Review
Chronic Obstructive Pulmonary Disease and Left Ventricle

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The mechanisms involved in COPD are complex and multifactorial, involving both intrinsic and extrinsic factors. The disease is characterized by airway obstruction due to chronic inflammation and injury to the airway walls. This leads to increased airway resistance and decreased lung function, resulting in dyspnea, chronic cough, and sputum production. The pathophysiology of COPD is characterized by various processes, including acute and chronic inflammation, mucus hypersecretion, airway remodeling, and structural changes in the airways and bronchiolar walls. These processes can lead to hyperinflation, which is a hallmark of COPD and is associated with reduced lung compliance and increased work of breathing. Additionally, COPD is often accompanied by systemic inflammation, which can contribute to the development of comorbidities such as cardiovascular disease, diabetes, and osteoporosis. The high prevalence of these comorbidities in COPD patients highlights the need for comprehensive care and management strategies to improve outcomes in this population.
not statistically significant (P=.06). This structural alteration may also be detrimental to LV filling.

**Left Ventricular Defects in Chronic Obstructive Pulmonary Disease and Their Clinical Consequences**

The morphological description of the heart chambers in COPD using echocardiography raises the issue of suboptimal quality if hyperinflation and diaphragmatic flattening coexist. Despite this, various echocardiographic series have been published in the last 20 years showing alterations in structural and functional parameters over the entire spectrum of disease severity (Table 1). The variability in the findings reported depends, in some cases, on the inclusion of “selected” patients (no CVRF except smoking), the presence of associated PH, the setting (specialist clinic/primary care) and the degree of airflow obstruction. There are also studies with other imaging techniques that are less commonly used in routine clinical practice, such as MRI and nuclear medicine techniques.

**Left Ventricular Hypertrophy**

As shown above, ventriculography and autopsy studies in patients with chronic bronchitis and emphysema show LV hypertrophy (LVH) and increased ventricular mass. In addition to the study by Smith et al., which describes an association between pulmonary hyperinflation and LV mass independent of other CVRF, Anderson et al. using echocardiography, reported a prevalence of LVH of 21.4% in men and 43.2% in women with normoxic COPD and no underlying PH; the LV mass was significantly larger than that of controls. These findings indicate an independent effect of COPD on LVH that is not related with PH. The authors suggested sympatetic activation as the possible mechanism, mainly through the renin–angiotensin–aldosterone system.

LVH is a pivotal factor in cardiovascular events, and preventive treatment has been shown to reduce cardiovascular morbidity and mortality to a large extent. LVH is considered an arrhythmogenic factor and can result in the eventual onset of ventricular dysfunction (both diastolic and systolic), and atrial fibrillation (AF) and dilatation. Moreover, LVH reduces the coronary reserve, increasing the risk of ischemic heart disease. Controlling ventricular remodeling as far as possible has thus become one of the therapeutic targets in the management of chronic diseases in which LVH is prevalent, such as diabetes mellitus and chronic renal failure.

**Diastolic Ventricular Dysfunction**

During diastole, the LV receives blood from the left atrium, which is subsequently ejected into the systemic circulation. In simple terms, the efficiency of LV filling can be measured as the ability to receive a large volume of blood at rapid filling rate but under lower pressures. Consequently, various physiological parameters interact in LV diastole, principally relaxation, ventricular distensibility and atrial contraction (Table 2). Among the most common causes of diastolic dysfunction are PH, senility and CAD.

Various studies in COPD patients describe a high rate of LV diastolic dysfunction (LVDD) compared to age-matched controls, even in those without CVRF. Its prevalence also varies considerably, reaching 90% in COPD patients with severe airflow limitation. The most frequently described pattern is slow relaxation, which is characterized by a reduced E wave (due to a decrease in the relaxation velocity of the myocardial fibers) and an increased A (atrial contraction) wave with an E:A ratio <1. This impaired ventricular filling can be a major complication in patients with AF, a very prevalent arrhythmia in COPD, due to both loss of atrial systole and shortening of the filling period.

