Bangalore Baptist Hospital
QUALITY WITH COMPASSION SINCE 1973

# Early Repolarisation Syndrome

- **BENIGN or LETHAL?**
- **HOW to DIFFERENTIATE?**

**Disclaimer: No conflicts of interest to disclose.**


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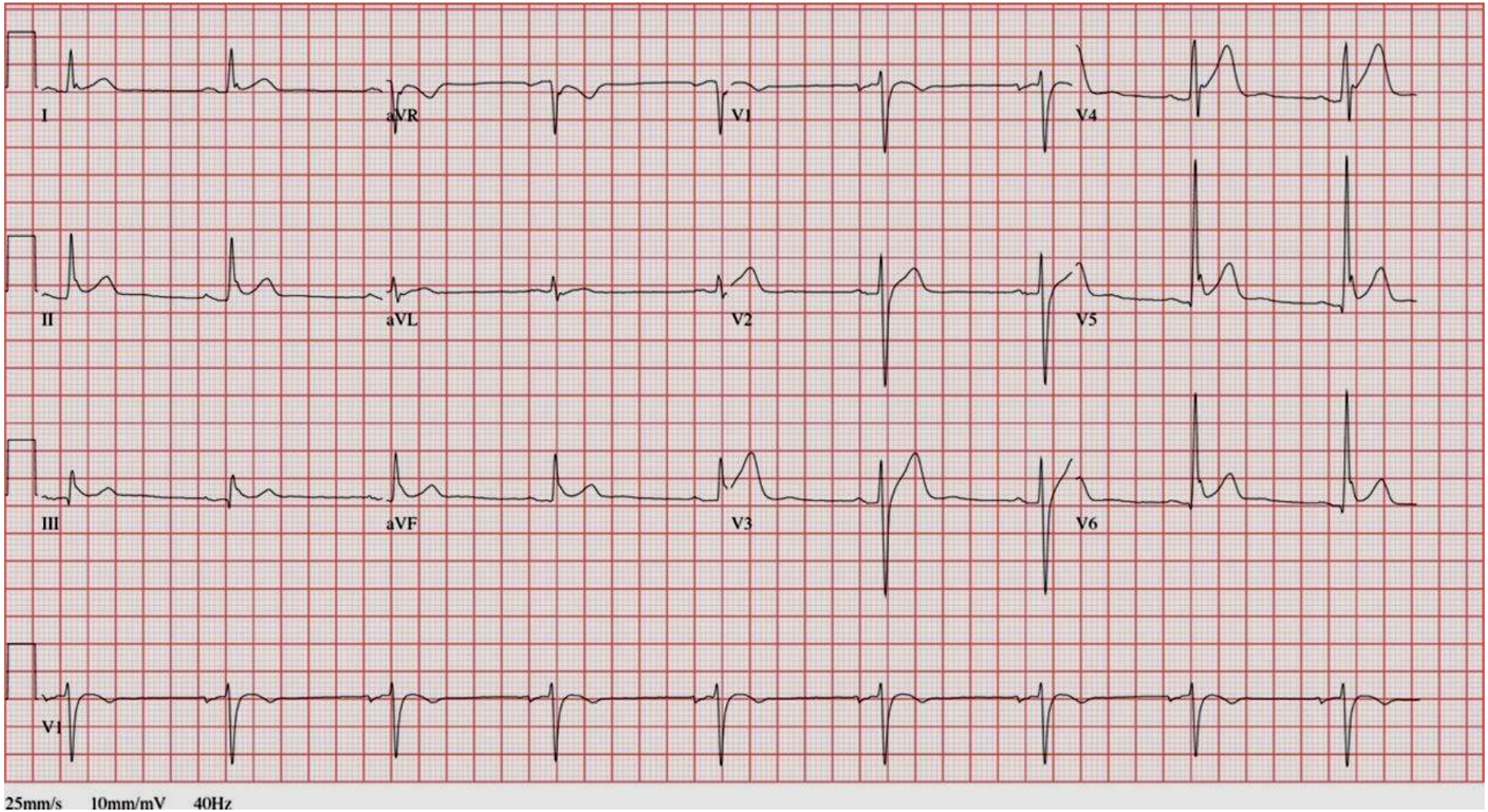

I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
V1
25mm/s 10mm/mV 40Hz

# What is ERS?

American Heart Journal

Volume 11, Issue 3, March 1936, Pages 325-345

Original communication

The four-lead electrocardiogram in two hundred normal men and women R.A.ShipleyM.D.W.R.HallaranM.D.

