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Impulse oscillometry may be of value in detecting early manifestations of COPD

S. Frantz [a,*], U. Nihlén [b], M. Dencker [a], G. Engström [c], C.G. Löfdahl [b], P. Wollmer [a]

[a] Clinical Physiology and Nuclear Medicine Unit, Department of Clinical Sciences, Malmö, Lund University, Sweden
[b] Respiratory Medicine and Allergology Unit, Department of Clinical Sciences, Lund, Lund University, Sweden
[c] Cardiovascular Epidemiology Research Group, Department of Clinical Science, Malmö, Lund University, Sweden

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KEYWORDS
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Summary
Background: Spirometry is used to diagnose chronic obstructive pulmonary disease (COPD). The Impulse oscillometry system (IOS) allows determination of respiratory impedance indices, which might be of potential value in early COPD, although previous experience is limited. We examined pulmonary resistance and reactance measured by IOS in subjects with or without self-reported chronic bronchitis or emphysema or COPD (Q+ or Q−) and subjects with or without COPD diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (G+ or G−).
Methods: From a previous population-based study 450 subjects were examined with spirometry and IOS and answered a questionnaire on respiratory symptoms and diseases.
Results: Seventy-seven subjects were Q+, of whom 34 also were G+. Q+/G− subjects ($n = 43$) reported respiratory symptoms more frequently (35–40% vs 8–14%) but had higher FEV_1 (100% vs 87%) than Q−/G+ subjects ($n = 90$), $p < 0.05$ for both comparisons. Q+ subjects had higher pulmonary resistance and lower pulmonary reactance than Q− subjects ($p < 0.01$ for all comparisons). The same pattern was seen both in G+ subjects ((Q+/Q−) R5 0.39/0.32, R5–R20 0.10/0.07, X5 0.13/0.09, AX 0.55/0.27, $p < 0.05$ for all) and G− subjects ((Q+/Q−) R5 0.35/0.29, R5–R20 0.08/0.06, X5 0.10/0.08, AX 0.31/0.19 $p < 0.05$ for all) except for R20 (adjusted for gender and age).
Conclusions: Self-reported chronic bronchitis or emphysema or COPD was associated with higher pulmonary resistance and lower pulmonary reactance measured by IOS, both among subjects with and without COPD according to GOLD criteria. IOS may have the potential to detect pathology associated with COPD earlier than spirometry.

* Corresponding author. Clinical Physiology and Nuclear Medicine Unit, Department of Clinical Sciences, Skåne University Hospital, 205 02 Malmö, Sweden. Tel.: +46 40 338733; fax: +46 40 338768.
E-mail address: sophia.frantz@med.lu.se (S. Frantz).

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Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by chronic, progressive airway obstruction and can be diagnosed by spirometry.[1] Major treatment guidelines, e.g. the global initiative for obstructive lung disease (GOLD 2010) recommend that COPD should be identified as early as possible in order to increase the opportunity to affect disease progression.[1] Most COPD patients experience respiratory symptoms such as dyspnoea, cough and sputum production, but the role of symptoms in early detection of COPD is unclear. Studies by de Marco et al.[2] and Lindberg et al.[3] suggest that the presence of chronic cough/phlegm identifies subjects at risk of COPD independent of smoking habits. However, longitudinal data from the Copenhagen Heart Study did not show that productive cough was a predictor of COPD development.[4] Furthermore, respiratory symptoms may not always be adequately reported and there is also a poor relationship between respiratory symptoms and spirometric variables.[1,5]

Respiratory mechanics can also be measured by forced oscillation measurements.[6–8] A commercially available method is provided by the Impulse Oscillometry System (IOS) (MasterScreen IOS, Viasys GmbH, Hoechberg, Germany). IOS assesses pulmonary resistance (Rrs) and reactance (Xrs), which are the real and imaginary part of respiratory impedance (Zrs), at various frequencies. Oscillometry has been proposed to be able to reflect more distal airway function[9] compared to spirometry[10,11] and distal airways are a major site for airway obstruction in COPD.[12–15] A clinical advantage of this method is that it is performed during tidal breathing and requires no forced manoeuvres. The relevance of this method in COPD is still somewhat unclear, but an association between reactance and FEV_1 in COPD patients has been shown.[16] Another study showed a correlation between IOS measurements and health status and dyspnoea among COPD patients.[17] These studies did not include control groups, and it is not clear what information IOS contributes in subjects with symptoms of COPD but normal spirometry.

