J Wave Syndromes an Undate

Andrés Ricardo Pérez-Riera, MD PhD
Design of Studies and Scientific Writing Laboratory at the ABC School of Medicine, Santo André, São Paulo, Brazil
Dear Pedro, 
I wonder what is your personal opinion about the so-called J-wave syndrome. In other words justified this new syndrome? Thank in advance 
Andres.

Dear Andres, 
It has become very silent after the first publication. We have found many patients with J waves that a have a positive ajmaline test (an ajmaline test was not obligatory in the publication of Haissaguerre). There is certainly something, but J waves are very prevalent in normal individuals (30% of the athletes we test have them). Time will tell! Un saludo cordial!
Prof. Dr. Pedro Brugada. 
Chairman, Cardiovascular Division. 
Free University of Brussels (UZ Brussel) VUB.

Dear Andres, it is interesting that you ask. I have no problem with the terminology in itself as long as one doesn't imply that the pathophysiological mechanisms are identical. My personal view is that it helps to group disease entities into categories and there are certainly a lot of similarities between ERS and BrS (as the two entities in the J-wave syndromes). But there are also major differences and we think they rebate to the different underlying pathophysiological mechanisms. 
Hope this answers your question.
very best
Arthur A Wilde
University of Amsterdam – Department of Cardiology
Amsterdam
The Netherlands
Electrocardiogram waves classification

I. Constant and visible
   a) P-wave
   b) QRS complex: Q/q; R/r; S/s; R'/r'; S'/s'
   c) T-wave

II. Constant and invisible
   a) T-a or T-P-wave

III. Inconstant
   a) The “enigmatic” U-wave (Pérez-Riera 2008)

1. ECG Normal waves

2. ECG Pathological waves

I. Delta (δ) – wave of ventricular preexcitation (Wolff-Parkinson-White (WPW) syndrome)

II. Pseudo delta (δ) – waves:
   a) Wolffian PVCs: PVCs from basal portion of the ventricles – QRS complexes predominantly positive in all precordial leads (V1-V6) (Rosenbaum 1969)
   b) Epicardial ventricular tachycardias
   c) Slurred QRS upstroke mimicking delta (δ) waves in hypertrophic cardiomyopathy (Marine 2013)

III. J-wave, J deflection, "the camel's hump“/ camel-hump sign, “late δ wave”, elevated J-point, hathook junction, hypothermic wave, K wave, H wave, current of injury, or Osborn wave: a J wave is defined as either notching or a slur at the QRS terminal > 0.1 mV above the isoelectric line or without ST segment elevation at least in two contiguous leads.

IV. Lambda (λ)-wave or Gussak wave (Gussak 2004): Peculiar shape of J wave?

V. Epsilon (ε) wave, epsilon potential or Fontaine wave
J Point: end of ST segment and beginning of QRS complex
J Point: end of QRS complex and beginning of ST segment
QRS slurring without STSE producing a positive hump

QRS notching without STSE + a positive Deflection(hump) inscribed on terminal QRS complex

Classical definition of ERP: STSE associated with concave upward ST-segment elevation and prominent T waves in at least two contiguous leads.

Without J-wave

With J-wave

V_2

J-point

ST elevation

J-wave

J-point

New definition of early repolarization pattern: without ST segment elevation

Slurred QRS downstroke without STE

J-wave or the new “J-point elevation” without STE

New J-point
QRS slurring without STSE producing a positive hump
Clinical causes of J-wave or elevated J-point

1. Hypothermic J-wave or Osborn wave: hypothermia mediated VT/VF

2. Normothermic states
   ❖ ERS. ER a J-point elevation, notching or slurring of the terminal portion of the R wave (J wave) QRS slurring or notching in at least 2 contiguous inferior or lateral leads.
     □ Type 1: Early Repolarization Pattern (ERP) only in the lateral precordial leads (V4-V6).
       ✓ ST elevation limited to the precordial leads. Reciprocal depression only in aVR.
       ✓ Age range: 20 to 40 years old. Healthy black young adult male athletes;
       ✓ HR: sinus bradycardia/phasic sinus arrhythmia is frequent;
       ✓ ECG changes usually stable over time (i.e. non-progressive)
       ✓ Axes of QRS, ST segment and T wave, are oriented in the same direction in the FP;
       ✓ Deep and narrow Q waves followed by R wave of great voltage in left precordial leads;
       ✓ Notch or slurring of R wave descending branch;
       ✓ Transition area in precordial leads of sudden occurrence;
       ✓ J point and ST segment elevation, usually < 2 mm (exceptionally it may be > 5 mm) of superior concavity in middle and/or left precordial leads and possibly in inferior leads;
       ✓ Possible reduction in J point and ST segment elevation by sympathetic action and sympathomimetic drugs;
       ✓ Absence of reciprocal or mirror image (exception in VR lead);
       ✓ Symmetrical T waves, with great width and polarity matching QRS.
In early repolarization, there is a voltage gradient, however, no dispersion of duration of action potentials in ventricular wall thickness. For this reason, these patients showed ST segment elevation with no tendency to develop arrhythmias.

