



Apnoea-hypopnoea-index comparing the 2007 and 2012 American Academy of Sleep Medicine criteria in chronic obstructive pulmonary disease/obstructive sleep apnoea overlap syndrome

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Contributions: (I) Conception and design: B He, J Steier; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: None; (V) Data analysis and interpretation: B He, M Al-Sherif, Y Wu, S Higgins; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Background: In 2007 and 2012, the American Academy of Sleep Medicine (AASM) updated their scoring criteria for nocturnal respiratory events. We hypothesised that this could have led to changes in the apnoea-hypopnoea index (AHI) of patients with chronic obstructive pulmonary disease (COPD)/obstructive sleep apnoea (OSA) overlap syndrome.

Methods: In a retrospective study, polysomnographic (PSG) recordings of 34 patients with COPD/OSA overlap syndrome were independently analysed using the AASM criteria from 2007 (AASM₂₀₀₇) and 2012 (AASM₂₀₁₂). The primary outcome was the difference in AHI, the secondary outcomes were frequency of hypopnoeas, diagnosis of overlap syndrome and differences between the AASM 2007 recommended (AASM_{2007Rec}) and altered (AASM_{2007Alt}) classifications. Data are presented as mean (standard deviation) if normally distributed, and as median (interquartile range) if non-normally distributed.

Results: The PSGs of 34 elderly [aged 67 (7.0) years] and predominantly male (m:f, 31:3) patients with COPD [FEV₁%pred 48.4% (19.6%)] were analysed. The AHI using AASM_{2007Rec} criteria was 5.9 (2.0, 15.1) events/hour *vs.* 20.4 (11.5, 28.0) events/hour using the 2012 criteria (P<0.001); with the AASM_{2007Alt} criteria, the AHI was 15.0 (9.3, 26.3) events/hour (P<0.001). Using the 2012 classification, the number of scored hypopnoeas increased by +48% compared to the AASM_{2007Rec} criteria (P<0.001), 92% of these events were associated with arousal. Although statistically non-significant, using the AASM_{2007Alt} classification, 12% of our cohort would not have been diagnosed with COPD/OSA overlap syndrome (P=0.114), this was also the case for 47% of the cohort when the AASM_{2007Rec} classification was used (P<0.01).

Conclusions: The use of the AASM₂₀₁₂ scoring rules results in a significantly higher AHI compared to the AASM₂₀₀₇ criteria in patients with COPD/OSA overlap syndrome, mostly due to an increased number of arousal-associated hypopnoeas. These observations are important for the definition of the COPD/OSA overlap syndrome.

Keywords: Polysomnography; classification; hypopnoea; arousal; desaturation

Submitted May 15, 2020. Accepted for publication Jul 27, 2020.

doi: 10.21037/jtd-cus-2020-008

View this article at: <http://dx.doi.org/10.21037/jtd-cus-2020-008>

Introduction

Sleep-disordered breathing is a common problem in the general population, the most common form of which is obstructive sleep apnoea (OSA) (1,2). In addition, chronic obstructive pulmonary disease (COPD) affects more than 250 million people according to a recent report (3). A high prevalence of the combination of both COPD and OSA has been reported since its description as “overlap syndrome” by Flenley in 1985 (4,5).

The apnoea-hypopnoea index (AHI) is a key component in the diagnosis, the classification of severity and the assessment of any treatment response of sleep-disordered breathing, in particular of OSA (6). However, the criteria for scoring apnoeas and hypopnoeas, which are required to calculate the AHI, have recently changed, particularly for hypopnoea events (7).

In 2007, the American Academy of Sleep Medicine (AASM) published the manual for the scoring of sleep and associated events mostly adopted in clinical practice, which included “recommended” (AASM_{2007Rec}) and “alternative” (AASM_{2007Alt}) scoring criteria (8). The hypopnoea definitions of AASM_{2007Rec} require a reduction of 30% or more in the nasal pressure signal, associated with a $\geq 4\%$ desaturation, and those of AASM_{2007Alt} require a 50% or more reduction in nasal pressure signal associated with a $\geq 3\%$ desaturation or an arousal. With the objective of improvement, the AASM published an update of the 2007 manual in 2012 (known as the AASM₂₀₁₂ Manual), particularly considering the implications for lean people and OSA associated outcomes (7). The AASM₂₀₁₂ criteria recommendations define the scoring criteria for a hypopnoea in case of a $\geq 30\%$ reduction in nasal pressure flow associated with a $\geq 3\%$ desaturation or an arousal.

