

Cardiovascular Comorbidities in COPD Patients

Roever L* and Resende ES

Department of Clinical Research, Federal University of Uberlandia, Brazil

*Corresponding author: Leonardo S Roever-Borges, MHS, Department of Clinical Research, Federal University of Uberlandia, Av. Para, 1720-Bairro Umuarama Uberlandia - MG - CEP 38400-902, Brazil, Tel: +553488039878; E-mail: leonardoroever@hotmail.com

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Abstract

Chronic obstructive pulmonary disease (COPD) is a cause of morbidity and mortality worldwide. Patients with COPD and the metabolic syndrome, sedentary lifestyle, skeletal muscle dysfunction, systemic inflammation, oxidative stress, hypoxemia, endothelial dysfunction have increased risk of morbidity and mortality due to cardiovascular disease (CVD). CVD contributes to hospitalization in patients with COPD and to mortality. This review describes the various components of CVD and its impact in COPD patients.

Keywords: Chronic obstructive pulmonary disease; Cardiovascular diseases; Risk factors

Introduction

More than 14 million of Americans have been diagnosed with COPD, and another 12 million likely have COPD but have not been diagnosed. A systematic review and meta-analysis of studies carried out in 28 countries, provide evidence that the prevalence of COPD is appreciably higher in smokers and ex-smokers, in those over 40 years of age, and more in men [1,2]. The PLATINO study reported the prevalence of COPD increased steeply with age, with the highest prevalence among those over age 60, and higher in men than in women [3].

Patients with COPD are at higher risk of CVD and die from cardiovascular cause [4-12]. Cardiovascular conditions that have been reported to occur with a greater frequency in patients with COPD are coronary artery disease (CAD), heart failure (HF), peripheral vascular disease (PVD), and arrhythmias [13]. The evidence has implicated systemic and pulmonary inflammation as the common link between COPD and certain comorbid conditions, such as lung cancer, CVD and cachexia [14-16]. Low grade systemic inflammation is linking COPD with cardiovascular disease, including C-reactive protein (CRP), IL-6, IL-8, IL-10, nuclear factor (NF)- κ B, fibrinogen, circulating leukocytes and TNF- α [17].

The reduced of FEV1 is a risk factor for cardiovascular mortality in patients of COPD, 10% decrease in FEV1 increases all-cause mortality by 14%, cardiovascular mortality by 28%, and nonfatal coronary event by almost 20%, after adjustments for relevant confounders such age, sex, smoking, and treatment assignment [18-20]. In this review, we consider as common comorbidities all previously described diseases that frequently observed in COPD correlated with cardiovascular disease.

Cardiovascular Comorbidities

Hypertension

Hypertension affects more than 76 million adults in the United States \geq 20 years of age and around one billion individuals worldwide.

Hypertension is common in COPD patients, and is related to the increased systemic inflammation, with higher dyspnea scores, reduced capacity for physical activity, and airflow obstruction. Since the lungs are damaged, the amount of oxygen that goes to the blood is reduced, and this produces high blood pressure in the blood vessels from the heart to the lungs, and makes it even more difficult for the heart to pump much needed blood [21, 22].

Diabetes

Diabetes worsens mortality in COPD patients, and has been reported to be a frequent COPD comorbidity, with prevalence as high as 18.7% among COPD patients [23-27]. COPD may be considered as a novel risk factor for new onset type 2 diabetes mellitus via multiple pathophysiological alterations such as: inflammation and oxidative stress, insulin resistance, weight gain and alterations in metabolism of adipokines. Diabetes is associated with an increased risk of pulmonary infections, acute exacerbations and worsened COPD outcomes. Diabetes patients worsen the outcomes of COPD by affecting a number of parameters: reducing six- minute walking distance, risk of death during exacerbations, increasing Medical Research Council dyspnea scores, shortening time to first hospitalization and increasing hospitalization [28-30].

Metabolic syndrome

The prevalence of metabolic syndrome (MetS) is reported to be up to 22.5% in COPD patients. These diseases are a result of common risk factors, like smoking, and also the synergic effect of systemic inflammation mediated by common cytokines [31-33]. One studied reported the association between the components of MetS and airflow obstruction in 129,965 men. MetS was associated with low FEV1 (odds ratio (OR) 1.28; 95% confidence interval (CI) 1.20-1.37) and FVC (OR 1.41; 95% CI 1.31-1.51). Abdominal obesity was strongly associated with low FEV1 (OR 1.94; 95% CI 1.80-2.09) and FVC (OR 2.11; 95% CI 1.95-2.29) [34]. Another studied enrolled 38 subjects with COPD and 34 controls to test whether MetS in COPD patients. Overall 47% of COPD patients had three or more MetS components in comparison with 21% of control subjects, and the prevalence of obesity was approximately two times higher in the COPD group [35].

