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SELECTED ABSTRACTS

Congress Abstract, Spring Meeting 2025, Young Researchers

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Phenoage and phenoageaccel do not outperform chronological age in predicting physical function decline and mortality in community-dwelling older adults

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Aim: Chronological age is a strong predictor of physical decline and mortality but fails to capture inter-individual variability in health and aging. Biological age metrics, such as PhenoAge and PhenoAgeAccel, integrate clinical biomarkers (e.g., inflammatory markers) to better reflect physiological aging. While these measures may predict well inflammation-driven outcomes, their utility for broader functional outcomes in general older populations remains unclear. This study compares their predictive power for physical function decline and all-cause mortality to chronological age in community-dwelling older adults.

Methods: Data from the InCHIANTI study were analyzed[3]. Participants aged ≥65 years with complete biomarker data for PhenoAge calculation (creatinine, albumin, glucose, C-reactive protein, red cell distribution width, mean corpuscular volume, lymphocyte percentage, white blood cell count, and alkaline phosphatase) and baseline Short Physical Performance Battery (SPPB) assessments were included (N=979; median age 73 years; 56% women). PhenoAgeAccel was calculated as the difference berween PhenoAge and chronological age. Physical function was assessed using the Short Physical Performance Battery (SPPB). Linear mixed models and Cox regression assessed associations with longitudinal changes in a continuous rescaled score of SPPB (rSPPB) and 10-year all-cause mortality. Logistic regression examined, in a subset of participants with normal physical function at baseline (N=504) the associations of these metrics with the onset of compromised physical function, defined as a drop in SPPB score from normal (≥10) at baseline to impaired (<10) at 6-year follow-up.

Results: Chronological age showed the strongest association with rSPPB decline (-0.50 points/10 years, p<0.001) and all-cause mortality (HR 1.15, p<0.001). PhenoAge and PhenoAgeAccel were associ-

ated with physical function decline (-0.32 and -0.15 points/10 years, respectively; p<0.001) and mortality (HR 1.10 and 1.09, respectively; p<0.001) but did not outperform chronological age. For the onset of compromised physical performance, chronological age demonstrated the strongest association and the highest predictive accuracy (OR 1.17, AUC=0.71) compared to PhenoAge (OR 1.10, AUC=0.69) and PhenoAgeAccel (OR 1.05, AUC=0.55).

Conclusions: While significantly associated with physical function decline and mortality, PhenoAge and PhenoAgeAccel do not surpass chronological age as predictive tools for these outcomes in general older populations. These outcomes are likely influenced by a complex interplay of factors – including musculoskeletal, psychosocial, and environmental determinants – that extend beyond those captured by these measures biomarker panels. These findings highlight the need for more comprehensive biological aging metrics to improve risk stratification and intervention planning in geriatric populations.

Circulating mitochondrial DNA signature in cardiometabolic patients

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Aim: Circulating mitochondrial DNA (mtDNA) profiles could refine risk stratification, but current methods do not account for different fractions of circulating mtDNA. We aimed to explore whether patients with cardiometabolic disease have a specific signature of the total circulating mtDNA profile.

Methods: We performed a complete clinical assessment, including blood tests, 12-lead ECG and ultrasound at rest and during cardiopulmonary exercise. Ultrasound congestion was defined at rest as inferior vena cava of ≥21 mm, lung B-lines ≥4, or discontinuous renal venous flow. In fasting whole blood and plasma samples collected at rest, we simultaneously measured the copy number of the cellular and cell-free components of mtDNA by real-time quantitative polymerase chain reaction. We calculated the ratio of cell mtDNA to cell-free mtDNA as an index of mitochondrial efficiency.

Results: We enrolled 120 consecutive patients: 42% with HF and preserved ejection fraction (HFpEF), 33% with HF and reduced ejection fraction (HFrEF) and 25% at risk of developing HF; 35% had diabetes. Cell-free mtDNA was increased in patients with HF (and higher in HFrEF than HFpEF) and with diabetes. Cell-free mtDNA was higher in patients with systemic inflammation (high-sensitivity C-reactive protein [hs-CRP] ≥0.2 mg/dL with neutrophil-lymphocyte ratio [NLR] >3) and more ultrasound signs of congestion. The mtDNA ratio showed opposite trends (all p<0.05). Cell-free mtDNA and mtDNA ratio independently predicted the presence of ≥2 ultrasound signs of congestion and effort intolerance (peak oxygen consumption <16 mL/kg/min) at ROC analysis and using multivariable regressions after adjustment for age, sex, hs-CRP, NLR, high-sensitivity Troponin T and NT-proBNP.

Conclusions: Cardiometabolic patients have an altered circulating mtDNA signature characterised by higher cell-free mtDNA and lower mtDNA ratio. Both are associated with impaired response to exercise, higher systemic inflammation and increased congestion. Circulating mitochondrial profile could be a new biomarker of mitochondrial status in cardiometabolic diseases.