High Hypopnea/Apnea Ratio (HAR) in Extreme Obesity

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Study Objectives: The study was performed to evaluate the hypothesis that the extremely obese manifest sleep disordered breathing with a preponderance of hypopneas and relative paucity of obstructive apneas.

Methods: Retrospective review of 90 adults with obstructive sleep apnea-hypopnea syndrome (OSAHS) matched for age and gender, comparing two groups, Group A: body mass index (BMI) < 35, Group B: BMI ≥ 45. Exclusion criteria: age < 18 years, pregnancy, ≥ 5 central apneas/hour, BMI ≥ 35 < 45.

Primary Outcome Measure: Hypopnea/apnea ratio (HAR); secondary measures: obstructive apnea-hypopnea index (AHI), obstructive and central apnea indices, hypopnea index (HI), oxygen saturation (SpO₂) nadir, end-tidal carbon dioxide tension (PetCO₂), and presence of obesity-hypoventilation syndrome (OHS). Statistical methods: *t*-test for independent samples; Mann-Whitney, linear regression with natural log transformation, and Kruskal-Wallis χ^2 . Descriptive statistics were expressed as interquartile range, median and mean ± standard deviation, *p* < 0.05 considered significant.

Results: Group A (*n* = 45): age = 50.6 ± 11.5 years, BMI = 28.9 ± 4 kg/m²; Group B (*n* = 45): age = 47.4 ± 12.7 years, BMI = 54.5 ± 8 kg/m². HAR was significantly higher in Group B (38.8 ± 50.7) than Group A (10.6 ± 16.5), *p* = 0.0006, as was HI (28.7 ± 28.6 in B vs 12.6 ± 8.4 in A, *p* = 0.0005) and AHI (35.5 ± 33.8 vs 22 ± 23, *p* = 0.03), but not apnea index. HAR was significantly higher in Group B regardless of race, gender, or presence of OHS. The BMI was the only significant predictor of HAR (adjusted *r*² = 0.138; *p* = 0.002) in a linear regression model with natural log transformation of the HAR performed for age, gender, race, BMI, and PetCO₂.

Conclusion: Extremely obese patients manifest OSAHS with a preponderance of hypopneas.

Keywords: Obesity, obstructive sleep apnea, hypopnea, obesity-hypoventilation syndrome, gender differences, sleep-disordered breathing, hypopnea/apnea ratio.

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Obesity is one of the major risk factors for obstructive sleep apnea-hypopnea syndrome (OSAHS),¹ which may be defined as an apnea-hypopnea index (AHI) ≥ 5 apneas+hypopneas/hour of sleep, accompanied by symptoms of excessive sleepiness, difficulty sleeping, or non-refreshing sleep. The prevalence of obesity in the USA has increased by 33% during the last decade, with 40% of men and 55% of women aged 25 years or older being overweight or obese.² OSAHS has a higher prevalence among obese subjects than among the general population.³ The prevalence of OSAHS (AHI ≥ 15) in obese (body mass index [BMI] ≥ 32-59 kg/m²) adults is 32%⁴ and is significantly higher in men with morbid obesity (BMI ≥ 39 kg/m²) with 40% having an apnea index > 20 apneas/hour.⁵ The prevalence of OSAHS among hospitalized patients has been reported to be 60% in the morbidly obese.⁶ Complete upper airway collapsibility is generally expected to occur in morbidly obese subjects with sleep disordered breathing, resulting in both apneas and hypopneas. However, different mechanisms may be involved in the pathophysiology of apneas with static upper airway obstruction in contrast to hypopneas with dynamic upper airway obstruction.⁷ Some patients have a distinct pattern of sleep disordered breathing characterized predominantly by hypopneas with a paucity of apneas. Based on the above and as a result of observations with nocturnal polysomnography (NPSG), we hypothesized that extremely obese patients manifest OSAHS with an unusual preponderance of hypopneas and

BRIEF SUMMARY

Current Knowledge/Study Rationale: Different pathophysiological mechanisms may underlie the generation of apneas (static obstruction) and hypopneas (dynamic obstruction). These different mechanisms appear to be reflected in those with extreme obesity (BMI ≥ 45 kg/m²), who exhibit sleep disordered breathing with very high numbers of hypopneas and relatively few apneas.

