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CONSENSUS REPORT

The View of the Turkish Thoracic Society on the Report of the GOLD 2017 Global Strategy for the Diagnosis, Management, and Prevention of COPD

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Abstract

Since the Global Initiative for Obstructive Lung Disease (GOLD) published its first guidelines on chronic obstructive pulmonary disease (COPD) in 2001, much has changed till 2017. Previous versions of GOLD guidelines mentioned the forced expiratory volume in one second (FEV_1)-based approach for staging and treatment modalities. Since 2011, a composite multi-dimensional approach has been introduced to cover various aspects of the disease. Unfortunately, this approach was not found to be correlated with mortality as well as the FEV_1-based approach, despite the fact that it was better for estimating exacerbation rates. Although this assessment tool has been considered as a big step in personalized medicine, the system was rather complex to use in daily practice. In 2017, GOLD introduced a major revision in many aspects of the disease. This mainly includes a revised assessment tool and treatment algorithm. This new ABCD algorithm has excluded spirometry for guiding pharmacological therapy. Treatment recommendations are mainly based on symptoms and exacerbation rates. Escalation and de-escalation strategies have been proposed for the first time. The spirometric measurement has only been retained to confirm the diagnosis and lead to nonpharmacological therapies. In this report, the Turkish Thoracic Society COPD assembly aimed to summarize and give an insight to the Turkish interpretation of GOLD 2017.

KEYWORDS: Chronic obstructive pulmonary disease, diagnosis, management, prevention, Global Initiative for Obstructive Lung Disease guidelines

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the leading cause of morbidity and mortality worldwide. It causes a considerable burden on the quality of life, public health, and the health economy [1].

Global Initiative for Obstructive Lung Disease (GOLD) has been established to increase awareness of COPD and form guidelines for its prevention, diagnosis, and treatment. Between 2001 and 2011, the committee released guidelines mainly based on spirometric grading. Since 2011, a multi-dimensional assessment tool was proposed as a step forward in personalized medicine. However, treatment recommendations were not based on high-quality evidence; therefore, since then, the guidelines were named as "strategy documents." The current GOLD document was released on November 16, 2016. It has a major revision in evaluation and treatment recommendations. However, in general, the document has been heavily criticized.

The Turkish Thoracic Society (TTS) COPD assembly published a consensus report on the prevention, diagnosis, and treatment of COPD in 2014. After the publication of the new 2017 GOLD document, the TTS COPD assembly decided to publish a Turkish consensus report with the interpretation, criticism, and adaptation of the GOLD 2017 COPD report in regards with the Turkish Health System in March 2017. This current report comprised an executive summary of the Turkish view of the GOLD 2017 COPD report.

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Definition of COPD

COPD had been defined in 2016 GOLD document as "a common preventable and treatable disease which is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients" [2].

In GOLD 2017, the definition has been revised to "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" [1].

In GOLD 2017, there has been an emphasis on the importance of recognizing chronic respiratory symptoms that can precede the development of airflow obstruction and may be associated with the development of acute respiratory events. A considerable number of smokers can have structural abnormalities of emphysema and airway wall thickening without airflow limitations [1].

A major revision in the definition of COPD is the replacement of the term "inflammation" and putting additional emphasis on "respiratory symptoms." The committee did not provide an explanation for this change. Although COPD is still considered a chronic inflammatory disorder, an effective anti-inflammatory strategy has not yet been discovered. It appears that systemic inflammation only exists in a small percentage of COPD patients and that there is no information about the existence of inflammation in patients having insufficient lung development. This would be a rational explanation behind the removal of word "inflammation" from the definition. However, in general medicine, there is a tendency to define diseases with underlying mechanisms. Therefore, "both inflammation and severe airway abnormalities with emphysema" can be mentioned in the definition.