**Theoretical electrophysiological explanation for ST segment elevation in ECGs in athletes**

- **Notch or slurring in R wave descending branch**
- **J point and ST Segment elevation from 1 to 4 mm from the isoelectric line**
- **Voltage Gradient**
- **T waves of great voltage and polarity matching QRS**
- **ST segment upwardly concave**
Typical ECG of early repolarization syndrome in an athlete with bradycardia

Name: DAS       Age: 24y       Sex: Male       Race: Black       Weight: 82 kg
Height: 1.91 m       Biotype: Athletic       Profession: professional basketball player

**ECG diagnosis:** sinus bradycardia, (HR 50 bpm). J point and ST segment with elevation > 4 mm in precordial leads from V₃-V₅ of superior concavity. Notch or slurring of terminal portion of the QRS complex (J point). ST segment elevation > 4mm in precordial leads V₃, V₄ and V₅.

**Conclusion:** sinus bradycardia, early repolarization syndrome.
The figure shows V4 precordial lead with STSE concave to the top followed by large positive T wave that resembles a "smiling face".

Mirror image or reciprocal changes only in aVR lead
There are not final broad S wave in left leads (V5-V6):

There are not IRBBB

PSEUDO IRBBB

ST: SADDLE TYPE
Genetic forms

J-wave syndromes: a group of clinical entities that share similar molecular, ionic and cellular mechanism and marked by amplified J wave on the ECG and a risk of PVT/VF.

- Without apparent structural heart disease
  - **J-wave Syndromes**
    - BrS: J-wave in the right precordial leads V1-V3
    - Overlapping between BrS and ERS
    - Idiopathic VF
    - SQTS; LQTS

- With structural heart disease
  - Concealed forms of Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia (ARVC/D) (*Nava 1988*)

Acquired forms

- Ischemia- mediated VT/VF: Vasospastic angina, Prinzmetal J waves/ Ischemic J-Waves
- Miscellaneous
  - Hypercalcemia
  - Brain injury
    - Subarachnoid hemorrhage
    - Acute intracranial hypertension
    - Transient postictal hemiplegia (Todd's paralysis) (*O'Connell 2013*)
  - Damage to sympathetic nerves in the neck: or spinal cord injury leading to loss of sympathetic tone
  - Cardiopulmonary arrest from over sedation (*Shinde 2007*)
  - Accessory third papillary muscle with a prominent J-wave
  - Hypervagotonia.

I. Ventricular repolarization components on the electrocardiogram

- Transmural voltage gradient during early ventricular repolarization: phases 1 and 2 of AP
- Electrical heterogeneity among ventricular endocardium and epicardium during repolarization.
- The ventricular epicardium denotes an AP with a prominent transient outward K⁺ current ($I_{to}$)-mediated notch.
- The AP of the endocardium shows a much smaller $I_{to}$ current.
- J waves are associated with Phase 2 reentrant arrhythmias.

II. Ventricular depolarization components on the electrocardiogram

- QRS fragmentation (fQRS)
- QRS duration ≥120 ms in V2 and II
- Epsilon wave
- Right End Conduction Delay
- Parietal block
- QT peak
- QT end
- r-J interval
- Late potentials (LPs)
Transmembrane APs from epicardium, endocardium and midmyocardium (M cells): repolarization mechanism

A prominent AP notch in the epicardium mediated by $I_{to}$ channels is responsible for the appearance of J wave on the ECG of BrS, IVF.
Early repolarization mechanism in Brugada syndrome repolarization mechanism

Gene mutations SCN5A and other

Fever
Ischaemia
Multiple Drugs
Cocaine
Alcohol
Hypokalaemia
Hypothermia

Type 1 Brugada Pattern

Short-coupled PVCs/
Polymorphic VT
Phase 2 reentry VT

Self-terminating
VT/VF

Sustained VF


downarrow Na;
downarrow Ca;
downarrow Na; downarrow Ca

uparrow Ito; uparrow IK-ATP

Epi Endo
Depolarization mechanism

I. QRS fragmentation or fragmented QRS complex (fQRS): defined as ≥ 2 notches of the R wave or in the nadir of the S wave in at least 2 consecutive leads.

