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Editorial

COPD Assessment: Back to the Future

Valoración de la EPOC: regreso al futuro

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In medicine it is usual that old techniques or concepts that were forgotten for years reappear with great force at a certain time and be reincorporated into clinical practice. Sometimes, these comings and goings are merely fashions, in other cases, they are ideas that were correct at the outset and were abandoned due to the impossibility of implementing them in clinical practice. The development of new technologies may bring about changes in our understanding or treatment of diseases and make these forgotten procedures viable.

Currently, the SEPAR-ALAT, American Thoracic Society (ATS)-ERS and Global Initiative for Obstructive Lung Diseases (GOLD) guidelines define COPD and assess its severity using spirometric criteria, and tend to make us think that we must focus our efforts on trying to achieve good values for expired forced volume in the first second (FEV_1) and relegate the patient to second place.[1] This excessive weighting of forced spirometry values has limited the design of strategies adapted to the patient, both in the clinical field and in research. The question we must ask ourselves at this moment is the following: Should we treat a 50 year old patient with 50% FEV_1 in the same way as an 80 year old patient with the same lung function? This same question is equally valid for the presence or absence of emphysema, for the presence or absence of "asthmatic features", etc. For this reason, during the next few years, the main challenge in the treatment of COPD will be the identification of different disease phenotypes, which will make it possible to perform better clinical assessments, make changes in therapeutic protocols and acquire a better knowledge of COPD pathogenic pathways.[2]

This way of understanding COPD which may seem novel and which has been supported recently by the American NHLBI, implies casting our minds back. Laennec, in his classical description of the symptoms of emphysema, observed 2 large groups of patients in relation to their degree of cough and expectoration, with a notable mix between both. Half a century ago, at the CIBA Symposium, the concept of non-specific chronic lung disease made its appearance, and was used to refer to the clinical term chronic bronchitis and generalized obstructive disease. This last, was divided into emphysema and asthma. In 1975 the term COPD appeared, the ATS and the American College of Chest Physicians defined it as a disease of uncertain aetiology characterized by a persistent slowing of airflow during forced expiration. In 1987 the ATS adds a morphological concept to the functional definition, this consists of a structural alteration that affects airways and lung parenchyma. At that time, mention is also made of the phenotype related to chronic bronchitis and emphysema. For several decades all the guidelines and textbooks have continued to make references to the "different types of COPD": However, after the publication of GOLD in 2001, key aspects related to the heterogeneity of the disease have been eliminated and the simplicity of spirometric values is dominant. This way of understanding COPD has been useful at a certain time to transmit simple messages to large populations, but currently it is conditioning progress in the treatment of this disease. It is difficult to advance with research if it is going to be based on the cut-off value of spirometry readings and not on the patients. To improve our knowledge of COPD, it will be necessary to approach it from several angles (images, biological markers, respiratory function tests, clinical variables, etc.). Following this line of work, one of our first objectives is to clarify the role of lung emphysema in COPD.

Although in many texts COPD and pulmonary emphysema are considered the same, Thurlbeck more than 3 decades ago,[3] observed that approximately 20% of the subjects with more than 30% of their lung tissue affected by emphysema lesions did not have COPD. Furthermore, approximately 40% of the patients with the most severe forms of emphysema (scored by using the panel system above 65%) did not have clinically relevant COPD. More recently, Hogg[4] has observed that the extension and the severity of macroscopic emphysema do not correlate with the degree of obstruction measured preoperatively in 407 patients who underwent lung resection. When assessment was performed by means of CT scans instead of histology, authors such as Gelb[5] have described a poor correlation between presence of emphysema and FEV_1 values. This data supports the need for

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studies that analyse the contribution of lung emphysema to airflow limitation.

