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Review Article

Applications of impulse oscillometry in the diagnosis and monitoring of preschool asthma

Alberto Vidal[1,*]

[1]Department of Pediatric Pulmonology, Clínica MEDS, Santiago, Chile

*Author for correspondence: Email: aevgmd@yahoo.es

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Abstract

Impulse oscillometry is a lung function test that has become more widely used over the past 30 years. It is particularly useful in patients who have difficulty performing forced respiratory maneuvers, such as preschool children, who have shorter expiration times, less strength to inhale, less coordination and shorter attention spans than older children or adults. At preschool age, oscillometry has a higher success rate than spirometry and is more sensitive in detecting changes in lung function in the diagnosis and monitoring of asthma. This review summarizes the available scientific evidence supporting its use in the diagnosis, measurement of control, severity, monitoring and follow-up of preschool asthma.

Keywords: Asthma, Preschool, Impulse oscillometry

Introduction

Impulse oscillometry (IOS) is a lung function test derived from the forced oscillation technique (FOT) described in 1956 by Dubois [1]. In 1994, Voegel and Smith presented it to the international scientific community, which allowed the German laboratory Jaeger® to begin its development and commercialization for both children and adults worldwide [2]. In the last 30 years its use has expanded globally, having a particular utility in the diagnosis and monitoring of respiratory diseases in children and adults [3]. In simple terms, IOS uses a loudspeaker to transmit square-shaped sound waves in constant pulses of at least 5 times per second that travel in an oscillating manner superimposed on the normal respiratory flow at different frequencies, allowing pressure and flow to be determined by transducers and transmitting this information to software to calculate Impedance (Zrs), Resistance (Rrs) and Reactance (Xrs) and other parameters of the respiratory system (**Table 1**). These parameters are useful for diagnosis and monitoring of different diseases affecting the respiratory system [4]. Technical and interpretation recommendations for IOS for children and adults have recently been published [5,6]. The parameters measured in the IOS may vary due to different factors, among which the most important are age, height and ethnicity; which may contribute to the underrepresentation of some populations [7]. Recently, predictive equations for healthy people from 2.7 to 90 years of age were published, which will allow more accurate measurements of lung function throughout life in the future [8]. IOS is a noninvasive technique, easy to perform, without complex maneuvers, which makes it ideal for young children. It has been shown that only 80% of children are able to perform the forced spirometric maneuver, unlike 100% who can perform IOS [9]. In addition, it is a fast, reliable and sensitive technique for small changes in lung function, which allows diagnosis of small airway obstruction, a site of the respiratory system that in recent years has been recognized as the target for the treatment of asthma in the first years of life [10,11]. Recent evidence highlights preschool IOS as one of the best techniques to identify children at highest risk of future lung function decline [12].

Table 1. Common parameters in impulse oscillometry.

Parameter	Definition
Respiratory Impedance (Zrs)	Respiratory Resistance plus Respiratory Reactance.
Respiratory Resistance (Rrs)	Energy to propagate a pressure wave through the airways.
Resistance at 5 Hertz (R5)	Reflects the total resistance of the airway.
Resistance at 20 Hertz (R20)	Reflects proximal airway resistance.
Difference between 5 and 20 Hertz Resistance (R5-R20)	Reflects the resistance of the distal airway.
Respiratory Reactance (Xrs)	Energy generated by the recoil of the lungs after distension by a pressure wave, composed of inertance and elastance.
Reactance at 5 Herz (X5)	Reactance at low frequency where the elastance effect predominates.
Reactance Area (AX)	Area under the curve between values of X5 and Fres, also called the Goldman triangle.
Resonance frequency (Fres)	Point where reactance is equal to zero, where elastic forces are equivalent to inertial forces.

Furthermore, IOS has been shown to be a cost-effective technique for the diagnosis of asthma when compared with spirometry in preschool children [13]. The objective of the present study was to describe the scientific evidence available regarding the usefulness of IOS in preschool asthma.