Coronary heart disease

COPD and coronary heart disease share a common major risk factor, which is smoking. The coexistence has been reported to be as high as 30% or even higher in COPD patients [36]. Both diseases are characterized by chronic inflammation and coagulopathy. The mediator of this sustained inflammation in COPD is elevated C-reactive protein levels, which maintain bronchial constriction and increase the risk for coronary disease [37,38].

Atrial fibrillation

The COPD are associated with increased risk for atrial fibrillation (AF)/atrial flutter and non-sustained ventricular tachycardia (NSVT). The prevalence of atrial fibrillation and NSVT among COPD patients has been reported to be as high as 23.3% and 13.0%, respectively [39,40]. Reduced FEV1 in COPD is associated with a higher incidence of AF [41,42]. Hospitalization mortality in severe COPD patients with arrhythmia has been reported to be as high as 31%, and the prolonged conduction time in the right atrium and typical atrial flutter are commonly observed in COPD patients with AF [43,44].

Congestive heart failure

CHF and COPD are associated with smoking, studies report a 3.8% to 16% [45,46]. CHF is among the leading causes of hospitalization and death for patients with COPD and worsens their prognosis. COPD is an independent risk factor for death in patients with CHF [47,48]. Coexistence of COPD and CHF worsens right ventricular dysfunction, when compared with non-COPD patients. Left ventricular dysfunction is present in around 20% of COPD patients [48,49].

Stroke

COPD patients increased risk for ischemic stroke, because of common risk factors, like age, smoking, systemic inflammation and coagulopathy caused by COPD [50,51]. The studies reported a linear correlation between stroke risk and airflow obstruction. In the total of 8% of all COPD patients have a history of stroke and 4 % of all deaths in COPD patients are related to an incident of ischemic stroke [52-54].

Peripheral arterial disease

Previous study reported the risk of PAD in patients with COPD and showed adjusted RR estimates of 1.11 (range: 1.05-1.19) and 5.50 (range: 4.90-6.18) in patients with COPD as compared with those without COPD [55].

Endothelial dysfunction and carotid intima-media thickness

The obstructive sleep apnea (OSA) causing vessel inflammation as well as hypoxia, induced by difficulties in the passage of air through the upper airways. In one study the authors enrolled 63 patients (49 males and 14 female, mean age: 54 ± 10 years) subdivided into four groups: high cardiovascular risk factors, no CPAP therapy, CPAP therapy started less- and more than 3 months before. This study shows the importance of administering CPAP therapy for more than 3 months in patients suffering from OSA to improve endothelial function to a level equal to high cardiovascular risk subjects probably due to a recovery from the systemic hypoxia [56].

In another study the authors enrolled 156 patients (125 men, mean age: 60 ± 12 years) affected by OSA of different severity: 111 (71%)

were in CPAP therapy; some of the population were also affected by hypertension (65%), dyslipidemia (33%) and diabetes (24%). The authors found a statistically significant higher carotid intima-media thickness (IMT) value in patients with longer-lasting disease (OSA duration in IMT < 0.9 mm: 120 (60-192) months versus OSA duration in IMT ≥ 0.9 mm: 200 (120-310) months; $p < 0.001$), and too a positive relationship between IMT and OSAS duration ($r = 0.34$; $p < 0.001$) and between apnea-hypopnea index and IMT ($r = 0.51$; $p < 0.001$) [57].

The same group evaluated the relationship between carotid intima-media thickness (cIMT) and inflammatory markers plasma levels in OSA patients (80 OSA and 40 controls). High-sensitive C-Reactive Protein (hsCRP), interleukin (IL)-6, tumor necrosis factor (TNF)- α and pentraxin (PTX)-3 serum concentrations were detected. cIMT was higher in OSA patients than controls (0.89 ± 0.13 mm vs. 0.65 ± 0.1 mm, $p < 0.01$). OSA patients showed increased cIMT, CRP, IL-6, TNF- α , and PTX-3 levels. Inflammatory markers levels are correlated to cIMT in OSA patients [58].

Vitamin D deficiency

Vitamin D deficiencies strongly interact with different pathogenic mechanisms in COPD, and too linked with a higher risk for cardiovascular disease [59].

Endocrinological Derangements

The mechanisms by which COPD alters endocrine function are incompletely understood but likely involve hypoxaemia, hypercapnia, systemic inflammation and glucocorticoid administration. Several mechanisms, including decreased protein anabolism, increased protein catabolism, nonenzymatic glycosylation and activation of the rennin-angiotensin-aldosterone system [60]. Nonthyroidal illness syndrome is the most common in COPD, being reported in 20% of stable patients and 70% of patients experiencing an exacerbation [61]. Hyperthyroidism causes inspiratory and expiratory muscle weakness in COPD patients [62].

The COPD is associated cardiovascular comorbidities. Prevention and treatment should be implemented in these patients aiming at reducing morbidity and mortality.

Disclosure

The authors report no conflicts of interest in this work.

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