St George's
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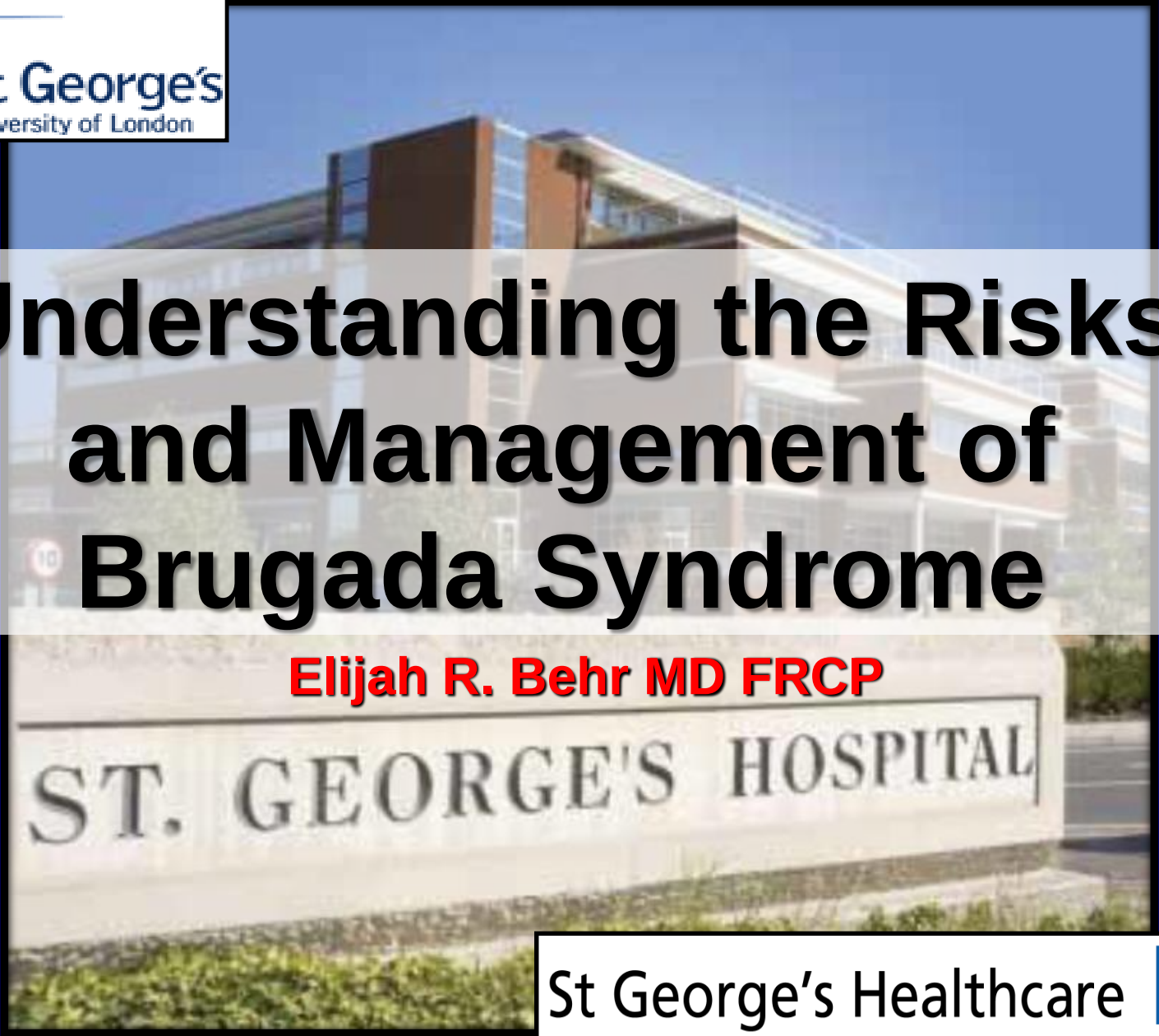
Understanding the Risks and Management of Brugada Syndrome

Elijah R. Behr MD FRCP



St George's Healthcare NHS
NHS Trust

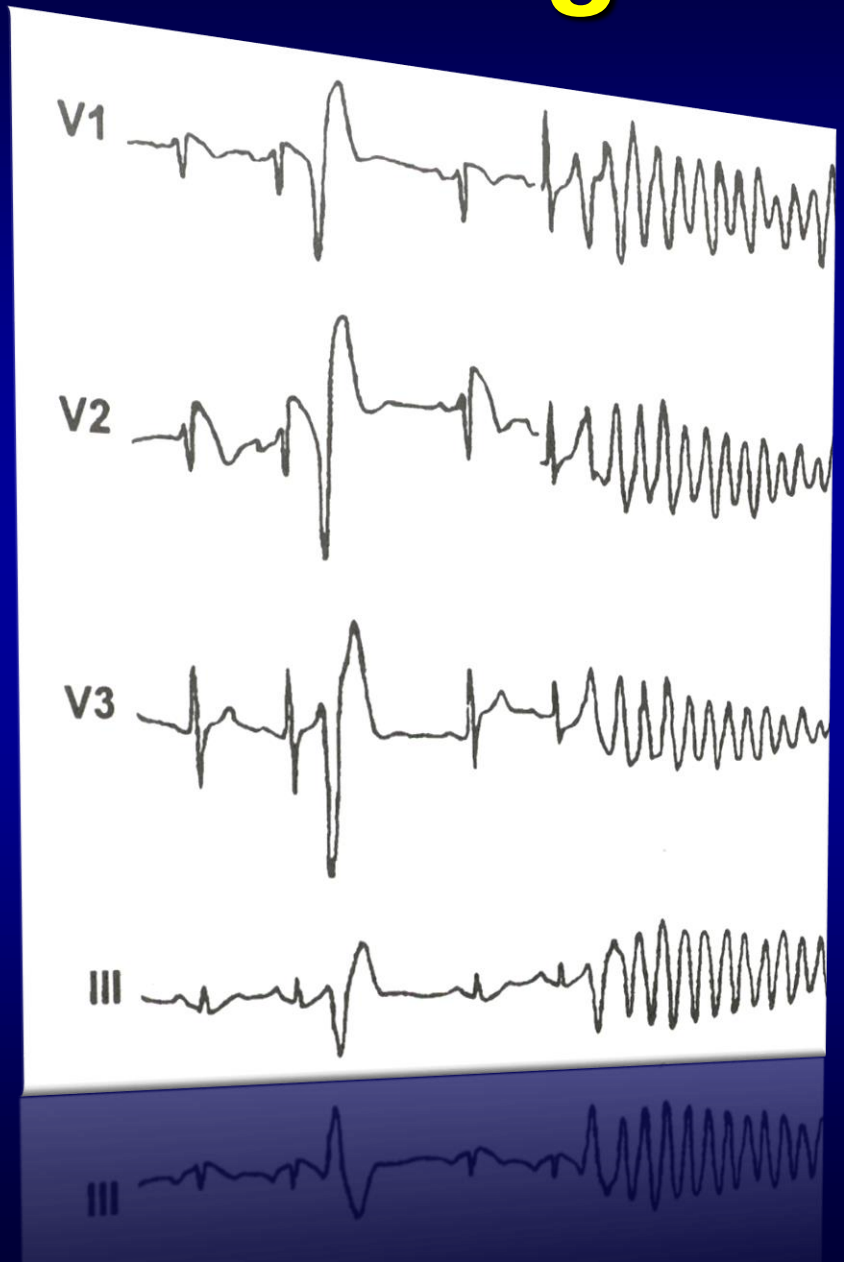
Europace (2013) **15**, 1389–1406
doi:10.1093/europace/eut272

HRS/EHRA/APHRS CONSENSUS STATEMENT

Executive summary: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes

Silvia G. Priori, (HRS Chairperson)[1], Arthur A. Wilde, (EHRA Chairperson)[2], Minoru Horie, (APHRS Chairperson)[3], Yongkeun Cho, (APHRS Chairperson)[4], Elijah R. Behr[5], Charles Berul[6], Nico Blom[7]*, Josep Brugada[8], Chern-En Chiang[9], Heikki Huikuri[10], Prince Kannankeril[11]‡, Andrew Krahn[12], Antoine Leenhardt[13], Arthur Moss[14], Peter J. Schwartz[15], Wataru Shimizu[16], Gordon Tomaselli[17]†, Cynthia Tracy[%18]

Brugada Syndrome



Primary electrical disorder

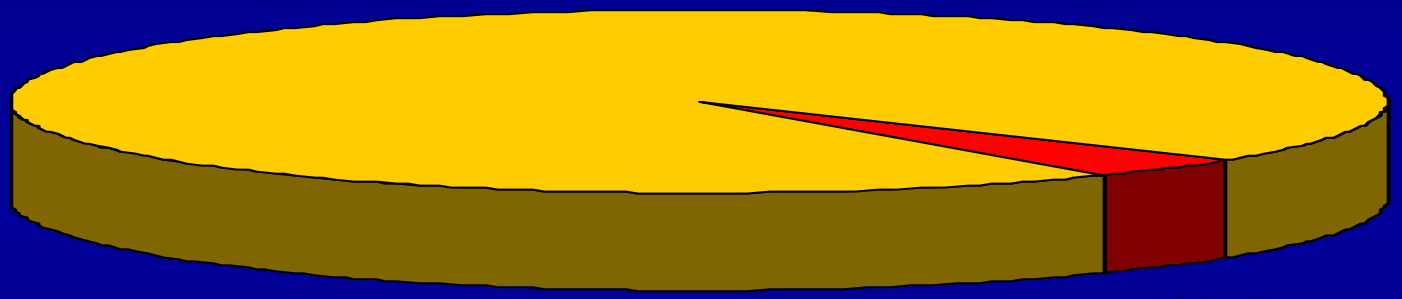
ECG diagnosis

Characteristic ECG
- **Persistent**
- **Transient**
- **Provoked**

Prevalence:
- **1 in 2000 West**
- **1 in 500 SE Asia**

Sudden Cardiac Death due to Brugada Syndrome

50-100,000 p.a.



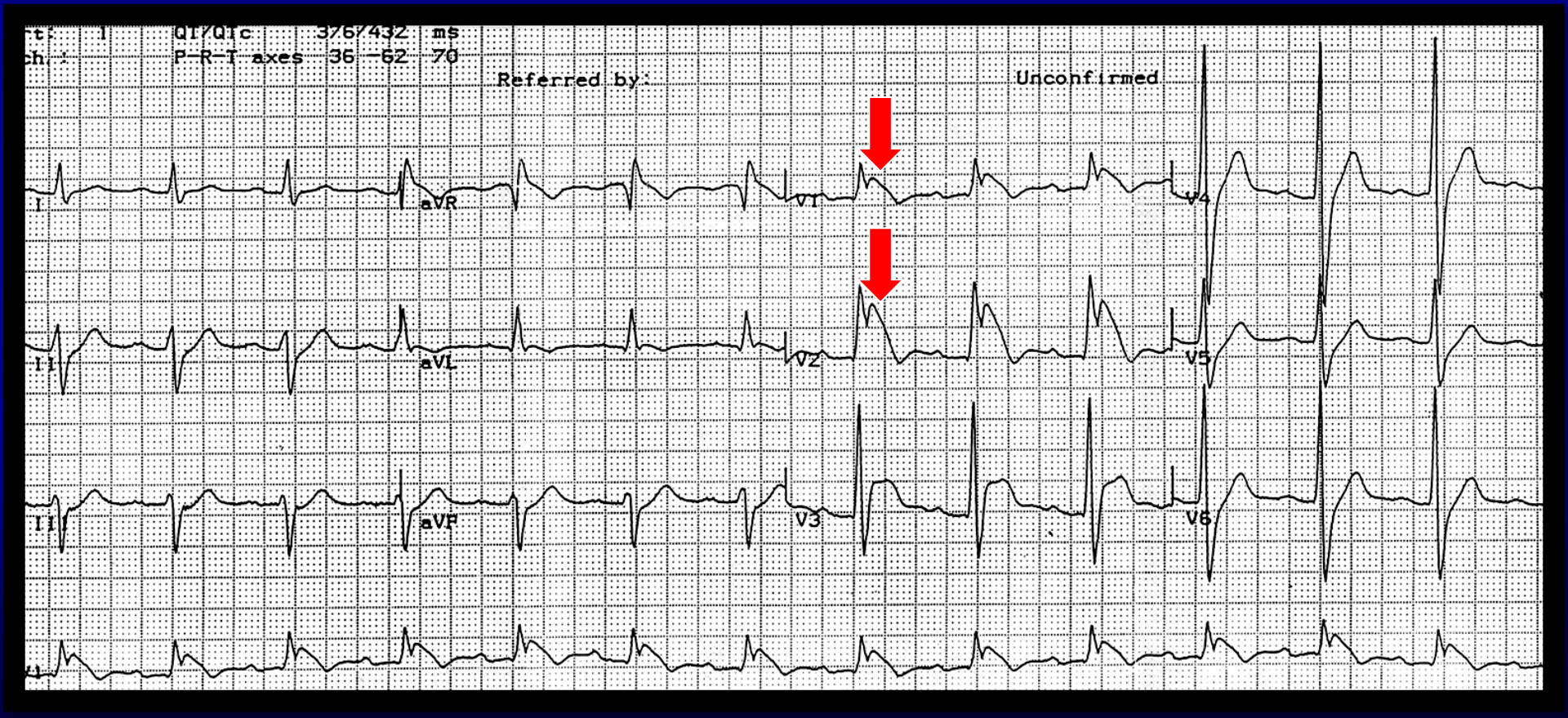
4% Brugada

2-4,000 p.a. ?

