Sleep Medicine 54 (2019) 159–163

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

# P-wave dispersion as a simple tool for screening childhood obstructive sleep apnea syndrome

Chutima Kraikriangsri, Anant Khositseth*, Teeradej Kuptanon

*Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University Bangkok, Thailand*

ARTICLE INFO

*Article history:*
Received 22 February 2018
Received in revised form
25 September 2018
Accepted 27 September 2018
Available online 7 November 2018

*Keywords:*
Obstructive sleep apnea
Electrocardiography
Arrhythmia
Children

ABSTRACT

*Introduction:* The gold standard for the diagnosis of childhood obstructive sleep apnea syndrome (OSAS) diagnosis is polysomnography; however, electrocardiography (ECG) may provide a simpler alternative. P-wave dispersion (PWD), the difference between the maximum and minimum P-wave duration measured by 12-lead ECG, is increased in adult OSAS but has not been researched in childhood OSAS. The aims of this study were to determine the PWD and cut-off value for the diagnosis of childhood OSAS and its association with severity.

*Methods:* A total of 77 children with confirmed OSAS and 44 control participants underwent surface 12-lead ECG. P-wave duration was measured using a digital caliper by a researcher blinded to the groups.

*Results:* Median (interquartile range) PWD in children with OSAS (median age = 82.8 months, range = 24–194 months) was significantly higher than that in the control group (median age = 73.4 months, range = 12–156 months): 38.3 (29.7–50.5) vs 25.5 (20.5–30.5) milliseconds, respectively ($p < 0.0001$). Subgroup analysis according to OSAS severity categorized by the apnea–hypopnea index from polysomnography demonstrated that PWD in the severe OSAS group ($n = 24$) was significantly higher than that in the mild-to-moderate OSAS group ($n = 53$): 48.5 (34.7–67.4) vs 35.5 (28.2–47.8) milliseconds, respectively ($p = 0.006$). A cut-off value of PWD at 26.5 ms from the receiver operating characteristic curve for the diagnosis showed the area under the curve to be 0.839, with a sensitivity of 89.6% and a specificity of 61.4%.

*Conclusion:* PWD was significantly increased in children with OSAS, particularly in severe cases. PWD could be a useful tool for screening childhood OSAS.



## 1. Introduction

Obstructive sleep apnea syndrome (OSAS) is a form of common sleep-disordered breathing that has various physiological consequences, including neurocognitive deficits, behavioral abnormalities, and cardiovascular morbidities [1]. The incidence of cardiovascular diseases is significantly higher, especially in adult OSAS. Observations associated with OSAS include an increase in heart rate, corrected QT interval (QTc), P-wave duration, and P-wave dispersion (PWD). Although OSAS has been studied in adults, there are limited studies in children [2–6].

Previous studies in adults have demonstrated a positive association between atrial conduction and OSAS, including P-wave duration and PWD [7]. PWD is defined as the difference in the maximum and minimum P-wave, which indicates prolongation of intra-atrial, inter-atrial conduction time and the inhomogeneous propagation of sinus impulses that are well known electrophysiologic characteristics of the atrium and a marker of atrial fibrillation [8]. The gold standard for diagnosis of OSAS is polysomnography (PSG) in a sleep laboratory, but this requires considerable time and expense. Low-cost and simplified screening methods using electrocardiography (ECG) have been reported in previous adult studies [6,8] and may provide an alternative means for OSAS diagnosis in children.

We hypothesized that PWD in childhood OSAS might increase relative to that in controls, as observed in adults. The aims of the study were to evaluate PWD in childhood OSAS compared with that in normal healthy children without snoring and to assess the effect of severity of OSAS on PWD.

