REVIEW

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Summary of the Chronic Obstructive Pulmonary Disease Clinical Practice Guideline Revised in 2014 by the Korean Academy of Tuberculosis and Respiratory Disease

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Chronic obstructive pulmonary disease (COPD) results in high morbidity and mortality among patients both domestically and globally. The Korean clinical practice guideline for COPD was revised in 2014. It was drafted by the members of the Korean Academy of Tuberculosis and Respiratory Diseases, as well as participating members of the Health Insurance Review and Assessment Service, Korean Physicians' Association, and Korea Respiration Trouble Association. This revised guideline covers a wide range of topics, including the epidemiology, diagnosis, assessment, monitoring, management, exacerbation, and comorbidities of COPD in Korea. We drafted a guideline on COPD management by performing systematic reviews on the topic of management with the help of a meta-analysis expert. We expect this guideline will be helpful medical doctors treating patients with respiratory conditions, other health care professionals, and government personnel in South Korea.

Keywords: Pulmonary Disease, Chronic Obstructive; Guideline; Diagnosis; Treatment

Introduction

According to a survey conducted by the Korean Academy of Tuberculosis and Respiratory Diseases in 2008, people over the age of 40 years have a high chronic obstructive pulmonary disease (COPD) prevalence rate of 13%[1]. According to the National Statistical Office, COPD is one of the 10 major causes of death in South Korea[2]. The World Health Organization (WHO) expects that the prevalence and mortality rates of COPD will increase worldwide[3]. The WHO also emphasizes the importance of prevention, early diagnosis, and proper treatment of COPD by selecting it as one of the five non-infectious diseases that must be managed worldwide. In 2012, the Korean Academy of Tuberculosis and Respiratory Diseases published the COPD clinical practice guideline (in Korean), which could be used in clinical practice. In 2014, the revised version of the COPD guideline (in Korean) was published on the basis of the

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findings of new studies published over the previous 2 years[4]. This revision has been made not only by the Korean Academy of Tuberculosis and Respiratory Diseases but also by the Health Insurance Review and Assessment Service, Korean Physicians' Association, and Korea Respiration Trouble Association. Therefore, the revised clinical practice guideline is more advanced than the original one. We expect this guideline would be helpful not only to medical doctors treating patients with respiratory conditions but also to other health care professionals and government personnel in South Korea.

Definition, Epidemiology, Cause, and Mechanism

COPD can be defined as follows.

"It is a pulmonary disease with irreversible air inflow limitation and is induced by damage to the airway and lung parenchyma due to chronic inflammation." The most important cause of chronic inflammation is smoking, but it can also be induced by occupational exposure, indoor air contamination, and infection. As it is a very common disease, it has a severe socioeconomic influence. It generally progresses, but prevention and treatment are possible. Acute exacerbation occurs frequently and comorbid diseases are comparatively more common in the general population, influencing the severity and prognosis of COPD.

COPD is a leading cause of morbidity and mortality worldwide[3,5]. The prevalence of COPD has increased over the decades. This phenomenon is due to consistent exposure to COPD risk factors and global population aging, and it is anticipated to continue into the future. A study by the WHO estimated that in 2007, the global number of patients with COPD was 210 million[6]. As for the COPD prevalence in Korea, 13.4% of the population over 40 years of age has COPD based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (forced expiratory volume in 1 second/forced vital capacity [FEV_1/FVC] <0.7), with 19.4% of the male population and 7.9% of the female population having COPD based on the 2008 Korean National Health and Nutrition Examination Survey[7]. However, among 353 patients diagnosed with COPD, only nine (2.4%) were diagnosed with COPD by a doctor, and only eight (2.1%) received treatment. This suggests that most Korean patients with COPD are not diagnosed and treated. COPD is an important cause of mortality in most countries. According to the Global Burden of Disease Study conducted in 1990, COPD ranked sixth among the global causes of death, but it is anticipated to rank third in 2020 and fourth in 2030[8]. According to Statistics Korea, the total number of deaths from COPD, based on disease code, was 3,329 in the year 2000 (2,120 among men and 1,209 among women), and 5,002 in the year 2010 (3,526 among men and 1,476 among women). In 2010, chronic lower airway disease ranked seventh among the overall causes of death, accounting for a total of 7,092 deaths (4,473 among men and 2,619 among women)[8]. In an aging population, the risk of death from COPD has been increasing, and it ranks fifth among the overall causes of death in the age group of 80 years or older, with a mortality rate of 3,732 per 100 thousand.