Study Impact: This study confirms the high hypopnea/apnea ratio (HAR) in extremely obese subjects with obstructive sleep apnea. This is a consequence of very high BMI and is independent of gender, race or the presence of obesity-hypoventilation syndrome. This supports the possibility of different mechanisms in the generation of hypopneas and apneas, and may lead to specific goal-directed therapy aimed at those with hypopnea-dominated sleep disordered breathing.

paucity of apneas, possibly based on a different pathophysiology than that of less obese subjects.

METHODS

Study Design and Methods

The objective of our study was the comparison of the hypopnea/apnea ratio (HAR) in the extremely obese (BMI ≥ 45 kg/m²) with that in a less obese (BMI < 35 kg/m²) population, matched for age and gender. After obtaining permission (HSC-MS-11-0178) from the Committee for the Protection of Human

Table 1—Baseline demographics

	Group A (BMI < 35) n = 45	Group B (BMI ≥ 45) n = 45
Gender (M:F)	24:21	20:25
Age (years)	50.6 ± 11.5	47.4 ± 12.7
Weight (lbs)	188 ± 35	347 ± 75.7
BMI (kg/m ²)	28.9 ± 4	54.5 ± 8
Smoking Hx	4	9
COPD	1	1
Caucasian	29 (64%)	15 (33%)
African American	9 (20%)	23 (51%)
Hispanic	4 (9%)	6 (13%)
Asian	2 (4%)	0 (0%)
Other/mixed	1 (2%)	1 (2%)

Subjects of the University of Texas Health Science Center at Houston, the study was conducted as a retrospective review of all adult NPSGs over an 18-month period (from June 1, 2009, to December 31, 2010) at an academic sleep disorders center accredited by the American Academy of Sleep Medicine (AASM). Among the 900 adult charts reviewed, we found 45 meeting our inclusion criteria for Group B, and then accepted the first 45 patients who were studied contemporaneously who met criteria for Group A matched for age and gender with Group B. All NPSGs were scored according to 2007 AASM guidelines⁸ by the same registered polysomnographic technologist and interpreted by a board-certified sleep specialist. The NPSGs were computerized, attended recordings (Rembrandt Manager System-Medcare, Amsterdam, Netherlands) with monitoring of EEG (C3/A2, C4/A1, Fp2/A1, Fp1/A2, O1/A2, O2/A1), EOG (right and left), chin, anterior tibialis, and intercostal EMG, ECG, body position, nasal pressure (Pn), nasal-oral thermistor, thoracic, and abdominal excursion by respiratory inductance plethysmography, oxygen saturation by pulse oximetry (SpO₂), continuous capnometry with end-tidal carbon dioxide tension (PetCO₂), and continuous audio and video recordings by means of infrared cameras. Hypopneas were scored with ≥ 30% decrease in Pn ≥ 10 sec, accompanied by ≥ 4% decrease in SpO₂. Alternative scoring of hypopneas by version 2.0.2 AASM criteria⁹ with 3% desaturation or arousal was additionally performed in 51 of the 90 subjects. Apneas were scored with ≥ 90% decrease in peak oro-nasal thermal sensor for ≥ 10 seconds. Apneas were classified as obstructive if respiratory effort continued and were classified as central if respiratory effort was absent.

The study population consisted of 90 adult patients who were diagnosed with obstructive sleep apnea with an AHI ≥ 5. The first 45 consecutive patients with BMI ≥ 45 kg/m² were categorized as Group B, and another 45 consecutive patients with BMI < 35 kg/m² matched for age and gender constituted Group A. We excluded patients below 18 years of age, patients with ≥ 5 central apneas/h, pregnant patients, and patients with BMI between ≥ 35 and < 45 kg/m². The primary outcome measure was the comparison of hypopnea/apnea ratio (HAR) in the 2 study groups, and the secondary measures were the apnea-hypopnea index (AHI), obstructive apnea index (AI), hypopnea index (HI), SpO₂ nadir, central apnea index (CAI), baseline

PetCO₂ peak PetCO₂, percentage of sleep time with PetCO₂ > 50 torr, and presence of obesity-hypoventilation syndrome (OHS), which was defined as (1) baseline awake PetCO₂ > 45 torr, (2) BMI ≥ 30 kg/m², (3) sleep disordered breathing (either obstructive sleep apnea or sleep related hypoventilation⁸ with ≥ 10 torr rise in sleep PetCO₂ over wake value), and (4) absence of other causes of hypoventilation. Data were analyzed between groups using R software for statistical computing (version 3.0.2) with the *t*-test for independent samples, the Mann Whitney test, linear regression with natural log transformation, and Kruskal-Wallis χ^2 . Our results were expressed as interquartile range, median and mean ± standard deviation (SD). The statistical level of significance was defined as *p* < 0.05.