In the new definition, respiratory symptoms were included for the first time in the GOLD guidelines. In this definition, symptoms with airflow limitation are considered mandatory. However, in the chapters on "diagnosis and assessment," the same document mentions airflow limitation with or without symptoms for making a diagnosis. There are people with risk factors and airflow limitation but no symptoms and there are people with symptoms but no airflow limitation. Although the definition requires both symptoms and airflow limitation, making a diagnosis requires airflow limitation on the background of either symptoms or risk factors. This discrepancy should be justified by the GOLD committee. The reason of why symptoms were included in the definition would be a justification for symptom-based treatment strategy, which will be discussed later.

A symptom-based definition and assessment can result in several limitations. Symptoms can be perceived and expressed differently in different populations depending on sex, ethnicity, and the social, cultural, and economic status. Patients can underestimate their symptoms and exacerbations. In contrast, in some groups such as women, patients having a low socioeconomic status, minority groups, and immigrants, the symptoms may be overexpressed. Approximately 25% of COPD patients are asymptomatic, and around 50% of smokers have symptoms without having airflow limitations. Hence, symptoms may be related to comorbid conditions [3-6]. For example, in a patient with a forced expiratory volume in one second (FEV_1) of <30%, severe dyspnea is expected. However, patients may slow-down their walking pace and therefore they may deny that they have dyspnea. In contrast, in a patient with a preserved FEV_1, disproportionate symptoms may occur due to comorbid conditions.

Burden of COPD

Based on epidemiological studies, the estimated number of COPD patients was 384 million in 2010, with a global prevalence of 11.7%. Globally, there are 3 million deaths due to COPD annually, and by 2030, this number is expected to increase to 4.5 million. COPD-related mortality is mainly driven by smoking, reduced mortality from other common causes of death, aging of the world's population, and the scarcity of effective disease-modifying therapies [1].

The Global Burden of Disease study revealed that COPD is the fifth leading cause of disability-adjusted life years lost in 2013 [7].

Factors Influencing Disease Development and Progression

Cigarette smoking is the most well-studied risk factor; however, nonsmokers can also develop COPD. Epidemiological studies have shown that never-smokers had milder disease, fewer symptoms and lower systemic inflammation. They did not have increased risk of lung cancer or cardiovascular disease [8]. There are no data that monitor the entire course of the disease including the pre- and perinatal periods. The perinatal period may be very important in developing COPD.

Cigarette smoking is the leading risk factor for COPD. However, fewer than 50% of smokers develop COPD [9]. The socioeconomic status may be linked to a child's birth weight. Although controversial, some studies have suggested that women are susceptible to tobacco smoke [10-12].

Any factor that affects lung growth during gestation and childhood, which is termed "childhood disadvantage factors," has the potential for increasing the risk of COPD. A recent study showed that 50% of patients developed COPD due to abnormal lung growth with a normal decline in the FEV_1 [13].

Occupational exposure to organic and inorganic dusts and fumes are underestimated risk factors for COPD. The proportion of COPD cases attributable to workplace exposure is 19.2%. The risk from occupational exposure in less regulated areas is likely to be much higher than reported [1].

Worldwide, 3 billion people use biomass and coal as their main source of energy. Indoor air pollution is a very important risk factor for COPD. The role of outdoor air pollution as a risk factor for COPD is unclear; however, this has an impact on impaired lung growth [14,15].

A lower socioeconomic status is associated with an increased risk of developing COPD. Asthma, bronchial hyper-reactivity, chronic bronchitis, HIV, and tuberculosis increase the risk of developing COPD [1].

GOLD 2017 has gathered epidemiological findings from mostly developed countries. However, over 90% of COPD patients live in low- and middle-income countries [16]. The Burden of Obstructive Lung Disease study revealed that airway obstruction was correlated with smoking rate but not mortality. However, restrictive spirometric impairment, as a consequence of poverty and poor lung development, was well correlated with mortality. This restrictive impairment was more common in low–middle-income countries. One of the best predictors of mortality in COPD is the gross national income (GNI) per capita [17]. The mortality rate increases particularly in countries that have a GNI per capita of below US$ 20000 [18]. People in the low socioeconomic status have 14-times more respiratory system disorders [17]. The social determinants of health (income, housing, lifestyle and working conditions, and access to qualified education and health services) are the best predictors of the risk of COPD [19]. It appears that the GOLD 2017 report did not evaluate the social determinants of health and thoroughly assessed the underlying mechanisms of childhood disadvantage factors, indoor and outdoor air pollution.

