

Brugada syndrome

Ji-Eun Ban, MD.

Ewha University Medical Center

Seoul, Korea



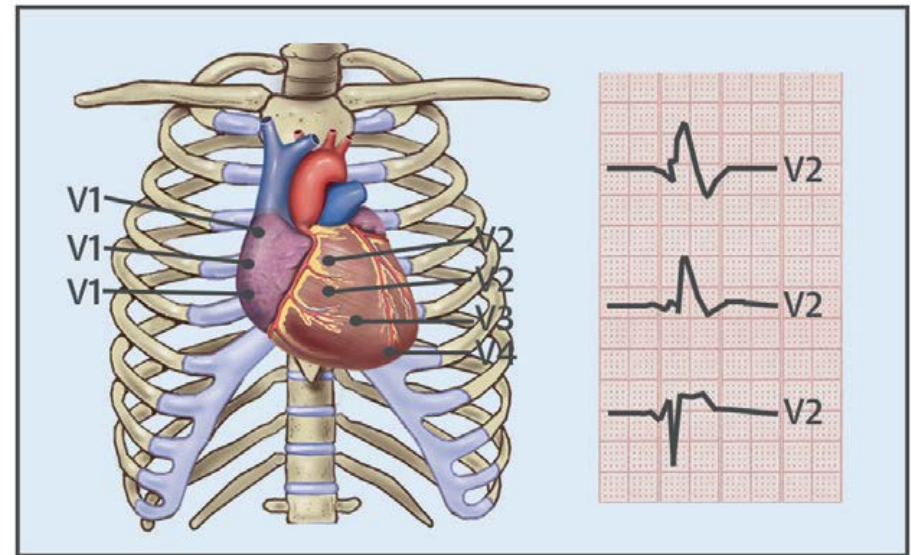
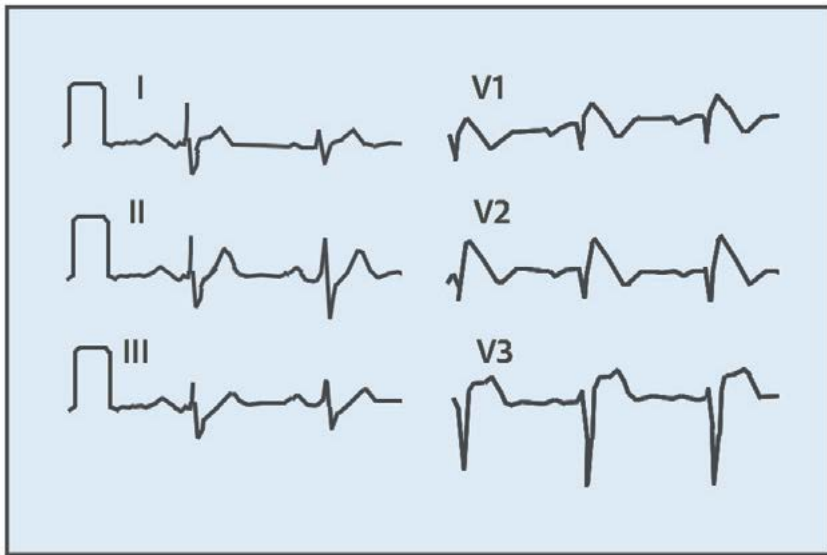
- Conflict of interest : non declared



Brugada Syndrome

1992, 1st report

Brugada, J. et al. J Am Coll Cardiol. 2018;72(9):1046–59.



Coved type ST-segment in V1-V2

V1-V2 positioned in the 2nd, 3rd or 4th ICS

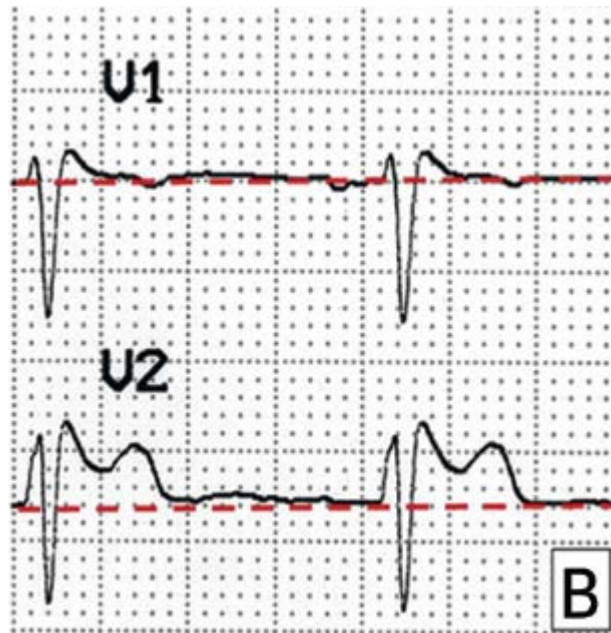
- spontaneously or provocative drug test with iv sodium-channel blockers (ajmaline, flecainide, procainamide, or pilsicainide)

Electrocardiographic Patterns

Type 1 ("coved type")



Type 2 ("saddle-back type")



