Updates on Brugada Syndrome

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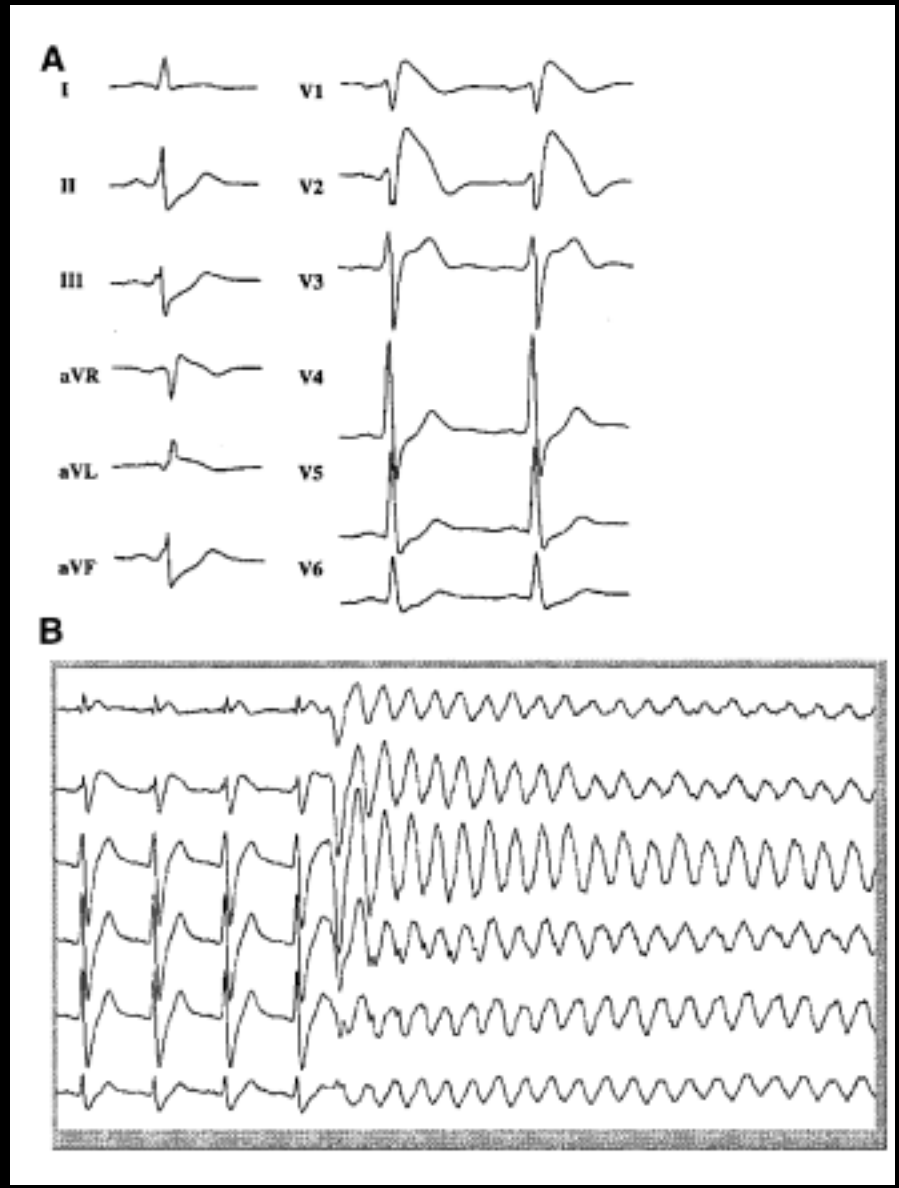
Asan Medical Center

