

Brugada Syndrome

Subjects: Genetics & Heredity

Contributor: Peter Tang

Brugada syndrome is a condition that causes a disruption of the heart's normal rhythm. Specifically, this disorder can lead to irregular heartbeats in the heart's lower chambers (ventricles), which is an abnormality called ventricular arrhythmia. If untreated, the irregular heartbeats can cause fainting (syncope), seizures, difficulty breathing, or sudden death. These complications typically occur when an affected person is resting or asleep.

Keywords: genetic conditions

1. Introduction

Brugada syndrome usually becomes apparent in adulthood, although it can develop any time throughout life. Signs and symptoms related to arrhythmias, including sudden death, can occur from early infancy to late adulthood. Sudden death typically occurs around age 40. This condition may explain some cases of sudden infant death syndrome (SIDS), which is a major cause of death in babies younger than 1 year. SIDS is characterized by sudden and unexplained death, usually during sleep.

Sudden unexplained nocturnal death syndrome (SUNDS) is a condition characterized by unexpected cardiac arrest in young adults, usually at night during sleep. This condition was originally described in Southeast Asian populations, where it is a major cause of death. Researchers have determined that SUNDS and Brugada syndrome are the same disorder.

2. Frequency

The exact prevalence of Brugada syndrome is unknown, although it is estimated to affect 5 in 10,000 people worldwide. This condition occurs much more frequently in people of Asian ancestry, particularly in Japanese and Southeast Asian populations.

Although Brugada syndrome affects both men and women, the condition appears to be 8 to 10 times more common in men. Researchers suspect that testosterone, a sex hormone present at much higher levels in men, may account for this difference.

3. Causes

Brugada syndrome can be caused by mutations in one of several genes. The most commonly mutated gene in this condition is *SCN5A*, which is altered in approximately 30 percent of affected individuals. This gene provides instructions for making a sodium channel, which normally transports positively charged sodium atoms (ions) into heart muscle cells. This type of ion channel plays a critical role in maintaining the heart's normal rhythm. Mutations in the *SCN5A* gene alter the structure or function of the channel, which reduces the flow of sodium ions into cells. A disruption in ion transport alters the way the heart beats, leading to the abnormal heart rhythm characteristic of Brugada syndrome.

Mutations in other genes can also cause Brugada syndrome. Together, these other genetic changes account for less than two percent of cases of the condition. Some of the additional genes involved in Brugada syndrome provide instructions for making proteins that ensure the correct location or function of sodium channels in heart muscle cells. Proteins produced by other genes involved in the condition form or help regulate ion channels that transport calcium or potassium into or out of heart muscle cells. As with sodium channels, proper flow of ions through calcium and potassium channels in the heart muscle helps maintain a regular heartbeat. Mutations in these genes disrupt the flow of ions, impairing the heart's normal rhythm.

In affected people without an identified gene mutation, the cause of Brugada syndrome is often unknown. In some cases, certain drugs may cause a nongenetic (acquired) form of the disorder. Drugs that can induce an altered heart rhythm include medications used to treat some forms of arrhythmia, a condition called angina (which causes chest pain), high

blood pressure, depression, and other mental illnesses. Abnormally high blood levels of calcium (hypercalcemia) or potassium (hyperkalemia), as well as unusually low potassium levels (hypokalemia), also have been associated with acquired Brugada syndrome. In addition to causing a nongenetic form of this disorder, these factors may trigger symptoms in people with an underlying mutation in *SCN5A* or another gene.

3.1. The genes associated with Brugada syndrome

- CACNA1C
- HCN4
- SCN5A
- TRPM4

4. Inheritance

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. In most cases, an affected person has one parent with the condition. Other cases may result from new mutations in the gene. These cases occur in people with no history of the disorder in their family.

5. Other Names for This Condition

- bangungut
- idiopathic ventricular fibrillation, Brugada type
- Pokkuri death syndrome
- sudden unexpected nocturnal death syndrome
- sudden unexplained death syndrome
- SUDS
- SUNDS

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