

Derek T. Connelly

Consultant Cardiologist

Glasgow Royal Infirmary and

West of Scotland Heart & Lung Centre

Golden Jubilee National Hospital

Devices In Inherited Cardiac Conditions:

BRUGADA SYNDROME

October 2011

- ① 26-year-old ♂ orthopaedic surgical SHO
- ① Presented with non-specific chest pain
- ① No previous symptoms
- ① ECGs:

G442025

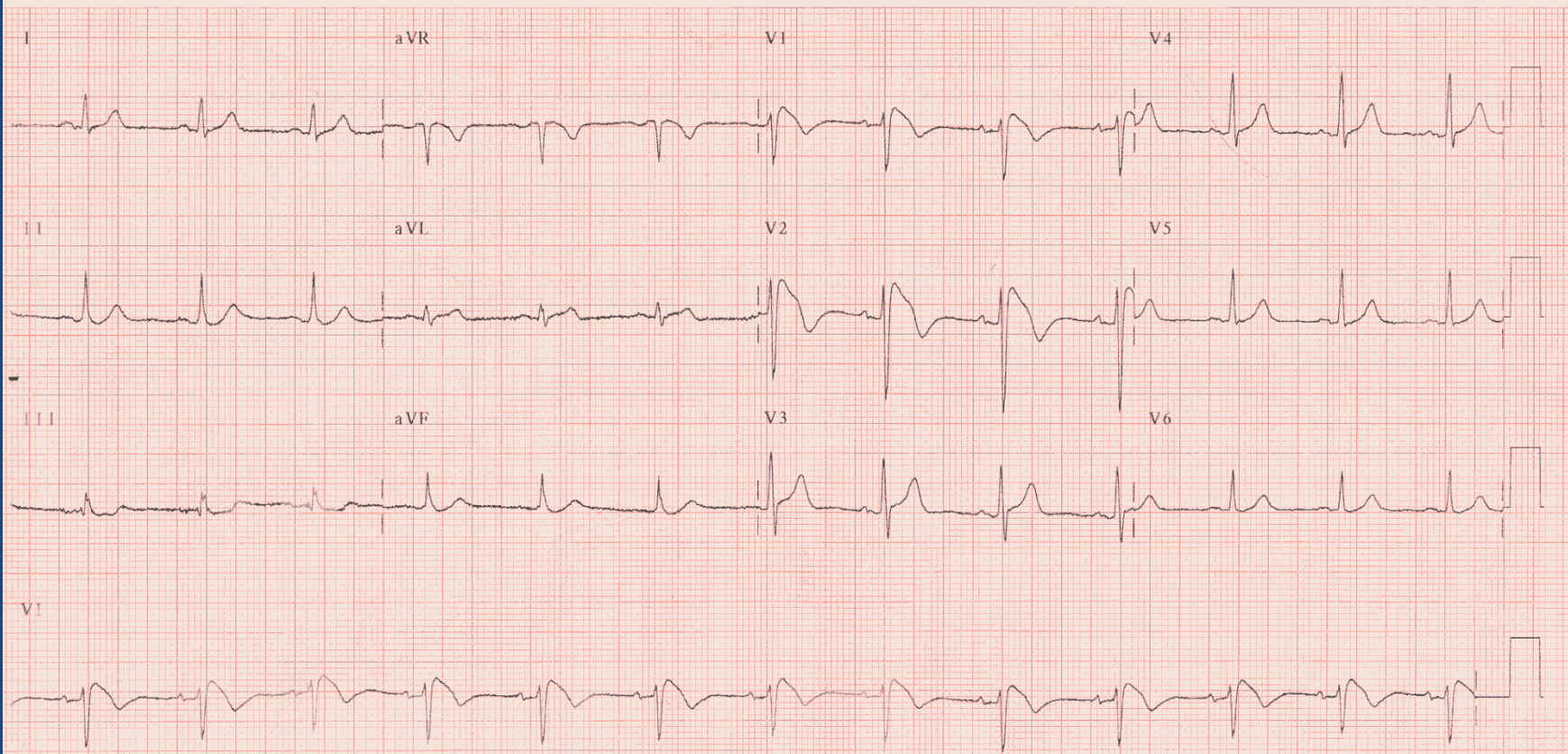
01/03/2002 09:28:41
26 years Male

GLAN CLWYD E.C.G DEPARTMENT

Dept: CCU

Oper: VP

Requested by:
CMB



LOC 00000-5839 Speed: 25 mm/sec Lim 0 mm/mV Chest: 10 mm/mV

50 μ 0.05-150 Hz

02078

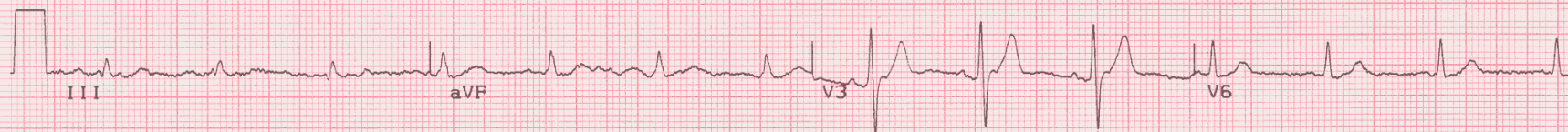
1:3:02

25mm/s Med:
10mm/mV Age: Ht: Wt: NORMAL SINUS RHYTHM
40Hz Sex: Race: NORMAL ECG
Pgm 007B Loc: Room: COPD
v206

Vent. rate 82 BPM
PR interval 132 ms
QRS duration 76 ms
Cart: 1 QT/QTc 344/401 ms
Tech.: P-R-T axes 10 42 30