RESULTS

Age, weight, gender, and racial data are summarized in **Table 1**. The mean BMI in Group A was 28.9 ± 4 kg/m² and in Group B was 54.5 ± 8 kg/m² (*p* < 0.0001). The primary and secondary endpoint results are summarized in **Table 2**. The HAR was significantly higher (*p* = 0.0006) in Group B (38.8 ± 50.7) than in Group A (10.6 ± 16.5), as were the AHI (35.5 ± 33.8 vs 22 ± 23, *p* = 0.03) and HI (28.7 ± 28.6 vs 12.6 ± 8.4, *p* = 0.0005), but not the AI (6.7 ± 13.6 vs 11.2 ± 23.5, *p* = 0.25), as seen in **Figures 1** and **2**. The median HAR was 3.5 for Group A and 23 for Group B, with interquartile range (IQR) of 9.27 and 43.3, respectively (*p* < 0.0001 by Kruskal-Wallis χ^2 ; *p* < 0.01 by Mann-Whitney test). The oxygen saturation (SpO₂) nadir was lower in Group B (79.1% ± 7.1% vs 83.1% ± 6.7%, *p* = 0.007). The baseline PetCO₂ was higher in Group B (43.2 ± 6.1 vs 40.7 ± 4.7, *p* = 0.04). The maximum PetCO₂ in Group B was 53.7 ± 7.5 vs 50.9 ± 5.6 in Group A (*p* = 0.052). There were no significant differences in percentage of sleep time spent with PetCO₂ > 50 torr or in CAI. As seen in **Table 2**, there were no significant differences in the sleep architecture, although the total sleep time was longer in Group A (*p* = 0.02). Specifically, there was no significant difference in REM sleep between the groups (*p* = 0.16). The amount of continuous positive airway pressure (CPAP) required to eliminate apneas and hypopneas was higher (*p* = 0.003) in Group B (13.2 ± 3.7 cm H₂O) vs Group A (10.05 ± 2.4 cm H₂O).

Among the entire 90 subjects, there was no significant difference between men and women in HAR (29.7 ± 52.4 vs 19.8 ± 22.6, *p* = 0.25). Within the extremely obese Group B, the HAR was higher in men (55.3 ± 67.9) than women (25.5 ± 25.6), but this did not meet statistical significance (*p* = 0.07). There was a significantly higher HAR in Group B than Group A for men (55.3 ± 67.9 vs 8.4 ± 16.8, *p* = 0.0067), and of borderline significance in women (25.5 ± 25.6 vs 13.1 ± 16.6, *p* = 0.054). Thus, the preponderance of hypopneas over apneas was more robust in extremely obese men than women (**Table 3**). There was no significant difference in mean BMI between men (55.1 ± 8.5 kg/m²) and women (54.1 ± 7.9 kg/m²) in Group B or Group A (29 kg/m² for both).

When racial characteristics were examined, there were more African Americans in Group B (51% vs 20%), and there was a significantly higher BMI in African Americans than Caucasians (47.8 ± 14.4 vs 37.4 ± 12.8 kg/m², *p* = 0.0015), but there were no significant differences in the HAR between Caucasians and

Table 2—Polysomnographic findings

	Group A: BMI < 35 (n = 45)	Group B: BMI ≥ 45 (n = 45)	p value
Hypopnea-apnea ratio (HAR)	10.6 ± 16.5	38.8 ± 50.7	0.0006
Apnea hypopnea index (AHI)	22 ± 23	35.5 ± 33.8	0.03
Hypopnea index (HI)	12.6 ± 8.4	28.7 ± 28.6	0.0005
Obstructive apnea index (AI)	11.2 ± 23.5	6.7 ± 13.6	0.25
Central apnea index (CAI)	0.45 ± 0.85	0.27 ± 0.66	0.265
Oxygen saturation nadir	83.1 ± 6.7	79.1 ± 7.1	0.007
Baseline PetCO ₂ (torr)	40.75 ± 4.7	43.3 ± 6.1	0.04
% sleep time PetCO ₂ > 50 torr	10.5 ± 22.5	19.2 ± 28	0.11
Peak PetCO ₂ (torr)	50.9 ± 5.6	53.7 ± 7.5	0.052
% Stage N1 sleep	9.1 ± 11.9	12.3 ± 15.5	0.32
% Stage N2 sleep	67.9 ± 14.2	69.2 ± 16.1	0.70
% Stage N3 sleep	9.5 ± 11	6.15 ± 10.2	0.17
% REM sleep	9.5 ± 11	12.7 ± 8.5	0.16
Total sleep time (h)	5.9 ± 1.2	5.2 ± 1.6	0.02
Sleep efficiency (%)	79.1 ± 14.7	74.9 ± 15	0.21

Bold type, statistically significant.

