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Review

Total management of chronic obstructive pulmonary disease (COPD) as an independent risk factor for cardiovascular disease

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ABSTRACT

Patients with cardiovascular disease (CVD) often have multiple comorbid conditions that may interact with each other, confound the choice of treatments, and reduce mortality. Chronic obstructive pulmonary disease (COPD) is one of the most important comorbidities of CVD, which causes serious consequences in patients with ischemic heart disease, stroke, arrhythmia, and heart failure. COPD shares common risk factors such as tobacco smoking and aging with CVD, is associated with less physical activity, and produces systemic inflammation and oxidative stress. Overall, patients with COPD have a 2–3-fold increased risk of CVD as compared to age-matched controls when adjusted for tobacco smoking. Chronic heart failure (HF) is a frequent and important comorbidity which has a significant impact on prognosis in COPD, and vice versa. HF overlaps in symptoms and signs and has a common comorbidity with COPD, so that diagnosis of COPD is difficult in patients with HF. The combination of HF and COPD presents many therapeutic challenges including beta-blockers (BBs) and beta-agonists. Inhaled long-acting bronchodilators including beta2-agonists and anticholinergics for COPD would not worsen HF. Diuretics are relatively safe, and angiotensin-converting enzyme inhibitors are preferred to treat HF accompanied with COPD. BBs are only relatively contraindicated in asthma, but not in COPD. Low doses of cardioselective BBs should be aggressively initiated in clinically stable patients with HF accompanied with COPD combined with close monitoring for signs of airway obstruction and gradually up-titrated to the maximum tolerated dose. Encouraging appropriate and aggressive treatment for both HF and COPD should be recommended to improve quality of life and mortality in HF patients with COPD.

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Introduction

Chronic obstructive pulmonary disease (COPD), a common preventable and treatable disease, is characterized by persistent airflow limitation and respiratory symptoms that is usually progressive and associated with airway and/or alveolar abnormalities caused by significant exposure to noxious particles or gases [1]. By 2020, COPD is predicted to cause over 6 million deaths annually worldwide, thus becoming the third leading cause of death in the world.

Tobacco smoking is the most important cause of COPD. Almost all smokers experience a progressive decline in lung function in a dose- and duration-dependent manner. Tobacco smoking is a common risk factor for many comorbidities, including cardiovascular disease (CVD) [2]. Many numbers of inflammatory cell types such as macrophages, neutrophils, and T-cells in the airway and the lung are involved in the pathophysiology of COPD [3]. In addition to the lung inflammation, chronic systemic inflammation is observed in COPD, but the origin of this inflammation remains unclear. The systemic inflammation of COPD causes a multisystem disease associated with the high frequency of major comorbidities including diagnosed and subclinical CVD independently of the patients' advanced age and shared risk factors [1]. CVD including hypertension, ischemic heart disease (IHD), stroke, atrial fibrillation (AF), and heart failure (HF) is the most frequent and most important comorbidity in COPD because of the worsening prognosis in patients with COPD, and vice versa [4].

In particular, COPD is a frequent co-morbidity in chronic HF with its prevalence ranging between 20% and 30% [2]. Accordingly, the objective of this review is to clarify COPD as a main comorbidity of CVD, and to discuss the diagnostic and therapeutic approach for HF patients accompanied with COPD.

Clinical features of COPD

COPD is a major cause of morbidity and mortality so that its diagnosis should be considered in any patient who has dyspnea, chronic cough, or sputum production with a history of smoking [1]. Spirometry is required to make a clinical diagnosis of COPD. The presence of the ratio of forced expiratory volume in 1 s (FEV₁) to forced vital capacity (FVC) < 0.70 with a post-bronchodilator indicates airflow limitation caused by COPD. Tobacco smoking is the most important cause of COPD, which causes lung inflammation that induces parenchymal tissue destruction, leading to air trapping and progressive airflow limitation.

COPD should be treated based on an individualized assessment of disease in order to reduce current symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance. Smoking cessation, non-pharmacologic therapies including pulmonary rehabilitation, and pharmacologic therapies are recommended based on an individual patient's symptoms, airflow limitation, and severity of exacerbations.

Pharmacologic therapies for COPD are used to reduce symptoms, avoid exacerbations, and improve health status and exercise tolerance. Inhaled bronchodilator medications are indicated for the

symptomatic management of COPD. The principal bronchodilator treatments to prevent or reduce symptoms are anticholinergics, beta₂-agonists, or combination therapy. These treatments should be decided according to each patient's individual response and relative contraindication. Long-acting inhaled bronchodilators are more convenient and effective for symptom relief, and have fewer adverse effects on the cardiovascular system than short-acting bronchodilators.

COPD is considered a complex, heterogeneous, and multicomponent disease because of many comorbidities and extrapulmonary manifestations as well as structural and functional abnormality of the lungs [4]. Extrapulmonary comorbidity should be aggressively treated to improve regular physical activity as well as mortality for patients with COPD.

COPD on cardiovascular disease

COPD often coexists with CVD and has a significant impact on prognosis [4]. Overall, patients with COPD have a 2–3-fold increased risk of CVD compared to age-matched controls when adjusted for tobacco smoking [5]. In a multicenter observational prospective study conducted at 17 cardiology clinics across Japan, the prevalence of airflow limitation compatible with COPD was observed in 995 cardiac outpatients with a smoking history (Fig. 1) [6]. The overall prevalence of airflow limitation compatible with COPD was 27.0%, and 87.7% of those patients did not have a prior diagnosis of COPD.

Cardiovascular comorbidities are common at any severity of COPD and have the most serious consequences in patients with COPD, but they are most frequently undiagnosed and untreated.

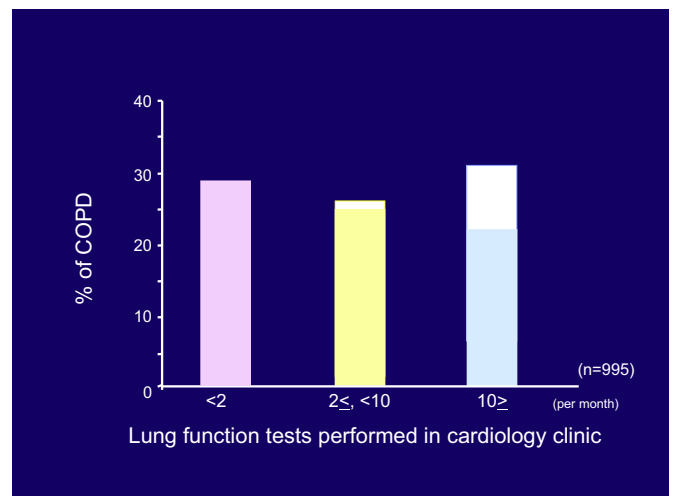


Fig. 1. The prevalence of airflow limitation and a previous diagnosis of COPD in cardiology clinic. The amount of airflow limitation and a previous diagnosis of COPD observed in 995 cardiac outpatients with a smoking history. Lung function tests performed in cardiology clinic often (10_≥), less often (2_≤, <10), and seldom (<2). Color squares show airflow limitation, and white squares show a previous diagnosis of COPD. COPD, chronic obstructive pulmonary disease.

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