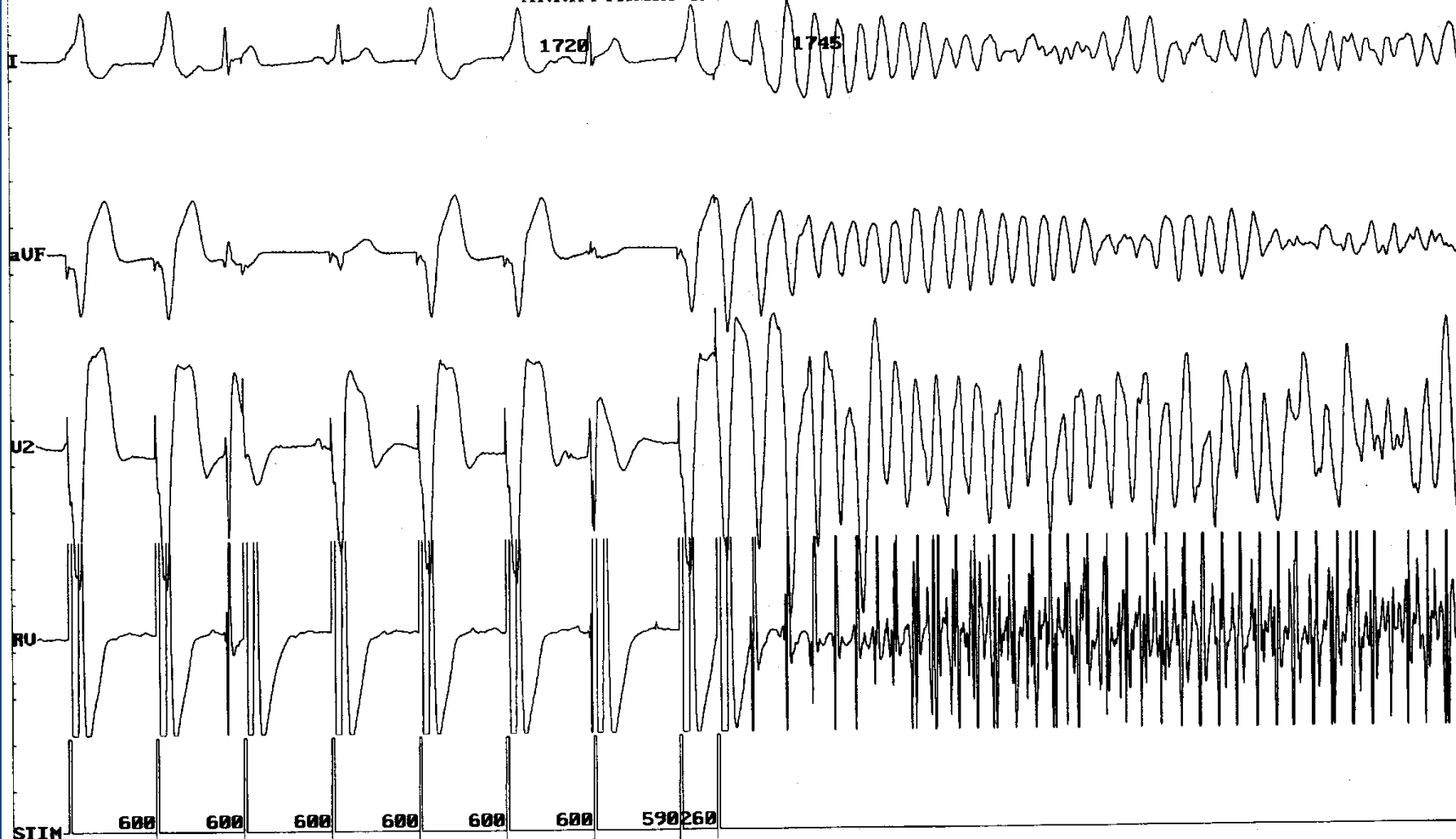
Referred by: DTC

Unconfirmed



Page 2

ARRHYTHMIA INDUCTION RV S1=600 S2=260



Asymptomatic Brugada Syndrome: Is EP study necessary?

- 443 patients studied (180 symptomatic)
- Standardised protocol (RV apex, 2 rates, 2 VPB)
- VT/VF inducible in 217 cases (49%)
 - 70% of symptomatic cases, 34% of asymptomatic subjects
- Follow-up: spontaneous VF in 28% of inducible patients; 2% of non-inducible patients

Brugada et al *J Cardiovasc Electrophysiol* 2003; 14: 455

Asymptomatic Brugada Syndrome: Is EP study necessary?

- Clinical data on 200 patients (152 ♂)
- SCN5A mutations identified in 28/130 patients and 56/121 family members
- Kaplan-Meier analysis: no association between inducibility and spontaneous occurrence of VF
 - 14% cardiac arrest rate in “non-inducible” patients
- Multivariate analysis: after adjusting for sex, family history of sudden death and SCN5A mutations, the combined presence of ST \uparrow V₁₋₃ and syncope identified subjects at risk of cardiac arrest (HR 6.4, 95% CI 1.9 – 21)

Priori et al *Circulation* 2002; **105**: 1342-7

Brugada syndrome – types 1,2 & 3

Wilde et al Brugada Syndrome: Diagnostic Criteria

TABLE 1. ST-Segment Abnormalities in Leads V₁ to V₃

	Type 1	Type 2	Type 3
J wave amplitude	≥2 mm	≥2 mm	≥2 mm
T wave	negative	positive or biphasic	positive
ST-T configuration	coved type	saddleback	saddleback
ST segment (terminal portion)	gradually descending	elevated ≥1 mm	elevated <1 mm

1 mm=0.1 mV. The terminal portion of the ST segment refers to the latter half of the ST segment.