Figure 1—Apnea-hypopnea index (AHI) with composite apnea index and hypopnea index.

There were significant differences in the AHI ($p = 0.03$), hypopnea index ($p = 0.0007$) and the hypopnea/apnea ratio ($p = 0.0006$) between groups. There was no significant difference in apnea index ($p = 0.26$). BMI, body mass index.

Figure 2—Hypopnea/apnea ratio.

Hypopnea/apnea ratio (HAR) ± SEM in Group B subjects with extreme obesity (BMI ≥ 45 kg/m²) was significantly higher ($p = 0.0006$) than in those in Group A (BMI < 35 kg/m²). BMI, body mass index.

African Americans either for the whole population (21.7 ± 40.4 vs 33.4 ± 43.6 , $p = 0.235$) or within Group B (40.4 ± 61.2 vs 42.2 ± 48.1 , $p = 0.92$). The HAR was higher in Group B than Group A for all racial groups (**Table 3**), reaching statistical significance for Caucasians and African Americans. There were only 10 Hispanics (4 in Group A, 6 in Group B) and 2 Asians (both in Group A).

We also evaluated the differences in HAR based on the presence or absence of OHS in these subjects (**Table 3** and **Figure 3**). Among the 90 subjects in the study, 15 (16.7%) met criteria for OHS, 4 from Group A and 11 from Group B, with 8 males and 7 females. These consisted of 7 African Americans, 5 Caucasians, and 3 Hispanic subjects. The OHS subjects had a higher AHI (44 ± 38.8 vs 25.7 ± 26.6 , $p = 0.027$; **Figure 3**), but there was no significant difference in HAR between OHS and non-OHS subjects, even when matched for BMI. Within the more obese Group B alone, there was also no significant difference in HAR

between OHS and non-OHS subjects. The HAR was significantly higher in Group B for both the OHS (43.3 ± 52.8 vs 5.4 ± 6.2 , $p = 0.04$) and non-OHS (37.3 ± 50.7 vs 11.1 ± 17.3 , $p = 0.007$) subjects (**Table 3**). The oxygen saturation nadir was significantly lower in the OHS subjects ($76.3\% \pm 6.25\%$ vs $82.05\% \pm 7\%$, $p = 0.004$). As might be expected, subjects in the OHS group had a higher baseline (awake) PetCO₂ (50 ± 5.4 vs 40.3 ± 3.8 torr, $p < 0.0001$), higher percentage of sleep time with PetCO₂ > 50 torr ($47.8\% \pm 34.6\%$, vs $8.35\% \pm 17.5\%$, $p < 0.001$), and higher maximum PetCO₂ (61.2 ± 6.5 vs 50.65 ± 5.3 torr, $p < 0.0001$). While wake and sleep PetCO₂ were recorded on all subjects, arterial blood gases were done on 17 patients, among whom those with OHS had higher arterial carbon dioxide tension (PaCO₂) awake (54 ± 18.9 vs 40.8 ± 4.9 torr, $p < 0.05$). The only significant difference in sleep architecture was a lower percentage of REM sleep in the OHS subjects ($8.9\% \pm 9.2\%$ vs $14.2\% \pm 8.1\%$, $p = 0.036$).

Table 3—Subgroup differences in hypopnea/apnea ratio (HAR)

	n	BMI < 35, HAR ± SD	BMI ≥ 45, HAR ± SD	p value
Total	90	10.6 ± 16.5	38.8 ± 50.7	0.0006
Men	44	8.4 ± 16.8	55.3 ± 67.9	0.0067
Women	46	13.1 ± 16.6	25.5 ± 25.6	0.054
Caucasians	44	12.1 ± 18.8	40.4 ± 61.2	0.026
African Americans	32	10.85 ± 15.4	42.2 ± 48.1	0.009
Hispanics	10	5.5 ± 3.8	27.8 ± 37.7	0.21
Asians	2	3.3 ± 2.2		
OHS	15	5.4 ± 6.2	43.3 ± 52.8	0.04
Non-OHS	75	11.1 ± 17.3	37.3 ± 50.7	0.007

Figure 3—Apnea-hypopnea index (AHI) with composite apnea index and hypopnea index in obesity-hypoventilation syndrome (OHS) and non-OHS subjects.

