

Chronic Obstructive Pulmonary Disease in Life and Death

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“Dead, he’s dead...but it’s tough to die of COPD!”

Anonymous pathologist

Chronic obstructive pulmonary disease (COPD) represents a considerable worldwide health burden in both absolute and relative terms. Worldwide mortality projections calculated in 1990¹ and recently updated² confirm that COPD, which was the fifth cause of death in 1990, has become the fourth since 2000, and is expected to be the third by 2020. The most recently available data for Spain, dating from 2002, published by the National Institute of Statistics in December 2004, indicate that COPD is the fourth cause of death among men, with an annual mortality rate of 60 per 100 000 population, and the seventh among women, with an annual mortality rate of 71 per 100 000 population.³

As occurs with other chronic smoking-related diseases, the distribution of COPD depends on 2 main factors: the effects of exposure to tobacco smoke and the gradual aging of the population. For this reason, it appears logical to predict that in the coming years we will be experiencing a veritable COPD epidemic in Spain, if we define an epidemic as a greater number of cases in time and space than expected. Such predictions are supported by the fact that we are, unfortunately, the country with the highest percentage of adolescent smokers in Europe and with one of the highest in the world of women smokers.⁴ Furthermore, the population of Spain is expected to reach maximum growth in 2050, with 53 million inhabitants and to have its maximum average age in 2060.³

The epidemiology and distribution of COPD among the general population is still an issue for concern. Several recent international initiatives, led by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) and other organizations,⁵ have been launched in order to obtain much needed population-based evidence. In Spain, this need was filled by the IBERPOC study,⁶ perhaps the most widely cited internationally for the distribution of COPD in the general population. This study found a 9.1% prevalence of COPD (defined by a postbronchodilator ratio of forced expiratory volume in 1 second to forced vital capacity of less than 88% of predicted in men and less than 89% of predicted in women between the ages of 40 and 69 years, without bronchial reversibility). Surprisingly, 80% of the patients had not yet been diagnosed, and 50% of patients with severe obstruction had not been prescribed any respiratory treatment for COPD. Unfortunately, these discouraging figures, obtained during the period from 1996 to 1997, have not improved in recent years.⁷ It is estimated that 18 000 people in Spain die of COPD each year.³ Both prevalence and mortality are probably underestimated, and, although it has been reported that smoking-related deaths decreased for the first time in 2001,⁸ prevalence and mortality rates for COPD can only increase in the coming years, as will COPD-related costs.^{9,10}

Until quite recently COPD was considered an irreversible disease of scant therapeutic interest. Therapy was symptomatic only, and apart from smoking cessation,¹¹ there were no interventions that could alter the natural history of the disease or increase survival.¹² This pessimistic perspective is reflected in guidelines for the handling and treatment of COPD, in which a decrease in mortality is identified as the seventh objective.^{13,14} This situation may change if the results of the TORCH study⁵ are favorable. TORCH, the acronym for “Towards a Revolution in COPD Health,” is a multicenter, randomized, parallel-group, double-blind, placebo-controlled trial. Approximately 6200 patients with moderate to severe COPD were randomized to receive treatment with a combination of salmeterol and fluticasone propionate (50/500 µg),

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fluticasone propionate (500 µg), salmeterol (50 µg), or placebo for 3 years. In Spain 13 centers have participated, randomizing 250 patients. The main objective of the TORCH study is to determine the differences in mortality from any cause between the group receiving the combination of salmeterol plus fluticasone propionate and the group receiving placebo. The many secondary objectives include the study of exacerbations and of variations in state of health as measured by the St George's Respiratory Questionnaire.

If the results of the recent meta-analysis of clinical trials on the effect of inhaled corticosteroids compared to placebo in COPD¹⁶ are confirmed by the TORCH study, the impact on survival may be much greater than that observed with other pharmacological interventions that have been introduced into routine clinical practice in primary care as well as into such specialties as cardiology and oncology.¹⁷ We may expect one of the greatest difficulties in the interpretation of the results of the TORCH study, which will soon become available, to be the identification of the specific causes of death in COPD patients. Even when death occurs in the hospital environment, determining the precise cause of death in a patient with COPD is a challenge for the clinician. The difficulty of identifying the cause of death correctly has been mentioned by several authors who have described series of COPD patients.¹⁸

The study of the circumstances that characterize the final period of the lives of COPD patients is unexplored territory. This is due in part to the presence of comorbidities and to the fact that data registers usually reflect only the main cause of death.¹⁹ The commonly held belief that the majority of COPD patients die of respiratory failure is erroneous and stems from the fact that early studies were biased. They were based on patients whose COPD was in an advanced stage, who presented respiratory failure (PaO₂<60 mm Hg [<8.0 kPa]), and who were receiving oxygen therapy.²⁰ In the initial phases of COPD, cardiovascular disease and lung cancer are, in fact, the most frequent causes of death.¹¹

In the coming years it will be necessary to study in detail the association of COPD with various comorbidities and with other causes of death. Although it has been suggested that pulmonary and systemic inflammation may trigger ischemic heart disease and/or lung cancer, the mechanism responsible for this is still unknown.

The results of the TORCH study will soon be available and, among other things, we may expect them to confirm that death with COPD is and will be more frequent than death from COPD.

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