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Review Article

Assessment of Hypoxemia in Patients with Obstructive Sleep Apnea Hypopnea Syndrome using Weighted Percent of the Total Recorded Time Spent Desaturation

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Abstract

Objective: To develop a quantitative index named weighted percent of the total recorded time spent desaturation (WTS) to assess the severity of hypoxemia in patients with obstructive sleep apnea hypopnea syndrome (OSAHS).

Methods: A group of 237 patients with complete polysomnography (PSG) data was reviewed. Multiple indices, including descriptions of various oxygen desaturation (SaO_2) levels (e.g. awake ($ASaO_2$), lowest ($LSaO_2$), lowest SaO_2 in the longest apnea duration ($LASaO_2$), lowest SaO_2 in the longest hypopnea duration ($LHSaO_2$)), percent of the total time spent below various levels of oxygen saturation (TS%) at thresholds <90 (TS90), <85 (TS85), <80 (TS80), <75 (TS75), <70 (TS70), <65% (TS65), and WTS calculated using the weighting method in mathematics, were recorded. All indices were compared in patients with varying degrees of OSAHS using one-way analysis of variance firstly. Then all indices were compared with apnea-hypopnea index (AHI) and Epworth Sleepiness Scale (ESS) using simple linear correlation analysis and multiple linear stepwise regression analysis. In addition, another group of 103 patients with OSAHS was reviewed. The coincidences between the degree of AHI (DA) and degree of hypoxemia (DH) which was assessed using traditional hypoxemia indices such as $LSaO_2$, TS90, and WTS were observed.

Results: In the first group, multiple indices, including $LSaO_2$, $LASaO_2$, $LHSaO_2$, TS90, TS85, TS80, TS75, and WTS, were associated with the degree of OSAHS. Among them, WTS index is the most consistently reported parameter associated with AHI and ESS. In the second group, the coincidences were 72.8% between DH assessed using WTS and DA, 57.3% between DH assessed using TS90 and DA, 42.7% between DH assessed using $LSaO_2$ and DA.

Conclusion: WTS index, combining time and severity of desaturation, may have high coincidence with AHI, and provide additional useful data in the study of hypoxemia, compared to other traditional indices. Such data may be important in future studies of physiological variables.

Keywords: Sleep; Sleep apnea; Hypoxemia; Hypoxia; Polysomnography; Evaluation

Introduction

The gold standard in the diagnosis of obstructive sleep apnea hypopnea syndrome (OSAHS) is polysomnography (PSG), and the severity of OSAHS has traditionally been described by the number of apnea-hypopnea index (AHI) and lowest oxygen saturation ($LSaO_2$) as determined by the results of PSG. But the coincidence between severity of AHI and $LSaO_2$ is not good [1-3]. More and more data have showed that hypoxemia is a key factor to cause a series of clinical symptoms [4-6]. In order to determine the relationship of the physiologic consequences of the disorder, however, quantification of hypoxemia is important. Although many publications have presented a wide variety of methods used to describe the severity of hypoxemia [7-10], there is still no accepted method of quantifying the severity of hypoxemia. Slutsky et al. [11]. proposed the concept that analysis of the cumulative degree of hypoxemia would be more valid than the following techniques which identified only time of desaturation: reporting single points ($LSaO_2$), selected averaging (mean oxygen saturation ($MSaO_2$)), or calculating the percent of the total time spent below various levels of oxygen saturation (TS%). Chesson et al. [12,13]. reported that saturation impairment time (SIT) index which integrated time and degree of desaturation could be used to evaluate hypoxemia. But it is difficult to establish the measurement of SIT index and not suitable for clinical application. A suitable method integrating time and degree of desaturation for evaluating hypoxemia is required.

