

Apnoeic and Hypopnoeic Load in Obstructive Sleep Apnoea: Correlation with Epworth Sleepiness Scale

Joel CI Goh,¹ MBBS, Joyce Tang,² MBBS, MRCS (Edinburgh), MMED (ORL), Jie Xin Cao,³ BM BCh, Ying Hao,⁴ PhD, Song Tar Toh,^{2,5,6} MMED (ORL),
MMED (Sleep Medicine), FAMS (ORL)

Abstract

Introduction: Patients with obstructive sleep apnoea (OSA) often present with excessive daytime sleepiness (EDS) as measured by the Epworth Sleepiness Scale (ESS). However, the relationship between EDS and OSA severity as measured by the apnoea-hypopnoea index (AHI) remains inconsistent. We hypothesise that this may be due to the usage and equal weightage of apnoea and hypopnoea events used in determining AHI and that apnoea and hypopnoea load as measured by their total durations may be a better metric to use. We sought to investigate if apnoea or hypopnoea load can display better correlation with ESS. **Materials and Methods:** Retrospective analysis of 821 patients with AHI ≥ 5 , who underwent in-laboratory polysomnogram for suspected OSA from January 2015 - December 2015, was performed. Objective factors on polysomnogram were correlated with ESS. **Results:** ESS was correlated with age ($r = -0.148$, $P < 0.001$), number of apnoeas ($r = 0.096$, $P = 0.006$), apnoea load ($r = 0.102$, $P = 0.003$), apnoea index ($r = 0.075$, $P = 0.032$), number of desaturations ($r = 0.081$, $P = 0.020$), minimum SpO₂ ($r = -0.071$, $P = 0.041$), time SpO₂ $< 85\%$ ($r = 0.075$, $P = 0.031$) and REM sleep duration ($r = 0.099$, $P = 0.004$). Linear regression analysis found age ($P < 0.001$), apnoea load ($P = 0.005$), REM ($P = 0.021$) and stage 1 sleep duration ($P = 0.042$) as independent factors correlated to ESS. The apnoea load calculated using duration in apnoea correlate with ESS in patients with severe OSA by AHI criteria compared to the mild category. **Conclusion:** AHI does not correlate with ESS. Younger age, longer apnoea, stage 1 and REM sleep were independently related to higher ESS though the correlations were weak. Apnoea load should be taken into account when determining OSA severity.

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Key words: Apnoea duration, Epworth sleepiness scale

Introduction

Obstructive sleep apnoea (OSA) is a common disorder, estimated to affect up to 15-30% of the Singaporean population.^{1,2} It is characterised by recurrent collapse of the upper airways during sleep, resulting in transient airflow cessation, intermittent nocturnal hypoxaemia and sleep fragmentation, factors linked to increased day time sleepiness.^{3,4}

The Epworth Sleepiness Scale (ESS) was developed in 1991 to quantify daytime sleepiness.⁵ Since its inception,

it has gained in popularity and is commonly used to assess excessive daytime sleepiness (EDS) and OSA. EDS is known to contribute to increased motor vehicular accidents, impaired social functioning and reduced quality of life.⁶⁻⁸ Although a prominent symptom of OSA patients,⁹ studies have failed to find a consistent relationship between EDS and OSA severity as measured by the apnoea-hypopnoea index (AHI) or respiratory disturbance index (RDI).¹⁰⁻¹²

We postulate that this could be the result of criteria set for scoring apnoea or hypopnoea and that respiratory events are

¹Yong Loo Lin School of Medicine, National University of Singapore, Singapore

²Sleep Apnoea Surgery Service, Department of Otolaryngology, Singapore General Hospital, Singapore

³Oxford University Medical School, University of Oxford, United Kingdom

⁴Health Services Research Unit, Singapore General Hospital, Singapore

⁵Sleep Disorders Unit, Singapore General Hospital, Singapore

⁶Singhealth Duke-NUS Sleep Centre, Singapore

Address for Correspondence: Dr Toh Song Tar, Department of Otolaryngology, Singapore General Hospital, Outram Road, Singapore 169608.

