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Obesity - Important Risk Factor for Sleep Apnea Syndrome

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Abstract
Sleep apnea syndrome is a common pathology with negative consequences on cardiovascular and metabolic diseases. The relationship between obesity and OSAS is complex, multifactorial and bidirectional; that leads to a negative mutual influence of the two pathologies. The main purpose of this study is to evaluate the risk associated with obesity and the occurrence of the apnea phenomenon, as well as, to compare the various polysomnographic parameters and to compare them with obesity. 100 patients took part to this study. 60 % of the patients were diagnosed with OSAS. 71 % of the patients had varying degrees of obesity. Significant statistic differences were revealed between: the Mean variation of the BMI in patients with and without apnea (T Test p= 0,007 < 0,05); the dorsal AHI Mean of the non-obese group as against to the dorsal AHI Mean of the obese group (T Test p= 0,002), the AHI Mean in other positions of the non-obese group as against to the AHI Mean in other positions of the obese group (T Test p= 0,000) and the Mean of the arousal index of the non-obese group as against to the Mean of the arousal index of the obese group (T Test p= 0,009). The current study revealed that the arousals associated with breathing events and the position during sleep, especially in obese patients, worsen the consequences of OSAS.

Keywords: apnea; obstructive; arousal; obesity.

Introduction

The obstructive sleep apnea syndrome (OSAS) is an ordinary disease which has negative medical and public health consequences [1]. This is a serious pathology of sleep, with an increased prevalence in society, which can damage the quality of life and can cause car accidents, hypertension, cardiovascular and cerebrovascular diseases, insulin resistance, and dyslipidemia [2]. Among the risk factors of this pathology may be numbered: sex (especially males), age (especially the elderly) [3], smoking [4, 5], alcohol [6], the craniofacial morphology [3], the genetic predisposition, the shape of the upper airway, the hormonal influence and the phenotype APOE420 [7].

The obesity, a chronic condition, characterized by the excess of the adipose tissue, regarded as a metabolic dysfunction and the inflammation of the adipose tissue, able to generate and maintain inflammation at the clinical level, constituting the unifying hypothesis of the metabolic alterations

of obesity and the atherosclerotic vascular pathology, is associated with many different comorbidities, including sleep apnea syndrome [8]. Sleep fragmentation, present in patients with OSAS, is a common cause of excessive daytime sleepiness and is considered to be a risk factor for obesity. Van Cauter and his co-workers showed a clear and direct impact of the decrease sleep time on metabolism, favoring weight gain, increased appetite and insulin resistance [9].

The prevalence of obesity is increasing in Western societies [9]. Sleep apnea syndrome (SAS) is common in obese middle-aged men [10]. The relationship between obesity and OSAS is complex, multifactorial and bidirectional leading to a mutual symptomatic worsening of the two pathologies.

Obesity is the promoter of metabolic syndrome, and the primary objective of the OSAS treatment will be to reduce weight and to maintain the new weight, along with maintaining the control of the other cardiovascular risk factors. Busetto and his co-workers discovered that reducing with 15 % the body mass index (BMI) increases substantially the pharyngeal cross-sectional area of the neck and thus decreases the severity of OSAS [8]. A moderate weight reduction, of 5 to 10% of the present weight, corresponding to approximately 30% of visceral adipose tissue, is followed by significant improvement in cardiovascular risk factors (blood pressure, lipid profile and glucose, pro-thrombotic state).

There are a multitude of risk factors involved in the occurrence of OSAS, their combination contributing to worsening the severity of sleep apnea syndrome. Therefore experts should be encouraged to systematically evaluate psychosomatic abnormalities in OSAS and vice versa.

The present study intends to: evaluate the relation between obesity and the occurrence of the apnea phenomenon; calculate the prevalence of obesity to patients who have addressed the Alps-Leman Sleep Laboratory in France; compare the severity of sleep apnea syndrome and its correlation with obesity.

