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Title: Inspiratory resistive loading exacerbates calf vasoconstriction in patients with coexisting COPD-CHF compared to COPD and healthy controls

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Body: Rationale: Sympathetic overstimulation is a marker of chronic heart failure (CHF) and might also be present in advanced chronic obstructive pulmonary disease (COPD). Inspiratory resistive loading (IRL) can trigger a sympathetically-mediated metaboreflex which increases peripheral vascular resistance, leading to impaired blood flow. Coexistence of COPD and CHF is likely to potentiate these abnormalities. Objective: To investigate the effects of IRL on calf blood flow (CBF) and resistance (CVR) in patients with COPD presenting or not with CHF as a co-morbidity and healthy controls. Methods: Twelve patients with COPD on isolation (FEV_1= 42 ± 14 % pred), 10 patients with coexisting COPD-CHF (FEV_1= 46 ± 10 % pred, left ventricular ejection fraction < 45%) and 10 age-matched controls breathed through an inspiratory resistance at 60% of maximal inspiratory pressure (MIP) to task failure. CBF was measured by venous occlusion plethysmography. Results: COPD-CHF had significantly lower MIP than COPD and controls ($p<0.05$). The former group, however, stopped earlier the IRL trials (185 ± 35 s vs. 284 ± 82 s vs. 365 ± 88 s, respectively; $p<0.01$). COPD-CHF had lower CBF and higher CVR in this former group. In addition, IRL led to greater decrements in CBF and increases CVR in COPD-CHF compared to either COPD or controls ($p<0.05$). CVR during IRL was inversely related to MIP across the groups ($r= -0.66$, $p<0.01$). Conclusions: CHF as a co-morbidity of COPD exacerbates peripheral vasoconstriction induced by inspiratory muscle overloading. This might contribute to further impair muscle blood flow during exercise in this patient sub-population.