Brugada’s Syndrome and Sudden Cardiac Death

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Survival Incidence (cases/year)

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<th>Incidence (cases/year)</th>
<th>Survival</th>
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<tbody>
<tr>
<td>Worldwide</td>
<td>3,000,000</td>
<td>&lt;1%</td>
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<tr>
<td>U.S.</td>
<td>450,000</td>
<td>5%</td>
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<tr>
<td>W. Europe</td>
<td>400,000</td>
<td>&lt;5%</td>
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Magnitude of Sudden Cardiac Death (SCD) in United States

SCD claims more lives each year than these other diseases combined.

80% Coronary Artery Disease
5% Other*
15% Cardiomyopathy

Causes of Sudden Cardiac Death

* ion-channel abnormalities, valvular or congenital heart disease, other causes


3 2002 Heart and Stroke Statistical Update, American Heart Association.
**Cardiomyopathy**

- Dilated Cardiomyopathy
- Hypertrophic Cardiomyopathy (HCM)
- Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)
- Left Ventricular Non-compaction
- Restrictive Cardiomyopathy

**Cardiac Channelopathies**

- Brugada Syndrome
- Long QT Syndrome (LQTS)
- Short QT Syndrome
- Catecholamine induced Polymorphic Ventricular Tachycardia (CPVT)
- Short coupled Torsades
- Idiopathic VF

**Brugada Syndrome**

- First described in 1992 in 8 patients with aborted sudden cardiac death
- Characterized by:
  - ECG findings of RBBB and persistent ST segment elevation in V₁-V₃
  - Structurally normal hearts
  - Propensity for life threatening ventricular arrhythmias

**Brugada Syndrome: ECG**
Brugada: Clinical Features

Incidence and Distribution

- Unexpected sudden death
- Syncope, seizures
- Agonal nocturnal respirations
- Affects male patients predominately (8:1)
- Cases reported worldwide

Brugada: Clinical Features

Incidence and Distribution

- Responsible for up to 50% of sudden death in victims with structurally normal hearts in Thailand
- Recognized in Asia for decades:
  - Bangungut: “scream followed by sudden death during sleep” (Philippines)
  - Lai tai: “death during sleep” (Thailand)
  - Pokkuri: “unexpected death during sleep” (Japan)

Brugada Syndrome: ECG

Type 1  Type 2  Type 3

Brugada Syndrome: Before (A) and After (B) Procainamide
Factors / Drugs that enhance ECG Pattern

- Na+ channel blockers
- Alpha agonists, Vagotonic agents, Beta-blockers
- Fever
- Tricyclic antidepressants, antihistaminics
- Hypercalcemia, Hyperkalemia
- Alcohol, Cocaine
- Severe ischemia
**Brugada Syndrome: Other Arrhythmias**

- 20% Atrial Fibrillation
- Prolonged PR interval (prolonged HV interval)
- AV nodal reentrant tachycardia
- WPW

**Brugada Syndrome: Genetics**

- Autosomal dominant
- 60 different mutations in the SCN5A (chromosome 3) gene have been linked to the syndrome.
- Failure of alpha subunit of Sodium channel to express
- Shift in voltage and time dependence of $I_{NA+}$ activation, inactivation or reactivation

**Brugada: Pathophysiology**

**Variation Between LV and RV Action Potentials**

*More pronounced AP notch (red arrow) due to greater $I_{to}$ mediated outward current in RV*

**Brugada: Pathophysiology**

**Heterogeneous Loss of Action Potential Dome**

*Transmural voltage gradient
Endocardium
Epicardium
Transmembrane dispersion of repolarization
Epicardial dispersion of repolarization*
Brugada: Diagnosis

- Symptoms: syncope, SCD (usually during sleep)
- Physical exam: normal
- Family history: strong history of SCD
- ECG: best test to identify Brugada patients
  - May require Flecainide or Procainamide to bring out typical findings
  - ST elevation more predictive of SCD than RBBB
- Imaging tests: usually no underlying structural disease
- Stress tests: symptoms and ECG findings not usually reproducible with exercise
- SAECG: can show late potentials in 80%

Brugada Syndrome: Diagnostic Criteria

Major criteria
1. Presence of the ECG marker of Brugada syndrome in patients with structurally normal heart
2. Appearance of the ECG marker of Brugada syndrome after administration of sodium channel blockers

Minor criteria
1. Family history of sudden cardiac death
2. Syncope of unknown origin
3. Documented episodes of ventricular tachycardia/ventricular fibrillation
4. Positive programmed electrocardiostimulation test on ventricular tachycardia/ventricular fibrillation
5. Genetic mutations of ion channels

Brugada: Prognosis

Recurrence of VF or SCD in Asymptomatic vs. Symptomatic Patients

- Risk factors for asymptomatic individuals
  - Male - 5.5 fold
  - Spontaneous positive ECG - 7.7 fold
  - Inducible VT/VF - 8 fold
- Asymptomatic, drug induced type 1 Brugada ECG pattern and no inducible VT during Electrophysiology study - 0.5% probability of event
- Asymptomatic, Spontaneous type 1 Brugada ECG pattern and inducible sustained VT during EP study - 14% probability of event
- Syncope, Spontaneous type 1 Brugada ECG pattern, and inducible sustained VT during EP study- 27% probability of event

Risk Stratification

- Male
- Spontaneous positive ECG
- Inducible VT/VF
- Asymptomatic, drug induced type 1 Brugada ECG pattern and no inducible VT during Electrophysiology study
- Asymptomatic, Spontaneous type 1 Brugada ECG pattern and inducible sustained VT during EP study
- Syncope, Spontaneous type 1 Brugada ECG pattern, and inducible sustained VT during EP study

**Brugada: Treatment**

- Symptomatic patients with the disease: ICD
- Asymptomatic patients with a family history of SCD: with normal ECG and negative EP study **OBSERVE**
- Asymptomatic pt with prolonged H-V interval, and inducible VT/VF: controversial ICD

**Potential antiarrhythmic drugs in Brugada Syndrome**

- Quinidine (non specific $I_{to}$ blocker)
- Isoproterenol (open L type calcium channel)
- Cilostazol (augment $I_{ca}$)
- Tedisamil ($I_{to}$ blocker)

**Brugada Syndrome: Summary**

- Sudden Cardiac Death in Southeast Asia
- Characteristic ECG pattern
- ICD implantation in symptomatic patients