Material and Method

The present study is a case – control study conducted during six months in the Sleep Laboratory of the "Alpes Léman" Hospital from France.

The criteria for inclusion were: in the present study were included patients aged between 18 and 80 years; with a total duration of sleep ≥ 180 minutes; patients with negative or positive diagnose of OSAS, but with at least one of the following pathologies associated: cardiovascular disease (hypertension, stroke, arrhythmias, coronary artery disease), respiratory diseases (chronic obstructive pulmonary disease, bronchial asthma), metabolic and hormonal diseases (dyslipidemia, diabetes, hypothyroidism), otorhinolaryngology (ORL) changes (micrognatism, retrognathia, enlargement of the tonsils / palate / uvula).

For each patient was made an individual assessment scheme, including demographic data (age, sex, height, weight), a history of pathological and polysomnographic data (type of apnea, the dorsal apnea- hypopnea index (AHI), the AHI in other positions, the arousal index). Through the ratio weight (kg) / height (m^2) was calculated the BMI. The weight levels were interpreted according to BMI, as recommended by the World Health Organization, namely: overweight: BMI = 25- 29.9 kg/m^2; obesity level 1: BMI= 30- 34.9 kg/ m^2; obesity level 2: BMI= 35- 39.9 kg/ m^2; obesity level 3: BMI ≥ 40 kg/ m^2.

The diagnosis of sleep apnea- hypopnea syndrome (SAHS) was performed using the standard method, polysomnography. This was done with the „Morpheus" polysomnograph, which had the following channels: 8 channels for electroencephalogram (EEG), 2 channels for electro- oculogram (EOG), 2 channels for electromyogram (EMG) chin and 4 channels for EMG legs, 3 channels for ECG (electrocardiogram), Pulse Oximeter, laryngeal microphone to record snoring, the respiratory flow nasal cannula, piezoelectric sensors for thoracic and abdominal respiratory movements, integrated sensor in patient unit for body position during sleep, integrated light sensor for measuring the time spent in bed. The analysis of each polysomnography was made manually using the "Rembrandt" programme. Sleep staging was divided into 30 seconds eras, and the breathing events into 4 minutes gaps according to the classification criteria of Rechtschaffen-Kales and American Academy of Sleep Medicine from 2007. The diagnosis of OSAS was given if the patient had over 5 breathing pauses/

hour of sleep or respiratory flow decreases with 30-50% for at least 10 seconds, with significant desaturation (decrease of SaO2 with 3 %) and/or associated arousal. The assessment of the severity of OSAS was established according to the international validated criteria: the mild form: AHI = 5-14/ hour of sleep, the moderate form: AHI = 15- 29/ hour of sleep, the severe form: AHI > 30/ hour of sleep.

Statistics. It was conducted a case-control study between apnea and obesity. The descriptive analysis of the individual parameters was performed and also the possible connections between them: medium on groups/ scatter / frequency diagrams (pie). To describe the qualitative variables were used: frequency tables, contingency tables, column or structure charts (pie). The comparison of the observed distribution with the theoretical one was made with the following statistical tests: Chi2 test and Fisher's accurate test. To describe the quantitative variables were used: the Mean, the standard deviation (SD), the median (Me), the interquartilic interval Q25, Q75, frequency tables, histograms and box-plot charts. In order to compare Means were applied: "t" Student test for independent samples or ANOVA variance analysis in accordance with the requirements of independence, normality plots and when these conditions were not met it was applied the Mann-Whitney or Kruschal-Wallis test for a confidence level of 95%.

Results

Based on the inclusion criteria, were included in this study 100 patients aged 18 to 80 years, in November 2012 – April 2013. Males were present in 57%, and the female in 43%.

The SAHS was diagnosed in 60% of the cases. Pure obstructive apnea was noted in 44% of patients, and the positional obstructive apnea in 11% of patients. Mild, moderate and severe SAS was found in 2%, 21% and 37% of the cases.