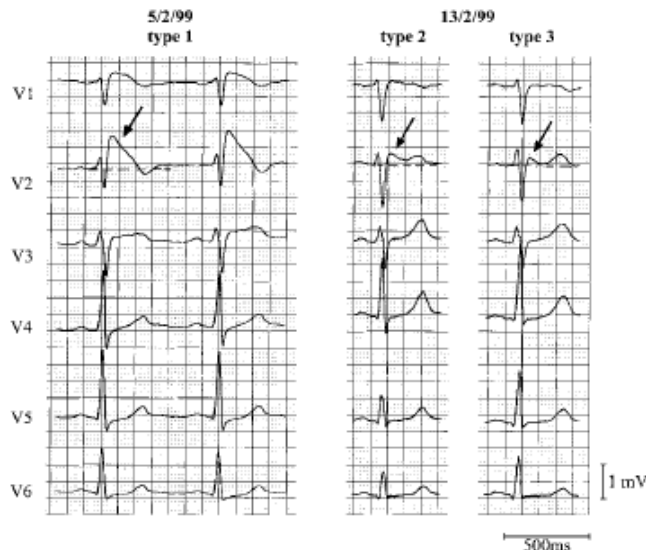


Figure 1. Precordial leads of a resuscitated patient with Brugada syndrome. †

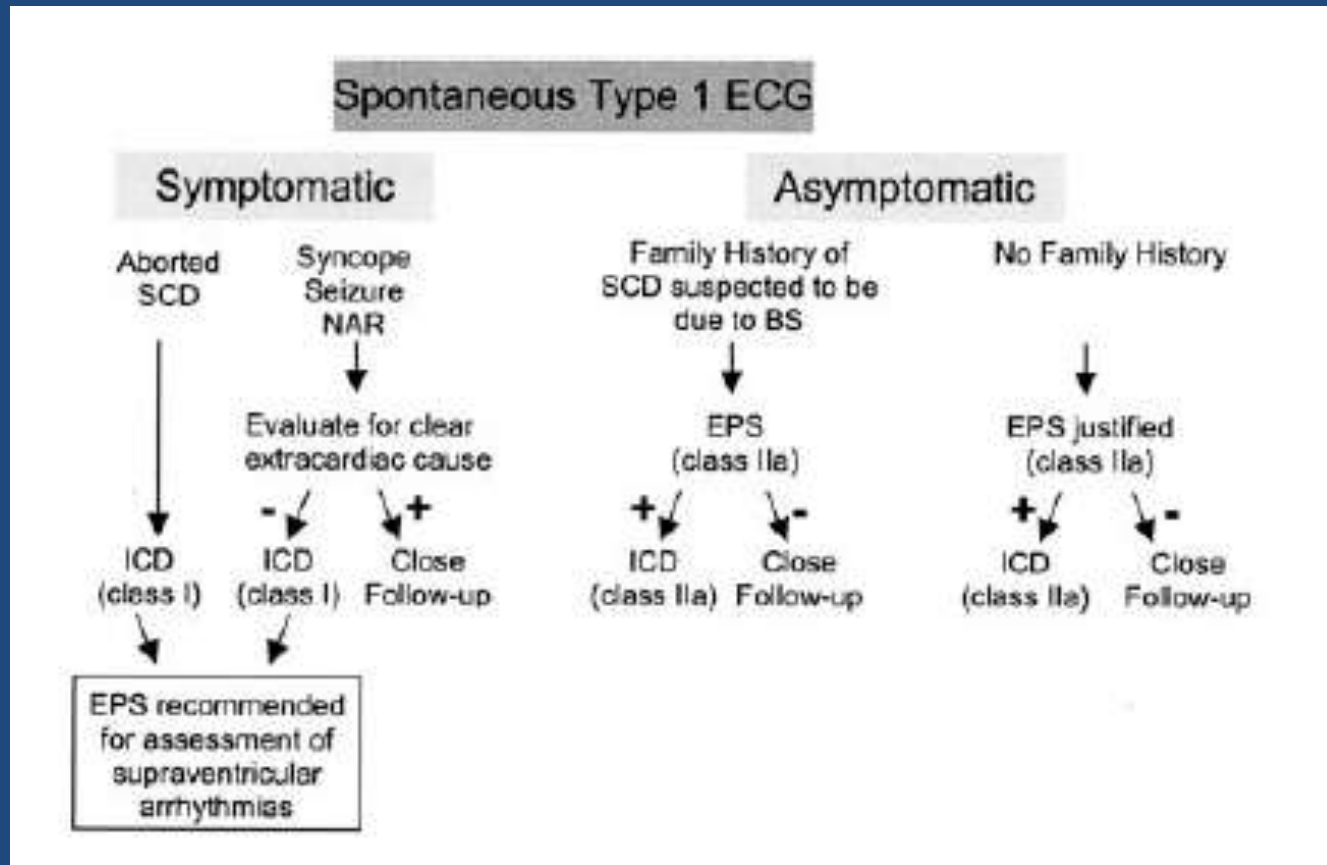
Diagnostic Criteria –
Consensus Report
Circulation 2002; 106:
2514-9

Brugada Syndrome – NICE Guidance

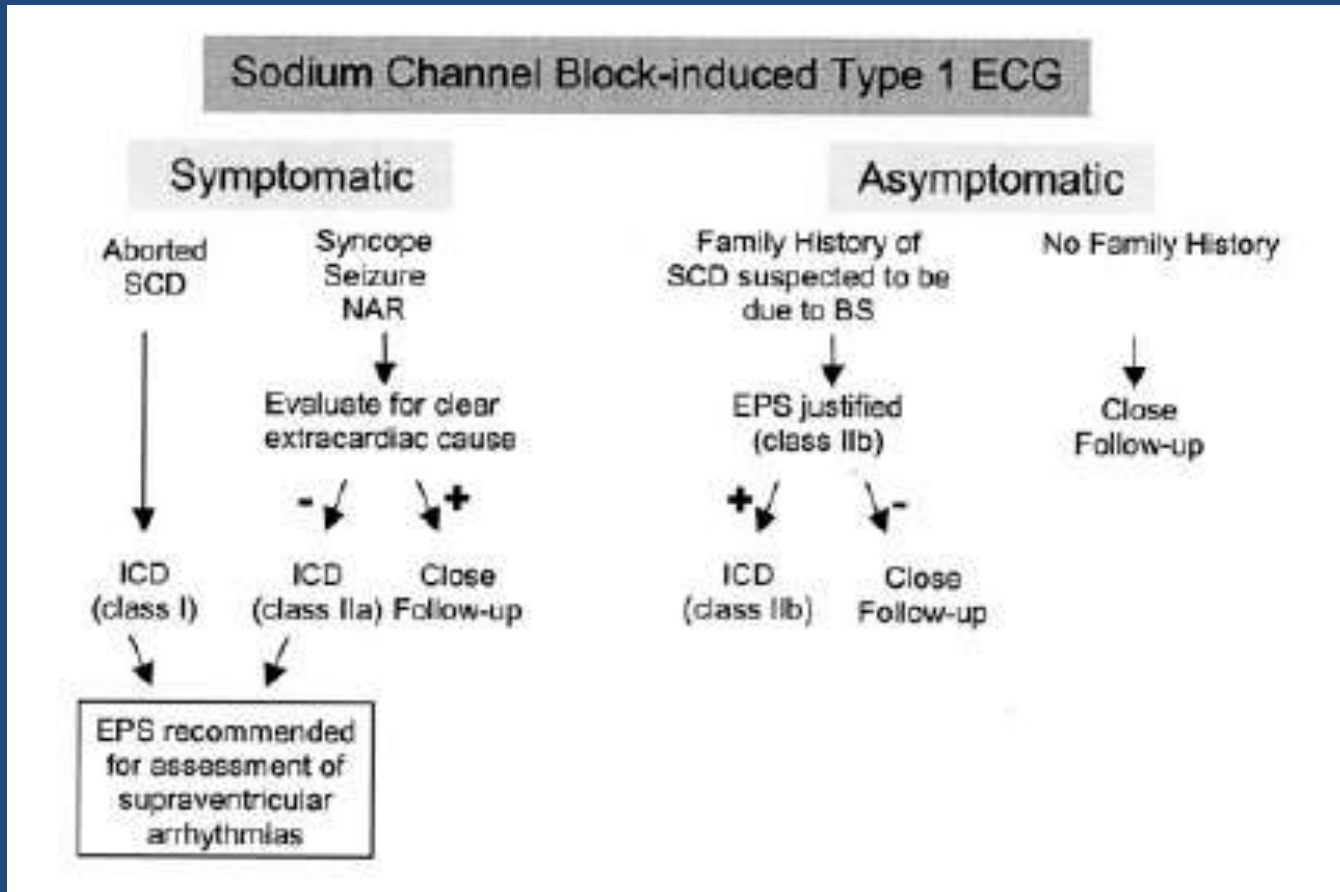
Primary prevention ICD indicated in patients with

- a familial cardiac condition with a *high risk of sudden death*, including long QT syndrome, hypertrophic cardiomyopathy, **Brugada syndrome**, arrhythmogenic right ventricular dysplasia (ARVD) and following repair of congenital heart disease.