Pathogenesis and Pathophysiology

The inhalation of cigarette smoke and other noxious particles such as biomass smoke cause lung inflammation. In response to chronic inflammation, repeated injury and repair cause pathological changes in the airways, lung parenchyma, and pulmonary vasculature. Although some patients develop COPD without smoking, the nature of the inflammatory response is still unknown. Lung inflammation persists after smoking cessation. The GOLD 2017 report has mentioned that peribronchiolar and interstitial fibrosis may occur in COPD patients, which may contribute to small airway limitation [1].

Diagnosis and Assessment

Diagnosis

GOLD 2017 reports that COPD should be considered in any patient who has dyspnea, chronic cough, or sputum production and/or a history of exposure to risk factors. Spirometry is required for making a diagnosis. Comorbidities should be actively sought and appropriately treated.

In the previous version of GOLD, symptoms with risk factors were considered as main factors for suspecting the diagnosis of COPD. However in GOLD 2017 report, symptoms or risk factors are sufficient to make a diagnosis. This approach has advantages and disadvantages. As discussed in the "Definition" chapter, the expression of symptoms can depend on several factors. In addition, symptoms can occur due to other comorbid conditions or asthma. Therefore, in the absence of predisposing risk factors, clinicians should be careful in the interpretation of symptoms. In contrast, some patients who have risk factors but no symptoms may be found out with the spirometry screening. These patients should be followed up carefully to check whether they will develop symptoms and require treatment along with the natural course of the disease. They should be encouraged to stop smoking and avoid other risk factors and be physically active. Public spirometric screening cannot be recommended until a precise advantage of screening is shown [1,20]. Additionally, it is well known that some patients can have symptoms without airflow limitation; they were referred to as GOLD 0 in the past. Later on, GOLD 0 was removed from GOLD staging based on evidence that such patients did not necessarily develop airflow limitation. However, chronic bronchitis symptoms may precede the development of airflow obstruction [21].

Spirometry is the most reproducible and objective measurement of airflow limitation. Good-quality spirometry is possible in health care settings, and all healthcare workers who care for COPD patients should have access to spirometry. A post-bronchodilator $FEV_1/FVC<70\%$ is required for making a diagnosis of COPD. It is simple and independent of reference values and has been used in numerous clinical trials. This criterion may lead an over- and underestimation of airflow obstruction depending on age compared with the lower limit of normal (LLN) values [22,23]. In concordance with GOLD, the TTS has encouraged clinicians to perform spirometry. All doctors should be able to assess the spirometry results for diagnosing COPD. Spirometry should be performed according to standardized criteria [24,25]. Recently, normal spirometry has been defined using a new approach from the Global Lung Initiative (GLI) using GLI equations. The GLI requires a single parameter called z-score. A z-score below -1.64 denotes an LLN at the fifth percentile of normal distribution [26,27]. GLI criteria need more supportive data before any recommendation can be made.

Assessment

Since 2011, GOLD has recommended a multi-dimensional approach for evaluating patients. It comprises three components: spirometry, symptom level, and number and severity of exacerbations. The high risked patients were decided on by either FEV_1 or the number of exacerbations. This approach was considered rather complex by busy clinicians.

In the new assessment tool, FEV_1 is not a part of the staging evaluation, although this is not underestimated for the diagnosis and evaluation for the nonpharmacological approach. Although St George's Respiratory Questionnaire score 25 is well correlated with COPD Assessment Test 10 and modified Medical Research Council (mMRC) 1, the recommended cut-off point of the mMRC is still 2. In the definition of exacerbation, exacerbation that requires emergency department admission is considered as a severe exacerbation. Pharmacological therapy is tailored by ABCD assessment tool (Figure 1).

