

# Functional and radiological characteristics of asthma combined chronic obstructive pulmonary disease overlap

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**Background** Persons with asthma–chronic obstructive pulmonary disease (COPD) overlap (ACO) are a crucial but poorly characterized group. In spite of the numbers of patients with ACO have increased, there is minimal confirmed evidence regarding diagnostic features and choices of treatment. So, the aim of this study was to identify the physiological and radiological characteristics of patients with ACO.

**Patients and methods** This study was performed on 200 patients classified into 38 patients diagnosed as having asthma, 132 patients diagnosed as having COPD, and 30 patients diagnosed as having ACO, who were chosen based on clinical features. All patients underwent pulmonary function tests, and multislice computed tomography imaging.

**Results** The mean age of our study population was 61 years. The mean age in COPD group was higher compared with asthma and ACO groups (63.9±7.8 vs. 44.84±12.2 and 56.7±8, respectively), with a predominance of males in COPD and females in asthma, with a higher smoking index in patients with COPD than those with ACO and asthma (47.05±37.7, 13.53±2.2, and 2.47±1.46, respectively). Measurements of forced expiratory volume in 1 s (FEV<sub>1</sub>) by liters before bronchodilator therapy is greater in patients with asthma than ACO and COPD groups (1.89±0.42, 1.52±0.39, and 1.35±0.4, respectively), with highly significant difference ( $P<0.001$ ). With airway reversibility, it is also greater in patients with asthma than ACO and COPD groups (2.85±0.49, 1.99±0.47, and 1.41±0.39, respectively), with a highly significant difference ( $P<0.001$ ). Airway internal diameter of patients with COPD is greater than ACO and asthma groups (4.03±0.3, 3.92±0.17, and 2.82±0.31, respectively), with a

highly significant difference ( $P<0.001$ ). On the contrary, airway external diameter of patients with COPD is greater than asthma and ACO groups, with a highly significant difference ( $P<0.001$ ). Airway wall thickness of patients with asthma is greater than ACO and COPD groups, with a highly statistical difference ( $P<0.001$ ). There is no relation between thickness of airway wall and airway obstruction, expressed as FEV<sub>1</sub> % predicted, in patients with asthma and COPD. This study results confirmed the correlation between the thickness of airway wall and airway obstruction, expressed as FEV<sub>1</sub> % predicted, in patients with ACO.

**Conclusion** Bronchial wall thickness measured by chest high resolution computed tomography (HRCT) is increased in patients with asthma than those with ACO and COPD, with a high statistical significance.

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**Keywords:** asthma–chronic obstructive pulmonary disease overlap, asthma, chronic obstructive pulmonary disease

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## Introduction

Asthma and chronic obstructive pulmonary disease have been identified as two separate diseases that usually overlap [1]. The Global Initiative for Asthma (GINA) and Chronic Obstructive Lung Disease (GOLD) have proposed a consensus document reaching to improve the characterization and description of these patients [2]. Individuals with asthma–chronic obstructive pulmonary disease overlap (ACO) are often identified as asthmatics with a history of smoking who show partial reversible airflow limitation or individuals with COPD who develop characteristics of asthma [3].

A joint project of GINA and GOLD provides a clinical identification of ACO as follows: ACO is characterized by persistent limitation of airflow with many criteria often associated with asthma and many criteria often associated with COPD. Therefore, ACO

is described by the criteria that it shares with both asthma and COPD [2]. As ACO has overlapping features of asthma and COPD, ACO may be a particular phenotype of a spectrum of chronic obstructive airway diseases, in which both asthma and COPD are at the two opposite ends. ACO is poorly characterized regarding genetic risk factors, underlying mechanisms, clinical criteria, pathological features, response to treatment, and outcome [4].

Patients with the overlap phenotype have more respiratory symptoms, worse lung function, and a lower health-related quality of life than either

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disease alone. Recently, the diagnostic features for the overlap phenotype have been confirmed by the consensus of a group of experts. However, this is restricted to patients with COPD but not for the asthma with fixed airflow obstruction [5].

The aim of our study is to analyze lung function tests and radiological characteristics of the overlap phenotype of asthma with COPD characteristic compared with age-matched and sex-matched patients with only COPD and patients with only asthma.

## Patients and methods

This prospective study was performed on 200 patients recruited randomly from chest department between May 2015 and May 2017. They were classified into 38 patients diagnosed as having asthma, 132 patients diagnosed as having COPD, and 30 patients diagnosed as having ACO according to diagnostic criteria.

The diagnosis of asthma, COPD, and ACO was dependent on GINA and GOLD [6]. Participants with asthma had reversible airflow obstruction with a post-bronchodilator forced expiratory volume in 1 s ( $FEV_1$ )/forced vital capacity (FVC) at least 70% and post-bronchodilator  $FEV_1$  more than 80% of predicted. Individuals with COPD had incompletely reversible airflow obstruction with a post-bronchodilator  $FEV_1$ /FVC less than 70% and post-bronchodilator  $FEV_1$  less than 80% of predicted.

