HCT Medical Policy

Cardiac Risk Assessment Laboratory Tests

Policy # HCT111
Current Effective Date: 10/30/2014

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Policy Statement

Lipid and non-lipid risk factors as an adjunct to measurement of LDL cholesterol, or other tests including panels that include lipid and non-lipid cardiovascular risk markers for risk assessment of cardiovascular disease are considered experimental, investigational and unproven. There is insufficient evidence in the peer reviewed medical literature regarding the diagnostic value and clinical utility of the following tests for cardiac risk assessment: (not an all-inclusive list)

- Angiotensin II
- Apolipoproteins
- Cystatin C
- Cystine and homocystine, urine, qualitative
- Fibrinogen; antigen
- HDL subclass
- Homocysteine
- Leptin
- LDL subclass
- Lipoprotein remnants: intermediate density lipoproteins (IDL) and small density lipoproteins
- Lipoprotein(a) enzyme immunoassay
- Lipoprotein-associated phospholipase A2 (Lp-PLA2) (PLAC)
- VAP cholesterol test
- VLDL cholesterol
Overview

Several cardiovascular risk prediction tests, including biomarkers, have been developed to help identify individuals who are at risk of cardiovascular disease. These tools propose to assist clinicians in clinical disease management, particularly in cases where early therapeutic interventions, such as lifestyle modification and/or pharmacological treatment regimens might be helpful. Biomarkers are largely thought to provide independent diagnostic or prognostic value by reflecting an underlying disease or condition. For cardiac heart disease, biomarkers need to reflect the underlying biology of the vessel walls and the atherosclerotic process. The clinical utility of a biomarker depends on its ability to determine a significant proportion of individuals at increased risk and to add pertinent data to the traditional risk factors. These tests include the following:

- Angiotensin II (Ang II) is an octapeptide hormone that plays a central role in mediating hypertension, heart failure, cardiac remodeling, diabetes, and the proliferative and inflammatory responses to arterial injury and has been studied to establish if it has any relationship with the development of cardiovascular disease.

- Cystatin C: Cystatin C or cystatin 3 is a protein encoded by the CST3 gene and is typically used as a biomarker of kidney function. Cystatin C has been recently studied for its role in predicting the risk of new-onset cardiovascular disease because of the relationship between renal disease and cardiovascular disease.

- Fibrinogen: Fibrinogen is a clotting protein in circulation that is synthesized in the liver and is a precursor of fibrin. Serum fibrinogen levels increase during periods of inflammation. Fibrinogen has been used as an inflammatory marker and has been studied as a cardiovascular disease risk factor.

- HDL subclass: It has been proposed that various subclasses of HDL may have a role in protection from atherosclerosis. Particles of HDL can be characterized based on size/density and/or on the apolipoprotein composition. Using size/density, HDL can be classified into HDL2, the larger, less dense particles that may have the greatest degree of cardio-protection, and HDL3, which are smaller, more dense particles. HDL contains two associated apolipoproteins, i.e., A-I and A-II. HDL particles can also be classified by whether they contain apolipoprotein A-I (apo A-I) only or whether they contain both
apo A-I and A-II. There has been increasing interest in determining whether subclasses of HDL can be used to provide additional information on cardiovascular risk compared to HDL alone.

- **Homocysteine**: is a chemical in the blood that is produced when an amino acid called methionine is broken down in the body. Elevated homocysteine levels may cause irritation of the blood vessels and has been studied to establish if it shows increased risk for atherosclerosis.

- **Leptin**: Leptin is a protein secreted by fat cells that has been found to be elevated in heart disease and has been studied to establish if it has any relationship with the development of cardiovascular disease.

- **Lipoprotein-associated Phospholipase A2**: Lipoprotein-associated phospholipase A2 (Lp-PLA2), also known as platelet-activating factor acetylhydrolase, is an enzyme that hydrolyzes phospholipids and is primarily associated with low density lipoproteins. Evidence has suggested that Lp-PLA2 is a biomarker of coronary artery disease and may have a pro-inflammatory role in the progression of atherosclerosis.

- **LDL subclass**: There are two main subclass patterns of LDL, called A and B. In subclass pattern A, the particles have a diameter larger than 25 nm and are less dense, while in subclass pattern B, the particles have a diameter less than 25 nm and a higher density. Subclass pattern B is a commonly inherited disorder with associated dyslipidemia.

- **VAP Test**: The VAP Test is an expanded lipid panel that directly measures total cholesterol, HDL, LDL, and triglycerides, along with intermediate-density lipoprotein (IDL), LDL pattern density, HDL subtypes, and very low-density lipoprotein (VLDL), including their components, subclasses, and LDL pattern size.

- **VDRL**: A lab test that measures very low density lipoprotein. Lipoproteins are made up of cholesterol, triglycerides, and proteins and have been studied to establish if it has any relationship with the development of cardiovascular disease.

**Scientific Rationale**
The peer reviewed medical evidence from a number of large prospective group and case-control studies have demonstrated a positive association of some biomarkers with coronary
heart disease (CHD) events, and this association appears to be independent of most other risk factors. However, the overall magnitude of the evidence varied considerably and was inconclusive as to whether test results might lead to appropriate preventive and/or therapeutic measures in at-risk patients. There is insufficient evidence in the peer reviewed medical literature regarding the diagnostic value and clinical utility of these tests for cardiac risk assessment. 2-4 6-9

The ACC/AHA Guidelines for cardiovascular risk do not recommend the measurement of lipid parameters, including lipoproteins, apolipoproteins, particle size, and density, beyond a standard fasting lipid profile for cardiovascular risk assessment in asymptomatic adults. 1 5

The National Academy of Clinical Biochemistry Laboratory Medicine Practice guidelines state that “Heart disease and stroke continue to be the leading causes of death in the United States. As a result, investigators continue to look for new and emerging biomarkers of disease risk. Because many of these emerging biomarkers are not as well documented as those of conventional lipid and lipoprotein risk factors, their value in clinical practice needs to be critically appraised and appropriate guidelines developed for their proposed use.” 10

The U.S. Preventive Services Task Force (USPSTF) concludes that the evidence is insufficient to assess the balance of benefits and harms of using the nontraditional risk factors discussed in this statement to screen asymptomatic men and women with no history of CHD to prevent CHD events. 14

**Related Codes**

82163: Angiotensin II  
82172: Apolipoprotein, each  
82610: Cystatin C  
82615: Cystine and homocystine, urine, qualitative  
83090: Homocysteine  
83695: Lipoprotein (a)  
83698: Lipoprotein-associated phosolipase A2 (Lp-PLA)  
83700: Lipoprotein, Blood; electrophoretic separation and quantitation  
83701: Lipoprotein, Blood; high resolution fractionation and quantitation of lipoproteins including lipoprotein subclasses when performed (eg, electrophoresis, ultracentrifugation)  
83704: Lipoprotein, Blood; quantitation of lipoprotein particle numbers and lipoprotein particle subclasses (eg, by nuclear magnetic resonance spectroscopy)  
83718: Lipoprotein, direct measurement; high density cholesterol (HDL cholesterol)  
83719: Lipoprotein, direct measurement; VLDL cholesterol  
84999: Unlisted chemistry procedure
References


Document History

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<th>Date</th>
<th>Action</th>
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