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Towards a new definition of non-cystic fibrosis bronchiectasis

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One of the most obvious peculiarities of bronchiectasis is that it is an enormously heterogeneous disease in its presentation and evolution,[1] as well as being complex in nature in terms of both phenotype[2] and endotype.[3] This is probably due, at least in part, to the fact that dozens of different pulmonary and extra-pulmonary etiologies[4] are capable of causing irreversible damage to the bronchial wall and the variable pulmonary and systemic clinical picture,[5,6] including exacerbations,[7,8] that characterizes this disease.

Since the 1990s, High-resolution CT (HRCT) scan has been the gold standard in the diagnosis of bronchiectasis and a series of radiological diagnostic criteria have been established. These criteria have been used to this day, in both clinical practice and trials, and basically include the following: an increase in the diameter of the bronchial lumen relative to that of the adjacent vessel—this is the most widely used criterion (a broncho-arterial ratio > 1); lack of bronchial tapering; and the presence of dilated bronchi adjacent to the pleura.[9] However, the increasing use of HRCT and improved interpretation of HRCT images have also revealed several additional problems. First, dilated bronchi with a broncho-arterial ratio ≥ 1 may be found in up to 20% of individuals older than 70 years of age with no comorbidities or respiratory symptoms,[10] and something similar seems to be found in individuals living at high altitude. Second, some interstitial or post-infectious diseases (probably including bronchiectasis following COVID-19 pneumonia) as well as diseases with an emphysematous component may also be associated with areas of traction bronchiectasis and little or no clinical component.[11] Third, as a consequence of the variation in the diameter of the vessels adjacent to the bronchus in patients with chronic pulmonary diseases, bronchiectasis may be either underdiagnosed (due to an increase in vessel diameter in patients with pulmonary hypertension) or overdiagnosed (in patients with hypoxic vasoconstriction).[12] Fourth, the visualization and quantification of the thickening of the bronchial wall (a reflection of the underlying inflammatory process of the airways), with a subsequent increase in the diameter of the bronchus, has been constantly improving. Finally, on top of all that, there have been disparities in the radiological interpretation of images, depending on the readers and the specialist skills available at a given centre.

Obviously, the aforementioned issues undoubtedly have an impact on both the daily clinical management of such individuals and the homogeneity of their inclusion in clinical trials, the results of which, to a great extent, will be included in guidelines for clinical practice.

Accordingly, a large group of experts (including both clinicians and radiologists) from all over the world have recently come together to agree on a definition of bronchiectasis that is based on a combined radiological and clinical perspective. Although this definition may vary over time, it does ensure homogeneity of diagnosis for both clinical and research purposes.[13]

Perhaps the key point of this agreed definition is the assertion that the diagnosis of bronchiectasis must include both radiological and clinical factors. This reflects the fact that the so-called "asymptomatic radiological bronchiectasis", which usually includes the bronchiectasis observed in healthy individuals or in fibrotic lung diseases, does not have any clear meaning and does not require, for the moment, any type of therapeutic approach.[13]

The criteria established from a radiological perspective are similar to those that are already well known, with the most relevant change probably being the addition of the thickness of the bronchial wall to the diameter measurement. Accordingly, a broncho-arterial ratio of the inner diameter (only the diameter of the bronchial lumen) and the outer diameter (the diameter of the bronchial lumen plus the thickness of the bronchial wall) ≥ 1 can be considered bronchiectasis if it is accompanied by related symptoms. In any case, from a purely radiological point of view, the greatest diagnostic certainty has been set at a broncho-arterial ratio ≥ 1.5, in an attempt to avoid as much as possible small bronchial dilatations in healthy subjects (although, from a clinical point of view, those are not usually active). From a scientific perspective, centralized reading of the images is recommended.[13]

There are greater discrepancies in clinical criteria, since there are no characteristic, easily recognizable symptoms attributable to bronchiectasis. Assuming this limitation, the presence of at least two of the following symptoms or signs has been established as a criterion: a cough most days of the week, sputum production most days of the week, and a history of exacerbations. In any case, a series of considerations are necessary in this regard. First, the aforementioned agreed definition has a fundamentally scientific purpose, i.e., its application is recommended above all for the homogenization of the type of patient who is suitable for inclusion in a clinical trial. Although the parameters can be used in a clinical setting, cases need to be individualized, since patients may present with other symptoms or signs related to radiologically relevant bronchiectasis, and these symptoms or signs may be modified by treatment. Second, the symptoms described must be attributable to bronchiectasis, so it is important to make every effort to identify both the

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possible etiologies of bronchiectasis and the lung diseases frequently associated with it, such as COPD and asthma. Third, with time and increasing knowledge of bronchiectasis, changes may occur in the clinical interpretation of this disease and the relative impact of each symptom on the patient.[13]

In short, it is very important to be able to find homogeneity in heterogeneity, and few lung diseases are more heterogeneous than bronchiectasis. This point is absolutely essential when comparing the results of clinical trials that will be the basis for guidelines that will inform diagnostic and therapeutic actions for most of our patients in clinical practice. However, we must not lose the perspective of common sense and of our own experience, and we must be aware that each patient has a unique clinical phenotype and should be treated on an individualized basis.

AUTHOR CONTRIBUTIONS

The authors equally contributed to this work.

CONFLICT OF INTEREST

None declared.

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