Brugada syndrome

Characteristic ECG

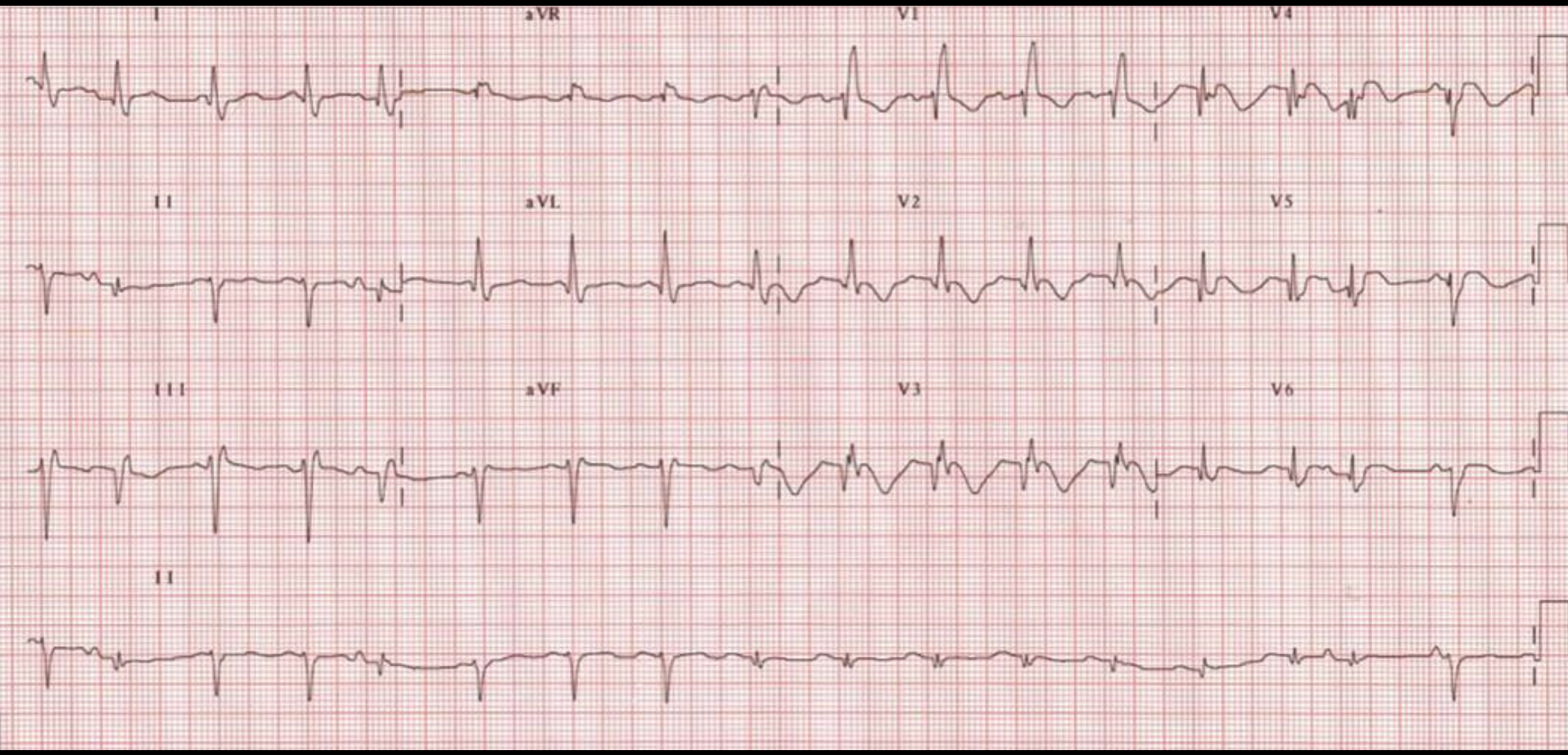
Dramatic clinical manifestation

Basic and clinical research



Brugada-like Precordial ST Elevation on ECG by Anterior Mediastinal Infective Mass Lesion

