# BRUGADA SYNDROME

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## I DEFINITION, GENETICS AND ECG CLASSIFICATION (ESC 2022 VA/SCD GUIDELINES)

- **Definition:** Brugada Syndrome (BrS) is an inherited primary electrical channelopathy (8:1 male predominance; highest prevalence in South and Southeast Asia) predisposing to nocturnal or fever-triggered **polymorphic Ventricular Tachycardia (pVT), Ventricular Fibrillation (VF), and Sudden Cardiac Death (SCD)** in the absence of overt structural heart disease.
- **Genetic and Cellular Substrate:** Loss-of-function pathogenic variants in ***SCN5A*** (encoding the alpha-subunit of the cardiac Nav1.5 sodium channel) are identified in **20 to 30 percent** of probands (the only gene with definitive ClinGen monogenic causality, though **polygenic risk scores** strongly modulate penetrance), causing either a transmural **Phase 1 repolarization gradient** (unopposed epicardial *Ito* current -> Phase 2 re-entry) or **delayed conduction and micro-fibrosis in the epicardial Right Ventricular Outflow Tract (RVOT)** (depolarization hypothesis).
- **ECG Classification (Only the Type 1 Pattern is Diagnostic):**
  - **Type 1 ("Coved-Type") Brugada ECG Pattern: J-point and coved ST-segment elevation of 2 mm (0.2 mV) or greater** gradually descending into a **negative (inverted) symmetric T wave** with little or no isoelectric separation in **at least one right precordial lead (V1 and/or V2)** placed in the **standard 4th, 3rd, or 2nd intercostal space (High Right Precordial Leads)**.
  - **Type 2 (and Historical Type 3) ("Saddleback") Pattern:** J-point elevation >=2 mm with a saddleback ST-segment remaining >=1 mm (Type 2) or <1 mm (Type 3) above baseline and a positive or biphasic T wave. **Not diagnostic of BrS** unless converted to a Type 1 pattern during fever or a **Sodium Channel Blocker Challenge (Ajmaline 1 mg/kg, Flecainide 2 mg/kg, or Procainamide 10 mg/kg IV)**.

## II THE SHANGHAI SCORING SYSTEM AND ESC 2022 DIAGNOSTIC CRITERIA

- **Why Scoring is Required:** Because a **drug-induced Type 1 ECG** can occur in 2 to 4 percent of healthy individuals (false-positive provocation), the **Shanghai Brugada Score** and **2022 ESC Guidelines** require clinical, family, or genetic corroboration when the Type 1 pattern is not spontaneous:
- **Spontaneous Type 1 ECG (3.5 points):** Diagnostic of BrS on its own in patients with no other heart disease (**Class I** in ESC 2022).
- **Fever-Induced (3.0 points) or Drug-Induced (2.0 points) Type 1 ECG:** Requires **additional clinical features** (survived cardiac arrest/documented VF [3.0 pts], suspected arrhythmic syncope [2.0 pts], nocturnal agonal respiration [2.0 pts], or definite family history of BrS [2.0 pts]) to reach a **Probable/Definite Shanghai Score of >= 3.5 points** (Class I in ESC 2022 if survivor of cardiac arrest; Class IIa if accompanied by arrhythmic syncope or family history).

| Shanghai Score Category | Specific Diagnostic Criterion (Select Highest Single Item per Category) | Points Awarded |
|---|---|---|
| **I. ECG (12-Lead / Ambulatory)** | **Spontaneous Type 1** Brugada ECG at nominal or high (2nd/3rd ICS) leads | **3.5 points** |
| | **Fever-induced Type 1** Brugada ECG | **3.0 points** |
| | **Sodium-channel blocker-induced Type 1** Brugada ECG | **2.0 points** |
| **II. Clinical History** | Unexplained cardiac arrest or documented VF / polymorphic VT | **3.0 points** |
| | Nocturnal agonal respirations | **2.0 points** |
| | Suspected arrhythmic syncope | **2.0 points** |
| **III. Family History** | First- or second-degree relative with definite BrS (unexplained SCD <45 yr with negative autopsy scores only 0.5) | **2.0 points** |
| **IV. Genetic Test Result** | Pathogenic mutation in a BrS susceptibility gene (***SCN5A***) | **0.5 points** |
| **Diagnostic Threshold** | **>= 3.5 Points = Probable/Definite BrS**; **2.0–3.0 Points = Possible BrS** | Requires >=1 ECG finding |

