Association between mean platelet volume and obstructive sleep apnea-hypopnea syndrome in children

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Abstract

To evaluate the correlation between mean platelet volume (MPV) and obstructive sleep apnea-hypopnea syndrome (OSAHS) in children, and to explore the diagnostic value of MPV for OSAHS. Children with OSAHS diagnosed by polysomnography (PSG) at Fuyong People's Hospital of Bao'an District/Shenzhen Children's Hospital from January 2020 to January 2021 were enrolled in this study. MPV in peripheral venous blood of the enrolled children was detected. Based on the PSG results (apnea-hypopnea index [AHI] and lowest oxygen saturation [$LSaO_2$]), illness severity was classified, and correlations between the 2 parameters were statistically analyzed. A total of 190 children (males = 135, females = 55) with OSAHS were enrolled in the study. There were no significant correlations between AHI, $LSaO_2$, white blood cell count, red blood cell count, blood platelets, hemoglobin, and packed cell volume ($P > .05$), but there was a significant positive correlation between AHI and MPV ($R > 0$, $P < .05$). There was a significant negative correlation between the $LSaO_2$ index and MPV ($R > 0$, $P < .05$). In addition, the receiver operating characteristic (ROC) curve indicated that the best cutoff value for MPV to diagnose mild and moderate-to-severe disease conditions was 9.35 fl, and the coincidence rates for these 2 disease conditions were 93% and 80%, respectively. The ROC curve was also optimal for the diagnosis of mild and moderate-to-severe hypoxia. The critical value was 8.85 fl, and the coincidence rates for these 2 conditions were 96.4% and 76.3%, respectively. In children with OSAHS, MPV is positively correlated with AHI and negatively correlated with the $LSaO_2$ index of PSG. Based on the results of ROC curve analysis, MPV can be used as an auxiliary diagnostic index to judge the severity of OSAHS and the degree of hypoxia in children.

Abbreviations: AHI = apnea-hypopnea index, $LSaO_2$ = lowest oxygen saturation, MPV = mean platelet volume, OSAHS = obstructive sleep apnea-hypopnea syndrome, PSG = polysomnography, RBC = red blood cell count, ROC = receiver operating characteristic.

Keywords: hypoxemia, mean platelet volume, obstructive sleep apnea-hypopnea syndrome

1. Introduction

Obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common clinical disease condition in pediatric otolaryngology, with an incidence rate as high as 3% to 5%.[1,2] The main cause of this condition is the pathological collapse of the upper respiratory tract, especially blockage caused by tonsils and adenoid hypertrophy. This disease condition is mainly characterized by intermittent partial or complete upper airway obstruction, which leads to sleep-disordered breathing in children, resulting in prolonged chronic hypoxia.[3,4] Chronic hypoxia in childhood can stimulate systemic inflammation, cause endothelial damage and atherosclerosis, and increase the incidence of cardiovascular disease in adulthood.[5] Current studies have shown that OSAHS is an independent risk factor for cardiovascular disease-related mortality and morbidity, such as hypertension,

coronary artery disease, and stroke.[6,7] Therefore, an accurate diagnostic assessment of OSAHS can help formulate effective treatment plans to prevent its detrimental effect on children's growth and development.

Currently, polysomnography (PSG) is the gold standard for the clinical diagnosis of OSAHS. PSG mainly monitors changes in the chest and abdominal movement and airflow through the nose and mouth during sleep, as well as indicates OSAHS severity according to blood oxygen saturation and the number of sleep apneas. The main indicators are the apnea-hypopnea index (AHI) and the lowest oxygen saturation ($LSaO_2$).[8,9] However, it is difficult to obtain PSG results in some cases: First, it is difficult to configure the PSG detector and children'hisleep monitoring room in primary medical institutions; Second, PSG examination requires children to sleep all night and the results cannot provide a timely feedback. Therefore,

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Table 1

General information of children with different grades of AHI.

| Severity | n | Gender | | Age (yr) | Weight (kg) |
		Female	Male		
Mild	111	38 (34.23%)	73 (65.77%)	5.64 ± 2.20	20.22 ± 2.67
Moderate-to-severe	79	17 (21.52%)	62 (78.48%)	6.07 ± 2.23	20.18 ± 2.37
χ^2/t		$\chi^2 = 3.628$		$t = -1.302$	$t = 0.091$
P		.057		.195	.927

some otolaryngologists only subjectively judge the condition and the degree of hypoxia based on the size of the tonsils at the initial diagnosis, and then perform surgical treatment. Previous studies have shown that there are inconsistencies in the association of the size of the tonsils alone with the severity of the disease and the degree of hypoxia.[10] Thus, identifying a simple and easy-to-obtain outpatient index that matches the PSG results will be helpful for otolaryngologists to initially assess the condition and formulate follow-up diagnosis and treatment plans. Thus, in this study, we aimed to explore a new detection indicator that can preliminarily assess the severity/degree of OSAHS in children.

