Impulse oscillometry in COPD: Identification of measurements related to airway obstruction, airway conductance and lung volumes

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Spirometry;
Body Plethysmography

Summary
Background: Impulse oscillometry system (IOS) assesses pulmonary resistance and reactance. We set out to investigate which IOS measurements are related to airflow obstruction, airway conductance and lung volumes in chronic obstructive pulmonary disease (COPD).

Methods: Ninety-four COPD patients were recruited and 58 agreed to follow up after 1 year. IOS measurements (R5, R20, X5 & Fres), body plethysmography (sGaw, FRC, TLC, RV & IC) and spirometry (FEV1) were performed. Pearson or Spearman correlation determined the relationships between IOS and other measurements.

Results: R5, X5 and Fres were all significantly associated (p < 0.05) with FEV1, sGaw, TLC, RV and IC. However, R20 was not related to any of these measurements except for RV. The strongest associations were observed between FEV1 and the reactance measurements X5 (r = 0.48) and Fres (r = −0.44), and sGaw with X5 (r = 0.47) and Fres (r = 0.51). The r values for the associations with TLC and IC were all <0.25.

There was no statistically significant change in the FEV1, R5, X5 or Fres after 1 year, but R20 significantly increased over the year. The changes in R5 and R20 did not significantly correlate with the changes in FEV1. In contrast, X5 changes were significantly related to FEV1 changes over 1 year (r = −0.27, p = 0.05), while for Fres changes there was a trend to statistical significance (p = 0.08).

Conclusions: IOS reactance measurements are more closely related than resistance measurements to other pulmonary function measurements in COPD patients. The IOS reactance...
Introduction

Chronic obstructive pulmonary disease (COPD) is defined by poorly reversible airflow limitation caused by the inhalation of noxious particles such as cigarette smoke.\(^1\) COPD patients display heterogeneous pathophysiological abnormalities including small airway disease, hyperinflation and mucus hypersecretion, all of which may cause airflow obstruction.\(^2\)

Spirometry is the 'gold standard' by which airflow obstruction is assessed in COPD patients. Forced expiration is used as part of spirometry in the diagnosis and staging of COPD. This procedure can be difficult for patients to perform as it is effort dependent and can alter bronchomotor tone. Body plethysmography is an alternative pulmonary function technique, allowing assessment of airways resistance and conductance. However, it can be technically demanding for patients to perform as it requires complex ‘panting’ manoeuvres. Thus, there is a need for easy to perform but physiologically accurate methods to assess pulmonary mechanics in COPD patients.

The forced oscillation technique (FOT) was developed in 1956 to measure the impedance of the respiratory system through application of small pressure oscillations at the mouth during normal breathing.\(^3\) FOT systems use pseudorandom noise signals to enable the simultaneous measurement of respiratory resistance (Rs) and reactance (Xs). It has been reported that FOT measurements are associated with traditional lung function measurements in patients with obstructive lung disease.\(^4,5\) In COPD patients specifically, it has been shown that FOT resistance measurements can be used to sensitively diagnose mild COPD, but that reactance measurements are better for grading severity of disease.\(^6\) The authors of this paper point out that FOT provides unique data on respiratory mechanics that is complimentary to spirometry. However, they also point out that there is little consensus in the literature as to the best FOT parameters for evaluating respiratory mechanics.

The impulse oscillometry system (IOS)\(^7\) is a type of FOT but with 2 important differences; rectangular waveform impulses are applied instead of pseudorandom noise signals, and the IOS has a different set of data outputs. IOS has been used in clinical trials to examine drug effects\(^8,9\); COPD and asthma studies have shown IOS measurements to be more sensitive than FEV\(_1\) for measuring the pulmonary effects of bronchodilator drugs.\(^10–12\) Additionally, IOS measurements can be used to sensitively diagnose obstructive lung disease.\(^13,14\) Hellinckx et al.\(^15\) reported that IOS gives similar but not identical respiratory resistance and reactance measurements compared to FOT, underscoring that these techniques may give different results.

While there is information for FOT using pseudorandom noise generation\(^4,6\) it is not known which IOS parameters are the most informative when assessing the severity of COPD. Importantly, we need to understand which IOS measurements are related to the degree of airflow obstruction as measured by forced expiratory volume in 1 s (FEV\(_1\)), and which are related to the degree of hyperinflation measured by lung volumes. This paper describes the relationship of IOS measurements to other pulmonary function measurements in a large cohort of COPD patients (n = 94). We followed up these patients for 1 year, and then compared the changes in IOS and FEV\(_1\) measurements over 1 year.