Brugada Syndrome 2nd Consensus Conference 2005



Brugada Syndrome 2nd Consensus Conference 2005



ICDs in Brugada Syndrome

Table 1 Cardiac event rates per annum from different study populations for different clinical presentations of Brugada syndrome calculated from available data

	Brugada et al. ⁴¹	Sacher et al. ⁵⁰	Takagi et al. ⁴⁹	Sarkozy et al. ⁵¹	Probst et al. ⁴⁸
Total patient numbers	334	220	188	47	1029
Prior cardiac arrest	13.8%	10.7%	9.8%	Not studied	7.7%
Previous syncope	8.8%	3.15%	1.9%	2.9%	1.9%
Asymptomatic	(72% FH) 3.74%	(54% FH) 1.7%	(10% FH) 0%	(57% FH) 4.8%	(37% FH) 0.5%
Asymptomatic spontaneous type 1 ECG	6.4%	2.54%	0%	Unavailable	0.81%
Asymptomatic drug-induced type 1 ECG	0%	0.73%	0%	Unavailable	0.35%

Event rates are rates per annum of sudden cardiac death, ventricular fibrillation, or (in patients with ICDs) appropriate shocks per annum.

Garratt, Elliott, Behr et al *Europace* 2010; 12: 1156-75

ICDs in Brugada Syndrome

- Brigham & Women's Hospital experience
- 33 consecutive patients 1995-2008
 - Type 1 n=18, type 2 n=12, drug-induced n=3
 - 3 patients had a history of VF arrest, 70% syncope, 56% VT/VF inducible at EPS
- During 7.9 ± 3.6 years of follow-up, only 2 patients had appropriate ICD shocks
 - Both had prior history of VF arrest
- 5 patients (15%) had inappropriate shocks
- 8 patients (24%) developed 11 major device-related complications

Role of EP study – meta-analysis

- ⊙ 15 studies, 1036 patients
 - 18% VF survivors, 23% syncope, 59% asymptomatic
- ⊙ VT/VF inducible in 548
- ⊙ VT/VF during follow-up in 141 patients
- ⊙ Except for one study, the OR for VT/VF during follow-up in relation to VT/VF inducibility was non-significant
 - (OR 1.5; P = ns).

Paul et al *Eur Heart J* 2007; **28**: 2126-33

Risk stratification – meta-analysis

- ⊙ 30 studies, 1545 patients
- ⊙ Relative risk of SCD, syncope or ICD shock assessed
- ⊙ Overall event rate 10% at 32 months
 - ↑ risk in pts with history of syncope or VF (RR 3.24)
 - ↑ risk in ♂ v ♀ (RR 3.47)
 - ↑ risk with spontaneous type 1 pattern (RR 4.65)
- ⊙ No increase in risk with
 - FH of SCD
 - SCN5A mutation
 - Inducibility at EPS

Gehi et al *J Cardiovasc EP* 2006; 17: 577-83

Brugada Syndrome – long-term prognosis

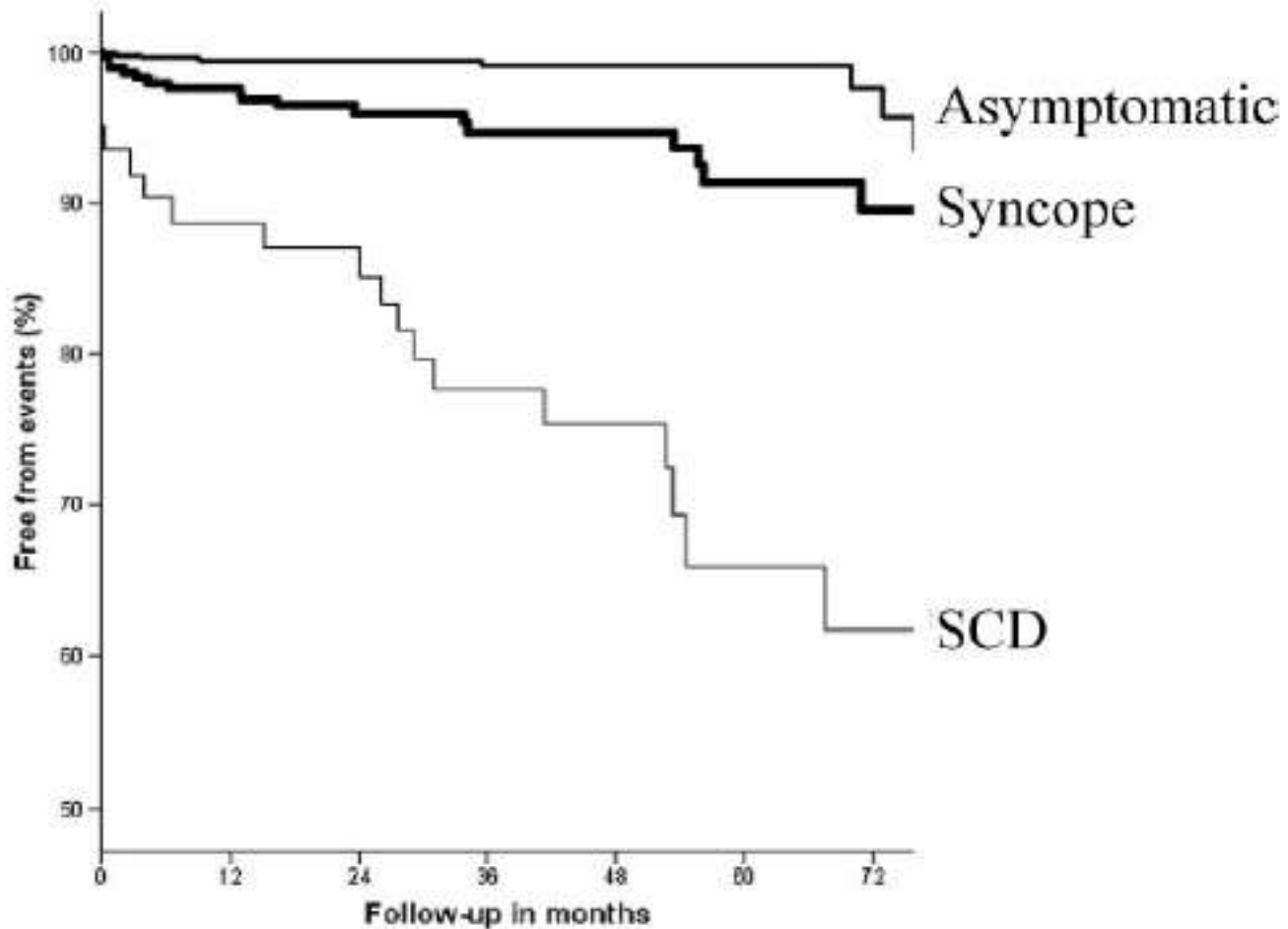
- ◎ FINGER Registry (France, Italy, Netherlands, GERmany): largest series to date
- ◎ 1029 consecutive subjects, 72% ♂, median age 45
- ◎ 6% aborted SCD, 30% syncope, 64% asymptomatic
- ◎ Median follow-up 32 months
 - 51 events (7 deaths, 44 appropriate ICD shocks)

