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Advantage of impulse oscillometry over spirometry to diagnose chronic obstructive pulmonary disease and monitor pulmonary responses to bronchodilators: An observational study

Constantine Saadeh[1,2], Charles Saadeh[1], Blake Cross[3], Michael Gaylor[2] and Melissa Griffith[2]

Abstract

Objectives: This retrospective study was a comparative analysis of sensitivity of impulse oscillometry and spirometry techniques for use in a mixed chronic obstructive pulmonary disease group for assessing disease severity and inhalation therapy.

Methods: A total of 30 patients with mild-to-moderate chronic obstructive pulmonary disease were monitored by impulse oscillometry, followed by spirometry. Lung function was measured at baseline after bronchodilation and at follow-up (3–18 months). The impulse oscillometry parameters were resistance in the small and large airways at 5 Hz (R5), resistance in the large airways at 15 Hz (R15), and lung reactance (area under the curve X; AX).

Results: After the bronchodilator therapy, forced expiratory volume in 1 second (FEV_1) readings evaluated by spirometry were unaffected at baseline and at follow-up, while impulse oscillometry detected an immediate improvement in lung function, in terms of AX ($p = 0.043$). All impulse oscillometry parameters significantly improved at follow-up, with a decrease in AX by 37% ($p = 0.0008$), R5 by 20% ($p = 0.0011$), and R15 by 12% ($p = 0.0097$).

Discussion: Impulse oscillometry parameters demonstrated greater sensitivity compared with spirometry for monitoring reversibility of airway obstruction and the effect of maintenance therapy. Impulse oscillometry may facilitate early treatment dose optimization and personalized medicine for chronic obstructive pulmonary disease patients.

Keywords

Bronchodilator, chronic obstructive pulmonary disease, impulse oscillometry, spirometry

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Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by a gradual decline in lung function and debilitating respiratory symptoms that include dyspnea, sputum production, and chronic coughing.[1] Contrary to asthma, COPD primarily targets the small airways, which are gradually and irreversibly damaged by inflammation and remodeling, and presents as chronic bronchitis and emphysema. While lung function measurement by spirometry remains the gold standard in most clinical practices for patients with asthma and COPD,[2] our growing understanding of these complex diseases warrants the adoption of strategies capable of monitoring the status of both the large and small airways.

In the past decade, impulse oscillometry (IOS) has been proposed as an alternative for the measurement of treatment

[1]Texas Tech University Health Sciences Center, Lubbock, TX, USA
[2]Amarillo Center for Clinical Research (ACCR), Allergy A.R.T.S. (Asthma, Rheumatology Treatment Specialists), Amarillo, TX, USA
[3]Texas College of Osteopathic Medicine, University of North Texas, Denton, TX, USA

Corresponding author:
Constantine Saadeh, Amarillo Center for Clinical Research (ACCR), Allergy A.R.T.S. (Asthma, Rheumatology Treatment Specialists), 6842 Plum Creek Dr, Amarillo, TX 79124, USA.
Email: csaadeh@allergyarts.com

efficacy and disease progression in COPD patients. It is able to assess both small and large airway reactance as well as resistance capacitance of the lung.[3] In contrast to traditional spirometry, this technique is noninvasive, relatively effort independent, and minimally intrusive (requires spontaneous normal tidal breathing).[4–8] The most relevant measurements of IOS include R5, which is the resistance in small and large airways (at 5 Hz); R15 (resistance at 15 Hz) or higher, which is the resistance in larger airways; and AX (area of reactance), which is low frequency integrated impedance reactance at 5 Hz and above, similar to forced expiratory volume in 1 s (FEV_1) spirometry.[8,9]

Comparative studies have shown higher sensitivity of IOS over FEV_1 for the early detection of COPD symptoms.[4,10–12] IOS is able to specifically evaluate chronic bronchitis and emphysema as an increase in pulmonary resistance and a decrease in pulmonary reactance in patients with normal spirometry.[12] However, the aforementioned studies investigated the sensitivity and reliability of IOS during a long-term follow-up of COPD patients under a specific bronchodilator treatment.