Methods

Subjects

Ninety-four patients with COPD were recruited from primary care by media advertising into our cohort for measurement of pulmonary function (see Table 1 for demography). All patients were invited to attend 1 year later; 58 patients agreed to participate, with the remainder unable to do so or having withdrawn consent. COPD was diagnosed according to current GOLD guidelines,\(^1\) based on a smoking history of at least 10 pack years together with typical symptoms (one or more of productive cough, breathlessness and wheeze) and evidence of airflow obstruction. Patients with a clinical history of asthma, an exacerbation or any change in their COPD therapy within 4 weeks of the study, or a history of lung cancer were excluded. Written informed consent was obtained and the local ethics committee approved the study.

Study design

Each patient performed pulmonary function tests in the following order; impulse oscillometry system (IOS), body plethysmography (including measurement of lung volumes) and spirometry.

Pulmonary function measurements

IOS (Masterscreen IOS, Erich Jaeger, Hoechberg, Germany) measurements were performed as previously described.\(^12\)

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient demographics at baseline.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, male/female</td>
<td>63/31</td>
</tr>
<tr>
<td>Age (years)(^b)</td>
<td>63.81 (7.76)</td>
</tr>
<tr>
<td>Current/Ex Smokers</td>
<td>35/59</td>
</tr>
<tr>
<td>Smoking history (pack years)(^b)</td>
<td>42 (35–53.5)</td>
</tr>
<tr>
<td>ICS use/no use</td>
<td>52/42</td>
</tr>
<tr>
<td>LABA use/no use</td>
<td>43/51</td>
</tr>
<tr>
<td>LANC use/no use</td>
<td>17/77</td>
</tr>
<tr>
<td>Methylxanthines use/no use</td>
<td>7/87</td>
</tr>
</tbody>
</table>

There were no patients on oral corticosteroids. Abbreviations: ICS, inhaled corticosteroids; LABA, long acting bronchodilator; and LANC, long acting anticholinergic.

\(^a\) Data represented as mean (SD).

\(^b\) Data represented as median (IQR).
and the actual values of respiratory resistance at 5 and 20 Hz (R5 and R20, respectively), reactance at 5 Hz (X5) and resonant frequency (Fres) were recorded. sGaw, functional residual capacity (FRC), vital capacity (VC) and inspiratory capacity (IC) were measured in a constant volume plethysmograph (Sensormedics Vmax 6200). Total lung capacity (TLC) and residual volume (RV) were then calculated from these parameters. IOS and body plethysmograph measurements were performed in triplicate and the mean used for further analysis. FEV1 was measured using the spirometry system on the Masterscreen. Readings were again performed in triplicate, with the highest FEV1 recorded.

**Statistical analysis**

The Kolmogorov–Smirnov test was applied to determine the normality of data. Non-parametric data was natural log transformed, X5 and R5 data remained non-parametric despite natural log transformation. Data is represented as means and 95% confidence intervals (95% CI) unless otherwise specified. Pearson correlation or Spearman correlation was applied to determine the relationships between the baseline IOS and pulmonary function measurements and the relationships between the change in FEV1 and change in IOS over 1 year. Paired t test or the Wilcoxon matched pair test was performed to determine the differences between the 2 visits over a year. P < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS (Chicago; USA).

**Results**

Baseline patient demographics and pulmonary function measurements are shown in Tables 1 and 2, respectively. The study population was composed of patients with moderate disease severity with a mean FEV1% predicted of 57.9%.

**Relationships between IOS and other pulmonary function measurements**

R5, X5 and Fres were all significantly associated with FEV1, with the reactance measurements X5 \( (r = 0.48) \) and Fres \( (r = -0.44) \) showing the strongest degree of association (Fig. 1). R20 did not correlate with FEV1.

TLC (Fig. 2), IC (Fig. 3) and sGaw (Fig. 4) were significantly associated with R5, X5 and Fres, but not R20. The \( r \) values for the associations with TLC and IC were all < 0.25. In contrast there was a stronger degree of association for sGaw, particularly for Fres \( (r = 0.51) \). RV was significantly correlated with R5 \( (r = 0.35, p = 0.0007) \), R20 \( (r = 0.20, p = 0.05) \), X5 \( (r = -0.36, p = 0.0002) \) and Fres \( (r = 0.31, p = 0.003) \). None of the IOS measurements were significantly correlated with FRC \( (p > 0.05) \).

**Comparison of FEV1 and IOS measurements over 1 year**

To compare changes in FEV1 and IOS measurements over 1 year in 58 patients at follow up, we considered changes in group statistics and changes within each individual. For the overall group mean or median values, there was no statistically significant change in the FEV1, R5, X5 or Fres after 1 year (Table 3). However, R20 significantly increased over the years.

