



CPVT

Catecholaminergic Polymorphic Ventricular Tachycardia

A Guide for Patients

Catecholaminergic Polymorphic Ventricular Tachycardia

What is CPVT?

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a condition that affects the ability of your heart to beat regularly, particularly when you experience physical or emotional stress. CPVT is caused by a problem in the regulation of your heartbeat but not by any structural heart abnormalities. Therefore, this heart disease may not be detectable with a routine heart examination. When you are physically active or experience intense emotional stress, your body releases hormones such as adrenaline. Adrenaline is a type of hormone known as a catecholamine. Normally catecholamine results in an increase in your heart rate. If you have CPVT, your heart does not respond to catecholamine correctly and beats irregularly and too quickly, a condition known as tachycardia. During tachycardia, the heart beats so fast that it can cause dizziness and fainting. In some cases, CPVT can cause cardiac arrest and sudden death. About 1 in 10,000 people have CPVT.

What are the symptoms of CPVT?

Symptoms of CPVT include:

- Fainting (syncope)
- Dizziness
- Rapid or irregular heartbeats (tachycardia or arrhythmia)
- Sudden cardiac death

The most common symptoms of CPVT are dizziness and fainting that occur with physical activity or emotional stress. If you have CPVT, these symptoms usually occur in childhood, although they can develop later. Since symptoms of CPVT are similar to other heart problems, it is crucial for you to see your doctor for a medical evaluation if you think you may have CPVT or any heart condition.

What causes CPVT?

CPVT is caused by an abnormality (mutation) in one of your genes. Mutations in two genes (Table 1) are known to be associated with about 60 % of CPVT cases. Most commonly, CPVT is inherited in an autosomal dominant manner, so if you have CPVT there is a 50 % chance of passing the genetic disorder on to each of your children. Less frequently, CPVT is inherited as an autosomal recessive condition and may affect your siblings but is unlikely to affect your children.

TABLE 1

GENE	GENE NAME
RYR2	Ryanodine receptor 2
CASQ2	Calsequestrin 2

How is CPVT diagnosed?

Your physician will use an electrocardiogram (ECG) to diagnose CPVT. However, since CPVT does not show up when you are resting, your doctor will need to monitor your heart rhythm during activity, such as exercise. Your personal and family histories can provide additional clues to the diagnosis of CPVT. Genetic testing can help confirm a diagnosis.

How is CPVT treated?

The clinical management of your CPVT varies and depends on the severity of your disease and symptoms. Medications may include beta-blockers. Beta-blockers work by preventing the abnormal heart rhythm (tachycardia) that can lead to fainting and death. Some high-risk patients may need surgery to have a defibrillator placed. The defibrillator constantly monitors your heartbeat and uses an electrical shock if necessary to restore a regular heartbeat. Avoiding competitive sports and strenuous exercise is often recommended.

Genetic Testing for CPVT

How is genetic testing for CPVT performed?

The CPVT genetic test is a blood test ordered by your physician. At GeneDx, we will extract your DNA and analyze it by specifically searching for mutations in the genes that are associated with CPVT. After the test is complete (in about eight weeks), the results will be sent to your physician, who will explain the test results to you.

What makes the GeneDx test different from others?

Identifying the genetic cause of your CPVT is important, as it can help your physician determine the best way to monitor and treat your condition. If GeneDx finds a genetic variant that we cannot yet interpret, another member of your family with CPVT, if available, will be tested at no additional cost. GeneDx will also evaluate a large panel of clinically normal individuals to determine if the genetic variant is a normal genetic variation seen in individuals who do not have CPVT.

Who should have genetic testing for CPVT?

- Anyone with a clinical diagnosis of CPVT
- Family members of the person who has a disease-causing mutation

How is genetic testing for CPVT helpful?

- Confirms your clinical diagnosis of CPVT, especially if the diagnosis is unclear
- Identifies your family members who are at risk of developing CPVT
- Allows you to make informed personal and family health decisions

How long does it take to complete the genetic test?

It usually takes eight weeks to complete the test (from the time the lab receives the blood sample to the time your physician receives the results). It can take longer if GeneDx has to study clinically normal individuals or test family members to interpret results.

What type of test results can I expect?

Three types of results are possible:

- **A positive result** indicates that we identified a disease-causing mutation in one of your genes associated with CPVT. This finding confirms the diagnosis of CPVT and provides valuable information to you and your family members. A genetic confirmation of CPVT can help your physician in identifying activities and behaviors to avoid and may be useful in determining your risk of experiencing a life-threatening cardiac event. All first-degree relatives (children, siblings, parents) may then be offered diagnostic or predictive genetic testing to clarify the risk for CPVT. If a family member is found to be positive for the familial mutation, this individual is considered to be at risk for CPVT and should be referred for cardiac evaluation. It is important to note that there is variability in symptoms even within families.
- **A negative result** indicates that we did not identify a disease-causing mutation in one of your genes associated with CPVT. However, this does not rule out CPVT or a genetic cause of CPVT, and you should be managed according to your clinical symptoms. Possible reasons for a negative result could be (1) you may have a mutation in a gene not covered in the testing panel, or (2) you may have a mutation in a part of a CPVT gene that was not covered in the test. When a genetic test result is negative, predictive genetic testing of family members will not be informative

and therefore not helpful. Careful review of your family history may help determine if your disease is hereditary, so that other family members can have their hearts monitored by their doctor.