Additionally, COPD results in a huge socioeconomic burden. In Korea, based on the 2010 data of the Health Insurance Review and Assessment Service, about 284 billion Korean won is spent on the medical treatment of COPD[1]. According to the 2009 data of the Health Insurance Review and Assessment Service, the medical fee per individual is as high as 3.23 million won, and it has been increasing rapidly in recent years. Moreover, in 1990, COPD ranked 12th among the cause of disability-adjusted life years (DALYs) loss in the world, but it is anticipated to rank seventh in 2030[3]. In Korea, DALYs from COPD have rapidly increased from 270 years per 100 thousand in 2002 (ranking 10th) to 550 years per 100 thousand in 2007 (ranking seventh)[9].

The most important and well-known risk factor for COPD is smoking. Other risk factors include occupational dust, chemical materials, air pollution, low socioeconomic status, chronic bronchitis, and respiratory infection. Host factors related to COPD include genetics, age, sex, lung growth, and airway hypersensitivity[10,11]. Smoke and harmful substances induce lung inflammation, and lung parenchyma damage from such inflammation and disruption of the normal repair system can induce emphysema and small airway fibrosis[12]. Such pathologic alteration induces air trapping and airflow limitation.

Diagnosis and Assessment

A person over the age of 40 years exposed to cigarette smoke or other risk factors and showing symptoms of dyspnea, cough, and sputum production should be suspected of having COPD[13].

To diagnose COPD, a patient should undergo spirometry

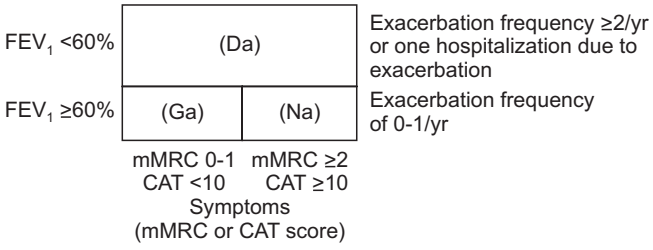

Figure 1. Classification of patients with chronic obstructive pulmonary disease (COPD). FEV_1: forced expiratory volume in 1 second; mMRC: modified Medical Research Council dyspnea score; CAT: COPD assessment test score. Adapted with permission from the Korean Academy of Tuberculosis and Respiratory Diseases[4].

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that determines the FEV_1, FVC, and the ratio of FEV_1/FVC. FEV_1/FVC <0.7 confirms an airflow limitation, which is an objective diagnostic evidence of COPD. More importantly, spirometry should be performed after short-acting bronchodilator inhalation to confirm the airflow limitation in COPD.

For COPD treatment, spirometry, symptom grade, and exacerbation history should be assessed (Figure 1). First, the severity of COPD on spirometry should be classified into two categories: FEV_1 ≥60% versus FEV_1 <60%. Second, the symptom grade should also be classified into two categories: the modified Medical Research Council dyspnea scores (mMRC) 0–1 versus mMRC ≥2, or the score of the COPD assessment test score (CAT) <10 versus CAT ≥10. Third, the exacerbation frequency should be classified as follows: 0–1/yr versus ≥2/yr. According to this assessment, patients with COPD are classified into three groups: Ga, Na, and Da (Figure 1). When patients with COPD show other accompanying diseases, such as cardiovascular disorders, osteoporosis, depression, or lung cancer, their prognosis is poor. Therefore, the comorbid diseases accompanying COPD should be evaluated.

Patients with asthma-COPD overlap syndrome exhibit features of both asthma and COPD. Experts suggest that treatment for both asthma and COPD should be administered to such patients.

An mMRC dyspnea grade of 2 refers to the situation where a patient walks slower on ground level than a similarly aged person because of shortness of breath, or when a patient stops for breathing when walking at his or her own pace on ground level.

FEV_1 of 50% predicted value, the cut-off threshold in the GOLD documents, is an arbitrary one. For the treatment of stable COPD patients, one of the important medications is an inhaled corticosteroid (ICS). ICS has been proven to be effective in COPD patients with FEV_1 less than around 60% of predicted value. So, we decided the cut-off FEV_1 value of 60%.

