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## Editorial

## Bronchiectasis in COPD and Asthma. More Than Just a Coincidence<sup>☆</sup>



Bronquiectasias en EPOC y asma. ¿Algo más que una casualidad?

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Asthma and chronic obstructive pulmonary disease (COPD) are the two most common obstructive airway diseases (asthma affects more than 300 million people worldwide and more than 250 million people have  $COPD^2$ ). The incidence of both entities is increasing. The high prevalence and morbidity of these diseases also generates high healthcare costs (in Spain, 2% of public health resources are spent on asthma and 2.5% on COPD). The third most common airway disease, bronchiectasis, also carries a heavy healthcare burden, with an estimated mean cost per exacerbation of around  $\in 5,350.3$ 

Although the pathophysiological and clinical features of asthma, COPD, and bronchiectasis differ, they can coexist in the same patient in the form of overlap syndromes, either by chance (as all these diseases are very prevalent), or perhaps because they are connected in some way. There is growing evidence of the existence of a clinical phenotype, COPD and bronchiectasis, that presents with its own clinical characteristics. However, studies have failed to demonstrate a causal association between these diseases,<sup>4–7</sup> and even less scientific evidence is available on the relationship between asthma and bronchiectasis. Although bronchiectasis appears to be linked with more severe asthma, the impact of bronchiectasis on the progress of asthma, the possible pathophysiological mechanism that could explain this association, and any causal relationship between these entities<sup>8</sup> remain to be clarified. Some authors believe that because COPD, asthma, and bronchiectasis share certain risk factors, etiological features, and pathophysiological pathways, COPD and asthma could be responsible for the development of bronchiectasis in susceptible individuals.7

Bronchiectasis is the consequence of a complex vicious circle of infection, inflammation, and mucociliary damage. 9,10 Failure to resolve the inflammation-infection binomial leads to chronicity, with a cycle of destruction and repair of the bronchial wall that causes irreversible injuries. This mechanism is intensified periodically during exacerbations, possibly accelerating disease

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progression. Many of these factors have also been observed in COPD, triggered or magnified by tobacco smoke and other toxic gases. It is not surprising, therefore, that according to some studies, 4,5 between 30% and 50% of patients with moderate-severe COPD have bronchiectasis. Patients with both COPD and bronchiectasis tend to be mainly men, older, and with a greater accumulated smoking index. They also have more respiratory symptoms (increased hypersecretion, more purulent sputum, and worse dyspnea), poorer lung function, more airway colonization by potentially pathogenic microorganisms (especially *Pseudomonas aeruginosa* [*P. aeruginosa*]), more serious and more frequent exacerbations, and higher mortality rates. 4-7,11,12

SEPAR bronchiectasis guidelines recommend performing a high-resolution CT scan to rule out bronchiectasis in patients with moderate-severe COPD with multiple exacerbations and/or repeated isolation of potentially pathogenic microorganisms in respiratory samples (or *P. aeruginosa* on a single occasion) in a clinically stable phase.<sup>8</sup>

Since the 1990s, we have known that asthma and bronchiectasis coexist in a high percentage of patients, 13 but it is only now, probably in the light of results in COPD, that interest in this phenomenon has been rekindled, and efforts are being directed at determining the characteristics of these patients and the possible prognostic and therapeutic implications of this combination. Most studies that have attempted to determine the prevalence of bronchiectasis in asthma patients are retrospective or cross-sectional; they use different methodologies; high-resolution computed tomography is not always performed in all patients<sup>14</sup>; and they have other important biases, such as the inclusion of smokers<sup>15</sup> and patients with allergic bronchopulmonary aspergillosis 16 or other diseases causing bronchiectasis. For all these reasons, the reported incidence of bronchiectasis varies greatly, from 2% to 80% of cases. However, higher quality studies report a prevalence of bronchiectasis in patients with severe asthma of around 25%-30%.<sup>17</sup>

A recent study by our group, <sup>18</sup> designed to analyze the association between asthma and bronchiectasis while avoiding the biases of previous studies, prospectively included 398 patients, non-smokers with uncontrolled moderate or severe asthma, followed up in a specialized high-complexity SEPAR-accredited asthma unit. All study subjects underwent high-resolution computed tomography. In total, 28.4% had bronchiectasis (20.6% with moderate asthma vs 33.6% with severe asthma, *P*<0.001). Asthma patients

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with bronchiectasis (compared to those without bronchiectasis) were older, had poorer lung function and lower levels of FeNO, and a greater percentage had severe asthma, chronic expectoration, purulent sputum and exacerbations, more emergency room visits, and a higher use of antibiotics. The presence of bronchiectasis was associated with more severe asthma, chronic expectoration, at least 1 previous episode of pneumonia, and lower levels of FeNO (at a cut-off point of 20.5 ppb). All this suggests that these are a special type of patients, with their own particular characteristics.

There is still a long way to go and many questions must be answered about inflammatory airway diseases before we understand the complex causative pathophysiological processes, their correlation, and the clinical, prognostic, and therapeutic implications of bronchiectasis in patients with asthma or COPD. These diseases remain a challenge for the treating physician, even more so in the era of personalized medicine.

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