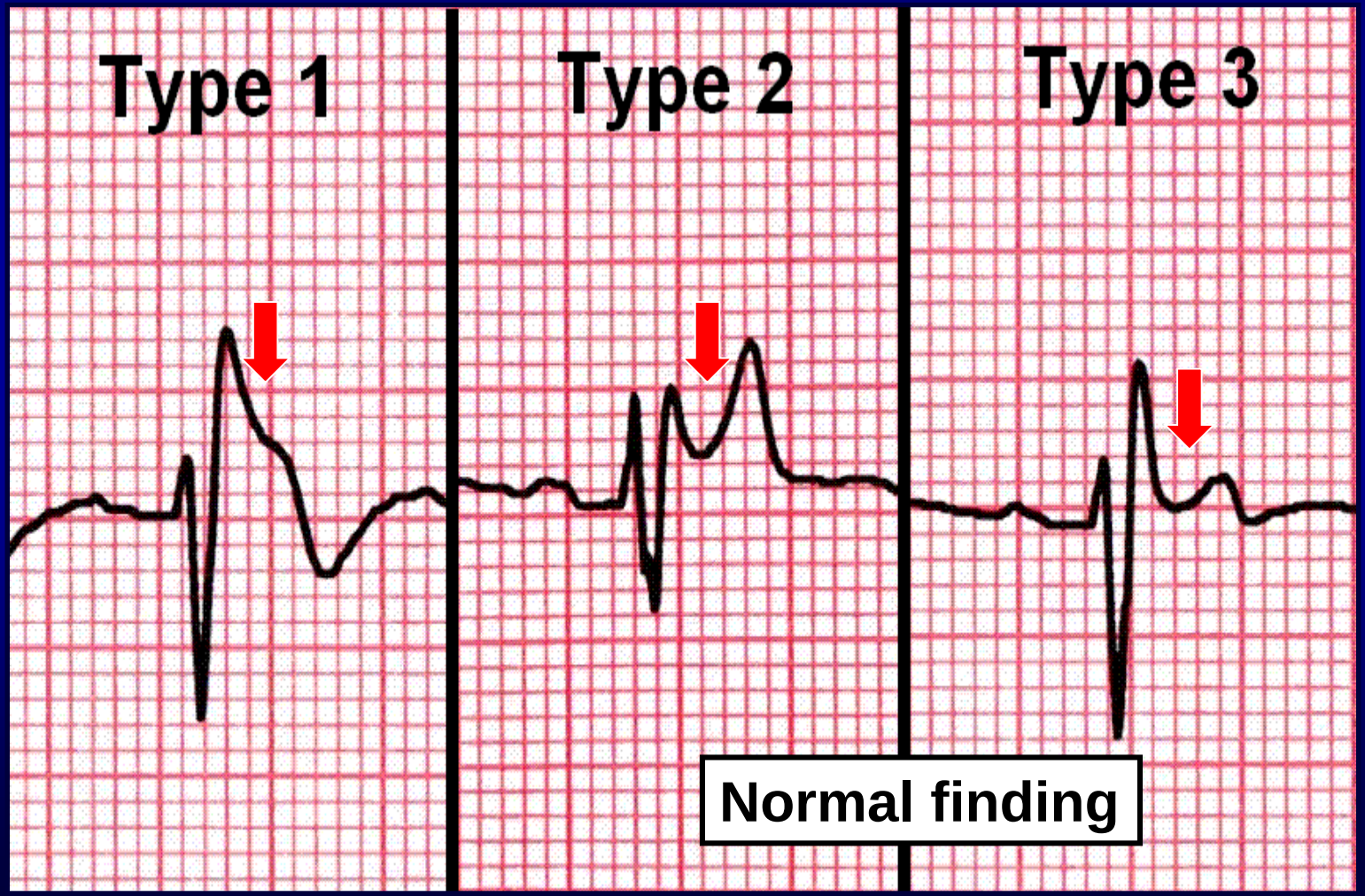
SCD in the UK

Est. Incidence: **5-66/100,000 p.a.**
1/1,000 p.a. Laos

Brugada syndrome: Spontaneous Type 1 ECG Pattern

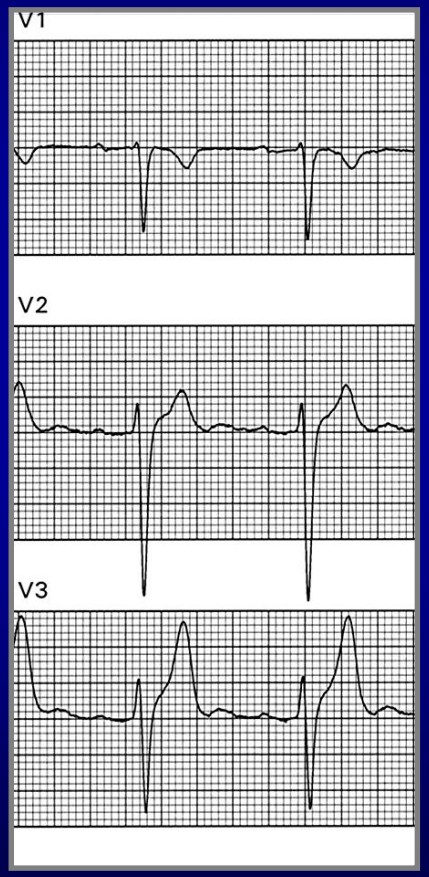


The Brugada ECG

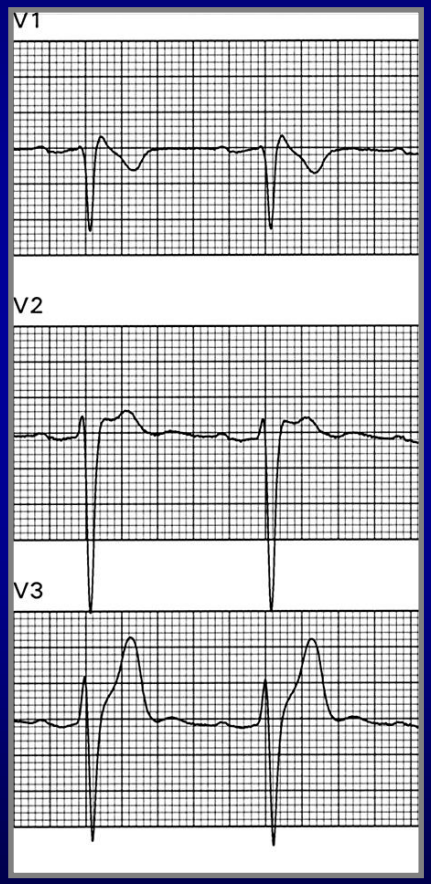


The Ajmaline Test

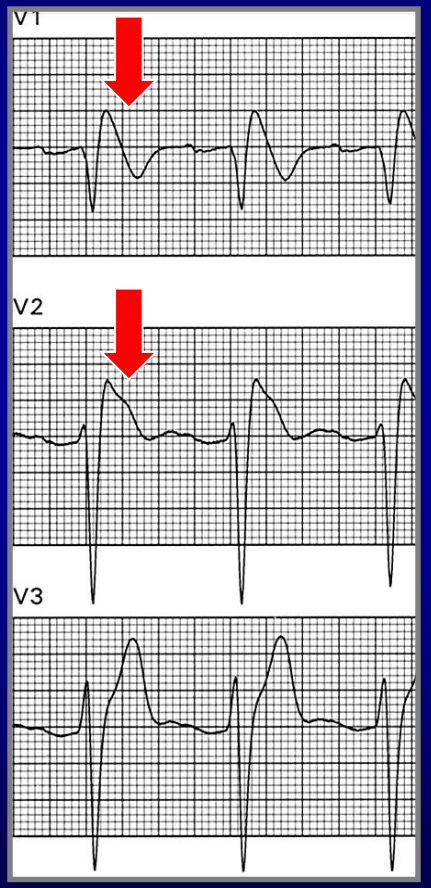
Baseline



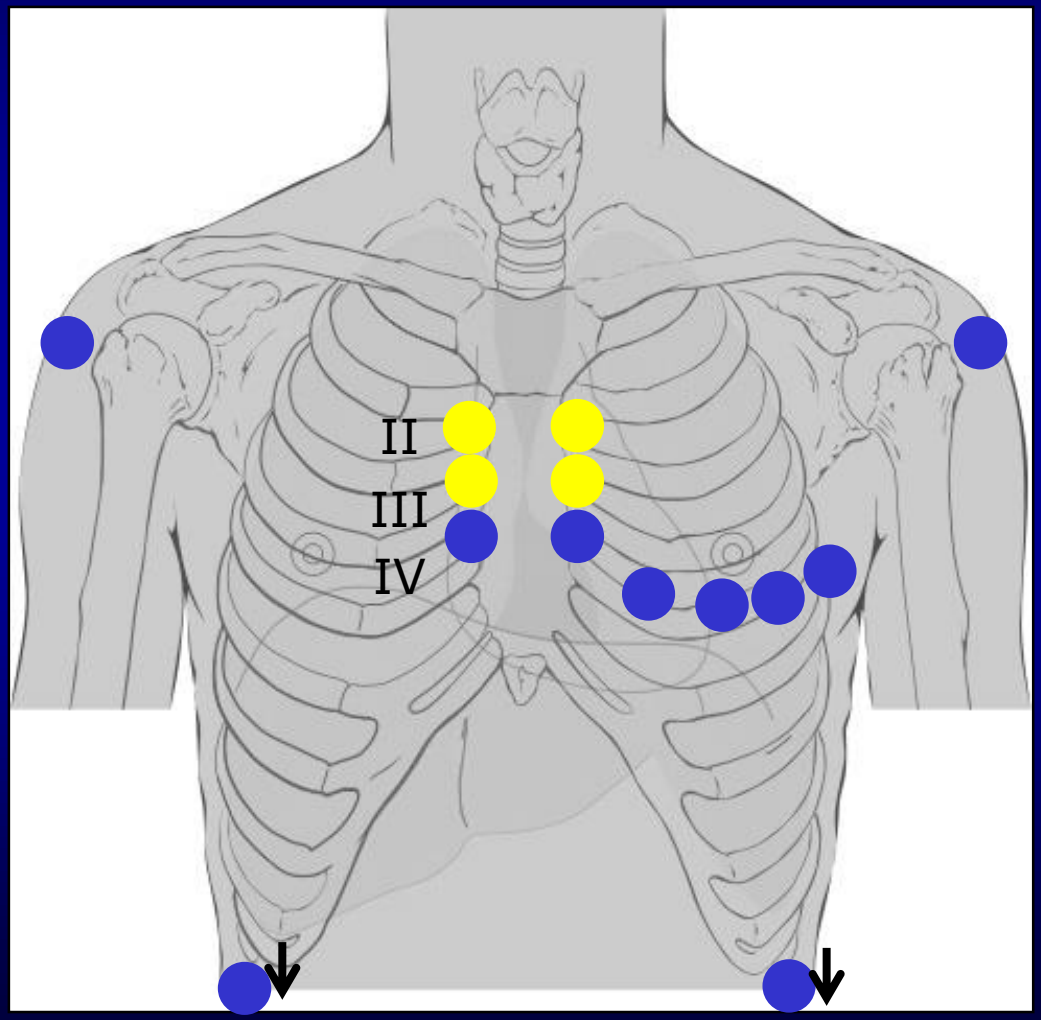
2 mins

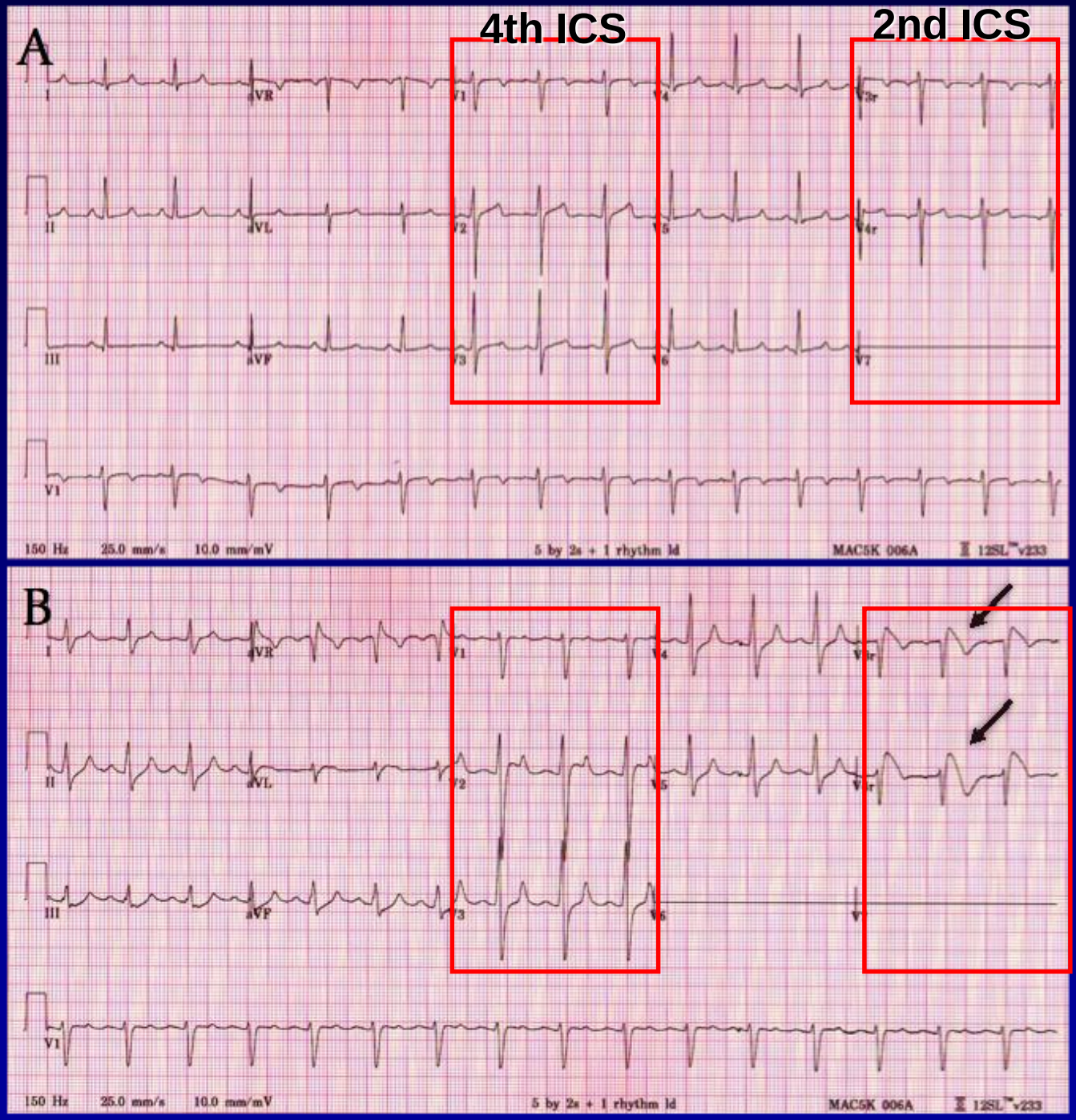


3 mins



High RV leads and RVOT





Baseline

Ajmaline

Europace (2013) **15**, 1389–1406
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HRS/EHRA/APHRS CONSENSUS STATEMENT

Executive summary: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes

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Brugada syndrome

1. BrS ***is diagnosed*** in patients with ST segment elevation with type 1 morphology ≥ 2 mm in ≥ 1 lead among the right precordial leads V1, V2 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 V1, V2 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 1 ECG morphology

New Consensus Document

Europace
doi:10.1093/europace/euw235

J-Wave syndromes expert consensus conference report: Emerging concepts and gaps in knowledge

Endorsed by the Asia Pacific Heart Rhythm Society (APHRS), the European Heart Rhythm Association (EHRA), the Heart Rhythm Society (HRS), and the Latin American Society of Cardiac Pacing and Electrophysiology (Sociedad Latinoamericana de Estimulación Cardíaca y Electrofisiología [SOLAECE])

Drug-induced Type 1 ECG

PLUS at least one of

- **Documented VF or polymorphic VT**
- **Arrhythmic syncope**
- **A family history of:**
  - **SCD at <45 years old with negative autopsy**
  - **Coved-type ECGs**
- **Nocturnal agonal respiration**
