

Pneumologia

Sleep apnoea syndrome in patients with chronic obstructive pulmonary disease and obesity – hypoxic load, comorbidities

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Abstract

English:

Introduction: We analyse anthropometric, somnopolygraphic and comorbidities data in patients with OSA syndrome, OSA with COPD, and OSA with COPD and obesity.

Material and method: 2644 OSA patients, three groups: I – OSA (2112 pts., 79.9%); II – OSA and COPD (116 pts., 4.4%); III – OSA, COPD and obesity (416 pts., 15.7%).

Results: significantly older ($p < 0.01$, $p = 0.01$, $p < 0.01$); more men: 68.4% vs. 80.2% vs. 78.8%; smokers 59.4% vs. 70.7% vs. 74.3%; larger neck circumference: 42.74 ± 5.08 cm vs. 40.57 ± 3.97 cm vs. 45.90 ± 4.92 cm; higher BMI; lower O₂ saturation: $p < 0.01$, $p = 123$, $P < 0.01$; higher desaturation index: 30.65 ± 26.96 vs. 18.94 ± 20.28 vs. 42.28 ± 29.02 ; lowest O₂ saturation: ($p < 0.01$, $p = 0.024$, $p < 0.01$); higher AHI: $p = 0.001$, $p < 0.01$, $p < 0.01$; coronary artery disease: $p < 0.01$, $p = 195$, $p < 0.01$; heart failure: $p < 0.01$, $p = 760$, $p < 0.01$; arrhythmias: $p < 0.01$, $p = 796$, $P < 0.01$; stroke: insignificant; diabetes mellitus: $p = 0.252$, $p = 0.007$, $p = 0.794$; systemic hypertension: $p < 0.01$, $p = 0.786$, $p < 0.01$.

Conclusion: COPD in OSA is more severe, with more diabetes and longer hypertension duration, but not significantly different for O₂ saturation, CAD, heart failure, arrhythmia, stroke and systemic hypertension. Obesity adds to overlap OSA–COPD significant burden for all recorded data, with the exception of stroke and diabetes.

Keywords

COPD • obstructive sleep apnoea • obesity • hypoxic burden • comorbidities

Sindromul de apnee in somn la pacientii cu bronhopneumopatie cronica obstructiva si obezitate- povara hipoxica si comorbiditati

Rezumat

Romanian:

Apneea obstructivă în somn (OSA) este o tulburare tot mai frecventă, caracterizată prin colaps repetat al căilor respiratorii superioare în timpul somnului, ducând la desaturări și somn perturbat. În această lucrare, ne-am propus să analizăm parametrii antropometrici, somnopoligrafici și comorbiditățile la pacienții cu sindromul de apnee obstructivă în somn (OSA) comparativ cu cei cu OSA și boală pulmonară obstructivă cronică (BPOC), respectiv cu cei cu OSA, BPOC și obezitate.

Material și metodă: Retrospectiv, 2644 de pacienți cu OSA (2005–2019) au fost distribuiți în 3 grupuri: grupul I - OSA (2112 pacienți, 79.9%); grupul II - OSA și BPOC (116 pacienți, 4.4%); grupul III - OSA, BPOC și obezitate (416 pacienți, 15.7%).

Rezultate: Vârsta a fost de 51.80 ± 13.08 ani vs 56.50 ± 14.35 ani vs 56.23 ± 10.39 ani ($P < 0.01$, $P = 0.01$, $P < 0.01$). Bărbați: 68.4% vs 80.2% vs 78.8% ($P < 0.01$, $P = 0.22$, $P < 0.01$). Fumat: 59.4% vs 70.7% vs 74.3% ($P < 0.01$, $P = 0.55$, $P < 0.01$). Intensitatea fumatului în ani-pachet: 17.28 ± 15.88 vs 27.84 ± 17.43 vs 30.92 ± 19.69 ($P < 0.01$, $P = 0.01$, $P < 0.01$). Circumferința gâtului: 42.74 ± 5.08 cm vs 40.57 ± 3.97 cm vs 45.90 ± 4.92 cm ($P < 0.01$, $P < 0.01$, $P < 0.01$). Obezitate - indicele de masă corporală (IMC) > 30 kg/m² (70.2% vs 11.2% vs 100% ($P < 0.01$, $P < 0.01$, $P < 0.01$). Saturația medie a fost de 92.10 ± 6.15 vs

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92.65 ± 7.80 vs 85.59 ± 6.62 ($P < 0.01$, $P = 123$, $P < 0.01$). Indexul de desaturare a fost de 30.65 ± 26.96 vs 18.94 ± 20.28 vs 42.28 ± 29.02 ($P < 0.01$, $P < 0.01$).