- **A variant of unknown significance (VOUS) result** indicates an inconclusive finding. This happens when we find a new DNA variation (i.e., one that has never been seen before), but it is unclear if that change causes CPVT. A VOUS result is reported only after GeneDx has confirmed that no individual in a large panel of normal controls carries the variant. To further clarify the clinical significance of the VOUS, it may be helpful to test other family members. If an affected relative also has the variant, it is more likely that the variant causes disease. The more affected family members who carry the VOUS, the greater the likelihood that the VOUS is responsible for CPVT in your family.

How will I learn my test results?

Your physician will share your results with you and discuss them in the context of your health care.

Will my insurance cover this test?

GeneDx accepts all commercial insurance. GeneDx will bill your insurance company and appeal for payment. Currently, GeneDx does not accept Medicare or Medicaid. For more information, please visit our website at: www.genedx.com/cardiology or call us at 301-519-2100, x 6727.

What if I do not have insurance?

If you do not have health insurance or cannot afford to pay the full cost of testing, GeneDx provides a generous financial assistance program including a significantly discounted price. For more information, call us at 301-519-2100, x 6106.

Do my family members need to be tested?

If you have a disease-causing mutation in one of the CPVT genes, your family members can be tested for that specific mutation. If you have a VOUS, GeneDx may ask to test your family members at no additional cost if it is necessary to interpret your test results.

Does GeneDx test family members?

Yes, GeneDx offers mutation-specific testing (for a known mutation) for family members of anyone who has been shown by GeneDx to have a genetic mutation. For more information, please call one of our genetic counselors at 301-519-2100. If a family member has been tested at another lab, we can still test you or other family members, but we require blood from the previously tested relative be sent along with your sample for confirmation.

How does testing of family members differ from full CPVT panel testing in a patient?

The first CPVT patient in a family to be tested typically requires analysis of two genes in the CPVT panel. Once a disease-causing mutation is identified in a specific gene, family members are tested only for that specific mutation. The cost and turnaround time are significantly reduced when family members get tested only for a specific mutation instead of the full gene panel.

Does GeneDx perform prenatal testing?

Yes, GeneDx can provide prenatal testing for a known familial mutation in any gene for families who have had previous testing at GeneDx. For more information, please call one of our genetic counselors at 301-519-2100.

Can my health insurer or employer discriminate against me based on my test results?

No, The Genetic Information Nondiscrimination Act of 2008, also referred to as GINA, is a federal law that protects Americans from discrimination by health insurance companies and employers based on their genetic information. The President signed the act into federal law on May 21, 2008. The parts of the law relating to health insurers took effect on May 2009, and those relating to employers took effect on November 2009. **However, this law does not cover life insurance, disability insurance, or long-term care insurance.** For more information, please visit <http://www.genome.gov/10002328>.

How can I order this test?

Your physician can order this test by taking the following steps:

- Download cardiology requisition forms from the GeneDx website: www.genedx.com/cardiology
- Complete all forms with the required information
- Ship completed forms along with 2-5ml blood in EDTA (purple/lavender top tube) to the following address:

*GeneDx
207 Perry Parkway
Gaithersburg, MD 20877*

We also provide shipping kits to physicians when requested. To order a cardiology shipping kit, you can call us at 301-519-2100 or email us at zebras@genedx.com.

Where can I find more information?

You can find more information at the following websites:

- GeneDx cardiology page: www.genedx.com/cardiology
- Gene Reviews, a database of genetic diseases: www.geneclinics.org
- National Society of Genetic Counselors, to help you find a counselor near you: www.nsgc.org
- Sudden Arrhythmia Death Syndromes (SADS) Foundation, a patient support organization: www.sads.org
- Cardiac Arrhythmias Research and Education Foundation (C.A.R.E.), a patient support organization: www.longqt.org
- The Canadian Sudden Arrhythmia Death Syndromes (SADS) Foundation, a patient support organization in Canada: www.sads.ca
- Sudden Cardiac Arrest Association, a patient support organization: www.suddencardiacarrest.org

About GeneDx

GeneDx is a highly respected company that specializes in genetic testing for rare inherited disorders. Two scientists from the National Institutes of Health (NIH) founded the company in the year 2000 to address the needs of patients and clinicians concerned with rare inherited disorders. Currently, GeneDx offers testing for more than 350 rare Mendelian disorders, using DNA sequencing and deletion/duplication analysis of the associated gene(s). GeneDx also offers oligonucleotide microarray-based testing for detecting chromosomal abnormalities, testing for autism spectrum disorders, and testing for various inherited cardiac disorders. At GeneDx, our technical services are matched by our scientific expertise and customer support. Our growing staff includes more than 12 experts in molecular and clinical genetics as well as 12 genetic counselors who are just a phone call or email away. We invite you to visit our website www.genedx.com to learn more about us and the services we offer.

www.genedx.com