Regarding the type of apnea and its severity, there was a statistical difference between the group with the absence of apnea and the group with present apnea with a value of $p = 0.000 < 0.05$.

In the study group, 46 patients had a dorsal AHI lower or equal to 8, and the remaining 54 patients had a dorsal AHI over 8.4 / hour of sleep. 62 patients experienced a non-dorsal AHI ≤ 9.95 / h, and 38 patients had a non-dorsal AHI ≥ 9.96 / hour of sleep.

Figure 1 shows the statistical difference between the dorsal AHI Mean of the group without apnea compared to the dorsal AHI Mean of the group with apnea (Levene Test and T Test for independent groups with unequal variations: $p = 0.000 < 0.05$). The variations of the non-dorsal AHI Mean of the two groups of patients were unequal (Levene Test: $p=0,000 < 0,05$). There were statistical differences between AHI Mean in other positions in the group without apnea compared to AHI Mean in other positions in the group with apnea (T test for independent groups with unequal variations: $p = 0.000 < 0.05$) represented in Figure 2.

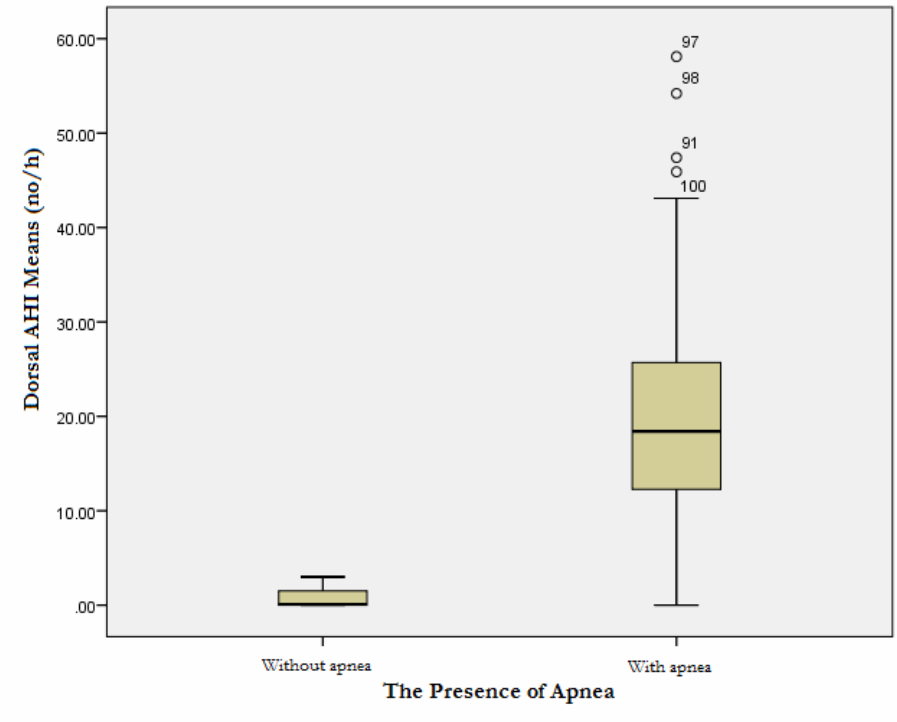

Figure 1. The comparison of the dorsal AHI Means (no/h) to patients with and without apnea.