Saturația O₂ minimă: $76.43 \pm 13.43\%$ vs $78.88 \pm 11.60\%$ vs 71.52 ± 15.32 ($P < 0.01$, $P = 024$, $P < 0.01$). Indexul de apnee hipopnee (AHI): $37.79/\text{hr} \pm 18.12$ vs 52.61 ± 26.33 vs 44.73 ± 25.59 ($P = 0.001$, $P < 0.01$, $P < 0.01$). Boala coronariană: $P < 0.01$, $P = 195$, $P < 0.01$. Insuficiență cardiacă: $P < 0.01$, $P = 760$, $P < 0.01$. Aritmii: $P < 0.01$, $P = 796$, $P < 0.01$. Accident vascular cerebral: $P = 208$, $P = 0.770$, $P = 0.22$. Diabetul zaharat: $P = 0.252$, $P = 0.007$, $P = 0.794$. Hipertensiunea sistemică: $P < 0.01$, $P = 0.786$, $P < 0.01$.

Concluzie: BPOC la pacienții cu SAOS sunt semnificativ diferite în ceea ce privește antropometria, AHI și indicele de desaturare, cu mai mult diabet și o durată mai lungă a hipertensiunii, dar nu diferă semnificativ pentru media saturației de O₂, boala coronariană, insuficiența cardiacă, aritmie, accident vascular cerebral și hipertensiunea sistemică. Am constatat că există un efect aditiv semnificativ al obezității în suprapunerea SAOS-BPOC pentru toate datele înregistrate, cu excepția accidentului vascular cerebral și diabetului.

Cuvinte-cheie

BPOC • apnee • obezitate • povara hipoxica • comorbidități

Introduction

Obstructive sleep apnoea (OSA) is an increasingly common disorder of repeated upper airway collapse during sleep, leading to oxygen desaturation and disrupted sleep. Common symptoms are snoring, witnessed apnoea, and sleepiness. Risk factors include obesity, male sex, age, menopause, fluid retention, adenotonsillar hypertrophy and smoking. OSA causes sleepiness, road traffic accidents and probably systemic hypertension, myocardial infarction, congestive heart failure, stroke and diabetes mellitus (1).

The global prevalence of OSA is almost 1 billion people, exceeding 50% in some countries, and effective diagnostic and treatment strategies are needed to minimise the negative health impacts and to maximise cost-effectiveness (2).

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease that is characterised by persistent respiratory symptoms and airflow limitation attributable to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases (3). Using the Global Obstructive Lung Disease (GOLD) definition, the number of people worldwide aged 30–79 years having COPD in 2019 has been ascertained at 391.9 million, and owing to the fact that there is extensive under-diagnosis and misdiagnosis where COPD is concerned, a situation is caused wherein patients receive no treatment or incorrect treatment (4).

Obesity is a complex chronic disease in which abnormal adiposity impairs health, increases the risk of long-term medical complications and reduces lifespan; and the prevalence is increasing globally. Obesity is defined using the body mass index (BMI; weight/height²), as a BMI exceeding 30 kg/m², and is sub-classified into classes 1 (30–34.9 kg/m²), 2 (35–39.9 kg/m²) and 3 (≥ 40 kg/m²) (5).

OSA and COPD are among the most prevalent chronic diseases and represent a major economic burden for healthcare systems worldwide (6). The clinical presentation of OSA–COPD ‘overlap syndrome’ compared to OSA alone remains undefined and more research is needed to elucidate how the association of both diseases exercises an impact on cardiovascular (CV) health (7).

The objective of this paper was to study the main differences between OSA in patients with OSA alone, compared to OSA and COPD and to OSA, COPD and obesity.

Materials and methods

The present work consists of a descriptive, retrospective study, which utilised data pertaining to a total of 2644 patients who were diagnosed with OSA between 2005 and 2019 at the Pulmonology Department, Victor Babes Hospital, Timisoara. The database provides selected information about the patient's physical examination, history, symptoms, comorbidities and sleep test results.

