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The triad of obstructive sleep apnea syndrome, COPD, and obesity: sensitivity of sleep scales and respiratory questionnaires

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Study carried out at the Ambulatório de Pneumologia, Hospital Regional de Presidente Prudente; Faculdade de Fisioterapia e Faculdade de Medicina, Universidade do Oeste Paulista – Unoeste – Presidente Prudente (SP) Brasil; and at the Hospital das Clínicas, Faculdade de Medicina de Botucatu, Universidade Estadual Paulista, Botucatu (SP) Brasil.

ABSTRACT

Objective: To investigate whether the presence of obstructive sleep apnea syndrome (OSAS) alters the perception of respiratory symptoms and quality of life in COPD patients, by using specific questionnaires, as well as to determine whether scales for assessing daytime sleepiness and for screening for OSAS can be used in the triad of OSAS, COPD, and obesity. **Methods:** We included 66 patients diagnosed with mild-to-moderate or severe COPD and presenting with a body mass index > 27 kg/m^2. After polysomnography, patients completed the Epworth sleepiness scale (ESS), the Berlin questionnaire (BQ), the modified Medical Research Council (mMRC) scale, the Baseline Dyspnea Index (BDI), and the Saint George's Respiratory Questionnaire (SGRQ). **Results:** Patients were first divided into two groups: COPD + OSAS (n = 46); and COPD-only (n = 20). The COPD + OSAS group was subdivided into a COPD + mild-to-moderate OSAS group (n = 32) and a COPD + severe OSAS group (n = 14), all of which were compared with the COPD-only group. There was a significant difference in mean FEV_1 (L) between the COPD + OSAS groups and the COPD-only group (p = 0.073). The presence of the triad did not lead to significantly higher ESS scores, and scores > 10 had a specificity of 0.58. The BQ did not identify high risk for OSAS in the presence of the triad (specificity of 0.31). There were no significant differences in domain or total scores of the SGRQ between the COPD + OSAS groups and the COPD-only group. **Conclusions:** The confounding factors present in the triad of OSAS, COPD, and obesity prevented the perception of increased daytime sleepiness and high risk for OSAS. We observed no worsening of dyspnea perception or quality of life.

Keywords: Sleep apnea, obstructive; Pulmonary disease, chronic obstructive; Obesity; Surveys and questionnaires.

INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by intermittent partial or complete obstruction of the airways during sleep, being called OSA syndrome (OSAS) when it is associated with daytime/nighttime symptoms and/or comorbidities, such as systemic arterial hypertension or diabetes mellitus.[1] The prevalence of OSAS is as high as 32%[2] in the general population, ranges from 1% to 20% in subjects with COPD (overlap syndrome),[1,3] and is reported to be greater than 60% in subjects with COPD and obesity (triad of COPD, OSAS, and obesity).[4,5] The major daytime symptom of OSAS is sleepiness,[1] which can be assessed by the Epworth sleepiness scale (ESS).[6] The likelihood of having OSAS can be determined by the Berlin Questionnaire,[7] which has been used as a screening instrument; however, the gold standard for diagnosis is overnight polysomnography (PSG).[1,2]

COPD is characterized by lower airway airflow limitation that is not fully reversible,[1] and its prevalence ranges from 8% to 10% in subjects over 40 years of age in developed countries, although it can be as high as 15%.[8,9] The progressive impairment of pulmonary function can proportionally increase exertional dyspnea, which causes changes in and limits activities of daily living (ADL) and leads to functional disability; this has been assessed by the modified Medical Research Council (mMRC) scale[10] and the Baseline Dyspnea Index (BDI).[11] Quality of life in COPD patients has been assessed by the Saint George's Respiratory Questionnaire (SGRQ),[12] and there have been reports of worsening in (increased scores on) all domains of assessment.[13,14]

A combination of diseases can limit the use of sleep scales and respiratory questionnaires. COPD and obesity can contribute to the presence of dyspnea and the sensation of fatigue or tiredness in patients suspected of having OSA.[15] They act as confounding factors that could affect the accuracy of those scales and questionnaires.

