familial hypertrophic cardiomyopathy

Familial hypertrophic cardiomyopathy is a heart condition characterized by thickening (hypertrophy) of the heart (cardiac) muscle. Thickening usually occurs in the interventricular septum, which is the muscular wall that separates the lower left chamber of the heart (the left ventricle) from the lower right chamber (the right ventricle). In some people, thickening of the interventricular septum impedes the flow of oxygen-rich blood from the heart, which may lead to an abnormal heart sound during a heartbeat (heart murmur) and other signs and symptoms of the condition. Other affected individuals do not have physical obstruction of blood flow, but the pumping of blood is less efficient, which can also lead to symptoms of the condition. Cardiac hypertrophy often begins in adolescence or young adulthood, although it can develop at any time throughout life.

The symptoms of familial hypertrophic cardiomyopathy are variable, even within the same family. Many affected individuals have no symptoms. Other people with familial hypertrophic cardiomyopathy may experience chest pain; shortness of breath, especially with physical exertion; a sensation of fluttering or pounding in the chest (palpitations); lightheadedness; dizziness; and fainting.

While most people with familial hypertrophic cardiomyopathy are symptom-free or have only mild symptoms, this condition can have serious consequences. It can cause abnormal heart rhythms (arrhythmias) that may be life threatening. People with familial hypertrophic cardiomyopathy have an increased risk of sudden death, even if they have no other symptoms of the condition. A small number of affected individuals develop potentially fatal heart failure, which may require heart transplantation.

Frequency

Familial hypertrophic cardiomyopathy affects an estimated 1 in 500 people worldwide. It is the most common genetic heart disease in the United States.

Genetic Changes

Mutations in one of several genes can cause familial hypertrophic cardiomyopathy; the most commonly involved genes are *MYH7*, *MYBPC3*, *TNNT2*, and *TNNI3*. Other genes, including some that have not been identified, may also be involved in this condition.

The proteins produced from the genes associated with familial hypertrophic cardiomyopathy play important roles in contraction of the heart muscle by forming muscle cell structures called sarcomeres. Sarcomeres, which are the basic units of muscle contraction, are made up of thick and thin protein filaments. The overlapping

thick and thin filaments attach to each other and release, which allows the filaments to move relative to one another so that muscles can contract. In the heart, regular contractions of cardiac muscle pump blood to the rest of the body.

The protein produced from the *MYH7* gene, called cardiac beta (β)-myosin heavy chain, is the major component of the thick filament in sarcomeres. The protein produced from the *MYBPC3* gene, cardiac myosin binding protein C, associates with the thick filament, providing structural support and helping to regulate muscle contractions.

The *TNNT2* and *TNNI3* genes provide instructions for making cardiac troponin T and cardiac troponin I, respectively, which are two of the three proteins that make up the troponin protein complex found in cardiac muscle cells. The troponin complex associates with the thin filament of sarcomeres. It controls muscle contraction and relaxation by regulating the interaction of the thick and thin filaments.

It is unknown how mutations in sarcomere-related genes lead to hypertrophy of the heart muscle and problems with heart rhythm. The mutations may result in an altered sarcomere protein or reduce the amount of the protein. An abnormality in or shortage of any one of these proteins may impair the function of the sarcomere, disrupting normal cardiac muscle contraction. Research shows that, in affected individuals, contraction and relaxation of the heart muscle is abnormal, even before hypertrophy develops. However, it is not clear how these contraction problems are related to hypertrophy or the symptoms of familial hypertrophic cardiomyopathy.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Rarely, both copies of the gene are altered, leading to more severe signs and symptoms.

In most cases, an affected person has one parent with the condition.

Other Names for This Condition

- familial asymmetric septal hypertrophy
- HCM
- hereditary ventricular hypertrophy
- heritable hypertrophic cardiomyopathy
- idiopathic hypertrophic subaortic stenosis

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Familial hypertrophic cardiomyopathy 1
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3495498/
- Genetic Testing Registry: Familial hypertrophic cardiomyopathy 2
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1861864/
- Genetic Testing Registry: Familial hypertrophic cardiomyopathy 4
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1861862/
- Genetic Testing Registry: Familial hypertrophic cardiomyopathy 7
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1860752/

Other Diagnosis and Management Resources

- Cleveland Clinic
  http://my.clevelandclinic.org/health/articles/hypertrophic-cardiomyopathy
- GeneReview: Hypertrophic Cardiomyopathy Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1768
- MedlinePlus Encyclopedia: Hypertrophic Cardiomyopathy
  https://medlineplus.gov/ency/article/000192.htm
- Stanford University Hospitals and Clinics
  https://stanfordhealthcare.org/medical-conditions/blood-heart-circulation/hypertrophic-cardiomyopathy.html
- The Sarcomeric Human Cardiomyopathies Registry (ShaRe)
  https://thesharereg istry.org/

