

# Comparing frequencies of asthma-chronic obstructive pulmonary disease overlap in patients with stable chronic obstructive pulmonary disease

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**Context** Asthma and chronic obstructive pulmonary disease (COPD) may share some physiological features and coexist as asthma-chronic obstructive pulmonary disease overlap (ACO).

The prevalence of ACO differs according to the diagnostic criteria and study design. In patients with COPD, the prevalence of ACO varies from 5 to 55%.

This study aims to examine the effect of using different diagnostic criteria on the resulting frequency of ACO in patients with COPD.

**Settings and design** This cross-sectional observational study enrolled 60 patients with COPD randomly selected from outpatient clinics of Chest Department of Minia Cardio-Thoracic University Hospital during the period from September 2015 to September 2016.

**Patients and methods** History, clinical examination, spirometry, and sputum cytology were done.

The frequency of ACO among the 60 patients with stable COPD was separately studied based on five different diagnostic criteria (Hardin's, Menezes, combined Hardin and Menezes, Spanish consensus, and Global Initiative for Asthma-Global Initiative for Chronic Obstructive Lung Disease criteria).

**Statistical analysis** Statistical analysis was performed using statistical package for social science software ( $\chi^2$  test and independent sample *t* test).

**Results** The frequency of ACO in COPD was 40, 23.3, 16.7, 13.3, and 10% on applying combined Hardin and Menezes, Hardin's alone, Menezes alone, the Spanish consensus, and Global Initiative for Asthma-Global Initiative for Chronic Obstructive Lung Disease criteria, respectively.

**Conclusion** The frequency of ACO in patients with COPD decreases when using more restrictive diagnostic criteria.

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

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## Background

Asthma and chronic obstructive pulmonary disease (COPD) are two major obstructive airway diseases. Although they have different pathogeneses, they may share some physiological features and coexist in the so-called asthma-chronic obstructive pulmonary disease overlap syndrome (ACOS) [1,2].

A joint project of Global Initiative for Asthma (GINA) and Global Initiative for Chronic Obstructive Lung Disease (GOLD) defined ACOS as persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD [3].

GINA-GOLD criteria and Spanish consensus are two famous diagnostic criteria used in defining ACOS. However, there are many other diagnostic criteria [4].

Several studies reported that asthma is a significant risk factor for the future development of COPD and that the more severe the COPD, the more likely people were to predispose to a diagnosis of asthma [5,6].

Other studies used spirometry-defined asthma as positive bronchodilator reversibility and spirometry-defined COPD as postbronchodilator forced expiratory volume (FEV)/forced vital capacity (FVC) less than 70% in diagnosis of ACOS; in these studies, prevalence ranged from 13 to 55.2% [7,8].

In reviewing previous studies, the prevalence of ACOS varies considerably because it has been diagnosed using different criteria, which depend on the study design and the population. In patients with COPD, the prevalence of ACOS varies from 5 to 55% [9].

Asthma and COPD are not a single phenomenon but in contrast, they have different pathogenetic mechanisms. Moreover, the clinical features are highly diverse. As a result, it has been recommended

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that the term 'syndrome' be dropped and that the disease name be changed to ACO [10].

In this paper, the disease that shares several features of both asthma and COPD will be referred to as ACO.

#### Aim of the study

This study aims to examine the effect of using different diagnostic criteria in the resulting frequency of ACO in patients with COPD.

#### Patients and methods

This cross-sectional observational study enrolled 60 patients with COPD randomly selected from patients who sought medical advice in the outpatient clinics of Chest Department of Minia Cardio-Thoracic University Hospital during the period from September 2015 to September 2016.

The study was approved by Faculty of Medicine Ethics Committee, Minia University. All patients provided written informed consent.

