ORIGINAL ARTICLE

Small airway dysfunction in asthma: concordance and discordance between spirometry and oscillometry in real-life

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Summary

Background. Small airway dysfunction (SAD) is increasingly recognized as a key feature in asthma, influencing control, exacerbations, and severity. Spirometry remains the gold standard for lung function assessment but mainly reflects large airways, whereas impulse oscillometry (IOS) offers complementary insights into peripheral airway function. **Methods.** A retrospective analysis was conducted on 218 patients referred for asthma-like symptoms or untreated mild asthma to the Allergy and Clinical Immunology Unit of L. Sacco Hospital (Milan). All underwent spirometry and IOS; 169 also completed bronchodilator testing. Concordance, discordance, and correlations were evaluated using chi-square tests, logistic regression, and Pearson's coefficient. **Results.** Among 218 patients (mean age 40 years, 62% female), SAD was detected in 24 by spirometry and 52 by IOS, with significant overall concordance ($p < 0.001$), particularly in patients with asthma-like symptoms. Discordance was associated with older age, female sex, and higher body mass index. Bronchodilator testing showed discordant responses, correlating with exertional symptoms and lower Asthma Control Test (ACT) scores. **Conclusions.** IOS and spirometry provide complementary insights into airway physiology. IOS is more sensitive to peripheral airway abnormalities and can detect distinct bronchodilator responses, whereas spirometry remains the standard assessment tool. Their combined use improves detection and monitoring of small airway dysfunction, especially in early or mild asthma, potentially guiding more personalized management strategies.

Key words
Asthma; small airway dysfunction; oscillometry; spirometry; bronchodilator response

Impact statement: This study highlights the complementary value of spirometry and oscillometry in detecting small airway dysfunction, supporting their combined use to improve early diagnosis, monitoring, and personalized management of asthma.

Introduction

The involvement of peripheral airways in asthma has become increasingly relevant. Traditionally considered a disease of central airways, growing evidence shows that small airways are important sites of inflammation and obstruction (1). These airways, <2 mm in diameter and including terminal and respiratory bronchioles, conduct air to alveoli but, due to their size, are more prone to obstruction (2). In healthy lungs they contribute little to resistance ("silent zone"), but in asthma inflammation and remodeling cause small airway dysfunction (SAD), associated with poor control, exacerbations, nocturnal and exercise-induced asthma (3, 4). SAD is also a hallmark of chronic obstructive pulmonary disease (COPD), linked to higher exacerbation risk and mortality (5). It can occur at all Global Initiative for Asthma (GINA) stages, making its assessment important for personalized therapy, as a treatable trait (6–8).

Different methods exist to evaluate peripheral airways. Biomarkers of inflammation (studied through biopsies, resection samples, exhaled nitric oxide) and imaging (high-resolution computed tomography, gas-enhanced magnetic resonance imaging) provide insights but are rarely used in routine practice (9, 10).

Regarding functional parameters, spirometry remains the most commonly used method. Forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) mainly assess large airways, while indices such as forced expiratory flow at 50% (FEF50) and at 75% (FEF75) of FVC, and especially the average flow over the 25–75% range (FEF25-75) reflect peripheral obstruction (11). However, FEF25–75 lacks standardized cut-offs (ranging from 60% to 75%) and depends on FVC and expiratory time (12, 13).

Impulse oscillometry (IOS), derived from the forced oscillation technique, measures airway resistance and reactance by applying external oscillatory pressure at frequencies between 5 and 20 Hz. Resistance at 20 Hz (R20) represents large airway resistance, while resistance at 5 Hz (R5) reflects total airway resistance, and R5-R20 indicates small airway resistance. Reactance at 5 Hz (X5) can be sensitive to air trapping and ventilation heterogeneity, and, along with the reactance area (AX), describes the elastic recoil and lung distensibility. R5–R20 is the primary parameter in IOS to evaluate the frequency dependence of resistance and is considered pathological if it exceeds 0.07 $kPa \cdot s \cdot L^{-1}$, even though different cut-offs (>0.10 $kPa \cdot s \cdot L^{-1}$) have been proposed in recent years (16, 17).
IOS is a simple, non-invasive technique that does not require forced maneuvers, only tidal breathing, making it suitable across all age groups. Additionally, IOS can detect airway obstruction earlier than spirometry, offering a valuable tool for evaluating lung function, particularly when spirometry falls short in assessing SAD (18, 19). In addition to obstructive diseases, IOS has also been shown to be potentially useful in restrictive lung diseases (20, 21). IOS can further assist in evaluating bronchodilator or bronchoconstriction response in patients presenting with asthma-like symptoms, thereby contributing to the diagnostic work-up of bronchial asthma. Spirometry remains the gold standard for assessing bronchodilator response and airway hyperresponsiveness, with a positive response defined as >10% increase in predicted FEV_1 or FVC (22). For IOS, recent studies suggest that in adults, significant reversibility can be defined as a relative decrease of ≥32% in R5 and a relative increase of ≥44% in X5. However, no validated reversibility cut-offs currently exist for R5–R20 or AX, although a recent international Delphi study suggested that a change in the Z-score for X5 of > +1.4 and for R5 of > –1.4 may indicate a significant bronchodilator response (17, 23, 24).
The aim of the present study is to evaluate the concordance and discordance between spirometry and IOS in assessing SAD in a cohort of patients with asthma-like symptoms or bronchial asthma not receiving treatment at the time of the evaluation. Additionally, in patients who underwent both pre- and post-bronchodilator testing, bronchodilator responses with both techniques were compared. Moreover, the correlation between key spirometric and oscillometric parameters was analyzed across all subjects.

