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Comparative evaluation of impulse oscillometry and spirometry for the detection of small airway disease in patients with obstructive airway diseases

Kamendra Singh Pawar,[1] Rohit Kumar,[1] Shibdas Chakrabarti,[2] Neeraj Kumar Gupta,[1] Tanmaya Talukdar,[1] Pranav Ish,[1] Nitesh Gupta,[1] Rajnish Kaushik[1]

[1]Department of Pulmonary, Critical Care and Sleep Medicine, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi; [2]Department of Respiratory Medicine, SGT Medical College and Hospital, Gurgaon, Haryana, India

Correspondence: Kamendra Singh Pawar, Department of Pulmonary, Critical Care and Sleep Medicine, Vardhman Mahavir Medical College and Safdarjung Hospital, NH-48, Ansari Nagar West, 110029, New Delhi, India.
Tel.: +91-8462076012. E-mail: kamendrasinghpawar@gmail.com

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Abstract

Although there is some evidence supporting a correlation between impulse oscillometry (IOS) and spirometry for detecting small airway disease (SAD), in many cases, discordant results are observed. IOS has not yet been established as a standard method for routine pulmonary function assessment in clinical practice. We did this study with the primary objective of diagnosing SAD in patients with obstructive airway diseases (OAD) using IOS and comparing it with spirometry. This cross-sectional, comparative study was conducted from July 2023 to December 2024. Adult patients (≥18 years of age) with diagnosed stable OADs [asthma, chronic obstructive pulmonary disease (COPD), and bronchiectasis] were included in the study (n=118). Maximum expiratory flow 25-75 with a Z score of <-1.64 and resistance at 5 Hz - resistance at 20 Hz (R5-R20) >150% were criteria used for defining small airway obstruction in spirometry and IOS, respectively, and were compared. As secondary outcomes, correlation of severity of SAD across COPD groups, Global Initiative for Asthma (GINA) steps using IOS, and comparison of bronchodilatation responsiveness (BDR) were also done. In pre-BDR, IOS and spirometry diagnosed SAD in 94.91% and 82.20% of patients, respectively (p=0.069). There was poor agreement (κ=0.155) between these modalities pre-BDR; however, post-BDR, there was fair agreement (κ=0.277) between these modalities, and both modalities for the detection of SAD were significantly related (p=0.003). Across various Global Initiative for Chronic Obstructive Lung Disease groups, there was no significant difference in the severity of SAD, while across various GINA steps, there was a significant difference in the severity of SAD, especially GINA step 1-2 and step 5. There was poor agreement between these modalities for the BDR test. In conclusion, both modalities performed differently in pre-BDR (discordant) and post-BDR (concordant) settings. For the BDR test, both modalities are not exchangeable. Further research is warranted to determine the optimal setting (pre-BDR *vs*. post-BDR).

Key words: impulse oscillometry, spirometry, small airway disease, obstructive airway disease, bronchodilatation responsiveness.

Introduction

Asthma and chronic obstructive pulmonary disease (COPD) represent the majority of the obstructive airway disease (OAD) burden. COPD is primarily regarded as a small airway disease (SAD), while there is growing recognition that SAD is also a significant component of asthma [1,2]. Small airways are those with a diameter of less than 2 mm lack cartilage in their walls and extend from approximately the 8th generation to the alveoli [3]. The small airways are prone for obstruction and various pathologies owing to small size [4]. The physiological consequences of small airway obstruction may include increased airway resistance, reduced airflow, air trapping, and ventilation mismatches [5].

Spirometry is the most commonly used modality in practice for assessing SAD due to its availability and ease of use. Forced expiratory flow 25-75% (FEF25-75%) is more sensitive than forced expiratory flow in one second (FEV1) for assessing small airway function. It is less effort-dependent than FEV1 and is useful in measuring SAD [6]. However, spirometry requires active patient cooperation, which can be challenging to obtain in children, elderly, and frail patients.

Impulse oscillometry (IOS) is simple, safe, noninvasive modality requiring minimal patient cooperation, based on principles of forced oscillation technique that uses sound waves to measure respiratory mechanics. IOS can identify subtle changes in the small airways even when spirometry results are normal, providing valuable information for the early diagnosis and monitoring of airway diseases [7].

