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Original Article

Impedance differences between chronic obstructive pulmonary disease and Asthma patients with the same airflow limitation severities

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Abstract: Objective: Chronic obstructive pulmonary (COPD) disease and asthma are both chronic lung diseases that limit airflow. The aim of this study was to compare IOS parameters of COPD and asthma patients with the same airflow limitation levels. Then evaluate the application value of IOS parameters to identify these two diseases. Methods: A total of 155 patients, including 35 normal subjects, 60 COPD patients, and 60 asthma patients, were enrolled in this study. The COPD and asthma patients were divided into three subgroups according to their airflow limitation stages. Each subgroup contained 20 subjects. We compared the IOS parameters of the normal subjects, COPD patients, and asthma patients. The IOS parameters in each paired COPD and asthma subgroup with the same airflow limitations were also compared. ROC and discriminant analysis were used to evaluate the power of IOS parameters to differentiate between asthma and COPD patients. Results: The IOS parameters including Z_5, R_5, R_{20} and R_{5-20} of both the COPD and asthma patients were greater than those of the normal subjects. The above IOS parameters were greater in the asthma patients than the COPD patients, although the FEV_1 values were not significantly different. When the IOS parameters were compared between the paired asthma and COPD subgroups, the results were the same as those for the whole COPD and asthma groups. ROC analysis showed Z_5, R_5, R_{20} alone were valuable to distinguish with COPD and asthma with the same airflow limitation, whose AUCs were all greater than 0.7. Discriminant analysis showed that more than 75% patients can be correctly classified when combining spirometry and IOS parameters. Conclusion: The respiratory impedance indices of asthma patients are greater than those of COPD patients, although the airflow limitations of these patients are similar. These differences may provide help to distinguish with COPD and asthma patients.

Keywords: Impedance, impulse oscillometry, asthma, chronic obstructive pulmonary disease, lung function

Introduction

Chronic obstructive pulmonary disease (COPD) and asthma are very common chronic airway diseases [1]. During the exacerbation of these conditions, airflow limitations can be detected in both COPD and asthma patients [2, 3]. The forced expiratory volume in 1 second (FEV_1) is the most important index of the severity of airflow limitation and is measured by spirometry [4]. However, when performing spirometry, the subjects are required to have to breathe in a hard manner. Currently, many lung function tests [4] that can reflect other pathological aspects of diseases [5, 6] are widely used in clinical practice [7], whereas the conventional pulmonary function test (cPFT) is not. Some of these lung function tests do not require hard breathing, and the breathing patterns during the measurements are similar to those of daily life [5, 6]. The parameters of these tests reflect pathological changes in tidal breathing [8] and may differ between COPD and asthma patients who endure the same level of airflow limitation.

Impulse oscillometry (IOS) was introduced by Dubois [9] and is considered to be a forced oscillation technique (FOT) in which only normal breathing is required [10]. IOS allows for the collection of respiratory impedance indices including the respiratory impedance at 5 Hz (Z_5), respiratory resistance at 5 Hz (R_5), respiratory resistance at 10 Hz (R_{10}), respiratory resist-

ance at 20 Hz (R_{20}), the difference in resistances at 5 Hz and 20 Hz (R_{5-20}), and the reactance at 5 Hz (X_5) [11]. Based on these indices, we know that respiratory resistance and reactance are located in different parts of the airway [12]. Since IOS was introduced, many studies have revealed that some respiratory resistance is well correlated with FEV_1 in both COPD and asthma patients [11, 13-17]. Furthermore, IOS has been confirmed to possess the ability to detect the airflow limitation stage in obstructive lung disease [6, 18-20]. Moreover, in contrast to spirometry measurements, the performance of IOS does not require hard respiration. When the measurements are initiated, the subject's breathing pattern is similar to the breath pattern of daily life. So the parameters from IOS can reflect respiratory resistance in tidal breathing [21-23]. Therefore, although COPD and asthma patients occasionally endure the same levels of airflow limitation, the impedance indices from IOS in these patients may differ.

In the present study, sixty COPD patients and sixty asthma patients were selected. We compared their respiratory impedances in each airflow limitation stage to observe the impedance differences between the COPD and asthma patients. Further more, we observed the power of IOS parameters to differentiate COPD and asthma.

