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Dynamic pulmonary hyperinflation occurs without expiratory flow limitation in chronic heart failure during exercise☆

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ABSTRACT

To assess the occurrence of tidal expiratory flow limitation (EFL) and/or dynamic pulmonary hyperinflation (DH) in chronic heart failure (CHF) during exercise 15 patients with stable systolic CHF, aged 69 ± 6 yr, underwent pulmonary function testing and incremental cardio-pulmonary exercise testing. They subsequently performed constant load exercise testing at 30, 60 and 90% of respective maximum workload. At each step the presence of EFL, by negative expiratory pressure technique, and changes in inspiratory capacity (IC) were assessed. Ejection fraction amounted to 36 ± 6% and $\dot{V}_{O_2}$, peak (77 ± 19% pred.) was reduced. EFL was absent at any step during constant load exercise. In 6 patients IC decreased more than 10% pred. at highest step. Only in these patients TLC, FRC, RV $FEF_{25-75\%}$ and DL_{CO} were decreased at rest. $\dot{V}_{O_2}$, peak correlated with DL_{CO}, TLC and IC at rest and with IC ($r^2 = 0.59$; $p < 0.001$) and decrease in IC ($r^2 = 0.44$; $p < 0.001$) at 90% of maximum workload. During exercise CHF patients do not exhibit EFL, but some of them develop DH that is associated with lower $\dot{V}_{O_2}$, peak.

1. Introduction

Patients with chronic heart failure (CHF) exhibit reduced tolerance to physical effort due to the occurrence of unbearable lower limb muscle fatigue and/or dyspnea. An inadequate increase of cardiac output during exercise can explain the former, while the latter, apart from an early onset of anaerobic metabolism with higher ventilatory request, might also arise from abnormalities on either gas exchange or pulmonary mechanics caused by the presence of secondary lung involvement, the so called “cardiac lung”.

Chronic left ventricular systolic dysfunction, today more frequently due to ischemic or idiopathic cardiomyopathy, may influence lung function by increasing lung stiffness and airflow resistance with consequent both restrictive and obstructive ventilatory defect (Agostoni et al., 2002; Ries et al., 1986).

In fact, a reduction of total lung capacity (TLC) and functional residual capacity (FRC) may occur in CHF patients, caused by greater heart size, decreased static lung compliance, due to chronic interstitial fluid accumulation and fibrosis, and reduced inspiratory muscles strength. Moreover, airway narrowing can be observed because of peri-bronchiolar cuffing, greater cholinergic bronchial tone and airway hyper-responsiveness in CHF patients (Ries et al., 1986). In addition, breathing at lower FRC with risk of closure of dependent small airways during tidal breathing (Torchio et al., 2006), can further reduce expiratory flow reserve at low lung volumes, favoring tidal expiratory flow limitation (EFL) that actually was reported in these patients when supine (Duguet et al., 2000; Pecchiari et al., 2009).

Moreover, besides a lower lung diffusion capacity, ventilation/perfusion mismatch may alter pulmonary gas exchange in CHF patients (Guazzi, 2000).

Such abnormalities have repeatedly been shown in these patients at rest, but could be mostly relevant in determining different exercise tolerance and maximal physical performance in CHF patients who exhibit similar baseline systolic dysfunction.

The purpose of the present study was to establish the occurrence of EFL and dynamic pulmonary hyperinflation during exercise in patients suffering from stable systolic CHF and see whether the changes in lung mechanical properties were associated with the reduction of exercise capacity.

☆ The authors disclose any relationship with industries and financial association from within the past 2 yrs that might pose a conflict of interest in connection with this work.

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2. Methods

2.1. Subjects

Patients with CHF secondary to chronic ischemic or idiopathic cardiomyopathy were consecutively admitted to our Laboratory. The diagnosis of CHF was based on a complete clinical evaluation, laboratory testing, trans-thoracic echocardiography and coronary angiography. The respective functional class was established according to the New York Heart Association (NYHA) scale. Inclusion criteria required a left ventricular ejection fraction at rest less than 40%, measured by trans-thoracic echocardiography within 3 months preceding the study, clinically stable conditions (defined as no change in symptoms, clinical status and drug administration in the last 3 months), capacity of performing an exercise test, and absence of pulmonary, endocrine, hematologic or neuromuscular diseases.

According to the study design, each patient underwent pulmonary function testing, symptom-limited incremental cardiopulmonary exercise test and 3 consecutive constant-load exercise tests at 30%, 60% and 90% of respective maximum workload to assess tidal EFL by the negative expiratory pressure (NEP) technique and measure inspiratory capacity (IC) changes.

The study was approved by the local Ethic Committee (number 10-00274) and each patient gave a written informed consent.