The diagnosis of ACO was based on a joint statement reported by the GINA and the GOLD guidelines. Participants with ACO had respiratory symptoms, increased airflow variability [asthma, i.e. bronchial hyperresponsiveness (AHR) or Bronchodilator response (BDR)], and incompletely reversible airflow obstruction (COPD): post-bronchodilator  $FEV_1$ /FVC less than 70% and post-bronchodilator  $FEV_1$  less than 80% of predicted. ACO diagnosis was made when a patient had diagnostic features for both asthma and COPD [2].

Exclusion criteria were as follows: (a) any obvious abnormal pulmonary parenchymal lesions, including interstitial pneumonia; (b) pulmonary tumor; (c) congestive heart failure; (d) infectious disease including pulmonary tuberculosis; (e) other obstructive pulmonary illness such as diffuse panbronchiolitis; (f) cystic disease; (g) previous thoracotomy; (h) peripheral vascular disease; (i) thromboembolic disease (acute and chronic); (j) liver cell failure; and (k) any cognitive disorder.

The study was approved by the local ethical committee of our university, to evaluate and publish information. After explaining to the patients, a written consent was taken from all patients.

## Pulmonary functions test

Pulmonary function testing was done for all patients according to American Thoracic Society criteria [7] using Medical Equipment Europe (Abteilung Entwicklung, Hammelburg, Germany). The largest  $FEV_1$  and FVC were recorded after examining all of the acceptable curves.  $FEV_1$  and FVC were measured in liters and percentage predicted before and after bronchodilator therapy.  $FEV_1$ /FVC% was measured by dividing actual  $FEV_1$  in liters over actual FVC in liters. American Thoracic Society criteria [7] require a rise in  $FEV_1$  of at least 200 ml or 12% from baseline values, and a similar change in FVC of 200 ml or 12%, to indicate a response to a bronchodilator. Post-bronchodilator  $FEV_1$ /FVC less than 0.70 indicates irreversible airflow obstruction [6].

## Multislice computed tomography

The multislice computed tomography (MSCT) of chest was done to evaluate MSCT features of asthma, COPD, and ACO and correlate these features with clinical and pulmonary function tests (spirometry).

MSCT was performed using 16-CT high-speed advantage scanner (Siemens, Erlangen) Somatom, made in Germany. Noncontrast high resolution computed tomography (HRCT) scanning was done at full inspiration with 1-mm collimation at 120 kVp (200 MAS) and matrix size of 512×512, and scans were taken at 10-mm interval with window setting appropriate for the lungs (window level from 700 to 900 HU, width from 800 to 1000 HU).

The lungs were scanned from the apex to the base with the patient lying in the supine position and holding his breath at full inspiration. Three reconstruction planes (axial, coronal, and sagittal) were automatically obtained.

The computed tomography (CT) images were enlarged (magnification, ×10). Cross-sections of bronchi with external diameter range 1–5 mm were known and submitted for analysis. Only cross-sections perpendicular to the long airway axis were chosen. Regions of interest were traced manually. The external (D) and internal diameters of bronchi (L) were assessed by standard software analysis for distance measurement expressed in millimeters (mm). All measurements were

performed by a radiologist blinded to the patient's diagnosis. After D and L measurements, the following parameters were calculated: (a) WT, wall thickness, with the assumption that the bronchial wall thickness (BWT) is constant on the cross section [ $WT=(D-L)/2$ ], and (b) BWT, outlined as the ratio of the wall thickness to the external diameter ( $BWT=WT/D$ ) [8].

Scans were obtained at two selected levels: the trunk of the apical bronchus of the right upper lobe and the trunk of the posterior basal bronchus of the right lower lobe. We therefore decided to measure airway wall dimensions at only one of two sites in this study: the origin of the apical bronchus of the right upper lobe. This site was selected because of its more convenient orientation for obtaining a tangential view of the airway and an outer perimeter view of the airway not abutted by vessels or other bronchi.

### Statistical analysis

Results are expressed as mean±SD for quantitative data and by number (%) for qualitative data. Comparisons between the groups were conducted by independent sample *t*-test for parametric data and by Mann–Whitney test for nonparametric data.  $\chi^2$ -Test was used to test the significance between groups regarding qualitative data, and Fisher exact test was used instead of the  $\chi^2$ -test when the expected count in any cell found less than 5. *P* value less than 0.05 was considered as significant. Data entry and all statistical analyses were performed using statistical package for the social sciences (SPSS) version 21 under Windows 7 operating system (SPSS Inc., Chicago, Illinois, USA).

