BMJ Best Practice

# Brugada syndrome

Straight to the point of care

Last updated: Mar 19, 2024

# Table of Contents

# Summary

Brugada syndrome (BrS) (also known as sudden unexplained [or unexpected] nocturnal death syndrome and as idiopathic ventricular fibrillation) should be suspected in any patient with a past history of any one or more of unexplained cardiac arrest, ventricular arrhythmia (e.g., documented polymorphic ventricular tachycardia or ventricular fibrillation) of unknown cause, or cardiogenic syncope. Be aware that patients may also present asymptomatically with incidental findings of Brugada pattern on ECG, or through family screening.

Diagnosis of BrS is considered probable or definite if spontaneous type 1 Brugada pattern is recorded on ECG from the 2nd to 4th intercostal spaces. Induced type 1 Brugada pattern (e.g., by fever, medications such as sodium-channel blockers, or by psychotropic drugs, alcohol, or illicit drugs) or type 2 or 3 Brugada pattern on the ECG is not diagnostic, and requires further investigation. However, diagnosis of BrS should be made by a specialist, and requires synthesis of ECG findings and features of the history (which should include relevant family history) and physical exam.

Treatment consists of conservative management and primary and secondary prevention of serious arrhythmic events. This aims to prevent serious arrhythmic events, while avoiding potential complications of any treatments. Nonconservative treatments include implantable cardioverter defibrillator (ICD), pharmacologic therapy, and radiofrequency catheter ablation.

# Definition

Brugada syndrome (BrS) (also known as sudden unexplained [or unexpected] nocturnal death syndrome and as idiopathic ventricular fibrillation) is an inherited channelopathy characterized by a typical pattern of ST-segment elevation in the precordial leads V1-V3, and is associated with increased risk of serious arrhythmic events such as ventricular arrhythmias and cardiac arrest.[1] BrS is typically first diagnosed in young- to middle-aged patients and is rare in children.[1] [2] [3]

The diagnosis and management of BrS in children is not covered in this topic.

THEORY

# Epidemiology

The true prevalence of Brugada syndrome (BrS) is difficult to determine because the diagnosis requires specific ECG findings (which are often intermittent), and many patients are asymptomatic.[1] [7] [8] [9] However, prevalence of BrS with type 1 Brugada pattern on the ECG is thought to be around 1 in 2000.[1] [4] [8][9] [10] Prevalence of a type 2 or type 3 Brugada pattern on the ECG (which is not diagnostic of BrS, but requires further investigation) is around 1 in 500.[1]

BrS is most commonly diagnosed in young- to middle-aged men; it is around 8 to 10 times more prevalent in men than in women.[1] [10] [11] The phenotypic expression of BrS appears to be age dependent because it is rare in children, with a prevalence of around 1 in 20,000.[1] [2] [3] However, BrS is thought to be the cause of around 4% to 12% of sudden cardiac deaths in children and young athletes, and around 20% of sudden explained deaths in young people in general.[12] Note that children are not covered elsewhere in this topic.

BrS occurs more commonly in Asia than in Europe and the US.[1] [13] It is particularly common in Southeast Asia, where nocturnal sudden death syndrome in young men was clinically reported by a variety of local names (e.g., bangungut, lai-tai, pokkuri, bei gui ya) in countries such as Philippines, Thailand, Japan, and China, prior to the formal classification of BrS.[14] It is the leading cause of death in men under age 40 years in Southeast Asia.[4]

# Etiology

Brugada syndrome (BrS) is a condition that is inherited through an autosomal dominant pattern of transmission with variable expression.[1] [4] [15] [9] Mutations of many genes have been implicated in BrS, but only SCN5A gene variants are considered definitely disease-causing.[1] [7] However, identifiable SCN5A variants are only found in approximately 20% to 30% of patients with BrS.[1] [16][17] [18] Mutations of other genes may account for around 2% to 5% of cases.[14] [16] [17][19]

Features of BrS may be apparent only when induced by certain factors.[1] [7] Inducible features of BrS are particularly important to identify in asymptomatic patients (i.e., those who do not have a past history of unexplained cardiac arrest, ventricular arrhythmias, or syncope), but may also be present in symptomatic patients. These include:[1] [7]

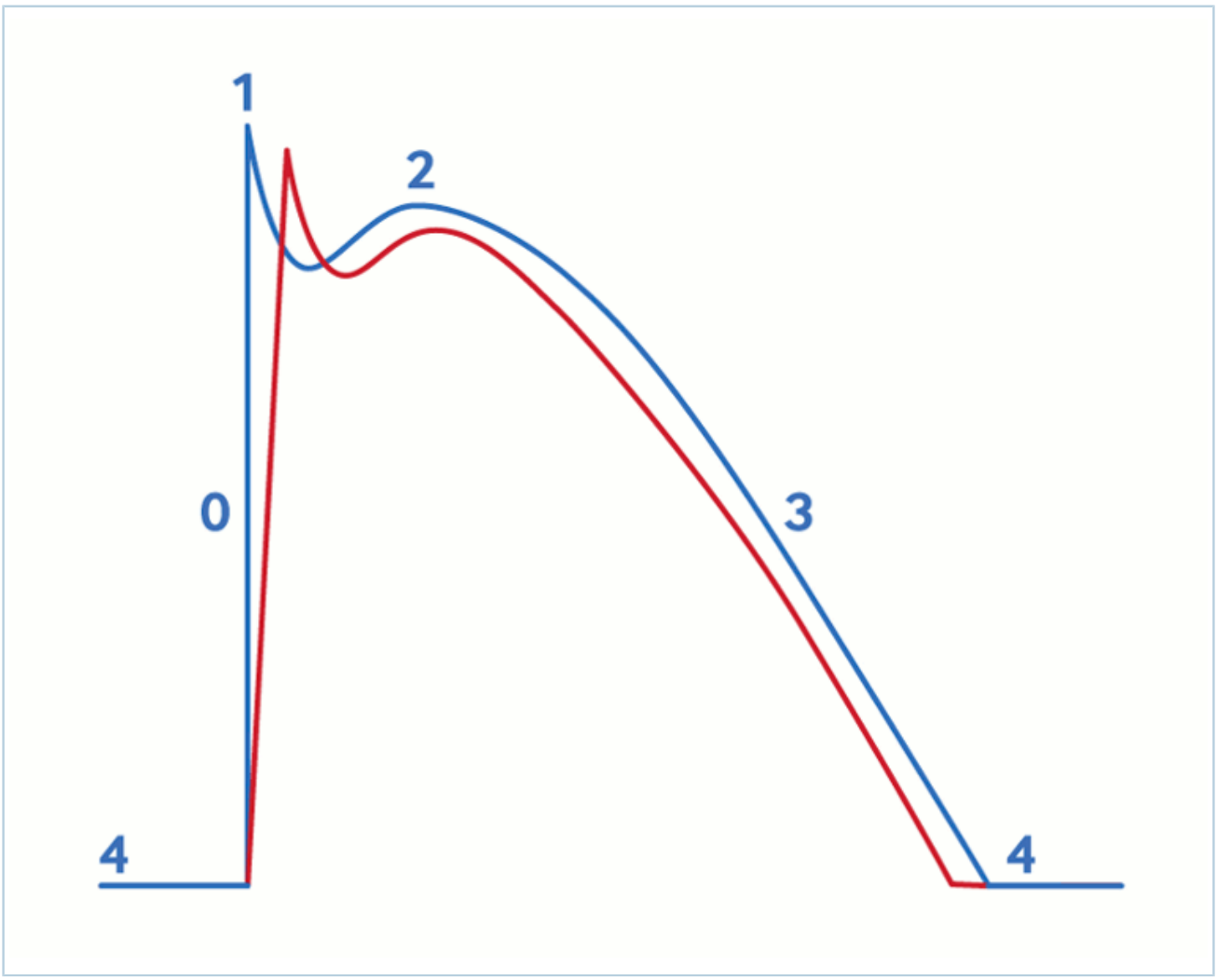
- Febrile illness. This is known to induce type 1 Brugada pattern on ECG and precipitate arrhythmic events.[1] [7] In endemic regions, the prevalence of BrS in patients presenting with febrile illness for any reason has been reportedly as high as 4%, around 20-fold greater than a nonfebrile control group in one Thai cross-sectional study of 401 patients.[20] [21] While in isolation fever is not specific for BrS, in a patient with suspected BrS, it has implications for both diagnosis and management.[1] [7]
- Medications.[1] [7] [18] These include sodium-channel blockers (e.g., flecainide, procainamide), psychotropic medications (e.g., tricyclic or tetracyclic antidepressants, lithium), and local anesthetics. These are known to induce type 1 Brugada ECG changes and may also precipitate arrhythmic events.[1] [7] [18]
- Illicit drugs or alcohol.[1] [7] These are known to induce type 1 Brugada ECG changes and may also precipitate arrhythmic events.[1] [7] [18]

# Pathophysiology

The underlying pathophysiology of Brugada syndrome (BrS) remains unclear.[1] It is likely that there are a number of contributing factors that lead to the typical Brugada pattern on ECG, rather than a single mechanism, because of the range of clinical manifestations and phenocopies.[1]

Around 20% to 30% of people with BrS have identifiable inherited mutations of the SCN5A gene, which causes dysfunctional cardiac voltage gated NaV1.5 sodium channels.[1] [7] [16] [17] [18] These defective sodium channels shorten the duration of the cardiac action potential, leading to a reduction of the peak influx of sodium ions and a slowing in the upstroke (phase 0) of the cardiac action potential.[1] Over 300 mutations of the SCN5A gene have been discovered so far.[22] This range of genetic mutations may cause differences in electrophysiologic abnormalities, which could explain the different clinical manifestations of BrS.[23] [24]

Experimental studies have shown that the function of NaV1.5 sodium channels is also affected by changes in temperature, with additional shortening of the cardiac action potential at higher temperatures.[1]




*Cardiac action potential in Brugada syndrome. Blue line indicates normal ventricular action potential; red line indicates delayed upstroke of action potential in Brugada syndrome. Action potential phases: 0, rapid depolarization; 1, rapid/early repolarization; 2, plateau; 3, terminal repolarization; 4, resting potential*

*Krahn AD et al. JACC Clin Electrophysiol 2022 Mar;8(3):386-405; used with permission*

Other genes that have been implicated in BrS (although their significance is disputed; only SCN5A gene variants are considered definitely disease-causing) include SCN10A (which encodes for the a-subunit of the NaV1.8 sodium channel), those that encode for NaV1.5 b-subunits, those involved in NaV1.5 trafficking or expression, and potassium and calcium channel genes.[1] [17] [19][25] [26] [27] [28] [29] [30] [31]

There is debate about whether BrS is due to a primary repolarization disorder, a primary depolarization disorder, or both.[1] [32] [33] The argument for a primary repolarization disorder is supported by the fact that patients with BrS have a conduction delay in the right ventricular outflow tract, which is associated with late action potentials.[1] This conduction delay results in heterogeneity of depolarization around the right ventricular outflow tract, which is thought to predispose the patient to arrhythmias.[1] The argument for a primary depolarization disorder is supported by evidence that has shown a dispersion of transmural (epicardial-endocardial gradient) action potentials in canine models of pharmacologically induced BrS.[1] [33] [34] Heterogeneity of repolarization between the epicardium and endocardium is thought to cause arrhythmias by phase 2 re-entry.[1] [34] In addition, both repolarization and depolarization abnormalities have been demonstrated in people with BrS, although it is suggested that these repolarization changes occur secondary to a primary depolarization disorder.[1]

Some studies have shown that people with BrS have functional changes in the epicardial aspect of the right ventricle.[1] [35] [36] There have also been histologic changes identified in the anterior right ventricular outflow tract that are associated with areas of low voltage and the presence of abnormal fractionated electrograms on electrophysiologic studies.[1] These changes include increased collagen and fibrosis, presence of inflammatory infiltrates, and a reduction in connexin-43 (a gap junction protein that provides electrical coupling between myocytes).[1] [37][38] Ablation that is targeted to these areas can result in correction of the typical Brugada pattern ECG changes and prevention of ventricular arrhythmias.[1] [22] [37] [38]

# Classification

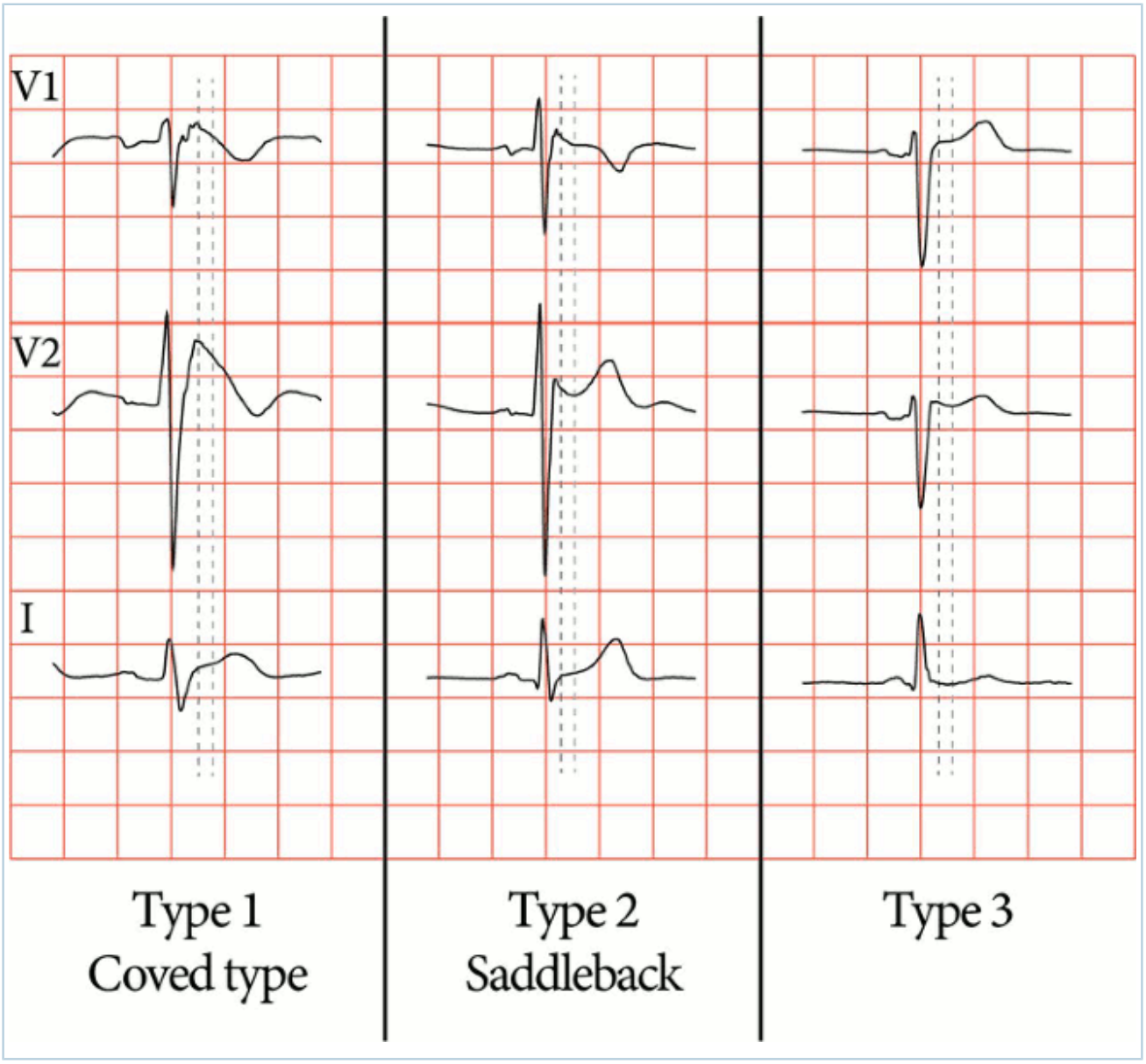
## ECG classification

Type 1

Coved ST-segment elevation (J-point elevation with a gradual down-sloping ST-segment) ≥2 mm with a negative T-wave in the right precordial leads.[1] [4] [5] [6] Type 1 Brugada pattern may be spontaneous, or induced (e.g., by factors such as fever or sodium-channel blockers).[1] [5] [7]

Type 2 or 3

Saddleback ST-segment configuration with variable levels of ST-segment elevation.[1] [4] [6]




*Electrocardiographic patterns in Brugada syndrome showing type 1 (diagnostic) and types 2 and 3 (non-diagnostic) patterns. Type-1 (diagnostic): coved STT morphology in lead V2 with J-point elevation (dark gray line) of ≥0.2 mV (≥2 mm) and a terminal ST-segment elevation (light gray line, J+60 ms) also ≥0.2 mV (≥2 mm). Note the PR interval and wider QRS complex, wide and deep S in lead I, and fractionation in the right precordial ECG leads. Type-2 (non-diagnostic): saddleback STT morphology in lead V2 with J-point elevation (dark gray line) of ≥0.2 mV (≥2 mm) and a terminal ST-segment elevation (light gray line, J+60 ms) ≥0.1 mV (≥1 mm), followed by a positive T wave. Note the less wide and deep S-wave in lead I, less prominent fractionation. Type-3 (non-diagnostic): saddleback STT morphology in lead V2 with J-point elevation (dark gray line) of ≥0.2 mV (≥2 mm) and a terminal ST-segment elevation (light gray line, J+60 ms) <0.1 mV (<1 mm)*

*Marsman EMJ et al. Heart 2022 May;108(9):668-75; used with permission*

THEORY

# Case history

## Case history #1

A 33-year-old man presents with palpitations and a recent episode of fainting while at the gym. An ECG with standard lead positions is unremarkable, aside from occasional premature ventricular complexes. Repeat ECG with high precordial leads shows ST segment elevation that is coved-type and >2 mm in amplitude, and inverted T-waves in the right precordial leads. The patient reports that his uncle passed away unexpectedly in his early 40s when his car went off the road unexpectedly while driving during the daytime. The patient has a past medical history of depression, for which he is taking a selective serotonin-reuptake inhibitor, but no other medical problems. He is a non-smoker but occasionally drinks 5-10 alcoholic beverages in one sitting while watching sports.

## Case history #2

A 19-year old student who is a college athlete is undergoing preparticipation evaluation and noted to have a type I Brugada pattern pattern on ECG. The student is asymptomatic, but states that his uncle died aged 38 in his sleep in Southeast Asia.