Small airway involvement in COPD, as assessed by IOS, is observed in up to 74% of cases and is present in both COPD phenotypes [8]. A recent review reported that 50-60% of asthma patients have small airway disease [9].

SAD in asthma has been linked to more severe exacerbations, poor asthma control, and increased airway hyperresponsiveness [10]. The presence of SAD in COPD is also linked to air trapping, poorer spirometric function, and worse health status, highlighting the importance of small airways as a key treatment target [11]. Spirometric bronchodilator responsiveness (BDR) primarily measures the responsiveness of proximal airway obstruction. In a large proportion of OAD, small airways are involved, the clinical significance of small airway BDR remains unclear [12]. A recent review summarized that forced oscillation may detect significant BDR that spirometric parameters might miss, although there can be issues with the reproducibility of IOS [13].

Although there is some evidence supporting a correlation between IOS and spirometry for

detecting SAD, impulse oscillometry has not been established as a standard method for routine pulmonary function assessment in clinical practice [14,15]. In many cases, discordant results are observed. There is relative paucity of literature and further studies are needed to compare IOS and spirometry for detecting SAD, in order to bridge the knowledge gaps related to this important small airway target. The present study was undertaken with aim to compare IOS and spirometry in diagnosing small airway involvement in patients with obstructive airway diseases.

Materials and Methods

Study design and study population

The present study was cross sectional, comparative study conducted at our tertiary care teaching hospital from July 2023 to December 2024. Adult patient ≥ 18 years of age with diagnosed stable OADs namely asthma, COPD and bronchiectasis as per existing guidelines were included in study [16-18]. Patient with any contraindications for performing spirometry and IOS, acute exacerbations in previous four weeks and having pulmonary infections or malignancies were excluded.

Aim of the study

Primary objective was to diagnose SAD in patient with OAD using IOS and compare with spirometry. Secondary objectives were 1. Correlate severity of SAD across Global Initiative for Asthma (GINA) steps in asthma using IOS 2. Correlate severity of SAD across Global initiative for Chronic Obstructive Lung disease (GOLD) groups in COPD using IOS 3. Compare BDR between IOS and spirometry across OAD.

Methodology

Patients diagnosed with OAD who met the inclusion criteria underwent a comprehensive clinical and demographic evaluation. Each patient underwent IOS and spirometry, with a BDR test conducted using both methods [17]. For BDR test 4 puffs of 100ug pressurized metered dose inhaler salbutamol was used. Bronchodilation response was assessed 10-15 minutes later. If patients were using bronchodilators, these were withheld according to current recommendations prior to performing the maneuver and BDR test [19]. First, patient performed IOS using available IOS system (The tremoflo® C-100 airwave oscillometry system by schiller healthcare pvt ltd Switzerland) as per standard protocol [20].

Demonstration of technique was done by trained technician. Minimum acquisition time was 30 seconds. There was repeating acquisitions until at least three measurements have been recorded that are free of artefacts (both pre and post bronchodilatation). The coefficient of variation (Cov) between replicates was to be ⩽10%. The average of measurable IOS parameter from three measurements was taken up for analysis. The resistance at 5Hz (R5), resistance at 20 Hz (R20), R5-R20, reactance at 5 Hz (X5) and area under curve reactance (AX) was taken up for interpretation. The value of R5-R20 greater than 150% predicted was taken as abnormal and defining for small airway obstruction. For defining positive BDR, −40% in R5, +50% in X5 and −80% in AX was taken in account [20].

Next, Spirometry was performed with available spirometry system (GANSHORN LFX 1.9 with Power Cube Spiro+ by Ganshorn Medizin Electronics GmbH Germany).

Patient preparation, instructions, demonstration, maneuver was done as per standard protocol of spirometry [19]. Test was repeated for a minimum of three maneuvers. Acceptability and repeatability criteria were checked. Maneuver with largest sum of FEV1 and forced vital capacity (FVC) was taken up for interpretation [19]. For defining obstruction for COPD, post bronchodilator FEV1/FVC <0.7 was taken [17]. For assessing severity of obstruction in asthma and bronchiectasis, Z scores was used as: Mild: (−1.65 to −2.5) Moderate: (−2.51 to −4.0) and Severe: (<−4.1). Maximum Expiratory Flow 25-75 (MEF25-75) was used with Z score < -1.64 taken as abnormal and defining for small airway obstruction in spirometry test. For defining positive BDR test during spirometry, change >10% of predicted value in FEV1 or FVC was considered [21]. A comparison between IOS and spirometric parameters for detecting small airway obstruction was made using R5-R20 and MEF25-75.

