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Comparison of invasive intubation and noninvasive mechanical ventilation in patients with chronic obstructive pulmonary disease and obstructive sleep apnoea syndrome

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Abstract

Objective: The concurrence of chronic obstructive pulmonary disease (COPD) and obstructive sleep apnoea syndrome (OSAS) is defined as overlap syndrome (OS), but investigations into predictors of OS in patients with COPD remain limited. Here, potential markers of OS in patients with COPD were investigated, and results of intubation were compared between patients with COPD only or OS.

Methods: This retrospective study included patients with COPD who were divided according to OS diagnosis: COPD only (COPD group) or OS (OS group).

Results: Among 206 patients with COPD, 120 were diagnosed with OS. Mean body mass index (BMI) was significantly higher in the OS versus COPD group (28.95 $\pm$ 2.96 versus 23.84 $\pm$ 4.06, respectively). Receiver operating characteristic curve analyses revealed that BMI was associated with OS (area under the curve, 0.835). The rate of invasive intubation within 48 h was lower in

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the OS versus COPD group (9.2% versus 20.9%, respectively), and the duration of noninvasive ventilation was longer in the OS versus COPD group.
Conclusions: BMI may be a predictor of OS in patients with COPD. The duration of noninvasive ventilation was longer in patients with OS than in patients with COPD alone.

Keywords
Chronic obstructive pulmonary disease, obstructive sleep apnoea syndrome, overlap syndrome, body mass index, intubation, noninvasive ventilation

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Introduction

Patients with chronic obstructive pulmonary disease (COPD) experience nocturnal hypoxia and hypoventilation during the rapid eye movement phase of sleep, due to intercostal muscle relaxation and decreased chest wall mobility. Patients with obstructive sleep apnoea syndrome (OSAS) often experience apnoea and hypopnea, resulting in nocturnal awakenings and excessive daytime sleepiness, mainly through upper airway collapse, intrathoracic pressure reduction and activation of the sympathetic nervous system.[1] Overlap syndrome (OS) was first proposed by Flenley in 1985,[2] to describe the combination of OSAS and COPD in an individual.[2,3]

In patients with OS, the concurrence of COPD and OSAS aggravates daytime symptoms, and COPD has been associated with higher rates of snoring, apnoea and daytime sleepiness.[4,5] The concurrence of COPD and OSAS also aggravates hypoxaemia and hypercapnia during sleep, and reduces sleep time and quality.[6] In addition, OSAS can increase the frequency and degree of acute exacerbation in patients with COPD, leading to higher rates of respiratory failure in patients with OS.[7]

The concurrence of COPD and OSAS in patients with OS may have an impact on complications and prognosis through hypoxia, inflammation and oxidative stress response. Compared with patients with COPD or OSAS alone, patients with OS are shown to be more prone to nocturnal hypoxaemia, and to have a higher incidence of cardiovascular events, atherosclerosis, pulmonary hypertension, new onset atrial fibrillation, and right ventricular remodelling. OS has also been associated with worse prognosis, lower life quality, increased medical resource usage and economic expenditure, and even increased death risk versus COPD or OSAS alone.[8–11]

To date, studies investigating potential predictors of OSAS in patients with COPD remain limited, and study conclusions are controversial.[12–14] In this context, the aim of the present study was to retrospectively investigate potential markers associated with OS in patients with COPD. In addition, rates of invasive tracheal intubation and duration of noninvasive mechanical ventilation were compared between patients with OS and patients with COPD only.

Patients and methods

Study population

In this retrospective observational cohort study, medical records of patients with COPD who were admitted to the Department of Respiratory and Critical

Care Medicine, Harrison International Peace Hospital, between October 2019 and October 2020, were reviewed.

Patients eligible for study inclusion met the following criteria: aged ≥18 years; diagnosis of COPD according to 2017 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines;[15] met the requirements of noninvasive ventilator-assisted ventilation; received timely endotracheal intubation and invasive mechanical ventilation treatment, as required; and had undergone sleep monitoring for assessment of sleep apnoea or hypopnea within one week after the clinical condition was stable.