Since then, several studies have assessed the impact of different hypopnoea definitions on the AHI and diagnosis of OSA in the general population (9,10). BaHammam *et al.* demonstrated that the AASM₂₀₁₂ criteria could lead to a higher AHI when compared to the AASM₂₀₀₇ criteria (10). Recently, Duce *et al.* further confirmed that the AASM₂₀₁₂ criteria were generally associated with higher AHIs than the 2007 criteria, but led to similar AHI and diagnostic outcomes as the 1999 manual (9). In a large population-based study using home polysomnography (PSG) in more than 2,000 people, applying different scoring rules for hypopnoea resulted in a large difference in the prevalence of OSA and a twofold difference in an AHI threshold associated with hypertension (11).

However, there are no studies to report the impact of the changed classification on the AHI and diagnosis of OSA in patients with COPD, the COPD/OSA overlap syndrome. Generally, COPD patients with severe emphysema may be more likely to be lean and elder than the general population and, due to a lower oxygen saturation and hypoventilation, more prone to frequent nocturnal oxygen desaturations. Thus, we hypothesised that the AASM₂₀₁₂ criteria could have led to significant changes in the AHI and the diagnosis of patients with COPD associated OSA due to a change in the definition of hypopnoea. We present the following article/case in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/jtd-cus-2020-008>).

Methods

This was a retrospective study preformed in the Sleep Disorders Centre at Guy’s & St Thomas’ NHS Foundation Trust, King’s College London, UK and the First Affiliated Hospital of Guangzhou Medical University. All consecutive stable patients diagnosed with COPD by respiratory specialists (post-bronchodilator FEV₁/FVC ratio of < 0.7) and OSA (AHI ≥ 5 events/hour in an overnight PSG) between August 2013 and April 2019 were eligible. In the British cohort, all patients with COPD/OSA Overlap Syndrome who underwent PSG between August 2013 and April 2019 were screened, but in the Chinese cohort, the first 26 patients screened backwards were selected. To ensure a reliable analysis, patients were not included if any primary PSG channel (nasal pressure, pulse oximetry, all EEG, respiratory effort) contained artefacts during more than 30% of total sleep time, or the total sleep time was too short (< 2.8 hours). This study was approved by the review board of Guy’s & St Thomas’ NHS Foundation Trust of King’s College London and the First Affiliated Hospital of Guangzhou Medical University (the registered service review: 2019/9662). This retrospective study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The requirement for informed consent was waived because of the retrospective study design. All eligible patients were reviewed by a respiratory consultant through the ‘electronic patient record’ system to obtain basic information such as age, body mass index (BMI), spirometry (forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC) and the ratio of FEV₁ to FVC (FEV₁/FVC)) and Epworth sleepiness scale (ESS). The PSG data of all eligible patients were re-analysed by experienced sleep

technicians.

Outcome parameters

The primary outcome of this retrospective study was the difference in AHI using 2007 *vs.* 2012 criteria. Secondary outcomes were frequency of hypopnoeas, diagnosis of overlap syndrome, and differences between the AASM 2007 recommended (AASM_{2007Rec}) and altered (AASM_{2007Alt}) classifications.