II. QRS duration ≥120 ms in V2 and II, f-QRS are powerful depolarization marker for VF/SCD is a significant S-wave (≥0.1 mV and/or ≥40 ms) in lead I in patients with BrS (Calò 2016)

III. QT-interval prolongation in right precordial leads (Pitzalis 2003)

IV. Presence of LPs on SAECG: 1) Total filtered QRS duration (f-QRS) ≥114 ms; 2) Root Mean Square voltage (RMS40) of the terminal 40 ms of the f-QRS complexes ≥20 μV; and 3) Duration of low-amplitude signals 40 μV of the f-QRS complexes (LAS40) ≥38 ms. LP is identified when 2 of the criteria are satisfied. 5) Right End Conduction Delay on VCG
r–J interval, defined as the time between the earliest deflection of the QRS complex and J wave
RECD on right posterior quadrant: Depolarization mechanism.

T-loop: Rounded, small, with symmetrical velocity of inscription of afferent and efferent limbs and a 1:1 length/width ratio: Repolarization mechanism.

Type 1 Brugada pattern
T LOOPS CHARACTERISTICS IN ALL THREE GROUPS

GROUP I
Type-1 Brugada ECG Pattern
Frontal Plane

GROUP II
IRBBB
Frontal Plane

GROUP III
CRBBB
Frontal Plane

Horizontal Plane

Afferent limb
+60° CW

Efferent limb

Horizontal Plane

Afferent limb

Efferent limb

Horizontal Plane

Afferent limb

Efferent limb

Horizontal Plane

Afferent limb

Efferent limb

CW: Clockwise Rotation, CCW Conterclockwise Rotation
The 10 to 20ms initial forces are directed to left and downward (in LAFB this forces are directed to right and downward). Counterclockwise rotation (CCWR) with extreme left axis deviation, SII>SIII, prominent final R wave in aVR and prolonged R-peak time in this lead.
Abnormal expression of cardiac neural crest cells in heart development (Elizari 2007) in fact this theory is also eclectic because it admits both mechanisms: depolarization and repolarization. The cardiac neural crest (CNC) cells are a subpopulation of cranial neural crest discovered nearly 33 years ago by ablation of premigratory neural crest. The CNC cells are necessary for normal cardiovascular development.

Cardiac neural crest (CNC) cells migrate from the neural tube to the circumpharyngeal ridge (i.e., circumpharyngeal crest), caudal pharyngeal arches (third, fourth, and sixth), and outflow tract (OFT) just before asymmetrical remodeling of the aortic arch arteries. Some of the CNC cells migrate in and envelop the nascent aortic arch arteries, while others continue to migrate and eventually colonize to later form the aorticopulmonary septum.
1. Hypothermic J-wave or Osborn wave ECG features

**Concept:** Hypothermia is defined as the condition where central temperature (rectal, esophageal or tympanic) is below 35°C. Hypothermia may be accidental, metabolic, or therapeutic.

Accidental hypothermia is more frequent in countries with cold weather, during winter season. The hypothermal state is characterized by drop in basal metabolism, decrease in \( \text{O}_2 \) consumption and greater production of \( \text{CO}_2 \).

During hypothermia, a gradual decrease of heart rate is observed and systolic volume, with progressive drop of blood pressure later, which becomes significant when central temperature values close to 23°C are reached.

- **Sinus bradycardia**, but in the initial phase tachycardia by release of adrenaline
- **Atrial fibrillation** (50% of cases), temperature < 32°C.
- **Artifacts:** fluctuation in the baseline caused by the muscular trembling. Only in the initial phase (of struggle), when body temperature is between 36 and 32°C.

![J Wave and End of QRS](image)

- **PR interval** prolongation
- **QRS complex:** decrease in voltage and increase in duration.
- **QT and QTc intervals** prolongation.
- Both supraventricular and ventricular arrhythmias
- Very characteristic extra wave, called J wave between the end of QRS complex and ST segment onset, not pathognomonic (may be observed in normothermia conditions, positive and prominent in \( V_5 \) and \( V_6 \)). Inverse correlation between J wave voltage (mm) and central temperature.
Inverse and significant correlation between J wave voltage (mm) and central temperature in hypothermia.
The tracing was obtained during cooling of the blood before a surgical procedure of the heart. Although the ECG obtained was somewhat expected, what was striking is that the progressive development and augmentation of the J wave was recorded. Most of the hypothermia cases are published in the moment when the patient is rescued and after recovery. On the other hand, in this case we can see the time course of changes up to the simulation of a monophasic action potential. Additionally, significant bradycardia is observed and the QT interval was too prolonged, something that usually is not given much attention in the published cases.

Courtesy from Prof. Dr. Raimundo Puerta from Cuba
2. Normothermic states

J-wave syndromes: a group of clinical entities that share similar molecular, ionic and cellular mechanism and marked by amplified J wave on the ECG and a risk of PVT/VF.