Probst et al *Circulation* 2010; **121**: 635-643

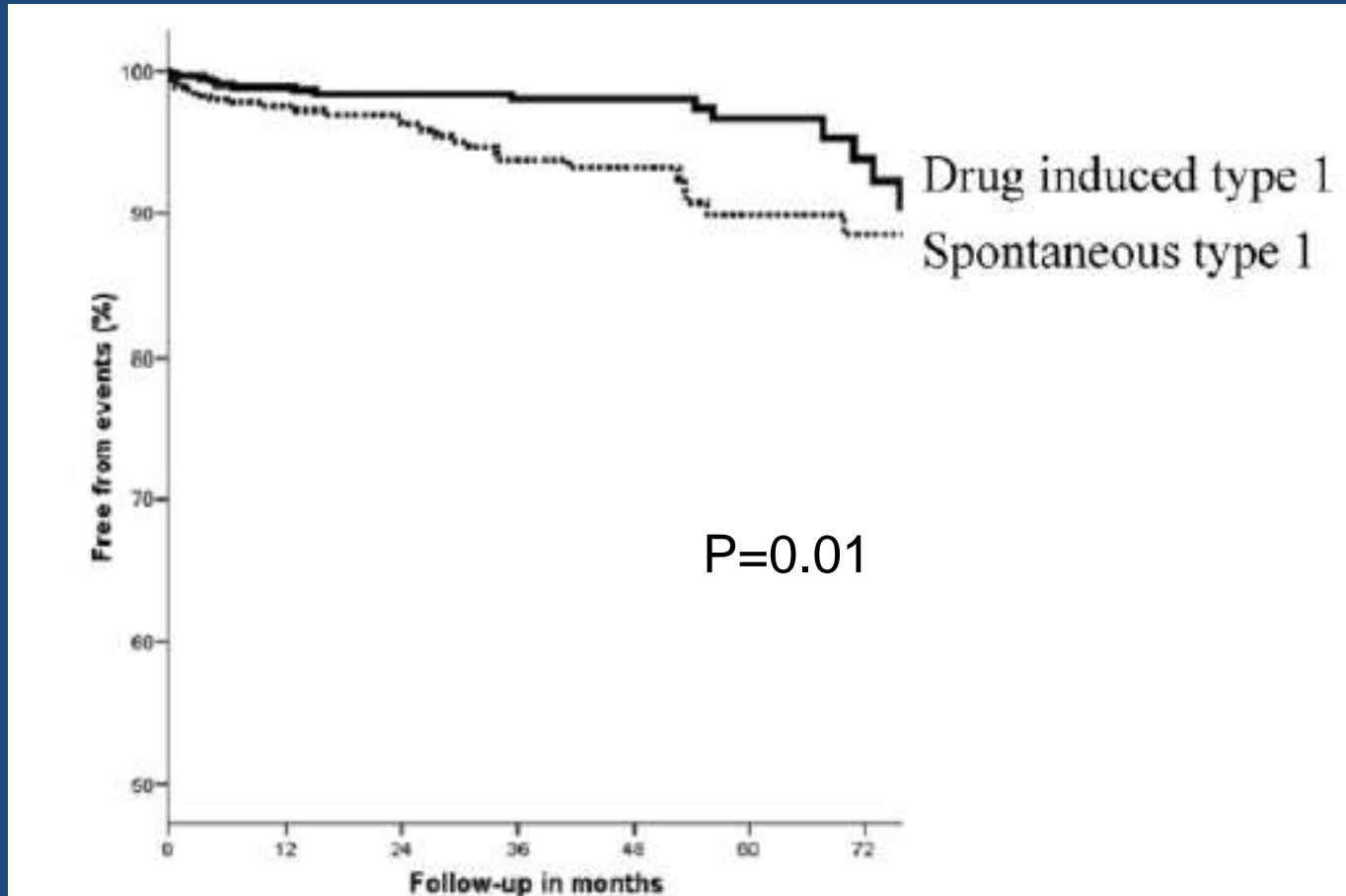
Brugada Syndrome – long-term prognosis

- ⊙ Event rate per year
 - 7.7% in patients with aborted SCD
 - 1.9% in patients with syncope
 - 0.5% in asymptomatic patients
- ⊙ Arrhythmic events commoner in patients with symptoms & with spontaneous type 1 ECG
- ⊙ Gender, family history, inducibility at EPS, SCN5A mutation not predictive of events