The new assessment system to lead pharmacological therapy is quite simple and comprises two modifiable components of the disease: symptoms and the number of exacerbations in the previous year. FEV_1 is not a component of this assessment. [1]. However, spirometry is already underused in practice. In addition, making a differential diagnosis still requires spirometry, and it is still beneficial during follow-up. Therefore, we recommend spirometry in each follow-up visit to monitor disease activity and for making a differential diagnosis when needed. The definition of exacerbation that requires health care utilities is not an optimal approach for the evaluation of exacerbation severity. In Turkey, sometimes, emergency room (ER) admissions and even hospitalizations can occur with a wide range of indications. Sometimes, patients may be admitted to the ER to be treated with only short-acting agents.

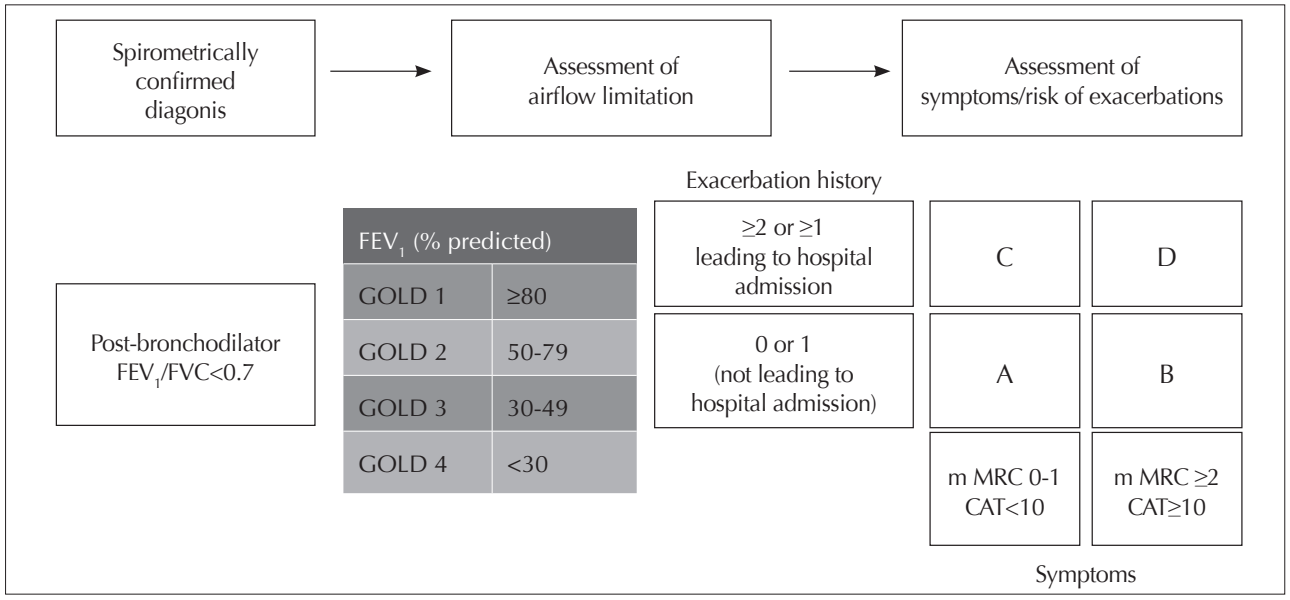

Figure 1. The new ABCD assessment tool for staging COPD [1]

Therefore, symptom severity and physical findings should be taken into consideration for the evaluation of exacerbation severity, and ER admission itself can be considered in the moderate exacerbation.

Evidence supporting prevention and maintenance therapy

Smoking cessation has the greatest capacity to influence the natural history of COPD [1]. Every clinician should assess the smoking status and refer smokers to smoking cessation clinics. E-cigarettes are being increasingly used as a form of nicotine replacement therapy. Their efficacy is controversial, and the overall safety profile has not been defined. Vaccination is recommended for both influenza and pneumococcal disease [1]. Influenza vaccinations are recommended to all COPD patients, and pneumococcal vaccinations are recommended to patients over 65 years [1]. An adult vaccination schedule has just been published in Turkey. Accordingly, there is no age restriction regarding to pneumococcal vaccination in COPD patients in Turkey [28].