Several authors attributed this impairment to the phenomenon of ventricular interdependence. Funk et al., however, described LVDD in COPD patients without PH, demonstrating that its development may be due to the interaction of other mechanisms, as described above.

Impaired ventricular filling has been negatively associated with exercise tolerance assessed using the 6-min walk test and with a reduction in physical activity.
<table>
<thead>
<tr>
<th>First author/year</th>
<th>n/Controls</th>
<th>Population</th>
<th>Mean age</th>
<th>FEV₁ (% pred); PO₂ (mmHg); SpO₂ (%)</th>
<th>CVRF excluded</th>
<th>Main findings</th>
<th>Comments</th>
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<tr>
<td>Schena et al., 1998</td>
<td>30</td>
<td>CRF, cor pulmonale, PH</td>
<td>62</td>
<td>FEV₁ 37; PO₂ 51; HT, valvular heart disease, cardiomyopathy</td>
<td></td>
<td>Correlation between mPAP and diastolic and systolic eccentricity of the LV and E/A ratio of LV filling despite a normal systolic phase</td>
<td>RV pressure overload induces an alteration in LV filling despite a normal systolic phase.</td>
</tr>
<tr>
<td>Tutar et al., 1999</td>
<td>40/20</td>
<td>Cor pulmonale</td>
<td>60</td>
<td>FEV₁ 35; PO₂ 47; HT, CAD, valvular heart disease</td>
<td></td>
<td>HT, CAD, valvular heart disease</td>
<td>Relationship with sPAP: E/A ratio and IRT of sPAP correlated with LV filling and IRT velocity.</td>
</tr>
<tr>
<td>Boussuges et al., 2006</td>
<td>34/20</td>
<td>Stable COPD</td>
<td>60</td>
<td>FEV₁ 42; PO₂ 54; HT, ischemic heart disease, valvular heart disease</td>
<td></td>
<td>&lt;E, &gt;A, E/A ratio compared to controls (75% vs 35%)</td>
<td>Prevalence of HF in COPD compared with data from population aged &gt;65 years.</td>
</tr>
<tr>
<td>Ozer et al., 2001</td>
<td>48/59</td>
<td>Group 1: 25 (with PH) Group 2: 23 (without PH) Stable COPD</td>
<td>57/55</td>
<td>FEV₁ 39/PO₂ 45; FEV₁ 45/PO₂ 59; FEV₁/FVC 64%</td>
<td>Heart disease, valvular heart disease, HF</td>
<td>COPD with PH: &lt;E, &gt;A, Em/Am</td>
<td>Prevalence of HF in COPD compared with data from population aged &gt;65 years.</td>
</tr>
<tr>
<td>Rutten et al., 2005</td>
<td>405</td>
<td>Group 1: 24 (without PH) Group 2: 20 (without PH) Stable COPD</td>
<td>64/65</td>
<td>FEV₁ 50/PO₂ 74; FEV₁ 42/PO₂ 67; FEV₁ 40/PO₂ 74; Song et al., 2007</td>
<td>HT, heart disease, valvular heart disease, HF</td>
<td>No</td>
<td>Prevalence of HF in COPD compared with data from population aged &gt;65 years.</td>
</tr>
<tr>
<td>Funk et al., 2008</td>
<td>22/22</td>
<td>Group 1: 25 (without PH) Group 2: 22 (with PH) Stable COPD</td>
<td>59</td>
<td>FEV₁ 1.8; PO₂ 71</td>
<td>E/A, Em/Am</td>
<td>Correlation between mPAP and IRT of sPAP correlated with LV filling and IRT velocity.</td>
<td></td>
</tr>
<tr>
<td>Acikel et al., 2010</td>
<td>47/20</td>
<td>Group 1: 25 (without PH) Group 2: 22 (with PH) Stable COPD</td>
<td>61/58</td>
<td>FEV₁ 52/PO₂ 61; FEV₁ 40/PO₂ 56</td>
<td>HT, valvular heart disease, AF, heart disease, branch block</td>
<td>E/A, Em/Am</td>
<td>Patients with LVD had higher all-cause mortality compared to those without LVD at 2-year follow-up.</td>
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<td>Sabit et al., 2010</td>
<td>36/14</td>
<td></td>
<td>66</td>
<td>FEV₁ 57</td>
<td>Previous history of heart disease</td>
<td>The mean strain and strain rate was lower than in the control group, P &lt; 0.05.</td>
<td>Relationship of the IRT with aortic pulse wave.</td>
</tr>
<tr>
<td>Flu et al., 2010</td>
<td>1005 vascular surgery patients</td>
<td></td>
<td>367</td>
<td>FEV₁ 56; PO₂ 69</td>
<td>No</td>
<td>Sub-clinical LVD: 47% LVSD (LVEF&lt;50%); 12% Heart failure: 14%</td>
<td>Patients with CI/TLC&lt;0.25 impaired ventricular filling compared to those with CI/TLC&gt;0.25. Inverse correlation of CI/TLC with cardiac chamber size. LVSD has direct correlation with severity of FEV₁.</td>
</tr>
<tr>
<td>Watz et al., 2010</td>
<td>138</td>
<td>GOLD I-IV</td>
<td>63</td>
<td>FEV₁ 56; PO₂ 69</td>
<td>CAD, AF; LVEF&lt;50%</td>
<td>CAD, AF, LVEF&lt;50%</td>
<td>Patients with CI/TLC&lt;0.25 impaired ventricular filling compared to those with CI/TLC&gt;0.25. Inverse correlation of CI/TLC with cardiac chamber size. LVSD has direct correlation with severity of FEV₁.</td>
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Table 1 (Continued)

