Nocturnal hypoxemia and obstructive sleep apnea (OSA) are common comorbidities in patients with chronic obstructive pulmonary disease (COPD). The authors sought to develop a strategy to interpret nocturnal pulse oximetry and assess its capacity for detection of OSA in patients with stage 3 to stage 4 COPD. A review of consecutive patients with COPD who were clinically prescribed oximetry and polysomnography was conducted. OSA was diagnosed if the polysomnographic apnea-hypopnea index was $\geq 15$ events/h. Comprehensive criteria were developed for interpretation of pulse oximetry tracings through iterative validation and interscorer concordance of $28\%$. Criteria consisted of visually identified desaturation ‘events’ (sustained desaturation $\geq 4\%$, $1$ h time scale), ‘patterns’ ($\geq 3$ similar desaturation/saturation cycles, $15$ min time scale) and the automated oxygen desaturation index. The area under the curve (AUC), sensitivity, specificity and accuracy were calculated. Of $59$ patients ($27$ male), $31$ had OSA ($53\%$). The mean forced expiratory volume in $1$ s was $46\%$ of predicted (range $21\%$ to $74\%$ of predicted) and $52\%$ of patients were on long-term oxygen therapy. Among $59$ patients, $35$ were correctly identified as having OSA or not having OSA, corresponding to an accuracy of $59\%$, with a sensitivity and specificity of $59\%$ and $60\%$, respectively. The AUC was $0.57$ ($95\%$ CI $0.55$ to $0.59$). Using software-computed desaturation events (hypoxemia $\geq 4\%$ for $\geq 10$ s) indexed at $\geq 15$ events/h of sleep as diagnostic criteria, sensitivity was $60\%$, specificity was $63\%$ and the AUC was $0.64$ ($95\%$ CI $0.62$ to $0.66$). No single criterion demonstrated important diagnostic utility. Pulse oximetry tracing interpretation had a modest diagnostic value in identifying OSA in patients with moderate to severe COPD.

Key Words: Chronic obstructive pulmonary disease; Nocturnal hypoxemia; Obstructive sleep apnea; Oximetry

L’examen des tracés de saturométrie pour dépister l’apnée obstructive du sommeil chez les patients atteints de maladie pulmonaire obstructive chronique avancée

L’hypoxémie nocturne et l’apnée obstructive du sommeil (AOS) sont des comorbidités courantes chez les patients atteints de maladie obstructive chronique (MPOC). Les auteurs ont cherché à élaborer une stratégie pour interpréter la saturométrie nocturne et en évaluer la capacité de dépister l’AOS chez les patients atteints de MPOC de stade 3 à 4. Ils ont effectué une analyse des patients consécutifs atteints de MPOC à qui on avait prescrit une oxymétrie et une polysomnographie en clinique. L’AOS était diagnostiquée si l’indice polysomnographique apnée-hypopnée était supérieur à $15$ événements à l’heure. Les auteurs ont établi des critères détaillés pour interpréter les tracés de saturométrie par validation itérative et concordance interévaluateur d’au moins $80\%$. Ces critères consistaient à déterminer visuellement les « événements » de désaturation (désaturation soutenue d’au moins $4\%$, échelle d’une heure), les « profils » (au moins trois cycles similaires de désaturation/saturation, échelle de $15$ minutes) et la mesure automatique de l’indice de désaturation en oxygène. Ils en ont calculé l’aire sous la courbe (ASC), la sensibilité, la spécificité et la précision. Sur $59$ patients (27 de sexe masculin), $31$ étaient des AOS ($53\%$). Le volume expiratoire maximal moyen par seconde était de $46\%$ (plage de $21\%$ à $74\%$) de la valeur prévue, et $52\%$ des patients étaient sous oxygénothérapie à long terme. Chez ces $59$ patients, les auteurs ont établi correctement que $35$ étaient ou non de l’AOS, pour une exactitude de $59\%$, une sensibilité de $59\%$ et une spécificité de $60\%$. L’ASC était de $0.57$ ($95\%$ IC $0.55$ à $0.59$). Après avoir indexé dans les critères diagnostiques les événements de désaturation informatisé (hypoxémie d’au moins $4\%$ pendant au moins dix secondes) à au moins $15$ événements par heure de sommeil, la sensibilité s’élevait à $60\%$, la spécificité, à $63\%$, et l’ASC, à $0.64$ ($95\%$ IC $0.62$ à $0.66$). Aucun critère unique n’en démontrait une utilité diagnostique importante. L’interprétation du tracé de saturométrie avait une valeur diagnostique modeste pour dépister l’AOS chez les patients atteints de MPOC modéré à grave.
recognition of prespecified patterns was performed prospectively for the analysis outcomes: mean oxygen saturation (SpO₂), highest/lowest