### Results

The general characteristics of patients are shown in Table 1. Male percentage was higher among COPD

group compared with asthma and ACO groups (90.1 vs. 36.8 and 46.7%, respectively). The female percentage was high among asthma compared with COPD and ACO groups (63.2 vs. 9.1 and 53.3%, respectively), with a highly significant difference among these groups ( $P<0.001$ ). There is a highly significant difference regarding age among COPD group compared with asthma and ACO groups (63.9 vs. 44.84 and 56.7, respectively). The table also demonstrates no significant difference regarding BMI ( $P>0.05$ ), whereas the same table illustrates a highly significant difference regarding disease duration less than 0.001. This table also clarifies high significant difference according to smoking index among COPD group compared with ACO and asthma groups (47.05 vs. 13.53 and 2.47, respectively).

Measurements of FEV<sub>1</sub> in liters before bronchodilator therapy is greater in asthma patients than ACO and COPD groups (1.89±0.42, 1.52±0.39 and 1.35±0.39, respectively), with a high significant difference ( $P<0.001$ ). With reversibility also it is greater in patients with asthma than ACO and COPD groups (2.85±0.49, 1.99±0.47 and 1.41±0.4, respectively), with a high significant difference ( $P<0.001$ ; Table 2). Measurements of FVC in liters before bronchodilator therapy is greater in patients with asthma than ACO and COPD groups (3.9±0.47, 3.84±0.65 and 3.43±0.63, respectively), with a statistically significant difference ( $P<0.049$ ). Reversibility was also greater in patients with asthma than ACO and COPD groups (4.08±0.38, 3.87±0.58 and 3.53±0.67, respectively), with a high statistically significant difference ( $P<0.001$ ).

Airway internal diameter of patients with COPD is greater than ACO and asthma groups (4.03±0.3, 3.92±0.17 and 2.82±0.31, respectively), with a high statistically significant difference ( $P<0.001$ ). On the

**Table 1 Comparison of baseline clinical characteristics of the studied groups**

Parameters	Asthma (N=38)	COPD (N=132)	ACO (N=30)	<i>P</i> value
Age (mean±SD) (years)	44.84±12.2	63.9±7.8	56.7±8	<0.001**
Sex [N (%)]				<0.001**
Males	14 (36.8)	120 (90.9)	16 (53.3)	
Females	24 (63.2)	12 (9.1)	14 (46.7)	
Disease duration (mean±SD)	14.26±8.7	11.24±6.6	21.4±8.48	<0.001**
BMI (mean±SD)	27.5±3.07	26.68±3.03	27.9±3.3	0.56
Smoking history [N (%)]				0.7
Never	8 (21.1)	12 (9.1)	2 (6.6)	
Ex-smoker	18 (47.3)	74 (56.1)	14 (46.7)	
Smoker	12 (31.6)	46 (34.8)	14 (46.7)	
Smoking index (pack-year) (mean±SD)	2.47±1.46	47.05±37.7	13.53±2.2	<0.001**

ACO, asthma–chronic obstructive pulmonary disease overlap; COPD, chronic obstructive pulmonary disease. \*\**P* value is highly significant.

**Table 2 Comparison of pulmonary function parameters (before and after bronchodilator therapy) among asthma, chronic obstructive pulmonary disease and asthma–chronic obstructive pulmonary disease overlap groups**

	Pulmonary function tests	Before bronchodilator therapy (mean±SD)	After bronchodilator therapy (mean±SD)	P value
Asthma	FEV <sub>1</sub> (l)	1.85±0.42	2.85±0.49	<0.045*
	%Predicted	64.26±16.63	100.58±22.98	<0.003*
	FVC (l)	3.89±0.47	4.09±0.38	0.69
	%Predicted	115.6±26.18	120.8±24	0.45
	FEV <sub>1</sub> /FVC%	47.84±8.39	73.63±7.24	0.31
COPD	FEV <sub>1</sub> (l)	1.35±0.4	1.41±0.39	0.062
	%Predicted	48.67±13.76	48.68±13.08	0.98
	FVC (l)	3.34±0.63	3.53±0.67	<0.001**
	%Predicted	90.5±19.43	96.9±21.66	<0.001**
	FEV <sub>1</sub> /FVC%	40.3±10.17	41.09±8.93	0.33
ACO	FEV <sub>1</sub> (l)	1.52±0.39	1.99±0.47	<0.001**
	%Predicted	56.67±15.7	73.9±18.27	<0.001**
	FVC (l)	3.84±0.66	3.87±0.58	<0.001**
	%Predicted	40.07±9.35	50.7±28.7	<0.001**
	FEV <sub>1</sub> /FVC%	40.07±9.35	51.8±11.98	<0.001**

ACO, asthma–chronic obstructive pulmonary disease overlap; COPD, chronic obstructive pulmonary disease; FEV<sub>1</sub> (l), forced expiratory volume 1 per liters; FVC (l), forced vital capacity per liters. \*P value is significant. \*\*P value is highly significant.

contrary, airway external diameter of patients with COPD is greater than asthma and ACO groups, with a high statistically significant difference ( $P<0.001$ ). Airway wall thickness of patients with asthma is greater than ACO and COPD groups, with a high statistically significant difference ( $P<0.001$ ).