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Hypertrophic Cardiomyopathy
  https://medlineplus.gov/ency/article/000192.htm
- Health Topic: Cardiomyopathy
  https://medlineplus.gov/cardiomyopathy.html

Genetic and Rare Diseases Information Center

- Familial hypertrophic cardiomyopathy
  https://rarediseases.info.nih.gov/diseases/7229/familial-hypertrophic-cardiomyopathy

Additional NIH Resources

- National Heart, Lung, and Blood Institute: Types of Cardiomyopathy
  https://www.nhlbi.nih.gov/health/health-topics/topics/cm/types

Educational Resources

- Cleveland Clinic
  http://my.clevelandclinic.org/health/articles/hypertrophic-cardiomyopathy
- Disease InfoSearch: Primary familial hypertrophic cardiomyopathy
  http://www.diseaseinfosearch.org/Primary+familial+hypertrophic+cardiomyopathy/9162
- KidsHealth from Nemours: Arrhythmias
  http://kidshealth.org/en/parents/arrhythmias.html
- KidsHealth from Nemours: Heart and Circulatory System
  http://kidshealth.org/en/parents/heart.html
- MalaCards: mybpc3-related familial hypertrophic cardiomyopathy
  http://www.malacards.org/card/mybpc3_related_familial_hypertrophic_cardiomyopathy
- MalaCards: myh7-related familial hypertrophic cardiomyopathy
  http://www.malacards.org/card/myh7_related_familial_hypertrophic_cardiomyopathy
- MalaCards: tnni3-related familial hypertrophic cardiomyopathy
  http://www.malacards.org/card/tnni3_related_familial_hypertrophic_cardiomyopathy
- MalaCards: tnnt2-related familial hypertrophic cardiomyopathy
  http://www.malacards.org/card/tnnt2_related_familial_hypertrophic_cardiomyopathy

- My46 Trait Profile
  https://www.my46.org/trait-document?trait=Hypertrophic%20cardiomyopathy&type=profile
- Orphanet: Rare familial disorder with hypertrophic cardiomyopathy
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=99739
- Stanford University Hospitals and Clinics
  https://stanfordhealthcare.org/medical-conditions/blood-heart-circulation/hypertrophic-cardiomyopathy.html

Patient Support and Advocacy Resources

- American Heart Association
  http://www.heart.org/HEARTORG/Conditions/More/Cardiomyopathy/Hypertrophic-Cardiomyopathy_UCM_444317_Article.jsp
- Championship Hearts Foundation
  http://www.champhearts.org/
- Sudden Arrhythmia Death Syndromes (SADS) Association: Living with SADS
  http://www.sads.org/living-with-sads#.Vds7Z5dGdD8
- The Sarcomeric Human Cardiomyopathies Registry (ShaRe)
  https://theshareregistry.org/

GeneReviews

- Hypertrophic Cardiomyopathy Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1768

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22familial+hypertrophic+cardiomyopathy%22+OR+%22Cardiomyopathy%2C+Hypertrophic%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Cardiomyopathy,+Hypertrophic,+Familial%5BMAJR%5D%29+AND+%28familial+hypertrophic+cardiomyopathy%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 1
  http://omim.org/entry/192600
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 2
  http://omim.org/entry/115195
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 3
  http://omim.org/entry/115196
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 4
  http://omim.org/entry/115197
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 6
  http://omim.org/entry/600858
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 7
  http://omim.org/entry/613690
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 8
  http://omim.org/entry/608751
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 9
  http://omim.org/entry/613765
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 10
  http://omim.org/entry/608758
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 11
  http://omim.org/entry/612098
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 12
  http://omim.org/entry/612124
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 13
  http://omim.org/entry/613243
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 14
  http://omim.org/entry/613251
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 15
  http://omim.org/entry/613255
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 16
  http://omim.org/entry/613838
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 17
  http://omim.org/entry/613873
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 18
  http://omim.org/entry/613874

- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 19
  http://omim.org/entry/613875
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 20
  http://omim.org/entry/613876
- CARDIOMYOPATHY, FAMILIAL HYPERTROPHIC, 21
  http://omim.org/entry/614676

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https://ghr.nlm.nih.gov/condition/familial-hypertrophic-cardiomyopathy

Reviewed: August 2015
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services