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What do patients with chronic obstructive pulmonary disease die from?

Na co umierają chorzy na przewlekłą obturacyjną chorobę płuc?

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Chronic obstructive pulmonary disease (COPD) is a condition characterised by a duration of several decades. The main cause of mortality due to COPD in developed countries is smoking and the main feature of this disorder is a progressive decrease in ventilatory reserve of the lungs of the obstructive type.

Over the decades-long course of the disease forced expiratory volume in one second (FEV₁) decreases by an average of 40 ml per year. When FEV₁ drops below 50% predicted the patient may develop respiratory failure — a condition in which the lungs are unable to supply sufficient amounts of oxygen to the tissues and to remove excess carbon dioxide from the tissues. Respiratory failure is a complication of COPD and is the main cause of death, which usually occurs during an acute exacerbation of the disease [1].

Chronic hypoxia caused by respiratory failure is the underlying cause of another complication of COPD: hypoxic pulmonary hypertension, also referred to as cor pulmonale. According to the data collected by the Epidemiology Department of the Institute of Tuberculosis and Lung Diseases in Warsaw, Poland [2], cor pulmonale was the cause of death in 10,524 patients in Poland in 1980. The frequency of this cause of death is rapidly decreasing. In 2009, a total of 706 patients died from cor pulmonale in Poland.

If COPD patients had no co-morbidities, they would most commonly die from the above complications. This, however, is not the case. COPD is very prevalent. In some countries, it is the fourth most common cause of death. The two main causes of mortality in developed countries, namely

cardiovascular disease and cancer, are commonly seen in COPD patients for the very reason of their high prevalence. Myocardial infarction and lung cancer have been shown to be several times more prevalent in COPD patients than in smokers with normal lung function [3].

Interesting data on the causes of death in patients with COPD are provided in this issue of “Pneumonologia i Alergologia Polska”, in the paper by Rubinsztajn and Chazan [4], in which the causes of death in COPD patients hospitalised at a university hospital pulmonary department were analysed.

Medical records of 266 consecutive COPD patients who were admitted to the department and died during hospitalisation were analysed. The mean age was 73 ± 8 years. The most common cause of death (30% of the patients) was acute exacerbation of COPD, followed by pneumonia (25%), followed by lung cancer (19%). The fourth and fifth most common causes of death were ischaemic heart disease (7%) and heart failure (5%), respectively.

The results of the study by Rubinsztajn and Chazan [4] confirm that even in the advanced stage of COPD one fourth of the patients die from heart disease and lung cancer. Of note is the fact that the youngest were patients dying from lung cancer, while the oldest were those dying from pneumonia. A serious general condition on admission and its further deterioration were the reasons why the authors did not have spirometry results, which would have allowed them to make an attempt at relating the cause of death to the degree of ventilatory dysfunction of the lungs.

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In the largest and longest prospective study of patients with mild to moderate COPD, a total of 5887 subjects aged 35 to 60 years were followed up for 14.5 years. Of the 731 deaths during this period nearly a half (55%) was caused by heart disease or cancer [5].

Patients with severe respiratory failure requiring home oxygen therapy are at the other end of the severity spectrum. In a large multicentre European analysis of 215 patients with COPD receiving home oxygen therapy [6], 72% of the subjects died from exacerbation of respiratory failure or cor pulmonale. Myocardial infarction or lung cancer were the cause of death in 13% of the patients. Similar causes of death were identified by Rubinsztajn and Chazan [4] in the subgroup of patients receiving home oxygen therapy.

The relationships between age and the cause of death and between the severity of the disease and the cause of death presented above could be one of the explanations of the widespread finding in epidemiological studies, namely that patients with mild to moderate disease account for 80% of all COPD patients, while only 20% progress to severe and very severe disease [7]. A large proportion of patients with mild to moderate COPD die from co-morbidities, mainly heart disease and cancer. I have intentionally used the word “co-morbidities” in order to keep a certain reserve regarding the opinion according to which COPD is a systemic inflammatory disease that affects the development of many disorders seen in COPD patients [8].

One of the findings confirming the inflammatory hypothesis is the correlation between the levels of markers of systemic inflammation, such as C-reactive protein (CRP), interleukin-6 (IL-6) and tumour necrosis factor- α (TNF- α), in patients with COPD and the severity of the features of lung distension, an indirect sign suggestive of emphysema [9]. The presence of similar correlations does not mean that they are clinically relevant and they may be purely accidental.

