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THE UNIVERSITY OF BRITISH COLUMBIA



Brugada Syndrome: Understanding Diagnostic Tests And Who Is At Risk?

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October 16 - 18
14th EDITION **2015**





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**NO CONFLICT OF
INTEREST TO
DECLARE**

Hot Topics in EP!

Venice Arrhythmia 2013

Hereditary Arrhythmogenic Syndromes

11.00-13.00

THE “BOXING RING” OF ARRHYTHMIC SYNDROMES. THE HOTTEST DEBATES IN ELECTROPHYSIOLOGY (1)

Chairmen: S.G. Priori / Pavia, Italy - D.P. Zipes / Indianapolis, USA

The pathophysiology of Brugada syndrome, “re” or “de”:

- Brugada syndrome is a repolarization disease
C. Antzelevitch / Utica, USA
- Brugada syndrome is a depolarization disease
A.A. Wilde / Amsterdam, The Netherlands

Electrophysiologic studies (EPS) in Brugada syndrome

- EPS are crucial for selecting therapy
J. Brugada / Barcelona, Spain
- EPS are useless for selecting therapy
S. Viskin / Tel Aviv, Israel

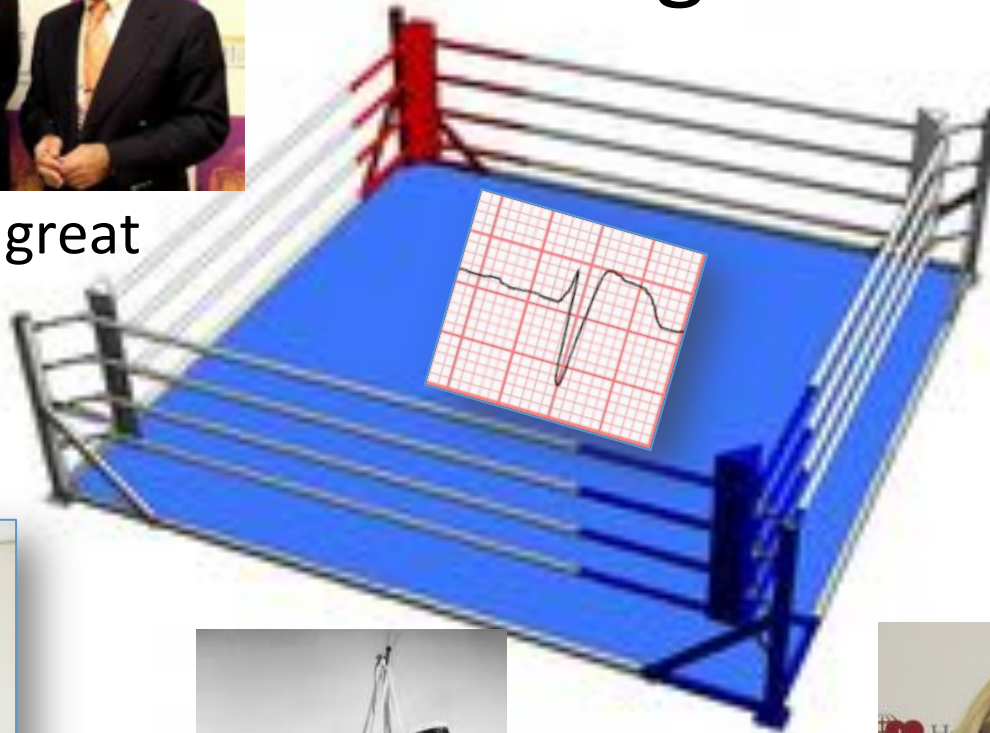
Brugada Boxing



EP testing is great



Brugada is Repol



EP testing is
not useful



Brugada is Depol



Case Presentation

- 37 year old male presents to the emergency room with a productive cough and pleuritic chest pain, and an ECG was performed.
- He is otherwise well, and experienced syncope in the shower 18 months ago when he was suffering from gastroenteritis symptoms
- On examination, he looks unwell with a frequent minimally productive cough of clear sputum. Temperature 37.8 °C
- He has no family history of sudden death, and he has 2 children that are 8 and 6 years old. He has a brother with epilepsy.

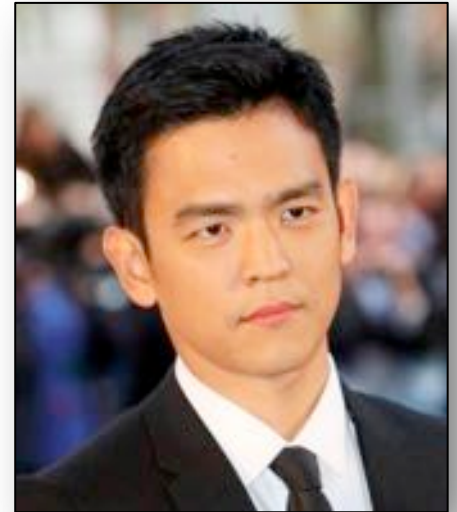


Resting ECG with Fever



The Brugada Syndrome

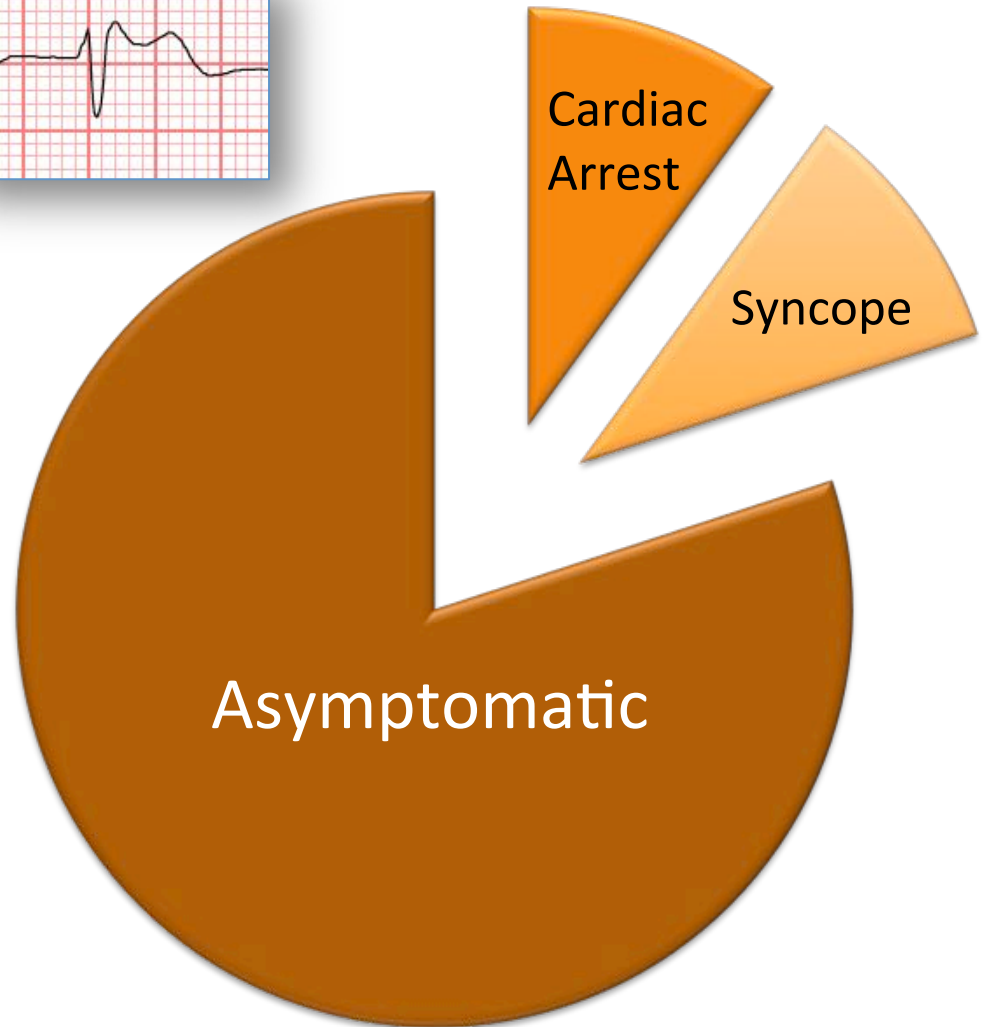
- Sudden death (due to VF) often at night or rest
- Much more common in males (9:1), SE Asian men (SUDS)
- J point elevation in V_1 - V_3 and “RBBB” not always present; exacerbated by Na^+ channel block, β -blockers; improved by isoproterenol/exercise.
- Syncope/SCD may be provoked by fever, large meals, alcohol.
- SCN5A mutations causing loss of I_{Na} function— now identified in ~20% of affected subjects.
- Other genes: GPD1L, SCN1B, calcium channel genes, KCNE3, SCN3B.



