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Title: Muscle phenotypes in COPD patients: An exploratory cluster analysis

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Body: Peripheral muscle dysfunction is a key outcome in chronic obstructive pulmonary disease (COPD) and has been well characterized by reductions in fiber cross-sectional area (CSA) and type I fiber proportion. However, it is currently unknown if these two features are linked and consequence of common factors (like the oxidative stress), because of a great heterogeneity in the patients muscle histo-morphology, which overlaps with sedentary healthy subjects (SHS). We therefore tested whether the clustering of COPD patients and SHS would reveal reductions in fiber CSA and type I proportions in distinct or same sub-groups. Then, we aimed to model the occurrence of fiber atrophy and/or reduced type I fiber proportion in a decision tree. Principal component analysis of functional and histo-morphological muscle parameters revealed two clusters of COPD patients. As compared with the two clusters of SHS, both clusters had a reduction in the type I fiber proportion ($p<0.05$). Reduced fiber CSA and increased protein carbonylation were found only in the most severe cluster of patients ($p<0.05$). Yet, clusters of patients had the same age (60.4±8.8 yrs vs. 60.8±9.0 yrs; $p=0.87$). Last, an algorithm including 6-minute walking distance, ventilatory threshold, and body mass index accurately classified 57% of the individuals according to fiber atrophy and/or type I fiber regression. These clusters may indicate distinct COPD phenotypes, as they are related to clinical outcome (muscle/fiber atrophy). Moreover, patho-biological mechanism and time course may have differed in the two clusters of COPD patients. Decision trees may improve the identification of COPD patients with distinct muscle features.