There was no significant difference in the hypopnea/apnea ratio (HAR) between groups ($p = 0.37$), but the AHI was higher in those with OHS ($p = 0.027$).

A linear regression model with natural log transformation of the HAR was performed for age, gender, race, BMI and baseline and peak PetCO_2 . The BMI remained the only significant predictor of HAR (adjusted $r^2 = 0.138$; $p = 0.002$). We also rescored hypopneas according to the 2013 AASM Version 2.0.2 scoring criteria⁹ with 3% desaturation or arousal in 51 of these subjects: 25 in Group A and 26 in Group B. Using these scoring criteria, the HAR remained statistically higher in the extremely obese. The mean HAR was 12.99 ± 16.88 for Group A and 55.14 ± 92.64 for Group B ($p = 0.02$ with t-test). The median HAR was 7.08 for Group A and 23.67 for Group B, with IQR of 12.07 and 47.07, respectively ($p < 0.01$ by both Kruskal-Wallis χ^2 and Mann-Whitney test).

DISCUSSION

In our study, very obese patients ($\text{BMI} \geq 45 \text{ kg/m}^2$) with OSAHS, matched for age and gender with less obese ($\text{BMI} < 35 \text{ kg/m}^2$) subjects, manifested a significantly higher ratio of hypopneas to apneas (HAR). The preponderance of hypopneas over apneas may be due to different pathophysiological mechanisms of static and dynamic obstruction in the extremely obese. A

difference between static and dynamic obstruction was shown by Farre and his group using a collapsible resistor model with continuous positive airway pressure (CPAP) and different gases: air and 79% helium/21% oxygen (He- O_2 or Heliox).⁷ Using the equation $\dot{V}_{\text{max}} = (P_n - P_{\text{crit}})/R_{\text{up}}$ (where $\dot{V}_{\text{max}}$ = maximal inspiratory airflow, P_n = nasal pressure, P_{crit} = minimal intraluminal airway pressure to keep the collapsible segment open, R_{up} = upstream resistance and CPAP_{opt} = optimal CPAP, the level at which flow limitation disappears and the airway is completely open), apneas occur due to static obstruction in the absence of flow and are dependent on the P_{crit} . Hypopneas represent flow limitation due to dynamic obstruction associated with inspiratory flow and are dependent on $\text{CPAP}_{\text{opt}} - P_{\text{crit}} = R_{\text{up}}$ (i.e., the additional increase in nasal pressure required to normalize breathing). In a study on patients with OSAHS, Farre et al. were able to modify the severity of dynamic obstruction by altering the density of the breathing gases and were able to lower CPAP_{opt} and R_{up} significantly when they substituted He- O_2 for air.⁷ Substituting He- O_2 for air did not, however, change static obstruction (P_{crit}) significantly. This suggests that different mechanisms may be involved in the generation of apneas and hypopneas. There have been additional prior data that suggest that P_{crit} and R_{up} may be altered independently.¹⁰ This is consistent with our findings that a higher CPAP was required to eliminate sleep disordered breathing in the extremely obese Group B with hypopnea-dominant sleep disordered breathing.

Our findings might also be related to varying propensity toward oxygen desaturation in different weight groups with consequent effects on scoring hypopneas.^{11,12} Scoring rule changes that have been made over the years which place less emphasis on arousals and more emphasis on oxygen desaturations may lead to leaner patients with OSAHS having fewer or less severe oxygen desaturations with scorable hypopneas when compared to obese patients, presumably related to less ventilation/perfusion mismatch and higher functional residual capacity in the leaner patients, although they still present with the other cardinal features of flow reduction and arousal. This possibility is reflected in the fact that in our study the oxygen saturation nadir was significantly lower in the more obese Group B subjects. However, when we rescored the hypopneas using the 2013 AASM Version 2.0.2 scoring criteria with 3% desaturation or arousal, the higher HAR in the extremely obese remained statistically significant. This makes it unlikely that oxygen desaturation is the only determining factor, especially

since these hypopneas could be scored with only arousals even without desaturation. In addition, this does not explain the relative paucity of apneas in this group. The technology utilized in our study (intercostal EMG and impedance plethysmography) has a limited capacity to distinguish between obstructive and central hypopneas, and it is possible that some hypopneas may have been of central origin. An algorithm to assist in distinguishing central from obstructive hypopneas has been reported,¹³ and this may be of use in future studies. The fact that all had significant obstructive apnea and those with central apnea were excluded should mitigate this possibility.