- **BrS**: J-wave in the right precordial leads V1-V3
- **IVF**
- **SQTS**
- **LQTS**

**J-wave syndromes**

- Type 2: ERP in the inferior (II, III, aVF) or inferolateral leads (II, III, aVF, V5-6). Intermediate risk.
- Type 3: ERP global (inferior, lateral, and right precordial leads). Highest risk.

**Brugada syndrome**

**Concept**

Clinical and electrocardiographic entity (without apparent structural heart disease) hereditary heterogeneous pattern with autosomal dominant transmission (33% of cases) or sporadic (67%), mainly caused by mutation in the SCN5A gene encoding the α subunit of Na+ channel (Na (v) 1.5) located on the short arm of chromosome 3 (locus: 3p21). Until present date, 20 types of genes affected are known.

Clinically manifested by a tendency to syncope and/or sudden death in 60-80% of cases during night rest, with great male predominance (8:1), endemic in Southeast Asia (Thailand, Philippines) and Japan, predominantly in productive life time (young adult).

**Diagnosis criteria**

1. Absence of apparent structural heart disease
2. Absence of drugs effects, electrolyte disturbance and CHD
3. Documented PVT/VF
4. Family history of SCD at <45 years in first-degree relatives
5. Type 1 ECG Brugada pattern (coved-type) in proband and family members
6. Induction of VT/VF with Programmed Electrical Stimulation
7. Syncope, cardiac arrest or nocturnal agonal respiration.
Clinical diagnosis: Syncope. Positive familiar background of sudden death in young (≤35 y/o) first-degree relative. Genetic research performed: negative.

ECG diagnosis: Sinus bradycardia (HR <60 bpm), Brugada type 1 ECG pattern, prolonged QRS duration, aVR signal: final R wave of aVR lead >3 mm, fQRS in V1-V2.

Extreme left axis deviation: Left anterior fascicular block? or Right superior fascicular block?
ECG/VCG correlation in the frontal plane

Name: MK; Age: 38 y/o; Gender: Male; Ethnic Group: Asian; Weight: 68 kg; Height: 1,70 m

Broad final R wave

RECD on right Superior quadrant: RVOT
Depolarization mechanism

CCW Rotation

Round, small T-Loop Repolarization mechanism

Extreme Left Axis Deviation + CCW = LAFB
SIII>SII
ECG/VCG correlation horizontal plane

Name: MK; Age: 38 y/o; Gender: Male; Ethnic Group: Asian; Weight: 68 kg; Height: 1.70 m.
Twelve-lead ECG from the same 20-year-old man, recorded 72 hours later. The ERP persists, and there is now sinus bradycardia with a Brugada type 1 ECG pattern (coved type) in leads V1 to V3. The ST-segment elevation seen in lead aVR has been identified as a potential high-risk marker for ventricular arrhythmia in patients with BrS.
Classical case of ERS Type 3

J wave in all precordial leads
Reciprocal change or 
Mirror image

J wave insinuation

Normal QRS axis +60°
A: Basal tracing. We observe J-wave across all precordial and inferior leads.

**Example of idiopathic ventricular fibrillation with “malignant” Early Repolarization Syndrome type 3**
Comments: The drug reduces the magnitude of the Ito channel – mediator of phase 1 and consequently normalize the elevation of the ST segment. Additionally, it could improve repolarization due to its vagolytic effect (M2 muscarinic receptor block) and to the exacerbation of reflex sympathetic tone.

B: ECG after two days after oral quinidine 1500 mg/day

HR 83 bpm
Inferolateral early repolarization patterns and magnitude of risk of sudden cardiac death. Estimated prevalence in the general population is manifested by width of the pyramid. Highest risk is on the top of the pyramid, and lowest on the bottom (Junttila MJ et al Eur Heart J. 2012 Nov;33:2639–43.).

1. J-point with rapidly ascending ST segment followed by tall T wave considered a Benign form.

2. J-point with horizontal or descending ST segment, considered a Malignant form.
## Common features of early repolarization and Brugada syndrome

<table>
<thead>
<tr>
<th>Early repolarization</th>
<th>Brugada syndrome</th>
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<tbody>
<tr>
<td>Average age of first event 35 years</td>
<td>Average age of first event 30–40 years</td>
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<tr>
<td>Male predominance: 75%</td>
<td>Male predominance: 80%</td>
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<tr>
<td>Temporal variation in the expression of the ECG pattern</td>
<td>Temporal variation in the expression of the ECG pattern</td>
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<td>Vagally mediated accentuation of ECG pattern</td>
<td>Vagally mediated accentuation of ECG pattern</td>
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<tr>
<td>Pattern with ascending ST-segment after J-point: lower risk</td>
<td>Pattern with ascending ST-segment after J-point, i.e. Type II and III ECG: lower risk</td>
</tr>
<tr>
<td>Normalization during quinidine exposure</td>
<td>Normalization during quinidine exposure</td>
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</tbody>
</table>
Short QT syndrome with early repolarization