With respect to airway dynamics, IOS offers the advantage of measuring bronchomotor tone in COPD patients, with daily variations even when spirometry results are unchanged. It is also helpful in assessing asymptomatic individuals with peripheral airway dysfunction.[13] This fact encouraged us to evaluate the IOS and spirometry data of a mixed group of COPD patients at our clinic. The patients presented at different stages and severity of COPD but were evaluated uniformly both at baseline, following nebulizer treatment, and during follow-up.

The aim of this retrospective study was to evaluate whether IOS has specific advantages over spirometry in detecting reversibility of airflow obstruction and improvement in lung function in COPD patients following inhalation therapy. Lung function was measured in these patients at baseline, after the first dose of bronchodilator therapy, and at follow-up conducted 3–18 months later (conducted after maintenance therapy with inhaled corticosteroids, beta-2 agonists, and/or anticholinergics). Our efforts were centered on monitoring the AX, R5, and R15 parameters of IOS and FEV_1 of spirometry at diagnosis and after maintenance therapy in stable COPD outpatients in routine clinical practice.

Methods

Study design

This retrospective study included routine outpatient COPD patients treated at the Allergy ARTS (Asthma, Rheumatology Treatment Specialist) facility after their initial diagnosis using spirometry and IOS (Masterscreen; Erich Jaeger, Germany). The data for the entire study were collected between 2010 and 2012. Institutional Review Board approval was obtained with regard to the approach for compiling, reviewing, and analyzing the data presented in this article. The study was approved by IntegReview ethical review board, Austin, Texas, US, and the study patients had provided consent for use of their clinical charts for research purposes.

Patients

The inclusion of patients in this retrospective analysis was based on chart review of patients diagnosed with COPD by a physician. Decreased FEV_1 (i.e. FEV_1 of 80% of that predicted or less) with less than 10% reversibility was considered suggestive, but not a definite criterion for the diagnosis of COPD. Patients with a $\geqslant$10-year history of smoking at least 1 pack per day and shortness of breath along with its progressive worsening, with or without sputum production, were included. Other diagnostic criteria were chest X-ray findings of hyperinflation and increased intercostal space. Duration of the diagnostic symptoms ranged from 3 months to more than 5 years in all patients. These patients received standard treatment for COPD (inhaled corticosteroids, anticholinergics, or bronchodilators). Patients received bronchodilator therapy in two forms. First, long-acting beta agonists were used in combination with cortical steroid inhalation as maintenance therapy. Second, rescue inhalers were used as emergency treatment; they either included albuterol formulations or levalbuterol hydrochloride.

IOS and spirometry data were collected at diagnosis, before and after bronchodilator inhalation, which represented the start of the observation period. The commonly used bronchodilator was levalbuterol hydrochloride (Xopenex®; Sepracor Inc.). Same assessments were conducted again after 3 months. The bronchodilator therapy was not given at the time of follow-up measurement to allow an unbiased and absolute comparison with baseline (prior to bronchodilator inhalation).

Pulmonary function tests

Baseline IOS and spirometry were repeated after the first dose of inhalation therapy (levalbuterol or albuterol) to compare the capacity of the two techniques to detect a change in initial treatment responses or reversibility of airflow obstruction in newly diagnosed COPD patients. For IOS, the resistive frequencies at 4 to 32 Hz indicated both small and large airway resistance.[14] IOS measured the parameters, AX, R5, and R15 or higher. AX was reflective of the reactance of the lungs in response to loudspeaker stimuli and indicated the integral summation of small airway reactance, that is, an index of small airway response to the external application of multiple frequency signals from the transducer. X5 is a specific point to indicate reactance and is equivalent to AX; however, pure AX reflects physiological integration of small frequency signals. In this study, we chose AX to reflect reactive measurement. R5 is a reflection of the summation of small and large airways. R15 is a reflection of the larger