Polysomnography recording and scoring

Inpatient PSGs were recorded in the sleep laboratory using Rembrandt polysomnography system (Embla, Broomfield, CO, USA) in the UK, and Alice 5 diagnostic equipment (Respironics Inc., Murrysville, PA, USA) in China. The recording montage consisted of EEG (F3A2, F4A1, C3A2, C4A1, O1A2, O2A1), eye movements (E1M2 & E2M1), muscle tone (electromyogram of chin and both legs), oxygen saturation (finger pulse oximeter), chest and abdominal wall movement (thoracic and abdominal inductance plethysmography), airflow (thermistor and nasal pressure transducer), and snoring (microphone). Sleep stages and arousals of the British cohort (n=8) and the Chinese cohort (n=26) were analyzed by a trained PSG scorer (UK: SH, China: YXW). These PSGs were randomly assigned to three PSG scorers (BTH, MS, YXW) to be re-analysed for respiratory events. Respiratory events were independently re-analysed three times in random order, and scored using either the AASM_{2007Rec}, AASM_{2007Alt} or AASM₂₀₁₂ criteria. The hypopnoea definitions of AASM_{2007Rec} require a reduction of 30% or more in the nasal pressure signal, associated with a $\geq 4\%$ oxygen desaturation, and those of AASM_{2007Alt} require a $\geq 50\%$ reduction in nasal pressure signal associated with a $\geq 3\%$ desaturation or an arousal (8). The AASM₂₀₁₂ criteria recommendations define the scoring criteria for a hypopnoea as a $\geq 30\%$ reduction in nasal pressure flow associated with a $\geq 3\%$ desaturation or an arousal (7).

Statistical analysis

Statistical analysis was performed using SPSS 16.0 (Chicago, IL/USA) following collection of the data in MS Excel 2010 (Microsoft, Seattle, WA/USA). The data are presented as mean [standard deviation (SD)] if normally distributed,

and as median [interquartile range (IQR)] if non-normally distributed. Group data were compared using the paired *t*-test or the Friedman test, with the Tukey's honestly significant difference (HSD) post hoc test for multiple comparisons. The diagnosis of OSA and severity of disease in the patient cohort, as defined by using the different scoring criteria, were compared using the Chi-Square test. The agreement of the different criteria was further compared using Bland-Altman plots. Stepwise multiple linear regression analysis was performed to investigate predictors of the AHI (2012 *vs.* 2007Alt, 2012 *vs.* 2007Rec) including age, gender, BMI, and severity of COPD. In all analyses, a $P < 0.05$ was considered statistically significant.

Results

Patient characteristics

Seven patients' PSGs were excluded due to bad signals of PSGs (n=4) and the lack of spirometry result (n=3). Thirty-four patients were included in the analysis. A summary of patient's characteristics and PSG results are presented in *Table 1*. The 26 patients from China were older (69 ± 5 *vs.* 61 ± 10 years, $P < 0.01$) and leaner (BMI, 20 ± 3 *vs.* 33 ± 9 kg/m², $P < 0.001$), and had more severe airway obstruction (FEV₁ %pred, $45\% \pm 14\%$ *vs.* $60\% \pm 30\%$, $P = 0.046$) than the eight patients from the UK.

Differences in AHI and hypopnoea-index (HI) according to scoring criteria

The AHI and HI were significantly different between AASM₂₀₁₂ criteria, AASM_{2007Alt} and AASM_{2007Rec} ($P < 0.001$; *Table 2*). The AASM₂₀₁₂ criteria resulted in an increase in the AHI of 12% (9%, 26%) and 64% (38%, 86%) compared to AASM_{2007Alt} and AASM_{2007Rec}, respectively. Bland-Altman analyses for AHI₂₀₁₂, AHI_{2007Alt} and AHI_{2007Rec} showed a bias of 3.5 (95% CI, -2.0 to 8.9) events/hour and 11.7 (95% CI, -1.0 to 24.4) events/hour in the AASM₂₀₁₂ criteria when compared to AASM_{2007Alt} and AASM_{2007Rec}, respectively (*Figure 1*). There was an increase of 25% in the number of hypopnoeas scored by the AASM₂₀₁₂ criteria when compared to AASM_{2007Alt} ($P < 0.001$) due to the change of rules from $\geq 50\%$ to $\geq 30\%$ flow reduction. The AASM₂₀₁₂ criteria resulted in an increase in the number of hypopnoeas events of 48% compared to the AASM_{2007Rec} criteria ($P < 0.001$); 92% of these events were associated with arousal.