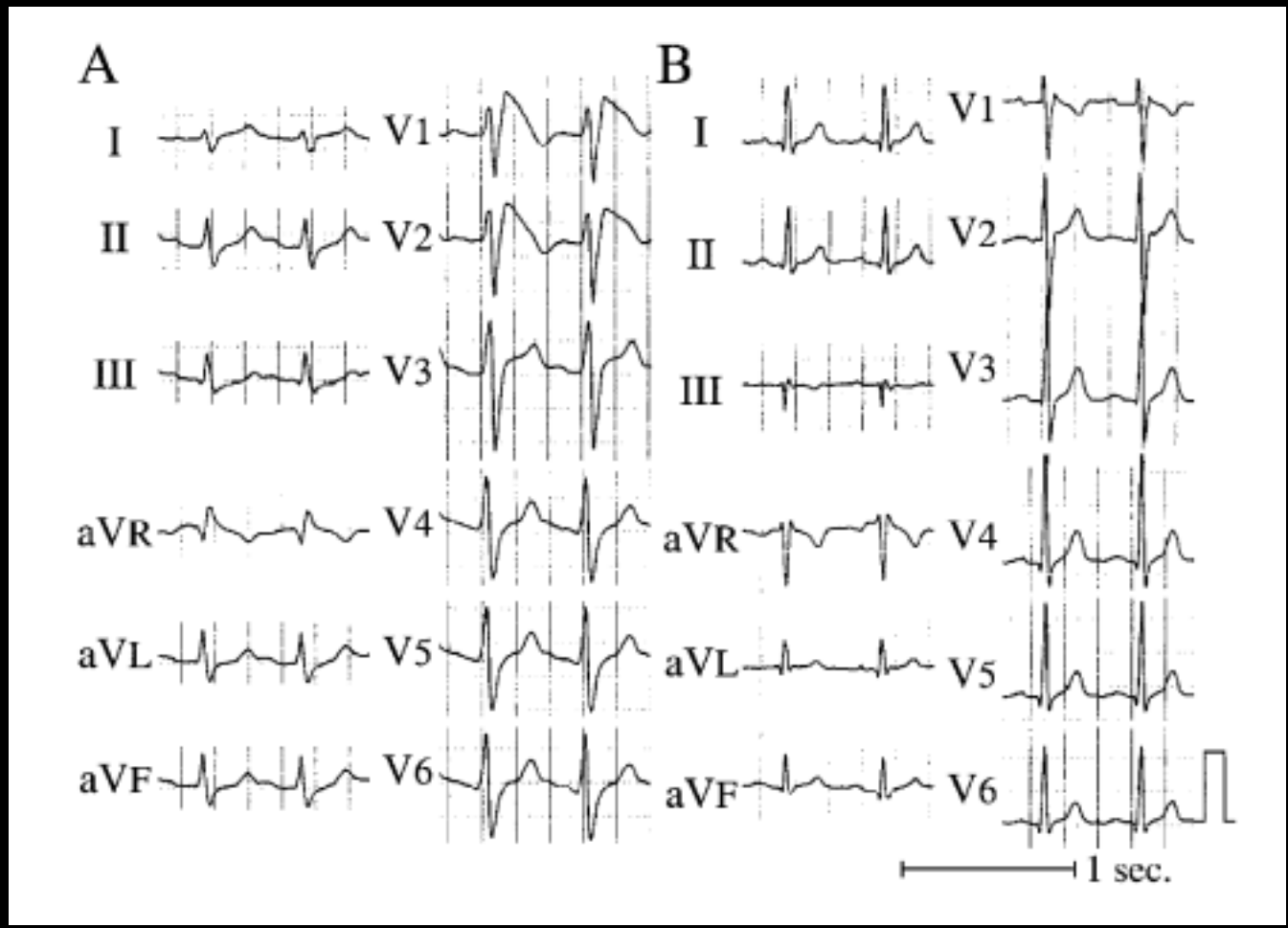
Indian Pacing Electrophysiol. J. 2003;3(3):184


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

A 33-year-old man was successfully resuscitated from an out-of-hospital episode of ventricular fibrillation…

Drug overdose (nortriptyline)