The main features of congenital SQTS are:

➢ Absence of structural heart disease

➢ Familial clinical-electrocardiographic entity

➢ Autosomal dominant inheritance or sporadic, and genetically heterogeneous

➢ Constant and uniform very short QT and QTc intervals (QTc interval \(\leq 330\) ms)

➢ Positive family history for sudden cardiac death (SCD)

➢ Manifested by syncope, sudden death, dizziness and high tendency to appearance of episodes of paroxysmal runs of atrial fibrillation (AF)

➢ The response to exercise testing is a slight reduction of the QT interval during the increase in heart rate.

➢ Short refractory periods and tendency for inducible AF and VF were seen in electrophysiology studies (EPSs).

➢ Autopsy did not reveal any structural heart disease
Clinical diagnosis: Congenital short QT syndrome with mutation in Caveolin-3 (SQT7).

ECG diagnosis: Sinus rhythm, HR = 68 bpm; P wave: SÂP + 32º, PR interval duration: 120 ms, PR segment depression (>0.5 mm) in II and V5, absence of ST segment, positive-negative T wave or “minus-plus T wave sign” in aVF, and QT = 280 ms; QTc = 295 ms.
El primer punto de inflexión de la rampa descendente de la onda R es considerado el punto J real. En estos casos el método de la “línea tangente” es ideal. Elevación del segmento ST = 0,8 mm. Consideramos una variante tipo C atípica de patrón de repolarización precoz. El aspecto de lambda es un marcador de arritmias fatales.
J-wave syndrome with structural heart disease
1. Concealed forms of arrhythmogenic dysplasia of the right ventricle

36-year-old patient, episode of VF

The authors interpreted this tracing as early repolarization pattern. Today we know that this is the typical type 1 ECG Brugada pattern, which from the vectorcardiographic point of view is diagnosed as RECD by one of the RB fascicles of the RBB (Nava 1988).
Clinical diagnosis: 56-year-old female who presented to the emergency department with a decreased level of consciousness following intensification of a two-week long worsening headache. The patient's past medical history was significant for hypertension for which she was on no medication. On physical exam, she was unconscious (Glasgow Coma Scale (GCS) 6).

**ECG diagnosis:** Wide-complex QRS VT (160 ms) at a rate of 294 bpm with visible fusion and capture beats. Monophasic R-waves in leads V1–V2 indicated left ventricular origin.

2. Brain injury - ECG at admission (08:32 A.M.) - Massive J-waves in the context of intracranial hemorrhage
ECG diagnosis: The patient was electrically cardioverted and a second ECG performed after 8 minutes demonstrated rapid AF at 188 bpm and massive J-waves (maximal amplitude: 0.47 mV in lead II) with ST-segment elevation in the inferolateral leads and ST-segment depression in the anterior leads (V1–V4).
Computed tomography of the brain showing a massive intraparenchymal hematoma.
Clinical diagnosis: ECG performed subsequent postictal confusion/hemiplegia with left-sided upper and lower extremity hemiparesis: cerebral and cardiac hypoperfusion (ischemia) following a postictal event with an increase in sympathetic tone.

ECG diagnosis: Lambda waves in the setting of cerebral injury such as trauma or hemorrhage; however, ECG evidence of a dynamically displaced J-point has not been previously described in the setting of postictal hemiplegia.
3. Ischemia-mediated VT/VF: 3-A) Vasospastic angina, Prinzmetal J waves/Ischemic J-Waves

During myocardial ischemia in patients with Prinzmetal vasospastic angina, J-wave augmentations caused by myocardial ischemia during coronary spasms has lambda wave morphology. The presence and augmentation of J waves, especially prominent J waves with the characteristic ST-elevation patterns, were associated with VF (Sato 2012).

We show a continuous Holter monitoring below belonging to a man who had coronary revascularization a time ago, during an episode of angina and concomitant ST segment elevation and ischemic giant J-wave "lambda-like type" associated with Premature Ventricular Contractions with Bigeminy sequence and very short coupling. The PVCs disappear immediately after cessation of vasospastic ischemia with administration of sublingual nitrate.