This study had two objectives concerning a new method for measuring the cumulative severity of hypoxemia in patients with OSAHS. The first objective was to establish the expected values and distributional properties of the new index named weighted percent of the total recorded time spent desaturation (WTS) for patients with OSAHS. The second was to demonstrate the potential of the proposed WTS index to offer information that is different from that provided by the traditional hypoxemia indices. To accomplish these objectives, we studied 237 patients with OSAHS firstly and compared the standard measurement of AHI and Epworth Sleepiness Scale (ESS) with the traditional hypoxemia indices and newly developed measure of quantitative hypoxemia, the WTS index. Finally, we reselected 103 patients with OSAHS. The coincidences between the degree of AHI (DA) and degree of hypoxemia (DH) which was assessed using traditional hypoxemia indices such as $LSaO_2$, TS90, and WTS were observed.

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Methods

Participants

We analyzed data we had previously collected from PSG studies of 340 consecutive male patients who were referred to our hospital with suspected OSAHS. The data was divided into two groups according to the time of the examination: the first group (237 patients, from January 2012 to December 2013) and the second group (103 patients, from January 2014 to June 2012). Inclusion criteria included: (1) obtaining at least 7h of nocturnal PSG with concurrent computerized and manual analysis of oxygen saturation (and without major periods of signal loss due to probe off or persistent EEG signal loss which would make PSG scoring and computerized acquisition incomplete); (2) having sufficient history, physical examination, and PSG data to establish the presence of OSAHS; and (3) finding no additional medical problems that would alter oximetry findings beyond the alterations expected for the diagnosis of OSAHS.

Polysomnography

The Polywin PSG system (Respironics Inc, USA) was used for sleep monitoring in all patients. The standard PSG montage consisted of monitoring of the electroencephalogram (EEG, C_4-M_1, C_3-M_2, O_2-M_1, and O_1-M_2), electrooculogram (EOG, ROC-M_1, LOC-M_2), sub mentalist and anterior tibialis electro myograms (EMG), electrocardiogram with surface electrodes, thermostats for nasal and oral airflow, thoracic and abdominal excursion, finger pulse oximetry, and body position. All epochs were analyzed and sleep stages were scored according to the international criteria of American Academy of Sleep Medicine (AASM) [1]. An apnea was identified as more than 90% reduction in airflow for at least 10 sec; hypopnea as 30% or more reduction of airflow for at least 10 sec associated with 4% or more reduction in SaO_2. An EEG arousal was also scored according to the criteria of AASM.

OSAHS was considered to be present if AHI was 5 or greater. Patients were grouped by their total AHI. AHI ranged from 5 to 14.9 for mild OSAHS, from 15 to 29.9 for moderate OSAHS, and 30 or greater for severe OSAHS [2].

Acquisition and analysis of oxygen saturation data

After the PSG studies were completed, multiple indices, including awake SaO_2 ($ASaO_2$), $LSaO_2$, lowest SaO_2 in the longest apnea duration ($LASaO_2$), lowest SaO_2 in the longest hypopnea duration ($LHSaO_2$), and percent of the total sleep time spent below various levels of oxygen saturation (TS%) at thresholds <90 (TS90), <85 (TS85), <80 (TS80), <75 (TS75), <70 (TS70), and <65% (TS65) SaO_2, were recorded respectively.

In addition, time spent <90 but >85% SaO_2 (t9085), time spent <65% SaO_2 (t65L), and total sleep time (TST) were recorded. The definitions of t8580, t8075, t7570, and t7065 were equal to that of t9085. Percent of the total time spent <90 but >85% SaO_2 (TS9085) was calculated as follows: TS9085 = t9085/TST × 100%. The definitions of TS8580, TS8075, TS7570, TS7065, and TS65L were equal to that of TS9085.