- **Inducibility of VT/VF with 1 or 2 extrasystole**

Shanghai score

Score (requires at least 1 ECG finding)

≥3.5 points: Probable/definite BrS

2–3 points: Possible BrS

<2 points: Nondiagnostic

I. ECG (12-Lead/Ambulatory)

A. Spontaneous type 1 Brugada ECG pattern at nominal or high leads	3.5
B. Fever-induced type 1 Brugada ECG pattern at nominal or high leads	3
C. Type 2 or 3 Brugada ECG pattern that converts with provocative drug challenge	2

**Only award points once for highest score within this category. One item from this category must apply.*

II. Clinical History*

A. Unexplained cardiac arrest or documented VF/ polymorphic VT	3
B. Nocturnal agonal respirations	2
C. Suspected arrhythmic syncope	2
D. Syncope of unclear mechanism/unclear etiology	1
E. Atrial flutter/fibrillation in patients <30 years without alternative etiology	0.5

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

III. Family History

A. First- or second-degree relative with definite BrS	2
B. Suspicious SCD (fever, nocturnal, Brugada aggravating drugs) in a first- or second-degree relative	1
C. Unexplained SCD <45 years in first- or second- degree relative with negative autopsy	0.5

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

Brugada Syndrome Prognosis

BS patients with typical ECG

Cardiac arrest

20% within 1 year

SUCD

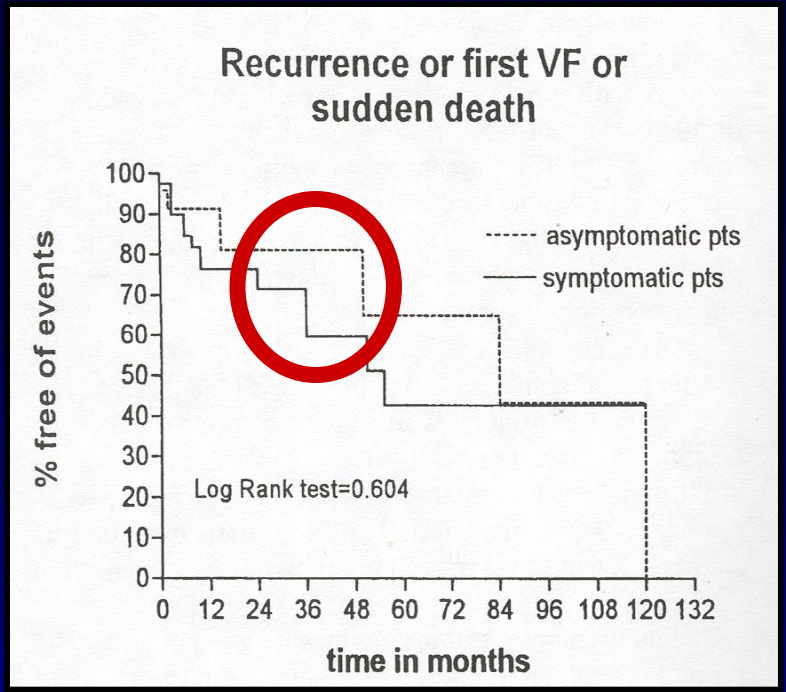
40% in 4 years

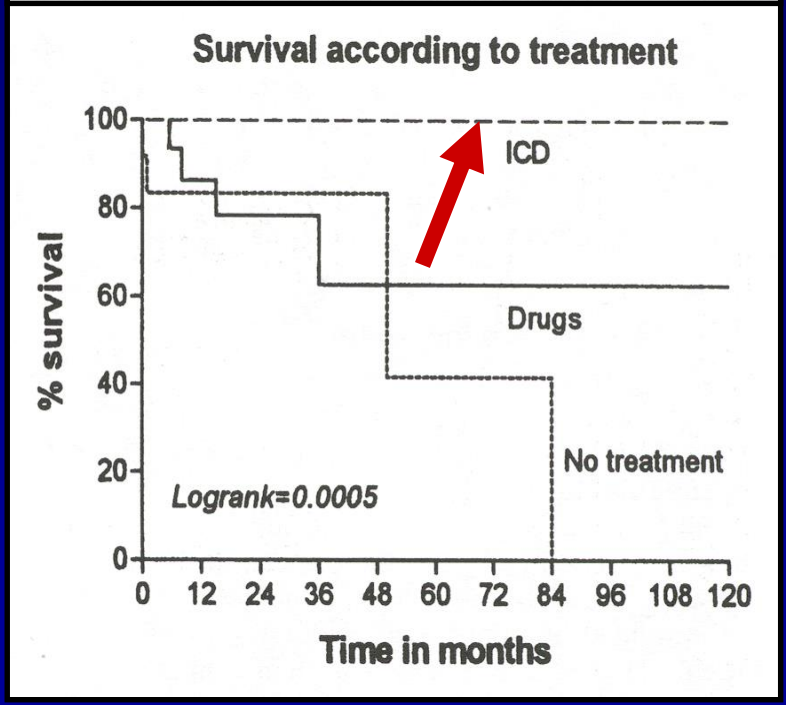
Asymptomatic = Symptomatic

ICD = fully protective

Drugs = ineffective

Brugada et al, Circulation 1998





Population Follow-up Studies

Atarashi et al JACC 2001

Japanese factory population (~10,000):

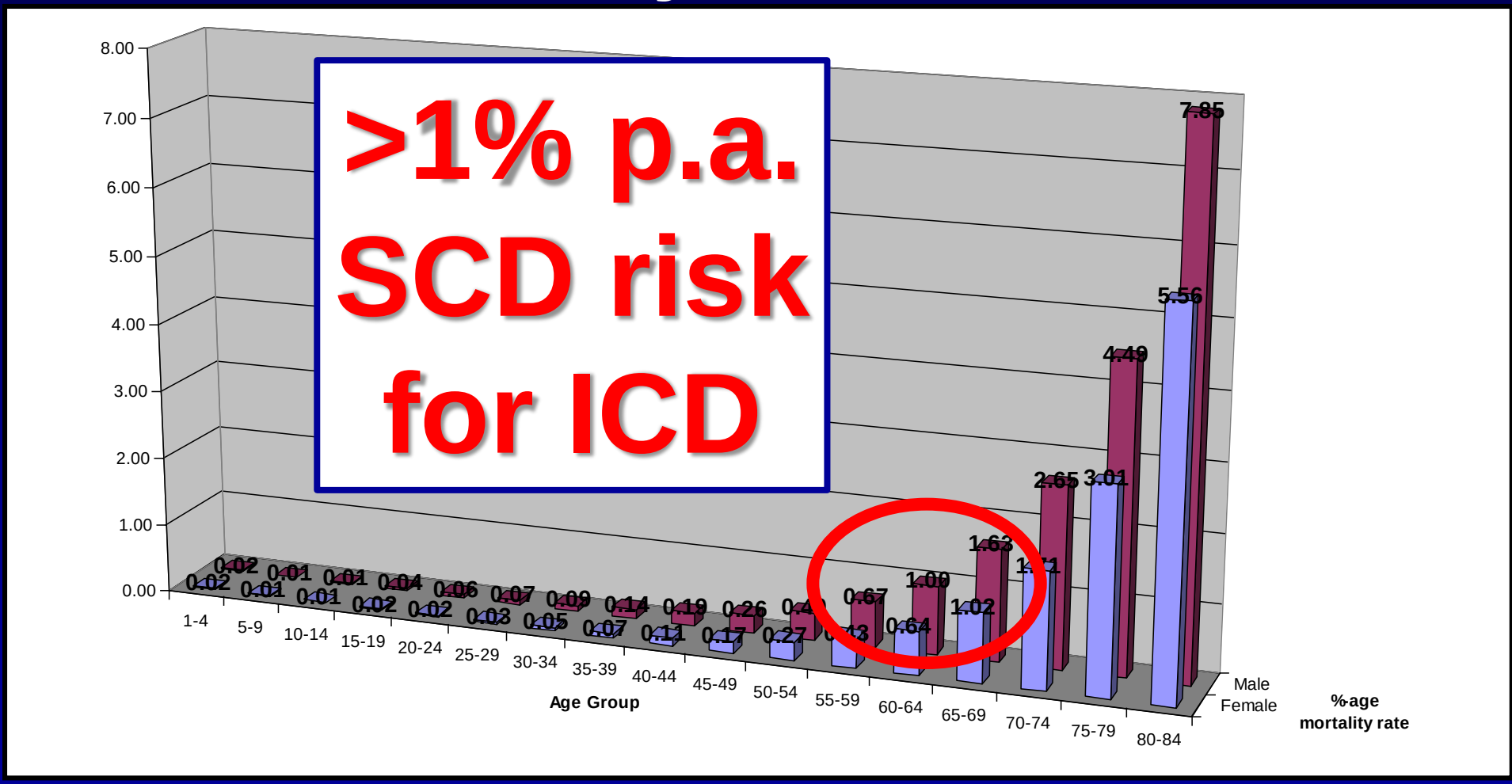
- Prevalence 0.16%
- 90% male
- 3 year follow-up
- 1.5% cardiac event rate