# Approach

Brugada syndrome is usually diagnosed through a combination of clinical features, risk factors, and ECG findings, although the diagnosis is considered probable or definite if spontaneous type 1 Brugada pattern is recorded on ECG from the 2nd to 4th intercostal spaces.[1] [4][7] [51] Refer all patients with type 1 Brugada pattern (spontaneous or induced) to a cardiologist or cardiac electrophysiologist for further investigation. Key differentials, such as acute coronary syndrome, should be excluded. The proposed Shanghai score may also be used to aid diagnosis.[1]

| Factor - ECG (12-lead/ambulatory)[b] | Points |
|---|---|
| Spontaneous type 1 Brugada pattern on standard or Brugada ECG | 3.5 |
| Fever-induced type 1 Brugada pattern on standard or Brugada ECG | 3 |
| Type 2 or 3 Brugada ECG pattern that converts with sodium channel-blocking drug challenge | 2 |
| **Clinical history[a]** | |
| Unexplained cardiac arrest or documented ventricular fibrillation/polymorphic ventricular tachycardia | 3 |
| Nocturnal agonal respirations | 2 |
| Suspected arrhythmic syncope | 2 |
| Syncope of unclear mechanism or unclear etiology | 1 |
| Atrial flutter or fibrillation in patients <30 years without alternative etiology | 0.5 |
| **Family history[a]** | |
| First- or second-degree relative with definite BrS | 2 |
| Suspicious SCD (during fever, at night, or when taking Brugada-aggravating drugs) in a first- or second-degree relative | 1 |
| Unexplained SCD <45 years in a first- or second-degree relative with negative autopsy | 0.5 |
| **Genetic test result** | |
| Probable pathogenic mutation in BrS susceptibility gene | 0.5 |
| **Total score (requires ≥1 ECG finding)** | |
| ≥3.5 points: Probable or definite BrS | |
| 2-3 points: Possible BrS | |
| <2 points: Non-diagnostic | |

**BrS** Brugada syndrome, **ECG** electrocardiogram, **SCD** sudden cardiac death
**a** This table was adapted from an original table as reported by Antzelevitch et al.
**b** Only award points once for highest score within each category

*Proposed Shanghai Score for diagnosis of Brugada syndrome*

*Adapted from Peltenburg PJ et al. Neth Heart J. 31. 10.1007/s12471-022-01723-6; used with permission*



| At risk | Evaluation and testing | Diagnostic criteria |
|---|---|---|
| Symptomatic<br>• Cardiogenic syncope<br>• Ventricular arrhythmias<br>• Resuscitated cardiac arrest<br>Asymptomatic<br>• Type 1 ECG<br>• Type 2/3 ECG<br>• Family screening of first-degree relatives | Initial<br>• Clinical: syncope, family history, medical history, medications<br>• ECG with high leads<br>• Echocardiogram: exclude structural abnormalities<br>Discretionary<br>• SCB provocation<br>• Holter monitor<br>• Further cardiac imaging as indicated<br>• EP study<br>• Cardiac MRI | Definite<br>• Spontaneous type 1 ECG changes in $V_1$-$V_2$ at ICS2-4<br>Probable<br>• Type 1 ECG changes in $V_1$-$V_2$ at ICS2-4 with fever or SCB provocation |

*Diagnosis summary for Brugada syndrome [IMAGE KEY: EP = Electrophysiology; ICD = Implantable cardioverter defibrillator; ICS = Intercostal space; MRI = Magnetic resonance imaging; SCB = Sodium-channel blocker]*

*Krahn AD, et al. Brugada syndrome. JACC Clin Electrophysiol 2022 Mar;8(3):386-405; used with permission*

## History

Take a detailed history of any patient with suspected BrS to identify clinical features of BrS, risk factors for BrS and sudden cardiac death, and other potential differentials. This is particularly important for the diagnosis of BrS in patients with type 1 Brugada pattern on ECG that is induced by triggers (e.g., fever, medications such as sodium-channel blockers or psychotropic drugs, alcohol, or illicit drugs), and in asymptomatic patients with type 2 or 3 Brugada pattern on ECG.[1] [7]

Clinical features

Consider a diagnosis of symptomatic BrS if a patient has a past history of any one or more of the following:

- Unexplained cardiac arrest, or documented polymorphic ventricular tachycardia (PMVT), or ventricular fibrillation (VF)[1] [5] [7]
  - There are many causes of sudden cardiac arrest, PMVT and VF, but BrS should be considered as a differential, particularly if there is Brugada pattern on ECG and one or more risk factors for BrS (see below).
  - Patients may also present with monomorphic VT, but this is rare and should prompt investigation of other arrhythmogenic cardiomyopathies.[5] [52] [53]
- Cardiogenic syncope
  - Up to one third of patients with BrS present with, or have a history of, syncope at the time of diagnosis.[54]

- Take a careful history to differentiate cardiogenic from noncardiogenic causes of syncope.[1] [7] The Shanghai score for the diagnosis of BrS assigns 2 points to patients with suspected cardiogenic syncope, and 1 point to those with an unclear cause of syncope.[1] [49]
- Patients with BrS who have a history of cardiogenic syncope are also at 2.5 to 5-fold greater risk of serious arrhythmic events compared with those with noncardiogenic syncope.[47] [48] [55] [56] [57] Patients with noncardiogenic syncope have not been shown to have an increased risk for serious arrhythmic events.[58]

Other clinical features of BrS may include:

- Atrial fibrillation or flutter in a patient <30 years.[1] [59] [60]
  - Concomitant atrial arrhythmias are common in patients with BrS, with a prevalence of approximately 10%, although these are not specific for diagnosis of BrS.[61]
  - Use of sodium-channel blockers may unmask the Brugada pattern in some of these patients.[61]
- Nocturnal agonal respirations.[1] [7]
  - The Shanghai score for BrS assigns 2 points to patients with nocturnal agonal respirations.[1] [49]
  - In a Danish national survey, prevalence of nocturnal agonal respirations in patients with BrS was 14%, but this is likely to be greater in endemic areas.[62]
  - Nocturnal agonal respirations were described in early reports from Southeast Asia (Philippines, Thailand, Japan, China, and others) of sudden unexpected nocturnal death syndrome (SUNDS), a syndrome which is thought to be genetically, phenotypically, and functionally the same as BrS.[63]

Risk factors

Identify any of the following risk factors which are associated with, or increase the risk of, BrS and subsequent sudden cardiac death:[1]

- Age 30 to 50 years[1]
  - BrS is typically first diagnosed in young to middle-aged patients.[1]
  - Patients ages 30 to 50 years with BrS are also at high risk of serious arrhythmic events.[39] This is also typically the age at which patients with BrS may present with their first serious arrhythmic event.[1] However, serious arrhythmic events have also been reported in children as young as <1 year old.[21] [40] [41] Women in particular may be more likely to have their first SAE in childhood, or later in life.[1] [39]
  - Patients >50 years who have BrS experience significantly fewer serious arrhythmic events compared with younger patients, and for those ≥55 years at the time of BrS diagnosis, annual mortality is similar to that of the general population.[41] [42] [43] However, it remains unclear whether these observations are due to protective effects acquired through aging or simply represent selection bias.
- Male sex[1]



- BrS is more common in men compared with women.[1] [39] Men account for up to 90% of cases of BrS in some cohorts.[1] [39]
- Evidence has shown that men with BrS are also at increased risk of serious arrhythmic events.[44] [45] [46] However, this finding remains controversial, and has not been confirmed with complete adjustment for potential confounding factors.[47] [48]

- Asian ancestry[1]
  - BrS occurs more commonly in Asia compared with Europe and the US.[1] [13] BrS is particularly common in Southeast Asia, where a nocturnal sudden death syndrome in young men was clinically reported by a variety of local names in countries such as Philippines, Thailand, Japan, and China, prior to the formal classification of BrS.[14]
- Positive family history
  - Determine the following features (which form part of the Shanghai score) in any first or second degree relative of the patient:[1] [49]
    - Definite BrS
    - Suspicious sudden cardiac death (febrile, nocturnal, confounded by BrS-associated drug)
    - Unexplained sudden cardiac death <45 years with noncontributory autopsy.
  - Bear in mind that, although family history is a standard and important part of any diagnostic evaluation, limited evidence exists to support a family history of sudden death as a risk factor for BrS-associated arrhythmic events.[50]

Asymptomatic patients

Features of BrS may only be apparent when induced by certain factors.[1] [7] Inducible features are particularly important to identify in asymptomatic patients (i.e., those who do not have a past history of unexplained cardiac arrest, ventricular arrhythmias, or syncope), but may also be present in symptomatic patients. These include:[1] [7]

- Febrile illness
  - Known to induce type 1 Brugada pattern on ECG and precipitate arrhythmic events.[1] In endemic regions, the prevalence of BrS in patients presenting with febrile illness for any reason has been reportedly as high as 4%, around 20 times greater than a non-febrile control group in one Thai cross-sectional study of 401 patients.[20] [21] While in isolation fever is not specific for BrS, in a patient with suspected BrS, it has implications for both diagnosis and management.[1]
- Medications
  - These include sodium-channel blockers (e.g., flecainide, procainamide), psychotropic medications (e.g., tricyclic or tetracyclic antidepressants, lithium), and local anesthetics.
  - Known to induce type 1 Brugada ECG changes, and may also precipitate arrhythmic events.[1] [18]
- Illicit drugs or alcohol

- Known to induce type 1 Brugada ECG changes and may also precipitate arrhythmic events.[1] [18]

## Physical examination

Perform a full cardiovascular examination to identify other causes of the patient's clinical presentation. These include:

- Acute coronary syndrome
- Arrhythmogenic cardiomyopathy
- Athlete's heart
- Hemodynamically significant valvular disease
- Pectus excavatum
- Incomplete right bundle branch block.

Although the physical examination is valuable in the overall evaluation of any patient, it is not useful to rule out or rule in a diagnosis of BrS.

Check whether the patient has a fever, which may unmask features of BrS.[1]

## Initial investigations

ECG

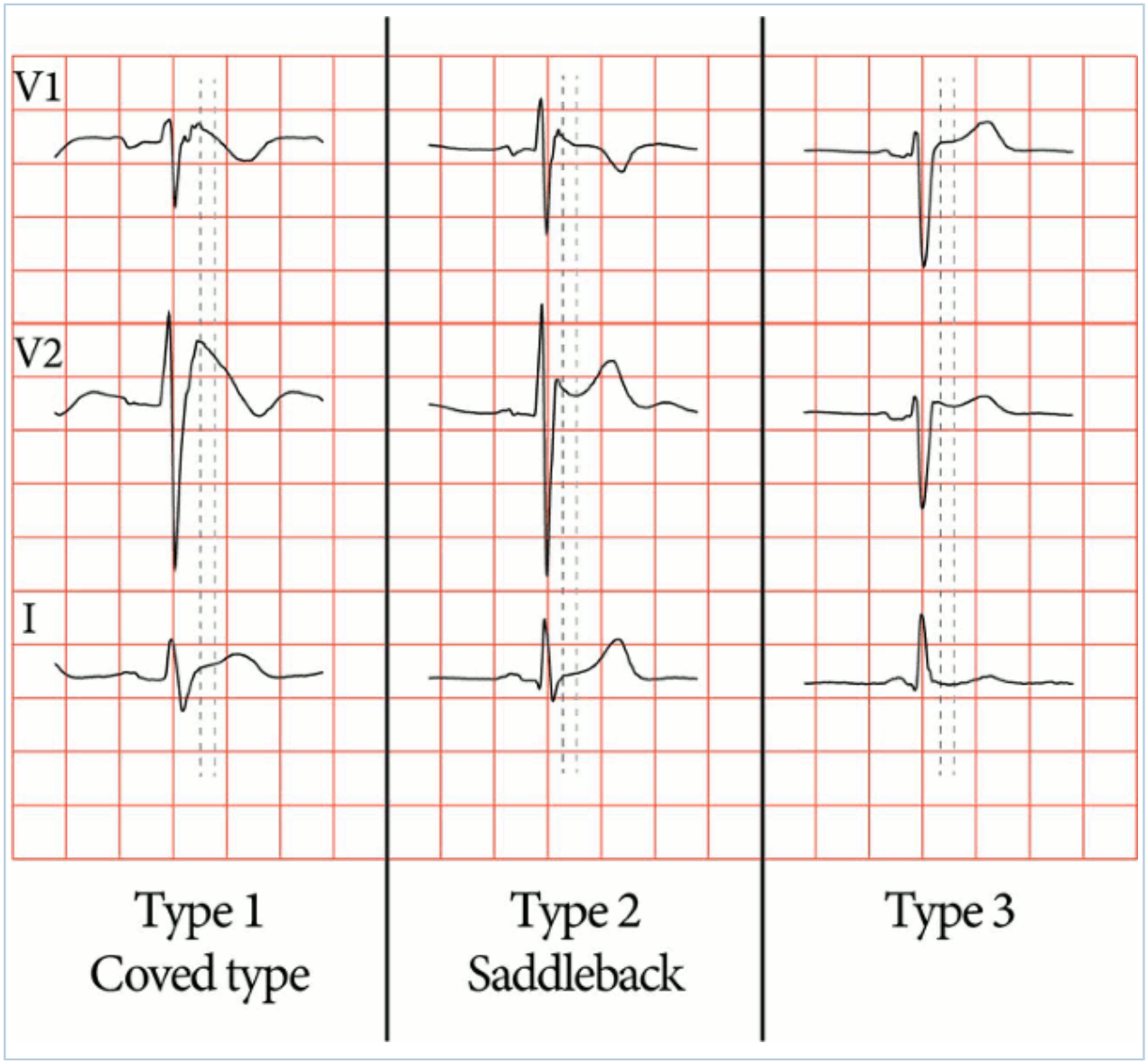
Perform an ECG as the first line investigation for any patient with suspected BrS.[1][5] [7] [18] [64] Look for the following patterns that may indicate BrS:[1] [7]

- Type 1: coved ST-segment elevation (J-point elevation with a gradual down-sloping ST-segment) ≥2 mm with a negative T-wave in the right precordial leads.[1] [4] [5] [7] [51]
    - Type 1 Brugada pattern may be spontaneous, or induced (e.g., by factors such as fever or sodium-channel blockers).[1] [5] [7]
- Type 2 or 3: saddleback ST-segment configuration with variable levels of ST-segment elevation.[1] [4] [51]

Consider high precordial lead testing if ECG using standard lead placement is not conclusive and you have a high clinical suspicion of BrS. High precordial lead testing increases diagnostic yield by accounting for anatomic variations in right ventricular outflow tract anatomy.[1] [4] [5] [65] [66] [67]

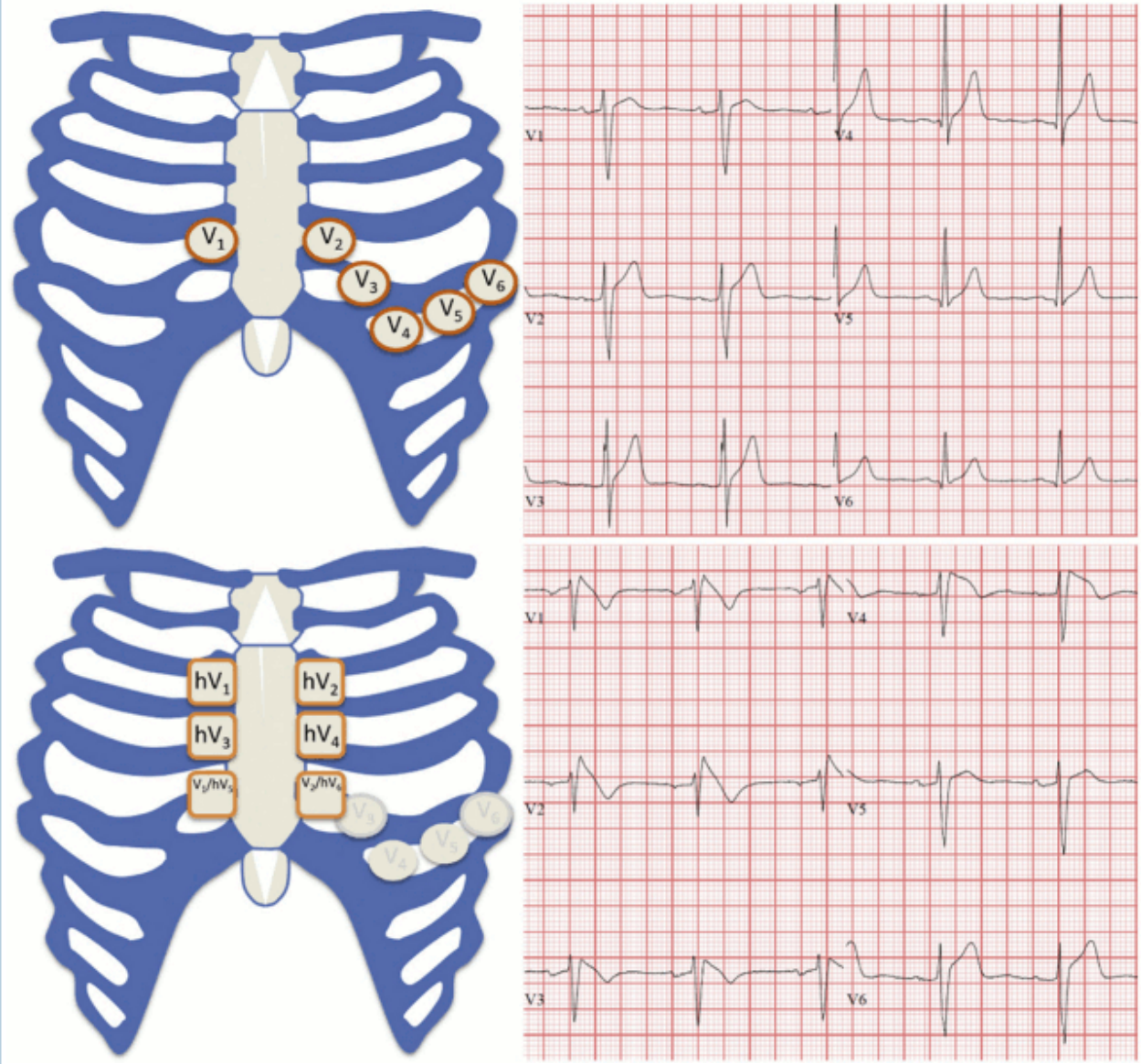





*Electrocardiographic patterns in Brugada syndrome showing type 1 (diagnostic) and types 2 and 3 (non-diagnostic) patterns. Type-1 (diagnostic): coved STT morphology in lead V2 with J-point elevation (dark gray line) of ≥0.2 mV (≥2 mm) and a terminal ST-segment elevation (light gray line, J+60 ms) also ≥0.2 mV (≥2 mm). Note the PR interval and wider QRS complex, wide and deep S in lead I, and fractionation in the right precordial ECG leads. Type-2 (non-diagnostic): saddleback STT morphology in lead V2 with J-point elevation (dark gray line) of ≥0.2 mV (≥2 mm) and a terminal ST-segment elevation (light gray line, J+60 ms) ≥0.1 mV (≥1 mm), followed by a positive T wave. Note the less wide and deep S-wave in lead I, less prominent fractionation. Type-3 (non-diagnostic): saddleback STT morphology in lead V2 with J-point elevation (dark gray line) of ≥0.2 mV (≥2 mm) and a terminal ST-segment elevation (light gray line, J+60 ms) <0.1 mV (<1 mm)*

*Marsman EMJ et al. Heart 2022 May;108(9):668-75; used with permission*




*Standard- and high-lead electrocardiogram positions. (Top) Standard-lead ECG positions and corresponding precordial ECG in a patient with Brugada syndrome. (Bottom) High-lead ECG positions and corresponding ECG in the same patient. Note that hV5 and hV6 on the high-lead ECG correspond with V1 and V2 on the standard-lead ECG.*

*Krahn AD, et al. Brugada syndrome. JACC Clin Electrophysiol 2022 Mar;8(3):386-405; used with permission*

Refer all patients with type 1 Brugada pattern (spontaneous or induced) to a cardiologist or cardiac electrophysiologist.

- The diagnosis of BrS is considered probable or definite if spontaneous type 1 Brugada pattern is recorded on ECG from the 2nd to 4th intercostal spaces.[1] [4] [7] [51] However, these patients require diagnostic evaluation by a specialist.
- Ensure you establish the patient's clinical history in all patients with type 1 Brugada pattern.[4]
- This is essential, because distinguishing type 1 Brugada pattern from other causes of ST elevation using ECG alone can be difficult, even for an experienced cardiologist.[4]



- If the patient has induced type 1 Brugada pattern, additional information is key to aid diagnosis of BrS (e.g., relevant clinical history or family history, and/or genetic testing).[1]

If the patient has type 2 or 3 Brugada pattern, consider provocative drug testing with sodium channel blockade (see below).[1] [18]

Echocardiogram

Organize an echocardiogram for any patient being evaluated for BrS to assess for underlying structural heart disease and to rule out other causes of their presentation.[1] [49] Echocardiogram is often normal in BrS or may demonstrate mild structural abnormalities in the right ventricle or right ventricular outflow tract.

## Other investigations

Provocative drug testing with sodium channel blockade

Consider provocative drug testing with sodium-channel blockers (e.g., procainamide, flecainide) for any patient with both:[1] [7] [13] [18][49]

- Type 2 or 3 Brugada pattern on ECG

  AND
- Suspected BrS due to relevant clinical signs, symptoms, or family history.

The diagnosis of BrS is considered probable in these patients if type 1 Brugada ECG pattern is provoked during drug testing with sodium-channel blockers; this scores two points on the Shanghai score.[1] Refer these patients to a cardiologist or cardiac electrophysiologist.

Due to an associated risk of inducing life-threatening ventricular arrhythmias, provocative drug testing should only be performed by experts under optimal circumstances.[68]

Sodium-channel blocker test is not recommended in patients with a prior type I Brugada pattern.[7]

Genetic testing

Arrange genetic testing in patients with type 1 Brugada pattern on ECG (spontaneous or induced); this helps facilitate family screening of first degree relatives.[1] [18] [69] However, the presence of a susceptible gene mutation is not diagnostic of BrS. This is in part due to only 50% penetrance of genetic variants. Clinical presentation remains central to diagnosing Brugada syndrome.[1]

Probable pathogenic mutation in a BrS susceptibility gene also scores 0.5 points on the Shanghai score.[1] Mutations of many genes have been implicated in BrS, but only SCN5A gene variants are considered definitely disease-causing.[1] [7] However, identifiable SCN5A variants are only found in approximately 20% to 30% of patients with BrS.[1] [7] [16] [17] [18][64] Mutations of other genes only account for around 2% to 5% of cases.[14] [16] [17][19]

Advanced cardiac imaging (MRI or CT)

Consider other advanced imaging modalities, such as cardiac MRI or CT, if the diagnosis of BrS is uncertain to help differentiate BrS from other differentials, such as arrhythmogenic cardiomyopathy.[36] [70] See Differentials .

Invasive electrophysiological (EP) study with inducibility testing for ventricular arrhythmias

Invasive EP studies with inducibility testing (including measurement of baseline intervals, programmed electrical stimulation [PES], and electroanatomic mapping) may be considered following consultation with an electrophysiologist or cardiologist with expertise in managing BrS if the patient has asymptomatic BrS and is deemed intermediate risk on risk stratification. See Management approach for more information about risk stratification.[7] [64] Although there is debate regarding the prognostic value of PES in primary electrical diseases, there is some evidence to consider its use in BrS.[64] [71]

Invasive EP assessments have demonstrated voltage abnormalities recorded from the right ventricular epicardium of patients with BrS in the absence of cardiac MR or CT structural abnormalities.[38] This highlights the importance of expert consultation if you suspect BrS, but the diagnosis is unclear.