Patients were excluded if they had received invasive ventilation immediately after admission due to severe pulmonary encephalopathy or contraindications for noninvasive ventilation; had uncontrollable pulmonary hypertension, severe arrhythmia, cardiogenic shock, myocardial infarction, acute pulmonary embolism, pneumothorax, a large amount of pleural effusion, or malignant lung tumour; had upper gastrointestinal perforation, digestive tract obstruction, massive bleeding, recent gastrointestinal surgery, or major diseases of other systems (such as acute cerebral infarction, autoimmune system disease, blood system disease, uraemia, malignant tumour, or cirrhosis); had undergone tracheotomy; or did not complete treatment.

Patients who met the following two criteria were diagnosed with OSAS: (I) occurrence of at least one listed symptom: daytime drowsiness, no recovery of energy after waking, fatigue, or insomnia; night waking due to suffocation, wheezing or suffocation, habitual snoring and respiratory interruption, hypertension, coronary heart disease, stroke, heart failure, atrial fibrillation, type 2 diabetes, emotional disorders, and cognitive impairment; and (II) an apnoea hypopnea index (AHI) of ≥5 times/h according to portable monitoring, and occurrence of mainly obstructive events. Patients with an AHI of ≥15 times/h, without other above-mentioned clinical symptoms, were also diagnosed with OSAS.

This study was conducted according to the Declaration of Helsinki (revised in 2013), and was approved by the ethics review board of Harrison International Peace Hospital Affiliated to Hebei Medical University. All patient details were de-identified for this retrospective observational cohort study, and as such, the requirement for informed consent was waived by the review board. The reporting of this study conforms to STROBE guidelines.[16]

Procedures

Data regarding baseline patient demographic and clinical characteristics were extracted from medical records, including age, sex, body mass index (BMI), smoking history within 6 months, COPD assessment test (CAT) score, acute exacerbation frequency during previous year, pulmonary function classification, complications, blood gas analysis (pH, partial pressure of CO_2 [PCO_2]), leukocyte counts, and haemoglobin, procalcitonin, C-reactive protein (CRP), and albumin level. Data regarding hospitalization tracheal intubation status, duration from admission to intubation, and duration of noninvasive mechanical ventilation were also extracted.

For patients who needed invasive intubation within 48 h after hospitalization, the pulmonary function records within 6 months before hospitalization were extracted. In patients with multiple lung function test results within 6 months, the mean value was calculated. In patients with no pulmonary function test results within 6 months, results of a pulmonary function test performed within one week after stabilization of the patient's condition (after extubation) were extracted.

Statistical analyses

Patients were divided into two groups for analyses: patients with COPD only (COPD group) and patients with coexisting COPD and OSAS (OS group). Statistical analyses were conducted using SPSS software, version 22.0 (IBM, Armonk, NY, USA). Categorical data are presented as *n* (%) prevalence and were compared between groups using χ^2-test. Continuous variables are presented as mean ± SD or median and between-group comparisons were performed by Student's *t*-test. Ordinal data were analysed using Wilcoxon signed–rank test. Potential associations between a variable and OS were analysed by receiver operating characteristic (ROC) curve. A P value <0.05 was considered to be statistically significant.

Results

A total of 493 patients with COPD were admitted to Harrison International Peace Hospital between October 2019 and October 2020, of whom, 227 were excluded based on enrolment inclusion and exclusion criteria. Among the remaining 266 patients with COPD, 39 self-discharged from hospital during treatment, 13 required tracheal intubation but refused treatment by invasive ventilator assisted ventilation, and eight experienced severe complications during treatment (defined in the exclusion criteria). Therefore, a total of 206 patients with COPD were eligible for study inclusion, of whom, 120 patients (58.3%) were diagnosed with concurrent OSAS. Thus, the study population comprised 86 patients in the COPD group (COPD only) and 120 patients in the OS group.

Following active symptomatic supportive care, the condition of patients was found to be relatively stable, and patients received further sleep monitoring within one week of hospital admission.