Recovery



Tada et al., JCE 2001;12:275

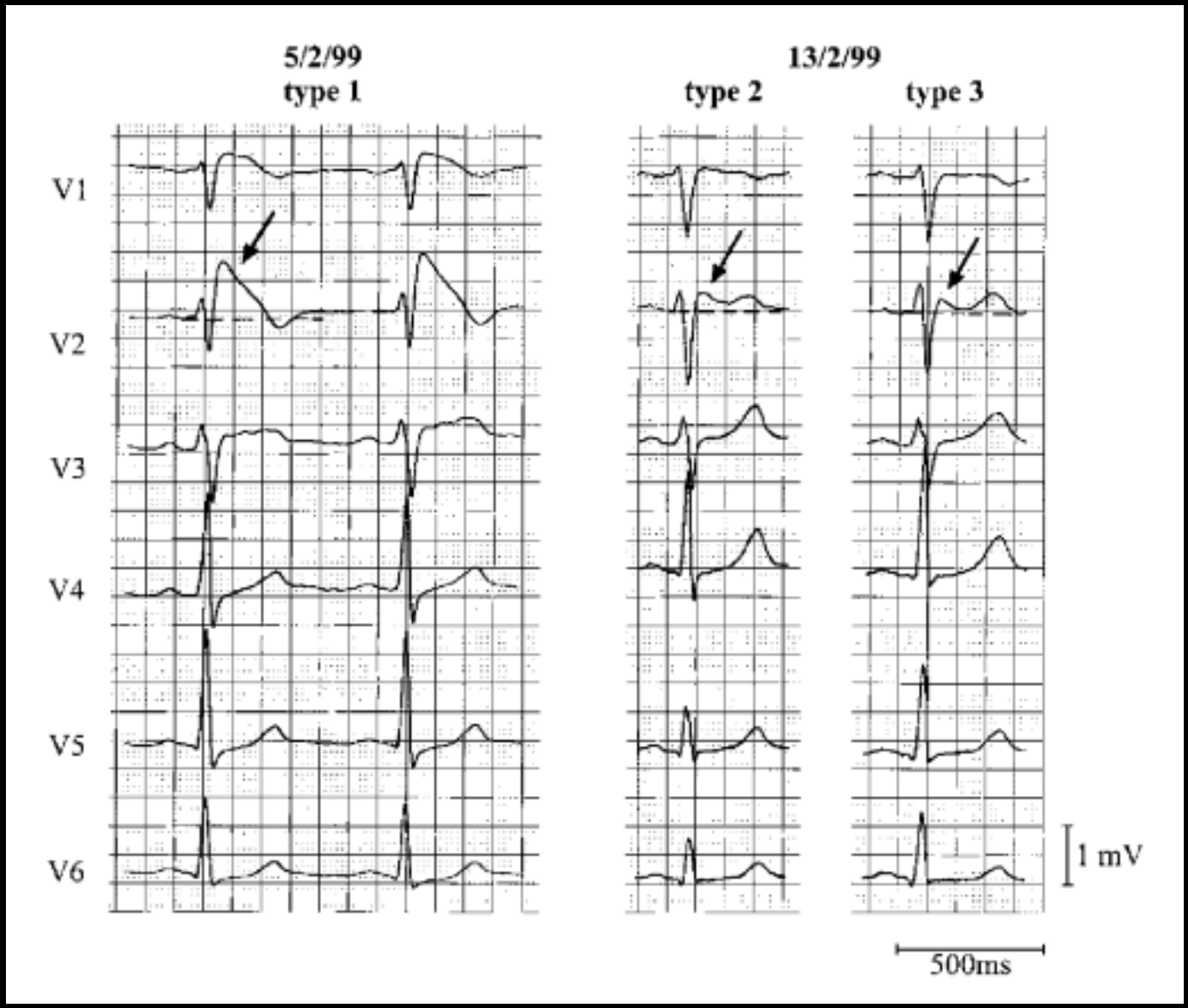
ST-Segment Elevation in the Right Precordial Leads

Right or left bundle branch block, left ventricular hypertrophy
Acute myocardial ischemia or infarction
Acute myocarditis
Right ventricular ischemia or infarction
Dissecting aortic aneurysm
Acute pulmonary thromboemboli
Various central and autonomic nervous system abnormalities
Heterocyclic antidepressant overdose
Hypercalcemia, Hyperkalemia
Cocaine intoxication
Mediastinal tumor compressing RVOT
Arrhythmogenic right ventricular dysplasia/cardiomyopathy
Long-QT syndrome, type
Early repolarization syndrome
Other normal variants (particularly in men)

Circulation 2002;106:2514

Prevalence

Miyasaka	0.1 mV, coved	0.12 %
Hermida	0.1 mV, coved	0.1 %
	0.1 mV,saddle back	6.0 %
Matuo	0.1 mV, coved	0.15 %
IVF investigator	0.1 mV, coved or saddle	0.16 %
Furuhashi	0.1 mV, coved or saddle	0.14 %
	0.1 mV, coved	0.05 %
Sakabe	0.2 mV, coved or saddle	2.1 %



