Obesity in association with Sleep Apnea Syndrome as predictor for coronary-vascular comorbidities

Obezitatea în asociere cu sindromul de apnee în somn ca predictor pentru comorbiditățile coronaro-vasculare

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Abstract

Background and aims: *Sleep apnea syndrome (SAS) is a common disorder with growing awareness. We sought to evaluate if the presence of obesity in patients with SAS is associated with a high risk for development of coronary-vascular comorbidities.*
Methods: *We performed a retrospective study that included 1370 patients (30, 3% female and 69, 7% male) diagnosed with SAS from May 2005 to May 2012. The collected data included body mass index (BMI), waist/hip ratio, abdominal, neck, hip circumference and Epworth Sleepiness Scale. The positive diagnostic of SAS was based on apnea-hypopnea index (AHI) provided by polysomnography, and patient comorbidities were obtained from the sleep laboratory records.*
Results: *From the total of 1370 patients, 989 (72%) had grade I to III obesity, 305 (22%) were overweight and only 76 (6%) had a normal weight. Cardiovascular comorbidities were presented in 60.6% of patients, with coronary disease ranking first (34.2%) followed by heart failure (22.6%) and stroke (3.8%). The predictors for cardiovascular comorbidities were coronary disease (OR 2.1, 95% CI 1.20 – 3.39, p=0.0063), heart failure (OR 3.44, 95% CI 1.60 – 7.74, p<0.001) but not stroke (OR 2.3 95% CI 0.57 – 13.84, p=0.357). Analyzing the polysomnography parameters we found a strong correlation for AHI (p<0.0001), oxygen desaturation index (p<0.0001) and mean average oxyhaemoglobin saturation (p<0.0001).*
Conclusions: *Overweight and obese patients with SAS have a poor outcome, being at high risk of developing other comorbidities like coronary disease and heart failure.*
Keywords: ***sleep apnea, obesity, cardiovascular risk, coronary disease, heart failure, stroke***

Rezumat

Introducere și scop: *Sindromul de apnee în somn (SAS) este o patologie comună a cărei conștientizare este în continuă creștere. Am căutat să evaluăm dacă obezitatea prezentă la pacienții cu SAS este asociată cu un risc crescut de a dezvolta boli cardiovasculare (BCV).*
Metode: *Am efectuat un studiu retrospectiv care a inclus 1370 pacienți (30,3%femei și 69,7%bărbați) diagnosticați cu SAS în perioada mai 2005–mai 2012. Datele colectate au inclus indicele de masă corporală (IMC), raportul talie/bazin (șold), circumferința abdomenului, bazinului și gâtului, precum și scorul Epworth. SAS a fost diagnosticat prin polisomnografie pe baza indexului de apnee-hipopnee (IAH) iar comorbiditățile pacienților au fost preluate din baza de date a laboratorului de somnologie.*
Rezultate: *Din lotul total de 1370 pacienți, 989 (72%) au avut obezitate gradul I-III, 305 (22%) au fost supraponderali si76 (6%) au fost normoponderali. BCV au fost prezente în 60,6% din cazuri, din care bolile coronariene 34,2%, insuficiența cardiacă 22,6% și accidentele vasculare cerebrale (AVC) 3,8%. Predictorii pentru BCV au fost boala coronariană (OR 2.1,95% CI 1.20–3.39,p=0.0063), insuficiența cardiacă (OR 3.44,95% CI 1.60–7.74,p<0.001) însă nu și AVC (OR 2.3 95%CI 0.57–13.84,p=0.357). Analizând parametrii polisomnografici am găsit o corelație puternică pentru IAH (p<0.0001), indexul de desaturare (p<0.0001) și saturatia medie a oxihemoglobinei (p<0.0001).*
Concluzii: *Pacienții supraponderali și obezi cu SAS au un prognostic mai rezervat, fiind la risc înalt de a dezvolta alte comorbidități ca boală coronariană și insuficiență cardiacă.*
Cuvinte-cheie: ***apnee în somn, obezitate, risc cardiovascular, boală coronariană, insuficiență cardiacă, accident vascular cerebral***

