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Role of body mass index (BMI) on the oxygen saturation and apneic spells in obstructive sleep apnea (OSA)

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Data from the sleep disorders institute (SDI) showed that subjects with similar apnea hypopnea index (AHI) but different body mass index (BMI) had no difference in oxygen saturation in rapid eye movement (REM) or non-rapid eye movement (NREM) sleep. Only 6 pairs of subjects were evaluated in the study and they were not age-matched. The objective of this study was to evaluate, in age-matched subjects, if there were any differences in oxygen saturation and duration of apenic spells in subjects with similar AHI but different BMI. Ninety eight (98) subjects paired for AHI within one event/hour and BMI differences of 5 and above were grouped in 9 groups. Subjects belonged mainly to normal, mild and moderate AHI groups. Diagnostic nocturnal polysomnography (NPSG) inclusion criteria were normal REM sleep and total sleep time of 5 h. Oxygen saturation was continuously assessed throughout the nocturnal polysomnography (NPSG), and was calibrated for each NPSG study, and was visually identified by sleep physician and artifacts were eliminated from the analyses. For all age groups, differences between matched pairs on BMI were regressed on the following factors: baseline oxygen saturation, lowest oxygen saturation, average oxygen saturation difference between pairs, apnea maximum and mean durations. Mean BMI differences between age- and AHI-matched pairs were 10.2 ± 5.7 (range 5.0 to 29.0). Stepwise regression indicated that BMI differences between pairs best predicted minimum oxygen saturation ($p = 0.008$, 1-tail). One-way analysis of variance (ANOVA) showed that age differences contributed to the robust finding regarding how BMI differences predicted lowest oxygen saturation. Using a very conservative Bonferroni correction for multiple comparisons, lowest saturation differed only between lower age groups [group 1 < group 2 ($p = 0.3$) < group 3 ($p = 0.001$) and < group 4 ($p = 0.02$)]. Difference in BMI (when AHI is matched), especially between ages 25 and 44 years old, predicts differences in minimum oxygen saturation. Caution is warranted as severe apneics were not evaluated in small sample sizes in subject older than 40.

Key words: Obstructive sleep apnea (OSA), apnea hypopnea index (AHI), body mass index (BMI), nocturnal polysomnography (NPSG), oxygen saturation, sleep disorder.

INTRODUCTION

Sleep disordered breathing comprises a spectrum of conditions ranging from simple snoring and upper airway resistance syndrome to obstructive sleep apnea (OSA). OSA is a severe form of sleep-related disorders.

OSA is a chronic disease characterized by sleep apneas, hypopneas, daytime sleepiness, fatigue and disturbed sleep. It is usually diagnosed using a full night in-lab polysomnography study [NPSG] (gold standard), though split night and portable in-home monitoring options are also available. The Apnea-hypopnea index (AHI) and respiratory disturbance index (RDI) are calculated from the NPSG.

AHI is the total number of complete cessations (apnea) and partial obstructions (hypopnea) of breathing occurring per hour of sleep. These apneas and hypopneas must last for at least 10 s and be associated with a decrease in oxygenation of the blood. RDI is the total number of events including apneas, hypopneas, and respiratory effort related arousals (RERAs) per hour of sleep. RDI is usually slightly higher than the AHI, because it also includes the frequency of RERAs.

OSA diagnostic criteria in adults (American Academy of Sleep Medicine, 2005) ≥ 15 apneas, hypopneas, or respiratory effort related arousals per hour of sleep (that is, AHI or RDI ≥15) in an asymptomatic patient with more than 75% of apneas and hypopneas being obstructive. OR ≥ 5 apneas, hypopneas, or respiratory effort related arousals per hour of sleep (that is, AHI or RDI ≥5) in a symptomatic patient with more than 75% of apneas and hypopneas being obstructive.

OSA is further classified on the basis of AHI as mild (AHI 5 to 15), moderate (AHI 15 to 30) and severe (AHI >30). Prevalence of OSA has increased tremendously in the past few decades and this is partly due to the growing of the number of obese population (Young et al., 1993). Moreover, there is evidence that prevalence of OSA increases in patients with morbid obesity (Foster et al., 2009).

In the pathophysiology of OSA in obesity, patients with OSA are able to maintain their airway while awake by increasing the upper airway muscle tone (Schwab et al., 2003); but when asleep the airway muscle tone decreases and hence they fail to maintain their airway patency. This is further complicated in obese patients, in whom the gross enlargement of pharyngeal soft tissue structures (Horner et al., 1989; Shelton et al., 1993) along with increased fatty tissue in the soft palate, uvula, tongue and mandibular structures (Schwab et al., 2003; Stauffer et al.,1989) leading to further narrowing of the airway. In addition to the airway disorder, the lung volume is also additionally affected by the reduction in tracheal tractional and pharyngeal wall tension forces (Isono, 2012). More so, obesity related reduction of leptin responsiveness further interferes with breathing via neuro-anatomical interference (Polotsky et al., 2012).

