Pulse Transit Time as a Screening Test for Pediatric Sleep-Related Breathing Disorders

Scott E. Brietzke, MD, MPH; Eliot S. Katz, MD; David W. Roberson, MD

Objectives: To evaluate a noninvasive measure of arousal, the pulse transit time (PTT), as a screening tool for obstructive sleep apnea/hypopnea syndrome (OSAHS) in an unselected population of symptomatic children, compared with overnight polysomnography (PSG). A secondary objective included comparing the diagnostic performance of PTT with continuous pulse oximetry recorded during PSG.

Design: Prospective, blinded diagnostic comparison study using the gold standard of overnight PSG.

Setting: Tertiary-care children's hospital sleep laboratory.

Patients: An unselected, volunteer sample of 59 patients (mean age, 7.8 years) with and without adenotonsillar tissue undergoing PSG and simultaneous PTT, including patients with obesity and craniofacial syndromes.

Main Outcome Measures: The relationship between the PTT and polysomnographic measures of OSAHS to include pulse oximetry using correlation coefficients and receiver operating characteristic curve analysis.

Results: The correlation coefficient between the PTT arousal index and PSG apnea-hypopnea index (AHI) was 0.70 ($P<.001$). Linear regression resulted in a good fit ($R^2=0.73$) between PTT arousal index and AHI. With the use of an AHI of 1 or greater (35.6% prevalence of OSAHS) as a criteria for OSAHS, the area under the receiver operating characteristic curve was 0.86 (95% confidence interval, 0.76-0.96). The optimal PTT arousal index threshold was 5.4 events per hour, which translated into a sensitivity of 81% and a specificity of 76%.

Conclusions: The PTT arousal index is highly correlated with the PSG-derived AHI and demonstrated excellent diagnostic utility for moderate and severe OSAHS. However, for mild OSAHS, PTT was barely adequate and did not significantly outperform pulse oximetry. Pulse transit time may be a useful tool to evaluate moderate to severe sleep-related breathing disorders in children.

Obstructive sleep apnea/hypopnea syndrome (OSAHS) in children is an increasingly prevalent and important public health problem. Pediatric snoring is estimated to affect 3.2% to 12.1% of children, and OSAHS is estimated to affect 0.7% to 10.3% of children. In children, OSAHS has a detrimental effect on neurocognitive development and school performance. The accurate diagnosis of OSAHS is problematic because clinical history and examination is not reliable in making a definitive diagnosis either before or after adenotonsillectomy (TA). The gold standard for diagnosis, overnight polysomnography (PSG), is expensive, inconvenient, and not available for all children who might benefit. There is thus a need for a useful screening test. Screening tests for OSAHS including heart rate variability, pulse oximetry, audiocassettes, and videotaping have produced unimpressive results, owing to either inaccuracy or inconvenience, and therefore have not been widely used.

The pulse transit time (PTT) is a novel measure of respiratory effort and arousal that has shown promise in the diagnosis of sleep-related breathing disorders in adults. The PTT is the interval between the R-wave of the electrocardiogram and the arrival of the photoplethysmographic pulse at the finger. The travel time of the pulse wave is inversely proportional to arterial wall stiffness, which is determined by blood pressure. Therefore, the PTT is a noninvasive index that is inversely related to blood pressure. The utility of the PTT as a diagnostic tool in sleep-related breathing disorders stems from alterations in blood pressure patterns associated with respiratory arousal from sleep. Arousal at the termination of an obstructive event leads to a marked, transient increase in blood pressure. This results in
a decrease in the PTT. Thus, PTT can be used to evaluate arousal from sleep that results from apneas and/or hypopneas. The typical stand-alone PTT device is small and portable and requires only 2 electrocardiogram chest leads and a pulse oximeter probe. Thus, a portable, take-home PTT device could be an effective and efficient screening tool for pediatric OSAHS.

