Mitochondrial oxidative capacity and oxidative stress in chronically inactive elderly patients

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ï»¿Adverse health outcomes in the elderly population commonly result in extended periods of immobilization. Prolonged bed rest periods exacerbate the natural reduction in skeletal muscle mass and function that occurs with ageing (English & Paddon-Jones, 2010).This results in sarcopenia, insulin dysfunction and increased morbidity and mortality. Simultaneously, mitochondrial oxidative capacity is reduced and an increase in oxidative stress from accumulated reactive oxygen species (ROS) is observed (Kalyani *et al.*, 2014). However, the molecular mechanisms underlying this decrease in mitochondrial function are unknown. The aim of this study was to investigate the protein levels of markers of mitochondrial oxidative phosphorylation and ROS production in an elderly population (60-80 years old) following a 7-day bed rest model of inactivity.

Thirteen elderly patients (aged 67±1.45 years, BMI 26.3±0.7) were admitted three days preceding the 7 days of bed rest for dietary control, exercise and body composition testing. On day one of inactivity, patients underwent muscle biopsies and Oral Glucose Tolerance Tests (OGTT). These measures were repeated at the end of the inactivity period and following 7 days of rehabilitation. Mitochondrial respiration was assessed in permeabilized muscle fibres using an OROBOROS® O2K oxygraph. Markers of mitochondrial oxidative phosphorylation (Mitochondrial Oxidative Phosphorylation System, OXPHOS, primary anti-body cocktail) and ROS production (Superoxide dismutase 2, mitochondrial (SOD2) and Catalase) were assessed using Western blotting.

Seven days of bed-rest induced specific decreases in OXPHOS flux, which were restored after 7 days of rehabilitation. The protein expression levels of the members of the electron transport chain CV–ATP5a, CIII–UQCRC2 and CI–NDUFB89 were not affected by bed-rest or rehabilitation. Similarly, the protein expression levels of SOD2 and Catalase, which play a protective role against ROS damage, were not affected by bed-rest or rehabilitation.

Chronic inactivity in elderly patients decreases mitochondrial respiration without altering mitochondrial-associated protein expression. This might reflect a delay between the acute effects of inactivity on oxidative capacity and longer-term impacts on the mitochondrial oxidative machinery. In addition, qualitative changes in the OXPHOS process, or regulators of mitochondrial respiration (*e.g.* NOS and NO) might partly account for the observed decrease in respiration rates. Identifying the pathways that contribute to skeletal muscle dysfunction is essential to preserve mitochondrial oxidative capacity and reduce oxidative stress during extended periods of inactivity.

English KL & Paddon-Jones D. (2010) Protecting muscle mass and function in older adults during bed rest. *Current Opinion in Clinical Nutrition and Metabolic Care* **13:** 34-39.

Kalyani RR, Corriere M & Ferrucci L. (2014) Age-related and disease-related muscle loss: the effect of diabetes, obesity, and other diseases. *The Lancet Diabetes & Endocrinology* **2:** 819-829.