## III LIFESTYLE, PHARMACOLOGICAL AND DEVICE MANAGEMENT (ESC 2022 GUIDELINES)

- **Mandatory Lifestyle Measures in All BrS Patients (Class I):**
  - **Immediate Aggressive Treatment of Fever:** High body temperature prematurely inactivates mutant Nav1.5 channels; any fever must be treated immediately with antipyretics (**Paracetamol/Acetaminophen**), and febrile patients with a Type 1 ECG require hospital telemetry monitoring.
  - **Strict Avoidance of Offending Drugs and Triggers:** Avoid all Class I antiarrhythmics (Flecainide, Propafenone, Ajmaline, Procainamide), tricyclic antidepressants, lithium, high-dose propofol/bupivacaine (complete list at **brugadadrugs.org**), cocaine, cannabis, and **excessive alcohol intake or large heavy meals** (which heighten vagal tone).
  - **Implantable Cardioverter-Defibrillator (ICD) Indications:**
  - **Secondary Prevention (Class I):** Mandatory in survivors of **aborted cardiac arrest** or patients with documented **spontaneous sustained VT/VF** (Subcutaneous ICD [S-ICD] is an attractive option in young BrS patients without pacing needs or monomorphic VT).
  - **Primary Prevention in Syncope (Class IIa):** Recommended in patients with a **spontaneous Type 1 ECG and a history of arrhythmic syncope**. (An **Implantable Loop Recorder [ILR]** is Class IIa when syncope is of uncertain/vasovagal origin.)
  - **Asymptomatic Patients:** Routine ICD is not recommended in asymptomatic drug-induced BrS; in asymptomatic patients with a **spontaneous Type 1 ECG**, **Programmed Electrical Stimulation (PES)** up to two extrastimuli may be considered (Class IIb) for risk stratification.
  - **Pharmacotherapy:**
  - **Quinidine (Class IIa):** Blocks the outward potassium current (***Ito***), restoring the epicardial action potential dome. Indicated in patients with **recurrent ICD shocks, electrical storm**, or when an ICD is contraindicated or refused.
  - **Intravenous Isoproterenol (Class IIa for Electrical Storm):** Continuous infusion (**1 to 2 mcg/min**) augments inward L-type calcium current (***ICa-L***) and increases heart rate, acutely abolishing ST-segment elevation and **VF electrical storm**.

## IV EPICARDIAL RVOT SUBSTRATE ABLATION AND THE INDIAN CONTEXT

- **Epicardial RVOT Substrate Catheter Ablation (Nademanee / Pappone Technique — ESC 2022 Class IIa):**
  - **Mechanism:** High-density 3D mapping identifies low-voltage, prolonged, fractionated late potentials localized on the **anterior epicardial surface of the RVOT** (unmasked completely by IV ajmaline/flecainide or warm saline infusion into the pericardium).
  - **Evidence (BRAVO Registry, *Circulation* 2023):** Percutaneous **epicardial radiofrequency ablation** of all abnormal RVOT substrate electrograms aims to **normalize the Type 1 Brugada ECG** (normalization independently predicted a VF-free outcome) and achieved **VF freedom in 81 percent after one procedure and 96 percent after repeat procedures** (n = 159, mean follow-up ~4 years); ablation carries a **Class IIa recommendation** in the 2022 ESC Guidelines for patients with **recurrent appropriate ICD shocks or electrical storm refractory to/intolerant of Quinidine**.
  - **Practical Considerations in the Indian Context:**
  - **Tropical Febrile Infections (Dengue, Malaria, Enteric Fever, Viral Pyrexia):** In India, acute tropical febrile illnesses are a common trigger unmasking a **Fever-Induced Type 1 Brugada ECG** and precipitating VF arrest; immediate antipyretics, correction of hypokalemia, and telemetry monitoring until defervescence are mandatory.
  - **Pharmacological Alternatives When Quinidine is Unavailable:** Because oral **Quinidine** has limited commercial availability in India, oral **Cilostazol** (100 mg BD; a PDE-3 inhibitor that increases *ICa-L* and heart rate) or **Theophylline** is occasionally used as an empirical bridge alongside **Epicardial RVOT Catheter Ablation** in tertiary Indian EP centers for patients with recurrent ICD shocks.

KEY REFERENCES


- **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, *European Heart Journal*, 2022.
- **Antzelevitch C, Yan GX, Ackerman MJ, et al.:** J-Wave syndromes expert consensus conference report: Emerging concepts and gaps in knowledge (Shanghai Score), *Heart Rhythm / Europace*, 2016.
- **Nademanee K, Chung FP, Sacher F, et al. (BRAVO Registry Investigators):** Long-Term Outcomes of Brugada Substrate Ablation: A Report from BRAVO (Brugada Ablation of VF Substrate Ongoing Multicenter Registry), *Circulation*, 2023.