Patients with asthma were categorized in as per GINA steps 1-5 [16]. Similarly patient with COPD was categorized as per ABE assessment tool [17].

Ethical considerations

Ethical clearance was obtained from the institutional ethical committee and written informed consent from each patients were obtained before enrollment.

Statistical analysis

Data was entered in MS Excel and was analyzed in SPSS (statistical package for the social sciences) version 25 (IBM Corp. Armonk, NY, United States). Continuous data were

expressed as mean ± standard deviation (if normal distribution) or median (IQR) (if non normal distribution). Categorical data were expressed as frequency and percentage. Comparisons between quantitative variables was done using the T test/Mann– Whitney U tests. For comparing categorical data, chi-square ($\chi 2$) test/Fisher's exact test was performed. Correlations between quantitative variables was done using Pearson/Spearman rank correlation coefficient. Interrater agreement between impulse oscillometry and spirometry was taken out. P value ≤ 0.05 was considered statistically significant.

Results

In present study, total 118 patient included for final analysis. There were 41 (34.74%) patients with COPD, 61 (51.69%) patients with asthma, and 16 (13.55%) patients with bronchiectasis, constituting a heterogeneous patient population.

Baseline characterstics

Majority of patients in our study were males (N=70, 59.32%), however in the asthma group, females were predominant in number (N=36, 59.0%). The average age of the patient was 48.43 ± 15.66 years. The COPD patients were slight older as compared to other disease groups (mean age 57.73 years). The majority of patients were non-smokers (N=75, 63.55%), although in the COPD group, 80.48% had a history of smoking, with a mean pack years of 15.80. The mean serum AEC was 246.48 ± 171.17 per microliter (see *Supplementary Tables 1 and 2*). The R5-R20 (cmH2o.s/L) and MEF 25-75 ((L/s) values were worse in COPD patient compared to asthma patient (2.94 vs 2.37 and 0.49 vs 1.60, respectively).

However, in the bronchiectasis group, IOS parameters such as R5 (cmH2o.s/L) (7.54 vs 6.72 vs 6.74) and R5- R20 (cmH2o.s/L) (3.29 vs 2.94 vs 2.37) were worse compared to COPD and asthma patients respectively (*Supplementary Tables 3 and 4*). Majority of COPD patient belonged to group E (N= 17, 41.46%). Majority of asthma patient were having allergic phenotype (N= 25, 40.98%). In bronchiectasis patient, the most common etiology was idiopathic, found in 6 patients (37.5%), followed by post infectious in 5 patients (31.25%).

Primary objective analysis

Pre BDR analysis of OAD patient for diagnosis and comparison revealed, SAD was diagnosed using IOS in 112 (94.91%) patients, while spirometry diagnosed SAD in 97 (82.20%)

patients (P value = 0.069, nonsignificant).

The kappa value was 0.155, indicating poor agreement between the two diagnostic modalities for detecting SAD, which was statistically significant (P value = 0.034) (Table 1).

Post BDR analysis of OAD patients for diagnosis and comparison revealed, in 104 (88.13%) patients, SAD was diagnosed using IOS, while in 91 (77.11%) patients, SAD was diagnosed with spirometry (P value = 0.003, statistically significant).

The kappa value was 0.277, indicating fair agreement between the two modalities for detecting SAD, which was statistically significant (P value = 0.001) (Table 2).

Further subgroup analysis pre and post BDR shown in *Supplementary Tables 5 and 6*.

There was moderate negative correlation which is statistically significant between R5-R20 and MEF 25-75 both pre BDR and post BDR (r -0.55, p value <0.001 and r -0.56, p value <0.001 respectively).

