Pneumologia
REVISTA SOCIETĂȚII ROMÂNE DE PNEUMOLOGIE

Predictors of daytime sleepiness in patients with obstructive sleep apnea

Predictori ai somnolenței diurne la pacienții cu sindrom de apnee în somn obstructiv

Alexandru Corlateanu[1], Serghei Pylchenko[2], Victoria Sircu[1], Victor Botnaru[1]

1. Department of Respiratory Medicine, State University of Medicine and Pharmacy "Nicolae Testemitanu", Chisinau, Moldova

2. São João Hospital Center, Porto, Portugal

Corresponding author:
Alexandru Corlateanu, MD, PhD
Department of Respiratory Medicine, State University of Medicine and Pharmacy "Nicolae Testemitanu", Chisinau, Moldova
Stefan cel Mare street 165, 2004 Chisinau, Republic of Moldova
E-mail: alexandru_corlateanu@yahoo.com

Abstract

Background. *The main symptomatic criterion to diagnose obstructive sleep apnea (OSA) is the level of daytime sleepiness. The Epworth Sleepiness Scale is a simple, self-administered questionnaire which provides a measurement of the subject's general level of daytime sleepiness. The aim of this study was to investigate the factors that can predict daytime sleepiness in patients with sleep apnea.*
Methods. *50 consecutive patients with obstructive sleep apnea were enrolled into the study. Age, gender, anthropometric and polygraphic data were thoroughly analyzed. In all subjects daily sleepiness was assessed by Epworth Sleepiness Scale.*
Results. *The mean age of the subjects was 54.7±12.8 years, 82% males. The mean BMI was 31.9±6 kg/m^2. Pearson correlation coefficient analysis demonstrates a significant positive correlation between the Epworth Sleepiness Scale and the desaturation index (r=0.31, p<0.01) and arterial hypertension (r=0.32, p<0.01). The forward stepwise regression analysis shows that the apnea hypopnea index and desaturation index are important predictors of daytime sleepiness in patients with obstructive sleep apnea which explains 40% of the Epworth Sleepiness Scale score.*
Conclusion. *The desaturation index showed the strongest correlation with the Epworth scale. According to the results of the backward stepwise multiple regression and logistic regression, the predictors for the level of daytime sleepiness are oAHI and index of desaturation. According to the analysis of the ROC curve, desaturation index is a predictor of a high specificity.*
Keywords: *sleep apnea, Epworth Sleepiness Scale, daytime sleepiness*

Rezumat

Introducere: *Principalul simptom al sindromului de apnee în somn obstructiv (SASO) este somnolența diurnă. Scala Epworth este un chestionar simplu, autoadministrat ce cuantifică gradul de somnolență diurnă a pacinetului. Scop: investigarea factorilor ce pot prezice somnolența diurnă la pacienții cu SASO*
Material și metodă: *50 de pacienți cu SASO au fost înrolați. S-au măsurat vârsta, sexul, date antopometrice, datele poligrafiei. La toți subiecții s-a aplicat chestionarul Epworth.*
Rezultate: *Vârsta medie a fost de 54,7±12,8, dintre care 82% bărbați. Media indicelui de masă corporală a fost de 21,9±6kg/m2. Coeficientul de corelație Pearson a demonstrat o corelație pozitivă între rezultatul chestinarului Epworth și indiele de desaturare (r=0.31, p<0.01) și tensiunea arterială (r=0.3, p<0.01). Indicele de apnee/hipopnee și cel de desaturare sunt factori de predicție ai somnolenței diurne la pacienți cu SASO, ceea ce explică 40% din scorul înregistrat pe scara Epworth.*
Concluzii: *indicele de desaturare s-a corelat puternic cu scala Epworth. Nivelul somnolenței diurne este influențat de indicele de desaturare și indicele de apnee/hipopnee. Indicele de desaturare este un predictor cu o mare specificitate.*
Cuvinte-cheie: *SASO, scala Epworth, somnolență diurnă*

Introduction

OSAS is a chronic respiratory disorder that is associated with significant morbidity and mortality including cardiovascular, metabolic, neurocognitive alterations and increased cancer-related deaths[1]. Polysomnography is considered the gold standard for the diagnosis of respiratory syndromes associated with sleep disorders, including obstructive sleep apnea[2]. However, this study requires a highly specialized technical staff to carry it out, as well as to make calculation and interpretation of the data obtained. This method is expensive and is of great discomfort towards the patient. Therefore, it is believed that for the most patients with obstructive sleep apnea syndrome it is not necessary to carry out such a thorough checkup as polysomnography. Proposals were developed for a number of portable monitoring devices that can be used in ordinary hospitals or at the patient's home[3].