* Corresponding author. Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, 270 Rama VI Road, Ratchathewi, Bangkok 10400, Thailand.
*E-mail address:* anant.kho@mahidol.ac.th (A. Khositseth).

https://doi.org/10.1016/j.sleep.2018.09.032
1389-9457/

## 2. Methods

This cross-sectional study included patients with a confirmed diagnosis of OSAS by polysomnography and age- and sex-matched controls. Controls were recruited from a well-baby clinic who had no history of snoring and had been screened using the Obstructive Sleep Apnea–18 (OSA-18) questionnaire, in which a score of <60 is considered normal [9]. All participants in the control group had an OSA-18 score of less than the cut-off score. Patients with underlying heart disease, craniofacial anomalies or syndromic disorders, neuromuscular diseases, or treatment with continuous positive airway pressure were excluded. All patients with confirmed diagnosis of OSAS by polysomnography, along with age- and sex-matched control participants, underwent 12-lead ECG. Baseline characteristics including age, gender, weight, height, body mass index (BMI), *Z*-score, and the percentage of participants with obesity (defined as BMI *Z*-score greater than +2) [10] were recorded. The study was approved by the institutional ethics committee. Written informed consent was obtained from the parents of each participant in the study and control groups.

### 2.1. 12-Lead ECG parameters

All participants underwent 12-lead ECG recording after a 10-min resting period in the supine position at a paper speed of 50 mm/s with standard 1 mV/10 mm and frequency of 150 Hz, using PageWriter TC70/TC50/TC30 Cardiograph PHILIPS portable ECG machine. Fully trained staff performed 12-lead ECG in each participant using the same method for placement of 10 international standard electrode pads. Placement was at V1 (fourth intercostal space [ICS] to the right of the sternum); V2 (fourth ICS to the left of the sternum); V3 (midway between V2 and V4); V4 (fifth ICS at the midclavicular line) but we used V4R which is located on the right side symmetrically instead; V5 (anterior axillary line at the same level as V4); V6 (mid-axillary line at the same level as V4 and V5); right leg (anywhere above the right ankle and below the torso); right arm (anywhere between the right shoulder and the wrist); left leg (anywhere above the left ankle and below the torso; and, finally, left arm (anywhere between the left shoulder and the wrist). The duration of running the ECG paper was 12 s. The paper ECG recording was scanned into an electronic file as a portable document format (PDF) file. An Iconico screen caliper (version 4.0) was used to measure all the intervals from the screen of PDF file, including the P-wave duration (from onset to end of the P-wave) in all leads, R- and S-waves in V1, and S-wave in V6 by one investigator (C.K.) who was blinded to the study and control groups. PWD was defined as the difference between the maximum and minimum P wave durations in the 12-lead ECG. The QTc interval was recorded from the computerized value read on the echocardiogram.

### 2.2. Polysomnography

Polysomnography was performed in all patients according to the recommendations and guidelines of the American Thoracic Society [11–14]. The apnea–hypopnea index (AHI) was defined as the number of apneic and hypopneic events per sleep hour [12]. OSAS was diagnosed when patients had AHI score ≥1.5 events/h. The severity of OSAS was categorized into mild ($1.5 \leq AHI \leq 5$), moderate ($5 < AHI \leq 10$), and severe ($AHI > 10$) OSAS [12].

### 2.3. Statistical analyses

Statistical analyses were performed using SPSS version 11 software (SPSS Inc., Chicago, IL). Categorical data were expressed as numbers and percentages. Continuous data were expressed as median and interquartile range (IQR). For comparison of continuous data, the Mann–Whitney *U* test was used. Categorical data were compared using the $\chi^2$ test. All data were checked for normality using the Kolmogorov–Smirnov test and *F*-test for equality of variances. To assess the influence of OSAS severity on ECG parameters, Spearman rank correlation coefficients were calculated to identify independent predictors. To analyze the potential as a diagnostic tool, a receiver operating characteristic (ROC) curve was used. Bias and precision were calculated from the Bland–Altman graph [15] to evaluate the agreement between interpersonal and intrapersonal measurements. A $p$ value <0.05 was considered to be statistically significant.