Materials and methods

Study design

Healthy volunteers, COPD patients and asthma patients were selected if they met the inclusion criteria. Each enrolled subject was taught to correctly perform IOS and spirometry. IOS was tested first to the collect the respiratory impedance indices. Subsequently, spirometry was tested to detect the airflow limitation level. IOS was always performed before spirometry. Finally, the collected data were used for the analyses.

Ethics statement

The Ethics Committee of the Shanghai Pudong New Area People's Hospital approved the study protocol, and informed consent was obtained from each participant.

Subjects

Thirty-five healthy volunteers, sixty asthma patients and sixty COPD patients were enrolled in this study. All subjects were selected according to the inclusion and exclusion criteria detailed below.

The healthy volunteers were selected from among subjects with normal lung function and without histories of smoking, recent respiratory tract diseases, or cardiopulmonary disease.

COPD was diagnosed according to the Global Initiative for Obstructive Lung Disease criteria [2], and asthma was diagnosed according to the Global Initiative for Asthma criteria [1]. The patients did not use long-acting bronchodilators for at least twenty-four hours prior to the test and abstained from short-acting bronchodilators for at least six hours before the test.

The exclusion criteria included other diseases that affect lung function and comparable disabilities. Patients with FEV_1s < 35% Pred were not included.

The COPD patients were divided into the following 3 groups: a mild COPD group ($FEV_1 \geq 60\%$ predicted [Pred], n = 20), a moderate COPD group (50% Pred $\leq FEV_1 <$ 60% Pred, n = 20), and a severe COPD group (35% Pred $\leq FEV_1 <$ 50% Pred, n = 20). The asthma patients were also divided into 3 groups: a mild asthma group ($FEV_1 \geq 60\%$ Pred, n = 20), a moderate asthma group (50% Pred $\leq FEV_1 <$ 60% Pred, n = 20), and a severe asthma group (35% Pred $\leq FEV_1 <$ 50% Pred, n = 20). These classifications were performed according to the ATS/ERS-2005 guidelines [24]. In this study, the mild and moderate stages according to the ATS/ERS-2005 guidelines were combined to form the mild asthma group and the mild COPD group. The moderate COPD group and moderate asthma group were in the moderate-severe stages according to the ATS/ERS-2005 guidelines. The severe COPD group and severe asthma group were in the severe stages according to the ATS/ERS-2005 guidelines.

Impedance measurement

In the present study, the impedance indices included Z_5, R_5, R_{10}, R_{20}, R_{5-20}, and X_5. These indices were measured with a MasterLab IOS

Table 1. Comparison of the baseline characteristics and spirometry parameters and IOS parameters between the COPD, asthma, and healthy groups

	Healthy	Asthma	COPD	F (X^2)	P
N	35	60	60		
Sex (male/female)	24/11	41/19	45/15	0.773	0.679
Age (yrs)	56.91±9.09	58.25±9.63	60.73±9.12	2.104	0.126
Height (cm)	163.89±6.83	163.98±8.49	164.58±4.96	0.153	0.858
Weight (kg)	65.84±8.74	64.77±12.80	64.18±11.07	0.240	0.787
FEV_1 (%Pred)	102.15±11.33	56.04±13.46*	54.43±10.91*	143.748	0.000
FEV_1/FVC (%)	88.36±5.48	60.55±9.86*	60.38±8.62*	143.748	0.000
Lg Z_5	-0.5080±0.1195	-0.0714±0.1465*	-0.1791±0.1566*,†	102.607	0.000
(Z_5 (kPa/L/sec))	(0.3220±0.8824)	(0.8965±0.2990)	(0.7078±0.2788)	---	---
Lg R_5	-0.5255±0.1229	-0.1143±0.1265*	-0.2281±0.1274*,†	119.204	0.000
(R_5 (kPa/L/sec))	(0.3100±0.0876)	(0.8007±0.2281)	(0.6172±0.1859)	---	---
Lg R_{20}	-0.6057±0.1234	-0.3503±0.9735*	-0.4412±0.0936*,†	68.798	0.000
(R_{20} (kPa/L/sec)	(0.2577±0.0727)	(0.4580±0.1096)	(0.3703±0.0792)	---	---
Lg $R_{5\text{-}20}$	-1.3351±0.2561	-0.5179±0.2320*	-0.6956±0.3374*,†	93.958	0.000
($R_{5\text{-}20}$ (kPa/L/sec))	0.0523±0.0350	0.3425±0.1568	0.2468±0.1348	---	---
Lg $\lvert X_5 \rvert$	-1.1102±0.1680	-0.4995±0.2645*	-0.5994±0.3017	64.99	0.000
(X_5 (kPa/L/sec))	-0.0837±0.0351	-0.3792±0.2389	-0.3192±0.2487	---	---

