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Short Communication

Diagnostic Accuracy of a Mathematical Model to Predict Apnea-Hypopnea Index using Nighttime Pulse Oximetry

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Keywords

- Oxygen desaturation index
- Sleep apnea
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- Sensitivity
- Specificity

Abstract

Purpose: The intent of this study is to develop a predictive model to convert an oxygen desaturation index (ODI) to an apnea and hypopnea index (AHI). This model will then be compared to actual AHI to determine its precision.

Methods: 1467 subjects given polysomnograms with concurrent pulse oximetry between April 14, 2010 and February 7, 2012, were divided into model development (n=733) and verification groups (n=734) in order to develop a predictive model of AHI using ODI. Quadratic regression was used for model development.

Results: The coefficient of determination (r^2) between the actual AHI and the predicted AHI (PredAHI) was 0.80 (r=0.90), which was significant at a $p<0.001$. The areas under the ROC curve ranged from 0.96 for AHI thresholds of ≥10 and ≥15/hr. to 0.97 for thresholds of ≥5 and ≥30/hr.

Conclusions: The algorithm described in this paper provides a convenient and accurate way to convert ODI to a predicted AHI. This tool makes it easier for clinicians to understand oximetry data in the context of traditional measures of sleep apnea.

INTRODUCTION

Obstructive sleep apnea (OSA) is a condition that involves multiple episodes of airway closure and/or reduction in airflow that affects 2-4% of the population [1]. OSA has been associated with adverse medical conditions including congestive heart failure [2], stroke [3], pulmonary [4] and systemic [5] hypertension, cancer [6], and increased mortality [7]. Traditionally, sleep apnea has been assessed via a nighttime polysomnogram. This diagnostic procedure continues to be the gold standard for the evaluation of sleep apnea.

Numerous studies have looked at the role of pulse oximetry in the assessment of OSA [8-14]. These previous investigations have developed several methods for predicting AHI from oximetry data, these include: cumulative time below an oxyhemoglobin saturation (SaO_2) of 90% (CT90) [8], the number of SaO_2 events that drop either 3% or 4% (ODI) [9,10,15],a measure of SaO_2 variability (Δ index) [11,12], a central tendency measure [13], and a multilayer perceptron neural network [16]. However, in our review of the literature, we uncovered only two other studies that have attempted to convert oximetry to an apnea-hypopnea index (AHI) [14,16]. In the Magalang et al study, both Δ index and a composite measure of various oximetry indexes were found to have coefficients of determination of 0.60 and 0.70 respectively. The Marco et al study produced a more accurate predictive formula than Magalang *et al.,* However, scoring of the polysomnograms did not appear to utilize the updated guidelines recommended by the American Academy of Sleep Medicine(AASM) [17].

Therefore, the goal of this study is to develop a new predictive model of AHI using Oximetry data by utilizing more recent pulse oximetry technology, a large sample size, and the 2007 AASM scoring guidelines to evaluate the gold standard attended polysomnograms. We believe that by taking into account these factors we will be able to develop a new predictive model that out performs all previous models. Our predictive model will focus on ODI since it appears to be the most sensitive and specific oximetry index [9,18], and is therefore an ideal target for conversion to AHI.

METHODS

Patient Population

Approval for the study was granted by the institutional review board at Weill Cornell Medical College. 1467 subjects given

attended polysomnograms with concurrent pulse oximetry at the Center for Sleep Medicine, Weill Cornell Medical were utilized for this retrospective analysis (see table 1 for demographic data). Most of these subjects were suspected of OSA, a minority were suspected of other sleep disorders including (but not limited to) periodic limb movements, narcolepsy, sleep walking, and REM behavior disorder. All subjects ≥18 years old studied between April 14, 2010 and February 7, 2012, who had not received PAP therapy and/or supplemental oxygen therapy on their polysomnogram were included in this analysis. Subjects were randomized by assigning each case a random number, ordering the numbers in an ascending fashion, and splitting the randomly ordered cases into a model development group (n=733), and a verification group (n=734).

No significant differences were found between the model development and validation groups on any variable listed above at a $p<0.05$ using independent t-tests.