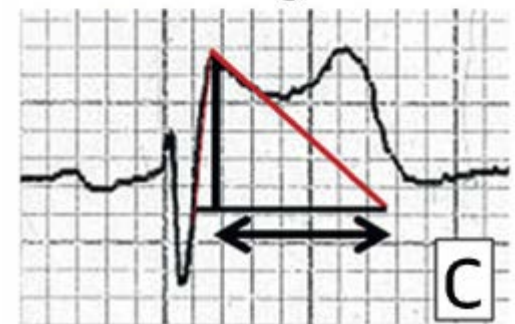
: only suggestive of BrS

Additional criteria

β angle $\geq 58^\circ$

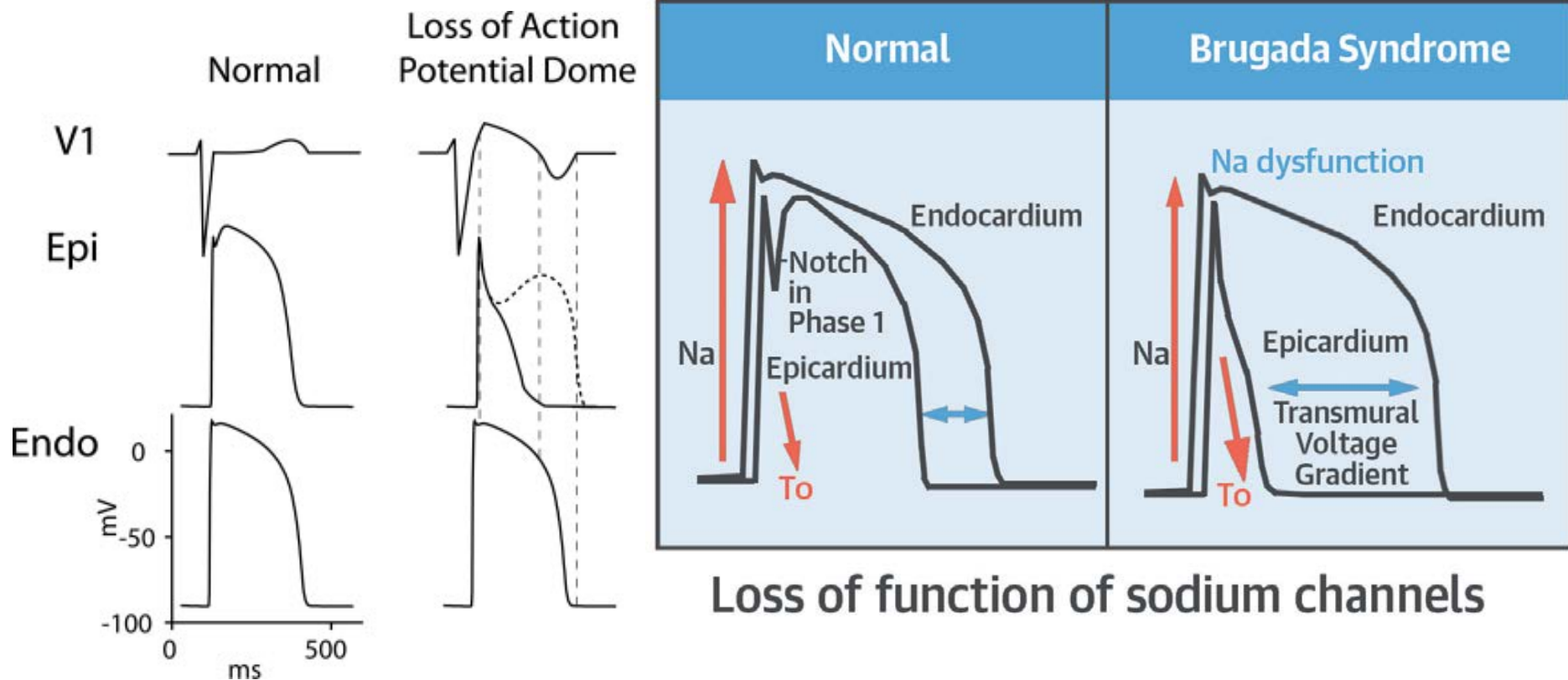


Base of triangle ≥ 4 mm

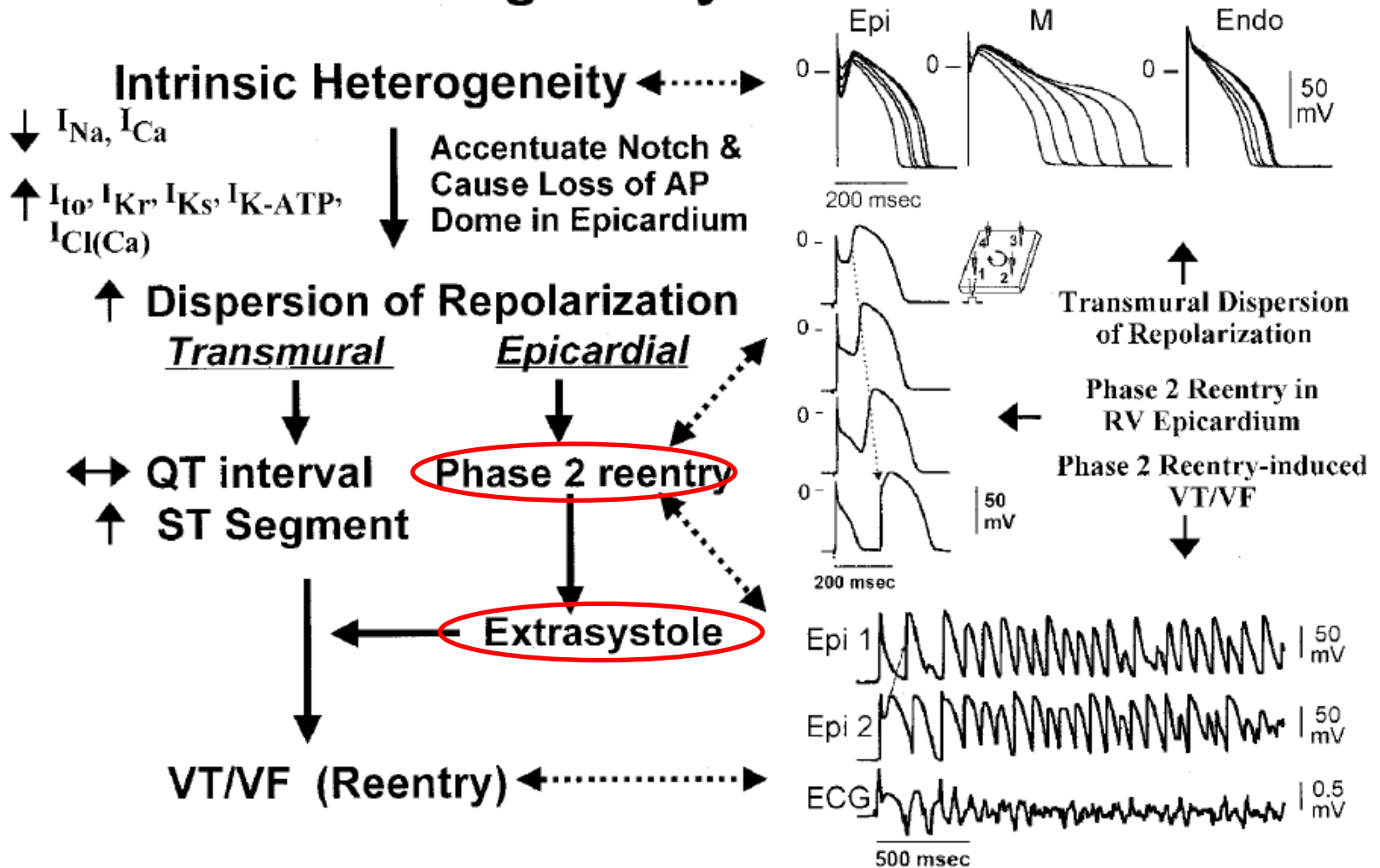


Mechanisms of the Brugada ECG pattern.

