

The **Brugada syndrome** is a [genetic disease](#) that is characterised by abnormal [electrocardiogram](#) (ECG) findings and an increased risk of [sudden cardiac death](#). It is also known as [Sudden Unexpected Death Syndrome](#)^[1] (**SUDS**), and is the most common cause of sudden death in young men without known underlying cardiac disease in [Thailand](#) and [Laos](#)^[2].

Although the ECG findings of Brugada syndrome were first reported^[3] among survivors of cardiac arrest in [1989](#), it was only in 1992 that the Brugada brothers^[4] recognised it as a distinct clinical entity, causing sudden [death](#) by causing [ventricular fibrillation](#) (a lethal [arrhythmia](#)) in the [heart](#).

Approximately 20% of the cases of Brugada syndrome have been shown to be associated with mutation(s) in the [gene](#) that encodes for the [sodium ion channel](#) in the [cell membranes](#) of the muscle cells of the heart (the [myocytes](#)). The gene, named [SCN5A](#), is located on the short arm of the third [chromosome](#) (3p21). Loss-of-function mutations in this gene lead to a loss of the action potential dome of some epicardial areas of the right ventricle. This results in transmural and epicardial dispersion of repolarization. The transmural dispersion underlies ST-segment elevation and the development of a vulnerable window across the ventricular wall, whereas the epicardial dispersion of repolarization facilitates the development of phase 2 reentry, which generates a phase 2 reentrant extrasystole that captures the vulnerable window to precipitate ventricular tachycardia and/or fibrillation that often results in sudden cardiac death. At present time however, all the reported patients died because of the disease and submitted to detailed necropsy study, have shown a structural right ventricular pathology underlying the syndrome.

Over 160 mutations in the SCN5A gene have been discovered to date, each having varying mechanisms and effects on function, thereby explaining the varying degrees of penetration and expression of this disorder. ^[7]

An example of one of the mechanisms in which a loss of function of the sodium channel occurs is a mutation in the gene that disrupts the sodium channel's ability to bind properly to [ankyrin-G](#), an important protein mediating interaction between ion channels and cytoskeletal elements. Very recently a mutation in a second gene, [Glycerol-3-phosphate dehydrogenase 1-like gene](#) ([GPD1L](#)) has been shown to result in Brugada Syndrome in a large multigenerational family (London, 2006). This gene acts as an ion channel modulator in the heart, although the exact mechanism is not yet understood.

Recently Antzelevitch has identified mutations in the [L-type calcium channel](#) subunits ([CACNA1C](#) (A39V and G490R) and [CACNB2](#) (S481L)) leading to ST elevation and a relatively short QT interval (below 360 msec).^[8]

This condition is inherited in an [autosomal dominant](#) pattern and is more common in males. In addition it has a higher prevalence in most Asian populations.

Electrocardiography

In some cases, the disease can be detected by observing characteristic patterns on an [electrocardiogram](#), which may be present all the time, or might be elicited by the administration of particular drugs (e.g., Class IC antiarrhythmic drugs that blocks sodium channels and causing

appearance of ECG abnormalities - ajmaline, flecainide) or resurface spontaneously due to as yet unclarified triggers. The pattern seen on the ECG is persistent ST elevations in the electrocardiographic leads V₁-V₃ with a [right bundle branch block](#) (RBBB) appearance with or without the terminal S waves in the lateral leads that are associated with a typical RBBB. A prolongation of the PR interval (a conduction disturbance in the heart) is also frequently seen. The electrocardiogram can fluctuate over time, depending on the autonomic balance and the administration of antiarrhythmic drugs. Adrenergic stimulation decreases the ST segment elevation, while vagal stimulation worsens it. (There is a case report of a patient who died while shaving, presumed due to the vagal stimulation of the carotid sinus massage) The administration of class Ia, Ic and III drugs increases the ST segment elevation, and also fever. Exercise decreases ST segment elevation in some patients but increases it in others (after exercise when the body temperature has risen). The changes in heart rate induced by atrial pacing are accompanied by changes in the degree of ST segment elevation. When the heart rate decreases, the ST segment elevation increases and when the heart rate increases the ST segment elevation decreases. However, the contrary can also be observed.