In order to integrate time and degree of desaturation, we established a weighting coefficient N and developed a new parameter named WTS which could be calculated using the following formula:

$$WTS = TS9085 + TS8580 \times (1 + n) + TS8075 \times (1 + 2n) + TS7570 \times (1 + 3n) + TS7065 \times (1 + 4n) + TS65L \times (1 + 5n)$$

Epworth sleepiness scale

All patients accomplished the validated Chinese version of ESS which is a self-administered questionnaire designed to measure the general level of daytime sleepiness [14]. Patients rate on a scale of 0-3 their likelihood of falling asleep in eight different situations commonly encountered in daily life. Total ESS score ranges from 0 to 24 and higher scores indicate more subjective sleepiness.

Statistical analysis

Statistical analysis was carried out with the SPSS v16 program (SPSS Inc, Chicago, IL). Statistical significance was accepted as $P < 0.05$. In the first group, one-way analysis of variance (ANOVA) was used to test for significant differences in continuous variables among mild, moderate, and severe groups. Simple linear correlation analysis was used to compare all indices with AHI and ESS. Pearson correlation was used when linearity, independence, normality, and homogeneity of the variances of the variables were met. If not, Spearman's coefficient was performed. Finally, the stepwise multiple linear regression analysis was carried out to compare all indices with AHI and ESS further.

The severity of hypoxemia was classified by using traditional hypoxemia indices such as $LSaO_2$, TS90 and WTS, respectively. The classification criterion of $LSaO_2$ referred to the diagnosis foundation and criterion of Chinese Medical Association Otolaryngology Branch [3]. The classification criterions of TS90 and WTS were founded according to the severity of 237 patients with OSAHS in the first group. In the second group, the coincidences between the degree of AHI and degree of hypoxemia which was assessed using $LSaO_2$, TS90, and WTS were observed, respectively.

Results

Patient demographics

In the first group, all of the 237 patients were male. To find the best parameter to evaluate hypoxemia, the correlations between all parameters of assessing the severity of hypoxemia and AHI and ESS were observed according to simple linear correlation and regression analysis in this group. Based on a cut-off point of 5 for AHI, these 237 patients were diagnosed as OSAHS by PSG. The average age was 41.1 (range, 19-62). The mean BMI was 28.5 (range, 18.7-36.6). The mean AHI was 40.2 (range, 6-91.3). In these patients, 33 (13.9%) had an AHI 5 or greater and less than 14.9 (mild), 74 (31.2%) had an AHI greater than 15 and less than 29.9 (moderate), 130 (54.9%) had an AHI 30 or greater (severe). The characteristics of all 237 patients are shown in Table 1. There was no significant difference in age and BMI among the different severity groups of OSAHS, but significantly higher ESS score was reported with increasing severity of OSAHS ($P < 0.001$).

In the second group, all of the 103 patients were male. The coincidences between all parameters and AHI were observed. The best parameter which has been selected from the first group was compared with other parameters in this group. The average age was 43.0 (range, 20-67). The mean BMI was 27.86 (range, 19.49-35.92). The mean AHI was 41.40 (range, 5.01-96.2). In these patients, mild, moderate and severe cases were 14 (13.6%), 24 (23.3%) and 65 (63.1%), respectively.

Table 1: Summarized Characteristics of the First Group (N = 237).

Variables	Mild	Moderate	severe	One-Way ANOVA
Number of patients (%)	33 (13.9)	74 (31.2)	130 (54.9)	
Age (yr)	41.7 ± 14.2	41.3 ± 10.2	39.4 ± 11.6	NS
BMI (kg/m^2)	27.6 ± 4.65	29.3 ± 6.21	28.3 ± 3.25	NS
ESS	13.55 ± 5.91	11.16 ± 5.47	16.88 ± 5.58	P < 0.001

Data are presented as mean ± standard deviation. ANOVA: Analysis of Variance; BMI: Body Mass Index; AHI: Apnea-Hypopnea Index; NS: Not Significant; ESS: Epworth Sleepiness Scale.