Email: songtar@gmail.com/toh.song.tar@singhealth.com.sg

counted without weightage consideration for duration of the respiratory events. For example, an apnoea of duration of 10 seconds or an apnoea of 30 seconds are both scored as 1 event and given equal weightage. Theoretically, more weightage should be given to an apnoea of duration of 30 seconds because it can be associated with a greater degree of oxygen desaturation, and because the 30 seconds would result in greater respiratory effort disturbance and energy consumption due to the longer duration of exaggerated breathing via an obstructed upper airway. These factors are not reflected in the AHI. An AHI of 30.0/hour can consist theoretically of thirty 10-seconds apnoea per hour, thirty 20-seconds apnoea per hour or thirty 30-seconds per hour. Intuitively, a patient with AHI of 30.0/hour consisting of all 30-seconds apnoea should have a higher disease burden than one with AHI of 30.0/hour with all 10-seconds apnoea. The issue is further complicated by the addition of hypopnoea into the equation and AHI calculation which has greater controversy because of different criteria, either arousals or degrees of oxygen desaturation used to score such events.

As such, we sought to investigate if the apnoea or hypopnoea duration can display better correlation to ESS. Our literature search did not reveal other studies that looked at this aspect.

Materials and Methods

A retrospective review of prospectively collected data was performed of all patients who underwent polysomnography (PSG) for suspected OSA in 2015 in Singapore General Hospital, an academic tertiary centre. A total of 821 patients were included in the data analysis.

The diagnosis of OSA in patients was made based on the criteria outlined in the American Association of Sleep Medicine (AASM 2012) guidelines.¹³ Exclusion criteria included factors that have an impact on daytime sleepiness. This included: 1) medical, psychiatric conditions and relevant medications related to daytime sleepiness; 2) known diagnosis of OSA; 3) receiving treatment for OSA; and 4) other sleep disorders such as circadian rhythm disorders, restless leg syndrome, periodic limb movement disorders and rapid eye movement (REM) sleep behaviour disorders (Fig. 1).

Prior to PSG evaluation, patients completed the ESS to evaluate the degree of daytime sleepiness. The scale ranges from 0 to 24, with higher scores indicating greater sleepiness during daily activities. EDS was defined as a score of greater than 10. Clinical data collected included demographic information, medical comorbidities and treatment history.

The overnight PSG was performed by trained PSG technicians and sleep physicians in accordance to AASM 2012 guidelines for overnight PSG.¹⁴ Polysomnographic

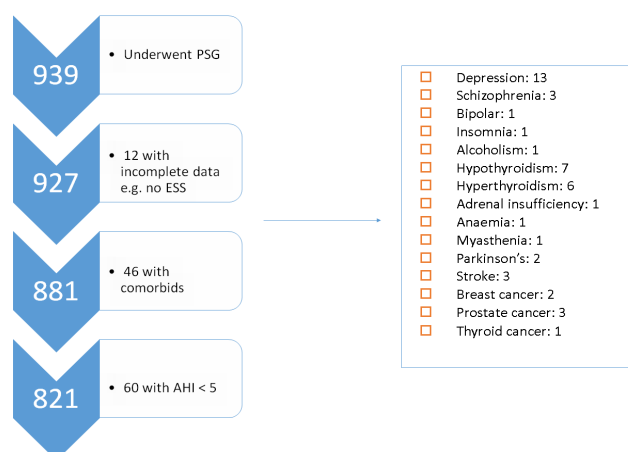


Fig. 1. A total of 939 patients underwent PSG in 2015 in Singapore General Hospital with 12 patients having incomplete data, 46 patients with comorbidities affecting daytime sleepiness and 60 patients with AHI < 5. 821 patients were included in the final analysis. AHI: Apnoea-hypopnoea index; ESS: Epworth sleepiness scale; PSG: Polysomnogram

data collected included sleep architecture and respiratory parameters including apnoea index, hypopnoea index, respiratory effort related arousals index, respiratory disturbance index, and oxygenation parameters during sleep, including the lowest oxygen saturation, oxygen desaturation indices (ODI), and time spent in hypoxia (oxygen saturation less than 90%). The PSG results were defined as per the criteria outlined in the AASM 2012 guidelines and scoring manual.