The objective of this study was to examine pulmonary resistance and reactance measured by IOS in subjects with or without self-reported chronic bronchitis or emphysema or COPD (according to a questionnaire on respiratory diseases and symptoms, Q+/Q−) and subjects with or without COPD diagnosed according to the GOLD criteria (G+/G−). Our primary hypothesis was that pulmonary resistance is higher and reactance lower among subjects reporting respiratory symptoms in a group of subjects not fulfilling the spirometric criteria for COPD according to GOLD and that this may indicate early manifestations of COPD.

Methods

This was a cross sectional study including one clinic visit at the Department of Clinical Physiology, Malmö University Hospital (UMAS) in Malmö.

Study population

The invited study population consisted of 870 invited subjects, who comprised a sub-population to a postal respiratory questionnaire survey ("Questions about the lungs") performed in a population-based cohort in 1992 as well as 2000.[18,19] Three different groups of subjects all residing in the area of Malmö, Southern Sweden were recruited; (1) Lung healthy never-smokers = subjects who did not report any respiratory symptoms and never had smoked (2) Lung healthy current smokers = subjects who did not report any respiratory symptoms and were current smokers and (3) Subjects with COPD = subjects who responded that they had or had had a diagnosis of chronic bronchitis or emphysema or COPD.

At the study visit, subjects were classified according to their current smoking habits (current smokers, ex-smokers and never-smokers), their answers to the repeated questionnaire and their spirometry results according to the GOLD 2010 criteria.

Ethic approval

The study was approved by the Ethics Committee of Lund University and participants signed an informed consent before any study related procedure.

Questionnaire

Questions about the lungs

This questionnaire was used both for study recruitment purposes and for classification of several respiratory symptoms at the study visit. "Questions about the lungs" is a questionnaire about respiratory diseases and symptoms that has been used in several previous surveys and is described elsewhere.[18]

Self-reported chronic bronchitis or emphysema or COPD

Self-reported chronic bronchitis or emphysema or COPD (Q+) was defined as a positive answer to any of the questions "Do you have or have had chronic bronchitis or emphysema or chronic obstructive pulmonary disease (COPD)?" and "Did you get the diagnosis chronic bronchitis or emphysema or chronic obstructive pulmonary disease (COPD) by a physician?"

Chronic bronchitis, long-standing cough and use of pulmonary medication

Symptoms of chronic bronchitis (CB) were defined as a positive answer to "Have you had periods of 3 months with cough with phlegm during 2 years in a row during the last years?". Long-standing cough was defined as a positive answer to "Have you had long-standing cough during the last 12 months?". Any use of pulmonary medication was defined as a positive answer to "Do you regularly take or have taken any pulmonary medication?".

Smoking habits

Subjects who currently smoked or had stopped smoking within the last 12 months prior to the study visit were classified as smokers. Subjects who had stopped smoking more than 12 months prior to the study visit were classified as ex-smokers. Subjects who had never been smoking daily for more than one month were classified as never-smokers. The total tobacco consumption was calculated in pack-

years (one pack year = 20 cigarettes smoked per day for one year).

Lung function tests

All lung function measurements were made 15–45 min after inhalation of 1.0 mg of terbutaline (Bricanyl Turbuhaler).

Spirometry

Spirometry was performed according to the standards of the European Respiratory Society (ERS)[20] and European reference values were used.[20] A spirometer (Master Screen, Viasys GmbH – Erich Jaeger, Hoechberg, Germany) was used to measure forced expiratory volume in one second (FEV_1) and vital capacity (VC).

IOS

The pulmonary resistance and reactance was measured using IOS (MasterScreen IOS, Viasys GmbH, Hoechberg, Germany). The device consists of a loudspeaker that generates pressure oscillations composed of multiple frequencies, which are superimposed during 30 s of normal tidal breathing. This allows the assessment of resistance and reactance at several frequencies simultaneously, ranging from 5 to 35 Hz. Subjects sat upright, had a nose clip and firmly supported their cheeks with their hands. A minimum of three trials were performed. The following variables were evaluated: I. Respiratory resistance at 5 Hz (R5), which is assumed to reflect total airways resistance, II. Respiratory resistance at 20 Hz (R20), which is assumed to reflect central airways resistance, III. The fall in resistance from R5 to R20 (R5–R20) was used as a surrogate for the frequency dependence of respiratory resistance, which increases with increasing inhomogeneity of peripheral airways,[10,11] IV. Distal capacitive reactance at 5 Hz (X5), which is assumed to reflect peripheral airways function and V. An area index of low frequent reactance (AX). This parameter incorporates the area, which ranges from the negative reactance between 5 Hz and resonant frequency to the zero line.

