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Review

Chronic Obstructive Pulmonary Disease and Left Ventricle☆

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ABSTRACT

Several studies have shown that the interaction between chronic obstructive pulmonary disease (COPD) and cardiovascular comorbidity is complex and bidirectional, since each of these diseases complicates the prognosis of the other.

Recent advances in imaging technology have led to better characterization of cardiac chambers and allowed the relationship between certain cardiac function parameters and COPD clinical and functional variables to be explored.

Although cardiac abnormalities in COPD have been mainly associated with the right ventricle, several studies have reported that the left ventricle may also be affected in this disease. A better understanding of the mechanisms involved and their clinical implications will establish diagnostic and therapeutic strategies for patients with both these conditions.

Enfermedad pulmonar obstructiva crónica y ventrículo izquierdo

Palabras clave:
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RESUMEN

Numerosos estudios han puesto de manifiesto que la interacción entre la enfermedad pulmonar obstructiva crónica (EPOC) y la comorbilidad cardiovascular es compleja y bidireccional, puesto que cada una de estas entidades complica el pronóstico de la otra.

El avance en las técnicas de imagen ha dado paso a una mejor caracterización de las cavidades cardíacas, hecho que ha permitido el estudio de la relación que existen entre ciertos parámetros de función cardíaca con variables clínicas y funcionales en la EPOC.

A pesar de que las alteraciones cardíacas en la EPOC han sido adscritas fundamentalmente al ventrículo derecho, diversos estudios han descrito que el ventrículo izquierdo también se puede afectar en esta enfermedad. Una mejor compresión de los mecanismos involucrados y de sus implicaciones clínicas permitirá establecer estrategias de abordaje diagnóstico y terapéutico en los pacientes donde coexistan estas 2 entidades.

Introduction

The anatomical and functional relationship between the heart and lungs is so close that dysfunction of one of these systems can affect the other.[1] There are neurological, humoral and mechanical interactions between both organs, and various mechanisms that lead to structural or functional ventricular alterations can coexist in patients with respiratory disease. Several studies have shown that cardiovascular events are more common in patients with chronic obstructive pulmonary disease (COPD) compared to smokers without the disease.[2–4] However, whether this is simply due to the higher prevalence of traditional cardiovascular risk factors (CVRF) (hypertension [HT], diabetes mellitus, reduced physical activity and dyslipidemia)[5] in COPD patients, or whether there is a particular pathophysiological connection is still widely debated. While some authors propose systemic inflammation as the etiological pathway to atherosclerosis, recent studies indicate that sustained systemic inflammation occurs in only a proportion of patients with COPD.[6] Thus, the association between cardiovascular

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diseases (CVD) and COPD is much more complex, and may involve other factors: biological (hypoxemia, endothelial dysfunction, increased platelet activation, arterial stiffness),[7–9] mechanical and/or functional (deterioration in the forced expiratory volume in the first second, emphysema, hyperinflation),[10,11] neurohumoral (excess sympathetic nerve activity)[12] and genetic (polymorphisms of the metalloproteinases, telomere shortening).[13,14]

There is growing interest in the as yet poorly characterized contribution of cardiovascular factors such as dyspnea and exercise intolerance to the symptomatology of COPD. Indeed, various studies with large patient cohorts have identified a cardiovascular phenotype in COPD that presents with a different clinical course and prognosis.[15–17]

The cardiac abnormality related with COPD has traditionally been right ventricular (RV) dysfunction, despite publications in the last century already reporting pathological left ventricle (LV) changes found in the autopsied hearts of COPD patients.[18] At present, thanks to advances in imaging techniques, various LV abnormalities in these patients that appear to affect certain clinical and functional variables of the disease have been verified. In this review, we will analyze the mechanisms linking LV dysfunction and COPD, their manifestation in imaging studies, and their clinical consequences.

Mechanisms Involved

Physiological Stress

Patients with COPD can have sustained (patients with chronic respiratory failure), or intermittent hypoxia (during exercise, exacerbations, or during sleep). Hypoxia can cause abnormalities in ventricular relaxation and contraction due to changes in the myocyte cell metabolism.[19] It can also affect the pathogenesis of atherosclerosis by various mechanisms, including increased vascular and systemic inflammation, elevated C-reactive protein and increased oxidative stress.[20,21] Furthermore, it can induce hemodynamic stress by increasing the heart rate and activating the sympathetic nervous system.[22,23] Finally, hypoxia is involved in pulmonary vascular remodeling that increases pulmonary vascular resistance, which may negatively affect LV diastolic filling by the phenomenon of ventricular interdependence, described below.