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Introduction

Sleep apnea syndrome (SAS) is a common medical condition that occurs in 5-15% of the general adult population and that is characterized by recurrent episodes of apnea and/or hypopnea during sleep caused by pharyngeal collapse[1,2]. These are followed by frequent awakenings, disrupted sleep, hypoxemia and variations of intrathoracic pressure, all leading to alterations of the sympathetic nervous system, blood pressure and heart rate. There are numerous studies that show that patients with SAS have a high incidence of coronary disease compared with those without SAS[3]. Obesity is one of the most important risk factor for SAS, being at the same time the only reversible one. With body mass index (BMI) and fat distribution correlating with the odds of having SAS[4], it is estimated that the risk of developing SAS increases by twofold for

every 10 kg increment in weight, and with fourfold with each increase in hip or waist circumference by 13-15cm[5,6]. Recent studies show that SAS may be involved in stroke and transient ischemic attacks, with high mortality and morbidity and also associated with coronary heart disease, heart failure, and cardiac arrhythmias[7].

Methods

Subjects

The study was performed on 1370 consecutive patients aged 21 and above, referred to Victor Babes Hospital Timisoara sleep laboratory from May 2005 to May 2012 and diagnosed with central, obstructive or mixed SAS, without CPAP treatment. We evaluated mostly patients with obstructive SAS and excluded those with central SAS over 5/h. Written informed consent was obtained from each patient.

Data collection

Anthropometric data was collected and included body mass index, waist/hip ratio, abdominal, neck and hip circumference. Patients completed the Epworth Sleepiness Scale to assess daytime somnolence. Data regarding patient comorbidities was obtained from the sleep laboratory data base, and the presence of stroke, heart failure or coronary disease was noted. We performed sleep studies using a polisomnography device Alice 5 Respironics, and polygraphic devices: Stardust from Respironics, Porti 7 from F+G and Poly Mesam 4. The numeric variables collected for this study were: mean heart rate, apnea-hypopnea index (AHI), oxygen desaturation index and mean average oxyhaemoglobin saturation. We performed both polisomnography and poligraphy, with a ratio of PSG/PG 3,5/1.

SAS was defined accordingly to AASM 2007 (American Academy of Sleep Medicine), that scores an apnea when all the following criteria are met: **1)** There is a drop in the peak thermal sensor excursion by ≥90% of baseline, **2)** The duration of the event lasts at least 10 seconds and **3)** At least 90% of the events duration meets the amplitude reduction criteria for apnea[16].

Statistical analysis

The current study is an observational and descriptive, retrospective one; the statistical analysis was performed using EPIINFO vs. 6, Microsoft Excel 2007, R vs. 2141 and Boxplot. Results were considered significant for p values < 0.05 and adjusted odds ratios with 95% confidence intervals were determined for all variables. Correlation between variables was accomplished using contingency 2x2 tables.

Results

Out of the 1370 patients, 415 (30,3 %) were female and 955 (69,7%) were male. They were divided based on BMI into 5 groups (Figure 1) as followed:

- G 1 – Normal weight BMI between 19 and 24.9 kg/cm^2,
- G 2 – Overweight BMI between 25 and 29.9 kg/ cm^2,
- G 3 – Grade I obesity BMI between 30 and 34.9 kg/cm^2,
- G 4 – Grade II obesity BMI between 35 and 39.9 kg/cm^2,
- G 5 – Grade III obesity BMI over 40 kg/cm^2.

The majority of the patients had grade I obesity (31%), followed by grade II obesity (24%), overweight (22%), grade III obesity (17%) and only 6% had a normal weight.

