

Evidence Based Guideline

High-Density Lipoprotein Subclass Testing in Cardiac Disease Risk Assessment

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Description of Procedure or Service

A large body of epidemiologic literature has demonstrated an inverse relationship between levels of high-density lipoprotein (HDL) and cardiovascular risk, indicating that HDL may have a protective role against cardiovascular disease. HDL particles exhibit considerable heterogeneity, and it has been proposed that various subclasses of HDL may have a greater 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 cardioprotection, 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 substantial interest in determining whether subclasses of HDL can be used to provide additional information on cardiovascular risk compared to HDL alone.

An alternative to measuring the concentration of subclasses of HDL, such as HDL₂ and HDL₃, is direct measurement of HDL particle size and/or number. Particle size can be measured by nuclear magnetic resonance (NMR) spectroscopy or by gradient-gel electrophoresis. HDL particle numbers can be measured by NMR spectroscopy. Several commercial labs offer these measurements of HDL particle size and number.

More recently, measurement of apo A-I has used measurement of HDL particle number as a surrogate, based on the premise that each HDL particle contains one apo A-I molecule. Direct measurement of apo A-I has been proposed as more accurate than the traditional use of HDL level in evaluation of the cardioprotective, or “good,” cholesterol. In addition, the ratio of apo B/apo A-I has been proposed as a superior measure of the ratio of proatherogenic (i.e., “bad”) cholesterol to anti-atherogenic (i.e., “good”) cholesterol.

Traditional lipid risk factors such as total HDL and low-density-lipoprotein cholesterol (LDL-C), while predictive on a population basis, are weaker markers of risk on an individual basis. Only a minority of subjects with elevated LDL and cholesterol levels will develop clinical disease, and up to 50% of cases of coronary artery disease (CAD) occur in subjects with “normal” levels of total and LDL cholesterol. Thus, there is considerable potential to improve the accuracy of current cardiovascular risk prediction models.

*****Note: This Evidence Based Guideline is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Evidence Based Guideline for high-density lipoprotein subclass testing in cardiac disease risk assessment

Subclassification of high-density lipoproteins may not be appropriate in the screening, diagnosis, and management of cardiovascular disease.

Medical Evidence regarding high-density lipoprotein subclass testing in cardiac disease risk assessment:

Numerous measures have been used in HDL subclass testing. The current evidence generally supports the contention that HDL subclass testing is as good as or better than currently used measures, although not all studies have come to this conclusion. Some experts argue that the apo B/apo A-1 ratio is superior to the LDL/HDL ratio as a predictor of cardiovascular risk, and should supplement or replace traditional lipid measures as both a risk marker and a treatment target. However, there is substantial uncertainty regarding the degree of improvement that these measures provide. The evidence suggests that any incremental improvement in predictive ability over traditional measures is likely to be small and of uncertain clinical significance.

Furthermore, improved risk prediction does not by itself result in better health outcomes. To improve outcomes, clinicians must have the tools to translate this information into clinical practice. Such tools for linking HDL subclasses to clinical decision-making, both in risk assessment and treatment response, are currently not available. HDL subclassification has not been incorporated into quantitative risk assessment models or treatment guidelines that can be used in clinical practice, such as the Adult Treatment Panel III (ATP III). The ATP III practice guidelines continue to tie clinical decision-making to conventional lipid measures, such as total cholesterol, LDL-C, and HDL-C. Therefore, it is not yet possible to conclude that these measures improve outcomes or that they should be adopted in routine clinical care.

Benefits Application

Please refer to certificate for availability of benefit. This guideline relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore certificate language should be reviewed before applying the terms of the guideline.

Billing/Coding/Physician Documentation Information

This guideline may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: No specific code.

CPT code 82664 (electrophoretic technique, not otherwise specified) or 83701 (lipoprotein, blood; high resolution fractionation and quantitation of lipoproteins including lipoprotein subclasses when performed [e.g., electrophoresis, ultracentrifugation]) may be used.

There is a CPT code for lipoprotein particle number and subclass quantification by nuclear magnetic resonance spectroscopy that is also not specific to HDL: 83704 (Lipoprotein, blood; quantification of lipoprotein particle numbers and lipoprotein particle subclasses [e.g., by nuclear magnetic resonance spectroscopy]).

Policy: High-Density Lipoprotein Subclass Testing in Cardiac Disease Risk Assessment

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.24, 4/24/09

Senior Medical Director review 9/2009

Policy Implementation/Update Information

10/26/09 New evidence based guideline issued. Subclassification of high-density lipoproteins may not be appropriate in the screening, diagnosis, and management of cardiovascular disease. (adn)

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