*Compared with the healthy controls, $P < 0.05$, †compared with the asthma patients, $P < 0.05$. Z_5, respiratory impedance at 5 Hz; R_5, respiratory resistance at 5 Hz; R_{10}, respiratory resistance at 10 Hz; R_{20}, respiratory resistance at 20 Hz; $R_{5\text{-}20}$, difference in resistance between 5 Hz and 20 Hz; X_5, reactance at 5 Hz; FEV_1, forced expiratory volume in 1 s; FVC forced expiratory volume; Pred, predicted; yrs years; cm centimetres; kg, kilogram; kPa, kilopascal; L, litre; sec, seconds; Lg, logarithmic transformation.

System (Erich Jaeger GmbH, Hoechberg, Germany). The system was calibrated using a 3-L syringe for volume calibrations and a reference resistance of 0.2 KPa/L·(s^{-1}) for the pressure calibrations. Body temperature and saturated gas pressure calibrations were also performed. When performing IOS, all subjects wore a nose clip, and they were seated in an upright position. The patients breathed spontaneously through a mouthpiece. The subjects supported their cheeks and chins with their hands to decrease the shunt compliance of the cheeks. The impulse was applied for 30 seconds in each IOS test. We excluded artefacts which were caused by coughing, swallowing and breath-holding.

Airflow limitation measurement

The airflow limitations were measured using a computerised spirometer (Erich Jaeger GmbH, Hoechberg, Germany). Calibration for the body temperature and the saturated gas pressure and volume were performed. Each subject was coached how to performe standard forced expiratory manoeuvres. The indices of airflow limitation included the FEV_1 and FEV_1/FVC.

Data analysis

The data were analysed with SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). The indices of the COPD, asthma and healthy groups were compared with 1-way analysis of variance (ANOVA), and LCD tests were performed to compare the differences between pairs of groups. Some of these indices were compared by their logarithmic transformations because of the heterogeneity of variance. Because the impedance indices in the COPD and asthma subgroups were not normally distributed, we also compared them with independent t-tests following logarithmic transformations. The gender distributions were compared with Chi-square analyses. Receiver Operating Characteristic curve was used to analysis the power of IOS parameters to differentiate COPD from asthma patients. At last, we used discriminant analysis to obtain the correct classification of COPD and asthma patients using spirometary and IOS parameters.

Table 2. Comparison of the baseline characteristics and spirometry parameters and IOS parameters between the mild COPD and mild asthma subgroups

	Mild COPD	Mild asthma	t (X^2)	P
n	20	20		
Sex (male/female)	16/4	14/6	0.533	0.358
Age (yrs)	54.75±9.81	51.90±7.46	1.034	0.308
Height (cm)	165.35±4.39	164.15±8.93	0.539	0.593
Weight (kg)	64.10±10.67	69.15±12.86	-1.362	0.181
FEV_1 (%Pred)	66.68±6.17	71.29±9.74	-1.786	0.082
FEV_1/FVC (%)	64.00±7.72	68.53±7.28	-1.908	0.064
Lg Z_5	-0.2979±0.1157	-0.1694±0.1435	-3.116	0.003
(Z_5 (kPa/L/sec))	0.5225±0.1597	0.7150±0.2570	---	---
Lg R_5	-0.3260±0.1084	-0.1951±0.1329	-3.413	0.002
(R_5 (kPa/L/sec))	0.4875±0.1389	0.6685±0.2200	---	---
Lg R_{20}	-0.4847±0.1070	-0.3976±0.0805	-2.910	0.006
(R_{20} (kPa/L/sec))	0.3370±0.0824	0.4070±0.0776	---	---
Lg R_{5-20}	-0.8994±0.3568	-0.6595±0.2776	-2.350	0.024
(R_{5-20} (kPa/L/sec))	0.1505±0.1004	0.2615±0.1543	---	---
Lg $\lvert X_5 \rvert$	-0.8225±0.2497	-0.6715±0.2486	-1.916	0.063
(X_5 (kPa/L/sec))	-0.1755±0.1066	-0.2490±0.1486	---	---

