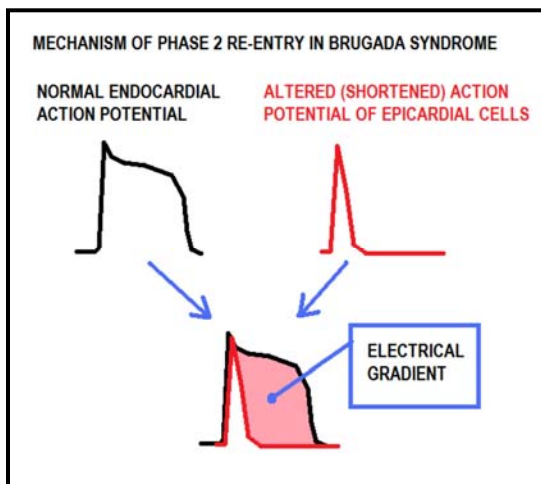


BRUGADA SYNDROME

Brugada Syndrome is a genetically determined disorder affecting the cardiac electrical system and causes paroxysmal episodes of polymorphic ventricular tachycardia. When the polymorphic VT terminates spontaneously, patients may experience palpitations, lightheadedness and syncope. In sustained episodes, VT degenerates into ventricular fibrillation, resulting in mortality. Current studies indicate that Brugada Syndrome is responsible for up to 12% of all unexpected sudden deaths, and up to 50% of all sudden deaths in patients with a structurally normal heart. This disease usually afflicts individuals in their 30s; however patients ranging in ages from 6 months to 74 years have been diagnosed with the disorder. Brugada syndrome is statistically more prevalent in males of Southeast Asian descent.

Although Brugada Syndrome has no relationship with coronary artery disease and ACS, this recently discovered and lesser-known condition warrants inclusion in this curriculum because patients may present for medical help after suffering from Brugada Syndrome induced syncope, with ACS being suspected as a primary diagnosis, especially when ST segment elevation – a common finding – is noted on the 12 Lead ECG. If clinicians are familiar with patient profiles and the typical clinical presentation associated with Brugada Syndrome, accurate diagnosis will most likely occur; patients will be treated appropriately, and mortality will be prevented. It is unknown how many patients suffering from Brugada Syndrome-mediated syncope have sought medical help, been evaluated for ACS, and have been “medically cleared” without being correctly diagnosed with Brugada Syndrome.



Brugada Syndrome has been linked to a mutation of gene SCN5A, which encodes for the cardiac sodium channel. This mutation alters repolarization of epicardial cells, predominantly of the right ventricle, significantly shortening their refractory period. The resulting electrical gradient between abnormal epicardial cells and normal endocardial cells provides the ideal substrate for arrhythmias based on phase 2 re-entry. (See diagram to left).

The degree of repolarization aberrancy fluctuates, and is affected by changes in the body's *autonomic system*, *temperature*, *electrolytes*, and the *presence of antiarrhythmic medications*. The result is that the characteristic ECG markers of Brugada Syndrome are known to present *intermittently*, with periods where the patient's ECG is normal. Also, there are patients with “concealed” versions of Brugada Syndrome, whose ECGs always present as normal. It should also be noted that while antiarrhythmic drugs such as beta blockers and Amiodarone may mask the ECG markers of Brugada Syndrome, most do not protect against sudden cardiac death; the most effective treatment currently is the implantation of a cardio-defibrillator (ICD). Recent studies indicate Quinidine, a class Ia sodium channel blocker, may effectively prevent VF in patients with Brugada Syndrome.¹

HISTORY: The first known case of Brugada Syndrome occurred in 1986, involving a three year old boy from Poland. The patient presented after experiencing several episodes of unconsciousness, and had been resuscitated by his father. The boy's older sister had died suddenly at the age of two. At the time of her death, she was receiving Amiodarone, and had a ventricular pacemaker implanted. The ECGs of both siblings featured the ECG abnormalities which have become known as the “typical patterns” of Brugada Syndrome. The identification of two more patients resulted in presentation of these cases at the North American Society of Pacing and Electrophysiology (NASPE) conference in 1991.

