JACC: Telomere length in circulating blood cells does not predict asymptomatic atherosclerosis

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Half of patients with CVD show no above-normal risk of developing the disease on the basis of classical risk factors, such as high cholesterol, smoking, lack of exercise, and high blood pressure

Cardiovascular disease (CVD) is the main cause of death in the world, killing 17.5 million people every year according to WHO figures. Prevention strategies based on risk prediction are now a top public health priority, and there is great interest in developing new biomarkers of cardiovascular risk that allow a more accurate risk predication than classical risk factors such as high cholesterol, smoking, physical inactivity, and high blood pressure. One possible biomarker is telomere length, but a new study suggests that leukocyte telomere length (LTL) in circulating blood does not effectively predict CVD risk in individuals without disease symptoms. The results of the study, conducted at the *Centro Nacional de Investigaciones Cardiovasculares Carlos III* (CNIC) and led by Drs. Valentín Fuster and Vicente Andrés, are published in *The Journal of the American College of Cardiology* (JACC).

Despite the lack of an association, Dr. Andrés, an investigator in the Instituto de Salud Carlos III Cardiovascular Research Network, emphasizes the need to interpret these results with caution. “These results are rather like taking a snapshot at a single point in a person’s lifetime, and we still need to determine if atherosclerosis progresses faster in people who start with shorter leukocyte telomeres, have a higher proportion of very short telomeres, or in whom telomeres shorten at a faster rate during the aging process.” But Dr. Andrés also emphasizes that “we expect these important questions to be answered during the follow-up investigation planned for the participants in this subproject of the PESA study.”

Some epidemiological studies have reported shorter telomeres in the leukocytes of patients with coronary artery disease, heart attack, or stroke

Telomeres are complex structures located at the ends of chromosomes, whose function is to maintain genomic stability and cell viability. Numerous studies have demonstrated that telomere DNA shortens progressively as we age, leading to genomic instability and eventually cell death, especially when the telomeres become “critically” short. Telomere DNA shortening has come to be viewed as a marker not only of aging, but also of an individual’s general state of health, and this has generated great interest in the possibility that telomere length in circulating white blood cells might predict the risk of CVD. This idea is supported by epidemiological studies demonstrating shorter LTL in patients suffering coronary artery disease, myocardial infarction, or stroke. However, the results obtained to date are inconclusive, especially in relation to subclinical atherosclerosis. Moreover, there is a lack of information about the possible association of CVD with a high proportion of very short telomeres.

Classical risk factors

An estimated half of CVD patients do not have a high risk profile based on classical risk factors such as high cholesterol, smoking, lack of exercise, and high blood pressure. Moreover, many individuals who score high for these risk factors do not develop the disease. There is therefore a clear need to find new biomarkers to enable the early identification of individuals who do not yet show disease symptoms but are at high risk of developing atherosclerosis and suffering a heart attack or stroke. Experts believe that this would allow the implementation of appropriate preventative strategies in individuals at high risk, improving quality of life and reducing the health care and societal costs linked to CVD.

The new study published in JACC included 1459 volunteers participating in the PESA (Progression of Early Subclinical Atherosclerosis) clinical trial. In the study, the CNIC research team explored whether mean LTL and the proportion of critically short telomeres show an association with the presence and extent of subclinical atherosclerosis (before the appearance of disease symptoms). The team analyzed the presence and extent of atherosclerosis in different vascular territories using noninvasive imaging techniques: 2D and 3D ultrasound in the carotid and iliofemoral arteries and the abdominal aorta, and computed tomography to quantify calcification in the coronary arteries. LTL was measured by researchers led by Dr. María Blasco at the Centro Nacional de Investigaciones Oncológicas (CNIO), using the HT-QFISH technique.

In line with previous studies, the results show an association between increasing age and a lower mean LTL and a higher proportion of short telomeres (defined arbitrarily as those measuring less than 3 kilobases). However, study authors Drs. Juan M. Fernández-Alvira and Beatriz Dorado point out that none of these parameters showed any association with the presence or extent of subclinical atherosclerosis in the PESA cohort.

Dr. Valentín Fuster, lead investigator on the PESA study, concludes that “the combination of noninvasive imaging techniques and HT-QFISH analysis has allowed us to conclusively evaluate whether telomere length in circulating leukocytes is a useful biomarker for identifying asymptomatic individuals at high risk of developing a cardiovascular disease in the future. Thanks to the PESA study,” adds Dr. Fuster, “we will now be in a position to determine if the rate of progressive telomere shortening can predict the development of subclinical cardiovascular disease.”

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