OSA diagnosis

Using the AASM_{2007Rec} classification, 48% of the AASM₂₀₁₂ overlap syndrome cohort would not have been diagnosed with COPD/OSA overlap syndrome if using the diagnostic criteria of an AHI ≥ 5 events/hour ($P < 0.01$); this was also the case for 12% of the cohort when the AASM_{2007Alt}

Table 1 Summary of demography, spirometry and polysomnography result

Parameter	Mean \pm SD
n	34
Age (years)	67.0 \pm 7.0
Sex M/F	31/3
Body mass index (kg/m ²)	23.0 \pm 6.9
FEV ₁ (%pred)	48.4 \pm 19.6
FEV ₁ /FVC (%)	49.5 \pm 12.7
ESS (points)	8.0 \pm 5.4
Total sleep time (h)	4.7 \pm 1.1
Sleep efficiency (%)	57.2 \pm 14.5
Stage N1 (%)	31.1 \pm 16.5
Stage N2 (%)	44.1 \pm 16.2
Stage N3 (%)	8.2 \pm 13.4
Stage R (%)	16.5 \pm 6.9
AI (events/h)	23.5 \pm 9.7
4% ODI (events/h)	12.0 \pm 15.3
Wake SpO ₂ (%)	94.7 \pm 1.7
Mean SpO ₂ (%)	94.0 \pm 2.3
Nadir SpO ₂ (%)	86.4 \pm 5.6
Time with SpO ₂ <90% (min)	21.8 \pm 37.9
% of TST with SpO ₂ <90% (%)	6.7 \pm 11.1

SD, standard deviation; ESS, Epworth Sleepiness Scale; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; AI, arousal index; ODI, oxygen desaturation index.

Table 2 AHI and HI using the AASM₂₀₁₂, AASM_{2007Alt}, or AASM_{2007Rec} criteria

Parameter	AASM ₂₀₁₂	AASM _{2007Alt}	AASM _{2007Rec}	P
AHI (events/hour)	20.4 (11.5, 28.0)	15.0 (9.3, 26.3)	5.9 (2.0, 15.1)	<0.001
HI (events/hour)	16.1 (10.1, 21.3)	11.8 (8.0, 17.9)	2.4 (0.68, 6.9)	<0.001

Data were presented as median (interquartile range). AASM, American Academy of Sleep Medicine; AHI, apnoea-hypopnoea index; HI, hypopnoea index.

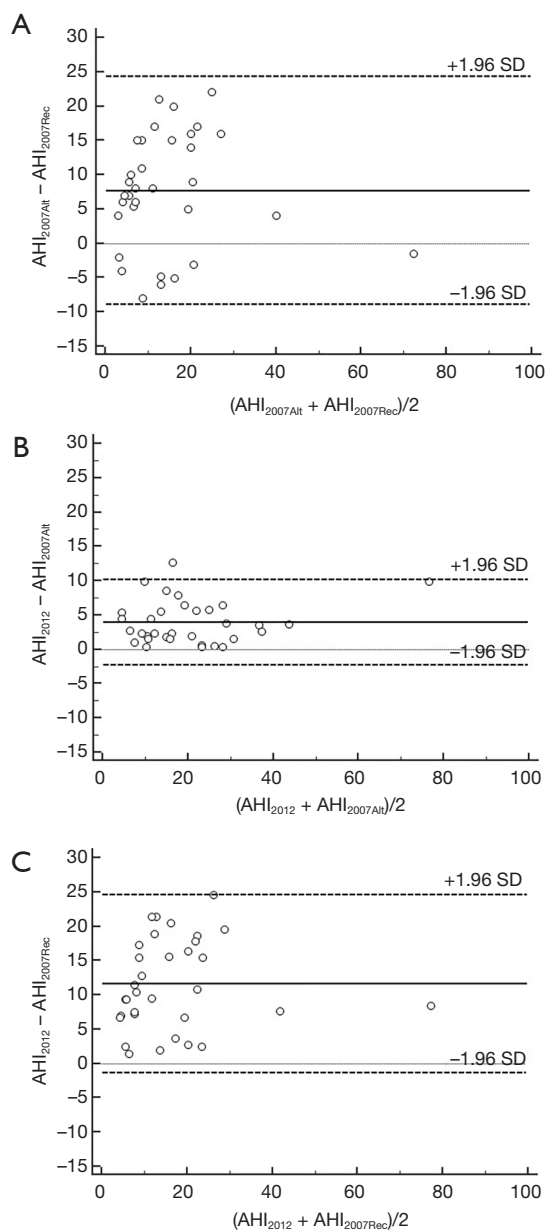


Figure 1 Bland-Altman agreement plots. The thick line represents the mean difference. The dashed lines represent ± 1.96 standard deviation.