CLINICAL PRESENTATION: Formal components of the Brugada Syndrome include: *right bundle branch block*, *ST segment elevation in leads V1, V2 and sometimes V3*, and *sudden death*. Patient presentations range from those who are asymptomatic, to those with sudden death. Asymptomatic patients may be discovered by presentation of the “typical Brugada pattern ECG” during a routine examination. Others are discovered during ECG evaluation after the sudden death of a family member is found to have the disease. Typical complaints of symptomatic Brugada Syndrome patients who present to emergency departments and physician's offices are of episodic “lightheadedness, dizziness, palpitations,” and/or “fainting,” secondary to runs of polymorphic ventricular tachycardia.

¹ B. Belhassen, MD et al, Circulation, 2004;110:1731-1737

According to recommendations published on www.brugada.org, the website maintained by the Ramon Brugada, Senior Foundation, **Brugada Syndrome should be ruled out in patients who present with:**

1. syncopal episodes of unknown cause or vaso-vagal origin or have a diagnosis of idiopathic ventricular fibrillation and/or
2. incidence of sudden, unexpected death of genetically (blood) related family member(s), and/or
3. ECG findings characteristic of Brugada Syndrome (see the examples on page 275).

DIAGNOSIS can be easily made in cases where patients present with characteristic ECG markers for Brugada Syndrome. (See examples on pages 273-274). In cases of where the ECG is normal, a Drug Study Protocol should be administered, using Ajmaline, Flecainide, or Procainamide infusions; either of these agents will "unmask" the ECG markers of Brugada Syndrome. Genetic testing for Brugada Syndrome is conducted by the Ramon Brugada, Senior Foundation. For information about the Drug Study Protocol and/or genetic testing for Brugada Syndrome, visit www.brugada.org.

PROGNOSIS: An online PubMed search for "Mortality from Brugada Syndrome" nets 108 published scientific papers on this subject. The summary of what I have extrapolated from this material is:

1. There is a clear relationship between patients with Brugada Syndrome and Sudden Death.
2. The highest degree of risk of sudden death (10.2 – 38% annual fatal arrhythmic events)^{2,3} correlates with patients whom are symptomatic (syncope) with ECG presence of a Brugada ECG pattern, or test positive in the Brugada drug study (see "DIAGNOSIS," above).
3. The lowest degree of sudden death risk, according to two studies, is in the subgroup of patients whom are asymptomatic. In one study, 2 previously asymptomatic patients out of 105 suffered sudden death at night during a 5.6 year follow-up.⁴ In the second study, conducted by Probst et al, the event rate for sudden death in asymptomatic patients was 0.5% per year.⁵

According to information posted by the Brugada Foundation, prognosis for individuals not treated for Brugada Syndrome is poor: one third of all patients who suffered from syncopal episodes or were resuscitated from a near-death experience presented with new episodes of polymorphic VT within two years. Incidentally, one-third of all asymptomatic patients discovered to have characteristic Brugada Syndrome markers on their ECG experienced polymorphic VT within the two year follow-up period.

The Brugada Foundation (www.brugada.org) recommends that patients who present with **family histories of sudden, unexpected death** and/or those who present with complaints of **syncope of unknown etiology** should be screened for Brugada Syndrome. The screening process should include:

1. ECG studies
2. Brugada Drug Study Protocol
3. EP Study for inducible VT/VF
4. Genetic testing for the SCN5A mutation.

TREATMENT: At present, ICD implantation has proven to be 100% effective. Current literature suggests that Quinidine may be an effective therapy for VF prevention in asymptomatic Brugada Syndrome patients. A clinical study (NIH Study #NCT00789165) is in progress for the use of Quinidine in asymptomatic Brugada Syndrome patients.⁶

In patients who underwent ICD implantation, there was a 0% mortality during a mean 5.6 year follow-up period,⁷ and a 0% mortality rate at up to 10 years, as reported by Brugada et al.

