The relationship of walking speed metrics to phosphorus magnetic resonance spectroscopy (^{31}P-MRS) bioenergetic measurements in the Baltimore Longitudinal Study of Aging (BLSA)

Seongjin Choi[1], David A. Reiter[2], Kenneth W. Fishbein[2], Eleanor M. Simonsick[1], Richard G. Spencer[2], and Luigi Ferrucci[3]

[1]*Translational Gerontology Branch, NIH/National Institute on Aging, Baltimore, Maryland, United States,* [2]*Laboratory of Clinical Investigation, NIH/National Institute on Aging, Baltimore, Maryland, United States,* [3]*Intramural Research Program, NIH/National Institute on Aging, Baltimore, Maryland, United States*

Target Audience: Researchers in the field of geriatric bioenergetics and clinical applications of ^{31}P MRS

Purpose: To examine the association between post-exercise bioenergetic recovery rate constant (k_{PCr}) and walking speed metrics, and to test the hypothesis that the known reduction in walking speed with increasing age can be explained by diminished mitochondrial recovery rate as assessed by k_{PCr}.

Methods: We investigated relationships among walking speed metrics incorporating varying distance and pace and phosphocreatine (PCr) recovery rate post-exercise, k_{PCr}, in the Baltimore Longitudinal Study of Aging (BLSA) participants (n = 126, mean age 72±12 years, male = 53, female = 73). In vivo ^{31}P-MRS measurements were obtained from the vastus lateralis muscle using a 3T Philips Achieva MR scanner (Philips, Best, NL) and a 10 cm ^{31}P-tuned surface coil (PulseTeq, Surrey, UK). All participants performed ballistic knee extension exercise in the MR scanner, following a protocol similar to that described by Jubrias et al [1]. ^{31}P MRS data were acquired at rest, during exercise, and during post-exercise recovery. The pulse sequence consisted of single adiabatic pulses of 90-degree flip angle applied with TR=1.5 s. Four scans were averaged for each time point, resulting in a 6 s interval between measurement time points. 75 time points were acquired for a total acquisition time of 7.5 minutes. Acquired spectra were processed using jMRUI [2] and quantified using a nonlinear least squares algorithm (AMARES) [3]. Phosphocreatine recovery rate constant was estimated by fitting the time-course of PCr concentration during post-exercise recovery to a mono-exponential function: $PCr(t) = PCr(0) + \{PCr_{rest} - PCr(0)\}\{1 - \exp(-t/\tau_{PCr})\}$; τ_{PCr}, the time constant of PCr recovery, is recognized as a marker for mitochondrial synthetic capacity [4], with $k_{PCr} = 1/\tau_{PCr}$. Gait speed measurements were performed over 6 m and 20 m courses in an uncarpeted corridor within three days of the ^{31}P-MRS measurements. Participants were instructed to walk at their normal pace for usual gait speed (UGS-6m) measurements, and at their maximal pace for rapid gait speed (RGS-6m) measurements over a 6-m long course. Usual gait speed for 150s (UGS-150s) was assessed by asking each participant to walk "at your usual comfortable pace" over a 20-m course marked by cones at each end of an uncarpeted corridor for 2.5 minutes (150 s). The distance walked in meters was recorded and used to calculate the speed. 400m-rapid-gait-speed (RGS-400m) was assessed by asking each participant to walk "as quickly as you can over the full 10 laps" over the same 20-m course. A linear regression model was applied to evaluate the associations between k_{PCr}, age and the four different walking metrics described above.

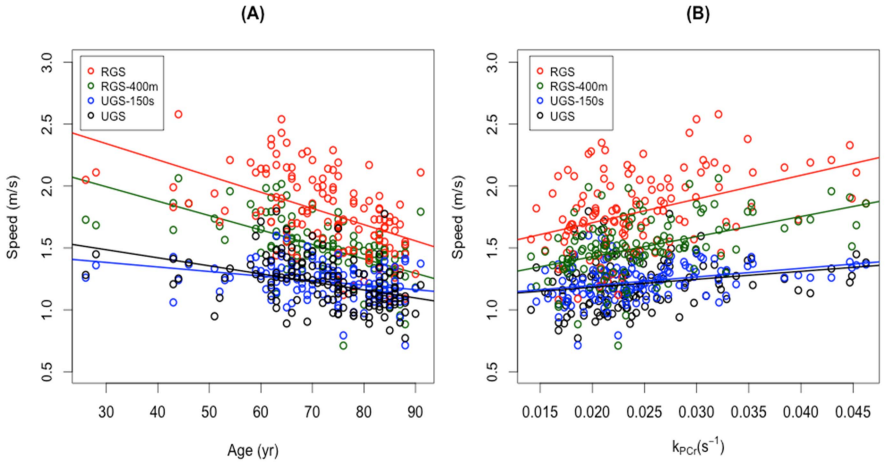

Fig. 1: Simple linear regression analysis for (A) walking metrics versus age and B) walking metrics versus k_{PCr}.

Results: Walking speeds at maximum pace exhibited a stronger dependence on k_{PCr} and age [Fig. 1] than walking speeds at usual pace and were more highly statistically correlated with both age and bioenergetic recovery rate k_{PCr} [Table 1]. Further, RGS-6m and RGS-400m decreased more rapidly with increasing age and increased more rapidly with increasing k_{PCr}. RGS-400m was best associated with both age and k_{PCr} [Table 1].

Discussion: These cross-sectional results from the BLSA demonstrate that strenuous ambulatory exercise (rapid gait) is better-associated with bioenergetic recovery in skeletal muscle than is non-strenuous (usual gait) exercise, likely reflecting, at least in part, a limitation in exercise performance due to decreased mitochondrial synthetic capacity. Similar results were obtained for the correlations between exercise and age. Thus, RGS walking metrics may serve as surrogates for bioenergetic capacity. Ongoing work with the BLSA cohort will permit the inclusion of other important physiological endpoints into the analysis, including whole-body oxidative capacity, body composition, muscle strength, and intramyocellular lipid (IMCL) content acquired using ^{1}H MRS. Most importantly, given the longitudinal and long-term design of the BLSA, the ^{31}P NMR measurements described here will provide a means of directly evaluating the influence of mitochondrial function on mobility and morbidity in the aging population.

Walking metrics	vs. Age	vs. k_{PCr}
UGS-6m	$R^2 = 0.154$, $p < 0.001$	$R^2 = 0.047$, $p = 0.015$
UGS-150s	$R^2 = 0.098$, $p < 0.001$	$R^2 = 0.108$, $p < 0.001$
RGS-6m	$R^2 = 0.254$, $p < 0.001$	$R^2 = 0.169$, $p < 0.001$
RGS-400m	$R^2 = 0.352$, $p < 0.001$	$R^2 = 0.212$, $p < 0.001$

Table 1: Coefficients of determinants and p-values corresponding to Fig. 1.

Conclusion: Long-distance walking at maximum pace (RGS-400m), the most physically challenging of the exercises evaluated, was the best paradigm for yielding walking speed measurements that were well-correlated with post-exercise mitochondrial synthetic capacity and with age.

References: [1] Jubrias et al. J Physiol 2003, 553(Pt. 2): 589-599, [2] Naressi et al. Comput Biol Med 2001, 31: 269-286, [3] Vanhamme et al. JMR 1997, 129: 35-43, [4] Conley et al. J Physiol 2000, 526(Pt.1): 203-210