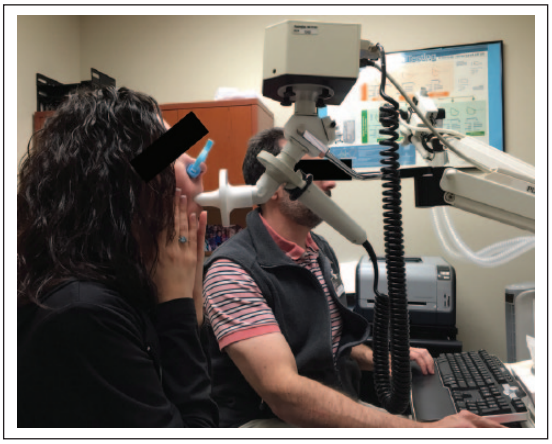

Figure 1. Image of the impulse oscillometry apparatus.
Both individuals in the photograph provided signed consent to be photographed for the purpose of publication.

airways. The difference between R5 and R15 is the true measurement of small airways. R15 indicated the measurement of larger airways at 15 Hz. Both R5 and R15 were calculated in cm H_2O. Furthermore, for individuals aged 13 years and older, the reference range included R5, 3 cm H_2O or less; R15 or above, 2 cm H_2O or less; and AX, 3 cm H_2O or less.[6,14]

The IOS technique was performed as previously described.[6,14] Briefly, patients were seated comfortably in a nonswivel chair (Figure 1). Nose clips were applied and a special mouthpiece was used. For IOS measurements, patients were advised to cradle their cheeks with their hands. Patients were allowed to breathe normally while the loudspeaker delivered intermittent multi-frequency impulses over a minimum of a 30-s period. A trained technician guided and assisted the patient during the procedure, which involved three to five sinusoidal readings, depending on the incidence of cough, swallowing, and holding of breath. The recordings with the best coherence at frequencies from 5 to 30 Hz were chosen. The technician was also trained to capture subclinical leaks through the mouthpiece, and leaky recordings were discarded. The pre- and post-bronchodilator assessments took at least 10 min and used ultrasonic nebulizer. The IOS parameters measured were R5, R15, and AX. Spirometry was performed after IOS in the same setting. FEV_1 was recorded, and the results were analyzed according to the American Thoracic Society guidelines. Follow-up patient data were evaluated after a minimum of 3 months and represented the next best repeat measurements of FEV_1 and IOS.

Statistical analysis

The reversibility of airflow limitation with the bronchodilator was measured at baseline and compared with follow-up using the Wilcoxon signed-rank test, which is the nonparametric equivalent of the paired *t*-test. The parameters analyzed were FEV_1, AX, R5, and R15. $p \leqslant 0.05$ was considered statistically significant.

Results

Patient demographics and baseline characteristics

Of the 30 patients diagnosed with COPD, data from 26 (mean age (standard deviation (SD)): 63.80 years (8.22 years)) were included for analysis. Four patients were excluded from analysis owing to lack of follow-up data. About 46% of the included patients were male, and a 10-year smoking history could be confirmed for only 77% patients. These patients had been exposed to smoking since approximately 10 pack-years. Six patients had less than 10 years of experience with smoking; however, they were identified as smokers. All patients were treated with corticosteroids (Advair®, Alvesco®, Asmanex®, Flovent®, Pulmicort®, Qvar®, or Symbicort®) and beta-2 agonists (levalbuterol or albuterol) after study entry. A total of 19 patients were also treated with anticholinergic medication (Spiriva®). The follow-up duration before the next best IOS and spirometry data were available ranged from 3 to 18 months. The variation in time to follow-up was owing to differences in baseline disease severity and other comorbid conditions among the patients. None of the patients were hospitalized during the 18 months of follow-up.

Patients' response

After the maintenance therapy with inhaled corticosteroids, beta-2 agonists, and/or anticholinergics, all patients exhibited improvement in symptoms of COPD, without any exacerbation of the disease.

IOS and spirometry

The mean (SD) and median of % FEV_1/predicted FEV_1 were 71.05 (12.33) and 71.94, respectively. At baseline, there was no significant change in FEV_1 values evaluated by spirometry after albuterol/levalbuterol inhalation ($p = 0.064$; Table 1). In contrast, IOS was able to detect an improvement in lung function in terms of AX ($p = 0.043$), but not R5 ($p = 0.148$) or R15 ($p = 0.198$; Table 2). A typical trace showing noticeable improvement in AX for a COPD patient after the first dose of bronchodilator is displayed in Figure 2.