## 3. Results

A total of 77 patients with a confirmed diagnosis of OSAS by polysomnography were categorized into mild OSAS ($n = 26$), moderate OSAS ($n = 27$), and severe OSAS ($n = 24$). A total of 44 children were included as controls. Age and gender did not differ between groups [median age in the study group = 82.8 months (IQR = 24–194) vs controls = 73.4 months (IQR = 12–156)]; proportion of males in the study group = 58% vs controls = 41%. However, weight, height, and BMI *Z*-score in the study group were significantly higher than in the control group [30.7 kg (13–120) vs 20.9 kg (11–58), $p = 0.005$; 121.3 cm (89–172) vs 111.3 cm (78–153), $p = 0.016$; and 1.02 (−0.73 to +2.24) vs −0.05 (−1.61 to +1.05), $p = 0.021$, respectively]. The percentage incidence of obesity tended to be greater in the study group (29% vs 14%, $p = 0.06$) Subgroup analyses by OSAS severity demonstrated that the percentage incidence of obesity was significantly higher in severe OSAS than in mild and moderate OSAS (Table 1). The median (IQR) of AHI, the lowest oxygen saturation, arousal index, respiratory disturbance index, and highest end-tidal $CO_2$ were 6.6 events/h (3.9–12.7), 90% (86–93), 22 events/h (18.1–27.2), 6.6 events/h

**Table 1**
Demographic characteristics of the controls and obstructive sleep apnea syndrome (OSAS) subgroups analyzed according to the severity of OSAS.

| Characteristic | Controls ($n = 44$) | Severity of OSAS[a] | | | $p$[b] |
|---|---|---|---|---|---|
| | | Mild OSAS ($n = 26$) | Moderate OSAS ($n = 27$) | Severe OSAS ($n = 24$) | |
| Age (mo) | 73 (12–15) | 78 (24–194) | 95 (38–185) | 75 (26–156) | NS |
| Male:female | 18:26 (41%) | 13:13 (50%) | 19:8 (70.4%) | 13:11 (54.2%) | NS |
| BW (kg) | 21 (11–58) | 25 (13–72) | 34 (13–120) | 32 (13–98) | NS |
| Height (cm) | 111 (78–153) | 117 (89–155) | 127 (94–163) | 119 (90–172) | NS |
| BMI *Z* score | −0.05 (−1.61 to 1.05) | 0.14 (−0.56 to −1.66) | 1.05 (1.01–2.17) | 1.68 (−0.7 to −4.47) | NS |
| Obesity[c] | 6 (14%) | 3 (11.5%) | 8 (29.6%) | 11 (45.8%) | 0.03 |

Data shown as median (interquartile range) except for Male:female and Obesity ($n$, %).
BMI, body mass index; BW, body weight.
[a] Severity of OSAS: categorized according to apnea–hypopnea index (AHI) into mild ($1.5 \leq AHI \leq 5$), moderate ($5 < AHI \leq 10$), and severe ($AHI > 10$).
[b] Comparisons were conducted among the OSAS severity groups.
[c] Obesity was defined as a BMI *Z* score greater than +2.

**Table 2**
Respiratory parameters from the polysomnography recordings in children with obstructive sleep apnea syndrome (OSAS) according to severity.[a]

| Variable | Mild OSAS ($n = 26$) | Moderate OSAS ($n = 27$) | Severe OSAS ($n = 24$) |
|---|---|---|---|
| AHI (events/h) | 3.2 (2.5–3.9) | 6.6 (6.1–8.1) | 17.9 (12.9–29.8) |
| Lowest oxygen (%) | 92 (89–94) | 91 (85–93) | 87 (80–89) |
| Arousal index (events/h) | 18.1 (12.9–21.0) | 23.6 (19.9–27.3) | 27 (20.3–38.8) |
| Respiratory disturbance index (events/h) | 3.4 (2.6–4.1) | 7.4 (6.1–8.4) | 15.9 (12.6–29.5) |
| $EtCO_2$ (mm Hg) | 51.6 (48.2–54.1) | 49.9 (48.5–52.0) | 52.2 (50.0–54.7) |

Data shown as median (interquartile range). AHI, apnea–hypopnea index; $EtCO_2$, end-tidal carbon dioxide.
[a] Severity of OSAS was categorized according to AHI into mild ($1.5 \leq AHI \leq 5$), moderate ($5 < AHI \leq 10$), and severe ($AHI > 10$).

