

Corporate Medical Policy

Genetic Testing for Predisposition to Inherited Hypertrophic Cardiomyopathy

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Description of Procedure or Service

Familial hypertrophic cardiomyopathy (HCM) is an inherited condition that is caused by a mutation in one or more of the cardiac sarcomere genes. HCM is associated with numerous cardiac abnormalities, the most serious of which is sudden cardiac death. Genetic testing for HCM-associated mutations is currently available through a number of commercial laboratories.

Familial hypertrophic cardiomyopathy (HCM) is the most common genetic cardiovascular condition, with a phenotypic prevalence of approximately 1 in 500 adults (0.2%). It is the most common cause of sudden cardiac death (SCD) in adults younger than 35 years of age, and is probably also the most common cause of death in young athletes. The overall death rate for patients with HCM is estimated to be 1% per year in the adult population.

The genetic basis for HCM is a defect in the cardiac sarcomere, which is the basic contractile unit of cardiac myocytes composed of a number of different protein structures. Nearly one-thousand individual mutations in at least 14 different genes have been identified to date. These genetic defects are inherited in an autosomal dominant pattern with rare exceptions. In patients with clinically documented HCM, genetic abnormalities can be identified in approximately 60%. Most patients with clinically documented disease are demonstrated to have a familial pattern, although some exceptions are found presumably due to *de novo* mutations.

The clinical diagnosis of HCM depends on the presence of left ventricular hypertrophy (LVH), measured by echocardiography or MRI, in the absence of other known causative factors such as valvular disease, long-standing hypertension, or other myocardial disease. In addition to primary cardiac disorders, there are systemic diseases that can lead to LVH and thus “mimic” HCM. These include infiltrative diseases such as amyloidosis, glycogen storage diseases such as Fabry disease and Pompe disease, and neuromuscular disorders such as Noonan’s syndrome and Friederich’s ataxia. These disorders need to be excluded before a diagnosis of familial HCM is made.

HCM is a very heterogenous disorder. Manifestations range from subclinical, asymptomatic disease to severe life-threatening disease. Wide phenotypic variability exists among individuals, even when an identical mutation is present, including among affected family members. This variability in clinical expression may be related to environmental factors and modifier genes. A large percentage of patients with HCM, perhaps the majority of all HCM patients, are asymptomatic or have minimal symptoms. These patients do not require treatment and are not generally at high risk for SCD. A subset of patients has severe disease that causes a major impact on quality of life and life expectancy. Severe disease can lead to disabling symptoms, as well as complications of HCM, including congestive heart failure (CHF) and malignant ventricular arrhythmias.

Genetic Testing for Predisposition to Inherited Hypertrophic Cardiomyopathy

Diagnostic screening of first-degree relatives and other family members is an important component of HCM management. Guidelines have been established for clinically unaffected relatives of affected individuals. Screening with physical examination, electrocardiography, and echocardiography is recommended every 12-18 months for individuals between the ages of 12 to 18 years, and every 3 to 5 years for adults. Additional screening is recommended for any change in symptoms that might indicate the development of HCM.

Genetic testing has been proposed as a component of screening at-risk individuals, in order to determine predisposition to HCM among those patients at risk. Patients at risk for HCM are defined as individuals who have a close family member with established HCM. Results of genetic testing may influence management of at-risk individuals, which may in turn lead to improved outcomes. Furthermore, results of genetic testing may have implications for decision-making in the areas of reproduction, employment, and leisure activities.

Regulatory Status

There are no assay kits approved by the U.S. Food and Drug Administration (FDA) for genetic testing for HCM, nor are any kits being actively manufactured and marketed for distribution. Clinical laboratories may develop and validate tests in-house (“home-brew”) and market them as a laboratory service; such tests must meet the general regulatory standards of the Clinical Laboratory Improvement Act (CLIA). The laboratory offering the service must be licensed by CLIA for high-complexity testing. While the FDA has technical authority to regulate home-brew tests, there is currently no active oversight nor any known plans to begin oversight. Home-brew tests may be developed using reagents prepared in-house or, if available, commercially manufactured analyte-specific reagents (ASRs). ASRs are single reagents “intended for use in a diagnostic application for identification and quantification of an individual chemical substance or ligand in biological specimens” and must meet certain FDA criteria but are not subject to premarket review.

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

Policy

BCBSNC will provide coverage for genetic testing for predisposition to inherited hypertrophic cardiomyopathy (HCM) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Genetic Testing for Predisposition to Inherited Hypertrophic Cardiomyopathy (HCM) is covered

Genetic testing for predisposition to hypertrophic cardiomyopathy (HCM) may be considered medically necessary for individuals who are at risk for development of HCM, defined as having a first-degree relative with established HCM, when there is a known pathogenic gene mutation present in that affected

Genetic Testing for Predisposition to Inherited Hypertrophic Cardiomyopathy

relative. (See policy guidelines).

When Genetic Testing for Predisposition to Inherited Hypertrophic Cardiomyopathy (HCM) is not covered

Genetic testing for predisposition to HCM is considered not medically necessary for patients with a family history of HCM in which a first-degree relative has tested negative for pathologic mutations.

Genetic testing for predisposition to HCM is considered investigational for all other patient populations, including but not limited to individuals who have a first-degree relative with clinical HCM, but in whom genetic testing is unavailable.

Policy Guidelines

For individuals at risk for HCM (first-degree relatives) genetic testing is most useful when there is a known mutation in the family. In this situation, genetic testing will establish the presence or absence of the same mutation in a close relative with a high degree of certainty. Absence of this mutation will establish that the individual has not inherited the familial predisposition to HCM and thus has a similar risk of developing HCM as the general population. These patients no longer need ongoing surveillance for the presence of clinical signs of HCM. Therefore, genetic testing may be considered medically necessary for first-degree relatives of individuals with a known pathologic mutation. .

For at-risk individuals without a known mutation in the family, the evidence does not permit conclusions of the effect of genetic testing on outcomes, since there is not a clear relationship between testing and improved outcomes. Genetic testing is considered investigational for this purpose. For at-risk individuals who have a family member with HCM who tests negative for pathologic mutations, genetic testing is not indicated. Genetic testing is considered not medically necessary in this situation.

Billing/Coding/Physician Documentation Information

This policy 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: S3865, S3866

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.02.28, 12/2011

Gersh BJ, Maron BJ, Bonow RO et al. 2011 ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2011. Retrieved on January 9, 2012 from <http://circ.ahajournals.org/content/124/24/2761.full>

Genetic Testing for Predisposition to Inherited Hypertrophic Cardiomyopathy

BlueCross BlueShield Association Technology Evaluation Center (TEC). Genetic testing for predisposition to inherited hypertrophic cardiomyopathy. 2009 TEC Assessments; Volume 24, Tab 11.

Policy Implementation/Update Information

- 1/24/11 New policy. “Genetic testing for predisposition to hypertrophic cardiomyopathy (HCM) may be considered medically necessary for individuals who are at risk for development of HCM, defined as having a first-degree relative with established HCM, when there is a known pathogenic gene mutation present in that affected relative. (See policy guidelines). Genetic testing for predisposition to HCM is considered not medically necessary for patients with a family history of HCM in which a first-degree relative has tested negative for pathologic mutations. Genetic testing for predisposition to HCM is considered investigational for all other patient populations, including but not limited to individuals who have a first-degree relative with clinical HCM, but in whom genetic testing is unavailable.” Reviewed by Medical Director. (mco)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.