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<th>Main findings</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Gupta et al., 2011&lt;sup&gt;8&lt;/sup&gt;</td>
<td>40</td>
<td>GOLD I-IV</td>
<td></td>
<td>FEV₁ 59; PO₂ 87</td>
<td>HPV, DM, heart disease, SAHS</td>
<td>7.5% LVSD 47.5% LVDD LVH 22.5% A-E &lt;E/A ratio; &gt;I/RT; &gt;EDT</td>
<td>Relationship of LVD with severity of FEV₁</td>
</tr>
<tr>
<td>Malerba et al., 2011&lt;sup&gt;14&lt;/sup&gt;</td>
<td>55/40</td>
<td>GOLD I-IV</td>
<td>59/56</td>
<td>FEV₁ 59; PO₂ 87</td>
<td>HPV, DM, heart disease, SAHS</td>
<td>Prevalence of LVDD 70.9% in COPD vs 27.5% in controls LVDD 59.26%</td>
<td></td>
</tr>
<tr>
<td>Bhattacharyya et al., 2012&lt;sup&gt;15&lt;/sup&gt;</td>
<td>21</td>
<td>GOLD I-IV</td>
<td>63</td>
<td>FEV₁ 25</td>
<td>IHD, HT, DM, hypothyroidism</td>
<td>Myocardial perfusion imaging was performed in patients with LVDD; 50% showed reversible perfusion defects in LV inferol wall</td>
<td></td>
</tr>
<tr>
<td>Macchia et al., 2012&lt;sup&gt;16&lt;/sup&gt;</td>
<td>218</td>
<td>GOLD I-IV</td>
<td>70</td>
<td>FEV₁ 39</td>
<td>No</td>
<td>13.7 LVSD LVDD</td>
<td>Patients with LVD had a tendency to mortality with HR 2.34 (95% CI, 0.99–5.54; P=0.053) at 2 year follow-up</td>
</tr>
<tr>
<td>Freixa et al., 2013&lt;sup&gt;17&lt;/sup&gt;</td>
<td>342</td>
<td>GOLD I-IV</td>
<td>68</td>
<td>FEV₁ 52; PO₂ 74</td>
<td>Previous history of severe heart disease</td>
<td>LVH 6% LVDD 13% LVDD 12%</td>
<td></td>
</tr>
<tr>
<td>Anderson et al., 2013&lt;sup&gt;18&lt;/sup&gt;</td>
<td>93/34</td>
<td></td>
<td>68</td>
<td>FEV₁ 70; SpO₂ 97</td>
<td>HT excluded by 24 h monitoring</td>
<td>The LV mass in COPD was greater than in controls (P&lt;0.17)</td>
<td></td>
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<tr>
<td>Lopez-Sanchez et al., 2013&lt;sup&gt;19&lt;/sup&gt;</td>
<td>71</td>
<td>GOLD III</td>
<td>66</td>
<td>FEV₁ 38.5; PO₂ 68</td>
<td>CAD, valvular heart disease, peripheral artery disease, AF, Charlson index&lt;5 SAHS, ischemic heart disease, DM, HF</td>
<td>LVDD 90%</td>
<td></td>
</tr>
<tr>
<td>Caram et al., 2013&lt;sup&gt;20&lt;/sup&gt;</td>
<td>50</td>
<td>GOLD I-IV</td>
<td>67</td>
<td>FEV₁ 57; SpO₂ 93</td>
<td>Heart disease History of cardiovascular disease</td>
<td>LVDD 88% COPD I-II had more ventricular contractility abnormalities (P&lt;0.05) LVDD associated with severity of FEV₁</td>
<td></td>
</tr>
<tr>
<td>Schoos et al., 2013&lt;sup&gt;21&lt;/sup&gt;</td>
<td>90</td>
<td>GOLD I-IV</td>
<td>69</td>
<td>FEV₁/SpO₂ I: 85/95 II: 58/96 III: 40/95 IV: 26/93</td>
<td>Heart disease History of cardiovascular disease</td>
<td>LVDD 66% The LV ejection volume and diastolic function were inversely correlated with the FEV₁ value, while the CF had a direct relationship (&gt;CF, lower FEV₁)</td>
<td></td>
</tr>
</tbody>
</table>