Materials and methods

In this study, 218 subjects evaluated at the Allergy and Clinical Immunology Unit of L. Sacco Hospital (Milan) between June 2024 and June 2025, were retrospectively analyzed. The selected population included individuals attending their first consultation due to respiratory symptoms, undergoing both spirometry and IOS—regardless of whether they received a new diagnosis of bronchial asthma—as well as patients with a prior diagnosis of bronchial asthma who were not receiving treatment at the time of evaluation (GINA stages 1–2). IOS was systematically performed prior to spirometry in all subjects. A subset of patients also underwent a bronchodilator reversibility test, with measurements taken 15 minutes after administration of salbutamol 400 mcg, and compared to pre-bronchodilator values.

The parameters recorded for each patient included age, sex, ethnicity, height, weight, body mass index (BMI), smoking status, presence of gastroesophageal reflux, atopy and sensitization to perennial or seasonal allergens, previous diagnosis of bronchial asthma, presence of symptoms at the time of the visit—specifically nocturnal awakenings or exertional symptoms—and symptom severity according to the ACT score (Asthma Control Test) (25).

IOS was performed using the Tremoflo device (Thorasys) at frequencies ranging from 5 to 20 Hz. Standard spirometry was carried out using the Quark PFT device (Cosmed). The analysis considered FVC, FEV_1, FEV_1/FVC, and FEF25-75 for spirometry, as well as R5, R5-R20, X5, and AX for IOS. To evaluate peripheral airway dysfunction, pathological cases were defined as those with FEF25-75% <65% in spirometry and R5-R20 >0.07 $kPa \cdot s/L$ in IOS (16, 26). Concordance and discordance between IOS and spirometry in assessing peripheral airways were analyzed. Additionally, in patients who underwent bronchodilator testing, differences in bronchodilator responsiveness between IOS and spirometry were assessed. According to the updated 2022 ERS/ATS guidelines, a bronchodilator response on spirometry was considered positive when there was an increase of >10% in predicted FEV_1 or FVC (22). For IOS, bronchodilator response was considered positive if there was a relative change of -32% in R5 or +44% in X5, with either parameter alone being sufficient to indicate a positive response (17, 23). Finally, FEF25–75, R5–R20, X5, and AX values were compared as indicators of peripheral airway function.

Statistical analysis was performed using the chi-square test to evaluate associations between categorical variables. Univariate logistic regression was applied to assess the association between each covariate and discordant patients, reporting estimated coefficients (β_1) and predicted probabilities. Correlations between spirometry and IOS parameters were assessed with Pearson's correlation coefficient, and effect sizes were interpreted according to Cohen's guidelines. A p-value < 0.05 was considered statistically significant. Python 3.11 was used for statistical analysis.

Results

Population characteristics

A total of 218 patients were included in this analysis, comprising 135 women and 83 men. The majority of participants (93%) were of Caucasian ethnicity. The mean age of the cohort was 40 years and 201 (92%) had atopy. Among the subjects with atopy, 98% had allergic rhinitis as a comorbidity. In addition, 83 individuals (38%) had a prior diagnosis of bronchial asthma and were not receiving treatment at the time of the visit. Table I provides a detailed descriptive analysis of the participants, including spirometric and oscillometric values.

