

Susceptibility to exacerbation in chronic obstructive pulmonary disease – Data from the ECLIPSE study

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Chronic obstructive pulmonary disease (COPD) has a natural history with many episodes of acute worsening of symptoms, called exacerbations. These exacerbations seem to accelerate the decline in lung function, therefore determining reduced physical activity, poor quality of life, increased risk of death and higher healthcare costs. Exacerbations are important outcomes in clinical trials and their prevention is a significant part of COPD management. Until now, relatively few studies focused on the incidence, the determinants and the effects of exacerbations, in patients with different stages of COPD.

The presented study is based on data collected as part of the ECLIPSE (Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints) observational study. Inclusion criteria were: age 40-75 years, history of smoking 10 or more pack-years, forced expiratory volume in 1 second (FEV1) less than 80% of predicted value after bronchodilator use, ratio FEV1 to forced vital capacity (FVC) of 0.7 or less after bronchodilator use.

At baseline patients underwent standard spirometry (after inhaled albuterol) and chest CT scan (evaluation of emphysema). The clinical

condition of the patients was graded using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) scale. Patients were followed for 3 years.

Exacerbations were considered a critical outcome and were defined functionally, based on the decision by the clinician or study personnel to prescribe, alone or in combination, antibiotics or systemic corticosteroids.

The results of the study are the following: the severity and frequency of exacerbations were directly related to the severity of COPD. Exacerbation rates in the first year were 0.85/person in patients with stage 2 COPD, 1.34 for patients with stage 3 and 2 in patients with stage 4 COPD. 22% of patients with stage 2, 33% with stage 3 and 47% with stage 4 had frequent (2 or more/ year) exacerbations. The single best predictor of exacerbations, independently of the GOLD stage, was the history of exacerbations. The frequent-exacerbation phenotype was defined, associated with more severe disease and prior exacerbation. Also, this phenotype was independently associated with a history of gastroesophageal reflux or heartburn, poorer quality of life, and elevated white-cell count.

The presented study confirms previous observations that the severity of exacerbations is directly proportional with the severity of underlying COPD. The most important determinant of frequent exacerbations is the history of exacerbations. Patients with more frequent exacerbations, some of them with milder forms of disease, may have a distinct susceptibility phe-

notype, with relative stability over time. Although exacerbations become more frequent and more severe with COPD progression, the rate at which they occur seems to reflect an independent susceptibility phenotype. This should be taken into consideration when using exacerbation-prevention strategies in different stages of the disease. □



Comment on a paper:

JR Hurst, J Vestbo, A Anzueto et al – Susceptibility to Exacerbation in Chronic Obstructive Pulmonary Disease, *N Engl J Med* 2010; 363:1128-1138