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Inspiratory loading and limb blood flow in COPD: The modulating effects of resting lung hyperinflation

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ABSTRACT

Inspiratory resistive loading (IRL) may have deleterious cardiocirculatory effects leading to poor peripheral perfusion in severely-hyperinflated patients with COPD. Nineteen patients (13 severely-hyperinflated with inspiratory capacity/total lung capacity ratio ≤ 0.28) underwent calf blood flow (CBF) measurements by venous occlusion plethysmography at rest and during IRL at 60% maximal inspiratory pressure. Severely-hyperinflated patients had lower resting CBF and greater calf vascular resistance (CVR) than moderately-hyperinflated patients ($p < 0.05$). All severely-hyperinflated patients had markedly reduced CBF ($p = 0.01$). Opposite to our main hypothesis, however, IRL did not further reduce CBF in these patients ($p > 0.05$). Conversely, it significantly decreased CBF and increased CVR in moderately-hyperinflated patients; in fact, end-trial CBF and CVR did not differ between the groups ($p > 0.05$). In conclusion, marked impairments in resting appendicular blood flow in severely-hyperinflated patients with COPD were seen only after acute IRL in less hyperinflated patients. These findings set the stage for studies investigating the effects of lung deflation on peripheral hemodynamics in patients with severe hyperinflation.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by varied abnormalities on the airways, lung parenchyma, and pulmonary vasculature which might have important negative cardiocirculatory consequences (O'Donnell et al., 2014; Boerrigter et al., 2012; Tyberg et al., 2000). In fact, there is growing recognition that the cardiocirculatory consequences of COPD are not only relevant to patients' functioning but also to mortality across the spectrum of disease severity (Sin and Man, 2005).

Central hemodynamic consequences of lung hyperinflation (Jörgensen et al., 2003; Jorgensen et al., 2007; Barr et al., 2012; Watz et al., 2010) and sympathetically mediated peripheral vasoconstriction, secondary to fatiguing contractions of respiratory muscles (St Croix et al., 2000; Sheel et al., 2001), may compromise peripheral blood flow in COPD. For instance, reduced right ventricle (RV) preload and increased RV afterload due to lung hyperinflation are known to negatively influence stroke volume and cardiac output (Jorgensen et al., 2007; Barr et al., 2012; Watz et al., 2010). In fact, static hyperinflation (inspiratory capacity/total lung capacity; IC/TLC) showed stronger associations with cardiac chamber sizes than airway obstruction or lung diffusion capacity. Patients with more severe lung hyperinflation also showed significantly impaired left ventricular diastolic filling pattern and myocardial performance (Watz et al., 2010). In addition to these negative effects of hyperinflation on central hemodynamics, volitional efforts against an inspiratory resistance have been found to increase vascular resistance and reduce resting calf blood flow (CBF) in COPD (Chiappa et al., 2014). Thus, in similarity with heathy subjects (St Croix et al., 2000; Sheel et al., 2001), fatiguing voluntary inspiratory efforts against resistance may increase muscle sympathetic nerve activity thereby decreasing blood flow to the resting limb in these patients.

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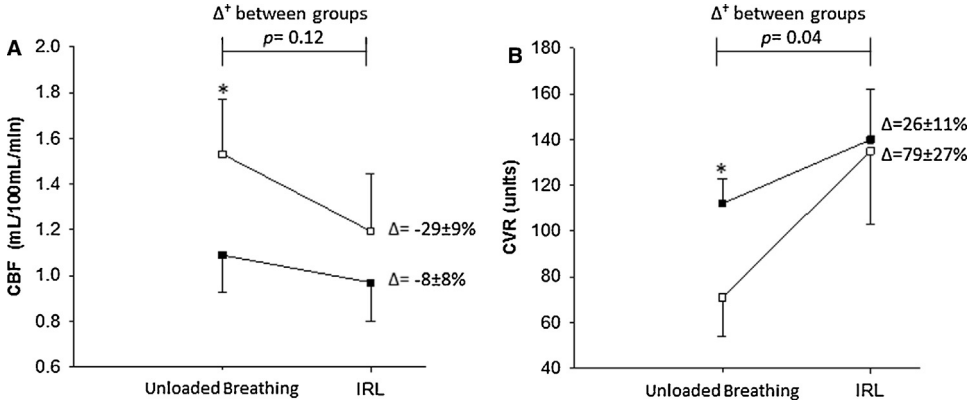

Fig. 1. Calf blood flow (CBF) (*panel A*) and calf vascular resistance (CVR) (*panel B*) at baseline and at the end of inspiratory resistive loading (IRL) in severely- (closed squares) and moderately-hyperinflated (open squares) patients with COPD.
Values in mean ± SE. † Δ = End-Baseline. *p < 0.05 for intergroup comparisons at a given point.

