Oximetry spectral analysis in the diagnosis of obstructive sleep apnoea

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ABSTRACT

Using spectral analysis of oximetry data, we prospectively evaluated the validity of this methodology in patients clinically suspected of suffering from obstructive sleep apnoea (OSA). A total of 233 outpatients were studied. Nocturnal oximetry was performed simultaneously with conventional polysomnography for all participants. The power density of oxygen saturation was analysed using Fast-Fourier transformation of the oximetric signal. Nocturnal oximetry test results were considered as abnormal (suspicion of OSA) if a peak in the spectrum between the period boundaries 30 and 70 s was observed. A normal test result was defined as the absence of the 30–70 s peak from the spectrum. Single-blind evaluation was performed by three independent observers, and agreement of two or more of these was considered definitive. The peak amplitude and the ratio of the area enclosed in the 30–70 s peak to the total area of the spectrum ($r_S$) were measured. The presence of a peak has a sensitivity of 78%, a specificity of 89%, a positive predictive value of 89% and a negative predictive value of 78%. Apnoea–hypopnoea indexes were correlated significantly with peak amplitude ($r_{fl} = 0.74; P < 0.001$) and with $r_S$ ($r_{fl} = 0.69; P < 0.001$). For a peak amplitude threshold of 0.7%2, the sensitivity was 94% and the specificity was 65% for OSA diagnosis. Using a threshold for $r_S$ of 0.15, the sensitivity was 91% and the specificity was 67%. Thus the spectral analysis of nocturnal oximetry and identification of a peak at 30–70 s could be useful as a diagnostic technique for OSA subjects.

INTRODUCTION

Obstructive sleep apnoea (OSA) is a disorder in which repetitive apnoeas occur during sleep; these are associated with hypoxaemia, bradycardia, arousals and fragmented sleep [1]. The prevalence of OSA in middle-aged populations is currently estimated to be 2% in women and 4% in men [2]. The morbidity and mortality in untreated subjects [3] can be diminished with effective treatment [4], and thus early diagnosis is warranted. Polysomnography is the standard diagnostic test for OSA; however, it is expensive and time consuming. The high prevalence of the disease and the inconvenience of polysomnography for the patient make simplified techniques desirable for diagnosing OSA. Simplified diagnostic techniques can also allow the physician to prioritize polysomnographic testing [5].

OSA is frequently accompanied by repetitive oxygen desaturation [6–11] and cyclical variations in heart rate [12], which can be useful for detecting the condition.

Key words: diagnostic test, obstructive sleep apnoea, oximetry, polysomnography, spectral analysis.

Abbreviations: AHI, apnoea–hypopnoea index; BMI, body mass index; CI, confidence intervals; ODI, oxygen desaturation index; OSA, obstructive sleep apnoea; PA, peak amplitude; P30–70, peak in the spectrum at 30–70 s; ROC, Receiver Operating Characteristics; $r_S$, ratio of the area enclosed in P30–70 to the total area of the spectrum; $\Delta S\alpha_2$, arterial oxygen saturation.

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Although several studies have examined heart rate variation using spectral analysis techniques under different conditions [13–17] and in OSA [18–20], few studies have concentrated on variations of oxygen saturation in samples from OSA subjects using this technique [19,20]. Furthermore, no studies have examined the diagnostic utility of spectral analysis in the measurement of oxygen saturation levels in OSA patients.

The aim of our study was to prospectively evaluate the spectral characteristics of nocturnal variations in arterial oxygen saturation (\(aO_2\)) as a possible diagnostic technique of OSA.

**METHODS**

**Patients**

A total of 240 subjects (191 men, 49 women), clinically suspected of having OSA, were referred to our sleep clinic by general practitioners. Subjects ranged in age from 21 to 82 years, and had a body mass index (BMI) of 30.4 ± 5.8 kg/m² (mean ± S.D.). All subjects were suspected of having OSA because of daytime hypersomnolence, loud snoring, nocturnal choking and awakenings, or apnoeic events (or all four) reported by the subject or a bedmate.

