Telomere growth predicts reduced chance of death from heart disease

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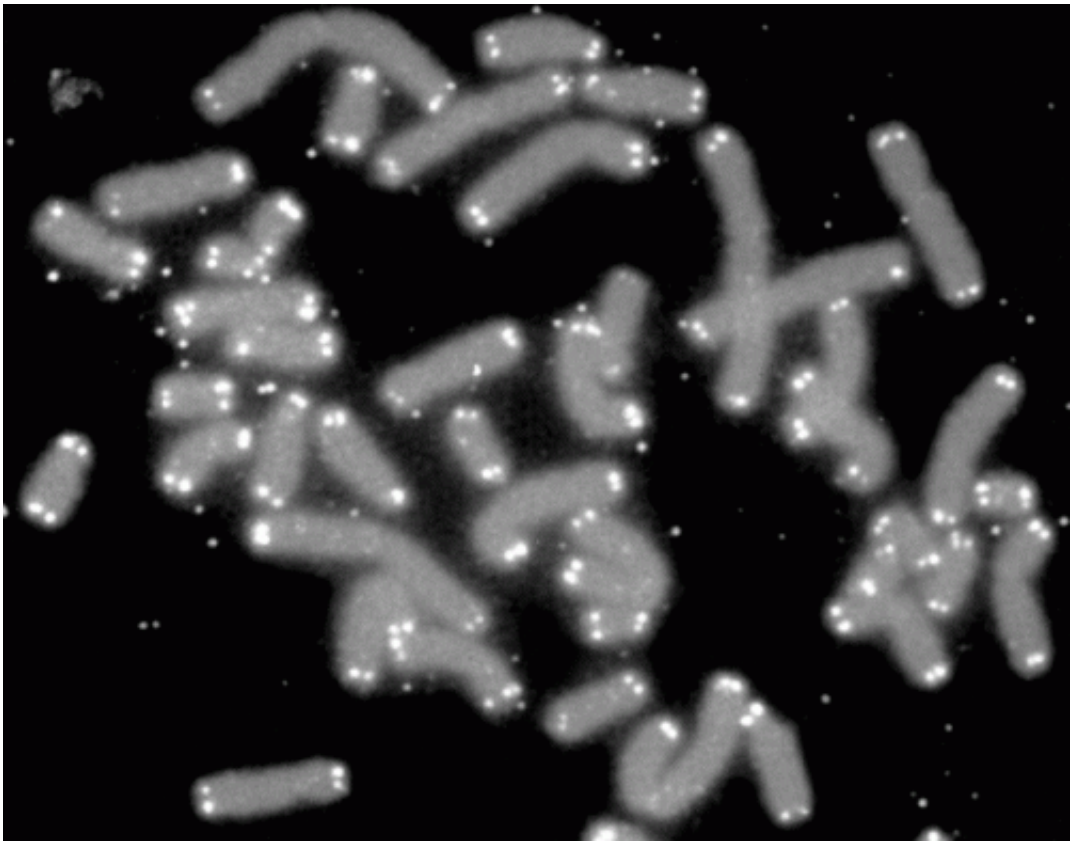

Human chromosomes (grey) capped by telomeres (white). Credit: PD-NASA; PD-USGOV-NASA

Short telomeres—the protective caps on the ends of chromosomes—have been previously linked to increased risk of death from heart disease. Now, research by scientists at UC San Francisco and

the Veterans Affairs Medical Center in San Francisco has found that change in telomere length over time is also important: heart disease patients whose telomeres shrank over time had a worse short-term prognosis than those whose telomeres stayed stable, and those whose average telomere length grew over the course of the study had a higher chance of survival.

The research, published online in *PLoS One* on October 26, 2016, was directed by Mary Whooley, MD, a professor of medicine and of epidemiology and biostatistics at UCSF and director of cardiac rehabilitation for the UCSF-affiliated San Francisco VA Health Care System.

Telomere length has emerged as a leading biomarker of aging, and predicts early onset of cardiovascular disease. In older people with stable heart disease, longevity can vary widely, but a number of studies have suggested that telomere length appears to be a good predictor of a patient's likely health span—their number of healthy years of life remaining. However, previous studies evaluating telomere length in white blood cells called leukocytes as a predictor of mortality have produced inconsistent findings, only sometimes predicting mortality.

In the new study, Whooley and colleagues asked whether the rate of telomere change—rather than absolute telomere length—might be a better predictor of health span in heart disease patients.

The team tracked health outcomes over nine years for 608 men and women with stable cardiovascular disease who were enrolled in the UCSF-led Heart and Soul Study. The researchers measured patients' leukocyte telomere length at the start of the study and again five years later, and then examined whether the difference between these measurements predicted which patients were most likely to die over the next four years.

Overall, one quarter of patients had died by the end of the study, but only 12 percent of patients whose telomeres had lengthened during the five-year observation period were among this group. In contrast, 39 percent of patients whose telomeres had shrunk in the five-year observation period died within the next four years. Of those whose telomere length had remained stable, 22 percent had died by the end of the study.

The researchers found that these three groups were similar in traditional cardiovascular risk factors such as blood pressure, BMI, and cholesterol levels. However, those whose telomeres shortened over the course of the study also showed higher abdominal fat, worse kidney function, and lower overall fitness. Controlling for these and other factors, the researchers found that those whose telomeres shortened over five years were 32 percent more likely to die during the next four years than those whose telomeres stayed the same, and those who experienced telomere lengthening were 56 percent less likely to die.

"This study goes beyond telomere length as a single measure and shows that the rate of change may also be an important predictive factor," Whooley said. "It also shows, rather surprisingly, that a substantial number of people had telomere lengthening, and that this appeared to be protective."

So far, the mechanism of telomere lengthening is unknown, the authors say. An earlier UCSF study found that greater exposure to stressful events predicts telomere shortening over one year, but that participants who maintained a healthy lifestyle—including sufficient sleep, a healthy diet, and regular exercise—did not show the shortening.

"While we have observed in several studies that average telomere length can get longer over the period of a year or two, we think the more common process is that a healthy lifestyle protects telomeres and leads to

less shortening, more stability, and thus better telomere maintenance over the years," said study co-author Elissa Epel, PhD, a professor of psychiatry and director of the Aging, Metabolism, and Emotions Lab at UCSF.

"Telomere lengthening appears to happen in people, and may be a meaningful phenomenon," said co-author Elizabeth Blackburn, PhD, a professor emeritus at UCSF, president of the Salk Institute for Biological Studies in San Diego and 2009 recipient of the Nobel Prize in Physiology or Medicine for her co-discovery of the telomerase enzyme. "Fortunately there are multiple ways to protect telomere length throughout the lifespan."

Among the research-vetted ways to protect telomeres, the authors cite avoiding smoking, getting at least 150 minutes of moderate exercise or 75 minutes of vigorous exercise per week, and maintaining a healthy, low-fat diet.

More information: Sarah E. Goglin et al. Change in Leukocyte Telomere Length Predicts Mortality in Patients with Stable Coronary Heart Disease from the Heart and Soul Study, *PLOS ONE* (2016). DOI: 10.1371/journal.pone.0160748

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