Analysis of secondary objectives

Analysis of severity correlation among COPD groups, result showed the mean values of R5-R20 (cmH2o.s/L) in Group A, Group B, and Group E was 2.91, 2.84, and 3.03, respectively, in the pre-BDR group. In both pre and post BDR, no significant intergroup difference in the severity of R5-R20 was seen (ANOVA test, P value = 0.931, and P value = 0.738 respectively). Similarly, no significant intergroup difference in the severity of MEF25-75 (both pre and post BDR) was seen (ANOVA test P value = 0.107, P value = 0.263 respectively) (Table 3).

For analysis of severity correlation among GINA steps, the mean values of R5-R20 (cmH2o.s/L) for GINA Step 1-2, Step 3, Step 4, and Step 5 were 1.49, 2.25, 2.89, and 2.87, respectively (ANOVA test, P value = 0.008), indicating a significant intergroup difference in the pre-BDR group. In the post hoc Tukey HSD test, a significant difference was observed between GINA Step 1-2 and Step 4 (P value = 0.019) and between GINA Step 1-2 and Step 5 (P value = 0.021). In post BDR, a significant intergroup difference was seen (ANOVA P value = 0.024). In the post hoc Tukey HSD test, a significant difference was observed between GINA Step 1-2 and Step 5 (P value = 0.011). Similarly a significant intergroup difference was seen for MEF25-75 both pre and post BDR across GINA steps (ANOVA test P value = 0.013, P value = 0.009) (Table 4).

Analysis of comparison of BDR between two modalities result showed, BDR was detected using IOS in 19 (16.10%) patients, while in 23 (19.49%) patients, BDR was detected using

spirometry (P value = 0.055, nonsignificant). The kappa value was 0.191, indicating poor agreement between the two modalities for detecting BDR, which was statistically significant (P value = 0.037) (Table 5).

Discussion

Primary objective of our study was to diagnose and compare IOS and spirometry for detection of SAD in patients with OAD. In 94.91% and 82.20% of patients, SAD was diagnosed using IOS and spirometry respectively in pre BDR group however difference between the two methods was not statistically significant (P value= 0.069). The inter rater agreement between this both modalities was poor in pre BDR group (κ 0.155 P value= 0.034) implying that while both methods are used to diagnose SAD, they may not always identify the condition in the same individuals. Our data in the pre BDR group suggest that there is no additional advantage of IOS over spirometry for SAD detection. IOS is not easily accessible due to cost concerns, whereas spirometry is widely available.

In the post-BDR group, there was a slight decrease in the number of patients diagnosed with SAD using IOS (88.13%) and spirometry (77.11%), possibly due to the effect of bronchodilation consistent with other studies however post BDR between both modalities difference was significant indicating a statistically significant relationship between IOS and spirometry for diagnosing airway disease [22]. This suggests that, in this context, the results from both tests are more likely to be related and consistent. The inter rater agreement between this both modalities suggests fair agreement (κ 0.277 p value 0.001) between the two tests in diagnosing SAD post BDR. This suggests that the two methods are more aligned in their results compared to the pre BDR values. This change post BDR suggests that the small airways, which might have been constricted or less responsive pre-BDR, are now more accessible, in fact reversible and both tests can detect this change more effectively. Considering this difference pre and post BDR, its preferable to use both IOS and spirometry complimentary to each other and further research and studies are needed to identify optimal settings (pre BDR vs post BDR). Other studies also found slight agreement between spirometry and IOS in the diagnosis of SAD, results are similar to our study seen post BDR [23,24]. There was a moderate negative correlation between the variables R5-R20 and MEF25-75 , which is statistically significant both pre and post BDR in our study. Similar result has been seen in previous studies [14,15,24-26]. The prevalence of SAD is high (94.91% and 82.20% pre-BDR) as detected by both tests in OAD patients in our

study. In an Indian study [27], SAD, as measured by R5-R20 >150%, was found in 27.3% of patients, despite being recruited from GINA step 4 and 5. In another study [28], using a cut-off of R5-R20 >0.075 kPa.L-1s, the prevalence of SAD was 77% in non-fixed airway obstruction (FAO) asthma, 95% in FAO-asthma, and 68% in the COPD group. The prevalence of SAD varies across studies and depends on the modality used for detection and cut off used. Our study contributes to this observation, highlighting the differences in detection rates based on the methods employed.

The prevalence of SAD in COPD group A, B and E does not steadily increased in our study as measured by IOS in contrast to previous studies [8]. There was no inter group difference in severity of SAD as assessed by IOS and spirometry both pre and post BDR in our study. Other studies has reported increase in respiratory resistance values as GOLD stage increases [8,26].