Circ Arrhythm Electrophysiol. 2010;3:283-290



Ionic Basis and Arrhythmia Mechanisms



Antzelevitch C. *J Cardiovasc Electrophysiol* 2001; 12:268-272

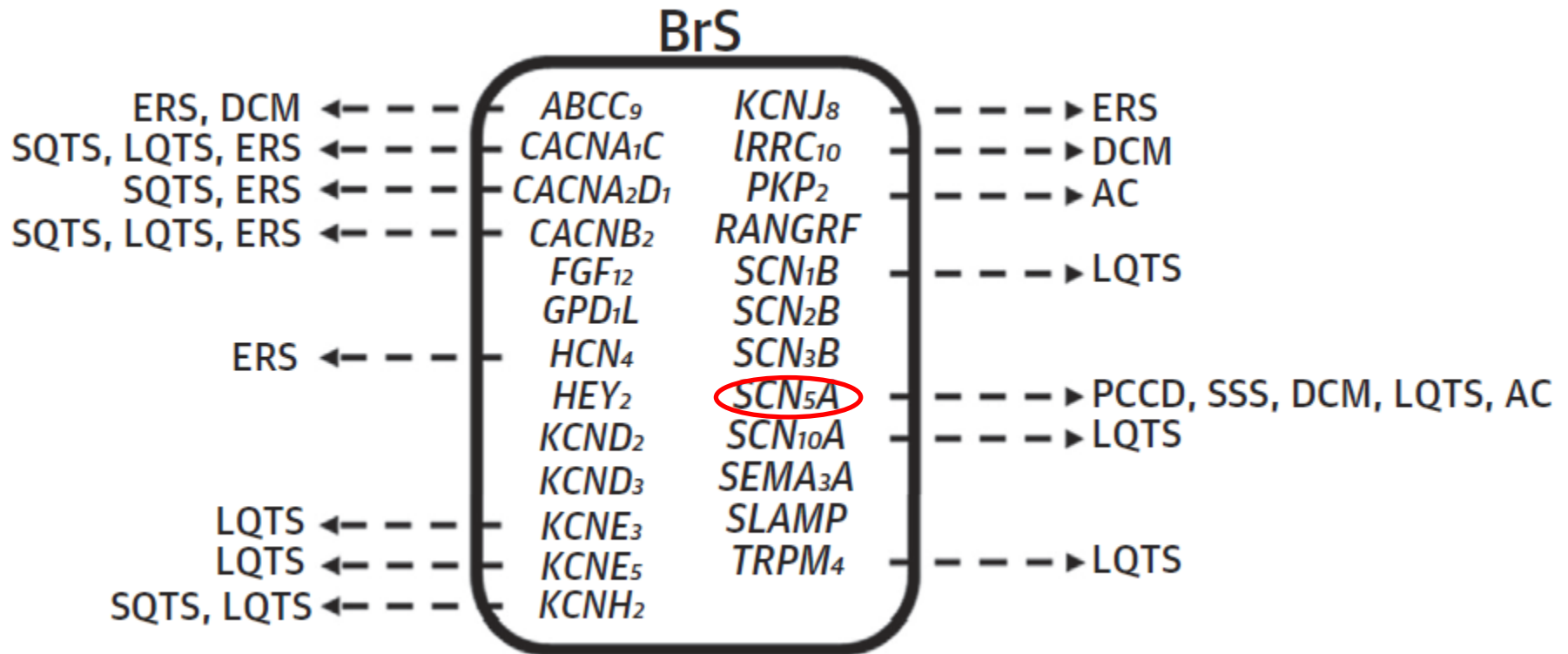


Genetic basis

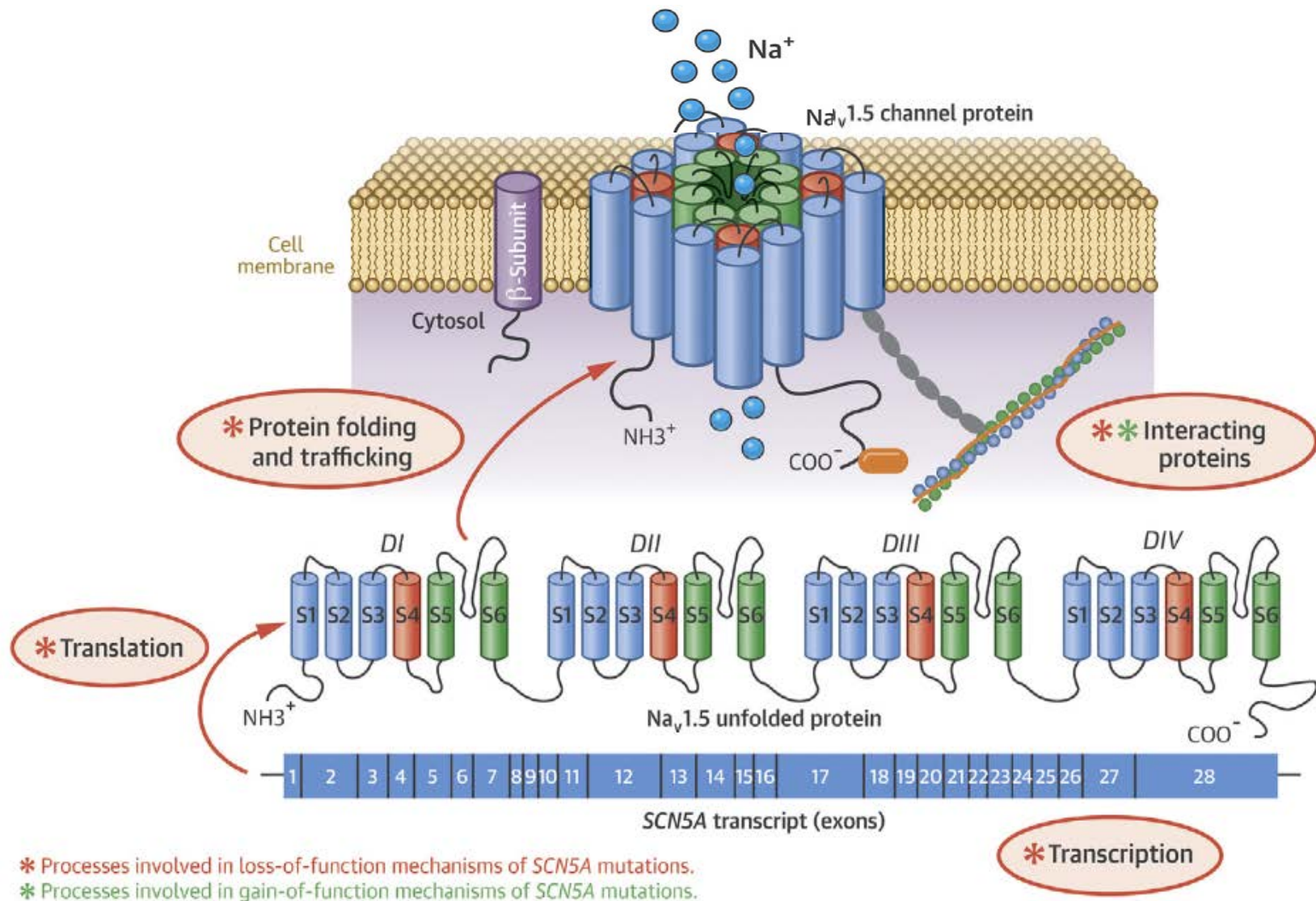
Brugada, J. et al. J Am Coll Cardiol. 2018;72(9):1046–59.

Genetic mutations alter ion channel functions.

Chen Q et al. 1998 Nature



Molecular structure of the SCN5A transcript

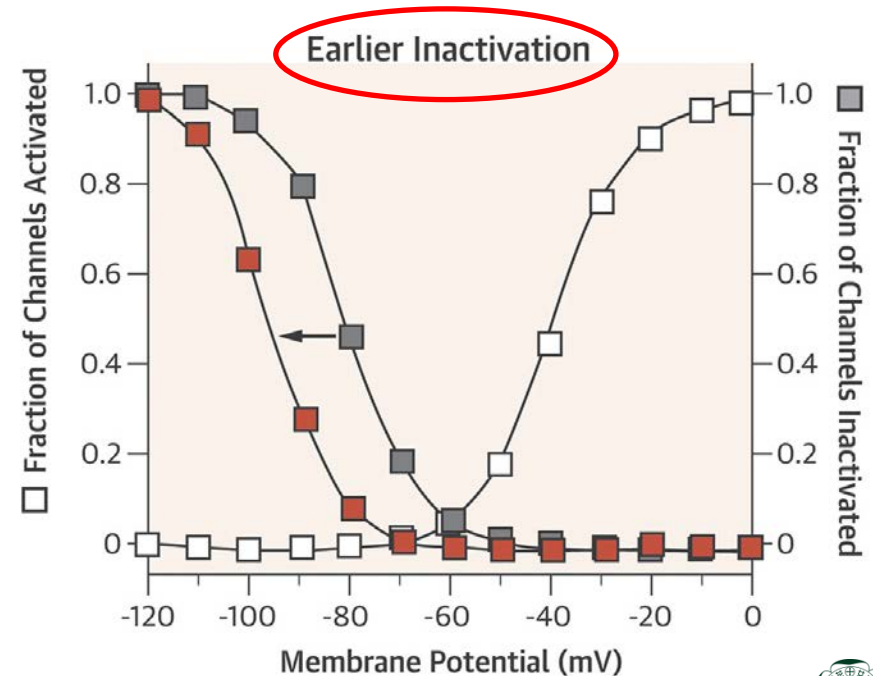
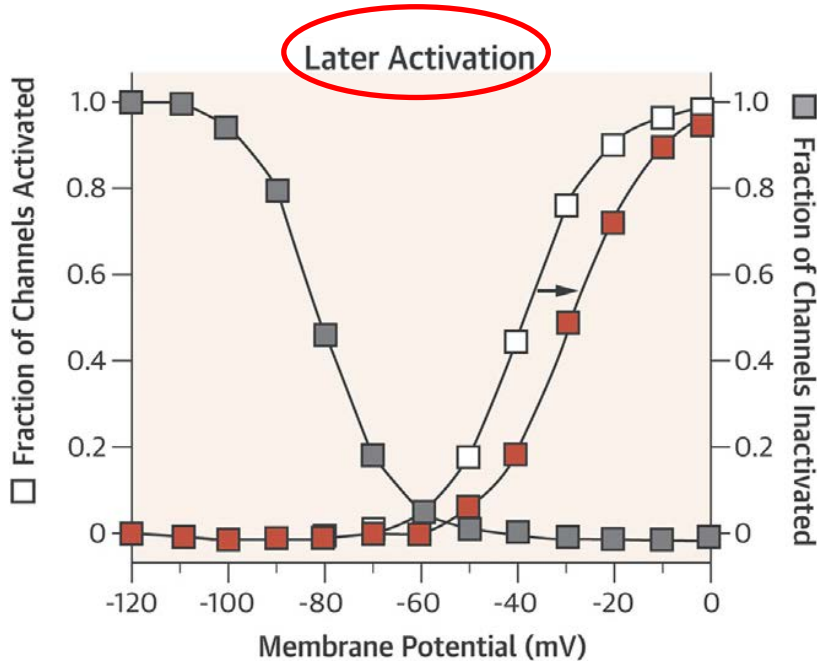
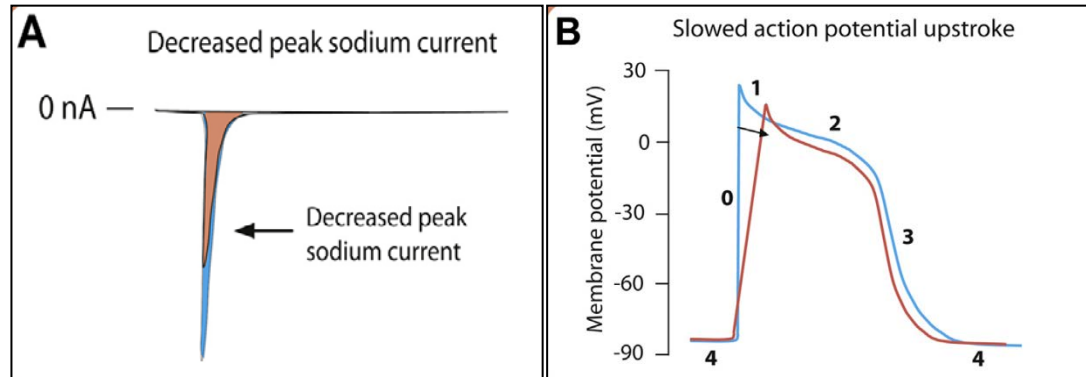


Wilde, A.A.M. et al. *J Am Coll Cardiol EP*. 2018;4(5):569–79.