We have defined the Da group which is an analogy of the combination, both GOLD group C and D. As for the GOLD group C, the proportion of it is very small in a clinical practice setting and the recommended medications are similar to those of the GOLD group D. So, we decided the combined group, Da.

Management of Stable COPD

The goals of management of stable COPD are to reduce both current symptoms and future risks with minimal side effects from treatment. Ongoing monitoring should ensure that the treatment goals are being met, and it should include continuous evaluation of exposure to risk factors and monitoring of disease progression, the effect of treatment and possible adverse effects, exacerbation history, and comorbidities. Identification and reduction of exposure to risk factors are important in the treatment and prevention of COPD.

1. Pharmacologic management

Appropriate pharmacologic therapy can reduce symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance. To date, none of the existing medications for COPD has been shown to modify disease progression or reduce mortality[14-16].

Table 1. Available inhaled bronchodilators in Korea (2014)

	Formulation	Dose (μg/dose)	Dosage	Action duration (hr)
SABA				
Salbutamol	MDI	100–200	1–2 puffs/dosage	4–6
Evohaler			Maximum 8 puffs/day	
Salbutamol nebulizer	Nebulizer	2.5 mg/2.5 mL 2.5 mL/ampule	20–60 mL/day	4–6
LABA				
Indacaterol	Capsule	150, 300	1 capsule/day	24
SAMA				
Ipratropium	Nebulizer	250 μg/mL/1 mL/A 500 μg/mL/A		6–8
LAMA				
Handihaler	Capsule	18	1 capsule/day	24
Respimat	SMI	2.5	2 puffs/day	24

Adapted with permission from the Korean Academy of Tuberculosis and Respiratory Diseases[4].
SABA: short-acting β2-agonist; MDI: metered-dose inhaler; LABA: long-acting β2-agonist; SAMA: short-acting muscarinic agent; LAMA: long-acting muscarinic agent; SMI: soft mist inhaler.

1) Bronchodilators

Bronchodilators are the cornerstone of pharmacological treatment in COPD (Table 1). Inhalation therapy is preferred over oral, subcutaneous, or intravenous administration, because inhalation therapy can maximize the bronchodilator's effect on the airway with least systemic side effects. When treatment is administered via inhalation, attention is essential to ensure effective drug delivery and training in inhaler technique. A metered-dose inhaler, dry powder inhaler, soft mist inhaler, or nebulizer can be used for inhalation therapy, according to the patient's clinical situation.

(1) β2-agonists: Short-acting β2-agonists (SABAs) are recommended as needed for the relief of dyspnea and exercise limitation[17]. Many trials have proven the clinical benefits of long-acting β2-agonists (LABAs) in COPD, including the improvement of health status, FEV_1, FVC, and exercise capacity. Therefore, regular treatment with LABAs is more highly recommended than irregular usage of SABAs on an as-needed basis to address the airflow limitation in COPD. Indacaterol is a once daily β2-agonist with a duration of action of 24 hours. This bronchodilator's effect is significantly greater than that of formoterol and salmeterol, and similar to that of tiotropium. Indacaterol has significant effects on breathlessness and health status[18,19].

(2) Anticholinergic agents: Long-acting muscarinic agents (LAMAs) provide clinically significant improvements in lung function, reduce acute exacerbation, and improve health status and the effects of pulmonary rehabilitation in patients with COPD[20,21]. A large, long-term clinical trial on patients with COPD showed no effect of tiotropium added to other standard therapies on the rate of lung function decline and no evidence of cardiovascular risk[22]. In another large trial, tiotropium was found to be superior to salmeterol in reducing exacerbations, even though the difference was negligible[23,24]. The long-acting anticholinergics aclidinium[25-29] and glycopyrronium[30-32] seem to have a similar action as tiotropium on lung function and breathlessness; however, far less data are available for other outcomes.

