Impaired tissue O2 delivery during exercise in chronic obstructive pulmonary disease: does coexisting heart failure worsen peripheral muscle fatigue ?

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Résumé

Background. In healthy humans, impaired tissue O2 delivery is commonly associated with exaggerated exercise-induced peripheral muscle fatigue (Amann et al., 2006). From a clinical standpoint, chronic obstructive pulmonary disease (COPD) and heart failure (HF) are two diseases that frequently coexist (Rutten et al., 2005). Each condition may impair muscle O2 delivery through distinct respiratory or cardiocirculatory mechanisms. In COPD, this is primarily due to impaired gas exchange and ventilatory mechanical abnormalities (O'Donnell et al., 2019), while it stems from reduced cardiac output and peripheral vasoconstriction in HF (Del Buono et al., 2019). Importantly, those conditions may synergistically interact to further compromise O2 transport (Neder et al., 2019), as evidenced by lower muscle blood flow and oxygenation *vs* isolated diseases (Oliveira et al., 2016). It remains unknown, however, whether such abnormalities may lead to exacerbated peripheral muscle fatigue during exercise in COPD-HF overlap.

Methods. Ten patients with COPD and HF with reduced left ventricular ejection fraction ((LVEF), 8 males, 68±8 years, forced expiratory volume in 1s=71±20% predicted, LVEF= 41±4%) and 10 patients with COPD individually matched for sex, age and lung function (LVEF=60±2%) underwent an incremental cycling exercise test to determine peak work rate (WRPEAK). On a separate visit, patients with COPD-HF performed a constant work-rate exercise test (70% WRPEAK) to symptom limitation (TLIM); COPD patients exercised up to TLIM of their matched COPD-HF counterpart. Arterialized blood gas, leg discomfort and *vastus lateralis* muscle oxygenation were respectively assessed by earlobe blood samples,

*Intervenant

Borg CR-10 scale and near-infrared spectroscopy. The pre-to-post exercise fall in *quadriceps* force response to magnetic nerve stimulation (twitch, Tw*quad*) which quantified the extent of muscle fatigue, was normalized to the external work performed (kJ=(work rate (W) TLIM (s))/1000).

Results. Patients with COPD-HF showed lower exercise tolerance than COPD (e.g., WRPEAK= 70±33 *vs* 117±47 W, respectively; p= 0.020). Consequently, they exercised at lower WR (49±23 *vs* 82±33W) during constant-load cycling (TLIM=468±302s, external work= 19 (20) *vs* 32 (21)kJ; p=0.243). Of note, end-exercise arterialized O2 saturation was similar between groups (94±2% in both; p=0.870). Patients with COPD showed numerically larger increase in total hemoglobin concentration (20.7±7.3 *vs* 16.5±9.3 μmol; p=0.294) and significantly greater decrease in tissue saturation index (-9±5 *vs* -3±6%; p=0.042). Greater post-exercise Tw*quad* fall (-1.55 (1.47) *vs* -0.60 (0.57)%/kJ; p=0.053) and leg discomfort (6±2 *vs* 4±2; p=0.016) were observed in COPD-HF.

Discussion. Our results suggest that coexisting heart failure is associated with lower hyperemic response and O2 extraction capacity on exertion in COPD which may worsen skeletal muscle fatigability, and overall, impede exercise tolerance in COPD-HF. Importantly, these preliminary findings were observed at strictly similar O2 saturation implying that between-group differences in muscle fatigue may thus not be attributed to "hypoxic" hypoxia.

Perspectives. Interventions aimed at increasing perfusive and/or diffusive O2 delivery to lessen peripheral muscle fatigue may prove useful to enhance exercise tolerance in COPD-HF overlap. The potential, beneficial effects of O2supplementation on these outcomes is currently under investigation in our research group.

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