In this context, it is necessary to clarify the use of respiratory questionnaires (quality of life and dyspnea) and sleep scales (sleepiness and risk for OSAS) in the triad of COPD, OSAS, and obesity. The combination of COPD, obesity, and OSAS makes it difficult to use the

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Berlin Questionnaire as a screening tool for OSAS, as well as making the ESS lose its specificity. Assessment of functional capacity by the mMRC scale and the BDI, as well as assessment of quality of life by the SGRQ, will be compromised by the presence of OSAS and obesity in combination with COPD.

The objective of the present study was to investigate whether the presence of OSAS alters the perception of respiratory symptoms and quality of life in COPD patients, by using specific questionnaires, as well as to determine whether scales for assessing daytime sleepiness and for screening for OSAS can be used in the triad of OSAS, COPD, and obesity.

METHODS

This study was approved by the Research Ethics Committee of the *Universidade do Oeste Paulista* (Unoeste, Western São Paulo State University), located in the city of Presidente Prudente, Brazil, and by the Research Ethics Committee of the São Paulo State University Botucatu School of Medicine, located in the city of Botucatu, Brazil (*Plataforma Brasil*; Registration no. 0905.1212.7.0000.551). All patients gave written informed consent.

We included 66 COPD patients presenting with a body mass index (BMI) > 27 kg/m^2 and treated at the pulmonology outpatient clinics of either the Regional Hospital of Presidente Prudente or the Unoeste Schools of Medicine and Physiotherapy, or at the Botucatu School of Medicine *Hospital das Clínicas*. COPD severity was classified (as moderate or severe) on the basis of spirometry results, in accordance with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2016 criteria,[16] with moderate COPD (GOLD II) being defined as 50% ≤ FEV_1 < 80% and severe COPD (GOLD III) being defined as 30% ≤ FEV_1 < 50%.

Patients completed the ESS and the Berlin Questionnaire, which assess sleepiness and risk for the presence of OSAS, respectively. The ESS determines the likelihood of dozing off in eight situations involving ADL, and scores > 10 points correspond to daytime sleepiness.[6] The Berlin Questionnaire comprises questions that investigate snoring, tiredness/fatigue, and the presence of systemic arterial hypertension or obesity, and that are grouped into categories. High risk for OSAS is defined as a positive score on two or more categories.[7] In addition, patients completed the mMRC scale[10] and the BDI[11] to assess the sensation of dyspnea, as well as the SGRQ[12] to measure quality of life.

The first component of the BDI assesses the magnitude of the task triggering dyspnea. The second and third components assess the magnitude of the effort leading to dyspnea and the functional impairment caused by dyspnea, respectively. The total score is obtained by summing the scores for each of the three domains and ranges from 0 to 12. Lower scores indicate greater severity of dyspnea.[11] The mMRC scale, which ranges from 1 to 4, measures the level of dyspnea in four everyday situations. Higher scores indicate greater severity of dyspnea.[10] The SGRQ comprises three domains: symptoms (problems caused by respiratory symptoms); activities (activity restrictions caused by dyspnea); and psychosocial impact (impact of the disease on daily life). The score ranges from 0 (no reduction in quality of life) to 100 (maximum reduction in quality of life).[12]

All patients underwent overnight PSG to confirm the diagnosis of OSAS. On the basis of the PSG results, patients were first divided into two groups: COPD + OSAS (overlap syndrome); and COPD-only; in addition, the overlap syndrome group was subdivided on the basis of the severity of OSAS into COPD + mild-to-moderate OSAS—defined as an apnea-hypopnea index (AHI) between 5 and 30 events/h—and COPD + severe OSAS—defined as an AHI > 30 events/h.[17]

Statistical method

Descriptive statistics were calculated using frequencies and proportions for qualitative variables and using means and standard deviations or medians and interquartile ranges for quantitative variables.

The chi-square test or Fisher's exact test, as appropriate, was used to test the association between the outcome variable and the explanatory variables of interest.