(3) Methylxanthines: Methylxanthines may act as nonselective phosphodiesterase inhibitors, but they have also been reported to have a range of nonbronchodilator actions, whose significance has been disputed. Theophylline is the most commonly used methylxanthine. Theophylline is less effective and less well tolerated than are inhaled long-acting bronchodilators, and it is not recommended if the latter drugs are available and affordable. The addition of theophylline to salmeterol produced a greater improvement in FEV_1 and breathlessness than did salmeterol alone[33]. Low-dose theophylline reduces exacerbations but does not improve postbronchodilator lung function.

(4) Combination bronchodilator therapy: Combining bronchodilators with different mechanisms and durations of action may increase the degree of bronchodilation with equivalent or lesser side effects. The combination of a β2-agonist, an anticholinergic, and/or theophylline may produce additional improvements in lung function and health status. Combinations of a LABA and a long-acting anticholinergic have shown a significant improvement in dyspnea and health status, as well as an increase in lung function compared with that shown by monotherapy; however, the prevention of exacerbation of COPD is still limited[34,35].

2) Corticosteroids

(1) Inhaled corticosteroids: Regular treatment with ICSs improves symptoms, lung function, and quality of life, and reduces the frequency of exacerbations in patients with COPD having an FEV_1 <60% predicted[36,37]. Withdrawal from treatment with ICSs may lead to exacerbations in some patients. However, regular treatment with ICSs does not modify the long-term decline of FEV_1 or mortality in patients with COPD[14,16,38,39].

(2) Combination of ICSs and long-acting bronchodilators: An ICS combined with a LABA is more effective than the individual components in improving lung function and health status and reducing exacerbations in patients with moderate to very severe COPD[36,37]. However, a large, prospective clinical trial failed to demonstrate a statistically significant effect of combination therapy on mortality[38]. Moreover, combination therapy is associated with an increased risk of pneumonia. The addition of a LABA/ICS combination to tiotropium improves lung function and quality of life, and may further reduce exacerbations. Nevertheless, more studies on triple therapy are needed[40].

3) Phosphodiesterase-4 inhibitors

Roflumilast is recommended for patients with COPD with severe airflow limitation (postbronchodilator FEV_1/FVC, 0.7; FEV_1 <50%), symptoms of chronic bronchitis, and a history of exacerbations, in whom the disease is not adequately controlled by long-acting bronchodilators[41-48]. The most frequent adverse effects are nausea, reduced appetite, weight loss, abdominal pain, diarrhea, sleep disturbances, and headache[41-45].

4) Other pharmacologic treatments

(1) Vaccination: Influenza vaccination and pneumococcal vaccination are recommended for patients with COPD.

(2) Antibiotics: Although studies have shown some effects of antibiotics on exacerbation rate[49-52], the role of this treatment is unclear. Prophylactic antibiotic treatment is not recommended because of an unfavorable balance between the benefits and side effects.

2. Pharmacologic treatment algorithms based on the Korean COPD classification (Figure 2)

1) Group Ga patients

SABA is recommended as a first-line therapy since SABA can improve lung function and decrease dyspnea. If dyspnea (mMRC ≥2) or acute exacerbation develops despite medical treatment, LABA or LAMA can be tried. However, not enough trials have been conducted on group Ga COPD.

2) Group Na patients

LABA or LAMA is recommended as a first-line therapy. Randomized controlled trials comparing ultra LABA and LAMA have shown no significant difference in the outcomes such as pulmonary function, symptomatic improvement, and health status. The choice of long-acting bronchodilators should depend on the patient's perception of symptom relief, side effects, and clinician's discretion. For patients with severe breathlessness, the alternative is a combination of long-acting bronchodilators. Combination therapy with LAMA and LABA can be provided for patients who show no improvement of symptoms with single therapy or undergo frequent exacerbation.

3) Group Da patients

Single therapy with LAMA or ultra LABA, or combination therapy with LABA+LAMA or ICS+LABA can be administered as a first-line therapy. If dyspnea (mMRC ≥2) or acute exacerbation develops despite first-line treatment, combination therapy with ICS, LABA, and LAMA or addition of a phosphodiesterase-4 (PDE4) inhibitor can be tried. In a *post-hoc* analysis of the UPLIFT trial, triple therapy with LABA+LAMA+ICS resulted in less hospitalization and more improvement of pulmonary function and quality of life than did combination therapy with ICS+LABA, but without a significant difference in mortality between the two groups. PDE4 inhibitors can be administered to this group of patients with COPD and chronic bronchitis phenotype who undergo frequent exacerbations, if the side effects of PDE4 inhibitors, including nausea, diarrhea, and weight loss, are not serious. Theophylline should not be added to PDE4 inhibitors.