² Y. Miyasaka, MD et al, J Am Coll Cardiol, 2001; 38:771-774

³ S. Kamakura et al, Circ Arrhythm Electrophysiol. 2009 Oct;2(5):495-503

⁴ G. Veerakul et al, Circulation. 2008;118:S_982

⁵ V Probst, et al; Circulation 2010 Feb 9;121(5):635-43

⁶ Sami Viskin, MD & C. Antzelevitch, www.clinicaltrials.gov (Study Identifier: NCT00789165)

⁷ G. Veerakul et al,

CASE STUDY 18 -- BRUGADA SYNDROME

CHIEF COMPLAINT and SIGNIFICANT HISTORY:

37 y/o FEMALE patient arrives via EMS after being involved in a low speed motor vehicle accident. Per EMS crew, patient was the driver and sole occupant of a car that struck a tree. Patient does not recall accident. Upon further questioning, patient admits to other episodes of syncope and near-syncope. Patient denies feeling any chest pain / pressure or shortness of breath. She states she "felt great" today, until just before the the accident, when she "suddenly felt lightheaded and must have blacked-out."

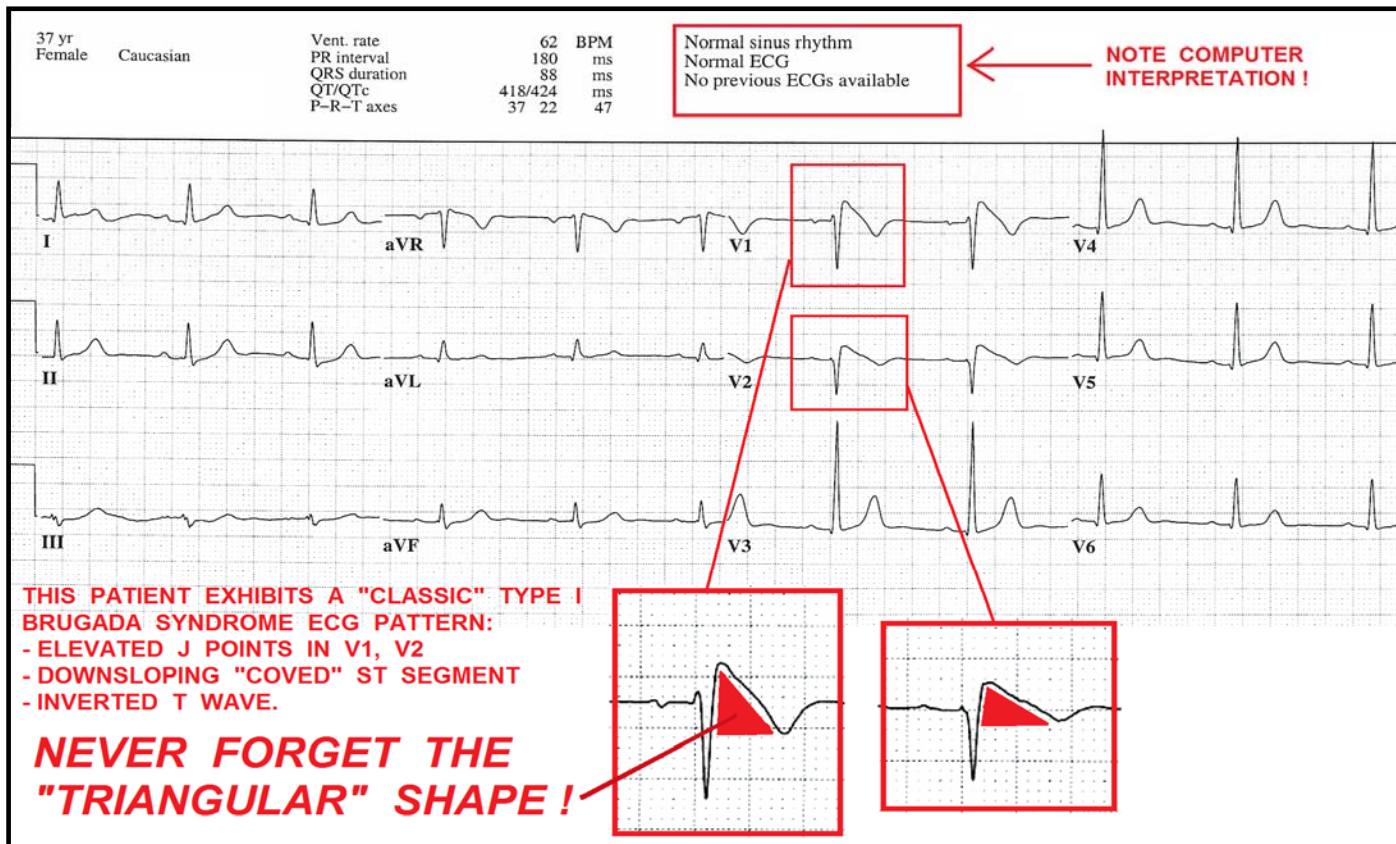
RISK FACTOR PROFILE:

🔥 **FAMILY HISTORY: MATERNAL AUNT DIED AT AGE 31, UNEXPECTEDLY. WAS RULED AS A "HEART ATTACK." THERE WAS NO PRIOR KNOWN HISTORY OF CAD.**

PHYSICAL EXAM: Pt. CAO x 3, skin warm, dry, color normal. Abrasions /contusions on face (airbag deployment). Patient appears to be in excellent physical condition, states she exercises several times per week (aerobics, weight training, swimming).

VITAL SIGNS: BP: 112/66, P: 62, R: 20, SAO2: 100% on room air.

LABS: TROPONIN: < .04 BMP and CBC: all values within normal limits.



Patient was admitted to the hospital and received implantable cardio-defibrillator (ICD) prior to hospital discharge.

33 y/o FEMALE

Vent. rate	129	BPM	Undetermined rhythm
PR interval	*	ms	Incomplete right bundle branch block
QRS duration	112	ms	Right ventricular hypertrophy
QT/QTc	398/583	ms	ST elevation consider anterior injury or acute infarct
P-R-T axes	* 121	-2	***** ACUTE MI *****

Abnormal ECG
No previous ECGs available

PT. BROUGHT TO EMERGENCY DEPARTMENT BY EMS AFTER SUFFERING SPONTANEOUS CARDIAC ARREST. PATIENT DID NOT EXPERIENCE ANY SYMPTOMS PRIOR TO COLLAPSE. HAD SEVERAL EPISODES OF NEAR-SYNCOPE IN THE PAST 10 YEARS. CARDIAC CATHETERIZATION REVEALED NO EVIDENCE OF CARDIOVASCULAR DISEASE. NORMAL LV FUNCTION.
DIAGNOSIS: BRUGADA SYNDROME. PT. RECEIVED ICD PRIOR TO HOSPITAL DISCHARGE.
VISIT: www.BRUGADA.org FOR MORE INFORMATION.

42 y/o FEMALE

Vent. rate	86	BPM	Normal sinus rhythm with sinus arrhythmia
PR interval	200	ms	Right bundle branch block
QRS duration	148	ms	ST elevation consider anterior injury or acute infarct
QT/QTc	414/495	ms	***** ACUTE MI *****
P-R-T axes	64 114	17	Abnormal ECG

No previous ECGs available

D.O.S.: _____ Confirmed By: _____

BRUGADA SYNDROME.
PATIENT HAD HISTORY of SYNCOPE of UNKNOWN ETIOLOGY.
FAMILY HISTORY of SUDDEN DEATH of YOUNG, HEALTHY ADULTS.
VISIT: www.BRUGADA.org FOR MORE INFORMATION !

THE ONLY KNOWN TREATMENT FOR BRUGADA SYNDROME is IMPLANTATION of an ICD. THIS PATIENT HAD ICD IMPLANTED PRIOR TO HOSPITAL DISCHARGE.