Profile of Brugada



- Most patients with a Brugada referral will have an asymptomatic type 2 ECG
- Most will not have a positive family history or affected family members
- Most will not have a positive genetic test

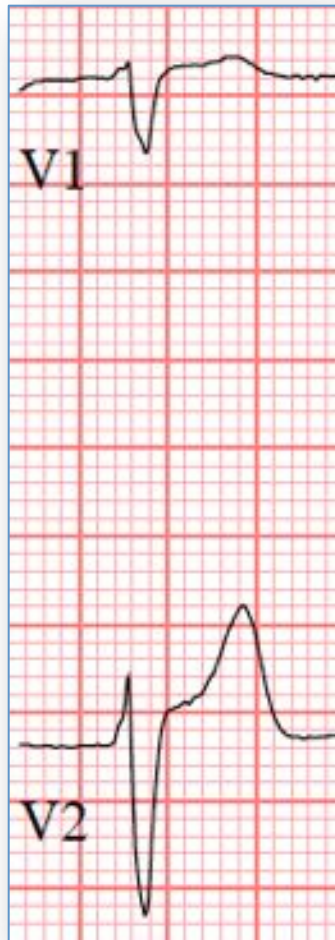


Brugada Referral to the Inherited Arrhythmia Clinic

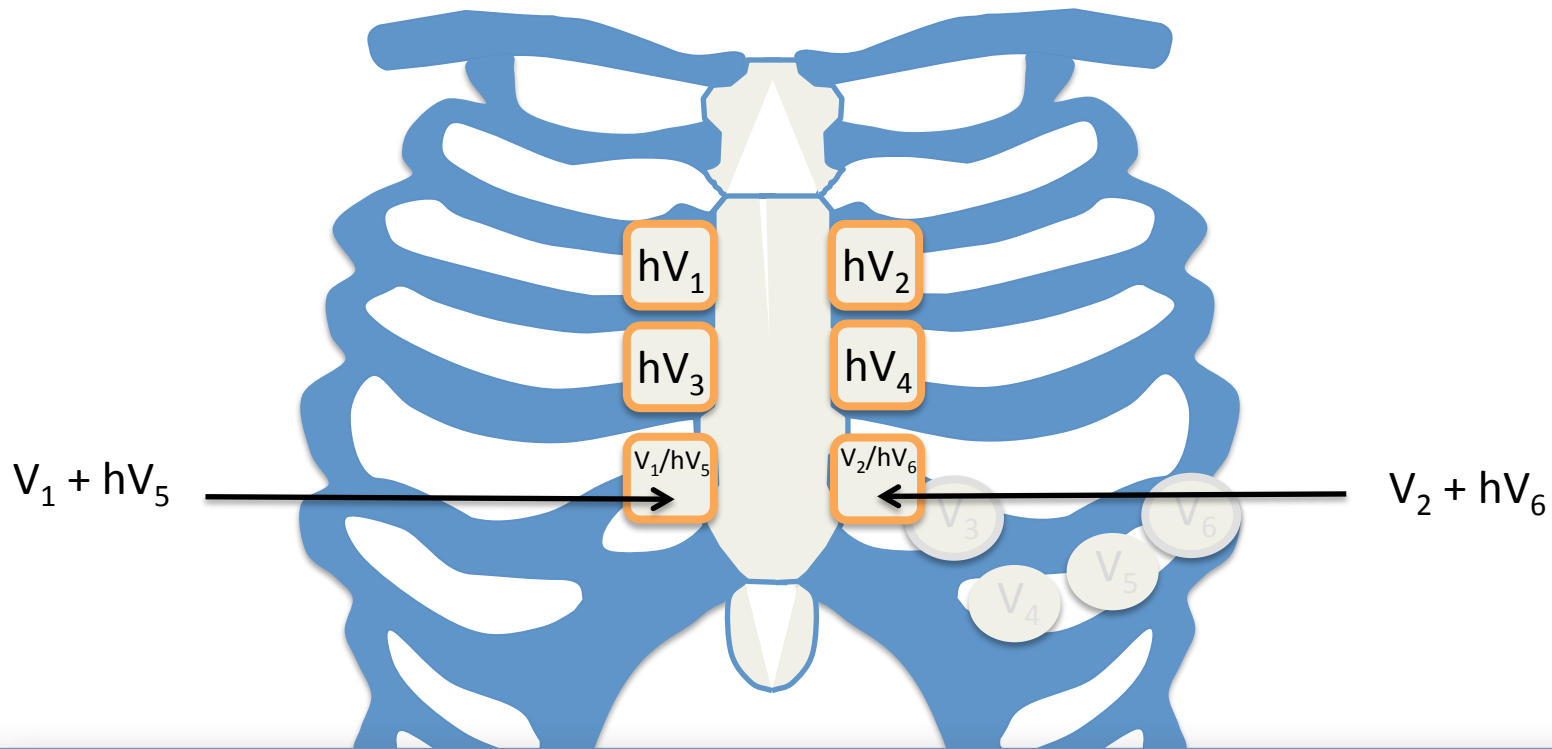
- Medical history
- Record review of all ECGs
- Formal 3 generation pedigree
- Standard 12 lead ECG
- High precordial lead ECG
- Signal averaged ECG
- Echo if not performed



