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COPD 2020 Guidelines — what is new and why?

To the editor

The new year dawns with new guidelines. Global Initiative for Obstructive Lung Disease (GOLD 2020) has some major and few minor changes to offer for the management of COPD. The significant changes include defining the role of inhaled corticosteroids (ICS) and vitamin D levels [1].

Definition — the definition remains the same. "Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases". However, there may be significant lung pathology (emphysema) in the absence of airflow obstruction, which warrants a detailed assessment. This stems from the ancient concept of GOLD 0, where there were structural changes but no obstruction. Being a clinically common scenario, the entity of emphysema without obstruction has been re-introduced.

Epidemiology — the predicted mortality by 2030 of 4.5 million deaths annually from COPD and related conditions has been extrapolated to over 5.4 million deaths annually by 2060 [2]. Among risk factors, documented Pseudomonas infection is a new addition. The rationale is a large observational study which documented that *Pseudomonas aeruginosa* colonization independently predicted an increased risk of hospitalization for exacerbation and all-cause mortality [3]. The utility of biomarkers in COPD has a new comment. The guidelines advocate the use of serum C-reactive protein (CRP) and procalcitonin in restricting antibiotic usage during exacerbations [1]. However, the observed sputum color remains highly sensitive and specific for a high bacterial load during such episodes. The SUMMIT trial failed to show the benefit of using CRP, SPD, s RAGE, CC-16, and fibrinogen to predict forced expiratory volume in 1st second (FEV_1) decline, hospitalization, or exacerbation [4]. Continued cautious and realistic interpretation of the role of biomarkers in the management of identified clinical traits is needed.

A caution on the use of e-cigarettes has been mentioned in the new guidelines citing a lack of safety data. Eosinophilic pneumonias, acute lung injury, diffuse alveolar hemorrhage and respiratory bronchiolitis have been linked to their use [5]. The CDC and FDA are investigating this, around 1604 illnesses and 34 deaths have been reported up to October 2019. Certain countries including India have recently banned the use of e-cigarettes citing unproven safety profile.

Diagnosis and treatment plan — the treatment algorithm emphasizes on using the ABCD assessment to determine initial treatment only. The follow-up treatment utilizes the management cycle changes as per dyspnea or exacerbation, similar to 2019 guidelines. The management of persistent dyspnoea with add-on bronchodilators and recurrent exacerbation with add-on inhaled steroids is identical to the GOLD 2019 guidelines [1].

The role of inhaled steroids (ICS) in the GOLD 2020 guidelines has been clarified. The history of ≥ 2 moderate exacerbations or hospitalization(s) attributable to exacerbation, serum

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DOI: 10.5603/ARM.2020.0080
Received: 22.01.2020

ISSN 2451–4934

eosinophilia (> 300 cells/μL) or concomitant asthma are factors that strongly support the use of ICS. The factors unfavorable to ICS use are recurrent pneumonia, history of mycobacterial infection, and eosinophils (<100 cells/μL) [6]. The new guidelines do mention that recent trials using triple therapy, showing a mortality benefit. However, as mortality was not the primary endpoint of any of the studies, hence, the mortality benefit warrants further evaluation [6, 7].

GOLD 2020 guidelines recommend all patients hospitalized for exacerbations should be assessed and investigated for the severe Vitamin D deficiency (< 10 ng/mL or < 25 nM), followed by supplementation if required. The rationale is similar to all chronic diseases; vitamin D levels are lower in COPD than in health. A recent meta-analysis showed that vitamin D supplementation reduced exacerbation rates in patients with low baseline vitamin D levels [8]. However, in unselected patients, the decline is not documented. Theophylline use in COPD has an unchanged recommendation. A trial in 2018, using low dose theophylline found no benefit in reducing exacerbation rates, and hence efficacy for the same remains doubtful [9].

The guidelines draw on the importance of phenotyping COPD patients. Four phase 3 studies evaluated the efficacy of mepolizumab and benralizumab in patients with severe COPD. The inclusion criteria were recurrent exacerbations and peripheral blood evidence of eosinophilic inflammation despite high intensity inhaled therapy. There was a 15–20% reduction in the rate of severe exacerbations, but, it was variable between studies and doses. There was no effect on FEV_1 or quality of life scores and no consistent relationship between the response to treatment and the peripheral blood eosinophil count. A posthoc analysis of the mepolizumab trial showed a more significant benefit against oral corticosteroid treated exacerbations [10, 11]. Thus, raising the possibility of this treatment might gain a role in a highly selected subgroup of patients with eosinophilic COPD and frequent requirement for oral corticosteroids. Further studies are required to investigate this.

Non-medical management — interventional procedures like endobronchial valves recommended according to appropriate indication. The rationale stemmed from the EMPROVE trial reporting a significant benefit in FEV_1, hyperinflation, dyspnoea, and health status [12]. However, the possibility of considerable pneumothorax warrants the need for the procedure performed at expert centers only. The current guidelines document the additional role of pulmonary rehabilitation in the reduction of anxiety and depression.

Acute exacerbation — the classification and management protocol of acute exacerbation episodes is unchanged. The clinical suspicion and investigative workup of the differential diagnosis of an exacerbation are listed in present guidelines. Thus, stress on systemic disease evaluation and comorbidities in diagnosis are explicit.

Clinical impact and future directives — the GOLD 2020 document presents a global resource as an evidence-based review and guide for the diagnosis, management, and prevention of COPD. The importance of COPD is magnified by the increasing global burden of this disease with estimated increased mortality by 2060. The new guidelines recognize the role of ICS as an individualized decision with a detailed evaluation of risks and benefits. The position of triple inhaled therapy, biologics, lung volume reduction, need for biomarkers, and assessment of vitamin D deficiency have been explicitly stated. Even though these differences are subtle, they provide the future directive of research.

Certain limitations include the specification that persistent symptoms are required to make the diagnosis which leaves outpatients with varying day-to-day traits. Additional updates regarding novel pharmacotherapeutic options, asthma-COPD overlap phenotype, recommendations around e-cigarette use, and further guidance for referral for lung transplantation are the need of the future.

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