Protocol
A consecutive chart review of the inpatient pulmonary rehabilitation service from January 1, 2006 to November 1, 2010 at Mount Sinai Hospital (Montreal, Quebec) was conducted. Patients were electively admitted for three to four weeks for pulmonary rehabilitation to improve functional capacity. Stable COPD was defined in patients who did not experience an exacerbation over a period of six weeks. Patients were identified and included if medical records’ coding for COPD, overnight pulse oximetry and PSG were present. This included patients who were undergoing long-term oxygen therapy (LTOT). The present study was approved by the Mount Sinai Hospital Ethics Committee.

With overnight PSG, the presence or absence of OSA was determined at a prespecified apnea/hypopnea index (AHI) cut-off of >15 events/h sleep. PSG recording and scoring followed the current standards of the American Academy of Sleep Medicine (AASM) (8) and used software for manual analysis of digital files (Sandman, Tyco, Canada and Nihon Kohden America, USA) that included the standard recordings of electro-oculogram, electroencephalogram, electrocardiogram and submental electromyography, with concurrent monitoring of respiratory variables during sleep including thermistor and nasal pressure waves, pulse oximetry and inductance plethysmography (9). Apneas were scored with at least 10 s of a 90% reduction in airflow according to thermistor. Hypopneas were scored using the official AASM alternative criteria when accompanied by at least a 3% desaturation or electroencephalogram arousal to avoid false-negative polysomnographic diagnoses of OSA in patients with a low body mass index or short times with sleep in the supine position. The overnight pulse oximetry (Respironics 920N + Oximeter, Respironics, USA) procedure was performed on a separate night within two weeks using a transcutaneous ear probe for a minimum of six continuous hours while the patient slept in his/her hospital bed. This procedure was repeated if sleep was observed to be disturbed by patient or environmental factors, or if the recording was of poor quality as determined by the care team. An electronic recording (ProFox Oximetry Standard 0103.12S, Respironics, USA) was then produced with the following automated interpretation protocol

METHODS

A web-based ROC calculator with an ordinal rating scale format was used for analyses (10). The ordinal rating scale format enabled the calculation of a confidence value (1 to 6) for ranges of AHI scores derived from PSG results such that a rating of 1 = definitely no OSA (AHI range of 0 to 5) and 6 = definitely OSA (AHI >30). The sensitivity, specificity, accuracy and area under the curve (AUC) are reported with relevant 95% CIs. Statistical significance was defined at the two-sided 0.05 level.

RESULTS

Baseline characteristics and pulmonary function data are summarized in Table 1. Of 59 patients (27 male), 31 (53%) had OSA. The mean forced expiratory volume in 1 s (FEV₁) was 46% of predicted (range 21% to 74% of predicted) and 52% of patients were on LTOT (oxygen was prescribed and used 18 h to 24 h per day) at rates ranging from 1 L/min to 4 L/min to help maintain saturations ≥92%. There were no significant differences in nocturnal saturation profiles between those diagnosed with OSA and those without OSA (Table 2).