# History and exam

## Key diagnostic factors

### past history of unexplained cardiac arrest or documented PMVT or VF (common)

- Consider a diagnosis of symptomatic Brugada syndrome (BrS) if a patient has a past history of unexplained cardiac arrest, or documented polymorphic ventricular tachycardia (PMVT), or ventricular fibrillation (VF).[1] [5] [7]
- 
  - There are many causes of sudden cardiac arrest, PMVT and VF, but BrS should be considered as a differential, particularly if there is Brugada pattern on ECG and one or more risk factors for BrS.
  - Patients may also present with monomorphic VT, but this is rare and should prompt investigation of other arrhythmogenic cardiomyopathies.[5] [52] [53]

### cardiogenic syncope (common)

- Consider a diagnosis of symptomatic Brugada syndrome (BrS) if a patient presents with, or has a past history of cardiogenic syncope.
- 
  - Up to one third of patients with BrS present with, or have a history of, syncope at the time of diagnosis.[54]
  - Take a careful history to differentiate cardiogenic from noncardiogenic causes of syncope.[1] [7] The published Shanghai score for BrS assigns two points to patients with suspected cardiogenic syncope, and one point to those with an unclear cause of syncope (see Criteria ).[1] [49]
  - Patients with BrS who have a history of cardiogenic syncope are also at 2.5 to 5-fold greater risk of serious arrhythmic events compared with those with noncardiogenic syncope.[48] [47] [56] [57] Patients with cardiogenic syncope have not been shown to have an increased risk for serious arrhythmic events.[58]

## Other diagnostic factors

### inducible features of Brugada syndrome (common)

- Features of Brugada syndrome (BrS) may only be apparent when induced by certain factors.[1] [7] Inducible features are particularly important to identify in asymptomatic patients (i.e., those who do not



have a past history of unexplained cardiac arrest, ventricular arrhythmias, or syncope), but may also be present in symptomatic patients. These include:[1] [7]

- Febrile illness. This is known to induce type 1 Brugada pattern on ECG and precipitate arrhythmic events.[1] In endemic regions, the prevalence of BrS in patients presenting with febrile illness for any reason has been reportedly as high as 4%, approximately 20-fold greater than a nonfebrile control group in one Thai cross-sectional study of 401 patients.[20] [21] While in isolation fever is not specific for BrS, in a patient with suspected BrS, it has implications for both diagnosis and management.[1]
- Medications. These include sodium-channel blockers (e.g., flecainide, procainamide), psychotropic medications (e.g., tricyclic or tetracyclic antidepressants, lithium), and local anesthetics. These are known to induce type 1 Brugada ECG changes and may also precipitate arrhythmic events.[1] [18]
- Illicit drugs or alcohol. These are known to induce type 1 Brugada ECG changes and may also precipitate arrhythmic events.[1] [18]

### atrial arrhythmias (uncommon)

- Consider a diagnosis of Brugada syndrome (BrS) in a patient <30 years who has atrial fibrillation or flutter.[1] [59] [60] Concomitant atrial arrhythmias are common in patients with BrS, with a prevalence of approximately 10%, although these are not specific for diagnosis of BrS.[61] [64] Use of sodium-channel blockers may unmask Brugada pattern on ECG in some of these patients.[61]

### nocturnal agonal respirations (uncommon)

- Can be a feature of Brugada syndrome (BrS).[1] [7]
- The Shanghai score for BrS assigns 2 points to patients with nocturnal agonal respirations (see Criteria ).[1] [49]
- In a Danish national survey, prevalence of nocturnal agonal respirations in patients with BrS was 14%, but this is likely to be greater in endemic areas.[61]
- Nocturnal agonal respirations were described in early reports from Southeast Asia (Philippines, Thailand, Japan, China, and others) of sudden unexpected nocturnal death syndrome (SUNDS), a syndrome which is thought to be genetically, phenotypically, and functionally the same as BrS.[63]

## Risk factors

### Weak

#### age 30 to 50 years

- Brugada syndrome (BrS) is typically first diagnosed in young to middle-aged patients.[1]
- Patients aged 30-50 years with BrS are also at high risk of serious arrhythmic events.[39] This is also typically the age at which patients with BrS may present with their first serious arrhythmic event.[1] However, serious arrhythmic events have also been reported in children as young as <1 year old.[21] [40] [41] Women in particular may be more likely to have their first SAE in childhood, or later in life.[1] [39]
- Patients >50 years who have BrS experience significantly fewer serious arrhythmic events compared with younger patients, and for those ≥55 years at the time of BrS diagnosis, annual mortality is similar to that of the general population.[41] [42] [43] However, it remains unclear whether these observations are due to protective effects acquired through aging or simply represent selection bias.

### male sex

- Brugada syndrome (BrS) is more common in men compared with women.[1] [39] Men account for up to 90% of cases of BrS in some cohorts.[1] [39]
- Evidence has shown that men with BrS are also at increased risk of serious arrhythmic events.[44] [45] [46] However, this finding remains controversial, and has not been confirmed with complete adjustment for potential confounding factors.[47] [48]

### Asian ancestry

- Brugada syndrome (BrS) occurs more commonly in Asia compared with Europe and the US.[1] [13] BrS is particularly common in Southeast Asia, where a nocturnal sudden death syndrome in young men was clinically reported by a variety of local names in countries such as Philippines, Thailand, Japan, and China, prior to the formal classification of BrS.[14]

### family history of BrS or suspicious or unexplained cardiac death

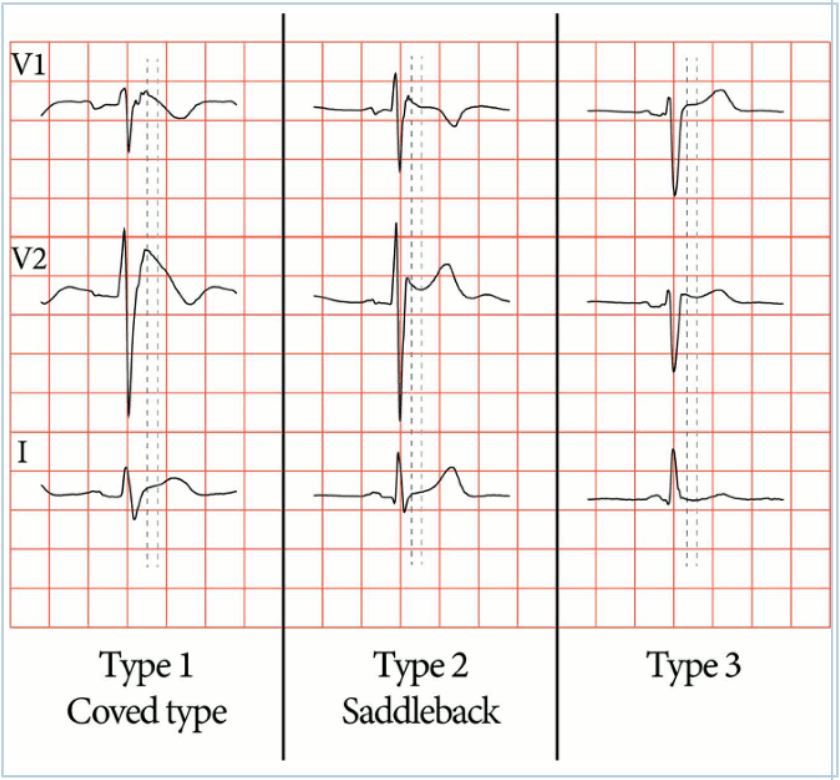
- Determine the following features (which form part of the Shanghai score; see Criteria ) in any first- or second- degree relative of the patient.[1] [49]
  - Definite Brugada syndrome (BrS)
  - Suspicious sudden cardiac death (febrile, nocturnal, confounded by BrS-associated drug)
  - Unexplained sudden cardiac death <45 years with non-contributory autopsy.
- Bear in mind that, although family history is a standard and important part of any diagnostic evaluation, limited evidence exists to support a family history of sudden cardiac death as a risk factor for BrS-associated arrhythmic events.[50]



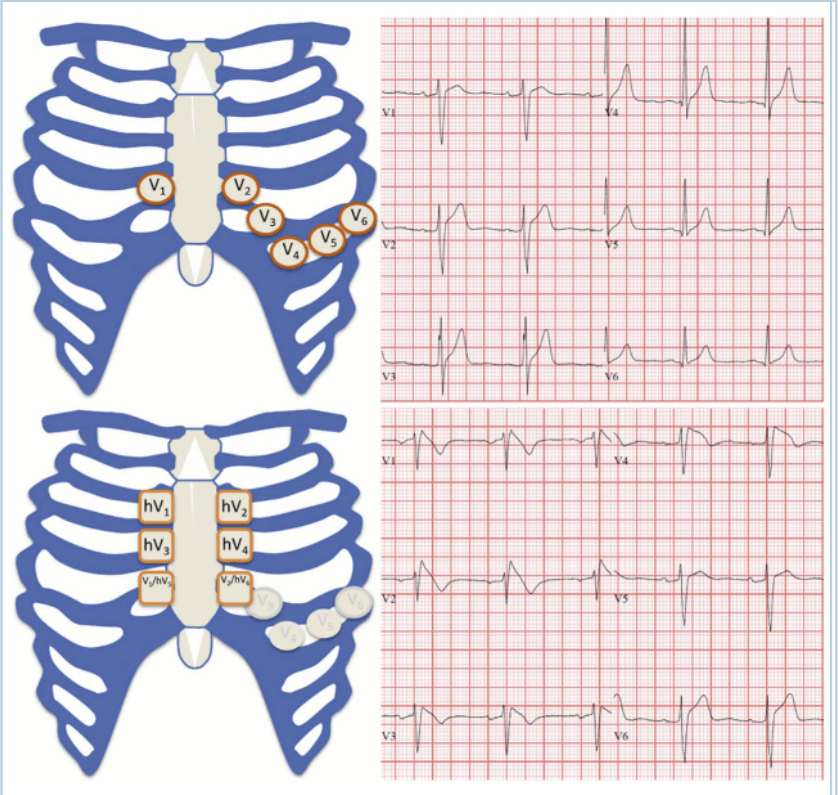
# Investigations

## 1st test to order

| Test | Result |
|---|---|
| **ECG**<br>• Perform an ECG as the first line investigation for any patient with suspected Brugada syndrome (BrS).[1][5] [7] [18] [64] Look for type 1, 2, or 3 Brugada patterns, which may indicate BrS.[1]<br>• Type 1 Brugada pattern may be spontaneous or induced (e.g., by factors such as fever or sodium-channel blockers).[1] [5] [7]<br>• Consider high precordial lead testing if ECG using standard lead placement is not conclusive and you have high clinical suspicion of BrS. High precordial lead testing increases diagnostic yield by accounting for anatomic variations in right ventricular outflow tract anatomy.[1] [4] [5] [65] [66] [67]<br>•  | **Type 1 Brugada pattern: coved ST-segment elevation (J-point elevation with a gradual down-sloping ST-segment) ≥2 mm with a negative T-wave in the right precordial leads.[1] [4] [5] [7] [51]**<br>**Type 2 or 3 Brugada pattern: saddleback ST-segment configuration with variable levels of ST-segment elevation.[1] [4] [51]** |

*Electrocardiographic patterns in Brugada syndrome showing type 1 (diagnostic) and types 2 and 3 (non-diagnostic) patterns. Type-1 (diagnostic): coved STT morphology in lead V2 with J-point elevation (dark gray line) of ≥0.2 mV (≥2 mm) and a terminal ST-segment elevation (light gray line, J+60 ms) also ≥0.2 mV (≥2 mm). Note the PR interval and wider QRS complex, wide and deep S in lead I, and fractionation in the right precordial ECG leads. Type-2 (non-diagnostic): saddleback STT morphology in lead V2 with J-point elevation (dark gray line) of ≥0.2 mV (≥2 mm) and a terminal ST-segment elevation (light gray line, J+60 ms) ≥0.1 mV (≥1 mm), followed by a positive T wave. Note the less wide and deep S-wave in lead I, less prominent fractionation. Type-3 (non-diagnostic): saddleback STT morphology in lead V2 with J-point elevation (dark gray line) of ≥0.2 mV (≥2 mm) and a terminal ST-segment elevation (light gray line, J+60 ms) <0.1 mV (<1 mm)*

*Marsman EMJ et al. Heart 2022 May;108(9):668-75; used with permission*

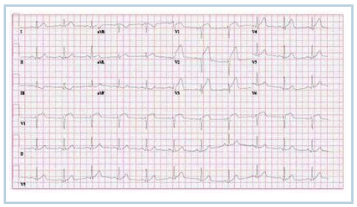
| Test | Result |
|---|---|
|  *Standard- and high-lead electrocardiogram positions. (Top) Standard-lead ECG positions and corresponding precordial ECG in a patient with Brugada syndrome. (Bottom) High-lead ECG positions and corresponding ECG in the same patient. Note that hV5 and hV6 on the high-lead ECG correspond with V1 and V2 on the standard-lead ECG.* *Krahn AD, et al. Brugada syndrome. JACC Clin Electrophysiol 2022 Mar;8(3):386-405; used with permission*<br>• Refer all patients with type 1 Brugada pattern (spontaneous or induced) to a cardiologist or cardiac electrophysiologist.<br>• <br>  • The diagnosis of BrS is considered probable or definite if spontaneous type 1 Brugada pattern is recorded on ECG from the 2nd to 4th intercostal spaces.[1][4] [51] [7] However, these patients require diagnostic evaluation by a specialist.<br>  • Ensure you establish the patient's clinical history in all patients with type 1 Brugada pattern.[4] This is essential, because distinguishing type 1 Brugada pattern from other causes of ST elevation using ECG alone can be difficult, even for an experienced cardiologist.[4]<br>  • If the patient has induced type 1 Brugada pattern, additional information is key to aid diagnosis of BrS (e.g., relevant clinical history or family history, and/or genetic testing).[1] [7]<br>• If the patient has type 2 or 3 Brugada pattern, consider provocative drug testing with sodium channel blockade (see below).[1] | |
| **echocardiogram**<br>• Organize an echocardiogram for any patient being evaluated for Brugada syndrome (BrS) to assess for underlying structural heart disease and to rule out other causes of their presentation.[1] [49] | **normal; mild structural abnormalities in the right ventricle or right ventricular outflow tract** |

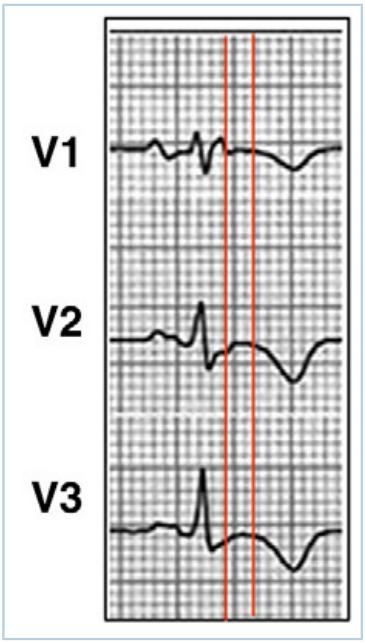
## Other tests to consider

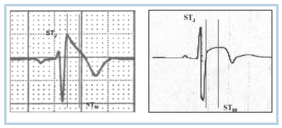
| Test | Result |
|---|---|
| **provocative drug testing with sodium channel blockade**<br>• Consider provocative drug testing with sodium-channel blockers (e.g., procainamide, flecainide) for any patient with both:[1] [7] [13] [49]<br>• Type 2 or 3 Brugada pattern (Brugada pattern) on<br>AND<br>• Suspected BrS due to relevant clinical signs, symptoms, or family history.<br>• The diagnosis of BrS is considered probable if type 1 Brugada pattern is provoked on ECG during drug testing with sodium-channel blockers; this scores 2 points on the Shanghai score (see Criteria ).[1] Refer these patients to a cardiologist or cardiac electrophysiologist.<br>• Due to an associated risk of inducing life-threatening ventricular arrhythmias, provocative drug testing should only be performed by experts under optimal circumstances.[68]<br>• Sodium channel blocker testing is not recommended in patients with a prior type I Brugada pattern.[7] | **development of type 1 Brugada pattern on ECG: coved ST-segment elevation (J-point elevation with a gradual down-sloping ST-segment) ≥2 mm with a negative T-wave in the right precordial leads.[1] [4] [5] [51]** |
| **genetic testing for BrS**<br>• Arrange genetic testing in patients with type 1 Brugada ECG pattern (spontaneous or induced); this helps facilitate family screening of first degree relatives.[1] [18] [69] However, the presence of a susceptible gene mutation is not diagnostic of BrS. This is in part due to only 50% penetrance of genetic variants. Clinical presentation remains central to diagnosing Brugada syndrome.[1] Probable pathogenic mutation in a BrS susceptibility gene also scores 0.5 points on the Shanghai score (see Criteria ).[1]<br>• Mutations of many genes have been implicated in BrS, but only SCN5A gene variants are considered definitely disease-causing.[1] [7] However, identifiable SCN5A variants are only found in approximately 20% to 30% of patients with BrS.[1] [7] [16] [17] [18] [64] Mutations of other genes only account for around 2% to 5% of cases.[14] [16] [17][19] | **positive for known pathogenic mutation associated with Brugada syndrome (e.g., SCN5A)** |
| **advanced cardiac imaging (MRI or CT)**<br>• Consider other advanced imaging modalities, such as cardiac MRI or CT if the diagnosis of Brugada syndrome (BrS) is uncertain to help differentiate BrS from other differentials, such as arrhythmogenic cardiomyopathy.[36] [70] See Differentials . | **may demonstrate cardiac structural changes, particularly in the right ventricular outflow tract** |
| **invasive electrophysiological (EP) study with inducibility testing for ventricular arrhythmias**<br>• Invasive EP studies (including measurement of baseline intervals, programmed electrical stimulation [PES], and electroanatomical mapping) with inducibility testing may be considered following consultation with an electrophysiologist or cardiologist with expertise in managing BrS if the patient has asymptomatic Brugada syndrome (BrS) and is deemed intermediate risk on risk stratification - see Management approach for more information about risk stratification.[7] [64] Although there is debate regarding the prognostic | **inducible ventricular tachycardia or fibrillation in patients with asymptomatic BrS** |

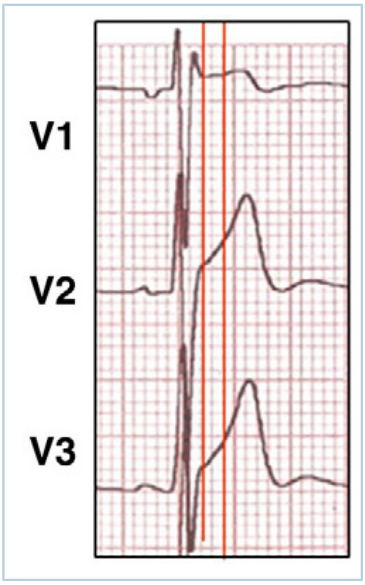
| Test | Result |
| --- | --- |
| value of PES in primary electrical diseases, there is some evidence to consider its use in BrS.[64] [71]<br>• Invasive EP assessments have demonstrated voltage abnormalities recorded from the right ventricular epicardium of patients with BrS in the absence of cardiac MR or CT structural abnormalities.[38] This highlights the importance of expert consultation if you suspect BrS, but the diagnosis is unclear. | |