Miyasaki et al JACC 2001

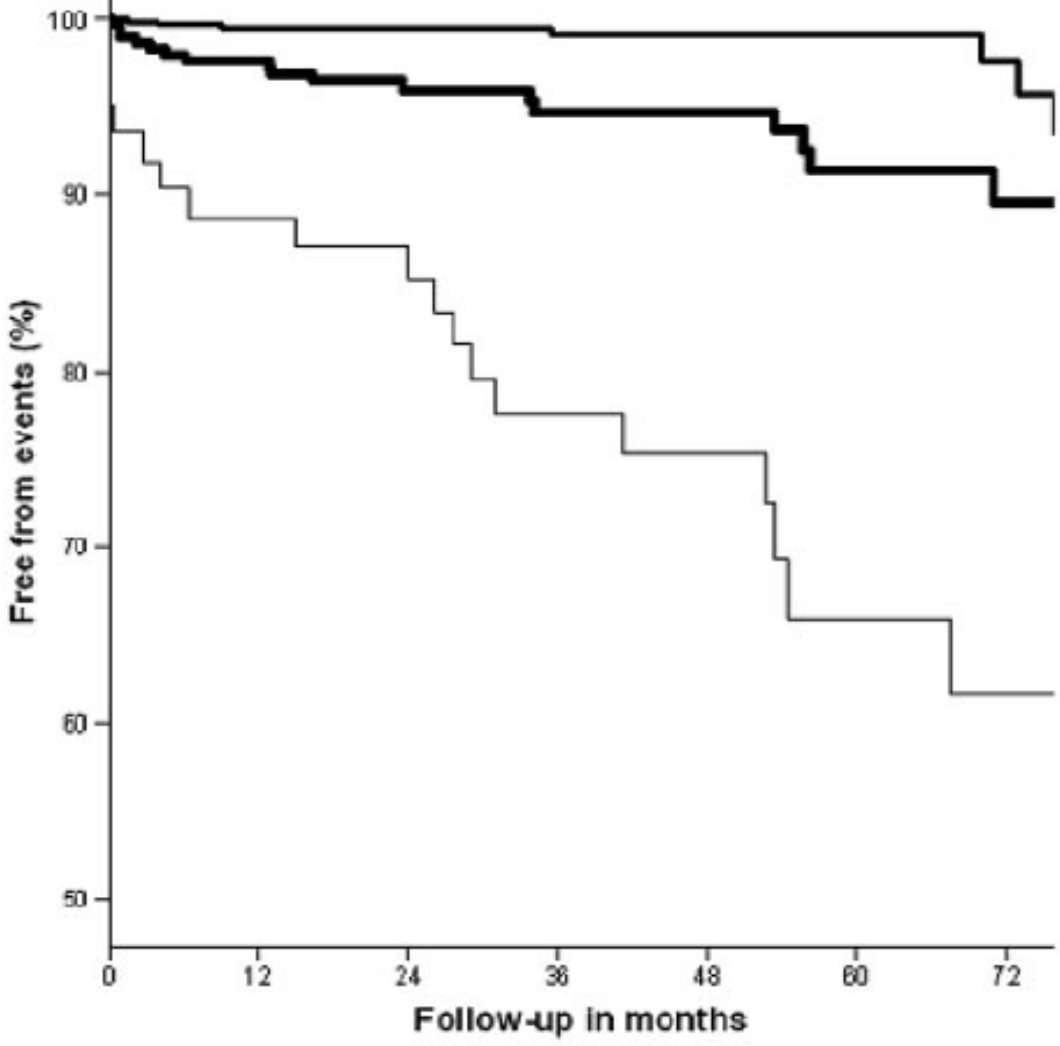
Japanese urban health screen (~14,000) :

- Prevalence 0.12%
- 81% male
- 2.6 years follow-up
- 1.0% mortality rate

UK General Population Annual Mortality Rates 2009



FINGER study: Symptoms



0.5% p.a.

1.9% p.a.

7.7% p.a.

Lifestyle

Class I

1. The following lifestyle changes ***are recommended*** in all patients with diagnosis of BrS:

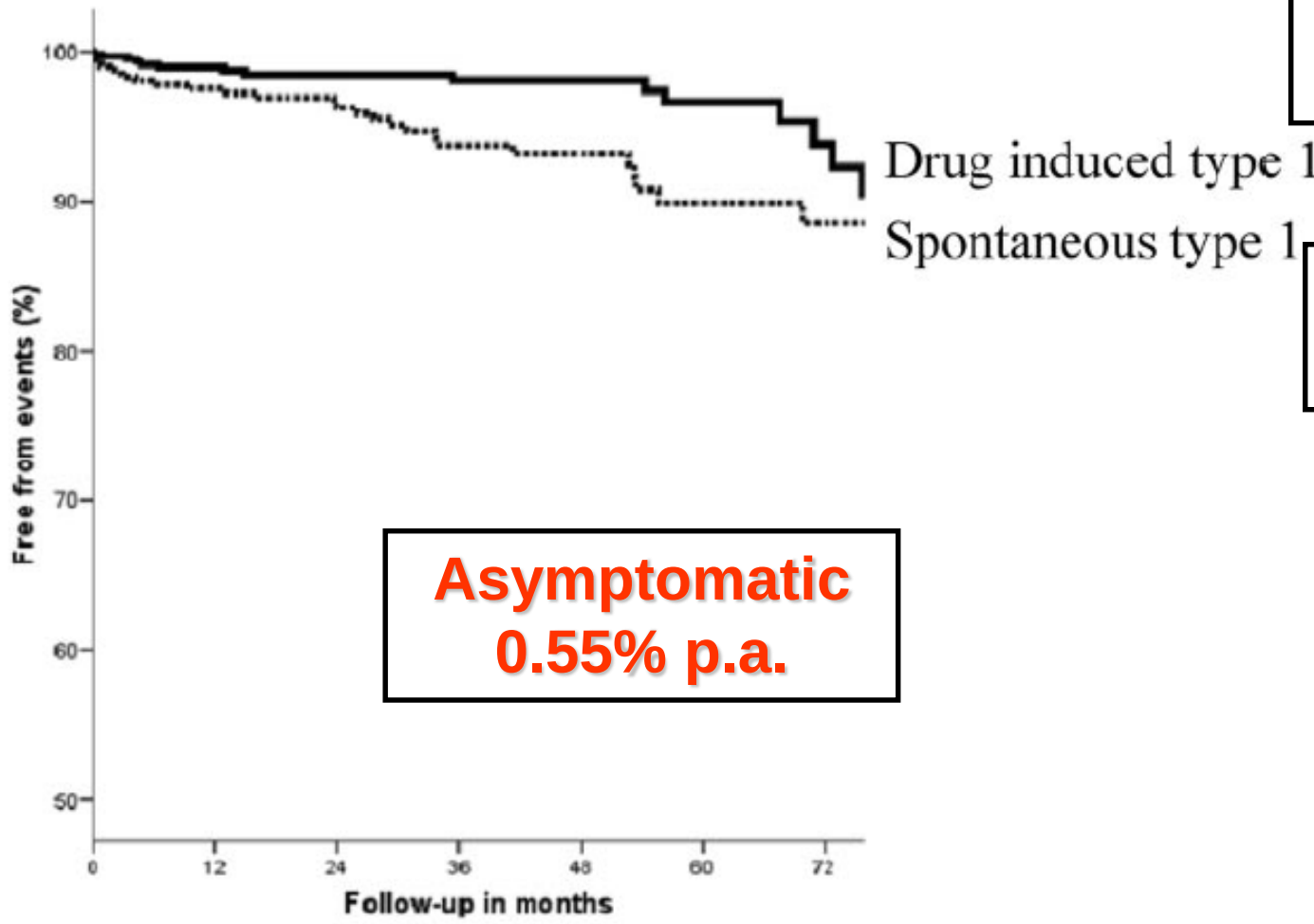
a) Avoidance of drugs that may induce or aggravate ST segment elevation in right precordial leads (Brugadadrugs.org),

b) Avoidance of excessive alcohol intake,

c) Immediate treatment of fever with antipyretic drugs.

Class	ICD Recommendations
Class I	ICD implantation **is recommended** in patients with a diagnosis of BrS who: • Are survivors of a cardiac arrest, and/or • Have documented spontaneous sustained VT with or without syncope.
Class IIa	ICD implantation **can be useful** in patients with a spontaneous diagnostic Type I ECG who have a history of syncope judged to be likely caused by ventricular arrhythmias.

FINGER Study: ECG appearance



1.7% p.a.

2.3% p.a.

Asymptomatic 0.55% p.a.

SADS Victims with Brugada Syndrome

The majority of sudden deaths in familial Brugada syndrome would not be predicted by current accepted markers

Nu	5
Type 1 I A	0 / 0

FINGER Study

Median follow-up 31.9 (14 to 54.4) months
51 arrhythmic events

- **Appropriate ICD shocks 44 patients**
- **SCD 7 patients**

Only 10 in the asymptomatic group
SURVIVOR BIAS?

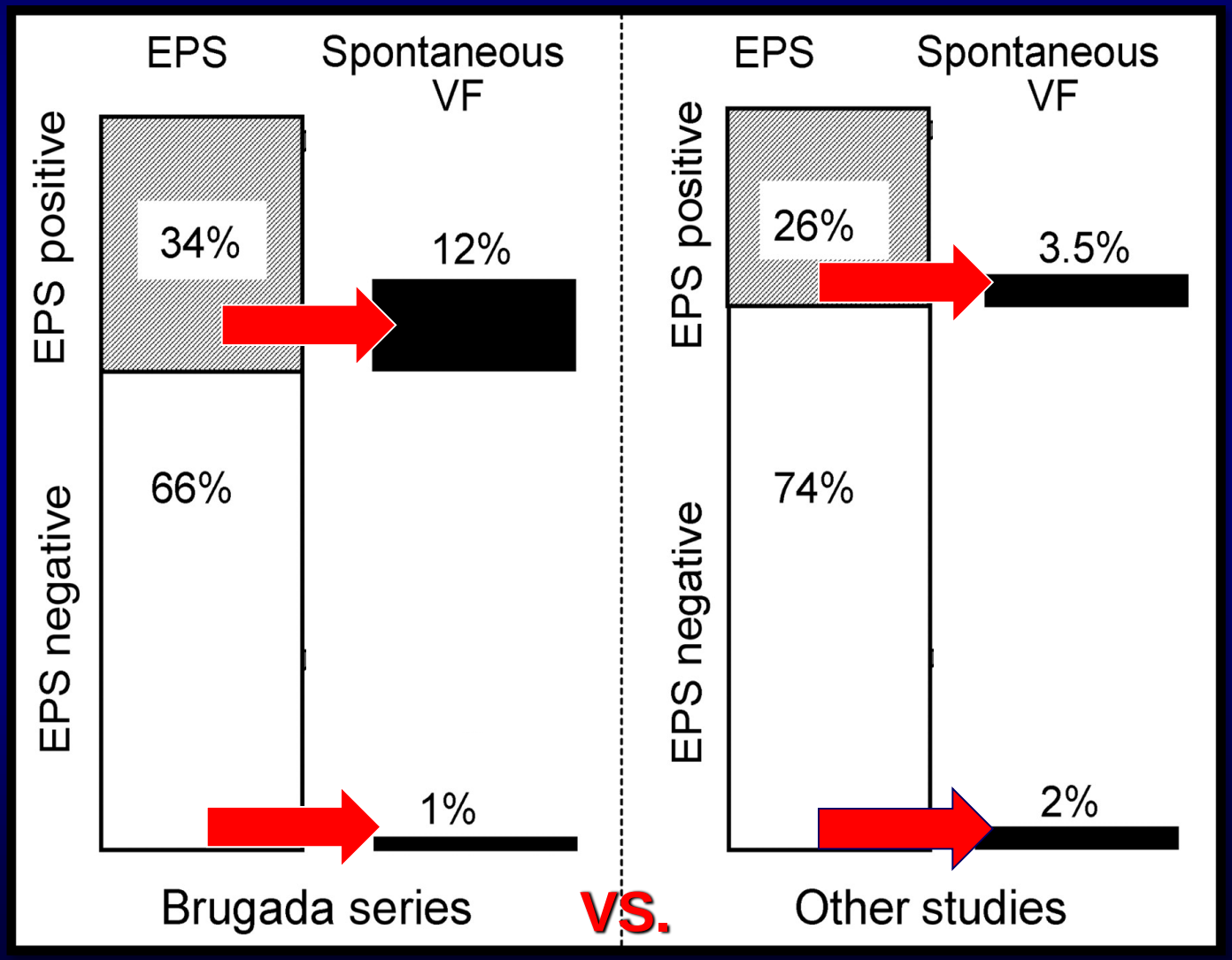
Raju et al JACC 2011

Primary Prevention: 2002/5 Consensus Recommendations

Class IIa:

Inducibility of sustained VT/VF at EP study *can be useful* as an indication for ICD implantation.

Primary Prevention: EP studies to Risk Stratify?



