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FEASIBILITY OF THE ELABORATED WEIGHTED SCORE FOR PREDICTING POSTOPERATIVE COMPLICATIONS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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ДОЦІЛЬНІСТЬ РОЗРОБЛЕНОГО ЗВАЖЕНОГО БАЛУ ДЛЯ ПРОГНОЗУВАННЯ ПІСЛЯОПЕРАЦІЙНИХ УСКЛАДНЕНЬ У ПАЦІЄНТІВ З ОБСТРУКТИВНИМ АПНОЕ СНУ

Амвросій Т., Шандру С., Тазлаван Т.

Обструктивне апное сну (OSA) – це розлад сну, який включає припинення або значне зменшення потоку повітря через верхні дихальні шляхи, незважаючи на наявність дихального зусилля. Це найпоширеніший тип розладу дихання уві сні, який характеризується повторюваними епізодами колапсу верхніх дихальних шляхів під час сну [1]. Пацієнти з OSA розвивають періопераційні ускладнення значно частіше, ніж пацієнти без OSA. Таким чином, важливо визначити демографічні та клінічні параметри, які можуть бути використані для прогнозування пацієнтів із високим ризиком OSA, щоб періопераційні стратегії зниження ризику періопераційних ускладнень і побічних явищ були оцінені та застосовані далі.

Ключові слова: обструктивне апное сну, періопераційні ускладнення, фактори ризику.

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Obstructive sleep apnea (OSA) is a sleep disorder that involves the cessation or significant decrease of airflow through the upper airways despite the presence of respiratory effort. This is the most common type of sleep-disordered breathing and is characterized by recurrent episodes of upper airway collapse during sleep [1]. Patients with OSA develop perioperative complications significantly more frequently than those without OSA. Therefore, it is important to define the demographic and clinical parameters that could be used to predict patients at high risk of OSA, so that perioperative strategies to reduce the risk of perioperative complications and adverse events are further evaluated and applied.

Key words: obstructive sleep apnea, perioperative complications, risk factors.

Introduction

Depending on the territorial region, obstructive sleep apnea can affect more than 75% of surgical patients. A growing number of research supports the association between OSA and perioperative complications, but some valuable research does not indicate any differences between the relationship of patients with OSA versus without OSA and perioperative complications. Many of these patients are asymptomatic, despite the presence of sleep apnea [2]. Patients after bariatric surgery have been shown to have a rate of up to 77.5% [3]. But patients after orthopedic surgery have been shown to have a slightly higher OSA rate than the general population [4]. This wide range of prevalence rates may be related to the diverse distribution of risk factors for OSA, such as obesity based on body mass index, age, and/or comorbidities (eg., stroke and myocardial infarction). Further research is needed to assess whether the surgical population has a higher risk of OSA independent of these factors.

Therefore, it is important to define the demographic and clinical parameters that could be used to predict patients at high risk of OSA, so that perioperative strategies to reduce the risk of perioperative complications and adverse events are further evaluated and applied. The aim of this analysis was to evaluate the value of risk factors in the prediction of OSA.

Material and methods

Prospective cohort study, descriptive-analytical. Positive opinion of the Research Ethics Committee (meeting of 24.03.2014). Written informed consent. Analyzed 400 complete data sets from patients scheduled for surgery.

Inclusion criteria in the study were:

1) adult patients (≥18 years), who gave informed consent to be enrolled in the study;
2) able to read and complete the proposed screening questionnaires;
3) scheduled for surgery on the abdomen or extremities.

Exclusion criteria from the study were:

1) the patient's desire to withdraw from the study;
2) interventions on two segments simultaneously or on pre-existing septic land;
3) low-quality or incomplete completion of questionnaires;
4) the need for reintervention.

According to the score given by the Berlin questionnaire, this sample of 400 patients was divided into “patients at increased risk of OSA” (OSA [+]) and “patients without OSA risk” (OSA [-]). The data in Table 1 show that the study groups are homogeneous.