The HAR did not appear to be influenced by the presence or absence of hypoventilation. The HAR findings were the same for those with and without OHS, with no significant differences, so that OHS does not appear to be a fundamental part of the pathophysiological mechanism. The differences in baseline PetCO_2 (40.75 ± 4.7 vs 43.3 ± 6.1 torr, $p = 0.04$) and maximum PetCO_2 (50.9 ± 5.6 vs 53.7 ± 7.5 torr, $p = 0.052$) between groups A and B were of borderline significance, and there was no significant difference in the percentage of sleep time with $\text{PetCO}_2 > 50$ torr. Caution must be advised regarding conclusions about OHS, however, because of the small numbers of OHS subjects in our study. The 15 OHS patients out of 90 OSAHS subjects (16.7%) in our study are consistent with the published data on OHS prevalence in obstructive sleep apnea patients. There is a calculated prevalence of 0.24% for OHS in the general population and 15.75% in patients with OSAHS based on prospective studies.¹⁴⁻¹⁷

The weight-dependent difference in HAR was more robust in men than women, and there was a trend toward higher HAR in men compared to women within the more obese Group B. Men have a higher P_{crit} than women,¹⁸ but this should render men more susceptible to apneas rather than hypopneas preferentially. Gender differences in sleep disordered breathing are not explained by ventilatory chemoresponsiveness, post-hypoxic ventilatory drive or ventilatory response to hypocapnic hypoxia.¹⁹ Men have longer pharyngeal airway length than women,²⁰ and this may lead to increased R_{up} , which might lead to increased susceptibility to dynamic obstruction with more hypopneas when the extra burden of extreme obesity is added. Our findings do not appear to be dependent on race or ethnic differences, but Asians and Hispanics were underrepresented in our population compared to Caucasians and African Americans.

The genioglossal muscle is the most important pharyngeal dilator muscle in humans, and it plays a major role in the pathogenesis of obstructive sleep apnea. There is increased genioglossal fatigability in non-obese patients with OSAHS, but genioglossal endurance in obese patients with OSAHS is indistinguishable from normal.²¹ This suggests that there may be different pathophysiological mechanisms involved in the development of OSAHS in the different weight categories. Perhaps preserved endurance of genioglossal muscle function in the extremely obese may allow more dynamic obstruction from high R_{up} without the complete collapse resulting in apnea. The retained genioglossal endurance may be an adaptation of the extremely obese to continued high R_{up} throughout the day, rather than only during sleep. In addition to adipose tissue deposition, weight gain can result in increased muscle mass in the upper airway,²² with larger percentage of muscle in the uvula in obesity.²³ This might

also cause a higher R_{up} with less effect on the P_{crit} . These presumably adaptive changes of the obese may be more pronounced and/or consistent in the extremely obese because of greater demands to maintain upper airway patency throughout the day.

Our study reinforces our hypothesis that the extremely obese ($\text{BMI} \geq 45 \text{ kg/m}^2$) have a distinctive pattern of severe sleep disordered breathing characterized by hypopneas rather than apneas. It appears to be different from the very mild sleep disordered breathing characterized by hypopneas and respiratory effort-related arousals seen in younger, leaner subjects because of its severity with high AHI and hypoxemia, yet also different from the more usual form of obstructive sleep apnea because of the relative paucity of apneas and abundance of hypopneas. The possibility of a distinctive pathophysiology of sleep disordered breathing in these extremely obese patients remains to be further explored. If these findings are confirmed, alternative therapeutic modalities might be developed to address this form of sleep disordered breathing.