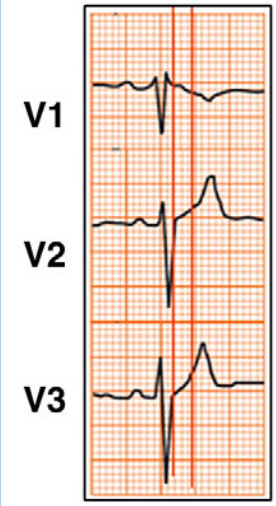
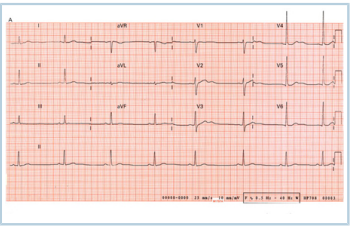
# Differentials

| Condition | Differentiating signs / symptoms | Differentiating tests |
|---|---|---|
| **Acute coronary syndrome** | • A careful history is key to determine features of acute coronary syndrome such as chest pain, sweating, or nausea.<br>• In addition, the patient may have risk factors for coronary artery disease such as smoking, hypertension, or diabetes. | • Right coronary artery or left anterior descending artery ischemia in particular may produce precordial lead changes with ST segment elevation on ECG which may be confused for Brugada pattern (BrP).<br>• Cardiac biomarkers will be elevated with ST-elevation myocardial infarction (MI) and non-ST elevation MI.<br>•  <br>*12-Lead ECG with ST-segment elevation lead V1 to V4*<br>*From the personal collection of Dr Mahi Ashwath; used with permission* |
| **Arrhythmogenic cardiomyopathy** | • Inherited cardiomyopathy resulting from defective desmosomal proteins[49]<br>• • Fibrofatty replacement of myocytes lead to scar-related ventricular arrhythmias, often in the young<br>• Up to 16% of patients with had a positive sodium-channel blocker challenge in one study.[72] | • Cardiac MRI assessment may show structural right ventricular or right ventricular outflow tract changes with arrhythmogenic right ventricular cardiomyopathy (AVRC), whereas in Brugada syndrome (BrS) structural abnormalities may not be easily detected.<br>• There may also be differences seen in the precordial leads on ECG, particularly leads V1 and V2. With ARVC T-wave inversion in right precordial leads usually has no preceding or mildly upward ST-segment, with BrS there is characteristically a high take off and ST segment elevation that is downsloping.[73] There may also be epsilon waves with ARVC. ECG changes are |

| Condition | Differentiating signs / symptoms | Differentiating tests |
|---|---|---|
| | | typically fixed with AVRC, rather than dynamic.<br>•  *3-lead ECG showing findings suggestive of arrhythmogenic right ventricular cardiomyopathy* *Bayés de Luna A et al. J Electrocardiol. 2012 Sep;45(5):433-42; used with permission* |
| **Athlete's heart** | • Typically seen in male endurance athletes without cardiac symptoms.<br>• No family history of HCM or sudden death.<br>• Hypertrophy will regress with cessation of exercise.[74] | • ECG: There will be upsloping ST segment elevation of early repolarization whereas in type 1 Brugada syndrome coved ST segment elevation would be seen, resulting in a broad R wave. The "Corrado index" measures the ST elevation at the start of the ST segment/J-point (STJ) and 80 ms after the start of the ST segment (ST80). The downsloping ST segment will have a STJ/ST80 ratio >1 in type 1 Brugada syndrome, but <1 in the athlete.[75]<br>• Echocardiography: Will characteristically show increased left ventricular (LV) chamber dimension (LV end-diastolic dimension or LV end-diastolic >55 mm), symmetric left ventricular hypertrophy (LVH) with a |

| Condition | Differentiating signs / symptoms | Differentiating tests |
|---|---|---|
| | | homogeneous-appearing myocardium.<br>• Wall thicknesses may occasionally exceed upper normal limits (12 mm).<br>• LV filling pattern is most often normal.[74]<br>  <br>*Brugada type 1 ECG (left) in comparison to early repolarization with "convex" ST segment elevation in a trained athlete (right). [Vertical lines mark the J-point (STJ) and 80 ms after the J-point (ST80). The "downsloping" ST segment elevation in Brugada pattern has an STJ/ST80 ratio >1. Early repolarization patterns in the athlete shows an initial "upsloping" ST segment elevation with STJ/ST80 ratio <1].*<br>*Drezner JA et al. Br J Sports Med 2017 May;51(9):704-31; used with permission* |
| **Pectus excavatum** | • A congenital chest wall deformity may be seen on examination. | • ECG findings in pectus excavatum may include a negative P wave in V1 (with V1 lead in the standard position i.e., fourth intercostal space to the right of the sternum), a well defined, peaked R wave in V1 which may be followed by a mildly elevated ST segment. The T wave is usually negative or biphasic in V1 and positive in V2 with pectus excavatum. |

| Condition | Differentiating signs / symptoms | Differentiating tests |
|---|---|---|
| | | • CT scan will show depression of the sternum.<br>•  *3-lead ECG showing findings suggestive of pectus excavatum* *Bayés de Luna A et al. J Electrocardiol. 2012 Sep;45(5):433-42; used with permission* |
| **Incomplete right bundle branch block (RBBB)** | • Diagnosis is primarily distinguished from Brugada syndrome (BrS) on ECG rather than clinical findings. | • On ECG look for the following features of RBBB:<br>• • Peaked positive terminal R wave. In type 2 Brugada pattern, the R wave is rounded, wide, and usually of relatively low voltage compared with RBBB.<br>• Identical QRS complex duration in leads V1-V2 to that observed in lead V6.<br>• Characteristic widened S wave, which is absent in most cases of Brugada syndrome.[76] |

| Condition | Differentiating signs / symptoms | Differentiating tests |
|---|---|---|
| | |  *3-lead ECG showing right bundle branch block* *Bayés de Luna A et al. J Electrocardiol. 2012 Sep;45(5):433-42; used with permission* |
| **Hypokalemia** | • Hypokalemia can produce ECG patterns that mimic the Brugada ECG patterns but is clinically distinct from BrS.[77] The cause of hypokalemia is often apparent from the history, this may include the use of known causative medications (such as diuretics, corticosteroids, beta-2 agonists, amphotericin B, chloroquine or theophylline toxicity, laxatives), a history of gastrointestinal losses (such as vomiting or diarrhea), or underlying medical conditions leading to urinary loss of potassium (such as renal tubular acidosis). | • Serum potassium levels <3.5 mmol/L (<3.5 mEq/L).<br>• The ECG in patients with hypokalemia may typically show ST segment depression, decrease in the amplitude of the T wave, and an increase in the amplitude of U waves (often seen in the lateral precordial leads V4 to V6).<br>•  *12-lead ECG demonstrating prominent U-waves in a patient with hypokalemia* *From: Lin HW, Chau T, Lin CS, Lin SH, Recurring paralysis, BMJ Case Reports 2009; doi:10.1136/ bcr.07.2008.0577* |

| Condition | Differentiating signs / symptoms | Differentiating tests |
|---|---|---|
| | | Other patterns of arrhythmias with hypokalemia, include sinus bradycardia, premature atrial and ventricular beats, paroxysmal atrial or junctional tachycardia, atrioventricular block, ventricular tachycardia, or fibrillation.[78] |

# Criteria

## Shanghai score[49]

Consider using the proposed Shanghai score to aid diagnosis of Brugada syndrome.[1]

| Factor - ECG (12-lead/ambulatory)[b] | Points |
|---|---|
| Spontaneous type 1 Brugada pattern on standard or Brugada ECG | 3.5 |
| Fever-induced type 1 Brugada pattern on standard or Brugada ECG | 3 |
| Type 2 or 3 Brugada ECG pattern that converts with sodium channel-blocking drug challenge | 2 |
| **Clinical history[a]** | |
| Unexplained cardiac arrest or documented ventricular fibrillation/polymorphic ventricular tachycardia | 3 |
| Nocturnal agonal respirations | 2 |
| Suspected arrhythmic syncope | 2 |
| Syncope of unclear mechanism or unclear etiology | 1 |
| Atrial flutter or fibrillation in patients <30 years without alternative etiology | 0.5 |
| **Family history[a]** | |
| First- or second-degree relative with definite BrS | 2 |
| Suspicious SCD (during fever, at night, or when taking Brugada-aggravating drugs) in a first- or second-degree relative | 1 |
| Unexplained SCD <45 years in a first- or second-degree relative with negative autopsy | 0.5 |
| **Genetic test result** | |
| Probable pathogenic mutation in BrS susceptibility gene | 0.5 |
| **Total score (requires ≥1 ECG finding)** | |
| ≥3.5 points: Probable or definite BrS | |
| 2-3 points: Possible BrS | |
| <2 points: Non-diagnostic | |

**BrS** Brugada syndrome, **ECG** electrocardiogram, **SCD** sudden cardiac death
**a** This table was adapted from an original table as reported by Antzelevitch et al.
**b** Only award points once for highest score within each category

*Proposed Shanghai Score for diagnosis of Brugada syndrome*
*Adapted from Peltenburg PJ et al. Neth Heart J. 31. 10.1007/s12471-022-01723-6; used with permission*

DIAGNOSIS

# Screening

Screen all first-degree relatives of patients diagnosed with Brugada syndrome (BrS) or unexplained sudden cardiac death.[1] [79] Be aware that familial screening is primarily done through clinical rather than genetic screening.[1] This is because:[1]

- The presence of a pathogenic variant in a BrS susceptibility gene in isolation is not diagnostic for BrS
- If a pathogenic variant is identified in a family, the penetrance is approximately 50%, and conversely family members who do not have the variant may still have BrS.

Clinical screening should include standard- and high-lead ECG testing and consideration of provocative drug testing with sodium channel blockade.[1] [7]

- For adult family members, screening does not usually need to be repeated if provocative sodium channel blockade testing is negative.[1]
- Pediatric family members should undergo standard- and high-lead ECG screening at age 3 years.[1] If this is negative, they should undergo additional screening every 3 years until age 15 years.[1] Provocative sodium channel blockade testing should not be used until they are age >15 years due to higher risk of adverse events compared with adults.[1] If provocative sodium channel blockade testing is negative in a person >15 years, screening does not need to be repeated.[1]

Arrange genetic testing in all patients with type 1 Brugada pattern on ECG (spontaneous or induced) to facilitate family screening.[1] [18] [69][79] However, the presence of a susceptible gene mutation is not diagnostic of Brugada syndrome. This is in part due to only 50% penetrance of genetic variants. Clinical presentation remains central to diagnosing Brugada syndrome.[1]

- Probable pathogenic mutation in a BrS susceptibility gene also scores 0.5 points on the Shanghai score (see Criteria ).[1]
- Mutations of many genes have been implicated in BrS, but only SCN5A gene variants are considered definitely disease-causing.[1] [7][79] However, identifiable SCN5A variants are only found in approximately 20% to 30% of patients with BrS.[1] [7][16] [17] [18]
- Mutations of other genes only account for around 2% to 5% of cases.[14] [16] [17][19]

# Approach

Treatment for patients with Brugada syndrome (BrS) consists of conservative management and primary and secondary prevention of serious arrhythmic events.[1] This aims to prevent serious arrhythmic events, while avoiding potential complications of any treatments.[1] Potential treatments include implantable cardioverter defibrillator (ICD), pharmacologic therapy, and radiofrequency catheter ablation.[1] [7]

Note that the distinction between confirmed and probable BrS is not significant in determining the management; this is guided by the patient's presentation, particularly whether they are symptomatic or asymptomatic. Most patients who are asymptomatic require conservative management only.[1] [18]

| Conservative | Pharmacological | Interventional |
|---|---|---|
| Avoid Brugada drugs and triggers, and promptly treat fever<br>• For all patients with definite BrS<br>• Recommended for all patients with probable BrS<br>Re-evaluation<br>• Yearly follow-up with cardiologist<br>Other considerations<br>• Promptly report any episodes of syncope or seizures<br>• Inform and screen family members | Quinidine<br>• Recurrent shocks with appropriate ICD therapies<br>• Consider for patients who qualify for ICD but decline<br>• Consider for medical management of atrial arrhythmias<br>• Consider low-dose therapy to prevent side effects<br>• Requires regular blood count monitoring<br>• Use may be limited due to a lack of drug availability<br>Isoproterenol<br>• During acute ventricular arrhythmias | ICD<br>• Secondary prevention for resuscitated cardiac arrest<br>• Recommended for primary prevention in patients with spontaneous type 1 ECG and syncope<br>• Consider for primary prevention in patients with provoked type 1 ECG and syncope<br>• Consider for primary prevention in asymptomatic patients with spontaneous type 1 ECG and additional high-risk features<br>Ablation<br>• Quinidine intolerance<br>• Arrhythmic events despite quinidine |

*Management summary for Brugada syndrome*

*Adapted from Krahn AD et al. J Am Coll Cardiol#EP. 2022 Mar,#8 (3) 386-405; used with permission*

## Acute ventricular arrhythmia

Intravenous isoproterenol should be given during an acute ventricular arrhythmia, including electrical storm (>2 episodes of ventricular tachycardia or ventricular fibrillation in 24 hours) if the mechanism is due to short-coupled premature ventricular complex-induced ventricular fibrillation.[1] [18] [51]

Quinidine should also be considered for patients who experience electrical storm.[1] [5] [51] [80] In practice, this is given once they have been stabilized with isoproterenol.

- Difficulty in obtaining quinidine can limit its use; phosphodiesterase-III inhibitors (cilostazol or milrinone) may be considered as an alternative, although supportive data are limited.[1] [7]

## Risk stratification

Risk stratify all patients to identify those who are at increased risk of serious arrhythmic events.[1] Risk stratification can aid decision making for the management of Brugada syndrome, particularly when considering an ICD for primary prevention of serious arrhythmic events.[1] [64]

There are currently no risk stratification tools that have proved effective in clinical practice.[1] The Sieira risk score has been proposed for predicting sudden death in patients with BrS, but has not been externally validated.[57] [81] [82][83] However, established features that are associated with the greatest risk of serious arrhythmic events are:[1] [84] [85] [86] [87]

- Resuscitated cardiac arrest
- History of cardiogenic syncope
- Spontaneous type 1 Brugada pattern on ECG.

Other features that are associated with increased risk of serious arrhythmic events are:[1]

- Sudden cardiac death in a young (<35 years) first-degree relative
- Greater "Brugada burden" on ECG, which includes:
    - Presence of type 1 Brugada pattern ECG in the peripheral leads in addition to the right precordial leads
    - Higher proportion of spontaneous type 1 Brugada pattern on ECGs during follow-up
- Other ECG markers such as early repolarization pattern and QRS fragmentation.[7] [64] [88]

Age and sex have limited effect on risk of serious arrhythmic events, although age ≥55 at diagnosis is associated with a more benign prognosis, with no increased mortality compared with the general population.[1]

Consider an electrophysiological study with programmed ventricular stimulation using up to two extrastimuli for further risk stratification in some patients, although this remains controversial.[1][7] [18]

- It should not be used routinely because it is invasive and puts the patient at risk of complications, as well as having issues around reproducibility of results.[1] One multicenter pooled analysis showed that in patients with BrS, arrhythmias induced with electrophysiologic studies were associated with a higher future risk of ventricular arrhythmia.[89]
- However, it may be useful in certain circumstances (e.g., where the decision to use an implantable cardioverter defibrillator for primary prevention is unequivocal).[1] [18]

## Conservative management

Use conservative management for all patients with definite/probable or suspected BrS, although some patients may need other additional treatments alongside this.[1] [7] Asymptomatic patients with inducible (particularly drug-induced) Brugada pattern on ECG usually require conservative management only.[1] [18]

Conservative management includes:[1] [7]



- Avoidance of drugs that could exacerbate the Brugada pattern (for further information see: [BrugadaDrugs.org: safe drug use and the Brugada syndrome] (https://www.brugadadrugs.org) ).[18] [51] These include:
    - Antiarrhythmics (particularly sodium-channel blockers)
    - Psychotropic drugs
    - Anesthetics
    - Certain over-the-counter drugs (e.g., antihistamines)
    - Illicit drugs (e.g., cannabis, cocaine).
- Prompt treatment of fever[18] [51]
- Avoidance of metabolic disturbance (e.g., hypokalemia, hyperkalemia, metabolic acidosis)
- Avoidance of alcohol intoxication[18] [51]

## Implantable cardioverter defibrillator (ICD)

An ICD is recommended for all patients with BrS who have been resuscitated from cardiac arrest for secondary prevention of sudden cardiac death.[1] [7] [18] [51]

However, the decision to use an ICD for primary prevention of sudden cardiac death due to BrS is less clear cut and needs to weigh up the risk of serious arrhythmic events with the risk of ICD-related complications.[1]

- ICD is generally recommended for patients who have:
    - Spontaneous type 1 Brugada pattern on ECG and a history of cardiogenic syncope, particularly if this is likely to be due to ventricular arrhythmias[1][7] [18]
    - Documented spontaneous sustained ventricular tachycardia with or without syncope.[7] [18] [51]
- ICD should be considered in patients who:
    - Have provoked type 1 Brugada pattern on ECG and a history of cardiogenic syncope[1] [7] [18]
    - Are asymptomatic and have a type 1 Brugada pattern on ECG, with high-risk features that are considered relevant after consultation with an expert.[1] [7] In general, ICD should be avoided in those patients without high risk features.[1] [51]
    - Develop ventricular fibrillation during electrophysiological study with programmed ventricular stimulation.[7] [51]

The patient's life expectancy should also be taken into account; ICD may not be appropriate if meaningful survival is <1 year.[18]

Regarding choice of ICD, a dual chamber system is recommended in most patients, particularly those prone to atrial arrhythmias (e.g., those carrying the SN5CA gene).[1] However, a subcutaneous device may be preferred in young patients who don't require pacing, because this has a lower risk of intravascular infection.[1]

## Pharmacologic therapy

Quinidine

Quinidine is a class 1a antiarrhythmic agent that has many effects.[1] The most significant of these is inhibition of the cardiac transient outward potassium current, which prolongs the refractory period.[1]

Quinidine is useful to suppress ventricular arrhythmias, and may also be used for medical management of atrial arrhythmias.[1] [51] It should be considered in patients who:[1] [5]

- Have an ICD and experience recurrent shocks[7] [18]
- Decline or are unsuitable for an ICD[7] [18] [51]
- Experience electrical storm (>2 episodes of ventricular tachycardia or ventricular fibrillation in 24 hours).[51] See "Acute ventricular arrhythmia" above
- Are asymptomatic but have a spontaneous type I Brugada pattern on ECG[51]
- Experience asymptomatic ventricular arrhythmia.[68]

Be aware that significant adverse effects and difficulty in obtaining the drug can limit its use.[1] [5]

- Monitor the patient's CBC for anemia and thrombocytopenia.[1]

Phosphodiesterase-III inhibitors

Phosphodiesterase-III inhibitors (cilostazol or milrinone) may be considered for patients with BrS (as an alternative to quinidine); however, supportive data are limited.[1] [7]

## Radiofrequency catheter ablation

Radiofrequency catheter ablation is indicated in patients who:

- Have recurrent ICD shocks, particularly if these are refractory to medical therapy[1] [5] [7] [18] [51]
- Experience serious arrhythmic events despite optimized medical therapy[1] [5]
- Are intolerant to, or would prefer not to have, medical therapy, or medical therapy is ineffective[1] [5]
- Have spontaneous type 1 Brugada pattern on ECG and symptomatic ventricular arrhythmias who are unsuitable for, or decline an ICD[18]
- Have a history of electrical storms.[51]

Significant contraindications to ablation include:[38]

- Ventricular tachycardia or fibrillation caused by myocardial ischemia, fever, or hypokalemia
- Presence of structural heart disease
- Brain anoxic encephalopathy from cardiac arrests caused by ventricular tachycardia or fibrillation.

A combined endocardial and epicardial approach has been shown to modify triggers and substrate for ventricular arrhythmias.[1]

## Genetic counseling

Arrange genetic counseling for all patients to facilitate screening of relatives.[1] [7] [18] [79] See Screening .

# Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

| Initial ( summary ) | | |
|---|---|---|
| **with acute ventricular arrhythmia** | | |
| | **1st** | **isoproterenol** |
| | **adjunct** | **quinidine or phosphodiesterase-III inhibitor** |

| Acute ( summary ) | | |
|---|---|---|
| **asymptomatic** | | |
| | **1st** | **conservative management** |
| | **plus** | **genetic counseling** |
| | **adjunct** | **implantable cardioverter defibrillator (ICD)** |
| | **adjunct** | **quinidine or phosphodiesterase-III inhibitor** |
| **symptomatic** | | |
| **with previous cardiac arrest** | **1st** | **conservative management** |
| | **plus** | **genetic counseling** |
| | **plus** | **implantable cardioverter defibrillator (ICD)** |
| | **adjunct** | **quinidine or phosphodiesterase-III inhibitor** |
| | **adjunct** | **radiofrequency catheter ablation** |
| **without previous cardiac arrest** | **1st** | **conservative management** |
| | **plus** | **genetic counseling** |
| | **adjunct** | **implantable cardioverter defibrillator (ICD)** |
| | **adjunct** | **quinidine or phosphodiesterase-III inhibitor** |
| | **adjunct** | **radiofrequency catheter ablation** |

# Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

## Initial

### with acute ventricular arrhythmia

**1st** **isoproterenol**

#### Primary options

» isoproterenol: consult specialist for guidance on dose

» Intravenous isoproterenol should be given during an acute ventricular arrhythmia, including electrical storm (>2 episodes of ventricular tachycardia or ventricular fibrillation in 24 hours) if the mechanism is due to short-coupled premature ventricular complex-induced ventricular fibrillation.[1] [7][18][51]

**adjunct** **quinidine or phosphodiesterase-III inhibitor**

Treatment recommended for SOME patients in selected patient group

#### Primary options

» quinidine sulfate: consult specialist for guidance on dose

#### Secondary options

» cilostazol: consult specialist for guidance on dose

**OR**

» milrinone: consult specialist for guidance on dose

» Quinidine should be considered in addition to isoproterenol for patients who experience electrical storm.[1][5] [51] [80] In practice, this is given once they have been stabilized with isoproterenol.