Observation: the pattern is very similar with ECG-2 from the present case because we have f-QRS + lambda wave.
Association of f-QRS in at least two contiguous leads on the 12-lead ECG + Wide QRS complexes + J-waves ≥0.1 mV combined with a descending/horizontal ST segment constitute a malignant ER pattern (Misuzawa 2014). Identifying patients with higher risk of fatal arrhythmias after CABG surgery. All are components of multifactorial risk for increased morbidity and mortality, sudden cardiac death and recurrent cardiovascular events.
4. Hypercalcemia

Comparative of monophasic action potential with surface ECG in normal conditions and in hypercalcemia

- **QTc interval shortening**: interval from Q wave onset to T wave onset corrected according to HR.
- **Q-aT interval decrease**: interval between QRS onset to T wave apex. Values below 270 ms are diagnostic.

Almost absent ST segment
J-waves in hypercalcaemia are presumably due to an increase in the calcium-activated outward current and a decrease in the inward calcium current. This leads to all-or-none repolarization of the action potential (end of Phase 1 in the epicardium), creating an Ito channel-mediated transmural voltage gradient during ventricular repolarization.
Algorithm for diagnosis, risk stratification, and treatment of Brugada syndrome

**Symptomatic**
- Aborted SCD → ICD
- Documented VT with/without syncope → ICD
- Spontaneous type 1 BrP + syncope → ICD
- Electrical storm → Isoprot. + (hydro) quinidine

**Asymptomatic**
- VT/VF induced by PVS → ICD
- Spontaneous type 1 ECG BrP → (Hydro) quinidine
- Drug-induced type 1 BrP + posit. fam. hist. → ICD not indicated

**Definitive diagnosis**
Type 1 ECG, BrP, in V1 or V2 in standard position or higher (up to 2nd ICS), spontaneous or induced (ajmaline)

**General treatment measures**
- Avoid drugs (brugadadrugs.org)
- Reduce fever immediately (paracetamol)
- Avoid excessive alcohol consumption
Indication for therapy of patients with BrS. Recommendations with class designation are taken from Priori et al (Antzelevitch 2016). Recommendations without class designation are derived from unanimous consensus of the authors.

**Type 1 Brugada pattern**

- Avoid drugs that may induce or aggravate ST segment elevation in right precordial leads (www.brugadadrugs.org)
- Avoid cocaine and excessive alcohol intake
- Immediately treat fever with antipyretic drugs (Class I)

Symptomatic

- Electrical storm
- Prior cardiac arrest
- Sustained VT

- Isoproterenol ± quinidine (Class IIa)
- Presumably arrhythmic origin
- ICD (Class I)
- ICD (Class IIa)
- Close follow-up with/without ILR
- Repeated appropriate shocks
- Quinidine (Class IIa)
- RVOT ablation (Class IIb)
- cilostazol

Asymptomatic

- Syncope seizure
- NAR

- Based on patient and ECG characteristics (age, gender, Jp amplitude, QRS fragmentation...)
- Inducible VT/VF with up to 2 ES
- Close follow-up
- Quinidine
- ICD
- ICD (Class IIb)

- Spontaneous and fever-induced type 1 Brugada pattern
- Type 1 Brugada pattern induced by Na channel blocker
- Close follow-up

Quinidine, if ICD indicated but refused or contraindicated (Class IIa)

ES: extra stimulus at right ventricular apex; ICD: implantable cardioverter defibrillator; ILR: implantable loop recorder; NAR: nocturnal agonal respiration; RVOT: right ventricular outflow tract; VF: ventricular fibrillation; VT: ventricular tachycardia
## Proposed Shanghai Score System for diagnosis of early repolarization syndrome

<table>
<thead>
<tr>
<th>I. Clinical history</th>
<th>Points</th>
</tr>
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<tbody>
<tr>
<td>A. Unexplained cardiac arrest, documented ventricular fibrillation or polymorphic ventricular tachycardia</td>
<td>3</td>
</tr>
<tr>
<td>B. Suspected arrhythmic syncope</td>
<td>2</td>
</tr>
<tr>
<td>C. Syncope of unclear mechanism/unclear etiology</td>
<td>1</td>
</tr>
</tbody>
</table>

*Only award points once for highest score within this category*

<table>
<thead>
<tr>
<th>II. Twelve-lead ECG</th>
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<tbody>
<tr>
<td>A. Early repolarization ≥0.2 mV in ≥2 inferior and/or lateral ECG leads with horizontal/descending ST segment</td>
<td>2</td>
</tr>
<tr>
<td>B. Dynamic changes in J-point elevation (≥0.1 mV) in ≥2 inferior and/or lateral ECG leads</td>
<td>1.5</td>
</tr>
<tr>
<td>C. ≥0.1 mV J-point elevation in at least 2 inferior and/or lateral ECG leads</td>
<td>1</td>
</tr>
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*Only award points once for highest score within this category*

<table>
<thead>
<tr>
<th>III. Ambulatory ECG monitoring</th>
<th></th>
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<tbody>
<tr>
<td>A. Short-coupled premature ventricular contractions with R on ascending limb or peak of T wave</td>
<td>2</td>
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</table>