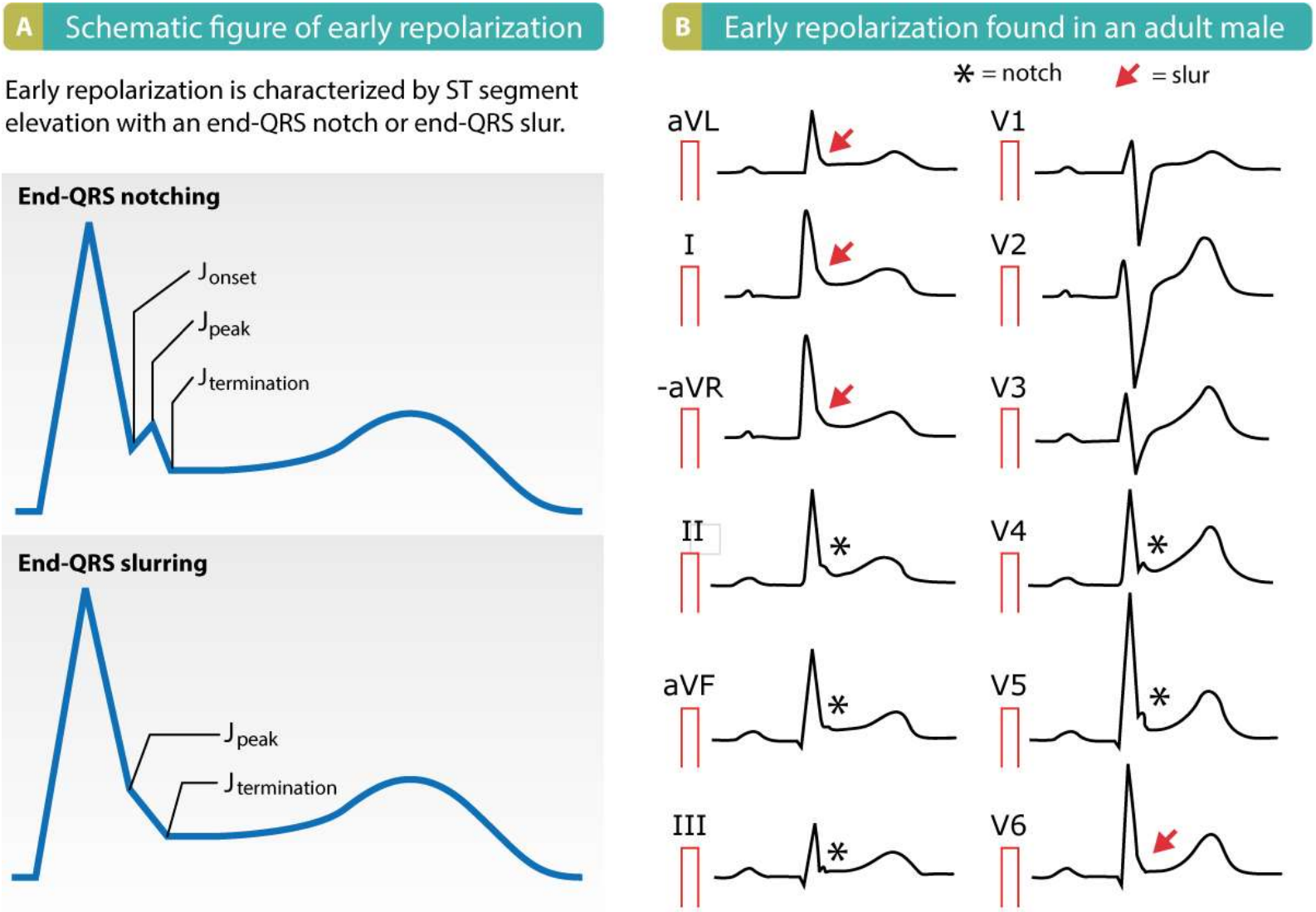
3. **Slurring and notching of QRS were common in Leads III and IV, were occasionally seen in Leads I or II, but were not encountered in Leads I and II together or in all three limb leads.**

**5. Slight deviations of the S-T level were common. The limits of deviation measured from the P-R level were 1 mm. above this level and 0.5 mm. below in Leads I, II, and III, except in cases of a deeply depressed P-R level when the elevation sometimes slightly exceeded 1 mm. The limits of deviation in Lead IV (left leg and apex) were 0.6 mm. above the line and 2.0 mm. below.**

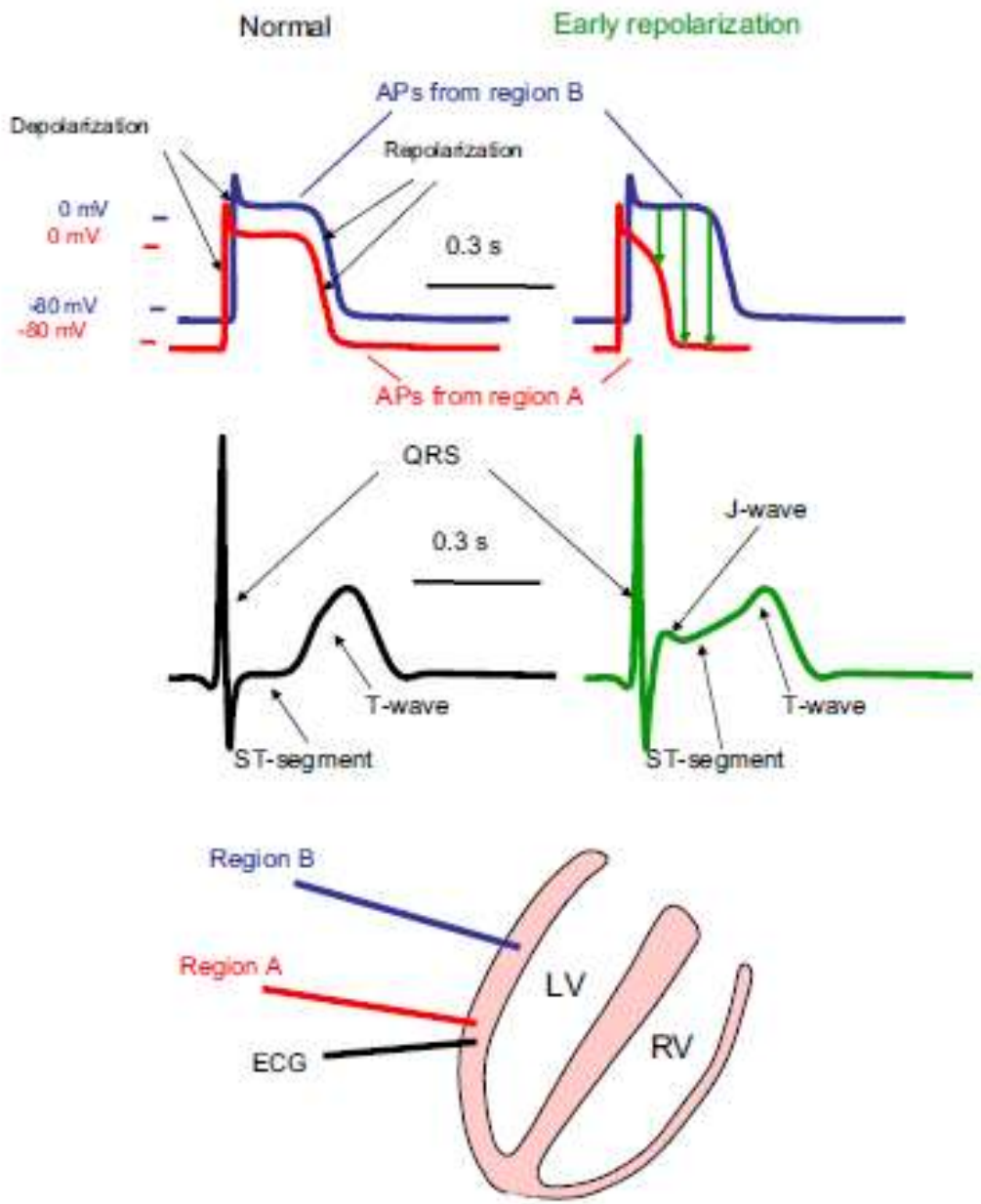
***Michel Haïssaguerre-2008 (STUDY OF 206 SCD FROM Idiopathic VF-ERS SEEN IN 31% VS 5% IN MATCHED CONTROLS)***