Method

A review of the scientific evidence on the use of IOS in asthmatic preschoolers was conducted. The search for articles was carried out between September 2024 in the Medline (PubMed), Web of Science (WOS), EBSCO Host, Science Direct and SCOPUS databases. MeSH terms and free terms in their English version were used. The terms were grouped into two dimensions: i) Impulse oscillometry ii) preschool asthma. The Boolean operator "and" was used to integrate the two dimensions. In addition, abstracts of publications published at the congresses of the American Thoracic Society (ATS) and the European Respiratory Society (ERS) were reviewed. The articles found were grouped into three categories: oscillometry in the diagnosis of preschool asthma, oscillometry in control and severity of preschool asthma, and oscillometry for monitoring and follow-up of preschool asthma.

Oscillometry in the diagnosis of preschool asthma

Preschoolers with early or late wheezing have been shown to have significantly higher baseline values of the reactance area (AX), the difference between the resistance at 5 Hertz (R5) and the resistance at 20 Hertz (R20) measured in Kilopascals (R5-R20) or percentage (R5-R20%) compared to healthy preschoolers [14]. Prebronchodilator R5 and R5-R20 values have been found to be significantly higher in preschoolers whose mothers reported more

Table 2. Impulse oscillometry studies in the diagnosis of preschool asthma.

Author	Type of study	Population	Age	Result
Kinitiä *et al.* [14]	Cross-sectional	Early wheezing, late wheezing, bronchopulmonary dysplasia vs healthy	Average 5 to 6 years	In early and late wheezing preschoolers, the z-scores of R5-20, R5-20% and AX were significantly higher than in healthy subjects (p<0.001 for all comparisons).
Medeiros *et al.* [15]	Cross-sectional	Preschoolers with or without respiratory symptoms	3 to 6 years	R5 baseline (symptoms 1.03 vs. no symptoms 0.92, p=0.018); R5-R20 baseline (symptoms 0.37 vs. no symptoms 0.29, p=0.009)
Da Silva Sena *et al.* [16]	Prospective	Preschoolers with a history of hospitalization for moderate to severe bronchiolitis	3 to 6 years	R5>1.65 Adjusted RR=3.11 and X5<-1.65 Adjusted RR=2.11 in preschoolers with maternal asthma and rhinovirus bronchiolitis
Hellinckx *et al.* [17]	Cross-sectional	Asthmatic vs. healthy preschoolers	2.7 to 6.6 years	Average post-bronchodilator decrease in R5 was -12% in healthy preschoolers with an upper range up to 40%
Nielsen *et al.* [18]	Cross-sectional	Asthmatic vs. healthy preschoolers	2 to 5 years	Post-bronchodilator decrease in R5 (S=76%, E= 65%, PPV=76%, NPV=65%)
Marotta *et al.* [19]	Cross-sectional	Asthmatic vs. healthy preschoolers	4 years	Δ R5 (asthma -27% vs no asthma 17%; P=0.02) y Δ10 asthma (24% vs no asthma 16%; P=0.03)
Song *et al.* [20]	Cross-sectional	Asthmatic vs. healthy preschoolers	3 to 6 years	R10 (asthma 0.8 kPa/L/s vs healthy controls 0.7 kPa/L/s, p=0.035). Bronchodilator response to detect clinical asthma (AUC ΔR5=0.663, AUC Δ R10=0.609)

