Study finds heart healthy behaviors may help reverse rapid cell aging

May 29 2024

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The benefit of better heart health may be associated with the positive impact of heart healthy lifestyle factors on biological aging (the age of the body and its cells), according to research published in the *Journal of the American Heart Association*.

"Our study findings tell us that no matter what your actual age is, better heart-healthy behaviors and managing heart disease risk factors were associated with a younger biological age and a lower risk of heart disease and stroke, death from heart disease and stroke and death from any cause," said Jiantao Ma, Ph.D., senior study author and an assistant

professor in the division of nutrition epidemiology and data science at the Friedman School of Nutrition Science and Policy at Tufts University in Boston.

This study analyzed whether a chemical modification process known as DNA methylation, which regulates gene expression, may be one mechanism by which cardiovascular disease health factors affect cell aging and the risk of death. DNA methylation levels are the most promising biomarker to estimate biological age. To some degree, biological age is determined by your genetic makeup, and it can also be influenced by lifestyle factors and stress.

Researchers examined health data for 5,682 adults (mean age of 56 years; 56% of participants were women) who were enrolled in the Framingham Heart Study, an ongoing, large, multigenerational research project aimed at identifying risk factors for heart disease.

Using interviews, physical exams and laboratory tests, all participants were assessed using the American Heart Association's Life's Essential 8 tool. The tool scores cardiovascular health between 0-100 (with 100 being the best) using a composite of four behavioral measures (dietary intake, physical activity, hours slept per night and smoking status) and four clinical measurements (body mass index, cholesterol, blood sugar and blood pressure).

Each participant was also assessed using four tools that estimate biological age based on DNA methylation and a fifth tool that assesses a person's genetic tendency towards accelerated biological aging. Participants were followed for 11–14 years for new-onset cardiovascular disease, cardiovascular death or death from any cause.

The analysis found:

- For each 13-point increase in an individual's Life's Essential 8 score, the risk of developing cardiovascular disease for the first time was reduced by about 35%, death from cardiovascular disease was reduced by 36% and death from any cause was reduced by 29%.
- In participants with a genetic risk profile making them more likely to have an accelerated biological age, the Life's Essential 8 score had a larger impact on outcomes potentially via DNA methylation, i.e., DNA methylation accounted for 39%, 39%, and 78% reduction in the risk of cardiovascular disease, cardiovascular death and all-cause death, respectively.
- Overall, about 20% of the association between Life's Essential 8 scores and cardiovascular outcomes was estimated to be due to the impact of cardiovascular health factors on DNA methylation; in contrast, for participants at higher genetic risk, the association was almost 40%.

"While there are a few DNA methylation-based, biological age calculators commercially available, we don't have a good recommendation regarding whether people need to know their epigenetic age," Ma said. "Our message is that everyone should be mindful of the eight heart disease and stroke health factors: eat healthy foods; be more active; quit tobacco; get healthy sleep; manage weight; and maintain healthy cholesterol, blood sugar and blood pressure levels."

Randi Foraker, Ph.D., M.A., FAHA, co-author of the Life's Essential 8: Updating and Enhancing the American Heart Association's Construct of Cardiovascular Health, said the findings are consistent with prior research.

"We know that modifiable risk factors and DNA methylation are independently associated with cardiovascular disease. What this study adds is that DNA methylation may serve as a mediator between risk

factors and cardiovascular disease," said Foraker, who is a professor of medicine at the Institute for Informatics, Data Science and Biostatistics and director of the Center for Population Health Informatics, both at Washington University School of Medicine in St. Louis, Missouri.

"The study highlights how cardiovascular health can impact biological aging and has important implications for healthy aging and prevention of cardiovascular disease and potentially other health conditions."

Study details, background and design:

- The study analyzed health data for a subgroup of participants who attended the Framingham Heart Study exams in the offspring group from 2005 to 2008 and the third-generation group from 2008 to 2011.
- Participants were followed for an average of 14 years for children of original participants and 11 years for the grandchildren.
- Health outcomes for the analysis included the development of cardiovascular disease (coronary heart disease, heart attack, stroke or heart failure), death from any cardiovascular disease or death from any cause.
- Results were adjusted for sex, age and alcohol use. Results for all-cause death were adjusted for the presence of cancer (excluding non-melanoma skin cancer) or heart disease at study enrollment. Participants already diagnosed with heart disease at study enrollment were excluded from the analysis of new-onset cardiovascular disease.
- The four tools to measure DNA methylation-based epigenetic age scores were based on established algorithms for DunedinPACE Score, PhenoAge, DNAmTL and GrimAge. A fifth tool, GrimAge PGS, assessed genetic tendency towards accelerated biological aging.

Because the study is an analysis of previously collected health data, it cannot prove a cause-and-effect relationship between cardiovascular health risk factors and DNA methylation. In addition, DNA methylation measures were from a single time point, which limits the validity of the mediation effect. The study's findings are also limited because the participants were predominantly of European ancestry, so the interactions of Life's Essential 8 and genetic aging found in this study may not be generalizable to people of other races or ethnicities.

"Currently, we are expanding our research to include people of other racial and ethnic groups to further investigate the relationship of cardiovascular risk factors and DNA methylation," Ma said.

According to the American Heart Association's 2024 Heart Disease and Stroke Statistics, heart disease and stroke claimed more lives in the U.S. in 2021 than all forms of cancer and chronic lower respiratory disease combined, and also accounted for approximately 19.91 million global deaths.

More information: Epigenetic Age Mediates the Association of Life's Essential 8 With Cardiovascular Disease and Mortality, *Journal of the American Heart Association* (2024). DOI: 10.1161/JAHA.123.032743

Provided by American Heart Association