***Defined as an elevation of the QRS–ST junction of at least 0.1 mV from baseline in the inferior or lateral lead, manifested as QRS slurring or notching.***

**In 1953; Osborn described the classic J-wave in experimental hypothermia resulting from increased dispersion of repolarization caused by a disproportionate abbreviation of the epicardial action potential compared to the endocardium**




Early repolarization characteristics associated with SCD include 1) High - amplitude J-point elevation 2) horizontal and/or down slopping ST segments and 3) Inferior and/or Lateral leads location.


Normal
Early repolarization
APs from region B
Depolarization
Repolarization
0 mV
0 mV
0.3 s
-80 mV
-80 mV
APs from region A
QRS
0.3 s
J-wave
T-wave
T-wave
ST-segment
ST-segment
Region B
Region A
ECG
LV
RV

# ERS- Epidemiology

- **1,342,512,706**
- 1.342 Billion
- ERS seen in 3% to 24% of general population (5 to 32 million Indians)
- 75% Male preponderance.
- 0.07% absolute risk for SCD-(up to 22400 SCD events in India)

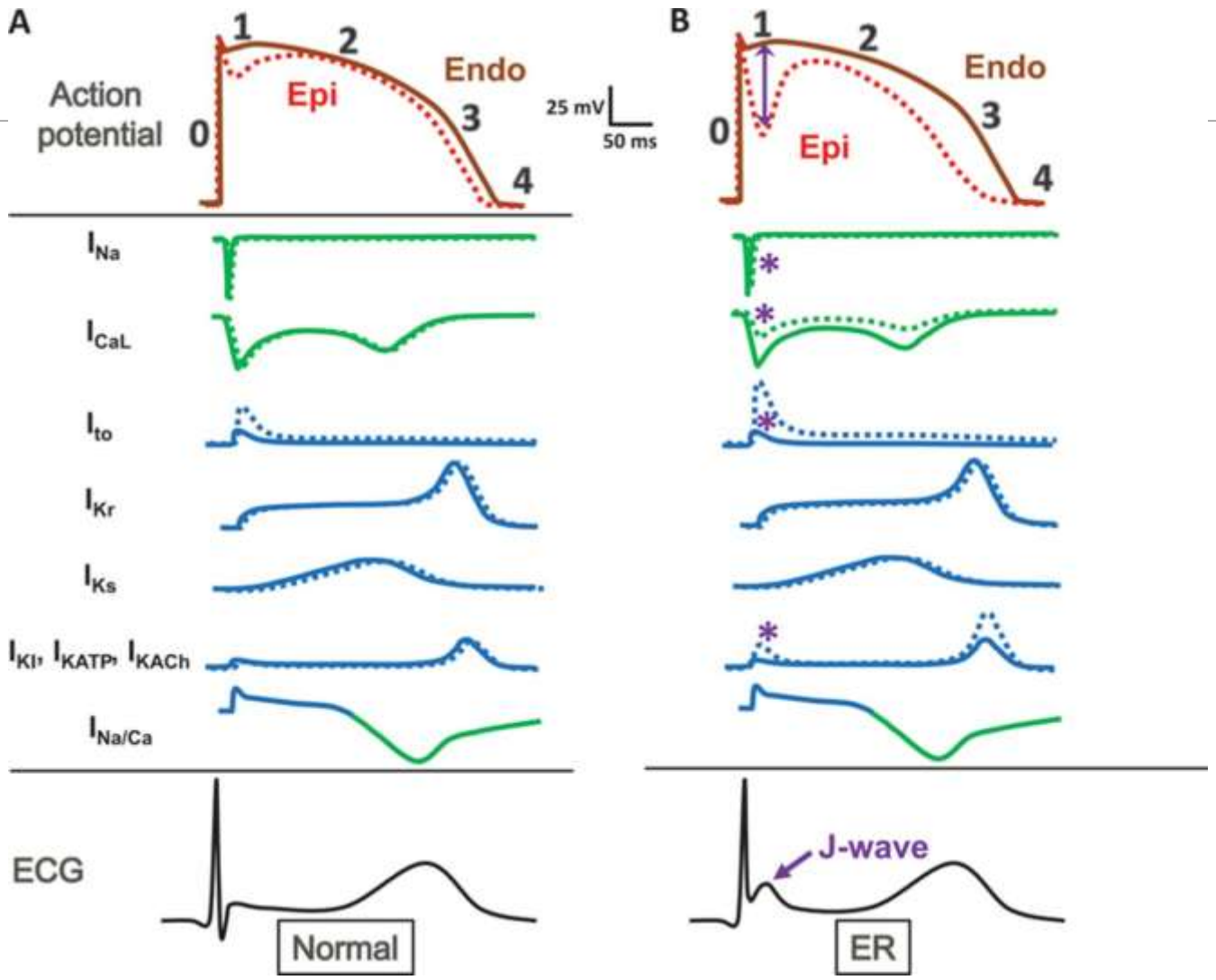
# ERS- BENIGN Vs MALIGNANT

- **The degree of J-point elevation determines SCD risk.**
- **Increases in J-wave amplitude often has been shown to precede VF episodes.**
- **A small study (of 9 SCD and 200 “benign” ER subjects) suggested an association of malignant ER with terminal-QRS “notching” versus “slurring” in left precordial leads (V4 to V5).**
- **This has not been confirmed for ER affecting inferior leads, where the degree of J-point elevation appears to be the only risk predictor.**
- **Localization of the ER pattern has prognostic implications.**
- **Case-control studies have associated aborted SCD with ER in inferior and, less commonly, lateral leads.**
- **In asymptomatic individuals, ER is most prominent in mid–precordial leads (V2 to V4), a pattern that is common among athletes and has a benign prognosis**