Shin *et al.* [21]	Cross-sectional	Preschoolers with stable asthma vs healthy controls	Average 4.6 years	Δ FEV1 ≥ 9% + ΔR5 ≥ -29% (S=63%, E=93%, LR+ 9.14)
Meoli *et al.* [22]	Retrospective	Preschoolers with asthma	3 to 6 years	Δ R5 -25.7% (AUC 0.77, p=.03) and Δ X5 25.7% (AUC 0.75, p=0.04) achieve the best sensitivity and specificity for FEV1 ≥ 12% and/or ≥ 200 ml
Jee *et al.* [23]	Cross-sectional	Preschoolers with asthma and controls with chronic cough	2 to 6 years	PC_{80}X5 was the best cut-off point to differentiate asthma from controls (S=80%, E=82.9%).
Schulze *et al.* [24]	Cross-sectional	Preschoolers with suspected asthma	3 to 6 years	Increase in R5 by 45% and/or reduction in X5 by 0.69 kPa/L/s detect a drop in FEV_1 by 20% (S=72% and E=73%; S=80% and E=76%, respectively)
Kalliola *et al.* [25]	Cross-sectional	Preschoolers with early-onset wheezing, late-onset wheezing, bronchopulmonary dysplasia, and healthy controls	3 to 8 years	40% increase in R5 with methacholine (late wheezing 77% vs healthy controls 21%, p<0.001)
Choi *et al.* [26]	Prospective	Preschoolers with asthma	3 to 6 years	Reproducibility coefficient (C_{80}X5=2.56, C_{30}R5=1.54)
Arikoglu *et al.* [27]	Cross-sectional	Recurrent wheezing with or without positive mAPI	3 to 6 years	R5-R20% in predicting recurrent wheezing positive mAPI (OR=1.4, p=0.02, AUC=0.655, p=0.003, S=75%, E=53%))
Hu *et al.* [28]	Cross-sectional	Preschoolers with or without cough as a variant of asthma	3 to 6 years	AUC for the diagnosis of cough as a variant of asthma (X5=0.657, FeNO=0.779, X5 + FeNO=0.809)
Chen *et al.* [29]	Prospective	Preschoolers with or without asthma	3 to 6 years	R5 + X5 + FeNO in the prediction of asthma (AUC=0.94, S=0.89, E=0.88, PPV=0.88 NPV=0.9)

Δ: Variation in Bronchodilator Response; AUC: Area Under the Curve; S: Sensitivity; E: Specificity; PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR+: Positive Likelihood Ratio; OR: Odds Ratio; RR: Relative Risk, mAPI: Modified Asthma Predicted Index; FeNO: Exhaled Fraction of Nitric Oxide

respiratory symptoms suggestive of asthma than those with fewer symptoms [15]. The IOS has also been shown to be useful for confirming abnormalities in preschoolers at high risk of asthma. One study showed that preschoolers with a history of maternal asthma and moderate to severe rhinovirus bronchiolitis had significantly higher baseline R5 and 5 Hertz reactance (X5) values on the IOS than preschoolers without this history [16]. Bronchodilator response (BDR) in IOS has also been studied in the diagnosis of preschool asthma. The first study that measured the utility of BDR in IOS demonstrated that post-bronchodilator decrease of R5 ≥ -40% could be a good parameter to differentiate between preschoolers with asthma and healthy children [17]. It was subsequently reported that decreases ≥ -27% or -29% in R5 could be good cut-off points to differentiate between preschool asthma and healthy controls [18]. A controlled study compared preschoolers with or without asthma at age 4 years, showing that the post-bronchodilator fall in R5 and 10 Hertz Resistance (R10) were the best parameters to discriminate between preschoolers with asthma and healthy ones. In this study, it was proposed that a decrease in post-bronchodilator resistance of -20 to -25% in R5 and/or -10 to -15% in R10 would be the best cut-off points to diagnose asthma among atopic preschoolers [19]. Another study found significantly higher baseline values of R10 in asthmatic preschoolers compared to healthy controls, as well as greater post-bronchodilator decreases in R5, R10, R20 and resistance at 35 Hertz (R35), differences that were not found in spirometry. Furthermore, this study reported that these differences were found in both atopic and non-atopic asthmatics compared to healthy controls [20]. The addition of the IOS BDR to the spirometry BDR has been shown to increase the accuracy in diagnosing preschool asthma, with this combination being superior to each parameter alone [21]. A recent retrospective evaluation of the BDR measured by IOS and spirometry in preschoolers diagnosed with asthma was performed. This evaluation found that the decrease in R5 and the increase in X5 after the bronchodilator would be the best parameters to identify the BDR in spirometry [22]. The IOS has also been used to measure bronchial hyperresponsiveness (BHR) with methacholine in the diagnosis of asthma, with the percentage change in X5 with respect to the predicted value being the parameter with the highest sensitivity and specificity [23]. A study showed that for the diagnosis of BHR with methacholine and IOS, the combination of an increase in R5 with the decrease in X5 was the one that had the best sensitivity to detect the 20% drop in the expiratory volume of the first second in spirometry [24]. It has been shown that the increase in R5 during the methacholine test can differentiate preschoolers with current asthma symptoms from healthy controls, a parameter that has been termed PD_{40}R5, i.e. the dose of methacholine with which the 40% increase in R5 is caused [25]. BHR measured with methacholine and IOS has been found in up to 97% of patients studied with R5 and X5, the latter parameter being the most reproducible [26]. In asthma diagnosis, the utility of the IOS combined with clinical predictive algorithms or biomarkers in respiratory diseases has been measured. It has been shown that baseline values of R5-R20% are increased in recurrent wheezers with a positive modified asthma predictive index (mAPI) compared to those with a negative algorithm, which may help to identify recurrent wheezers at high risk of asthma [27]. Other investigations have combined parameters of the IOS with the fraction of exhaled nitric oxide (FeNO). One study found that the best combination of markers for the diagnosis of cough-variant asthma was X5 less than -4.15 $cmH_2O/L/s$ plus FeNO over 18 ppb [28]. A 1-year follow-up study was recently published that was able to create a predictive model for preschool asthma, showing that the combination of R5, X5, and FeNO is able to differentiate with a high degree of accuracy preschoolers with or without asthma, with the combined model being superior to each parameter individually [29].