Portable monitoring (PM) stands out for its relatively low costs, portability, serviceability and simplicity of installation for the patient. There is no need for the patient to sleep in the specialized laboratory, and in case of an error in exploitation or data loss the checkup can be easily repeated. Moreover, many studies prove the specificity and sensitivity of the method[4-6].

Data obtained by portable monitoring are always evaluated in conjunction with the symptoms of the disease. The main symptomatic criterion to diagnose obstructive sleep apnea (OSA) is the level of daytime sleepiness. Most commonly it is determined by special scales, such as Epworth Sleepiness Scale (7) or Berlin Questionnaire Scale[8]. They are widespread, and are considered to be simple and universal methods of identifying and evaluating daytime sleepiness. Therefore, the goal of finding out the relationship between the scales data of daytime sleepiness and the results of polygraphy is relevant nowadays.

In our research the main emphasis will be placed on identifying with a portable monitor SOMNOcheck micro (Weinmann, Germany) those parameters that are more closely associated with the results of the Epworth scale and are so called predictors for the level of daytime sleepiness.

Aim

The purpose of this study was to identify predictors of daytime sleepiness in patients with obstructive sleep apnea, to detect correlation between the results of Epworth questionnaires, polygraphy parameters and anthropometry data, to evaluate sensitivity and specificity of the revealed predictors using the ROC (receiver operating characteristic) curves method.

Materials and Methods

The study involved 50 patients with obstructive sleep apnea. The anthropometric data included age, height, weight, neck circumference. Additionally, patients were examined by using the Epworth scale of daytime sleepiness, and an outpatient night portable monitoring was carried out by the use of the SOMNOcheck micro device (Weinmann, Germany).

The initial selection of patients was based on anamnestic data. Patients complained of daytime symptoms (daytime sleepiness, fatigue, impaired concentration) and nocturnal symptoms (snoring, restless sleep, frequent awakenings). All the patients were subjected to an anthropometric examination.

In order to determine the level of daytime sleepiness a questionnaire was carried out using the Epworth scale. The overnight portable monitoring was carried out by the SOMNOcheck micro device (Weinmann, Germany) to diagnose OSA.

Ethical Considerations

This study was conducted according to the principles of the Declaration of Helsinki. The protocol of this study was approved by our Institutional Review Boards (State University of Medicine and Pharmacy "Nicolae Testemitanu", 6 April 2015), and written informed consent was obtained from all of the patients before enrollment.

Statistical analysis

Statistical analysis was performed by using the applications StatSoft STATISTICA 7.0 and MedCalc ver. 11.5. The results were expressed as mean ± standard deviation or as an absolute number (percentage). The correlation analysis of the variables was performed with the use of Pearsons correlation coefficient (when the variables were normally distributed). T-test was used to analyze the parameters resulting from the estimation of the linear regression model; the statistical model was validated using the coefficient of determination (R square). In all the analyses, p values below the 5 percent level, two-tailed, were regarded as the significant ones.

Statistical methods used in the STATISTICA 7 program: Descriptive statistics (mean, standard deviation, median, the 25th and 75th percentiles); the Spearman correlation coefficient; backward stepwise multiple regression method. Statistical methods used in the program MedCalc ver. 11.5: logistic regression (logit regression): the calculation of odds ratio and the ROC curves analysis.

Results

41 men and 9 women were enrolled in the study. The mean age of the patients was 54.7 ± 12.8 years. The mean weight was 94.8 ± 18.1 kg and the mean height was 172.4 ± 8.5 cm. The mean BMI was 31.9 ± 6 kg/m2. The mean index value of the Epworth scale was 8 ± 4.9 points. According to the survey the 38% of patients suffered from excessive daytime sleepiness. The mean AHI (apnea-hypopnea index) value was 18.4 ± 17.7 events per hour, the mean duration of sleep apnea was 17 seconds, and the mean index of desaturation was 12.1 ± 14.2 events per hour. Desaturation index is the only index that correlates with the Epworth scale of daytime sleepiness (r = 0.3) (Table 1).