Classification and staging of COPD

COPD was diagnosed according to the GOLD (Global initiative for chronic Obstructive Lung Disease) criteria (www.goldcopd.org, version 2010). Also staging of COPD severity was performed according to the GOLD criteria with stage I (mild): $FEV_1 \geq 80\%$ of predicted normal (PN), stage II (moderate): $50\% \leq FEV_1 < 80\%$ PN, stage III (severe): $30\% \leq FEV_1 < 50\%$ PN, and stage IV (very severe COPD): $FEV_1 < 30\%$ PN.

Statistical analyses

IBM SPSS Statistics 18 (SPSS Inc., Chicago, Illinois 60606) was used for the statistical analyses. One-way ANOVA was used for comparisons of continuous variables. Continuous variables not normally distributed (IOS variables) were log-transformed before the analyses. The mean values of IOS variables in the four study groups were adjusted for age and gender and compared in a general linear model. As the IOS variables had skewed distributions the variables were log-transformed before the general linear model analysis. Log-transformed values were back transformed after the statistical analyses and presented as geometric means.

Categorical variables were compared using Chi-squared analysis. A p-value of <0.05 was considered statistically significant.

Results

Participation

Of the 870 invited subjects 450 subjects (52%) participated. The participation rates for lung healthy never-smokers, lung healthy current smokers and subjects with self-reported COPD were 50% ($n = 60$), 50% ($n = 282$) and 57% ($n = 108$), respectively.

Characteristics of the study population

At the study visit subjects were classified into four different groups based on spirometry results and current answers to the questionnaire: Q–/G–, Q–/G+, Q+/G– and Q+/G+ (Fig. 1). Thirty-one participants were excluded from the analyses due to incomplete answers to the questionnaire. The characteristics of the study population are shown in Table 1. Overall more women than men participated.

Subjects with COPD according to the GOLD criteria (G+) were older than subjects with no COPD according to the GOLD criteria (G–), regardless of concomitant self-reported chronic bronchitis or emphysema or COPD (Q+) or not (Q–) ($p < 0.01$).

Q–/G+ subjects had smoked more in terms of pack-years compared with Q+/G– ($p < 0.01$). The proportion of ex-smokers was significantly higher in both of the groups of

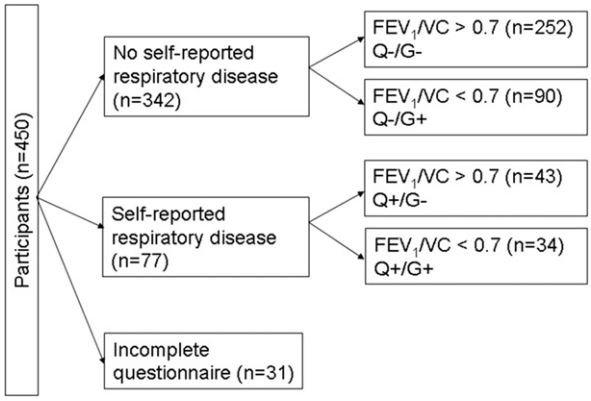

Figure 1 Flow chart demonstrating the classification of participants. Among subjects with no self-reported respiratory disease ($n = 342$) 252 subjects did not fulfil the spirometric criteria for COPD according to GOLD (Q–/G–) and 90 subjects did (Q–/G+). Among subjects with self-reported respiratory disease ($n = 77$) 43 subjects did not fulfil the spirometric criteria for COPD according to GOLD (Q+/G–) and 34 subjects did (Q+/G+).

Table 1 General characteristics of the study population. Numbers and percentages are shown for categorical variables and means with standard deviations are shown for continuous variables. (Q+/− = self-reported chronic bronchitis or emphysema or COPD or not, G+/− = COPD according to GOLD or not).