After 3–18 months of inhalational corticosteroid, beta-2 agonist, and/or anticholinergic therapy, FEV_1 still did not show any significant improvement in comparison to baseline ($p = 0.43$; Table 3). However, all IOS parameters had significantly improved compared to baseline at the time of follow-up, with a 37% decrease in impedance (AX; $p = 0.0008$), 20% decrease in overall airway resistance, that is, small and large airways (R5; $p = 0.0011$), and 12% decrease in resistance in the larger airways (R15; $p = 0.0097$).

Table 1. Baseline spirometry evaluation of COPD patients.

Age (years)	Inhaled steroid/beta-2 agonist	Inhaled anticholinergic	Baseline FEV_1	Post-bronchodilator FEV_1	% change
66	Budesonide and Formoterol	Tiotropium	0.64	0.73	13.0%
65	Mometasone	None	2.74	2.85	4.0%
60	Fluticasone and Salmeterol	None	2.42	2.52	4.3%
59	Fluticasone and Salmeterol	None	1.47	1.52	3.2%
62	Fluticasone and Salmeterol	Tiotropium	1.17	1.32	12.4%
49	Budesonide and Formoterol	Tiotropium	2.07	2.01	−3.0%
59	Budesonide and Formoterol	Tiotropium	2.27	2.13	−6.1%
75	Budesonide	Tiotropium	0.93	0.95	2.2%
70	Fluticasone and Salmeterol	Tiotropium	1.33	1.48	11.4%
68	Fluticasone and Salmeterol	None	1.37	1.41	3.2%
65	Fluticasone and Salmeterol	Tiotropium	1.80	1.79	−0.7%
79	Mometasone	Tiotropium	3.35	–	–
61	Budesonide	Tiotropium	1.12	1.29	14.5%
59	Fluticasone and Salmeterol	Tiotropium	2.06	2.22	7.8%
79	Mometasone	None	2.51	2.67	6.4%
57	Fluticasone and Salmeterol	Tiotropium	2.40	2.50	4.0%
78	Beclomethasone	Tiotropium	1.14	1.22	6.8%
55	Fluticasone and Salmeterol	Tiotropium	1.84	1.30	−29.3%
62	Budesonide	Tiotropium	2.90	3.04	4.9%
66	Fluticasone	Tiotropium	1.67	2.01	20.2%
69	Beclomethasone	Tiotropium	2.50	2.76	10.4%
47	Fluticasone and Salmeterol	Tiotropium	1.39	1.29	−7.1%
62	Fluticasone and Salmeterol	None	1.91	1.80	−6.1%
57	Ciclesonide	None	2.81	2.98	6.0%
69	Budesonide	Tiotropium	1.53	1.52	−0.3%
61	Budesonide and Formoterol	Tiotropium	2.58	–	–
		Mean (SD)	1.92 (0.6)	1.88 (0.6)	0.03 (0.09)

FEV_1: forced expiratory volume in 1 s; Budesonide and Formoterol: Symbicort®; Mometasone: Asmanex®; Fluticasone and Salmeterol: Advair®; Budesonide: Pulmicort®; Beclomethasone: Qvar®; Fluticasone: Flovent®; Ciclesonide: Alvesco®; Tiotropium: Spiriva®; SD: standard deviation.