Do Not Forget to Review all ECGs: Brother with BS



High Precordial Leads for Procainamide Infusion

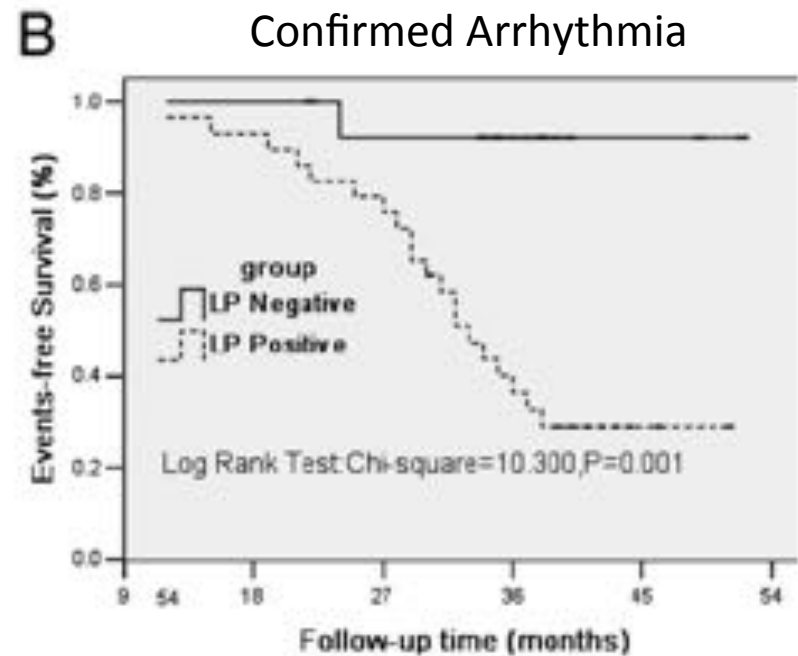
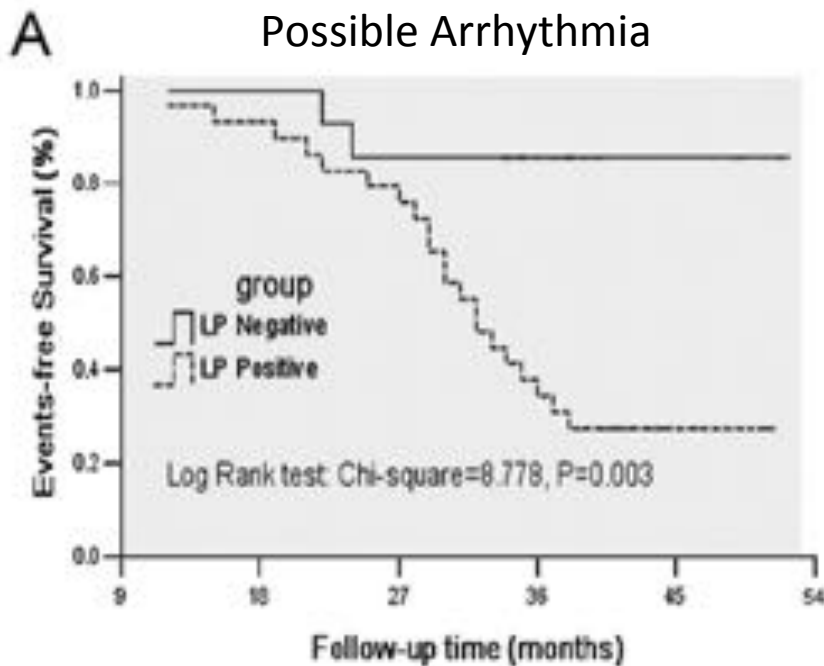


3. Brugada Syndrome (BrS) Expert Consensus Recommendations on Brugada Syndrome Diagnosis

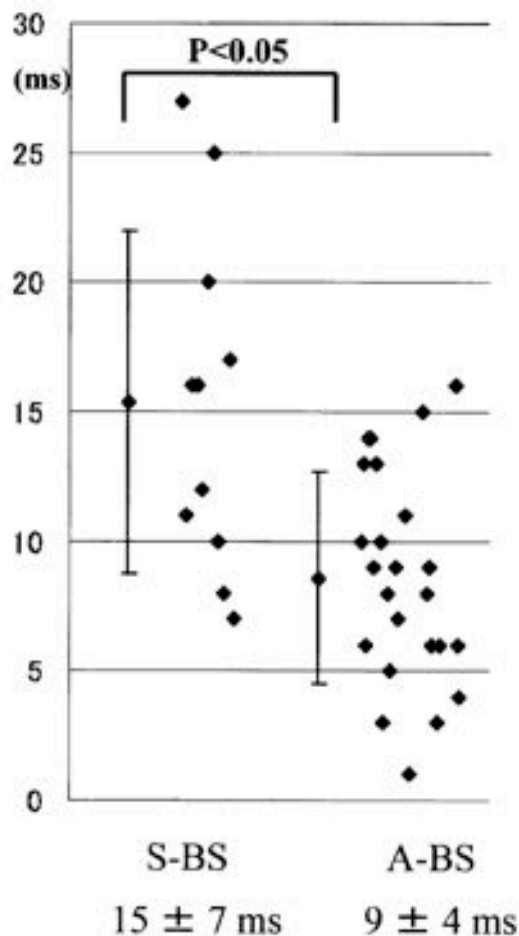
1. BrS is *diagnosed* in patients with ST-segment elevation with type 1 morphology ≥ 2 mm in ≥ 1 lead among the right precordial leads V_1 , V_2 , positioned in the 2nd, 3rd or 4th intercostal space occurring either spontaneously or after provocative drug test with intravenous administration of Class I antiarrhythmic drugs.
2. BrS is *diagnosed* in patients with type 2 or type 3 ST-segment elevation in ≥ 1 lead among the right precordial leads V_1 , V_2 positioned in the 2nd, 3rd or 4th intercostal space when a provocative drug test with intravenous administration of Class I antiarrhythmic drugs induces a **type I** ECG morphology.

Signal Averaged ECG

42 patients with BS, divided into symptomatic and asymptomatic, with events ascertained over 34 months