**Table 3**
Electrocardiographic parameters in OSAS and control.

| ECG Parameters | OSAS Group | Control Group | *P* value |
|---|---|---|---|
| $Pdur_{max}$ (ms) | 100 (90–108) | 84 (81–87) | <0.0001 |
| $Pdur_{min}$ (ms) | 59 (50–66) | 74 (67–80) | 0.001 |
| Pamp in $V_1$ (mV) | 0.7 (0.4–0.8) | 0.5 (0.5–1.0) | 0.021 |
| Ramp in $V_1$ (mV) | 4.3 (2.8–6.3) | 6.5 (4.0–8.0) | 0.015 |
| R/S ratio in $V_1$ | 0.6 (0.4–1.0) | 0.7 (0.5–1.0) | NS |
| Samp in $V_6$ (mV) | 2.5 (1.3–4.0) | 2.0 (1.0–4.5) | NS |
| QTc (ms) | 426 (413–441) | 426 (419–441) | NS |

ECG, electrocardiography; max, maximum; min, minimum; NS, not significant; OSAS, obstructive sleep apnea syndrome; Pamp, P-wave amplitude; Pdur, P-wave duration; QTc, corrected QT interval; Ramp, R-wave amplitude; Samp, S-wave amplitude.
Data shown as median (interquartile).

(3.9–12.1), and 50.8 mm Hg (48.8–53.0), respectively. All respiratory data from the polysomnography are shown by subgroup according to OSAS severity (Table 2).

ECG parameters in the OSAS and control groups are shown in Table 3. The maximum P-wave duration in the OSAS group was significantly higher than in the control group. The minimum P-wave duration in the OSAS group was significantly lower than in the control group, resulting in higher PWD in the OSAS group [median = 38.3 ms (29.7–50.5)] than in the control group [median = 25.5 ms (20.5–30.5)], $p < 0.0001$ (Fig. 1). Subgroup analyses showed that the PWD in the severe OSAS group [median = 48.5 ms (34.7–67.4)] was significantly higher than in the mild OSAS group [median = 34.7 ms (28.3–48.3)], $p = 0.02$ and higher than in the moderate OSAS group [median = 36.7 ms (27.9–46.5)]. However, there was no significant difference between mild and moderate OSAS ($p = 0.957$) (Fig. 1). There was no correlation between PWD and severity of OSAS.

As the percentage incidence of obesity in the OSAS group and the control group differed significantly, a further subgroup analysis was conducted in which all participants with obesity were excluded. Nonetheless, PWD was still significantly higher in the OSAS group than in the control group ($p < 0.0001$) (Fig. 2).

The receiver operating characteristic (ROC) curve analysis demonstrated that a PWD of 26.5 ms as the cut-off point for diagnosis of OSAS had sensitivity of 89.6% and specificity of 61.4% with an area under the curve of 0.839 (Fig. 3).

A measurement system by digital caliper was used to ensure accuracy. Randomized P-wave duration measurement (30 participants) was repeatedly measured by one of the authors (C.K.; intrapersonal errors). A Bland–Altman plot demonstrated bias (mean) and precision (standard deviation) of 0.43 ± 5.8 ms. Randomized P-wave duration measurement (30 participants) was measured by two of the authors (C.K. and A.K.; interpersonal errors). A Bland–Altman plot demonstrated bias (mean) and precision (standard deviation) of 1.8 ± 4.8 ms.

## 4. Discussion

Our study demonstrated higher maximum P-wave duration and lower minimum P-wave duration that resulted in higher PWD in the childhood OSAS group than in the control group. Moreover, PWD in severe OSAS was higher than in mild and moderate OSAS.