After disease establishment, prevention strategies would not be a certain solution. Besides smoking, dusts and noxious particles from workplace exposure, biomass smoke fumes, and outdoor pollution should be avoided in population settings. Public policies, local and national resources, cultural changes, effective ventilation, and nonpolluting cooking stoves are feasible measures worldwide [1]. Healthy intrauterine growth, easy access to health care facilities, and healthy housing and workplace are the most powerful prevention tools for COPD [29-32]. GOLD 2017 did not emphasize on the social determinants of health for primary prevention. The GOLD 2017 report may have prioritized pharmacological treatment strategies rather than disease prevention, which is actually considered to be the main treatment strategy.

Pharmacological therapy for stable COPD

Pharmacological therapy is used to reduce symptoms, improve the health status, and reduce the frequency and severity of exacerbations. There is no conclusive evidence to show that pharmacological therapy modifies the long-term decline in lung function. The report mentions that each treatment regimen needs to be individualized for symptoms, airflow limitation, and severity of exacerbations [1].

In the new document, pharmacological therapies have been placed according to the new ABCD assessment tool. For the first time in history of GOLD, the committee recommended preferential therapy and escalation and de-escalation management (Figure 2) [1]. In each visit, patients should be questioned about risk factors, healthy life style, physical activity, and vaccination. Inhaler techniques should be checked particularly using the teach-back method. Adverse drug events, comorbidities, and the exacerbation of history should be checked (1). The committee has declared that escalation therapy has not been systematically tested and that trials of de-escalation are limited [1]. Evidence for therapeutic recommendations for patients in groups C and D are not strong enough for frequent exacerbations; therefore, recommendations will be re-evaluated as additional data become available [1].

Group A: GOLD 2017 recommends either short- or long-acting bronchodilators according to the persistence of symptoms. A change in different groups is possible. Treatment should be continued if the benefit is persistence [1].

Group B: GOLD 2017 recommends either long-acting beta-2 agonists (LABA) or long-acting antimuscarinics (LAMA) for initial therapy. For patients with persistent symptoms, a combination (dual bronchodilation) is recommended. For severely symptomatic patients, an initial combination is recommended [1].

Group C: Initial therapy should consist of LAMA. Patients with further exacerbations a LABA could be added to LAMA (GOLD recommendation) or therapy could be switched to inhaled corticosteroids (ICS)+LABA. ICS+LABA is not the first choice due to the risk of excessive pneumonia [1].