#### Inclusion criteria

The following were the inclusion criteria:

- (1) COPD was diagnosed based on the GOLD criteria [11].
- (2) Age more than 40 years and of any sex.
- (3) All patients stopped bronchodilators and corticosteroid therapy 2 weeks before the study.
- (4) The frequency of ACO among the 60 patients with stable COPD was separately studied based on five different diagnostic criteria:
  - (a) Hardin's criteria [1]: postbronchodilator FEV/FVC less than 70% and history of bronchial asthma before the age of 40 years.
  - (b) Menezes criteria [8]: postbronchodilator FEV/FVC less than 70% and reversibility of FEV<sub>1</sub> after bronchodilator more than or equal to 200 ml and 12% plus wheezy chest in the past year.
  - (c) Combined Hardin and Menezes criteria: postbronchodilator FEV/FVC less than 70% and history of bronchial asthma before the age of 40 years or reversibility of FEV<sub>1</sub> after bronchodilator more than or equal to 200 ml and 12% plus wheezy chest in the past year.
  - (d) Spanish consensus criteria [12]: ACO is defined when a patient fulfills two major or one major and two minor criteria of the following:

Major criteria: very positive bronchodilator test, improvement in FEV<sub>1</sub> more than or equal to 400 ml and 15%, sputum eosinophilia, or a previous diagnosis of asthma before the age of 40 years. Minor criteria: increased total serum immunoglobulin E, previous history of atopy, or a positive bronchodilator test.

- (e) GINA-GOLD, 2015 criteria: which diagnoses ACO when patient had similar number of features for asthma and COPD [3].

#### Exclusion criteria

Patients with acute exacerbation of COPD at the time of the study, any obvious abnormal lung parenchymal lesions, lung cancer, and congestive heart failure were excluded.

Patients were subjected to the following:

- (1) History overview, especially history of bronchial asthma before the age of 40 years.
- (2) The grade of dyspnea was determined by using the modified Medical Research Council dyspnea scale [13].
- (3) Chest radiography.
- (4) Spirometry FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC ratio (prebronchodilator and postbronchodilator) was measured using a spirometer (ZAN 300, Oberthulba, Germany). Spirometry was done by the same apparatus for all included participants. All patients stopped bronchodilators and corticosteroid therapy 2 weeks before the study.
- (5) Sputum cellular analysis:

Eosinophilic inflammation is considered if sputum eosinophils are more than or equal to 2.4% [9].

#### Statistical analysis

Statistical analysis was performed using the statistical package for social science software, version 20 (SPSS Inc., Chicago, Illinois, USA) on a personal computer. A statistical analysis was performed using  $\chi^2$  test, and independent sample *t* test was used to assess differences between proportions.

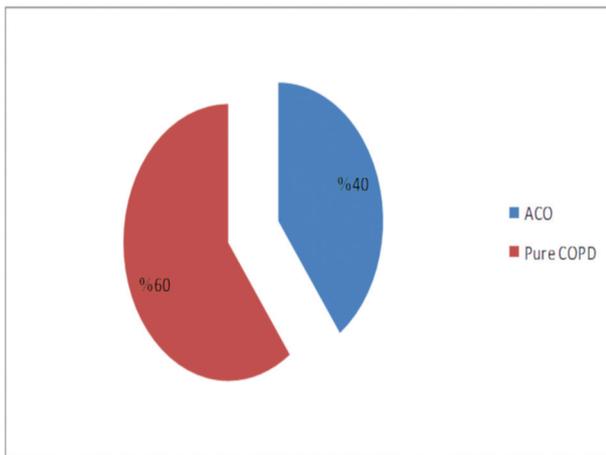
#### Results

The demographic data of patients with COPD are shown in Table 1. Regarding the frequency of ACO, 24 (40%) patients fulfilled the combined Hardin and Menezes criteria (Fig. 1), 14 (23.3%) patients fulfilled Hardin criteria, and 10 (16.7%) patients fulfilled Menezes criteria (Fig. 2).

**Table 1 Demographic data of the patients with chronic obstructive pulmonary disease**

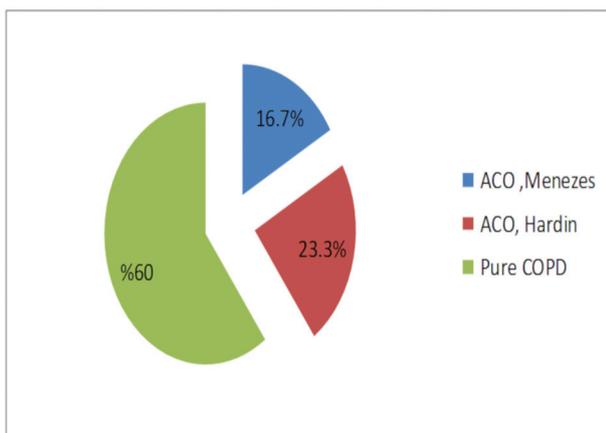
Variables	n (%)
Age (years)	
Range	46–84
Mean±SD	63.05±7.64
Sex	
Male	47 (78.3)
Female	13 (21.7)
Smoking	
Nonsmokers	17 (28.3)
Smoker	43 (71.7)

**Figure 1**



The frequency of ACO using combined Hardin and Menezes criteria. ACO, asthma-chronic obstructive pulmonary disease overlap.