The Pearson correlation test was used for numeric variables and multiple linear regression analysis was performed on variables with a P value of <0.05 on univariate analysis. Statistical analysis was performed using the SPSS statistical package (v 19.0; IBM Corporation, Armonk, NY, USA), and all P values reported were two-sided, with P values of <0.05 considered statistically significant. The institutional review board of Singapore General Hospital approved this study and the collection of data and waived the requirement for patient informed consent for the collected data.

Results

The demographics of the patient population stratified by OSA severity are presented in Table 1. When comparing the groups based on OSA severity, we found patients who were older ($P = 0.005$), male ($P < 0.001$), with higher BMI ($P < 0.001$) and larger neck circumferences ($P < 0.001$) were significantly associated with more severe OSA. Mean ESS ($P = 0.846$) and EDS ($P = 0.736$) were found to be comparable between the groups. The presence of comorbidity does not affect ESS.

There is statistically significant increase in apnoea and hypopnoea load as the severity of OSA by AHI criteria increases, and there are observed overlaps in apnoea and

Table 1. Clinical Characteristics of 821 Patients Stratified by Severity of OSA

	Mild OSA	Moderate OSA	Severe OSA	P Value
n	167	231	423	NA
Mean age, years (SD)	45.0 (15.7)	48.6 (14.9)	49.3 (13.9)	0.005
Sex, n (%)				<0.001
Male	93 (55.7)	159 (68.8)	329 (77.8)	
Female	74 (44.3)	72 (31.2)	94 (22.2)	
Ethnicity, n (%)				0.375
Chinese	137 (82.0)	184 (79.7)	338 (79.9)	
Malay	17 (10.2)	21 (9.1)	41 (9.7)	
Indian	5 (3.0)	20 (8.7)	30 (7.1)	
Others	8 (4.8)	6 (2.6)	14 (3.3)	
Mean BMI, kg/m ² (SD)	26.2 (5.1)	27.1 (5.0)	31.2 (17.4)	<0.001
Comorbidity, n (%)				
Hypertension	29 (17.4)	60 (26.0)	113 (26.7)	0.051
Dyslipidaemia	36 (21.6)	72 (31.2)	135 (31.9)	0.038
Diabetes	17 (10.2)	14 (6.1)	48 (11.3)	0.087
Mean neck circumference, cm (SD)	36.7 (3.5)	37.8 (3.8)	40.0 (4.3)	<0.001
Mean Epworth Sleepiness Scale, (SD)	9.3 (4.8)	9.1 (4.9)	9.1 (4.8)	0.846
≥11 (%)	62 (37.1)	79 (34.2)	157 (37.1)	0.736
Mean sleep quantity, hours (SD)	6.4 (1.0)	6.4 (1.1)	6.3 (1.1)	0.482
Mean Apnoea-Hypopnoea Index (SD)	10.3 (3.0)	21.8 (4.2)	54.2 (19.7)	NA
Mean Respiratory Disturbance Index (SD)	10.2 (2.9)	21.5 (4.2)	53.4 (19.4)	<0.001
Mean Oxygen Desaturation Index (SD)	5.2 (4.0)	12.7 (6.7)	43.5 (22.4)	<0.001
Mean minimum arterial oxygen saturation, % (SD)	88.2 (4.8)	83.8 (7.6)	73.6 (11.5)	<0.001
Mean total arousal index (SD)	10.9 (7.3)	16.5 (6.1)	41.4 (20.0)	<0.001
Mean total apnoea load, min (SD)	4.2 (5.4)	16.3 (18.8)	86.6 (80.2)	<0.001
Mean longest apnoea, min (SD)	0.5 (0.3)	0.7 (0.4)	1.0 (0.4)	<0.001
Mean total hypopnoea load, min (SD)	29.5 (13.6)	55.3 (23.3)	78.9 (47.5)	<0.001
Mean longest hypopnoea, min (SD)	1.2 (0.4)	1.4 (0.5)	1.2 (0.5)	<0.001

BMI: Body mass index; NA: Not applicable; OSA: Obstructive sleep apnoea; SD: Standard deviation

hypopnoea load between the groups. Patients with mild OSA may have higher apnoea or hypopnoea load than one with moderate OSA, and patients with moderate OSA may have apnoea or hypopnoea load higher than one with severe OSA (Table 1).