Determination of the value of weighting coefficient N

By substituting each value of n (n = 0.1, 0.2, 0.3,..., 1.0) into the formula, ten WTS values were obtained and compared with AHI using simple linear correlation analysis (Table 2). The results showed that all WTS values had significant positive correlations with AHI ($P < 0.001$ for all). However, the correlation coefficient changed obviously as the n value increased until n = 0.5. Conversely, the correlation coefficient change was small when n > 0.6. So the value of n was substituted by 0.5 in this study.

Comparison of parameters of hypoxemia among the different severity groups of OSAHS

The parameters of assessing the severity of hypoxemia among the different severity groups of OSAHS are shown in Table 3. Apart from $ASaO_2$, TS70, and TS65, the parameters of nocturnal hypoxemia measured by $LSaO_2$, $LASaO_2$, $LHSaO_2$, TS90, TS85, TS80, TS75, and WTS demonstrated that nocturnal hypoxemia progressively aggravated with increasing severity of OSAHS ($P < 0.01$).

Simple linear correlation and regression analysis

Simple linear correlation analysis was performed to evaluate the correlations between AHI, ESS and multiple parameters of nocturnal hypoxemia (Table 4). The results showed that multiple parameters, including $LSaO_2$, $LASaO_2$, TS90, TS85, TS80, TS75, and WTS, significantly correlated with AHI and ESS with the strongest association with WTS (r = 0.580 and r = 0.670 with AHI and ESS, respectively, all $P < 0.001$). By using the stepwise multiple linear regression analysis to further evaluate these correlations and their relative importance, only one variable, WTS, significantly correlated with AHI and ESS (β=0.580 and β=0.670 for AHI and ESS, respectively, all $P < 0.001$).

Verification of parameters for assessing the severity of hypoxemia in another group of OSAHS patients

WTS index was selected as the best parameter to assess the severity of hypoxemia based on the data in the first group. To verify this, we compared WTS with traditional parameters such as TS90 and $LSaO_2$ in another group of OSAHS patients (the second group).

The classification criterion of traditional parameter $LSaO_2$ for assessing the severity of hypoxemia referred to the diagnosis foundation and criterion of Chinese Medical Association Otolaryngology Branch [3]. In order to achieve reference values, 237 WTS values were arranged from lowest to highest. According to the number of patients in different severity of OSAHS (33 Mild,

Table 2: The simple linear correlation analysis between AHI and WTSs.

		WTS									
		n=0.1	n=0.2	n=0.3	n=0.4	n=0.5	n=0.6	n=0.7	n=0.8	n=0.9	n=1.0
AHI	r	0.552	0.570	0.575	0.579	0.580	0.581	0.581	0.581	0.581	0.580
	P	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

AHI: Apnea-Hypopnea Index; WTS: Weighted percent of the total recorded Time Spent desaturation.

Table 3: The parameters of assessing the severity of hypoxemia among the 3 groups.

Variables	Mild	Moderate	severe	Comparison One-Way ANOVA
$ASaO_2$ (%)	93 ± 2	93 ± 2	93 ± 2	NS
$LSaO_2$ (%)	79 ± 9	73 ± 12	61 ± 14	P < .001
$LASaO_2$ (%)	90 ± 4	86 ± 19	76 ± 20	P < .001
$LHSaO_2$ (%)	75 ± 37	87 ± 18	87 ± 14	P = .004
TS90 (%)	21.3 ± 24.4	17.9 ± 20.1	44.2 ± 18.7	P < .001
TS85 (%)	3.5 ± 10.5	6.0 ± 12.8	17.9 ± 12.6	P < .001
TS80 (%)	0.04 ± 0.09	3.95 ± 9.92	8.78 ± 8.96	P < .001
TS75 (%)	0.00 ± 0.00	2.60 ± 7.11	3.95 ± 5.21	P = .001
TS70 (%)	0.00 ± 0.00	1.77 ± 5.32	1.34 ± 2.33	NS
TS65 (%)	0.00 ± 0.00	0.18 ± 0.77	0.18 ± 0.53	NS
WTS (%)	23.6 ± 29.4	22.1 ± 29.5	42.0 ± 32.8	P < .001

