Patient Information

Brugada Syndrome

1. The Normal Heart

The heart is a specialized muscle that contracts regularly and continually, pumping blood around your body. The pumping action of your heart is caused by a flow of electrical signals through the heart that repeats itself in a cycle. Each cycle is one heartbeat. This electrical activity of the heart can be measured on an electrocardiogram (ECG). When the electrical activity of the heart is disturbed, known as an arrhythmia, it can affect your heart's ability to pump properly.

2. Brugada Syndrome

Brugada syndrome (BrS) is a rare inherited heart disease in which the flow of electrical signals through the heart is disturbed. This is because the movement of sodium into heart cells is damaged. This can lead to life-threatening arrhythmias.

3. Prevalence & Inheritance

Somewhere between 1 in every 2000 and 1 in every 5000 persons has BrS (the prevalence of the disease). BrS may be a genetic disease. This means that BrS can be caused by a defect (a mutation) in a gene that can be passed through families. A gene is part of our DNA which contains a code for making a molecule (a protein). Every person has two copies of each gene that can be linked to BrS. BrS can be caused by mutations in the gene that contains the code for sodium channels in the heart. This gene is called SCN5A. SCN5A lies on one of the autosomal chromosomes. If BrS is caused by a mutation in the SCN5A gene, then it is called an autosomal dominant disease.

This means that a mutation in only one of the two copies of the SCN5A gene (from father or from the mother) is enough to develop BrS (the mutation is dominant). A person with a mutation in SCN5A gene has a 50 percent (1 in 2) chance of passing the mutation to each child. The chance that a child will not inherit the mutation is also 50 percent. In some cases, a new (de novo) mutation can occur in the egg or sperm cells or in an embryo. In these cases, the child's parents do not have the mutation and BrS, but the child does have BrS and can pass the mutation to his or her own children.

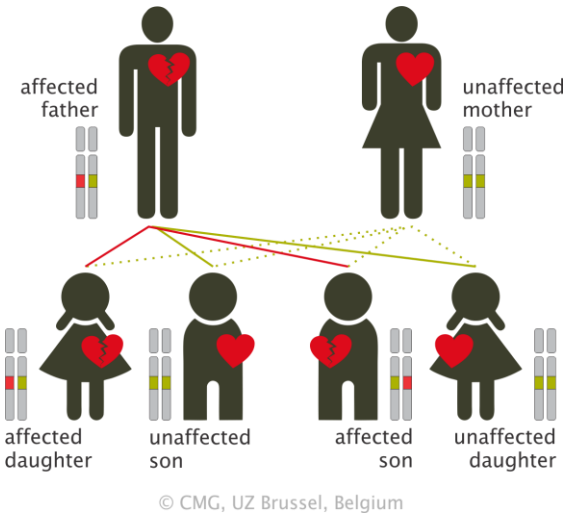

Figure 1. Autosomal dominant inheritance

4. Symptoms

The symptoms can include dizziness, palpitations, fainting, and sometimes sudden death. However, there are also a lot of asymptomatic patients.

5. Diagnosis

The most common tools to make the diagnosis of BrS are the medical and family history, physical examination, a heart electrical tracing (the electrocardiogram or ECG), an Ajmaline or Flecainide test, a heart ultrasound scan (echocardiogram), exercise testing, and heart rhythm monitor (Holter). Usually, BrS can be diagnosed on an the ECG. Patients with BrS can have **three different types of ECG patterns** (Figure 3). The diagnosis of BrS is only made if a person has

an obvious type 1 ECG pattern (known as a spontaneous pattern). In some people a type 1 ECG pattern is not present spontaneously, but can be brought out by a slow injection of a medicine (the Ajmaline or Flecainide test). These people also need to have other problems to make the diagnosis (for example a cardiac arrest or a family history of BrS). If a person has no symptoms and has only a type 2 or 3 ECG pattern, even after an Ajmaline test, then a diagnosis of BrS cannot be made and regular follow-up by a heart doctor (cardiologist) is advised.

5.1. ECG (electrocardiogram)

This is the most basic test. Small sticky patches (electrodes) are put onto the chest and sometimes to arms and legs. These are connected by wires to an ECG recording machine, which picks up the electrical activity for a few seconds that makes the heartbeat. Sometimes additional or repeated ECG-tests are necessary.

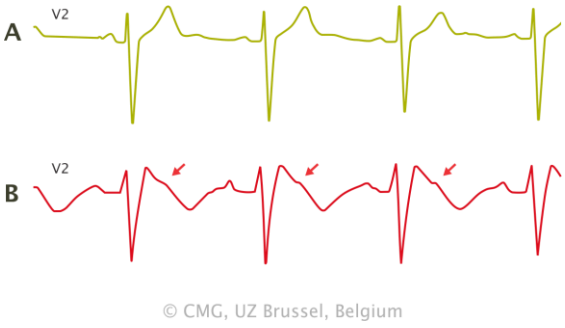

Figure 2. Brugada pattern.

This image shows a normal ECG-pattern in A. and typical signs of a Brugada-ECG in B. with ST-segment elevation (as pointed by the red arrow).