The study included 27 patients with underlying lung disease (24 with chronic obstructive pulmonary disease and three with restrictive disease). These subjects had a mean age of 56.6 ± 12.9 years (± S.D.) and a BMI of 30.1 ± 5.6 kg/m²; 23 (85%) were male.

The Review Board on Human Studies at our institution approved the protocol, and each subject gave his or her informed consent to participate in the study.

**Interventions**

Sleep studies were carried out in our Sleep Unit, usually from 00.00 to 08.00 hours. Patients were prospectively evaluated by a single-night nocturnal oximetry test in conjunction with a simultaneous conventional polysomnographic study. This technique consisted of continuous monitoring using a polygraph (Ultrasom Network, Nicolet, Madison, WI, U.S.A.) and included EEG, electro-oculogram, chin electromyogram, air flow (three-port thermistor), ECG and measurement of chest wall movements.

The polysomnographic register was analysed over periods of 30 s and during sleep phases I, II, III, IV and rapid eye movement, according to the system of Rechtschaffen and Kales [21]. Apnoea was defined as the absence of air flow for more than 10 s, and hypopnoea was defined as a decrease in respiratory flow of at least 50%, accompanied by a ≥ 4% decrease in the saturation of haemoglobin. The average apnoea–hypopnoea index (AHI) was calculated for hourly periods of sleep [22]. In this study, an AHI of 10 or more was considered as diagnostic of OSA. If the subject had less than 3 h of total sleep, the sleep study was repeated [23].

Recording of \(aO_2\) was carried out using a Criticare 504 oximeter (CSI, Wankeska, WI, U.S.A.) with a finger probe, with sampling at a frequency of 0.2 Hz (one sample every 5 s). We studied the oximetric tracing and oxygen desaturation indices (ODIs) per h of recording. The computer calculated the number of falls in \(aO_2\) of 4% or more, 3% or more and 2% or more from baseline. Baseline was set initially as the mean level in the first 3 min of recording [9]. ODI4 was calculated for events with falls in \(aO_2\) of ≥ 4%/h, ODI3 was calculated for events with falls of \(aO_2\) of ≥ 3%/h, and ODI2 was calculated for events with falls of \(aO_2\) of ≥ 2%/h. The percentage of time during which \(aO_2\) was below 90% was also calculated. In addition, we tested the system to be sure that spectral power at frequencies near and over 0.1 Hz was negligible. Stored data were played back on a computer for analysis. The power density of oxygen saturation was analysed using the Fast-Fourier transformation of the Hamming-windowed signal:

\[
y_i = X_i[0.54 - 0.46 \cos(\omega)]
\]

where \(\omega = 2\pi/n\), and \(n\) is the number of elements in the input sequence. The Hamming window was used in order to minimize the transition edges of the sampled signal to reduce leakage when performing Fourier analysis on a signal of finite length (\(X_i\)) [24]. Analysis was performed by using Labview 3.11 (National Instruments Corp. Austin, TX, U.S.A.) and Anadat 5.2 (Infodat, Montreal, PQ, Canada) software.

The power contents of the signal were plotted against the period:

\[
t(s) = 1/\text{frequency (Hz)}
\]

The presence of a peak in the spectrum at 30–70 s
Spectral analysis in sleep apnoea

Figure 2 Typical spectrum of a non-OSA subject
The power contents of the signal were plotted against the period: \( f(t) = 1/\text{frequency (Hz)} \). Ampl. amplitude.

(P30–70) was determined in each study [19,20], and the peak amplitude (PA) and the ratio of the area enclosed in the spectrum between the frequency boundaries of P30–70 to the total area of the spectrum (\( r_s \)) were measured (Figure 1).

Single-blind evaluation of oximetry recordings was carried out by three independent observers, and the agreement of two or more observers was considered to be definitive. Oximetry data were classified as abnormal (suspicion of OSA) in the presence of P30–70 (Figure 1), normal in the absence of P30–70 (Figure 2), and uninterpretable when at least two observers were doubtful about interpretation. Seven oximeter recordings were rejected because of artifacts or technical problems.