Oximetry tracing interpretation protocol

After review of the literature on the waveforms used to identify OSA with oximetry, a comprehensive set of criteria was developed for interpretation of pulse oximetry tracings through iterative validation and interobserver concordance ≥80% (author AS and acknowledged RC). Criteria consisted of quantification of visually identified desaturation ’events’ (continuous desaturation ≥4% lasting ≥30 min, viewed in a 2 h time scale window), saturation ’patterns’ (≥3 similar desaturation/saturation cycles, in a 15 min time scale window) and mean saturation within each pattern was reported (Appendix 1). Using this method, a patient is identified to have OSA if the following criteria are met: A mean SpO₂ ≥90% and at least one of the following – number of events ≥4 and/or number of patterns ≥12. Both ’events’ and ’patterns’ could coexist in the same tracing. To determine whether more or fewer events or patterns influenced the diagnostic accuracy, further ROC analysis was performed for each component of the interpretation criteria as well as the automated ODI provided by the software counting 4% desaturations. The oximetry tracings were scored blind of the PSG results. These findings were then prospectively compared with the PSG diagnosis. Examples of an excluded oximetry recording are shown in Figure 1, in which ≥20% of the total tracing time contains breaks (ie, a desaturation ‘event’ [Figure 2]), whereby an average desaturation of ≥4% from the baseline average was observed. The oxygen desaturation/resaturation ‘pattern’ depicted in Figure 3 is marked by a rise and fall of at least three similar saturation cycles (see Appendix 1 for greater detail regarding tracing exclusion, desaturation event and pattern recognition).

Statistical analysis

Descriptive statistics (means, SDs, counts and frequencies in percent) were used to present patients’ baseline characteristics. Differences between patients diagnosed with OSA and no OSA were tested using unpaired t tests. Contingency analysis and calculation of ROC curves were performed to assess the detection capacity of various oximetry indexes to identify OSA. A web-based ROC calculator with an ordinal rating scale format was used for analyses (10). The ordinal rating scale format enabled the calculation of a confidence value (1 to 6) for ranges of AHI scores derived from PSG results such that a rating of 1 = definitely no OSA (AHI range of 0 to 5) and 6 = definitely OSA (AHI >30). The sensitivity, specificity, accuracy and area under the curve (AUC) are reported with relevant 95% CIs. Statistical significance was defined at the two-sided 0.05 level.

Figure 1) An example of an excluded oximetry tracing with time frame of 1 h

Figure 2) An example of a desaturation ‘event’ from an oxygen saturation oximetry tracing with a time frame of 1 h

Figure 3) An example of an oxygen saturation ‘pattern’ from an oximetry tracing with a time frame of 15 min
The ROC analysis was performed for each component of the interpretation criteria and the standard oximetry variables (Table 3). When using an ODI with a cut-off ≥15 events/h, the sensitivity and specificity were 60% and 63%, respectively, and AUC 0.64 (95% CI 0.62 to 0.66) (ROC curve presented in Figure 4). A subgroup analysis of oximetry tracings performed in patients undergoing LTOT and in patients on room air was analyzed separately; the ROC analyses were similar (Table 3). Accuracy for interpretation of tracings on room air was 67%, while only 57% accuracy was achieved for the tracings from oxygen-dependent patients. No important differences were observed between the OSA and non-OSA groups with regard to pulmonary function, pulse oximetry (Table 2) and event and pattern count (data not shown). The OSA group spent a greater mean percentage of nocturnal time below 90% oxygen saturation; however, this did not reach statistical significance (P=0.06) (Table 2).

**DISCUSSION**

In the present study, we demonstrated that an explicit approach to interpretation of pulse oximetry tracings can provide a modestly reliable strategy for diagnosis or selection of patients who would most benefit from further polysomnographic assessment for sleep-related breathing disturbances. An interpretation tool, as presented herein, uses observations of predefined desaturation ‘events’ as well as ‘patterns’ of oxygen desaturation/resaturation. These visual criteria, in concert with the average oxygen saturation during these patterns, have modest diagnostic accuracy to identify patients who may have OSA. The interpretation criteria enabled us to correctly identify OSA in 55% of individuals with diagnosed OSA on PSG and to exclude 64% without a diagnosis OSA – an overall test accuracy of 59%. This result translated into a detection test with a similar rate for sensitivity and specificity of 60%. When we used an ODI generated by the software, the test became slightly more robust but nonetheless modest in its performance, with a 61% chance of correct detection.