Loss of function mutations in SCN5A

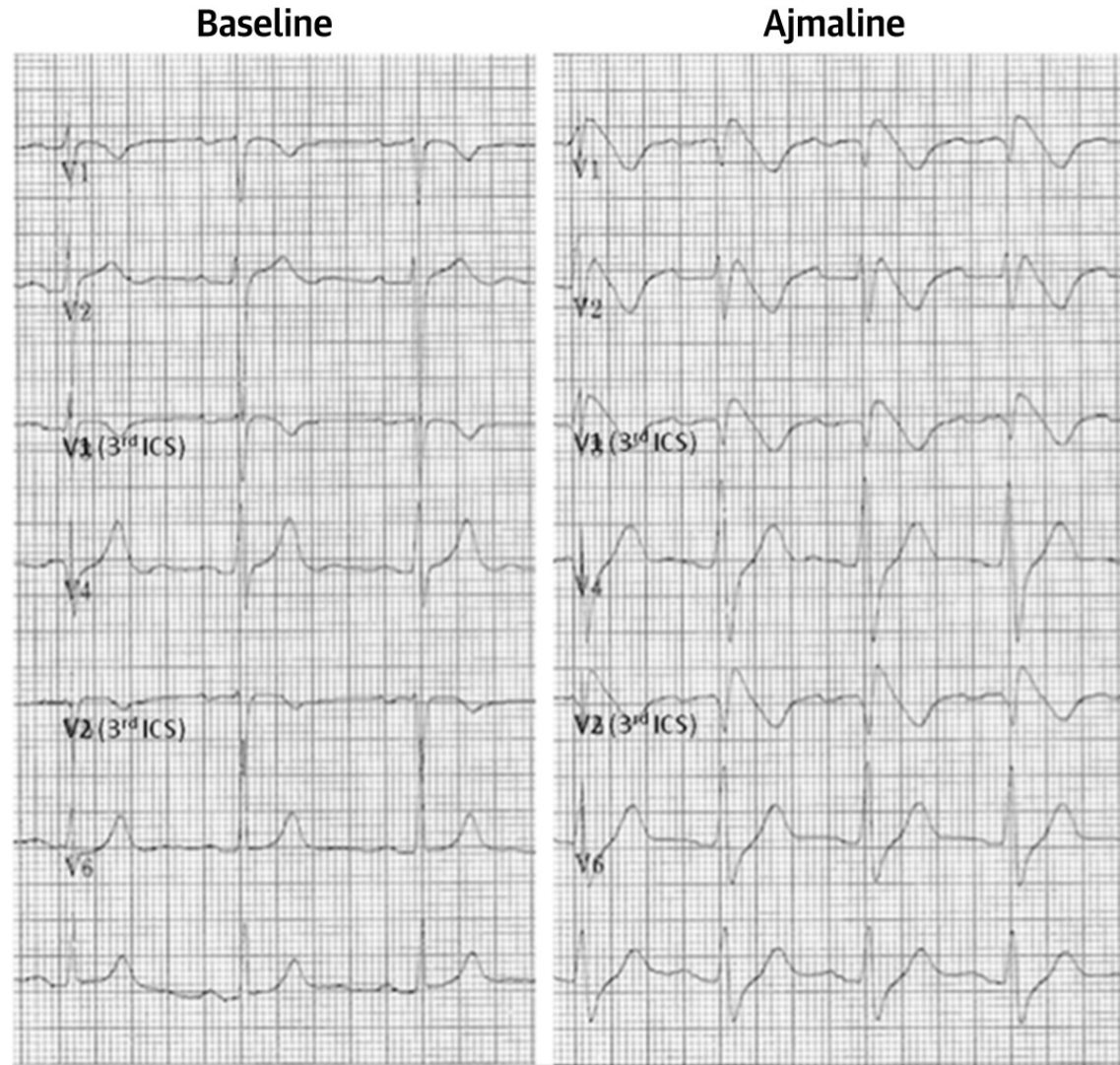
Wilde, A.A.M. et al. *J Am Coll Cardiol EP*. 2018;4(5):569–79.



Pharmacological Test

sodium-channel blocking agent

- Intravenous Ajmaline, and flecainide
 - Iv Procainamide
 - po flecainide, propafenone
- 25% of false-negative



Clinical manifestations

*Sx often occur during rest or sleep, during a febrile state or with vagotonic conditions, but rarely during exercise

(syncope or SCD, 17-42 %)

*Mean age of sudden death of 41 ± 15 years

* Male predominance ($\uparrow 8-10$ times)



febrile-induced VF in type 1 ECG

Morita H. HR 2018

- 1st : 2-year-old boy with influenza
 - VT of various configurations during febrile episode
- More than 100 reports of fever induced VF
- Frequent in **pediatric** patients
- Frequently associated with an **SCN5A mutation**.

***Mechanism of fever-induced ECG change and arrhythmia in BrS**

- changes in sodium channel function
 - : Sodium current reduction during hyperthermia
 - change the action potential morphology & promote VF



Gender differences and their mechanisms

- Male predominance

J Arrhythm 2016, HR 2018

-Asian countries : 90%– 96%, European : 60%–70%

- women had lower incidences of Sx and spontaneous type 1 ECG pattern.

Benito et al. 2008 JACC

- Mechanism

Morita H. HR 2018

long QT syndrome

: gain of function

Female predominance

Estrogen- ↑QT interval by decreasing I_{to} , I_K , and I_{K1} and increasing I_{Ca-L} .

Brugada syndrome

: loss of function

Male predominance

Testosterone- ↑ outward currents (I_{to} , I_{K1} , and I_{Ks}), decreases I_{Ca-L} , and ↓QT interval

→ action potential changes

→ repolarization heterogeneity & phase 2 reentry

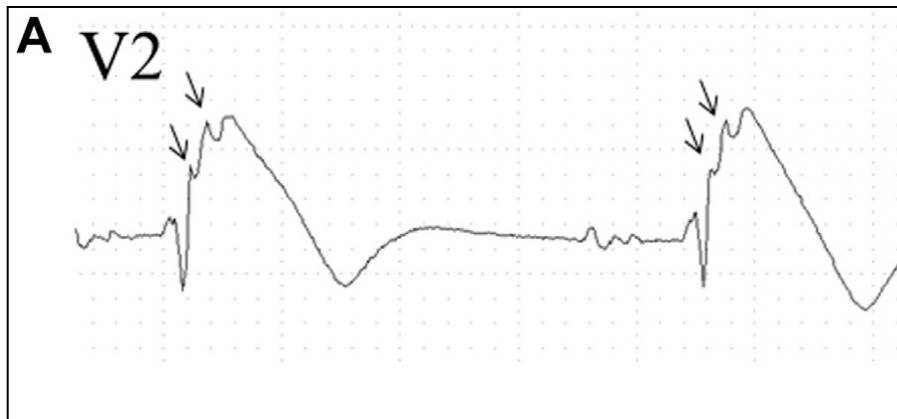


Risk stratification

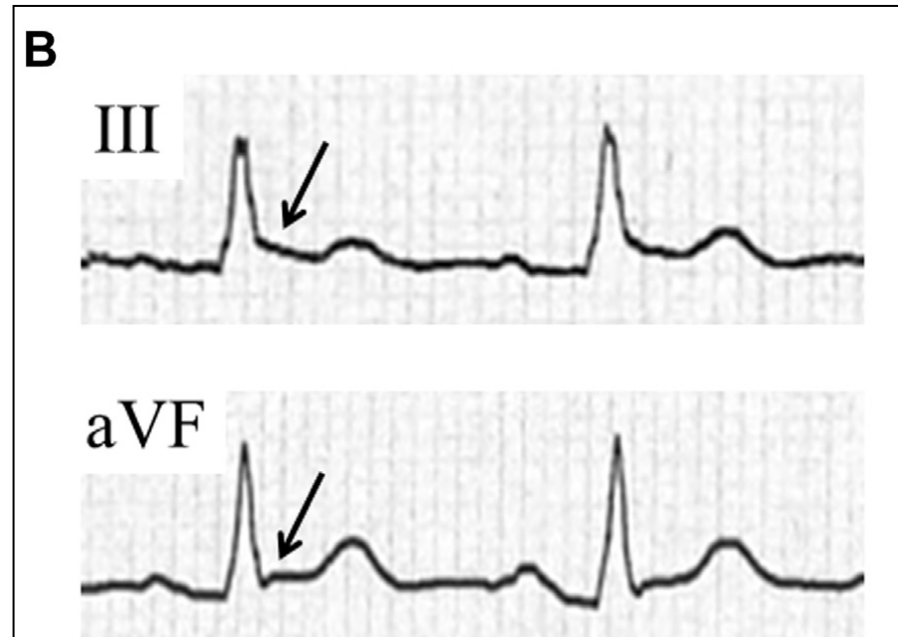
Electrocardiographic Parameters and Fatal Arrhythmic Events

