

Project title: Skeletal muscle determinants of functional deterioration in COPD: new biomarkers for evaluating disease severity and acute exacerbations?

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Chronic obstructive pulmonary disease (COPD) is a major burden for health systems and may negatively affect the patients' health status, quality of life and life expectancy. **Skeletal muscle dysfunction** is a major contributor to exercise intolerance, a key feature of the disease, and it is associated with worse outcomes. The pathogenesis of skeletal muscle dysfunction remains unclear, and the potential use of peripheral biomarkers to assess the **severity of COPD** and its **acute exacerbations** has not been investigated. The issue is relevant because COPD is a chronic and progressive disease characterized by frequent acute exacerbations, which are the main cause of progressive clinical deterioration in patients.

Muscle biopsy data explaining the underlying molecular mechanisms of muscle impairments induced by acute exacerbations of COPD are scarce, mainly based on cross-sectional study designs, and inconsistent results have been reported. Longitudinal studies are lacking.

The main aim of the present study is to identify skeletal muscle determinants of functional impairment in COPD patients with different disease severity and acute exacerbations, in order to assess their potential use as biomarkers of COPD severity and acute exacerbations.

Biomarkers of skeletal muscle oxidative metabolism, mitochondrial respiration, presence of inflammation, oxidative stress, muscle atrophy and skeletal muscle wasting will be assessed.

Biomarkers of impairment will be compared between patients with different disease severity and a group of controls (**cross-sectional study**) and, in each patient, at baseline and during acute exacerbations (**longitudinal study**). This approach will help to elucidate the pathophysiological mechanisms of impairment and, ideally, to define, personalized therapeutic or rehabilitation interventions in the future.