Z_5, respiratory impedance at 5 Hz; R_5, respiratory resistance at 5 Hz; R_{20}, respiratory resistance at 20 Hz; R_{5-20}, difference in resistance between 5 Hz and 20 Hz; X_5, reactance at 5 Hz; FEV_1, forced expiratory volume in 1 s; FVC, forced expiratory volume; Pred, predicted; yrs, years; cm, centimetres; kg, kilogram; kPa, kilopascal; L, litre; sec, seconds.

Table 3. Comparison of the baseline characteristics and spirometry parameters and IOS parameters between the moderate COPD and moderate asthma subgroups

	Moderate COPD	Moderate asthma	t (X^2)	P
n	20	20		
Sex (male/female)	15/5	15/5	0.000	1.000
Age (yrs)	63.50±6.95	60.90±9.79	0.968	0.339
Height (cm)	164.48±4.59	166.85±7.73	-1.181	0.245
Weight (kg)	63.88±9.94	64.20±13.79	-0.085	0.932
FEV_1 (%Pred)	54.05±1.91	54.25±2.52	-0.275	0.784
FEV_1/FVC (%)	61.21±6.16	57.66±7.69	-0.275	0.784
Lg Z_5	-0.1827±0.1163	-0.0668±0.1329	-2.935	0.006
(Z_5 (kPa/L/sec))	0.6785±0.1739	0.8970±0.2832	---	---
Lg R_5	-0.2231±0.1016	-0.1170±0.1074	-3.210	0.003
(R_5 (kPa/L/sec))	0.6135±0.1380	0.7865±0.1994	---	---
Lg R_{20}	-0.4474±0.0748	-0.3519±0.0937	-3.562	0.001
(R_{20} (kPa/L/sec))	0.3620±0.0625	0.4550±0.1034	---	---
Lg R_{5-20}	-0.6297±0.1708	-0.5141±0.1780	-2.096	0.043
(R_{5-20} (kPa/L/sec))	0.2515±0.0944	0.3310±0.1327	---	---
Lg $\lvert X_5 \rvert$	-0.5998±0.2194	-0.4832±0.2546	-1.553	0.129
(X_5 (kPa/L/sec))	-0.2805±0.1256	-0.3935±0.2685	---	---

Z_5, respiratory impedance at 5 Hz; R_5, respiratory resistance at 5 Hz; R_{20}, respiratory resistance at 20 Hz; R_{5-20}, difference in resistance between 5 Hz and 20 Hz; X_5, reactance at 5 Hz; FEV_1, forced expiratory volume in 1 s; FVC, forced expiratory volume; Pred, predicted; yrs, years; cm, centimetres; kg, kilogram; kPa, kilopascal; L, litre; sec, seconds.

Results

Comparisons of the baseline characteristics, FEV_1s and FEV_1/FVCs between the COPD, asthma, and hHealthy groups

There were no differences in sex, age, weight, or height between the COPD, asthma, and healthy groups. Meanwhile, the FEV_1 and FEV_1/FVC values exhibited no differences between the COPD and asthma groups, though they were both decreased compared with health group (**Table 1**). In the asthma group, the impedance indices, including Z_5, R_5, R_{20}, and R_{5-20} which were compared by their logarithmic transformations, were significantly greater than those in the COPD group ($P < 0.05$).

Comparison of the impedance indices between the COPD and asthma subgroups at each airflow limitation level

The sex, age, weight, height, FEV_1, and FEV_1/FVC values did not differ significantly between the mild COPD and mild asthma subgroups. However, the Z_5, R_5, R_{20}, and R_{5-20} values in the mild asthma subgroup were greater than those of the mild COPD subgroup (**Table 2**).

