



Arrhythmogenic Right Ventricular Cardiomyopathy

A Guide for Patients

Arrhythmogenic Right Ventricular Cardiomyopathy

What is arrhythmogenic right ventricular cardiomyopathy?

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a condition that changes the muscle in your heart, affecting the ability of your heart to beat regularly and effectively. Irregular heartbeats are known as arrhythmias. In ARVC, your normal heart muscle cells (called cardiac myocytes) are weakened, mostly affecting the right heart chamber (right ventricle). Arrhythmogenic right ventricular cardiomyopathy therefore means that there is a disorder of the muscle cells in your heart's right ventricle, causing irregular heartbeats and potential enlargement of the right ventricle. Sometimes ARVC is called ARVD (arrhythmogenic right ventricular dysplasia), but they are the same condition. ARVC affects 1 in 2,500 individuals, although some individuals may have ARVC and not develop symptoms. Men and women are equally at risk, although men are more likely to show symptoms.

What are the symptoms of ARVC?

Symptoms of ARVC include:

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

If you have symptoms of ARVC, they usually develop by the time you are 20 to 40 years old, although symptoms have been seen at all ages. Since symptoms of ARVC 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 ARVC or any heart condition. ARVC may also manifest as sudden cardiac arrest in athletes.

What causes ARVC?

ARVC is caused by an abnormality (mutation) in one of your genes. The known genes associated with ARVC are listed in Table 1. Mutations in these seven genes have been identified in 40%–50% of individuals with ARVC. ARVC is inherited in an autosomal-dominant manner, so if you have ARVC there is a 50% chance of passing on the genetic disorder to each of your children. Not all individuals who carry an ARVC mutation will have symptoms. Moreover, not all individuals with ARVC will have a genetic cause of their disease, and environmental factors or physical activity can influence the disorder.

TABLE 1

GENE	GENE NAME
DSC2	Desmocollin 2
DSP	Desmoplakin
DSG2	Desmoglein 2
PKP2	Plakophilin 2
RYR2	Ryanodine receptor 2
JUP	Plakoglobin
TMEM43	Transmembrane protein 43

How is ARVC diagnosed?

ARVC is usually diagnosed using noninvasive tests to look at the structure of your right ventricle and to measure how it is functioning. Your physician may use echocardiography (which uses sound waves to get an image of your heart) or cardiac magnetic resonance imaging (cardiac MRI). Additionally, a 24-hour Holter monitor may be obtained to look for any irregularities in how your heart is beating. Sometimes, additional tests are also necessary, such as electrophysiological testing, right ventricular angiography and endomyocardial biopsy. Your physician will also review your medical and family histories. Genetic testing can be used to confirm your doctor's clinical diagnosis.

How is ARVC treated?

The clinical management of ARVC 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. Medications may include β -blockers and/or anti-arrhythmic drugs, such as sotalol or amiodarone. Heart transplantation is rare, but may be considered if standard medical treatment does not manage your symptoms and progressive heart failure develops. Triggers of sudden cardiac arrest in ARVC include vigorous physical activity. Avoiding competitive sports and strenuous exercise is often recommended.

Genetic Testing for ARVC

How is genetic testing for ARVC performed?

The ARVC 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 ARVC. 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 a comprehensive genetic test for ARVC. Identifying the genetic cause of your ARVC 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 ARVC, 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 ARVC.

Who should have genetic testing for ARVC?

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

How is genetic testing for ARVC helpful?

- Confirms your clinical diagnosis of ARVC, especially if the diagnosis is unclear
- Identifies your family members who are at risk of developing ARVC
- 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 associated with ARVC in one of your genes. This finding confirms the diagnosis of ARVC and provides valuable information to you and your family members. A genetic confirmation of ARVC can help your physician identify 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 ARVC. If a family member is found to be positive for the familial mutation, this individual is considered to be at risk for ARVC and should be referred for cardiac evaluation. It is important to note that symptoms may vary even within families.
- **A negative result** indicates that we did not identify a disease-causing mutation associated with ARVC in one of your genes. **However, this does not rule out ARVC or a genetic cause of ARVC, and your health care 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 an ARVC 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 ARVC. **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 greater the number of affected family members who carry the VOUS, the greater the likelihood that the VOUS is responsible for ARVC 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 can't afford to pay the full cost of testing, GeneDx provides a financial assistance program that includes 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 ARVC 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 this 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 ARVC panel testing in a patient?

The first ARVC patient in a family to be tested typically requires analysis of all seven genes in the ARVC 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.

References

- 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 Syndrome (SADS), 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