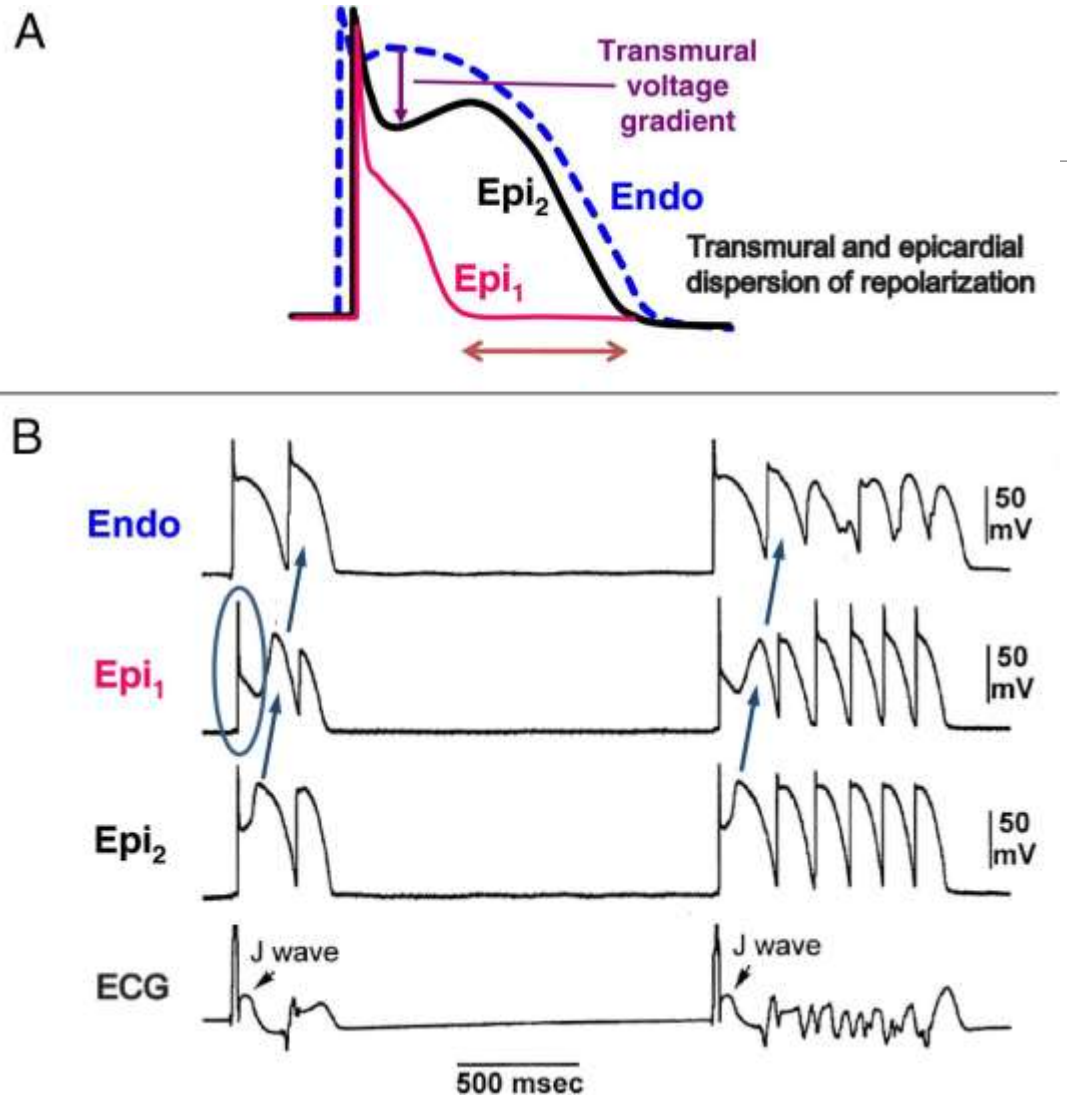
# ERS ECG Pattern is labile!

- **Autonomic tone and heart rate play major roles in ER variability.**
- **ER-associated VF events are more likely to occur in vagal contexts such as sleeping or after meals and J-wave amplitude increases at night.**
- **Adrenergic stimulation suppresses ER and associated arrhythmic events.**
- **Whether autonomic influences are mediated exclusively via heart-rate change or by direct actions on ion currents is unclear.**
- **Time-dependent recovery of Ito from inactivation could explain decreased J-wave amplitude with increased heart rate.**
- **Temperature can also modulate J waves and ST-segment elevation; hypothermia classically induces prominent J waves ("Osborn waves")**