Table 1

Comparison of groups uniformity according to the Berlin questionnaire

Variables	OSA [+] Group n=309	OSA [-] Group n=91	p
Men/Women, %	29.4%/70.5%	45%/54.9%	0.007
Age, years	57.0 (56.1–58.3)	52.0 (50.5–54.0)	0.0001
Height, cm	166.0 (165.7–167.7)	168.0 (166.7–170.6)	0.06
Body mass, kg	88.0 (86.7–90.7)	75.0 (73–8–79,3)	0.0001
BMI (Body Mass Index) kg/m²	31.0 (31.3–32.7)	27.0 (26.1–27.6)	0.0001
Neck Circumference, cm	40.0 (39.8–40.7)	38.0 (37.1–38.6)	0.0001
Abdomen Circumference, cm	106.0 (104.6–108.1)	93.5 (90.9–96.0)	0.0001
Distance C7 vertebra-coccyx, cm	56.0 (55.4–56.8)	58.0 (56.3–58.6)	0.06
Distance occiput protuberance-C7 vertebra, cm	16.0 (15.6–16.2)	15.0 (15.0–16.1)	0.3
Duration of hospitalization, days	9.0 (10.1–11.8)	7.0 (8.4–11.0)	0.1
Preoperative FEV (Forced Expiratory Volume)	300.0 (297.8–323.6)	340.0 (318.8–368–7)	0.01
Postoperative FEV	250.0 (232.7–258–3)	280.0 (270.4–326.6)	0.0002

For each AOS [+] and AOS [-] series, postoperative complications were recorded: of cardiovascular origin (arterial hypertension, arterial hypotension, cardio-vascular instability, cardiac arrhythmia, myocardial infarction); of respiratory origin (respiratory insufficiency, the need to ventilate artificially the lungs postoperatively ≥ 60 min, pneumonia, laryngospasm); other adverse events and complications (unplanned transfer to the intensive care unit, difficult intubation, stroke, postoperatively fever [≥38.5°C]. Hypertension was defined as an increase in systolic blood pressure ≥ 25% from the values initial for a duration of at least 5 min. Hypotension was defined as a drop in systolic blood pressure ≤ 90 mmHg for a duration of at least 5 min.

The following parameters were tested: assessment of the presence of the risk of obstructive sleep apnea (patients being tested by means of the Berlin questionnaire), body mass index, sex, age, neck and abdomen circumference, the “round” morphotype for women and the “endomorph” morphotype for men, FEV determined preoperatively, the distance between the occipital protuberance and the spinous apophysis of the C7 vertebra, the presence of arterial hypertension as a comorbidity and smoking. Then these parameters were included in the logistic regression analysis to evaluate the value of the risk factors in the prediction of OSA. The next step was to determine the sensitivity and specificity of the variables with the aim of diagnosing postoperative complications and adverse events. In order to investigate the balance between sensitivity and specificity in the current study, ROC (Receiver operating characteristic) curves were constructed.

The primary results from the questionnaires were entered into a Microsoft Excel table. The obtained data were processed with the help of IBM/PC, using the statistical processing software “Statistical Package for the Social Sciences” SPSS 22 for Windows

(SPSS, Chicago, IL, USA) and "GraphPad PRISM® 4.0" for Windows 4.0 (GraphPad Software, Inc.). The results are presented as absolute and relative values (binary data), or as mean and 95% confidence interval (continuous data).

Result

In the logistic regression analysis, 11 demographic and clinical variables were included, associated with the development of postoperative complications and events in patients with obstructive sleep apnea, detected during the OR evaluation. After performing the multiple logistic regression analysis, which took into account the interaction between the independently studied factors, the following variables were established as relevant: age older than 50 years, the presence of hypertension as a comorbidity and BMI greater than 35 kg/m^2, were associated with postoperative cardiovascular complications in the studied population (Table 2).

In the current study, it was observed that these variables were predictive for postoperative cardiovascular complications in patients who underwent surgery.

These 3 variables can then be used to calculate the probability of cardiovascular complication for OSA patients who will undergo surgery:

$P = \frac{e^y}{1+e^y}$, where *e* – mathematical constant = 2.718

In the case of the presence of all positive prognostic variables, we obtain the following equation:

y = -2.046 + (Age > 50 years × 1) + (preoperative hypertension × 1) + (BMI >35 kg/m^2× 1)

y = -2.046 + (0.792 × 1) + (1.560 × 1) + (1.095 × 1) = 1.401

$$P = \frac{2{,}718^{1{,}401}}{1+2{,}718^{1{,}401}} = 0{,}802$$

Thus, the probability of developing cardiovascular complications in the patient with OSA in which all the named variables are present is equal to 0.802 or 80.2%.