The clinical significance of identifying patients with OSA lies in the fact that it has been associated with high rates morbidity and mortality, mostly from cardiovascular causes and road traffic accidents (Marin et al., 2005).

The sleep disorders institute (SDI) study shows that subjects with similar AHI but different BMI have no difference in oxygen saturation in rapid eye movement (REM) or non-rapid eye movement (NREM) sleep. This study determines if it remains consistent once the subjects are age and BMI matched (Khan et al., 2009).

MATERIALS AND METHODS

Patient population

A retrospective study was conducted at SDI in New York City. The protocol was approved by the institutional review board (IRB) and ethics committee of the institution. Seven hundred and fifty six (756) charts were reviewed and 203 subjects who were selected met inclusion and exclusion criteria. Of these 203 patients, 98 patients were selected, based on AHI and BMI; and these 98 pairs of patients were compared. Charts were reviewed from January, 2007 to June, 2009. Patients were selected based on the following criteria [inclusion criteria]: age more than 18 years, having received a diagnosis of OSA confirmed through NPSG, total sleep time (TST) of 5 h and normal or within 90% of REM sleep]. Exclusion criteria: REM disorders, parasomnias, insomnia, current smokers or ex-smokers who quit within ≤6 months, lung surgeries [lobectomy, pneumonectomy], neuromuscular diseases, seizure disorders, chronic obstructive lung disease patients, previous cardiovasular accident or transient ischemic attacks, kyphosis, scoliosis, peripheral vascular disease patients (Raynaud's disease), interstitial lung disease (sarcoidosis, idiopathic pulmonary fibrosis) and pregnant women.

Experimental

BMI for each subject was obtained by dividing weight in kilograms by height in meters squared. Subjects were categorized by weight status based on their BMI: normal [between 20 and 24.9 kg/m^2], overweight [BMI between 25 and 29.9 kg/m^2], obese [BMI between 30 and 39.9 kg/m^2] (NIH Publication, 2000).

Polysomnography was performed using the standard method. The standard NPSG montage included measurement of the left and right anterior tibialis muscle electromyography (EMG) lead: two respiratory effort monitoring devices (RIP sensors): one on the abdomen at the navel level or below, and the other on the chest, nipple level or above; 3 chin EMG electrodes; electrocardiogram (ECG) electrodes used for modified Lead II; electroencephalogram (EEG) electrodes F3, F4, C3, C4, O1, and O2 using the international 10 - 20 system; reference electrodes at M1 (left mastoid) and M2 (right mastoid), and a ground electrode at Fpz; electrooculogram (EOG) leads with E1 (left eye) 1 cm below the left outer canthus and E2 (right eye) 1 cm above the right outer canthus; oronasal thermal sensor and nasal air pressure transducer with vibration sensor to detect snoring; and an oximeter probe placed on the patient's finger. The pulse oximeter model used was Ohmeda 3000. Electrode impedances were checked and biocalibrations performed to ensure signal integrity and absence of artifact.

During the data collection process, body position, and snoring

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status were recorded. Oxygen saturation was continuously assessed throughout the NPSG. Unusual movements and behaviors were documented by the technician. In this study, oxygen saturation was continuously assessed throughout the NPSG, and was calibrated for each NPSG study and was visually identified by the sleep physician and artifacts were eliminated from the analyses. Periodic impedance checks were made and documented to ensure signal strength and integrity. Sleep stages were classified according to the American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications (AASM Manual for the Scoring of Sleep and Associated Events, 2007).

Airflow was measured using a nasal cannula connected to a pressure transducer, and peripheral oxygen saturation (SpO^2) was measured using an Ohmeda 3000 pulse oximeter. Apnea was defined as a reduction in airflow to ≤10% of the baseline value for 10 s or more, and hypopnea was defined as reductions in airflow of ≥30% accompanied by awakening and a ≥4% drop in SpO^2. (AASM Manual for the Scoring of Sleep and Associated Events, 2007). AHI was calculated by dividing the total number of apnea-hypopnea episodes by the number of hours of sleep. Based on the AHI, OSA severity was classified as mild [<15], moderate [15 to 30] or severe [>30] (The Report of American Academy of Sleep Medicine Task Force, 1999).