The prevalence of SAD across various GINA steps as measured by IOS was 81.25% to 100% and 68.75% to 100% in pre and post BDR groups respectively in our study. Other studies shown similar trend [25], but the ATLANTIS study showed that the prevalence of SAD increased as the severity of asthma worsened across GINA steps 1-5 [29]. There was significant intergroup difference in severity of SAD across all GINA steps both pre and post BDR as assessed with any of modalities (ANOVA P value <0.05) in our study. In post hoc analysis using Tukey HSD test, the significant difference was seen between GINA step 1-2 vs step 4 and step 5. Other studies result also showed small airway resistance progressively increased with the increasing GINA steps and was significantly higher in steps 4–5 compared to others [25].

There was statistically not-significant difference (P value=0.055) and poor agreement (κ 0.191) between this modalities for detection of BDR in our study. Other studies have shown similar results [30,31]. Due to poor agreement between IOS and spirometry, IOS cannot be considered suitable alternative for spirometry and both should not be used interchangeably as well. The poor agreement is more likely related to different airway physiology and principle that these modalities actually detect and utilize respectively as postulated before [30].

There are certain limitations to our study, first, this is a cross-sectional study predominantly consisting of asthmatic patients which may hamper generalizability of our findings, particularly in relation to COPD and bronchiectasis. However most of previous studies done included either asthma or COPD or bronchiectasis patient, heterogeneous nature of patient

population makes our study novel in this regards. Second, currently, there are no universal diagnostic criteria for SAD in either spirometry or IOS. To enhance interpretive accuracy, the MEF25-75 Z score was used. Similarly, R5-R20 needs to be more widely accepted for detecting SAD and defining abnormalities using various parameters, such as predefined cutoffs, z-scores, and percent predicted values, remains a subject of debate. Third, although there is no gold standard noninvasive test for SAD detection, we lacked confirmatory tests for small airway dysfunction like HRCT chest.

Conclusions

Our study demonstrates a high prevalence of SAD across various obstructive airway diseases. There was difference in performance of IOS and spirometry pre and post BDR. Our study highlights that IOS and spirometry should be used in conjunction with each other in diagnosis of SAD and further research and studies are needed to identify optimal settings (pre BDR vs post BDR).

Across various GOLD groups, there was no significant difference in severity of SAD while across various GINA steps, there was significant difference in severity of SAD especially GINA step 1-2 and step 5. There was poor agreement between these modalities for BDR test. Our study also highlights that for BDR testing, IOS and spirometry are not exchangeable.

Since there is high prevalence of SAD in OAD groups, identification of SAD in routine clinical practice should get more attention as emerging evidence suggest SAD is associated with worse symptom control and quality of life. IOS and spirometry are not to be considered as replacement of each other but used and interpreted complimentary to each other for SAD detection. Further studies and research are needed for defining role of both modalities in SAD detection in established cases of OAD and optimal setting (pre BDR vs post BDR).

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Online supplementary material:

Supplementary Table 1. Demographical and clinical characteristics of the study participants.

Supplementary Table 2. Respiratory and treatment characteristics of the study participants.

Supplementary Table 3. Spirometric and impulse oscillometry parameters among obstructive airway disease and chronic obstructive pulmonary disease patients (pre- and post-bronchodilatation responsiveness).

Supplementary Table 4. Spirometric and impulse oscillometry parameters among asthma and bronchiectasis (pre- and post-bronchodilatation responsiveness).

Supplementary Table 5. Small airway disease (pre-bronchodilatation responsiveness) diagnosis and comparison using impulse oscillometry and spirometry across chronic obstructive pulmonary disease patients, asthma and bronchiectasis.

Supplementary Table 6. Small airway disease (post BDR) diagnosis and comparison using IOS and spirometry across COPD, asthma and bronchiectasis.

Table 1. Small airway disease (pre-BDR) diagnosis and comparison using IOS and spirometry in OAD patients.