Analysis of ESS with Demographics

Age showed a negative correlation with ESS. ($r = -0.148$, $P < 0.001$) while body mass index (BMI) did not (Table 2A). Younger patients demonstrate a higher degree of ESS.

Analysis of ESS with Respiratory Events, Oxygen Desaturation Indices and Sleep Architecture

ESS was correlated with respiratory events (Table 2B), apnoea load and hypopnoea load in sleep architecture (Table 2C) and different severity of OSA (Tables 2D, E, F).

ESS was found to be positively correlated with duration of apnoea ($r = 0.102$, $P = 0.003$) but not hypopnoea ($P = 0.162$). This positive correlation ($r = 0.181$, $P < 0.001$, Table 2F) was seen especially in the group of patients with severe obstructive sleep apnoea by AHI criteria. The following parameters were found not to be correlated with ESS: AHI ($P = 0.584$), RDI ($P = 0.553$) and ODI ($P = 0.298$).

ESS was negatively correlated with minimum SpO₂ values ($r = -0.071$, $P = 0.041$) and positively correlated with the number of desaturations ($r = 0.081$, $P = 0.020$), time spent below 85% ($r = 0.075$, $P = 0.031$) and 90% ($r = 0.072$, $P = 0.038$) SpO₂.

Total sleep ($r = 0.119$, $P = 0.001$), non-rapid eye movement (NREM) ($r = 0.092$, $P = 0.009$), rapid eye movement (REM) ($r = 0.099$, $P = 0.004$) and stage 1 sleep time ($r = 0.070$, $P = 0.045$) were positively correlated with ESS.

Table 2. Correlation between ESS and A: Patient Clinical Characteristics; B: Polysomnographic Variables; C: Sleep Architecture Variables; D: Apnoea and Hypopnoea Load in Mild OSA; E: Apnoea and Hypopnoea Load in Moderate OSA; F: Apnoea and Hypopnoea Load in Severe OSA

	Pearson's Rho with ESS	P Value
A: Correlation between ESS and Patient Clinical Characteristics		
Age	-0.148	<0.001
BMI	-0.005	0.880
B: Correlation between ESS and PSG Variables		
Apnoea-Hypopnoea Index	0.019	0.584
Respiratory Disturbance Index	0.021	0.553
Oxygen Desaturation Index	0.036	0.298
Apnoea load, mins	0.102	0.003
Hypopnoea load, mins	-0.049	0.162
Number of desaturations	0.081	0.020
Minimum SpO ₂	-0.071	0.041
Time spent at SpO ₂ <85, mins	0.075	0.031
Time spent at SpO ₂ <90%, mins	0.072	0.038
Time spent at SpO ₂ <95%, mins	-0.015	0.663
C: Correlation between ESS and Sleep Architecture Variables		
Total sleep time, mins	0.119	0.001
NREM sleep time, mins	0.092	0.009
REM sleep time, mins	0.099	0.004
Stage 1 sleep, mins	0.070	0.045
Stage 2 sleep, mins	0.045	0.196
Stage 3 sleep, mins	-0.012	0.723
D: Correlation between ESS and Apnoea and Hypopnoea Load in Mild OSA		
Apnoea load, mins	-0.110	0.158
Hypopnoea load, mins	0.094	0.226
E: Correlation between ESS and Apnoea and Hypopnoea Load in Moderate OSA		
Apnoea load, mins	0.051	0.360
Hypopnoea load, mins	0.115	0.082
F: Correlation between ESS and Apnoea and Hypopnoea Load in Severe OSA		
Apnoea load, mins	0.181	<0.001
Hypopnoea load, mins	-0.110	0.023

BMI: Body mass index; ESS: Epworth sleepiness scale; NREM: Non-rapid eye movement; OSA: Obstructive sleep apnoea; PSG: Polysomnogram; REM: Rapid eye movement; SpO₂: Oxygen saturation

Multivariate Analysis

Using multivariate analysis, we found that age ($P < 0.001$), duration of apnoea ($P = 0.020$), stage 1 ($P = 0.001$) and REM ($P = 0.042$) sleep time were found to be factors independently correlated with ESS. Table 3 summarises the multivariate analysis.