If COPD was indeed an inflammatory disorder, one could expect that anti-inflammatory drugs (antibiotics, steroids) would affect its natural history and disease-related mortality. So far no such relationship has been demonstrated [10]. The discussion about the inflammatory hypothesis in COPD is not only academic in nature. Its practical result is the use of anti-inflammatory drugs in each stage of COPD [11].

How to reduce mortality related to chronic obstructive pulmonary disease in Poland?

In their paper, Rubinsztajn and Chazan point to the fact that within the next 10 years COPD will have become the third most common cause of de-

ath in the United States [4]. A success of Polish pneumonologists would be to reduce COPD-related mortality. Unfortunately the COPD-related mortality rate in 2009 was the highest in history (20.5 per 100,000) [12]. Below I discuss the suggested courses of action which will most certainly reduce mortality attributable to COPD in Poland.

An increasing body of evidence has accumulated over the past 30 years to demonstrate that complete cessation of smoking reduces COPD-related mortality [5]. Home oxygen therapy [13] and non-invasive ventilation during hypercapnic respiratory failure with uncompensated respiratory acidosis [14] have also been shown to prolong survival in patients with COPD. Both treatments are insufficiently used in Poland [15–17].

Active diagnosis of COPD should be intensified. Unfortunately, despite the ten years of efforts to disseminate spirometry testing in groups of patients at high risk of COPD in Poland [18] a recent study to assess the prevalence of COPD in general practice has shown that only 24% of about 1000 subjects investigated (55% of whom were smokers and 90% of whom were over 40 years of age) had previously undergone spirometry [19]. At the same time, the quality of spirometries performed at GP surgeries needs improving [20]. Patients with COPD are predominated by those with primary-level education and low income. Such patients seek medical active at a very late stage [21]. Active diagnosis of the disease could improve the situation.

Spirometry combined with permanent smoking cessation counselling leading to a definitive cessation of smoking is the best way to stop the progression of COPD and to prevent other smoking-related conditions. Two long-term and very large studies investigating the effects of smoking cessation on annual reduction of FEV₁ have shown that patients with COPD who continue to smoke lose twice as much of their FEV₁ than those who managed to quit smoking. Over a period of 11 years, patients with mild to moderate COPD who continued to smoke lost an annual of 60 ml of FEV₁, while those who permanently quitted smoking lost annually 26 ml [22]. Another study of patients with moderate to severe disease who were followed up for 4 years has shown that patients who were not smoking during the study lost annually of 23 ml of their FEV₁, while those who were smoking lost 51 ml of their FEV₁ per year. This means that smoking cessation stops the progression of the disease at any stage, even at the stage of severe COPD [23]. Polish pneumonologists should therefore force the National Health Fund to adopt new rules for the

operation of smoking cessation clinics, both in terms of the type of services provided and the pricing of the procedures.

Non-invasive ventilatory support, i.e. the use of a ventilator connected with the patient through a mask, is a survival-prolonging treatment in COPD patients. The method, improved and disseminated by pneumonologists from the very beginning, has considerably developed in Europe in the past 30 years. Used in the management of exacerbations of hypercapnic respiratory failure with uncompensated respiratory acidosis, the method reduces mortality by 50% compared to traditional treatment (oxygen, antibiotics, bronchodilators and systemic steroids) [14]. Compared to Western European countries, non-invasive ventilatory support is very rarely used in Poland [16], most commonly at academic facilities. Reduced mortality of COPD patients during acute exacerbations may be expected after the accessibility to non-invasive ventilatory support is increased during exacerbations of the disease at hospitals, followed by continuation of this form of treatment in some of the patients at home [17]. At each pneumonology ward and department in Poland it is necessary to create an intensive pulmonary care unit with three monitored beds where non-invasive ventilatory support can be provided.

This year marks the 25th anniversary of implementation of home oxygen therapy in Poland. Over these 25 years the rate of patients on home oxygen therapy has reached 21 per 100,000 inhabitants. It is estimated that when the need for this form of therapy is met this number should increase to 50 per 100,000. Although home oxygen therapy is the simplest and the most accessible method of treatment, it is not fully taken advantage of by Polish pneumonologists. Home oxygen therapy prolongs survival, improves the quality of life, reduces the number of acute exacerbations of COPD and decreases hospitalisation rate. Who else, if not Polish pneumonologists, should make every effort to render this reimbursed method of treatment fully utilised?

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