Quantitative variables were tested for normality of distribution, and, for variables that had a normal distribution, ANOVA with Tukey's post hoc test was used for multiple comparison among the groups (COPD + OSAS vs. COPD + mild-to-moderate OSAS vs. COPD + severe OSAS vs. COPD-only). For variables that had a non-normal distribution, a generalized linear model adjusted to gamma distribution was used.

Values of $p < 0.05$ were considered significant. We used the Statistical Analysis System, version 9.3 (SAS Institute Inc., Cary, NC, USA).

RESULTS

We included 66 COPD patients, 46 (69.70%) of whom were diagnosed with overlap syndrome (COPD + OSAS) by PSG. The patients with overlap syndrome were subdivided on the basis of the severity of OSAS into a COPD + mild-to-moderate OSAS group (n = 42; 48.48%) and a COPD + severe OSAS group (n = 14; 21.21%). The groups were homogeneous regarding gender and BMI (Table 1).

All of the selected patients had obstructive lung disease on spirometry. The mean FVC, FEV_1, and FEV_1/FVC ratio, and their respective standard deviations, can be seen in Table 2. Although the mean FVC in L was lowest in the COPD-only group, the mean FVC in % of predicted showed statistical similarity among the groups. The mean FEV_1 in L and the mean FEV_1 in % of predicted were similar among the groups (Table 2).

A diagnosis of overlap syndrome did not lead to statistically significantly higher ESS scores (11.77 ± 4.89 vs. 9.68 ± 5.58), and scores > 10 had an accuracy of 0.57, with a sensitivity and specificity of 0.61 and 0.58, respectively. The Berlin Questionnaire did not identify patients diagnosed with overlap syndrome, although it had a sensitivity of 0.83 for recognition of OSAS and of 100% for recognition of severe OSAS, with a very low specificity and accuracy, 0.31 and 0.63, respectively (Tables 3 and 4). These data suggest that the ESS and the Berlin Questionnaire have no or low accuracy for identification of the overlap syndrome.

ADL-limiting dyspnea was assessed by the mMRC scale, and the values obtained were similar between COPD patients with and without OSAS, regardless of severity. Distribution by BMI category also did not indicate significant differences among the groups.

All domains of the SGRQ had high scores in the different groups evaluated. However, the presence or greater severity of OSAS did not affect the quality of life scores determined by the questionnaire (Table 5).

DISCUSSION

The present study investigated the presence of OSAS in COPD patients, as well as whether a diagnosis of overlap syndrome would worsen the perception of dyspnea, quality of life, and daytime sleepiness, making a research questionnaire a potential tool in the identification of the overlap syndrome. In the present study sample, the ESS was unable to identify increased sleepiness, and the Berlin Questionnaire did not identify increased risk for OSAS, considering the triad of COPD, obesity, and OSAS. The combination of OSAS and obesity in COPD patients did not increase the severity of dyspnea as assessed by the mMRC scale, nor did it increase functional disability as assessed by the BDI. The scores on the domains of the SGRQ were similar between patients with and without OSAS.

The present study found similar ESS scores between patients with and without OSAS, with little likelihood of identifying increased daytime sleepiness. There are controversial data in the literature. In a study by Marin et al.,[18] the mean ESS score was 12 ± 4 and 6 ± 3, respectively, in the presence of overlap

Table 1. Characteristics of the study sample by group.[a]

Variable	Group				p
	COPD + OSAS (n = 46)	COPD + mild-to-moderate OSAS (n = 32)	COPD + severe OSAS (n = 14)	COPD-only (n = 20)	
Prevalence, %	69.70	48.48	21.21	30.30	
Male gender, n (%)	26 (56.52)	16 (50.0)	10 (71.43)	4 (20.0)*	0.006
Age, years	61.56 ± 11.30	63.78 ± 10.82	56.50 ±11.13	59.75 ±9.68	0.163
BMI, kg/m^2	34.00 ± 5.67	32.95 ± 5.34	36.41 ± 5.84	33.89 ±6.75	0.157
AHI, events/h	18.35 (11.05-39.62)	12.95 (9.75-19.97)*	68.55 (41.25-61.22)	1.70 (0.65-2.40)*	0.006

OSAS: obstructive sleep apnea syndrome; BMI: body mass index; and AHI: apnea-hypopnea index. [a]Values expressed as mean ± SD or as median (interquartile range), except where otherwise indicated. *p < 0.05.