Statistical analysis
Data from the oximetry sleep study were used to determine the sensitivity, specificity and likelihood ratios for oximetry in the detection of OSA. For specificity and sensitivity calculations, indeterminate data were treated as a negative result. Receiver Operating Characteristics (ROC) curves were constructed, representing the comparative course of sensitivity and \( (1 - \text{specificity}) \) at different thresholds [25]. \( \kappa \) statistics were calculated for the measurement of inter- and intra-observer agreement [26,27].

Clinical and spectral characteristics of the subjects were expressed as means ± S.D., or as percentages (95% confidence intervals (95% CI)). A Mann–Whitney test was used for comparison between groups. Correlations were investigated using Spearman correlation analysis. A \( P \) value of < 0.05 was considered significant.

RESULTS

The diagnosis of OSA was confirmed in 124 (53%) of a total of 233 subjects included in the study. Anthropometric data, AHIs by polysomnography and spectral analysis characteristics are shown in Table 1. The OSA group had significantly higher values of \( r_s \) and PA than the non-OSA group.

Oximetry was normal in 105 (45%), abnormal in 109 (47%) and uninterpretable in 19 (8%) subjects. The three observers agreed on 182 out of 233 occasions (75%). The overall value of \( \kappa \) was 0.73 (\( P < 0.001 \)) (Table 2), while the concordance between two interpretations for the same observer was 0.95. The presence of P30–70 in the oximetry test had a sensitivity of 97 \( \pm \) 124, or 78.2% (95% CI 69.7–84.9), a specificity of 97 \( \pm \) 109 or 89.0% (95% CI 81.2–93.9), a positive predictive value of 97 \( \pm \) 109 or 89.0% (95% CI 81.2–93.9), and a negative predictive value 97/124 or 78.2% (95% CI 69.7–84.9).

Overall results and likelihood ratios for the nocturnal oximetry and polysomnography testing are detailed in Table 3. Of the 22 OSA subjects that had a negative diagnosis by oximetry, 18 had an AHI lower than 20, and the elevated value was principally because of hypopnoea. Of the 12 subjects that were diagnosed with OSA by oximetry, but were found by polysomnography not to suffer from OSA, five were older than 70 years, one had chronic obstructive pulmonary disease, two were obese with a BMI of > 35 kg/m² and four had an AHI higher than 8 and lower than 10. Sixteen (59%) patients with underlying disease presented with OSA.

The usefulness of the traditional methods (visual pattern recognition of \( \text{SaO}_2 \) recording, different desaturation indices and the total time spent with \( \text{SaO}_2 \) below 90%) in the diagnosis of OSA is shown in Table 4.

ROC analyses for PA and \( r_s \) are shown in Figure 3. For a PA threshold of 0.7%, the sensitivity was 94% and the

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Table 3  Likelihood ratios for nocturnal oximetry in relation to polysomnography

<table>
<thead>
<tr>
<th>Category</th>
<th>OSA</th>
<th>Non-OSA</th>
<th>Likelihood ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Proportion</td>
<td>n</td>
</tr>
<tr>
<td>Negative</td>
<td>22</td>
<td>0.177</td>
<td>83</td>
</tr>
<tr>
<td>Uninterpretable</td>
<td>5</td>
<td>0.040</td>
<td>14</td>
</tr>
<tr>
<td>Positive</td>
<td>97</td>
<td>0.782</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>124</td>
<td></td>
<td>109</td>
</tr>
</tbody>
</table>

Table 4  Usefulness of conventional oximetric methods in the diagnosis of OSA: oximetry inspection of $\delta O_2$ recording, the different ODIIs and the total time for which $\delta O_2$ is below 90%

CT90 > 1%, percentage of time spent with $\delta O_2$ below 90% representing > 1% of the total recording; PPV, positive predictive value; NPV, negative predictive value; LRPOS, likelihood ratio for a positive test; LRNEG, likelihood ratio for a negative test.