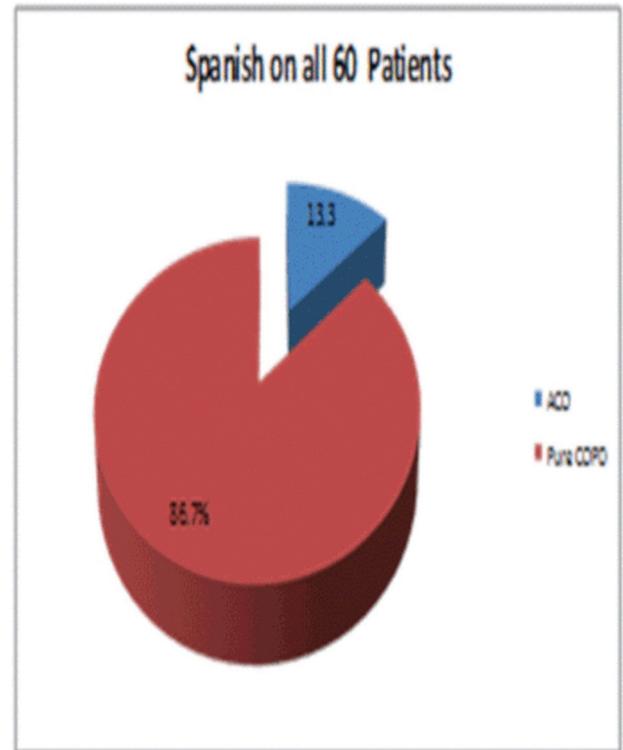
**Figure 2**



The frequency of ACO in our study by separately using Hardin or Menezes criteria. ACO, asthma-chronic obstructive pulmonary disease overlap.

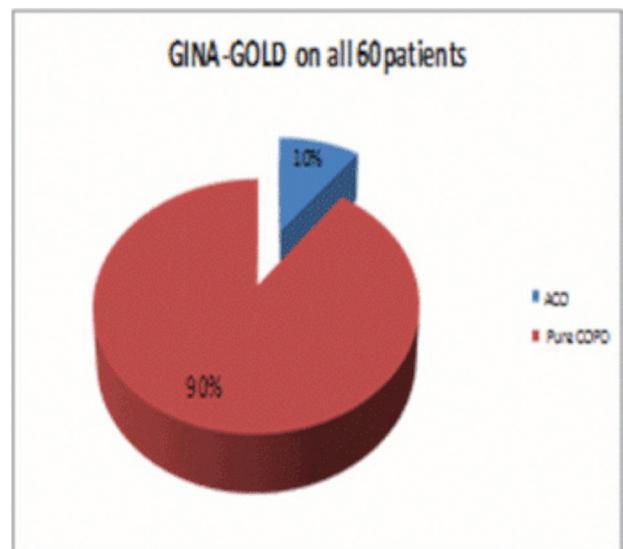
On applying both Spanish consensus and GINA criteria on all 60 patients with COPD, the frequency of ACO decreased to 13.3 and 10%, respectively (Figs 3, 4).

**Figure 3**



Applying the Spanish consensus on all patients with COPD. COPD, chronic obstructive pulmonary disease.

**Figure 4**



Applying the GINA-GOLD criteria on all patients with COPD. COPD, chronic obstructive pulmonary disease; GINA-GOLD, Global Initiative for Asthma-Global Initiative for Chronic Obstructive Lung Disease.

**Discussion**

Asthma–COPD overlap is identified in clinical practice by the features that it shares of both asthma and COPD. This is not a definition but a description for clinical use, as asthma–COPD overlap includes

several different clinical phenotypes, and there may be also several different underlying mechanisms: the disease that shares several features of both asthma and COPD will be referred to as ACO [14].

The prevalence of the overlap phenotype within the context of COPD differs according to different criteria used for diagnosis of ACO [4].

In a study taking 3099 adult cohorts, it was established that participants with active asthma had significantly higher hazard ratios than nonasthmatic patients for acquiring COPD [15].

