Connors et al,[9] each patient with OSA was classified with one of these three types of OSA:

(1) REM OSA (ROSA): Mild OSA that occurred almost exclusively during REM sleep and defined by AHI/TST >10 and <25 and AHI/REM/AHI non REM >2 and AHI/NONREM <10.
(2) Supine OSA (SOSA): OSA occurring almost exclusively in the supine position.
(3) OSA independent of sleep stage or sleep position (IOSA).

Respiratory function

Arterial blood samples were drawn from the brachial or the radial artery for blood gas analysis, after the patient had been in the supine position for at least 3 min. Arterial blood $PaCO_2$, PaO_2, pH and base excess were analyzed with an automatic acid-base analyser (ABL 30 radiometer, Copenhagen, Denmark). The measurement was performed in the evening, just before the sleep study.

Statistical analysis

Statistical analysis was performed using the STATISTICA 6.0 for Windows, StatSoft Inc. (1995) software (Tulsa, OK, USA). Results are presented as mean ± standard deviation (SD). Comparisons between two groups were performed using Student's *t*-test for unpaired data, or chi-square test when appropriated. A *P* value less than or equal to 0.05 was considered to be of statistical significance.

Results

Anthropometric characteristics, PaO_2 and $PaCO_2$ values, AHI and ESS of 20 obese females with OSA, compared with 25 obese males with OSA are shown in Table 1. There was no significant difference in terms of age (42.9±13.5 vs 45.0±10.3), BMI (39.6±6.7 vs 40.0±10.3), but the women had a significantly smaller neck circumference (38.3±6.6 vs 45.7±3.4), lower AHI (41.6±29.2 vs 57.3±22.9) and $PaCO_2$ (37.7±4.3 vs 40.9±5.3). Evident hypercapnia ($PaCO_2$ >45 mmHg) was present in 4 males (16%) and 1 female (5%). In Table 2 we compared the data of the sleep profile of females and males. Both the groups presented a typical profile, consistent with OSA (reduced SL, low SE, high WASO, reduced S3 + S4, low REM stage, high AI) but the women had, despite a lower AHI, significantly higher TWT (52.4±29.4 vs 33.9±26.7, $P<0.05$), WASO (92.7±52.4 vs 58.1±45.2, $P<0.05$), and AWI (15.5±3.6 vs 10.2±6.19, $P<0.001$) and a lower SE (69.6±15.9 vs 80.3±14.0, $P<0.05$). Even if there was no statistically

Table 1 Antropometric and respiratory function data in male and female obese with OSA.

	Male	Female	*P*-value
Age (yr)	45.0±10.3	42.9±13.5	Ns
BMI (K/m^2)	40.1±10.3	39.7±6.7	Ns
Neck (cm)	45.7±3.4	38.3±6.6	<0.0001
PaO_2 (mmHg)	79.4±13.1	82.2±10.4	Ns
$PaCO_2$ (mmHg)	40.9±5.3	37.7±4.3	<0.05
AHI (n)	57.3±22.9	41.6±29.2	<0.05
ESS	11.1±6.6	8.2±4.6	Ns

BMI: body mass index, AHI: apnea/hypopnea index; ESS: Epworth sleepiness scale.

Table 2 Sleep architecture of male and female obese with OSA.

	Male	Female	*P*-value
TB (min)	371.3±54.1	366.1±60.7	Ns
SL (min)	9.6±8.2	12.2±9.6	Ns
TST (min)	312.1±69.9	273.4±69.4	Ns
SE (%)	80.3±14.0	69.6±15.9	<0.05
WASO (min)	58.2±45.2	92.6±52.4	<0.05
TWT (min)	33.9±26.7	52.4±29.4	<0.05
S1 + S2 (%)	35.1±13.2	33.9±9.3	Ns
S3 + S4 (%)	7.6±7.3	7.1±5.1	Ns
REM duration (min)	53.2±42.9	44.4±25.6	Ns
REM duration (%)	14.5±10.1	17.0±9.1	Ns
AI (n/h)	39.4±21.1	29.9±22.3	Ns
AWI	10.2±6.215	15.5±3.6	<0.001

TB: time spent in bed; SL: sleep latency, TST: total sleep time; SE: sleep efficiency; WASO: wake after sleep onset; TWT: total wake time; AI: arousal index; AWI: number of awakenings.