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<tr>
<th>IV. Family history</th>
<th></th>
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<tbody>
<tr>
<td>A. Relative with definite early repolarization syndrome (ERS)</td>
<td>2</td>
</tr>
<tr>
<td>B. ≥2 first-degree relatives with a II.A.ECG pattern</td>
<td>2</td>
</tr>
<tr>
<td>C. First-degree relative with a II.A. ECG pattern</td>
<td>1</td>
</tr>
<tr>
<td>D. Unexplained sudden cardiac death &lt;45 years in a first- or second-degree relative</td>
<td>0.5</td>
</tr>
</tbody>
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*Only award points once for highest score within this category*

<table>
<thead>
<tr>
<th>V. Genetic test result</th>
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<tbody>
<tr>
<td>A. Probable pathogenic ERS susceptibility mutation</td>
<td></td>
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<tr>
<td>Score (requires at least 1 ECG finding) - ≥5 points: Probable/definite ERS; 3–4.5 points: Possible ERS &lt;3 points: Nondiagnostic</td>
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Differential diagnosis of early repolarization pattern

Other causes of early repolarization pattern include the following:

- Juvenile ST pattern
- Pericardial disease (pericarditis, pericardial cyst, pericardial tumor)
  - Hypothermia
- Hyperthermia
- Myocardial tumor (lipoma)
- Hypertensive heart disease
- Athlete’s heart
- Myocardial ischemia
- ST segment elevation myocardial infarction (i.e., anteroseptal myocardial infarction)
- Fragmented QRS (terminal notching)
- Hypocalcemia
- Hyperpotassemia
- Thymoma
- Aortic dissection
- Arrhythmogenic right ventricular cardiomyopathy
- Takotsubo cardiomyopathy
- Neurologic causes (intracerebral bleeding, acute brain injury)
- Myocarditis
- Chagas disease
- Cocaine use
## J-wave syndromes

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Inherited</th>
<th>Acquired</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ERS type 1</td>
<td>ERS type 2</td>
<td>ERS type 3</td>
<td>BrS</td>
</tr>
<tr>
<td>Average age of first event</td>
<td>healthy black male athletes</td>
<td>35 years</td>
<td>30-40 years</td>
<td>40-50 years</td>
</tr>
<tr>
<td>Anatomic location</td>
<td>Lateral LV</td>
<td>Inferior LV</td>
<td>Both ventricles</td>
<td>RVOT</td>
</tr>
<tr>
<td>Leads displaying J point/J wave</td>
<td>I, V4-6</td>
<td>II, III, aVF</td>
<td>Global</td>
<td>V1-3</td>
</tr>
<tr>
<td>Response of J wave/ST elevation to</td>
<td>Bradycardia or pause</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td></td>
<td>Na-channel blockers</td>
<td>↓ →</td>
<td>↓ →</td>
<td>↓ →</td>
</tr>
<tr>
<td>Male predominance</td>
<td>75%</td>
<td></td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>Sex dominance</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>VT/VF</td>
<td>Rare common in healthy athletes</td>
<td>Yes</td>
<td>Yes, electrical storms</td>
<td>Yes</td>
</tr>
</tbody>
</table>

ERS: Early repolarization syndrome; BrS: Brugada syndrome; LV: Left ventricle; RVOT: Right ventricular outflow tract; VT: Ventricular tachycardia; VF: Ventricular fibrillation;
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Inherited</th>
<th>Acquired</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ERS type 1</td>
<td>ERS type 2</td>
</tr>
<tr>
<td>Response to quinidine</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>J wave/STSE</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>VT/VF</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Response to isoproterenol</td>
<td>Limited data</td>
<td></td>
</tr>
<tr>
<td>J wave/STSE</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>VT/VF</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Gene mutations</td>
<td>CACNA1C, CACNB2B</td>
<td>KCNJ8, CACNA1C, CACNB2B</td>
</tr>
</tbody>
</table>

ERS: Early repolarization syndrome; BrS: Brugada syndrome; STSE: ST segment elevation; VT: Ventricular tachycardia; VF: Ventricular fibrillation
## Diagnosis of BrS (proposed Shangai score system)

