



## Editorial

## How can Patients With Asthma-COPD Overlap Syndrome in Clinical Practice be Identified? ☆



### ¿Cómo podemos identificar a los pacientes con fenotipo mixto asma-EPOC (ACOS) en la práctica clínica?

Miriam Barrecheguren,<sup>a</sup> Cristina Esquinas,<sup>a</sup> Marc Miravittles<sup>a,b,\*</sup>

<sup>a</sup> Servicio de Neumología, Hospital Universitari Vall d'Hebron, Barcelona, Spain

<sup>b</sup> Cíber de Enfermedades Respiratorias (CIBERES), Spain

In a recent consensus meeting of 26 Spanish specialists, 85% of the participants were in agreement about the existence of a mixed COPD-asthma phenotype, known as asthma-COPD overlap syndrome (ACOS). However, there was less agreement on the characteristics that defined this phenotype and how it can be identified in routine clinical practice.<sup>1</sup>

The need for an agreement on the significance of ACOS led to the first consensus meeting aimed at defining ACOS as a COPD phenotype. This was necessary in view of the emerging body of evidence on COPD patients with asthmatic characteristics who respond better to treatment with inhaled corticosteroids (ICS). In this meeting, major and minor criteria for the diagnosis of ACOS were defined<sup>2</sup>; however, subsequent studies have shown that these criteria were excessively restrictive, and that they applied to only a small proportion of patients who may have ACOS.<sup>3</sup>

Compared to the excessively restrictive criteria of the Spanish consensus, the recent criteria from the Global Initiative for Asthma (GINA) and the Global Initiative for Obstructive Lung Disease (GOLD) appear imprecise and ambiguous. These organizations provide a list of characteristics associated with asthma and another list of characteristics associated with COPD. Doctors are expected to tick the characteristics which apply to the patient, and if the number of ticks in each list is similar, the patient probably has ACOS.<sup>4</sup> There is no indication of how many ticks are required, and all ticks have the same weight, even though not all characteristics have the same value when identifying asthma or COPD. Returning to the opinion of the Spanish experts, we find that the most relevant ACOS diagnostic criteria were: prior diagnosis of asthma in a COPD patient (according to 88% of experts); significant tobacco consumption (73%); and post-bronchodilator FEV1/FVC < 0.7 (69%).<sup>1</sup>

In contrast, other characteristics listed in the GINA-GOLD document, such as respiratory symptoms or daily variability in these symptoms,<sup>4</sup> did not appear among the criteria proposed by the Spanish consensus group.<sup>1,5</sup>

From the perspective of COPD, a diagnosis of ACOS is based on the presence of asthmatic characteristics in COPD patients. In contrast, from an asthma perspective, the identification of COPD is not so clear: an asthma patient cannot be diagnosed as having ACOS simply because they have incomplete reversibility of airflow obstruction (post-bronchodilator FEV1/FVC < 0.7). If that patient has never smoked, they should be classified as having chronic, severe or not completely reversible asthma, but asthma nevertheless. Similarly, neutrophilic asthma would still be asthma, not ACOS.

In any case, a prerequisite for diagnosis of ACOS is an overlap between COPD and asthma, and we must therefore be able to identify COPD and asthma in a patient with this possible diagnosis. The most common type of ACOS patient is an asthmatic who is, or who used to be a heavy smoker, who has developed incomplete reversibility of airflow obstruction. In this case, smoking does not cure the asthma, rather it is an added risk factor for the development of incomplete reversibility of airflow obstruction with underlying asthmatic inflammation. Another common pattern is the smoker with COPD who has characteristics reminiscent of asthma, such as reversible airflow obstruction, signs of atopy, rhinitis and/or elevated peripheral eosinophilia.<sup>6</sup> This patient may also be a smoker with asthma, perhaps mild or previously undiagnosed. Despite these considerations, it is curious that 31% of participants in the Spanish consensus meeting did not view incomplete reversibility of airflow obstruction as an essential criterion for the diagnosis of ACOS.<sup>1</sup>

From a clinical point of view, the identification of ACOS in patients previously labelled asthmatic has no impact on management, since these patients should be treated as for asthma. In contrast, in COPD, a diagnosis of ACOS will require the immediate introduction of ICs (combined with long-acting bronchodilators). This is a very significant difference with respect to other COPD

☆ Please cite this article as: Barrecheguren M, Esquinas C, Miravittles M. ¿Cómo podemos identificar a los pacientes con fenotipo mixto asma-EPOC (ACOS) en la práctica clínica?. Arch Bronconeumol. 2016;52:59–60.