Table 3 Gender differences in apnea/hypopnea index during different sleep stage and position.

	Male	Female	*P*-value
AHI $_{NREM}$ (n/h)	57.4±24.5	40.4±31.1	<0.05
AHI $_{REM}$ (n/h)	50.9±26.4	39.9±22.3	ns
AHI $_{supine\ TST}$ (n/h)	65.3±23.3	42.2±33.6	<0.01

Table 4 Prevalence of different type of obstructive sleep apnea in male and female.

	Male	Female	P-value
REM OSA (n)	1/25	7/20	<0.05
S OSA (n)	7/25	6/20	Ns
I OSA (n)	17/25	7/20	<0.05

significant difference, the AI was higher among the males (39.4±21.1 vs 29.9±22.3, $P=0.4$) while the REM stage percentage was higher among the females (17.0±9.1 vs 14.5±10.1, $P=0.2$).

In Table 3 we show the characteristics and the distribution of SRDB in REM and non REM stage and in supine position. AHI/NREM was significantly higher among the men (57.4±24.5 vs 40.4±31.1 $P<0.05$), while AHI/REM was similar into the two groups. (50.9±26.4 vs 39.9±22.3, $P=0.6$).

AHI/sup was significantly higher among the males (65.3±23.3 vs 41.1±33.6, $P<0.01$).

Among the males the AHI/sup was significantly higher than AHI/nsup (65.3±23.3 vs 39.8±32.0, $P<0.005$) while among the females the difference was no statistically significant (42.2±33.6 vs 37.4±27.4, $P=0.7$).

The prevalence of the different types of OSA is shown in Table 4. Among the obese women there was a greater prevalence of REM OSA (35%) in comparison with the males (4%). Supine OSA was similarly frequent among the men and the women (respectively, 28% vs 30%).

In Table 5 we reported the gender differences in terms of prevalence and severity of the different types of SRDB.

The females had a significantly greater proportion of hypopneas (70.9% vs 56.9%, $P<0.05$), while among the males we found a significantly greater proportion of mixed apnea (9.3% vs 0.6%, $P<0.05$). No statistical difference there was in terms of obstructive apnea and central apnea.

The mean duration of apnea (19.7±6.3 vs 16.1±2.5) and the mean desaturation during sleep (7.8±5.1 vs 4.8±4.5) were greater among the men but only in the first case there was a statistically significant difference ($P<0.05$).

Finally nocturnal hypoventilation (NHP) was present in 15% of women and in 36% of men ($P=0.6$).

Discussion

The present study is the first analysis of gender difference in the sleep architecture in severely obese patients with OSA.

The most important result of our study shows that, despite a lower AHI, a group of obese women with OSA has similar polysomnographic parameters in comparison with a group of men matched by age

Table 5 Gender difference in prevalence of different type of SRDB.

	Male	Female	*P*-value
Central apnea (%)	2.8	2.9	ns
Obstructive apnea (%)	30.9	25.5	ns
Mixed apnea (%)	9.3	0.6	<0.001
Hypopnoea (%)	56.9	70.9	<0.05
MDA (s)	19.7 ± 6.3	16.1 ± 2.5	<0.05
MDS (%)	7.8 ± 5.2	4.8 ± 4.5	ns
TST $<$ 90% (%)	31.2 ± 25.7	19.2 ± 25.5	ns
NHP	9/25	3/20	ns

MDA: mean duration apnea; MDS: mean desaturation; TST $<$ 90%: total sleep time with oxyemoglobine saturation $<$ 90%; NHP: nocturnal hypoventilation.

and weight; even better we found among the women a greater disturbance of the sleep architecture with a more severe sleep disruption.

Secondly the distribution of the respiratory events in REM stage was similar and more than 60% of the apneas among the women was related to the REM stage and the supine position.

Finally another important finding is that among the men the severity (in terms of duration and desaturation) of the respiratory events and the prevalence of nocturnal hypoventilation was greater, while among the women we found a wider proportion of hypopneas.

It is known that patients with severe OSA have significant abnormalities of the sleep architecture. Moreover, according with Vgontzas et al.[15] we demonstrated that even morbid obesity is associated with significant sleep disturbances.[16] However no information exists in relation to the gender difference in the sleep pattern of severely obese subjects with OSA.