Table 2. Spirometric parameters for the study participants by group.[a]

Variable	Group				p
	COPD + OSAS (n = 46)	COPD + mild-to-moderate OSAS (n = 32)	COPD + severe OSAS (n = 14)	COPD-only (n = 20)	
FVC, L	2.54 ± 0.76	2.37 ± 0.68	2.92 ± 0.82[a]	2.16 ± 0.77*	0.002
FVC, % predicted	70.16 ± 17.47	70.38 ± 18.46	69.59 ± 15.23	67.30 ± 21.65	0.522
FEV_1, L	1.63 ± 0.54	1.54 ± 0.48	1.84 ± 0.63	1.39 ± 0.52	0.073
FEV_1, % predicted	56.00 (48.75-65.25)	56.50 (51.25-64.75)	53.50 (37.25-71.75)	51.50 (41.25-64.50)	0.824
FEV_1/FVC, %	65.00 (48.75-65.25)	65.00 (60.00-73.00)	63.50 (58.00-67.25)	63.50 (55.75-73.50)	0.476

OSAS: obstructive sleep apnea syndrome. [a]Values expressed as mean ± SD or as median (interquartile range). *p < 0.05.

Table 3. Results of the Berlin Questionnaire and the Epworth sleepiness scale for the study participants by group.[a]

Variable	Group				p
	COPD + OSAS (n = 46)	COPD + mild-to-moderate OSAS (n = 32)	COPD + severe OSAS (n = 14)	COPD-only (n = 20)	
Berlin Questionnaire, %					
Positive	89	84	100	68	
Negative	11	16	0	31	
ESS, score	11.77 ± 4.89	11.08 ± 4.81	13.50 ± 4.90	9.68 ± 5.58	0.217

OSAS: obstructive sleep apnea syndrome; and ESS: Epworth sleepiness scale. [a]Values expressed as mean ± SD, except where otherwise indicated.

syndrome and in COPD patients with no OSAS. The mean AHI, which was higher in the study by Marin et al.[18] (34 events/h) than it was in our study, may have influenced the observed level of sleepiness. In our study, the COPD + severe OSAS group also had higher scores, but the difference did not reach significance, probably because of the small number of patients in this group (n = 14). In a study by Venkateswaran & Tee,[19] ESS scores were compared in patients diagnosed with OSAS, those diagnosed with overlap syndrome, and those diagnosed with COPD (11.39 vs. 13.89 vs. 4.84) and were found to be highest in the overlap syndrome group. Shiina et al.[20] reported no such finding. In their study, including 524 individuals with OSAS, 64 patients (12%) were diagnosed with overlap syndrome, with a mean ESS of 9.0 (range, 6.0-13.0) in the OSAS group and a mean ESS of 7.0 (range, 4.5-11.0) in the overlap syndrome group ($p < 0.05$). The mean BMI of the patients in the overlap syndrome group was 24.8 kg/m^2, which is different from that found in our study, and may have contributed to the finding of lower scores. Steveling et al.[21] found only 20% of patients with ESS scores > 10 in the population diagnosed with overlap syndrome, although it included only obese patients with an AHI > 10 events/h. In a study by Faria et al.,[22] 40% of the patients had that characteristic, but the mean BMI in the overlap syndrome group was considered normal. In our sample, daytime sleepiness was found not only in patients with overlap syndrome, with 60% of our population having ESS scores > 10, but also in patients with no OSAS (in 40%). We believe that our study included patients with more severe COPD, with overlap of limitation of daytime activities and the subjective perception of sleepiness.