Polysomnogram

Previously described standard techniques were employed on all-night attended sleep recordings using Grass Technologies Twin® digital polysomnographs with an integrated Nonin clip Oximetry (see below for additional details on Oximetry). Standard polysomnogram montage and digital filter settings recommended by the AASM were employed [19]. Respiratory effort was measured by Sleep sense® inductive plethysmography belts placed around the rib cage and abdomen. Airflow was determined by the Pro-Tech PTAF lite® pressure transducer on the baseline study. The nasal cannula for the pressure transducer was placed at the level of the upper lip in midline position. A continuous electrocardiogram recorded heart rate and rhythm. Respiratory events were classified according to AASM criteria: an apnea was defined as a decrease in peak nasal pressure of >90% of baseline, lasting at least 10 seconds. Hypopnea was defined by a decrease of >30% of the baseline nasal pressure, lasting at least 10 seconds and associated with a ≥4% drop in the oxyhemoglobin saturation. All records were reviewed by board certified sleep specialists and scored by registered polysomnographic technicians.

Pulse Oximetry

The oximeter used was the Nonin Xpod® model 3011 with an adult finger clip senor (Nonin 8000AA) utilizing Pure SAT® technology that automatically adjusts to provide pulse to pulse averaging of three seconds or faster (based on pulse rates 60 BPM and greater). ODI was calculated by the number of ≥4% drops in oxyhemoglobin saturation over total recording time.

Statistical Analysis

SPSS version 21 and R version 3.2.1 were used for statistical analysis. Linear, multivariate adaptive sp lines, segmented, and quadratic regression modeling was used to develop the predictive models of AHI using ODI. A log transformed (to address a non-normal distribution of the residuals) quadratic regression model provided the best fit compared to the other models. Therefore, the results listed below are only based on the transformed quadratic model. The regression algorithm was developed with 733 subjects. Verification of the model was performed using a separate group of 734 subjects (see Table 1 for demographic information on the subject groups). Sensitivity and specificity are shown for AHI break points of ≥5/hr., ≥10/hr., and ≥15/hr. due to the frequent use of these threshold levels in clinical practice to

Table 1: Demographic information.

		Subject group (n=1467)			
		Model development group		Model validation group	
		Mean±SD	Count	Mean ± SD	Count
Gender	Female		288		273
	Male		444		460
Age (Years)		48.47±16.17		49.8±16.81	
BMI (kg / m^2)		28.20±6.90		27.94±6.56	
Epworth Score		8±5		8±5	
ODI Total (Events / h)		8.5±12.7		7.9±10.3	
AHI Total (Events / h)		14.7±19.6		14.00±17.3	
Avg O2 Sat Total (%)		94.5±6.4		94.5±6.4	
Avg O2 Sat Wake (%)		92.5±16.5		93.5±13.3	
Avg O2 Sat NREM (%)		92.0±15.7		93.1±12.3	
Avg O2 Sat REM (%)		87.3±25.5		89.7±64	
Average HR Total (BPM)		64±11		64±10	
Sleep Efficiency (% TST)		74.4±20.1		74.8±18.1	
Total Sleep Time (Min)		346±106		351±103	

Demographic information about the 1467 subjects

Abbreviations: BMI: Body Mass Index; H: Hours; Avg: Average; 0_2 Sat: Oxygen Saturation; NREM: Non-Rapid Eye Movement Sleep; REM: Rapid Eye Movement; HR: Heart Rate; BPM: Beats Per Minute; TST: Total Sleep Time; Min: Minute

No significant differences were found between the model development and validation groups on any variable listed above at a $p<0.05$ using independent t-tests.

determine the need for treatment of sleep apnea. In addition, an AHI threshold of ≥30/hr. is also shown to illustrate the role of our predictive model in identifying subjects with severe sleep apnea. Confidence intervals (CI) are all listed as 95%.

RESULTS

The coefficient of determination (r^2) between the actual AHI and the predicted AHI (Pred AHI) was 0.80 (r=0.90), which was significant at a p<0.001.PredAHI determined a correct AHI ±5/hr. in 76% of subjects. The intra class correlation for single measures using an absolute agreement definition was 0.88 (CI 0.87-0.90). The subjects that had a Pred AHI greater than ±5/hr were significantly older t (732) = -5.311, p<0.001, had a higher AHI t(732)=-16.89, p<0.001, and a lower sleep efficiency t (732)=5.12, p<0.001.

The AUC was 0.97±0.005 (SE), CI 0.96-0.98 for an AHI of ≥5/hr., 0.96±0.007 (SE), CI 0.94-0.97 for an AHI ≥10/hr., 0.96±0.007 (SE), CI 0.95-0.98 for an AHI of ≥15/hr., and 0.97±0.008 (SE), CI 0.96-0.99 for an AHI of ≥30/hr. (see Figure 1 for ROC curves, and Table 2 for other measures of test precision). The asymptotic significance level for AUC at all tested thresholds was p<0.001.