246 pts (236 men; mean age, 47.6 ± 13.6 yrs) with a Brugada-type ECG

Fragmented QRS (f-QRS)

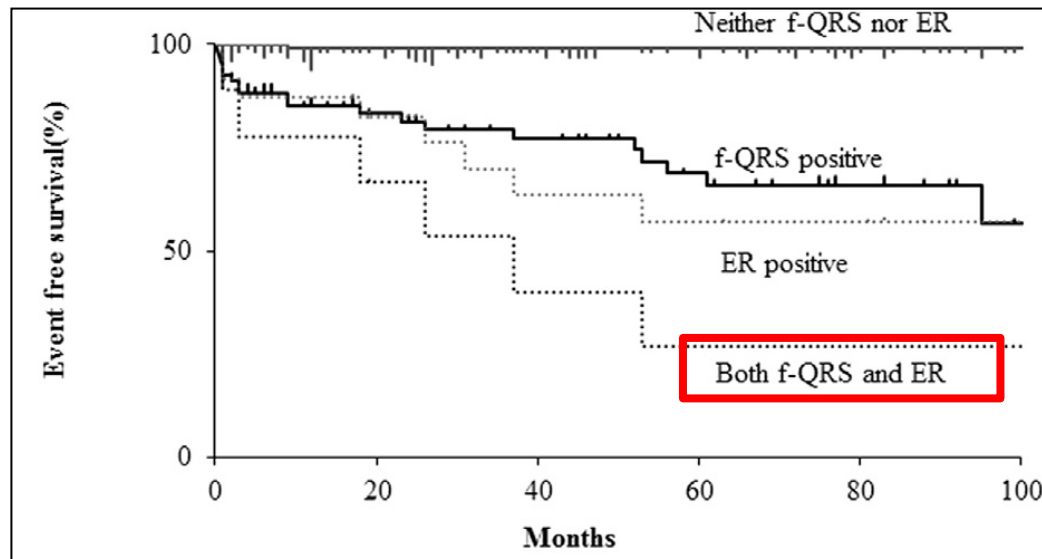
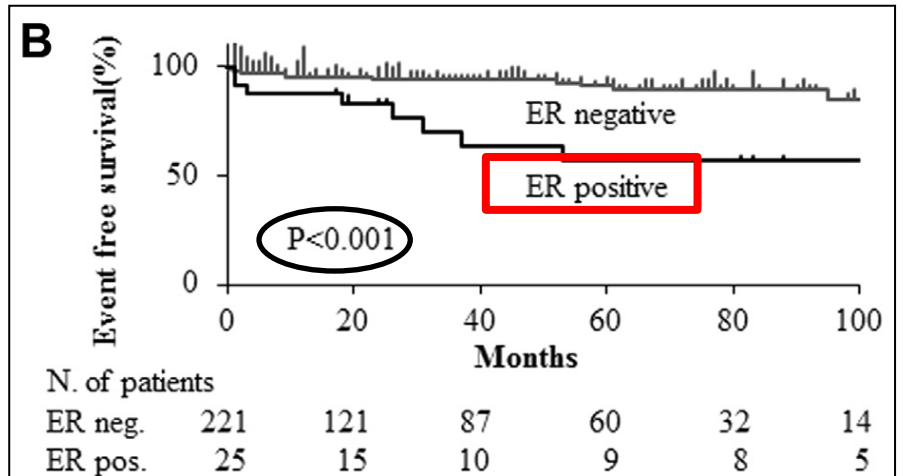
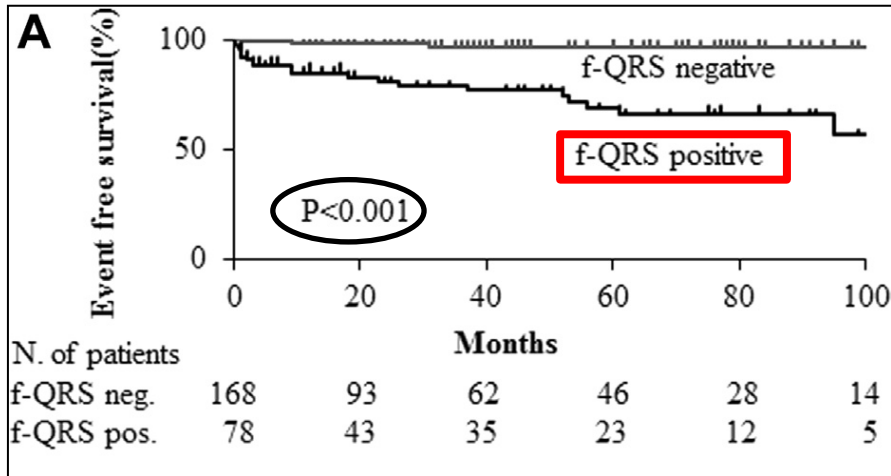


Early repolarization (ER)



Tokioka K et al. J Am Coll Cardiol 2014;63:2131-8

Kaplan-Meier Analysis of VF/SCD Events



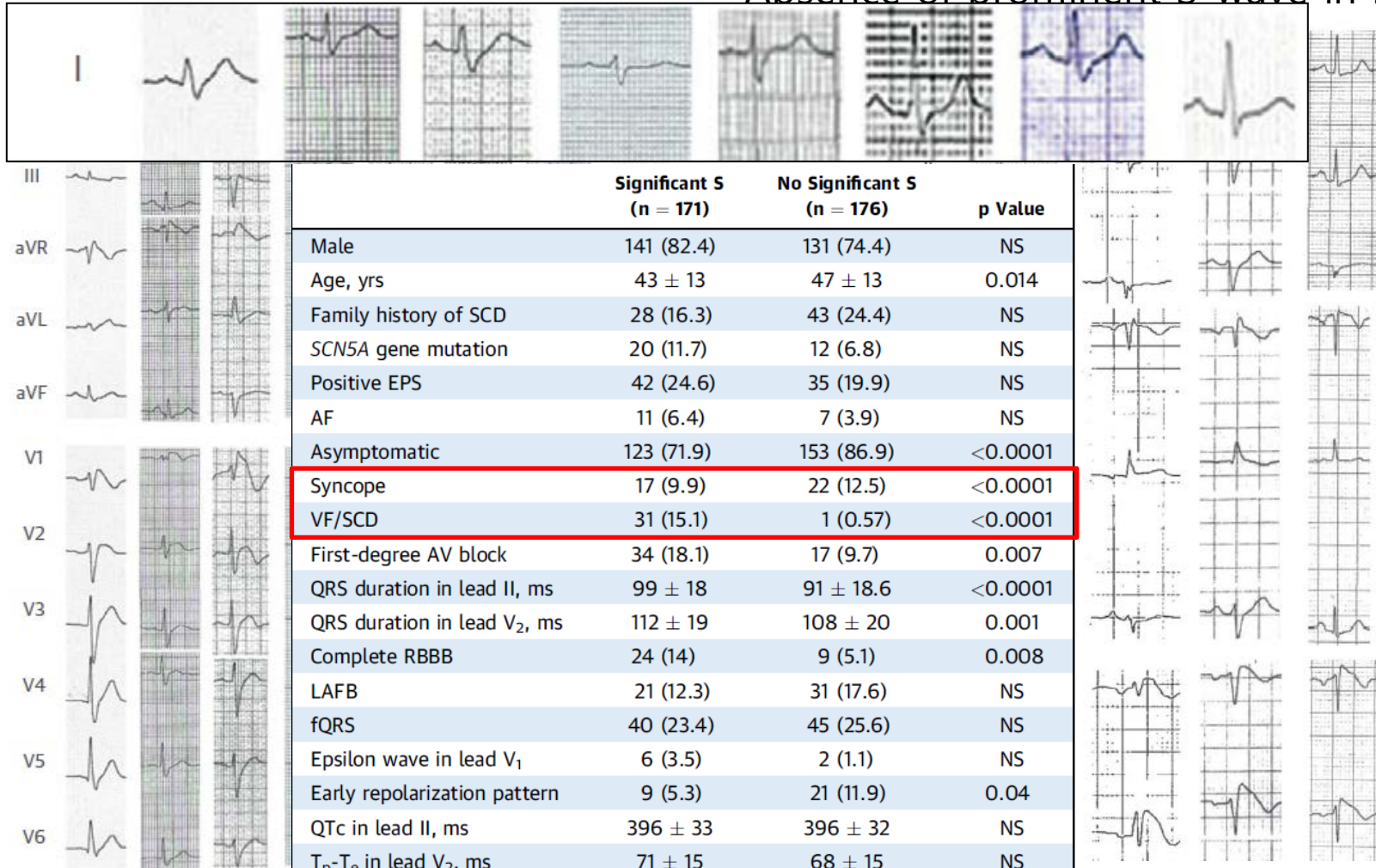
The combination of **depolarization and repolarization abnormalities** in BrS is associated with **later VF events**