For OSA, data were recorded using polysomnography and cardiorespiratory polygraphy devices. The cardiorespiratory polygraphy records oronasal airflow by thermistor, chest and abdominal respiratory movements, tracheal sounds, cardiac frequency, oxygen saturation, body position and continuous positive airway pressure (CPAP) level. Recordings were scored manually (8).

A complete cessation of the airflow signal of ≥ 10 s was defined as apnoea. Hypopnoea was defined as a discernible reduction of $\geq 50\%$ of the airflow signal for ≥ 10 s, accompanied by a decrease of $\geq 3\%$ in oxyhaemoglobin saturation.

The apnoea–hypopnoea index (AHI) was calculated as the sum of the number of episodes of apnoea and hypopnoea per hour of polygraphical recording (9).

As for the diagnostic routine that was used to establish the presence of COPD, an assessment of airway obstruction by spirometry was carried out based on the European Respiratory Society–American Thoracic Society criteria (ERS–ATS) criteria; specifically, an forced expiratory volume in one second/force vital capacity (FEV1/FVC) ratio below 0.7 after the application of bronchodilator was deemed to be an indication of COPD (10).

For obesity, patients were classified as obese when their BMI (a person's weight divided by the square of the person's height) exceeded 30 kg/m² (11).

Overlap syndrome was defined as AHI ≥5/hr, with an FEV1/FVC ratio of ≤70% plus FVC >80% (12).

Hypoxic burden was measured with three parameters: mean oxygen saturation, desaturation index (number of desaturation/hr) and the lowest desaturation.

Inclusion and exclusion criteria

The inclusion criteria were the following: (1) patients diagnosed with OSA and COPD; and (2) availability of complete data pertaining to BMI. The exclusion criteria were the following: (1) age <18 years old; or (2) incomplete or multiple measurements.

Statistical analysis

Descriptive data are reported as mean values and standard deviations, medians or percentages. *P* values under 0.05 are regarded as statistically significant. Variables were tested for normality using the Shapiro–Wilk test. *P* values for continuous variables showing a normal distribution were obtained using the student's *t* test, whereas *P* values for continuous variables not showing a normal distribution were obtained using the Mann–Whitney *U* test; further, *P* values for categorical variables were obtained using the chi-square test. Data analysis was performed using the programs Microsoft Excel 2016 and Real Statistics MedCalc 19.5.3 (MedCalc Software Ltd, Belgium) were used for statistical analysis.

Results

To facilitate an effective description, the patients were divided into three groups: Group I – 2112 patients (79.9%) with OSA only; Group II – 116 patients (4.4%) with OSA and COPD overlap; and Group III – 416 patients (15.7%) with OSA, COPD and obesity.

Anthropometrics

Patients were older in Groups II and III with a mean age distribution between all groups: 51.80 ± 13.08 years versus

56.50 ± 14.35 years versus 56.23 ± 10.39 years (*P* < 0.01 vs *P* = 0.001 vs *P* < 0.01). The male genre was predominant in all groups: 68.4% versus 80.2% versus 78.8% (*P* < 0.01 vs *P* = 0.022 vs *P* < 0.01). The mean AHI shows severe OSA patients in all three groups: 44.73 ± 25.59/hr versus 37.79 ± 18.12/hr versus 52.61 ± 26.33/hr (*P* < 0.01 vs *P* < 0.01 vs *P* < 0.01). The most severe cases were in the Group III overlap and obesity.

Smoking prevalence was the highest in Group III: 59.4% versus 70.7% versus 74.3% (*P* < 0.01 vs *P* = 0.055 vs *P* < 0.01). Smoking intensity as the number of packs/year postero-anterior (PA) was higher in the OSA–COPD overlap group: 17.28 ± 15.88 versus 27.84 ± 17.43 versus 30.92 ± 19.69 (*P* < 0.01 vs *P* < 0.001 vs *P* < 0.01). The neck circumference was 42.74 ± 5.08 cm versus 40.57 ± 3.97 cm versus 45.90 ± 4.92 cm (*P* < 0.01 vs *P* < 0.001 vs *P* < 0.01), with the highest values in the overlap and obesity groups. Obesity (defined as a BMI >30 kg/m²) was higher in the OSA alone group and low in the OSA–COPD overlap group: 70.2% versus 11.2% versus 100% (*P* < 0.01, *P* < 0.01, *P* < 0.01).