Oscillometry in control and severity of preschool asthma

Preschoolers with recurrent wheezing and a positive Asthma Predictive Index (API) who use inhaled corticosteroids have been reported to have a higher R20 than API-positive preschoolers who do not use inhaled corticosteroids. This would reflect the increased central airway resistance and indicate that they probably have greater asthma severity [30]. The X5 z-score has been reported as a parameter capable of differentiating between preschool asthma of different degrees of severity, defined by the risk of exacerbations with systemic corticosteroid use or the need for controller treatment [31]. The increase in R5-R20 measured during the methacholine test has been reported as a marker of the severity of exercise-induced bronchoconstriction (EIB) in preschoolers with suspected asthma [32]. A prospective one-year study in preschoolers with asthma demonstrated that R5, R5-R20, and X5 were the IOS parameters that best predicted asthma exacerbations [33]. The preschooler subgroup in a study spanning up to adolescence showed that X5 is better than FEF 25-75% as a parameter for predicting uncontrolled asthma [34]. Other studies in preschoolers with asthma demonstrated that the combination of R5, R5-R20, Fres or X5 in IOS with FeNO was the most accurate in discriminating between controlled and uncontrolled asthma [35,36]. AX, R5-R20 and R5 have also been reported to be the best parameters for predicting loss of asthma control in preschoolers after 8 to 12 weeks [37]. Reactance inversion (RI) is a recently described phenomenon in the IOS of asthmatic patients. RI can be identified with the corrected R5 (X5c) and has been found more frequently in preschoolers with decreased lung function on spirometry and peripheral airway obstruction with other IOS parameters such as AX and R5-R20 [38].

Oscillometry for monitoring and follow-up of preschool asthma

A follow-up study demonstrated that inhaled corticosteroid treatment of preschool asthma can be guided by a free-running exercise challenge test. In this study, The EIB measured by increases in R5 was significantly decreasing with treatment over 3 visits in 6 months [39]. Another study showed that in preschoolers, the IOS improves significantly after one year of controller treatment, however, it maintains a high percentage of significant BDR, which could reflect the severity of the disease. This study also showed that atopy, the degree of asthma control and significant improvement of some parameters that reflect peripheral airway obstruction would allow identifying preschool asthma phenotypes [40]. The decrease in R5 and R5-R20 during asthma treatment has also been shown to correlate significantly with improvement in asthma control as measured by questionnaires at 12 months of treatment [41]. Two recent studies have demonstrated the usefulness of preschool IOS in predicting asthma or impaired lung function at school age. The first was conducted in preschoolers with persistent asthma who were on average 4.9 years old at the first assessment and 7.9 years old at the second assessment three years later, showing that AX, R5-R20 and R5 were the best parameters to discriminate between normal and

Table 3. IOS studies in measuring preschool asthma control and severity.