Subjects	Q−/G− (n = 252)	Q−/G+ (n = 90)	Q+/G− (n = 43)	Q+/G+ (n = 34)	Total (n = 419)
Male gender	99 (39.3%)	49 (54.4%)	12 (27.9%)	13 (38.2%)	173 (41.3%)
Female gender	153 (60.7%)	41 (45.6%)	31 (72.1%)	21 (61.8%)	246 (58.7%)
Age, years	60.1 (7.5)	64.1 (6.9)	60.0 (7.5)	65.5 (6.2)	61.4 (7.6)
Height, cm	169.4 (8.8)	171.3 (8.6)	167.7 (8.4)	168.3 (8.6)	169.5 (8.8)
BMI, kg/m^2	26.2 (5.0)	26.0 (4.3)	29.3 (6.4)	27.2 (5.6)	26.6 (5.1)
Never-smokers	65 (25.8%)	3 (3.3%)	10 (23.3%)	1 (2.9%)	79 (18.9%)
Ex-smokers	58 (23.0%)	30 (33.3%)	25 (58.1%)	20 (58.8%)	133 (31.7%)
Current smokers	129 (51.2%)	57 (63.3%)	8 (18.6%)	13 (38.2%)	207 (49.4%)
Pack-years	19 (17)	32 (23)	19 (18)	30 (15)	23 (19)
COPD stage I	0	64 (71.1%)	0	18 (52.9%)	82 (19.6%)
COPD stage II	0	26 (28.9%)	0	10 (29.4%)	36 (8.6%)
COPD stage III−IV	0	0	0	6 (17.6%)	6 (1.4%)

Q+ subjects compared to any of the groups of subjects with Q− ($p < 0.05$).

A diagnosis of COPD according to the GOLD criteria was confirmed in 30% of the study population most subjects at GOLD stage I.

Spirometry and IOS results and report of respiratory symptoms in the study population

The crude mean levels of resistance and reactance over the full frequency range are plotted in Fig. 2 for the four different study groups. Especially for the measurement of resistance, both of the curves representing subjects reporting respiratory symptoms (Q+) are clearly separated from both of the curves representing symptom-free subjects (Q−). We wanted further to analyse these differences, comparing subjects with and without respiratory symptoms and with and without COPD according to GOLD.

Symptomatic subjects (Q+) had statistically significantly lower spirometry values (FEV_1, VC, FEV_1/VC) than non-symptomatic subjects (Q−) (Table 2a). Q+ subjects also had statistically significantly higher pulmonary resistance and lower (i.e. abnormal) reactance than Q− subjects.

Subjects fulfilling the spirometric criteria for COPD according to GOLD (G+) had significantly higher pulmonary resistance and lower pulmonary reactance than subjects not fulfilling the GOLD criteria (G−), except for unadjusted R20 (Table 2b). A higher proportion of G+ subjects reported use of any pulmonary medication, but no difference was seen between the groups regarding report of long-standing cough and symptoms characteristic of chronic bronchitis. As expected, G+ subjects had significantly lower FEV_1 and lower FEV_1/VC than G− subjects.

In Table 3 all 4 study groups are compared. This shows that among all G+ subjects, lung function variables according to spirometry were lower and pulmonary resistance was higher and pulmonary reactance was lower for Q+ subjects compared to Q− subjects (except for VC% PN, $p = 0.25$ and R20, $p = 0.11$) The same pattern was seen among G− subjects (except for FEV_1/VC% PN, $p = 0.84$).

G+ subjects had lower FEV_1 and FEV_1/VC than G− subjects, irrespective of symptoms.

While pulmonary resistance did not differ significantly between Q+/G+ subjects and Q+/G− subjects, pulmonary reactance was significantly lower among Q+/G+ subjects than Q+/G− subjects ($p < 0.05$). The measurements with forced oscillation thus identified differences between