Coved type ST segment elevation (J or ST $\geq$ 2 mm)
More than 1 electrode through V1-V3
Spontaneously or after Na channel blocker

Cir 2002;106:2514

Diagnosis of BS

Type I ECG

Clinical marker

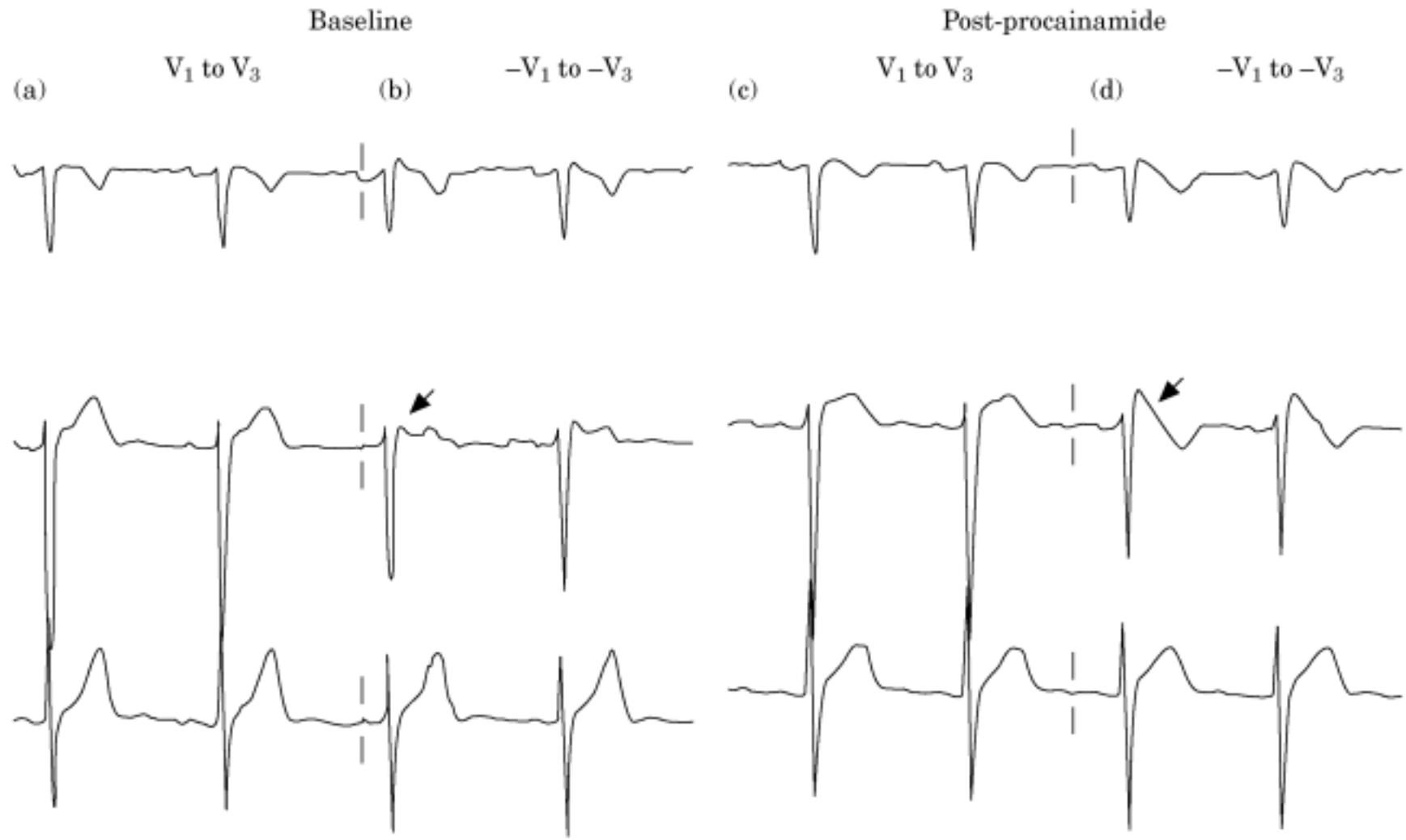
- **Documented ventricular fibrillation**
- **Self terminating polymorphic ventricular tachycardia**
- **A family history of SCD (<45 years)**
- **Coved type ECGs in family members**
- **Electrophysiological inducibility**
- **Syncope**
- **Nocturnal agonal respiration**