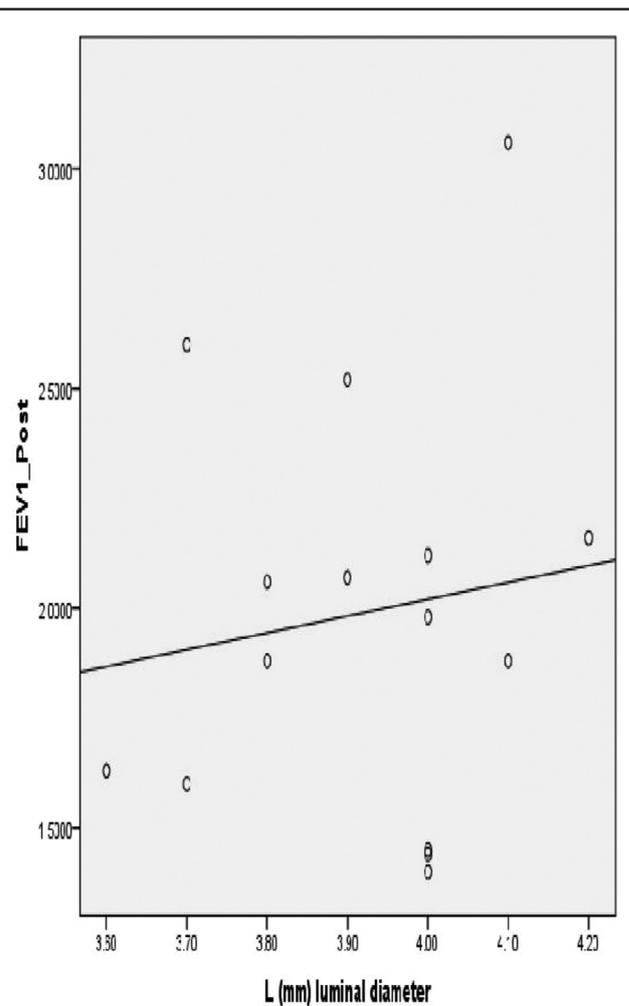
There is a high statistical significance in the correlation of post-bronchodilator FEV<sub>1</sub> with dimensions of airway assessed in HRCT among patients with ACO, whereas there is no statistical significance in the correlation of post-bronchodilator FEV<sub>1</sub> with dimensions of airway assessed in HRCT among patients with COPD and asthma (Figs 1–5 and Tables 3–5).

## Discussion

ACO was recently recognized by the GINA and the GOLD guidelines, which outlined this condition as being characterized by persistent airflow limitation together with many features often associated with asthma or COPD. The relatively recent identification of this condition has resulted in multiple definitions of ACO being used [9].

The prevalence of ACO varies from 1.6 to 4.5% in several studies all over the world [10]. If only individuals with asthma or COPD are included, the prevalence of ACO among patients with COPD varies from 12.1 to 55.2% and among patients with asthma from 13.3 to 61.0% [11].

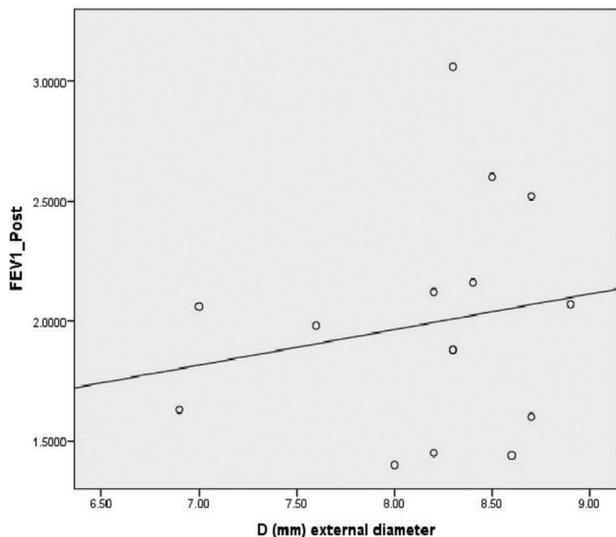
Patients with ACO experience additional severe symptoms than those with either asthma or COPD

**Figure 1**

Correlation of a forced expiratory volume in 1 s after bronchodilator therapy with airway internal diameter assessed in HRCT among patients with asthma–chronic obstructive pulmonary disease overlap.

