Back to the Roots of Chronic Obstructive Pulmonary Disease: The Severity of Respiratory Impairment Matters

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Chronic obstructive pulmonary disease (COPD) is a complex disease and, as such, it is commonly considered worthy of a comprehensive approach with a rapidly expanding list of 'omics' joining the broad series of factors, mainly non-respiratory factors, expected to shed light on its phenotypic variability and its clinical course. This dramatic conceptual and practical effort is commendable because it tries to identify associated diseases clustering under the umbrella definition COPD. However, it should not distract from classical, direct indicators of COPD severity in favor of multidimensional indexes, which not always sustain longer testing. Such an approach would carry the risk of disregarding prognostically important information, mainly in patients with an acute exacerbation. Indeed, since 1995 it is well known that the alveolar-arterial difference in oxygen, an index of gas exchange efficiency, is second only to age as prognostic indicator in patients with acutely exacerbated COPD [1]. On the other hand, multidimensional indexes are intended for long-term prediction and, thus, are unlikely to improve the prognostic definition of acutely exacerbated COPD with regard to classical indexes of respiratory impairment. In this perspective, the study by Matkovic et al. [2] in this issue of *Respiration* clearly shows that hypoxemia, hyper-capnia and frequent exacerbations identify patients more likely to experience a composite adverse outcome. Neither BODEx nor dose-modified indexes could improve the AUC of the ROC model when substituted for history of exacerbation in the previous year, with hypoxemia and hypercapnia being the other two components of the model. This finding points to a simpler prognostic model being preferable to a more articulated one, at least in the acute care setting. Moreover, it suggests that the collected history of exacerbation is the core prognostic information shared by these indexes. Finally, it stresses the role that frequent exacerbations, which may represent a phenotypic variant of COPD [3], have in conditioning the course of the disease.

The observation by Matkovic et al. [2] is to some extent biased by the relatively small sample size (n = 155), and, as the authors correctly acknowledge, the lack of information on selected and prognostically important comorbidities or complications of COPD such as chronic cor pulmonale [4]. However, its main limitation is an inclusion criterion shared with the vast majority of studies on COPD: the selection of patients able to satisfactorily perform spirometry likely guarantees that patients really having COPD are included, but it excludes a consistent

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fraction of patients, frequently with advanced COPD or important comorbidities, unable to perform spirometry. This is especially true for a population with a mean age of 70 years. In fact, even in optimal settings, 1 of 4 COPD subjects >64 years could not meet ATS/ERS standards for the quality of spirometry, and even the FEV_6, a simpler surrogate measure of FVC, could not be obtained in 1 of 5 [5, 6]. Thus, the true problem of this and almost all studies lies in the patients with COPD studied as a representative COPD population. Even large pharmacological trials have adopted so stringent exclusion criteria, ranging from long-term oxygen therapy to any comorbidity that could preclude participation in the study or interfere with study results, to select a population poorly representative of the 'usual' COPD population [7–9].

Despite these limitations, the study by Matkovic et al. [2] extended our view on COPD by stressing the short-term prognostic role of direct indicators of respiratory impairment and COPD severity. This reminds us that, at least when exacerbated, COPD affects the health status primarily as a respiratory disease. Then, a careful assessment and an optimal treatment of the respiratory problem is what the patient needs, at least in this clinical context. Accordingly, the caring physician should point at the origins of COPD. Conceptualizing complex disease entities might help to understand the place of COPD among chronic conditions and to clarify components of the umbrella definition, if any, but it is unlikely to provide prognostically important information and, possibly, improve management in the acute care setting.

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