The purpose of this study was to assess the utility of PTT as an ambulatory screening test for OSAHS in pediatric patients compared with laboratory-based PSG. A secondary objective of this study was to compare the diagnostic utility of PTT measurements with that of continuous pulse oximetry measurements recorded during overnight PSG.

**METHODS**

This study was approved by the institutional review board of Children’s Hospital Boston, Boston, Massachusetts. Signed, informed consent was obtained from the parent of each participating child. Patients aged from 2 to 18 years who presented for a routinely scheduled PSG at the Children’s Hospital Boston Sleep Laboratory were asked to participate. Patients with obesity, trisomy 21 syndrome, or any other craniofacial syndrome and with or without a history of tonsillectomy and/or adenoidectomy were included. The exclusion criteria consisted of (1) preexisting tracheostomy or (2) a PSG that was obtained for continuous positive airway pressure titration.

The study was designed as a blinded screening test study. Patients underwent simultaneous PTT testing and overnight multichannel PSG. Scorers of the PTT and the PSG were blinded as to the other result. The PTT measurements were recorded with an ambulatory device (Stowood Scientific Instruments, Oxford, England). A PTT arousal was defined as a decline in the 4-second moving time average PTT tracing of greater than 15 torr. Thus, PTT can be used to evaluate OSAHS if the optimal PTTAI cut point was excluded from the analysis.

Multichannel PSG was performed with Bio-logic hardware and software (Bio-logic Systems Corporation, Mundelein, Illinois) including electroencephalogram (C3-A2, O1-A2, and F1-A2); right and left electrocardiogram; submental electromyogram; tibial electromyogram; surface diaphragmatic electromyogram; electrocardiogram; end-tidal carbon dioxide; arterial oxygen saturation; and chest and abdominal wall motion (piezoelectric transducers). Nasal pressure was measured with a Pro-Tec transducer (Pro-Tech, Mukilteo, Washington) and oronasal airflow with a thermistor. Sleep architecture was assessed by standard techniques. An obstructive apnea was defined as the presence of chest-abdominal wall motion associated with a reduction of airflow of 80% or greater of the baseline rate, lasting for a duration of 2 breaths or longer. An obstructive hypopnea was defined as a discernible reduction in airflow associated with either a drop in oxygen saturation by a pulsoximetry of 4% or greater or a discernible reduction in airflow associated with either a drop in oxygen saturation by a pulse oximetry of 4% or greater or an arousal lasting for a duration of 2 breaths or longer. The apnea-hypopnea index (AHI) was defined as the total number of obstructive apneas and hypopneas per hour of total sleep time. Obstructive sleep apnea/hypopnea syndrome was defined as an AHI greater than 1 event per hour.

The primary outcome measures of the study were the correlation of the PTT arousal index (PTTAI) with the PSG-derived AHI and receiver operating characteristic (ROC) curve analysis of the PTTAI. Subgroup analysis consisted of looking at these outcome measures for subgroups of patients based on age, presence of craniofacial syndrome, and presence or absence of adenotonsillar tissue. A secondary analysis consisted of comparing PTT screening performance to PSG included pulse oximetry measurements in the diagnosis of OSAHS. Statistical analysis was performed with the assistance of STATA 8.2 software (StataCorp, College Station, Texas). The null hypothesis was rejected, with a probability of P < .05.

Fifty-nine patients were included in the study (63% male). The mean age was 7.8 years (range, 2-16 years), and the mean body mass index (calculated as weight in kilograms divided by height in meters squared) was 21.5 (range, 9.0-38.9). Of 59 patients, 11 (19%) had undergone previous TA and 15 (25%) had a craniofacial syndrome diagnosis (eg, trisomy 21 and Apert syndrome). The mean AHI was 4.5 events per hour (range, 0-69.3 events per hour). Diagnostic data for OSAHS included the following:

<table>
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<tr>
<th>OSAHS Criteria</th>
<th>No. (%) of Subjects (N=59)</th>
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<tr>
<td>AHI &gt; 1</td>
<td>21 (36)</td>
</tr>
<tr>
<td>AHI &gt; 3</td>
<td>14 (24)</td>
</tr>
<tr>
<td>AHI &gt; 5</td>
<td>12 (20)</td>
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The PTTAI overall was strongly correlated with the PSG AHI, with a Spearman rank coefficient of 0.70 (P < .001) (Figure 1). This trend of strong correlation was preserved among patients with (n=15; r=0.58, P=.02) and without (n=43; r=0.73, P < .001) craniofacial syndrome as well with (n=42; r=0.68, P < .001) and without (n=11; r=0.92, P < .001) adenotonsillar tissue. Simple linear regression was also performed resulting in an excellent fit between the PTTAI and AHI (R²=0.73) (Figure 2).

The ROC analysis was performed to determine the optimal threshold cut points for various OSAHS diagnostic criteria as well as to assess the overall value of the PTTAI as a screening measurement for pediatric OSAHS. Complete data are given in Table 1. For each diagnostic criterion, the area under the ROC curve (ROC area) was greater than 0.85, indicating excellent screening test performance with increasingly greater areas (Figure 3). Multivariate logistic regression was used to adjust for multiple potential confounders to include age, sex, body mass index, presence of craniofacial syndromes, and adenotonsillar tissue. Adjusted odds ratios of the risk of diagnosing OSAHS if the optimal PTTAI cut point was ex-
ceeded for each OSAHS diagnostic criteria level were significant (Table 2).

Comparative analysis was performed between PTT measurements and PSG pulse oximetry measurements. Pulse oximetry represents the only current, widely used screening test for pediatric OSAHS. Because PTT measurement incorporates pulse oximetry measurements as part of its algorithm, pulse oximetry data will always accompany PTT data. Specifically, the screening test performance of the PTTAI and the lowest pulse oximetry saturation measurement were compared in terms of ROC area and the optimal sensitivity and specificity as determined by ROC analysis. For each OSAHS diagnostic criteria, the PTTAI was superior to the pulse oximetry lowest oxygen saturation measurement in the ROC area and in optimal sensitivity and in optimal specificity for 2 of the 3 OSAHS criteria, although the 95% confidence intervals overlap slightly (Table 3). Direct statistical comparison of the ROC area for PTT and oximetry for each OSAHS diagnostic criteria could not reject the null hypothesis that they are equal ($P = .10$ for AHI $\geq 1$; $P = .37$ for AHI $\geq 3$; and $P = .33$ for AHI $\geq 5$). However, the reader should note that this study was designed and statistically powered to primarily evaluate the diagnostic validity of the PTTAI vs the gold standard of PSG-derived AHI and not for a diagnostic ROC comparison of PTTAI vs pulse oximetry. Therefore, the present study is significantly underpowered for this secondary analysis. For mild OSAHS (AHI $> 1$) the calculated power is only 13% (probability of type II error, 87%), with more than 500 subjects needed to achieve 80% power or better.

This study examines the utility of PTT measurements from an ambulatory device as a potential screening test for the diagnosis of pediatric OSAHS. The PTTAI was found to be highly correlated with the “gold standard” PSG-derived AHI. Multivariate logistic regression revealed no significant confounding of this relationship by age, sex, body mass index, presence of craniofacial syndrome, and status of adenotonsillar tissue, with no significant confounding identified. Using ROC curve analysis, we found that PTT measurements have excellent overall screening test performance compared with the PSG gold standard for a variety of diagnostic criteria for pediatric OSAHS. Lastly, PSG pulse oximetry measurements were compared with the PTTAI in terms of screening test performance, with the PTTAI showing a nonsignificant trend toward superior performance over pulse oximetry alone. However, the formal results of this analysis were inconclusive, likely owing to low power.