<table>
<thead>
<tr>
<th>Oximetry inspection</th>
<th>ODI4</th>
<th>ODI3</th>
<th>ODI2</th>
<th>CT90 &gt; 1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>70</td>
<td>57</td>
<td>60</td>
<td>68</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>85</td>
<td>84</td>
<td>80</td>
<td>78</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>79</td>
<td>81</td>
<td>77</td>
<td>78</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>77</td>
<td>63</td>
<td>64</td>
<td>68</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>78</td>
<td>70</td>
<td>69</td>
<td>72</td>
</tr>
<tr>
<td>LRPOS</td>
<td>4.7</td>
<td>3.7</td>
<td>3.0</td>
<td>3.1</td>
</tr>
<tr>
<td>LRNEG</td>
<td>0.4</td>
<td>0.5</td>
<td>0.5</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Figure 3  ROC analysis relating sensitivity and (1 – specificity) at different thresholds of PA and $r_s$

Figure 4  Scatter plot of AHI against PA
PA has undergone logarithmic transformation in order to reduce dispersion of the data. The horizontal line shows the best cut-off point of PA in the diagnosis of OSA. The vertical line establishes the cut-off for subjects with and without OSA.

Figure 5  Scatter plot of AHI against $r_s$
The horizontal line shows the best cut-off point of $r_s$ for the diagnosis of OSA. The vertical line establishes the cut-off for subjects with and without OSA.

DISCUSSION

It has been demonstrated that subjects with untreated OSA suffer from an increased incidence of cardiovascular morbidity [28,29] and mortality [3]. In addition, it is well known that OSA patients are at increased risk of automobile accidents [30]. Following international
standards, polysomnography is required to confirm an OSA diagnosis and to commence treatment [31]. However, the high prevalence of the disease, in addition to the cost and inconvenience of polysomnography, make simplified techniques desirable for diagnosing OSA. Using oximetric spectral analysis, the present study demonstrates that the presence of P30–70 in the oxygen saturation spectrum has a high degree of sensitivity and specificity in the diagnosis of OSA. In particular, our observations support the findings of previous studies demonstrating that the oximetric spectral characteristics of OSA patients differ significantly from those of non-OSA subjects [19,20]. We provide evidence indicating that PA is higher in OSA patients. Moreover, AHIs were correlated with PA (r = 0.74; P < 0.001) and rS (r = 0.69; P < 0.001). In a previous study, Keyl et al. [19] showed that a peak period around 33 s in the oxygen saturation spectrum was related to periodic breathing.

As a diagnostic test, this method is more sensitive than other methods currently available. Of the different oximetric methods used for the diagnosis of OSA, spectral analysis is the most sensitive (78%), and also maintains a high specificity (89%). Furthermore, this method gives more accurate values for likelihood ratios. Indeed, the likelihood ratio for a positive test was 7.11, while that for a negative test was 0.23, which is well within the range that some workers interpret as an indication of moderate predictive probability of the presence of disease [32]. However, when we used the traditional oximetric methods on the same subjects, the positive and negative likelihood ratios ranged from 2.5 to 4.7 and from 0.4 to 0.5 respectively. In the study of Gulay et al. [9], the sensitivity of oximetry inspection was 72%. In a study by Cooper and co-workers [7], oximeter records were analysed ‘blind’ by two experienced observers and classified in one of three categories: positive ‘sleep breathing present’, negative ‘sleep breathing absent’, and uninterpretable. A recording was classified as positive following ‘pattern recognition’ of repetitive falls in oxygen saturation of more than 5%. The two observers agreed on 27/41 occasions (66%). For an AHI of > 15, the sensitivity was 75%. In our work with 233 subjects, we reached a sensitivity of 78%, with three observers agreeing in 188 cases (75%). The use of clinical features has been shown to be of little value in predicting OSA. However, Deegan and McNicholas [33] found that a combination of clinical parameters and oximetry data improved predictive accuracy. Since spectral analysis has not been used previously for this aim, we chose to make only an analysis of oximetric data.

