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My46 Trait Profile

Arrhythmogenic Right Ventricular Cardiomyopathy

Other Names: Arrhythmogenic Right Ventricular Dysplasia

Arrhythmogenic Right Ventricular Cardiomyopathy is a heritable disease of the heart muscle in which the muscle is gradually replaced with fat and scar tissue. It can be caused by mutations in any one of many different genes.

Characteristics of Arrhythmogenic Right Ventricular Cardiomyopathy

ARVC is a heritable condition that affects about 1 in 1000 - 2500 people. ARVC is a disease of the heart muscle (cardiomyopathy), in which the muscle is gradually replaced with fat and scar tissue (fibrofatty replacement). The muscle of the right ventricle is usually most affected, however the left ventricle may also be affected. This reduces the ability of the heart to pump blood efficiently and lead to problems with how the heart beats (arrhythmias). The effects of ARVC are highly variable. In some people, ARVC causes very little to no symptoms. In other people, this condition can lead to heart failure and sudden cardiac death. It is estimated that approximately 20% of sudden cardiac deaths under that age of 35 years is due to ARVC. The most common presenting symptoms are feeling like your heart skips a beat (palpitations), dizziness or light-headedness and fainting (syncope). Most individuals with ARVC develop these symptoms in their 20s to 50s.

Diagnosis/Testing

ARVC is diagnosed clinically by established guidelines. These guidelines include criteria that look at the hearts structure and function, which is measured by both noninvasive testing and invasive testing. Noninvasive testing includes, ultrasounds of the heart (echocardiogram) and other imaging of the heart (MRI) and tests that measure the electrical activity of the heart (electrocardiogram/EKG, signal averaged EKG, holter monitor and stress test). A holter monitor measures the electrical activity of the heart for a long period of time, usually 24 hours. A stress test looks at the hearts electrical activity and structure before, during and after exercise. Invasive testing may include a biopsy (sample) of the heart tissue and other tests that require a heart catheterization (putting a thin tube into the heart). The guidelines also include family history and genetic testing. Because the clinical findings of ARVC can be so variable, not every person will meet diagnostic criteria.

Currently, there are at least 8 genes associated with ARVC that are available to test on a clinical basis. These genes are: DSC2, DSG2, DSP, JUP, PKP2, RYR2, TGFB3 and TMEM43. The majority of these genes are responsible for making parts of heart desmosomes. Desmosomes help provide strength to the heart cells and help signals pass between them. When there is a change or mutation in a desmosome gene, it is thought that the heart cells are predisposed to detach from each other and die. When this happens, the heart cells are replaced by fat and scar cells (fibrofatty replacement), which leads to the clinical signs and symptoms of ARVC.

Approximately 50% of individuals with a clinical diagnosis of ARVC will have a mutation identified on one of these eight genes. This means, that in about half of people with ARVC, no genetic cause is determined. This may be because there is no genetic cause or the responsible gene has not yet been discovered.

Management/Surveillance

Management of ARVC is aimed at the prevention of arrhythmias and sudden cardiac death. Management is tailored

to an individuals clinical features. Management can include the use of medications to reduce the chance of arrhythmias and placement of an implantable cardiac defibrillator (ICD). An ICD is a device that is placed in the chest that uses pulses or shocks to control arrhythmias that could lead to a sudden cardiac arrest. Rarely, a person with ARVC may need a heart transplant secondary to heart failure.

It is recommended that all family members that are found to have an ARVC causing mutation have non-invasive cardiac screening every 1 to 2 years. In children, screening should begin around puberty (10-12 years) and be obtained at least every year until the second decade of life. Should a family member choose not to have genetic testing or if a genetic cause cannot be identified in a family, they should obtain a baseline cardiac evaluation and, if normal, repeat every 2-3 years or as recommended by their cardiologist. There should also be a low threshold for evaluation of symptoms, including syncope, palpitations, dizziness or heart racing in all first-degree family members.

It is very important that individuals at risk for ARVC be evaluated by a cardiologist. Individuals without symptoms but who are still at risk for developing ARVC, either because of family history or mutation status, may still be at risk for sudden cardiac death, especially during strenuous activity. Healthcare providers may make recommendations regarding avoiding strenuous exercise and activities.

Mode of inheritance

ARVC is mainly inherited in an autosomal dominant pattern. This means inheriting one mutation is enough for an individual to be at risk to develop ARVC. A mutation can be inherited from a parent or it can occur brand new (de novo) in a person. It is estimated that up to 50% of people with ARVC have other family members with signs or symptoms of ARVC. There are also autosomal recessive forms of ARVC. This means that an individual has to inherit two mutations (i.e., one from each parent) to be at risk to develop ARVC. Usually, the autosomal recessive forms of ARVC are associated with other clinical findings of the skin and hair.

Risk to family members

The risk to family members depends on whether or not the individual with ARVC has a mutation that was passed down from a parent. If a parent also has a mutation, the risk of having a child who also has the mutation is 50% with each pregnancy. If a parent does not have the mutation, the risk of other siblings being affected is very low.

Not every person that inherits a mutation will develop ARVC. This is called reduced penetrance. However, their children are still at risk for inheriting the mutation and developing ARVC. Also, not every person that inherits a mutation will develop the same symptoms or be diagnosed at the same age as other people with the same mutation, even within their own family. This is due to variable expressivity. This may be due to other genetic or environmental factors that influence the progression of ARVC.

Special considerations

None

Resources

The Cardiomyopathy Association
http://www.cardiomyopathy.org/
SADS Foundation
http://www.cardiomyopathy.org/
Genetics Home Reference: Arrhythmogenic right ventricular cardiomyopathy
http://ghr.nlm.nih.gov/condition/arrhythmogenic-right-ventricular-cardiomyopathy

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