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Epigenetic Age Acceleration is Associated with Lower CD4 T-cell Count, Increased Mortality Risk, and Frailty in Older Adults with HIV

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Background and Objectives: With advancements in antiretroviral therapy, people with HIV (PWH) are living longer lives and often aging into geriatric care. PWH are more likely to experience medical co-morbidities and geriatric syndromes including frailty as they age, and epigenetic studies indicate a trend towards epigenetic age acceleration in PWH. We aimed to investigate the association between epigenetic aging and phenotypic measures of frailty, as well as epigenetic methylation signatures associated with frailty, in a population of older PWH.

Methods: Adults aged 50 and older in clinical care for HIV management at Weill Cornell were randomly recruited to participate a detailed biopsychosocial survey, and those age 55 and older were invited to complete an in-person study visit which included blood sample collection, electronic medical record review, and physical function testing including grip strength and gait speed to calculate the Fried Frailty Index. The Veterans Aging Cohort Study Index (VACS) was used to calculate estimated mortality risk. Genome-wide DNA methylation was measured from dried blood spots using the Illumina MethylationEPIC platform and analyzed using 6 established epigenetic age algorithms including DNAm PhenoAge. The epigenetic frailty risk score (eFRS) was calculated based on characteristic methylation loci.

Results: A total of 164 participants enrolled in the study, and of those, 158 had a dried blood spot sample for analysis of DNA methylation. Median age was 60 years (IQR 56-64), 52 (33%) identified as female, and 76 (50%) identified as Black. Epigenetic analysis indicated the median PhenoAge was 66 years (IQR 62-71) for an average epigenetic "age acceleration" (EAA) of 5.4 years (SD 6.6). EAA was inversely related to chronologic age (Beta = -0.31 [95%CI: -0.48, -0.14] (p<0.01)) and was associated with lower CD4 T-cell count (Beta = -0.84 [95% CI: -1.14, -0.53] for every 100 CD4+ T-cells (p<0.01)) and higher VACS index (Beta = 0.10 [95%CI: 0.05, 0.16] (p<0.01)) in unadjusted linear regression models. There was a trend towards higher EAA with more advanced frailty state by ANOVA (p= 0.13). In an ordinal logistic regression model that included EAA, age, sex and race, both age and EAA were associated with higher odds of more advanced Fried frailty category. EAA was associated with eFRS in a univariate linear regression model (p<0.01), but eFRS was not associated with frailty category in an ordinal logistic regression model (p=0.78).

Conclusion: In this study of older adults with HIV, the average epigenetic age acceleration was 5.4 years, as calculated by PhenoAge, and EAA was associated with lower CD4 T-cell counts and higher VACS indices. In a model that included age, sex and race, EAA was also associated with an epigenetic frailty risk score, frailty phenotype, and age. These results suggest epigenetic clocks are a valuable biomarker of aging-related pathologies including low T-cell count, frailty and mortality risk, and warrant further study.

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Frailty and the Area Deprivation Index as Indicator of Neighborhood Disadvantage among Older People with HIV in Colorado

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Background: Examining geographic neighborhood-level factors provides a critical framework for implementing HIV care. While social determinants of health (SDOH) have been highlighted as relevant for HIV care and frailty prevention, the specific impact of neighborhood disadvantage on frailty