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ORIGINAL ARTICLE

Lung Function Abnormalities are Highly Frequent in Patients with Heart Failure and Preserved Ejection Fraction

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Background Heart failure with preserved ejection fraction (HFPEF) is the most prevalent form of heart failure in outpatients. Yet, the pathophysiology of this syndrome is unclear and pharmacological treatment does not improve prognosis. Because breathlessness during activities of daily living is the most frequent complaint of patients with HFPEF, we hypothesised that lung function may be often abnormal in these patients due to either a direct effect of HFPEF and/or shared risk factors. In this study we explore the frequency, type and severity of lung function abnormalities in HFPEF.

Methods We measured forced spirometry, static lung volumes, pulmonary diffusing capacity (DL_{CO}) and arterial blood gases in 69 outpatients with newly diagnosed symptomatic HFPEF.

Results We found that 94% of the patients showed abnormalities in at least one of the lung function measurements obtained: spirometry was abnormal in 59%, DL_{CO} in 83% and arterial hypoxaemia was present in 62%. Their severity varied between patients, they were more prevalent in patients with NYHA functional class III/IV, and most often they were undiagnosed and untreated.

Conclusions Lung function abnormalities are very frequent in HFPEF patients. A greater awareness among clinicians may contribute to improve their management and health status.

Keywords Airway obstruction • Diastolic • Diffusing capacity • Dyspnoea • Heart failure

Introduction

Heart failure with preserved ejection fraction (HFPEF) is the most prevalent form of heart failure in outpatients, accounting for approximately 40–50% of patients with the clinical syndrome of heart failure (HF) [1–3]. The diagnosis of HFPEF is clinically challenging and requires the presence of: (1) signs and/or symptoms of HF; (2) normal or mildly abnormal left ventricle (LV) ejection fraction (LVEF > 50%) with LV not dilated; and (3) evidence of structural heart disease and/or diastolic dysfunction [4,5] at rest. The pathophysiology of HFPEF is still unclear. Age and arterial hypertension are its main risk factors but other mechanisms inducing myocardial remodelling, such as valvular heart disease, infiltrative myocardial illnesses, obesity and/or cardiac inflammation, can also contribute [6]. Importantly, and opposed to HF with reduced ejection fraction, pharmacological treatment of HFPEF does not improve prognosis [4].

Breathlessness during activities of daily living is the most frequent complaint of patients with HFPEF. This is thought

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to be the consequence of the increased capillary pressure and subclinical pulmonary oedema that is well described in other forms of HF [7]. However, lung function is not routinely investigated in patients with HFPEF, so the prevalence, type and severity of lung function abnormalities in this population is unknown. Further, patients with HFPEF share several risk factors, such as ageing, smoking and obesity, with other common respiratory diseases. It is likely, therefore, that the latter may occur in these patients independently of HFPEF. If this was the case, breathlessness during activities of daily living in patients with HFPEF may have multiple origins and may be amenable to different therapeutic strategies.

In this study, we hypothesised that lung function abnormalities occur often in patients with HFPEF, that most of them are not diagnosed, and that they can contribute to their symptomatology. To test this hypothesis, we sought to characterise lung function comprehensively in outpatients with newly diagnosed HFPEF in order to determine the frequency, type and severity of lung function abnormalities in this population, as well as their level of under-diagnosis.

Patients and Methods

Study Design and Ethics

This is a pilot and observational study. It complies with the Declaration of Helsinki, it was approved by the Ethics Committee of our institution and all participants provided written informed consent.

Patients

All consecutive outpatients with newly diagnosed HFPEF in the specialised HF clinic of our institution between April 2009 and December 2012 were included in the study. The organisation, procedures and population attended in this HF clinic have been previously published [8]. Exclusion criteria were age < 18 years, life expectancy < 1 year and/or inability to perform complete lung function tests. Breathlessness was graded according to the New York Heart Association (NYHA) functional classification [9].

Heart Function Measurements

The diagnosis of HFPEF was established according to international cardiology guidelines [9,10] and the algorithm proposed by Paulus et al. [5] that combines clinical history, chest X-ray, electrocardiogram, Doppler-echocardiography measurements of diastolic function and type-B natriuretic peptide (BNP) levels. The echocardiographic study was performed on a Vivid 7 (General Electric-Vingmed, Wisconsin, USA) and included: measurement of LV volumes and LVEF by Simpson methodology, left atrial volume (LAVol) and LV mass indexed by body surface, LV filling pressures in mitral valve (E, A) determined by pulsed-Doppler, lateral mitral annulus by tissue-Doppler (E′, A′) and pulmonary veins flow (S/D). Diastolic function was classified into four patterns: normal, impaired relaxation, pseudo-normal or restrictive. The E/E′ index was calculated and the pulmonary capillary wedge pressure (PCWP) and systolic pulmonary arterial pressure were estimated [11].

Lung Function Measurements

Lung function measurements (Jaeger, MasterScreen; Würzburg, Germany) included forced spirometry (FEV_1, FVC) before and after bronchodilation, static lung volumes (TLC, RV) by body plethysmography, carbon monoxide diffusing capacity corrected for haemoglobin (DL_{CO}) by the single breath test, and arterial blood gases (PaO_2, $PaCO_2$, $AaPO_2$; Ciba Corning 800, USA). All measurements were performed according to international recommendations [12,13] and reference values correspond to a Mediterranean population [14,15].

An obstructive ventilatory defect was diagnosed if the FEV_1/FVC ratio was lower than 0.7, and its severity was graded according to the FEV_1 value expressed as % of reference, following international recommendations (mild ≥80%; moderate 50–79%; severe 30–49%; or very severe <30%) [16]. Restrictive ventilatory defects were diagnosed when TLC was lower than 80% of reference (mild 70–80%; moderate 50–69%; severe 40–49%; or very severe <40%). A mixed ventilatory abnormality was defined by the presence of both obstructive and restrictive spirometric patterns. Impairment of DL_{CO} was graded as mild (60–80% reference), moderate (40–59% reference) or severe (<40% reference). Arterial hypoxaemia (PaO_2 ≤80 mmHg) was graded as mild (PaO_2 70–80 mmHg), moderate (PaO_2 60–69 mmHg) or severe (PaO_2 40–59 mmHg).

According to the 2013 GOLD guidelines [17], the diagnosis of COPD was established in individuals with symptoms (dyspnoea, chronic cough and/or sputum production) plus a history of exposure to risk factors for the disease (mostly tobacco smoking) plus the presence of non-fully reversible airflow limitation (FEV_1/FVC <0.7). Non-fully reversible airflow limitation indicates an FEV_1/FVC <0.7 after bronchodilation. Patients not fulfilling these criteria but still showing airflow limitation likely represent the co-existence of other pulmonary diseases and/or the effect of heart failure upon lung function, as discussed below.

Statistical Analysis

Results are shown as mean ± standard deviation, frequency distribution or proportions, as appropriate. The χ^2-test was used to compare categorical variables. Correlations between variables of interest were explored using the Pearson correlation test. A *p*-value lower than 0.05 (two sided) was considered significant.

Results

Demographics and Clinical Data

We originally recruited 79 patients with HFPEF, but 10 of them declined to participate, so lung function measurements were obtained in 69 of them. Patients were mostly elderly females (Table 1) with high body mass index (BMI). Two-thirds of them