Table 3 Patient diagnosis according to hypopnoea criteria

Diagnosis	AASM ₂₀₁₂	AASM _{2007Alt}	AASM _{2007Rec}
No OSA	0	4 (11.8%)	16 (47.1%)*
Mild OSA	12 (35.3%)	13 (38.2%)	9 (26.5%)
Moderate OSA	15 (44.1%)	12 (35.3%)	7 (20.6%)*
Severe OSA	7 (20.6%)	5 (14.7%)	2 (5.9%)

Values presented as absolute number of diagnoses (% of total number of patients). *, $P < 0.05$ compared to AASM₂₀₁₂. AASM, American Academy of Sleep Medicine; OSA, obstructive sleep apnoea.

Table 4 Stepwise multiple linear regression analysis of the discrepancy in the AHI (2012 vs. 2007Alt, 2012 vs. 2007Rec) (n=33)

Dependent variable	Statistically significant independent variables	B	SE B	P value	Non-significant independent variables	P value
Δ AHI _{2012-2007Alt}	BMI	0.190	0.054	0.001	Age	0.179
	Gender	4.165	1.455	0.008		
	Severity of COPD	-1.356	0.530	0.016		
Δ AHI _{2012-2007Rec}	BMI	-0.362	0.138	0.013	Age	0.781
	Gender	-9.355	3.931	0.024	Severity of COPD	0.218

B, the standardized regression coefficient; SE B, the standard error of beta; Δ AHI_{2012-2007Alt}, the discrepancy in the AHI between the 2012 criteria and the 2007Alt criteria; Δ AHI_{2012-2007Rec}, the discrepancy in the AHI between the 2012 criteria and the 2007Rec criteria; severity of COPD, classification by post-bronchodilator spirometry (1: FEV₁ %pred $\geq 80\%$; 2: FEV₁ %pred 50% to 79%; 3: FEV₁ %pred 30% to 49%; 4: FEV₁ %pred $< 30\%$); AHI, apnoea-hypopnoea index; BMI, body mass index; COPD, chronic obstructive pulmonary disease.

classification was used ($P=0.114$). Moreover, 38% of our cohort were above the threshold for moderate OSA with an AHI of 15 events/hour using the AASM₂₀₁₂, but not when using the AASM_{2007Rec} classification ($P < 0.05$; Table 3).

Multiple linear regression analysis

A stepwise multiple linear regression analysis was performed to investigate predictors of differences in the AHI (2012 vs. 2007Alt, 2012 vs. 2007Rec) entering age, gender, BMI, severity of COPD (Table 4). The regression model ($F=13.199$, $P < 0.001$) showed that about 58% of the variation between AHI₂₀₁₂ and AHI_{2007Alt} ($R^2=0.577$, $P < 0.001$) was explained by the BMI ($P=0.001$), gender ($P=0.008$) and severity of COPD ($P=0.016$). About 33% of the variation between the AHI₂₀₁₂ and AHI_{2007Rec} ($R^2=0.330$, $P < 0.05$) was associated with BMI ($P=0.013$) and gender ($P=0.024$) ($F=7.382$, $P < 0.05$).

