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ORIGINAL ARTICLE

Left ventricular diastolic dysfunction in patients with chronic obstructive pulmonary disease (COPD), prevalence and association with disease severity: Using tissue Doppler study

Abeer M. Rawy [a,*], **Diaa Fathalla** [b]

[a] *The Department of Chest, Faculty of Medicine, Benha University, Egypt*
[b] *The Department of Cardiology, Faculty of Medicine, Tanta University, Egypt*

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KEYWORDS

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Abstract *Background:* Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. It has some significant extra pulmonary effects that may contribute to its severity in individual patient. Among COPD patients, cardiovascular diseases (CVD) are responsible for approximately 50% of all hospitalizations and 20% of all deaths. Left ventricular diastolic dysfunction (LVDD) is a frequent condition in COPD patients. Inflammation is considered to be one of the systemic manifestations of COPD and provides an alternative hypothesis to explain the relationship between airflow limitation and cardiovascular risk. The present study aimed to assess the prevalence of LV diastolic dysfunction in COPD patients and its relation to the disease severity and presence of inflammatory markers.

Patient and methods: Forty nine (49) COPD patients were included in this study. All patients were subjected to full medical history, physical examination, chest roentgenogram, spirometry, laboratory blood testing for inflammatory mediators (C-reactive protein, matrix metalloproteinase-9 and tissue inhibitor metalloproteinase-1) and Echo Doppler study (conventional and tissue Doppler analysis).

Results: The results showed that 36 COPD patients had LVDD (73.3%). There was a good correlation between LVDD parameters and COPD severity across GOLD stages and inflammatory markers. MMP-9 was statistically high in COPD patient with increasing severity with a

* Corresponding author. Mobile: +20 1001756638.
E-mail addresses: abeer_rawy@yahoo.com (A.M. Rawy), diaa_fathalla@hotmail.com (D. Fathalla).

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p-value < 0.0001. Also LVDD parameters were correlated with MMP-9 (*p*-value < 0.00001). Other inflammatory markers were also correlated to the degree of airway obstruction (FEV1) and presence of LVDD.

Conclusion: There is a high prevalence of LVDD in COPD patients which is associated with increased disease severity and associated with high levels of inflammatory markers (serum MMP-9 and TIMP-1). It is important to exclude decompensated heart failure during COPD exacerbation.

Background

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. It has some significant extra pulmonary effects that may contribute to its severity in individual patient [1]. COPD is considered as a major cause of respiratory morbidity and mortality worldwide and reported to be fourth-leading cause of chronic morbidity and mortality worldwide [2]. The best-recognized comorbidities in COPD include lung cancer, cardiovascular diseases, malnutrition involving primarily the loss and dysfunction of skeletal muscles, osteoporosis, anemia, diabetes, increased gastroesophageal reflux, metabolic syndrome, obstructive sleep apnea, depression, and anxiety [3]. Smoking triggers a local inflammatory response throughout the whole tracheobronchial tree, and pathologic changes, a characteristic of COPD, are found in the proximal large airways, peripheral small airways, lung parenchyma, and pulmonary vasculature. A part from these local effects, smoking may significantly contribute to or cause systemic inflammation including the stimulation of the hematopoietic system with polymorph nuclear leukocyte release, the generation of systemic oxidative stress, and the endothelial dysfunction of peripheral vessels. These systemic effects due to smoking may account for the frequent concurrent presence of other chronic illnesses such as cardiovascular diseases and metabolic disorders in COPD patients [4].

Among COPD patients, cardiovascular diseases (CVD) are responsible for approximately 50% of all hospitalizations and 20% of all deaths [5]. However, population-based studies have suggested that regardless of smoking status, age or sex, a COPD diagnosis increases the risk of cardiovascular morbidity and mortality by approximately two folds [6]. Left ventricular diastolic dysfunction (LVDD) is a frequent condition in COPD patients. Inflammation is considered to be one of the systemic manifestations of COPD and provides an alternative hypothesis to explain the relationship between airflow limitation and cardiovascular risk [7–9]. However, the prevalence of LVDD in COPD patients according to inflammatory markers and disease severity has not yet been established in COPD patients [10]. Given the prognostic implications of cardiovascular disease in COPD, its detection could serve as a guide to appropriate treatment and eventually improve survival.

Echocardiographic evaluation of left and right ventricular function in patients with COPD is really challenging, mainly due to lung hyperinflation but may be improved using tissue Doppler echocardiography (TDE) to study regional systolic and diastolic function, myocardial and annular velocities to allow precise and quantitative measurement of myocardial function and can therefore detect subclinical changes [11].

COPD is a characterized by chronic inflammation with increased levels of inflammatory markers as serum CRP and matrix metalloproteinases (MMPs). MMPs are a family of calcium-dependent, zinc-containing endopeptidases that are structurally and functionally related [12]. They are secreted in an inactive (latent) form, which is called a zymogen or a pro-MMP. These latent MMPs require an activation step before they are able to cleave extracellular matrix (ECM) components [13]. Recent studies have shown that levels of MMPs, especially MMP-9, are elevated in the bronchial alveolar lavage (BAL) fluid from patients with COPD, compared to normal controls [14,15], and high levels of both MMP-9 and its cognate inhibitor TIMP-1 have been found in sputum from chronic bronchitis [16] and correlated with a decrease in lung function [17,18]. MMP-9 may play important physiologic roles in lung extracellular matrix remodeling and repair, and in regulating the lung inflammatory response to injury [19]. However, MMP-9 has also been implicated in the pathogenesis of various lung diseases including chronic obstructive pulmonary diseases [14,20,21].

The present study aimed to assess the prevalence of LV diastolic dysfunction in COPD patients and its relation to the disease severity and with high levels of inflammatory markers (serum CRP, MMP-9 and TIMP-1).

Patients and methods

Patients

Forty-nine (49) COPD patients were recruited from the Pulmonary Outpatient Clinic aged >35 years. The severity was categorized according to FEV1% of predicted referred to GOLD classification [1] to GOLD I (mild including 6 patients), GOLD II (moderate including 25 patients), GOLD III (sever including 15 patients) and GOLD IV (very sever including 3 patients). The exclusion criteria included a primary diagnosis of other respiratory diseases e.g., asthma, restrictive disorders (tuberculosis sequelae or interstitial fibrosis), sleep apnea/hypopnea syndrome or lung cancer. In addition, a primary diagnosis of unstable angina, congestive heart failure (New York Heart Association class III or IV), atrial fibrillation, previous diagnosis, treatment for or evidence of arterial hypertension at the clinical examination and patients with significant valvular heart disease (more than mild aortic or mitral