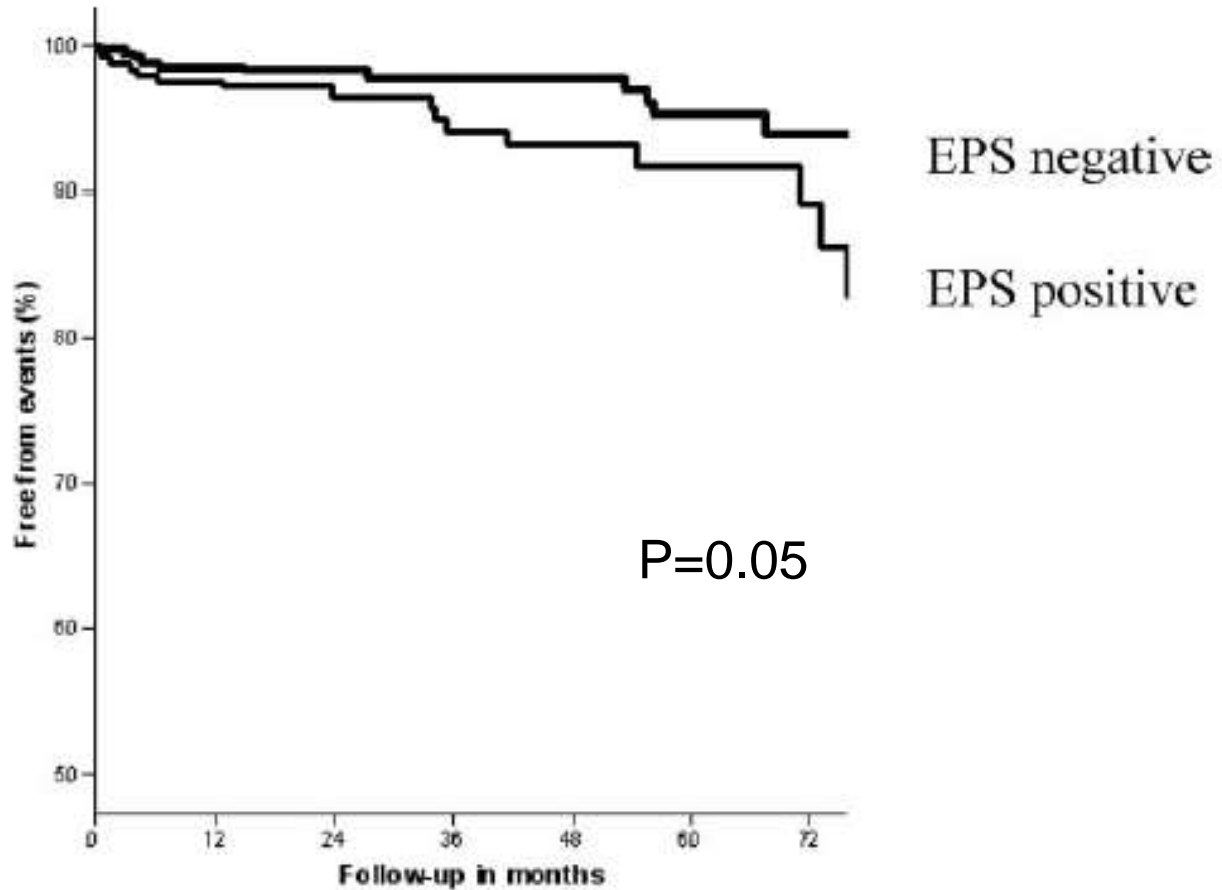
Probst et al *Circulation* 2010; **121**: 635-643



Probst et al *Circulation* 2010; **121**: 635-643



Probst et al *Circulation* 2010; 121: 635-643



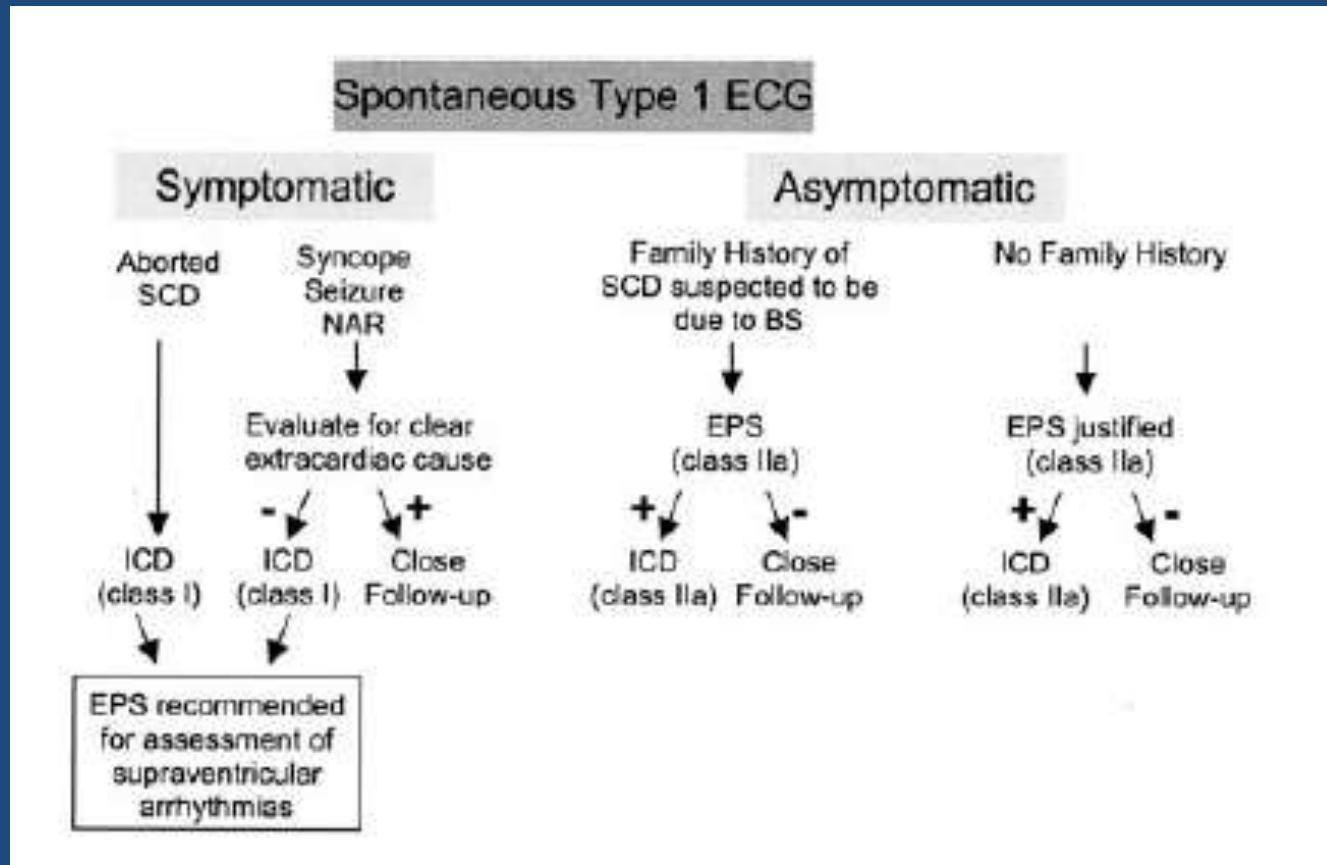
Probst et al *Circulation* 2010; 121: 635-643

