JAHA: Two novel blood biomarkers predict subclinical atherosclerosis and cardiovascular events

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A new study, published in the Journal of the American Heart Association*, shows that individuals with elevated levels of both proteins have twice the risk of cardiovascular events.*

Atherosclerosis is the progressive buildup of lipids, inflammatory cells, and fibrous tissue in the artery wall. It can progress silently for years, even decades, without causing symptoms. However, when one of these plaques ruptures or erodes, it can trigger the formation of a blood clot that abruptly blocks blood flow to vital organs such as the heart or brain. This process underlies most acute coronary syndromes and ischemic strokes, making atherosclerosis the leading cause of cardiovascular death.

Because atherosclerosis is silent and progressive, catching it early remains one of the biggest challenges in cardiovascular medicine today. Detecting the disease before serious clinical events occur offers a unique opportunity for early intervention, reducing the risk of heart attack, stroke, and other cardiovascular complications.

Cardiovascular risk assessment has traditionally relied on classic risk factors such as high blood pressure, high cholesterol, diabetes, smoking, and obesity. While these factors can estimate the likelihood of developing cardiovascular disease at a population level, they fall short of pinpointing which individuals are developing atherosclerosis early and silently.

Atherosclerosis can be detected using noninvasive imaging techniques such as ultrasound, which have been shown to improve cardiovascular risk stratification compared with conventional risk factor scores. However, cardiovascular imaging is not universally available, which has driven strong interest in developing other fast, noninvasive approaches—such as measuring plasma biomarkers—to improve the detection of atherosclerotic plaques and the prediction of cardiovascular events.

In an earlier study, the authors showed that elevated levels of haptoglobin (Hp) and immunoglobulin A2 (IgA2) could detect atherosclerosis in asymptomatic individuals across three different Spanish cohorts. Now, a study published in the *Journal of the American Heart Association* has confirmed the diagnostic value of these two biomarkers in a population of more than 5,000 US participants from the Bioimage study. The new study was conducted by researchers from four CIBERCV groups at the Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC) and the Investigación Sanitaria-Fundación Jiménez Díaz-Universidad Autónoma de Madrid (IIS-FJD-UAM), in collaboration with *The Binding Site* (Birmingham, UK) and funded by the "la Caixa" Foundation.

"Atherosclerosis is the underlying mechanism of most cardiovascular disorders, which are among the biggest health problems worldwide and place an enormous burden on health care systems. That's why it's so important to be able to identify the disease at its earliest stages, so we can prevent it before it develops," says Ana García-Álvarez, first author on the study and a researcher at CIBERCV and the CNIC.

The study also shows that these biomarkers can be used for prognostic purposes. As José Luis Martín Ventura, a CIBERCV researcher at the IIS-FJD-UAM, explains: "Elevated Hp and IgA2 levels double the risk of cardiovascular events, so measuring them could offer additional clues for understanding risk stratification in these patients." Jesús Vázquez, a principal investigator at CIBERCV and the CNIC, adds that "detecting Hp and IgA2 is a relatively simple, objective, and reproducible technique that's feasible in most hospitals, which would make it easy to implement in the clinic right away."

That said, the researchers point to the need for further research in this area: "From a clinical standpoint, further investigation is warranted to clarify the exact role of Hp and IgA2 as diagnostic and prognostic biomarkers, as well as their contribution to the pathogenic mechanisms of atherosclerosis," they conclude.

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Nicolás Pérez-García, Javier Sánchez-Gonzalez, Pieter Muntendam, Vicente Andrés , Luis Miguel Blanco-Colio, Jesús Vázquez , Borja Ibañez , Jose Luis Martin-Ventura. Haptoglobin and Immunoglobulin A2 predict cardiovascular risk in asymptomatic subjects: the Bioimage study. Journal of the American Heart Association 2026 Sep 9:e048286. doi: 10.1161/JAHA.125.048286