A Filtered QRS



B LAS 40

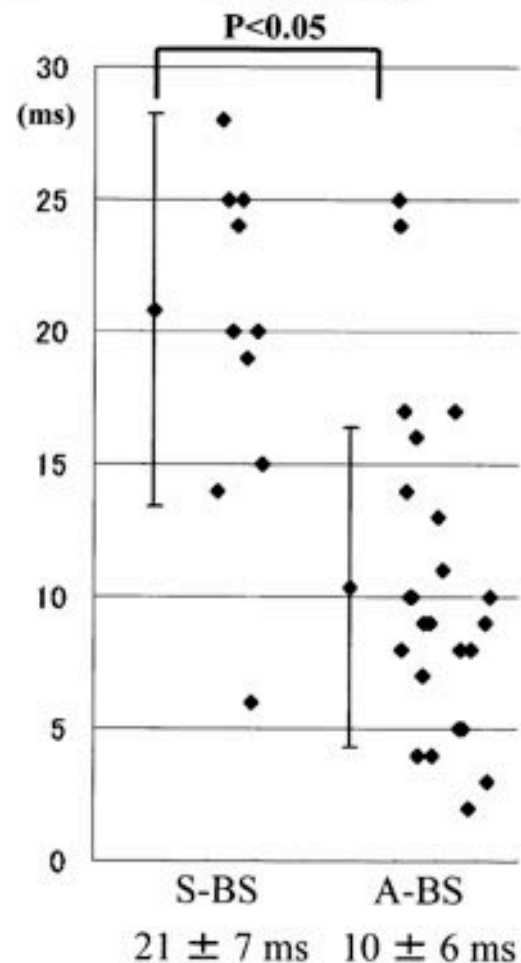
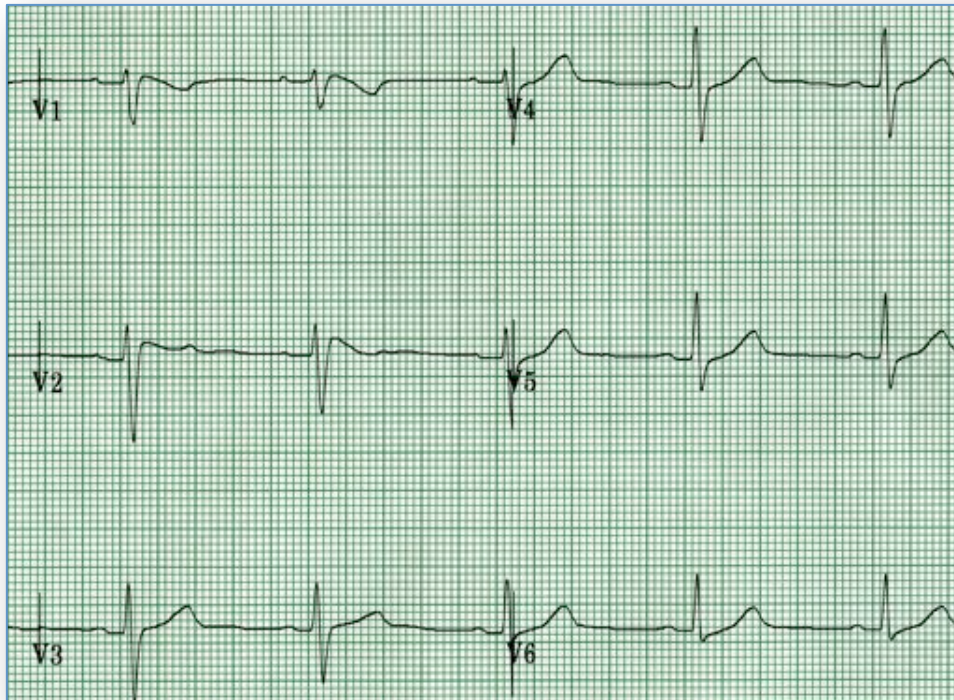
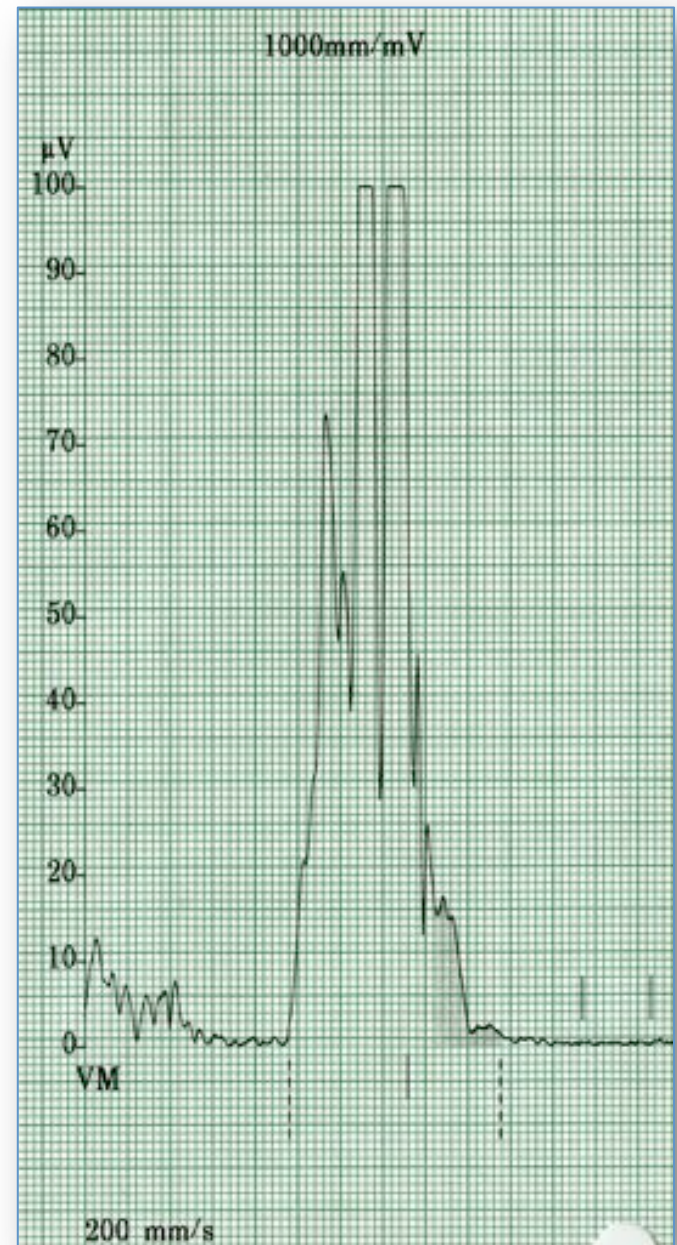


Figure 4. Differences in daily fluctuations of filtered QRS duration and LAS40 in SAECC between the two groups. A: Filtered QRS duration. B: LAS40. In S-BS, the daily fluctuations in filtered QRS and LAS40 were significantly larger than those in A-BS. A-BS = asymptomatic group; S-BS = symptomatic group.

Brugada SAECG



Analysis Filter : 40-250Hz
Std. QRS Duration (unfiltered) : 106 ms
Total QRS Duration (filtered) : 123 ms
Duration Of HFLA signals < 40 μ V : 54 ms
RMS Voltage in terminal 40 ms : 10 μ V
Mean Voltage in terminal 40 ms : 7 μ V



Fragmented QRS as a Marker of Conduction Abnormality and a Predictor of Prognosis of Brugada Syndrome

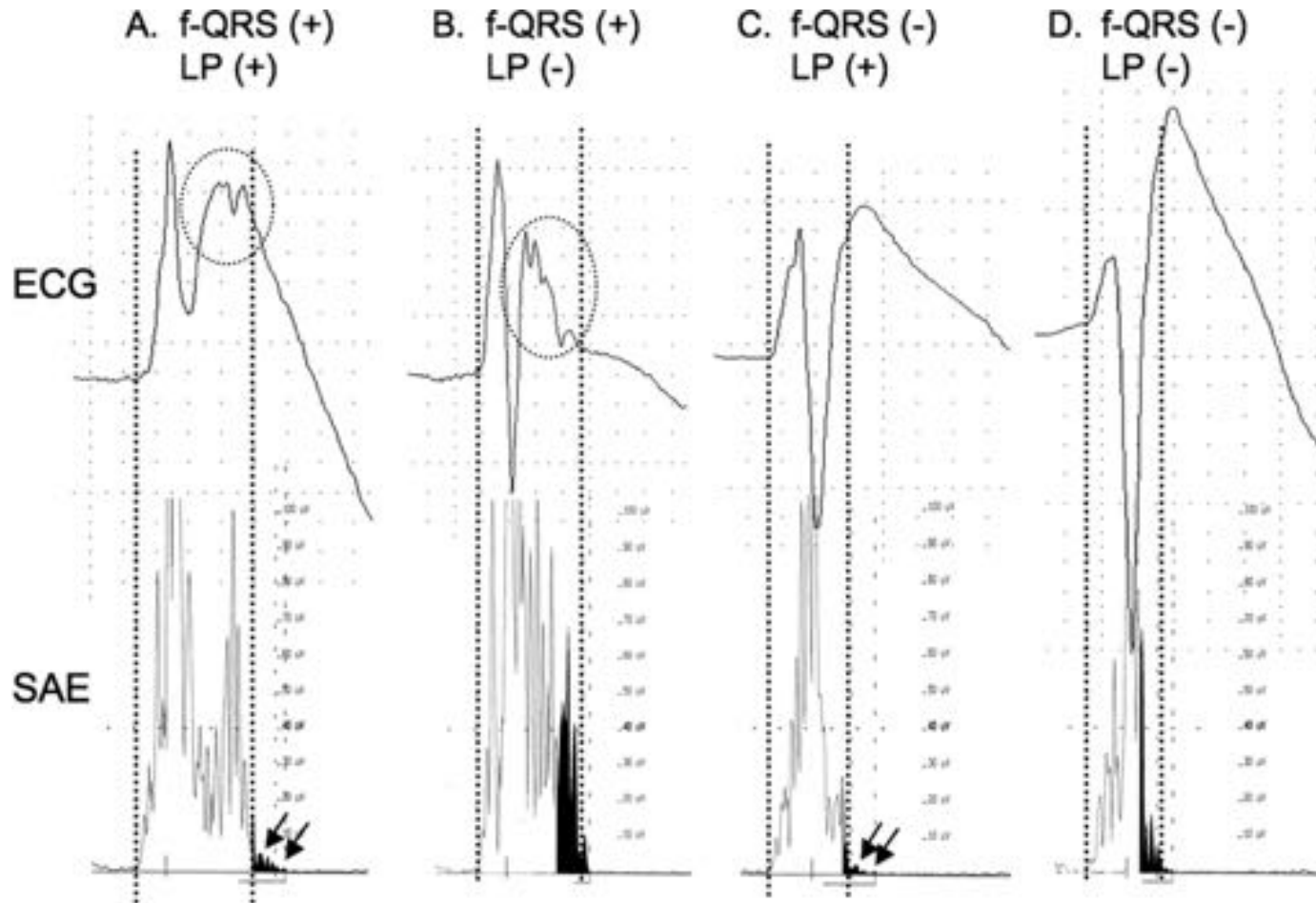
Hiroshi Morita, MD; Kengo F. Kusano, MD; Daiji Miura, PhD; Satoshi Nagase, MD;
Kazufumi Nakamura, MD; Shiho T. Morita, MD; Tohru Ohe, MD;
Douglas P. Zipes, MD; Jiashin Wu, PhD