Statistical analysis

Data were stored and analyzed using the program Statistical Package for Social Sciences (version number 20). Results are expressed as the number of cases, percentages, range, mean and standard deviation. Student's t-test was used for data analysis. Stepwise regression was used to evaluate for BMI differences between matched pairs. Analysis of variance (ANOVA) was used to analyze the differences between the group means for statistical significance. For comparison between multiple groups, Bonferroni correction method was used. Values of $p < 0.05$ were considered statistically significant.

RESULTS

A total of 98 subject pairs were reviewed; data are shown in Table 1. They were divided into 9 groups based on their age, at intervals of 5 years [group 1: 25 to 29 years, group 2: 30 to 34 years, group 3: 35 to 39 years, group 4: 40 to 44 years, group 5: 45 to 49 years, group 6: 50 to 54 years, group 7: 55 to 59 years, group 8: 60 to 64 years, group 9: >65 years].

Of the 98 pairs that were compared, there were 62 men and 44 patients were non-Caucasians. Each of the age groups were matched for AHI. The mean difference in BMI between age- and AHI- matched pairs were 10.2 ± 5.7 (range 5.0 to 29.0); data are shown in Table 2. Stepwise regression analysis indicated that BMI differences between the age and AHI matched pairs best predicted minimum oxygen saturation (p=0.008). One-way ANOVA showed that age differences contributed to how the BMI differences predicted lowest oxygen saturation. On further analysis using Bonferroni correction for multiple comparisons, the lowest saturation differed only between lower age groups [group 1 < group2 (p = 0.3) < group 3 (p = 0.001) and < group 4 (p = 0.02)]. These differences were not apparent at group 5 and above [age 45 and above].

DISCUSSION

In this retrospective study with OSA subjects, the effects of BMI on the disease were compared. This study suggests an inverse association between BMI and minimum nocturnal oxygen saturation in OSA patients. But the contribution of BMI (when age and AHI were matched) in predicting minimum oxygen saturation was seen only in subjects with OSA under 45 years of age. The BMI did not predict degree of nocturnal oxygen desaturation in OSA patients > 45 years.

Katz et al. (1990) noted that external neck circumference correlated with OSA but observed the need for further work to establish a strong co-relation with BMI. In a study by Knorst et al. (2008), the degree of obesity [assessed by BMI] had the greatest impact on the severity of OSA [AHI, percentage of total sleep time spent in apnea and minimum SPO^2]. This study not only confirms the findings of the aforementioned study, but also pointed out a lesser-known contribution of age to this effect. In other words, the directly proportional effect of BMI on worsening nocturnal oxygen desaturation on OSA subjects is limited to young subjects only [< 45 years of age]. In this study, groups were matched for age, AHI and other baseline characteristics; thus ensuring no confounding factors. Though the reason for this observation is not fully established, there is a possibility of craniofacial abnormality in the young adults being more severe (Johns et al., 1998). These anatomical abnormalities can become more pronounced with obesity. It can be hypothesized that with aging and associated changes in pharyngeal anatomy in the elderly, the degree of desaturation (thus the severity of OSA) can be low as compared to the young. Whether other age related factors in subjects > 45 years are contributing and compounding, the effect needs to be further studied.

Previous study noted as basis of our study: Dreher et al., 2012, A German study showed that in OSA patients with an equal AHI, the obese have fewer apneas, but more hypopneas, and a lower minimal oxygen saturation than normal weighted patients. Thirty two (32) normal weighted OSA patients (BMI ≤ 25 kg/m^2) were compared with 32 obese patients (BMI >25 kg/m^2). The patients had almost equivalent AHI. The mean AHI in both groups was 27.9 (BMI ≤ 25 kg/m^2) and 28.0 (BMI ≥ 25 kg/m^2), respectively. Sleep efficiency, relative percentages of sleep phases S1-S4 and REM, mean, minimal and maximal heart rates were not significantly different in statistic analysis in normal weighted and obese patients. Normal weighted OSA patients had a higher apnea index (11.4 versus 6.4, p=0.040), a higher minimal oxygen saturation (81.3% versus 71.7, p = 0.003) and mean (94.9% vs. 92.8%, p=0.007) oxygen saturation, but a

Table 1. Ninety-eight pairs of subjects' BMI, AHI and saturation difference.