In the logistic regression analysis of potential risk factors for respiratory complications in patients with obstructive sleep apnea (Table 3), only neck circumference >40 cm and BMI >35 kg/m^2 showed statistically significant values.

The presence or absence of these variables can then be used to calculate the probability of respiratory complications for OSA patients who will undergo surgery.

In the case of the presence of all positive prognostic variables, we obtain the following equation:

y = -3.549 + (Neck Circumference > 40 cm × 1) + (BMI >35 kg/m^2× 1)

y = -3.549 + (0.916 × 1) + (0.734 × 1) = -1.899

$$P = \frac{2{,}718^{-1{,}899}}{1+2{,}718^{-1{,}899}} = 0{,}13$$

The probability of developing respiratory complications in OSA patients is equal to 0.13 or 13%.

In the logistic regression analysis of potential risk factors for postoperative adverse events in patients with obstructive sleep apnea (Table 4), only preoperative FEV < 320 ml demonstrated statistically significant values. For the calculation of the probability of the development of adverse events in OSA patients, only one positive variable is not enough.

Table 2

Multiple logistic regression of potential risk factors for cardiovascular complications in patients with obstructive sleep apnea

Variabile	Coefficient (β)	ES	Wald Criterion (χ^2)	P
Male sex	-0.203	0.456	0.199	0.655
Age >50 years	0.792	0.352	5.052	0.025
Preoperative arterial hypertension	1.560	0.386	16.304	0.0001
Smoking	0.162	0.517	0.099	0.753
"Round" morphotype for women	0.706	0.374	3.567	0.059
"Endomorph" morphotype for men	0.688	0.508	1.836	0.175
Abdominal circumference >100 cm	-0.039	0.351	0.012	0.911
Neck circumference >40 cm	0.159	0.336	0.224	0.636
Occipital-C7 distance >15 cm	-0.174	0.290	0.358	0.550
BMI >35 kg/m²	1.095	0.356	9.472	0.002
Preoperative FEV <320 ml	-0.224	0.284	0.623	0.430
Constant	-2.046	0.550	13.820	

Table 3

Multiple logistic regression of potential risk factors for respiratory complications in patients with obstructive sleep apnea

Variabile	Coefficient (β)	ES	Wald Criterion (χ^2)	P
Male sex	-0.808	0.627	1.656	0.198
Age >50 years	0.882	0.496	3.159	0.075
Preoperative arterial hypertension	0.568	0.527	1.161	0.281
Smoking	0.440	0.588	0.561	0.454
"Round" morphotype for women	-0.163	0.485	0.112	0.738
"Endomorph" morphotype for men	0.300	0.651	0.212	0.645
Abdominal circumference >100 cm	-0.139	0.486	0.081	0.776
Neck circumference >40 cm	0.916	0.413	4.927	0.026
Occipital-C7 distance >15 cm	0.400	0.366	1.189	0.275
BMI >35 kg/m²	0.734	0.374	3.858	0,050
Preoperative FEV <320 ml	-0.122	0,356	0.117	0.732
Constant	-3.549	0.768	21.348	

The presence of this predictive variable can be used to calculate adverse effects in each OSA patient:

In the case of the presence of all positive prognostic variables, we obtain the following equation:

y = -1.909 + (preoperative FEV < 320 ml × 1)

y = -1.909 + (0.862 × 1) = -2.771

$$P = \frac{2,718^{-2,771}}{1 + 2,718^{-2,771}} = 0,06$$

Table 4

Logistic regression analysis of potential risk factors for adverse events in patients with obstructive sleep apnea

Variabila	Coeficientul (β)	ES	Criteriul Wald (χ^2)	P
Male sex	-1.132	0.793	2.036	0.154
Age >50 years	-0.233	0.450	0.268	0,605
Preoperative arterial hypertension	0.600	0.543	1.222	0.269
Smoking	0.562	0.643	0.763	0.382
"Round" morphotype for women	0.157	0.474	0.110	0.740
"Endomorph" morphotype for men	0.769	0.852	0.814	0.367
Abdominal circumference >100 cm	0.095	0.498	0.036	0.849
Neck circumference >40 cm	0.028	0.403	0.005	0.944
Occipital-C7 distance >15 cm	0.030	0.356	0.007	0.933
BMI >35 kg/m²	0.128	0,392	0,107	0.743
Preoperative FEV <320 ml	-0.862	0.408	4.464	0.035
Constant	-1.909	0.668	8.174	

Therefore, with the combination of several increased risk factors, the predictive value of preoperative FEV > 320 ml regarding the development of adverse effects in OSA patients is very low, constituting 0.06 or 6%.