# Electrophysiology of ERS

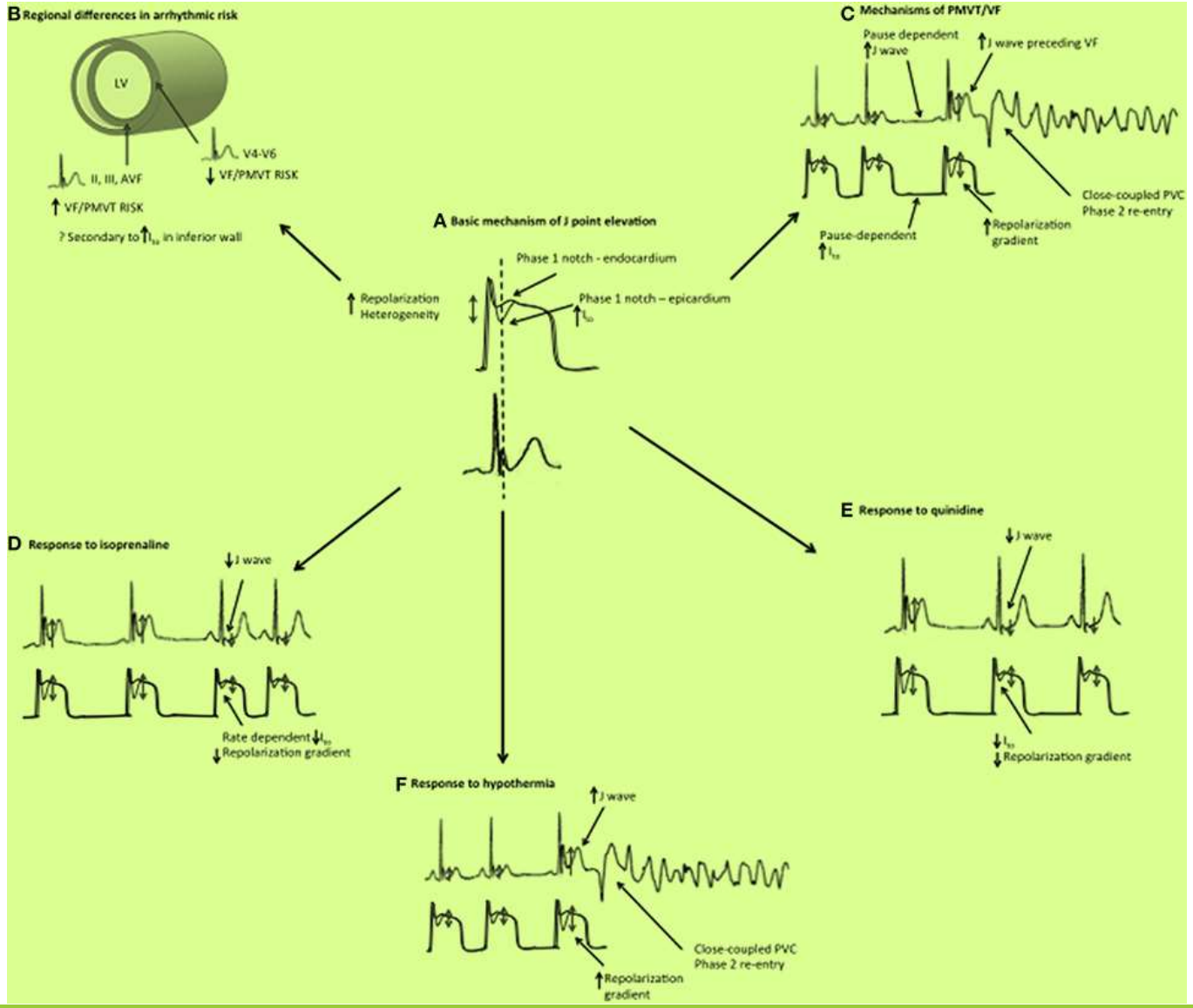


# Electrophysiology of ERS




**A) With enhanced repolarization in regions with prominent $I_{to}$, all-or-none repolarization can occur, creating a substrate for arrhythmias. (B) Simultaneous action potentials from 2 epicardial ($Epi_1$ and $Epi_2$) and 1 endocardial site (Endo), and surface ECG. A loss of the action potential dome in $Epi_1$, but not in $Epi_2$, leads to apparent propagation of the dome from $Epi_2$ to $Epi_1$, inducing re-entry.**

# Electrophysiology of ERS



# Genetic Basis of Ion Channel malfunction

- **The main underlying event is an inward–outward current imbalance, which is responsible for accelerated epicardial repolarization.**

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- **First report of a patient with the KCNJ8 S422L mutation was a case report of a 14-year-old female who experienced numerous episodes of idiopathic VF unresponsive to β-blockers, verapamil, and multiple antiarrhythmic medications. VF recurrences were associated with marked accentuation of ER. Subsequent functional studies demonstrated that compared with wild-type Kir6.1 channels, IKATP is increased (gain of function).**
- **This gain of function variant appears to be pathogenic in ER and idiopathic VF but is not present in the majority of cases of ER syndrome.**
- **Loss of function mutations of the cardiac L-type calcium channel have also been implicated (CACNA1C, CACNB2, and CACNA2D1 genes).**
- **Nonsynonymous variants affecting highly conserved residues of the *SCN5A* gene have been identified in 3 unrelated patients with ER and idiopathic VF (loss of Function mutation- cf Brugada Syndrome)**

# ERS Vs BRUGADA Syndrome

**Some features of ER resemble features of the Brugada ECG/syndrome such as**

1) **J-waves in ECG, 2) Pause/bradycardia dependent accentuation 3) the dynamic nature of the ECG pattern 4) local re-excitation via phase 2 re-entry, and 5) suppression of the ECG features and arrhythmia with isoproterenol and quinidine.**

