JACC: Cardiovascular Imaging: Cholesterol plaques in the neck and legs signal increased cardiac risk

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A study published today in JACC: Cardiovascular Imaging *shows that atherosclerosis (the build-up of colesterol plaques in the arteries) does not respect anatomical boundaries: once plaques appear, they tend to spread across different regions of the arterial system.*

Atherosclerosis does not respect anatomical territories. Once cholesterol plaques appear in the arteries, they tend to spread throughout different regions of the arterial system. A new analysis from the PESA (Progression of Early Subclinical Atherosclerosis) study, led by researchers at the *C*Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC) under the direction of principal investigator Dr. Valentín Fuster, shows that the presence and extent of plaques in the neck (carotid) and leg (femoral) arteries are closely associated with the presence, severity, and burden of atherosclerosis in the coronary arteries.

Subclinical atherosclerosis, the silent accumulation of cholesterol plaques in the arteries before symptoms appear, is a systemic disease that can affect multiple arterial territories throughout the body. The study, now published in JACC: Cardiovascular Imaging, shows that the presence and extent of atherosclerotic plaque in the carotid and femoral arteries, assessed by 3D vascular ultrasound, are robustly and independently associated with the presence, severity, and burden of coronary atherosclerosis, quantified by advanced contrast-enhanced coronary computed tomography angiography.

Atherosclerosis beyond individual vascular territories

Historically, atherosclerosis has been viewed through a territory-based lens: plaque in the coronary arteries as the principal determinant of myocardial infarction risk, plaque in the carotid arteries as a marker of stroke risk, and so on. The results of this study challenge that paradigm and propose an alternative perspective: atherosclerosis, regardless of where it is detected, represents a systemic manifestation of an arterial wall that is more vulnerable to cardiovascular risk factors. “Our data show that carotid and femoral artery plaques and coronary artery plaques are manifestations of the same underlying biological process and are closely interconnected,” explains Dr. Inés García Lunar, cardiologist and Group Leader at the CNIC and first author on the study.

The importance of early plaques before calcification

The imaging technique most widely used in clinical practice to assess silent coronary atherosclerosis is a non-contrast coronary CT scan, which detects calcium deposits in the coronary arteries. Although it involves exposure to radiation, the test is relatively simple because it does not require medication or contrast administration. However, calcification appears in more advanced stages of atherosclerosis, meaning that this approach cannot detect the earliest plaques which are composed mainly of cholesterol. Detecting non-calcified cholesterol plaques in the coronary arteries requires contrast-enhanced coronary CT angiography, in which contrast agent is administered intravenously. Although very safe, this procedure requires greater preparation and technical complexity than a non-contrast scan.

In the current study, approximately 12% of participants, all asymptomatic middle-aged adults with no history of cardiovascular disease, had non-calcified cholesterol plaques in their coronary arteries. These plaques could only be detected with contrast-enhanced coronary CT angiography. Most importantly, more than 90% of these individuals already had plaques in their peripheral arteries (carotid and femoral), detectable by vascular ultrasound.

“The absence of coronary calcification is reassuring, but it does not exclude the presence of atherosclerosis in its earliest stages, before plaques have calcified. In these cases, vascular ultrasound provides highly valuable additional information,” says Dr. Ana García-Álvarez, a cardiologist and Group Leader at the CNIC and coauthor on the study.

A hypothesis that inspired PESA

EstThese findings connect directly with one of the concepts that inspired the PESA study more than a

decade ago: atherosclerosis is not a disease of a single artery but of the entire arterial system. For this reason, PESA was designed from the outset to investigate multiple vascular territories simultaneously.

“The PESA study was founded on the conviction that atherosclerosis is a disease of the whole person, not of a specific vessel. To understand it properly, we needed to study it simultaneously across multiple arterial territories. This study confirms that vision,” says Dr. Fuster, CNIC General Director and principal investigator of the PESA cohort.

The study also opens the door to the use of vascular ultrasound as a tool for improving imaging-based cardiovascular prevention. In just a few minutes, this technique can provide a comprehensive assessment of the presence and volume of atherosclerotic plaques in the four principal peripheral arteries: the two carotid arteries and the two femoral arteries.

“Today, we can assess all four peripheral arterial territories in just five minutes using 3D vascular ultrasound and analyze the results in less than a minute with artificial intelligence–based tools under expert supervision,” explains Virginia Mass, a vascular ultrasound specialist and study coauthor.

The study findings highlight the potential of vascular ultrasound as a simple and efficient method for detecting atherosclerosis. Based on the associations observed, screening five individuals by vascular ultrasound identifies, on average, one person who also has calcified coronary plaque, while screening eight individuals identifies one person who also has non-calcified coronary plaque.

“Vascular ultrasound is emerging as an accessible, rapid, safe, and radiation-free tool for the large-scale early detection of atherosclerotic disease in asymptomatic individuals,” says Dr. Dr. Borja Ibáñez, CNIC Scientific Director and co-leader of the PESA study.

Dr. Ibáñez adds that “this study joins a growing body of evidence, from our group and others, supporting a paradigm shift toward precision medicine, in which primary prevention and the management of risk factors such as cholesterol and blood pressure are guided by the identification of silent disease through a simple ultrasound examination.”

- *García-Lunar I, Fuster V, Kofoed KF, Pérez-García CN, Larsen AF, Gómez-Talavera S, et al. Association Between Peripheral and Coronary Subclinical Atherosclerosis Burden in Midlife. JACC Cardiovasc Imaging. 2026 Nov 19. doi:10.1016/j.jcmg.2026.09.016*

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