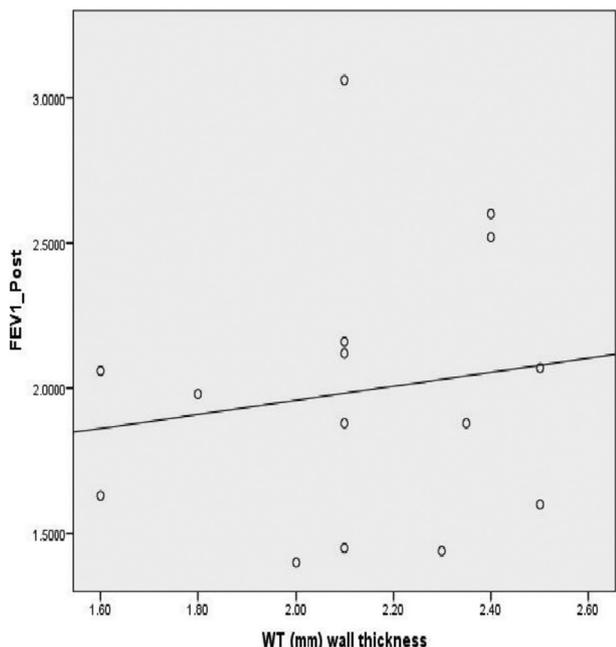
alone, with more frequent severe exacerbations and more frequent hospitalizations. Patients with ACO

Figure 2



Correlation of a forced expiratory volume in 1 s after bronchodilator therapy with airway external diameter assessed in HRCT among patients with asthma–chronic obstructive pulmonary disease overlap.

Figure 3



Correlation of a forced expiratory volume in 1 s after bronchodilator therapy with airway wall thickness assessed in HRCT among patients with asthma–chronic obstructive pulmonary disease overlap.

are significantly younger than those with COPD, with a higher BMI [12].

Regarding demographic data, the mean age of our study population is 61 years old, with high statistically significant difference among COPD compared with asthma and ACO groups ( $63.9 \pm 7.8$

vs.  $44.84 \pm 12.2$  and  $56.7 \pm 8$ , respectively). In agreement with our study, Ding and Small [13] and Gao *et al.* [14] found that COPD group is older than ACO and asthma. In contrast with our study, Kitaguchi *et al.* [15] found that the age has no statistical significant difference among COPD when compared with asthma and ACO groups ( $71.9 \pm 0.8$  vs.  $70.3 \pm 2.2$  and  $69.1 \pm 1.2$ , respectively).

Regarding sex, our study showed that males in ACO group were 53.3% and females were 46.7%, whereas males in COPD group were 90.1% and females were 9.9%, and males in asthma group were 36.8% and females were 63.2%, with predominance of males in COPD group and females in asthma group. In agreement with this study, Montes *et al.* [16], Ding and Small [13], and Gao *et al.* [17] had nearly similar results. In contrast with this study, Menezes *et al.* [11] and Kumbhare *et al.* [18] founded that females were predominant in all groups, and this may be owing to large numbers of populations included in these studies.

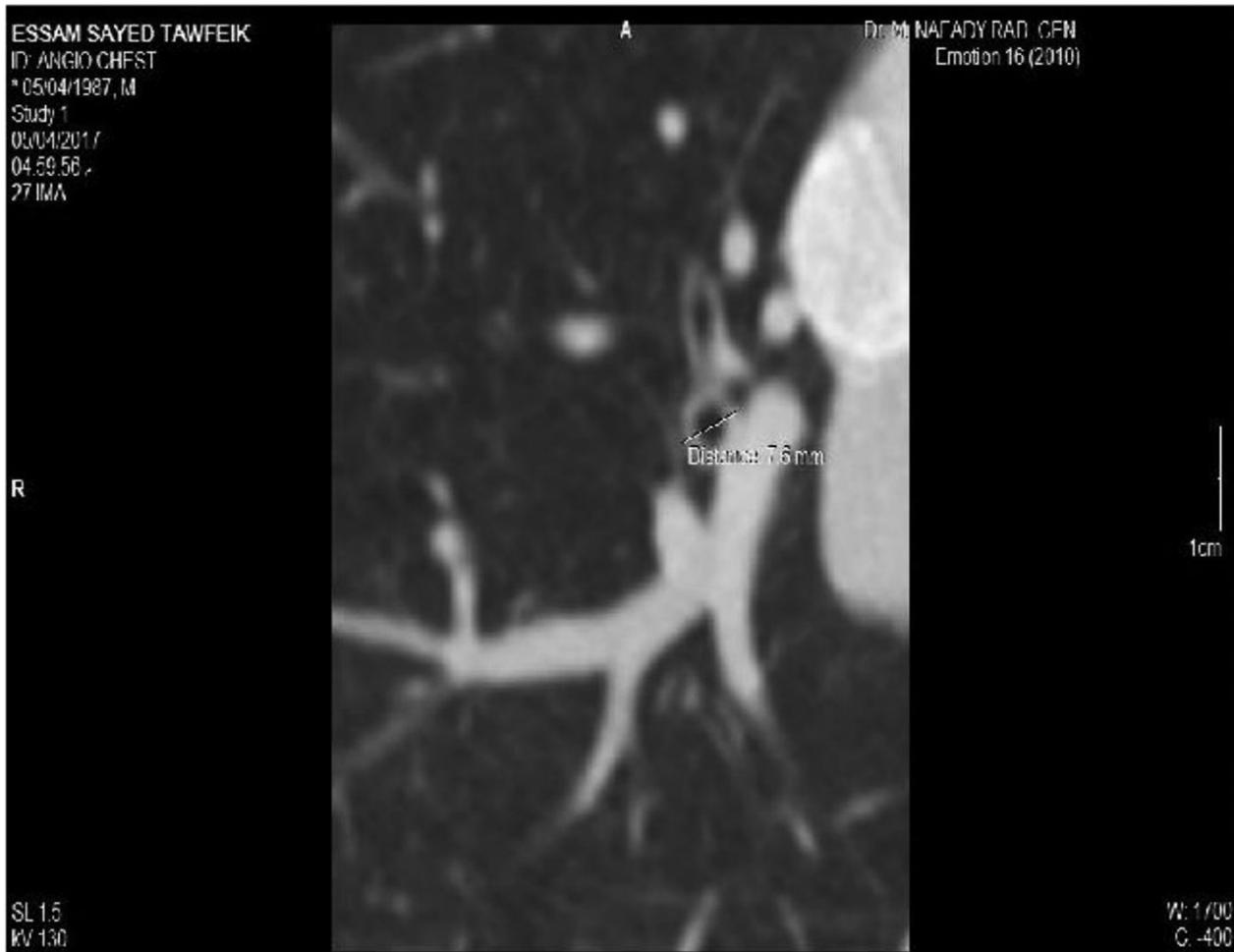
The relative prevalence of ACO decreases with age, whereas that of COPD alone increases with age. This decline is owing to increase rate of growth of the COPD cohort more than that of ACO population or an increase in ACO death rates [19].