Discussion

This retrospective study evaluated routine outpatient cases of COPD at diagnosis and after inhalational therapy, using IOS and spirometry. Change in FEV_1 in response to inhaled bronchodilators was evaluated by spirometry, and IOS parameters (AX, R5, and R15) were assessed at baseline and at follow-up, which was conducted 3–18 months later. The results showed that IOS indices, particularly AX, can effectively detect an abnormality in airway function or an acute bronchodilatory response in a mixed group of COPD patients with stable FEV_1. The IOS was able to detect changes in airway function immediately after the administration of bronchodilator inhalation as well as at follow-up, while FEV_1 remained unchanged in these patients. Furthermore, the improvement in AX after the first dose of bronchodilator suggests that this parameter could be used to adjust and customize the dose of medication for each patient.[14] The findings of this study are consistent with our previous findings associating greater precision of IOS parameters in estimating lung mechanics in asthmatic patients[15] and symptomatic patients with reactive airways.[16]

At diagnosis, there was no significant change in FEV_1 values after bronchodilator inhalation ($p = 0.064$), and IOS was able to detect an improvement in lung function in terms of AX ($p = 0.043$) only. Most importantly, after 3–18 months of maintenance therapy (inhalational corticosteroid and/or anticholinergic therapy), a symptomatic improvement in the COPD patients was observed: while FEV_1 still did not reflect any significant improvement from baseline ($p = 0.43$), all IOS parameters showed significant improvement, with a 39% decrease in impedance (AX; $p = 0.0008$), 31% decrease in overall airway resistance, that is, small and large airways (R5; $p = 0.0011$), and 15% decrease in resistance in the larger airways (R15; $p = 0.0097$). These results show the superior sensitivity of all three IOS parameters in monitoring bronchomotor responses that aligned with the subjective improvement observed in the patients after the maintenance therapy. We also observed a rise in patient compliance when IOS was used as opposed to spirometry. The ease of the administration of the test and the improvement in lung function experienced by the patients could have motivated this effect.

Table 2. Baseline impulse oscillometry evaluation of COPD patients.

Patient code	Baseline AX	Post-bronchodilator AX	% change	Baseline R5	Post-bronchodilator R5	% change	Baseline R15	Post-bronchodilator R15	% change
1	85.78	88.86	3.6%	8.95	8.99	0.5%	3.87	3.57	−7.7%
2	5.45	5.64	3.5%	2.72	3.25	19.3%	1.97	2.54	28.8%
3	17.69	9.71	−45.1%	3.73	3.02	−19.0%	2.25	2.03	−9.6%
4	19.81	13.24	−33.2%	4.47	3.30	−26.2%	2.50	2.13	−14.6%
5	29.19	21.96	−24.8%	4.55	4.30	−5.5%	2.49	2.29	−8.2%
6	11.20	10.26	−8.4%	3.70	3.50	−5.5%	2.55	2.28	−10.6%
7	16.52	24.81	50.2%	4.88	5.70	16.7%	2.80	3.05	8.9%
8	14.94	12.65	−15.3%	4.59	4.31	−6.1%	3.06	2.98	−2.6%
9	15.02	13.74	−8.5%	2.92	3.00	2.5%	2.00	1.86	−7.1%
10	9.98	20.82	108.6%	3.62	4.47	23.5%	2.46	2.63	7.0%
11	19.25	12.62	−34.5%	5.32	4.91	−7.8%	3.30	3.73	13.3%
12	1.23	–	–	1.48	–	–	1.18	–	–
13	22.37	19.89	−11.1%	3.60	3.81	5.9%	2.40	2.42	1.1%
14	38.58	23.04	−40.3%	8.09	6.29	−22.2%	5.25	4.41	−16.0%
15	7.37	6.95	−5.7%	2.55	2.84	11.3%	1.68	2.04	21.2%
16	7.15	7.79	9.0%	3.78	3.87	2.2%	3.09	2.90	−6.3%
17	43.55	23.71	−45.6%	5.26	3.83	−27.1%	3.13	2.72	−13.0%
18	15.13	8.04	−46.9%	7.50	4.69	−37.5%	6.50	4.07	−37.4%
19	14.56	11.86	−18.5%	4.34	4.01	−7.7%	2.99	2.85	−4.5%
20	9.49	7.02	−26.1%	2.54	2.17	−14.5%	1.50	1.44	−4.4%
21	9.96	7.67	−23.0%	3.24	3.35	3.3%	2.00	2.26	13.0%
22	32.33	45.23	39.9%	5.09	7.70	51.3%	3.01	4.22	40.2%
23	9.08	6.84	−24.6%	3.15	2.98	−5.4%	2.55	2.56	0.4%
24	13.27	11.28	−15.0%	2.94	2.82	−4.1%	1.69	1.67	−1.2%
25	26.48	16.00	−39.6%	4.87	3.94	−19.2%	2.82	2.52	−10.4%
26	12.74	–	–	3.55	–	–	2.38	–	–
Mean (SD)	19.54 (17)	17.90 (17)	−0.10 (0.3)	4.28 (2)	4.21 (2)	−0.02 (0.1)	2.74 (1)	2.71 (0.7)	−0.008 (0.1)