A: atrial contraction wave on the mitral Doppler flow; LA: left atrium; Am: diastolic velocity of the myocardium obtained by tissue Doppler during atrial contraction; IHD: ischemic heart disease; LVDD: left ventricular diastolic dysfunction; DM: diabetes mellitus; LVSD: left ventricular systolic dysfunction; LVED: left ventricular end-diastolic diameter; LVD: left ventricular dysfunction; E: early diastolic filling wave on the mitral Doppler flow; CAD: coronary artery disease; EDT: early deceleration time of the early ventricular filling wave; Em: diastolic velocity of the myocardium obtained by tissue Doppler during early filling; E/A: ratio between the E wave and the A wave on mitral Doppler flow; Em/Am: ratio between the Em wave and the Am wave; AF: atrial fibrillation; CF: cardiac frequency; FEV₁: forced expiratory volume in the first second; LVEF: left ventricular ejection fraction; CVRF: cardiovascular risk factors; PH: pulmonary hypertension; HR: hazard ratio; ST: systemic arterial hypertension; LVH: left ventricular hypertrophy; HF: heart failure; IC/TLC: ratio between the inspiratory capacity and total lung capacity; HFEF: heart failure with preserved ejection fraction; HIFF: heart failure with reduced rejection fraction; MI: myocardial infarction; CRF: chronic respiratory failure; OR: odds ratio; mPAP: mean pulmonary artery pressure; sPAP: systolic pulmonary artery pressure; PO₂: arterial oxygen pressure; IRT: left ventricular isovolumetric relaxation time; SAHS: sleep apnea–hypopnea syndrome; SpO₂: arterial oxygen saturation; 6MWT: 6-min walk test; RV: right ventricle; LV: left ventricle.