The next step was to determine the sensitivity and specificity of the variables with the aim of diagnosing postoperative complications and adverse events. The ideal model should have 100% sensitivity and 100% specificity, but in practice this is not possible, optimal would be the existence of a balance between sensitivity and specificity. In order to investigate the balance between sensitivity and specificity in the current study, ROC curves were constructed.

For the occurrence of cardiovascular complications in OSA patients, all studied variables have a statistically significant value for cardiovascular complications, except for the "endomorph" morphotype for men: AUC=0.456, p=0.127, 95% CI (0.399–0.513).

For the neck circumference > 40 cm variable, the following values were obtained: AUC=0.602, p=0.0001, 95% CI (0.547–0.657) (Figure 1).

The following values were obtained for the preoperative arterial hypertension variable: AUC=0.663, p=0.0001, 95% CI (0.609–0.717) (Figure 2).

For the age >50 years variable, the following values were obtained: AUC=0.629, p=0.0001, 95% CI (0.575–0.684) (Figure 3).

For the "round" morphotype variable for women, the following values were obtained: AUC=0.629, p=0.0001, 95% CI (0.574–0.684) (Figure 4).

For the abdominal circumference >100 cm variable, the following values were obtained: AUC=0.682, p=0.0001, 95% CI (0.630–0.734) (Figure 5).

The following variables are not relevant for the occurrence of respiratory complications in OSA patients: preoperative arterial hypertension – AUC=0.564, p=0.1, 95% CI (0.492–0.637), age > 50 years – AUC=0.529, p=0.4, 95% CI (0.459–0.598), of the "endomorph" morphotype for men – AUC=0.479, p=0.59, 95% CI (0.401–0.558).

For the neck circumference >40 cm variable, the following values were obtained: AUC=0.592, p=0.019, 95% CI (0.520–0.664) (Figure 6).