Background—Conduction abnormalities serve as a substrate for ventricular fibrillation (VF) in patients with Brugada syndrome (BS). Signal-averaged electrograms can detect late potentials, but the significance of conduction abnormalities within the QRS complex is still unknown. The latter can present as multiple spikes within the QRS complex (fragmented QRS [f-QRS]). We hypothesized that f-QRS could indicate a substrate for VF and might predict a high risk of VF for patients with BS.

Methods and Results—In study 1, we analyzed the incidence of f-QRS in 115 patients with BS (13 resuscitated from VF, 28 with syncope, and 74 asymptomatic). f-QRS was observed in 43% of patients, more often in the VF group (incidence of f-QRS: VF 85%, syncope 50%, and asymptomatic 34%, $P < 0.01$). *SCN5A* mutations occurred more often in patients with f-QRS (33%) than in patients without f-QRS (5%). In patients with syncope or VF, only 6% without f-QRS experienced VF during follow-up (43 ± 25 months), but 58% of patients with f-QRS had recurrent syncope due to VF ($P < 0.01$). In study 2, to investigate the mechanism of f-QRS, we studied in vitro models of BS in canine right ventricular tissues ($n = 4$) and optically mapped multisite action potentials. In the experimental model of BS, ST elevation resulted from a large phase 1 notch of the action potential in the epicardium, and local epicardial activation delay reproduced f-QRS in the transmural ECG.

Conclusions—f-QRS appears to be a marker for the substrate for spontaneous VF in BS and predicts patients at high risk of syncope. (*Circulation*. 2008;118:1697-1704.)

f-QRS and LP



Morita, H. et al. *Circulation* 2008;118:1697-1704

Early Repolarization in Brugada

ER patients more likely to be symptomatic and have a type 1 pattern

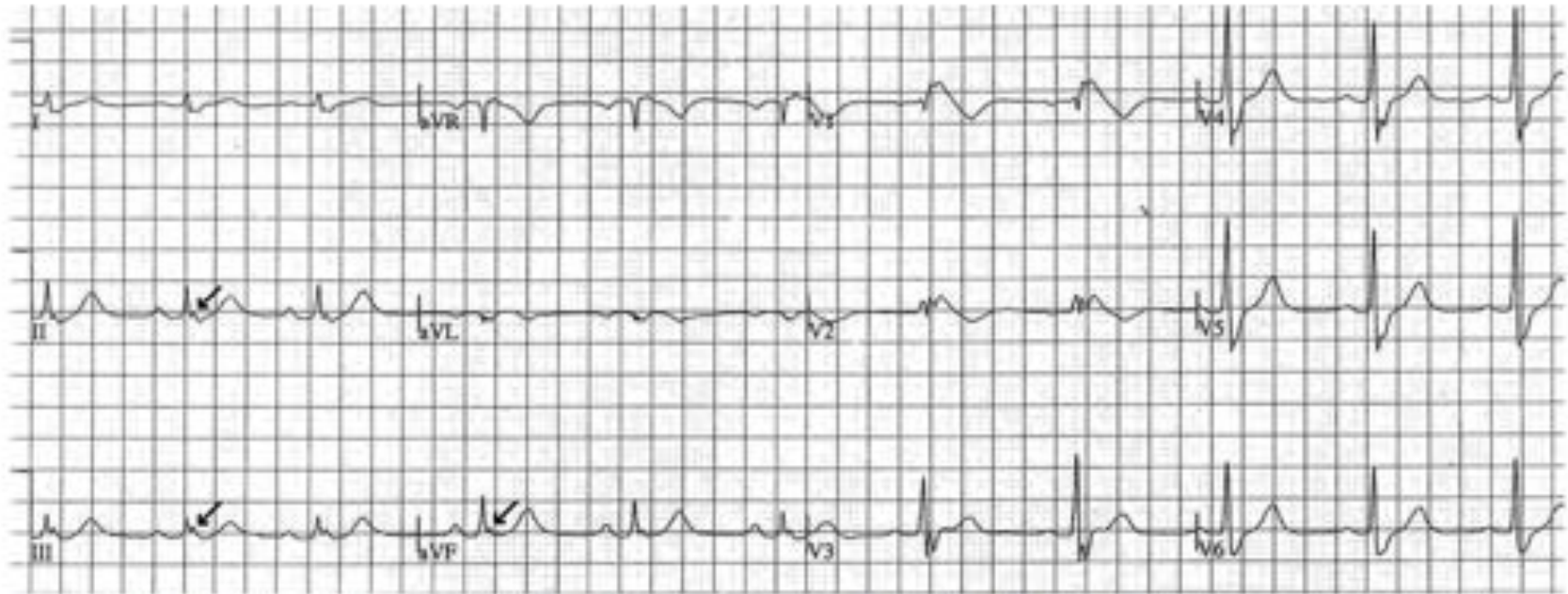


Figure 1. Example of spontaneous notched ≥ 1 -mm J wave in the inferior leads (arrows) in BS. The patient was a 75-year-old proband presenting with aborted sudden death. Note the diagnostic type I ECG in the right precordial leads and wide QRS complexes (QRS=140 ms).