Many current studies have revealed that mean platelet volume (MPV) is positively correlated with the severity of OSAHS, but most studies have focused on adult OSAHS.[11–15] Hence, we selected MPV, a blood biochemical indicator that is easily obtained in outpatient visits, as the diagnostic measure. Furthermore, we aimed to explore the correlation between MPV and PSG results (AHI and $LSaO_2$) in children, and we expect that MPV can be used to evaluate the condition and degree of hypoxia in these patients in the absence of PSG examination.

2. Methods

2.1. Data acquisition

The medical records of all pediatric patients diagnosed with OSAHS between January 2020 and January 2021 in the Department of Otolaryngology of Fuyong People's Hospital and Shenzhen Children's Hospital were examined in this study.

2.2. Ethical approval

This clinical study was approved by the Ethics Committee of Shenzhen Fuyong PeoplePe Hospital.

2.3. Inclusion criteria

The inclusion criteria were as follows: PSG (Contec RS01, Ginhuangdao, China)/(MegaHealth ZG-S01A, Shanghai, China) was used to monitor undisturbed sleep in children at night, which was in line with the standard "Draft Guidelines for the Diagnosis and Treatment of OSAHS in Children (Urumqi)" formulated by the Otolaryngology Branch of the Chinese Medical Association in 2007[16]; children with OSAHS who were born full term with no special circumstances in the feeding history and growth history; children with OSAHS who were aged between 3 and 15 years; and enrolled subjects, or their family members, who had voluntarily participated in the project and agreed to sign the informed consent form.

2.4. Exclusion criteria

The exclusion criteria were as follows: congenital anatomical abnormalities of the oropharyngeal cavity and nasopharyngeal cavity; severe neonatal asphyxia and hypoxic ischemic encephalopathy at birth; history of cerebral palsy and epilepsy after birth; severe hepatic and renal insufficiency; myasthenia gravis, periodic paralysis, and other muscle weakness disorders.

2.5. Degree of disease

According to the standard "Draft Guidelines for the Diagnosis and Treatment of OSAHS in Children (Urumqi)", the disease condition and degree of hypoxia in children with OSAHS were classified as follows: mild OSAHS: AHI (5–10 times/h); moderate-to-severe OSAHS: AHI (>10 times/h); mild hypoxemia: $LSaO_2$ (85%–91%); moderate-to-severe hypoxemia: $LSaO_2$ (<85%).

2.6. Laboratory data collected from the participants during hospitalization

After 8 hours of fasting, 2 mL of venous blood was drawn the next morning, and the blood sample was placed in an EDTA vacuum anticoagulant tube. White blood cell count, red blood cell count (RBC), blood platelets, MPV, hemoglobin, and packed cell volume were measured. Blood cells were analyzed within 30 minutes of sampling using an automatic blood cell analyzer (Minray BC-5390, China).

2.7. Statistical methods

SPSS 21.0 statistical software was used for data analysis. Measurement data are described as means ± standard deviation (x ± s), and t test was used for comparison between groups. The correlation between measurement data was analyzed using the Pearson correlation. Receiver operating characteristic (ROC) curves were used to evaluate the diagnostic efficacy of the indicators, and consistency between indicators was determined using the Kappa value. $P < .05$ indicated a statistically significant difference.

3. Results

3.1. Patient data

A total of 190 children with OSAHS were enrolled in the study. There were 135 male and 55 female pediatric patients, ranging in age from 3 to 13 years with a mean age of 5.82 ± 2.21 years.