Multiple correlation coefficient represents a close relationship between the revealed predictors and the Epworth scale (R = 0.7). Determination coefficient (R2= 0.4) indicates that the regression model describes the 40% of the Epworth scale ($p < 0.05$) (Table 2).

According to Table 3, the revealed predictors for the Epworth scale are desaturation index (beta coefficient = 1.3) and obstructive apnea-hypopnea index (oAHI) (beta coefficient = -0.9) ($p < 0.05$).

The relationship of desaturation index with Epworth is positive (beta coefficient = 1.3). That means that the increase in desaturation index results in the increase in Epworth scale indices. The relationship of the oAHI parameter with the Epworth scale results is negative (beta coefficient = -0.9). Consequently, the increase in this parameter leads to a decrease in Epworth indices.

Figure 1 shows that the spread of the 46 observations is within the range from -6 to 6 and 4 observations have values ranging from 7 to 13.5. These four values are overshoots and are recommended to be excluded to improve the regression model.

Exclusion of the residues from the model has significantly improved it. This model shows that the relationship between the revealed predictors and the Epworth scale is very strong (R = 0.9). According to the new determination coefficient the given model describes the 80% of Epworth scale (R2= 0.8) ($p < 0.05$) (Table 4).

Table 1 Correlation of the PM indices and anthropometric data with the Epworth scale

Index	Epworth	P
AHI (events per hour)	0.2	0.3
Respiratory disturbance index (RDI) (events per hour)	0.3	0.1
Desaturation index (events per hour)	0.3	< 0.01
Minimal saturation (events per hour)	0.2	0.2
Obstructive apnea-hypopnea index (oAHI) (events per hour)	0.2	0.3
Neck circumference (cm)	0.3	0.1

Table 2 Characteristics of the regression model

Index	Value
Multiple correlation coefficient R	0.7
Determination coefficient	0.4
p-level	< 0.01

Table 3 Predictors for the Epworth scale based on the results of multiple regression

Index	Beta coefficient	P
oAHI (events per hour)	-0.9	< 0.01
Desaturation index (events per hour)	1.3	< 0.01

Table 4 Characteristics of the multiple regression model

Index	Value
Multiple correlation coefficient R	0.9
Determinationcoefficient	0.8
p	< 0.01

Table 5 Predictors for Epworth scale based on results of multiple regression

Index	Beta coefficient	p
oAHI (events per hour)	-1,5	< 0.01
Desaturation index (events per hour)	1,7	< 0.01

According to table 5 the oAHI (beta coefficient = -1.5) (p <0,05) and the desaturation index (beta coefficient = 1.7) (p <0,05) have manifested themselves as stronger predictors than in the previous model, as they have bigger regression coefficients than in the previous model, where the oAHI beta coefficient is 0.9, and the desaturation index beta coefficient is 1.3.

Based on the results of the backward stepwise multiple regression, it can be concluded that the predictors for the daytime sleepiness level are oAHI (beta coefficient = -1.5) and desaturation index (beta coefficient = 1.7) (Table 5).

In the analyzed model the AUC = 0.9 (area under the curve), that indicates the excellent predictive power of the model. The model possesses a high statistical significance (p = < 0.01) and is included in the 95% confidence interval (Table 6).

Table 7 displays the regression coefficients (b) and their statistical significance. Desaturation index (b=0.7; p <0.05) possesses the highest and the only significant regression coefficient.

The only index that increases the chances (twice) of appearance of a high sleepiness level is desaturation index. Neck circumference has no effect on increasing the chanc-

Table 6 General characteristics of the logistic regression model

Index	Coefficient
Area under the curve (AUC)	0.9
p	< 0.01
95% confidence interval	0.8 – 1.0

Table 7 Predictors for Epworth scale based on results of logistic regression

Index	Coefficient (b)	Standard error	P
AHI (events per hour)	-0.1	0.3	0.7
Desaturation index (events per hour)	0.7	0.3	< 0.01
oAHI (events per hour)	-0.3	0.3	0.3
Neck circumference (cm)	0.0	0.2	1.0

Table 8 Odds ratio for logistic regression indices

Index	Odds ratio	95% confidence interval
AHI (events per hour)	0.9	0.5 – 1.5
Desaturation index (events per hour)	2.0	1.1 – 3.8
oAHI (events per hour)	0.7	0.4 – 1.2
Neck circumference (cm)	1.0	0.7 – 1.4

Table 9 Analysis of the ROC curve for desaturation index

Parameter	Value
AUC	0.7
95% confidence interval	0.5 – 0.8
p	0.02
Sensitivity	58%
Specificity	79%

es for appearance of a positive result. AHI and oAHI decrease the probability of a positive outcome (Table 8).