In our study, the frequency of ACO using the combined Hardin *et al.* [1] and Menezes *et al.* [8] criteria was 40% (Fig. 1).

This was close to Nguyen *et al.* [16], who diagnosed ACO in COPD based on either one of some parameters including history of bronchial asthma before age of 40 years, reversibility of FEV<sub>1</sub> after bronchodilator more than 200 ml and 12%, and sputum or blood eosinophilia. Using these criteria, the prevalence of ACO in patients with stable COPD obtained by Nguyen *et al.* [16] was 37%. The near similarity in the frequency of ACO between the present study and that of Nguyen and colleagues can be explained by the close proximity between the diagnostic criteria used by Nguyen and colleagues and the combined Hardin *et al.* [1] and Menezes *et al.* [8] criteria used in the present study.

When using Hardin's criteria alone not combined with Menezes, the frequency of ACO dropped from 40 to 23.3% (Fig. 2). This reduction in frequency can be explained by the reduction of factors that can transfer the patients from the COPD group to the ACO group.

Hardin *et al.* [1], Izquierdo-Alonso *et al.* [17], and Putcha *et al.* used history of asthma before 40 years alone as a reliable criterion to diagnose ACO in a patient with COPD, and they found prevalence of ACO phenotype in COPD patients reaching 16.7, 12.1, and 13%, respectively. The relatively higher frequency of ACO when using Hardin's criteria alone in the present study (23.3%) compared with the frequencies mentioned in the aforementioned three studies (16.7, 12.1, and 13) may be owing to a difference in the number of patients between studies or owing to self-reported physician diagnosis of asthma used in these studies, which may lead to a recall bias and may lead to overestimation or underestimation of asthma and thus difference in the diagnosis of ACO.

In the present study, when using Menezes criteria alone, the frequency of ACO was 16.7% (Fig. 2).

In a study by Marsh *et al.* who defined reversibility as 15% improvement in FEV<sub>1</sub>% postbronchodilator, the prevalence of ACO in patients with COPD was 55.2%. This difference observed from the present study may be explained by the fact that they defined reversibility as 15% improvement in FEV<sub>1</sub>% postbronchodilator but without using an absolute value of change in milliliters. We believed that we were more accurate in our study by matching the percentages of reversibility by a criterion of 200 ml in absolute value.

On applying the Spanish definition of ACO in our study, the prevalence of ACO was 13.3% (Fig. 3). In a study by Barrecheguren *et al.* [4], the prevalence of ACO among patients with COPD was 15.9% when used history of asthma before 40 years as a criterion. This was just like the diagnostic criteria used by Hardin *et al.* [1]. This frequency decreased to 3.6% when used the ACO diagnostic criteria of the Spanish consensus. The similarity between the present study and that of Barrecheguren *et al.* [4] lies in the acute drop of the frequency of ACO when shifting from Hardin criteria (or the combined criteria used in the present study) to the Spanish consensus definition.

Spanish consensus used more strict major criteria as a strong reversibility more than or equal to 400 ml and 15% or sputum eosinophilia which may play a role in the lower prevalence.

On applying GINA-GOLD [3], definition of ACO in our study, the prevalence of ACO dropped to 10% (Fig. 4). GINA-GOLD definition was based on presence of equal features of both asthma and COPD and that would result in lower prevalence when applied on patients with COPD only as the case in our study because all patients in the study have the basic features of COPD regarding history and examination. In a study of Rahul *et al.* [17], ACO represents 20% of patients with COPD when using GINA-GOLD criteria on patients previously diagnosed with COPD. The prevalence in this study was somewhat higher than the present study, and this can be explained by the higher number of patients with COPD, which was 101 in the study by Rahul *et al.* [17].

For future workup, a clear definition and precise diagnostic criteria of ACO and its sub-phenotypes, for example asthma-ACO and COPD-ACO, are urgently needed.

## Conclusion

In conclusion, this study demonstrated the following:

- (1) Patients with COPD with history of asthma before 40 years alone can be considered a diagnostic criteria of ACO.
- (2) When reversibility is used as a diagnostic criteria of ACO in COPD, both percent and milliliter changes should be considered.
- (3) The frequency of ACO in patients with COPD is decreased when we use more strict diagnostic criteria.

This study is limited by the small number of patients with COPD.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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