\* Corresponding author.

E-mail address: [mmiravittles@vhebron.net](mailto:mmiravittles@vhebron.net) (M. Miravittles).

patients, and for this reason, ACOS was included as one of the clinically relevant phenotypes in the Spanish COPD guidelines (GesEPOC).<sup>7</sup>

Consensus is growing on the limited efficacy of ICS in COPD, and the need for identifying responders to avoid overtreatment has been recognized.<sup>8</sup> ACOS patients respond well to ICS, as they typically present predominantly eosinophilic inflammation, and bronchial eosinophilic inflammation in COPD has been shown to be an excellent predictor of good response to ICS. However, the difficulty involved in analyzing eosinophils in sputum in daily practice has sparked interest in the potential of peripheral eosinophilia as a predictor of ICS response. A post hoc analysis of the results of 2 clinical trials found that the efficacy of an ICS (fluticasone furoate) plus a bronchodilator (vilanterol) in reducing COPD exacerbations had a dose–response relationship with the concentration of eosinophils in blood.<sup>9</sup> Confirmation of these findings in specifically designed prospective studies could herald the end of ACOS, which, being replaced by “eosinophilic COPD” as an identifier of patients with COPD who respond to ICS, would become obsolete. Until such time, our advice is to always ask COPD patients about any history of asthma (or asthmatic symptoms), since this may be a useful indication of the need to include the diagnosis of a possible ACOS in the evaluation of the patient.<sup>10</sup>

#### Conflict of interest

The authors state that they have no conflict of interest with regard to this manuscript.

#### References

1. Miravittles M, Alcázar B, Álvarez FJ, Bazús T, Calle M, Casanova C, et al. What pulmonologists think about the asthma-COPD overlap syndrome (ACOS). *Int J Chron Obstr Pulm Dis*. 2015;10:1321–30.
2. Soler-Cataluña JJ, Cosío B, Izquierdo JL, López-Campos JL, Marín JM, Agüero R, et al. Consensus document on the overlap phenotype COPD-asthma in COPD. *Arch Bronconeumol*. 2012;48:331–7.
3. Cosío BG, Soriano JB, López-Campos JL, Calle-Rubio M, Soler-Cataluña JJ, de-Torres JP, et al. Defining the asthma-COPD overlap syndrome in a COPD cohort. *Chest*. 2015. <http://dx.doi.org/10.1378/chest.15-1055> [Epub ahead of print].
4. GINA-GOLD. Diagnosis of disease of chronic airflow limitation: asthma, COPD and asthma-COPD overlap syndrome (ACOS). Available from: <http://www.goldcopd.org/asthma-copd-overlap.html> [accessed 5.07.15].
5. Fernández-Villar A, López-Campos JL. Mixed COPD-asthma phenotype: ACOS or CAOS? A reflection on recent guidelines and recommendations. *Arch Bronconeumol*. 2015. <http://dx.doi.org/10.1016/j.arbres.2015.07.005>.
6. Barrecheuren M, Esquinas C, Miravittles M. The asthma-chronic obstructive pulmonary disease overlap syndrome (ACOS): opportunities and challenges. *Curr Opin Pulm Med*. 2015;21:74–9.
7. Miravittles M, Soler-Cataluña JJ, Calle M, Molina J, Almagro P, Quintano JA, et al. Spanish guideline for COPD (GesEPOC). Update 2014. *Arch Bronconeumol*. 2014;50 Suppl. 1:S1–16.
8. Alcázar Navarrete B, Casanova C, Miravittles M, de Lucas P, Riesco JA, Rodríguez González-Moro JM. Correct use of inhaled corticosteroids in chronic obstructive pulmonary disease: a consensus document. *Arch Bronconeumol*. 2015;51:193–8.
9. Pascoe S, Locantore N, Dransfield M, Barnes NC, Pavord ID. Blood eosinophil counts, exacerbations and response to the addition of inhaled fluticasone furoate to vilanterol in patients with chronic obstructive pulmonary disease: a secondary analysis of data from two parallel randomized controlled trials. *Lancet Respir Med*. 2015;3:435–42.
10. Barrecheuren M, Román-Rodríguez M, Miravittles M. Is a previous diagnosis of asthma a reliable criterion for asthma-COPD overlap syndrome (ACOS) in a patient with COPD? *Int J Chron Obstr Pulm Dis*. 2015;10:1745–52.