Concordance between IOS and spirometry for the diagnosis of SAD

Out of 218 subjects analyzed, pathological spirometric values regarding the small airways were observed in 24 subjects, while pathological values for small airways in IOS were identified in 52 subjects (Table II). A chi-square test for independence was performed to assess concordance between spirometry and IOS, yielding a p value < 0.001 and indicating a significant statistical dependence between the two methods. When the analysis was performed separately, patients with known asthma showed no significant association between IOS and spirometry ($p = 0.225$). In contrast, in patients with asthma-like symptoms, with or without a previous asthma diagnosis, a strong statistical dependence between the two methods was observed ($p < 0.001$).

In patients in whom small airway dysfunction (SAD) was diagnosed as positive by only one of the two methods (IOS or spirometry), it was assessed whether such diagnostic discordance was associated with clinical and demographic features. Of all the factors considered, only age, sex, and BMI showed statistically significant p-values, as reported in Table III. None of the other factors, including smoking status and atopy, were identified as significant predictors in patients with discordant results. The estimated probability of discordance was then analyzed using logistic regression. The analysis showed that the probability of being discordant increased with age. Regarding sex, female sex was associated with a slightly higher probability of discordance. Finally, the analysis showed that the probability of discordance significantly increased with increasing BMI.

Concordance between IOS and spirometry in bronchodilator reversibility test

As a second main analysis of the study, the number of patients with a significant bronchodilator reversibility test by spirometry and IOS was investigated. Among patients with discordant results between the two methods, it was assessed whether there was a significant association with clinical and demographic factors. In the study, bronchodilation testing was performed on 169 patients. Bronchodilator reversibility was positive by spirometry in 39 subjects and by IOS in 20 subjects, as shown in Table IV. A chi-square test of independence was repeated and a p-value <0.001 was obtained, allowing the conclusion that the two testing methods are not independent. Subsequently, statistical analysis was conducted on patients with discordant results. Unlike previous findings, significant factors associated with discordance in bronchodilator reversibility test results between the two methods were exercise-induced symptoms and the ACT score (Table V). These results indicate that a lower ACT score (reflecting a higher presence of asthma-like symptoms) increased the likelihood of discordant results in the bronchodilator reversibility test between the two methods. This probability was further increased in the presence of exercise-induced symptoms.

Correlations between key spirometric and oscillometric parameters

An additional correlation analysis between spirometry and IOS parameters was performed using Pearson's correlation coefficient (Table VI). Specifically, potential linear relationships were investigated between the following predicted values: FEF25-75, R5-R20, X5, and AX. Correlation analysis of spirometric and oscillometric parameters revealed several notable relationships. The correlation between FEF25-75 and R5-R20 was moderate and negative ($r = -0.35$), suggesting that as R5-R20 increases, FEF25-75 tends to decrease, although this association was not particularly strong. Conversely, FEF25-75 and X5 showed a moderate positive correlation ($r = 0.35$), indicating a mild but consistent positive relationship. The correlation between FEF25-75 and AX was also negative and moderate ($r = -0.35$), pointing to a slight decrease in AX with increasing FEF25-75. A strong negative correlation was observed between R5-R20 and X5 ($r = -0.76$), implying a significant inverse relationship between these parameters. In contrast, R5-R20 and AX demonstrated a strong positive correlation ($r = 0.85$), indicating a robust direct association. Lastly, the correlation between X5 and AX was very strong and negative ($r = -0.94$), reflecting a pronounced inverse relationship, where increases in X5 were accompanied by sharp decreases in AX.

Discussion and conclusion

This retrospective study, conducted in 218 subjects with asthma-like symptoms or untreated asthma, offers a real-life perspective from an allergy center on the role of spirometry and IOS in assessing SAD and bronchodilator responsiveness. The study population was clinically and demographically heterogeneous, with a mean age of 40 years, a predominance of females and Caucasians, and only a minority belonging to other ethnic groups. Most participants were atopic (92%), almost all had concomitant allergic rhinitis (98%), and 22% were smokers. The inclusion of both untreated asthmatic patients and individuals with asthma-like symptoms allowed for the evaluation of small airway function without the confounding effect of pharmacological therapy.

The analysis demonstrated a significant degree of concordance between IOS and spirometry. Agreement was especially strong in patients with asthma-like symptoms ($p < 0.001$), suggesting that IOS may have a valuable role early in the disease course, when peripheral airway abnormalities are already present but have not yet substantially influenced traditional spirometric indices. In contrast, concordance was lower in patients with established asthma, likely reflecting disease heterogeneity, and airway remodeling, which cause the two modalities to capture different but complementary aspects of airway physiology.

Importantly, IOS identified a higher prevalence of SAD than spirometry (52 vs. 24 patients by R5–R20 and FEF25–75, respectively). This finding is consistent with previous literature indicating that oscillometry is more sensitive in detecting subtle or early abnormalities of the peripheral airways that do not necessarily impact spirometric indices (27, 28).