The center line of the plot represents the mean, the other two lines indicate ±2 SD. It shows data from 734 subjects (the validation set). The gold standard measure of AHI was derived from in-laboratory polysomnography scored according to AASM 2007 guidelines.

DISCUSSION

This analysis shows that an accurate prediction of AHI can be made using a regression formula derived from ODI, with areas under the ROC curve ranging from 0.96 for thresholds of ≥10 and ≥15/hr. to 0.97 for thresholds of ≥5 and ≥30/hr. This is better than most previously published comparisons of ODI to AHI [20,14,10]. Only one other study appears to outperform our model [9], however this study does not attempt to convert ODI to a predicted AHI. Moreover, our model was developed and compared to an AHI calculated using the AASM's currently recommended scoring guidelines for respiratory events [19], and therefore is more applicable for use today. In comparison to the Magalang *et al.,* models [14], which showed r^2'sof 0.60, and 0.70 for predicting AHI with Δ index alone and a composite measure of oximetry respectively, our model outperformed these algorithms with an r^2 of 0.80. The Marcos *et al.,* [16] model slightly out performed our model at an AHI of 15/hr (93% vs. 91%). However, our model was more accurate at AHI's of 5/hr. (84% vs. 91% and 10/hr. (87% vs. 90%). In addition, our model was very accurate at an AHI of 30/hr (Table 2).

Due to the fact that ODI cannot differentiate between central and obstructive events, we do not intend for this algorithm to

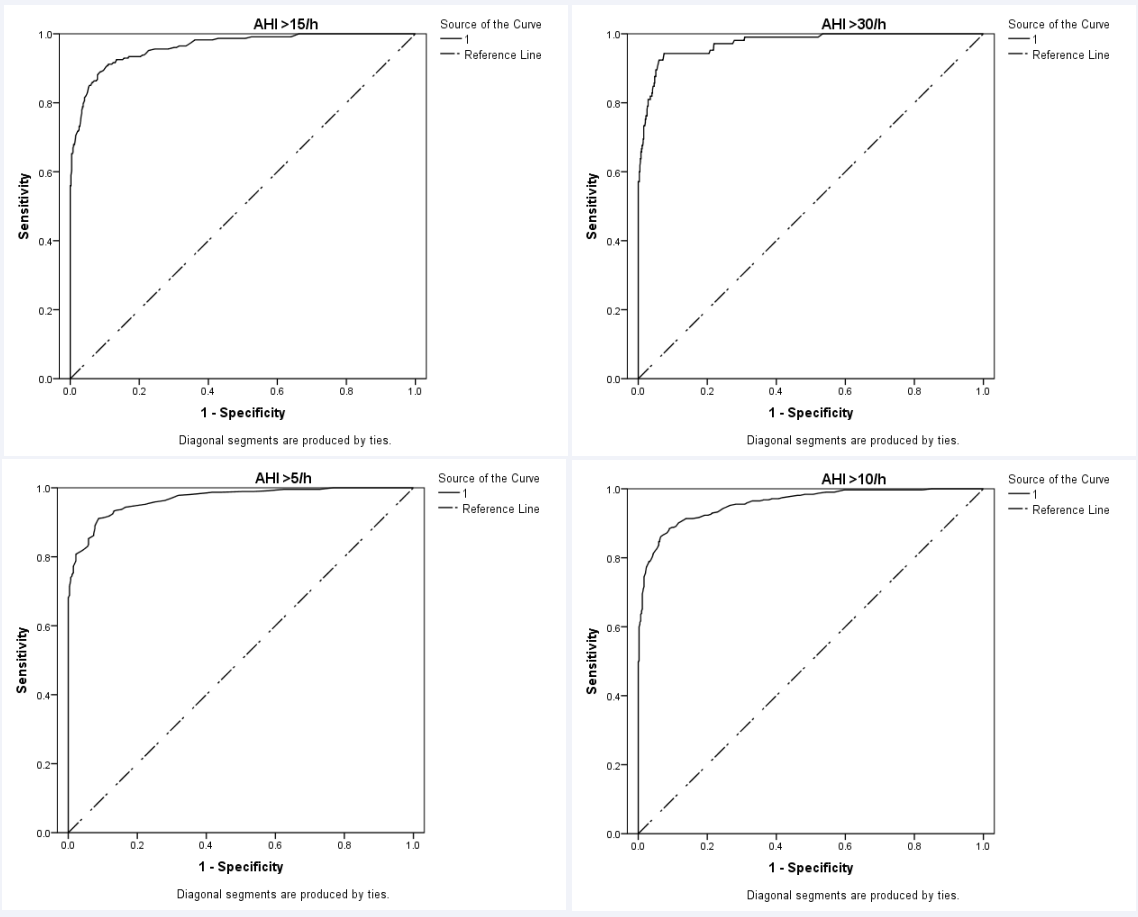

Figure 1 ROC Curve for Predicted AHI at Different Cutoff Points Compared to Polysomnography.

