Diagnosis of Pediatric Obstructive Sleep Apnea Syndrome in Settings With Limited Resources

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IMPORTANCE Although polysomnographic (PSG) testing is the gold standard for the diagnosis of obstructive sleep apnea syndrome (OSAS) in children, the number of pediatric sleep laboratories is limited. Developing new screening methods for identifying OSAS may reduce the need for PSG testing.

OBJECTIVE To evaluate the combined use of the sleep clinical record (SCR) and nocturnal oximetry testing for predicting PSG results in children with clinically suspected OSAS.

DESIGN, SETTING, AND PARTICIPANTS Prospective study over 10 months. A cohort of 268 consecutive children (mean [SD], age 6 [3] years) referred for clinically suspected OSAS was studied at a pediatric sleep center at a university hospital. Children with disorders other than adenotonsillar hypertrophy or obesity were excluded.

MAIN OUTCOMES AND MEASURES Mild OSAS (obstructive apnea–hypopnea index [AHI], 1-5 episodes/h) and moderate-to-severe OSAS (AHI, >5 episodes/h) were the main outcome measures. Sleep clinical record scores greater than or equal to 6.5 were considered positive, as were McGill oximetry scores (MOS) greater than 1, and these positive scores were the main explanatory variables in our study. Each participant was evaluated by the SCR, followed by pulse oximetry test the first night and PSG test in the sleep laboratory the second night.

RESULTS Of the total participants, 236 (88.1%) were diagnosed with OSAS, 236 (88.1%) had a positive SCR score, and 50 (18.7%) had a positive MOS. Participants with positive SCR scores had significantly increased risk of an AHI greater than or equal to 1 (adjusted odds ratio [AOR], 9.3; 95% CI, 3.7-23.2; P < .001). Children with an MOS greater than 1 were significantly more likely to have an AHI greater than 5 episodes/h than children with an MOS equal to 1 (AOR, 26.5; 95% CI, 7.8-89.2; P < .001). A positive SCR score had satisfactory sensitivity (91.9%) and positive predictive value (91.9%) but limited specificity (40.6%) and negative predictive value (40.6%) for OSAS. An MOS greater than 1 had excellent specificity (97.4%) and positive predictive value (94%) but low sensitivity (39.2%) and fair negative predictive value (60.8%) for moderate-to-severe OSAS among children with a positive SCR score. The combination of SCR scores and MOS correctly predicted primary snoring, mild OSAS, or moderate-to-severe OSAS in 154 of 268 (57.4%) participants.

CONCLUSIONS AND RELEVANCE The combined use of the SCR score and nocturnal oximetry results has moderate success in predicting sleep-disordered breathing severity when PSG testing is not an option.
Obstructive sleep-disordered breathing (SDB) is a common problem in childhood that ranges in severity from primary snoring to obstructive sleep apnea syndrome (OSAS). Obstructive sleep apnea syndrome is the most severe form of SDB, and it is characterized by snoring, obstructive and mixed apneas and hypopneas, gas exchange abnormalities, and frequent arousals from sleep. In contrast, children with primary snoring do not have any obstructive or hypopneic events, hypoxemia, hypercapnia or sleep disruption, and it is unclear whether they may benefit from any treatment interventions. Although polysomnographic (PSG) testing is the gold standard for the diagnosis of OSAS, sleep studies are labor intensive and inconvenient for children and their families. Furthermore, in many countries the availability of pediatric sleep laboratories is limited. The complexity and costs associated with PSG testing have spurred the quest for alternative diagnostic methods.

