

# Impulse oscillometry at preschool age predicts lung function by spirometry at school age

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In the current issue of *Pediatric Pulmonology*, Alberto Grell et al from Santiago, Chile, publish their interesting results on impulse oscillometry (IOS) at preschool age compared to flow-volume spirometry (FVS) at school age in 66 children with persistent asthma.<sup>1</sup> When measured at the mean age of 4.9 years, respiratory system resistance at 5 Hz (R5), resonance frequency (Fres), reactance area (AX) and the difference between resistance at 5 and 20 Hz (D5-20) were significant predictors of reduced forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC) and/or FEV1/FVC 3 years later, at the mean age of 7.9 years.<sup>1</sup> The parameters were analyzed also as categorized by limits obtained from international references. Increased AX, D5-20 and R5 had the highest positive likelihood ratios (LR+) of 50, 10, and 7.1, respectively, for reduced FEV1, FVC, and/or FEV1/FVC.<sup>1</sup> Increased R20, R5, and AX were the best predictors for 10% FEV1 rises after bronchodilation (BD), LR+s being 3.4, 2.9 and 2.8, respectively.<sup>1</sup> Roughly, LR+ >5 means, LR+ 3–5 may mean and LR+ <3 does not mean a clinically significant change from the pretest to the posttest probability. Thus, the presented LR+ values for FEV1 rises in the BD test may not be sufficient although the rises were statistically significant. The appropriate LR+ limits are dependent on the pretest probability, which depends on the severity of cases. In the study of Grell et al.<sup>1</sup> all children had persistent asthma. The authors do not report the associations between IOS and post-BD FVS parameters, but LR+ values for pre-BD parameters were so high, that probably, the conclusions would have been similar. Moreover, no data were available on confounding factors and adjusted analyses were not done. The potential current disease-modifying factors such as overweight and medication for asthma were rather similar between the IOS groups.

Two studies from Helsinki, Finland, have evaluated IOS at preschool age with FVS at school age in 154 and 121 children with asthma and/or asthma-like symptoms, respectively.<sup>2,3</sup> In the study of

Knihtilä et al.<sup>2</sup> baseline R5 and frequency-dependent respiratory system resistance (dR/df) at preschool age correlated with post-BD FEV1 at age 12–18 years, but the coefficients were low,  $-0.223$  and  $+0.234$ , respectively.<sup>2</sup> When the parameters were categorized by z-scores  $<1.65$  or  $>1.65$  standard deviations (SD) in the Finnish child population, increased R5 and decreased dR/df were associated with the decreased of-predicted FEV1 in multivariate logistic regression. In the study of Lajunen et al.<sup>3</sup> baseline R5 and Fres at preschool age correlated with baseline and post-BD FEV1 and FEV1/FVC at 12–18 years of age, but the coefficients were only low to modest. When the parameters were categorized by the limits of  $>1.65$  or  $<1.65$  SD, respectively, the significant associations were confirmed with multivariate logistic regression.<sup>3</sup>

A third Finnish study by Lauhkonen et al.<sup>4</sup> was done in Tampere, Finland, and included 64 children who performed IOS at the mean age of 6.3 and FVS at the mean age of 11.4 years. The children had been prospectively followed from hospitalization for bronchiolitis at  $<6$  months of age. Both baseline and post-BD measurements of IOS and FVS were available. The post-BD R5 showed a modest negative correlation with post-BD FEV1 and FEV1/FVC. The BD-induced decrease in R5 showed a modest positive correlation with the BD-induced increase in FEV1. Baseline and post-BD respiratory system reactance at 5 Hz (X5) showed modest correlations with baseline and post-BD parameters in FVS. All these correlations, although not better than modest, were statistically significant. Baseline X5 showed a strong correlation with baseline FVC ( $Rho = 0.61$ ,  $p < 0.0001$ ) and FEV1 ( $Rho = 0.59$ ,  $p < 0.001$ ). Preschool X5 was an independently significant predictor of FVS at teenage also in multivariate analyses.<sup>4</sup> These results based on both pre-BD and post-BD measurements confirm the value of IOS at preschool age, particularly that of X5, as a predictor of FVS at school age after infant bronchiolitis.

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The Chilean study,<sup>1</sup> in line with the two Finnish studies,<sup>2,3</sup> confirmed that IOS at preschool age in asthmatics was able to identify those patients who later had reduced FVS. Our postbronchiolitis cohort study<sup>4</sup> showed similar results in nonasthmatics, who constituted the great majority, 87% to 88%, of the cases at 6.2 and 12.3 years follow-up visits. The wide spectrum of cases including asthmatics and symptom-free nonasthmatics may explain the higher correlations in the study of Lauhkonen et al.<sup>4</sup> than in other Finnish studies done in asthmatics.<sup>2,3</sup>

An optimal design for the study comparing IOS performed at preschool and FVS performed at school age should include baseline measurements, exercise or other challenge tests, bronchodilatation tests and reporting of both baseline and post-BD IOS and FVS results. In addition, multivariate analyses are needed to manage the effects of confounders, as was done in the Finnish studies.<sup>2-4</sup> Some compromises are mandatory if the researchers want to do the measurements during the same 1-day outpatient visit. In two Finnish studies,<sup>3,4</sup> for example, bronchodilators were administered after the exercise challenge test, and therefore, the post-BD results may be biased to the direction of low FEV<sub>1</sub>, FVC, and/or FEV/FVC values.

To receive reliable results by FVS, the blows need to be maximally forced, and usually, this needs an age of 5–7 years. Instead, IOS is measured during tidal breathing, whereas lung function can be measured with IOS as early as at 2–3 years of age. Thus, IOS is the primary lung function method in preschool children, not only in wheezing or asthmatic children, but also as part of the

follow-up of lung function trajectories. The sensitivities and specificities of different IOS parameters may vary by the study population, such as asthmatic or wheezing children, or symptom-free former bronchiolitis patients.

#### AUTHOR CONTRIBUTION

**Matti Korppi:** Conceptualization; writing—original draft.

#### CONFLICT OF INTEREST STATEMENT

The author declares no conflict of interest.

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