



Brugada Syndrome

A Guide for Patients

Brugada Syndrome

What is Brugada syndrome?

Brugada syndrome (BrS) is a condition that affects the ability of your heart to beat normally and regularly. BrS may cause fainting and sudden cardiac arrest. An electrocardiogram (ECG) helps your physician determine if you have this condition. BrS affects 5 in 10,000 individuals from all ethnic backgrounds. Men are 8 to 10 times more likely than women to develop symptoms of Brugada syndrome.

What are the symptoms of Brugada syndrome?

Symptoms of BrS include:

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

If you have symptoms of Brugada syndrome, you will usually develop them by the time you are 20 to 40 years old, although symptoms have been seen at all ages. Symptoms of BrS occur more frequently when you are resting or asleep. Sometimes symptoms of BrS show up when you have a high fever. Since symptoms of BrS 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 Brugada syndrome or any other heart condition.

TABLE 1

GENE	GENE NAME
SCN5A	Sodium channel, voltage gated, type V alpha subunit
GPD1L	NAD-dependent glycerol-3-phosphate dehydrogenase
CACNA1C	Alpha-1C subunit of the L-type voltage-dependent calcium channel
CACNB2	Beta-2 subunit of the voltage-dependent L-type calcium channel
SCN1B	Voltage-gated sodium channel type 1 beta subunit
KCNE3	Potassium voltage-gated channel, Isk-related family, member 3
SCN3B	Beta subunit of voltage-gated type III sodium channel

What causes Brugada syndrome?

BrS is a heritable heart disorder. It is inherited in an autosomal dominant manner, so if you have BrS there is a 50% chance of passing the genetic disorder on to each of your children. BrS is caused by an abnormality (mutation) in one of your genes. The known genes associated with BrS are listed in Table 1. Mutations in five genes that are important for the normal electrical activity of your heart have been associated with 41% of individuals with this condition. Nevertheless, not all people who carry a BrS mutation will have symptoms.

How is BrS diagnosed?

BrS is usually diagnosed by an electrocardiogram (ECG) and physical examination. Your ECG and medical and family histories are essential in evaluating the likelihood of BrS. Genetic testing can be used to confirm your clinical diagnosis.

How is BrS treated?

The clinical management of BrS depends on the severity of your disease and symptoms. Some high-risk patients may need surgery to have a defibrillator placed. Your doctor will help determine if you need such treatment. Certain medications and drugs can cause BrS symptoms to worsen and should be avoided. High fevers may also cause complications, and your doctor may advise you how to manage any fever-related illnesses.

Genetic Testing for Brugada Syndrome

How is genetic testing for BrS performed?

The BrS 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 BrS. After the test is complete (in about six to eight weeks), the results are sent to your physician, who will explain the test results to you.

What makes the GeneDx test different from others?

GeneDx offers the most comprehensive genetic test for BrS. Identifying the genetic cause of your BrS is important, as it can help your physician determine the best way to monitor and treat your condition. If GeneDx finds a genetic variation that we cannot interpret, another member of your family with BrS will be tested at no additional cost. In such circumstances, 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 BrS.

Who should have genetic testing for BrS?

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

How is genetic testing for BrS helpful?

- To confirm your clinical diagnosis of BrS, especially if the diagnosis is unclear
- To identify your family members who are at risk of developing BrS
- To make informed personal and family health decisions

How long does it take to complete the genetic test?

It usually takes six to 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 associated with BrS in one of your genes. This finding confirms the diagnosis of BrS and provides valuable information to you and your family members. Knowledge of your specific genetic mutation can help your physician identify activities and behaviors that should be avoided 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 their risk for BrS. If a family member is found to be positive for the familial mutation, this individual is considered to be at risk for BrS and should be referred for cardiac evaluation including an ECG. Mutation-positive family members should have a baseline electrocardiogram, clinical evaluation by a cardiologist, and annual evaluations with a cardiologist. 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 associated with BrS in one of your genes. However, this does not rule out BrS or a genetic cause of BrS, 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 BrS 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 BrS. A VOUS report is sent 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 greater the number of affected family members who carry the VOUS, the greater the likelihood that the VOUS is responsible for BrS 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 BrS 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 BrS panel testing in a patient?

The first BrS patient in a family to be tested typically requires analysis of all five genes in the BrS 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 the forms with 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
- Ramon Brugada Senior Foundation: www.brugada.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
- Information on medications that may complicate Brugada syndrome: www.brugadadrugs.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