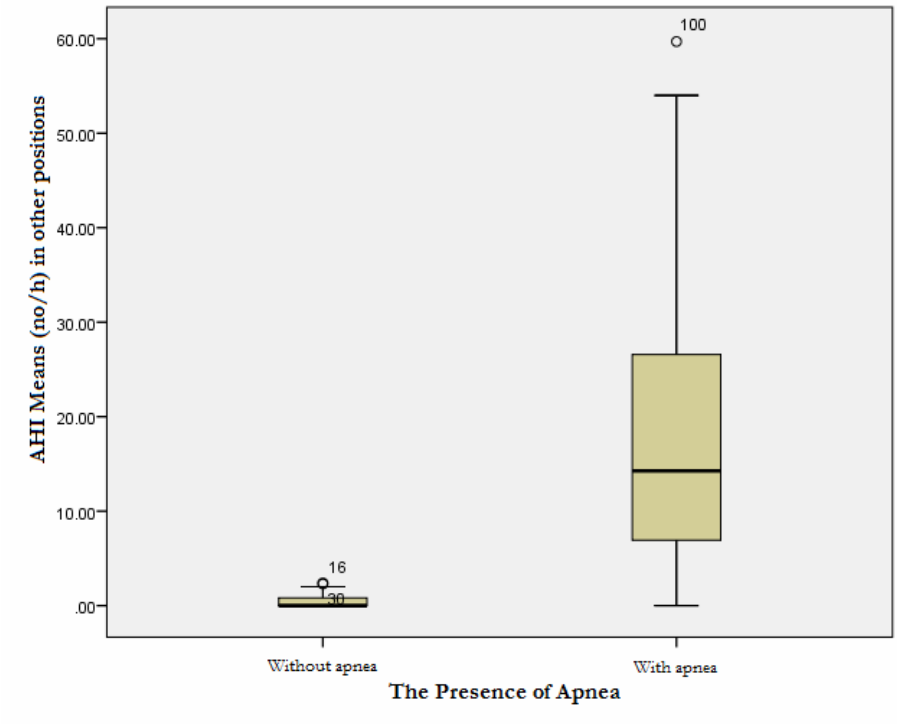

Figure 2. The Comparison of AHI Means (no/h) in other positions of the patients with and without apnea.

The arousals highlighted on EEG, that accompanied the respiratory events, were distributed as follows: 32 patients had below 10 arousals/hour of sleep, and the rest of 68 patients had over 10

arousals/hour of sleep. Of those 68 patients, only one had 78.09 arousals/ hour of sleep, 2 patients had 68.32 arousals/ hour of sleep, 3 patients had 58.56 arousals/ hour of sleep, 6 patients had 48.80 arousals/ hour of sleep, 7 patients had 39.04 arousals/ hour of sleep, 9 patients had 29.28 arousals/ hour of sleep and 40 patients had 19.52 arousals/ hour of sleep.

The comparison of variations of the arousals associated to respiratory events for patients with and without apnea using the Levene Test ($p=0.000 < 0.05$) was unequal. The application of T Test for independent groups with unequal variations revealed a $p = 0.000 < 0.05$. (Figure 3).