Considering the key role played by hyperinflation in overloading the respiratory muscles in patients with COPD (O'Donnell et al., 2014), this phenomenon, if present, would be particularly pronounced in more hyperinflated patients.

The aim of the present study, therefore, was to assess CBF during spontaneous breathing and inspiratory resistive loading (IRL) in moderate to severe COPD patients presenting with varied degrees of resting lung hyperinflation. We specifically hypothesized that, under these circumstances, CBF would be more reduced (and reciprocally calf vascular resistance (CVR) increased) in severely-hyperinflated patients with COPD. Understanding the deleterious effects of hyperinflation on the cardiovascular system is key to develop evidence-based strategies to mitigate the life-threatening cardiocirculatory consequences of COPD.

2. Material and methods

2.1. Patients

This study enrolled a convenience sample of consecutive COPD patients. All patients had clinical and functional diagnosis of COPD (forced expiratory volume in 1s (FEV_1)/forced vital capacity (FVC) < 0.7 and post-bronchodilator FEV_1 < 80% predicted) presenting with a long history of smoking (>20 pack-years). Patients were ex-smokers for at least 6 months and had stable disease with no exacerbations in the preceding 8 weeks. Patients were treated according to the current recommendations. (Vestbo et al., 2013) Main exclusion criteria were: current or previous cardiac disease (including previous acute coronary syndrome or known diagnosis of heart failure), long term oxygen therapy or arterial oxygen saturation <89% at rest, treatment with oral corticosteroids in the previous 3 months, neuromuscular disease, peripheral arterial disease, cancer or pulmonary rehabilitation in the preceding 12 months. The project was approved by Institutional Research Ethics Committees (No. 194.217) and all participants signed an informed consent.

2.2. Lung function tests

Spirometry (including IC measurements), body plethysmography (residual volume (RV) and TLC) and measurements of transfer factor (DL_{CO}) were performed using automated testing equipment (Eric Jaeger™, GmbH, Wüerzburg, Germany). According to IC/TLC ratio ("inspiratory fraction"), patients were separated into severely-hyperinflated (≤0.28) or moderately-hyperinflated groups, respectively (Albuquerque et al., 2006). Maximal

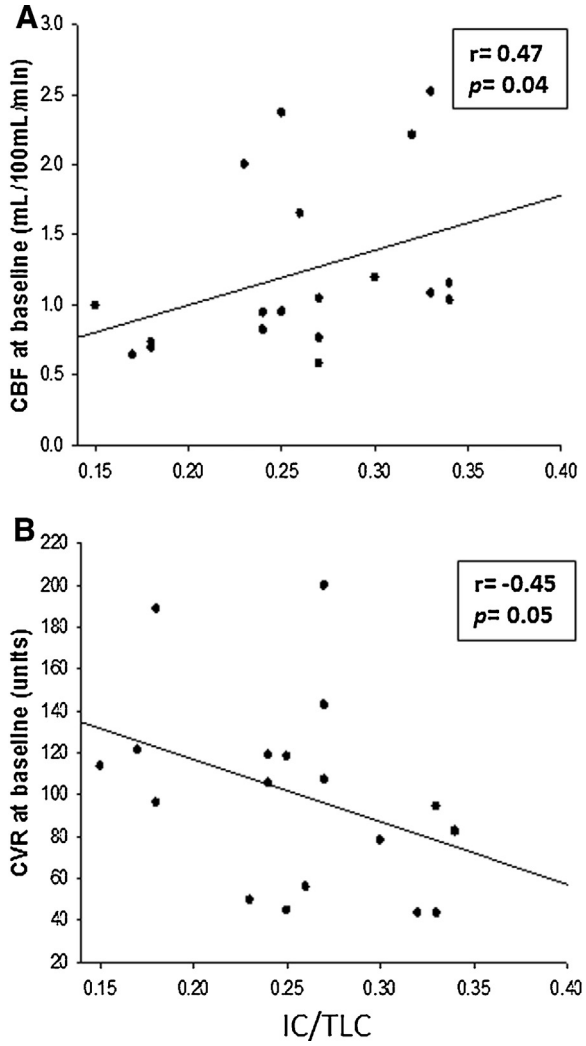

Fig. 2. Association between baseline calf blood flow (CBF) (*panel A*) and calf vascular resistance (CVR) (*panel B*) with lung hyperinflation (inspiratory capacity/total lung capacity; IC/TLC).

inspiratory pressure (MIP, cmH_2O) against an occluded airway with a minor air leak (2 mm) was obtained from RV (MVD-300™, Microhard System, Globalmed, Porto Alegre, Brazil). The highest pressure of five measurements was recorded (at least three reproducible, i.e.<10% between-maneuvers variation).