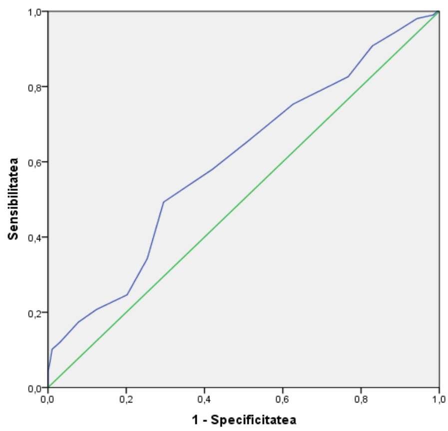

Fig. 1. ROC curve for the neck circumference >40 cm variable

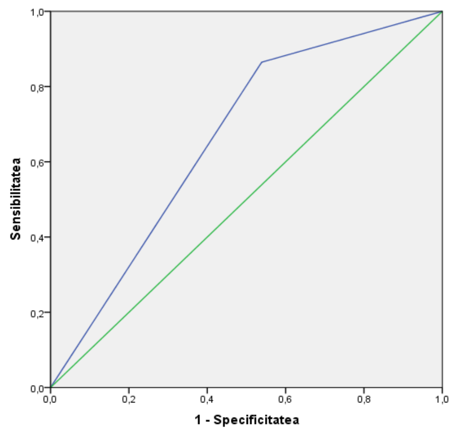

Fig. 2. ROC curve for preoperative arterial hypertension variable

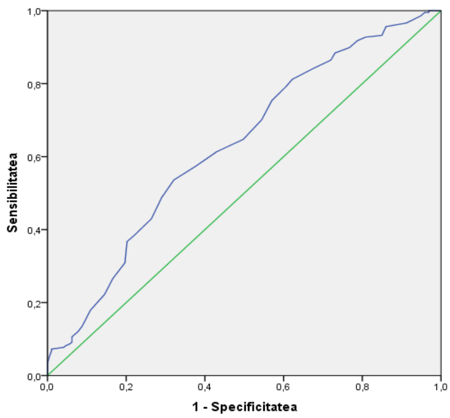

Fig. 3. ROC curve for age > 50 years variable

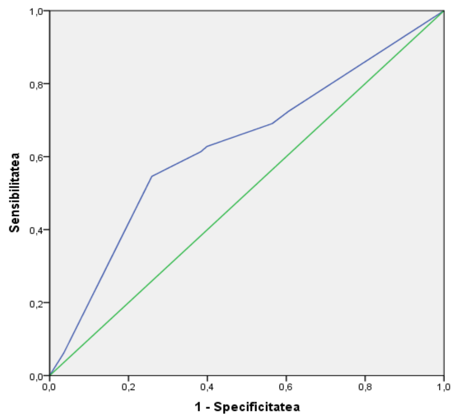

Fig. 4. ROC curve for "round" morphotype variable for women

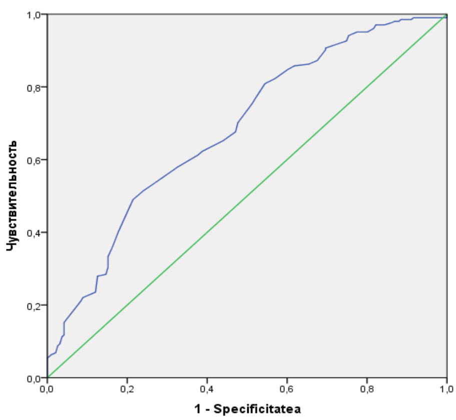

Fig. 5. ROC curve for the abdominal circumference >100 cm variable

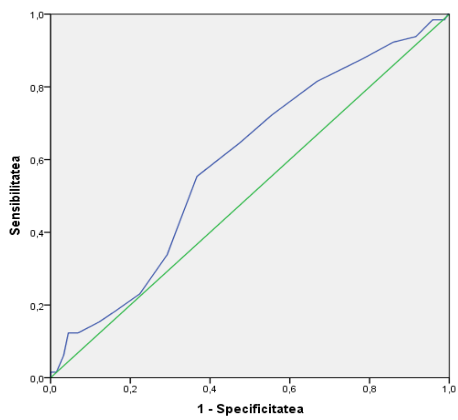

Fig. 6. ROC curve for the neck circumference >40 cm variable

For the “round” morphotype variable for women, the following values were obtained: AUC=0.586, p=0.028, 95% CI (0.507–0.665) (Figure 7).

For the abdominal circumference >100 cm variable, the following values were obtained: AUC=0.640, p=0.0001, 95% CI (0.568–0.712) (Figure 8).

In the ROC analysis of risk factors regarding the development of adverse events in OSA patients, the studied variables have no statistical significance, except for the “round” morphotype for women (Table 5).

For the “round” morphotype variable for women, the following values were obtained: AUC=0.650, p=0.0001, 95% CI (0.569–0.731) (Figure 9).

Despite the limited data on OSA as an independent perioperative risk factor, we can state that patients with OSA are in the category of increased risk of developing severe perioperative complications. Therefore, the identification and optimal perioperative management of OSA patients is mandatory.

Discussions

Obstructive sleep apnea has been recognized as a major health burden associated with hypertension and an increased risk of cardiovascular disease and death. Increased airway collapse and dysregulation of the ventilatory control response are the main pathological features of this disorder. Risk factors for obstructive sleep apnea include

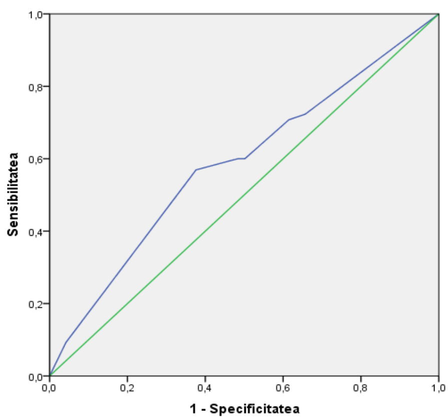

Fig. 7. ROC curve for the “round” morphotype for women variable

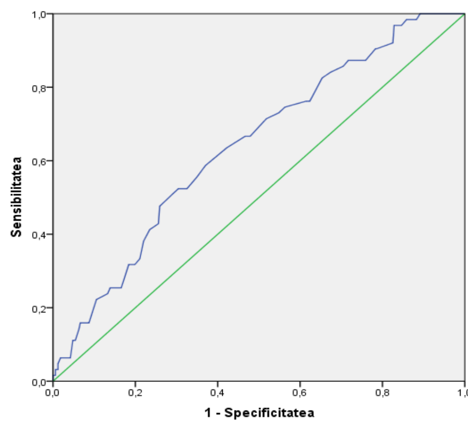

Fig. 8. ROC curve for the abdominal circumference >100 cm variable

Table 5

Characterization of the parameters of the ROC curves of the indicators tested for the diagnostic value of adverse events in patients with OSA