Poor positive predictive value

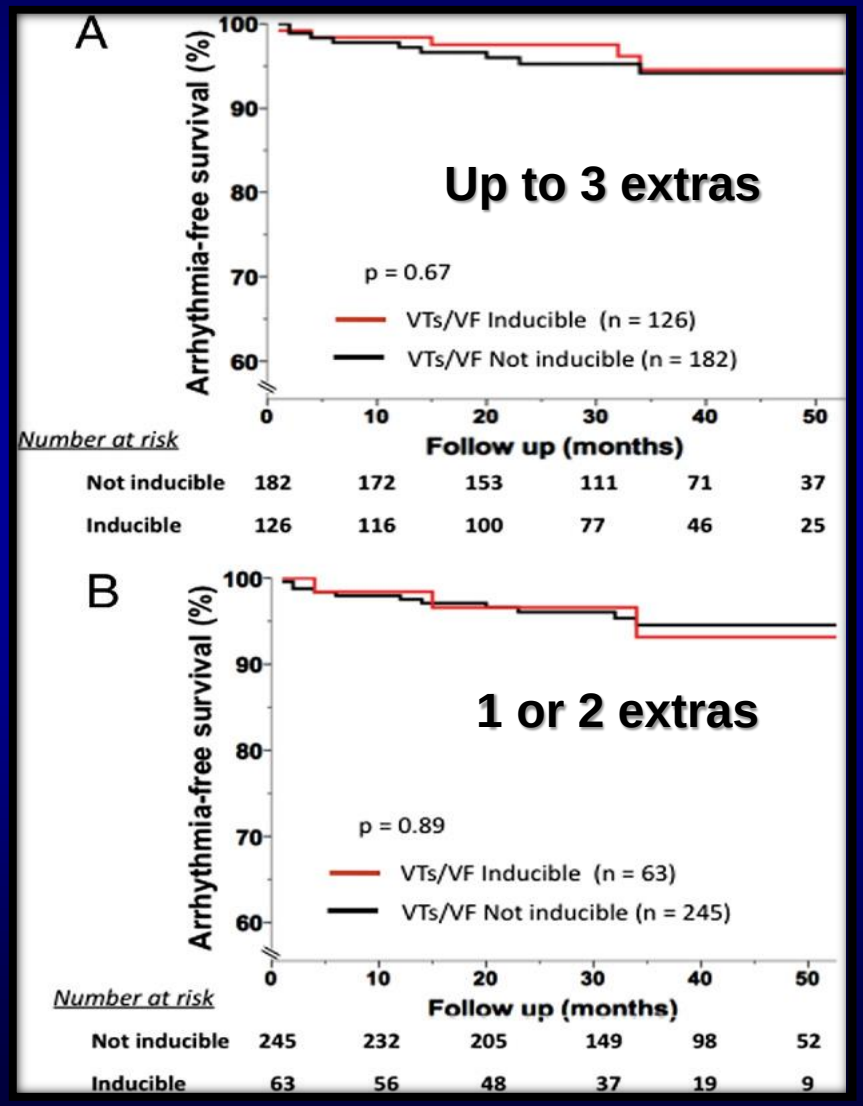
Good negative predictive value?

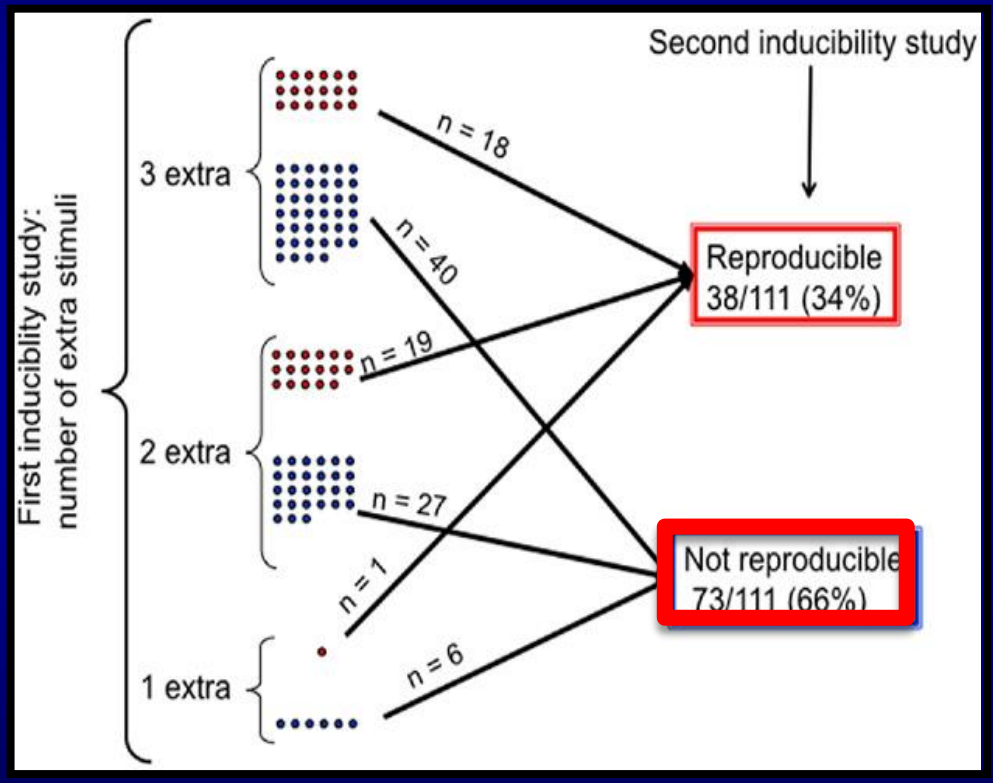
Low event rate

Short follow-up

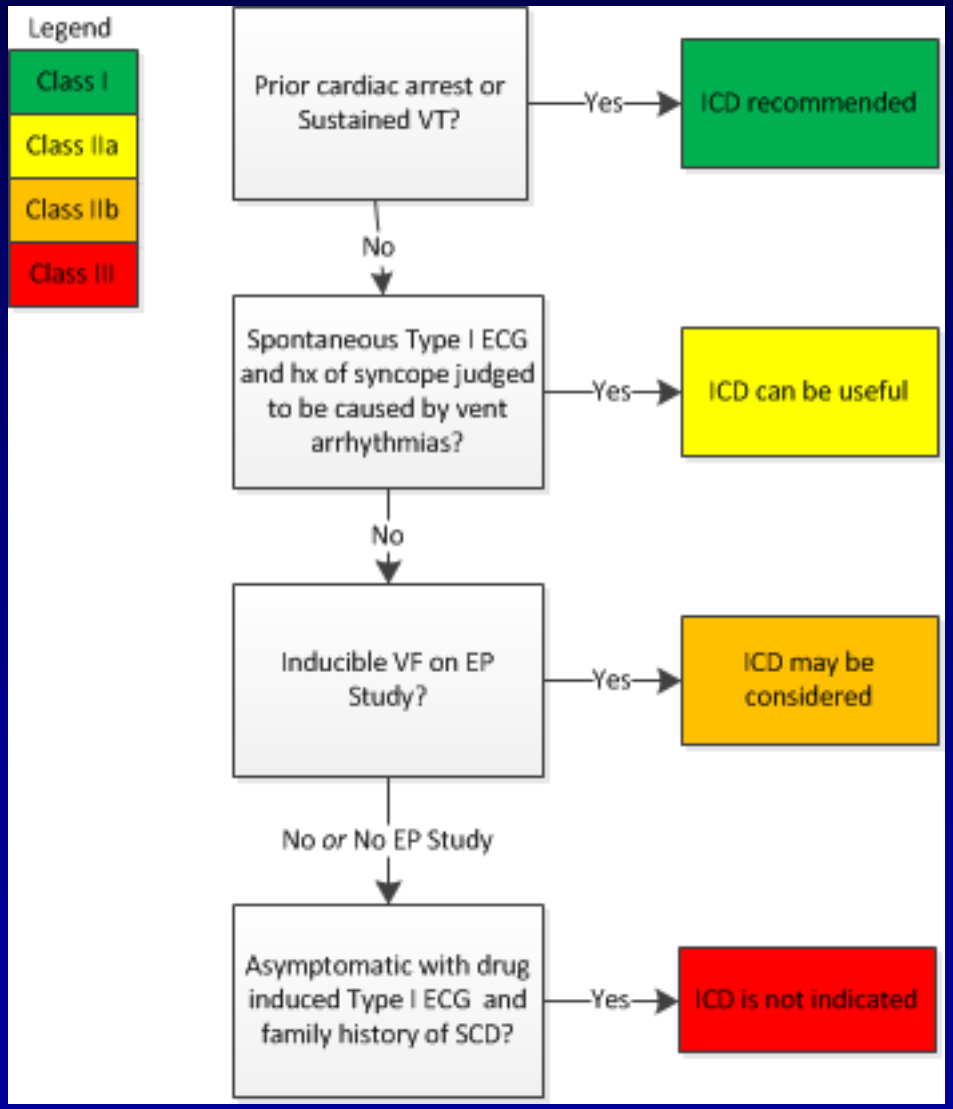
Viskin et al Europace 2007

PRELUDE study: Death Knell for EPS?

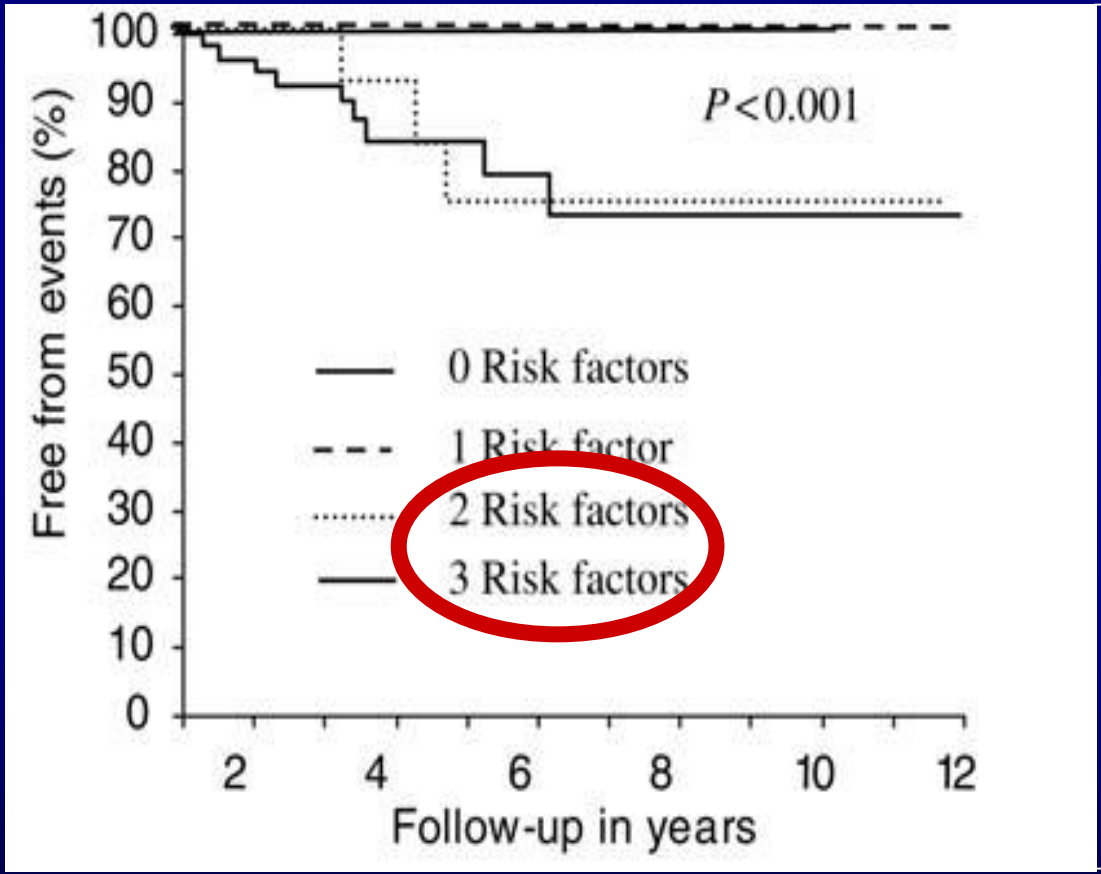




Priori et al JACC 2011


Legend
Class I
Class IIa
Class IIb
Class III
Prior cardiac arrest or Sustained VT?
Yes
ICD recommended
No
Spontaneous Type I ECG and hx of syncope judged to be caused by vent arrhythmias?
Yes
ICD can be useful
No
Inducible VF on EP Study?
Yes
ICD may be considered
No *or* No EP Study
Asymptomatic with drug induced Type I ECG and family history of SCD?
Yes
ICD is not indicated

BUT Parametric Score?



Risk factors:

Syncope

FH of SD

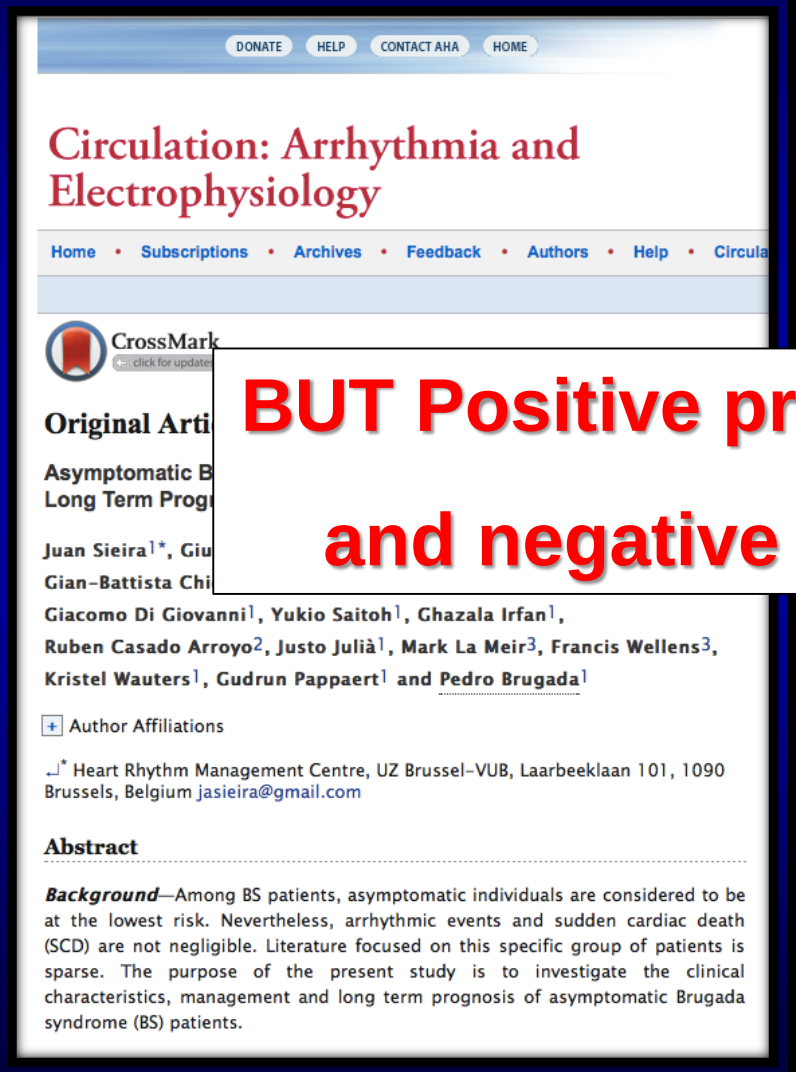
EPS positive

EP studies

NPV = 100%

Delise et al EHJ 2011

And…..