The relationships between changes in FEV1 and IOS measurements within each individual over 1 year are shown in Fig. 5. The changes in R5 and R20 did not significantly correlate with the changes in FEV1. In contrast, X5 changes were significantly related to FEV1 changes over 1 year \( (r = -0.27, p = 0.05) \), while for Fres changes there was a trend to statistical significance \( (p = 0.08) \).

**Discussion**

In our initial assessment of 94 COPD patients, we observed R5, X5 and Fres to be significantly associated with measures of airflow obstruction (FEV1), airway conductance (sGaw) and hyperinflation (TLC, RV and IC). However, R20 was not related to any of these measurements except for RV. The strongest associations were observed between reactance measurements and both FEV1 and sGaw. FEV1 is a well recognized measurement of airflow obstruction, while sGaw is a less commonly used but extremely sensitive measurement of airflow obstruction.\(^8\)\(^-\)\(^12\) Thus, the key novel finding of this study is that IOS reactance measurements are more informative than resistance measurements about the changes in pulmonary mechanics caused by airflow obstruction in COPD patients. Indeed, R20 appears to be unrelated to the severity of airflow obstruction.

Further evidence of the close association of reactance measurements to FEV1 was found when 58 patients were followed up at 1 year; changes in X5 and FEV1 over 1 year were significantly related, while there was a trend towards an association between Fres and FEV1 changes. Our data at the baseline visit and for the change over 1 year is similar to the findings of Di Mango et al.\(^6\) using FOT methods; they reported that reactance measurements were better than resistance measurements for grading severity of airflow obstruction in COPD. The novelty of the current study is that we have evaluated the IOS system which provides different data parameters to classic FOT systems and we have considered whether IOS measurements relate to hyperinflation or airway conductance in addition to the standard measurement of FEV1.
The strength of the correlations between FEV1 and reactance measurements ($r = 0.48$ for $X_5$ and $r = -0.44$ for $F_{res}$), and between $sGaw$ and reactance measurements ($r = 0.47$ for $X_5$ and $r = 0.51$ for $F_{res}$) suggests a moderate association between IOS airway reactance measurements and airflow obstruction, whether assessed by FEV1 or $sGaw$. IOS is therefore not a replacement for FEV1, but as previously pointed out for classic FOT methods provides complimentary information on respiratory mechanics. IOS reactance measurements provide insights into changes in pulmonary compliance associated with the severity of airflow obstruction. In contrast, IOS reactance measurements appear to be

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**Figure 1** Relationship between IOS measurements and FEV1 % predicted at the baseline visit (a) $R_5$ vs. FEV1 (b) $R_{20}$ vs. FEV1 (c) $X_5$ vs. FEV1 and (d) $F_{res}$ vs. FEV1. NS = not statistically significant ($p > 0.05$).

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**Figure 2** Relationship between IOS measurements and TLC % predicted at the baseline visit (a) $R_5$ vs. TLC (b) $R_{20}$ vs. TLC (c) $X_5$ vs. TLC and (d) $F_{res}$ vs. TLC. NS = not statistically significant ($p > 0.05$).
Respiratory reactance is thought to be a composite measurement of both lung compliance and inertiance. Inertiance measurements are usually clinically irrelevant, and reactance changes in pulmonary disease are dominated by respiratory compliance. \(^\text{16}\) Compliance is a measure of how easily the respiratory system can be inflated, and using the model of the respiratory system as an electrical circuit, reactance is thought to be related to the reciprocal of compliance. \(^\text{16}\) Reactance (X5) is numerically a negative value, and so reactance values that are more negative indicate reduced compliance. The overall respiratory compliance in COPD patients is reduced, \(^\text{10,12}\) presumably due to airways

![Figure 3](image1)

**Figure 3** Relationship between IOS measurements and IC (L) at the baseline visit (a) R5 vs. IC (b) R20 vs. IC (c) X5 vs. IC and (d) Fres vs. IC. NS = not statistically significant (p > 0.05).

![Figure 4](image2)

**Figure 4** Relationship between IOS measurements and sGaw % predicted at the baseline visit (a) R5 vs. sGaw (b) R20 vs. sGaw (c) X5 vs. sGaw and (d) Fres vs. sGaw NS = not statistically significant (p > 0.05).
obstruction, even though lung tissue compliance can be increased in emphysema patients due to parenchymal tissue destruction.

Fres is the point at which compliance and inertial reactance magnitudes are equal and opposite, thus X is zero. This occurs at a higher frequency with reduced respiratory compliance. Both Fres and X5 measurements were related to the degree of airflow obstruction (measured by FEV1), and the degree of hyperinflation (measured by lung volumes). Lung tissue destruction in emphysema patients causing hyperinflation should increase lung tissue compliance, but we have shown that hyperinflation is associated with decreased pulmonary compliance. Hyperinflation can cause airflow obstruction, which decreases pulmonary compliance. Our data therefore suggests that the associations between IOS reactance measurements and lung volumes are due to the airflow obstruction that occurs in patients with hyperinflation.