Subjective assessment of sleepiness with the ESS as a predictor of OSAS has been questioned in the literature. Ulasli et al.[23] found a sensitivity of 45% and a specificity of 60% in populations with OSAS, which were both even lower than those found in our study (62.8% and 57.8%, respectively), and questioned the applicability of the ESS as a screening tool. Similarly, in our study, the Berlin Questionnaire was found to be ineffective as a screening instrument for OSAS in COPD patients. Although the Berlin Questionnaire identified the presence of severe OSAS in COPD patients, it was unable to recognize patients without a diagnosis of overlap syndrome or those with mild-to-moderate OSAS. We believe that the questions regarding "fatigue" and "tiredness" (category 2) may be a confounding factor for COPD patients, who frequently have these complaints because of the limitation in performing ADL. Similar data were observed by Mahamoud et al.,[24] who identified high risk for OSAS in 70% of their sample of COPD patients. However, in the study by Faria et al.,[22] high risk for OSAS was identified in fewer patients (in 32.5% of the sample), which may be explained by the fact that all patients with overlap syndrome who were evaluated had normal BMI, which directly influences category 3 of the Berlin Questionnaire.

The presence or absence of OSAS did not influence the sensation of dyspnea or health status of COPD patients, as assessed by the mMRC scale. The mMRC scale is strongly related to dyspnea-induced limitations in ADL, and dyspnea is not a typical symptom in patients with OSAS.

The impact of dyspnea was similar as assessed by the BDI and the mMRC scale. A diagnosis of overlap syndrome did not lead to an increased sensation of dyspnea. Once again, it is clear that dyspnea is not a symptom commonly reported by individuals with OSAS.

In the three domains of assessment (symptoms, activities, and impact), as well as in the total score, quality of life as measured by the SGRQ was similar, regardless of the presence or severity of OSAS in the COPD patients. Scores > 25 were found, which is common among COPD patients,[13,14] and were also present in those with overlap syndrome. Therefore, the SGRQ was not sensitive enough to assess the presence of OSAS and obesity in combination with COPD.

Mermigkis et al.[25] observed that quality of life as assessed by the SGRQ was worse in patients with overlap syndrome than in COPD patients. However, the

Table 4. Accuracy, sensitivity, and specificity for the use of the Epworth sleepiness scale and the Berlin Questionnaire in the study sample of COPD patients with and without obstructive sleep apnea syndrome (n = 66).

Variable	Epworth sleepiness scale	Berlin Questionnaire
Accuracy	0.57	0.63
Sensitivity	0.61	0.83
Specificity	0.58	0.31

Table 5. Domain and total scores on the Saint George's Respiratory Questionnaire, by group.[a]

Variable	Group				p
	COPS + OSAS (n = 46)	COPD + mild-to-moderate OSAS (n = 32)	COPD + severe OSAS (n = 14)	COPD-only (n = 20)	
Symptoms domain	52.93 ± 24.43	49.36 ± 26.73	63.64 ± 11.51	48.96 ± 25.50	0.606
Activities domain	70.14 ±17.89	72.46 ±19.02	63.18 ± 12.84	73.56 ± 15.71	0.605
Impact domain	39.38 ± 16.03	40.20 ± 15.96	36.91 ± 17.49	45.74 ± 24.08	0.719
Total score	50.97 ± 15.99	51.47 ±17.10	54.72 ± 13.36	54.92 ±18.40	0.889

OSAS: obstructive sleep apnea syndrome. [a]Values expressed as mean ± SD.

mean FEV_1 in % of predicted was lower in the COPD group than in the overlap syndrome group (48.2% vs. 49.1%), which may have contributed to the worsened perception of quality of life.

The present study has various limitations. The study population is small in number, which may be a limitation for statistical analysis. We also believe that, because of the open invitation for participation in the study and the lack of randomization of outpatients, patients with more frequent symptoms and greater concern about having OSAS may have accepted the invitation, which would explain the high prevalence of overlap syndrome in our sample. However, data collection was blinded to the PSG results, which maintained the impartiality of the researchers.