Chinese and UK cohort

For patients with COPD from the UK, the AHI using

AASM_{2007Alt} criteria was significantly lower than when using AASM_{2007Rec} criteria [4.8 events/hour (1.8, 10.7) vs. 12.8 events/hour (5.8, 15.5), $P < 0.001$]. Using the AASM_{2007Alt} classification, the percentage of the British cohort that would not have been diagnosed as COPD/OSA overlap syndrome (AHI ≥ 5 events/hour) was 38% while this was true for 25% ($P=0.5$) using the AASM_{2007Rec} classification. In contrast to the British cohort, the AHI in the Chinese cohort using AASM_{2007Alt} criteria was significantly higher than when using AASM_{2007Rec} criteria [30.2 events/hour (21.9, 42.2) vs. 18.2 events/hour (17.1, 37.8), $P < 0.001$]. Using the AASM_{2007Alt} classification, the percentage of the Chinese cohort that would not have been diagnosed as COPD/OSA overlap syndrome (AHI ≥ 5 events/hour) was significantly lower than when using the AASM_{2007Rec} classification (4% vs. 54%, $P < 0.001$).

Discussion

The introduction of the AASM₂₀₁₂ scoring rules resulted in a significantly higher AHI compared to the AASM₂₀₀₇ criteria in patients with COPD/OSA overlap syndrome. This was

largely due to an increased number of arousal-associated hypopnoeas, and a significantly larger proportion of patients diagnosed with OSA when compared to AASM_{2007Rec} rather than AASM_{2007Alt}. In contrast to the overall trend the increase in the AHI and the proportion of patients diagnosed with OSA in the British cohort using the 2012 AASM criteria was when compared to AASM_{2007Alt}, rather than AASM_{2007Rec}. To the best knowledge of the authors, this is the first study to investigate the impact of the 2007 and 2012 AASM scoring criteria on the AHI in COPD/OSA overlap syndrome.

Clinical significance of findings

Previous studies have focused on the difference between AASM_{2007Alt}, AASM_{2007Rec}, and AASM₂₀₁₂ in the general population and OSA, but not in patients with COPD (9,10). They found that implementation of the 2012 AASM criteria increased the AHI and the diagnosis of OSA. However, the effect of the rule changes on the hypopnoea index in our study in COPD/OSA overlap syndrome differs to previous studies. The study of Duce *et al.* demonstrated that the inclusion of EEG arousals contributed almost equally to the change in the hypopnoea index as the decrease in SpO₂ desaturation requirement (9). In our study, the contribution of EEG arousal was significantly larger than that of the decrease in SpO₂ desaturation (92% *vs.* 8%) in COPD/OSA overlap syndrome. Bonnet *et al.* and Guilleminault *et al.* found that arousals are common in the elderly (12) and absence of SpO₂ desaturation often occurs in lean OSA patients (13). Hence, these differences between our results and others may be partially explained by the characteristics of our cohort, with elderly and leaner patients.

The studies of Marin *et al.* and Weitzenblum *et al.* demonstrate that patients with the overlap syndrome who suffer from more severe hypoxaemia and hypercapnia, may have a worse prognosis and higher mortality compared to patients with either condition alone (14,15). However, there are conflicting data about the association of oxygen desaturations (16,17) and clinically important outcomes (18,19) in the COPD/OSA overlap syndrome. Soler's and our previous studies showed that the prevalence of oxygen desaturations was similar between patients with isolated COPD and patients with overlap syndrome (16,17). Moreover, the clinical outcomes in patients on home mechanical ventilation for chronic respiratory failure is better in overlap syndrome compared to COPD alone in a recent report (18,19), with no difference in mortality (20).

This observation may be attributable to several factors. Different pathophysiological changes due to various phenotypes of overlap syndrome were reported in some studies (16). The change in the definition of hypopnoea by the AASM₂₀₁₂ criteria (7) could also result in an increased prevalence of overlap syndrome with predominant hypopnoea associated with arousals rather than severe desaturations, in particular for COPD patients according to the results of this study. Arousals are common in the elderly (12) which is a typical characteristic of patients with COPD. Moreover, a decrease of neural respiratory drive of COPD patients increases the chance of occurrence of hypopnoeas and hypoventilation (16,21). Thus, we believe that COPD patients have many hypopnoeas that are distinct from other nocturnal respiratory events caused by a collapsible upper airway in OSA, especially when hypopnoeas are scored based on a flow reduction accompanied by an arousal. In a study by Du *et al.*, OSA did not significantly impact on the mortality of patients with COPD (20). A recent cohort study suggested that COPD/OSA overlap syndrome is associated with a better prognosis than COPD alone (18,19). Hence, we should be careful to diagnose COPD/OSA overlap syndrome and treatment implications.