Coronary Artery Disease

Coronary artery disease (CAD) or atherosclerosis is the end result of the accumulation of atheroma plaques on the walls of the coronary arteries. Numerous epidemiological studies have shown that COPD patients have a high risk of developing CAD, with its inherent complications (ischemic heart disease, stroke, sudden death), and that this risk increases during exacerbations.[24–26] Some studies have found this association to be independent of smoking and other confounding factors, such as age. Sub-clinical atherosclerosis (the "early" phase of CAD) has also been described in smokers with airflow limitation and in emphysema patients.[27,28]

The etiology of CAD and COPD is complex and multifactorial, since they share common etiological factors apart from smoking (release of endothelial microparticles, changes in hemostasis and oxidative stress, among others).[29–31]

The precise prevalence of CAD in COPD is not known; estimates published to date vary widely (4.7%–60%).[32] Nevertheless, data from population studies indicate that it could be high.[33–35]

Other evidence that highlights the close relationship between CAD and COPD is the role of the latter as an independent factor for poor progress and mortality following coronary revascularisation.[36–38] COPD, together with 5 other major clinical variables including age, sex and LV ejection fraction (LVEF), is a predictor of mortality 4 years after revascularization in the SYNTAX score II (an angiographic grading tool to determine the complexity of CAD that helps clinicians decide the optimum revascularization method in patients with complex CAD).[39]

CAD can affect myocardial relaxation by decreasing arterial distensibility, and increasing central arterial pressure and LV afterload,[40] while subclinical atherosclerosis has been negatively associated with diastolic dysfunction parameters due to altered coronary reserve.[29]

Ventricular Interdependence

Right ventricular function and pulmonary hypertension (PH), usually only mild to moderate, are common in COPD. Both pulmonary vascular changes and pathological changes in the RV have been found even in early stages of the disease.[7,41] Ventricular interdependence describes the phenomenon in which both RV pressure and volume overload cause the interventricular septum to shift toward the LV, modifying its geometry ("D-shape"). The pathophysiological mechanisms involved are summarized in Fig. 1. Dilatation of the RV also increases the constrictive effect of the pericardium, all of which can result in a reduction in the distensibility and filling of the LV.[42] This mechanism may explain why a preserved ejection fraction can be observed in the LV, despite a sub-optimal filling phase.

Hyperinflation and Emphysema

Thanks to recent advances and the widespread availability of imaging techniques, the effect of emphysema and hyperinflation on LV dysfunction (LVD) is now understood in greater detail. Ten years ago, Jörgensen et al.[43–45] hypothesized that hyperinflated lungs and high intrinsic positive end-expiratory pressure will decrease intrathoracic blood volume and ventricular preload, resulting in "hypovolemic diastole". The authors showed through various studies that patients with severe emphysema had various functional and hemodynamic alterations, such as a decrease in the end-systolic and end-diastolic volumes of the LV, lower cardiac index and lower stroke volume index compared to a control group, and that furthermore, these parameters could improve after volume reduction surgery.[47]

In this respect, Watz et al.,[11] in an echocardiographic study of 138 patients with COPD of varying severity, observed that pulmonary hyperinflation (measured by the inspiratory capacity/total lung capacity [IC/TLC] ratio) was more strongly correlated with the decreased size of the heart chambers and impaired LV diastolic filling pattern than with airflow obstruction or the carbon monoxide diffusing capacity.

Barr et al.[10] provided solid evidence of the effect of emphysema on ventricular filling in the MESA study, an extensive population study in patients without CVRF. Emphysema detected by computed tomography (CT) and airflow obstruction were linearly and inversely correlated with the reduction in LV end-diastolic volume, systolic volume and cardiac output measured by magnetic resonance imaging (MRI). These associations were of greater magnitude among the active smokers than among former and never-smokers. These findings indicate that even in the early stages of COPD, the systolic volume and size of the LV are affected.[46] In 2 MESA sub-studies, Smith et al.[47] described an association between 2 pulmonary hyperinflation parameters (residual volume and the residual volume/TLC ratio) with a larger LV mass in 119 patients with COPD, while another study by the same group showed that the percentage of emphysema was inversely correlated with the diameter of the pulmonary veins,[48] which were narrower in COPD patients (GOLD I–III) than in controls, although the difference was