EP Testing

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Heart Rhythm Disorders

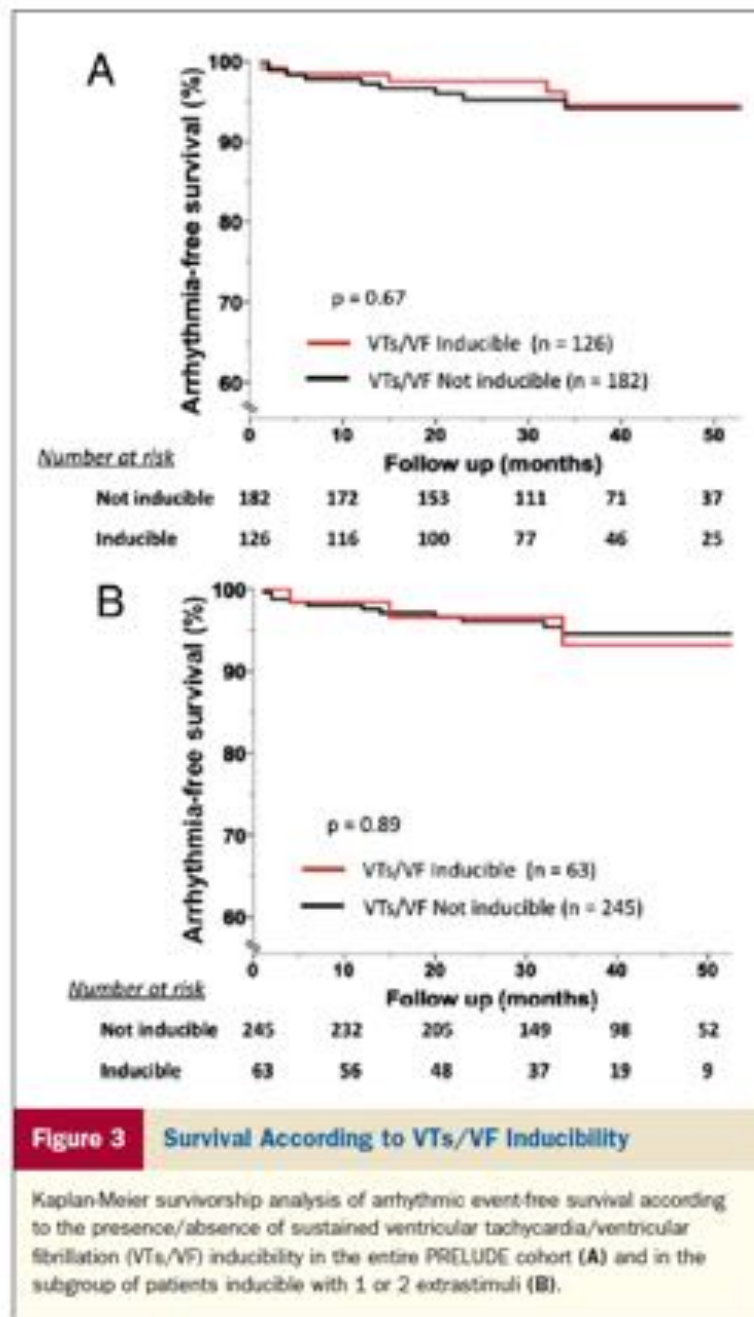
Risk Stratification in Brugada Syndrome

Results of the PRELUDE (PRogrammed ELectrical stimulation preDICTive valuE) Registry

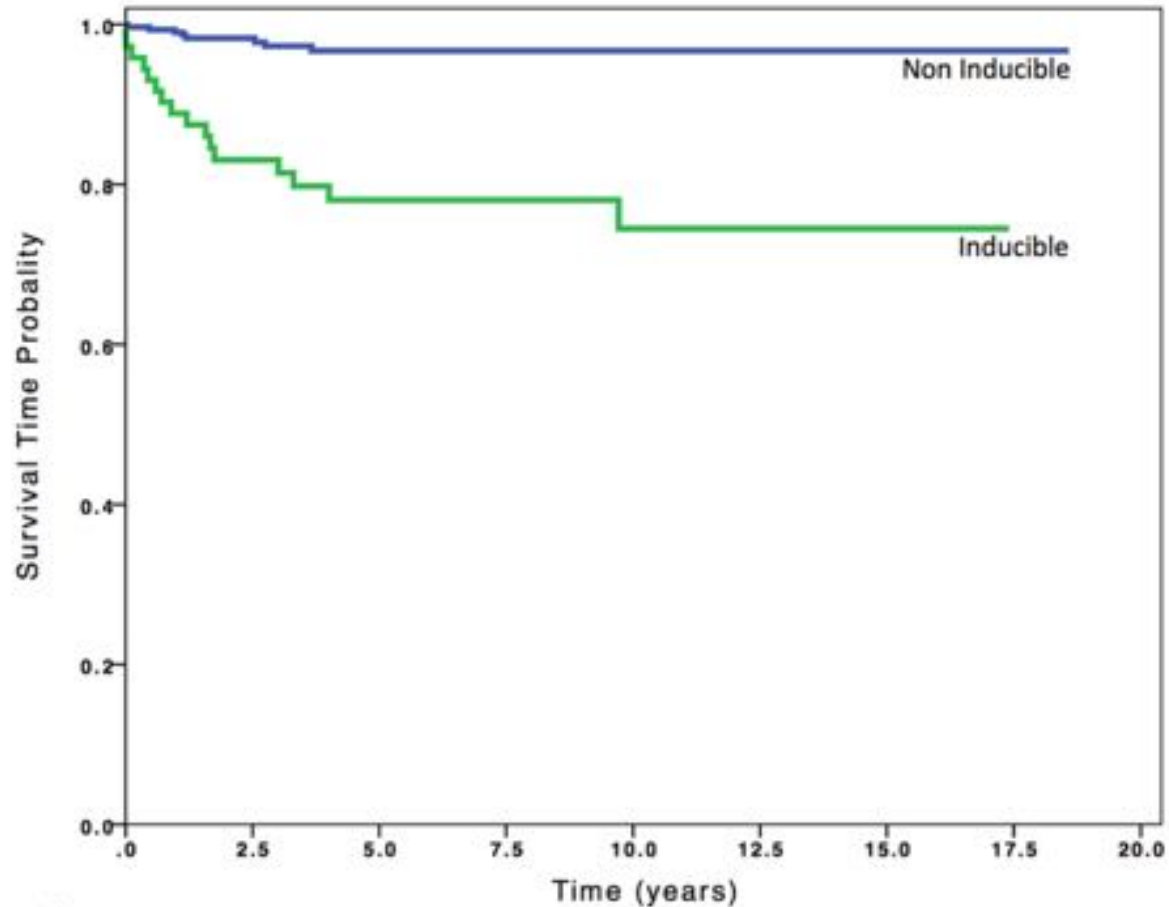
Silvia G. Priori, MD, PhD,*†‡ Maurizio Gasparini, MD,§ Carlo Napolitano, MD, PhD,*‡
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Roberto De Nardis MD,||| Mario Colombo, MS¶¶

*Pavia, Rozzano, Milano, Lido di Camaiore, Bentivoglio, Palermo, Ravenna, Bergamo, Cuneo,
and Vicenza, Italy; and New York, New York*

- 308 consecutive patients with Brugada (spontaneous or provoked) without previous cardiac arrest – 14 events over 34 months (4.5%)
- Predictors of events were previous syncope and spontaneous type 1