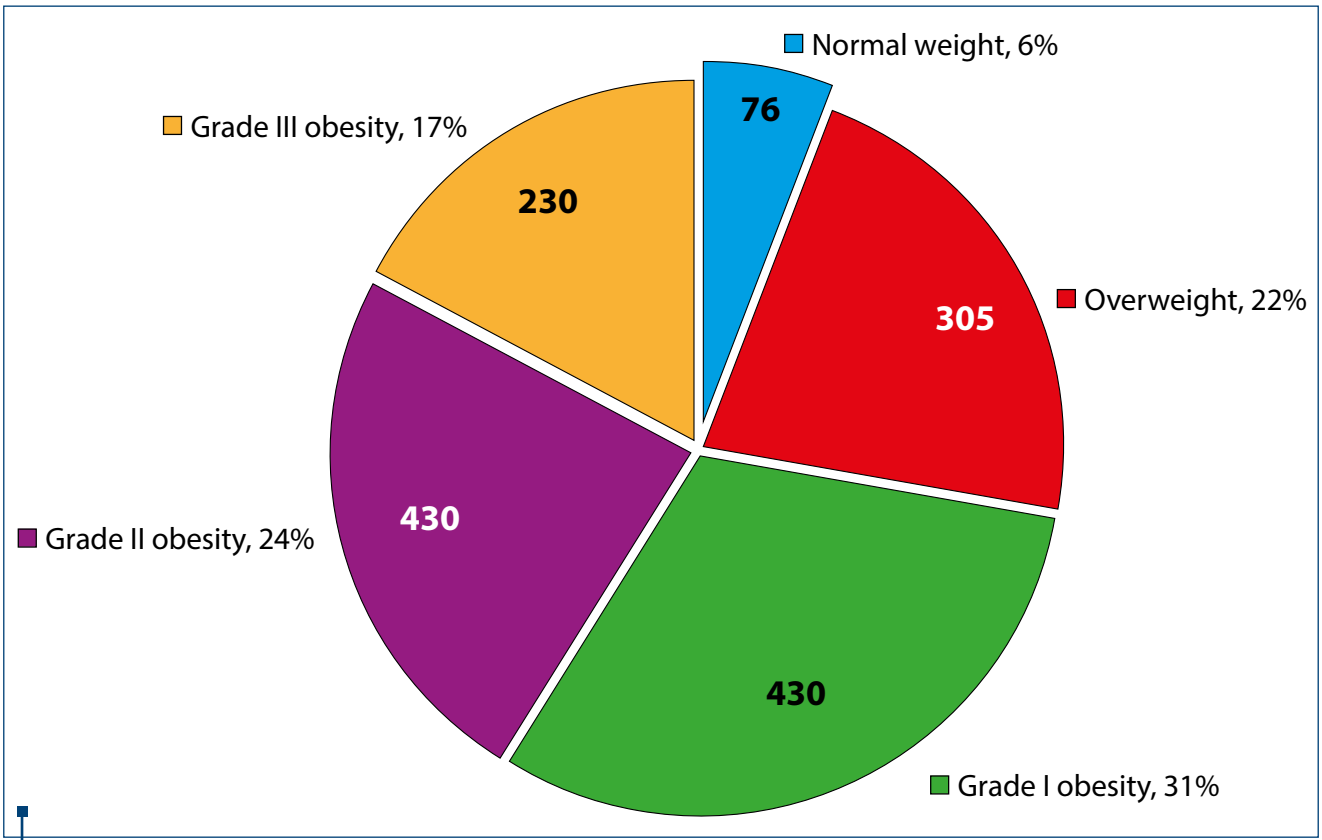

Figure 1. *Pie chart representing BMI (Body-mass index) distribution*

Table 1 Coronary-vascular comorbidities distribution

Patients (%) with coronary disease	Patients (%) with stroke	Patients (%) with heart failure	Patients (%) without comorbidities	Total (%)
468 pts.	52 pts.	310 pts.	540 pts.	**1370 pts.**
34.2%	3.8%	22.6%	39.4%	**100%**

Table 2 Apnea-Hypopnea Index in ANOVA analysis by BMI (Body-mass Index) groups

SUMMARY						
BMI Groups	**Count**	**Sum**	**Average**	**Variance**	**P value**	
Normal Weight	76	1,617.1	22.15	229		
Overweight	305	10,570	34.76	431	<0.0001	
Grade I obesity	430	18,333.6	43.54	581	<0.0001	
Grade II obesity	329	15,690.7	48.42	683	0.004	
Grade III obesity	230	14,338.4	58.05	970	<0.0001	
ANOVA						
Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	115,872.4	4	28,968.1	46.40	<0.0001	2.378453
Within Groups	851,406	1366	624.19			
Total	**967278,4**	**1370**				