3.2. Comparison of general data of children with different levels of AHI and $LSaO_2$

According to the results of AHI and $LSaO_2$, the degree of illness and degree of hypoxia in children with OSAHS were divided into the following 2 groups: mild and moderate-to-severe. There were no significant differences in gender composition, age, and weight between the groups with different grades of AHI and $LSaO_2$ ($P > .05$), as shown in Tables 1 and 2, respectively.

Table 2

General information of children with different grades of lowest oxygen saturation (LSaO$_2$).

| Severity | n | Gender | | Age (yr) | Weight (kg) |
		Female	Male		
Mild	85	23 (27.06%)	62 (72.94%)	5.60 ± 2.00	20.42 ± 2.60
Moderate-to-severe	105	32 (30.48%)	73 (69.52%)	6.00 ± 2.37	20.03 ± 2.49
χ^2/t			$\chi^2 = 0.267$	$t = -1.251$	$t = 1.050$
P			.606	.213	.295

Table 3

Correlation analysis of blood routine indicators and polysomnography (PSG).

| Indicators | $\bar{X} \pm s$ | AHI | | LSaO$_2$ | |
		r	P	r	P
WBC	7.94 ± 2.51	−0.095	0.193	−0.040	.584
RBC	4.80 ± 0.51	0.099	0.173	−0.114	.119
PLT	338.66 ± 80.80	−0.120	0.100	−0.140	.055
MPV	9.44 ± 1.05	0.350	0.000	−0.245	.001
HB	125.24 ± 10.61	0.006	0.935	−0.033	.653
PCV	38.41 ± 3.22	0.091	0.210	−0.081	.265

AHI = apnea-hypopnea index, HB = hemoglobin, LSaO2 = lowest oxygen saturation, MPV = mean platelet volume, PCV = packed cell volume, PCV = blood platelets, RBC = red blood cell count, WBC = White blood cell count.

3.3. Correlation analysis of blood routine indexes and PSG results (AHI and LSaO$_2$)

The Pearson correlation analysis of blood routine indexes and PSG results showed that there was no significant correlation between AHI, LSaO$_2$, white blood cell count, RBC, blood platelets, HB, and packed cell volume ($P > .05$), while AHI and MPV were significantly positively correlated ($R > 0$, $P < .05$). There was a significant negative correlation between the LSaO$_2$ index and MPV ($R < 0$, $P < .05$), as shown in Table 3.

3.4. ROC curve analysis

To further clarify the diagnostic value of MPV for OSAHS, we chose the ROC curve analysis. We used AHI as the "as thstandard" for judging the severity of OSAHS in children. AHI ≤ 10 times/h is considered mild, and AHI >10 times/h is considered moderate-to-severe. Considering LSaO$_2$ as the "gold standard" for the degree of hypoxia, LSaO$_2$ ≥85% is considered mild, and LSaO$_2$ <85% is considered moderate-to-severe. ROC curve analysis showed that the area under the curve values of MPV for AHI and LSaO$_2$ were 0.809 and 0.746 ($P < .05$), respectively, and the corresponding diagnostic cutoff values were 9.35 fl (AHI) and 8.85 fl (LSaO$_2$), respectively. These statistical results showed that MPV had a higher diagnostic value when AHI was used as the gold standard, especially in the diagnosis of moderate-to-severe disease (Fig. 1, Table 4).

3.5. Consistency analysis

To determine the diagnostic consistency between MPV and PSG results, we used the cutoff value obtained from the ROC diagnostic curve to classify MPV into mild and moderate-to-severe categories and conducted a consistency analysis with the severity of the 2 PSG indicators (AHI and LSaO$_2$). According to the Kappa consistency test, the coincidence rates for MPV and AHI were 93% and 80% for mild disease and moderate-to-severe disease, respectively, and the coincidence rates for MPV and LSaO$_2$ were 96.4% and 76.3% to judge mild hypoxia and moderate-to-severe hypoxia, respectively. This indicated that
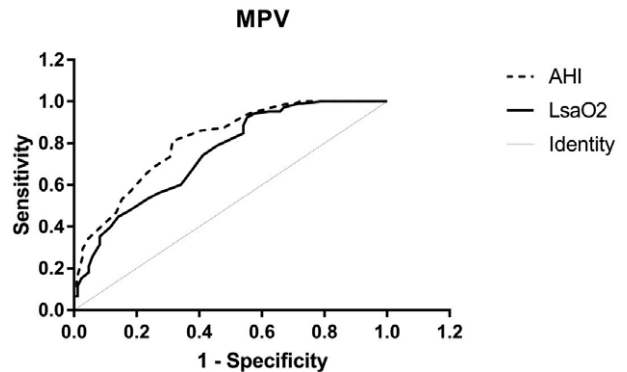

Figure 1. ROC curve of MPV. MPV = mean platelet volume, ROC = receiver operating characteristic.

the agreement between MPV and AHI was high (Kappa > 0.7), while the agreement between MPV and LSaO$_2$ was moderate (Kappa > 0.4) (Table 5).