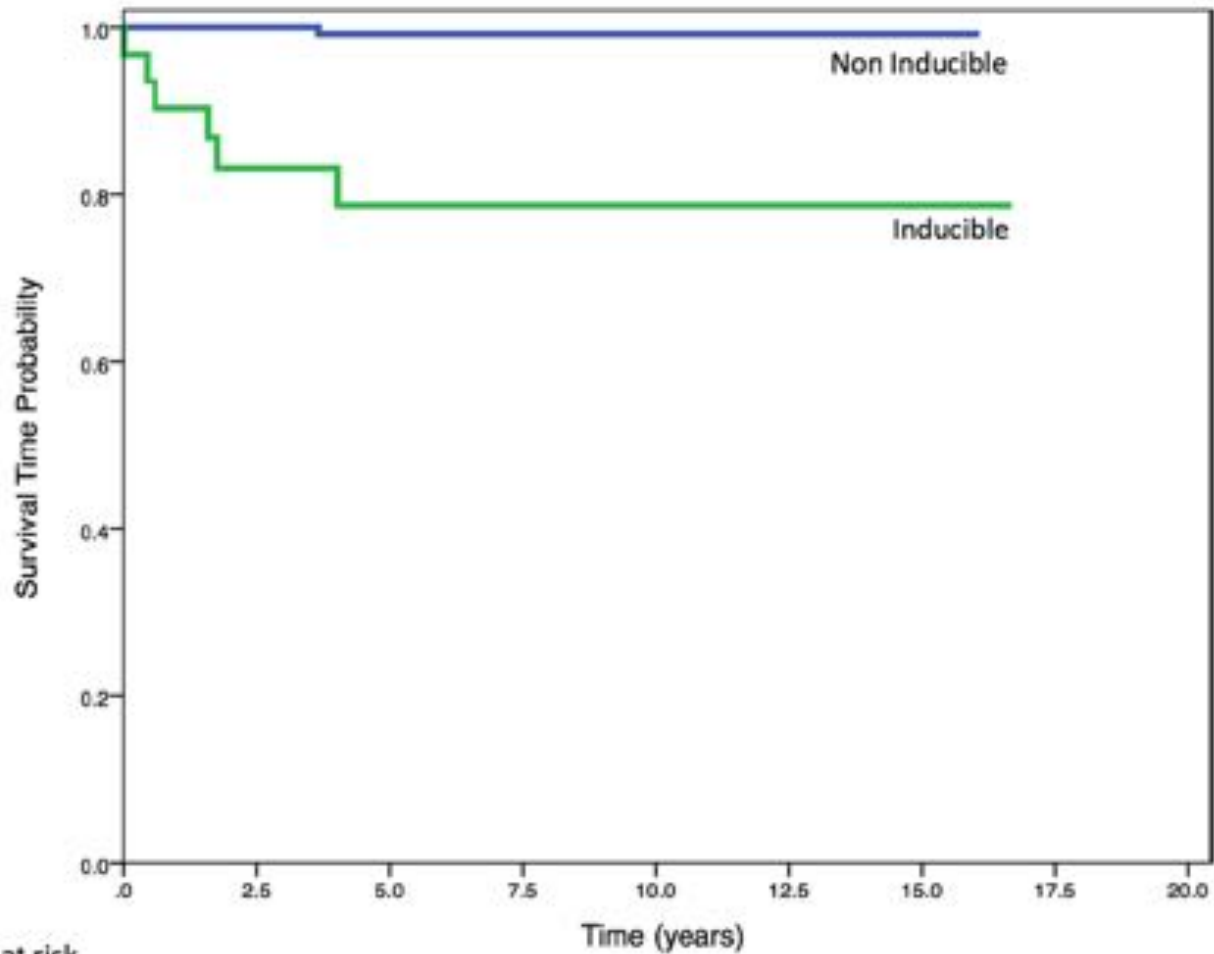
Counterpoint



Patients at risk

Inducible	73	53	43	32	21	10	5	0	0
Non Inducible	331	205	130	86	57	18	8	1	0

Asymptomatics!



Patients at risk

Inducible

32

21

17

13

5

3

1

0

0

Non Inducible

241

145

102

72

47

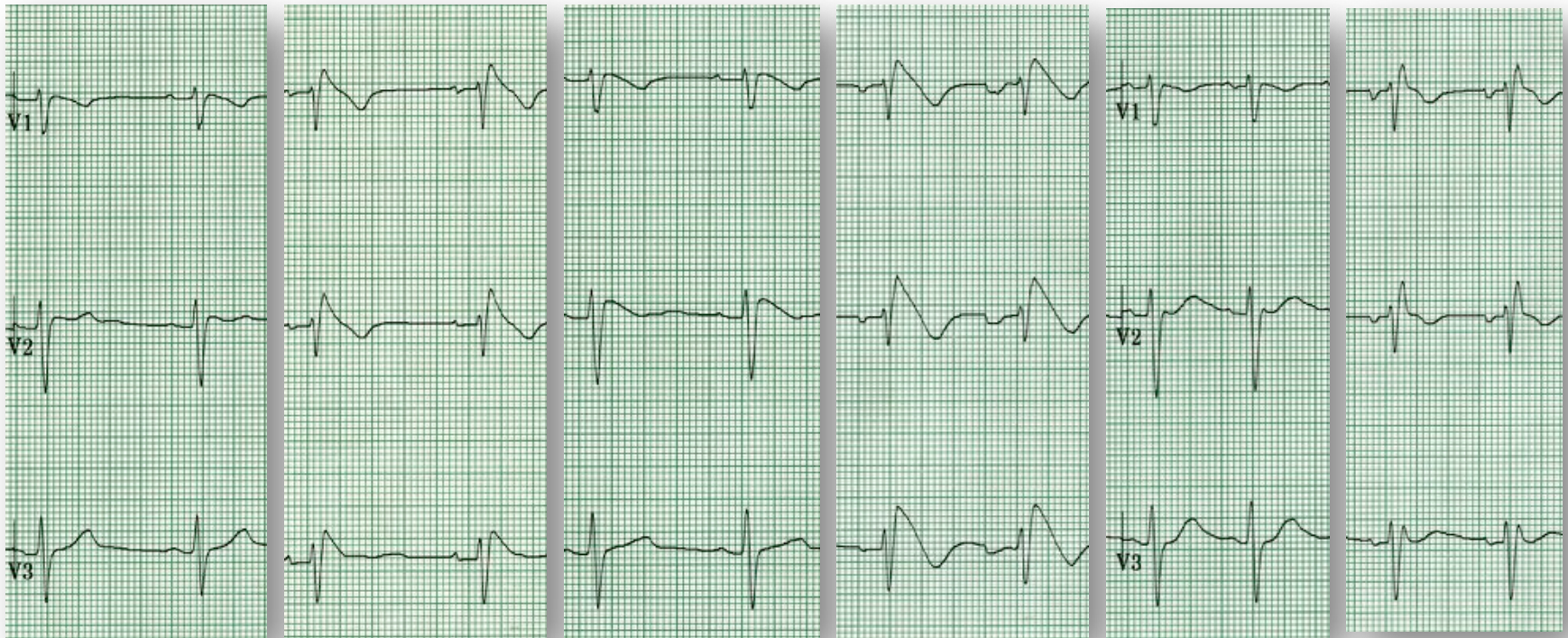
14

3

0

0

Brugada Procaainamide Infusion ECG Changes



baseline

high leads

procaainamide

procaainamide
high leads

isuprel

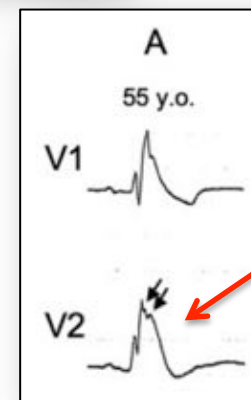
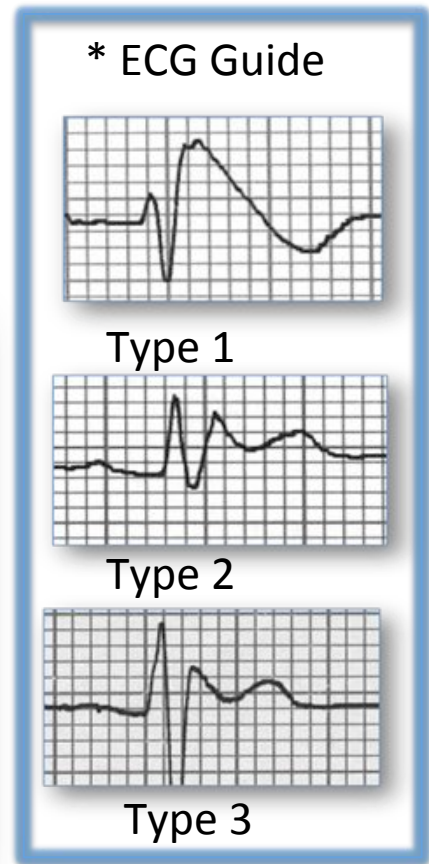
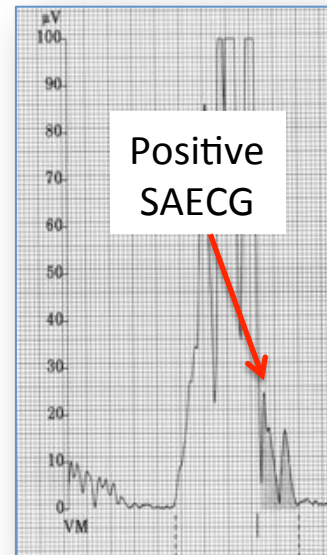
isuprel
high leads