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Asymptomatic B
Long Term Progr

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Abstract

Background—Among BS patients, asymptomatic individuals are considered to be at the lowest risk. Nevertheless, arrhythmic events and sudden cardiac death (SCD) are not negligible. Literature focused on this specific group of patients is sparse. The purpose of the present study is to investigate the clinical characteristics, management and long term prognosis of asymptomatic Brugada syndrome (BS) patients.

363 asymptomatic patients

11.3% spontaneous Type 1 pattern

88.4% underwent EPS

10% inducible

Follow-up 73.2±58.9 months

9 arrhythmic events

Annual incidence rate of 0.5%

BUT Positive predictive value was 18.2%

and negative predictive value 98.3%

1.8, p<0.01]

Spontaneous type 1 HR 4.0 [1.1–14.9, p=0.04]

Sinus node disease HR 8.0 [1.0 – 63.9, p=0.049]

Multivariate only inducibility significant HR 9.1, p<0.01

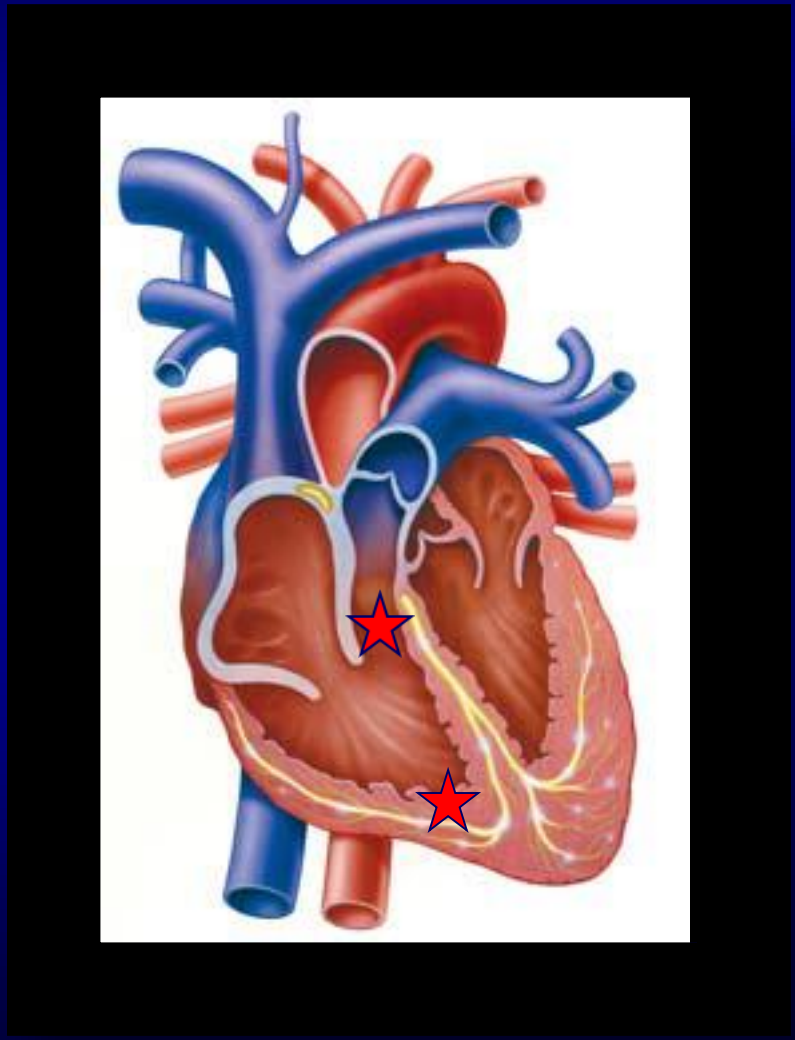
Why differences?

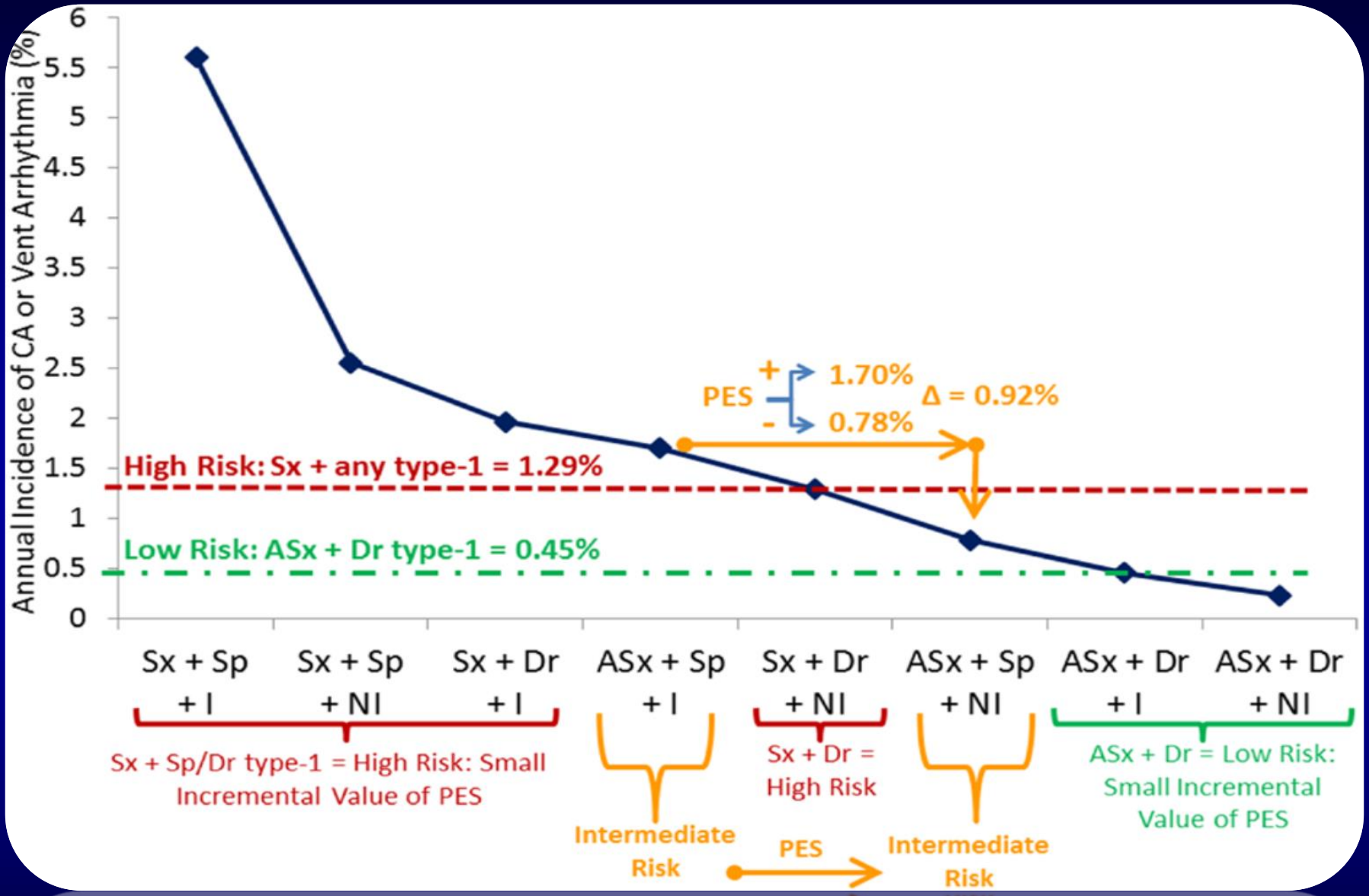
Pacing sites:

- RV apex
- RV outflow tract

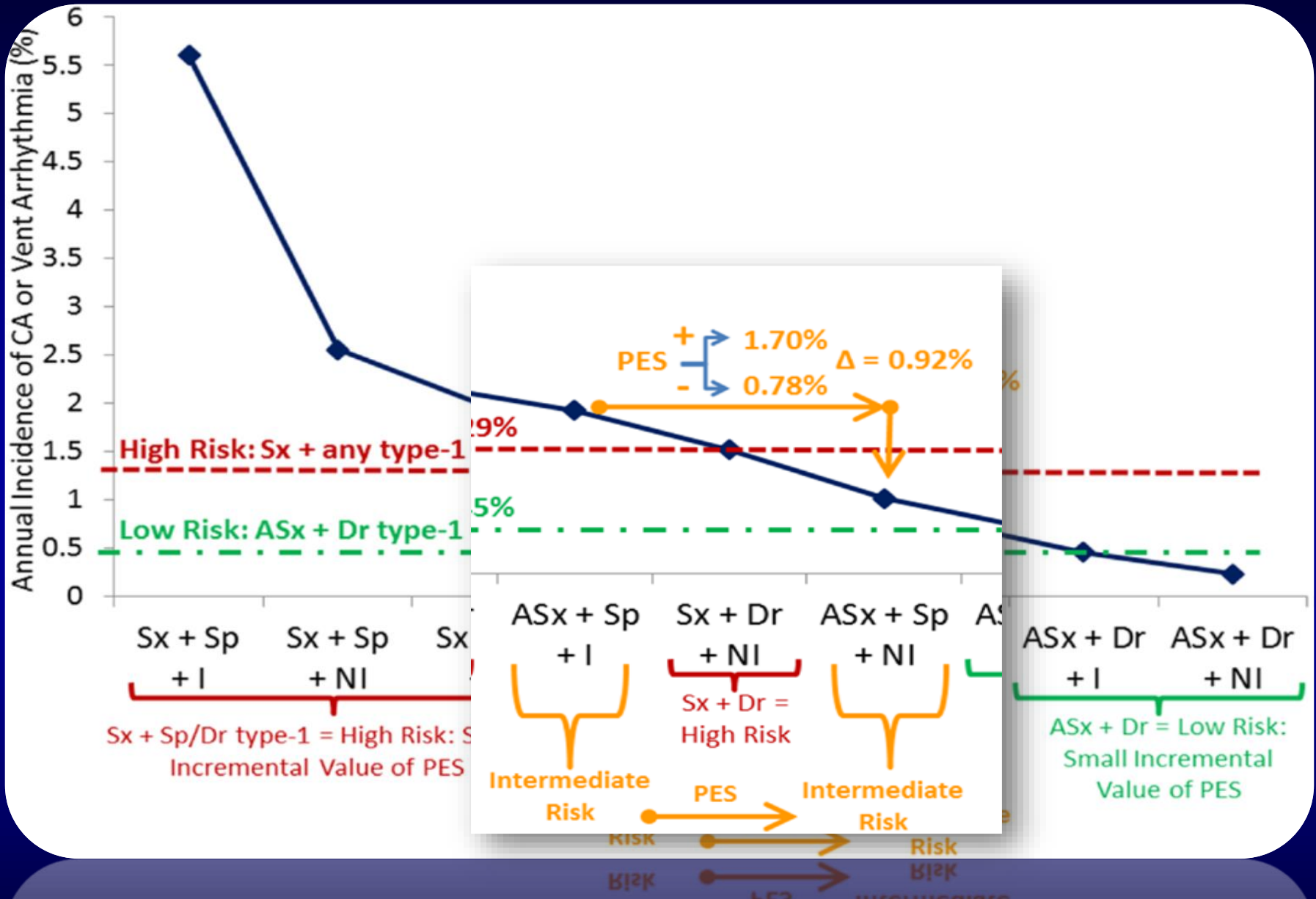
Extra-stimuli:

- Two vs Three
- Minimum coupling intervals (200ms)





Sroubek et al, Douad Circulation 2016



Sroubek et al, Douad Circulation 2016

Alternative Risk Markers?