	Spirometry (MEF 25-75 Z score<-1.64) SAD Absent N(%)	Spirometry (MEF25-75 Z Score <-1.64) SAD Present N(%)	Total
IOS (R5-R20 >150%)			
SAD absent N(%)	3 (2.54%)	3 (2.54%)	6 (5.08%)
SAD present N(%)	18 (15.25%)	94 (79.66%)	112 (94.91%)
Total	21 (17.79%)	97 (82.20%)	118 (100%)
p-value			0.069
Cohen's κ			0.155 (p=0.034)

SAD, small airway disease; IOS, impulse oscillometry; MEF25-75, maximum expiratory flow 25-75.

Table 2. Small airway disease (post-BDR) diagnosis and comparison using IOS and spirometry in OAD patient-

	Spirometry (MEF 25-75 Z score<-1.64) SAD Absent N(%)	Spirometry (MEF 25-75 Z Score <-1.64) SAD Present N(%)	Total
SAD IOS (R5-R20 >150%)			
SAD absent N(%)	8 (6.77%)	6 (5.08%)	14 (11.86%)
SAD present N(%)	19 (16.10%)	85 (72.03%)	104 (88.13%)
Total	27 (22.88%)	91 (77.11%)	118 (100%)
p-value			0.003
Cohen's κ			0.277 (p=0.001)

SAD, small airway disease; IOS, impulse oscillometry; MEF25-75, maximum expiratory flow 25-75.

Table 3. Severity correlation across COPD groups by IOS and spirometry.

COPD Group	R5-R20 (pre-BDR) Mean (SD)	MEF 25-75 (pre-BDR) Mean (SD)	R5-R20 (post-BDR) Mean (SD)	MEF 25-75 (post-BDR) Mean (SD)
A (N=10)	2.91 (1.22)	0.60 (0.23)	2.26(1.23)	0.61(0.20)
B (N=14)	2.84 (1.35)	0.51(0.26)	2.69(1.46)	0.55(0.35)
E (N=17)	3.03 (1.64)	0.40(0.19)	2.45(1.31)	0.44(0.23)
Total N=41	2.94 (1.41)	0.49(0.23)	2.48(1.32)	0.52(0.28)
p-value	0.931	0.107	0.738	0.263

MEF25-75 (L/s), maximum expiratory flow 25-75; BDR, bronchodilatation responsiveness; R5-R20 (cmH2o.s/L), difference of R5 and R20.

Table 4. Severity correlation across GINA steps in asthma by IOS and spirometry.

GINA Step	R5-R20 (pre-BDR) Mean (SD)	MEF 25-75 (pre-BDR) Mean (SD)	R5-R20 (post-BDR) Mean (SD)	MEF 25-75 (post-BDR) Mean (SD)
Step 1-2 (n=16)	1.49 (0.99)	2.22(0.88)	0.95 (0.76)	2.45(0.99)
Step 3 (n=14)	2.25(0.82)	1.77(1.46)	1.96(1.23)	1.87(1.36)
Step 4 (n=19)	2.89(1.59)	1.41(1.14)	1.65(1.58)	1.68(1.23)
Step 5 (n=12)	2.87(1.40)	0.88(0.54)	2.51(1.57)	0.96(0.61)
Total (n=61)	2.37(1.36)	1.60(1.15)	1.71(1.41)	1.78 (1.19)
p-value	0.008	0.013	0.024	0.009

MEF25-75 (L/s), maximum expiratory flow 25-75; BDR, bronchodilatation responsiveness; R5-R20 (cmH2o.s/L), difference of R5 and R20.

Table 5. Comparison of BDR between IOS and spirometry across OADs.

	OAD spirometry BDR		COPD spirometry BDR		Asthma spirometry BDR		Bronchiectasis spirometry BDR	
	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive
IOS BDR, n (%)								
Negative	83 (70.33),	16 (13.55)	28 (68.29)	9 (21.95)	41 (67.21	6 (9.83)	14 (87.5)	1 (6.25)
Positive	12 (10.16)	7 (5.93)	2 (4.87)	2 (4.87)	9 (14.75)	5 (8.19)	1 (6.25),	0 (0)
p-value	0.055		0.288		0.106		1.00	
Cohen's κ	0.191 (p=0.037)		0.144 (p=0.271)		0.248 (p=0.050)		-0.067 (p=0.79)	

BDR, bronchodilatation responsiveness; IOS, impulse oscillometry; OAD, obstructive airway disease.