Using spectral analysis, periodicities of ventilation have been found in elderly subjects both with and without OSA [34]. It has been shown previously that time-dependent variations in pulmonary gas exchange occur during the awake state [35] and during sleep [36]. However, these studies did not use quantitative methods to measure the periodicities, and the investigators did not address the issue of whether subjects with sleep apnoea showed more marked periodicities during apnoic episodes. Although similar ventilatory oscillations occur in subjects with and without OSA, the magnitude of the ventilatory oscillation differs between these groups [34]. This ventilatory oscillatory process can be reflected by SAO2, and can be studied by spectral analysis of oximetric measures. This was the theoretical motive for our study.

Our oximetric results and polysomnographic reference standards were assessed independently of each other. In addition, our criteria for assessing oximetric data were relatively strict, in that, for a record to be classified as positive, two out of three observers had to agree; recordings were classified as negative if two observers considered the saturation record as negative. Our results emerged from a good agreement between independent observers (κ = 0.73). Given that we recorded our indeterminate cases as negative, this method inevitably reduced the sensitivity and increased the specificity of our investigation. In a clinical context, technical errors or ambivalent results in any one subject would be regarded as a ‘negative’ outcome, and the study would be repeated. In addition, the sensitivity and specificity of oximetric data were studied at different PA and rS thresholds to obtain a ROC curve. An rS threshold of 0.15 and a PA threshold of 0.7 were selected as the best cut-off points for oximetric spectral analysis. The indeterminate recordings do not influence the sensitivity and specificity obtained by this method.

Despite our results, some technical or physiological difficulties are associated with using oximetry for recognizing OSA. For example, poor contact between the probe and the finger due to body movements or bad regional circulation occasionally produces signals resembling multiple decreases in oxygen saturation. In addition, patients with chronic airway disease may present periodic nocturnal oxygen desaturation. Such technical or physiological problems increase false-positive results and decrease the specificity of any diagnostic technique. Mindful of this, we examined our recordings before the analysis to see if they indicated technical problems. For example, we eliminated from our analysis all data that registered decreases to zero. From our experience, we knew that these falls were due to finger-probe disconnections. As regards the physiological difficulties, of the 12 subjects incorrectly diagnosed by oximetry as having OSA, five were > 70 years old, one had chronic obstructive pulmonary disease, two were obese with a BMI of > 35 kg/m² and four had an AHI higher than 8 and lower than 10. In addition, by
using a sampling frequency of 0.2 Hz, we have limited the spectral analysis to 0.1 Hz, according to the general theorem of discrete Fourier transformation. In practice, sampled functions are never limited completely in frequency content. Physical spectra tend to be smooth and approach zero asymptotically as \( w \) increases. Accordingly, to avoid aliasing, we chose a sampling interval \( t \) so that essentially all of the spectral content of the waveform is contained below \( \frac{1}{2} \) lengths (Niquist theorem), and a smoothing window that has the largest energy in the main lobe of its spectrum, with respect to its side-lobe amplitude. This procedure improves the detection of P30–70.

Some authors maintain that measurement of nocturnal oxygen saturation alone allows for confident recognition of moderate and severe OSA cases, but this is likely to be inadequate for excluding milder cases in clinical practice [10]. Out of the 22 OSA subjects undetected by oximetry, 18 had an AHI of < 20, mainly due to hypopnoeas. Oxygen saturation is an indirect parameter that reflects the consequences of breathing; hypopnoea periods are not always associated with a fall in oxygen saturation. Repeat oximetry or more detailed polysomnography will be required if clinical suspicion is high. We studied all subject types; therefore our study included subjects with mild and severe OSA.

In conclusion, we have shown that spectral analysis and peak detection of \( S_aO_2 \) could be useful as a first approach to the analysis of nocturnal oxygenation. Advantages of this technique are as follows: (1) the spectral characteristics of the \( S_aO_2 \) signal from OSA patients are significantly different from those of non-OSA subjects; (2) better diagnostic indices are obtained than with other traditional oximetric methods; (3) the good agreement reached between different observers may be due to the ease with which the peak in the spectrum can be seen; and (4) since both PA and \( r_\text{sp} \) have continuous distributions, the cut-off points can be adjusted to obtain greater sensitivity or specificity, depending on the desired aim.

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