According to the ROC curves analysis (Table 9), it can be concluded that the predictor of desaturation index has a good predictive power and high specificity.

Discussion

Presumably, the Epworth daytime sleepiness scale should correlate well with the main index of the portable monitoring, which is AHI. However, in our study we were faced with the fact that the AHI correlates worse with the Epworth scale than with some other indices. Perhaps this is due to the fact that the Epworth scale is a subjective method and imperfectly reflects the severity of OSA. There was a study carried out in 2000, which also shows a low correlation between AHI and the Epworth scale[9]. The main goal of that study was to find out how much the daytime sleepiness manifested in patients with varying degrees of obstructive sleep apnea severity. The study involved 30 patients and used polysomnography. The main severity criterion for OSA was a respiratory distress index (RDI). 15 patients had moderate OSA (RDI < 40). The other 15 were suffering from severe OSA (RDI > 40). The study found that the moni-

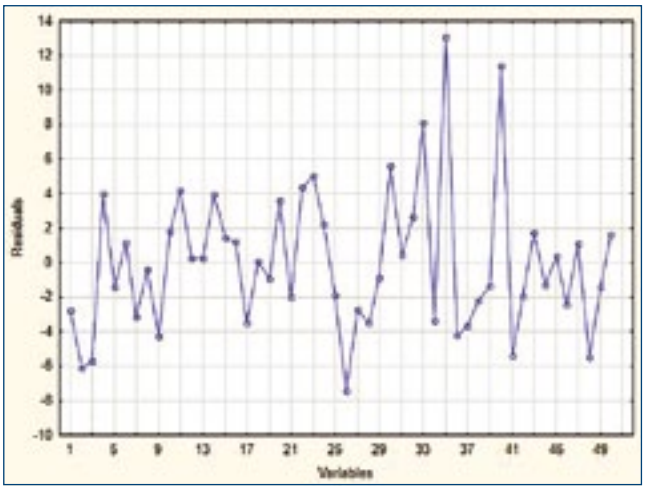

Figure 1. *Distribution diagram of residues according to the results of multiple regression*

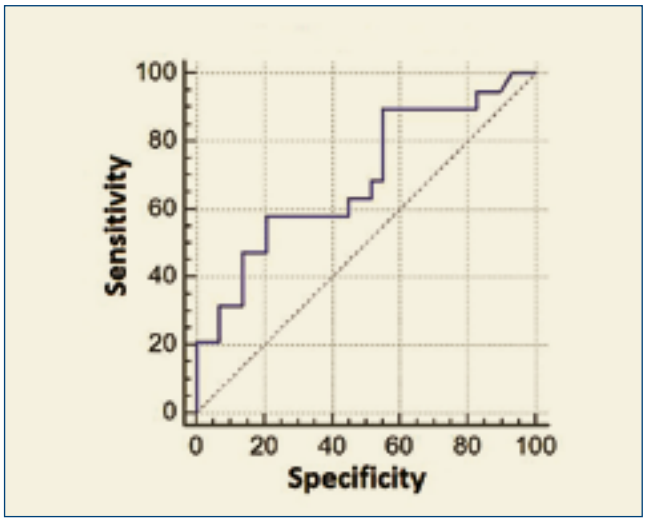

Figure 2. *ROC curve for desaturation index*

toring indices do not directly correlate with the level of daytime sleepiness. In our study, the oAHI did not display any significant correlation with the Epworth scale, however, it was identified as a predictor of the daytime sleepiness level. This result is similar to the results of that study and confirms that monitoring indices do not always correlate with the Epworth scale directly.