Regarding BMI, there is no significant statistical difference among the studied groups ( $P > 0.05$ ). In agreement with this study, Fu *et al.* [20] and McDonald *et al.* [21], supported this study, with no significant statistical difference among the studied groups ( $P > 0.05$ ). In contrast with this study, Ding and Small [13] and Kumbhare *et al.* [18] founded that ACO group has higher BMI than COPD and asthma groups, whereas Menezes *et al.* [11] founded that asthma group has higher BMI than ACO and COPD groups.

Regarding smoking index in our study, patients with COPD had higher smoking index than ACO and asthma groups ( $47.05 \pm 37.7$ ,  $13.53 \pm 2.2$ , and  $2.47 \pm 1.46$ , respectively). This was consistent with Marco *et al.* [22], who found that patients with COPD had higher smoking index than ACO and asthma groups. In contrast to our study, Montes *et al.* [16] and Gao *et al.* [17] founded that smoking index is higher in ACO group than COPD and asthma groups.

In most studies, patients with asthma had a lower smoking index in comparison with COPD and ACO groups, and this may be explained by the younger age of asthmatic patients and cannot stand smoking. However, patients with asthma and COPD

Figure 4



HRCT chest showing external diameter (D) of the apical bronchus of the right upper lobe measuring about 7.6 mm.

who were ex-smokers are more than who currently smoke and never smoking, but in ACO, the smoker is similar to ex-smoker and both more than never smoking. This is supported by Maria Montes *et al.* [16] which found nearly the same results. In contrast to the current study, Chung *et al.* [23] found that asthma and ACO groups had more current smokers, but COPD group had more never smoking.