Brugada syndrome – HRUK Guidelines

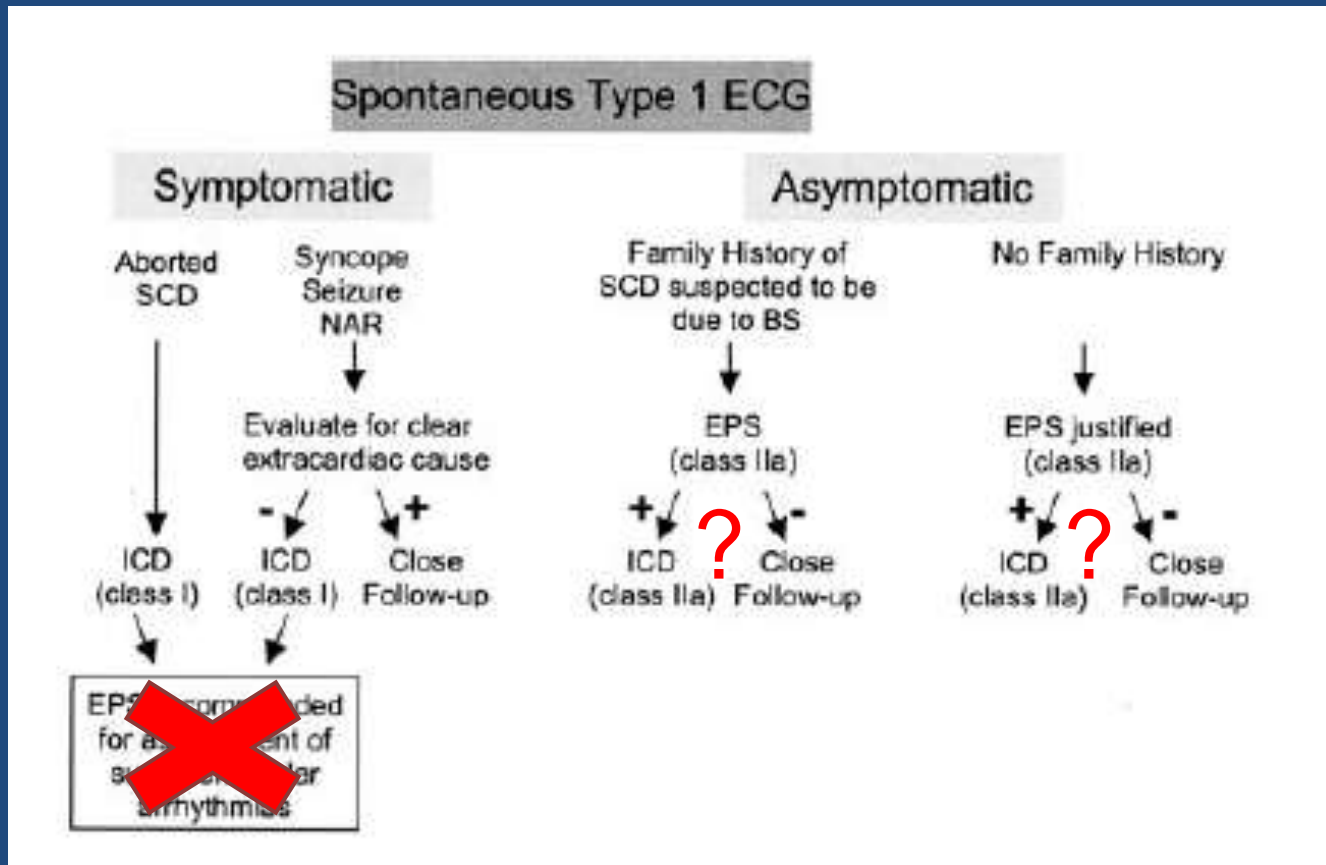
- BrS patients presenting with VF /cardiac arrest without reversible precipitant should undergo ICD implantation
- BrS patients with syncope (when VT/VF has not been excluded as the cause of syncope) should undergo ICD implantation
- Spontaneous type 1 ECG without symptoms: a firm recommendation cannot be made at this time
- Asymptomatic individuals who require a drug to induce the type 1 ECG pattern are at low risk of sudden death; risks of ICD likely to outweigh benefits

Garratt, Elliott, Behr et al *Europace* 2010; **12**: 1156-75

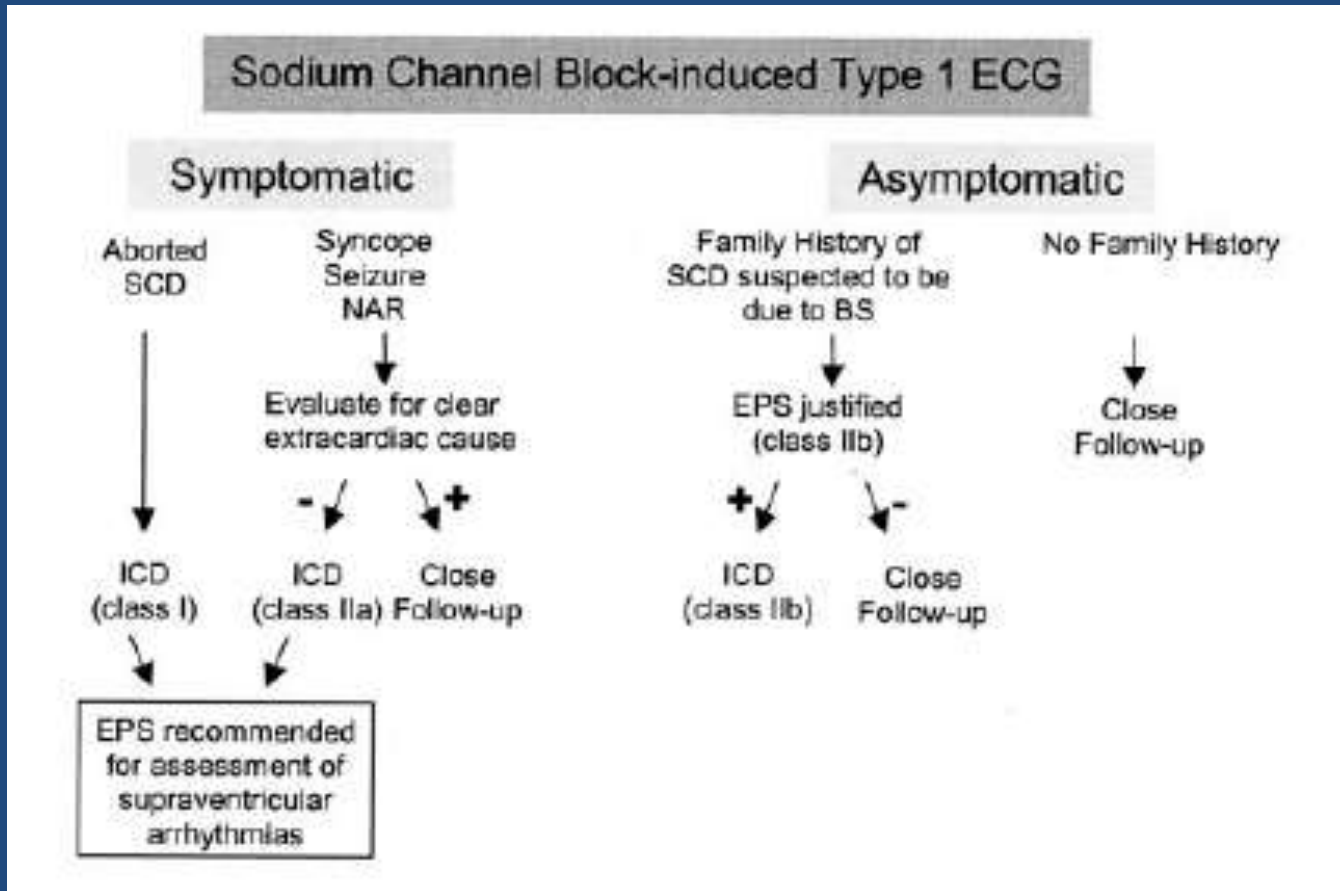
Brugada Syndrome 2nd Consensus Conference 2005