4. Discussion

OSAHS is a common type of sleep-disordered breathing in children. Intermittent or persistent upper airway blockage or even collapse during sleep at night affects gas exchange and leads to hypoxia, which in turn has a serious impact on the growth and development of multiple systems in children.[17,18] Thus, timely and accurate diagnosis of OSAHS is crucial for follow-up treatment for children.

Platelets, as the smallest cells in the peripheral blood, play an important role in thrombosis.[19,20] MPV is an important indicator of platelet activation. An increase in MPV indicates an increase in platelet volume. Larger platelets contain more dense granules, are more active in terms of enzymes and metabolism, and thus have greater prothrombotic potential.[21–23] Considering that currently, the diagnosis of OSAHS is mainly based on the results of PSG examination, it is necessary to explore the correlation between MPV and disease condition if there is a high

Receiver operating characteristic (ROC) results of mean platelet volume (MPV).

Gold Standard	AUC	SE	P	95%CI	Cutoff	Sensitivity	Specificity
AHI	0.809	0.030	.000	0.750–0.869	9.350	0.810	0.685
LSaO$_2$	0.746	0.035	.000	0.677–0.816	8.850	0.924	0.447

AHI = apnea-hypopnea index, AUC = area under the curve, LSaO2 = lowest oxygen saturation.

correlation with the main indicators of PSG (AHI and LSaO$_2$). Most scholars have focused on changes in MPV during different stages of adult OSAHS. Nena et al[11] observed that the MPV in adults with OSAHS (AHI ≥ 5 events/h) was significantly higher than that in the normal control group (AHI < 5 events/h), while Sökücü et al[12] found a positive correlation between MPV and AHI in adult patients with severe OSAHS (AHI ≥ 30 events/h) through a retrospective analysis, revealing that as the severity of the disease increased, MPV increased significantly. Xuesong et al[13] observed the levels of MPV in adult patients with OSAHS and found that the MPV in patients with severe OSAHS was significantly higher than that in the normal control group; they hypothesized that the inflammatory factors produced during OSAHS stimulated megakaryocyte ploidy, leading to platelet hyperplasia and a large increase in volume. Similar results were observed by Varol,[14,15] who reported that the correlation in adult males was significantly higher than in females. The underlying mechanism may be as follows. First, hypoxia causes an inflammatory response, which leads to an increase in interleukin-3 (IL-3) and IL-6 to promote the doubling of megakaryocytes. Then, long-term and repeated hypoxia at night causes a platelet thrombus that requires a large amount of platelets, stimulating the bone marrow to compensate for the production and release of larger reticulated platelets. In addition, further research found that MPV significantly decreased after 6 months of continuous positive airway pressure in patients with severe OSAHS, which indicated that the inflammation mediated by hypoxia may be effectively alleviated by improving hypoxia in the patient'atbody; thus, greatly reducing MPV.

Few studies have focused on the correlation of MPV and OSAHS in children. Erdim et al[24] found that MPV in the blood of obese children with OSAHS was not significantly correlated with the disease, but given the specific study population there was a selection bias. In addition, Onder et al[25] observed that MPV in children with OSAHS and adenoid hypertrophy was not necessarily correlated with upper airway obstruction. However, Kucur et al[26,27] found that MPV in children with adenoid hypertrophy was significantly higher than that in healthy children, and further tests showed that MPV in children after adenoidectomy was significantly lower than before surgery. In addition, Zicari et al[28] observed 67 children with sleep disordered breathing and found that MPV in these children was significantly higher than that in healthy children, and MPV in children with OSAHS was also significantly higher than that in patients with primary snoring. Their analysis suggests that the increase in platelet volume is due to the comprehensive effect of a systemic inflammatory response. In conclusion, the study of MPV in children with OSAHS is controversial; therefore, there is a significant need for further research.