» Phosphodiesterase-III inhibitors (cilostazol or milrinone) may be considered for patients with BrS (as an alternative to quinidine), however, supportive data are limited.[1] [7]

# Acute

## asymptomatic

**1st** **conservative management**

» Conservative management includes:[1] [7]

- Avoidance of drugs that could exacerbate the Brugada pattern (for further information see: [BrugadaDrugs.org: safe drug use and the Brugada syndrome] (https://www.brugadadrugs.org) ).[18] [51] These include antiarrhythmics (particularly sodium-channel blockers), psychotropic drugs, anesthetics, certain over-the-counter drugs (e.g., antihistamines), illicit drugs (e.g., cannabis, cocaine)
- Prompt treatment of fever[18] [51]
- Avoidance of metabolic disturbance (e.g., hypokalemia, hyperkalemia, metabolic acidosis)
- Avoidance of alcohol intoxication.[18] [51]

**plus** **genetic counseling**

Treatment recommended for ALL patients in selected patient group

» Arrange genetic counseling for all patients to facilitate screening of relatives.[1] [7] [18] [79] See Screening .

**adjunct** **implantable cardioverter defibrillator (ICD)**

Treatment recommended for SOME patients in selected patient group

» An ICD may be considered in asymptomatic patients if they have high-risk features that are considered relevant after consultation with an expert and who:

- Have a type 1 Brugada pattern on ECG[7] [1]
- Experience one or more episodes of documented spontaneous sustained ventricular tachycardia[51] [18] [7][68]
- Develop ventricular fibrillation during electrophysiologic study with programmed ventricular stimulation.[51] [7]

» The patient's life expectancy should also be taken into account; ICD may not be appropriate if meaningful survival is <1 year.[18]

» In general, ICDs should be avoided in patients without high risk features.[1] [51]

**adjunct** **quinidine or phosphodiesterase-III inhibitor**

## Acute

Treatment recommended for SOME patients in selected patient group

**Primary options**

» quinidine sulfate: consult specialist for guidance on dose

**Secondary options**

» cilostazol: consult specialist for guidance on dose

**OR**

» milrinone: consult specialist for guidance on dose

» Quinidine is a class 1a antiarrhythmic agent that has many effects.[1] The most significant of these is inhibition of the cardiac transient outward potassium current, which prolongs the refractory period.[1]

» Quinidine is useful to suppress ventricular arrhythmias.[1] [51] It should be considered in asymptomatic patients who:[1] [5]

- Have an ICD and experience recurrent shocks[7] [18]
- Decline or are unsuitable for an ICD[7] [18] [51]
- Have a spontaneous type I Brugada pattern on ECG[51]
- Experience asymptomatic ventricular arrhythmia.[68]

» Monitor the patient's CBC for anemia and thrombocytopenia.[1]

» Be aware that significant adverse effects and difficulty in obtaining the drug can limit its use.[1] [5]

» Phosphodiesterase-III inhibitors (cilostazol or milrinone) may be considered for patients with BrS (as an alternative to quinidine), however, supportive data are limited.[1] [7]

**symptomatic**

**with previous cardiac arrest** — **1st** — **conservative management**

» Conservative management includes:[1] [7]

- Avoidance of drugs that could exacerbate the Brugada pattern (for further information see: [BrugadaDrugs.org:

## Acute

safe drug use and the Brugada syndrome] (https://www.brugadadrugs.org) ).[18] [51] These include antiarrhythmics (particularly sodium-channel blockers), psychotropic drugs, anesthetics, certain over-the-counter drugs (e.g., antihistamines), illicit drugs (e.g., cannabis, cocaine)
- Prompt treatment of fever[18] [51]
- Avoidance of metabolic disturbance (e.g., hypokalemia, hyperkalemia, metabolic acidosis)
- Avoidance of alcohol intoxication.[18] [51]

**plus** **genetic counseling**

Treatment recommended for ALL patients in selected patient group

» Arrange genetic counseling for all patients to facilitate screening of relatives.[1] [7] [18] [79] See Screening .

**plus** **implantable cardioverter defibrillator (ICD)**

Treatment recommended for ALL patients in selected patient group

» An ICD is recommended for all patients with BrS who have been resuscitated from cardiac arrest for secondary prevention of sudden cardiac death.[1] [7] [18] [51]

- The patient's life expectancy should also be taken into account; ICD may not be appropriate if meaningful survival is <1 year.[18]

» Regarding choice of ICD, a dual chamber system is recommended in most patients, particularly those prone to atrial arrhythmias (e.g., those carrying the SN5CA gene).[1] However, a subcutaneous device may be preferred in young patients who don't require pacing, because this has a lower risk of intravascular infection.[1]

**adjunct** **quinidine or phosphodiesterase-III inhibitor**

Treatment recommended for SOME patients in selected patient group

### Primary options

» quinidine sulfate: consult specialist for guidance on dose

### Secondary options

» cilostazol: consult specialist for guidance on dose

MANAGEMENT

## Acute

**OR**

» milrinone: consult specialist for guidance on dose

» Quinidine is a class 1a antiarrhythmic agent that has many effects.[1] The most significant of these is inhibition of the cardiac transient outward potassium current, which prolongs the refractory period.[1]

» Quinidine is useful to suppress ventricular arrhythmias, and may also be used for medical management of atrial arrhythmias.[1] [51] It should be considered in patients who:[1] [5]

- Have an ICD and experience recurrent shocks[7] [18]
- Decline, or are unsuitable for, an ICD[7] [18] [51]
- Experience electrical storm (>2 episodes of ventricular tachycardia or ventricular fibrillation in 24 hours).[51] See "Acute ventricular arrhythmia" above.
- Experience asymptomatic ventricular arrhythmia.[68]

» Monitor the patient's CBC for anemia and thrombocytopenia.[1]

» Be aware that significant adverse effects and difficulty in obtaining the drug can limit its use.[1] [5]

» Phosphodiesterase-III inhibitors (cilostazol or milrinone) may be considered for patients with BrS (as an alternative to quinidine), however, supportive data are limited.[1] [7]

»

**adjunct** **radiofrequency catheter ablation**

Treatment recommended for SOME patients in selected patient group

» Indicated in patients who:

- Have recurrent ICD shocks, particularly if these are refractory to medical therapy[1] [5] [7] [18] [51]
- Experience serious arrhythmic events despite optimized medical therapy[1] [5]
- Are intolerant to or would prefer not to have medical therapy, or medical therapy is ineffective[1] [5]
- Have spontaneous type 1 Brugada pattern on ECG and symptomatic ventricular



## Acute

arrhythmias who are unsuitable for, or decline an ICD[18]
- Have a history of electrical storms.[51]

» Significant contraindications to ablation include:[38]

- Ventricular tachycardia or fibrillation caused by myocardial ischemia, fever, or hypokalemia
- Presence of structural heart disease
- Brain anoxic encephalopathy from cardiac arrests caused by ventricular tachycardia or fibrillation.

» A combined endocardial and epicardial approach has been shown to modify triggers and substrate for ventricular arrhythmias.[1]

**without previous cardiac arrest**

**1st** **conservative management**

» Conservative management includes:[1] [7]

- Avoidance of drugs that could exacerbate the Brugada pattern (for further information see: [BrugadaDrugs.org: safe drug use and the Brugada syndrome] (https://www.brugadadrugs.org) ).[18] [51] These include antiarrhythmics (particularly sodium-channel blockers), psychotropic drugs, anesthetics, certain over-the-counter drugs (e.g., antihistamines), illicit drugs (e.g., cannabis, cocaine)
- Prompt treatment of fever[18] [51]
- Avoidance of metabolic disturbance (e.g., hypokalemia, hyperkalemia, metabolic acidosis)
- Avoidance of alcohol intoxication.[18] [51]

**plus** **genetic counseling**

Treatment recommended for ALL patients in selected patient group

» Arrange genetic counseling for all patients to facilitate screening of relatives.[1] [7] [18] [79] See Screening .

**adjunct** **implantable cardioverter defibrillator (ICD)**

Treatment recommended for SOME patients in selected patient group

» The decision to use an ICD for primary prevention of sudden cardiac death due to BrS is less clear cut than in patients with BrS who have been resuscitated from cardiac arrest, and needs to weigh up the risk of serious arrhythmic events with the risk of ICD-related complications.[1]

## Acute

» An ICD is generally recommended for patients who have:

- Spontaneous type 1 Brugada pattern on ECG and a history of cardiogenic syncope, particularly if this is likely to be due to ventricular arrhythmias[1][7] [18]
- Documented spontaneous sustained ventricular tachycardia with or without syncope.[7] [18][51]

» An ICD should be considered in patients who:

- Have provoked type 1 Brugada pattern on ECG and a history of cardiogenic syncope[1] [18] [7]
- Develop ventricular fibrillation during electrophysiologic study with programmed ventricular stimulation.[7] [51]

» The patient's life expectancy should also be taken into account; ICD may not be appropriate if meaningful survival is <1 year.[18]

» Regarding choice of ICD, a dual chamber system is recommended in most patients, particularly those prone to atrial arrhythmias (e.g., those carrying the SN5CA gene).[1] However, a subcutaneous device may be preferred in young patients who don't require pacing, because this has a lower risk of intravascular infection.[1]

**adjunct** **quinidine or phosphodiesterase-III inhibitor**

Treatment recommended for SOME patients in selected patient group

### Primary options

» quinidine sulfate: consult specialist for guidance on dose

### Secondary options

» cilostazol: consult specialist for guidance on dose

**OR**

» milrinone: consult specialist for guidance on dose

» Quinidine is a class 1a antiarrhythmic agent that has many effects.[1] The most significant of these is inhibition of the cardiac transient outward potassium current, which prolongs the refractory period.[1]

## Acute

» Quinidine is useful to suppress ventricular arrhythmias, and may also be used for medical management of atrial arrhythmias.[1] [51] It should be considered in patients who:[1] [5]

- Have an ICD and experience recurrent shocks[7] [18]
- Decline or are unsuitable for an ICD[7] [18] [51]
- Experience electrical storm (>2 episodes of ventricular tachycardia or ventricular fibrillation in 24 hours)[51] See "Acute ventricular arrhythmia" above.
- Experience asymptomatic ventricular arrhythmia.[68]

» Monitor the patient's CBC for anemia and thrombocytopenia.[1]

» Be aware that significant adverse effects and difficulty in obtaining the drug can limit its use.[1] [5]

» Phosphodiesterase-III inhibitors (cilostazol or milrinone) may be considered for patients with BrS (as an alternative to quinidine), however, supportive data are limited.[1] [7]

**adjunct** **radiofrequency catheter ablation**

Treatment recommended for SOME patients in selected patient group

» Indicated in patients who:

- Have recurrent ICD shocks, particularly if these are refractory to medical therapy[1] [5] [7] [18] [51]
- Experience serious arrhythmic events despite optimized medical therapy[1] [5]
- Are intolerant to or would prefer not to have medical therapy, or medical therapy is ineffective[1] [5]
- Have spontaneous type 1 Brugada pattern on ECG and symptomatic ventricular arrhythmias who are unsuitable for or decline an ICD[18]
- Have a history of electrical storms.[51]

» Significant contraindications to ablation include:[38]

- Ventricular tachycardia or fibrillation caused by myocardial ischemia, fever, or hypokalemia
- Presence of structural heart disease.

MANAGEMENT

## Acute

» A combined endocardial and epicardial approach has been shown to modify triggers and substrate for ventricular arrhythmias.[1]

# Patient discussions

As part of conservative management, advise the patient to:[1] [7]

- Avoid drugs that could exacerbate the Brugada ECG pattern (for further information see: [BrugadaDrugs.org: safe drug use and the Brugada syndrome] (https://www.brugadadrugs.org) ).[18] [51]
    - Antiarrhythmics (particularly sodium-channel blockers)
    - Psychotropic drugs
    - Anesthetics
    - Certain over-the-counter drugs (e.g., antihistamines)
    - Illicit drugs (e.g., cannabis, cocaine).
- Treat any fever promptly[18] [51]
- Avoid alcohol intoxication.[18] [51]

In addition, patients should discuss new medications with their cardiologist as appropriate.

Reassure patients that exercise is not a normal trigger for ventricular arrhythmias in Brugada syndrome. However, a post-vagal state following exercise has been reported.

Advise patients to contact their care team urgently if they have palpitations, syncope, or seizures. In addition, if they have an implantable cardioverter defibrillator (ICD) they should also report any syncope or ICD shocks.

FOLLOW UP

# Monitoring

## Monitoring

Arrange yearly follow up with a cardiologist or electrophysiologist with expertise in Brugada syndrome.[1] In particular, symptoms such as palpitations, syncope, and seizures must be evaluated.

If a patient is taking quinidine, monitor their CBC for anemia and thrombocytopenia.[1]

# Complications

| Complications | Timeframe | Likelihood |
|---|---|---|
| **atrial arrhythmias** | **variable** | **medium** |
| Atrial arrhythmias occur in about 10% of patients with Brugada syndrome.[61] [93] [94] | | |
| **serious arrhythmic events** | **variable** | **low** |
| Brugada syndrome (BrS) is the cause of around 28% of cases of sudden cardiac death in patients with an apparently normal heart and around 5% to 10% of cases of resuscitated cardiac arrest.[1] [91] [92] Around 1 in 25 patients with BrS have a history of cardiac arrest at time of initial diagnosis.[1] [54] Incidence of sudden cardiac death in those without an ICD is approximately 0.19%.[83] Patients who have BrS and cardiogenic syncope have an annual incidence of a serious arrhythmic event of about 1.4%.[1] The most likely mechanism of serious arrhythmic events is ventricular fibrillation initiated by short-coupled premature ventricular complexes.[1] | | |
| **implantable cardioverter defibrillator (ICD)-related complications** | **variable** | **low** |
| Patients who require an ICD tend to be <50 years old and are at risk of ICD-related complications (e.g., lead fracture, infection) and unnecessary ICD shocks. One meta-analysis found a 4.5% annual rate of ICD-related complications and a 3.5% annual rate of inappropriate shocks.[95] | | |

# Prognosis

Patients with Brugada syndrome (BrS) who have genetic mutations of SCN5A tend to develop symptoms at a younger age, and have more pronounced electrophysiologic defects (e.g., higher rate of spontaneous type 1 ECG pattern, significant conduction or repolarization abnormalities, increased atrial vulnerability) and a more severe prognosis.[90]

Age ≥55 at diagnosis is associated with a more benign prognosis, with no increased mortality compared with the general population.[1]

Established features that are associated with the greatest risk of serious arrhythmic events in patients with BrS are:[1][40][85][86][87]

- Resuscitated cardiac arrest
- History of cardiogenic syncope
- Spontaneous type 1 Brugada pattern on ECG.

# Diagnostic guidelines

## International

### 2022 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Ventricular-Arrhythmias-and-the-Prevention-of-Sudden-Cardiac-Death) [7]

**Published by:** European Society of Cardiology **Last published:** 2022

### Genetic testing for inherited cardiovascular diseases: a scientific statement from the American Heart Association (https://www.ahajournals.org/doi/full/10.1161/HCG.0000000000000067) [79]

**Published by:** American Heart Association **Last published:** 2020

### Expert consensus on risk assessment in cardiac arrhythmias: use the right tool for the right outcome, in the right population (https://www.hrsonline.org/guidance/clinical-resources/ehrahrsaphrslahrs-expert-consensus-risk-assessment-cardiac-arrhythmias-use-right-tool-right-outcome) [64]

**Published by:** European Heart Rhythm Association; Heart Rhythm Society; Asia Pacific Heart Rhythm Society; Latin American Heart Rhythm Society **Last published:** 2020

### 2013 Executive summary: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes (https://academic.oup.com/europace/article/15/10/1389/532177) [51]

**Published by:** Heart Rhythm Society; European Heart Rhythm Association; Asia Pacific Heart Rhythm Society **Last published:** 2013

### Current electrocardiographic criteria for diagnosis of Brugada pattern: a consensus report (https://www.sciencedirect.com/science/article/abs/pii/S0022073612002026?via%3Dihub) [4]

**Published by:** International Society for Holter and Noninvasive Electrocardiology **Last published:** 2012

# Treatment guidelines

## International

### 2022 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Ventricular-Arrhythmias-and-the-Prevention-of-Sudden-Cardiac-Death) [7]

**Published by:** European Society of Cardiology **Last published:** 2022

### 2019 HRS/EHRA/APHRS/LAHRS expert consensus statement on catheter ablation of ventricular arrhythmias (https://www.heartrhythmjournal.com/article/S1547-5271(19)30210-3/fulltext) [5]

**Published by:** Heart Rhythm Society, European Heart Rhythm Association; Asia Pacific Heart Rhythm Society; Latin American Heart Rhythm Society **Last published:** 2019

### Management of asymptomatic arrhythmias: a European Heart Rhythm Association (EHRA) consensus document (https://academic.oup.com/europace/article/21/6/844/5382236?login=false) [68]

**Published by:** European Heart Rhythm Association (endorsed by: Heart Failure Association; Heart Rhythm Society; Asia Pacific Heart Rhythm Society; Cardiac Arrhythmia Society of Southern Africa; Latin America Heart Rhythm Society) **Last published:** 2019

### 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death (https://www.ahajournals.org/doi/10.1161/CIR.0000000000000549) [18]

**Published by:** American Heart Association; American College of Cardiology; Heart Rhythm Society **Last published:** 2017

### 2013 Executive summary: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes (https://academic.oup.com/europace/article/15/10/1389/532177) [51]

**Published by:** Heart Rhythm Society; European Heart Rhythm Association; Asia Pacific Heart Rhythm Society **Last published:** 2013

# Online resources

1. BrugadaDrugs.org: safe drug use and the Brugada syndrome (https://www.brugadadrugs.org) *(external link)*



REFERENCES

# Key articles


- Krahn AD, Behr ER, Hamilton R, et al. Brugada syndrome. JACC Clin Electrophysiol. 2022 Mar;8(3):386-405. Full text (https://www.sciencedirect.com/science/article/pii/S2405500X2101080X?via%3Dihub) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/35331438?tool=bestpractice.bmj.com)
- Cronin EM, Bogun FM, Maury P, et al. 2019 HRS/EHRA/APHRS/LAHRS expert consensus statement on catheter ablation of ventricular arrhythmias. Europace. 2019 Aug 1;21(8):1143-4. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7967791) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/31075787?tool=bestpractice.bmj.com)
- Priori SG, Wilde AA, Horie M, et al. HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes: document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013. Heart Rhythm. 2013;10(12):1932-63. Full text (https://www.heartrhythmjournal.com/article/S1547-5271(13)00552-3/fulltext) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/24011539?tool=bestpractice.bmj.com)
- Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Eur Heart J. 2022 Oct 21;43(40):3997-4126. Full text (https://academic.oup.com/eurheartj/article/43/40/3997/6675633?login=false) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/36017572?tool=bestpractice.bmj.com)
- Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm. 2018 Oct;15(10):e190-e252. Full text (https://www.heartrhythmjournal.com/article/S1547-5271(17)31249-3/fulltext) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/29097320?tool=bestpractice.bmj.com)
- Priori SG, Wilde AA, Horie M, et al. Executive summary: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes. Heart Rhythm. 2013;10(12):e85-108. Full text (https://core.ac.uk/reader/82269654?utm_source=linkout) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/23916535?tool=bestpractice.bmj.com)
- Nielsen JC, Lin YJ, de Oliveira Figueiredo MJ, et al. European Heart Rhythm Association (EHRA)/Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) expert consensus on risk assessment in cardiac arrhythmias: use the right tool for the right outcome, in the right population. J Arrhythm. 2020 Jun 15;36(4):553-607. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7411224) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/32782627?tool=bestpractice.bmj.com)


# References

1. Krahn AD, Behr ER, Hamilton R, et al. Brugada syndrome. JACC Clin Electrophysiol. 2022 Mar;8(3):386-405. Full text (https://www.sciencedirect.com/science/article/pii/S2405500X2101080X?via%3Dihub) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/35331438?tool=bestpractice.bmj.com)

2. Oe H, Takagi M, Tanaka A, et al. Prevalence and clinical course of the juveniles with Brugada-type ECG in Japanese population. Pacing Clin Electrophysiol. 2005;28(6):549-54. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/15955188?tool=bestpractice.bmj.com)

3. Yamakawa Y, Ishikawa T, Uchino K, et al. Prevalence of right bundle-branch block and right precordial ST-segment elevation (Brugada-type electrocardiogram) in Japanese children. Circ J. 2004;68(4):275-9. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/15056820?tool=bestpractice.bmj.com)

4. Bayés de Luna A, Brugada J, Baranchuk A, et al. Current electrocardiographic criteria for diagnosis of Brugada pattern: a consensus report. J Electrocardiol. 2012;45(5):433-42. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/22920782?tool=bestpractice.bmj.com)

5. Cronin EM, Bogun FM, Maury P, et al. 2019 HRS/EHRA/APHRS/LAHRS expert consensus statement on catheter ablation of ventricular arrhythmias. Europace. 2019 Aug 1;21(8):1143-4. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7967791) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/31075787?tool=bestpractice.bmj.com)

6. Priori SG, Wilde AA, Horie M, et al. HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes: document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013. Heart Rhythm. 2013;10(12):1932-63. Full text (https://www.heartrhythmjournal.com/article/S1547-5271(13)00552-3/fulltext) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/24011539?tool=bestpractice.bmj.com)

7. Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Eur Heart J. 2022 Oct 21;43(40):3997-4126. Full text (https://academic.oup.com/eurheartj/article/43/40/3997/6675633?login=false) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/36017572?tool=bestpractice.bmj.com)

8. Benito B, Brugada J, Brugada R, Brugada P. Brugada syndrome. Rev Esp Cardiol. 2009;62(11):1297-315. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/19889341?tool=bestpractice.bmj.com)

9. Antzelevitch C, Brugada P, Borggrefe M, et al. Brugada syndrome: report of the second consensus conference: endorsed by the Heart Rhythm Society and the European Heart Rhythm Association. Circulation. 2005;111(5):659-70. Full text (https://www.ahajournals.org/doi/10.1161/01.CIR.0000152479.54298.51?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/15655131?tool=bestpractice.bmj.com)

10. Jellins J, Milanovic M, Taitz DJ, Wan SH, Yam PW. Brugada syndrome. Hong Kong Med J. 2013;19(2):159-67. Full text (https://www.hkmj.org/abstracts/v19n2/159.htm) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/23535677?tool=bestpractice.bmj.com)

REFERENCES


11. Quan XQ, Li S, Liu R, Zheng K, Wu XF, Tang Q. A meta-analytic review of prevalence for Brugada ECG patterns and the risk for death. Medicine (Baltimore). 2016 Dec;95(50):e5643. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5268056) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/27977610?tool=bestpractice.bmj.com)

12. Behere SP, Weindling SN. Brugada syndrome in children - Stepping into unchartered territory. Ann Pediatr Cardiol. 2017 Sep-Dec;10(3):248-58. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5594936) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/28928611?tool=bestpractice.bmj.com)

13. Mizusawa Y, Wilde AA. Brugada syndrome. Circ Arrhythm Electrophysiol. 2012;5(3):606-16. Full text (https://www.ahajournals.org/doi/10.1161/CIRCEP.111.964577?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/22715240?tool=bestpractice.bmj.com)

14. Sarquella-Brugada G, Campuzano O, Arbelo E, Brugada J, Brugada R. Brugada syndrome: clinical and genetic findings. Genet Med. 2016;18(1):3-12. Full text (https://www.gimjournal.org/article/S1098-3600(21)04299-4/fulltext) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/25905440?tool=bestpractice.bmj.com)

15. Priori SG, Wilde AA, Horie M, et al. HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes: document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013. Heart Rhythm. 2013;10(12):1932-63. Full text (https://www.heartrhythmjournal.com/article/S1547-5271(13)00552-3/fulltext) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/24011539?tool=bestpractice.bmj.com)

16. Kapplinger JD, Tester DJ, Alders M, et al. An international compendium of mutations in the SCN5A-encoded cardiac sodium channel in patients referred for Brugada syndrome genetic testing. Heart Rhythm. 2010 Jan;7(1):33-46. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2822446) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20129283?tool=bestpractice.bmj.com)

17. Hu D, Barajas-Martínez H, Pfeiffer R, et al. Mutations in SCN10A are responsible for a large fraction of cases of Brugada syndrome. J Am Coll Cardiol. 2014;64(1):66-79. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4116276) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/24998131?tool=bestpractice.bmj.com)

18. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm. 2018 Oct;15(10):e190-e252. Full text (https://www.heartrhythmjournal.com/article/S1547-5271(17)31249-3/fulltext) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/29097320?tool=bestpractice.bmj.com)

19. Hosseini SM, Kim R, Udupa S, etal. Reappraisal of reported genes for sudden arrhythmic death: Evidence-based evaluation of gene validity for Brugada syndrome. Circulation. 2018 Sep 18;138(12):1195-205. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6147087) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/29959160?tool=bestpractice.bmj.com)

20. Adler A, Topaz G, Heller K, et al. Fever-induced Brugada pattern: how common is it and what does it mean?. Heart Rhythm. 2013;10(9):1375-82. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3832740) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/23872691?tool=bestpractice.bmj.com)

21. Rattanawong P, Vutthikraivit W, Charoensri A, et al. Fever-induced Brugada syndrome is more common than previously suspected: A cross-sectional study from an endemic area. Ann Noninvasive Electrocardiol. 2016;21(2):136-41. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6931454) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/26178440?tool=bestpractice.bmj.com)

22. Attard A, Stanniland C, Attard S,et al. Brugada syndrome: should we be screening patients before prescribing psychotropic medication? Ther Adv Psychopharmacol. 2022 Jan 28;12:20451253211067017. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8801628) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/35111298?tool=bestpractice.bmj.com)

23. Deschênes I, Baroudi G, Berthet M, et al. Electrophysiological characterization of SCN5A mutations causing long QT (E1784K) and Brugada (R1512W and R1432G) syndromes. Cardiovasc Res. 2000;46(1):55-65. Full text (https://academic.oup.com/cardiovascres/article/46/1/55/333556?login=true) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/10727653?tool=bestpractice.bmj.com)

24. Clancy CE, Kass RS. Defective cardiac ion channels: from mutations to clinical syndromes. J Clin Invest. 2002;110(8):1075-7. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC150807) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12393842?tool=bestpractice.bmj.com)

25. Behr ER, Savio-Galimberti E, Barc J, et al. Role of common and rare variants in SCN10A: results from the Brugada syndrome QRS locus gene discovery collaborative study. Cardiovasc Res. 2015;106(3):520-9. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4447806) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/25691538?tool=bestpractice.bmj.com)

26. Fukuyama M, Ohno S, Makiyama T, Horie M. Novel SCN10A variants associated with Brugada syndrome. Europace. 2016;18(6):905-11. Full text (https://academic.oup.com/europace/article/18/6/905/2467006?login=false) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/25842276?tool=bestpractice.bmj.com)

27. Riuró H, Beltran-Alvarez P, Tarradas A, et al. A missense mutation in the sodium channel β2 subunit reveals SCN2B as a new candidate gene for Brugada syndrome. Hum Mutat. 2013;34(7):961-6. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/23559163?tool=bestpractice.bmj.com)

28. Cerrone M, Lin X, Zhang M, et al. Missense mutations in plakophilin-2 cause sodium current deficit and associate with a Brugada syndrome phenotype. Circulation. 2014;129(10):1092-103. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3954430) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/24352520?tool=bestpractice.bmj.com)

29. Belbachir N, Portero V, Al Sayed ZR, et al. RRAD mutation causes electrical and cytoskeletal defects in cardiomyocytes derived from a familial case of Brugada syndrome. Eur Heart J. 2019 Oct 1;40(37):3081-94. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6769825) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/31114854?tool=bestpractice.bmj.com)

30. Giudicessi JR, Ye D, Tester DJ, et al. Transient outward current (I(to)) gain-of-function mutations in the KCND3-encoded Kv4.3 potassium channel and Brugada syndrome. Heart Rhythm.

2011;8(7):1024-32. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3150551) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/21349352?tool=bestpractice.bmj.com)

31. Burashnikov E, Pfeiffer R, Barajas-Martinez H, et al. Mutations in the cardiac L-type calcium channel associated with inherited J-wave syndromes and sudden cardiac death. Heart Rhythm. 2010;7(12):1872-82. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2999985) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20817017?tool=bestpractice.bmj.com)

32. Behr ER, Ben-Haim Y, Ackerman MJ, et al. Brugada syndrome and reduced right ventricular outflow tract conduction reserve: a final common pathway? Eur Heart J. 2021 Mar 14;42(11):1073-81. Full text (https://academic.oup.com/eurheartj/article/42/11/1073/6076711?login=false) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/33421051?tool=bestpractice.bmj.com)

33. Wilde AA, Postema PG, Di Diego JM, et al. The pathophysiological mechanism underlying Brugada syndrome: depolarization versus repolarization. J Mol Cell Cardiol. 2010;49(4):543-53. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2932806) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20659475?tool=bestpractice.bmj.com)

34. Yan GX, Antzelevitch C. Cellular basis for the Brugada syndrome and other mechanisms of arrhythmogenesis associated with ST-segment elevation. Circulation. 1999;100(15):1660-6. Full text (https://www.ahajournals.org/doi/10.1161/01.cir.100.15.1660?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/10517739?tool=bestpractice.bmj.com)

35. Iacoviello M, Forleo C, Puzzovivo A, et al. Altered two-dimensional strain measures of the right ventricle in patients with Brugada syndrome and arrhythmogenic right ventricular dysplasia/cardiomyopathy. Eur J Echocardiogr. 2011;12(10):773-81. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/21865227?tool=bestpractice.bmj.com)

36. Bastiaenen R, Cox AT, Castelletti S, et al. Late gadolinium enhancement in Brugada syndrome: A marker for subtle underlying cardiomyopathy? Heart Rhythm. 2017 Apr;14(4):583-9. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/27919765?tool=bestpractice.bmj.com)

37. Pieroni M, Notarstefano P, Oliva A, et al. Electroanatomic and pathologic right ventricular outflow tract abnormalities in patients with Brugada syndrome. J Am Coll Cardiol. 2018 Dec 4;72(22):2747-57. Full text (https://www.sciencedirect.com/science/article/pii/S0735109718386637?via%3Dihub) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30497561?tool=bestpractice.bmj.com)

38. Nademanee K, Veerakul G, Chandanamattha P, et al. Prevention of ventricular fibrillation episodes in Brugada syndrome by catheter ablation over the anterior right ventricular outflow tract epicardium. Circulation. 2011;123(12):1270-9. Full text (https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.110.972612?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/21403098?tool=bestpractice.bmj.com)

39. Milman A, Andorin A, Gourraud JB, et al. Age of first arrhythmic event in Brugada syndrome: Data from the SABRUS (Survey on Arrhythmic Events in Brugada Syndrome) in 678 patients. Circ Arrhythm

Electrophysiol. 2017 Dec;10(12):e005222. Full text (https://iris.unito.it/handle/2318/1660808) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/29254945?tool=bestpractice.bmj.com)

40. Gonzalez Corcia MC, Sieira J, Sarkozy A, et al. Brugada syndrome in the young: an assessment of risk factors predicting future events. Europace. 2017 Nov 1;19(11):1864-73. Full text (https://academic.oup.com/europace/article/19/11/1864/2194460?login=false) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/27738063?tool=bestpractice.bmj.com)

41. Minier M, Probst V, Berthome P, et al. Age at diagnosis of Brugada syndrome: Influence on clinical characteristics and risk of arrhythmia. Heart Rhythm. 2020 May;17(5 Pt A):743-9. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/31790831?tool=bestpractice.bmj.com)

42. Juang JM, Chen CY, Chen YH, et al. Prevalence and prognosis of Brugada electrocardiogram patterns in an elderly Han Chinese population: a nation-wide community-based study (HALST cohort). Europace. 2015 Oct;17(Suppl 2):ii54-62. Full text (https://academic.oup.com/europace/article/17/suppl_2/ii54/2802554?login=false) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/26842116?tool=bestpractice.bmj.com)

43. Kitamura T, Fukamizu S, Kawamura I, et al. Clinical characteristics and long-term prognosis of senior patients with Brugada syndrome. JACC Clin Electrophysiol. 2017 Jan;3(1):57-67. Full text (https://www.sciencedirect.com/science/article/pii/S2405500X16301062?via%3Dihub) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/29759696?tool=bestpractice.bmj.com)

44. Yuan M, Tian C, Li X, et al. Gender differences in prognosis and risk stratification of Brugada syndrome: A pooled analysis of 4,140 patients from 24 clinical trials. Front Physiol. 2018 Aug 22;9:1127. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6113678) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30246798?tool=bestpractice.bmj.com)

45. Sieira J, Brugada P. Brugada syndrome: Defining the risk in asymptomatic patients. Arrhythm Electrophysiol Rev. 2016;5(3):164-9. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5248661) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/28116080?tool=bestpractice.bmj.com)

46. Berthome P, Tixier R, Briand J, et al. Clinical presentation and follow-up of women affected by Brugada syndrome. Heart Rhythm. 2019 Feb;16(2):260-7. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30193851?tool=bestpractice.bmj.com)

47. Probst V, Veltmann C, Eckardt L, et al. Long-term prognosis of patients diagnosed with Brugada syndrome: Results from the FINGER Brugada Syndrome Registry. Circulation. 2010;121(5):635-43. Full text (https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.109.887026?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20100972?tool=bestpractice.bmj.com)

48. Delise P, Allocca G, Marras E, et al. Risk stratification in individuals with the Brugada type 1 ECG pattern without previous cardiac arrest: usefulness of a combined clinical and electrophysiologic approach. Eur Heart J. 2011;32(2):169-76. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3021386) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20978016?tool=bestpractice.bmj.com)

49. Antzelevitch C, Yan GX, Ackerman MJ, et al. J-Wave syndromes expert consensus conference report: Emerging concepts and gaps in knowledge. Heart Rhythm. 2016 Oct;13(10):e295-324. Full text

(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5035208) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/27423412?tool=bestpractice.bmj.com)

50. Kamakura S, Ohe T, Nakazawa K, et al. Long-term prognosis of probands with Brugada-pattern ST-elevation in leads V1-V3. Circ Arrhythm Electrophysiol. 2009;2(5):495-503. Full text (https://www.ahajournals.org/doi/10.1161/CIRCEP.108.816892?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/19843917?tool=bestpractice.bmj.com)

51. Priori SG, Wilde AA, Horie M, et al. Executive summary: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes. Heart Rhythm. 2013;10(12):e85-108. Full text (https://core.ac.uk/reader/82269654?utm_source=linkout) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/23916535?tool=bestpractice.bmj.com)

52. Rodríguez-Mañero M, Sacher F, de Asmundis C, et al. Monomorphic ventricular tachycardia in patients with Brugada syndrome: A multicenter retrospective study. Heart Rhythm. 2016;13(3):669-682. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/26538325?tool=bestpractice.bmj.com)

53. Eckhardt LL. Monomorphic ventricular tachycardia in Brugada syndrome: True-true but related?. Heart Rhythm. 2016;13(3):683-5. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/26632641?tool=bestpractice.bmj.com)

54. Casado-Arroyo R, Berne P, Rao JY, Rodriguez-Mañero M, et al. Long-term trends in newly diagnosed Brugada syndrome: Implications for risk stratification. J Am Coll Cardiol. 2016 Aug 9;68(6):614-23. Full text (https://pubmed.ncbi.nlm.nih.gov/27491905) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/27491905?tool=bestpractice.bmj.com)

55. Okamura H, Kamakura T, Morita H, et al. Risk stratification in patients with Brugada syndrome without previous cardiac arrest – prognostic value of combined risk factors. Circ J. 2015;79(2):310-17. Full text (https://www.jstage.jst.go.jp/article/circj/79/2/79_CJ-14-1059/_html/-char/en) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/25428522?tool=bestpractice.bmj.com)

56. Kawazoe H, Nakano Y, Ochi H, et al. Risk stratification of ventricular fibrillation in Brugada syndrome using noninvasive scoring methods. Heart Rhythm. 2016 Oct;13(10):1947-54. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/27424075?tool=bestpractice.bmj.com)

57. Honarbakhsh S, Providencia R, Garcia-Hernandez J, et al. A Primary prevention clinical risk score model for patients with Brugada syndrome (BRUGADA-RISK). JACC Clin Electrophysiol. 2021 Feb;7(2):210-2. Full text (https://www.sciencedirect.com/science/article/pii/S2405500X20308197?via%3Dihub) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/33602402?tool=bestpractice.bmj.com)

58. Olde Nordkamp LR, Vink AS, Wilde AA, et al. Syncope in Brugada syndrome: prevalence, clinical significance, and clues from history taking to distinguish arrhythmic from nonarrhythmic causes. Heart Rhythm. 2015;12(2):367-75. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/25311410?tool=bestpractice.bmj.com)

59. Schimpf R, Giustetto C, Eckardt L, et al. Prevalence of supraventricular tachyarrhythmias in a cohort of 115 patients with Brugada syndrome. Ann Noninvasive Electrocardiol. 2008;13(3):266-9. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6932135) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/18713327?tool=bestpractice.bmj.com)

60. Kusano KF, Taniyama M, Nakamura K, et al. Atrial fibrillation in patients with Brugada syndrome relationships of gene mutation, electrophysiology, and clinical backgrounds. J Am Coll Cardiol. 2008;51(12):1169-75. Full text (https://www.sciencedirect.com/science/article/pii/S0735109708000648?via%3Dihub) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/18355654?tool=bestpractice.bmj.com)

61. Giustetto C, Cerrato N, Gribaudo E, et al. Atrial fibrillation in a large population with Brugada electrocardiographic pattern: prevalence, management, and correlation with prognosis. Heart Rhythm. 2014;11(2):259-65. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/24513919?tool=bestpractice.bmj.com)

62. Holst AG, Jensen HK, Eschen O, et al. Low disease prevalence and inappropriate implantable cardioverter defibrillator shock rate in Brugada syndrome: a nationwide study. Europace. 2012;14(7):1025-9. Full text (https://core.ac.uk/reader/50680417?utm_source=linkout) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/22286273?tool=bestpractice.bmj.com)

63. Vatta M, Dumaine R, Antzelevitch C, et al. Novel mutations in domain I of SCN5A cause Brugada syndrome. Mol Genet Metab. 2002;75(4):317-24. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12051963?tool=bestpractice.bmj.com)

64. Nielsen JC, Lin YJ, de Oliveira Figueiredo MJ, et al. European Heart Rhythm Association (EHRA)/Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) expert consensus on risk assessment in cardiac arrhythmias: use the right tool for the right outcome, in the right population. J Arrhythm. 2020 Jun 15;36(4):553-607. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7411224) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/32782627?tool=bestpractice.bmj.com)

65. Veltmann C, Papavassiliu T, Konrad T, et al. Insights into the location of type I ECG in patients with Brugada syndrome: correlation of ECG and cardiovascular magnetic resonance imaging. Heart Rhythm. 2012;9(3):414-21. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/22119454?tool=bestpractice.bmj.com)

66. Sangwatanaroj S, Prechawat S, Sunsaneewitayakul B, et al. New electrocardiographic leads and the procainamide test for the detection of the Brugada sign in sudden unexplained death syndrome survivors and their relatives. Eur Heart J. 2001;22(24):2290-6. Full text (https://academic.oup.com/eurheartj/article/22/24/2290/512888?login=true) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/11728150?tool=bestpractice.bmj.com)

67. Govindan M, Batchvarov VN, Raju H, et al. Utility of high and standard right precordial leads during ajmaline testing for the diagnosis of Brugada syndrome. Heart. 2010;96(23):1904-8. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20962343?tool=bestpractice.bmj.com)

68. Arnar DO, Mairesse GH, Boriani G, et al. Management of asymptomatic arrhythmias: a European Heart Rhythm Association (EHRA) consensus document, endorsed by the Heart Failure Association

(HFA), Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS), Cardiac Arrhythmia Society of Southern Africa (CASSA), and Latin America Heart Rhythm Society (LAHRS). Europace. 2019 Mar 18;21(6):844–5. Full text (https://academic.oup.com/europace/article/21/6/844/5382236?login=false) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30882141?tool=bestpractice.bmj.com)

69. Gollob MH, Blier L, Brugada R, et al. Recommendations for the use of genetic testing in the clinical evaluation of inherited cardiac arrhythmias associated with sudden cardiac death: Canadian Cardiovascular Society/Canadian Heart Rhythm Society joint position paper. Can J Cardiol. 2011 Mar-Apr;27(2):232-45. Full text (https://www.onlinecjc.ca/article/S0828-282X(10)00094-2/fulltext) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/21459272?tool=bestpractice.bmj.com)

70. Heermann P, Fritsch H, Koopmann M, et al. Biventricular myocardial strain analysis using cardiac magnetic resonance feature tracking (CMR-FT) in patients with distinct types of right ventricular diseases comparing arrhythmogenic right ventricular cardiomyopathy (ARVC), right ventricular outflow-tract tachycardia (RVOT-VT), and Brugada syndrome (BrS). Clin Res Cardiol. 2019 Oct;108(10):1147-62. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30868222?tool=bestpractice.bmj.com)

71. Borgquist R, Haugaa KH, Gilljam T, et al. The diagnostic performance of imaging methods in ARVC using the 2010 Task Force criteria. Eur Heart J Cardiovasc Imaging. 2014;15(11):1219-25. Full text (https://academic.oup.com/ehjcimaging/article/15/11/1219/2399659?login=false) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/24939949?tool=bestpractice.bmj.com)

72. Peters S, Trümmel M, Denecke S, et al. Results of ajmaline testing in patients with arrhythmogenic right ventricular dysplasia-cardiomyopathy. Int J Cardiol. 2004 Jun;95(2-3):207-10. Full text (https://www.doi.org/10.1016/j.ijcard.2003.04.032) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/15193821?tool=bestpractice.bmj.com)

73. Wilde AA, Antzelevitch C, Borggrefe M, et al. Proposed diagnostic criteria for the Brugada syndrome: consensus report. Circulation. 2002;106(19):2514-9. Full text (https://www.ahajournals.org/doi/10.1161/01.cir.0000034169.45752.4a?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12417552?tool=bestpractice.bmj.com)

74. Pelliccia A, Maron BJ. Outer limits of the athlete's heart, the effect of gender, and relevance to the differential diagnosis with primary cardiac diseases. Cardiol Clin. 1997;15(3):381-96. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/9276164?tool=bestpractice.bmj.com)

75. Drezner JA, Sharma S, Baggish A, et al. International criteria for electrocardiographic interpretation in athletes: Consensus statement. Br J Sports Med. 2017 May;51(9):704-31. Full text (https://bjsm.bmj.com/content/51/9/704.long) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/28258178?tool=bestpractice.bmj.com)

76. Alings M, Wilde A. "Brugada" syndrome: clinical data and suggested pathophysiological mechanism. Circulation. 1999;99(5):666-73. Full text (https://www.ahajournals.org/doi/10.1161/01.cir.99.5.666?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/9950665?tool=bestpractice.bmj.com)

77. Anselm DD, Evans JM, Baranchuk A. Brugada phenocopy: A new electrocardiogram phenomenon. World J Cardiol. 2014;6(3):81-6. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3964189) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/24669289?tool=bestpractice.bmj.com)

78. Rose BD, Post TW. Clinical physiology of acid-base and electrolyte disorders, 5th ed. New York, NY: McGraw-Hill; 2001:836-56.