Data are presented as mean ± standard deviation. ANOVA: Analysis of Variance; AHI: Apnea-Hypopnea Index; $ASaO_2$: Awake Oxygen Saturation; $LSaO_2$: Lowest Oxygen Saturation; $LASaO_2$: Lowest Oxygen Saturation in the Longest Apnea Duration; $LHSaO_2$: Lowest Oxygen Saturation in the Longest Hypopnea Duration; WTS: Weighted percent of the total recorded Time Spent desaturation; TS90: Percent of the total time spent below various levels of oxygen saturation (T%) at thresholds <90% SaO_2; NS: Not Significant; The definitions of TS85, TS80, TS75, TS70, and TS65 were equal to that of TS90.

Table 4: The simple linear correlation between AHI, ESS and multiple parameters of hypoxemia.

		A SaO_2	L SaO_2	LA SaO_2	LH SaO_2	TS90	TS85	TS80	TS75	TS70	TS65	WTS
AHI	r	0.059	0.478	0.320	0.061	0.555	0.556	0.445	0.285	0.090	0.027	0.580
	P	0.362	0.000	0.000	0.331	0.000	0.000	0.000	0.000	0.167	0.679	0.000
ESS	r	0.094	0.477	0.298	0.153	0.651	0.620	0.443	0.333	0.205	0.098	0.670
	P	0.153	0.000	0.000	0.018	0.000	0.000	0.000	0.000	0.001	0.131	0.000

AHI: Apnea-Hypopnea Index; ESS: Epworth Sleepiness Scale; $ASaO_2$: Awake Oxygen Saturation; $LSaO_2$: Lowest Oxygen Saturation; $LASaO_2$: Lowest Oxygen Saturationi the Longest Apnea Duration; $LHSaO_2$: Lowest oxygen saturation in the longest Hypopnea duration; WTS: Weighted percent of the total recorded time spent desaturation; TS90: Percent of the total time spent below various levels of oxygen saturation (T%) at thresholds <90% SaO_2; The definitions of TS85, TS80, TS75, TS70, and TS65 were equal to that of TS90.

Table 5: The classification criterion of three parameters for assessing the severity of hypoxemia.

	Mild	Moderate	Severe
LaSO2	>0.85	0.84-0.65	<0.65
TS90	<5	6-25	>25
WTS	<6	7-33	>33

$LSaO_2$: Lowest Oxygen Saturation; WTS: Weighted percent of the total recorded time spent desaturation; TS90: Percent of the total time spent below various levels of oxygen saturation (T%) at thresholds <90% SaO_2.

74 Moderate, 130 Severe), the arrangement of WTS was divided into three parts: number 1 to 33, 34 to 107, and > 108 (Part 1, 2, and 3, respectively). WTS values ranged from 0 to 6 in part 1, from 7 to 33 in part 2, and 34 or greater in part 3. So we suggest that WTS values range from 0 to 6 for mild hypoxemia, from 7 to 33 for moderate hypoxemia, and 34 or greater for severe hypoxemia. The classification method of TS90 was the same as WTS. The classification criterions of three parameters for assessing the severity of hypoxemia are shown in Table 5.

The coincidences between the severity of hypoxemia determined by three parameters and the severity of OSAHS determined by AHI were observed. The results are shown in Table 6. The coincidences between LSO2, TS90 and WTS with AHI were 42.72% 57.3% and 72.82%, respectively. There were significant difference among three parameters (P<0.001).