3. Nonpharmacologic therapies

1) Smoking cessation

Smoking cessation is one of the most important interventions. It slows the rate of decline in FEV_1 with consequent benefits in terms of progression of symptoms and survival[39]. Pharmacotherapy and nicotine replacement reliably increase the long-term smoking abstinence rates.

2) Physical activity/pulmonary rehabilitation

The principal goals of pulmonary rehabilitation are to reduce symptoms, improve quality of life, and increase physical and emotional participation in everyday activities[53]. All patients who experience shortness of breath when walking on their own pace on level ground should be offered rehabilitation. Several studies have documented an effect of pulmonary rehabilitation in patients with breathlessness, usually mMRC > 1, and following acute exacerbations.

3) Oxygen therapy

The long-term administration of oxygen (>15 hr/day) to patients with chronic respiratory failure has been shown to increase survival in patients with severe resting hypoxemia[54]. Long-term oxygen therapy is indicated for patients who have the following conditions:

Partial pressure of oxygen (PaO_2) at or below 55 mm Hg

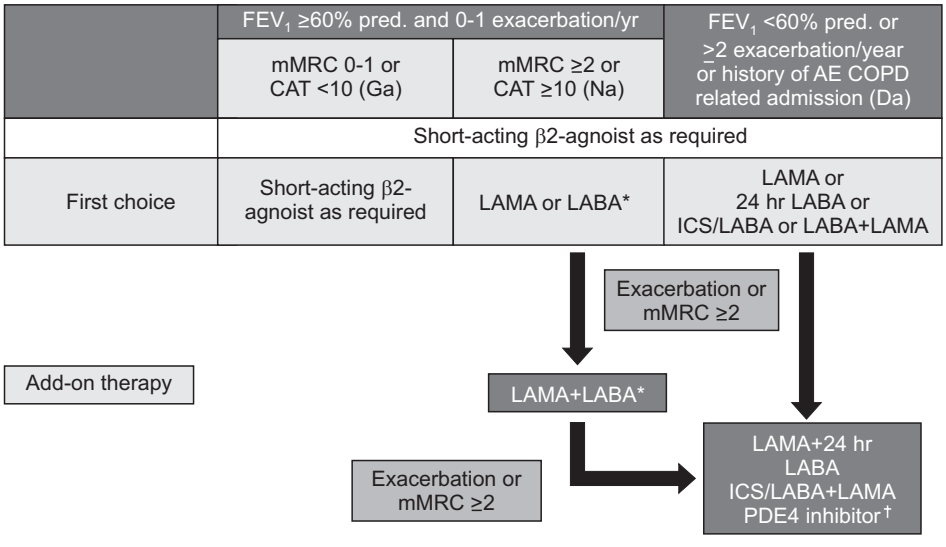

Figure 2. Pharmacologic treatment for stable COPD. *Including ultra LABA. †Postbronchodilator FEV_1/FVC, 0.7; FEV_1, <50%), symptoms of chronic bronchitis, and a history of exacerbations. FEV_1: forced expiratory volume in 1 second; mMRC: modified Medical Research Council dyspnea score; CAT: COPD assessment test score; AE COPD: acute exacerbation of chronic obstructive pulmonary disease; LAMA: long-acting muscarinic antagonist; LABA: long-acting β2-agonist; ICS: inhaled corticosteroid; PDE4: phosphodiesterase-4; FVC: forced vital capacity; COPD: chronic obstructive pulmonary disease. Adapted with permission from the Korean Academy of Tuberculosis and Respiratory Diseases[4].

or arterial oxygen saturation (SaO_2) at or below 88%, with or without hypercapnia confirmed twice over a 3-week period; or PaO_2 between 55 mm Hg and 60 mm Hg, or SaO_2 of 89%, if there is evidence of pulmonary hypertension, peripheral edema suggesting congestive cardiac failure, or polycythemia (hematocrit >55%).