Signal averaged ECG
Full stomach test
rJ interval in lead V1
QRS duration (lead V6)
Dynamic ST elevation
Heart rate variability (?)
S-wave in lead I
Severity of SCN5A mutation

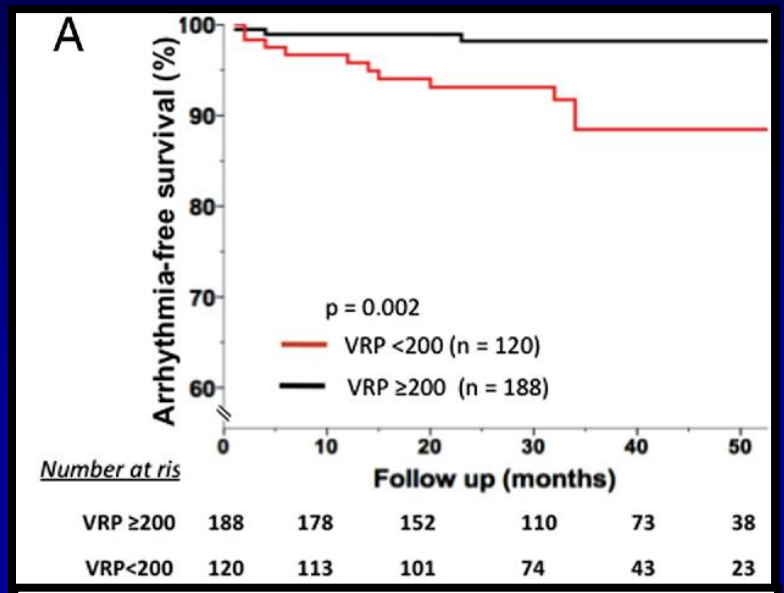
Higher risk: SE Asian

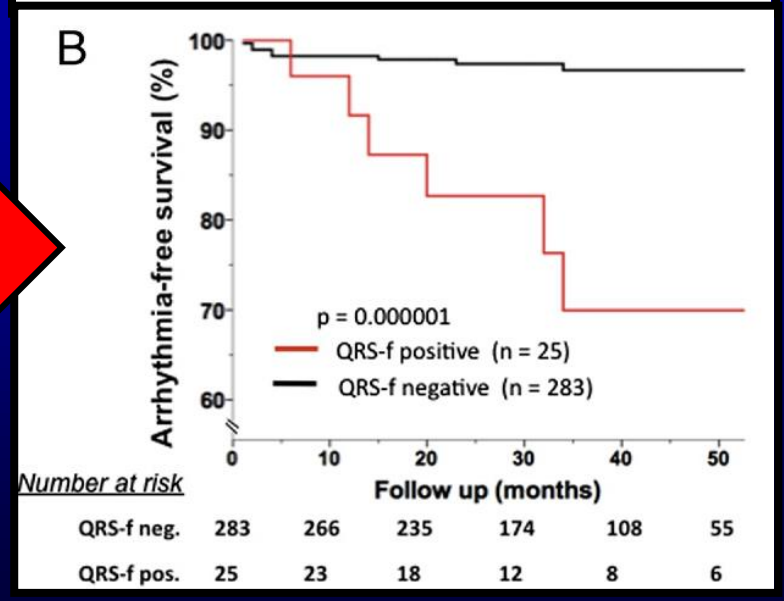
PRELUDE: QRS-f and VRP

Spontaneous type 1 and syncope

Sens 42.9% (19–69)

Spec 90.5% (89–92)

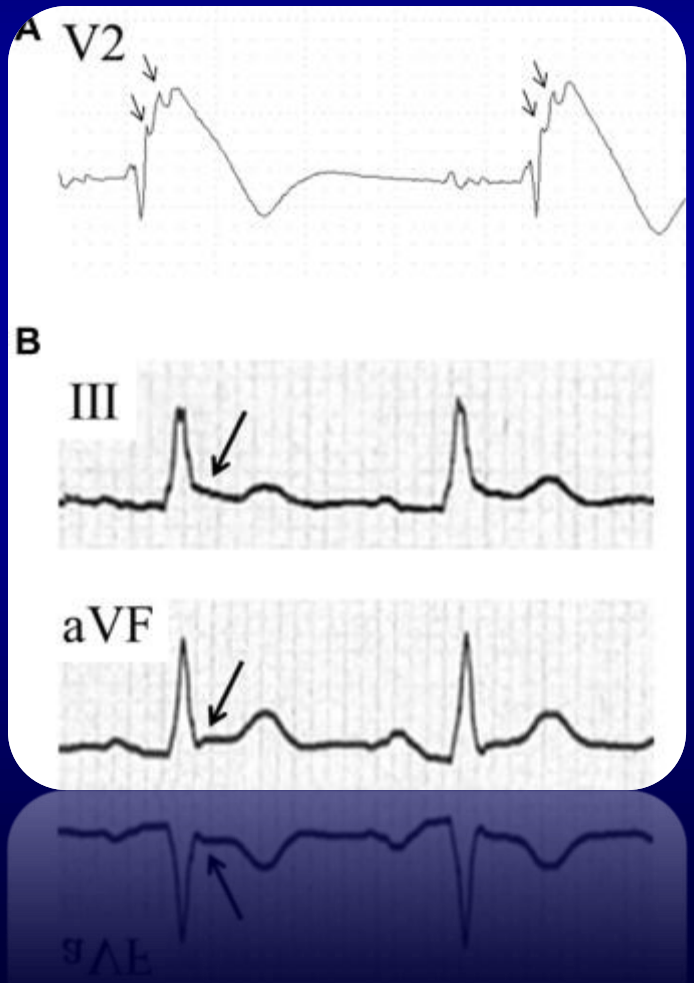




Priori et al JACC 2011

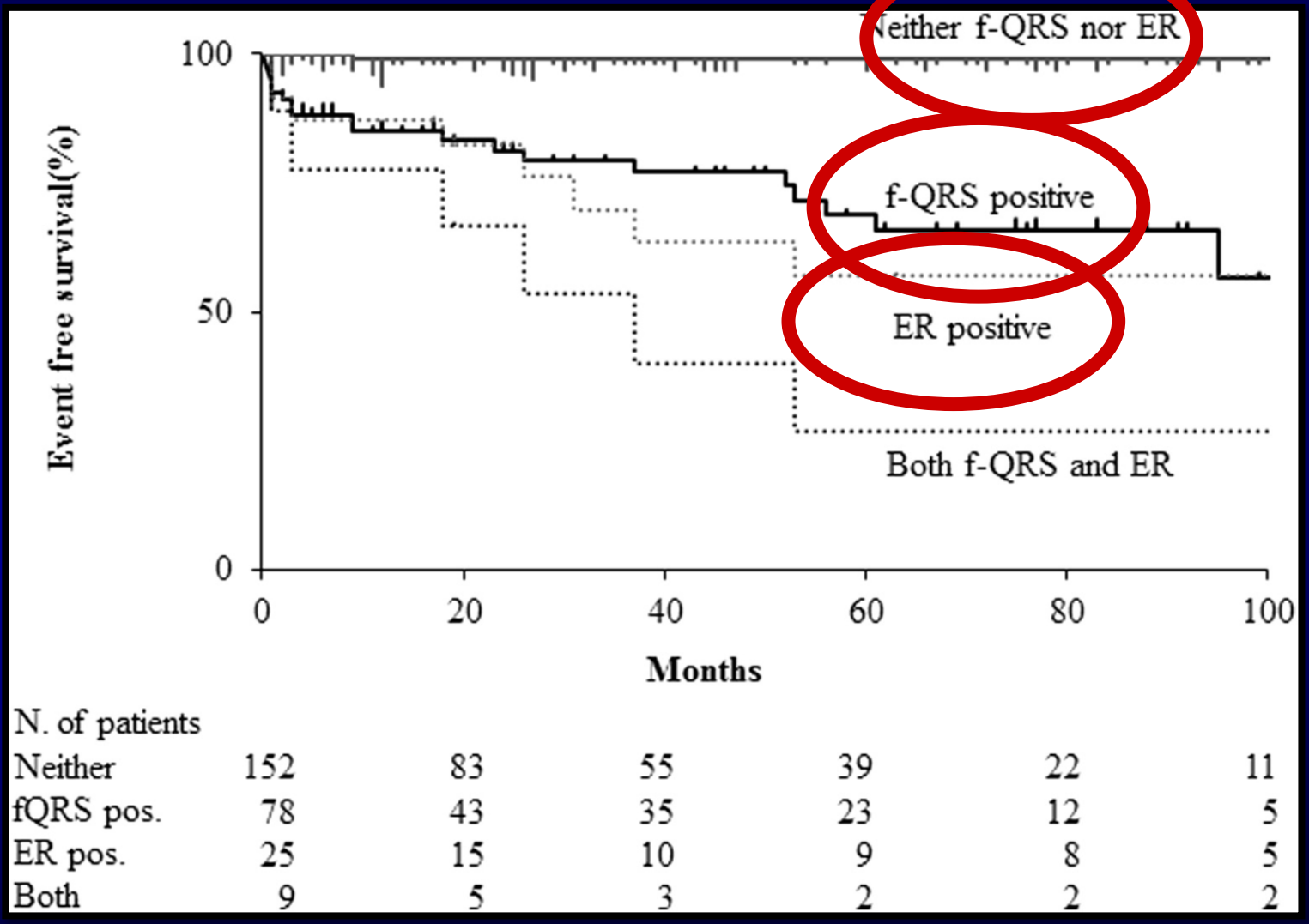
QRS-f and ERP

Male/female	236/10
Age, yrs	47.6 ± 13.6
Mean f-up period, mo	45.1 ± 44.3
History of syncope	40 (16.3)
History of VF episodes	13 (5.3)
Family history of SCD	69 (28.0)
PAF	44 (17.9)
Spontaneous type 1 ECG	156 (63.4)
ER pattern	25 (10.2)
f-QRS	78 (31.7)
Positive LP	166/235 (70.6)
SCN5A gene mutation	17/123 (13.8)
VF induction during EP study	71/155 (45.8)
ICD implantation	63 (25.6)
VF or SCD event during f-up	24 (9.8)



