EDITORIAL

Commentary on "Costs of pharmacotherapy of chronic obstructive pulmonary disease in relation to changing Global Initiative for Chronic Obstructive Lung Disease guidelines (2007, 2011, and 2017 updates)"

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Chronic obstructive pulmonary disease (COPD) is a complex and heterogenous disorder, characterized by high morbidity and mortality rates.[1] It represents a major social and economic burden for healthcare systems worldwide.[2] The reduction of risk factors, treatment of comorbidities, and prevention of acute exacerbations are key elements of proper disease management.

Forced expiratory volume in 1 second (FEV_1) is a marker of airflow obstruction. Due to its reliability and reproducibility, it has been frequently adopted as outcome in clinical research and for defining disease severity. However, observational studies, such as the ECLIPSE study (Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints), have clearly shown that FEV_1 poorly correlates with the patient's global performance and health-related variables, such as comorbidities, symptoms, quality of life,[3,4] exacerbations,[5] hospitalization, and mortality rates.[6,7]

To address this complexity, multiple multidimensional grading systems have been developed. The Global Initiative for Chronic Obstructive Lung Disease (GOLD), moved from a FEV_1-based severity grading (2007) to the ABCD classification, which stratifies patients according to symptoms and exacerbation history (2011). In the 2017 update of GOLD recommendations, spirometry was removed from the risk stratification and treatment algorithm, leaving FEV_1 alone for diagnostic purposes.[8]

Until now, no pharmacological treatment has proved to be significantly effective in modifying the progressive course of the disease, but available drugs are able to improve the patient's quality of life by reducing symptoms and frequency of exacerbations and increasing effort tolerability. On the one hand, this justifies the adoption of a severity grading system based on clinical features, but exclusion of functional parameters does not allow a precise patient's phenotyping. Conversely, it is a matter of fact that, although lung function measures show gradual progression towards an emphysema pattern in GOLD stage 3 and 4,[9] it is well known that bronchitis and emphysema can occur independently of the FEV_1 value and disease features. In the era of personalized medicine, it is clear that COPD cannot be managed with a sole therapeutic approach any longer, while focusing on the most appropriate treatment in any selected patient is increasingly deemed as a critical strategy.[10] In accordance with Safka et al,[11] a change from GOLD 2011 to 2017 criteria leads to a consistent shift of patients from higher (C and D) to lower (A and B) risk categories. This redistribution impairs in-between functional and clinical differences and might jeopardize the predictability of important patient-centered outcomes, such as mortality.[12] Obviously, this has economic implications.

Since healthcare system sustainability of chronic disorders, such as COPD, needs a well-defined management plan, the analysis performed by Brożek et al[13] provides relevant information. In a population sample of 2597 patients with COPD treated by a random population of Polish general practitioners, the authors simulated the impact of GOLD guideline updates on direct costs.

Three key messages could be drawn from this research. First of all, independently of

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the classification of severity adopted, the more severe forms of COPD are the most expensive. In contrast to asthma, we are not able yet to achieve the total control of COPD in its different stages. Worsening of lung function, dyspnea burden, and the rate of exacerbation lead to a step-up approach of pharmacotherapy. Two points need to be further explored: the ability of early combined long--term treatment with fixed doses of bronchodilators to reduce lung function decline, and the efficacy of target treatment (ie, biological drugs) in changing the natural history of the disease. We must also pay more attention to define the severity of the disease and the needs of our patients, since the change in classification parameters leads to switching of patients from one stage to another. In particular, GOLD 2017 considerably reduced the number of patients in C and D groups. Finally, a significant reduction of direct costs was observed at each update of GOLD guidelines.

As mentioned by the authors, the cost of pharmacotherapy represents only part of the total cost of COPD, but a proper therapeutic strategy can influence the indirect cost (ie, hospitalization due to disease exacerbations). In recent trials exploring the efficacy of single-inhaler triple therapy, patients treated in the context of a clinical trial where adherence to treatment is monitored have shown about 50% reduction of disease exacerbation during the follow-up in comparison with the previous year.[14,15] Furthermore, these trials were consistent in confirming that different combinations of drugs lead to different clinical effects in different patients. For example, IMPACT (Informing the Pathway of COPD Treatment) data[15] showed that the greater the rate of blood eosinophils, the greater the effect of inhaled corticosteroids on reducing the exacerbation. On the other hand, the benefits of inhaled corticosteroids in smokers were limited.

Fulfilling patient's needs, expressed as classification of disease severity and drugs' efficacy in specific groups of patients, is a matter of discussion. A recent release of the GOLD document[8] has further fueled this debate. The updated recommendation suggests considering the grade of obstruction (1 to 4) and the impact of symptoms and exacerbation risk (A, B, C, D) for defining the disease severity. This system should facilitate a better understanding of the impact of COPD at an individual level and provision of a tailored treatment. Concerning this point, there is a model for pharmacological management of COPD according to the individualized evaluation of symptoms and exacerbation risk following the ABCD assessment, although the lack of high-quality evidence supporting initial pharmacological treatment strategies in newly diagnosed COPD patients is evident. The document provides a separate algorithm for the follow-up treatment, where the escalation and de-escalation of drugs are still based on symptoms and exacerbations, but the recommendations do not depend on GOLD group classification at diagnosis.

ARTICLE INFORMATION

DISCLAIMER The opinions expressed by the author are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

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