In conclusion, the ESS and the Berlin Questionnaire as screening tools were unable to identify the presence of OSAS in patients with the triad of COPD, obesity, and OSAS in our sample. The mMRC scale and the BDI did not indicate poorer perception of dyspnea in ADL, nor was the SGRQ able to identify worsening of quality of life. Current instruments for clinical assessment of daytime sleepiness, risk for OSAS, effects of dyspnea on ADL, and quality of life do not allow recognition of the presence of OSAS in COPD patients, and its diagnosis depends on PSG.

REFERENCES

1. McNicholas WT. Chronic obstructive pulmonary disease and obstructive sleep apnoea-the overlap syndrome. J Thoracic Dis. 2016;8(2):236-42.
2. Tufik S, Santos-Silva R, Taddei JA, Bittencourt LR. Obstructive sleep apnea syndrome in the Sao Paulo Epidemiologic Sleep Study. Sleep Med. 2010;11(5):441-6. https://doi.org/10.1016/j.sleep.2009.10.005
3. Chaouat A, Weitzenblum E, Kessler R, Charpentier C, Enhart M, Schott R. A randomized trial of nocturnal oxygen therapy in chronic obstructive pulmonary disease patients. Eur Respir J. 1999;14(5):1002-8. https://doi.org/10.1183/09031936.99.14510029
4. Povitz M, James MT, Pendharkar SR, Raneri J, Hanly PJ, Tsai WH. Prevalence of Sleep-disordered Breathing in Obese Patients with Chronic Hypoxemia. A Cross-Sectional Study. Ann Am Thorac Soc. 2015:12(6):921-7. https://doi.org/10.1513/AnnalsATS.201412-551OC
5. Soler X, Gaio E, Powell LF, Ramsdell JW, Loredo JS, Malhotra A, et al. High Prevalence of Obstructive Sleep Apnea in Patients with Moderate to Severe Chronic Obstructive Pulmonary Disease. Ann Am Thorac Soc. 2015;12(8):1219-25.
6. Bertolazi AN, Fagondes SC, Hoff LS, Pedro VD, Menna Barreto SS, Johns MW. Portuguese-language version of the Epworth sleepiness scale: validation for use in Brazil. J Bras Pneumol. 2009;35(9):877-83. https://doi.org/10.1590/S1806-37132009000900009
7. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med. 1999;131(7):485-91. https://doi.org/10.7326/0003-4819-131-7-199910050-00002
8. Bednarek M, Plywaczewsk R, Jonczak L, Zielinsk J. There is no relationship between chronic obstructive pulmonary disease and obstructive sleep apnea syndrome: a population study. Respiration. 2005;72(2):142-9. https://doi.org/10.1159/000084044
9. Menezes AM, Perez-Padilla R, Jardim JR, Muiño A, Lopez MV, Valdivia G, et al. Chronic obstructive pulmonary disease in five Latin American cities (the PLATINO study): a prevalence study. Lancet. 2005;366(9500):1875-81. https://doi.org/10.1016/S0140-6736(05)67632-5
10. Kovelis D, Segretti NO, Probst VS, Lareau SC, Brunetto AF, Pitta F. Validation of the Modified Pulmonary Functional Status and Dyspnea Questionnaire and the Medical Research Council scale for use in Brazilian patients with chronic obstructive pulmonary disease. J Bras Pneumol. 2008;34(12):1008-18. https://doi.org/10.1590/S1806-37132008001200005
11. Mahler DA, Weinberg DH, Wells CK, Feinstein AR. The measurement of dyspnea. Contents, interobserver agreement, and physiologic correlates of two new clinical indexes. Chest. 1984;85(6):751-8. https://doi.org/10.1378/chest.85.6.751
12. Camelier A, Rosa FW, Salmi C, Nascimento OA, Cardoso F, Jardim JR. Using the Saint George's Respiratory Questionnaire to evaluate quality of life in patients with chronic obstructive pulmonary disease: validating a new version for use in Brazil. J Bras Pneumol. 2006;32(2):114-22. https://doi.org/10.1590/S1806-37132006000200006
