Algorithm for identification of asthma–COPD overlap: consensus between the Spanish COPD and asthma guidelines

To the Editor:

It was as early as 1959 that the report of the CIBA Symposium described the possible coexistence of different obstructive airway diseases, such as asthma, chronic bronchitis and/or emphysema, in the same individual. However, because there were no specific therapies for all these different expressions of lung disease, these overlaps were largely ignored by guidelines. In 1995, the American Thoracic Society chronic obstructive pulmonary disease (COPD) statement included a Venn diagram with the different possible overlaps of clinical presentation of obstructive lung diseases [1], but no specific recommendations of treatment were provided for them. It was not until 2007 that the Canadian COPD guidelines specified that: "if the asthma component (in COPD) is prominent, earlier introduction of inhaled corticosteroids (ICS) may be justified" [2]. Later, in 2010, the Japanese guidelines for COPD dedicated a chapter to "Treatment of COPD complicated by asthma" [3]. To the best of our knowledge, the Spanish guidelines for COPD (GesEPOC) in 2012 were the first to propose specific criteria for the identification of the so-called asthma–COPD overlap (ACO) [4, 5]. Because there was no internationally accepted definition of ACO, a group of experts proposed diagnostic criteria for ACO in COPD [6] and these were adopted in the document. The major criteria were as follows: a very positive bronchodilator response (>400 mL and >15% increase in forced expiratory volume in 1 s (FEV_1)), sputum eosinophilia or a previous diagnosis of asthma. Minor criteria were an increased total serum IgE, previous history of atopy or a positive bronchodilator test (>200 mL and >12% in FEV_1) on at least two occasions [6]. To be diagnosed with ACO, a patient must fulfil two major or one major and two minor criteria. Other national guidelines for COPD, such as the Finnish [7] and the Czech guidelines [8], followed this approach and proposed similar criteria for ACO.

However, it soon became evident that these criteria were very restrictive and identified <10% of COPD patients with ACO [9]. Therefore, variations of the criteria were investigated [9], and a new consensus was published that also included the point of view of asthma specialists [10]. In parallel, the Spanish guidelines for the management of asthma (GEMA, for *Guía Española de Manejo del Asma*) proposed some criteria for the diagnosis of ACO in the context of an adult patient with asthma [11]. Although the criteria proposed by GesEPOC and GEMA were similar, there were some practical differences that generated confusion among clinicians not specialised in asthma or COPD.

In 2014, the Global Initiative for Asthma (GINA) and Global Initiative for Chronic Obstructive Lung Disease (GOLD) published a joint document on ACO [12]. ACO was defined as the presence of persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD. The document presented a list of features of either asthma or COPD and suggested that ACO can be diagnosed when a similar number of features of asthma and COPD are identified in a given patient. Although this approach is intuitive, it is also quite imprecise, because it does not indicate how many of these features are necessary and/or whether they have the same relevance for the diagnosis of ACO.