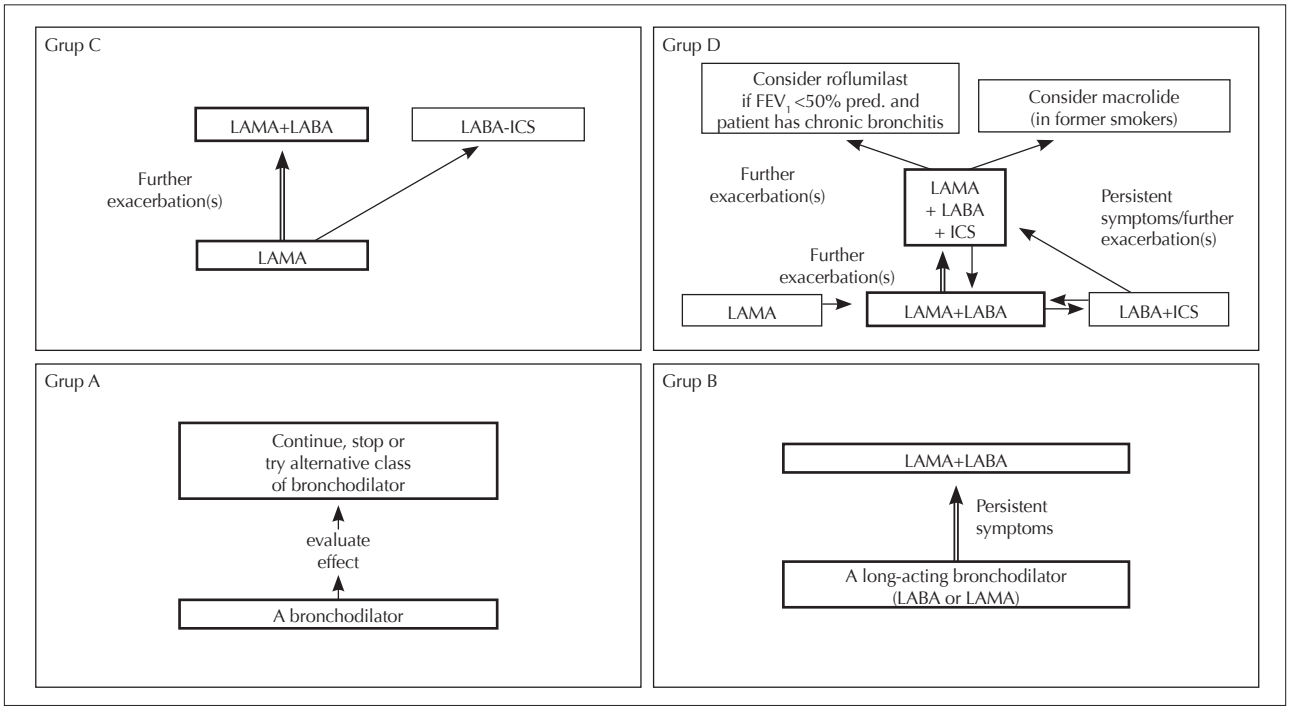

Figure 2. In patients with a major discrepancy between the perceived level of symptoms and severity of airflow limitation, further evaluation is warrented [1]
Preferred treatment: ⟹

Group D: Initial therapy should consist of LABA+LAMA. If patients continue to have exacerbations, escalation to LAMA+LABA+ICS can be offered (studies are underway). Switching to ICS+LABA can be done, although there is no evidence that switching results in better exacerbation prevention. A combination of LABA+ICS is recommended for asthma–COPD overlap patients as the first choice. If a monobronchodilator is chosen by clinicians, LAMA should be preferred. Patients with persistent symptoms with triple therapy (LAMA+LABA+ICS), roflumilast or macrolide could be added. Step-down is possible from LABA+LAMA+ICS to LABA+LAMA if there is no exacerbation [1].

The GOLD 2017 treatment recommendation has several limitations, particularly in groups C and D. There is no study that is fully designed prospectively on the definition of groups C or D. Most studies on exacerbation had recruited patients with one or more exacerbations. Only 19% of the population had two or more exacerbations in the FLAME study. In patients with severe exacerbations, both treatment arms (LABA+LAMA vs ICS+LABA) provided comparable results. Most exacerbations during the follow-up were mild in the FLAME study [33]. Considering these findings, the evidence on patients with two or more exacerbations were not strong enough to refer certain treatment strategy. On the other hand ICS are overused in Turkey [34]. Therefore, the TTS recommends starting pharmacological therapy with one bronchodilator (LABA or LAMA), and during follow-up, if the symptoms are persistent, the other group bronchodilator can be added. If the patient still has exacerbations (two moderate or one severe exacerbation), ICS can be added. This approach requires the close follow-up of patients. Withdrawal from ICS may be recommended when the patient is an infrequent exacerbator [1].

In the GOLD 2017 document, the blood eosinophil count has been discussed as a predictor of response to using ICS [1]. However, a prospective analysis is needed to raise clear conclusions and has not yet been considered for tailoring treatment.

Nonpharmacological therapy in COPD

A detailed chapter regarding nonpharmacological therapy such as rehabilitation, self-management, and behavioral changes in the management of COPD was mentioned in the GOLD 2017 report.

Pulmonary Rehabilitation

GOLD 2017 declares that pulmonary rehabilitation (PR) is the most effective therapeutic strategy for reducing symptoms and improving the health status and exercise intolerance [1]. It is appropriate for all COPD patients who are symptomatic. It can reduce readmission and mortality rates if it commenced early after hospital discharge. It is also one of the most cost-effective strategies [1]. Accessing and/or completing PR programs in Turkey are limited. The major barrier is the lack of awareness of its benefit. Limitations to access program, lack of finance, and transportation are the other barriers [1]. In Turkey, there are 35 rehabilitation centers. Home-based programs and having family practitioners incorporated into the program would be a solution for transportation problems and problems related to treatment adherence.