Exclusion of conditions that can account for ST elevation

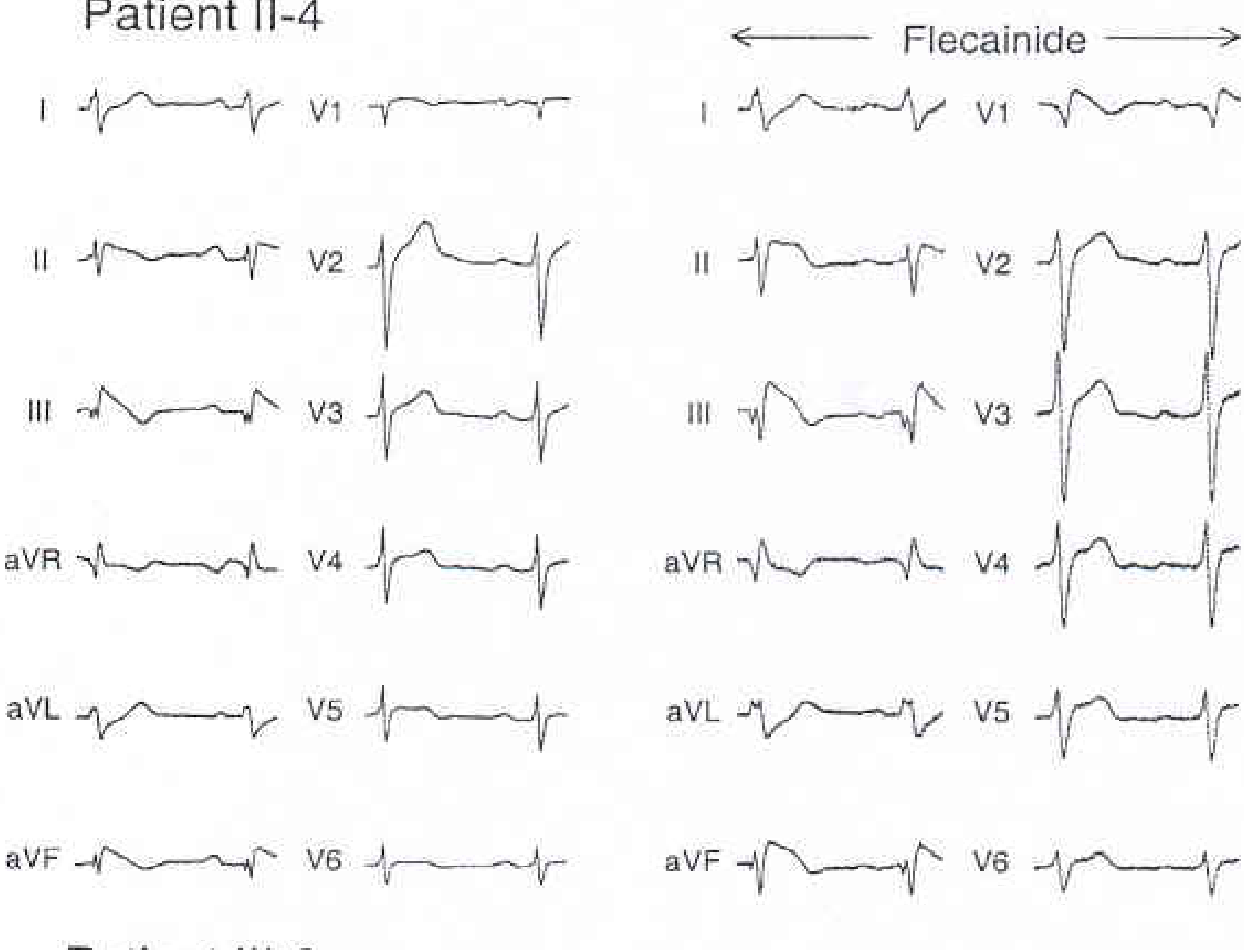
cf. Idiopathic Brugada ECG pattern