79. Musunuru K, Hershberger RE, Day SM, et al. Genetic testing for inherited cardiovascular diseases: A scientific statement from the American Heart Association. Circ Genom Precis Med. 2020 Aug;13(4):e000067. Full text (https://www.ahajournals.org/doi/full/10.1161/HCG.0000000000000067?rfr_dat=cr_pub++0pubmed&url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/32698598?tool=bestpractice.bmj.com)

80. Eifling M, Razavi M, Massumi A. The evaluation and management of electrical storm. Tex Heart Inst J. 2011;38(2):111-21. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3066819) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/21494516?tool=bestpractice.bmj.com)

81. Sieira J, Conte G, Ciconte G, et al. A score model to predict risk of events in patients with Brugada Syndrome. Eur Heart J. 2017 Jun 7;38(22):1756-63. Full text (https://academic.oup.com/eurheartj/article/38/22/1756/3098019?login=false) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/28379344?tool=bestpractice.bmj.com)

82. Chow JJ, Leong KMW, Yazdani M, et al. A multicenter external validation of a score model to predict risk of events in patients with Brugada syndrome. Am J Cardiol. 2021 Dec 1;160:53-9. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/34610873?tool=bestpractice.bmj.com)

83. Probst V, Goronflot T, Anys S, et al. Robustness and relevance of predictive score in sudden cardiac death for patients with Brugada syndrome. Eur Heart J. 2021 May 1;42(17):1687-95. Full text (https://academic.oup.com/eurheartj/article/42/17/1687/6027696?login=false) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/33289793?tool=bestpractice.bmj.com)

84. Gonzalez Corcia MC, Sieira J, Pappaert G, de Asmundis C, Chierchia GB, Sarkozy A, Brugada P. A Clinical Score Model to Predict Lethal Events in Young Patients (≤19 Years) With the Brugada Syndrome. Am J Cardiol. 2017 Sep 1;120(5):797-802. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/28728742?tool=bestpractice.bmj.com)

85. Andorin A, Behr ER, Denjoy I, et al. Impact of clinical and genetic findings on the management of young patients with Brugada syndrome. Heart Rhythm. 2016 Jun;13(6):1274-82. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/26921764?tool=bestpractice.bmj.com)

86. Priori SG, Gasparini M, Napolitano C, et al. Risk stratification in Brugada syndrome: results of the PRELUDE (PRogrammed ELectrical stimUlation preDictive valuE) registry. J Am Coll Cardiol. 2012;59(1):37-45. Full text (https://www.sciencedirect.com/science/article/pii/S073510971104530X?via%3Dihub) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/22192666?tool=bestpractice.bmj.com)

87. Priori SG, Napolitano C, Gasparini M, et al. Natural history of Brugada syndrome: insights for risk stratification and management. Circulation. 2002;105(11):1342-7. Full text (https://www.ahajournals.org/doi/10.1161/hc1102.105288?

url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/11901046?tool=bestpractice.bmj.com)

88. Conte G, de Asmundis C, Sieira J, et al. Prevalence and clinical impact of early repolarization pattern and QRS-fragmentation in high-risk patients with Brugada syndrome. Circ J. 2016 Sep 23;80(10):2109-16. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/27558008?tool=bestpractice.bmj.com)

89. Sroubek J, Probst V, Mazzanti A, et al. Programmed Ventricular Stimulation for Risk Stratification in the Brugada Syndrome: A Pooled Analysis. Circulation. 2016;133(7):622-30. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4758872) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/26797467?tool=bestpractice.bmj.com)

90. Chen C, Tan Z, Zhu W, et al. Brugada syndrome with SCN5A mutations exhibits more pronounced electrophysiological defects and more severe prognosis: A meta-analysis. Clin Genet. 2020 Jan;97(1):198-208. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30963536?tool=bestpractice.bmj.com)

91. Papadakis M, Papatheodorou E, Mellor G, et al. The diagnostic yield of Brugada syndrome after sudden death with normal autopsy. J Am Coll Cardiol. 2018 Mar 20;71(11):1204-14. Full text (https://www.sciencedirect.com/science/article/pii/S0735109718302420?via%3Dihub) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/29544603?tool=bestpractice.bmj.com)

92. van der Werf C, Hofman N, Tan HL, et al. Diagnostic yield in sudden unexplained death and aborted cardiac arrest in the young: the experience of a tertiary referral center in The Netherlands. Heart Rhythm. 2010;7(10):1383-1389 Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20646679?tool=bestpractice.bmj.com)

93. Sacher F, Probst V, Iesaka Y, et al. Outcome after implantation of a cardioverter-defibrillator in patients with Brugada syndrome: a multicenter study. Circulation. 2006;114(22):2317-24. Full text (https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.106.628537?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17116772?tool=bestpractice.bmj.com)

94. Kewcharoen J, Rattanawong P, Kanitsoraphan C, et al. Atrial fibrillation and risk of major arrhythmic events in Brugada syndrome: A meta-analysis. Ann Noninvasive Electrocardiol. 2019 Nov;24(6):e12676. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6931417) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/31353765?tool=bestpractice.bmj.com)

95. Dereci A, Yap SC, Schinkel AFL. Meta-analysis of clinical outcome after implantable cardioverter-defibrillator implantation in patients with Brugada syndrome. JACC Clin Electrophysiol. 2019 Feb;5(2):141-8. Full text (https://www.sciencedirect.com/science/article/pii/S2405500X18307424?via%3Dihub) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30784682?tool=bestpractice.bmj.com)

# Images

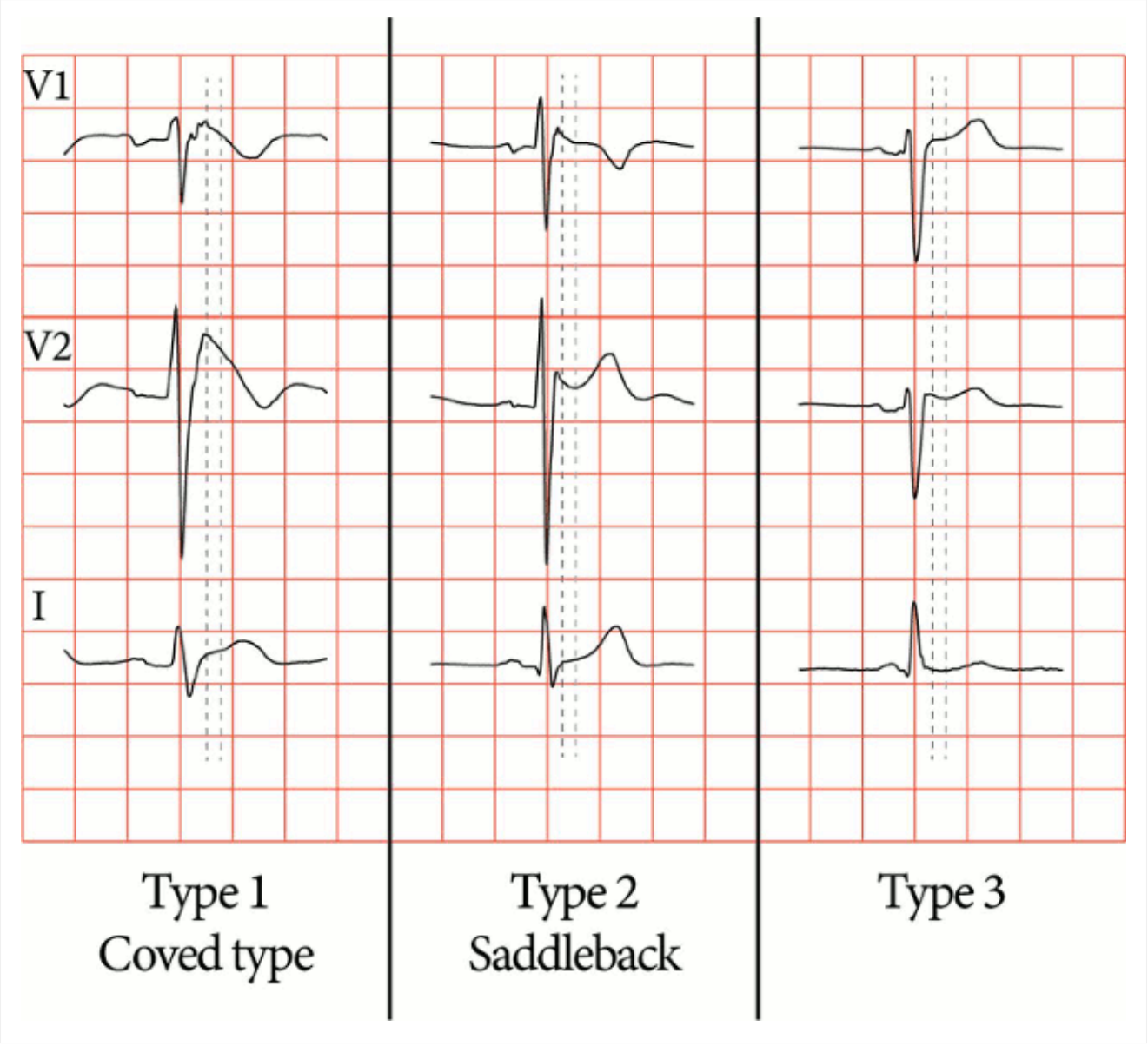



*Figure 1: Electrocardiographic patterns in Brugada syndrome showing type 1 (diagnostic) and types 2 and 3 (non-diagnostic) patterns. Type-1 (diagnostic): coved STT morphology in lead V2 with J-point elevation (dark gray line) of ≥0.2 mV (≥2 mm) and a terminal ST-segment elevation (light gray line, J+60 ms) also ≥0.2 mV (≥2 mm). Note the PR interval and wider QRS complex, wide and deep S in lead I, and fractionation in the right precordial ECG leads. Type-2 (non-diagnostic): saddleback STT morphology in lead V2 with J-point elevation (dark gray line) of ≥0.2 mV (≥2 mm) and a terminal ST-segment elevation (light gray line, J +60 ms) ≥0.1 mV (≥1 mm), followed by a positive T wave. Note the less wide and deep S-wave in lead I, less prominent fractionation. Type-3 (non-diagnostic): saddleback STT morphology in lead V2 with J-point elevation (dark gray line) of ≥0.2 mV (≥2 mm) and a terminal ST-segment elevation (light gray line, J+60 ms) <0.1 mV (<1 mm)*

*Marsman EMJ et al. Heart 2022 May;108(9):668-75; used with permission*

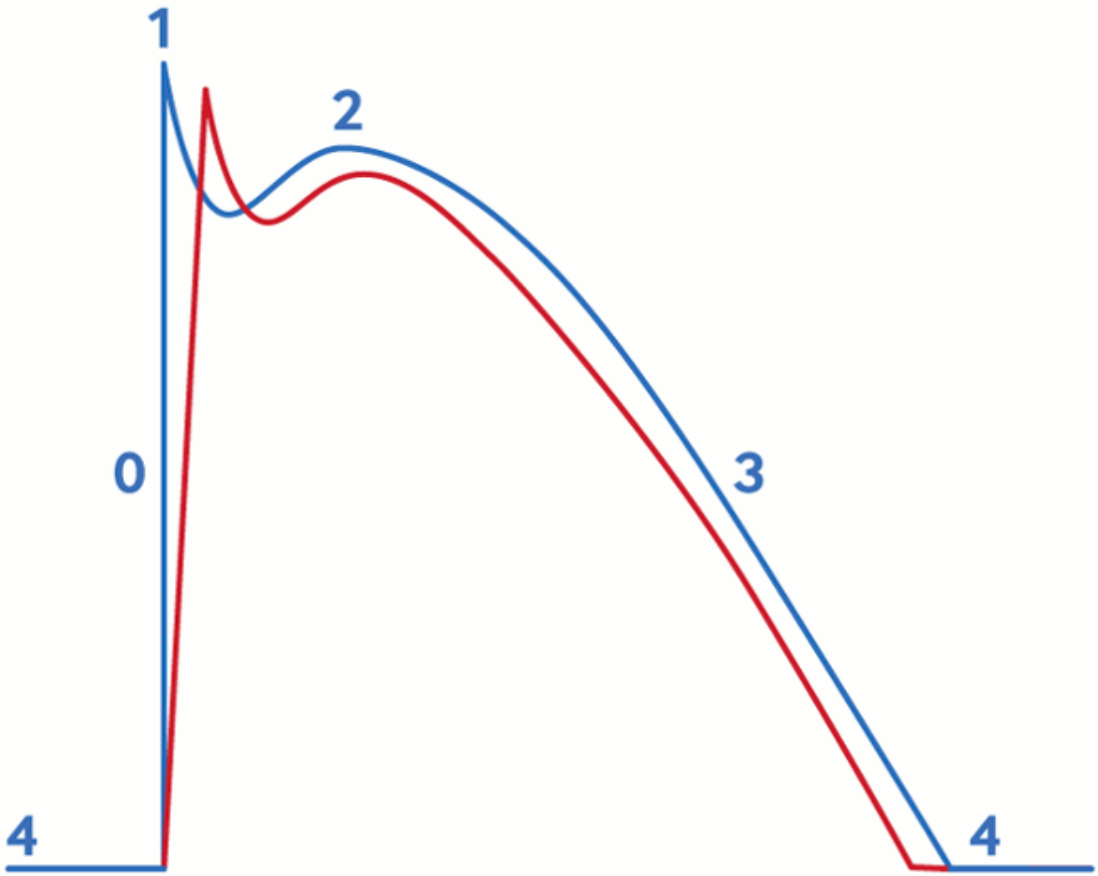



*Figure 2: Cardiac action potential in Brugada syndrome. Blue line indicates normal ventricular action potential; red line indicates delayed upstroke of action potential in Brugada syndrome. Action potential phases: 0, rapid depolarization; 1, rapid/early repolarization; 2, plateau; 3, terminal repolarization; 4, resting potential*

*Krahn AD et al. JACC Clin Electrophysiol 2022 Mar;8(3):386-405; used with permission*

| Factor - ECG (12-lead/ambulatory)[b] | Points |
|---|---|
| Spontaneous type 1 Brugada pattern on standard or Brugada ECG | 3.5 |
| Fever-induced type 1 Brugada pattern on standard or Brugada ECG | 3 |
| Type 2 or 3 Brugada ECG pattern that converts with sodium channel-blocking drug challenge | 2 |
| **Clinical history[a]** | |
| Unexplained cardiac arrest or documented ventricular fibrillation/polymorphic ventricular tachycardia | 3 |
| Nocturnal agonal respirations | 2 |
| Suspected arrhythmic syncope | 2 |
| Syncope of unclear mechanism or unclear etiology | 1 |
| Atrial flutter or fibrillation in patients <30 years without alternative etiology | 0.5 |
| **Family history[a]** | |
| First- or second-degree relative with definite BrS | 2 |
| Suspicious SCD (during fever, at night, or when taking Brugada-aggravating drugs) in a first- or second-degree relative | 1 |
| Unexplained SCD <45 years in a first- or second-degree relative with negative autopsy | 0.5 |
| **Genetic test result** | |
| Probable pathogenic mutation in BrS susceptibility gene | 0.5 |
| **Total score (requires ≥1 ECG finding)** | |
| ≥3.5 points: Probable or definite BrS | |
| 2-3 points: Possible BrS | |
| <2 points: Non-diagnostic | |

**BrS** Brugada syndrome, **ECG** electrocardiogram, **SCD** sudden cardiac death
**a** This table was adapted from an original table as reported by Antzelevitch et al.
**b** Only award points once for highest score within each category

*Figure 3: Proposed Shanghai Score for diagnosis of Brugada syndrome*

*Adapted from Peltenburg PJ et al. Neth Heart J. 31. 10.1007/s12471-022-01723-6; used with permission*



| At risk | Evaluation and testing | Diagnostic criteria |
|---|---|---|
| Symptomatic<br>• Cardiogenic syncope<br>• Ventricular arrhythmias<br>• Resuscitated cardiac arrest<br>Asymptomatic<br>• Type 1 ECG<br>• Type 2/3 ECG<br>• Family screening of first-degree relatives | Initial<br>• Clinical: syncope, family history, medical history, medications<br>• ECG with high leads<br>• Echocardiogram: exclude structural abnormalities<br>Discretionary<br>• SCB provocation<br>• Holter monitor<br>• Further cardiac imaging as indicated<br>• EP study<br>• Cardiac MRI | Definite<br>• Spontaneous type 1 ECG changes in $V_1$-$V_2$ at ICS2-4<br>Probable<br>• Type 1 ECG changes in $V_1$-$V_2$ at ICS2-4 with fever or SCB provocation |

*Figure 4: Diagnosis summary for Brugada syndrome [IMAGE KEY: EP = Electrophysiology; ICD = Implantable cardioverter defibrillator; ICS = Intercostal space; MRI = Magnetic resonance imaging; SCB = Sodium-channel blocker]*

*Krahn AD, et al. Brugada syndrome. JACC Clin Electrophysiol 2022 Mar;8(3):386-405; used with permission*

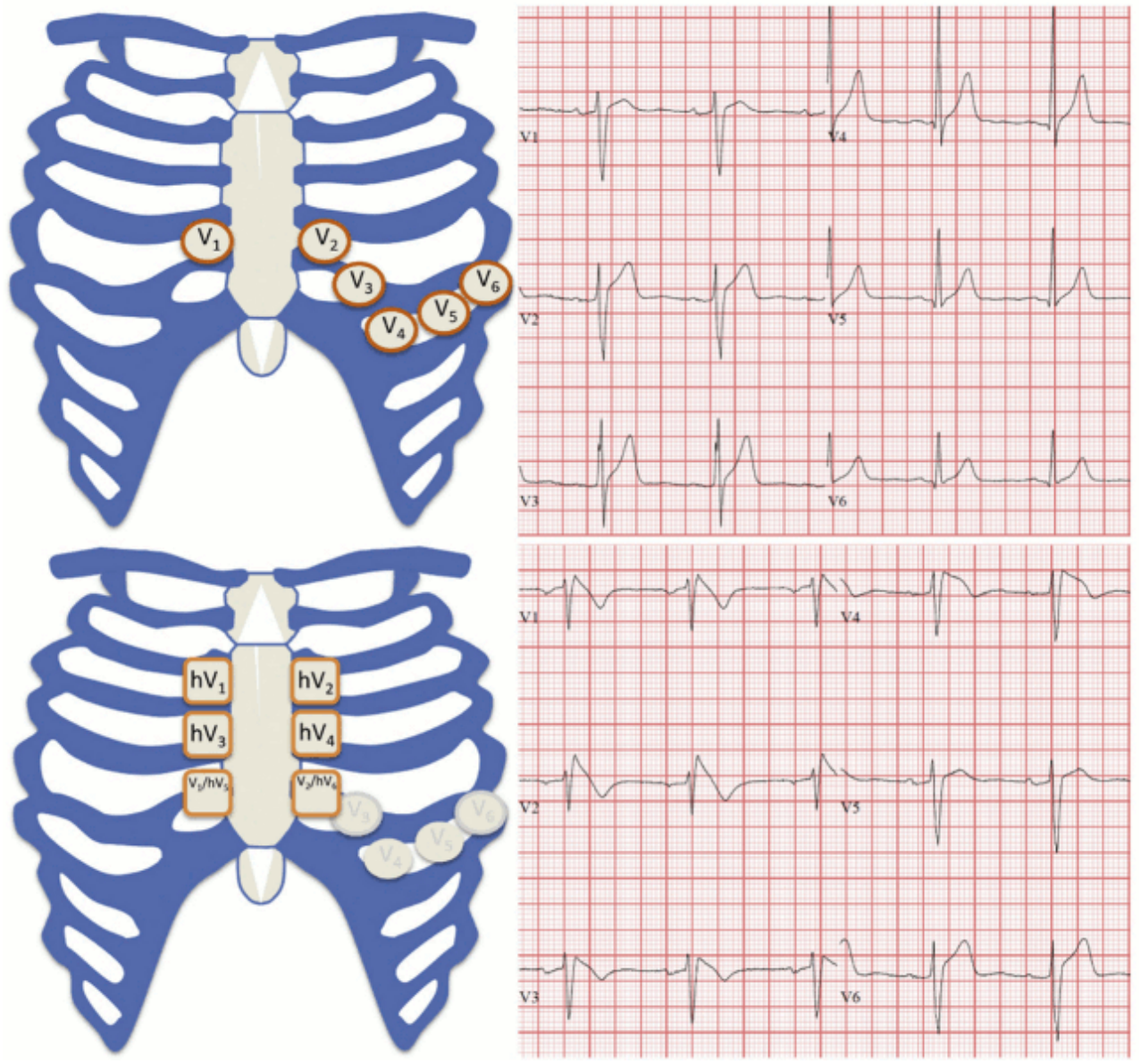



*Figure 5: Standard- and high-lead electrocardiogram positions. (Top) Standard-lead ECG positions and corresponding precordial ECG in a patient with Brugada syndrome. (Bottom) High-lead ECG positions and corresponding ECG in the same patient. Note that hV5 and hV6 on the high-lead ECG correspond with V1 and V2 on the standard-lead ECG.*