In the past, the relationship between the MPV and OSAHS was mainly focused on the correlation between AHI and MPV. However, clinical studies found that the relationship between AHI and LSaO$_2$ is often not parallel. Therefore, in our study, we explored the relationship between MPV and AHI and LSaO$_2$ separately. We found that all clinical blood biochemical indexes, except MPV, had no correlation with OSAHS. Among these indexes, MPV was significantly positively correlated with AHI and significantly negatively correlated with LSaO$_2$. This indicates that MPV is related to the disease condition, and it further confirms that MPV gradually increases with the progression of

Table 5

Analysis of consistency between MPV and polysomnography (PSG) [n (%)].

MPV	AHI		LSaO$_2$	
	Mild	Moderate-to-severe	Mild	Moderate-to-severe
Mild	93 (93.0)	7 (7.0)	53 (96.4)	2 (3.6)
Moderate-to-severe	18 (20.0)	72 (80.0)	32 (23.7)	103 (76.3)
Kappa	0.734		0.626	
P	.000		.000	

AHI Hlapnea-hypopnea index, LSaO2 Salowest oxygen saturation, MPV PVmean platelet volume.

the disease and aggravation of hypoxia. The increase in MPV in children due to this disease is not caused by a single factor but by the superposition of multiple factors. We analyzed the main reasons for this phenomenon. First, long-term chronic hypoxia leads to oxidative stress-induced damage to tissues and cells throughout the body and releases a large number of inflammatory factors that directly stimulate the bone marrow to produce larger platelets.[13,14] Thus, oxygen tolerance worsens and the platelet volume increases more significantly. This phenomenon is more common among children. Second, hypoxemia promotes the compensatory increase in RBCs, causing hemodynamic changes. Platelet thrombus formation subsequently occurs, requiring a large number of platelets; bone marrow-derived compensatory new platelets are significantly larger than mature platelets.[29] Third, MPV is a sign of platelet activation. Larger platelets can release more cytokines, such as serotonin, which can change the shape of platelets from double-concave to round, accompanied by pseudopodia, resulting in increased platelet volume. At the same time, serotonin can promote the formation of thrombus, thus creating a vicious circle.[30]

To further understand the relationship between MPV and the severity of OSAHS and the degree of hypoxia, we divided the children into mild and moderate-to-severe categories according to the AHI and LSaO$_2$ classification criteria. Our analyses of these groups showed that MPV determined that the optimal critical value for mild, moderate, and severe hypoxia was 8.85 fl. For example, when the MPV >8.9 fl, the child could be considered to be in a moderate to severe hypoxia state. The optimal critical value for mild and moderate-to-severe OSAHS was determined to be 9.35 fl. For example, when the child's MPV was >9.4 fl, the disease condition could be initially considered as moderate to severe OSAHS. In addition, it was found that MPV and AHI had 93% and 80% consistency in the diagnosis of mild and moderately severe disease, respectively, while MPV and LSaO$_2$ had 96.4% and 76.3% consistency in the diagnosis of mild and moderately severe hypoxia. These results suggest that it is possible to determine the severity of OSAHS using MPV as an indicator. Thus, based on the MPV > 9.4 fl, a child who has moderate to severe OSAHS with moderate to severe hypoxemia could receive a diagnosis and treatment plan. Our study further confirmed the correlation between the MPV and OSAHS disease stage. At the same time, quantifying the relationship between MPV and AHI and LSaO$_2$ enables the outpatient physicians to preliminarily determine the degree of disease and hypoxia in children based on the MPV level.

Given the exploratory nature of our study, there are certain limitations that should be acknowledged. Specifically, the classification of children with OSAHS is not exhaustive, and the sample size is not large enough.

5. Conclusion

These results suggest that in children with OSAHS, MPV is positively correlated with AHI and negatively correlated with the LSaO$_2$ index of PSG. According to the results of ROC curve analysis, MPV can be used as an auxiliary diagnostic index to judge the severity of OSAHS and the degree of hypoxia in children. However, more clinical data are needed in the future to confirm these findings.

Author contributions

Guo-hui Zeng designed/performed most of the investigation and data analysis, and wrote the manuscript; Guo Xu provided pathological assistance; Hong-yu Liu and Zhong Gao contributed to interpretation of the data and analyses. All of the authors have read and approved the manuscript.

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