AX: lung reactance (area under the curve X); R5: resistance in small and large airways at 5 Hz; R15: resistance in large airways at ⩾15 Hz; SD: standard deviation.

A forced oscillation technique whereby the machine delivers a regular square wave of pressure five times per second is now noted to be the standard IOS technique and is actually a modification of the old forced oscillation.[17] IOS may provide a more detailed characterization of respiratory function. It measures the properties of the lungs in response to external stimuli,[18] by applying pressure variation at the mouth of the subject via a loudspeaker. Respiratory impedance is then obtained as resistance that is R5 and above and reactance that is AX or X5.[14]

In this study, we observed that use of IOS in COPD patients may show reversibility of airflow limitation that is not detected by FEV_1. Bronchodilator response with IOS and spirometry is routinely evaluated in our clinic at diagnosis, to check for reversibility of bronchoconstriction. It is repeated at follow-up after these patients have been on different treatment regimens as maintenance therapy, making them a more heterogeneous population.

Furthermore, other than evaluation of the standard FEV_1 using spirometry, the mid-flow rate or forced expiratory flow (FEF) occurring in the middle 50% of the patient's exhaled volume (i.e. FEF 25%–75%) has been considered an indirect measure of small airway function. However, its reliability is questionable because the patient's efforts diminish with time.[9] For this reason, IOS may be considered a reasonable approach to assess patients with asthma and COPD. IOS is able to quantify respiratory resistance independent of respiratory frequency or effort.[5,9,11] In our study, R5 measurement was not only reflective of resistance in the small airways, but was also associated with good response to treatment without applying effort to breathing. It must be noted that while evaluating patients with COPD, IOS should be performed prior to spirometry. Initiating spirometry first may lead to falsely high AX or R5 due to increased airway resistance.[14] In our practice, we routinely perform IOS prior to spirometry.

A review of the literature suggests that IOS measurements have several uses. They may help differentiate between drug therapy response,[11,19,20] monitor small and large airway resistance in patients with asthma and cystic fibrosis independent of the upper airway shunt capacitance,[21] serve as useful correlates and adjuncts to nitric oxide measurements