In this paper we demonstrated that, despite a milder OSA, the women presented more important sleep disturbances than the men with similar age and BMI. Among the women the polysomnogram was characterized by a more severe sleep disruption: higher total wake time, higher wake after sleep onset, awakenings, lower sleep efficiency, and similar arousal index.

Recently Guilleminault et al.[17] found among the women a most relevant underlying psychological distress related to the obesity (characterized by the presence of tension and depression, by a different hormonal or metabolic configuration between obese women and obese man, by a higher prevalence of upper airways resistance syndrome (UARS) not apnea dependent and not associated with oxygen desaturation). This finding could explain the more severe disruption of the sleep architecture among the obese women when compared with the obese men.

The difference in the sleep profile between women and men could explain the difference in terms of reported symptoms.[18–20] In fact OSA among women is associated with uncommon and atypical symptoms (like fatigue, tension, depression and insomnia) while men with OSA report more frequently daytime sleepiness.[18,19] The misunderstanding of less common and more atypical symptoms has been considered the most important reason for under recognition, misdiagnosis or delayed diagnosis of OSA among women.

In our sample the women had lower AHI during N-REM sleep, but during REM sleep there was no statistically significant difference. These findings are consistent with O'Connor's work.[9] In addition our data confirm that OSA among women is usually milder and, in more than 60%, is REM or supine dependent, while among men this percentage is lower.

The reason for the higher prevalence and severity of OSA among men is only partially known,[21] but most likely it reflects gender differences in the structure and the function of upper airways. Although no study examined gender differences in airway sizes among obese men and women with and without OSA, it is known that men have a greater tendency to a fat distribution resulting in a larger neck circumference even if this fact, as Dancey demonstrated,[22] could explain only in part the increased prevalence of OSA among men.[23] In part the gender difference in OSA prevalence and in the distribution of the respiratory events would result from differences in upper airway muscle function during the different stages of sleep. In fact, during wakefulness women have greater genioglossus activity,[24] and the persistence of this difference during N-REM sleep, could prevent the upper airway collapse. This protective mechanism disappears[25] with the transition to REM sleep and could explain the high prevalence of REM OSA among women.

Another interesting result of our study is the analysis of sex influence on duration, severity, and specific pattern of the respiratory events. In literature there are few data on this subject. In any case our results are consistent with Leech et al.[26] and, more recently, with Ware et al.[10] who found that women have hypopnoeas rather than evident apneas in comparison with men and that among women the duration and the severity of events are lower. As suggested by Jordan, between men and women there would be not only a difference of upper airway collapsibility, but also a difference in terms of central and peripheral stimuli causing the end of apnea events.[27]

Finally in this study we found nocturnal hypoventilation in 36% of severely obese men with OSA with a higher, but not statistically significant, prevalence of NHP in comparison with women. These findings confirm our previous data obtained in a population of obese with and without OSA [8] and, although the diagnostic criteria of this trouble are still controversial,[14] these are the first studies in this field to our knowledge.

In conclusion, severely obese women with OSA, despite a milder OSA, present greater disturbances of the sleep architecture with a more severe sleep disruption in comparison with men matched by age and weight.

More than 60% of OSA among severely obese women is related to the REM stage and the supine position. The severity of the respiratory events is greater among men while women present a greater proportion of hypopneas than evident apneas.