Physical Activity

Physical inactivity is related to poor outcomes in COPD. It should be encouraged. However, information is lacking on required details for its optimization in standard care [1].

Education, Self-Management, and Integrative Care

Didactic sessions are insufficient for promoting self-management skills. Education is considered to be the first step for changing the behavior. Topics such as smoking cessation, correct use of inhalers, early recognition of exacerbation, decision-making and taking actions, and when to seek help and surgical interventions will be better dealt with using self-management interventions [1].

Self-management interventions improve the health status, but not overall mortality, in COPD patients. However, the issue possesses many unstandardized aspects. Heterogeneity among interventions, patient populations, follow-up times, and outcome measures make generalization difficult in real life [1]. In a limited experience of a Turkish institute without a case manager, self-management is considered to be ineffective in preventing exacerbation but is considered to improve treatment adherence (s study is in progress).

For the first time, GOLD 2017 has introduced a structured nonpharmacological approach in each category of ABCD staging. Dealing with risk factors, increasing physical activity and ensuring adequate sleep and a healthy diet are recommended for all COPD patients, and managing strategies for breathlessness and stress management are recommended for group B and D patients [1].

Although there has been a major interest to implement behavior-targeted interventions to improve physical activity, there is still no information on optimal quality assurance methods [1]. There is a continuous fear among patients to be physically active. However, every patient should be encouraged to be physically active. Patients should be encouraged to undergo a comprehensive rehabilitation program, and a maintenance home-based exercise program should be recommended after the completion of the rehabilitation program. Endurance, strength training, upper extremity exercise, and inspiratory muscle training (when needed) are the components of exercise training [1]. Motivational interventions that aiming to meet patient expectations, for gaining self-management skills, and end-of-life issues are the components of behavioral interventions [1]. Patient education alone does not change the behavior or motivate patients and has no impact on improving exercise performance or lung function; however, it can play a role for improving skills and being able to cope with illness and the health status [1].

Supportive, Palliative, End-of-Life Care

Palliative care is a term used for controlling symptoms as well as managing terminal patients close to death [1]. Nutritional support, palliative treatment for dyspnea, treatment for anxiety and depression, and end-of-life care and hospice services are needed in certain conditions. Turkey has a lack of structured supportive and end-of-life care services, hospice services, and related regularities. In Turkey, doctors managing COPD are neglected to give information to patients about their future risks. In particular, information on prognosis is not often discussed. Therefore, a majority of patients in Turkey are not aware of and provided the end-of-life care in practically.

Although malnutrition is a common problem and a prognostic factor, nutritional supplementation and dietary consultation are often neglected in COPD patients in Turkey. Doctors should be encouraged to support patients in this regard.

Oxygen Therapy and Ventilatory Support

Long-term oxygen therapy has been shown to increase the survival rate in patients with severe resting hypoxemia but not in those with moderate resting or exercise-induced hypoxemia [1]. Moderate-to-severe hypoxemic patients at sea level may be supplemented with 3 l/min of supplementary oxygen to provide 50 mmHg PaO_2 during air travel [1]. Noninvasive positive pressure ventilation (NPPV) is the standard care during acute respiratory failure; however, its benefit when used in chronic patients remains undetermined [1]. Poor adherence to NPPV is a major issue to solve. In COPD and obstructive sleep apnea patients, NPPV has a clear benefit in terms of both survival rates and risk of hospital admission [1].

Interventional Therapy

Lung volume reduction surgery (LVRS) increases elastic recoil, improves expiratory flow rates, and reduces exacerbations. It improves survival in patients with low post-rehabilitation exercise capacity. It has been shown to result in a higher mortality rate in patients with a FEV_1 of ≤20% and DLCO of ≤20% [1]. Bullectomy is required if the bullae cause compression and complications and if there is relatively preserved lung tissue. Hypercapnia, severe emphysema, and pulmonary hypertension are not absolute contraindications [1]. In appropriately selected patients, lung transplantation has been shown to improve the health status and functional capacity but not prolong survival. The median survival rate has increased to 5.5 years [1].

