



Test Information Sheet

Cardiology Genetics: Brugada Syndrome (BrS) Panel

Also known as: Sudden Unexplained Nocturnal Death Syndrome (SUNDS); Right Bundle Branch Block, ST Segment Elevation and Sudden Death Syndrome; Idiopathic Cardiac Conduction Defect

Mendelian Inheritance in Man Number: 601144

Clinical Features:

Brugada syndrome (BrS) is a genetic heart disorder due to abnormal ion channel function characterized by ST segment elevation on ECG (at leads V₁₋₃) in the absence of structural heart disease. It is associated with increased risk for syncope (unexplained fainting), ventricular tachyarrhythmia and sudden cardiac death. Brugada syndrome is thought to be responsible for 4-12% of unexpected sudden deaths and for up to 20% of all sudden death in individuals with an apparently normal heart.¹ Brugada syndrome occurs worldwide and is estimated to affect 5 per 10,000 individuals of all ethnicities, with some regional differences.² However, men are 8-10 times more likely than women to express symptoms of Brugada syndrome.³

The diagnosis of BrS is based on clinical history, ECG findings and family history. Typically, the disorder manifests in patients between ages 20 to 40, but symptoms have been reported from infancy through late life. Most individuals with BrS are asymptomatic. The most common clinical symptoms are syncope and cardiac arrest that occur at rest, during sleep, or with high fever. Some patients with BrS have supraventricular arrhythmias. Some patients will develop symptoms of BrS after taking certain medications such as sodium channel blockers. BrS may be present even in the absence of any clinical symptoms and in some patients sudden cardiac death occurs without any preceding symptoms and without an identifiable cause at autopsy. Additionally, many symptoms of BrS are similar to other heart conditions that could account for either the ECG findings or syncope seen in patients and could be included in a differential diagnosis. These include arrhythmogenic right ventricular cardiomyopathy (ARVC), atypical right bundle branch block, left ventricular hypertrophy, early repolarization, acute myocardial infarction, and acute pericarditis.

Inheritance Pattern: Brugada syndrome is inherited in an autosomal dominant manner, where by definition an affected individual with a disease-causing mutation has a 50% chance of transmitting this mutation to a child. Brugada syndrome has been seen to exhibit incomplete penetrance and variable expressivity among families.

Genetics:

Brugada syndrome is genetically heterogeneous with mutations in at least 5 genes being identified to date. Up to 41% of individuals with heritable BrS have an identifiable mutation in the SCN5A, GPD1L, CACNA1C, CACNB2 and SCN1B genes.⁴ Most of the disease-associated mutations have been found in genes encoding ion channel proteins that help regulate the movement of sodium and calcium ions in and out of cardiac cells. However, disease-causing mutations in BrS have been reported to display reduced penetrance and variable clinical expressivity, even within families. Most individuals diagnosed with BrS have an affected parent.¹ Molecular genetic testing also makes it possible to identify asymptomatic family members at risk for BrS.

<i>Genotype</i>	<i>Gene</i>	<i>Gene Name</i>
BrS1	SCN5A	Alpha subunit of voltage-gated sodium channel type V
BrS2	GPD1L	NAD-dependent glycerol-3-phosphate dehydrogenase
BrS3	CACNA1C	Alpha-1C subunit of the L-type voltage-dependent calcium channel
BrS4	CACNB2	Beta-2 subunit of the voltage-dependent L-type calcium channel
BrS5	SCN1B	Beta subunit of voltage-gated sodium channel type I