Author	Type of study	Population	Age	Result
Lezana *et al.* [30]	Cross-sectional	Preschoolers with API positive or negative asthma	24 to 72 months	API preschoolers (with CI R20 89% without corticosteroids 81%, p=0.047)
Shin *et al.* [31]	Cross-sectional	Preschoolers with intermittent, mild persistent, moderate-severe persistent asthma	2 to 5 years	Z-score X5 below the normal limit have highest need for medication (p=0.008) and highest combined severity (p=0.019)
Kalliola *et al.* [32]	Cross-sectional	Preschoolers with respiratory symptoms of suspected asthma	3 to 8 years	Increase R5-R20 in methacholine test (severe EIB vs no EIB p=0.036)
Schulze *et al.* [33]	Prospective	Asthmatic preschoolers	4 to 7 years	Prediction of exacerbations in one year (AUC R5=0.80, p<0.001, AUC R5-R20= 0.77, p<0.001, AUC X5=0.70, p=0.01)
Tirakitsoontorn *et al.* [34]	Retrospective	Subgroup of preschoolers with controlled and uncontrolled asthma	4 to 7 years	X5<3.8 cmH2O predicts uncontrolled asthma (AUC>0.7, S=68.8%, E=77.8%, PPV=64.7%, NPV=80.8%)
Zeng *et al.* [35]	Cross-sectional	Preschoolers with asthma (controlled and uncontrolled) and healthy controls	3 to 6 years	AUC of X5<-3.6 cmH2O, FeNO>27ppb and combination of both (0.75, 0.78 and 0.86, respectively)
Xiao *et al.* [36]	Prospective	Preschoolers with asthma (controlled and uncontrolled) and healthy controls	3 to 6 years	AUC for predicting uncontrolled asthma (R5-R20+FeNO=0.92, R5 + FeNO=0.91, X5 + FeNO=0.91, Fres + FeNO=0.91)
Zheng *et al.* [37]	Prospective	Preschoolers with asthma and healthy controls	3 to 6 years	Prediction of uncontrolled asthma with AUC (AX, R5-R20 and R5 = 0.88, 0.84 and 0.82, respectively)
González *et al.* [38]	Cross-sectional	Subgroup of persistent asthmatic preschoolers with and without reactance inversion	3 to 6 years	X5 vs X5c (FEV_1 1.28 vs 1.17, p<0.05, $FEV_{0.75}$ 1.16 vs 1.06, p<0.05, $FEV_{0.5}$ 0.97 vs 0.88, p<0.05,(AX 2.7 vs 4.4, p<0.01, R5-R20 0.24 vs 0.42, p<0.01)

API: Asthma Predicted Index; AUC: Area Under the Curve; S: Sensitivity; E: Specificity; PPV: Positive Predictive Value; NPV: Negative Predictive Value; EIB: Exercise-Induced Bronchodilator Restriction; FeNO: Exhaled fraction of nitric oxide

Table 4. IOS studies in the follow-up of preschool asthma.