13. Agusti A, Calverley PM, Celli B, Coxson HO, Edwards LD, Lomas DA, et al. Characterisation of COPD heterogeneity in the ECLIPSE cohort. Respir Res. 2010;11:122. https://doi.org/10.1186/1465-9921-11-122
14. Miravitlles M, Soriano JB, García-Rio F, Mu-oz L, Duran-Tauleria E, Sanchez G, et al. Prevalence of COPD in Spain: impact of undiagnosed COPD on quality of life and daily life activities. Thorax. 2009;64(10):863-8. https://doi.org/10.1136/thx.2009.115725
15. Koutsourelakis I, Perraki E, Bonakis A, Vagiakis E, Roussos C, Zakynthinos S. Determinants of subjective sleepiness in suspected obstructive sleep apnoea. J Sleep Res. 2008;17(4):437-43. https://doi.org/10.1111/j.1365-2869.2008.00663.x
16. Global Initiative for Chronic Obstructive Lung Disease - GOLD [homepage on the Internet]. Bethesda: Global Initiative for Chronic Obstructive Lung Disease [cited 2016 Jun 24]. Global Strategy for the Diagnosis, Management, and Prevention of COPD 2016. Available from: http://goldcopd.org/global-strategy-diagnosis-management-prevention-copd-2016/
17. American Academy of Sleep Medicine. The International Classification of Sleep Disorders. Diagnostic and Coding Manual. Westchester (IL): American Academy of Sleep Medicine; 2005.
18. Marin JM, Soriano JB, Carrizo SJ, Boldova A, Celli B. Outcomes in patients with chronic obstructive pulmonary disease and obstructive sleep apnea: the overlap syndrome. Am J Respir Crit Care Med. 2010;182(3):325-31. https://doi.org/10.1164/rccm.200912-1869OC
19. Venkateswaran S, Tee A. Overlap syndrome between chronic obstructive pulmonary disease and obstructive sleep apnoea in a Southeast Asian teaching hospital. Singapore Med J. 2014;55(9):488-92. https://doi.org/10.11622/smedj.2014117
20. Shiina K, Tomiyama H, Takata Y, Yoshida M, Kato K, Nishihata Y, et al. Overlap syndrome: additive effects of COPD on the cardiovascular damages in patients with OSA. Respir Med. 2012;106(9):1335-41. https://doi.org/10.1016/j.rmed.2012.05.006
21. Steveling EH, Clarenbach CF, Miedinger D, Enz C, Dürr S, Maier S, et al. Predictors of the overlap syndrome and its association with comorbidities in patients with chronic obstructive pulmonary disease. Respiration. 2014;88(6):451-7. https://doi.org/10.1159/000368615
22. Faria AC, da Costa CH, Rufino R. Sleep Apnea Clinical Score, Berlin Questionnaire, or Epworth Sleepiness Scale: which is the best obstructive sleep apnea predictor in patients with COPD? Int J Gen Med. 2015;8:275-81.
23. Ulasli SS, Gunay E, Koyuncu T, Akar O, Halici B, Ulu S, et al. Predictive value of Berlin Questionnaire and Epworth Sleepiness Scale for obstructive sleep apnea in a sleep clinic population. Clin Respir J. 2014;8(3):292-6. https://doi.org/10.1111/crj.12070
24. Mahamoud HA, Sallama SS, Ahmad AM. Validation of the Epworth sleepiness scale, Berlin, STOPBANG questionnaires and American Society of Anesthesiologists checklist as screening tools for obstructive sleep apnea in patients with chronic obstructive pulmonary disease, asthma and cardiovascular disease. Eur Respir J. 2013;42:P2032.
25. Mermigkis C, Kopanakis A, Foldvary-Schaefer N, Golish J, Polychronopoulos V, Schiza S, et al. Health-related quality of life in patients with obstructive sleep apnoea and chronic obstructive pulmonary disease (overlap syndrome). Int J Clin Pract. 2007;61(2):207-11. https://doi.org/10.1111/j.1742-1241.2006.01213.x