PADUA DAYS ON MUSCLE AND MOBILITY MEDICINE 2026

International Conference

March 3rd to 6th Euganean Thermae and Padua, Italy

LONGITUDINAL STUDY IN LOW AND HIGH FUNCTIONING OLDER HEALTHY ADULTS: PRELIMINARY DATA ON PLASMA METABOLOMICS AND MUSCLE DNA METHYLATION

Lecture of Xiaoxiao Wen, Jinying Zhao, Stephen Anton, Christiaan Leeuwenburgh

University of South Florida, Institute on Aging University of Florida, Gainesville, USA.

Mobility loss in older adults reduces quality of life and increases risks of falls, hospitalizations, and mortality. While low-functioning (LF) older adults experience faster mobility decline than their high-functioning (HF) peers, the biological mechanisms driving this remain unclear. Mitochondrial dysfunction is one hallmark linked to functional decline, but emerging evidence suggests that disrupted iron regulation, marked by altered iron-handling proteins, contributes to mitochondrial damage, senescence and inflammation. Although iron accumulation in aging muscle is emerging, its longitudinal impact on ferroptosis and activation of senescence pathways as well as on physical function remains understudied. The “Muscle Iron Flow Study” is a prospective, longitudinal observational study which enrolled low-functioning and high--functioning older adults (N= 114; age 75.8 ± 3.2 years, 64.9% female) and follows them for three years to examine links between ferroptosis, senescence, mitochondrial function, and physical performance. Functional capacity (Low vs High) was determined by Geriatric functional tests including walking speed. Biological blood samples (RNA, DNA, plasma serum), physical function tests, and behavioral measures (diet, activity, sleep, pain, medication use) were collected at baseline and annually, and muscle biopsies were conducted at baseline and year three. Cohort analysis between the Low vs. High functioning older adults have been initiated and functional, and biological measures (i.e., muscle DNA-methylation and plasma metabolomics) associations have been analyzed, but no longitudinal measures or outcomes have been completed. This study is among the first to investigate ferroptosis, senescence, mitochondrial dysfunction and various novel omics platforms and how they may contribute to future changes in physical function in LF and HF older adults. By integrating detailed molecular and functional assessments, the study aims to establish a foundation for examining how disrupted iron handling and mitochondrial health influence mobility trajectories. Findings may inform future biological targets to aid behavioral interventions to maintain mobility in our aging populations.

Keywords: *mitochondrial dysfunction, iron regulation, ferritin, inflammation, physical function, aging, muscle strength.*