REFERENCES

1. Malhotra A, White DP. Obstructive sleep apnoea. *Lancet* 2002;360:237-45.
2. Ogden CL, Carroll MD, Curtin LR, et al. Prevalence of overweight and obesity in the United States 1999-2004. *JAMA* 2006;295:1549-55.
3. Rajala R, Partinen M, Sane T, et al. Obstructive sleep apnea syndrome in morbidly obese patients. *J Intern Med* 1991;230:125-9.
4. Young T, Shahar E, Nieto FJ, et al. Predictors of sleep-disordered breathing in community-dwelling adults; the Sleep Heart Health Study. *Arch Intern Med* 2002;162:893-900.
5. Vgontzas AN, Tan TL, Bixler EO, Martin LF, Shubert D, Kales A. Sleep apnea and sleep disruption in obese patients. *Arch Intern Med* 1994;154:1705-11.
6. Palla P, Digiorgio M, Carpena N, et al. Sleep apnea in morbidly obese patients: prevalence and clinical predictivity. *Respiration* 2009;78:134-40.
7. Farre R, Rigau J, Montserrat JM, Buscemi L, Ballester E, Navajas D. Static and dynamic upper airway obstruction in sleep apnea: role of the breathing gas properties. *Am J Resp Crit Care Med* 2003;168:659-63.
8. Iber C, Ancoli-Israel S, Chesson A, Quan SF. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. Westchester, IL: American Academy of Sleep Medicine, 2007.
9. Berry RB, Brooks R, Gamaldo CE, et al. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. Version 2.0.2. www.aasmnet.org. Darien, IL: American Academy of Sleep Medicine, 2013.
10. Deebajah I, Demirovic F, Tarbichi A, Bard MS. Effect of long term facilitation on critical closing pressure in patients with sleep apnea. *Am J Respir Crit Care Med* 2002;165:A39.
11. Guilleminault C, Hagen CC, Huynh NT. Comparison of hypopnea definitions in lean patients with known obstructive sleep apnea hypopnea syndrome (OSAHS). *Sleep Breath* 2009;13:341-7.
12. Peppard PE, Ward NR, Morrell MJ. The impact of obesity on oxygen desaturation during sleep-disordered breathing. *Am J Respir Crit Care Med* 2009;180:788-93.
13. Randerath WJ, Trembl M, Priegnitz C, Stieglitz S, Hagmeyer L, Morgenstern C. Evaluation of a non-invasive algorithm for differentiation of obstructive and central hypopneas. *Sleep* 2013;36:363-8.
14. Kessler R, Chaouat A, Schinkewitch P, et al. The obesity-hypoventilation syndrome revisited: a prospective study of 34 consecutive cases. *Chest* 2001;120:369-376.
15. Resta O, Foschino Barbaro MP, Bonfitto P, et al. Hypercapnia in obstructive sleep apnoea syndrome. *Neth J Med* 2000;56:215-22.
16. Mokhlesi B, Tulaimat A, Faibussowitsch I, Wang Y, Evans AT. Obesity hypoventilation syndrome: prevalence and predictors in patients with obstructive sleep apnea. *Sleep Breath* 2007;11:117-24.
17. Trakada GP, Steiropoulos P, Nena E, Constantinidis TC, Bouros D. Prevalence and clinical characteristics of obesity hypoventilation syndrome among individuals reporting sleep-related breathing symptoms in northern Greece. *Sleep Breath* 2010;14:381-6.

18. Jordan AS, Wellman A, Edwards JK, Schory K, Dover L, MacDonal M. Respiratory control stability and upper airway collapsibility in men and women with obstructive sleep apnea. *J Appl Physiol* 2005;99:2020-7.
19. Tarbichi AGS, Rowley JA, Shkroukani MA, Mahadevan K, Badr MS. Lack of gender difference in ventilatory chemoresponsiveness and post-hypoxic ventilatory drive. *Respir Physiol Neurobiol* 2003;137:41-50.
20. Malholtra A, Huang Y, Fogel RB, et al. The male predisposition to pharyngeal collapse: importance of airway length. *Am J Respir Crit Care Med* 2002;166:1388-95.
21. Carrera M, Barbe F, Sauleda J, et al. Effects of obesity upon genioglossus structure and function in obstructive sleep apnea. *Eur Respir J* 2004;23:425-9.
22. Schwab RJ, Remmers JE, Kuna ST. Anatomy and physiology of upper airway obstruction. In Kryger MH, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine*. 5th ed. St. Louis, MO: Elsevier/Saunders, 2011:1162.
23. Stauffer JL, Buick MK, Bixler EO, Sharkey FE, Abt AB, Manders EK. Morphology of the uvula in obstructive sleep apnea. *Am Rev Respir Dis* 1989;140:724-8.

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