Bhattacharyya et al.<sup>25</sup> conducted a study to determine whether LVDD could be secondary to ischemic lesions that were not detected by conventional studies (electrocardiogram and echocardiography). They included patients with COPD GOLD III and IV with no risk factors for developing LVDD (HT, diabetes mellitus, history of ischemic heart disease or hypothyroidism). Patients diagnosed with LVDD by echocardiography were examined using myocardial perfusion single-photon emission computed tomography imaging. Reversible perfusion defects were found in 7 of the 14 patients studied (50%). On the basis of these findings, the
authors hypothesized that ischemic heart disease in these patients could also be a cause of LVDD. Further studies are required with a larger patient sample to confirm these results.

**Systolic Ventricular Dysfunction**

Left ventricular systolic dysfunction (LVSD) is defined as an LVEF <50%. The reported prevalence of LVSD in patients with stable COPD varies widely, and is related to the exclusion of CVRF in different series (0%–16% in COPD patients without CVRF). The frequency of this abnormality ranges from 8% to 25% in non-selected patients.

Analysis of ventricular deformation or strain and the ventricular deformation rate or strain rate are the new parameters that quantitatively assess the segmental contractility of the LV, irrespective of a normal LVEF. This can be done using tissue Doppler imaging, and more recently, using two-dimensional ultrasound speckle tracking. Sabit et al. found that these parameters were significantly reduced compared to controls in a series of 36 patients with COPD. Schoos et al. reported that these parameters were predictors of mortality by multivariate analysis in a series of 90 patients with COPD of varying severity.

LVSD (systolic and diastolic) was described as a predictor of survival in a cohort of COPD patients undergoing vascular surgery who were followed up for 2 years. Macchia et al. found higher mortality in COPD patients with this abnormality compared non-LVSD patients, although this difference did not reach statistical significance.

**Heart Failure**

Heart failure (HF) may not be suspected in patients with COPD, since the signs and symptoms are common and overlap in both diseases. The prevalence of HF in patients with COPD in different series ranges from 7.1% to 31.3%.

There are 2 patterns of HF: one involving preserved systolic function (HfPEF), more associated with HT, advanced age and extracardiac diseases, and the other involving a reduced ejection fraction (HFpEF), more related with ischemic heart disease.

Rutten et al. reported a prevalence of HF of 20.5% in a cohort of patients with stable COPD. During a 4-year follow-up period, mortality among patients diagnosed with HF was higher, regardless of other factors such as age, sex, history of ischemic heart disease or HT. Although there is little information in this respect, the prognosis in COPD patients with HF appears to be independent of LVEF.

Conversely, COPD is a common comorbidity in patients with HF, and has been described in up to one third of this population. Comorbid COPD has been shown to worsen the prognosis in HF, and COPD exacerbation is known to cause or precipitate acute HF. In a study comparing the impact of different comorbidities on prognosis in 2843 patients diagnosed with HfPEF and 6599 with HFpEF, COPD was the only comorbidity that acted as an independent variable of mortality for both groups. It is remarkable that, despite the importance of COPD as a comorbidity in HF, the latest HF guidelines do not include spirometry among the complementary tests recommended in the management of this entity.

**Conclusions**

LV defects can present in patients with COPD of any severity. The pathophysiological mechanisms involved can act independently or synergically, given the complex heart–lung interaction. While little information is currently available, studies have shown that LV defects in COPD negatively affect parameters as important as exercise capacity, physical activity and mortality. These findings pave the way for future research, and to new diagnostic and therapeutic strategies. However, it should be borne in mind that treatment and prevention of smoking has the greatest impact on the natural history of coexisting COPD and CVD. In view of recent research, it is essential that specialists in other fields contribute to the study of this association to find a comprehensive approach to the disease, in the certainty that COPD does not live (or die) by cor pulmonale alone.

**Conflict of Interests**

None declared.

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**References**