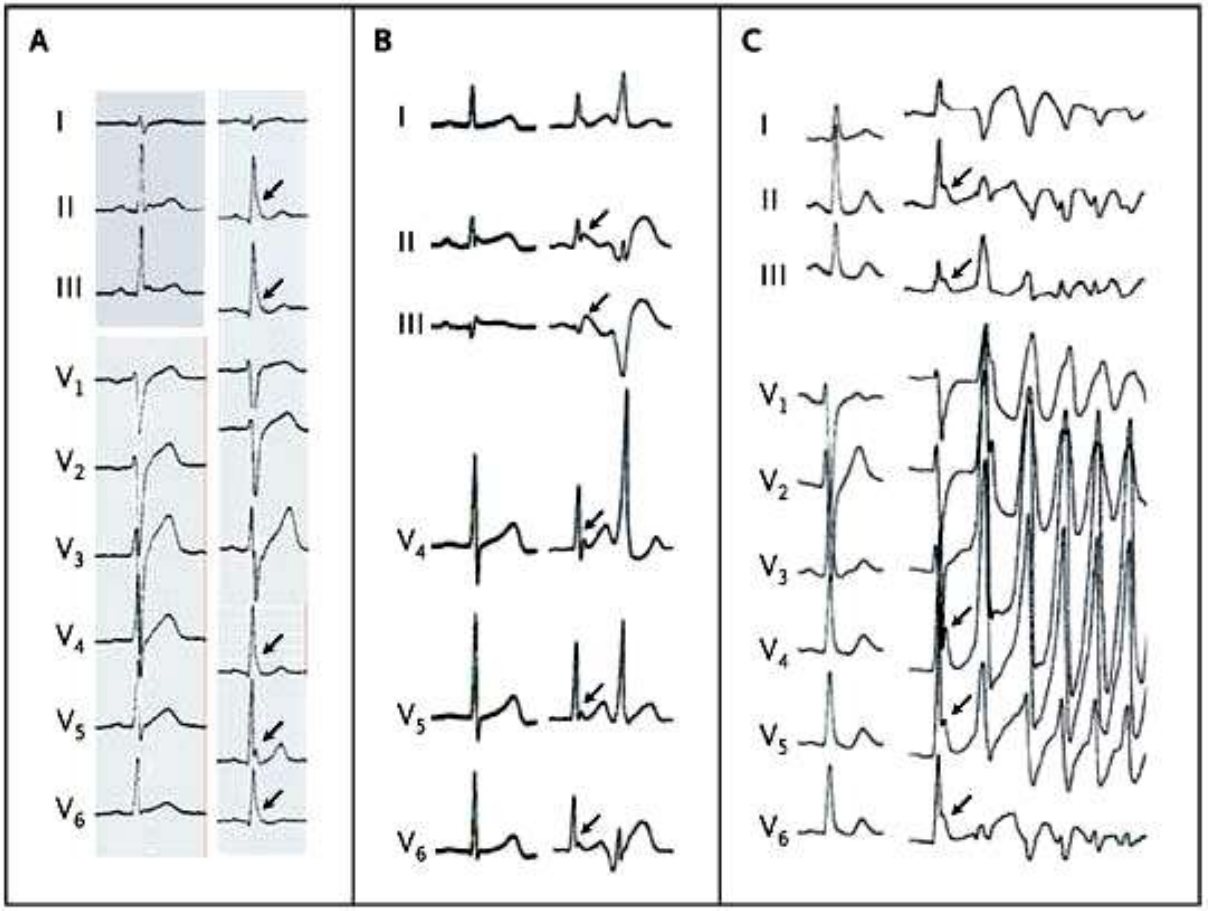
2) **However, Brugada feature of provocation by sodium channel blocker (Flecainide/Ajmaline) is not observed in ER.**

3) **No recognized structural counterpart in ER (like that recently described within the epicardium of the right ventricular outflow tract in malignant forms of Brugada syndrome).**

4) **About 12% of individuals with Brugada syndrome have been show to have co-existant ER.**

5) **There appear to be basic pathophysiological differences that delineate these 2 as possibly related but distinct entities.**

# Arrhythmia Induction in ERS- A Case study *(Michel Haisagurre et al)*



# Pharmacotherapy of ERS

**•Clinical experience with quinidine to prevent/treat VT is promising.**

**• Beta-adrenergic agonists (such as Isoprenaline) are beneficial in Idiopathic VF associated with ER, particularly for arrhythmic storm.**

**• Amiodarone has been reported effective in some patients, but its overall efficacy is limited .**

**• Several studies suggest that Na-channel blockers such as flecainide/ajmaline do not modify ER in contrast to the worsening typically seen in BrS.**

# Mechanistic review of useful interventions in ERS

- **Adrenergic activation with isoproterenol is effective in suppressing ER arrhythmias, likely by enhancing inward currents (particularly L-type Ca2+-current) that offset the net outward K+-current excess.**
- **Quinidine is a direct inhibitor of several potassium (outward) currents, particularly Ito and is effective in suppressing VT/VF in ERS.**
- **Vagal influences generally antagonize adrenergic effects and are probably responsible for events that are triggered by contexts like meals and during sleep.**

# Secondary prevention.

**ER patients resuscitated from IVF, ICD implantation is required.**

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**In patients with ICDs and frequent non-sustained VT and/or ICD shocks, adjuvant antiarrhythmic therapy with quinidine reduces arrhythmia burden.**

**No information is available about lifestyle modification, but it may be prudent to advise highly active patients with resting bradycardia and malignant ER to reduce physical-training programs.**

**Arrhythmic storm occurs in about 10% of patients with ER-related SCD . Isoproterenol infusion, titrated to increase heart rate beyond 90 and up to 120 beats/min, suppresses arrhythmic events as do other heart rate-increasing interventions (such as atrial or ventricular pacing).**

**In patients refractory to standard therapy, endocardial ablation of ectopic sources in the ER zone can be useful.**

# Primary prevention

- **Primary prevention of SCD in asymptomatic ER presents a major challenge. Few reliable criteria are available to stratify SCD risk.**

- **Inferior J-point elevation 2 mm predicts a 3-fold increase in SCD risk (Even this high-risk group does not diverge from the controls until at least 10 years after the index ECG!)**

- **The ER pattern diminishes and even disappears in response to exercise; Therefore, TMT does not provide prognostic information.**

- **ER patterns (especially in leads V2 to V6) occur in up to 90% of high-performance athletes . This ER pattern is particularly noted to be benign and therefore unreasonable to stop these athletes from training & participation.**

- **Unexplained syncope associated with an electrocardiographic ER pattern is a particular problem.**