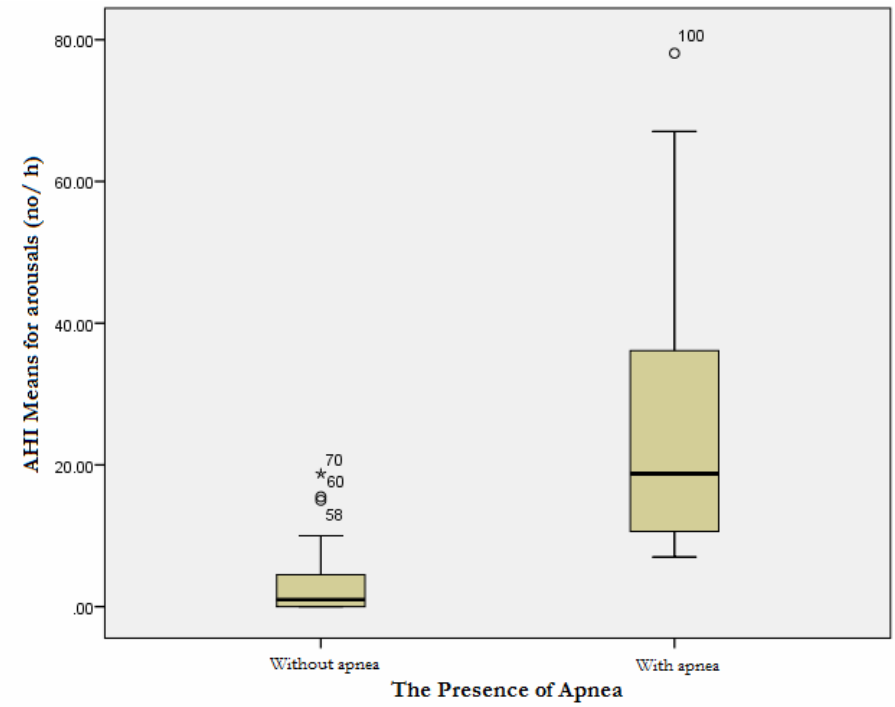

Figure 3. The Comparison of AHI Means for arousals (no/ h) of the patients with and without apnea.

In table 1 the Mean variations of the BMI of the 2 groups of patients were equal by applying the Levene Test ($p= 0.140 > 0.05$). The application of T Test for independent groups with equal variations revealed a $p= 0.007 < 0.05$.

Of all patients 71% were overweight and obese. The levels of obesity are represented in Figure 4.

Out of total number of overweight and obese patients only 47 were diagnosed with OSAS. So, out of 60 patients diagnosed with OSAS, 47 patients had a BMI > 25 kg/ m^2. In table 2 the presence of apnea was found to be dependent on obesity, emphasizing a $p= 0.048< 0.05$ of a Pearson Chi-Square test.

Statistical differences were found between: the dorsal AHI Mean of the non-obese group compared to the dorsal AHI Mean of the obese group (Levene Test: $p < 0.05$; T Test: $p= 0.002 < 0.05$), the AHI Mean in other positions of the non-obese group compared to the AHI Mean in other positions of the obese group (Levene Test: $p < 0.05$; T Test: $p = 0.000 < 0.05$) and the Mean of the arousal index of the non-obese group compared to the Mean of the arousal index of the obese group (Levene Test: $p < 0.05$; T Test : $p= 0.009 < 0.05$). All these relationships are presented in tables 3, 4 and 5.

Table 1. The results of statistical tests between the BMI means for the group without apnea versus the group with apnea.

Independent Samples Test										
		Levene's Test for Equality of Variances		T-Test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
BMI (kg/m)	Equal variances assumed	2.208	0.140	-2.769	98	0.007	-2.66108	0.96100	-4.56815	-.75402
	Equal variances not assumed			-2.973	97.831	0.004	-2.66108	0.89498	-4.43719	-.88498

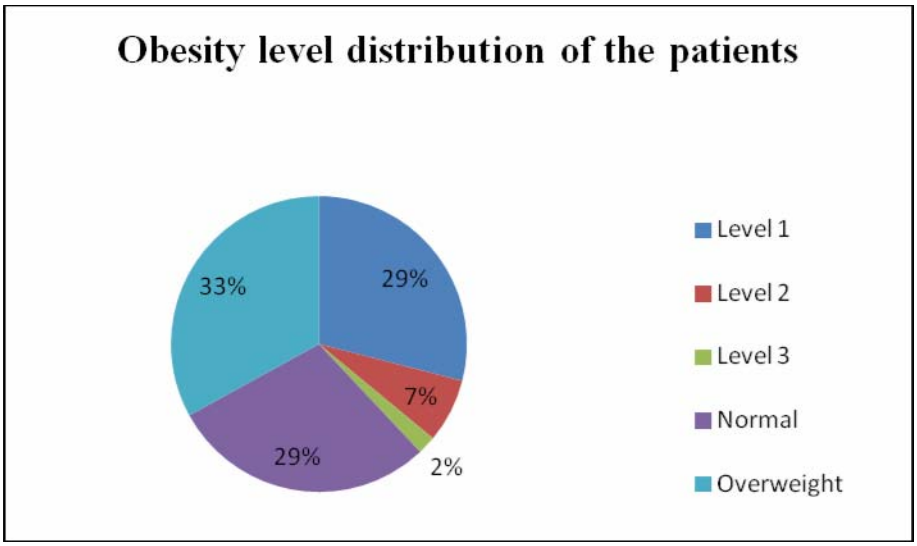

Figure 4. Obesity level distribution of the patients.