Table 3 Desaturation index in ANOVA analysis by BMI (Body-mass Index) group

SUMMARY						
BMI Groups	Count	Sum	Average	Variance	P value	
Normal Weight	76	664.7	9.49	238		
Overweight	305	4,915.9	16.60	385	0.0006	
Grade I obesity	430	10,733.1	26.9	610	<0.0001	
Grade II obesity	329	10,950.1	35.90	789	<0.0001	
Grade III obesity	230	10,158.3	44.16	1,049	0.001	
ANOVA						
Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	141,220	4	35,305.01	53.56	<0.0001	2.378801
Within Groups	853,509.3	1,366	659.08			
Total	**99,4729.3**	**1,370**				

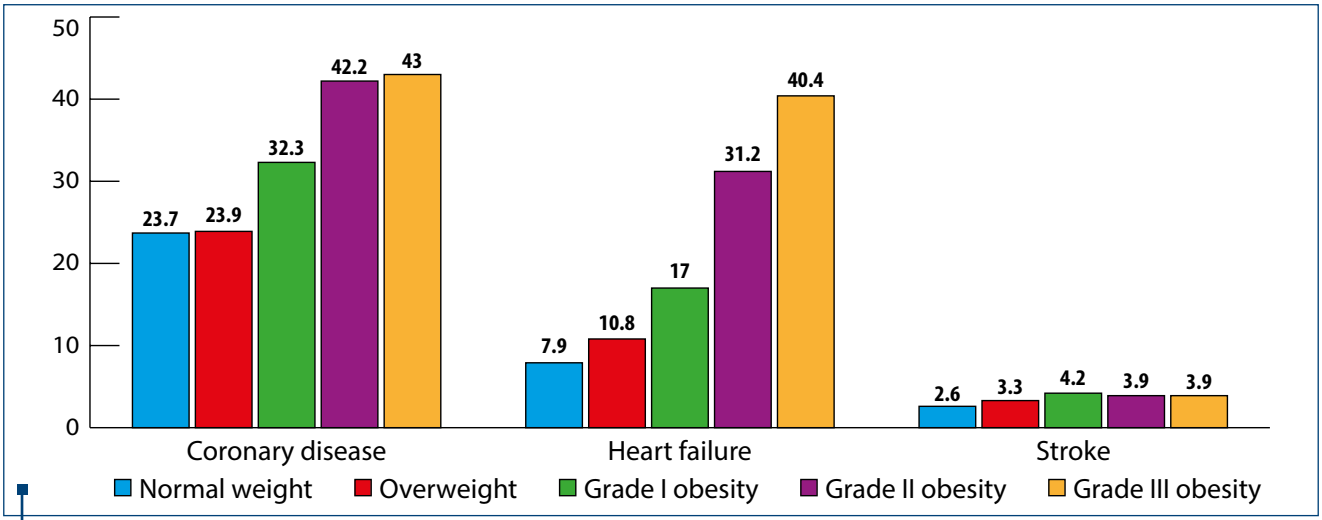

Figure 2. *Comorbidity distribution (%) by BMI (Body-mass index) groups*

Table 4 Mean oxygen desaturation in ANOVA analysis by BMI (Body-mass Index) groups

SUMMARY						
BMI Groups	Count	Sum	Average	Variance	P value	
Normal Weight	70	6,681	95.44	6		
Overweight	296	27,974	94.50	7	0.003	
Grade I obesity	399	37,235	93.32	29	<0.0001	
Grade II obesity	305	28,078	92.05	19	<0.0001	
Grade III obesity	230	20,785	90.36	29	<0.0001	
ANOVA						
Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	2,975.658	4	743,91	35,40	<0.0001	2,378801
Within Groups	27,206.72	1,366	21			
Total	**30,182.38**	**1,370**				

Table 5 Multivariate regression for coronary vascular comorbidities

	OR	95% CI	P value
Heart failure	3.44	1.60 - 7.74	<0.001
Coronary disease	2.01	1.20 - 3.39	0.0063
Stoke	2.3	0.54 - 13.84	0.357

Regarding the 830 patients (60, 6%) (Table 1), with coronary-vascular comorbidities the distribution was 34,2% for coronary disease, 22,6% for heart failure and 3,8% for stroke.

