Cardiovascular disease continues to be a leading cause of mortality and morbidity globally, with inherited cardiac disorders amongst those taking pride of place. In the early 1990s a newcomer joined their ranks. Named after the three Spanish physicians who first identified it, Brugada Syndrome can present in a variety of different ways, which creates significant challenges for risk stratification and management.

In the 20 years since the condition was first described, awareness of Brugada Syndrome has increased significantly within the medical and insurance professions, with an ever increasing number of cases identified at underwriting and claims stages.

The impetus for this article came from a recent spate of cases seen during the underwriting process: a trend that shows no sign of dropping off. In this article we explore the nature of this condition, its implications for risk management, consider its likely future incidence and conclude with a brief guide to the key issues around Brugada Syndrome in a Question and Answer section.

What is Brugada Syndrome?

The term was first used in 1992 to describe eight individuals who had survived recurrent episodes of sudden cardiac arrest (SCA). This occurs when uncoordinated electrical activity in the heart leads to life threatening abnormal rhythms. Brugada Syndrome with its capacity to disturb the heart’s normal electrical processes has since been identified in many different parts of the world, with
the highest incidence reported amongst young-to-middle-aged South East Asian males.

The number of affected individuals in the UK is estimated at 1:5,000-10,000. The youngest reported case was diagnosed at two days old, the eldest at 84.

Many of those diagnosed with Brugada have a positive family history of sudden cardiac death (SCD) or temporary loss of consciousness known as syncope. This, together with a clustering of initial symptoms between the ages of 30 and 50, suggests a genetic component to the disorder.

A genetic disease?

Several genetic mutations have been linked to Brugada Syndrome involving sodium channel, calcium encoding and potassium current genes. It is not always possible to establish a genetic association, with mutations identified in only 18 to 30% of those diagnosed. Genetic mutations occur equally in males and females; but males are 8 to 10 times more likely to show Brugada characteristics.

Symptoms vary from none to sudden cardiac death and include dizziness, palpitations, syncope with sweating, and rigidity or shaking of the limbs – potentially mistaken for epilepsy. All result from abnormal rhythms originating primarily, but not exclusively, in the lower chambers of the heart.

Diagram 1


Types

Brugada can also produce three distinctive electrocardiograph (ECG) patterns (illustrated in Diagram 1) which display in leads V1-V3. The Type 1 ECG pattern displays a prominent coved ST-segment as indicated by the arrow, followed by a negative T wave.

The Type 2 ECG pattern shows a high ST-segment take off with a saddleback configuration as denoted by the arrow, followed by a positive T wave.

The Type 3 ECG pattern features ST-segment elevation which may be saddleback or coved, with the possibility of displaying both forms.

These ECG patterns can occur spontaneously or following administration of sodium-blocking drugs like flecainide, procainamide and ajmaline. Brugada’s ECG signature is dynamic, with the ability to switch types or to disappear altogether from the trace. When Brugada is suspected but typical ECG patterns fail to exhibit, drug challenge testing with sodium channel blocking agents is often used.
The syndrome until recently was also considered to occur in structurally normal hearts with most of those diagnosed having no previous cardiac history and extensive investigative procedures often coming up empty. This view has since been challenged. Recent studies identify subtle, localised structural abnormalities in the right lower heart chamber on cardiac biopsies.

**How is Brugada diagnosed?**

An absence of overt structural defects tends to hinder diagnosis – as do sporadic genetic mutations, an often symptomless state and transient normalisation of ECG patterns.

A Type 1 ECG pattern that occurs spontaneously or following drug provocation testing with an ST elevation ≥ 2mm in more than 1 lead from V1 to V3 is considered diagnostic of Brugada Syndrome when combined with any of the following:

- A history of aborted sudden death or syncope
- Documented ventricular fibrillation or polymorphic ventricular tachycardia (often fatal abnormal heart rhythms)
- Family history of sudden cardiac death (<45 years)
- Coved type ECGs in family members
- Nocturnal agonal respiration
- Provocation of ECG changes or abnormal rhythms on electrophysiological testing or drug challenges

Type 2 and Type 3 ECG patterns are not considered diagnostic of Brugada Syndrome, merely suggestive. Electrocardiograms are the minimum standard investigation required to diagnose and evaluate Brugada Syndrome. To accurately appraise any application for insurance, or to assess any claim with a noted history of Brugada Syndrome, a general practitioner or attending cardiologist’s report is required including all relevant investigation results and electrocardiographic tracings.

Where Brugada is suspected based on family history or symptom presentation but characteristic ECG patterns do not spontaneously present, drugs can be administered to unmask diagnostic patterns or electrical stimulation testing can be performed as part of electrophysiological studies (EPS).

**What is the treatment?**

The treatment received for Brugada Syndrome is of major importance in both clinical and insurance risk management processes. The choice of treatment will depend on:

- The presence or absence of symptoms like syncope and aborted sudden cardiac death
- The individuals age
- Predisposition to ventricular arrhythmias during programmed electrical stimulation
- Worsening ST-segment elevation under drug challenge testing

Treatments include:

- Observation for those without symptoms and who have transient ECG abnormalities, or where electrical and pharmaceutical provocation fails to induce abnormal rhythms
- Pharmacological therapy such as beta-blockers, amiodarone or quinidine for those who are asymptomatic but in whom abnormal rhythms can be induced under testing
- Insertion of an automatic implantable cardiac defibrillator (AICD), in those with a past history of syncope and/or aborted cardiac arrest

Alternate procedures like radiofrequency ablation, cryosurgery and pacing have also been used, with inconclusive results.