Table 2. The results of the statistic tests between the presence of apnea and obesity.

Chi-Square Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.918[a]	1	0.048		
Continuity Correction[b]	3.078	1	0.079		
Likelihood Ratio	3.871	1	0.049		
Fisher's Exact Test				0.071	0.040
N of Valid Cases	100				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 11.60.

b. Computed only for a 2x2 table

Table 3. The results of the statistic tests between the dorsal AHI Means of the non-obesity group versus the obese group.

Independent Samples Test										
		Levene's Test for Equality of Variances		T-Test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Dorsal AHI (nr/h)	Equal variances assumed	5.409	0.022	2.732	98	0.007	8.01340	2.93346	2.19205	13.83475
	Equal variances not assumed			3.245	78.540	0.002	8.01340	2.46961	3.09732	12.92947

Table 4. The results of the statistic tests between the AHI Means in other positions of the non-obesity group versus the obese group.

Independent Samples Test										
		Levene's Test for Equality of Variances		T-Test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
AHI in other posi-tions(nr/h)	Equal variances assumed	25.13	0.000	3.650	98	0.000	10.08390	2.76306	4.60069	15.56710
	Equal variances not assumed			5.041	97.875	0.000	10.08390	2.00057	6.11377	14.05402

Table 5. The results of the statistic tests between the Means of the arousal index of the non-obese group versus the obese group.

Independent Samples Test										
		Levene's Test for Equality of Variances		T-Test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Arousal index (nr/h)	Equal variances assumed	14.12	0.00	2.030	98	0.045	7.56040	3.72420	0.16984	14.95096
	Equal variances not assumed			2.681	96.113	0.009	7.56040	2.82017	1.96249	13.15831

Discussion

Like other studies in the medical literature, males predominated in our study. The sleep apnea syndrome was diagnosed in a high percentage of 60%. Among the SAS types the predominant type was the obstructive one. In the study group there was a positional component of OSAS, which was found in 11%. According to literature, moderate and severe forms of the disease predominated in this study.

Dividing the subjects into groups of patients with and without apnea were found statistically significant differences between various polysomnographic parameters. These differences were highlighted between: type of apnea and its severity, the dorsal AHI Means, the AHI Means in other positions, the arousals Means associated to the breathing events, of the non-obese group versus the obese group. By applying the Levene Test and T Test, a statistically significant difference was also demonstrated between the BMI Mean of the non-apnea group compared to the BMI Mean of the apnea group.

To highlight a cause-effect relationship between obesity and apnea, a second division of patients was made, namely: subjects with and without obesity. In our study, the presence of apnea was found to be dependent on obesity. Compared to the total number of patients included in the study, overweight and obesity was seen in a high percentage of 71%. Most patients had BMI higher than 25 kg / m^2. The overweight and obese cases of 1^{st} degree have predominated in 33% and 29% of cases, being followed by 2^{nd} and 3^{rd} degree obesity, 7% and 2%. Obesity was present in varying degrees at a total of 47 patients with positive diagnosis of SAS.

Approximately 60% of adults in developed countries are overweight with a body mass index (BMI) higher than 25 kg / m^2 and one-third are obese with a BMI over 30 kg / m^2[9]. In a study of Health Improvement Network from Britain individuals with BMI> 40 kg / m^2 had a 27 times higher risk of being diagnosed with OSAS compared with those whose BMI was normal. Also, there was a significant percentage (40%) of the diagnosis of OSAS in people with BMI below 30 kg/ m^2 [11]. In one study it was found that the association between obesity and a severe type of SAS revealed a risk of death by 44% higher than that of single OSAS [8]. Obesity and sleep apnea syndrome frequently coexist: 40% of the obese persons have OSAS; over 70% of those diagnosed with OSAS are considered obese based on BMI status [12, 13]. Increases or decreases in body weight are known to be involved in affecting the severity of OSAS. Most adults with OSAS have central obesity and show an increase in visceral fat; the latter being associated with adiposity of the neck, with increased fat on upper airway and metabolic abnormalities appearance, even in subjects with normal weight [14]. In another study (Wisconsin Sleep Cohort Study), who used 700 subjects, 10% of patients had increases in weight which led to a 32% increase of AHI's, while the loss of 10% of body weight resulted in a decrease of 26% AHI score for a 4-year period [13].