The current gold standard diagnostic test for pediatric OSAHS is overnight multichannel PSG. Although the diagnostic accuracy of overnight PSG is considered superior to any other modality, its use is problematic in many ways. It is expensive, inconvenient for parents and children, and has limited availability in many areas. In contrast to high-tech PSG, the clinical history and physical examination are the most inexpensive and readily available tools to the otolaryngologist but are limited in their diagnostic accuracy.7 Therefore, identifying a screening test that is simple, inexpensive, and well correlated with

### Table 1. Pulse Transit Time Measurement Diagnostic Performance

<table>
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<tr>
<th>OSAHS Criteria</th>
<th>ROC Area (95% Confidence Interval)</th>
<th>Optimal Cut Point, Events per Hour</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
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<tr>
<td>AHI $&gt; 1$</td>
<td>0.86 (0.76-0.96)</td>
<td>5.4</td>
<td>81</td>
<td>76</td>
</tr>
<tr>
<td>AHI $&gt; 3$</td>
<td>0.97 (0.93-1.00)</td>
<td>7.4</td>
<td>93</td>
<td>91</td>
</tr>
<tr>
<td>AHI $&gt; 5$</td>
<td>0.96 (0.92-1.00)</td>
<td>8.1</td>
<td>92</td>
<td>89</td>
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Abbreviations: AHI, apnea-hypopnea index; OSAHS, obstructive sleep apnea/hypopnea syndrome; ROC area, area under the receiver operating characteristic curve.

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Figure 2. Scatterplot of the pulse transit time arousal index (PTTAI) and the apnea hypopnea index (AHI) with the results of simple linear regression interposed. The line represents the result of the regression analysis with the 95% confidence interval (CI) for the fitted values ($R^2 = 0.73$).

Figure 3. Receiver operating characteristic (ROC) curve for the pulse transit time arousal index vs polysomnogram-derived apnea-hypopnea index (AHI) as the gold standard with a criteria for obstructive sleep apnea/hypopnea syndrome of and AHI greater than 1.0 event per hour. The area under the ROC curve was 0.86 (95% confidence interval, 0.76-0.96). The dotted line represents the null area of 0.5.
the gold standard test could be extremely useful when evaluating patients for this very common pediatric public health problem.

When considering the most beneficial role of a potential screening test for OSAHS, would its role be better served if it was aimed at effectively screening in OSAHS or screening out OSAHS? Ruling out OSAHS as a diagnosis is probably clinically more important than being able to rule it in for 2 reasons. First, the clinical history and physical examination are more accurate in ruling in OSAHS as the probability that a patient with a positive history (snoring and gasping) and examination (large tonsils and adenoids) having a positive PSG result is very high. Second, there is mounting evidence that isolated snoring—even in the absence of OSAHS—can have clinically significant neurobehavioral consequences. This means that patients with normal PSG results but a strong clinical history could still potentially benefit from surgery. Thus, a potentially valuable screening test would primarily have the ability to accurately and consistently exclude pediatric OSAHS.

The particular limitations of the clinical history and physical examination center on its inability to effectively exclude (ie, rule out) OSAHS. The inability to effectively exclude OSAHS is particularly important because the first-line therapy for pediatric OSAHS, ie, TA, is only about 80% to 85% successful in normalizing PSG measurements. This means that 1 of 5 to 1 of 6 TA patients will likely have persistent OSAHS after surgery. How does one identify the patients with persistent OSAHS after TA? Using PSG to screen the hundreds of thousands of post-TA patients annually is impossible. Pulse oximetry has been repeatedly shown to be unable to consistently rule out OSAHS. This situation creates a large need for a simple, accurate screening test that can effectively rule out obstructive sleep apnea syndrome.