Discussion

Increasing evidence over the last few decades suggests that chronic intermittent hypoxia (CIH) in OSAHS is a major pathological element associated with daytime sleepiness, cardio respiratory diseases, insulin resistance, neurocognitive dysfunction, road traffic accidents and sudden death [15-20]. So CIH is a functionally important reason for causing the clinical features in patients with OSAHS [21-25]. Currently, $LSaO_2$ index obtained by PSG is the most common parameter which is used to assess the severity of hypoxemia, and the severity of $LSaO_2$ often does not agree with the severity of AHI. $LSaO_2$ index only reports the lowest point of oxygen saturation and ignores the duration of desaturation. Many scholars suggest that TS90 index is more appropriate than other indices [12,13]. However, the cumulative degree of desaturation may contribute more to hypoxemia than the time of desaturation. TS90 index reflects time of desaturation and ignores degree of desaturation. Although SIT index reported by Chesson et al. [13] integrates time and degree of desaturation, it is difficult to measure and has no reference value. Therefore, there is no desirable method of quantifying the degree and duration of the oxygen saturation.

This study established the WTS index which was an integration of time and degree of desaturation and compared this index with other indices which had been used to assess the severity of hypoxemia. By establishing a weighting coefficient n and substituting the value of n into the formula successively, ten WTS indices was calculated and compared with AHI. Finally, the most significant value (n = 0.5) of weighting coefficient was determined.

In our study, more severe OSAHS indeed had greater ESS, TS90, TS85, TS80, TS75, and WTS, and lower $LSaO_2$, $LASaO_2$, and $LHSaO_2$. There into, the traditional hypoxemia indices including TS90, TS85, TS80, TS75, $LSaO_2$, $LASaO_2$, and $LHSaO_2$ were significantly correlated with AHI and ESS, and TS90 ($r = 0.555$ and $r = 0.651$ with AHI and ESS, respectively, all $P < 0.001$) was stronger association than other traditional indices. These results support the hypothesis of Chaudhary et al. [9] that TS90 may be a method of expressing oxygen saturation changes during PSG better than other indices. However, in our results, WTS based on integrating time and degree of desaturation showed more significant correlation with AHI and ESS ($r = 0.580$ and $r = 0.670$ with AHI and ESS, respectively, all $P < 0.001$) than TS90 which only reflected time of desaturation. And the results of stepwise multiple linear regression analysis showed that only WTS significantly correlated with AHI and ESS ($\beta = 0.580$ and $\beta = 0.670$ for AHI and ESS, respectively, all $P < 0.001$). So we suggest that WTS index may be the best method of assessing the severity of hypoxemia.

In order to verify the accuracy of new parameter further, WTS was compared with traditional parameters in another group of OSAHS patients (the second group). The severity of hypoxemia was determined by using $LSaO_2$, TS90 and WTS, respectively. The coincidences between the severities of hypoxemia judged by $LaSO_2$, TS90 and WTS and severity of OSAHS judged by AHI were 42.72% 57.3% and 72.82%, respectively. This means WTS is the best method of assessing the severity of hypoxemia and worthy to use in clinical practices in future. In addition, PSG examination needs special equipment and large consumption of human and material resources. More and more doctors use nocturnal home pulse oximetry to predict or screen OSAHS. Traditional parameters such as LaSO2 and TS90 show low rate of accuracy, and WTS may be a better parameter to predict or screen OSAHS.

Table 6: The coincidences between three parameters and AHI.

	Coincidence	No Coincidence	Coincidence Rate
LSaO2	44	59	42.7%
TS90	59	44	57.3%
WTS	75	28	72.8%

$LSaO_2$: Lowest Oxygen Saturation; WTS: Weighted percent of the total recorded time spent esaturation; TS90: Percent of the total time spent below various levels of oxygen saturation (T%) at thresholds <90% SaO_2.

In addition, the value of WTS can be calculated in the computer in which the math equation is inputted and all the procedures can be finished during PSG. Therefore, the value of WTS can be acquired easily. However, all the patients in our study are male. We plan to include female OSAHS patients in the future work and observe the diagnostic significance of WTS for hypoxemia in female OSAHS patients.

In conclusions, WTS index, combining time and severity of desaturation, may provide additional useful data in the study of hypoxemia, and have high coincidence with AHI, compared to other traditional indices.

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