Baseline characteristics

Baseline demographic and clinical characteristics of the two groups were compared (Table 1). There were no statistically significant between-group differences in terms of age (68.31 ± 7.51 versus 70.07 ± 8.66, $P = 0.074$), sex (male, 74.4% versus 73.3%, $P = 0.861$), smoking history within 6 months (30.2% versus 30.0%, $P = 0.971$), CAT score (19.8 ± 7.23 versus 20.74 ± 7.47, $P = 0.460$), and acute exacerbation frequency within the previous 1 year (1.01 ± 0.98 versus 0.99 ± 1.10, $P = 0.193$).

There were no statistically significant between-group differences in pulmonary function classification ($P > 0.05$), or in reported complications (hypertension, coronary heart disease, diabetes, pneumonia; $P > 0.05$). In addition, there were no significant between-group differences in blood parameters: pH, PCO_2, leukocyte count, and haemoglobin, C-reactive protein, procalcitonin and albumin levels (all $P > 0.05$; Table 1). Mean BMI was significantly higher in the OS group than in the COPD group (28.95 ± 2.96 versus 23.84 ± 4.06, $P = 0.001$).

BMI as a potential marker associated with OS

Next, BMI was analysed as a potential marker associated with OS in patients with COPD. Receiver operating characteristic (ROC) curve analysis showed an area under the curve value of 0.835, with sensitivity of 0.775 and specificity of 0.894 (Figure 1).

Comparison of invasive intubation and noninvasive mechanical ventilation between COPD and OS groups

After hospitalization, patients in both groups required noninvasive ventilation due to their condition. Fewer patients in

Table 1. Baseline demographic and clinical characteristics in 206 patients with chronic obstructive pulmonary disease (COPD).

Characteristic	COPD group ($n = 86$)	OS group ($n = 120$)	Statistical significance
Age, years	68.31 ± 7.51	70.07 ± 8.66	NS
Sex, male	64 (74.4)	88 (73.3)	NS
Body mass index	23.84 ± 4.06	28.95 ± 2.96	$P = 0.001$
Smoking history within 6 months	26 (30.2)	36 (30.0)	NS
CAT score	19.8 ± 7.23	20.74 ± 7.47	NS
Acute exacerbation frequency within 1 year	1.01 ± 0.98	0.99 ± 1.10	NS
Pulmonary function classification, FEV1 % predicted			
Level I (≥80%)	2 (2.3)	4 (3.3)	NS
Level II (50–79%)	8 (9.3)	13 (10.8)	NS
Level III (30–49%)	39 (45.3)	49 (40.8)	NS
Level IV (<30%)	37 (43.0)	54 (45.0)	NS
Complication			
Hypertension	41 (47.7)	62 (51.7)	NS
Coronary heart disease	38 (44.2)	55 (45.8)	NS
Diabetes	20 (23.3)	34 (28.3)	NS
Mild pneumonia	40 (46.5)	50 (41.7)	NS
pH value	7.26 ± 0.63	7.25 ± 0.63	NS
PCO_2, mmHg	98.22 ± 14.26	102.19 ± 12.90	NS
Leukocyte count, $\times 10^9$/L	9.92 ± 2.72	9.53 ± 2.77	NS
Haemoglobin, g/L	118.17 ± 11.16	118.48 ± 11.43	NS
Albumin, g/L	30.43 ± 2.48	30.94 ± 2.28	NS
Procalcitonin, ng/ml	0.43 ± 0.25	0.44 ± 0.26	NS
Whole blood CRP, mg/L	59.57 ± 32.19	61.66 ± 31.29	NS

Data presented as *n* (%) prevalence or mean ± SD.
OS, overlap syndrome (COPD plus obstructive sleep apnoea syndrome); CAT, COPD assessment test; FEV1, forced expiratory volume in 1 s; PCO_2, partial pressure of CO_2; CRP, C-reactive protein.
NS, no statistically significant between-group difference ($P > 0.05$; χ^2-test or Student's *t*-test).

the OS group (11/120 [9.2%]) required invasive intubation within 48 h after hospitalization versus the COPD group (18/86 [20.9%]; $P = 0.017$; Figure 2). The median time interval between admission and invasive intubation was 6.0 h in the OS group and 5.5 h in the COPD group, with no statistically significant difference between the two groups (log-rank 0.708; $P = 0.400$; Figure 3A).