Similar to the above results, the sex, age, weight, height, FEV_1, and FEV_1/FVC values also exhibited no significant differences between the moderate subgroups or the between the severe subgroups. However, the Z_5, R_5, R_{20}, and R_{5-20} in values of the moderate and severe asthma subgroups were greater than

Table 4. Comparison of the baseline characteristics and spirometry parameters and IOS parameters between the severe COPD and severe asthma subgroups

	Severe COPD	Severe asthma	T (X^2)	P
N	20	20		
Sex (male/female)	14/6	12/8	0.440	0.371
Age (yrs)	63.95±7.54	61.95±8.49	0.787	0.436
Height (cm)	163.90±5.91	160.95±8.13	1.312	0.197
Weight (kg)	64.55±13.12	60.55±10.84	0.946	0.350
FEV_1 (%Pred)	42.56±4.62	42.60±4.77	-0.024	0.981
FEV_1/FVC (%)	55.94±9.89	55.46±9.31	0.157	0.876
Lg Z_5	-0.0566±0.1364	0.0222±0.0949	-2.119	0.041
(Z_5 (kPa/L/sec))	0.9225±0.3162	1.0775±0.2493	---	---
Lg R_5	-0.1352±0.0957	-0.0307±0.0793	-3.760	0.001
(R_5 (kPa/L/sec))	0.7505±0.1806	0.9470±0.1797	---	---
Lg R_{20}	-0.3914±0.0744	-0.3013±0.0963	-3.312	0.002
(R_{20} (kPa/L/sec))	0.4120±0.0756	0.5120±0.1214	---	---
Lg R_{5-20}	-0.5025±0.1698	-0.3810±0.1325	-2.525	0.016
(R_{5-20} (kPa/L/sec))	0.3385±0.1372	0.4350±0.1373	---	---
Lg $\lvert X_5 \rvert$	-0.3758±0.2593	-0.3437±0.1834	-0.452	0.654
(X_5 (kPa/L/sec))	-0.5015±0.3266	-0.4950±0.2257	---	---

Z_5, respiratory impedance at 5 Hz; R_5, respiratory resistance at 5 Hz; R_{20}, respiratory resistance at 20 Hz; R_{5-20}, difference in resistance between 5 Hz and 20 Hz; X_5, reactance at 5 Hz; FEV_1, forced expiratory volume in 1 s; FVC, forced expiratory volume; Pred, predicted; yrs, years; cm, centimetres; kg, kilogram; kPa, kilopascal; L, litre; sec, seconds.

those of the moderate and severe COPD subgroups (**Tables 3** and **4**).

ROC curve analysis between COPD and asthma patients

ROC curve analysis showed that AUC of most IOS parameters except R_{5-20} and X_5 were higher than 0.7 between each paired COPD and asthma group. Their sensitivity and specificity were shown in **Table 5** (**Table 5** and **Figure 1**).

Correct classification between COPD and asthma patients using FEV_1, FEV_1/FVC together with Z_5, R_5 and R_{20} through discriminant analysis

Combining *FEV_1, FEV_1/FVC and IOS parameters including Z_5, R_5 and R_{20}* eighty to ninety percent COPD patients can be correctly classified. However, the correct classification ratio of asthma patients was not so high. The whole classification ratio was more than seventy-five percent (**Table 6**).

Discussion

Many studies have utilised IOS values in investigations of asthma and COPD patients [25, 26]. As previously reported, IOS parameters can be used to detect expiratory flow limitations [15, 19, 27, 28], and some IOS parameters have also been confirmed to be well correlated with the FEV_1 and to be even more sensitive in some conditions [27-29]. However, few articles have reported on the differences in impedance measured with IOS between asthma and COPD patients with the same airflow limitation levels. In clinical practice, these differences may help us to distinguish between COPD and asthma to some extent.