# Patient with ER and Unexplained Syncope

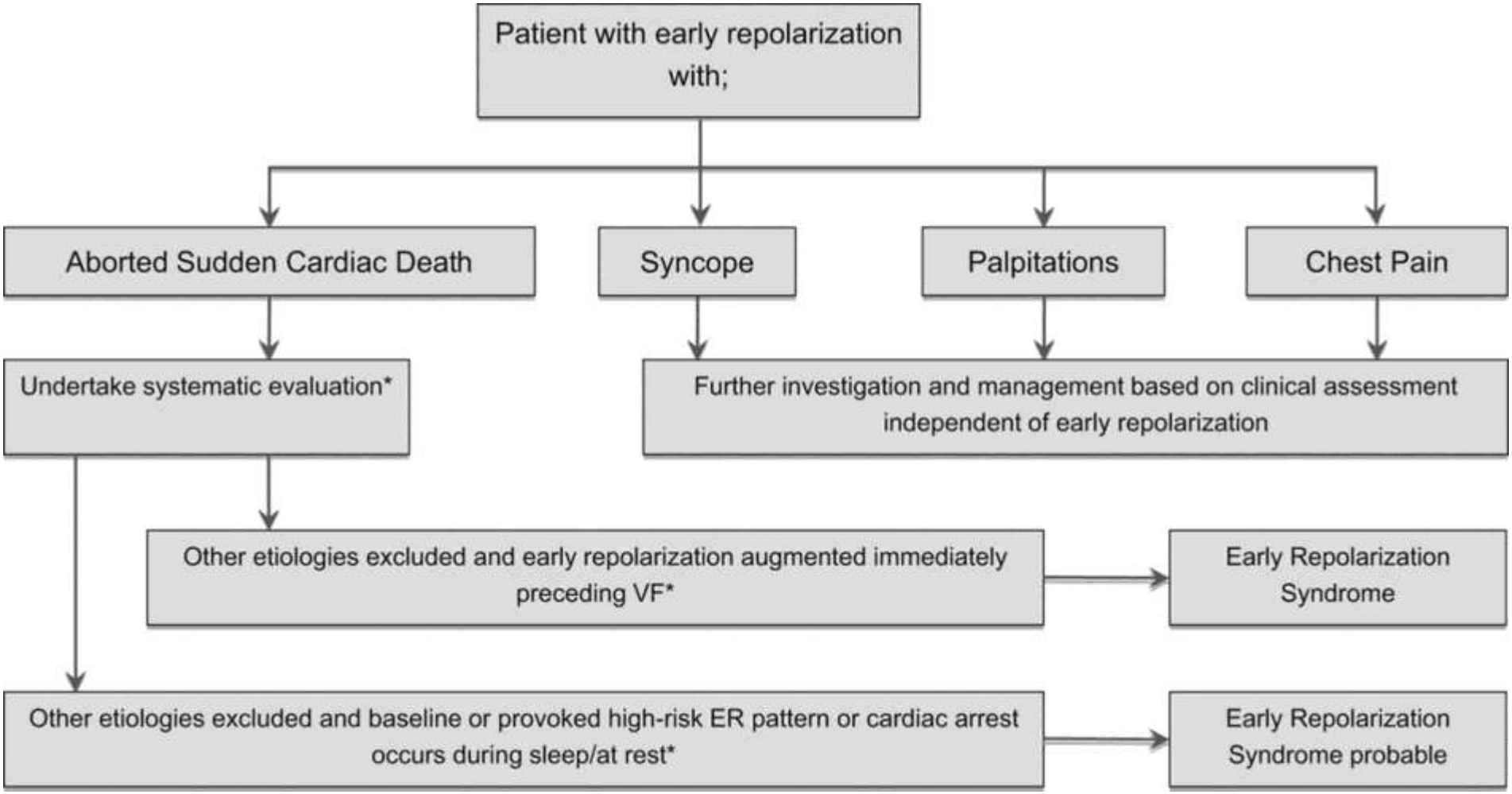
- Both ER and syncope are very common, affecting an average of 5% and 40% of the general population, respectively.

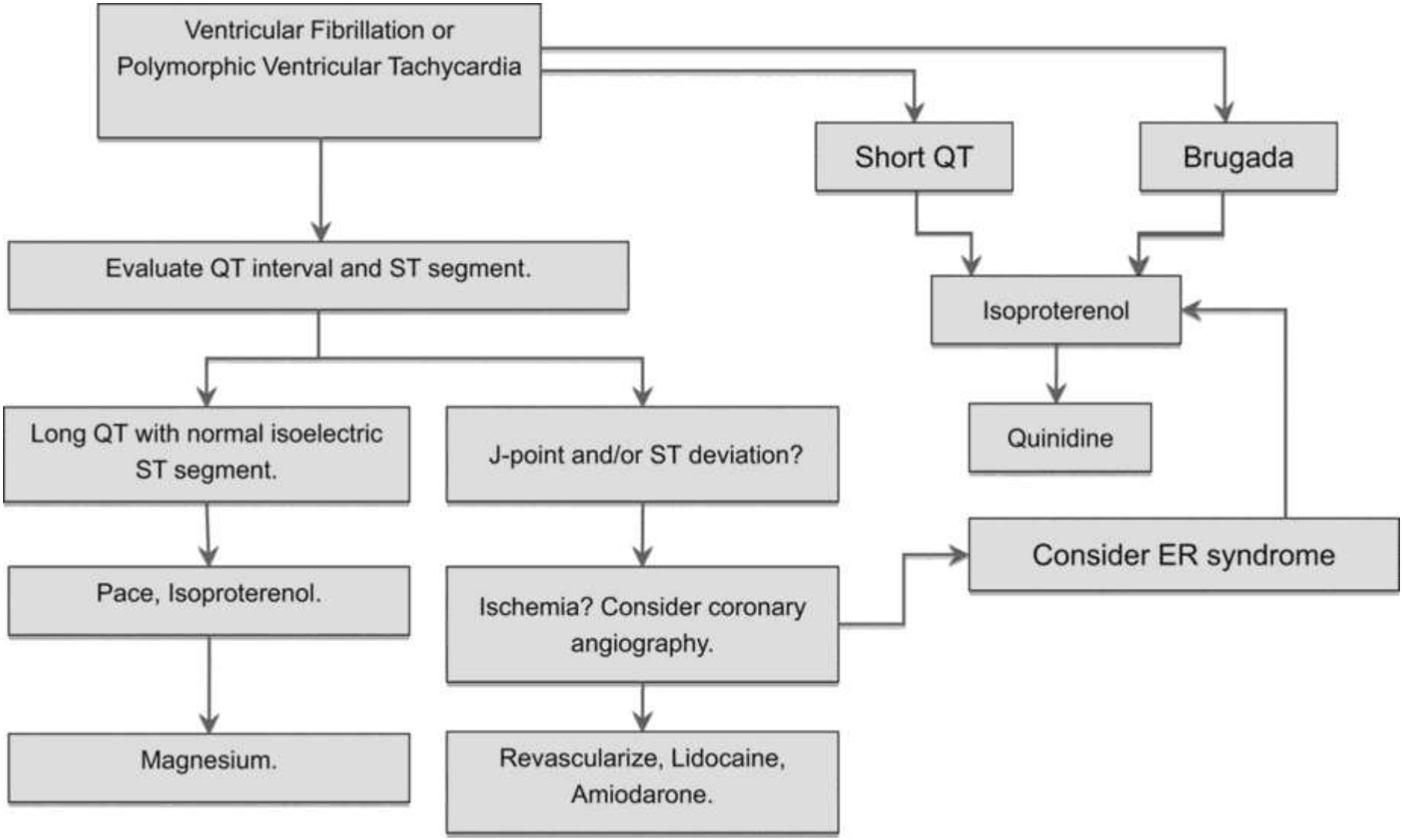
- **Usual high risk indicators in syncope evaluation should apply to this population.**