In this context, representatives of GesEPOC and GEMA understood the need to clarify and update the criteria for ACO. They developed a new strategy for its identification that was independent of the initial diagnosis, *i.e.* asthma or COPD, and that took into account the new evidence generated over the previous years. The objective was to provide simple and clear guidance for clinicians specialised or not in airways disease to help them identify ACO among patients with COPD or asthma. This proposal is illustrated in figure 1.
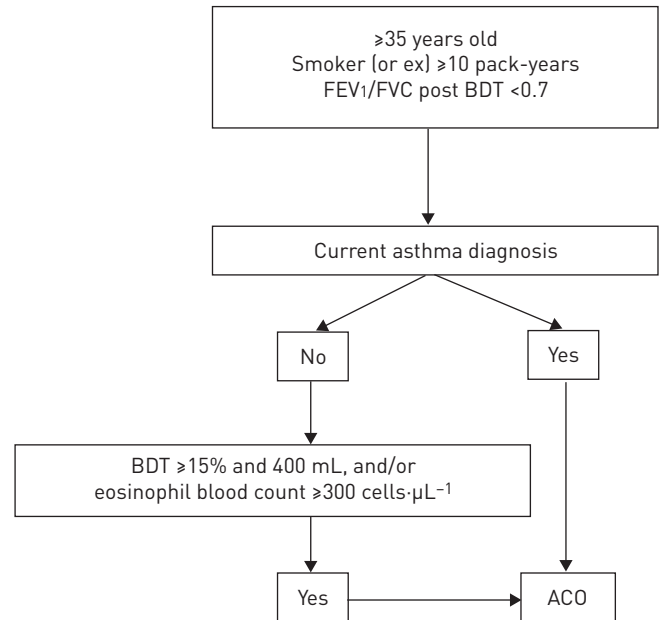
FIGURE 1 Diagnostic algorithm of asthma–COPD overlap (ACO). Persistent airflow limitation (FEV1/FVC <0.7) must be confirmed after treatment with bronchodilators and inhaled corticosteroids or after a course of oral corticosteroids, when required. BDT: bronchodilator test; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity.

The first criterion to be fulfilled is the diagnosis of COPD based on guidelines, *i.e.* age >35 years with significant exposure to smoking (or other inhalation agents) and persistent respiratory symptoms and airflow limitation [5, 12]. Once the diagnosis of COPD is established, the patient may also fulfil the diagnostic criteria for asthma [11, 12]. In this case there is no doubt about the diagnosis of ACO, because the patient fulfils the diagnostic criteria of both diseases. When the diagnostic criteria for asthma are not completely fulfilled, if the patient presents a very positive bronchodilator response (>400 mL and >15% in FEV1) and/or significant blood eosinophilia (>300 cells·mm^{-3}), that patient can also be included under the term ACO.

The main reason for diagnosing ACO in clinical practice is to identify patients with COPD who are likely to have a better response to inhaled corticosteroids (ICS); therefore, the term ACO proposed here is an umbrella term for symptomatic patients with COPD and either concomitant asthma or asthmatic trends that are associated with a better response to ICS. Consequently, we have extended the diagnosis of ACO beyond the coexistence of the diagnosis of both diseases to include patients with COPD and asthmatic trends, such as high reversibility and high blood eosinophil counts. Although not diagnostic, reversibility >400 mL and >15% in FEV1 is considered to be highly suggestive of asthma and has been used in a previous study to define ACO, identifying a subgroup of patients with COPD that matched the common characteristics of ACO [13]. Regarding high blood eosinophil counts, several studies have indicated that they are a promising biomarker for the response to ICS in COPD [14]. Although a clear threshold for a "high" count has not yet been established, the authors agreed upon a concentration of 300 cells·mm^{-3} in accordance with previous consensus [15]. Obviously these criteria must be validated in future prospective studies, but the limited existing evidence suggests that they can be used as an initial guide to select patients that should undergo more careful investigations to establish the definitive diagnosis of ACO.

The current proposal is very similar to a recent consensus [15] that also requires the diagnosis of COPD plus a previous diagnosis of asthma or increased reversibility in addition to one minor criterion: a documented history of atopy or allergic rhinitis, a positive bronchodilator test on at least two occasions, or a blood eosinophil count of >300 cells·mm^{-3}. Because one of the main objectives of our algorithm, from the point of view of the clinician, was to identify patients with symptomatic COPD who may require ICS treatment, we simplified these criteria by including only the best-documented factors associated with response to ICS in COPD: a current diagnosis of asthma and high blood eosinophilia. Although evidence for ICS response in patients with very high reversibility to airflow is less consistent, this small subgroup of COPD patients deserves particular attention. We believe that this simple diagnostic algorithm may be useful until new diagnostic biomarkers of ACO are available or until prospective studies definitely confirm the role of eosinophilia as a predictor of ICS response in COPD, in which case a blood eosinophil-based stratification would be easier and more useful for practising physicians than the ACO criteria.

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