2.2. Pulmonary function testing

On the first day of the study in each patient who wore a noseclip and breathed through a flanged mouthpiece, slow vital capacity (VC) and IC were measured twice using a bell spirometer at rest and in sitting position. Then, 3 acceptable and reproducible maximal full expiratory and inspiratory flow-volume curves were performed to obtain forced vital capacity (FVC), maximal expiratory volume in the first second (FEV_1), peak expiratory flow (PEF) and maximal expiratory and inspiratory flow rates. Subsequently, a multi-breath helium dilution technique in a closed circuit was used to measure functional residual capacity (FRC) and then total lung capacity (TLC) and residual volume (RV) were computed. Furthermore, lung diffusion capacity to carbon monoxide (DL_{CO}), alveolar volume (VA) and coefficient of diffusion (K_{CO}), was measured twice and corrected for hemoglobin. In each circumstance the best values were retained for analysis. All tests were performed according to the ERS-ATS recommendations (Miller et al., 2005), using BIOMEDIN instruments (Padoa, Italy). Predicted values of lung function parameters were those proposed by European Community for Coal and Steel (ECCS) (Quanjer et al., 1993) and the predicted values of IC were from Tantucci et al. (2006).

2.3. Cardiopulmonary exercise test

A symptom-limited, incremental cardiopulmonary exercise test (CPET) was performed by an electronically braked cycle-ergometer (60 rpm) with breath-by-breath in- and expiratory gas analysis and airflow measurements (Med Graphics cardio-metabolic system, St. Paul, MN). The system was calibrated with a gas mixture of known concentration before each test. The power was increased at a rate of 10 and 20 W/min according to the NYHA class to keep the CPET duration between 8 and 15 min. The first minute of pedaling was unloaded. All routine cardiopulmonary and respiratory parameters were measured during exercise and the anaerobic threshold was obtained by the V-slope method (Med Graphics cardio-metabolic system, St. Paul, MN). The predicted values were those obtained by the equations from Hansen et al. (1984) and Neder et al. (2001). Peripheral oxygen hemoglobin saturation was monitored by a pulse-oxymeter. ECG (12 leads) was recorded continuously and arterial blood pressure was measured every 2 min by a standard mercury sphygmomanometer. The patients were encouraged to exercise to exhaustion which occurred because of intolerable leg fatigue and/or dyspnea.

2.4. Constant-load exercise test

On the following day every patient performed a constant-load exercise test on the cycle ergometer in 3 consecutive steps, each lasting 6 min or at least 4 min, at a workload equal to 30%, 60% and 90% of the individual maximum workload achieved during the previous CPET. In the last minute of each step, a negative expiratory pressure (NEP) of 5 cmH_2O was applied at the mouth, while the patient was breathing through a flanged mouthpiece in a heated pneumotacograph (3830A Hans-Rudolph, Kansas City, MO) to check the occurrence of tidal EFL, as described by Koulouris et al. (1995).

Briefly, if the expiratory flow during NEP is always higher than the flow of the previous control expiration, tidal EFL is absent, while if part or all of the expiratory flow during NEP impinges on the flow of the previous control expiration, partial or complete tidal EFL occurs (Koulouris et al., 1995). Both automatic and visual analysis of flow tracings were performed to assess tidal EFL in different NEP tests. The NEP test was performed at least twice when patients were on the bicycle both at rest and at each step.

Subsequently, always at the end of each step, IC was measured twice, asking patients to perform a full inspiration. Assuming no change in TLC during exercise (Johnson et al., 2000), any change in IC is expected to reflect an equal and opposite change in FRC. Such approach has been validated in COPD patients (Yan et al., 1997). Therefore, any significant decrease in IC (more than 10% of predicted) was considered as clue of dynamic pulmonary hyperinflation. The mean IC value obtained in each step was used for analysis.

2.5. Statistical analysis

Data are presented as mean ± standard deviation. Unpaired *t*-tests were used for comparison of pulmonary function and exercise parameters. Correlation and determination coefficients were calculated by linear regression analysis. Stepwise (backward) multivariate regression analysis was performed using variables significantly related with oxygen uptake at peak exercise ($\dot{V}_{O_2}$, peak) at the univariate analysis. A p value <0.05 was considered as significant. All statistical analyses were performed using SPSS software (version 12.0.1, SPSS Inc. Chicago, IL)

3. Results

Fifteen patients (13 male) were enrolled in the study of whom 8 suffered from ischemic cardiomyopathy and 7 from idiopathic dilated cardiomyopathy. Nine were ex-smokers, one current smoker and 5 non-smokers. All patients were treated with selective beta-1 blockers.

Five were in NYHA 1 functional class and 10 in NYHA 2 functional class. The resting left ventricular ejection fraction was 36.1 ± 6.0%.

Anthropometric and functional parameters at rest and during exercise are shown in all patients in Table 1. Among baseline pulmonary parameters, on average, only DL_{CO} was reduced (<80% of predicted). Mean $\dot{V}_{O_2}$, peak was less than 80% of predicted and mean work efficiency ($\dot{V}_{O_2}$/watt slope) was lower than 10 ml/min/W.

Thirteen patients stopped exercise because of leg discomfort/fatigue, one because of leg discomfort and dyspnea and one because of thoracic pain. According to the Weber classification, 4 were in class A, 2 in class B, 8 in class C and one in class D,