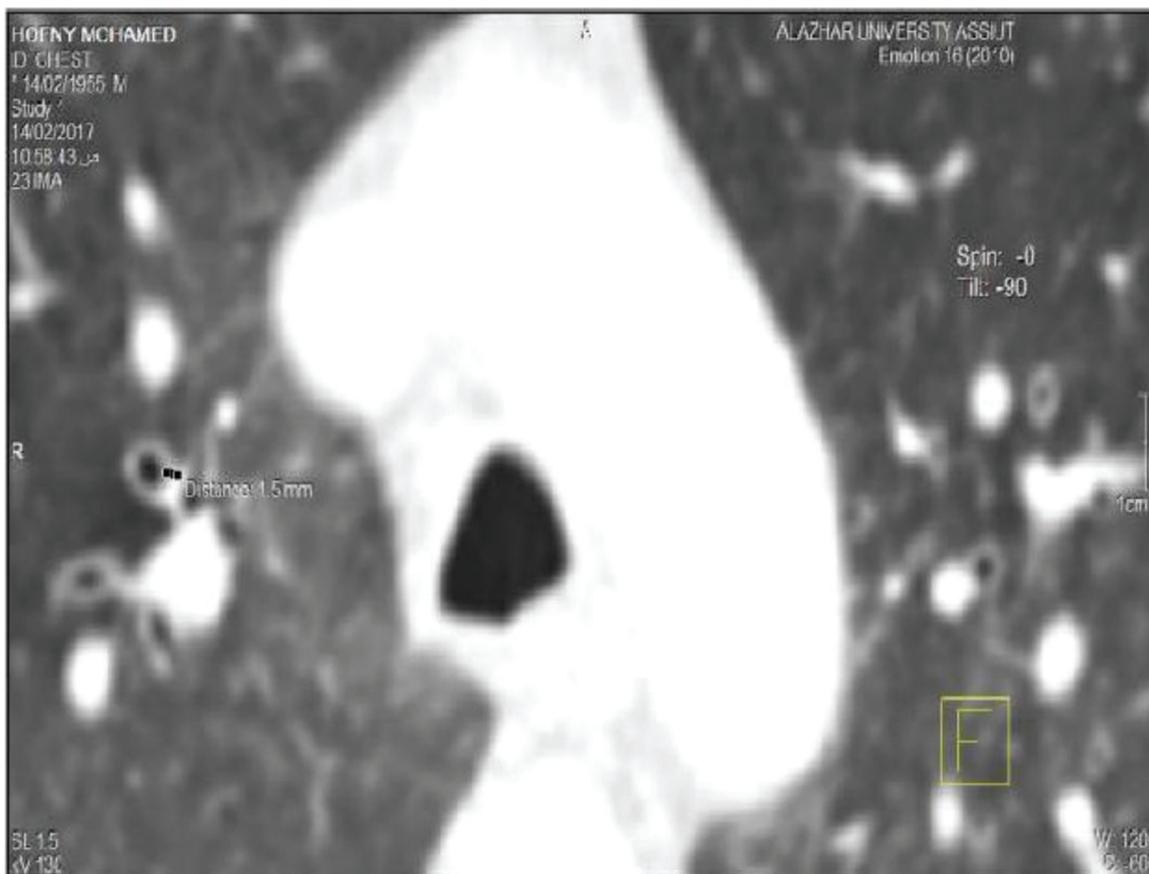
Spirometry is essential for the diagnosis and evaluation of obstructive pulmonary diseases that are characterized by decreased airflow related to increased resistance caused by narrowing of airway. These obstructions may occur either directly by the airway lumen narrowing or by reduced elasticity of the parenchyma surrounding the airways. FEV<sub>1</sub> and FEV<sub>1</sub>/FVC values of the spirometric test are the best indicators for obstruction of airway [24].

Our study evaluated the differences in the pulmonary physiology in patients with obstructive pulmonary diseases and founded that there were significant

differences in multiple parameters of pulmonary function tests among the COPD, asthma, and ACO groups. There were significant differences in the reversibility of airflow limitation in response to short-acting  $\beta_2$ -agonists among patients with COPD, ACO, and asthma, and the reversibility of airflow limitation was the greatest in patients with asthma. In agreement with our study, Menezes *et al.* [11] supported that the reversibility of airflow limitation was the greatest in patients with asthma, whereas Kitaguchi *et al.* [15] founded that the reversibility of airflow limitation was the greatest in patients with ACO.

HRCT is a valuable tool in assessment of thickness of airway wall and dimension of airway lumen. It enables a noninvasive, reproducible evaluation of the airways at the bronchioles level. A relationship between basement membrane thickness assessed in biopsy specimens and airway wall thickness assessed by HRCT was documented. On the contrary, HRCT has its limitations. It enables the imaging of the total

Figure 5



HRCT chest showing wall thickness (WT) of the apical bronchus of the right upper lobe measuring about 1.5 mm.

**Table 3 Comparison of forced expiratory volume in 1 s (%predicted), forced vital capacity (%predicted), and forced expiratory volume in 1 s/forced vital capacity% after bronchodilator therapy among the studied groups**

FEV <sub>1</sub> , FVC and ratio (%predicted)	Asthma (N=38)	COPD (N=132)	ACO (N=30)	P value
FEV <sub>1</sub> (l) after bronchodilator therapy	2.85±0.49	1.41±0.39	1.99±0.47	<0.001**
%Predicted	100.58±22.9	48.68±13.08	73.9±18.27	<0.001**
FVC (l) after bronchodilator therapy	4.08±0.38	3.53±0.67	3.87±0.58	<0.001**
%Predicted	120.8±24	96.9±21.66	50.7±28.8	<0.001**
FEV <sub>1</sub> /FVC% after bronchodilator therapy	73.6±7.23	41.09±8.3	51.8±11.98	<0.001**

ACO, asthma–chronic obstructive pulmonary disease overlap; COPD, chronic obstructive pulmonary disease; FEV<sub>1</sub> (l), forced expiratory volume 1 in liters; FVC (l), forced vital capacity in liters. \*\*P value is statistically highly significant.

