



SPECIAL ARTICLE

## Asthma-chronic obstructive pulmonary disease overlap syndrome – Literature review and contributions towards a Portuguese consensus

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### KEYWORDS

Asthma;  
Chronic obstructive  
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### Abstract

**Introduction:** Phenotypic overlap between the two main chronic airway pulmonary diseases, asthma and chronic obstructive pulmonary disease (COPD), has been the subject of debate for decades, and recently the nomenclature of asthma-COPD overlap syndrome (ACOS) was adopted for this condition. The definition of this entity in the literature is, however, very heterogeneous, it is therefore important to define how it applies to Portugal.

**Methods:** A literature review of ACOS was made in a first phase resulting in the drawing up of a document that was later submitted for discussion among a panel of chronic lung diseases experts, resulting in reflexions about diagnosis, treatment and clinical guidance for ACOS patients.

**Abbreviations:** ACOS, asthma-COPD overlap syndrome; BD, bronchodilation; CARAT, control of allergic rhinitis and asthma test; COPD, chronic obstructive pulmonary disease; FENO, fractional exhaled nitric oxide; FEV<sub>1</sub>, forced expiratory volume in 1 s; FVC, forced vital capacity; GINA, Global Initiative for Asthma; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICS, inhaled corticosteroid; IgE, immunoglobulin E; IL, interleukin; LABA, long acting beta agonist; LAMA, long acting muscarinic antagonist; LLN, lower limit of normal; mMRC scale, modified Medical Research Council scale; PEF, peak expiratory flow; RCT, randomized controlled trial; 6MWT, 6-min walking test.

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**Results:** There was a consensus among the experts that the diagnosis of ACOS should be considered in the concomitant presence of: clinical manifestations characteristic of both asthma and COPD, persistent airway obstruction (post-bronchodilator  $FEV_1/FVC < 0.7$ ), positive response to bronchodilator test (increase in  $FEV_1$  of  $\geq 200$  mL and  $\geq 12\%$  from baseline) and current or past history of smoking or biomass exposure. In reaching diagnosis, the presence of peripheral eosinophilia ( $> 300$  eosinophils/ $\mu$ L or  $> 5\%$  of leukocytes) and previous history of atopy should also be considered. The recommended first line pharmacological treatment in these patients is the ICS/LABA association; if symptomatic control is not achieved or in case of clinical severity, triple therapy with ICS/LABA/LAMA may be used. An effective control of the exposure to risk factors, vaccination, respiratory rehabilitation and treatment of comorbidities is also important.

**Conclusions:** The creation of initial guidelines on ACOS, which can be applied in the Portuguese context, has an important role in the generation of a broad nationwide consensus. This will give, in the near future, a far better clinical, functional and epidemiological characterization of ACOS patients, with the ultimate goal of achieving better therapeutic guidance.

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## Introduction

Asthma and COPD are chronic lung diseases which are highly prevalent and have significant socio-economic impact.<sup>1,2</sup> Data from a recent nationwide study indicate that the current asthma prevalence in the Portuguese population is 6.8%.<sup>3</sup> The national prevalence for COPD was estimated in 9.0% and 5.3% in 2 previous studies – in selected age groups ( $\geq 40$  years old in one study and between 35 and 69 years old in the other); there is also another study carried out in the Lisbon area that showed a prevalence of 14.2% (in patients of 40 years old or more).<sup>4,5</sup> Both asthma and COPD affect the airways and are characterized by the presence of bronchial obstruction.<sup>1,2</sup> Even though these pathologies are heterogeneous, they usually present quite characteristic clinical symptoms, functional changes and underlying physiopathology, which enables a straightforward diagnosis in a majority of patients.<sup>1,2,6</sup> However, there is a growing consensus that typical asthma and COPD characteristics can both exist simultaneously in one patient, especially in those who are older and have a history of smoking.<sup>6–8</sup> Data from the *INAsma* study clearly show that, in Portugal, asthmatic patients smoke in the same proportion as the non-asthmatic and that the passive exposure is even higher in the first group.<sup>9</sup> In reality, there are patients with severe asthma, that has evolved over a long period and frequently with smoking habits, that eventually develop fixed airway obstruction, a pattern usually seen in COPD.<sup>10,11</sup> On the other hand, a positive bronchodilator test, as seen in many asthma patients, can be found in a significant proportion of COPD patients, although not of same magnitude.<sup>12,13</sup> In this context, the concept of ACOS (asthma-COPD overlap syndrome) has been used to describe this set of patients that present concomitant asthma and COPD characteristics. It is important to highlight that in this group of patients, although they show a broad clinical heterogeneity, there are essentially two types of patients: the asthmatic patient that develops ACOS and the COPD patient that presents clinical characteristics of ACOS. It is, thus, important to be aware that in these cases there is an initial distinct physiological base

that culminates in an overlap of symptoms, which can have implications for diagnosis and therapy.

The way these patients are characterized by the several entities analysing this issue is very heterogeneous, which makes it difficult to apply the concept of ACOS to the clinical situation in Portugal. In this context, there is a need for a first step towards clarification of concepts applied to the national context, in order to develop, in the near future, a broader ACOS medical consensus. This paper is an indexed literature revision on the subject, complemented by a series of critical reflexions regarding diagnostic criteria, patient identification, therapeutic approaches and guidelines for future clinical investigation.

## Methods

A literature review was carried out via the PubMed database by searching for MeSH Terms (“asthma”, “chronic obstructive lung disease”, “overlap syndrome”). Articles between 2006 and 2016 were selected as relevant if they had epidemiological data, diagnostic criteria, clinical symptoms and impact and therapeutic approaches. In a second phase, a working meeting was held with medical experts from the chronic lung diseases field (Pulmonology, Immunoallergology, Family Medicine) where the several topics presented in this paper were discussed and proposals for recommendations on ACOS adapted to the Portuguese context drawn up.

## Clinical characterization and impact

The differentiation in terms of respiratory symptoms between asthma and COPD is, in many cases, quite difficult, because there are several areas where they can overlap, making the distinction more complicated. For example, the presence of chronic productive cough is more associated with COPD but can also be present in an asthmatic patient, which leads to a worse prognosis in terms of pulmonary function decline.<sup>14</sup> On the other hand, it is also common to have

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