



Editorial

Is Chronic Obstructive Pulmonary Disease Really a Progressive Disease?☆



¿Es realmente la enfermedad pulmonar obstructiva crónica una enfermedad progresiva?

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The Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines chronic obstructive pulmonary disease (COPD) as a disease characterized by usually progressive, irreversible airflow obstruction.¹

The degree of bronchial obstruction measured by volume exhaled during the first second of a forced expiratory maneuver (FEV₁) is the conventional method of evaluating disease “progression”. This implies that, according to the GOLD definition, most COPD patients have a progressive decline of lung function with a fall in FEV₁.

Recent studies^{2,3} indicate that not all patients have the same lung function decline. These publications show 3 different patterns of progress: rapid decliners, slow decliners, and those who even experience an improvement in lung function. These studies also confirm that only a small percentage of patients (20%–30%) are rapid decliners, and thus meet the definition of clear disease “progression”.

The idea that lung function declines over time implies that most COPD patients will inexorably “progress” after diagnosis to more severe disease stages. This would suggest that patients who are currently in GOLD spirometric stages I–II will progress to stages II–IV, if they manage to survive long enough. In contrast, it would also suggest that patients in GOLD spirometric stages III–IV would have previously progressed through stages of less severity in the natural course of their disease.

This ingrained concept of the progressive nature of the disease has recently been questioned in a study published by the BODE group in *PloSOne*.⁴ This group of investigators determined the proportion of patients with COPD whose GOLD stage changed over a prolonged follow-up period. They looked at a group of 318 patients who they called “survivors”, who were regularly monitored over at least 8 years, and another group of “non-survivors” who had died during the follow-up period, but who had been monitored for at

least 4 years before death. The “non-survivor” group was purposely included in order to avoid the modifying effect observed when only healthy subjects who “survive” are evaluated, as this latter group would be more resilient, and consequently slower decliners. This design also helped the authors explore what happens to patients in the years before death, so that those with a poorer prognosis, who presumably would be rapid decliners, also contributed to the analysis. All study patients received standard medical treatment according to GOLD guidelines.

One of the most important findings of the study was that 9% of survivors and 11% of non-survivors improved their GOLD stage during the follow-up period, suggesting that a certain proportion of patients really do show a highly favorable response to treatment. Moreover, among the survivors, the proportion of patients who progress reduces and the proportion who improve increases as the severity of the obstruction increases, while among non-survivors, the proportion of patients who progress appears to fall, but clearly the number who improve falls as the severity of their obstruction increases. This suggests the existence of 2 patient profiles: “responders” to standard medical treatment, who are consequently survivors, and “non-responders”, who are consequently “non-survivors”. GOLD stages also remained unchanged in approximately 70% of patients in both groups. In other words, most patients remained stable throughout the course of their disease. Some other aspects of these findings are of interest: (1) The 8-year follow-up (10–12 years in many cases) of survivors represents 40%–50% of the potential survival time of a patient diagnosed with COPD between the ages of 50–60 years, so it is probably truly representative of what happens in the “real-life” course of a COPD patient. (2) The percentage of patients who decline rapidly (and whose GOLD stage therefore worsens) is similar to figures published in other studies, adding external validity to the findings. The authors mention some limitations, the most important being that their population comprises mainly men; that during the follow-up period, new therapies appeared that probably affected the natural course of the disease; and that the yearly exacerbation rate of patients that might have an impact on lung function decline was not consistently collected.

The observation that a large proportion of patients remained in the same GOLD stage for a prolonged time is consistent with a recent report that found that almost half of patients with COPD

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are diagnosed without having experienced a rapid decline in lung function.⁵ The authors of this study suggested that in individuals with COPD without rapid FEV1 deterioration, the decline may have already occurred as a result of having started out with functional compromise from an early age, whether as a result of genetic problems or pulmonary insult during childhood caused by factors such as asthma and infections during the early postnatal period of lung growth. Finally, the fact that almost 10% of patients show improved lung function to the extent of dropping one grade on the GOLD scale is very significant. Is it possible that the lungs of these patients are really being repaired? To date, all our attention has been focused on slowing down the process of functional decline, but these findings oblige us to rethink our position and wonder if it is possible to recover lost function, at least partially.

These studies may have important implications in the interpretation of the course of COPD⁶ and the impact of treatment on patient progress. The participants in this observational study were treated according to the guidelines applicable at the time, and probably reflect the real life and progress of patients we see on a daily basis in our clinics. The findings underline that our day-to-day management of our patients has a real impact on their COPD progress, and

that most remain at the same stage of spirometric severity, and some even improve, overturning our nihilistic concept of a disease described in the current guidelines as “usually progressive”.

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