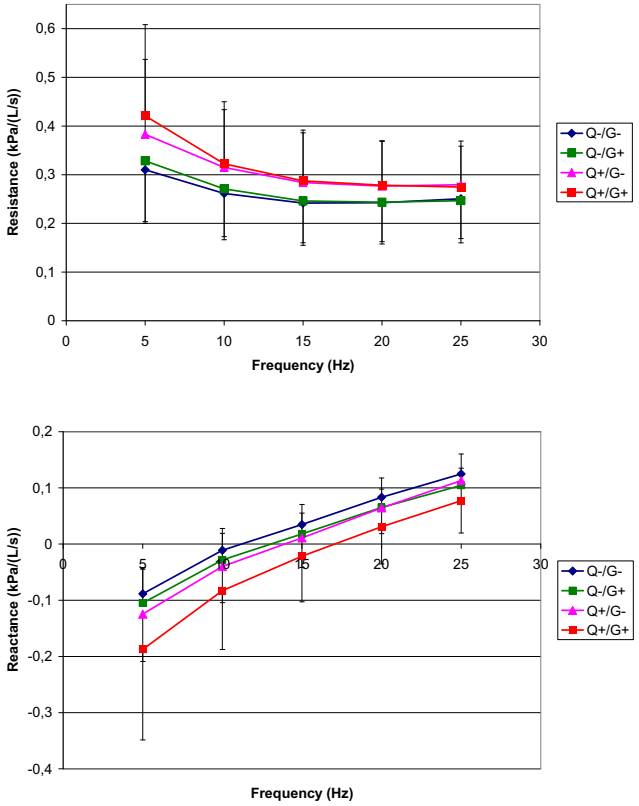

Figure 2 The crude mean values of resistance and reactance at different frequencies in the different study groups. (Q+/Q− = questionnaire positive or negative, G+/G− = fulfilling the spirometric criteria for COPD according to GOLD or not).

Table 2a Comparison of spirometry and IOS results between Q+ and Q− subjects (subjects with or without self-reported chronic bronchitis or emphysema or COPD). Means with standard deviations are shown for continuous variables and numbers and percentages are shown for categorical variables. Continuous variables not normally distributed (all unadjusted IOS values) are presented as medians and 80% central ranges. Geometric means are adjusted for gender and age. PN = predicted normal value. (Q+/− = self-reported chronic bronchitis or emphysema or COPD or not).

	Q+ (n = 77)	Q− (n = 342)	p-value
FEV_1% PN	90 (23)	101 (15)	<0.001
VC% PN	106 (19)	111 (14)	0.015
FEV_1/VC	0.70	0.74	0.003
FEV_1/VC% PN	90 (17)	97 (10)	<0.001
R5 (kPa/(L/s))	0.37 (0.23−0.57)	0.30 (0.19−0.47)	<0.001
R5 geometric mean	0.36	0.30	<0.001
R20 (kPa/(L/s))	0.26 (0.19−0.38)	0.23 (0.16−0.35)	0.004
R20 geometric mean	0.26	0.23	0.004
R5−R20 (kPa/(L/s))	0.11 (0.04−0.23)	0.06 (0.02−0.14)	<0.001
R5−R20 geometric mean	0.09	0.06	<0.001
X5 (kPa/(L/s))	−0.12 (−0.31 to −0.05)	−0.08 (−0.16 to −0.04)	<0.001
X5 geometric mean	−0.11	−0.08	<0.001
AX	0.49 (0.08−1.88)	0.20 (0.06−0.83)	<0.001
AX geometric mean	0.40	0.22	<0.001
Symptoms of CB	24 (31.2%)	30 (8.8%)	<0.001
Long-standing cough	30 (39.0%)	49 (14.3%)	<0.001
Any use of pulmonary medication	29 (37.7%)	12 (3.5%)	<0.001

symptomatic and asymptomatic subjects not revealed by spirometry. For pulmonary resistance and reactance, higher values for unadjusted R5 and R20 were observed for Q+/G− subjects than for Q−/G+ subjects ($p < 0.05$). After adjustments for gender and age, no differences were observed.

Discussion

Results from this study suggest that subjects with self-reported chronic bronchitis or emphysema or COPD (Q+) have a higher pulmonary resistance and lower pulmonary

Table 2b Comparison of spirometry and IOS results between G+ and G− subjects (subjects with or without COPD according to the GOLD criteria). Means with standard deviations are shown for continuous variables and numbers and percentages are shown for categorical variables. Continuous variables not normally distributed (all unadjusted IOS values) are presented as medians and 80% central ranges. Geometric means are adjusted for gender and age. PN = predicted normal value. (G+/− = COPD according to GOLD or not).