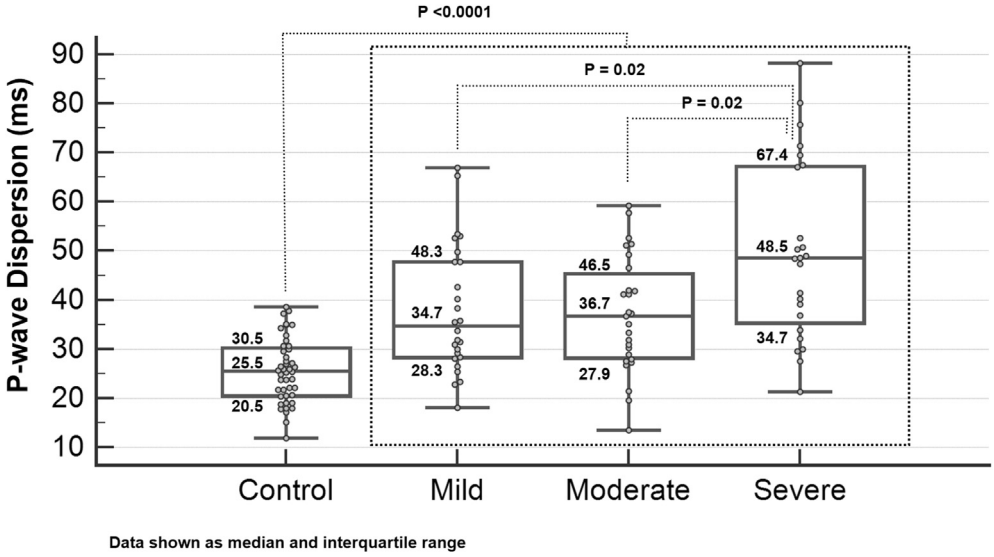


**Fig. 1.** Median and interquartile range of P-wave dispersion in patients with obstructive sleep apnea and controls. ms, milliseconds; OSAS, obstructive sleep apnea syndrome; PWD, P-wave dispersion.

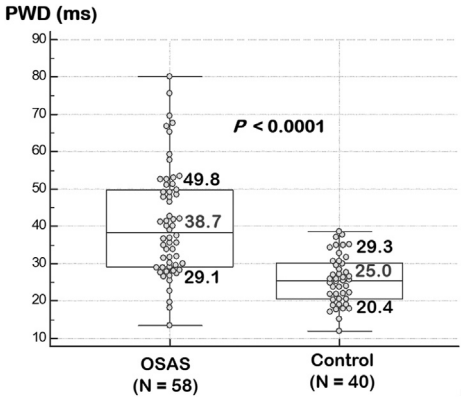


**Fig. 2.** Median and interquartile range of P-wave dispersion in patients with obstructive sleep apnea and controls (excluding participants with obesity in both groups). ms, milliseconds; OSAS, obstructive sleep apnea syndrome; PWD, P-wave dispersion.

Higher PWD may be related to atrial arrhythmia. Although the incidence of significant arrhythmia in childhood OSAS is quite low [16], there is higher QT dispersion (defined as the difference between the maximum and minimum QT interval in 12-lead ECG) in children with OSAS [17]. A higher QT dispersion may be a marker for the development of ventricular arrhythmia [18]. However, there is no cut-off QT dispersion that can be applied for the diagnosis of OSAS. Atrial arrhythmias including bradyarrhythmias and tachyarrhythmias are highly prevalent in moderate-to-severe adult OSAS [2,19]. OSAS has been demonstrated to be an independent risk factor for atrial arrhythmias likely to be caused by hypoxia, hypercapnia, autonomic dysfunction, atrial stretching, effect of negative intrathoracic pressure, and inflammation [5].