Bronchoscopic interventions

Endobronchial valve replacement and nitinol coil implantation are the main bronchoscopic interventions in emphysema treatment. In selected cases, treatment improves the 6-min walk distance, lung function, and health status. Major complications of coil therapy include pneumonia, pneumothorax, hemoptysis, and COPD exacerbations [1]. Endobronchial one-way valves may be considered if interlobar collateral ventilation is absent in computed tomography scans [1].

Patients with heterogeneous upper lobe predominant emphysema can be candidates for either LVRS or bronchoscopic volume reduction. However, homogenous emphysema patients are not routinely considered candidates for undergoing LVRS, but bronchoscopic therapy may be considered [1].

Endobronchial therapy has become popular in Turkey. However, treatment is very expensive and is not lack of complications; therefore, appropriate patient selection and close follow-up are required to see the long-term results.

Management of COPD exacerbations

In previous guidelines, COPD exacerbation was defined as "the worsening of respiratory symptoms that is beyond the normal day to day variation and leads to change in medication." However, in the new version, it has been defined as "acute worsening of respiratory symptoms that needs addi-

tional therapies." Exacerbations were classified as mild [treated with short-acting bronchodilators (SABDs) only], moderate (SABDs+antibiotics and or oral corticosteroids), or severe (patients require hospitalization or visits to the ER). A considerable amount of exacerbations are not reported to health care professionals and could be significantly important [1].

The GOLD 2017 definition of COPD exacerbation can lead to different limitations. Although the definition is adopted in clinical trials, in real life, it could lead to standardization problems according to the attending doctor or hospital policy. For example, in Turkey, ER admissions can take place for patients with less symptoms and could result in only SABD administration. ER admission can be considered moderate exacerbation in Turkey if it is not resulted in hospitalization.

GOLD 2017 also underlined the importance of the differential diagnosis of respiratory symptoms, respiratory virus-triggered exacerbations, and eosinophilia during exacerbations [1]. The strongest predictor of a patient's future exacerbation frequency is the number of exacerbations they had in the prior year. COPD patients showed a moderately stable phenotype, but a significant proportion has changed with the worsening of FEV_1 [1].

Corticosteroid administration is recommended to be via the oral route and with a dose of 40 mg daily for 5 days. The more expensive nebulized budesonide may be an alternative to oral corticosteroids in some patients [1]. Antibiotics are recommended according to Anthonisen criteria and patients on invasive or noninvasive ventilation. The optimal duration is 5–7 days. On the basis of the COPD Audit study, the GOLD 2017 report has underlined the importance of oxygen therapy, has described the detail of ventilator support, and has defined the criteria of hospital discharge and the care-bundle [1]. Early follow-up (within one month) following discharge should be performed when possible and is associated with less exacerbation-related readmissions [1].

Comorbidities of COPD

Comorbidities have a significant impact in over course of COPD. In general, comorbidities should be actively sought out and treated according their guidelines. The presence of comorbidities should not alter COPD treatment. Lung cancer and cardiovascular diseases are important prognostic comorbidities. Osteoporosis, anxiety and depression, and gastroesophageal reflux are commonly underdiagnosed and are associated with a poor health status and prognosis. Comorbidities may occur in any grade of COPD and influence mortality and hospitalization rates [1,35]. In an investigation in Turkey, Charlson's Comorbidity index has been found to be related with the long-term mortality of COPD patients [36]. Another study has shown that comorbidities are related to hospital readmission [37].

GOLD 2017 has taken a comprehensive section for comorbidities. The aging population is under the risk of multimorbidity mainly composed of obesity, cardiovascular disorders, metabolic syndrome, airway disease, and sleep disorders. When COPD is a part of it, it may be overlooked or underdiagnosed under the mask of restrictive conditions. Such patients are becoming a major burden in daily practice in Turkey, which might be the case in other countries.

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