also improves with exercise

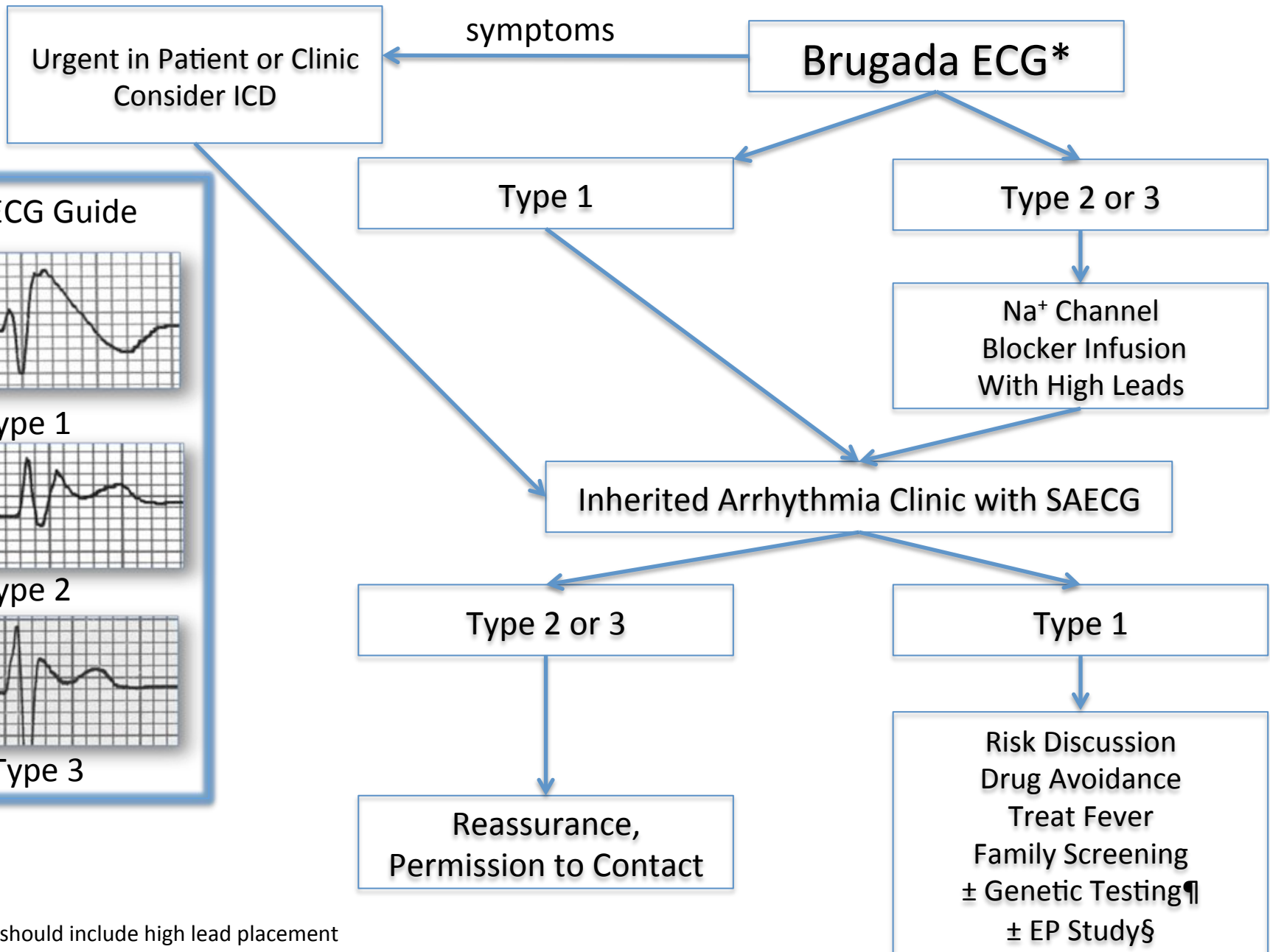
Brugada Risk Factor Checklist 2015

(not equally weighted or validated)

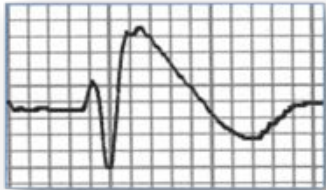
- Major
 - cardiac arrest
 - unexplained/arrhythmic syncope
 - spontaneous type 1
- Minor
 - fractionation/positive SAECG
 - ER pattern in the inferior leads
 - Male
 - Other considerations: AF, VERP<200 msec
- Not considered risk factors
 - family history (social RF)
 - SCN5A mutation



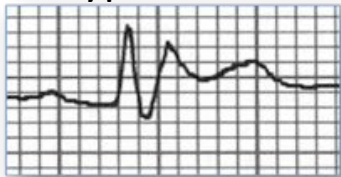
fractionation



*** ECG Guide**



Type 1



Type 2



Type 3

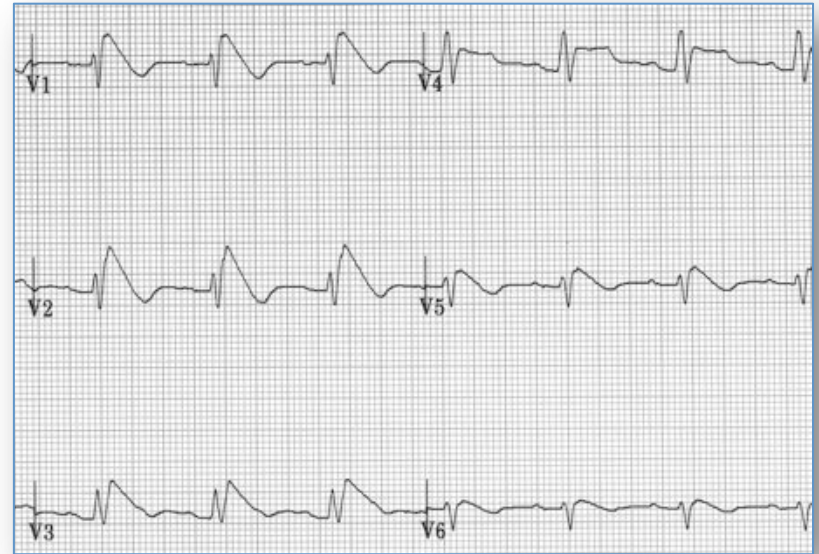
* ECG should include high lead placement

§ Discretionary EP testing, generally discouraged

¶ Guidelines recommend genetic testing, access to coverage for testing is variable

Back to our Case: Procainamide Infusion

- Positive infusion
- Positive SAECG
- No ER or fractionation
- Negative family history and SCN5A sequencing
- All first degree relatives “cleared” with standard and high leads
- Usual lifestyle advice (fever, drug avoidance, report symptoms)
- Registry follow-up





Conclusions



- Several clinically accessible tests are readily available to the clinician to risk stratify BS patients
- Incremental ECGs including a high precordial lead ECG should be performed in all patients
- Signal averaged ECGs may be helpful
- EP testing is not routine, but may play a role in borderline cases where an ICD is being contemplated (very few)
- Independent incremental effect of these tests on clinical decision making is uncertain since asymptomatic patients generally do not warrant an ICD

Important Websites

- www.qtdrugs.org
- www.brugadadrugs.org
-
- akrahn@mail.ubc.ca