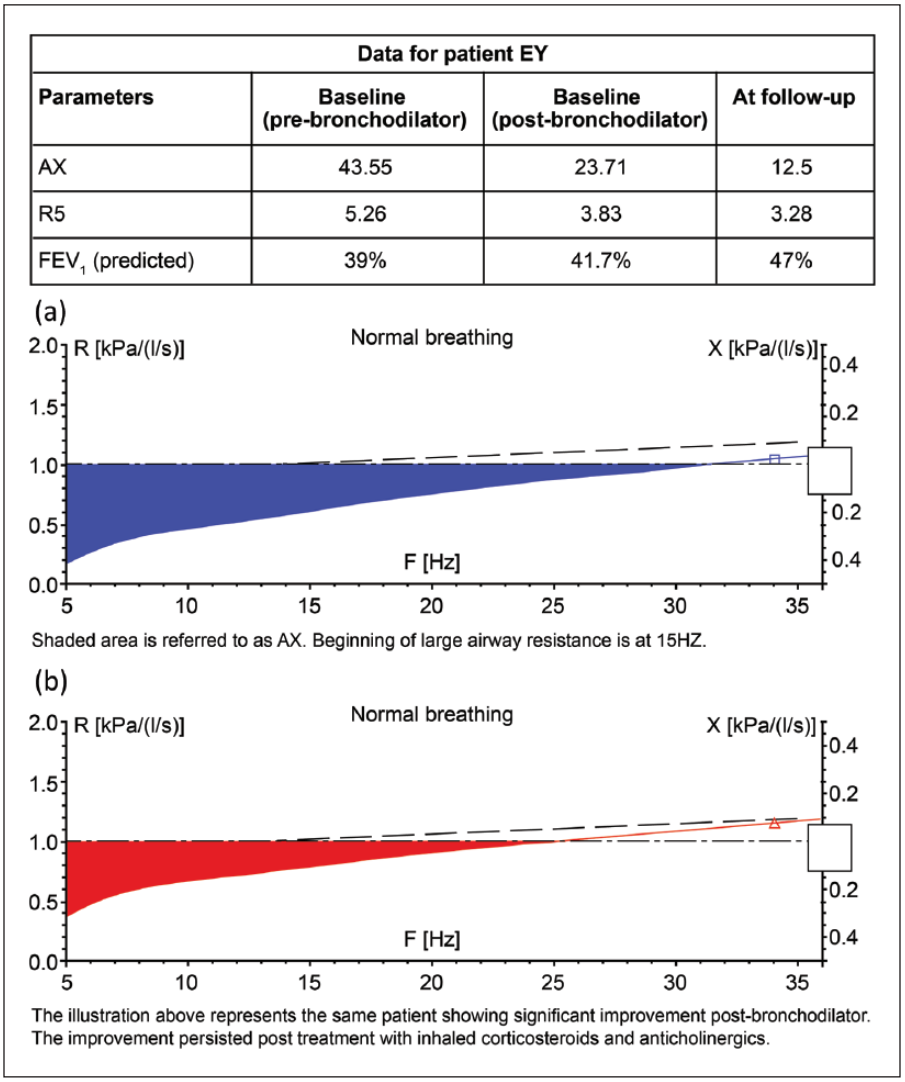

Figure 2. Impulse oscillation area of reactance (AX) detects bronchodilator efficacy in COPD patients after a single dose. Traces showing AX (a) before and (b) after the first dose of inhalation therapy. Airway resistance was measured over a range of intermittent frequency impulses (5–35 Hz) delivered by a loudspeaker. Thereafter, AX was calculated from the area under the x-axis. Large airway resistance was recorded at frequencies of ⩾15 Hz.

in asthma and COPD,[22] evaluate exercise response on the 6-min walk test in COPD patients, detect respiratory problems in pregnancy, evaluate response to the methacholine challenge test,[23,24] detect pathophysiological changes in accordance with the severity of COPD even when the FEV_1/forced vital capacity (FVC) is normal,[5] and study within-breath behavior of the oscillatory mechanics for evaluating disease severity.[25] However, in comparison to FEV_1, IOS measurements may not show statistically significant changes in R5 and X5 in patients with COPD at 1-year follow-up with maintenance therapy.[9] In terms of dynamic compliance, it seems that IOS is a noninvasive tool for assessing distal airway function even when spirometry is normal, particularly at stage 0 of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) COPD criteria.[4] Finally, Crim et al.[26] studied lung impedance with IOS in healthy nonsmokers, healthy former smokers, and patients with COPD. These parameters were correlated with spirometry and areas of low attenuation computed tomography, and it seemed that in a large number of patients, IOS showed good reproducibility over 3 months. Respiratory system impedance was worse when compared with control in patients with COPD stratified according to the GOLD criteria. However, there was some crossover to the normal range when the respiratory impedance was used by itself.[26]

In future, IOS could be utilized for respiratory impedance model measurements, heart failure models, intubated patients on mechanical ventilation, and sleep apnea.[27,28] Furthermore, with respect to airway dynamics, IOS offers the advantage of measuring bronchomotor tone in COPD patients, with daily variations even when spirometry results are unchanged.[13] Future studies should address a potential limitation: namely,

Table 3. Spirometry and impulse oscillometry evaluations at follow-up and their comparison with respect to baseline (pre-bronchodilator therapy).