Comorbidities

Comorbidities were identified in patients from the three groups of the study in different percentages, with the highest values in Group III (Table 1). Coronary artery disease distribution: 30.1% versus 38.8% versus 47.8% (*P* < 0.01 vs *P* = 0.195 vs *P* < 0.01). Heart failure: 24.8% versus 29.3% versus 44.5% (*P* < 0.01 vs *P* = 0.760 vs *P* < 0.01). Arrhythmias: 22.8% versus 23.3% versus 32.2% (*P* < 0.01 vs *P* = 0.796 vs *P* < 0.01). Stroke: 4.4% versus 5.2% versus 5.8% (*P* = 0.208 vs *P* = 0.770 vs *P* = 0.221) with no significant differences between groups. The percentage of diabetes was 32.7% versus 55.2% versus 67.3% (*P* = 0.252 vs *P* = 0.007 vs *P* = 0.794).

Systemic hypertension is highly prevalent: 67.3% versus 70.7% versus 80.5% (*P* < 0.01 vs *P* = 0.786 vs *P* < 0.01).

Regarding the time interval since the onset of arterial hypertension and the evaluation carried out for inclusion in the study, the statistical analysis revealed the existence of

Table 1. The percentage of comorbidities

Comorbidities	OSA (%)	OSA + COPD (%)	OSA + COPD + obesity (%)
Coronary artery disease	30.1	38.8	47.8
Heart failure	24.8	29.3	44.5
Arrhythmias	22.8	23.3	32.8
Stroke	4.4	5.2	5.8
Diabetes	32.7	55.2	67.3
Systemic hypertension	67.3	70.7	80.5

COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnoea.

percentage differences between the three groups of patients: 7.74 ± 7.54 years versus 6.10 ± 6.01 years versus 8.98 ± 7.74 years ($P = 0.131$ vs $P = 0.039$ vs $P = 0.006$).

Hypoxic load

Oxygen saturation is a parameter with clinical–therapeutic and prognostic implications in OSA. Mean O_2 saturation was for all three groups 92.10 ± 6.15% versus 92.65 ± 7.80% versus 85.59 ± 6.62% ($P < 0.01$ vs $P = 0.123$ vs $P < 0.01$), with the lowest in Group III. The desaturation index distribution was 30.65 ± 26.96 versus 18.94 ± 20.28 versus 42.28 ± 29.02 ($P < 0.01$ vs $P < 0.01$ vs $P < 0.01$), with the highest in the OSA group. The lowest saturation was 76.43 ± 13.43% versus 78.88 ± 11.60% versus 71.52 ± 15.32%, with the lowest in the obesity group ($P < 0.01$ vs $P = 0.024$ vs $P < 0.01$).

Comparing the groups, there is a significant additive effect in adding COPD to OSA (Group II) in terms of gender, age, BMI and smoking intensity and marginally in smoking, AHI, neck circumference, desaturation index, diabetes and hypertension duration but not significant differences for mean O_2 saturation, coronary artery disease, heart failure, arrhythmia, stroke and systemic hypertension (Table 2). Adding obesity to the overlap of OSA and COPD (Group III), there is a significant additive

effect for all recorded data, with the exception of stroke and diabetes (Table 2).

Discussions

The overlap of OSA–COPD was present in 4.4% of the patients, similar to observations made in the literature (12), but lower than those reported in other studies (13).

The male predominance was found in all groups. In general, male patients outnumber women in the diagnosis of OSA. Female patients had less severe disease compared to male patients and more frequently reported ‘atypical’ Sleep apnea syndrome (SAS) symptoms, while male patients more frequently reported ‘typical’ OSA symptoms (14).

In the case of smoking, the highest value of pack-years was recorded in the group of patients in whom there was an association between OSA, COPD and obesity. OSA patients with a history of smoking had an increased risk of hypertension, COPD, gastro-oesophageal reflux (GERD) and chronic pharyngitis (15).

Neck circumference is an important risk factor, because fat deposition around the pharyngeal airways is likely to increase their collapse. The adults, especially males with a large neck, are more likely to develop OSA (16).

Obesity is associated with functional impairment of the muscles of the upper respiratory tract. Shared risk factors between OSA and obesity, may, through multiple mechanisms, lead to deterioration of pulmonary function. The relationship between OSA and many chronic lung diseases is bidirectional, with a worsening of one disease process leading to a deterioration of the other, as seen in COPD (17).