The analysis of factors associated with discordance revealed that older age, female sex, and higher BMI were independent predictors. In patients with these characteristics, oscillometry detected a higher prevalence of SAD compared with spirometry (Table II). The greater likelihood of discordance with advancing age may reflect age-related structural and functional changes in the peripheral airways and lung parenchyma. In addition, spirometry can be more challenging to perform accurately in elderly patients, as it requires greater respiratory effort and coordination than IOS. In women, anatomical differences and lower lung volumes compared to men may reduce the reliability of FVC-based indices such as FEF25–75. Similarly, the association with higher BMI aligns with previous studies reporting more heterogeneous ventilation patterns and increased peripheral airway resistance in overweight and obese individuals (29, 30).

With regard to bronchodilator response, agreement between IOS and spirometry was statistically significant ($p < 0.001$) but incomplete. Spirometry identified a larger number of positive responders (39 vs. 20), yet IOS uniquely detected eight patients with a positive response based solely on oscillometric criteria, suggesting improvements localized to the peripheral airways not captured by conventional spirometric parameters. Conversely, 27 patients were positive only by spirometry, reinforcing the notion that the two methods assess different physiological domains. This finding contrasts with previous reports in adults, where oscillometry has often been found to detect bronchodilation more frequently than spirometry, with changes in X5 and AX correlating with spirometric responses and identifying a greater proportion of patients with poor asthma control compared to spirometry (31). The observation that spirometry identified more positive bronchodilator responders than IOS may have several explanations. Among these, the current criteria for IOS bronchodilator response could be too stringent in a mild asthma population, potentially underestimating reversibility in peripheral airways. Additionally, bronchodilation in this cohort may have predominantly occurred in the larger airways, better reflected by FEV_1. These findings highlight the need for further studies to refine IOS thresholds and to explore bronchodilator effects across the airways.

Discordance in bronchodilator testing was more frequent among patients with exertional symptoms and lower ACT scores, factors that may indicate a distinct clinical phenotype and warrant further exploration in future studies. Correlation analyses between oscillometric and spirometric parameters further underscored their complementary roles. Moderate negative correlations were observed between R5–R20 and FEF25–75, as well as between AX and FEF25–75, while the strong inverse relationship between X5 and AX confirmed the internal consistency of these oscillometric indices as robust markers of peripheral airway dysfunction. Collectively, these findings suggest that incorporating IOS into clinical practice could improve the detection and monitoring of SAD, particularly in patients with mild asthma discordant spirometric findings, or in those unable to perform forced expiratory maneuvers (32, 33). From a therapeutic perspective, the findings of this study support personalized management based on both spirometry and IOS results. In patients with pathological IOS, extra-fine formulations were preferred to optimize delivery to the peripheral airways. In treatment-naïve subjects with normal functional tests, clinical judgment guided the decision to either exclude asthma or initiate maintenance or on-demand therapy, with short-term follow-up to assess response.

The study has limitations, including its retrospective single-center design, lack of longitudinal follow-up, and reliance on a single cut-off for SAD, which may not fully capture the spectrum of airway dysfunction. The predominantly Caucasian population may limit generalizability, and selection bias cannot be excluded. SAD was defined using fixed cut-offs based on previous literature; however, FEF25−75 lacks standardized thresholds, and applying alternative definitions, such as the lower limit of normal, could substantially change the concordance between spirometry and IOS. Future research should involve larger, more diverse populations and refine oscillometric thresholds for diagnosis and bronchodilator response. Moreover, a key limitation in the field is the lack of a true gold standard for non-invasive assessment of SAD. In this study, spirometry and IOS were compared, demonstrating that they provide complementary information; however, in cases of discordant results, it remains unclear which method most accurately reflects small airway dysfunction.

In conclusion, IOS and spirometry play complementary roles in assessing small airway function. Spirometry remains the standard tool, but IOS offers greater sensitivity to peripheral abnormalities and unique insights into bronchodilator responsiveness. The observed discordance underscores their evaluation of distinct physiological domains, supporting their combined use in clinical practice. Prospective multicenter studies are needed to validate IOS cut-offs, define the prognostic significance of IOS-defined responses, and determine their impact on asthma management and outcomes.