Overnight oximetry tests are easily conducted and inexpensive. In settings where PSG testing is unavailable or there is a long waiting time, nocturnal pulse oximetry tests can be used to screen for the presence of OSAS. A 4-level severity classification scheme of hypoxemia, the McGill oximetry score (MOS), has been developed and validated by Nixon et al in the USA. An oximetry score greater than 1 indicates abnormal or positive oximetry and has high positive predictive value (97%) but has a sensitivity of 40% and a negative predictive value of 53.1% for recognizing an obstructive apnea-hypopnea index (AHI) greater than 1 episode/h. An AHI greater than 5 episodes/h indicates moderate-to-severe OSAS, and although the greatest improvement in PSG testing parameters postadenotonsillectomy occurs among children in this subgroup, this same subgroup is unlikely to experience spontaneous resolution of SDB if no treatment is implemented. The value of nocturnal oximetry for detecting moderate-to-severe OSAS has not been explored in the literature.

In addition, Villa et al developed the sleep clinical record (SCR), a simple PSG test-validated screening tool for OSAS that combines a patient’s history with findings from a physical examination. In contrast to the MOS, the SCR has satisfactory sensitivity (96.1%) and an acceptable positive predictive value (88.6%) for identifying children with OSAS without providing any information regarding disease severity (ie, mild OSAS [AHI 1–5 episodes/h] vs moderate-to-severe OSAS). Therefore, in the current study, we aimed to evaluate the predictive value of the SCR, a tool useful for the detection of an AHI greater than 1 episode/h, combined with nocturnal oximetry. We hypothesized that nocturnal oximetry may be sensitive for recognizing the subgroup of patients with moderate-to-severe OSAS among those with positive SCR scores, thus rendering further testing by PSG unnecessary in settings with limited resources.

Methods
Participants and Initial Clinical Evaluation
Consecutive children with clinically suspected OSAS who were referred to the Pediatric Sleep Disease Centre at S. Andrea Hospital, Sapienza University of Rome, from September 2013 to June 2014 were recruited prospectively. The study protocol was approved by the institutional ethics committee and written informed consent was obtained from parents and assent from children older than 8 years.

Children with craniofacial abnormalities, seizure disorder, neuromuscular disease, genetic syndromes, chronic lung or congenital heart disease, or previous treatment for OSAS were excluded from participation in the study. Baseline demographic and somatometric characteristics, including age, sex, and body weight, were recorded on recruitment in the study. The body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) was calculated and converted to a sex- and age-specific BMI z score. Children were categorized as obese if their BMI z score was greater than or equal to 1.645, representing the 95th percentile and above for age and sex.

Evaluation for SDB
Each participant was initially evaluated for the presence of OSAS by the SCR, followed by nocturnal pulse oximetry testing the first night and standard overnight PSG testing in the sleep laboratory the second night.

SCR
The SCR incorporates data from clinical history and physical examination aiming to predict OSAS. The SCR is comprised of 6 main parts. In the first 3 parts, the presence of oral breathing, nasal obstruction, nasal septum deviation, dental malocclusion, narrow palate, tonsillar hypertrophy, or pathological position of the mandible is explored. In the fourth part, the presence of a facial phenotype indicative of obesity or adenoidal hypertrophy is noted. The fifth part describes the patient’s subjective symptoms as summarized by the Brouillette OSAS score. The final part incorporates symptoms of inattention and hyperactivity that are identified by an attention-deficit/hyperactivity disorder rating scale completed by the parents. An SCR score greater than or equal to 6.5 is indicative of an AHI greater than or equal to 1 episode/h.

Nocturnal Pulse Oximetry
A pulse oximeter (Nonin 2500A; Nonin Medical) was used to obtain nocturnal oximetry recordings that were analyzed by a physician blinded to the patient’s SCR score using a software package (PROXYnet 10.1; MedicAir). Recordings with a duration of less than 6 hours were disregarded. An MOS of 1 to 4 was assigned to each recording. Oximetry recordings with at least 3 clusters of desaturation events and at least 3 dips in the oxygen saturation of hemoglobin below 90% were regarded as diagnostic for OSAS, indicating abnormal or positive oximetry and an MOS greater than 1. Recordings not meeting these diagnostic criteria were considered as negative or inconclusive for OSAS and indicated a MOS of 1. Oxygen desaturation greater than or equal to 3% of hemoglobin index was calculated as the number of oxygen saturation of hemoglobin drops greater than or equal to 3% per hour of artifact-free recording.
A positive SCR score is greater than or equal to 6.5 and indicates OSAS. Mild OSAS has an AHI of 1 to 5 episodes/h, and moderate-to-severe OSAS has an AHI of greater than 5 episodes/h. A positive MOS is greater than 1. An MOS equal to 1 indicates primary snoring and/or mild OSAS, and an MOS greater than 1 indicates moderate-to-severe OSAS. In step 1, an SCR score is determined for each patient in the cohort. In step 2, MOS are determined and used to identify the subgroup of children with positive SCR scores who are at high risk of moderate-to-severe OSAS. Children with MOS equal to 1 and positive SCR scores are at risk of mild OSAS. AHI indicates the obstructive apnea-hypopnea index; MOS, McGill oximetry score; OSAS, obstructive sleep apnea syndrome; SCR, sleep clinical record.