S-Wave in Lead I

347 pts (78.4% male; mean age 45 ±13.1 yrs) with spontaneous type 1 BrS

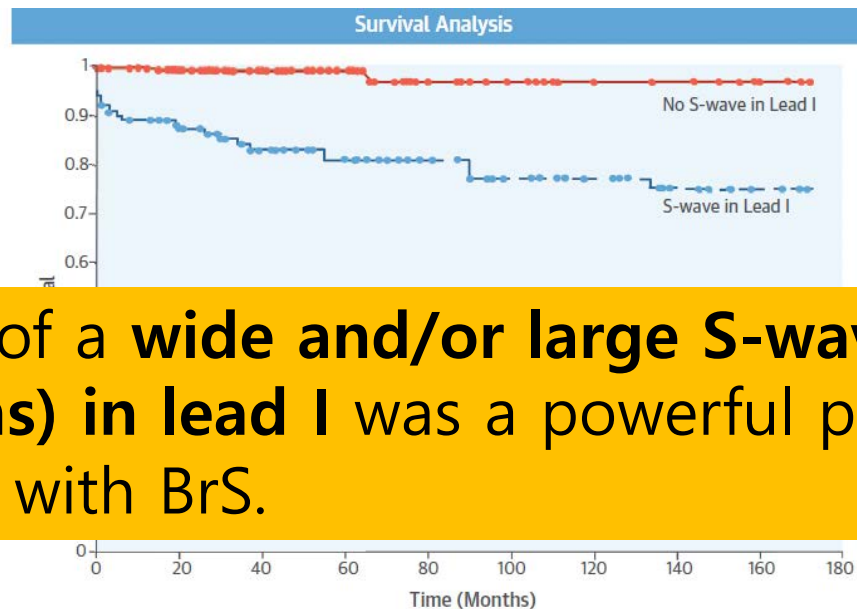
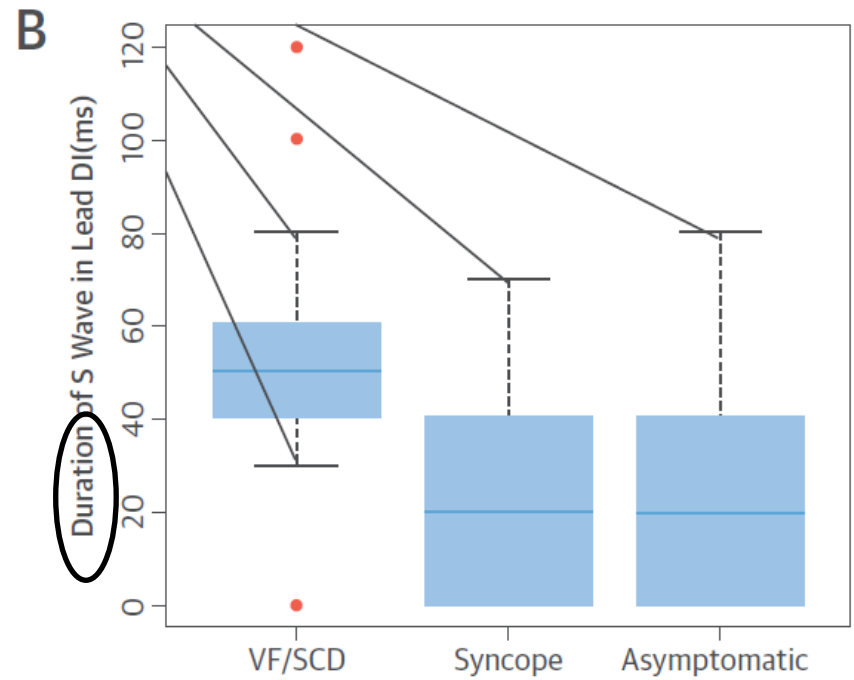
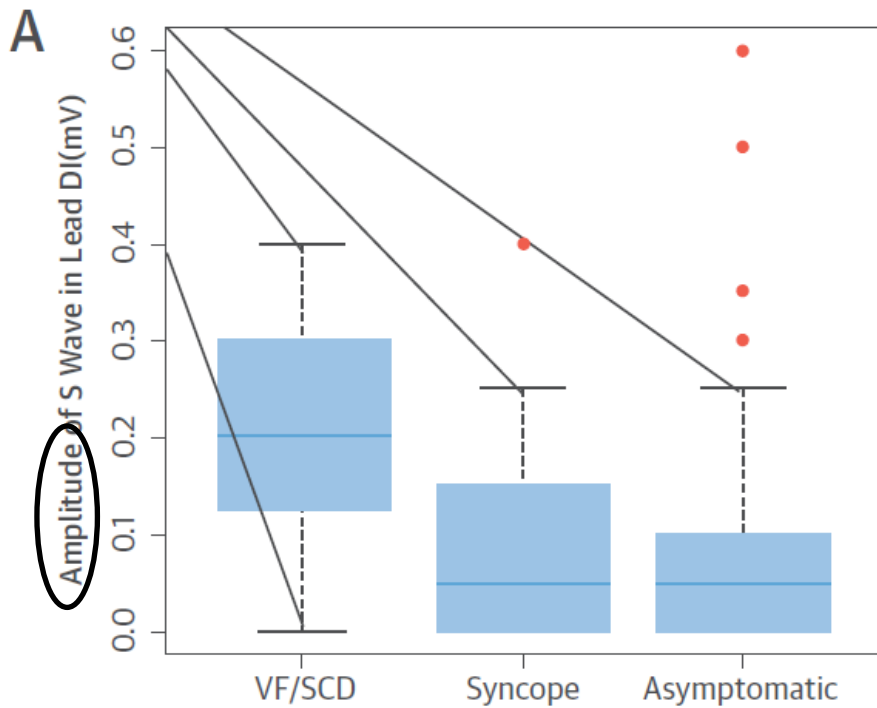
Prominent S-wave in lead I

Absence of prominent S-wave in lead I



Am J Cardiol 2016;67:1427-40





The presence of a **wide and/or large S-wave (≥ 0.1 mV and/or ≥ 40 ms)** in lead I was a powerful predictor for VF/SCD in pts with BrS.

Other risk factors

- An effective refractory period <200 ms

*J Am Coll Cardiol 2012;59:37–45.
Heart Rhythm 2012;9:242–248*

- Male gender

Benito et al. 2008 JACC

- Spontaneous AF (10-53 %)

*J Cardiovasc Electrophysiol 2006;17:577–583.
J Am Coll Cardiol 2008;51:1169–1175
J Am Coll Cardiol. 2016; 67(12):1427–40.*

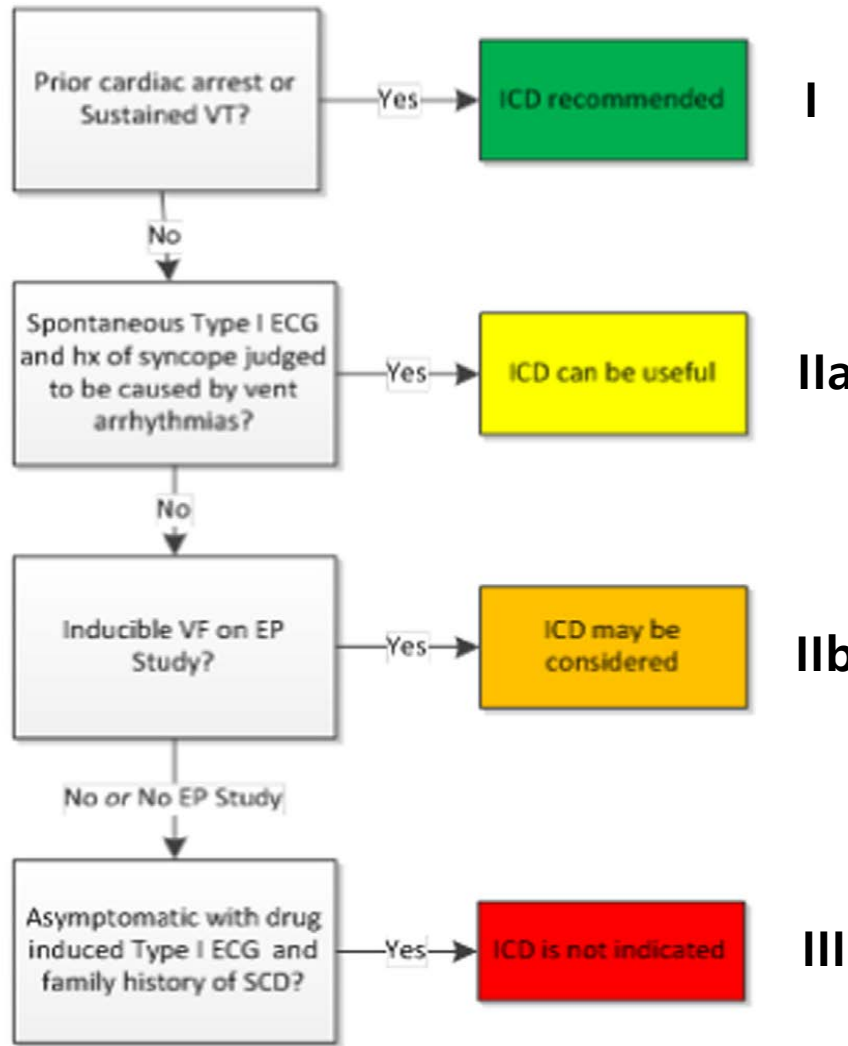
- Genetic analysis – no conclusive studies