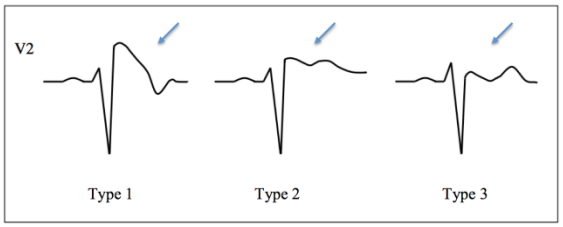

Figure 3. Brugada types 1,2, and 3.
(*Source: with permission from Centenary Institute, Australia)*

5.2. Ajmaline test

If a BrS is suspected on the ECG, but not completely sure (for example when type 2 or type 3 ECG pattern is present), then an Ajmaline test can be considered. Ajmaline is a medicine which can be given intravenously (by a slow injection known as an infusion) to a person to unmask the typical type 1 ECG pattern. If Ajmaline is not available, the test can also be performed with another medicine like Flecainide.

5.3. Exercise test (stress test)

Exercise test is the same as the ECG described above, but is recorded before, during and after exercising on a treadmill or an exercise bike. This records any changes in the electrical patterns that occur with exercise.

5.4. Holter monitoring

Holter monitoring involves a small digital machine, which can be worn on a belt round the waist. Four or six ECG electrodes from the machine are taped to the chest. It then records the electrical activity of the heart for 24-48 hours, or for up to seven days. During the monitoring all activities are listed in a 'diary'.

5.5 Cardiomemo and cardiac event recorders

These are more complicated versions of the Holter monitoring test described above. During any symptoms, the device can be triggered to record the heart's rhythm. The advantage of the cardiomemo is that it doesn't have any electrodes, so it just can be placed on the chest while having symptoms.

5.6. Echocardiogram (echo)

Echocardiogram uses ultrasound waves to look at the structures of the heart. An echocardiogram can detect different types of structural changes in the heart, for example heart muscle diseases and heart valve abnormalities. Areas of thinning of the heart muscle can also be identified. Patients with BrS don't have major structural abnormalities, but often an echo is performed once to confirm this.

5.7. Cardiac MRI

An MRI scan uses a magnetic field to create images of the heart. The scanner itself is a large tube with a table in the middle, allowing the patient to slide into the tunnel. The test takes about one hour. An MRI is very good at showing the structure of the heart and blood vessels, showing the condition of the heart muscle, and identifying any scarring within the heart. It's useful for patients with BrS in whom there is a suspicion of structural problems. In these patients, cardiac MRI can be used to look at the structure of the heart in more detail.

5.8 Genetic testing

In about 1 in 4 (25%) of the BrS families, a mutation can be found in the SCN5A-gene. In the remaining 75% of families with BrS, the genetic problem responsible for the disease is expected to be more complex, for example multiple mutations in different genes.

6. Therapy

Most people with BrS do not need treatment. In people with previous arrhythmias or an increased risk for arrhythmias the implantation of an internal cardiac defibrillator (ICD) can be considered. The ICD constantly monitors the electrical activity of the heart and can recognize severe arrhythmias. The ICD can be programmed specifically to each individual patient. It can treat severe and rapid arrhythmias by sending electrical impulses or give an electric shock, and return a normal heartbeat. An ICD consists of 2 parts: the battery (the device) and the electrical lead that monitors the electrical activity of the heart and provides electrical impulses or an electrical shock to the heart. The lead of an ICD can be placed in the right heart chamber (via blood vessels) or under the skin in an area of the chest overlying the heart.

7. Lifestyle & Sports

There are key recommendations for patients (and families) who are diagnosed with BrS, to prevent arrhythmias:

- avoid drugs that might worsen BrS. The list of drugs to avoid can be found at www.brugadadrugs.org

- during fever (temperature ≥ 38.5 degrees Celsius), it is important to go to the hospital to have an ECG. Some patients with BrS have important changes on their ECG during fever, with an increased risk of arrhythmias. When it is not possible to go the hospital, it is important to treat the fever quickly with paracetamol (to lower the body temperature and the risk of arrhythmias).

- avoid excessive alcohol intake

- encourage relatives to be screened

- usually patients with BrS can participate in sports.

However, if a person has had symptoms during physical activity, the expert physician can strongly advice not to exercise.

The diagnosis of BrS and the ability to pass on the condition can lead to anxiety and many other questions. Medical social workers or psychologists have experience with this and may be helpful for the patient and the family members.

8. Follow-up

Depending on the symptoms, age, and treatment there will be an advice for the frequency of follow-up to the cardiologist.

9. Family Screening

If a mutation in SCN5A gene is found in a patient with BrS (see Genetic testing), family members of this patient (to start with the first-degree family members: mother, father, brothers, sisters, children) can have genetic testing at a genetic heart clinic. Family members in whom the same mutation is found, are called 'mutation carriers' and will be followed by a cardiologist. Family members in whom the mutation is not found can sometimes also have BrS. The cause for BrS in these family members is not yet understood. But it is therefore important for family members without the mutation to see a cardiologist.
If a mutation in SCN5A is not found in a patient with BrS, family members of this patient (to start with the first-degree family members) are advised to see a cardiologist.

Although most patients don't have symptoms of BrS during childhood, there are patients who experience arrhythmias at a young age, often triggered by fever. These patients often have an abnormal ECG (for example a spontaneous type 1 ECG pattern). Therefore it is recommended that family members of BrS patients have an ECG in the first years of life, after which advice on follow-up can be given.

10. BrS and Pregnancy

There are no specific recommendations (others than reported in 'lifestyle and sports') for the mother and the baby during a pregnancy.

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