**PSG**

Computerized overnight PSG testing was performed using a polygraph (Grass Heritage; Grass Technologies). A PSG test was initiated at the patient’s usual bedtime and continued until spontaneous awakening. The recorded signals included electroencephalogram with at least 6 channels; bilateral frontal, central temporal, and occipital monopolar montages referred to the contralateral mastoid; bilateral electro-oculogram; submental electromyogram; and electrocardiogram with 1 derivation. Oral nasal airflow was detected by a thermocouple and a nasal pressure transducer. Oxygen saturation of hemoglobin was monitored by a pulse oximeter, and snoring was recorded by a microphone.

All recordings were scored visually by an investigator who was blinded to the patient’s SCR score and oximetry results. Sleep stages, central, obstructive, and mixed apnea and hypopnea events were scored according to the standard criteria of the American Academy of Sleep Medicine.11 Patient AHI was defined as the average number of obstructive and mixed apneas and hypopneas per hour of sleep time. Obstructive sleep apnea syndrome was diagnosed in the presence of an AHI greater than or equal to 1 episode/h. Children with snoring recorded during PSG tests and with an AHI less than 1 episode/h were diagnosed as having primary snoring.

**Data Analysis**

An AHI greater than or equal to 1 episode/h and greater than 5 episodes/h were the primary outcome measures of the study, whereas a positive SCR score and a positive MOS were the explanatory variables. Children with positive SCR scores were compared with those with negative SCR scores in terms of age, BMI z scores, frequency of female sex, tonsillar hypertrophy and obesity, MOS, AHIs obtained from PSG testing, oxygen desaturation (≥3%) of hemoglobin index calculated from oximetry, and prevalence of AHIs greater than or equal to 1 episode/h. Furthermore, participants with positive oximetry findings were compared with children with negative or inconclusive oximetry findings regarding age, BMI z scores, frequency of female sex, tonsillar hypertrophy, and obesity, AHIs, oxygen desaturation (≥3%) of hemoglobin index, prevalence of positive SCR scores, and AHIs greater than 5 episodes/h. A χ² test was applied for comparisons involving categorical variables and the t test for continuous variables. The Pearson correlation coefficient was applied to evaluate the association between oxygen desaturation of hemoglobin index and the AHI.

Odds ratios (ORs) and the corresponding 95% CIs for having an AHI of greater than or equal to 1 episode/h in children with positive SCR scores compared with patients with negative SCR scores were calculated using univariate logistic regression analysis. Multivariate logistic regression analysis was completed to adjust ORs for age, sex, and BMI z scores. Similarly, ORs and 95% CIs were calculated for having an obstructive AHI greater than 5 episodes/h in patients with positive oximetry results vs patients with negative or inconclusive oximetry results. Odds ratios and 95% CIs were also adjusted for age, sex, and BMI z scores.