References

1. Guilleminault C, Van den Hoed, Miler MM. Clinical overview of the sleep apnea syndrome. In: Guilleminault C, Dement WC, editors. *Sleep apnea syndromes*. New York: Alan R. Liss: Inc.; 1978. p. 1–3.
2. Guilleminault C, Quera-Salva MA, Partinen M, Jamieson A. Women and obstructive sleep apnoea syndrome. *Chest* 1988;**93**(1):104–9.
3. Block AJ. Sleep apnea, hypopnea and oxygen desaturation in normal subjects. A strong male predominance. *N Engl J Med* 1979;**300**(10):513–7.
4. Hoffstein V, Szalai P. Predictive value of clinical features in diagnosing obstructive sleep apnea. *Sleep* 1993;**16**(2): 118–22.
5. Young T, Hutton R, Finn L, Salfan B, Palta M. The gender bias in sleep apnea diagnosis. Are women missed because they have different symptoms? *Arch Intern Med* 1996;**156**: 2445–51.
6. Redline S, Kunp K, Tishler P, Browner I, Ferrette V. Gender differences in sleep disordered breathing in a community-based sample. *Am J Respir Crit Care Med* 1994;**149**: 722–6.
7. Bixler E, Vgontzas A, Lin HM, Have TT, Rein J, Vela-Bueno A, Kales A. Prevalence of sleep disordered breathing in women. *Effect of gender. Am J Respir Crit care Med* 2001;**163**: 608–13.
8. Resta O, Foschino-Barbaro MP, Legari G, Talamo S, Bonfitto P, Palumbo A, Minenna A, Giorgino R, De Pergola G. Sleep-related breathing disorders, loud snoring and excessive daytime sleepiness in obese subjects. *Int J Obesity* 2001; **25**:669–75.
9. O'Connor C, Thornley KS, Hanly P. Gender differences in the polysomnographic features of obstructive sleep apnea. *Am J Respir Crit Care Med* 2000;**161**:1465–72.
10. Ware JC, McBrayer RH, Scott JA. Influence of sex and age on duration and frequency of sleep apnea events. *Sleep* 2000;**23**(2):165–70.
11. Johns M. Rethinking the assessment of sleepiness. *Sleep Med Rev* 1998;**2**:3–15.
12. Rechtchaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep stage of human subjects. NIH publication no: 204. Washington, DC: US Government Printing Office; 1968.
13. Kopelman PG. Sleep apnoea and hypoventilation in obesity. *Int J Obes Relat Metab Disord* 1992;**16**(Suppl 2):S37–42.
14. Piper AJ, Sullivan CE. Pressure support ventilation. (Letter to the Editor). *Chest* 1995;**107**:591.
15. Vgontzas AN, Bixler EO, Tan TL, Kantner D, Martin LF, Kales A. Obesity without sleep apnea is associated with daytime sleepiness. *Arch Intern Med* 1998;**158**:1333–7.
16. Resta O, Foschino-Barbaro MP, Bonfitto P, Giliberti T, Pedalo A, Panaciulli N, De Pergola G. Low sleep quality and daytime sleepiness in obese patients without obstructive sleep apnoea syndrome. *J Intern Med* 2003;**253**:536–43.
17. Guilleminault C, Stoohs R, Kim Y, Chervin R, Black J, Clerk A. Upper airway sleep-disordered breathing in women. *Ann Intern Med* 1995;**122**:493–501.
18. Ambrogetti A, Olson LG, Saunders NA. Differences in symptoms of men and women with obstructive sleep apnea. *Aust N Z J Med* 1991;**21**:863–6.
19. Pillar G, Lavie P. Psychiatric symptoms in sleep apnea syndrome: effects of gender and respiratory disturbance index. *Chest* 1998;**114**(3):697–703.
20. Larsson LG, Lindberg A, Franklin KA, Lundback B. Gender differences in symptoms related to sleep apnea in a general population and in relation to referral to sleep clinic. *Chest* 2003;**124**:204–11.
21. Kapsimalis F, Kryger MH. Gender and obstructive sleep apnea syndrome, part 1: Clinical features. *Sleep* 2002;**25**(4): 412–8.
22. Dancey DR, Hanly PJ, Soong C, Lee B, Shepard J, Hoffstein V. Gender differences in sleep apnea. *Chest* 2003;**123**: 1544–50.
23. Millman RP, Carlisle CC, McGarvey ST, Eveloff SE, Levinson PD. Body fat distribution and sleep apnea severity in women. *Chest* 1995;**107**:362–6.
24. Popovic RM, White D. Influence of gender on waking genioglossal electromyogram and upper airway resistance. *Am J Respir Crit Care Med* 1995;**152**:725–31.
25. Trinder J, Kay A, Kleiman J, Dunai J. Gender differences in airway resistance during sleep. *J Appl Physiol* 1997;**83**: 1986–97.
26. Leech JA, Onal E, Dulberg C, Lopata MA. A comparison of men and women with occlusive sleep apnea syndrome. *Chest* 1988;**94**:983–8.
27. Jordan AS, Mcevoy RD. Gender difference in sleep apnea: epidemiology, clinical presentation, and pathogenic mechanism. *Sleep Med Rev* 2003;**7**(5):377–89.