	ROC Parameters		
Variabile	**AUC**	**Valoarea p**	**95% CI**
Neck circumference >40 cm	0.499	0.97	0.416–0,582
Preoperative hypertension	0.555	0.2	0,474–0,636
Age >50 years	0.536	0.4	0.448–0.625
“endomorph” morphotype for men	0.416	0.05	0.336–0.495
Abdominal circumference >100 cm	0.575	0.08	0.492–0.658

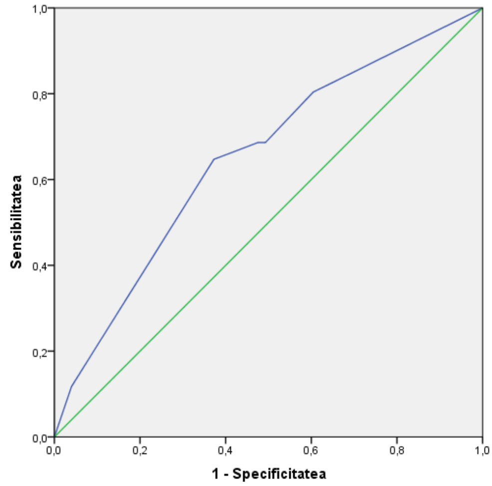

Fig. 9. ROC curve for the "round" morphotype for women variable

obesity, sex, age, menopause, family factors, craniofacial abnormalities, smoking and alcohol.

Age – The Heart Health Study shows a simple, positive, linear correlation between age and OSA until the age of approximately 65 years, at which point there is a plateau in prevalence [5]. In published studies regarding the prevalence of OSA in the elderly, ranges of 5.6%–70% are reported [6; 7]. Our research reports a prevalence of OSA in the elderly (> 65 years) of 16.7%, OSA [+] vs. AOS [-] being n=67 (90.5%) vs. n=7 (9.4%) (p=0.0001). In another analysis carried out in the elderly, a prevalence of OSA was found in men of 28%–62%, and in women of 19.5% – 60% [8], our study reports a prevalence of OSA in the elderly in men 4.7% and in women 12%.

Sex – OSA is more common in men, with a male-female ratio of 2–4:1 in epidemiological studies [9; 10] and approximately 10:1 in clinical studies [11]. Instead, our research reveals a male-female ratio of 1:2–3. The gender inconsistency between community and clinical prevalence of OSA can be explained by the fact that women often do not have classic OSA symptoms. Women are more likely to report morning headaches, difficulty initiating sleep, and fatigue, less likely to report restless sleep and confirmed apnea [12]. Moreover, women with OSA are more likely to be treated for depression, insomnia and hypothyroidism than men with the same degree of OSA [13].

A possible explanation of gender differences as a risk factor is the variation in the distribution of adipose tissue between men and women. Men are prone to the distribution of adipose tissue predominantly in the upper part of the body, including the neck (android), thus predisposing to the collapse of the upper airways, compared to women, who have a distribution predominantly in the lower part of the body (gynoid) [14]. In the research, the impact of the constitutional type on the manifestation of OSA was analyzed, thus a more frequent OSA prevalence was reported in men with the "endomorph" type compared to those without OSA n=44 (89.7%) vs. n=5 (10.2%) (p=0.0001), and in women the "round" constitutional type n=130 (90.9%) vs. n=13 (9.1%) (p=0.0001). Consistent with this observation, measurement of neck circumference and waist circumference is better correlated with OSA severity vs. BMI [5].

