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## **CIRCULATING HEMATOLOGIC SIGNATURES DISTINGUISH LOW VS HIGH PHYSICAL FUNCTION IN OLDER ADULTS**

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Iron is indispensable for multiple physiological processes in the human body including skeletal muscle function (1). Adequate iron availability is critical for muscle energetics and physical performance across the lifespan (2). Aging is associated with systemic and cellular iron dysregulation that may impair multiple processes and increase disease risk in older adults (3). However, the relationship between circulating iron biomarkers and physical function in older people, particularly among octogenarians, remains poorly defined. In this study, we examined the cross-sectional associations between iron biomarkers and with validated measures of physical function in 103 community-dwelling adults aged 70-80 years. Scores on the Short Physical Performance Battery (SPPB) were used to categorize participants into high (> 10) and low (<9) functioning groups. Blood samples were analyzed for serum iron, ferritin, transferrin saturation, soluble transferrin receptor, hepcidin and total iron binding capacity, as well as IL-6. Within-group correlations between iron biomarker levels and baseline SPPB functioning group and grip strength were calculated using Spearman correlation for continuous variables and rank-biserial correlation for binary-

-continuous variable pairs, and group comparisons of continuous variables were performed using the Wilcoxon rank-sum test. Participants had a mean age of 74.4 years, with no significant age differences by sex. Men demonstrated significantly higher handgrip strength and relative power, therefore, analyses were adjusted for sex. Individuals classified as low functioning had lower handgrip strength values, slower gait speed and higher IL-6 levels compared to high functioning participants. Iron biomarkers differed by functional status with low serum iron and low TSAT in low functioning participants. Correlation analysis revealed positive correlations between serum iron and TSAT with grip strength and an inverse relationship with IL-6 (Figure 1). In conclusion, in older adults including those approaching octogenarian age, circulating iron biomarkers are associated with physical function. Our findings support a link between iron availability, inflammation and functional outcomes in later life and underscore the importance of considering iron metabolism in studies of very old adults. Longitudinal studies are warranted to better understand the relationship between blood iron biomarker levels with physical function decline.

**Keywords:** *Circulating hematologic signatures, low vs high physical function, older adults.*