Other measures recommended include avoiding medications, such as certain anti-depressants, antihistamines and anti-arrhythmics, that can potentiate the development of accelerated heart rhythms, optimal control of fever which can influence ECG patterns, moderation of alcohol intake and ensuring potassium and calcium level stability.

The implications for risk management include the obvious threat of sudden death or cardiac arrest, the potential for harm caused by less sinister atrial arrhythmias and hazards associated with the various treatments.

Numerous clinical studies have focused on identifying those most at risk of sudden death, cardiac arrest and syncope. It is generally accepted that those with a prior
history of aborted sudden death or syncope have the highest propensity to experience future events. It is this subset of individuals for whom defibrillator insertion is recommended. AICDs are inserted into the chest, like pacemakers, where they monitor and correct abnormally fast heart rhythms by sending electrical charges to the heart.

**Prognosis**

The prognosis for those receiving AICD therapy for Brugada Syndrome is favourable, with a 0% mortality reported in many randomised clinical trials. Consequently these individuals are eligible for insurance, provided the implanted devices are in working order.

In those with a history of Brugada Syndrome displaying a Type 1 ECG pattern but no symptoms, the prognosis is poor without the security of an implanted AICD. The use of medications to treat Brugada Syndrome has proven less effective than AICD therapy. Cover would typically be declined in this segment of lives if AICD treatment is not undertaken.

Randomised clinical trials have also shown that asymptomatic persons who exhibit Type 2 or 3 Brugada ECG patterns are generally at lower risk of sudden death, cardiac arrest or syncopal episodes. However, the dynamic status of the syndrome means that sudden death, cardiac arrest or syncope remain possibilities for this group of lives. Insurance terms may be considered for this subset, depending on the medical evidence provided.

**Further Complications**

A further implication for risk management lies in Brugada’s capacity to cause abnormal heart rhythms originating in the upper chambers of the heart. Termed atrial arrhythmias, these constitute a lower level of hazard than those which cause sudden death or cardiac arrest, but are not without threat.

If persistent, these atrial arrhythmias can lead to the formation of clots which can travel beyond the heart to other parts of the body where they may produce damage, for example strokes. They can also cause a drop-off in blood pressure or degenerate into more adverse heart rhythms. Applicants or lives assured who have been treated with AICD therapy present no additional mortality or morbidity risk as a result of potential atrial arrhythmias, due to the AICD devices’ ability to terminate both atrial and ventricular heart rhythms.

Individuals with Brugada who go untreated or receive treatments other than AICD therapy are therefore at risk of atrial arrhythmias and their sequelae. Where insurance terms are available, use of extra mortality ratings or exclusion clauses can offset this added risk.

A number of hazards associated with treatments for Brugada can also have risk management implications. These include, but are not limited to:

- Drug toxicity or the capacity of some medications to cause abnormal heart rhythms
- AICD device malfunctions including lead failure and limited battery life requiring surgical revisions
- The risk of infection or clot formation linked to surgical interventions
- The psychological impact where treatments consist merely of a wait and see approach or – at the other extreme – where an inserted device repeatedly activates

As awareness of this syndrome grows among healthcare providers and the general public – and as increasingly sophisticated genetic profiling and clinical testing techniques become available – we can expect to see more cases diagnosed and encountered at the underwriting and claims stages.

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# Key questions and answers

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
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<tr>
<td>Can insurance terms be considered following diagnosis and treatment?</td>
<td>This will depend on the nature of treatment delivered, for example those who have received an AICD may be considered for terms, subject to receipt of full medical details. Moderate loadings or appropriately worded exclusion clauses may apply to some covers.</td>
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<tr>
<td>What action can be taken if a Brugada ECG pattern is suspected on routine insurance screening but no formal diagnosis established?</td>
<td>The suggested approach is to postpone all cover where a Type 1, 2 or 3 ECG pattern presents in the absence of a formal diagnosis or where no investigation has occurred.</td>
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<td>What evidence should be sought to assess Brugada Syndrome appropriately?</td>
<td>As a definitive diagnosis relies on the presentation of a Type 1 ECG pattern in combination with any one of a number of other criteria, it is recommended that a general practitioner report (GPR) inclusive of any investigative results and electrocardiographic tracings be obtained.</td>
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<td>Should we expect high volumes of Brugada cases applying for insurance or anticipate a poor claims experience?</td>
<td>As the highest incidence of Brugada Syndrome is in South East Asia and estimated numbers in the United Kingdom are 1:5,000-10,000 persons it is not anticipated that high volumes will be encountered at underwriting or claims stages. However, increased migration from developing countries to industrialised nations and advances in gene typing and clinical detection could mean, we will see more cases.</td>
</tr>
<tr>
<td>Where can I find out more about this syndrome?</td>
<td>From the Hannover Re UK Life Branch Underwriting &amp; Claims Strategy Team.</td>
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Summary

At Hannover Re UK Life Branch we will consider any insurance applications or claims submitted featuring a history of Brugada Syndrome. However, terms may only be available for a select group, depending on symptoms, diagnosis and treatment received. Similarly claims may be admitted provided the event bringing about the claim meets with specified definition wordings.

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infocus

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