A 2-step algorithm combining the SCR and MOS for predicting SDB severity was evaluated (Figure). In the first step, a positive SCR score was applied to recognize children at high
risk of OSAS (AHI ≥1 episode/h) and the respective sensitivity, specificity, positive predictive value and negative predictive value were calculated. In the second step, positive oximetry results were used to identify children at high risk of moderate-to-severe OSAS (AHI >5 episodes/h) among those patients with a positive SCR score, and the respective sensitivity, specificity, positive predictive value, and negative predictive value were also calculated. Finally, inconclusive or negative oximetry results were assessed as a tool for identifying mild OSAS among participants with a positive SCR score.

**Results**

**Patient Characteristics**
A cohort of 268 children, mean (SD) age, 6 (3) years (range, 0.9-17.2 years), with acceptable oximetry recordings were included. Of the included patients, 178 (66.4%) were male and 69 (25.7%) were obese. Thirty-four patients were younger than 3 years, 9 participants were older than 12 years, and the majority of children (n = 225) were aged 3 to 12 years. The majority of patients, 236 of 268 (88.1%), had an AHI greater than or equal to 1 episode/h on PSG results and were diagnosed with OSAS, whereas the remaining 32 (11.9%) children were given a diagnosis of primary snoring.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SCR Score, No. (%)</th>
<th>MOS, No. (%)</th>
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<tbody>
<tr>
<td></td>
<td>≥6.5 (n = 236)</td>
<td>&gt;1 (n = 50)</td>
</tr>
<tr>
<td></td>
<td>&lt;6.5 (n = 32)</td>
<td>1 (n = 218)</td>
</tr>
<tr>
<td></td>
<td><em>P</em> Value</td>
<td><em>P</em> Value</td>
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<tr>
<td>Age, y</td>
<td>5.93 (2.97) [0.91-17.16]</td>
<td>4.55 (2.30) [0.9 to 11.8]</td>
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<tr>
<td></td>
<td>6.68 (3.36) [1.67-14.5]</td>
<td>6.38 (3.07) [1 to 17.16]</td>
</tr>
<tr>
<td>Female</td>
<td>64 (35.6)</td>
<td>14 (28)</td>
</tr>
<tr>
<td></td>
<td>6 (18.7)</td>
<td>76 (34.9)</td>
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<tr>
<td>BMI z score</td>
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<td>0.34 (1.25) [-2.38 to 3.37]</td>
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<tr>
<td></td>
<td>0.9 (1.2) [-1.98 to 3.25]</td>
<td>0.59 (1.41) [-3.71 to 3.77]</td>
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<tr>
<td>Obesity</td>
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<td>9 (18)</td>
</tr>
<tr>
<td></td>
<td>7 (21.9)</td>
<td>60 (27.5)</td>
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<tr>
<td>Tonsillar hypertrophy</td>
<td>150 (63.6)</td>
<td>39 (78)</td>
</tr>
<tr>
<td></td>
<td>6 (18.8)</td>
<td>117 (53.7)</td>
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</table>

**Table 1. Characteristics and Statistical Comparisons of Patients**

- Continuous variables are expressed as mean (SD) [range].
- Obtained from polysomnography.
- Calculated from oximetry.

**SCR Score and MOS as Independent Predictors of OSAS**

The majority of the patients, 236 of 268 (88.1%), with snoring had a positive SCR score. Children with a positive SCR score differed significantly in the frequency of tonsillar hypertrophy and abnormal MOS and in terms of AHI and oxygen desaturation of hemoglobin index when compared with children with negative SCR score (Table 1). Children with a positive SCR score had an approximately 8-fold increased risk for AHI of greater than or equal to 1 episode/h (OR, 7.81; 95% CI, 3.35-18.2; *P* < .001). This association persisted after adjustment for age, sex, and BMI z score (OR, 9.3; 95% CI, 3.7-23.2; *P* < .001). An AHI calculated from a PSG test was significantly associated with oxygen desaturation of hemoglobin index as obtained from nocturnal oximetry results (*r* = 0.58; *P* < .001).
combined use of SCR and nocturnal pulse oximetry for predicting OSAS severity

In step 1 of the proposed algorithm, 32 children with snoring had a negative SCR score and were considered to be at low risk of OSAS, whereas 236 subjects with a positive SCR score were considered to have a high risk of mild or moderate-to-severe OSAS. All 32 children with SCR scores less than 6.5 had normal or inconclusive oximetry results and, thus, oximetry could not contribute further information regarding the presence or absence of OSAS (Table 2). An SCR score greater than or equal to 6.5 had satisfactory sensitivity (91.9%) and positive predictive value (91.9%) but limited specificity (40.6%) and negative predictive value (40.6%) for detecting OSAS irrespective of its severity (Figure).