	G+ (n = 124)	G− (n = 295)	p-value
FEV_1% PN	85 (18)	104 (14)	<0.001
VC% PN	110 (18)	110 (14)	0.629
FEV_1/VC	0.62	0.78	<0.001
FEV_1/VC% PN	81 (11)	102 (6)	<0.001
R5 (kPa/(L/s))	0.32 (0.20−0.57)	0.30 (0.19−0.49)	0.029
R5 geometric mean	0.34	0.30	0.002
R20 (kPa/(L/s))	0.23 (0.16−0.36)	0.24 (0.16−0.35)	0.505
R20 geometric mean	0.25	0.23	0.049
R5−R20 (kPa/(L/s))	0.08 (0.03−0.21)	0.06 (0.02−0.15)	0.013
R5−R20 geometric mean	0.07	0.06	0.023
X5 (kPa/(L/s))	−0.10 (−0.25 to −0.05)	−0.08 (−0.16 to −0.04)	<0.001
X5 geometric mean	−0.10	−0.08	<0.001
AX	0.34 (0.09−1.54)	0.20 (0.06−0.86)	<0.001
AX geometric mean	0.33	0.21	<0.001
Symptoms of CB	21 (16.9%)	33 (11.1%)	0.098
Long-standing cough	26 (21.0%)	53 (18.0%)	0.433
Any use of pulmonary medication	21 (16.9%)	20 (6.8%)	<0.001

Table 3 Spirometry, IOS and questionnaire results at the study visit. Means with standard deviations are shown for continuous variables and numbers and percentages are shown for categorical variables. For IOS variables geometric means (adjusted for gender and age) are shown. PN = predicted normal value. Letters a, b, c and d show pair wise significant comparisons between indicated groups ($p < 0.05$). (Q+/− = self-reported chronic bronchitis or emphysema or COPD or not, G+/− = COPD according to GOLD or not).

	Q−/G− (a) (n = 252)	Q−/G+ (b) (n = 90)	Q+/G− (c) (n = 43)	Q+/G+ (d) (n = 34)
FEV_1% PN	$105^{b,c,d}$ (13)	$87^{a,c,d}$ (13)	$100^{a,b,d}$ (15)	$78^{a,b,c}$ (25)
VC% PN	110^{c} (14)	111^{c} (16)	$105^{a,b}$ (16)	108 (22)
FEV_1/VC	$0.78^{b,d}$	$0.64^{a,c,d}$	$0.79^{b,d}$	$0.58^{a,b,c}$
FEV_1/VC% PN	$102^{b,d}$ (6)	$83^{a,c,d}$ (7)	$102^{b,d}$ (7)	$76^{a,b,c}$ (16)
R5 (kPa/(L/s))	$0.29^{b,c,d}$	$0.32^{a,d}$	0.35^{a}	$0.39^{a,b}$
R20 (kPa/(L/s))	$0.23^{c,d}$	0.24	0.25	0.27^{a}
R5−R20 (kPa/(L/s))	$0.06^{c,d}$	0.07^{d}	0.08^{a}	$0.10^{a,b}$
X5 (kPa/(L/s))	$0.08^{b,c,d}$	$0.09^{a,d}$	$0.10^{a,d}$	$0.13^{a,b,c}$
AX	$0.19^{b,c,d}$	$0.27^{a,d}$	$0.31^{a,d}$	$0.55^{a,b,c}$
Symptoms of CB	$18^{c,d}$ (7.1%)	12^{c} (13.3%)	$15^{a,b}$ (34.9%)	9^{a} (26.5%)
Long-standing cough	$36^{c,d}$ (14.3%)	$13^{c,d}$ (14.4%)	$17^{a,b}$ (39.5%)	$13^{a,b}$ (38.2%)
Any use of pulmonary medication	$5^{b,c,d}$ (2.0%)	$7^{a,c,d}$ (7.8%)	$15^{a,b}$ (34.9%)	$14^{a,b}$ (41.2%)

reactance than subjects without self-reported chronic bronchitis or emphysema or COPD (Q−), both in subjects with and without spirometry diagnosed COPD according to the GOLD criteria (G+ and G−). In addition, characteristics of Q+ subjects were associated with more frequent reports of symptoms characteristic of chronic bronchitis, long-standing cough and use of pulmonary medication compared with G+ subjects. Together these findings suggest that IOS could be of interest for getting increased understanding of relationships between underlying disease mechanisms of COPD, for example small airway disease and clinically important symptoms. IOS may be complementary to spirometry for this purpose. Furthermore, it seems conceivable that IOS would be of value for detection of individuals that already have developed typical pathological airway changes (i.e. small airway disease) for COPD, even though not yet meeting the GOLD diagnosis criteria.