**Table 4 Comparison of airway dimensions assessed in HRCT among the studied groups**

Parameters	Asthma (N=38)	COPD (N=132)	ACO (N=30)	P value
L (mm) internal diameter	2.82±0.31	4.03±0.3	3.92±0.17	<0.001**
D (mm) external diameter	7.8±0.7	8±0.36	7.17±0.58	<0.001**
WT (mm) wall thickness	2.78±0.38	1.99±0.2	2.1±0.34	<0.001**
WT/D	0.33±0.02	0.24±0.17	0.25±0.0.04	<0.001**
HRCT emphysema score	2.5±0.5	3.6±0.7	0.6±0.3	<0.035*

ACO, asthma–chronic obstructive pulmonary disease overlap; COPD, chronic obstructive pulmonary disease; D L, bronchial external diameter in millimeters; HRCT, high resolution computed tomography; L, bronchial internal diameter in millimeters; WT, wall thickness. \*P value is significant. \*\*P value is highly significant.

enlargement of the wall area or lumen area, but it does not provide with any information about each layer of the bronchial wall. Exposure of a patient to higher

doses of radiation, compared with conventional chest radiograph, is still an important limitation of the method [25].

**Table 5 Correlation of a forced expiratory volume in 1 s after bronchodilator therapy with airway dimensions assessed in HRCT among asthma, chronic obstructive pulmonary disease and asthma–chronic obstructive pulmonary disease overlap patients**

	Parameters	<i>r</i> value	<i>P</i> value
Asthma FEV <sub>1</sub> after bronchodilator therapy	L (mm) luminal diameter	−0.09	0.098
	D (mm) external diameter	0.012	0.96
	WT (mm) wall thickness	0.051	0.84
	WT/D	0.31	0.18
COPD FEV <sub>1</sub> after bronchodilator therapy	L (mm) luminal diameter	0.093	0.45
	D (mm) external diameter	−0.19	0.12
	WT (mm) wall thickness	−0.2	0.1
	WT/D	−0.19	0.12
ACOS FEV <sub>1</sub> after bronchodilator therapy	L (mm) luminal diameter	0.33	0.026*
	D (mm) external diameter	0.6	<0.001**
	WT (mm) wall thickness	0.51	<0.001**
	WT/D	0.41	<0.001**

ACO, asthma–chronic obstructive pulmonary disease overlap; COPD, chronic obstructive pulmonary disease; D L, bronchial external diameter in millimeters; FEV<sub>1</sub>, forced expiratory volume in 1 s; HRCT, high resolution computed tomography; L, bronchial internal diameter in millimeters; WT, wall thickness. \**P* value is significant. \*\**P* value is highly significant.

The greater thickness of airway wall in asthma can be partially explained by histological findings. The basement membrane thickness, smooth muscle layer, and the number of blood vessels in patients with asthma are greater than those in patients with COPD and ACO. Therefore, it is likely that airway remodeling results in a greater thickening of the airway wall in asthma when compared with COPD and ACO [26]. We did not find any relation between thickness of airway wall and airway obstruction, expressed as FEV<sub>1</sub> %predicted, in asthmatic patients. On the contrary, the results of some other studies suggest that there is a correlation between airway wall thickening and disease severity [27]. This study results confirm the correlation between the thickness of airway wall and airway obstruction, expressed as FEV<sub>1</sub> %predicted, in patients with ACO.

It should be noted, however, that airway wall remodeling is only one of the factors contributing to airflow limitation in asthma. Mucous membrane edema, inflammatory cell infiltration, increased mucus secretion, and smooth muscle constriction may influence airflow limitation. On the contrary, many

genetic and environmental factors can influence spirometric results and airflow limitation [28].

In this study, there is no relationship between thickening of airway wall and spirometric parameters in patients with COPD. The bronchial wall thickness measured by chest HRCT is increased in patients with asthma than those with ACO and COPD, with a high statistically significant difference. However, the percentage of BWT on chest HRCT was lower in patients with ACO than those with asthma. Kitaguchi *et al.* [15] supported these findings in their study. This study suggests that patients with ACO have a lower degree of airway remodeling owing to asthma than patients with asthma. This variable pattern of remodeling may reflect primary differences in the inflammatory processes in asthma and COPD and could affect the reversibility of airflow limitation [15].

Our study had several limitations. One of them was a relatively small number of patients with ACO and patients with asthma. However, our data were accurate and reproducible, because all parameters were assessed using the same equipment. Another limitation was the lack of a second radiologist evaluating the airway. Lastly, there were different definitions used for the diagnosis of ACO. A confirmation study with a larger sample size of patients with ACO who are selected based on clinical criteria is warranted.

## Conclusion

Obstructive airway diseases could be classified depending on clinical, radiological, and pulmonary function test findings into three groups including COPD, asthma, and ACO. Chest HRCT has a valuable tool in evaluating dimensions of small airway in patients with asthma, ACO and COPD. Lack of correlations between spirometric parameters and airway dimensions assessed in HRCT indicates that thickness of airway wall and lumen diameter are not the only factors that affect airflow limitation during forced expiration.

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