Management

2013 HRS/EHRA/APQRS Expert Consensus Statement

ICD



EPS inducibility

*PRELUDE registry
: fail to prove that
Lack of inducibility has
negative predictive value

*FINGER registry
: inducibility did not
predict arrhythmic events



Pharmacological Treatment

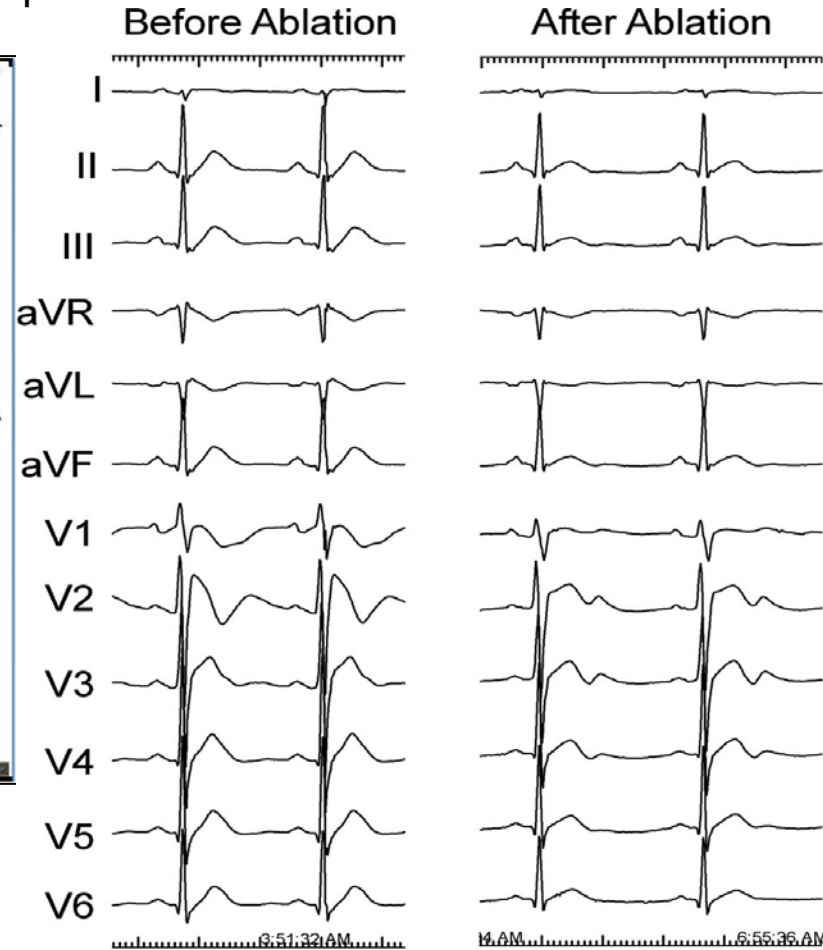
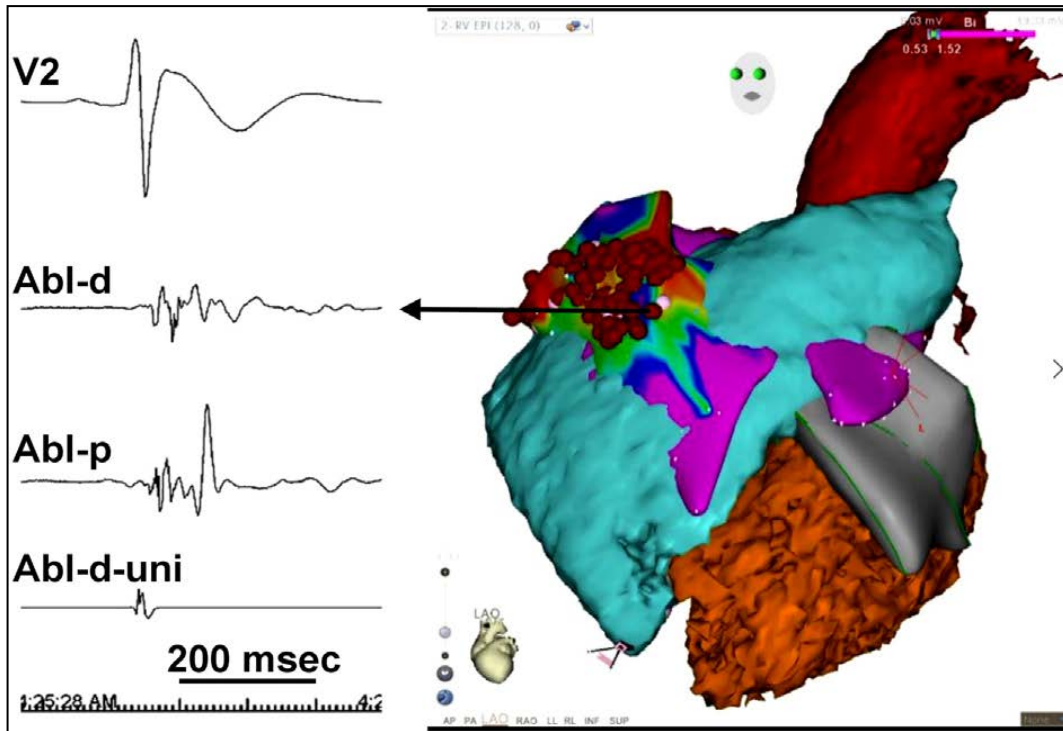
- **Isoproterenol** (: increases the L-type calcium current)
 - : Tx of electrical storm in BrS
 - controlled data are not available.
 - **Quinidine** (Class Ia : I_{to} and I_{Kr} blocker effects)
 - : prevent induction of VF
 - suppress spontaneous ventricular arrhythmias
- Ix (1) pts with multiple ICD shocks or arrhythmic storms
(2) an alternative to an ICD in children
(3) for the Tx of supraventricular arrhythmias

Belhassen B. Circ Arrhythm Electrophysiol 2016



Epicardial substrate ablation for Brugada syndrome

9 symptomatic pts with the BrS, recurrent VF episodes



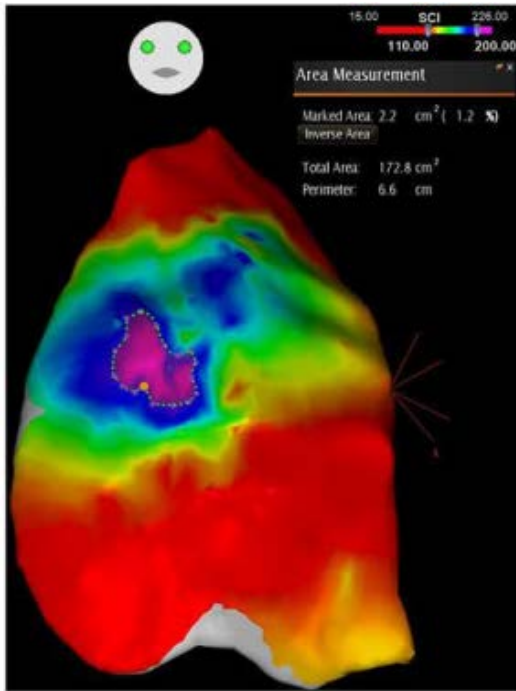
→VT/VF noninducibility (7/9), normalization of the Brugada ECG pattern (89%)