Age (Years)	pairs	BMI difference	AHI difference	Saturation baseline difference	Saturation minimum difference	Saturation average difference	AHI maximum difference	AHI average difference
	1	6.0	0.8	2.0	6.0	4.0	29.6	2.5
	2	5.0	0.7	1.0	6.0	7.0	11.9	11.9
	3	5.0	0.4	1.0	9.0	8	5.9	5.2
	4	21.0	0.1	0.0	16.0	16	13.1	4.9
	5	5.0	1.0	3.0	5.0	2	7	2.6
25-29	6	16.0	1.0	1.0	22.0	21	6.5	5.5
	7	6.0	0.2	1.0	1.0	0	19.6	17.4
	8	16.0	0.9	3.0	21.0	18	6.1	2.3
	9	17.0	0.0	0.0	21.0	21	14.6	6.5
	10	6.0	0.1	3.0	0.0	3	19.2	14.2
	11	7.0	0.8	0.0	0.0	0	27.7	18.4
	12	13.0	0.2	1.0	23.0	24	35.3	12.8
	13	11.0	0.4	1.0	0.0	1	51.5	15.9
	14	22.0	0.6	5.0	7.0	2	18.8	8
	15	16.0	0.6	3.0	1.0	2	7.6	5.7
	16	10.0	0.4	4.0	9.0	5	4.3	1.7
	17	16.0	0.2	3.0	7.0	4	17.7	4.3
	18	8.0	0.9	0.0	7.0	7	8.9	2.2
	19	17.0	0.1	1.0	4.7	3.7	12.6	5.1
	20	17.0	0.6	0.0	0.0	0	4	1.1
	21	10.0	0.4	0.0	6.0	6	25.1	6.4
	22	7.0	0.2	2.0	1.0	1	19.9	18.2
	23	6.0	0.6	6.0	0.0	6	10.2	9
	24	13.0	0.7	1.0	4.0	5	25.1	22
	25	5.0	0.9	3.0	2.0	1	14.4	12.4
	26	24.0	0.5	1.0	6.0	7	2.4	2
	27	11.0	0.8	1.0	2.0	1	14.4	12.4
	28	5.0	1.0	2.0	2.0	4	14.4	12.4
	29	25.0	0.8	1.0	1.0	2	0.1	2.2
	30	5.0	0.9	6.0	1.0	5	2	1.2
	31	12.0	1.0	1.0	3.0	4	16.9	14.2
	32	29.0	0.1	2.0	8.0	6	16.8	14.4
	33	7.0	0.0	3.0	2.0	1	14.8	14.3
	34	6.0	0.0	2.0	6.0	4	11.2	2.3
30-34	35	12.0	1.0	1.0	2.0	3	14.5	6.3
	36	6.0	0.4	2.0	0.0	2	2.1	3.7
	37	7.0	0.3	1.0	10.7	10	12.5	1.3
	38	7.0	1.0	0.0	6.0	6	21.1	5.3
	39	5.0	0.0	0.0	5.0	5	21.1	15.6
	40	22.0	0.1	1.0	6.0	7	2	0.1
	41	29.0	0.0	1.0	8.0	7	16.8	14.4
	42	6.0	1.0	1.0	8.0	7	2.8	4
	43	7.0	0.1	5.0	4.0	1	14.9	13
	44	7.0	0.1	2.0	2.0	4	14.8	14.3
	45	6.0	0.6	1.0	2.0	1	12.9	2.6
	46	19.0	0.2	2.0	5.0	3	36.1	13.4
	47	11.0	0.3	0.0	2.0	1	49.4	5
	48	12.0	0.7	1.0	3.0	2	2	0.2
	49	11.0	0.8	2.0	1.0	3	2.4	1.8
	50	5.0	0.2	1.0	2.0	1	1.2	2.6
	51	15.0	0.3	0.0	0.0	0	6	0.9
	52	6.0	0.2	1.0	5.0	5	10.9	10.8
	53	9.0	1.0	1.0	3.0	2	22	22
	54	6.0	0.1	1.0	4.0	5	1.9	4.1
	55	7.0	0.9	0.0	1.0	1	0.6	2.4
	56	12.0	0.6	2.0	3.0	1	2	2.2
	57	6.0	0.5	1.0	2.0	3	16.6	2.1
	58	16.0	0.5	0.0	1.0	1	1.3	1.3

