





Inflammatory Biomarkers and their Association with Atherosclerosis

Atherosclerosis is associated with specific inflammatory biomarkers, which can be measured to help evaluate a patient's risk for heart disease and cardiovascular events.



PAIRING ADVANCED LIPID ASSESSMENT WITH INFLAMMATION TO IDENTIFY CARDIOVASCULAR RISK

The risk of developing cardiovascular disease has traditionally been assessed by measuring low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C). Recent studies demonstrate that approximately 50% of heart attacks and strokes occur in patients with 'normal' cholesterol levels.¹ An advanced lipid assessment, or measuring the number of apolipoproteins or lipoprotein particles present, has been shown to better predict cardiovascular disease (CVD) risk than traditional lipid tests.^{2,3} Atherogenic particles can infiltrate the vessel wall contributing to macrophage activity, foam cell production, atherosclerotic plaque formation, and CVD events.

Although it is essential to assess cholesterol levels, adverse events (such as heart attack, stroke, or death) have been associated with inflammation,⁴ specifically vulnerable plaque related to increased white blood cell activation. The prominent clinical trials, JUPITER (2009) and CANTOS (2017), characterize inflammation as a critical component of atherosclerotic disease and cardiovascular risk, independent of lipids.^{5,6}

INFLAMMATION AND THE "RESPONSE TO INJURY HYPOTHESIS"

In 1976, world-renowned vascular biologist, Dr. Russell Ross, proposed the "Response to Injury Hypothesis", providing insight into the initiation and subsequent progression of cardiovascular disease.⁴ Risk factors such as smoking, hypertension, and diabetes can damage the vessel wall, making it more susceptible to penetration and accumulation of atherogenic cholesterol. The body responds to the injury with an inflammatory response designed to remove cholesterol from the artery wall. This process becomes dysregulated and ultimately potentiates the progression of cholesterol deposition and vulnerable plaque formation, placing an individual at increased risk of plaque rupture and subsequent heart attack or stroke.

INFLAMMATORY BIOMARKERS

Quest Diagnostic's Cleveland HeartLab Center of Excellence offers inflammatory biomarker testing to help practitioners evaluate cardiovascular risk in patients. This group of tests covers a patient's biomarker profile, which may result from lifestyle concerns (F_2 -IsopPs, OxLDL) to the development of cardiovascular disease (ADMA, Microalbumin, hsCRP) and formation of vulnerable plaque and increased risk for an adverse event (Lp-PLA₂, MPO).



F₂-Isoprostanes (F₂-IsoPs) are prostaglandin-like compounds used for measuring oxidative stress in the body. Elevated levels may be the result of excessive red meat intake,⁸ reduced activity levels,⁹ and smoking, and identify risk for atherosclerosis¹⁰ and cancer.^{11,12}

Oxidized LDL (OxLDL) is formed when the apolipoprotein B subunit on LDL particles becomes oxidized. Elevated levels may be the result of poor lifestyle choices and identify risk of metabolic syndrome.¹³



Asymmetric Dimethylarginine (ADMA) is a metabolite of L-arginine and can inhibit nitric oxide (NO) production. Elevated levels of ADMA are associated with endothelial dysfunction,¹⁴ insulin resistance,¹⁵ hypertension,¹⁵ and subclinical atherosclerosis.¹⁶

Urine Albumin is the quantification of small amounts of albumin (a serum protein) in the urine, to assess function and integrity of the kidneys. An elevated urine albumin/creatinine ratio is associated with endothelial dysfunction and risk of cardiovascular morbidity and mortality.¹⁷

High-Sensitivity C-Reactive Protein (hsCRP)

is an acute-phase protein released into the blood by the liver during inflammation. Elevated levels are associated with the risk of future adverse cardiovascular events in apparently healthy individuals¹⁸ and individuals with stable coronary artery disease.¹⁹



Lp-PLA₂ is a vascular-specific inflammatory enzyme that increases with the activation of macrophages in atherosclerotic lesions of the artery wall under the collagen cap. Increased Lp-PLA₂ Activity is associated with risk of coronary heart disease (CHD)²⁰ or a CHD event.²¹

Myeloperoxidase (MPO) is a vascular-specific inflammatory enzyme released by white blood cells into the bloodstream in response to vulnerable plaque, erosions, or fissures in the artery wall. Elevated MPO levels are associated with risk of cardiac events in subgroups otherwise characterized as low risk,^{22,23} and may assist cardiovascular risk prediction when used independently or alongside standard biomarker testing, such as hsCRP.²⁴

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