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Contribution ID: 386

Type: 1 - Scientific Poster

Mediating role of mitochondrial energetics on the associations between physical activity and muscle function in older adults: a moderated mediation analysis by cancer survivorship in the Study of Muscle, Mobility and Aging (SOMMA)

Background: Habitual physical activity (PA) is associated with preserved physical function in older adults, but underlying biological mechanisms remain unclear. We examined whether skeletal muscle mitochondrial energetics mediated associations of PA with concurrent and future physical function and if pathways differed by cancer survivorship status.

Methods: Participants were 879 adults aged ≥ 70 years enrolled in the Study of Muscle, Mobility and Aging (SOMMA). Wrist-worn accelerometry collected over 7 consecutive days captured sleep, inactivity, light PA (LPA), moderate-to-vigorous PA (MVPA) and steps. Physical function outcomes included 4m walking speed, 1RM leg strength, leg power, and grip strength. Mitochondrial energetics were assessed via in vivo ^{31}P -magnetic resonance spectroscopy ATPmax and ex vivo high-resolution respirometry maximal oxidative phosphorylation (max OXPHOS). Structural equation modeling examined cross-sectional and 3-year longitudinal mediation and moderated mediation associations, adjusting for demographic and clinical covariates. Cancer survivorship status was tested as a moderator.

Results: Cross-sectionally, MVPA and steps were associated with walking speed, leg strength and power, with both ATPmax and max OXPHOS mediating these associations (indirect effect β $p < 0.05$). Longitudinally, baseline MVPA and steps were only associated with future walking speed; each 30 min/d MVPA and 1,000 steps/d increase predicted a 0.012 m/s faster walking speed 3-years later ($\beta = 0.04$ SD; 1 SD = 0.3 m/s). Although baseline MVPA and steps were associated with ATPmax and max OXPHOS, neither mitochondrial measure mediated associations with future walking speed (indirect effect β $p > 0.05$). Results were unchanged after adjustment for D3Cr muscle mass. Cancer survivorship status did not modify the mediation pathways.

Conclusion: Higher PA was associated with improved walking speed 3-years later in older adults, but skeletal muscle mitochondrial energetics did not explain the longitudinal association. Mitochondrial energetics appear more strongly related to current rather than future physical function, suggesting alternative mechanisms underlie long-term functional benefits of habitual PA.

Keywords

sarcopenia; accelerometry; respirometry; longitudinal

Conflict of Interest & Ethical Approval

yes

Abstract submitters declaration

yes

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Session Classification: Poster Session