4) Bronchoscopic lung volume reduction

In a *post-hoc* analysis, bronchoscopic lung volume reduction (BLVR) in patients with COPD and severe airflow limitation (FEV_1, 15%–45% predicted), heterogeneous emphysema on computed tomography (CT), and hyperinflation (total lung capacity >100% and residual volume >150% predicted) induced modest improvements in lung function, exercise tolerance, and symptoms, at the cost of more frequent exacerbations of COPD, pneumonia, and hemoptysis after implantation[55]. Additional data are required to define the optimal BLVR technique and patient population.

Acute Exacerbation of COPD

1. Definition

Acute exacerbation of COPD can be defined as a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication[56].

2. Meaning and importance

Acute exacerbation of COPD can impact the natural course of COPD in the following ways:

- Worsening of quality of life
- Deterioration of symptoms and lung function (requiring a few weeks to recover)
- Acceleration of decline of lung function
- Increase in mortality rate
- Increase in socioeconomic burden

3. Etiology

The causes of COPD acute exacerbation are numerous. The most common cause is respiratory infection (viral and/or bacterial)[57,58]. Air pollution can also cause exacerbation. Discontinuing maintenance medication and poor adherence to COPD medication can also be causes. However, the cause of exacerbation cannot be identified in one-third of the cases. Diseases with similar symptoms (pneumonia, congestive heart failure, pneumothorax, pleural effusion, pulmonary thromboembolism, and arrhythmia) should also be differentiated from COPD exacerbations.

4. Symptoms and diagnosis

Symptoms for COPD acute exacerbations are aggravation of dyspnea, increase in cough and sputum volume, and change in sputum color. Diagnosis of COPD is based on the presence of symptoms that are beyond normal day-to-day variations.

5. Assessment of severity and criteria for hospitalization

Severity of exacerbation can be assessed using the following variables.

1) History

- History of previous exacerbation frequency and severity
- Degree of air-flow obstruction in the stable state
- Duration and severity of deterioration of symptoms
- Comorbidity (especially, cardiac disease)
- Current medication
- Home O_2 therapy

2) Physical examination

- Use of accessory muscle
- Paradoxical chest wall movement
- Cyanosis
- Peripheral edema
- Hemodynamic instability
- Decrease of mentality

3) Laboratory findings

- Pulse oximetry: If oxygen saturation is below 90%, hospitalization should be considered. If respiratory failure is suspected, arterial blood gas analysis (ABGA) should be performed.
- Chest plain radiography: If there is a clear difference in the findings between the initial and follow-up radiographs, hospitalization should be considered.
- Electrocardiography should be performed to check for concomitant heart disease.
- Complete blood count: To check for anemia, polycythemia, and leukocytosis.
- Blood chemistry: To check for electrolyte imbalance and hyperglycemia.
- Sputum study: The characteristics of the sputum should be checked because antibiotic treatment may be necessary if the sputum is purulent. Culture tests may be helpful in selecting the antibiotics.

6. Medication

1) Bronchodilators

SABA or short-acting muscarinic antagonist (SAMA) is recommended. Theophylline can be used if SABA and/or SAMA are not effective.

2) Steroids

Systemic steroids can reduce the recovery and admission periods. They also improve lung function and oxygen saturation. Systemic steroids can also reduce further exacerbation. Administration of 30–40 mg of prednisolone for 10–14 days is recommended. Intravenous administration is not superior to oral administration.

3) Antibiotics

Antibiotics are reported to reduce treatment failure and mortality. They are recommended when the sputum is purulent or for patients on mechanical ventilation[59].

7. Respiratory support

1) Oxygen

Oxygen therapy is a key component of management of COPD exacerbation. The target goal of saturation is 88%–92%. ABGA should be performed 30–60 minutes after oxygen therapy. However, too much oxygen can result in CO_2 retention.

2) Ventilatory support

Some patients require admission to the intensive care unit. Noninvasive positive pressure ventilation (NIPPV) or invasive mechanical ventilation (IMV) may be needed for such patients.

3) NIPPV

Success rate of NIPPV is reported to be 80%–85%. NIPPV improves respiratory acidosis, respiratory rate, and dyspnea. It also reduces complications, such as ventilator-associated pneumonia, and the duration of hospitalization. Moreover, NIPPV also reduces the IMV rate and mortality.