In step 2 of the proposed algorithm (Figure), nocturnal pulse oximetry was used to identify children at high risk of moderate-to-severe OSAS among the 236 remaining children with an SCR score greater than or equal to 6.5. An MOS greater than 1 had excellent specificity (97.4%) and positive predictive value (94%) but low sensitivity (39.2%) and fair negative predictive value (60.8%) for identifying an AH1 greater than 5 episodes/h among children with a positive SCR score. It is evident from Table 2 that almost all children with an SCR score greater than or equal to 6.5 and an MOS greater than 1 had an AH1 greater than 5 episodes/h, but several children (57.9%) with an AH1 greater than 5 episodes/h had positive SCR scores and negative oximetry results.

Conversely, normal or inconclusive oximetry results had excellent sensitivity (96.9%) and negative predictive value (94%) but low specificity (36%) and fair positive predictive value (50.5%) for identifying mild OSAS among children with a positive SCR score (Figure). Almost all children with an AH1 of 1 to 5 episodes/h had positive SCR scores and an MOS of 1, and very few patients with an AH1 of 1 to 5 episodes/h had an MOS greater than 1. Nevertheless, several children with positive SCR scores and negative oximetry results had either primary snoring (10.2%) or moderate-to-severe OSAS (39.2%) (Table 2).

The combined use of SCR scores and MOS, according to the proposed algorithm, allowed the correct classification of 154 of 268 participants (57.4%) with snoring as having primary snoring (n = 13), mild OSAS (n = 94); or moderate-to-severe OSAS (n = 47). Of note, among 126 patients with an AH1 greater than 5 episodes/h, 73 (57.9%) were misclassified as having mild OSAS and 6 (4.8%) as having primary snoring. When only children younger than 3 years were considered, application of the algorithm resulted in correct classification of OSAS severity in 21 of 34 (61.8%) participants. One case of primary snoring was correctly classified; 8, mild OSAS; and 12, moderate-to-severe OSAS.

Discussion

Recognizing moderate-to-severe OSAS is of clinical importance, because children with an AH1 greater than 5 episodes/h will get the most benefit from adenotonsillectomy, and they are at risk of persistent disease and development of morbidity if OSAS remains untreated. Although PSG testing is the gold-standard method for diagnosing OSAS and evaluating its severity, the number of pediatric sleep laboratories are limited in many European countries and other parts of the world. Although several screening tools for OSAS have been developed, they have not been widely validated.

In the current report and for the first time to our knowledge, the value of MOS in combination with SCR scores as a screening tool for moderate-to-severe OSAS was assessed. Of clinical importance, MOS did not facilitate the classification of children with snoring and negative SCR scores into a level of SDB severity (primary snoring, mild or moderate-to-severe OSAS), because in all such cases, nocturnal oximetry results were normal or inconclusive. Therefore, in the context of a negative SCR score, nocturnal oximetry results are unlikely to provide additional information about SDB severity, and are therefore redundant.

Another clinically useful finding is that the majority of children with an MOS greater than 1 had an AH1 greater than 5 episodes/h. This further supports the previous recommendation that children with symptoms of SDB and an MOS greater than 1 should undergo adenotonsillectomy without a PSG test. Taking into consideration the high positive predictive value of an MOS greater than 1 for moderate-to-severe OSAS, essentially no children with mild OSAS would be referred for surgery because of abnormal oximetry results. Overall, application of the proposed algorithm based on the combined use of SCR scores and pulse oximetry results allowed the correct diagnostic classification of approximately 60% of patients with snoring into the primary snoring, mild OSAS, or moderate-to-severe OSAS subgroups of SDB severity.