One novel aspect of the present study was that patients who underwent nocturnal oximetry while on oxygen were included in the analysis. When the oxygen and room air interpretations were analyzed separately, the accuracy was higher in the room air set of tracings; however, overall, the criteria performed similarly in both test groups, with an AUC of approximately 0.6. It may be expected that supplemental oxygen would limit the diagnostic value of this test; however, because both subsets performed similarly, it may be explained that significant OSA inhibits the adequate passage of low-flow oxygen in these patients with severely diminished pulmonary function. The present study was also unique in that interpretation criteria were based on examining the recording in gross detail using larger time scales (1 h and 2 h) as well as capturing more subtle changes through a 15 min time scale.

In the past two decades, there have been >20 articles published attempting to define criteria to detect sleep-related breathing disturbances, such as OSA, from pulse oximetry tracings in primarily non-COPD populations. In a review by Netzer et al (11), 11 studies were identified and diverse methodologies for oximetry interpretation were reported where available. The contingency analyses from these studies resulted in sensitivity and specificity ranging between 31% and 91%, and 41% to 100%, respectively. It should be noted that these studies involved adults with suspected sleep disorders and not specific to COPD. Only one study included pulmonary disease-specific nocturnal oximetry interpretation (12). In this small study, there were eight participants with COPD, three with restrictive lung disease and 15 with OSA syndrome. In this study, using a mathematical interpretation of the SaO₂ signal the number of apneas detected by PSG and the

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Baseline characteristics and pulmonary function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
<td>OSA (n=31)</td>
</tr>
<tr>
<td>Age, years</td>
<td>69.3±12.6</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>19 (46)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>36.4±9.4</td>
</tr>
<tr>
<td>FEV₁, L</td>
<td>1.7±0.7</td>
</tr>
<tr>
<td>FVC, % predicted</td>
<td>53.6±14.0</td>
</tr>
<tr>
<td>Supplementary O₂ therapy, %</td>
<td>48</td>
</tr>
<tr>
<td>FVC, L</td>
<td>1.1±0.6</td>
</tr>
<tr>
<td>FEV₁, % predicted</td>
<td>46.8±14.9</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD unless otherwise indicated. FEV₁ Forced expiratory volume in 1 s; FVC Forced vital capacity; OSA Obstructive sleep apnea.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Pulse oximetry characteristics for obstructive sleep apnea (OSA) and non-OSA subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurement</td>
<td>OSA (n=31)</td>
</tr>
<tr>
<td>Oxygen saturation, %</td>
<td>89.2±3.8</td>
</tr>
<tr>
<td>Highest oxygen saturation, %</td>
<td>97.6±2.4</td>
</tr>
<tr>
<td>Lowest oxygen saturation, %</td>
<td>66.7±15.7</td>
</tr>
<tr>
<td>High desaturation, %</td>
<td>90.2±6.9</td>
</tr>
<tr>
<td>Low desaturation, %</td>
<td>85.2±4.3</td>
</tr>
<tr>
<td>Desaturation events, n</td>
<td>204.3±180.6</td>
</tr>
<tr>
<td>Desaturation events/h</td>
<td>27.0±21.9</td>
</tr>
<tr>
<td>Oxygen desaturation events &lt;90%, n</td>
<td>204.3±180.6</td>
</tr>
<tr>
<td>% of time &lt;90% oxygen saturation</td>
<td>45.2±30.5</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD. *Comparison t test P=0.06