*Krahn AD, et al. Brugada syndrome. JACC Clin Electrophysiol 2022 Mar;8(3):386-405; used with permission*



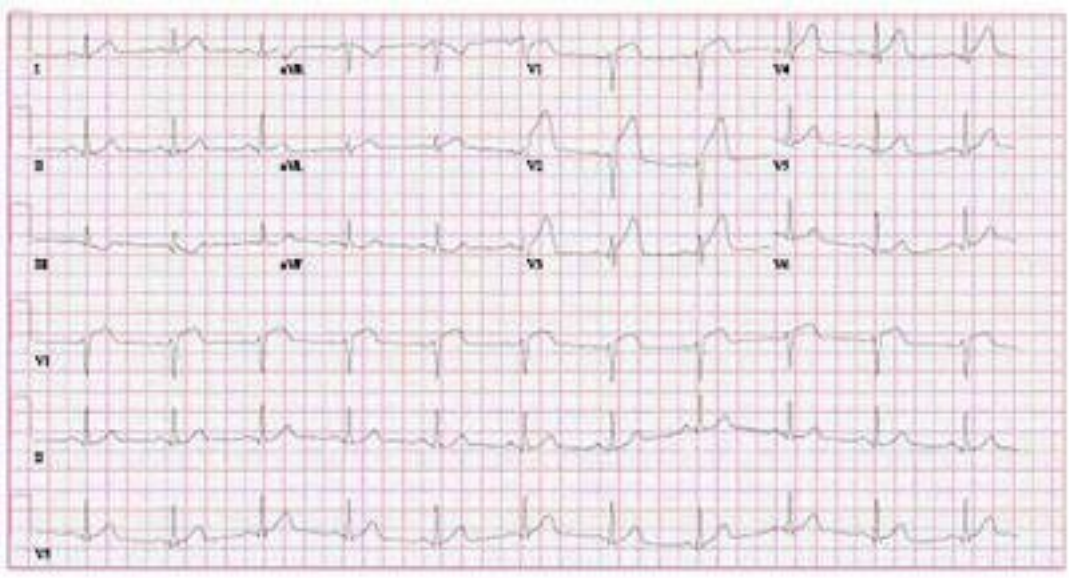


*Figure 6: 12-Lead ECG with ST-segment elevation lead V1 to V4*

*From the personal collection of Dr Mahi Ashwath; used with permission*

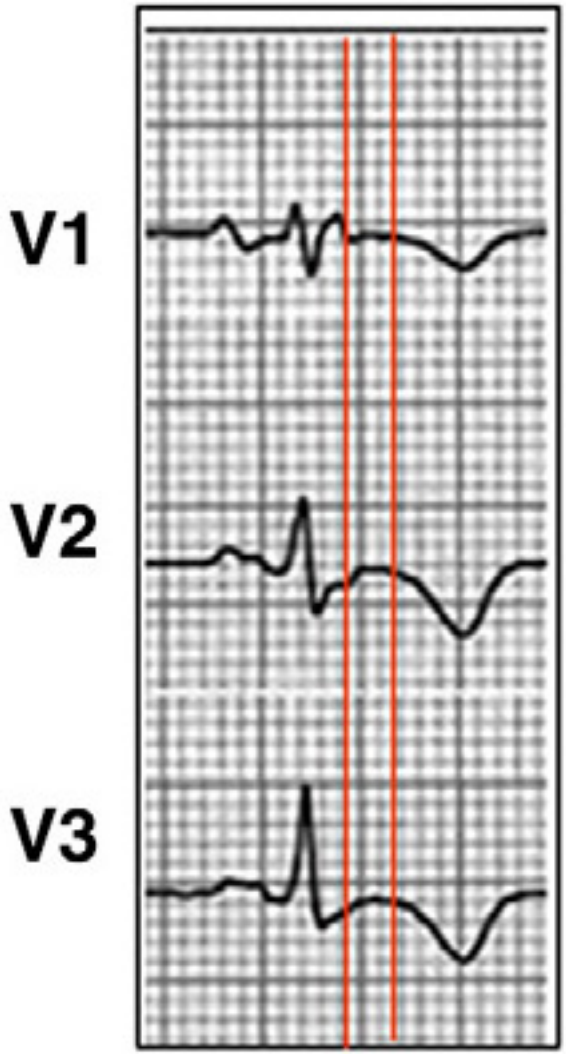



*Figure 7: 3-lead ECG showing findings suggestive of arrhythmogenic right ventricular cardiomyopathy*

*Bayés de Luna A et al. J Electrocardiol. 2012 Sep;45(5):433-42; used with permission*

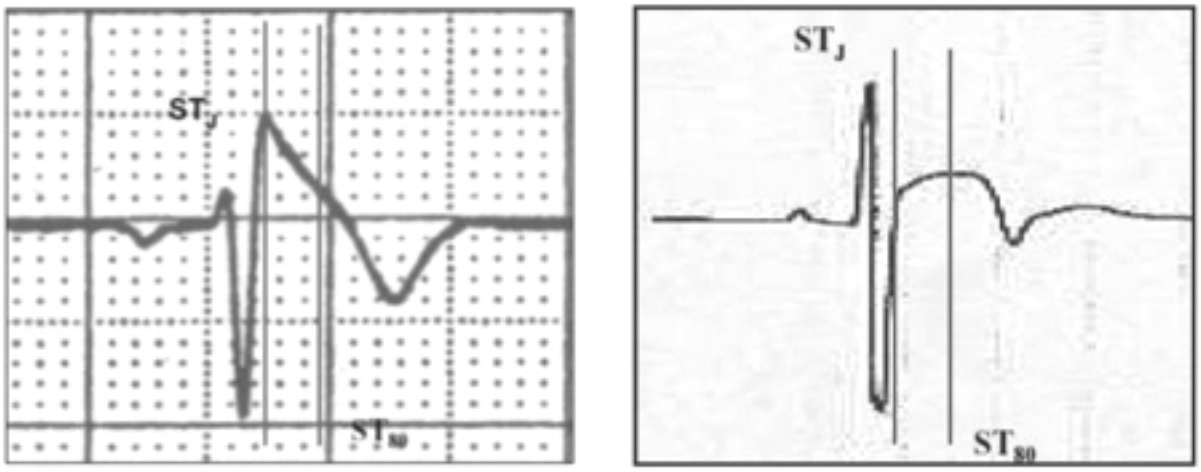



*Figure 8: Brugada type 1 ECG (left) in comparison to early repolarization with "convex" ST segment elevation in a trained athlete (right). [Vertical lines mark the J-point (STJ) and 80 ms after the J-point (ST80). The "downsloping" ST segment elevation in Brugada pattern has an STJ/ST80 ratio >1. Early repolarization patterns in the athlete shows an initial "upsloping" ST segment elevation with STJ/ST80 ratio <1].*

*Drezner JA et al. Br J Sports Med 2017 May;51(9):704-31; used with permission*

IMAGES

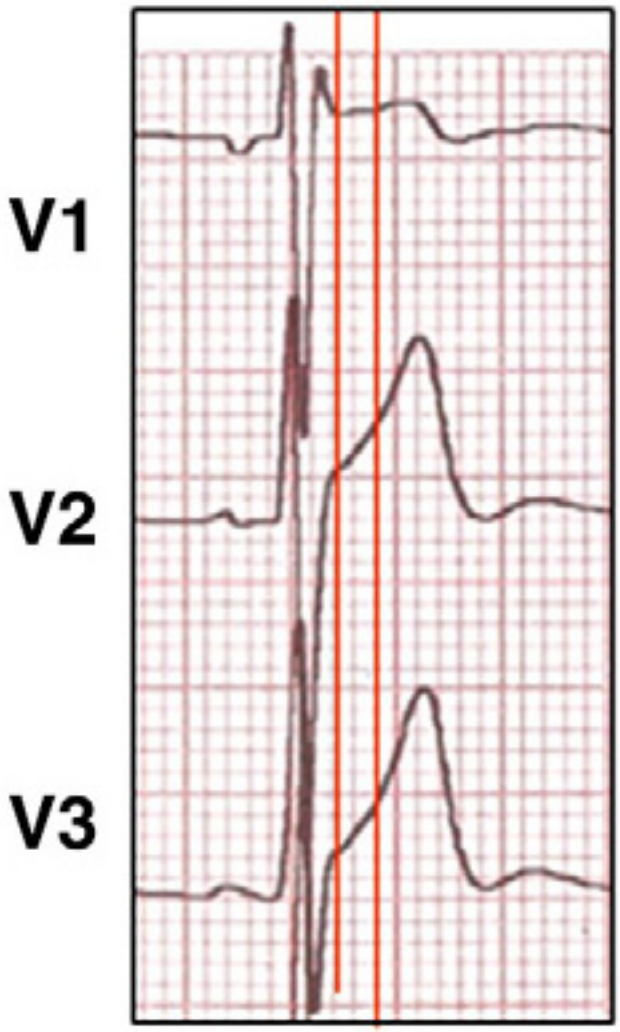



*Figure 9: 3-lead ECG showing findings suggestive of pectus excavatum*

*Bayés de Luna A et al. J Electrocardiol. 2012 Sep;45(5):433-42; used with permission*

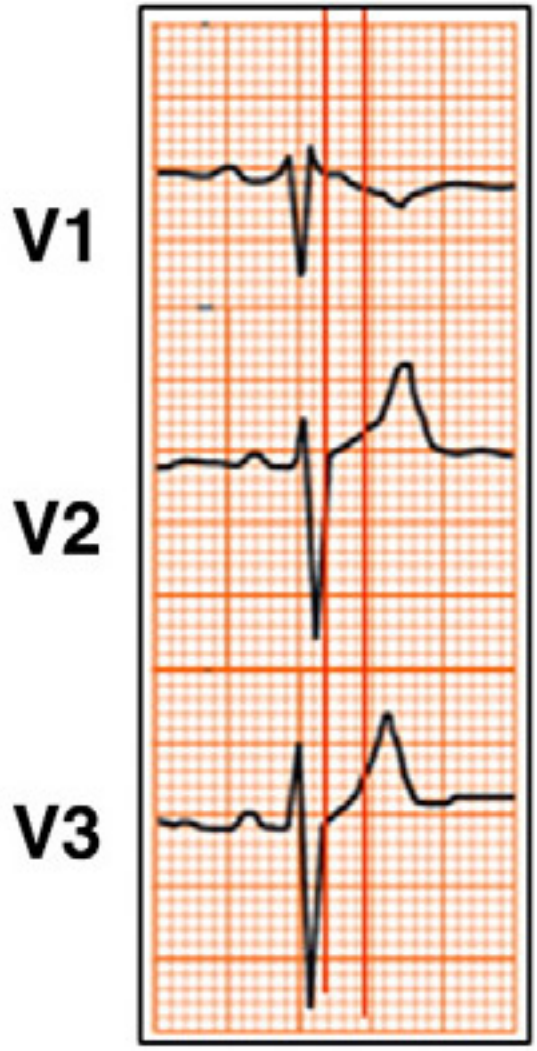



*Figure 10: 3-lead ECG showing right bundle branch block*

*Bayés de Luna A et al. J Electrocardiol. 2012 Sep;45(5):433-42; used with permission*

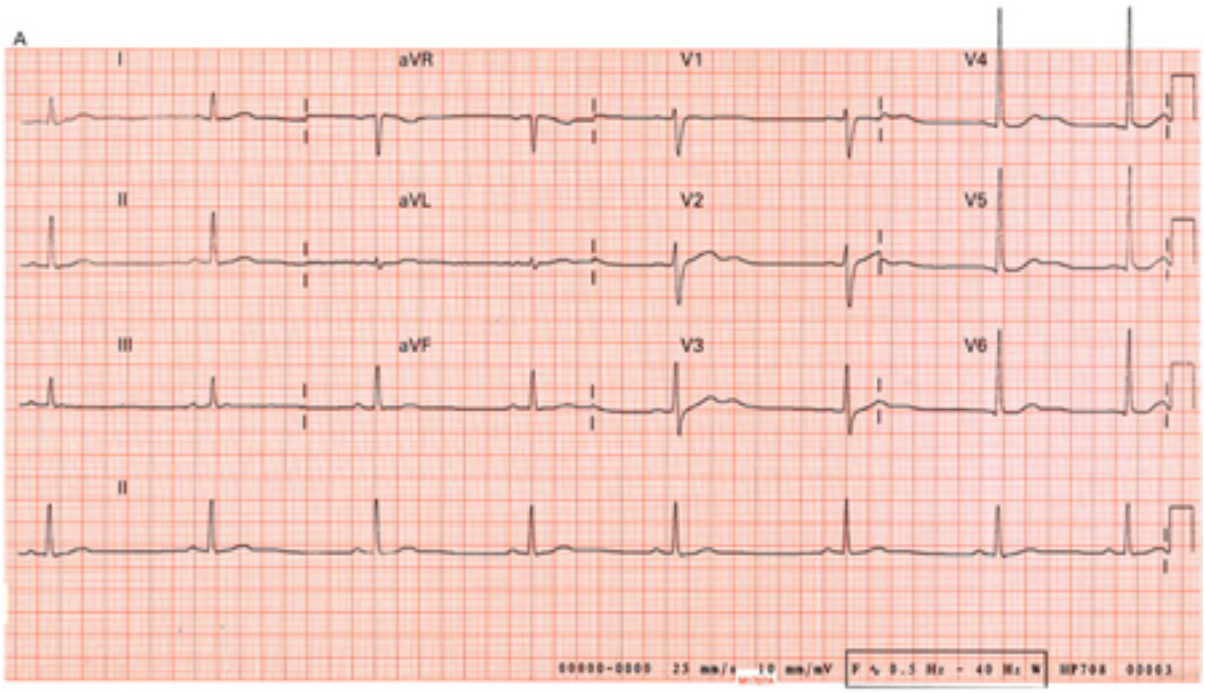



*Figure 11: 12-lead ECG demonstrating prominent U-waves in a patient with hypokalemia*

*From: Lin HW, Chau T, Lin CS, Lin SH, Recurring paralysis, BMJ Case Reports 2009; doi:10.1136/bcr.07.2008.0577*



| Conservative | Pharmacological | Interventional |
|---|---|---|
| Avoid Brugada drugs and triggers, and promptly treat fever<br>• For all patients with definite BrS<br>• Recommended for all patients with probable BrS<br>Re-evaluation<br>• Yearly follow-up with cardiologist<br>Other considerations<br>• Promptly report any episodes of syncope or seizures<br>• Inform and screen family members | Quinidine<br>• Recurrent shocks with appropriate ICD therapies<br>• Consider for patients who qualify for ICD but decline<br>• Consider for medical management of atrial arrhythmias<br>• Consider low-dose therapy to prevent side effects<br>• Requires regular blood count monitoring<br>• Use may be limited due to a lack of drug availability<br>Isoproterenol<br>• During acute ventricular arrhythmias | ICD<br>• Secondary prevention for resuscitated cardiac arrest<br>• Recommended for primary prevention in patients with spontaneous type 1 ECG and syncope<br>• Consider for primary prevention in patients with provoked type 1 ECG and syncope<br>• Consider for primary prevention in asymptomatic patients with spontaneous type 1 ECG and additional high-risk features<br>Ablation<br>• Quinidine intolerance<br>• Arrhythmic events despite quinidine |

*Figure 12: Management summary for Brugada syndrome*

*Adapted from Krahn AD et al. J Am Coll Cardiol#EP. 2022 Mar,#8 (3) 386-405; used with permission*

# Disclaimer

BMJ Best Practice is intended for licensed medical professionals. BMJ Publishing Group Ltd (BMJ) does not advocate or endorse the use of any drug or therapy contained within this publication nor does it diagnose patients. As a medical professional you retain full responsibility for the care and treatment of your patients and you should use your own clinical judgement and expertise when using this product.

This content is not intended to cover all possible diagnosis methods, treatments, follow up, drugs and any contraindications or side effects. In addition, since such standards and practices in medicine change as new data become available, you should consult a variety of sources. We strongly recommend that you independently verify specified diagnosis, treatments and follow-up and ensure it is appropriate for your patient within your region. In addition, with respect to prescription medication, you are advised to check the product information sheet accompanying each drug to verify conditions of use and identify any changes in dosage schedule or contraindications, particularly if the drug to be administered is new, infrequently used, or has a narrow therapeutic range. You must always check that drugs referenced are licensed for the specified use and at the specified doses in your region.

Information included in BMJ Best Practice is provided on an “as is” basis without any representations, conditions or warranties that it is accurate and up to date. BMJ and its licensors and licensees assume no responsibility for any aspect of treatment administered to any patients with the aid of this information. To the fullest extent permitted by law, BMJ and its licensors and licensees shall not incur any liability, including without limitation, liability for damages, arising from the content. All conditions, warranties and other terms which might otherwise be implied by the law including, without limitation, the warranties of satisfactory quality, fitness for a particular purpose, use of reasonable care and skill and non-infringement of proprietary rights are excluded.

Where BMJ Best Practice has been translated into a language other than English, BMJ does not warrant the accuracy and reliability of the translations or the content provided by third parties (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages). BMJ is not responsible for any errors and omissions arising from translation and adaptation or otherwise.Where BMJ Best Practice lists drug names, it does so by recommended International Nonproprietary Names (rINNs) only. It is possible that certain drug formularies might refer to the same drugs using different names.

Please note that recommended formulations and doses may differ between drug databases drug names and brands, drug formularies, or locations. A local drug formulary should always be consulted for full prescribing information.

Treatment recommendations in BMJ Best Practice are specific to patient groups. Care is advised when selecting the integrated drug formulary as some treatment recommendations are for adults only, and external links to a paediatric formulary do not necessarily advocate use in children (and vice-versa). Always check that you have selected the correct drug formulary for your patient.

Where your version of BMJ Best Practice does not integrate with a local drug formulary, you should consult a local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing before prescribing.

### Interpretation of numbers

Regardless of the language in which the content is displayed, numerals are displayed according to the original English-language numerical separator standard. For example 4 digit numbers shall not include a comma nor a decimal point; numbers of 5 or more digits shall include commas; and numbers stated to be less than 1 shall be depicted using decimal points. See Figure 1 below for an explanatory table.

BMJ accepts no responsibility for misinterpretation of numbers which comply with this stated numerical separator standard.

This approach is in line with the guidance of the International Bureau of Weights and Measures Service.

**Figure 1 – BMJ Best Practice Numeral Style**



5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

Our full website and application terms and conditions can be found here: Website Terms and Conditions.

**Contact us**

+ 44 (0) 207 111 1105
support@bmj.com

BMJ
BMA House
Tavistock Square
London
WC1H 9JR
UK

# Contributors:

## // Authors:

**Eugene H Chung, MD, MPH**

Professor of Internal Medicine
Director of Sports Electrophysiology Clinic, Massachusetts General Hospital, Harvard Medical School, Boston, MA
DISCLOSURES: EHC declares that he has no competing interests.

## // Acknowledgements:

Professor Eugene H Chung would like to gratefully acknowledge Dr Mohammed-Ali Jazayeri for his contribution to the initial drafts of this topic.
DISCLOSURES: MAJ declares that he has no competing interests.

## // Peer Reviewers:

**Sei Iwai, MD**

Section Chief, Cardiac Electrophysiology
Department of Cardiology, Westchester Medical Center Health Network, Valhalla, NY
DISCLOSURES: SI declares that he has no competing interests.

**Amanda Varnava, MA(Hons), MD, FRCP**

Consultant Cardiologist
Imperial College Healthcare Trust, London, UK
DISCLOSURES: AV declares that she has no competing interests.