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Title: Blunted muscle angiogenic response after exercise training in COPD patients

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Body: In chronic obstructive pulmonary disease (COPD) patients, the skeletal muscle impairment reduces the exercise capacity. Systemic factors (i.e oxidative stress, low grade inflammation ...) have been incriminated. Then, as for the muscle oxidative fibers, the muscle angio-adaptive response to training could also be blunted in COPD, like in other chronic conditions. Therefore, we aimed to compare the muscle functional response, myofiber remodeling and angio-adaptations to training in COPD patients and sedentary healthy subjects (SHS). 21 COPD patients and 23 SHS completed a 6-week rehabilitation program based on individualized moderate-intensity endurance and resistance training. Histomorphological muscle analysis and measurements of pro-angiogenic vascular endothelial factor-A (VEGF-A) and antiangiogenic thrombospondin-1 (TSP-1) were conducted before and after training. Both COPD patients and SHS improved their peak oxygen consumption (respectively, $+0.96 \pm 2.4$ and $+2.9 \pm 2.6$ mL/kg/min, $p < 0.001$) and muscle endurance (respectively, $+65\%$ and $+108\%$, $p < 0.001$), although improvements were lower in COPD patients (group-time interaction: $p < 0.05$ and $p = 0.06$ respectively). Whereas the capillary-to-fiber ratio (C/F) and the angio-adaptive VEGF-A/TSP-1 ratio increased in COPD patients and SHS (C/F: $p < 0.01$ and VEGF-A/TSP-1: $p < 0.05$), the improvement in C/F was significantly reduced in COPD patients vs. SHS ($p < 0.05$), and no fiber type switch occurred in patients. Absolute changes in C/F and in VO_{2SL} were correlated ($r = 0.51$, $p < 0.05$). The angiogenic response may drive the functional improvements. In addition to a lack of fiber switch, the angiogenic response to training was blunted in COPD patients.