Are PTT measurements suitable for this role of excluding OSAHS? Another way to look at this issue is to compare what the posttest probability of having residual OSAHS after TA is with no testing and after TA with a negative PTT screening test result. Is the probability with a negative test result lowered enough to make use of the test acceptable to otolaryngologists and/or parents? Using Bayes theorem (posttest probability = pretest probability × likelihood ratio), one can estimate this posttest probability. Estimating that the probability of having residual OSAHS after TA is approximately 15% (an optimistic estimate based on published systematic review data) and using an optimal negative likelihood ratio of 0.25 from the ROC analysis performed in this study for an OSAHS criteria of an AHI greater than 1.0, we found a posttest probability of 4.22% of having an AHI greater than 1.0. In other words, a patient who undergoes TA and has a postoperative PTT screening test result with an arousal index of less than 5.4 events per hour has only a 4.22% probability of having a postoperative AHI of greater than 1.0 compared with a 15% probability if the clinical examination alone is used. If we estimate conservatively that approximately 250 000 pediatric tonsillectomies are performed in the United States for OSAHS, the number of children with undiagnosed persistent OSAHS after TA would be reduced from 37 000 to approximately 10 000. As a point of comparison using the same calculations, if we apply a pulse oximetry cut point of less than 90% lowest saturation as a screening test result, an approximate 7.81% postoperative, posttest probability of having an AHI of greater than 1.0 after TA would result. This would reduce the number of children with undiagnosed, persistent OSAHS from 37 000 to approximately 19 500.

These estimates obviously assume ideal conditions. The present study represents a small pilot study of a diverse patient population in the ideal setting of a monitored sleep laboratory. A limited number of other small studies have been published evaluating the usefulness of PTT measurements in pediatric patients with sleep-related breathing disorders. The published data continue to support the diagnostic accuracy of PTT measurements in children compared with the gold standard of PSG, although none of the other studies have exclusively focused on the potential role of PTT as a stand-alone screening test for pediatric OSAHS. Katz et al reported that PTT measurements were a more sensitive measure of obstructive events in children than electroencephalography and were

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<th>Table 2. Adjusted Odds Ratios of the Probability of Meeting the Criteria for OSAHS for the Optimal PTT Arousal Index Cut Point</th>
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Abbreviations: AHI, apnea-hypopnea index; OSAHS, obstructive sleep apnea/hypopnea syndrome.

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<th>Table 3. Comparison of Diagnostic Performance Between Pulse Transit Time and Pulse Oximetry</th>
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Abbreviations: AHI, apnea-hypopnea index; OSAHS, obstructive sleep apnea/hypopnea syndrome; ROC area, area under the receiver operating characteristic curve; Sens, sensitivity (true positive %) for optimal cut point; Spec, specificity (true negative %) for optimal cut point.
sufficient to accurately distinguish primary snoring from upper airway resistance syndrome. Foo et al reported that PTT was superior to pulse oximetry alone in evaluating obstructive events and, in another report, that PTT measurements had a sensitivity of 90% and a specificity of 82% in detecting obstructive events. As more experience is gained, the next logical step would be to perform a clinical trial with the large-scale use of ambulatory PTT as a screening test for OSAHS after TA. In addition, the PTT indexes could be combined with measures of oxygen saturation to further enhance the identification of OSAHS.

Of course, the discussion above regarding post-TA residual OSAHS begs the question of what to do when residual OSAHS is identified and what level of residual apnea or hypopnea causes a genuine impact on the child's health. These are difficult questions for which there are no current well-accepted answers. Regardless, identifying the patients with this problem would be the initial step to further exploring these issues and determining the role of therapy vs observation.

In conclusion, the PTTAI is highly correlated with the gold standard PSG-derived AHI. Pulse transit time measurements demonstrate excellent screening test performance per receiver operating curve analysis and are possibly superior to pulse oximetry measurements. Pulse transit time may be a suitable ambulatory screening test for pediatric OSAHS.

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Author Contributions: Drs Brietzke, Katz, and Roberson had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Brietzke, Katz, and Roberson. Acquisition of data: Brietzke and Katz. Analysis and interpretation of data: Brietzke and Katz. Drafting of the manuscript: Brietzke and Katz. Critical revision of the manuscript for important intellectual content: Brietzke, Katz, and Roberson. Statistical analysis: Brietzke. Obtained funding: Brietzke. Administrative, technical, and material support: Katz. Study supervision: Katz and Roberson.

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REFERENCES