Table 2: Stratified results for predicting sleep apnea using the PredAHI algorithm.

	Sensitivity	Specificity	PPV	NPV	Accuracy
AHI >=5 h	.90	.92	.95	.85	.91
AHI >=10 h	.86	.94	.91	.90	.90
AHI >=15 h	.82	.96	.89	.92	.91
AHI >=30 h	.76	.98	.85	.96	.95

Abbreviations: PPV: Positive Predictive Value; NPV: Negative Predictive Value

replace traditional polysomnograms. However, this formula can be useful in diagnosing patients that have had either a home or in-laboratory sleep study, but the flow sensor data is unavailable. It is not uncommon in clinical practice to have patients remove the flow sensor because of discomfort; in these cases a predicted AHI can be calculated from the ODI, and the respiratory effort activity can be viewed to gain an estimate of central vs. obstructive apnea. This formula can also be used with pulse oximeters to convert nighttime oximetry data to AHI in order to determine if additional testing or treatment for sleep apnea is warranted.

As mentioned in the introduction, since the 1990's studies have shown the value of using oximetry in assessing apnea [8-14]. However, the use of oximetry indexes for clinical decision making in sleep disordered breathing remains uncommon. The ability to convert oximetry data to an AHI allows a more readily understandable metric that sleep specialists and most non-sleep specialists alike can interpret.

As seen in Figure 2, Pred AHI tends to underestimate AHI in the severe range. This is likely due to the fact that as the actual AHI becomes very high, the individual apneas tend to be shorter, resulting in fewer respiratory events resulting in ≥4% drop in blood oxygen saturation (e.g. If an average apnea length is 15 sec. the maximum AHI is 120/hr. vs. 90/hr. for an average apnea length of 20 sec.). However, the accuracy (Table 2) of Pred AHI at the ≥30/h AHI threshold is high at 95%. Differentiating whether a true AHI is 50/hr. vs. 90/hr. is not as important as determining if an AHI is in the severe range, therefore we do not believe this discrepancy will significantly affect clinical decisions to treat sleep apnea based on our formula. Another limitation of this study is the use of a single testing site. However, the heterogeneity of our patient population in New York City moderates this concern to some degree. Moreover, the use of a large sample size in both developing and validating our model gives confidence in its accuracy.

In summary, the algorithm described in this paper provides a convenient and accurate way to convert ODI to a predicted AHI. This tool makes it easier for clinicians to understand oximetry data in the context of traditional measures of sleep apnea. Our goal is to pair our formula with a commercially available pulse oximeter in order to provide a low cost screening tool for sleep apnea to determine the need for additional evaluation and/or treatment of sleep disordered breathing. We believe this instrument will be useful for trades such as the transportation industry, which is in need of a low cost and accurate way to asses for sleep apnea, or for patients living in rural or impoverished areas where traditional attended polysomnography may not be available or may be too costly.

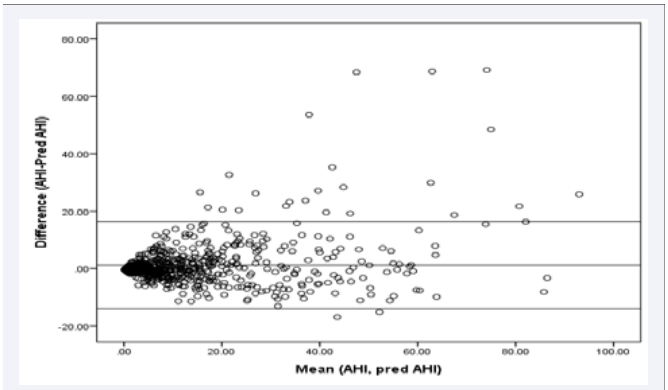

Figure 2 Bland-Altman plot showing the differences between in-laboratory polysomnography determined AHI and our predicted AHI based on oximetry.

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Dr. Matthew Ebben takes responsibility for the content of the manuscript, including the data and analysis.

Competing interests

The Cornell University technology commercialization office has licensed the formula described in the paper for Matthew R. Ebben and Ana C. Krieger. Matthew R. Ebben also works as a consultant for Apnostics, the company that has licensed the algorithm described in the paper from Cornell University.

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