Treatment

The cause of death in Brugada syndrome is [ventricular fibrillation](#). The episodes of syncope (fainting) and sudden death (aborted or not) are caused by fast polymorphic ventricular tachycardias or ventricular fibrillation. These arrhythmias appear with no warning. While there is no exact treatment modality that reliably and totally prevents ventricular fibrillation from occurring in this syndrome, treatment lies in termination of this lethal [arrhythmia](#) before it causes death. This is done via implantation of an [implantable cardioverter-defibrillator](#) (ICD), which continuously monitors the heart rhythm and will [defibrillate](#) an individual if ventricular fibrillation is noted. Some recently performed studies had evaluated the role of quinidine, a Class Ia antiarrhythmic drug, for decreasing VF episodes occurring in this syndrome. Quinidine was found to decrease number of VF episodes and correcting spontaneous ECG changes, possibly via inhibiting Ito channels.^[9] Those with risk factors for [coronary artery disease](#) may require an angiogram before ICD implantation.

References

- [^] Hong K, Berruezo-Sanchez A, Pongvarin N, et al (January 2004). "Phenotypic characterization of a large European family with Brugada syndrome displaying a sudden unexpected death syndrome mutation in SCN5A:". *J. Cardiovasc. Electrophysiol.* **15** (1): 64-9. [doi:10.1046/j.1540-8167.2004.03341.x](#). [PMID 15028074](#).
- [^] Brugada J, Brugada P, Brugada R (July 1999). "The syndrome of right bundle branch block ST segment elevation in V₁ to V₃ and sudden death--the Brugada syndrome". *Europace* **1** (3): 156-66. [doi:10.1053/eupc.1999.0033](#). [PMID 11225790](#).

- ^ [Martini B, Nava A, Thiene G, et al](#) (December 1989). "Ventricular fibrillation without apparent heart disease: description of six cases". *Am. Heart J.* **118** (6): 1203-9. [PMID 2589161](#).
- ^ [Brugada P, Brugada J](#) (November 1992). "Right bundle branch block, persistent ST segment elevation and sudden cardiac death: a distinct clinical and electrocardiographic syndrome. A multicenter report". *J. Am. Coll. Cardiol.* **20** (6): 1391-6. [PMID 1309182](#).
- ^ [Delpon E, Cordeiro JM, Núñez L, et al](#) (2008). "Functional Effects of KCNE3 Mutation and Its Role in the Development of Brugada Syndrome". *Circulation Arrhythmia and Electrophysiology* **1** (3): 209-18. [doi:10.1161/CIRCEP.107.748103](#).
- ^ [Watanabe H, Koopmann TT, Le Scouarnec S, et al](#) (June 2008). "[Sodium channel beta1 subunit mutations associated with Brugada syndrome and cardiac conduction disease in humans](#)". *J. Clin. Invest.* **118** (6): 2260-8. [doi:10.1172/JCI33891](#). [PMID 18464934](#).
- ^ [Napolitano C, Priori SG](#) (2006). "Brugada syndrome". *Orphanet journal of rare diseases* **1**: 35. [doi:10.1186/1750-1172-1-35](#). [PMID 16972995](#).
- ^ [Antzelevitch C](#) (2007). "Genetic basis of Brugada syndrome". *Heart rhythm : the official journal of the Heart Rhythm Society* **4** (6): 756-7. [doi:10.1016/j.hrthm.2007.03.015](#). [PMID 17556198](#).
- ^ [Belhassen B, Glick A, Viskin S](#) (2004). "Efficacy of quinidine in high-risk patients with Brugada syndrome". *Circulation* **110** (13): 1731-7. [doi:10.1161/01.CIR.0000143159.30585.90](#). [PMID 15381640](#).

External links

1. [GeneReviews: Brugada syndrome](#)

Algado et al:

http://www.medspain.com/ant/n13_jun00/Brugada.htm

Behr: [http://www.c-r-y.org.uk/long qt syndrome.htm](http://www.c-r-y.org.uk/long_qt_syndrome.htm)

[The Ramon Brugada Senior Foundation](#)

[http://digilander.libero.it/martini syndrome/](http://digilander.libero.it/martini_syndrome/)