A limitation of the proposed algorithm is that a proportion of children with moderate-to-severe OSAS (approximately 60%) had positive SCR scores and negative or inconclusive oximetry results, and they were misdiagnosed as having mild OSAS. Moreover, a smaller subgroup of participants with an AH1 greater than 5 episodes/h (approximately 5%) had both negative SCR scores and oximetry results,
and they were misdiagnosed as having primary snoring. However, severity of SDB is not the only criterion for determining the need for treatment interventions. Children with snoring and associated morbidity (eg, excessive daytime sleepiness, poor school performance, behavioral disorders, enuresis or delayed somatic growth rate) tend to improve postadenotonsillectomy even if they have an AHI less than 5 episodes/h.16-19 In a systematic review of 14 studies, the overall prevalence of enuresis among children with obstructive SDB was 31% and decreased by 50% postoperatively.20 Hence, the presence of OSAS-associated morbidity may also direct the clinical decision to offer treatment, especially in cases with negative oximetry results. Although the great majority of participants were aged 3 to 12 years, the algorithm was equally useful for predicting OSAS severity in children younger than 3 years. No solid conclusions can be made about the use of the SCR score and nocturnal oximetry results when applied to children with snoring older than 12 years because the number of such participants in the current study was limited.

Numerous studies have been conducted to identify a simple screening tool for OSAS.8,14,20,21 In the Childhood Adenotonsillectomy Trial (CHAT),22 African American race, obesity, and the Pediatric Sleep Questionnaire (PSQ) total score were associated with a higher AHI, but in the multivariable analysis, the significant variables explained less than 3% of the variance in OSAS severity as measured by PSG tests. Published evidence indicates that questionnaires alone do not provide a good diagnostic prediction of OSAS.14,21 The main limitation of clinical questionnaires is that in contrast to the SCR, they do not combine findings from both the child’s history and physical examination. Of interest, and in accordance with results of the current report, Chang et al24 performed a retrospective study to develop a screening process for OSAS using a combination of a symptoms questionnaire and the oxygen desaturation index as determined by nocturnal pulse oximetry. It was demonstrated that the oxygen desaturation index and the occurrence of observable apnea or mouth-breathing during sleep or restless sleep were significant predictors of OSAS in PSG tests.

Similar to the SCR, the Clinical Assessment Score-15 (CAS-15) described by Goldstein et al25 incorporates 10 history items (nighttime symptoms indicating upper airway obstruction, daytime hyperactivity, and symptoms related to adenotonsillar hypertrophy) and 5 physical examination items (mouth breathing, hyponasal voice, adenoid face, height of hard palate, and tonsillar hypertrophy).26 A CAS-15 score greater than or equal to 32 had a sensitivity of 77.3%, specificity of 60.7%, positive predictive value of 82.3%, and negative predictive value of 53.1% for identifying an AHI greater than 2 episodes/h. In the present study, an SCR score greater than or equal to 6.5 had better sensitivity (91.9%) and positive predictive value (91.9%) but inferior specificity (40.6%) and negative predictive value (40.6%) for detecting an AHI greater than or equal to 1 episode/h when compared with CAS-15.

Conclusions

The current study indicates that the combination of the SCR score and MOS, a tool that is based on symptoms, clinical examination, and overnight oximetry results, allows accurate classification of SDB severity in about two-thirds of patients 12 years or younger who are referred for suspected OSAS when PSG testing is not an option. However, PSG testing is the gold standard for determining OSAS severity, because oximetry misclassifies approximately two-thirds of children with moderate-to-severe disease into mild OSAS or primary snoring. Due to the high positive predictive value of the proposed algorithm for detecting an AHI greater than 5 episodes/h, no patients with mild OSAS will be misdiagnosed as having more severe OSAS. Additional presence of OSAS-associated morbidity can direct clinical decisions in cases of moderate-to-severe OSAS that will potentially be missed by oximetry testing.