Although these were small cohorts, there was an inverse trend in the Chinese and British cohorts between AASM_{2007Rec} and AASM_{2007Alt}. Our study demonstrated that the AHI using AASM_{2007Alt} criteria was significantly lower than when using AASM_{2007Rec} criteria in the Chinese cohort, but significantly higher in the British cohort. In other words, the hypopnoeas that occurred in the British cohort were mostly associated with desaturations rather than arousals. This difference might be explained by different phenotypes of COPD, such as pink puffers or blue bloaters (22,23). COPD patients with lower daytime SpO₂ are also more likely to experience more severe nocturnal desaturations (24). In our study, the British cohort was more represented by "blue bloaters" with higher BMI and lower daytime SpO₂ but also more preserved FEV₁ than the Chinese cohort, which included more "pink puffers".

Limitations

This study represented a small sample, in particular of any comparison between Chinese and British patients. Although we selected patients with COPD/OSA overlap syndrome diagnosed by the criteria using an "AHI ≥ 5 events/hour", there were limited subjects who were eligible for this study. The requirement of full PSG including the EEG signal

could be the main reason. Portable sleep monitors without EEG signal might be easier to use in the general population and in COPD patients to diagnose and assess patients with COPD/OSA overlap syndrome. Notwithstanding the above limitations, our study demonstrated that there was a clear effect of the new classification on the diagnosis of COPD/OSA overlap syndrome.

Conclusions

In summary, this study has demonstrated that the use of the AASM₂₀₁₂ scoring rules results in a significantly higher AHI compared to the AASM₂₀₀₇ criteria in patients with COPD/OSA overlap syndrome. The increase of hypopnoeas in patients with COPD/OSA overlap syndrome is mostly associated with arousals rather than desaturations. These findings should be considered in diagnosing COPD/OSA overlap syndrome and treatment decisions in these patients.

Acknowledgments

We gratefully acknowledge the support of the clinical team at the Lane Fox Unit and the Sleep Disorders Centre at Guy's, St Thomas' NHS Foundation Trust, London and Key National Laboratory for Respiratory Disease, Guangzhou Medical University, China.

Funding: This project was funded by National Key R&D Program of China (Grant Number: 2016YFC1304200) and National Natural Science Foundation of China (NSFC No. 81600064).

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Joerg Steier) for the series "5th Clinical Update Sleep" published in *Journal of Thoracic Disease*. The article was sent for external peer review organized by the Guest Editor and the editorial office.

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <http://dx.doi.org/10.21037/jtd-cus-2020-008>

Data Sharing Statement: Available at <http://dx.doi.org/10.21037/jtd-cus-2020-008>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/jtd-cus-2020-008>)

[org/10.21037/jtd-cus-2020-008](http://dx.doi.org/10.21037/jtd-cus-2020-008)). The series "5th Clinical Update Sleep" was commissioned by the editorial office without any funding or sponsorship. JS served as the unpaid Guest Editor of the series and serves as an unpaid editorial board member of *Journal of Thoracic Disease*. JS's contribution was partially supported by the National Institute for Health Research (NIHR) Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust and King's College London. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This retrospective study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the local review board at Guy's & St Thomas' NHS Foundation Trust, King's College London and the First Affiliated Hospital of Guangzhou Medical University (the registered service review: 2019/9662). The requirement for informed consent was waived because of the retrospective study design applying to subsequent patients that fulfilled the review criteria.

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Cite this article as: He B, Al-Sherif M, Wu Y, Higgins S, Schwarz EI, Luo Y, Said AF, Refat N, Abdel Wahab NH, Steier J. Apnoea-hypopnoea-index comparing the 2007 and 2012 American Academy of Sleep Medicine criteria in COPD/obstructive sleep apnoea overlap syndrome. *J Thorac Dis* 2020;12(Suppl 2):S112-S119. doi: 10.21037/jtd-cus-2020-008