PWD has been demonstrated to be a marker of paroxysmal atrial arrhythmia [20]. Increased PWD is related to the prolongation of atrial conduction, which is associated with OSAS [21,22]. Several potential mechanisms including negative intrathoracic pressure, left ventricular diastolic dysfunction from pulmonary hypertension, increased atrial stretch, left atrial dilatation, increased pro-inflammatory mediator of atrial fibrosis, and autonomic dysregulation explain prolonged P-wave duration (the propagation of delayed atrial conduction) are linked to the pathophysiological mechanisms that contribute to atrial fibrillation development in adult OSAS [5]. From our findings, it might be speculated that children with OSAS start to display abnormality in atrial conduction represented by increased PWD.

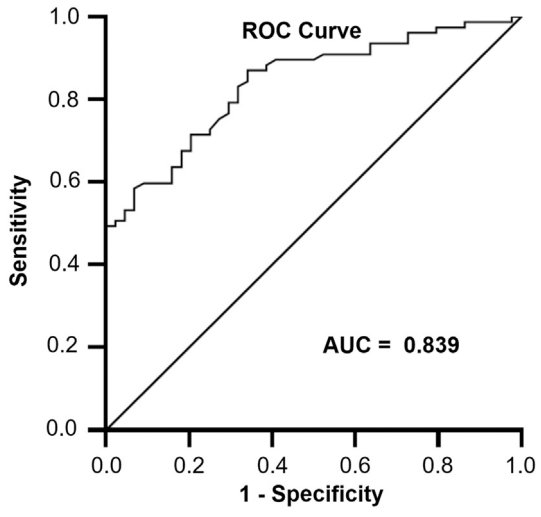


**Fig. 3.** Receiver operating characteristic (ROC) curve analysis of P-wave dispersion. AUC, area under the curve.

Notably, obesity might be one of the factors associated with increased PWD [23]. As the percentage of obesity in children with OSAS was higher than in controls in this study, we excluded all participants with obesity in a further analysis and found that the PWD in children with OSAS was still higher than in controls. This leads us to the conclusion that OSAS is the factor associated with higher PWD. The more severe OSAS, as categorized by AHI score, was associated with higher PWD. This could lead to a higher risk of atrial fibrillation (intra- and interatrial conduction delay) in the future. Whether or not the PWD decreases after treatment of OSAS is an interesting question and needs further study.

Assessment of PWD might be helpful in screening of childhood OSAS using the cut-off of 26.5 ms (sensitivity 89.6%, specificity 61.4%). Although the sensitivity is high, the specificity is low, and so we do not recommend this approach as a diagnostic tool. However, we do propose performing 12-lead ECG in all patients with a history of snoring and suspected OSAS and using this PWD cut-off as a screening tool. If patients have a PWD greater than this cut-off value, we recommend performing PSG to confirm the diagnosis of OSAS.

This study had some limitations. First, the small number of participants in the control group means that they might not represent the normal population. Second, all participants in the control group were recruited as healthy children visiting a well-baby clinic who had no history of snoring and were screened using the OSA-18 questionnaire. However, none underwent PSG to confirm that they did not have OSAS. Third, PWD might change during episodes of apnea; yet, in this study, all the participants underwent 12-lead electrocardiography during the daytime when they were awake.

## 5. Conclusion

In conclusion, PWD significantly increased in children with OSAS and was higher in severe OSAS than in mild and moderate OSAS. PWD might be helpful in screening for childhood OSAS, and particularly in cases of severe OSAS.

## Acknowledgements

This work was supported by Ramathibodi Research Grant, Faculty of Medicine Ramathibodi Hospital, Mahidol University. We thank all participants and their parents for their participation in this study; Savita Nonyai, Chutikan Chaiyawech, Sunantha Danwiwatdecha, and Uthan Bunmee for performing 12-lead electrocardiography; Anchalee Leejakpai and Vijittra Hongtong for performing polysomnography. We also thank Nattawut Unwanatham in helping with statistical analysis. We thank Catherine Deeprose, PhD, from Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

## Conflict of interest

None of the authors have any conflict of interest in regard to this work.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2018.09.032.