Table 1. Cont'd

	59	5.0	0.5	2.0	3.0	1	1.2	2
	60	6.0	1.0	1.0	1.0	0	14.3	14.3
	61	6.0	0.6	2.0	3.0	1	14.3	14.3
	62	6.0	0.1	0.0	2.0	8	46.8	22.9
	63	7.0	0.8	3.0	5.0	8	2.4	0.5
	64	17.0	0.5	1.0	8.0	7	3.4	2
	65	11.0	0.4	2.0	7.0	9	7.2	4
	66	21.0	0.0	0.0	5.0	5	15.9	11.1
	67	12.0	0.9	0.0	1.0	1	28	21.1
	68	15.0	0.6	2.0	1.0	1	8.2	6.7
	69	9.0	0.9	0.0	4.0	4	11.9	11.2
	70	6.0	0.6	2.0	6.0	4	8.1	2.2
	71	12.0	0.4	1.0	2.0	1	0	0
40-44	72	5.0	0.9	1.0	0.0	1	6.1	3.9
	73	7.0	0.9	0.0	1.3	4.3	31.6	25.5
	74	5.0	0.8	1.0	3.0	2	17.8	17.8
	75	7.0	0.8	0.0	1.0	1	3.4	2.9
	76	5.0	0.7	1.0	2.0	1	19.9	15
45-49	77	11.0	0.9	4.0	3.0	0.7	0.4	2.1
	78	13.0	0.6	2.0	1.0	3	2.2	4.4
	79	8.0	0.7	0.0	6.0	6	2.2	5.1
	80	6.0	1.0	0.0	2.0	2	16.5	10
	81	9.0	0.6	1.0	8.0	9	9.5	4
50-54	82	6.0	0.4	1.0	4.0	10	3.9	0.1
	83	8.0	0.5	4.0	3.0	7	20.8	1.3
	84	13.0	0.3	2.0	2.0	0	5.4	3.9
	85	7.0	0.1	1.0	2.0	3	19.3	10.9
	86	5.0	0.2	2.0	5.0	7	15.4	9.9
50-59	87	10.0	0.9	3.0	5.0	8	0.9	5.9
	88	6.0	0.3	1.0	2.0	7	15.9	12.5
	89	9.0	0.7	2.0	2.0	4	8.5	9.4
	90	9.0	0.8	1.0	7.0	2	0.7	1.4
60-64	91	5.0	0.2	2.0	1.0	3	23	0.2
	92	5.0	0.9	2.0	8.0	6	9	5.2
	93	8.0	1.0	0.0	4.0	4	18.3	1.9
	94	5.0	0.3	4.0	6.0	2	13.2	11.9
65+	95	11.0	0.5	2.0	7.0	9	1.5	5.6
	96	7.0	0.9	2.0	2.0	0	11.1	6.8
	97	16.0	0.4	0.0	1.0	1	9.6	4.8
	98	7.0	0.1	1.0	1.0	2	3.8	0.1

smaller hypopnea index (16.5 vs. 21.6, p = 0.047) and a lower index of snoring (175.2 versus 394.1, p < 0.001) than their obese counterparts.

The major limitations of this study were the lack of control group, severe apneics and absence of patients with BMI > 40 who fit the inclusion criteria. Also, the sample size for patients more than 40 years of age was small.

Previous studies have emphasized the need for OSA screening in subjects with obesity and the metabolic syndrome. It is important to keep in mind that traditional risk factors for OSA such as excessive daytime somnolence may not be present in a significant proportion of the patients (Resta et al., 2001). Although, there is a strong correlation between obesity and OSA, it is not clear why a significant proportion of obese patients, including severe forms of obesity, do not develop OSA. Comprehensive genetic studies with anatomic and functional upper airway assessment should be undertaken to elucidate protective mechanisms (Patel et al., 2008). Researchers have pointed out previously that though there is clear interaction between obesity and

Table 2. Patient groups according to age range and corresponding AHI range.

Group No.	No. of patients	Age range	Mean AHI ± SD	AHI range
1	11	25 - 29	4.1 ± 2.3	0.2 − 10.2
2	34	30 - 34	8.8 ± 8.7	1.1 − 35.9
3	26	35 - 39	5.0 ± 3.6	0.6 − 16.6
4	5	40 - 44	5.3 ± 3.8	1.7 − 12.6
5	5	45 - 49	12.3 ± 2.5	8.4 − 16.4
6	5	50 - 54	13.0 ± 0.2	12.8 − 13.3
7	4	55 - 59	7.7 ± 2.4	5.7 − 11.9
8	4	60 - 64	14.8 ± 11.4	3.5 − 25.8
9	4	65+	6.7 ± 3.8	4.2 − 13.1

OSA there are several gaps in the present knowledge (Ong et al., 2013).

Conclusion

In conclusion, this study shows that oxygen desaturation during sleep is correlated with BMI in younger subjects (< 45 years) when they are matched for AHI.

There is need for more studies to further explore the correlation of BMI in the elderly population (> 45 years).

It is of clinical significance both from a diagnostic and management perspective to keep in mind that BMI plays a more important role in the severity of OSA for younger population and one should be cautious when interpreting the significance of BMI in the elderly population.

Conflict of interest

Authors have none to declare.

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