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Title

Accelerated biological aging leads to the trajectory of cardiometabolic multimorbidity to dementia and mortality

Priority 1 (Research Category)

Screening, prevention, and health promotion

Presenters

Yu Jia, Xiaoyang Liao, MD

Abstract

Context: Cardiometabolic multimorbidity (CMM) and aging are increasing public health concerns. Objective: This study investigated the relationship between biological aging and the trajectory of CMM with dementia and mortality and the preventive value of Life's Essential 8 (LE8) for biological aging. Study design and setting: This prospective analysis was conducted using a UK Biobank study. CMM is the coexistence of at least two cardiometabolic diseases (CMD), including stroke, ischemic heart disease, and type 2 diabetes. Biological age was calculated using the KDM-BA and PhenoAge algorithms using a clinical index. Participants: The study included 415,147 individuals with an average age of 56.5 years. Main outcome measures: The primary outcomes of this study were CMDs, CMM, all-cause dementia (Alzheimer's disease, vascular dementia, and other causes), and all-cause mortality. The Cox proportional hazards model was used to examine the risk of adverse events associated with accelerated aging (biological age > chronological age). Results: During the average 11-year follow-up period, CMD-free individuals with accelerated aging had a significantly greater risk of developing CMD (KDM-BA, HR 1.456; PhenoAge, HR 1.404), CMM (KDM-BA, HR 1.952; PhenoAge, HR 1.738), dementia (KDM-BA, HR 1.243; PhenoAge, HR 1.212), and mortality (KDM-BA, HR 1.821; PhenoAge, HR 2.047) after adjustment for tridional risk factors ($P<0.05$ for all). Accelerated aging had adjusted HRs of 1.489 (KDM-BA) and 1.488 (PhenoAge) for CMM, 1.493 (KDM-BA) and 1.195 (PhenoAge) for dementia, and 1.951 (KDM-BA) and 1.985 (PhenoAge) for mortality in participants with CMD at baseline ($P<0.05$ for all). CMM significantly mediated accelerated aging's indirect effects on dementia by 13.7% (KDM-BA, HR) and 21.6% (PhenoAge); those on mortality were 4.7% (KDM-BA) and 5.2% (PhenoAge). The population attributable-risk of LE8 score (≥80 vs. <80) were 0.79 and 0.43 for KDM-BA and PhenoAge accelerated aging, respectively. Conclusions: Biological aging involves the entire trajectory of CMM from a CMD-free state to CMD, to CMM, and ultimately to dementia and death. LE8 may be a potential target to counter age acceleration.