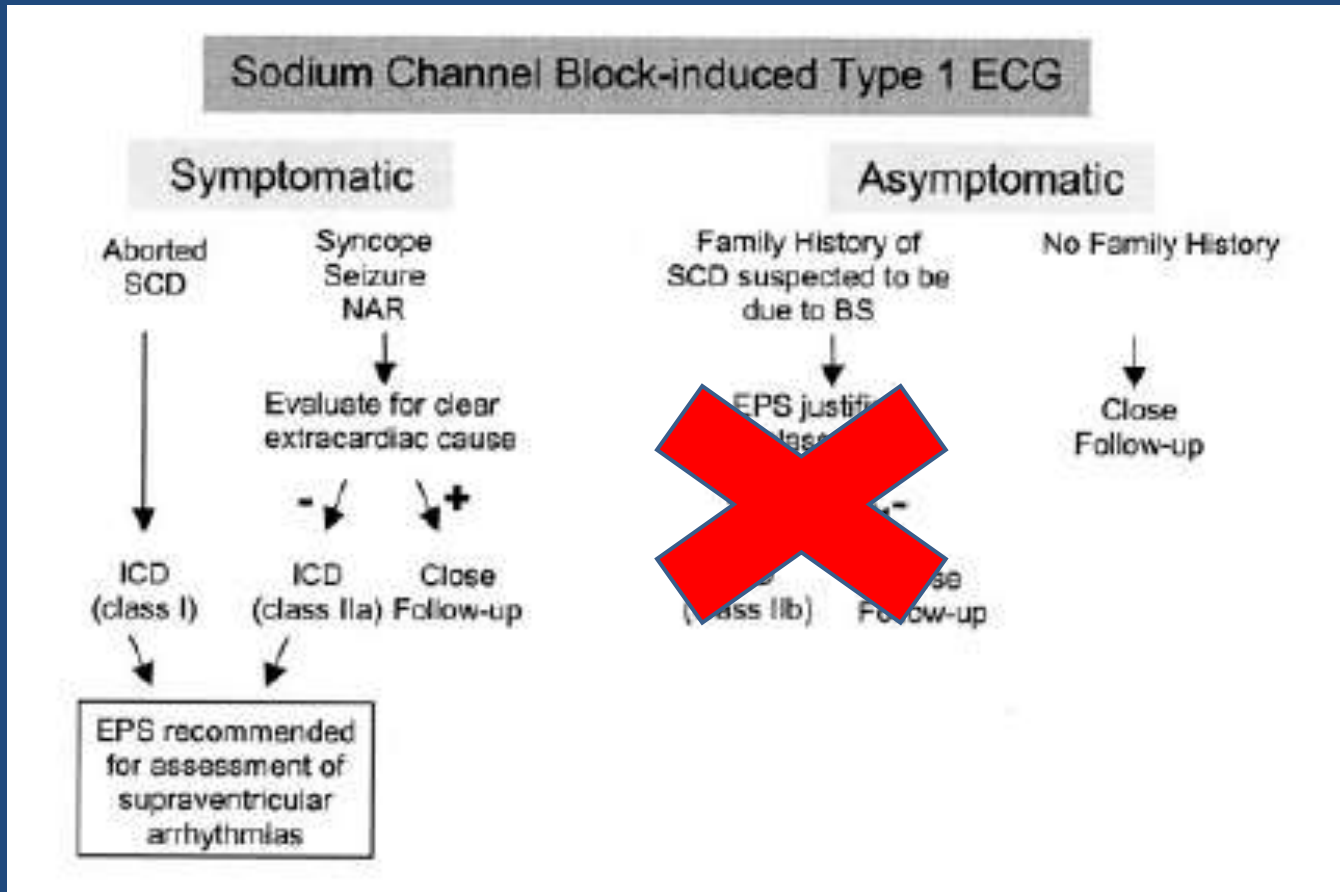
Brugada Syndrome 2nd Consensus Conference 2005



Brugada Syndrome 2nd Consensus Conference 2005



Brugada Syndrome 2nd Consensus Conference 2005



Do Brugada Syndrome patients with VF / SCD have history of “high-risk” features?

- Analysis of 2002 individuals in 49 families; 50 deaths
- Mean age at death 29 ± 10 years; 82% ♂
- Antemortem ECGs available for 5 probands
 - Only 1 had spontaneous type 1 BrS pattern
- 9 patients had had ≥ 1 syncopal event before fatal event
- 68% of probands would have been considered “low-risk” by current criteria
- Conclusion: We need better risk stratification criteria!

Raju et al *JACC* 2011; 57: 2340-5

Conclusions

- ⦿ New HRUK Guidelines are up-to-date
 - And written by a panel of experts!
- ⦿ BrS patients with a history of VT/VF or unexplained syncope should have an ICD
- ⦿ Asymptomatic patients with drug-induced type 1 BrS pattern do not need an ICD

Conclusions (2)

- Family history is not a useful predictor of SCD

Conclusions (2)

- Family history is not a useful predictor of SCD



Conclusions (3)

- ⊙ Asymptomatic patients with spontaneous type 1 BrS pattern have “intermediate” risk
 - Individual discussion with patient *re* possible risks v benefits of ICD
 - Possible role for EP study
- ⊙ Better risk stratification is needed!