**TABLE 3**

The performance of criteria and its components to identify obstructive sleep apnea (OSA)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>AUC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patterns</td>
<td>50</td>
<td>47</td>
<td>0.49 (0.46–0.51)</td>
</tr>
<tr>
<td>Events</td>
<td>58</td>
<td>55</td>
<td>0.59 (0.57–0.61)</td>
</tr>
<tr>
<td>SaO₂</td>
<td>57</td>
<td>59</td>
<td>0.55 (0.53–0.57)</td>
</tr>
<tr>
<td>ODI</td>
<td>60</td>
<td>63</td>
<td>0.64 (0.62–0.66)</td>
</tr>
<tr>
<td>RA tracings</td>
<td>67</td>
<td>67</td>
<td>0.59 (0.55–0.63)</td>
</tr>
<tr>
<td>O₂ tracings</td>
<td>59</td>
<td>62</td>
<td>0.61 (0.56–0.65)</td>
</tr>
</tbody>
</table>

ODI Oxygen desaturation index; O₂ Ability of criteria to detect OSA in the 30 patients using their usual long-term oxygen therapy; RA Ability of criteria to detect OSA in 29 patients on room air; SaO₂ Arterial oxygen saturation.

![Figure 4](image-url) ROC curve of oxygen desaturation index in predicting obstructive sleep apnea. The hash line indicates a hypothetical test equal to random guessing.

Can Respir J Vol 21 No 3 May/June 2014 173
calculated desaturation index from oximetry were correlated ($r^2=0.92$; $P<0.01$). Other authors have been successful using similar methodology to the present study in patients with congestive heart failure. Sériès et al (13) examined home nocturnal oximetry tracings for detection of sleep-related breathing disturbances in patients with chronic heart failure (n=50) and reported their analysis to be sensitive (85%) and specific (93%) for identifying OSA. A smaller study involving congestive heart failure patients (n=10) who were examined for ventilatory disturbances, such as Cheyne-Stokes breathing, concluded that pulse oximetry was effective in identifying sleep-related breathing changes, and was simple, inexpensive and well tolerated (14). Heart failure and COPD can coexist in patients with overlap of symptoms, thereby complicating diagnosis and treatment (15).

The coexistence of both OSA and COPD has been termed the ‘overlap syndrome’ (16). This occurs in approximately 5% to 10% of the population with obstructive airways disease, which represents approximately 0.5% to 1% of the general population ≥40 years of age (17). When the overlap syndrome has been identified, it has been found to be associated with poorer quality of sleep, lower quality of life, increased morbidity and increased mortality (17,18). It is clinically worthwhile to identify, as early as possible, this subgroup of patients with COPD given the interventions that exist and have proven beneficial (18). However, both diseases share common symptoms such as fatigue and nonrestorative sleep. Although clinicians may currently use the common indicators of disruptive snoring, excessive daytime sleepiness and an elevated body mass index to suspect OSA in a patient with COPD, many patients with OSA do not have these characteristics (18,19).

In this clinical setting, this becomes highly evident and problematic when we consider the variation in physician interpretation of nocturnal oximetry. A recent study addressed this question and revealed the wide inconsistency of physician opinions concerning the utility of oximetry and measurements they believed to be pertinent to the diagnosis and management of their patients (20). All subjects (pulmonary physicians) were asked to interpret three oximetry tracings and provide a diagnosis; approximately one-half of the physicians were able to. Diagnoses varied widely including sleep-related breathing disturbances, lung or cardiac disease, rapid eye movement-associated desaturation and neuromuscular disease. Management recommendations also varied among the physicians: the top three were PSG, nocturnal oxygen prescription and the need for more medical information. The top four physician-selected oximetry data chosen for relevancy included SpO2 waveform and pattern. Some other variables not measured by the oximetry that were considered to be important for interpretation were whether they had witnessed apneas, patient had known heart or lung disease, recording length and sleepiness status.