Patient code	Follow-up FEV_1	Follow-up AX	Follow-up R5	Follow-up R15	FEV_1 % change	AX % change	R5 % change	R15 % change
1	1.04	33.65	6.32	4.06	62.50%	−60.77%	−29.39%	4.91%
2	1.95	3.57	2.59	2.26	−28.83%	−34.50%	−4.78%	14.72%
3	2.45	8.54	2.82	1.89	1.24%	−51.72%	−24.40%	−16.00%
4	1.47	13.29	3.66	2.25	0.00%	−32.91%	−18.12%	−10.00%
5	1.49	19.19	3.66	2.16	27.35%	−34.26%	−19.56%	−13.25%
6	2.27	6.72	3.01	2.18	9.66%	−40.00%	−18.65%	−14.51%
7	2.40	8.54	3.51	2.30	5.73%	−48.31%	−28.07%	−17.86%
8	1.48	6.42	3.09	2.31	59.14%	−57.03%	−32.68%	−24.51%
9	1.72	4.77	2.27	1.88	29.32%	−68.24%	−22.26%	−6.00%
10	1.57	10.08	3.38	2.42	14.60%	1.00%	−6.63%	−1.63%
11	1.69	9.78	3.73	2.51	−6.11%	−49.19%	−29.89%	−23.94%
12	2.93	1.48	1.50	1.20	−12.54%	20.33%	1.35%	1.69%
13	1.27	18.79	3.38	2.23	13.39%	−16.00%	−6.11%	−7.08%
14	1.92	16.56	4.34	2.91	−6.80%	−57.08%	−46.35%	−44.57%
15	–	4.52	2.17	1.55	–	−38.67%	−14.90%	−7.74%
16	–	6.94	3.54	2.67	–	−2.94%	−6.35%	−13.59%
17	1.41	12.52	3.28	2.47	23.68%	−71.25%	−37.64%	−21.09%
18	1.80	5.85	3.45	2.86	−2.17%	−61.34%	−54.00%	−56.00%
19	3.20	8.86	3.21	2.23	10.34%	−39.15%	−26.04%	−25.42%
20	1.84	7.47	2.32	1.44	10.18%	−21.29%	−8.66%	−4.00%
21	–	4.02	2.40	1.87	–	−59.64%	−25.93%	−6.50%
22	1.42	45.52	6.48	3.50	2.16%	40.80%	27.31%	16.28%
23	2.16	1.14	1.48	1.23	13.09%	−87.44%	−53.02%	−51.76%
24	2.97	8.50	2.52	1.62	5.69%	−35.95%	−14.29%	−4.14%
25	1.78	11.31	3.45	2.20	16.34%	−57.29%	−29.16%	−21.99%
26	2.46	12.73	3.63	3.63	−4.65%	−0.08%	2.25%	52.52%
					$p = 0.43$	$p < 0.005$	$p < 0.005$	$p < 0.01$

AX: lung reactance (area under the curve X); FEV_1: forced expiratory volume in 1 s; R5: resistance in small and large airways at 5 Hz; R15: resistance in large airways at ⩾15 Hz.

that our study did not allow us to objectively correlate the improvement in patients' symptoms with the IOS measures owing to lack of data on patient symptoms.

In conclusion, this retrospective study shows that IOS has the ability to detect airway dysfunction with normal tidal breathing in COPD patients at diagnosis and after maintenance therapy. We have shown that although FEV_1 values were unchanged in some patients following bronchodilator treatment at diagnosis of COPD and after maintenance therapy (using inhaled corticosteroids, long-acting beta-2 agonists, and/or anticholinergics), IOS was able to detect an improvement in lung function in these patients, which aligned with the symptomatic improvement observed in these patients. Despite the unresponsive FEV_1, the ability of AX to detect acute changes in lung function after the first dose of bronchodilator may lead to early treatment dose optimization and personalized medicine for COPD patients. Future prospective trials with specific treatment for COPD should provide further insight into the role of IOS in the evaluation and follow-up of patients with COPD.

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Declaration of conflicting interests

All authors have no conflicts to declare.

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