In the present study, we first compared the impedance indices between the whole COPD and asthma groups and found that the impedance values (Z_5, R_5, R_{20}, and R_{5-20}) were significantly greater in the asthma patients than the COPD patients. In 2010, Shintarou Kandal et al. ever compared the impedances of asthma patients, COPD patients and healthy volunteers and found that the, FEV_1 % Pred in the COPD group (55.3±2.3) was smaller than that of the asthma group (79.5±2.9). However, the Z_5 and R_5 have not previously been observed to be greater in COPD patients than in asthma patients. The R_{20} value has been found to be higher in asthma patients [30]. According to the results of these authors, the impedance in asthma patients should be greater than that in COPD patients at the same levels of airflow limitation. Our results confirmed this hypothesis. There are two main factors leading to this phenomenon. As we know, indices of airflow limitation including FEV_1 and FEV_1/FVC are measured in a forced way. However, subjects should only breathe normally when performing IOS. The different measuring way may cause different IOS parameters' value between COPD and asthma patients,

Table 5. ROC curve analysis using IOS parameters in each paired COPD and asthma groups

Groups	IOS	AUC	Sensitivity	Specificity	Youden index
COPD-asthma	Z_5	0.700	0.817	0.517	0.334
	R_5	0.738	0.817	0.633	0.450
	R_{20}	0.754	0.717	0.733	0.450
	R_{5-20}	0.678	0.717	0.583	0.300
	X_5	0.597	0.300	0.867	0.167
Mild COPD-mild asthma	Z_5	0.781	0.750	0.750	0.500
	R_5	0.794	0.700	0.850	0.550
	R_{20}	0.748	0.850	0.600	0.450
	R_{5-20}	0.720	0.900	0.400	0.300
Moderate COPD-moderate asthma	Z_5	0.725	0.900	0.500	0.400
	R_5	0.761	0.750	0.700	0.450
	R_{20}	0.786	0.750	0.700	0.450
	R_{5-20}	0.659	0.950	0.400	0.350
Severe COPD-severe asthma	Z_5	0.711	0.600	0.900	0.500
	R_5	0.820	0.700	1.000	0.700
	R_{20}	0.786	0.650	0.900	0.550
	R_{5-20}	0.705	0.500	0.950	0.450

