70

Epigenetic clock-derived age acceleration is associated with lung function in the population-based Lifelines cohort study

Tigist Demssew Adane, Dr. Maaike de Vries, Dr. Judith M. Vonk

University Medical Center Groningen; Department of Epidemiology

Introduction: Lung function is an important marker of general health which naturally declines with aging. DNA methylation(DNAm) has been postulated as a marker of biological aging that can be estimated using epigenetic clocks. The difference between this estimated biological age and the chronological age is a measure of age acceleration(AA). Our study aimed to assess the association between AA and lung function and the mediation role of AA on the association between smoking and lung function.

Methods: We included 1618 study participants from the Lifelines cohort study. The lung function was measured with spirometry, and Forced Expiratory Volume in one second (FEV1) was used as the outcome. Skin Horvath, PhenoAge, DunedinPACE, and telomer length epigenetic clocks were used. Age acceleration was derived from the residuals of the regression of biological age on chronological age except for the DunedinPACE-clock. Linear regression and causal mediation analysis adjusted for confounders were used.

Results: Of 1618 participants, 927 (55%) were males with a mean age of 47 years. AA measured by PhenoAge and DunedinPACE epigenetic clocks was significantly associated with FEV1. FEV1 was 7.7ml lower (95% CI:-12.3,-3.19) for a one-year higher PhenoAge AA and 488.6 ml lower (95% CI:-728.83,248.39) for a one-year faster Dunedin pace of aging. Telomere length, Blup, and skin Horvath age acceleration were not associated with FEV1. PhenoAge AA and DunedinPACE mediated the well-known association between smoking and FEV1. PhenoAge AA explained 7% of the variance between smoking and FEV1, while DunedinPACE explained 29 %.

Conclusion: This study shows that age acceleration measured by the PhenoAge and DunedinPACE epigenetic clock is significantly associated with lower lung function. This suggests that faster biological aging accelerates natural lung function decline. Apart from the direct effect of smoking on the lungs, smoking leads to AA, and this AA leads to lower lung function.

Conflicts of interest to disclose: We declare no competing interests