There has recently been much focus on the overlap syndrome of OSA and COPD, with the constituents as well as the overlap being considered as independent risk factors for CV disease. There is an additive effect of COPD on the CV damages in patients with OSA-associated comorbidities. The complication of both has a worse prognosis compared with patients with only one of these diseases. However, the details of the underlying mechanisms of this worsened prognosis have not yet been elucidated (18).

In the group of patients with both OSA and COPD, there are some differences with regard to the comorbidities, but these are not significant for O_2 saturation, coronary artery disease, heart failure, arrhythmia, stroke and systemic hypertension. A cross-sectional study conducted in the French National Sleep Apnea Registry between January 1997 and January 2017 showed that in adults with moderate-to-severe OSA, overlap with COPD was minimally symptomatic, but exhibited higher

Table 2. *P* values between groups

Parameter	<i>P</i> value		
	Lot 1	Lot 2	Lot 3
Sex	<0.01	0.022	<0.01
Age	<0.01	0.001	<0.01
BMI	<0.01	<0.01	<0.01
Obesity	<0.01	<0.01	<0.01
Smoking	<0.01	0.055	<0.01
Smoking intensity (PA)	<0.01	<0.001	<0.01
AHI	<0.01	<0.01	<0.01
Neck circumference	<0.01	<0.01	<0.01
O_2 saturation (mean)	<0.01	0.123	<0.01
Desaturation index	<0.01	<0.01	<0.01
Lowest O_2 desaturation	<0.01	0.024	<0.01
Coronary artery disease	<0.01	0.195	<0.01
Heart failure	<0.01	0.760	<0.01
Arrhythmia	<0.01	0.796	<0.01
Stroke	0.208	0.770	0.221
Diabetes	0.252	0.007	0.794
Systemic hypertension	<0.01	0.786	<0.01
Hypertension duration	0.131	0.039	0.006

AHI, apnoea–hypopnoea index; BMI, body mass index.

odds for prevalent coronary heart disease, heart failure and peripheral arteriopathy (19).

Comorbidities, especially CV, in patients with overlap syndrome are at least as prevalent as in OSA only patients and may contribute to the overall severity and prognosis of the disease (20).

Nocturnal hypoxaemia is the hallmark of OSA, and a new quantitative marker, hypoxic burden, has been shown to be associated with CV mortality. Commonly used somnopolygraphy indices, such as AHI, desaturation index and T90% (time in minutes with O₂ less than 90%), are poor markers of CV insults induced by OSA (21). Mean oxygen saturation, desaturation index and the lowest desaturation were all significantly different, adding more hypoxic load to OSA, except for mean O₂ saturation in the OSA–COPD overlap.

Limitation

The study is a retrospective analysis. The patients were referred to be evaluated for OSA in a sleep clinic, with high probability of having a confirmed diagnosis. Furthermore, we evaluated the coexistence of two heterogeneous disorders, COPD and OSA. Both diseases are characterised by different clinical outcomes and prognoses, despite similar airway obstruction or AHI. Moreover, some of our COPD patients had spirometry values affected by obesity, which were not in total accordance with the Global Obstructive Lung Disease (GOLD) criteria for COPD.

Conclusions

Adding COPD to OSA makes a group of patients significantly different in terms of older age, a larger proportion of males, higher BMI, smoking intensity, higher AHI, larger neck circumference, desaturation index, a larger proportion of diabetics and longer hypertension duration but without significant differences for mean O₂ saturation, coronary artery disease, heart failure, arrhythmia, stroke and systemic hypertension. Adding obesity to overlap of OSA and COPD, there is a significant additive effect for all recorded data, with the exception of stroke and diabetes.

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Authors' contributions

1. Vlad Stupar: paper writing and reviewing data collection, analysis, endorsement of the final version. 2. Loredana Gligor: data collection, reviewing, endorsement of the final version, 3. Stefan Mihaicuta: conception, study design, data collection, analysis and interpretation; participation to paper writing and reviewing; endorsement of publishing the final version.

Conflicts of interest

The authors declare no conflict of interest.

Institutional review board statement

The study was conducted according to the Declaration of Helsinki's guidelines and approved by the local Ethical Commission. The Ethical Committee of Victor Babes Hospital, Timisoara approved the present research (10/12/10/2013).

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Data availability statement

Data used to support the findings of this study are available from the corresponding author upon request.

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