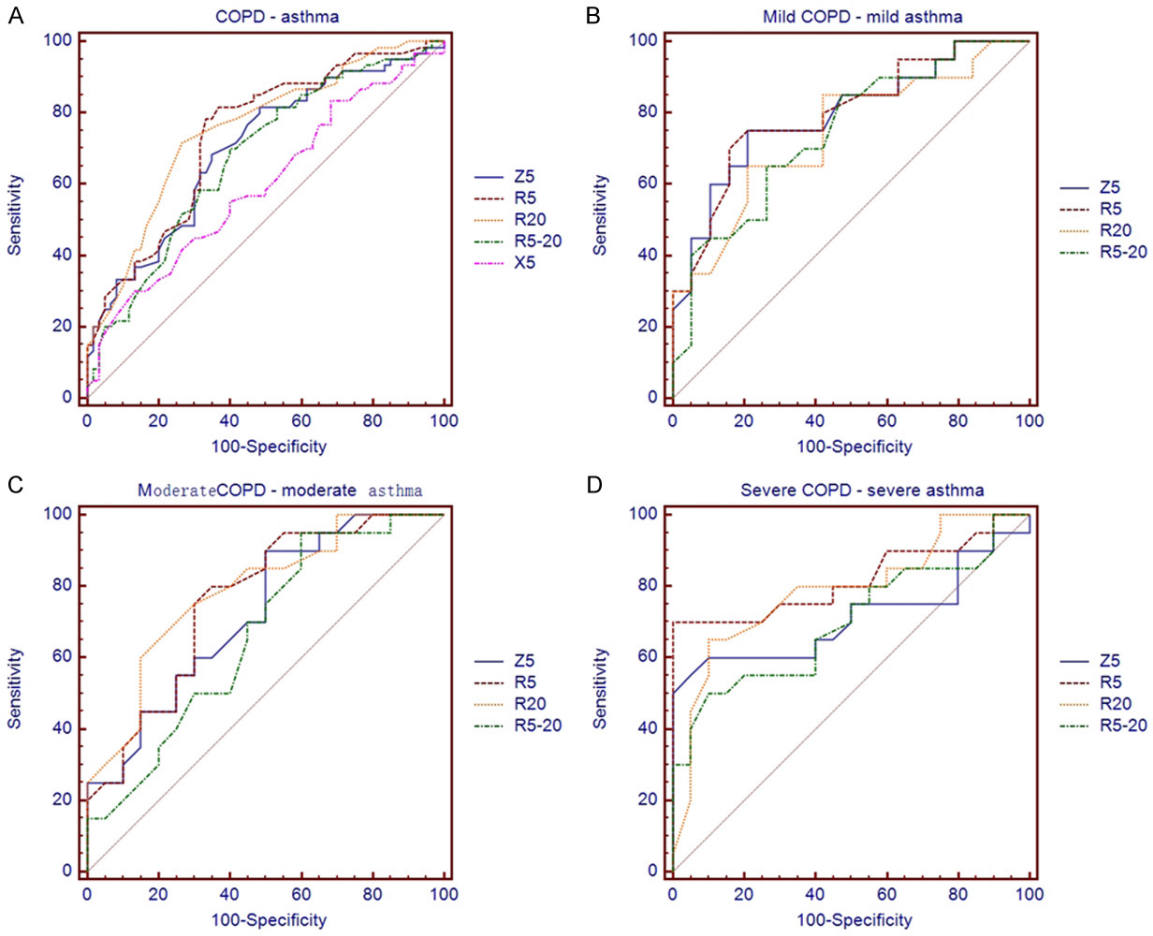

Figure 1. ROC curve analysis using IOS parameters in each paired COPD and asthma groups.

Table 6. The correct classification between COPD and asthma using spirometary and IOS parameters through discriminant analysis

Initial \ Predicted	COPD/Asthma (Correct classification)	Mild COPD/Mild asthma (Correct classification)	Moderate COPD/ Moderate asthma (Correct classification)	Severe COPD/ Severe asthma (Correct classification)
COPD	50/10 (83.3%)	18/2 (90.0%)	17/3 (85.0%)	18/2 (90.0%)
Asthma	19/41 (68.3%)	8/12 (60.0%)	6/14 (70.0%)	4/16 (80.0%)
Whole correct classification	75.8%	75.0%	77.5%	85.0%

although they share the same level of airflow limitation. On the other hand, no matter IOS parameters or limitation indices are influenced by more than one kind of pathological changes. Meanwhile, COPD and asthma patients not only share some common pathological changes, they also have lots of different changes. This factor can also lead to the results in our study.

To examine the differences of IOS parameters between asthma and COPD patients with different levels of airflow limitations, we divided the asthma and COPD patients into three subgroups. The baseline characteristics and airflow limitations of the COPD and asthma subgroups exhibited no significant differences, but the above IOS parameters' values of the asthma patients were greater than those of the COPD patients at each airflow limitation severity level, and these findings were consistent with results from the overall COPD and asthma groups. These results suggest that the impedances of asthma patients are greater than those of COPD patients at each airflow limitation level.

The differences make it possible to differentiate COPD and asthma patients by IOS measurement. Through ROC analysis, we found that Z_5, R_5 and R_{20} were valuable to distinguish COPD and asthma patients in each airflow limitation level, with all of their their AUCs greater than 0.7. Therefore, IOS parameters may provide help to identify these two obstructive lung diseases when spirometry cannot be performed in some patients. When combining spirometry and IOS parameters, more than 75 percent patients were correctly classified through discriminant analysis. And in severe patients, the percentage was as high as 85%, which suggested that the combination of IOS and spirometry have power to distinguish COPD and asthma patients with the same airflow limitation level.

The shortcoming of our study is that a relatively small number of patients were enrolled. Additional research involving larger samples should be performed for further analysis. Moreover, because IOS is applied extensively in clinical practice, changes of respiratory impedance should be observed with measures other than airflow limitation indices because these other measures may aid the elucidation of pathological aspects of diseases.

Conclusions

Although COPD and asthma are both obstructive lung diseases, these conditions exhibited differences in many aspects including aspects of lung function. The measurements of respiratory impedances require only normal breathing, and the results of such measurements were greater in the asthma patients than the COPD patients after controlling for the level of airflow limitation. The differences may provide help to differentiate between COPD and asthma patients.

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Disclosure of conflict of interest

None.

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