Some authors maintain that AHI is not the most demonstrative value for assessing severity of OSA[10]. In a study of the year 2005 in Pennsylvania, USA, Veasey made an attempt to correlate the level of daytime sleepiness in patients with OSA with the degree of their sleep fragmentation disorder. The researcher found out that oxygen saturation demonstrates the degree of sleep fragmentation better than AHI. Moreover, it better reflects the severity of nighttime and daytime symptoms in patients with OSA. In our study, desaturation index turned out to be the main predictor of the level of daytime sleepiness, too, that confirms the results of the researcher.

The insignificant relationship between AHI and level of daytime sleepiness is also explained by the fact that AHI is calculated on the basis of the number of events of apnea and hypopnea, but does not reflect their severity. There are studies that prove that excessive daytime sleepiness is more dependent on the number of awakenings, which indirectly reflect the number of apnea events, excluding hypopnea events from the calculation[11-13].

The main limitation of this study is small number of patients. In a small number of patients, any deviation from the mean value greatly affects the results of the statistical analysis. The smaller the group is, the less representative a sample is considered.

Another limitation is the fact that the Epworth scale is a subjective method and imperfectly reflects the real level of daytime sleepiness in patients.

Conclusions

The desaturation index showed the strongest correlation with the Epworth scale. According to the results of the backward stepwise multiple regression and logistic regression, the predictors for the level of daytime sleepiness are oAHI and index of desaturation. According to the analysis of the ROC curve, desaturation index is a predictor of a high specificity. ■

References

1. Corlateanu A, Botnaru V, Mathioudakis A, Sircu V, Siafakas N. Overlap Syndrome of Chronic Obstructive Pulmonary Disease and Obstructive Sleep Apnoea: A two-faced Janus. Current Respiratory Medicine Reviews. 2015;11(2):in press.
2. Collop NA, Anderson WM, Boehlecke B, Claman D, Goldberg R, Gottlieb DJ, et al. Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients. Portable Monitoring Task Force of the American Academy of Sleep Medicine. *J Clin Sleep Med.* 2007 Dec;3(7):737-47.
3. Flemons WW, Littner MR, Rowley JA, Gay P, Anderson WM, Hudgel DW, et al. Home diagnosis of sleep apnea: a systematic review of the literature. An evidence review cosponsored by the American Academy of Sleep Medicine, the American College of Chest Physicians, and the American Thoracic Society. *Chest.* 2003 Oct;124(4):1543-79.
4. Tonelli de Oliveira AC, Martinez D, Vasconcelos LF, Goncalves SC, Lenz MC, Fuchs SC, et al. Diagnosis of obstructive sleep apnea syndrome and its outcomes with home portable monitoring. *Chest.* 2009 Feb;135(2):330-6.
5. Whitelaw WA, Brant RF, Flemons WW. Clinical usefulness of home oximetry compared with polysomnography for assessment of sleep apnea. *Am J Respir Crit Care Med.* 2005 Jan 15;171(2):188-93.
6. Mulgrew AT, Fox N, Ayas NT, Ryan CF. Diagnosis and initial management of obstructive sleep apnea without polysomnography: a randomized validation study. *Ann Intern Med.* 2007 Feb 6;146:157-66.
7. The Epworth Sleepiness Scale. 2015; Available from: http://web.stanford.edu/~dement/epworth.html.
8. Berlin Score Questionnaire – Sleep Test. 2015; Available from: https://www.ukcpap.co.uk/info-questionnaire-berlin-score.php.
9. Sauter C, Asenbaum S, Popovic R, Bauer H, Lamm C, Klosch G, et al. Excessive daytime sleepiness in patients suffering from different levels of obstructive sleep apnoea syndrome. J Sleep Res. 2000 Sep;9:293-301.
10. Veasey SC. Obstructive sleep apnea: re-evaluating our index of severity. *Sleep Medicine.*7(1):5-6.
11. Yue HJ, Bardwell W, Ancoli-Israel S, Loredo JS, Dimsdale JE. Arousal frequency is associated with increased fatigue in obstructive sleep apnea. *Sleep Breath.* 2009 Nov;13:331-9.
12. Kingshott RN, Engleman HM, Deary IJ, Douglas NJ. Does arousal frequency predict daytime function? *Eur Respir J.* 1999 Dec;12:1264-70.
13. Roehrs T, Zorick F, Wittig R, Conway W, Roth T. Predictors of objective level of daytime sleepiness in patients with sleep-related breathing disorders. *Chest.* 1989 Jun;95:1202-6.