<table>
<thead>
<tr>
<th>Category</th>
<th>Points</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I. ECG (12 lead/ambulatory)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A) Spontaneous type 1 BrP at conventional or high levels</td>
<td>3.5</td>
<td></td>
</tr>
<tr>
<td>B) Fever induced type 1 BrP at conventional or high levels</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>C) Type 2 or 3 BrP that converts with provocative drug challenge</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><em>Only award points once for highest score within this category. One item from this category must apply.</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>II. Clinical history</strong>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A) Unexplained cardiac arrest documented VF/polymorphic VT</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>B) Nocturnal agonal respirations</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>C) Suspected arrhythmic syncope</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>D) Syncope of unclear mechanism/unclear etiology</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>E) Atrial flutter/fibrillation in patients &lt;30 years without alternative etiology</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td><em>Only award points once for highest score within this category. One item from this category must apply.</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>III. Family history</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A) First or second degree relative with definitive BrS</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>B) Suspicious SCD (fever, nocturnal, Brugada aggravating drugs) in a first or second degree relative</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>C) Unexplained SCD &lt;45 years in a first/second degree relative with negative autopsy</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td><em>Only award points once for highest score within this category. One item from this category must apply.</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>IV. Genetic test result</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A) Probable pathogenic mutation in BrS susceptibility gene</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td><strong>Score (requires at least one ECG finding)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥3.5 points: probable/definitive BrS; 2-3 points: possible BrS; &lt;2 points: nondiagnostic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Similarities between early repolarization syndrome and Brugada syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BrS</td>
<td>ERS</td>
<td>Possible mechanism(s)</td>
</tr>
<tr>
<td>Male predominance</td>
<td>Yes (&gt;75%)</td>
<td>Yes (&gt;80%)</td>
</tr>
<tr>
<td>Average age of first event</td>
<td>30-50</td>
<td>30-50</td>
</tr>
<tr>
<td>Associated with mutation of rare variants in KCNJ8, CACNA1C, CACNB2, CACNA2D, SCNSA, ABCC9, SCN110A</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Relatively short QT intervals in subjects with Ca channel mutations</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Dynamic of ECG</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>VF often occurs during sleep or at low level of physical activity</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>VT/VF trigger</td>
<td>Short-coupled PVC</td>
<td>Short-coupled PVC</td>
</tr>
<tr>
<td>Ameliorative response to cilostazol</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Effect of Na channel blockers on unipolar epicardial electrogram</td>
<td>Augmented J waves</td>
<td>Augmented J waves</td>
</tr>
<tr>
<td>Fever</td>
<td>Augmented J waves</td>
<td>Augmented J waves (rare)</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>Augmented J waves mimicking BrS</td>
<td>Augmented J waves</td>
</tr>
</tbody>
</table>
### Differences between BrS and ERS

<table>
<thead>
<tr>
<th>Region most involved</th>
<th>BrS: RVOT</th>
<th>ERS: Inferior LV wall</th>
<th>Possible mechanism(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leads affected</td>
<td>V1-V3</td>
<td>II, III, aVF, V4-V6, I, aVL</td>
<td>Higher levels of I&lt;sub&gt;o&lt;/sub&gt; and/or differences in conduction</td>
</tr>
<tr>
<td>Regional difference in prevalence</td>
<td>Asia</td>
<td>Europe</td>
<td>Both inferolateral</td>
</tr>
<tr>
<td>Incidence of late potentials in signal average ECG</td>
<td>Higher</td>
<td>Lower</td>
<td></td>
</tr>
<tr>
<td>Prevalence in atrial fibrillation</td>
<td>Higher</td>
<td>Lower</td>
<td></td>
</tr>
<tr>
<td>Effect on Na channel blocker on ECG</td>
<td>Increased J wave</td>
<td>Reduced J wave</td>
<td>Reduction of J wave in the setting is thought to be due largely to prolongation of QRS. Accentuation of repolarization defects predominates in BrS, whereas accentuation of depolarization defects predominates in ERS.</td>
</tr>
</tbody>
</table>

Structural changes, including mild fibrosis and reduced expression of Cx<sub>43</sub> in RVOT or fibrofatty infiltration in cases of ARVC. Imaging studies have also revealed wall motion abnormalities and mild dilatation in the region of RVOT. Higher in some forms of the syndrome

Some investigators have hypothesized that some of these changes may be the result of rater than the cause of the BrS substrate which may create a hibernation-like state due to loss of contractility in the RVOT secondary to loss of the AP dome.

<table>
<thead>
<tr>
<th>Male predominance</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age at initial presentation</td>
<td>Young adults</td>
<td>Old adults</td>
</tr>
<tr>
<td>Most common morphology</td>
<td>Dome-like smooth appearance</td>
<td>Relatively sharp appearance</td>
</tr>
<tr>
<td>Response to change in heart rate</td>
<td>Bradycardia- and pause-dependent augmentation of J wave, which may be accompanied by T-wave inversion</td>
<td>Tachycardia and prematurity-dependent augmentation of the notch</td>
</tr>
<tr>
<td>Structural heart diseases</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td></td>
<td>History of myocardial infarction and/or cardiomyopathy</td>
<td></td>
</tr>
</tbody>
</table>