Approximately 2 decades ago, the Montreal group proposed the hypothesis that lung emphysema seen in smokers may adopt 2 different destructive patterns (basically panacinar [PE] and centriacinar [CE]), with different mechanical behaviour; one (PE) with elevated lung distensibility and reduced elasticity, and the other (CE) with normal or reduced distensibility for similar values of elasticity.[6] Moreover, airways pathological findings are different in both processes, since the small airways in lungs with CE emphysema lesions have more pathological changes. The most important finding of these studies was that in CE airflow limitation depended on anomalies in the small airways, which explains the reason for the favourable therapeutic responses obtained with bronchodilators and even corticosteroids in patients with lung emphysema. On the contrary, the loss of lung elasticity is the main cause of ventilation limitation in PE emphysema. When both types of emphysema, CE and PE, coexist in the same patient, at least in 50% of cases, is that this pattern is maintained and one functional mechanism or another predominates according to the predominant lesion. The Vancouver group has confirmed these findings identifying specific peculiarities in patients with an alpha-1-antitrypsin deficit.[8] This information will help us to interpret the poor correlation between CT scan findings and FEV_1, and, at the same time, allow the development of image techniques to be of help when determining different aspects of COPD that may be key issues for understanding its pathogenesis, clinical expression and response to different treatments.

In CT images, emphysema appears as low density areas and it is possible to identify different patterns of destruction. In CE emphysema it is possible to see low density areas located near to blood vessels, in the centre of secondary lobes. In PE emphysema, destruction is uniform, with a tendency to locate in basal regions. Although there are authors who indicate that quantification of lung emphysema using densitometric parameters could be a sensitive and specific way to assess progress of the disease, most protocols do not assess this type of lesion and current evidence is insufficient to make recommendations on the use of CT scans for determining clinical treatment of emphysema. However, CT scans have been shown to be of use in concrete cases, such as the selection of patients for volume reduction surgery. The development of new techniques (new CTs, MRIs with hyperpolarized gasses, etc.) could be useful for a better identification of the changes seen in COPD and so improve the understanding of its pathogenesis. Recently, De Meo et al[9] have observed that apical or basal emphysematous destruction could be influenced by different genes. These observations support classical data which describe a greater predominance of CE lesions in upper lung fields and a predominance of PE lesions in lower lobes, lesions which are possibly mediated by different pathogenic mechanisms.[6]

In this number of the Archives of Bronchopneumology, Torres et al[10] analyse, using CT scans, the degree of emphysematous destruction using an analysis of the attenuation of lung density on inspiration and the degree of air entrapment caused by expiratory attenuation. The authors have also assessed regional differences in these changes and their correlation with FEV_1 and the BODE index. The main conclusion of this study, carried out on 55 male patients with stable COPD selected sequentially, is that airway obstruction parameters are correlated with lower lobe attenuation during expiration, whereas hyperinsufflation parameters are correlated with attenuation during inspiration. This relation was not seen with the BODE index.

The results presented by the authors in some paragraphs are difficult to interpret, since the data from different groups is not always consistent. Correlation with FEV_1 or with IC/TLC is significant but low, and the clinical relevance of these findings has not been established. One of the limitations of this study is the small size of the sample. If, additionally to analysing small groups, GOLD classification arbitrary cut-off points are used, the differences in FEV_1 between groups III and IV are very small (1.11L vs. 1.13L), it could be that lesion overlapping and technique variability make it difficult to obtain conclusive results. Previous studies with a larger number of subjects[11] have observed that the same severity of emphysema varies widely even in patients with the same stage of COPD. These same studies have observed that the patients with most emphysema had less BMI and worse quality of life, which contrasts with the absence of correlation with the BODE index seen in this study. The difficulties of applying the BODE index in concrete populations[12] and some of the methodological limitations detailed above may explain the results.

The study of regional variations can be extremely relevant for a better understanding of COPD. In this paragraph, the authors' data is also difficult to interpret. Additionally to having assessed density levels, a visual analysis, at least a semi-quantitative one,[11] could have increased the amount of information on the real presence or not of macroscopic emphysema and its histological predominance. Finally, this study was carried out on men, therefore the results may not be susceptible to extrapolation to the population in general, since women show peculiarities in their presentation of lung emphysema.[13]

Undoubtedly, new imaging techniques may revitalize the assessment of lung emphysema as they do not need to use histological studies, but to provide relevant information they need to be appropriately standardized. For 2 decades multiple cross-sectional studies have been published that have confirmed the poor correlation between FEV_1 and emphysema assessed by CT scans. To continue advancing it is necessary to look back at the past and keep in mind the heterogeneity, not only of COPD but of emphysema itself.[6,14] At the same time, we must look to the future by designing longitudinal studies that assess the clinical relevance of the findings obtained with imaging techniques. A clear example in this sense has been the NETT[15] study that has determined the importance of emphysema and its characteristics whatever the FEV_1.

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