Worldwide, COPD is underdiagnosed as well as detected too late in its course, due to factors such as underuse of spirometry and patient delay.[1,21,22] Early detection is of importance to get the best possibility to intervene pharmacologically and with other treatments. IOS seems to have the potential to evaluate further the occurrence of distal airway pathology, an important component of COPD,[12–14,23] by measuring resistance and reactance. Since IOS is a non-invasive method that requires minimal active engagement by the patient it could perhaps also be used routinely with the purpose of facilitate early detection of COPD. Since forced oscillations measurements are made during quiet breathing at functional residual capacity (FRC), forced breathing manoeuvres which may affect bronchial tone are avoided. In theory, elastic properties of the lung are reflected in the low frequencies of reactance (distal airways) and inertial properties are reflected in the high frequencies of reactance (central airways).[24] For resistance, the theory is that resistance at low frequencies represents total airway resistance, and resistance at high frequencies represents central airway resistance, proposing that the difference between these two is a surrogate for peripheral airway resistance.[9] Already in the 1980s Clément et al.[25] could separate healthy subjects from subjects with respiratory complaints, associated or not with a reduced FEV_1. This group also studied differences between smokers and non-smokers with normal spirometry without finding any significant differences in forced oscillation.[26] A previous study of respiratory impedance in a large sample of subjects referred for routine spirometry has shown that the impedance measurements contributed significantly to the discrimination between subjects with and without marked respiratory complaints.[27] A recent study has also shown that IOS measurements can be used to define different subgroups of COPD patients.[28]

Symptoms of long-standing cough and symptoms characteristic of chronic bronchitis were more frequent among Q+ subjects than G+ subjects. There was no significant difference concerning the report of long-standing cough and symptoms characteristic of chronic bronchitis comparing G+ and G− subjects.

It has been shown that subjects with respiratory symptoms have a high risk of developing COPD[2,3,29] although there are conflicting results.[4] Symptoms also have a predictive value among COPD patients, for example it has been shown that dyspnoea better predict 5-year survival than FEV_1 in this group.[30] Cough and sputum production may be symptoms of particular importance, since they may be independent risk factors for FEV_1 decline,[31] COPD hospitalisation and also overall mortality.[32,33]

The fact that there is a poor relationship between respiratory symptoms and spirometric variables[1,5] may be a further reason to use additional methods such as for example IOS for characterisation of lung physiology, particularly if these methods are validated, certified, non-invasive and user friendly. Concerning IOS, there is a need for more extensive studies of reference values.

A strength of this study is that the original study group is population-based. In a representative population-based sample, the prevalence of COPD is very low, and we therefore performed a stratified sampling to increase the

proportion of subjects with COPD. Interpretation of the information obtained by questionnaires always involves uncertainties, which is a limitation that this study shares with many other studies. Screening subjects for symptoms is difficult; therefore there is a need for sensitive and simple objective screening methods for future studies in this field.

The GOLD criteria for a COPD diagnosis are based on a fixed cut-off FEV_1/VC ratio of 0.7. This leads to a risk of overestimation of COPD especially in elderly men.[34] Still, we preferred to apply the fixed value since also subjects with an FEV_1/VC below 0.7 but above the lower limit of normal for the age-adjusted predictions appear to risk an unfavourable outcome.[34]

In conclusion, this study shows that subjects reporting respiratory symptoms differ in lung mechanics measured by the forced oscillation technique, whether they fulfil the GOLD criteria of COPD or not. This may indicate that IOS better captures changes in respiratory mechanics than spirometry. As forced oscillation measurements are considered better to reflect distal airway function than spirometry, IOS may be useful for early detection of COPD. Further research is, however, needed to establish this.

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Conflict of interest statement

Ulf Nihlén and Gunnar Engström are full-time employees at AstraZeneca. The other authors report no conflicts of interest.

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