The duration of noninvasive mechanical ventilation in the OS group (median, 8.0 days) was significantly longer than that of the COPD group (median 6.0 days; log-rank 30.856; $P < 0.001$; Figure 3b).

Discussion

In the present study, BMI was found to have a sensitivity of 0.775 and specificity of 0.894 in predicting OS in patients with COPD, suggesting that it may be a potential marker associated with OS in such patients. Patients with OS had a longer duration of noninvasive ventilation and a lower rate of invasive intubation within 48 h of hospitalization than those with COPD only. The time interval between admission and invasive intubation were similar between patients with OS or COPD only.

The reported incidence rate of OSAS in patients with COPD varies among different

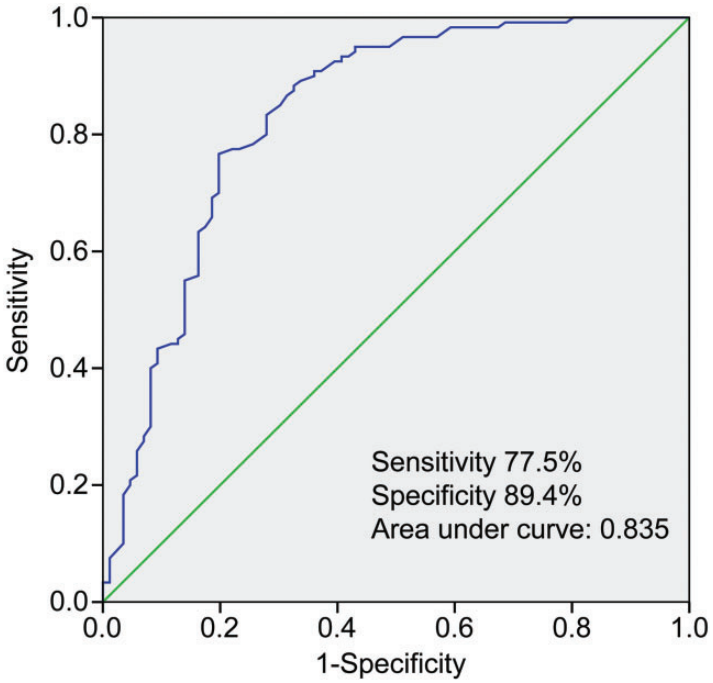

Figure 1. Receiver operating characteristic curve analysis of body mass index in predicting obstructive sleep apnoea syndrome in 206 patients with chronic obstructive pulmonary disease.

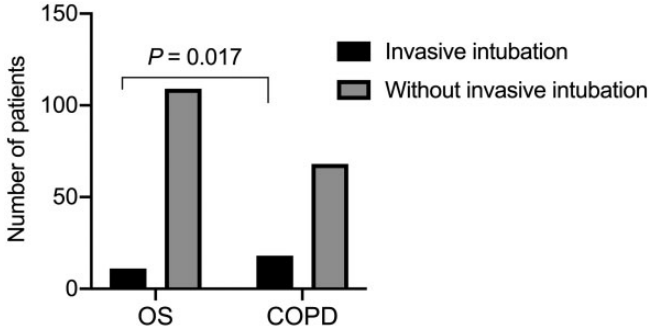

Figure 2. Rate of invasive intubation within 48 h of hospital admission in patients diagnosed with chronic obstructive pulmonary disease (COPD) only (COPD group, $n = 86$) or COPD plus obstructive sleep apnoea syndrome (overlap syndrome [OS] group; $n = 120$).

studies, but is high overall, ranging between 20% and 58%.[14,17–19] In the present study, 58.3% of patients with COPD were found to have OSAS. This variation between the current and previously published studies may be due to differences in race, disease severity, treatment condition, or sample size between the study populations.