Author	Type of study	Population	Age	Result
Burman *et al.* [39]	Prospective	Preschoolers diagnosed with asthma	4 to 7 years	R5 post-exercise 1st, 2nd and 3rd visit (61% vs 18% vs 13.5%, P<0.001)
González *et al.* [40]	Prospective	Persistent asthmatic preschoolers	3 to 6 years	IOS altered at baseline and after 12 months (80.6% vs 64.5%, p=0.04). BDR at baseline and after 12 months (77.4% vs 83.9, p=0.43)
Hu *et al.* [41]	Prospective	Preschoolers with asthma and exacerbations	2 to 6 years	C-ACT with R5% y C-ACT with R5-R20 (both r=-0.49, p<0.01), TRACK with R5% (r=-0.31, p=0.04) TRACK with R5-R20 (r=-0.33, p=0.02)
Grell *et al.* [42]	Prospective	Preschoolers with persistent asthma	3 to 5 years	LR+ for predicting abnormal spirometry (AX, R5-R20, R5 = 50, 10, and 7.1, respectively). AUC in predicting abnormal spirometry for AX, R5, R5-R20 (0.91, 0.9, and 0.79, respectively)
Kinitiä *et al.* [43]	Prospective	Preschoolers with asthma	3 to 8 years	Increased R5 at 4 years and decreased lung function at 8 years (β =-0.3; p<0.001 for FEV_1) or active asthma at 8 years (β=2.0; p=0.029)
Kinitiä *et al.* [44]	Retrospective	Asthmatic adolescents aged 12 to 18 with preschool IOS	2 to 7 years	Increased preschool R5 (decreased FEV_1 in adolescence, OR=5.9)
Lauhkonen *et al.* [45]	Prospective	Preschoolers with a history of hospitalization for bronchiolitis before 6 months of age	5 to 7 years	Post-BD X5 preschool has a strong correlation with post-BD FVC (rho = 0.61) and post-BD FEV1 (rho=0.59) in adolescence. One unit decrease in preschool X5 Z-score predicts 9.6% lower FEV_1 and 9.3% lower FVC in adolescence.
Lajunen *et al.* [46]	Prospective	Preschoolers with asthma	4 to 7 years	R5 abnormal preschool (in adolescence OR=9.2 for abnormal FEV_1/FVC, 9.2 for medication, and 9.9 for asthma symptoms)

BDR: Bronchodilator Response; C-ACT: Child-Asthma Control Test; r: Pearson Correlation; LR+: Positive Likelihood Ratio; AUC: Area Under the Curve; OR: Odds Ratio, rho: Spearman Correlation

abnormal spirometry at school age [42]. In the second study, lung function was measured with IOS in preschoolers aged 4, 5, 6 years and spirometry at 5, 6, 7 and 8 years. This study demonstrated that the increase in preschool R5 is able to predict which children will continue to have active asthma or impaired lung function at 8 years of age [43]. Other studies have linked alterations in preschool IOS with decreased lung function measured by spirometry in adolescence. One study showed that high R5 values in asthmatic preschoolers were associated with decreased post-bronchodilator FEV_1 in adolescence [44]. Another study showed that post-bronchodilator X5 values in preschool IOS have a strong correlation with post-bronchodilator FEV_1 and FVC in adolescents [45]. Finally, a prospective study in preschoolers showed that increased preschool R5 was associated with lower FEV_1/FVC, higher medication use, and asthma symptoms in adolescence after 10 years of follow-up [46].

Conclusion

There is evidence demonstrating the usefulness of baseline IOS and its bronchodilator response in the diagnosis of preschool asthma. Combining some parameters of the IOS with asthma predictive algorithms or biomarkers increases the ability to discriminate between preschoolers with asthma and healthy children. The IOS has also been shown to be useful in identifying uncontrolled preschool asthma, patients at risk of future exacerbations, and those who require more controller treatment or have decreased lung function by other methods such as spirometry, methacholine test, bronchial challenge test with exercise or FeNO. Recent evidence allows us to recommend the use of the IOS in preschool asthma to identify patients who will continue to have active asthma or decreased lung function at school age or adolescence. Despite the significant developments of preschool IOS, there are still some limitations, such as not having universal predictive values applicable to different populations or establishing clinically useful cut-off points for the bronchodilator response with the different IOS parameters.

Conflict of Interest

There is no conflict of interest in this study.

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