Obesity – the factors used in research such as BMI, the circumference of the abdomen and neck, the "endomorph" and "round" morphotype denote the nutritional status of the patient. Obesity causes physiopathological changes at the level of various organs and systems, changes responsible for the perioperative evolution of obese patients. Obesity indirectly contributes to narrowing of the upper airways, particularly in the hypotonic airways present during sleep, as lung volumes are significantly reduced through a combination of increased abdominal fat mass and dorsal posture. In turn, the reduced lung volume decreases the effort at the level of the trachea induced by the traction exerted by means of the mediastinal structures, by negative intrathoracic pressures, by the lowering of the diaphragm and by the increase in the thickness of the pharyngeal side walls with the narrowing of the airways.

Several types of cross-sectional studies have revealed a monotonic relationship between OSA and body weight, BMI, neck circumference, waist-to-hip ratio, and other measures of body composition [9]. Our research reports an increased prevalence among obese of OSA n=190 (92.2%) compared to obese without OSA n=16 (7.7%) (p=0,0001). In addition, fluctuations in body weight have demonstrated an influence on the severity of OSA. A 10% increase in body weight was associated with an approximately 30% worsening of OSA grade [15].

The postoperative complications reported in the obese in the research were: arterial hypertension n=108 (26.8%), arterial hypotension n=28 (6.9%), cardiovascular instability (the need to connect cardiotonics) n=11 (2.7%), cardiac arrhythmia n=35 (8.7%), myocardial infarction (followed by death) n=2 (0.4%), bradypnea n=28 (6.9%), need to ventilate postoperative artificial lungs ≥60 min n=12 (2.9%), pneumonia n=4 (0.9%), laryngospasm n=1 (0.2%), unplanned transfer to the ICU n=15 (3.7%), difficult intubation n=9 (2.2%), stroke n=2 (0.4%), fever [≥38.5°C] postoperatively n=6 (1.4%).

Smoking is a well-known risk factor for postoperative pulmonary complications, with a potential to be avoided and modified, depending on the patient's compliance. Smoking causes difficulties in sleep initiation, sleep fragmentation, and daytime sleepiness [16]. The physiopathological mechanism of smoking also includes the damage to the ciliated epithelium caused by the impairment of the tracheobronchial clearance, with the increase in the reactivity of the tracheobronchial system, the secretion of hyperviscous mucus and the narrowing of the small airways causing an increase in the closing volume [17].

Studies are inconsistent regarding the identification of smoking as a risk factor for OSA. In a cohort study, Wisconsin Sleep, a higher risk of snoring and OSA was observed in smokers compared to non-smokers or ex-smokers with a ratio of 2.29 and 4.44, respectively [18]. This finding was confirmed by another study where smokers were 2.5 times more likely to have OSA than non-smokers [19]. In the research, there were 44 (11%) smoking patients, of which 28 patients (63.6%) were in the group with high risk of OSA and 16 patients (36.3%) in the group with low risk of OSA. Thus, smokers were 1.7 times more likely to have OSA than non-smokers.

Arterial hypertension – During the research, 283 patients (70.7%) reported arterial hypertension as a comorbidity, of which there were 257 (90.8%) patients with OSA compared to those without OSA n=26 (9.1%) with p=0.0001. The main mechanism in the development of arterial hypertension in OSA is the hyperactivity of the sympathetic nervous system. It has been postulated that intermittent hypoxia and negative intrathoracic pressure lead to chemoreceptor activation with increased sympathetic activity and subsequent endothelial dysfunction, which predisposes to increased arterial stiffness and the development of arterial hypertension.

No publications were identified that revealed data regarding the influence as a risk factor on the occurrence of perioperative complications of FEV and the distance between the occipital protuberance and the C7 vertebra.

Conclusions

1. Patients with obstructive sleep apnea have postoperative complications and produce adverse events significantly more frequently than those with a reduced risk of obstructive sleep apnea, regardless of the spectrum of complications and adversities taken into consideration;
2. Risk factors have a different affinity to postoperative complications and adverse events.
3. Within the ROC analysis of the risk factors, the analysis showed that the studied variables have statistical significance regarding the development of postoperative cardiovascular complications in OSA patients. The probability of developing cardiovascular complications in patients with OSA is 80.2%.
4. The studied variables have less statistical significance for respiratory complications and postoperative adverse events, with a probability for respiratory complications of 13% and for adverse events of 6%.
5. Our research demonstrated that OSA patients are in the high risk category of developing severe perioperative complications. Therefore, the identification and optimal perioperative management of OSA patients is mandatory.

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