In the present study, patients with higher BMI were more likely to have concurrent OSAS. The sensitivity and specificity of BMI for predicting OSAS were 0.775 and

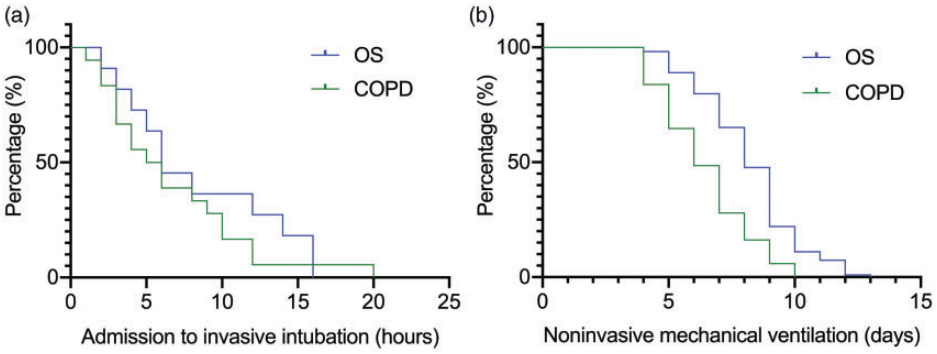

Figure 3. Log-rank probability curves showing: (a) time interval between hospital admission and invasive intubation; and (b) duration of noninvasive mechanical ventilation in both study groups. COPD, chronic obstructive pulmonary disease (patients with COPD only); OS, overlap syndrome (patients with concurrent COPD and obstructive sleep apnoea syndrome).

0.894, respectively, suggesting a potential use of BMI as one of the indicators for predicting OS. The present results were consistent with previous studies showing that BMI may be a positive predictor of OSAS in patients with COPD.[14] No significant differences in other baseline characteristics were found between patients with COPD only and those with OS. These results are in line with those of Hoflstein et al.,[13] who showed that smoking was not significantly associated with the presence of OSAS in a cohort of 3509 patients. However, another study reported that the proportion of patients who smoked was higher in those with OSAS than in those without.[12] Therefore, further investigations are warranted to evaluate the value of smoking in predicting OSAS in patients with COPD.

Noninvasive mechanical ventilation and invasive intubation have been widely used in clinical practice to effectively alleviate hypercapnia and respiratory failure. Long-term follow-up studies have shown that the effective use of noninvasive mechanical ventilation reduces intubation rate and intensive care unit length-of-stay in patients with COPD, and also reduces mortality rate.[20–24] The present study focused on comparing the time from admission to invasive tracheal intubation, the duration of noninvasive mechanical ventilation, and the final invasive tracheal intubation rate between patients with OS and those with COPD only. The rate of invasive tracheal intubation was found to be lower in patients with OS than in patients with COPD only, and the duration of noninvasive mechanical ventilation was significantly longer in patients with OS than in patients with COPD. One reasonable explanation may be that patients with OS had longer duration of chronic hypoxia than patients with COPD, and thus gradually tolerated hypoxia and carbon dioxide retention.[25] In addition, patients with OS were associated with higher BMI than patients with COPD alone, and obesity may be associated with better fitting of the face mask used in noninvasive ventilation, and thus, more effective treatment. Obesity may also be associated with reduced sensitivity of the central respiratory system to carbon dioxide. Thus, compared with patients with COPD alone, patients with OS may be less prone to pulmonary encephalopathy, leading to lower invasive respiratory rate in patients with OS.[26,27]

The results of the present study may be limited by several factors. First, the

retrospective design may be subject to selection and information biases. Secondly, the sample size was relatively small, which may introduce bias into the study conclusions. In addition, this was a single centre study, and may not be generalisable to the wider population. Therefore, further prospective, randomized studies, with larger sample sizes are warranted to validate the present results.

In conclusion, the current retrospective study demonstrated that BMI may be used as a predictor of OS in patients with COPD. The duration of noninvasive ventilation was longer and the rate of invasive intubation within 48 hours was lower in patients with OS than in patients with COPD alone. This study increases our knowledge in the field of diagnosing concurrent OASA in patients with COPD, and provides information regarding noninvasive ventilation and invasive intubation in such patients.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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