Previous oscillometry studies have demonstrated that peripheral airway obstruction is characterised by a greater increase in the resistance at low frequencies (R5) compared to the higher frequencies (R20), often called frequency dependence of resistance. Thus R5 is thought of as a measurement of peripheral airway obstruction. It is well documented that COPD patients demonstrate frequency dependence of resistance. The current study showed that R5, but not R20, was associated with FEV1 at the baseline visit. This adds further weight to the evidence that low frequency IOS resistance measurements can be used to assess peripheral airway obstruction in COPD patients. In contrast, R20 measurements appear to be unrelated to airflow obstruction in COPD patients, and the value of these measurements in COPD patients must be questionable. Our findings also support several studies in asthma and COPD patients where R20 was found to be less sensitive than R5 at detecting bronchodilation.9–13

Table 3 Comparison of FEV1 and IOS measurements between the baseline visit and year 1 visit.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Year 1</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (% predicted)</td>
<td>56.7 (13.1)</td>
<td>57.5 (13.3)</td>
<td>0.54</td>
</tr>
<tr>
<td>R5b (kPa L.s)</td>
<td>0.640 (0.557–0.856)</td>
<td>0.698 (0.564–0.932)</td>
<td>0.57</td>
</tr>
<tr>
<td>R20b (kPa L.s)</td>
<td>0.416 (0.383–0.451)</td>
<td>0.442 (0.413–0.474)</td>
<td>0.03</td>
</tr>
<tr>
<td>X5b (kPa L.s)</td>
<td>−0.308 (−0.453,−0.190)</td>
<td>−0.307 (−0.446,−0.187)</td>
<td>0.80</td>
</tr>
<tr>
<td>Fres (Hz)</td>
<td>26.5 (7.1)</td>
<td>26.7 (6.5)</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Data represented as mean (SD) unless otherwise specified. 
* Data represented as geometric mean (95% CI). 
** Data represented as median (IQR).

Figure 5 Relationship between the changes in IOS and FEV1 within each individual over a 1 year interval (a) Change in R5 vs. change in FEV1, (b) Change in R20 vs. change in FEV1, (c) Change in X5 vs. change in FEV1 and (d) Change in Fres vs. change in FEV1. NS = not statistically significant (p > 0.05).
At the 1 year follow up we found X5 was the only IOS measurement that significantly correlated with FEV1 changes. These findings further underscore the potential utility of X5 as an alternative measurement of pulmonary mechanics in COPD patients that is physiologically relevant and associated with changes in FEV1. Previous studies have shown that X5 is sensitive to the therapeutic effects of bronchodilators and that analysis of the differences between inspiratory and expiratory reactance can be used to identify COPD patients with expiratory flow limitation. We did not assess inspiratory and expiratory reactance. This does not negate the value of the current study, as IOS is often performed in clinical practice without assessment of inspiratory and expiratory values.

There are many practical issues that need to be considered when deciding which pulmonary function measurement will provide the best method of assessing COPD. Whilst spirometry is the widely accepted method to measure airflow obstruction, it can exhaust patients to perform and is effort dependent. Similar problems also exist for the body plethysmography. Alternatively IOS is an easy procedure to perform that requires only tidal breathing. However, there are other issues that should be further addressed before IOS is considered an alternative to FEV1 in clinical practice. Firstly, the 1 year follow up in the current study could be argued to be relatively short, and further assessment of changes in IOS parameters is warranted over longer periods and in a larger sample size with the inclusion of more severe patients. Secondly, the evaluation of IOS measurements in COPD patients during exacerbations would be interesting. These studies would allow IOS measurements to be compared to changes in FEV1 as well as other well recognized pulmonary function parameters such as IC and RV that categorize the severity of COPD.

Lastly, the actual values for IOS were used for analysis in this study, as one of the limitations of IOS in a clinical setting is the lack of definitive predictive equations, especially for adults. Although, there has been little variation in resistance values in the few studies that have reported reference values in healthy subjects, it should be noted that these studies were limited by selection criteria or sample size. Thus, the European Respiratory Society Task Force Report has recently highlighted the need for further large scale studies across a wider age range to validate existing reference values.

In summary, we have shown X5 and Fres to be the IOS measurements most closely associated with more traditional measurements of pulmonary function in COPD patients. These reactance measurements are related to the degree of airflow obstruction, and offer an alternative to FEV1. The ease of use of IOS and the sensitivity of this technique to measure the effects of therapeutic interventions in COPD patients should provide a sound basis for the increased use of this method in clinical practice.

Conflicts of interest statement

The authors have no financial or other potential conflicts of interest to disclose.

References