- **Familial SCD history, palpitations prior to syncope, and syncope in the supine position point to increased risk.**

- **The sensitivity of EP studies in ERS to predict SCD is very low at 34%.**

- **Subcutaneous implanted recording devices might prove useful**


Patient with early repolarization with;
Aborted Sudden Cardiac Death
Syncope
Palpitations
Chest Pain
Undertake systematic evaluation*
Further investigation and management based on clinical assessment independent of early repolarization
Other etiologies excluded and early repolarization augmented immediately preceding VF*
Early Repolarization Syndrome
Other etiologies excluded and baseline or provoked high-risk ER pattern or cardiac arrest occurs during sleep/at rest*
Early Repolarization Syndrome probable


Ventricular Fibrillation or Polymorphic Ventricular Tachycardia
Short QT
Brugada
Evaluate QT interval and ST segment.
Isoproterenol
Long QT with normal isoelectric ST segment.
J-point and/or ST deviation?
Quinidine
Consider ER syndrome
Pace, Isoproterenol.
Ischemia? Consider coronary angiography.
Magnesium.
Revascularize, Lidocaine, Amiodarone.

# ACC/AHA/HRS Guidelines on ERS

| | |
|---|---|
| Class I | 1. ICD implantation **is recommended** in patients with a diagnosis of early repolarization syndrome who have survived a cardiac arrest. |
| Class IIa | 2. Isoproterenol infusion **can be useful** in suppressing electrical storms in patients with a diagnosis of early repolarization syndrome.<br>3. Quinidine in addition to an ICD **can be useful** for secondary prevention of VF in patients with a diagnosis of early repolarization syndrome. |
| Class IIb | 4. ICD implantation **may be considered** in symptomatic family members of early repolarization syndrome patients with a history of syncope in the presence of ST segment elevation >1mm in 2 or more inferior or lateral leads.<br>5. ICD implantation **may be considered** in asymptomatic individuals who demonstrate a high-risk early repolarization ECG pattern (high J-wave amplitude, horizontal/descending ST-segment) in the presence of a strong family history of juvenile unexplained sudden death with or without a pathogenic mutation. |
| Class III | 6. ICD implantation **is not recommended** in asymptomatic patients with an isolated early repolarization ECG pattern. |

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# Early Repolarization Pattern and Risk for Arrhythmia Death

## A Meta-Analysis

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*Guangzhou, China*

**Objectives** A meta-analysis was performed to determine the risk and incidence rate of arrhythmia death, cardiac death, and all-cause death in the general population with the early repolarization pattern (ERP).

**Background** The ERP has recently been associated with vulnerability to ventricular fibrillation in case-control studies. However, the prognostic significance of the ERP in the general population is controversial.

**Methods** Relevant studies published through July 31, 2012, were searched and identified in the MEDLINE and Embase databases. Studies that reported risk ratio estimates with 95% confidence intervals (CIs) for the associations of interest were included. Data were extracted, and summary estimates of association were obtained using a random-effects model.

**Results** Of the 9 studies included, 3 studies reported on arrhythmia death (31,981 subjects, 1,108 incident cases during 726,741 person-years of follow-up), 6 studies reported on cardiac death (126,583 subjects, 10,010 incident cases during 2,054,674 person-years of follow-up), and 6 studies reported on all-cause death (112,443 subjects, 22,165 incident cases during 2,089,535 person-years of follow-up). The risk ratios of the ERP were 1.70 (95% CI: 1.19 to 2.42; $p = 0.003$) for arrhythmia death, 0.78 (95% CI: 0.27 to 2.25; $p = 0.63$) for cardiac death, and 1.06 (95% CI: 0.87 to 1.28; $p = 0.57$) for all-cause death. The estimated absolute risk differences of subjects with the ERP were 70 cases of arrhythmia death per 100,000 subjects per year. J-point elevation ≥ 0.1 mV in the inferior leads and notching configuration had an increased risk for arrhythmia death in subgroup studies.

**Conclusions** The ERP was associated with increased risk and a low to intermediate absolute incidence rate of arrhythmia death. Further study is needed to clarify which subgroups of subjects with the ERP are at higher risk for arrhythmia death. (J Am Coll Cardiol 2013;61:645–50) © 2013 by the American College of Cardiology Foundation

# Thank You