There have been several published methods regarding mathematical models to predict OSA from indexes of nocturnal pulse oximetry. An aggregated model developed a predictive calculation that was able to accurately detect OSA based on differences in saturation over 12 s intervals (delta index), desaturation events and data on time spent below various saturation thresholds (21). The main finding was that combining the variables of oximetry improved the precision of OSA diagnosis compared with using the delta index or desaturation indexes alone ($r^2=0.70$). This method was validated in a prospective cohort whereby the oximetry data were collected simultaneously during PSG and separated for independent analyses. Recently, an analysis was performed to evaluate four different statistical pattern recognition techniques of SpO2 signals to circumvent the need for PSG in the detection of OSA in otherwise normal patients (22). The most accurate classifier was derived by a linear discriminant analysis algorithm with spectral features (accuracy 87.6% and AUC 0.925). In contrast, a testing of two predictive models that included integration of a clinical score, pulmonary function results, arterial blood gas data and nocturnal pulse oximetry interpretation failed to be valid when used in a prospective population that was similar and selected in the same way (23). Other predictive methods used in patient populations with suspected OSA that integrated clinical features and/or questionnaires as well as oximetry data were found to have modest capacity for identifying OSA, with some success at eliminating patients without OSA as well as categorizing high-risk patients needing further investigation (24,25).

A limitation of the present study was that the oximetry interpretation analysis was performed retrospectively and would need to be validated prospectively to confirm its utility. The study included a limited number of subjects and would need to be further explored with a larger subset of patients. However, the 95% CIs for all the explicit oximetry criteria were relatively narrow, spanning ≤58% and excluded AUC ≥0.70. The subjectivity of the analytical method must also be considered when selecting a strategy for oximetry tracing interpretation and may warrant adequate training for those who use nocturnal oximetry in their management of patients with potential sleep-related breathing disturbances; however, our tracing visual analysis criteria were explicitly defined and demonstrated inter-rater concordance >80% before beginning the analysis of our patients with COPD.

Although our study appears to support the findings outlined in practice parameters for the indications for PSG, which states that oximetry lacks the specificity and sensitivity to be used as an alternative to PSG for diagnosing sleep-related breathing disorders (26), it does warrant further investigation. There remains an important need to use simplified diagnostic techniques for patients with severe COPD. Our data suggest that simple pulse oximetry appears to be neither sensitive nor sufficiently specific to stand alone as a diagnostic procedure. There appears to be more promise in the use of mathematical waveform interpretation rather than visual waveform analyses to risk stratify patients with suspected sleep-related breathing disturbances such as OSA. This has yet to be tested in patients with advanced COPD.

ACKNOWLEDGEMENTS: The authors thank Ryan Chan, an MSc candidate from the School of occupational and Physical Therapy at McGill University for his assistance in protocol development and data collection. AS and MB designed the research study, analyzed the data and wrote the manuscript. AS performed the research. NW reviewed the data and contributed to the writing and editing of the manuscript. The authors also acknowledge the ongoing support of the research fund at Mount Sinai Hospital Center.

APPENDIX 1: NOCTURNAL OXIMETRY TRACINGS

Protocol for the analysis and interpretation criteria

Gross exclusion:
- In a 1-hour time scale
  1) Exclude subject from analysis if ≥20% of the total tracing time contains breaks.
  2) A section of the tracing can be excluded from analysis if within a 30 minute period (in a 2 hour time scale), there are ≥6 breaks OR if there is no discernable pattern.

Events (within 2 hour time scale):
- A change in the tracing defined by the following:
  - Average desaturation of ≥4% from the baseline average
  - Minimal duration of 30 minutes with similar pattern magnitude/frequency.
- A second event can occur if during an event there is a progressive change in mean desaturation of 8% or greater from baseline.

Patterns (within 15 minute time scale):
(Must meet all of the criteria)
- Exclusion: Within a 5 minute period, there are ≥3 breaks.
- Pattern: A rise and fall of at least 3 similar saturation cycles
Use of oximetry tracings to identify OSA in COPD

OSA diagnosis:

- A case is identified as OSA if the following criteria are met:
  1. A mean SpO2 ≤ 90%
  2. At least one of the following:
     - # of events ≥ 4
     - # of patterns ≥ 12
- A case is identified as no-OSA if the previous criteria are not met.

REFERENCES