## References


[1] Tan HL, Gozal D, Kheirandish-Gozal L. Obstructive sleep apnea in children: a critical update. Nat Sci Sleep 2013;5:109–23.
[2] Gami AS, Pressman G, Caples SM, et al. Association of atrial fibrillation and obstructive sleep apnea. Circulation 2004;110:364–7.
[3] Filgueiras-Rama D, Arias MA, Iniesta A, et al. Atrial arrhythmias in obstructive sleep apnea: underlying mechanisms and implications in the clinical setting. Pulm Med 2013;2013:426758.
[4] Deng ZD, Poon CS, Arzeno NM, et al. Heart rate variability in pediatric obstructive sleep apnea. Conf Proc IEEE Eng Med Biol Soc 2006;1:3565–8.
[5] Maan A, Mansour M, Anter E, et al. Obstructive sleep apnea and atrial fibrillation: pathophysiology and implications for treatment. Crit Pathw Cardiol 2015;14:81–5.
[6] Cicek D, Lakadamyali H, Gokay S, et al. Effect of obstructive sleep apnea on heart rate, heart rate recovery and QTc and P-wave dispersion in newly diagnosed untreated patients. Am J Med Sci 2012;344:180–5.
[7] Jazi MH, Amra B, Yazdchi MR, et al. P wave duration and dispersion in Holter electrocardiography of patients with obstructive sleep apnea. Sleep Breath 2014;18:549–54.
[8] Dilaveris PE, Gialafos EJ, Sideris SK, et al. Simple electrocardiographic markers for the prediction of paroxysmal idiopathic atrial fibrillation. Am Heart J 1998;135:733–8.
[9] Franco Jr RA, Rosenfeld RM, Rao M. Quality of life for children with obstructive sleep apnea. Otolaryngol Head Neck Surg 2000;13:9–16.
[10] World Health Organization. Child growth standards. 2006. Available at: http://www.who.int/childgrowth/en/. [Accessed 1 August 2018].
[11] Grigg-Damberger MM. The AASM Scoring Manual four years later. J Clin Sleep Med 2012;8:323–32.
[12] Marcus CL, Brooks LJ, Draper KA, et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 2012;130:576–84.
[13] Trosman I. Childhood obstructive sleep apnea syndrome: a review of the 2012 American Academy of Pediatrics guidelines. Pediatr Ann 2013;42:195–9.
[14] Walz PC, Schroeder Jr JW. Pediatric polysomnography for sleep-disordered breathing prior to tonsillectomy: a guideline review. Pediatr Ann 2013;42:188–94.
[15] Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–10.
[16] Khositseth A, Chokechuleekorn J, Kuptanon T, et al. Rhythm disturbances in childhood obstructive sleep apnea during apnea-hypopnea episodes. Ann Pediatr Cardiol 2013;6:39–42.
[17] Khositseth A, Nantarakchaikul P, Kuptanon T, et al. QT dispersion in childhood obstructive sleep apnoea syndrome. Cardiol Young 2011;21:130–5.
[18] Pye M, Quinn AC, Cobbe SM. QT interval dispersion: a non-invasive marker of susceptibility to arrhythmia in patients with sustained ventricular arrhythmias? Br Heart J 1994;71:511–4.
[19] Roche F, Xuong AN, Court-Fortune I, et al. Relationship among the severity of sleep apnea syndrome, cardiac arrhythmias, and autonomic imbalance. Pacing Clin Electrophysiol 2003;26:669–77.
[20] Villani GQ, Piepoli M, Rosi A, et al. P-wave dispersion index: a marker of patients with paroxysmal atrial fibrillation. Int J Cardiol 1996;55:169–75.
[21] Ariyarajah V, Mercado K, Apiyasawat S, et al. Correlation of left atrial size with P-wave duration in interatrial block. Chest 2005;128:2615–8.
[22] Can I, Aytemir K, Demir AU, et al. P-wave duration and dispersion in patients with obstructive sleep apnea. Int J Cardiol 2009;133:e85–9.
[23] Kosar F, Aksoy Y, Ari F, et al. P-wave duration and dispersion in obese subjects. Ann Noninvasive Electrocardiol 2008;13:3–7.