



Functional lung imaging in chronic obstructive pulmonary disease phenotypes: a complementary vision

Imagen pulmonar funcional en los fenotipos de la enfermedad pulmonar obstructiva crónica: una visión complementaria

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In relation with the review article entitled «Lung Stereology in chronic obstructive pulmonary disease: pulmonary functional exploration imaging examination» which exposes and comments on the virtues of some of the advanced imaging techniques and their association with clinical and functional variables at an appropriate time, given the new and the old classifications of chronic obstructive pulmonary disease (COPD), rekindled and proposed in the last version of the GOLD Report 2023.¹

Within the current definition of COPD as a condition characterized by bronchitis/bronchiolitis and emphysema as the main causes of persistent, irreversible and progressive obstruction of the airway and, therefore, being the traditional diagnostic instrument the post-bronchodilator spirometry according to the ratio of the forced expiratory volume in one second on force vital capacity ($FEV_1/FVC < 0.70$),¹ it has been observed that this criterion shows limitations as it does not have a high sensitivity in the younger population under 50 years of age with an important subdiagnosis.²

Other functional respiratory tests have been analyzed in terms of their performance, such as the Carbon Monoxide Diffusing Capacity (DLCO), which when compared with the spirometry in smokers predicted better the occurrence of COPD in medium term.³

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With the new advanced imaging techniques that have given rise to spatial stereology (image by sections) and the great technological development of imaging of functional type (pulmonary ventilation and perfusion) in which structural changes have been described in subjects with normal spirometries and with COPD⁴ and who, in addition, show affectation in the other pulmonary function tests⁴ and present the same level of symptoms as individuals with COPD,⁵ we believe that this approach by imaging will provide data and validate, in a certain way, these classifications that have originated controversy, as to whether they represent the preamble of COPD and whether they should receive some type of intervention.¹

Early COPD¹ in biological terms refers to the onset of the mechanisms (inflammatory at the biochemical and cellular level)⁶ that lead to the typical lesions of the disease and that, it is accepted, may be present many years before irreversible obstruction is declared.⁷ This approach differs and is far from the early clinical onset of symptoms, the functional limitation and the evident structural abnormalities that may be set in long after the initial preclinical changes seen in «healthy» smokers (normal smokers).⁸

Functional pulmonary imaging (FPI) or stereology will clarify how these structural damages develop and associate them with inflammatory parameters, such as the dilemma of smokers with normal spirometry who show several forms of phenotypes⁸ discussed in the GOLD Report 2023¹ and that deserve to be discussed from this point of view.

Mild COPD should not be interpreted as an early stage of the disease in young people, but merely as a degree of severity that can occur at any age and progress or not over time.⁹ In this case, the potential stereological findings would

have more congruence because there is already a level of obstruction, even if it is mild.

Young COPD may include patients who never reached normal maximum pulmonary function in their youth or who begin premature functional decline from infections in childhood; it does not necessarily have to be a mild disease, rather it may have a major impact on the health.¹⁰ In this phenotype one would expect to find morphological changes of the airways and entrapment by densitometry, as well as incipient functional changes of diffusion and perfusion that needed to be defined.

Pre COPD is where there are symptom and structural or functional abnormalities detectable in presence of normal spirometry, which may or may not develop chronic obstruction (COPD) over time.¹¹ The term pre-COPD does not necessarily mean to evolve into the disease; (IPF), the diffusion and perfusion alterations, the changes of the airway and densitometry must be present to define and predict those who will become patients.

Finally, PRISm (preserved ratio impaired spirometry) describe a $FEV_1/FVC \geq 0.7$ but a $FEV_1 < 80\%$ post-bronchodilator; in a good proportion of patients, if not in the majority, it is associated with the development of COPD over time; and the more structural lesions observed on chest computed tomography (CT), the greater the risk of COPD installation.¹² In this situation, the challenge is to demonstrate the possible benefit of a treatment on the functional changes by IPF; perhaps this condition is the one that involves more structural alterations that influence the conversion to COPD.

For all these reflections, stereology or IPF opens a complementary portal to traditional pulmonary function tests by knowing the volumetry, air entrapment through densitometric analysis, the morphology of the airways (thickening of the wall and the area of the bronchial lumen), as well as other functional techniques to assess ventilation, diffusion and perfusion through dual energy CT, multi detector perfusion CT, perfusion magnetic resonance (with xenon, helium and krypton), positron emission tomography (PET) and single photon emission CT (SPECT), definitely, they will give more information for the study and approach of phenotypes and classifications where there are gaps in natural history and where spirometry does not finish defining what we should do.

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