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Spotlight on Health

Advanced Testing for Cardiovascular Disease

Despite improvements in atherosclerotic cardiovascular disease (ASCVD) outcomes in recent decades, heart disease remains the leading cause of death in the United States.[1,2] Key contributors to risk reductions include management of traditional risk factors (eg, smoking, high blood pressure)[2] and lowering low-density lipoprotein cholesterol (LDL-C)—the earlier the intervention, the greater the benefit.[2] Managing inflammation also plays an important role in reducing the buildup of cholesterol and reducing cardiovascular disease (CVD) risk.[3]

However, for some patients managing traditional risk factors and lowering LDL-C may not be enough. These patients have residual CVD risk (see Sidebar),[2,4-6] to which other factors may contribute.

Advanced laboratory testing for factors associated with residual CVD risk may help identify patients who would benefit from more intensive therapy.[2,7] This newsletter will discuss residual CVD risk, and testing for lipoprotein and inflammatory biomarkers.

ASCVD Development and Progression

ASCVD begins when too many cholesterol particles are trapped in the artery wall; a consequence of high levels of LDL-C in blood.[8] The accumulation of cholesterol particles causes inflammation, which damages the artery wall causing yet more cholesterol accumulation.[8] In conjunction, other traditional risk factors (such as high blood pressure, age, or smoking) accelerate the disease and can lead to major adverse CV events in many people.[2,4] On the other hand, high-density lipoprotein cholesterol (HDL-C) has a protective effect against the development of ASCVD.[2]

Lipoprotein Biomarkers

While measurement of LDL-C and HDL-C can help establish CVD risk, measurement of lipid particle number, size, and associated proteins can help determine residual CVD risk.

LDL-C particle number. Having a greater number of LDL-C particles has been associated with an increased risk of myocardial infarction (MI).[7] People can have elevated LDL-C particle numbers even if their LDL-C levels are within guideline-recommended ranges.[7]

LDL-C and HDL-C subclasses. LDL-C and HDL-C particles can be broadly classified as large and small. Large HDL-C particles participate in removing cholesterol from artery walls—a low level of large HDL-C particles has been associated with increased coronary heart disease (CHD) risk.[7] Small LDL-C particles are removed from the blood less effectively, are more adherent to the artery wall, and because of size and number, may enter the artery wall more readily than larger particles. Thus, they may cause faster plaque development. A predominance of small LDL-C particles is called the Pattern B lipid phenotype, which is associated with cardiovascular risk.[7]

Apolipoprotein B-100 (ApoB). ApoB is the primary apolipoprotein attached to atherogenic particles. A high level of ApoB is associated with increased risk of CHD.[7] The 2019 American College of Cardiology/American Heart Association

Residual CVD Risk

ASCVD is still a major cause of illness and death in the United States.[1] Importantly, CVD death rates have remained high in younger patients due to the epidemic of obesity and diabetes.[4]

The American College of Cardiology/American Heart Association (ACC/AHC) Guideline on the Primary Prevention of Cardiovascular Disease recommends modifying lifestyle (eg, smoking, diet, exercise) and treating elevated LDL-C levels with statins to reduce the risk of CVD and events.[2]

However, around 50% of patients hospitalized for first or recurrent CHD events have normal LDL-C levels,[5] suggesting that residual CVD risk is common.[2,6]

guidelines now endorse the use of ApoB testing to further define risk in intermediate risk patients.[2]

Lipoprotein(a). Lipoprotein(a) is an LDL particle to which an Apo(a) protein is attached. Lipoprotein(a) levels are genetically predetermined, and high levels are associated with an increased risk of coagulation and development of atherosclerosis.[7] As many as 1 in 5 people have an abnormal genetically determined lipoprotein(a) level.[9] Family members of individuals with elevated lipoprotein(a) may need to be tested.[9]

Inflammatory Biomarkers

Inflammation plays an important role in the development and progression of ASCVD and adverse CV events.[3] Measurement of inflammatory markers can help determine the presence of ASCVD, disease activity, and residual CVD risk. Some key markers are

High-sensitivity C-reactive protein (hsCRP). CRP is an acute-phase reactant that is increased in response to inflammation. A mild but sustained elevation of CRP is associated with CVD.[7] Lowering the CRP level decreases the risk of recurrent CV events, independent of lipid levels.[7]

Lipoprotein-associated phospholipase A2 (Lp-PLA2) activity. Lp-PLA2 is an enzyme produced by macrophages and foam cells in arterial plaques. Enzyme activity is correlated with disease activity within plaque.[7] Elevated Lp-PLA2 activity is associated with increased risk of developing CHD and having an adverse CV event, independent of non-HDL-C levels.[7]

Myeloperoxidase (MPO). MPO is an inflammatory enzyme that is a specific marker of vascular inflammation. An elevated MPO level is an independent predictor of CVD (eg, MI, need for coronary revascularization).[10]

How the Laboratory Can Help

The Quest Diagnostics-Cleveland HeartLab Cardiometabolic Center of Excellence offers a comprehensive menu of advanced lipid and inflammatory marker testing. Enhanced reports provide an in-depth assessment of cardiovascular risks to help you recommend the ideal, individualized treatment option for your patients.

The Advanced Lipid Panel with Inflammation, Cardio IQ® (test code 94220) includes standard lipid testing as well as advanced CVD markers in order to provide improved assessment of CVD risk. The panel includes cholesterol, total (test code 91717); HDL-C (test code 91719); triglycerides (test code 91718); non-HDL and calculated components; lipoprotein fractionation, ion mobility (test code 91604; including LDL-C particle number, LDL-C, and HDL-C subclasses); apolipoprotein B (test code 91726); lipoprotein (a) (test code 91729); hs-CRP (test code 91737); and Lp-PLA2 activity (test code 94218). Panel components can be ordered separately.

Additional inflammatory markers, including Cardio IQ Myeloperoxidase (test code 92814), F2-Isoprostane/Creatinine Ratio (test code 92771), OxLDL (test code 92769), and ADMA/SDMA (test code 94153), are also available to assist in determining CVD risk in low-risk individuals, as well as those with established CVD.

References

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