Discussion

Our study showed that younger age group, increased apnoea load, especially in the severe category of OSA by AHI criteria, longer REM and stage 1 sleep time during in-laboratory sleep study to be independently related to a higher degree of daytime sleepiness. The AHI does not correlate with ESS.

The ESS is an easily administered screening tool. As such, family physicians and other referring doctors rely on ESS scores to screen patients for EDS and subsequently refer onwards for investigation of possible OSA.^{15,16} However, the mechanism of EDS in OSA remains controversial. As evidenced in the Wisconsin Sleep Cohort Study,¹⁷ OSA patients have a higher prevalence of EDS. In our study, more than a third of patients with OSA had EDS. However, studies have not shown a consistent relationship between ESS and apnoea severity as defined by the AHI or RDI,^{10-12,18} which is also shown in our study. They argue that ESS is not an accurate predictor for OSA severity since EDS can even be present in simple snorers. These findings suggest that other factors besides the frequency or index of respiratory

Table 3. Results of Multiple Linear Regression for Variables Contributing to Daytime Sleepiness

	Non-Standardised Coefficient		Standardised Coefficient	T Statistic	P Value
	Beta	Standard Error			
Age	-0.049	0.011	-0.149	-4.301	<0.001
Apnoea load	0.006	0.003	0.089	2.329	0.020
REM sleep time	0.020	0.006	0.116	3.299	0.001
Stage 1 sleep time	0.010	0.005	0.079	2.037	0.042

REM: Rapid eye movement

events, have a role to play in the development of EDS.

OSA severity has classically been based upon the AHI, which measures the number of apnoea and hypopnoea events per hour. As defined by the AASM, obstructive apnoea is airflow cessation secondary to anatomic airway obstruction for at least 10 seconds and hypopnoea a drop in airflow of at least 30% as measured in from nasal pressure transducer associated with at least 3% desaturation or arousal.¹⁹ However, the AHI does not capture the severity or quality of respiratory events such as the lowest oxygen saturation nor the duration of apnoea and hypopnoea events respectively, factors shown to have effect on OSA severity and its resultant health consequences.²⁰ For example, an apnoeic event of 10 seconds is given equal weightage as an apnoeic event of 30 seconds, and apnoea is given equal weightage with hypopnoea, without consideration for the degree of oxygen desaturation or duration of the event. Hypothetically, an AHI of 30/hr can contain all apnoeas, all hypopnoeas (with desaturations or arousals), or mixture of apnoeas and hypopnoeas. The durations of each event or the degree of oxygen desaturation is not given considerable weightage. We hypothesised that this was the reason AHI correlated poorly with ESS. In our analysis, we found the total duration of apnoea to be positively correlated with ESS on both uni- and multivariate analysis, especially in the severe group of OSA by AHI criteria. However, total duration of hypopnoea, hypopnoea index, or even apnoea index were not found to be correlated to ESS after multivariate analysis. This reinforces the hypothesis that the nature and severity of the respiratory event, and not the mere frequency, might be more consequential to the development of EDS.

The correlations are, however, weak. This underscores the complexity of obstructive sleep apnoea as there maybe individual genetic susceptibility to the sleep quality or oxygen desaturations. Further studies should be conducted to incorporate the severity (duration and quality) of these respiratory events in the assessment of OSA severity, as well as to study individual genetic susceptibilities.

Our study found that younger patients displayed higher

degrees of ESS and thus, increased daytime sleepiness. Bixler et al have also identified this correlation and conclude that the young often have unmet sleep needs due to more active lifestyles and greater prevalence of depression, resulting in increased levels of daytime sleepiness.¹⁰ Although patients with depression were excluded from our analysis, clinicians should be aware of the possibility of depression in the evaluation of excessive daytime sleepiness in the young.