By correlating various parameters of the polysomnographic apnea and obesity in this study were highlighted statistically significant relationships. There have been compared: the dorsal AHI Mean, the AHI Mean in other positions, the arousal Mean associated with the breathing events of the obese group versus the dorsal AHI Mean, the AHI Mean in other positions, the arousal Mean associated with the breathing events of the non-obese group; the p value for these variables was considered statistically significant.

The close relationship between obesity and OSAS was replicated also in Sleep Heart Health Study and in Cleveland Family Study [13]. Knowing the link between OSAS and obesity is evolving and involves a two-way relationship, affecting both the contribution of obesity on OSAS and the contribution of the implications of OSAS on obesity [15]. It is possible that OSAS and obesity to interact and to potentate their own negative consequences [14].

Obesity is a strong risk factor influencing the development, maintenance and growth of OSAS to influence the severity of upper airway, involving neuromuscular control and production of adipokines [15]. OSAS and obesity share common mechanisms such as: activation of inflammation, oxidative stress and increased sympathetic activity [14]. Independently, obesity appears to affect upper airway control through multiple mechanisms, including alterations in upper airway structure and function, reducing their volume during sleep and causing adverse effects on respiratory flow.

Submission of fat especially around the neck can also contribute to increased susceptibility of OSAS.

The role of OSAS on obesity is less direct than the impact of obesity on the pathophysiology of OSAS. As described by Ong et al, OSAS has an impact on energy consumption and caloric intake and thus on total weight of the body in different ways, such as: 1) change in energy consumption during sleep and wakefulness; 2) increased preference for energy dense foods and high in calories; 3) alteration in hormonal regulation of appetite and satiety; 4) changes in sleep duration, which may decrease physical activity and may contribute to the appearance of lethargy and daytime sleepiness [15]. Recent studies have suggested that OSAS may worsen the effect of obesity on cardiovascular risk and could represent an additional burden on metabolic disorders associated with obesity [16].

Limitations of the study

Several potential factors, such as the neck and abdomen circumference were not measured in our study. Regarding positional OSAS the patients were not distributed in those with pure positional OSAS (dorsal AHI > 10/ h, AHI in other positions < 10/ h) or impure positional OSAS (dorsal AHI or AHI in other positions > 10/ h). We believe that further studies including these variables are needed to determine the impact of these observations on obese OSAS patients.

Conclusion

In conclusion, this study revealed that obesity is significantly associated with OSAS, which is a major risk factor for OSAS [9, 13, 14, 17]. SAS was found in a high percentage even in people with a BMI below 30 kg / m^2; that's way general practitioners should be open to OSAS diagnosis even to symptomatic persons who are not obese. Also the correlation of obesity with dorsal and non-dorsal AHI might suggest worsening OSAS in various positions during sleep especially in obese patients. Arousals associated with respiratory events in obese patients may worsen intermittent hypoxia and also increase the risk of cardiovascular and metabolic dysfunction.

List of abbreviations

AHI = apnea- hypopnea index
BMI = body mass index
EEG = electro- encephalogram
EOG = electro- oculogram
EMG = electro- myogram
ECG = electrocardiogram
OSAS = obstructive sleep apnea syndrome
SAHS = sleep apnea- hypopnea syndrome
SAS = sleep apnea syndrome

Conflict of Interest

The authors declare that they have no conflict of interest.

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