Nademanee K et al. Circulation. 2011;123:1270-1279

Heart Rhythm 2017;14:457-461

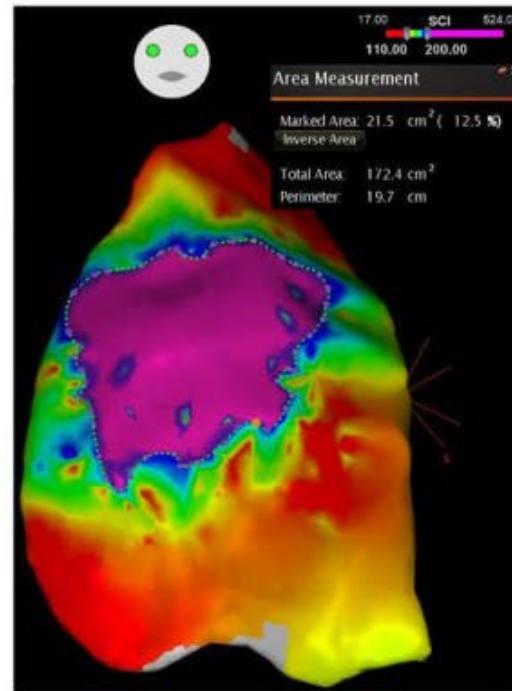
Effect of sodium channel blockers in identifying subtle epicardial substrate

Baseline



(2.2 cm²)

Ajmaline



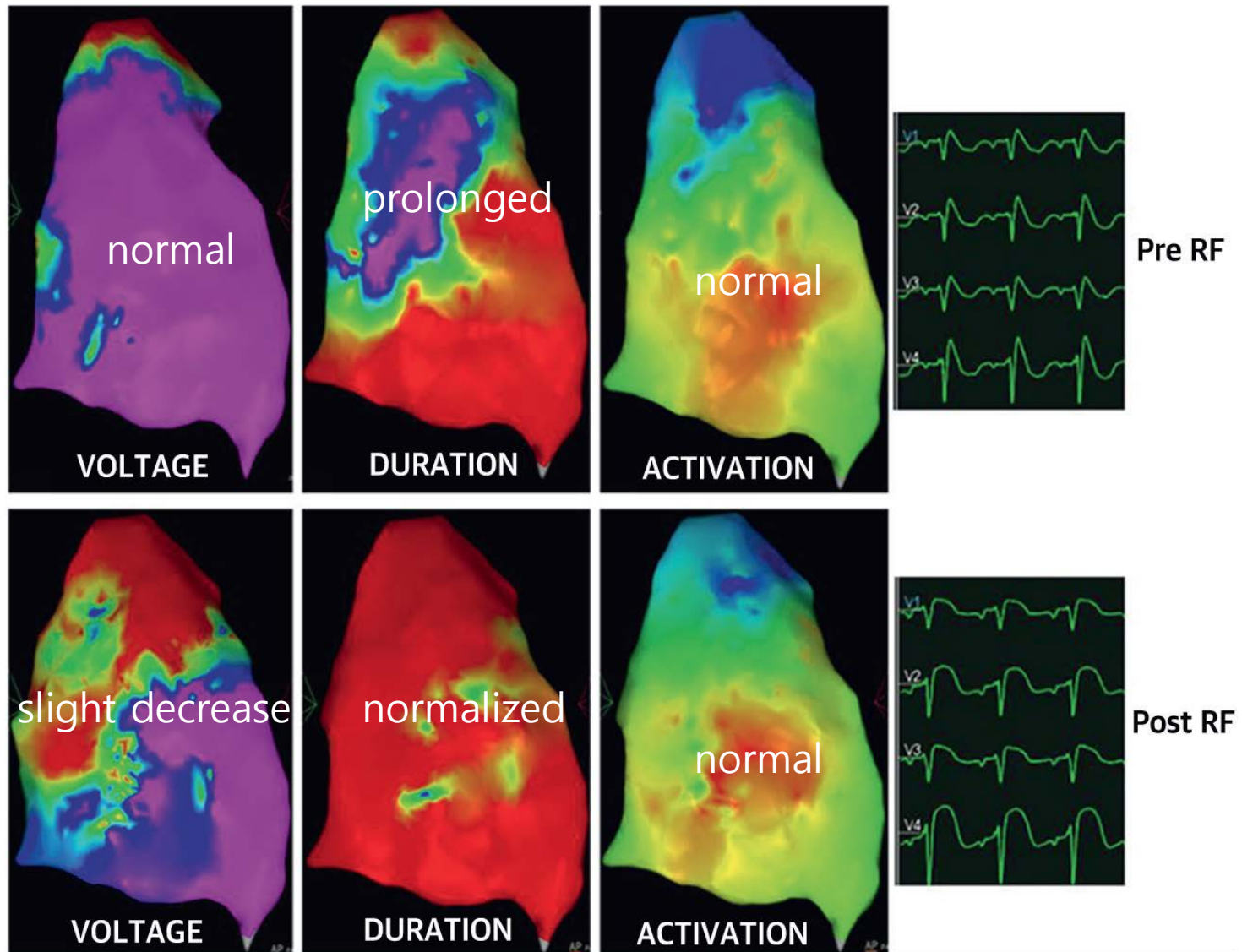
(21.5 cm²)

Epicardial color-coded duration maps

Circ Arrhythm Electrophysiol. 2017



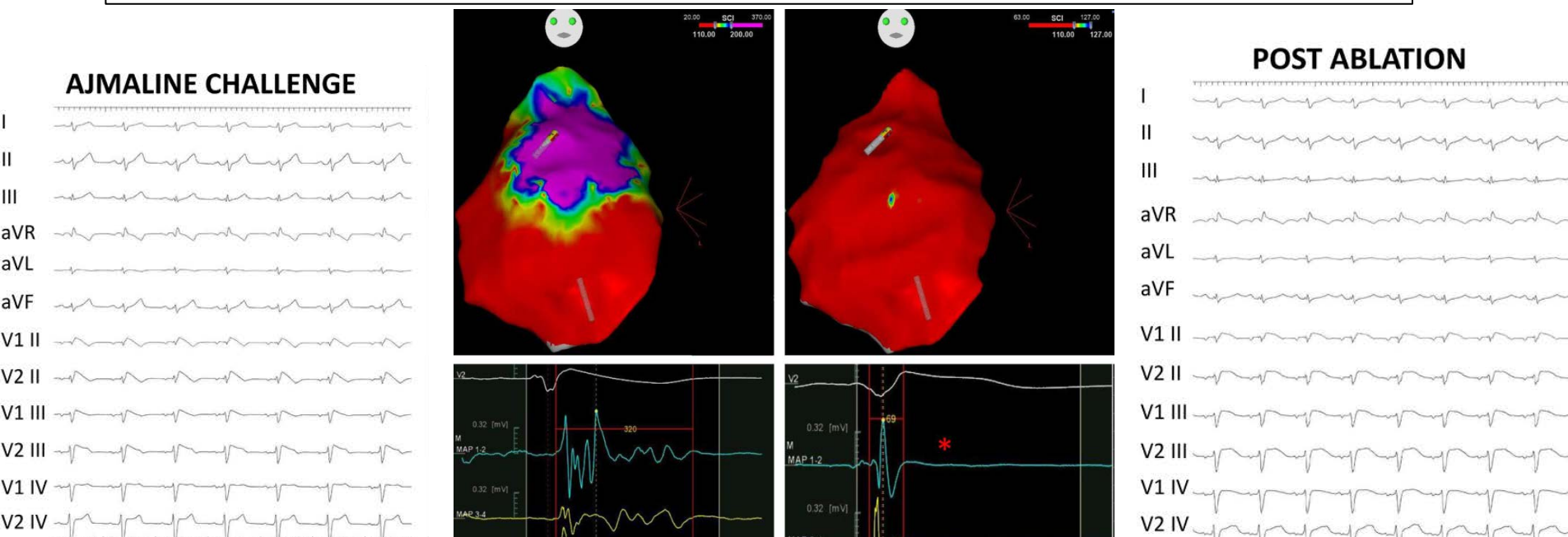
Voltage Mapping, Potential Duration Mapping, Activation mapping of the RV Epicardium



Electrical Substrate Elimination in 135 Consecutive Patients With Brugada Syndrome

Pappone C et al. Circ Arrhythm Electrophysiol. 2017

135 symptomatic Brugada syndrome pts having ICD
-63 pts, documented VT/VF (27 pts, multiple ICD shocks)
-72 pts, inducible VT/VF without ECG documentation



Substrate based-radiofrequency ablation results in ECG normalization and VT/VF noninducibility.

Summary

- In Brugada syndrome, SCN5A mutations are associated with $\text{Na}_v1.5$ loss-of-function leading to a decreased I_{Na} .
- Detection of high risk Brugada syndrome is an important issue in the clinical setting.
- the ICD is the most accepted therapy to protect patients at risk.
- Substrate based epicardial ablation in selected patients has been used as a new therapy.



Thank you for your attention !