4) Invasive mechanical ventilation

The indications of IMV are listed in (1) respiratory or cardiac arrest, (2) decreased mentality, (3) unable to remove secretion, (4) unable to tolerate NIPPV or NIPPV failure, (5) others.

8. Discharge and follow-up

Indications of discharge are listed in the indications of discharge are (1) patient can walk across the room, (2) patient can eat and sleep without frequent awakening, (3) patient can use long-acting bronchodilator±ICS properly, (4) stable result of arterial blood gas analysis for 12–24 hours, (5) others. Patients should use an inhaled long-acting bronchodilator±ICS before discharge. Education for smoking cessation, assessment of the effect of the inhaler, and follow-up measurements of lung function are needed.

9. Prevention

COPD can be prevented by nonpharmaceutical and pharmaceutical treatments.

1) Nonpharmaceutical treatment

- Pulmonary rehabilitation
- Smoking cessation
- Vaccination

2) Pharmaceutical treatment

- Inhaled long-acting bronchodilators: LABA or LAMA
- ICS
- PDE4 inhibitor

Comorbidities of COPD

Most patients with COPD have comorbidities, which have a significant impact on prognosis[60,61]. Table 2 shows the prevalence of comorbidities in Korean patients with COPD based on National Health Insurance data for 2009 provided by the Health Insurance Review and Assessment Service.

Comorbidities such as heart failure exaggerate or induce dyspnea and/or cough, which are symptoms similar to those in COPD exacerbation. The diagnosis of heart failure in patients with COPD could be delayed. Therefore, patients with COPD should be regularly evaluated for the presence of comorbidities.

The treatment of comorbidities in patients with COPD is not different from that in those without COPD. Treatment is equally important in both groups of patients.

Cardiovascular diseases are the most common and important comorbidities of COPD[62]. Ischemic heart disease, heart failure, atrial fibrillation, and hypertension are the most common cardiovascular diseases. Beta-blockers are one of the most important drugs for the treatment of ischemic heart

Table 2. Prevalence of comorbidities in Korean patients with chronic obstructive pulmonary disease (n=192,496)*

Comorbidity	No. of patients	Prevalence (%)
Hypertension	97,672	51
Diabetes mellitus	48,189	25
Ischemic heart disease	35,021	18
Heart failure	36,736	19
Metabolic syndrome	33,323	17
Osteoporosis	17,572	9
Depression	17,313	9

*Supported by the National Strategic Coordinating Center for Clinical Research.

disease and heart failure. If patients with COPD require beta-blockers, selective beta-1 inhibitors are the best choice, particularly for patients with severely impaired lung function[63,64].

Metabolic syndrome and type 2 diabetes mellitus are very common since most patients with COPD are elderly and current or former smokers. Weight reduction aimed at achieving a body mass index of less than 21 kg/m^2 is not recommended for patients with severe COPD, because it might increase respiratory mortality[65,66].

Gastroesophageal reflux disease is also a common comorbidity and seems to be one of the risk factors for COPD exacerbation[67-69]. In Korean patients with COPD, the prevalence of gastroesophageal reflux disease is 28%[68]. However, the preventive effect of proton pump inhibitors on COPD exacerbation has not yet been proven.

Although osteoporosis is one of the main comorbidities in COPD[62,70], it is sometimes neglected or its diagnosis is delayed[71]; this leads to general weakness and worse prognosis[70]. Since systemic corticosteroids are one of the well-known risk factors for osteoporosis, their overuse should be avoided.

Anxiety and depression are also common comorbidities[72]. The prevalence of depression in patients with COPD is higher than that in the general population[13]. Approximately 25% of the patients with COPD have depression[73-75]. Korean Patient Health Questionnaire-9 is recommended as a screening tool to diagnose depression in patients with COPD[76-78].

Lung cancer is another common comorbidity in patients with COPD[79]. Recently, a large, randomized controlled trial demonstrated the survival benefit of CT screening in patients with lung cancer[80]. However, the benefits of CT screening in patients with COPD have not yet been evaluated. Severe airflow limitation is an absolute contraindication for surgery, even though lung cancer is detected early.

Severe respiratory infection is also common in patients with COPD[81]. If a patient with COPD experiences recurrent pneumonia and has been taking an ICS, discontinuing the ICS should be considered[82].

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Acknowledgments

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