There have been increasing numbers of studies demonstrating the relationship between ESS and nocturnal hypoxaemia. Mediano et al found that lowest and mean arterial oxygen saturation (SpO_2) were related to EDS.¹⁵ Chen et al also reported that ODI was an independent determinant of ESS scores on multiple linear regression analysis.²¹ In contrast, Bausmer et al found no correlation between ESS and lowest SpO_2 . In a separate study published previously by Huang et al, ODI correlate better with ESS and quality of life measured by SF 36.²² In our study, ESS was negatively correlated to lowest SpO_2 on univariate analysis, and positively correlated with time spent with oxygen saturations below 85% and 90%. This supports the hypothesis of nocturnal hypoxaemia being a prominent determinant of EDS. However, the statistical significance was lost in multivariate analysis. These varied results in different studies highlight the fact that there are multiple factors besides nocturnal hypoxaemia which contribute to higher ESS scores.

Disrupted sleep architecture is another factor thought to impact daytime sleepiness. Typically, patients with OSA experience short sleep latency and multiple arousals. They maintain relatively more stage I and II sleep and less stage III and REM sleep. It is hypothesised that this lack of deep sleep results in symptoms of daytime sleepiness. Indeed, a local study by Lim et al reported that patients with more severe OSA experienced more light sleep with less deep and REM sleep.²³ In our study, univariate analysis showed ESS was positively correlated with stage 1, NREM, REM and total sleep duration. On multivariate analysis, only durations of stage 1 and REM sleep were found to be

statistically significant. Although the positive relation between ESS and REM sleep time is seemingly different from the abovementioned studies, it is postulated that the ratio of REM to total sleep time is decreased in patients with OSA as compared to those without. Indeed, the mean percentage of time spent in REM sleep in our study was 17% as compared to 25% in the normal population.²⁴

Although the exact mechanism is yet to be established, the current leading theory behind daytime sleepiness and neurocognitive dysfunction in OSA revolve around chronic nocturnal intermittent hypoxia.²⁵⁻²⁷ The recurrent episodes of airway obstruction lead to cycles of hypoxia and reoxygenation, disrupting energy metabolism pathways. This, in turn, causes an increase in oxidative stress and resultant inflammation response. Oxidative stress in susceptible regions of the brain triggers neuron injury resulting in neurocognitive dysfunction and sleepiness. Apart from continuous positive airway pressure (CPAP) management, there are ongoing studies studying the effect of antioxidants in preventing and reversing oxidative damage to the brain.²⁸

In recent years, subjective measures of apnoea severity have become increasingly popular. Ryu et al reported that daytime sleepiness was independently predicted by subjective OSA symptoms, measured by the Sleep Breathing Scale (SBS), but not objective apnoea severity as measured by PSG.²⁹ Similarly, Kang et al found that patients with OSA estimate their quality of life based on subjective sleep perception, measured by the Pittsburgh Sleep Quality Index, rather than AHI.³⁰ This highlights the importance of incorporating subjective measures of severity in the evaluation of the patient with OSA.

The retrospective nature of this study and its resultant potential for selection and recall bias is a limitation of this project. EDS was quantified subjectively with the Epworth sleepiness scale which is vulnerable to recall bias. Objective measures include the Multiple Sleep Latency test (MSLT). However, not only is it resource-intensive, but studies have also argued that ESS and MSLT measure different domains of EDS. ESS measures an individual's perception of sleepiness, whereas MSLT measures sleepiness in a controlled sleep laboratory.³¹ Lastly, our study population was limited to Asian patients who sought specialist care in a dedicated sleep unit and underwent inpatient sleep laboratory PSG, excluding those with level II and III home sleep studies. Extrapolating our results to other patient populations may not be accurate.

Conclusion

To our knowledge, this is the first study to compare the relation of ESS with apnoea and hypopnoea load and other PSG variables besides AHI to determine OSA severity. Our

study found that the younger age group, increased apnoea load, REM and stage 1 sleep time to be independently related to higher ESS scores though the correlations were weak. The apnoea load should be taken into account when determining OSA severity.

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