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Parameter	Value
Sex, F/M	135/83
Age, years	39.59 ± 15.30
BMI, kg/m²	24.68 ± 4.73
Ethnicity	Caucasian: 202, African: 6, Asian: 1, Hispanic: 8, Indian: 1
Atopy, yes (with rhinitis)/no	201(198)/17
Smoking habit, yes/no/former	49/147/22
Known asthma, yes/no	83/135
Asthma duration, years	12.87 ± 9.22
FVC, % pred	98.16 ± 15.14
FEV_1, % pred	99.02 ± 18.31
FEV_1/FVC, % pred	100.70 ± 12.62
FEF25-75, % pred	102.06 ± 32.95
R5-R20, kPa·s·L^{-1}	0.04 ± 0.06
X5, kPa·s·L^{-1}	-0.16 ± 0.09
AX, kPa·L^{-1}	0.97 ± 1.26

Table I: The table shows the mean values and standard deviations, where applicable, along with the distribution of categorical variables. BMI = body mass index; FVC = forced vital capacity; FEV_1 = forced expiratory volume in 1 second; FEF25-75 = forced expiratory flow between 25 and 75% of forced vital capacity; R5-R20 = difference between resistance at 5 Hz and 20 Hz; X5 = reactance at 5 Hz; AX = reactance area.

	Non-Pathological IOS	Pathological IOS (SAD)
Non-Pathological Spirometry	n=158	n=36
Pathological Spirometry (SAD)	n=8	n=16

Table II: n = number of subjects; Pathological Spirometry = FEF25-75 < 65%; Pathological IOS = R5-R20 >0.07 kPa·s/L; SAD = small airway dysfunction

Factors	**Estimated β_1 coefficient**	**p-value**	**95% confidence interval**
Age	0.034	0.002	[0.012, 0.055]
Sex	-1.057	0.009	[-1.849, -0.265]
Body mass index	0.098	0.004	[0.031, 0.165]

Table III: Factors significantly associated with discordance between spirometry and IOS in detecting SAD. Estimated logistic regression coefficients and corresponding p-values are shown. Positive coefficients indicate that higher values of the factor increase the likelihood of discordance, whereas negative coefficients indicate a decrease. In this analysis, the negative coefficient for sex indicates that female patients (coded as 0) have a slightly higher probability of discordance compared to male patients (coded as 1). For clarity, 95% confidence intervals for the estimated coefficients are also provided.

	Negative bronchodilator test on IOS	Positive bronchodilator test on IOS
Negative bronchodilator test on spirometry	122	8
Positive bronchodilator test on spirometry	27	12

Table IV: ***Patients with positive bronchodilator test results by both methods.*** n ***= number of subjects. IOS = impulse oscillometry. Positive bronchodilator test on spirometry defined as an increase of >10% in predicted*** FEV_1 ***or FVC after salbutamol administration. Positive bronchodilator test on IOS defined as a relative change of -32% in R5 or +44% in X5 after salbutamol administration.***

Factors	**Estimated β_1 coefficient**	**p-value**	**95% confidence interval**
Exertional symptoms	1.144	0.004	[0.369, 1.919]
Asthma Control Test (ACT)	-0.112	0.017	[-0.204, -0.020]

Table V: Factors significantly associated with discordance between positive bronchodilation tests on spirometry and IOS. Estimated logistic regression coefficients and corresponding p-values are shown. Positive coefficients indicate that higher values of the factor increase the likelihood of discordance, whereas negative coefficients indicate that higher values decrease it. For example, the negative coefficient for ACT indicates that lower ACT scores are associated with increased discordance. For clarity, 95% confidence intervals for the estimated coefficients are also provided.

	FEF25-75%, $kPa\cdot s\cdot L^{-1}$	R5-R20, $kPa\cdot s\cdot L^{-1}$	X5, $kPa\cdot s\cdot L^{-1}$	AX, $kPa\cdot s\cdot L^{-1}$
FEF25-75%	r= 1.000000	r= -0.354617	r= 0.347281	r= - 0.354348
R5-R20, $kPa\cdot s\cdot L^{-1}$	r= - 0.354617	r= 1.000000	r= - 0.764700	r= 0.853660
X5, $kPa\cdot s\cdot L^{-1}$	r= 0.347281	r= - 0.764700	r= 1.000000	r= - 0.942186
AX, $kPa\cdot s\cdot L^{-1}$	r= - 0.354348	r= 0.853660	r= - 0.94216	r= 1.000000

Table VI: Pearson's correlation analysis between spirometry and IOS. r = Pearson's correlation coefficient; FEF25-75 = forced expiratory flow between 25 and 75% of forced vital capacity; R5-R20 = difference between resistance at 5 Hz and 20 Hz; X5 = reactance at 5 Hz; AX = reactance area.