Tokioka et al , JACC 2014

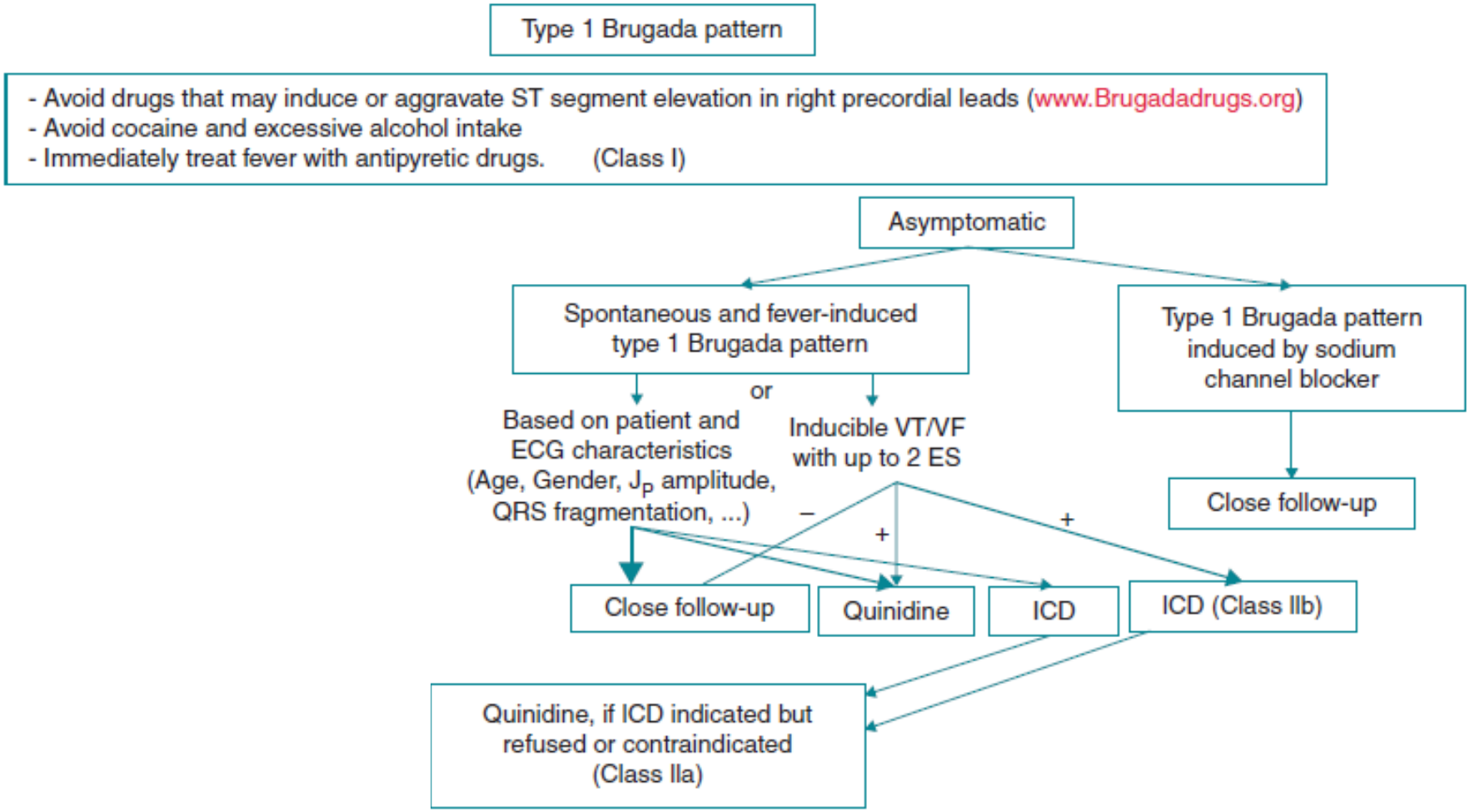
QRS-f and ERP



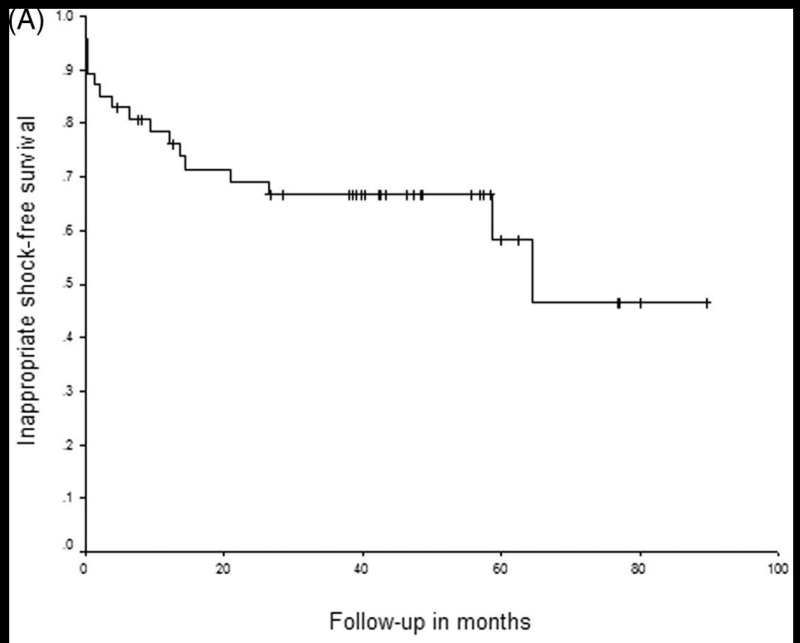
N. of patients						
Neither	152	83	55	39	22	11
fQRS pos.	78	43	35	23	12	5
ER pos.	25	15	10	9	8	5
Both	9	5	3	2	2	2

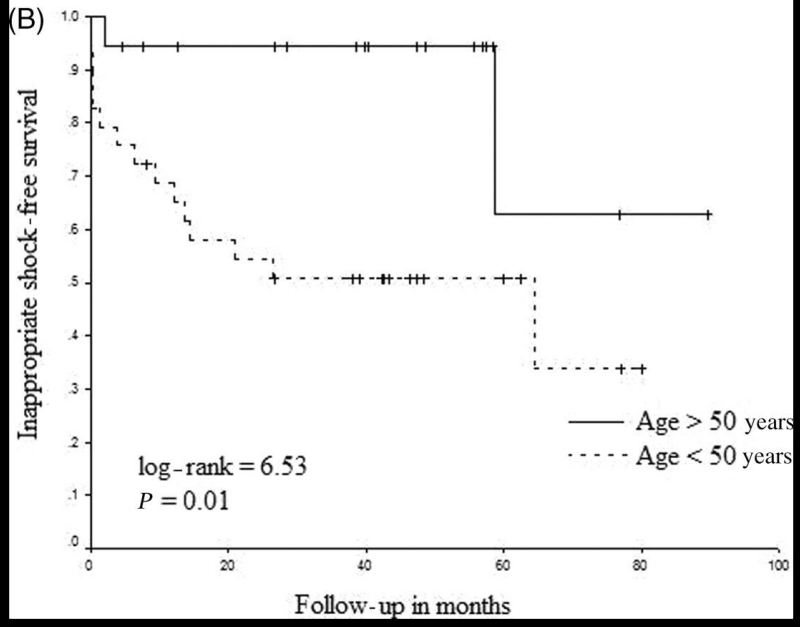
Tokioka et al , JACC 2014

Management


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)
Asymptomatic
Spontaneous and fever-induced type 1 Brugada pattern
or
Based on patient and ECG characteristics (Age, Gender, J_P amplitude, QRS fragmentation, ...)
Inducible VT/VF with up to 2 ES
Type 1 Brugada pattern induced by sodium channel blocker
Close follow-up
–
+
+
Close follow-up
Quinidine
ICD
ICD (Class IIb)
Quinidine, if ICD indicated but refused or contraindicated (Class IIa)

ICD complications in Brugada Syndrome





Sarkozy et al. Eur Heart J 2007

176 patients

Mean follow-up 83.8 ± 57.3 months

33 (18.7%) had inappropriate shocks

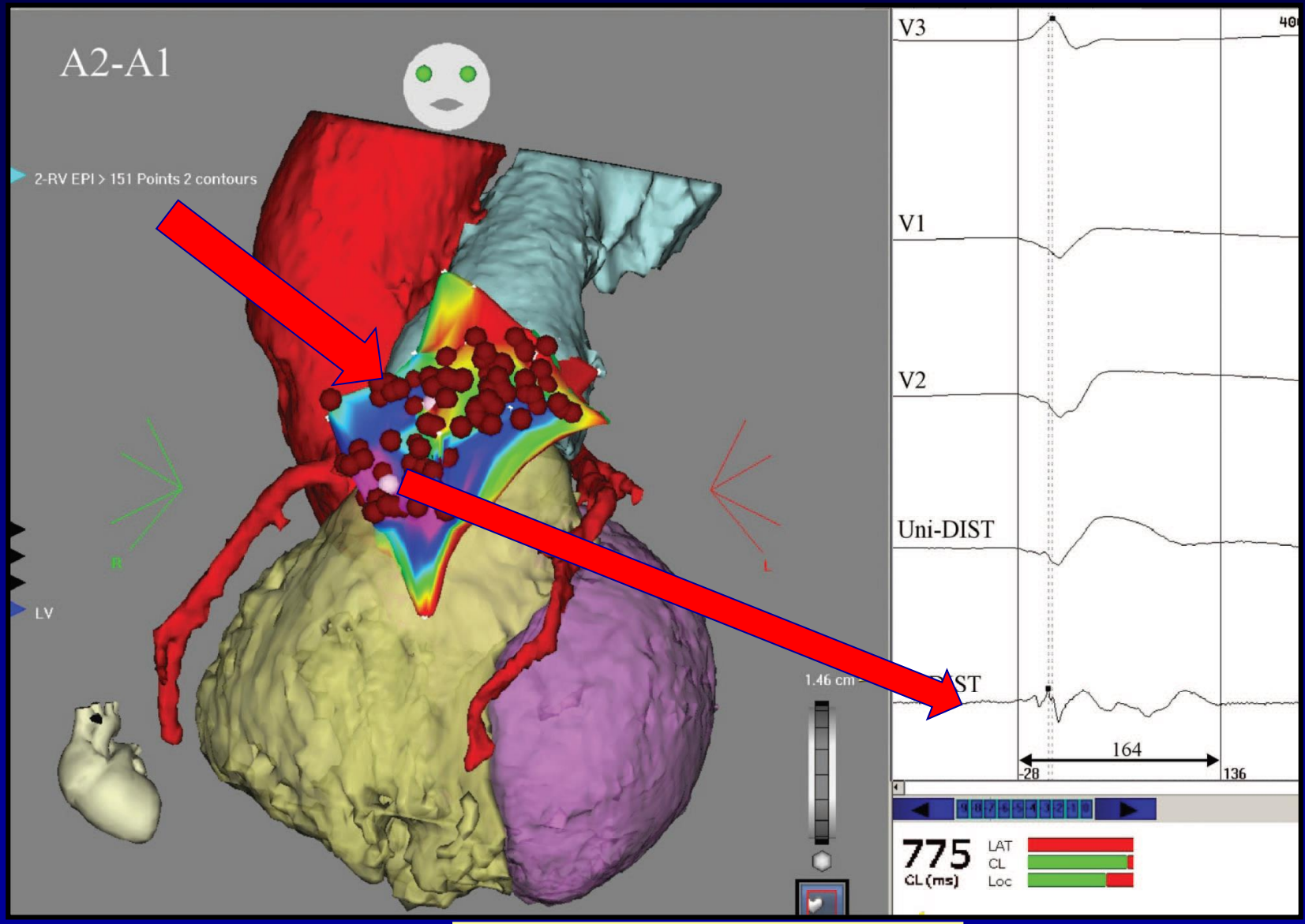
8 (15.9%) experienced device-related complications

Complications consisted of:

- **lead fracture 14**
- **lead dislocation 7**
- **generator migration 2**
- **device infections 5**

Conte et al. JACC 2015

Epicardial mapping and ablation



Nademanee et al Circ 2011

Summary: Risk Stratification

Cardiac Arrest and Syncope = High Risk

Asymptomatic drug-induced ECG = Low risk

BUT Largest group

May harbour many SCDs: How do we stratify?

Asymptomatic + Spontaneous Type 1 ECG = Risk intermediate

Conclusions

Risk stratification is still imperfect

Asymptomatic need better markers

EPS remain albeit class IIb: spontaneous type 1

New ECG/EP measures for risk: ECG/EP/Genomic risk score

Less and better ICD implantation!! S-ICD

Replace with substrate ablation?

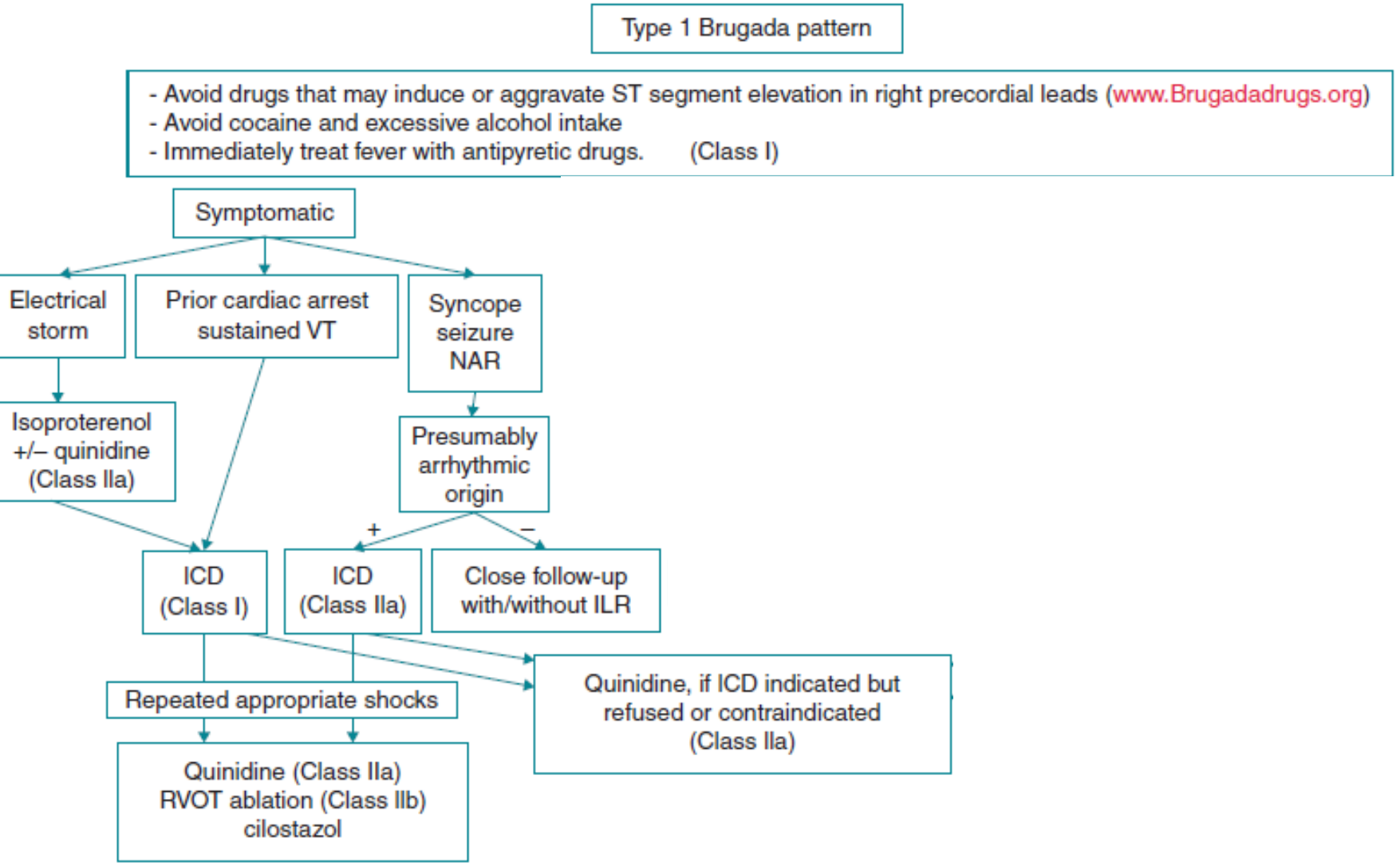
? QUESTIONS

Management

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)

Management


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
Syncope seizure NAR
Isoproterenol +/– quinidine (Class IIa)
Presumably arrhythmic origin
+
–
ICD (Class I)
ICD (Class IIa)
Close follow-up with/without ILR
Repeated appropriate shocks
Quinidine, if ICD indicated but refused or contraindicated (Class IIa)
Quinidine (Class IIa)
RVOT ablation (Class IIb)
cilostazol