Using ANOVA single factor data analysis, we evaluated the polysomnography parameters in relationship with the BMI groups as seen in table 2, table 3, table 4, and significant correlations were found. When the comorbidity distribution among the BMI groups (Figure 2.) were evaluated, we found a significant increase for heart failure (7,9% for normal weight and 40,4% for grade III obesity) and coronary disease (23,7% for normal weight and 43% for grade III obesity), but not for stroke (2,6% for normal weight and 3,9% for grade III obesity).

We implemented contingency 2x2 tables for all three diseases most associated with SAS as presented in Table 5.and found a strong correlation for coronary disease (OR 2.1, 95% CI 1.20 – 3.39, p=0.0063), heart failure (OR 3.44, 95% CI 1.60 – 7.74, p<0.001) but not stroke (OR 2.3 95% CI 0.57 – 13.84, p=0.357).

Discussion

A patient diagnosed with SAS will present 5 to over 100 apneas per hour, and every single one leads to a hypoxic episode. The underlying pathophysiology of SAS is complex, and through intricate mechanisms such as endothelial dysfunction, inflammation and oxidative stress, it exerts a negative cardiovascular effect that is not yet fully understood[8] . It has been showed that blood pressure rises throughout the sleep period by sympathetic activation episodes that are caused by the hypoxia that follows an apneic episode[9]. It is known that obesity and sleep apnea are strongly connected, and that the collapsibility shown in SAS may be attributed to nasal and peripharyngeal fluid accumulation, upper airway neuromuscular disturbance and resistance due to excessive fat deposits[10].

We found a strong correlation between polysomnographic parameters and BMI groups; oxygen desaturation index increases significant in grade III obesity compared to normal weight while mean average oxyhaemoglobin saturation decreases. The more severe the obesity, the lower the oxyhaemoglobin saturation will be.

The present study examined the relationship between obesity in patients with SAS and coronary-vascular comorbidities[11]. The results revealed a strong correlation between BMI and cardiovascular comorbidities such as ischemic heart disease and congestive heart failure, but not for stroke. We found that heart failure increases by fourfold in grade III obesity with OSA as compared to normal weight with SAS; also the percentage of coronary disease is increased by twofold in patients with SAS and grade III obesity compared to normal weight.

The association of SAS and a high BMI with ischemic heart disease is probably in relationship with carotid chemoreceptor stimulation that leads to sympathetic activation, vasoconstriction, increased fibrinogen levels with decreased fibrinolytic activity and platelet activation. These factors may contribute or aggravate an underlying ischemic heart disease[9]. Our study supports these findings, as coronary disease was significantly correlated with BMI (OR 2.1, 95% CI 1.20 – 3.39, p=0.0063) and SAS.

Another independent SAS association was found to be with heart failure, as confirmed by our study (OR 3.44, 95% CI 1.60 – 7.74, p<0.001). There is an increased mortality in such patients, mainly due to a high rate of arrhythmias, but also the fluid retention caused by heart failure leads to an aggravation of sleep apnea.

Although there are studies that show that the risk of stroke is increased with SAS, independent of other risk factors, including hypertension[12], we found no significant association with SAS (OR 2.3 95% CI 0.57 – 13.84, p=0.357). One explanation is that mean stroke age varies around 65-70 years old and patients with OSA usually have a life expectancy of 60 y.o. (with approximately 5 years added if treated)[13]. The age decrease the mortality risk in SAS and this may be explained by the cerebrovascular protection conferred by ischemic preconditioning due to hypoxia-reoxigenation cycles[14]. Increased SAS severity without obesity in very old patients needs to be confirmed and further studied[15]. Studies on rodent brain showed that repeated episodes of systemic hypoxia protects from subsequent ischemic damage; translating to humans, the preconditioning resulting from repeated hypoxias accompanying SAS could limit the damage of stroke[16].

Conclusions

Obesity has an impact on the evolution of SAS, with significant differences on the polysomnography parameters. Considering the strong correlation between BMI, SAS and cardiovascular disease shown in this study, and also confirmed by previous studies, we suggest that physical activity and weight loss has to become a priority and be recommended in all patients with SAS. Overweight and obese patients with SAS have a poor outcome, being at high risk of developing comorbidities like coronary disease and heart failure. ■

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