Circulation 2002;106:2514

BS ECG recorded in higher ICS



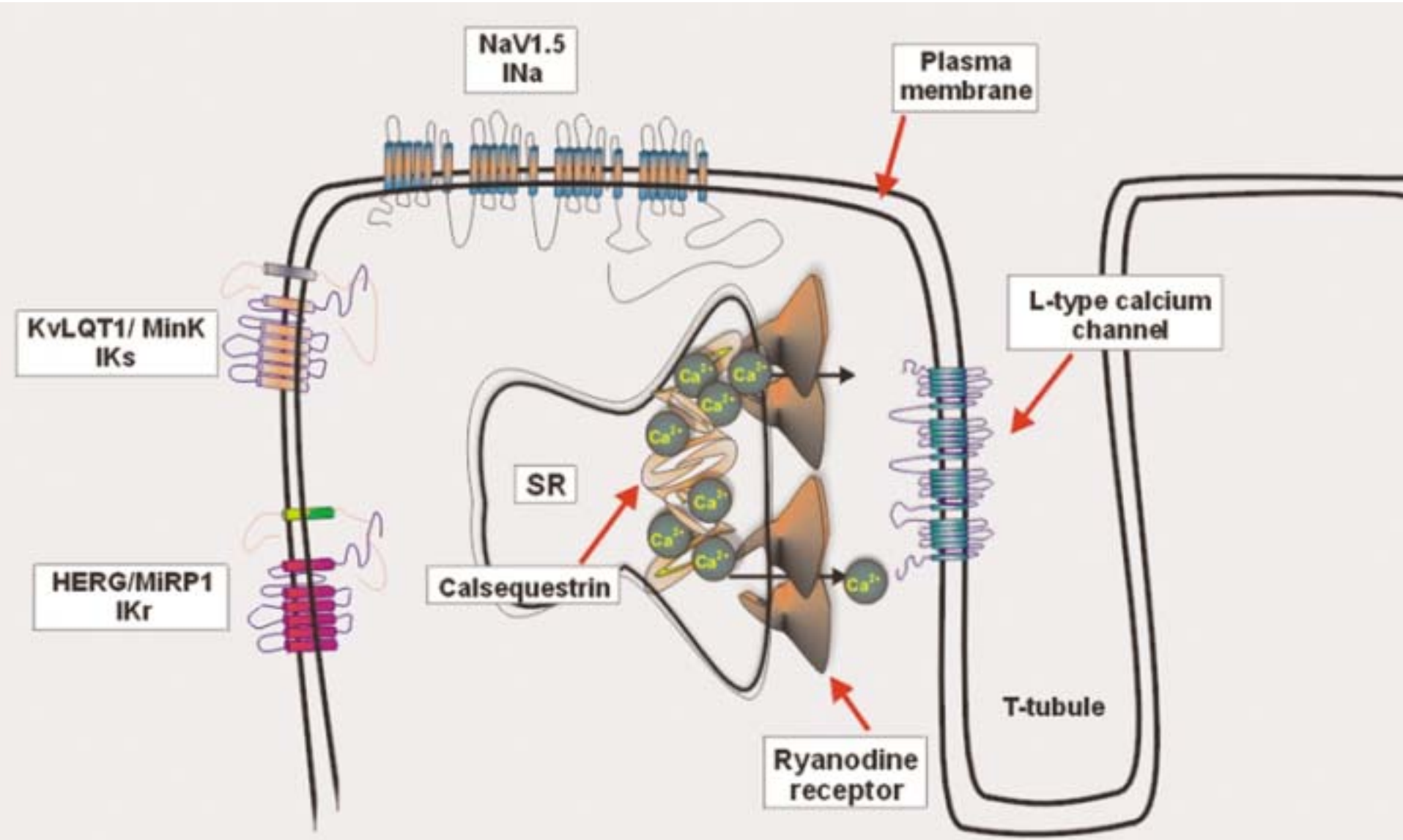
Sangwatanaroj et al.,
Eur Heart J 2001; 22: 2290

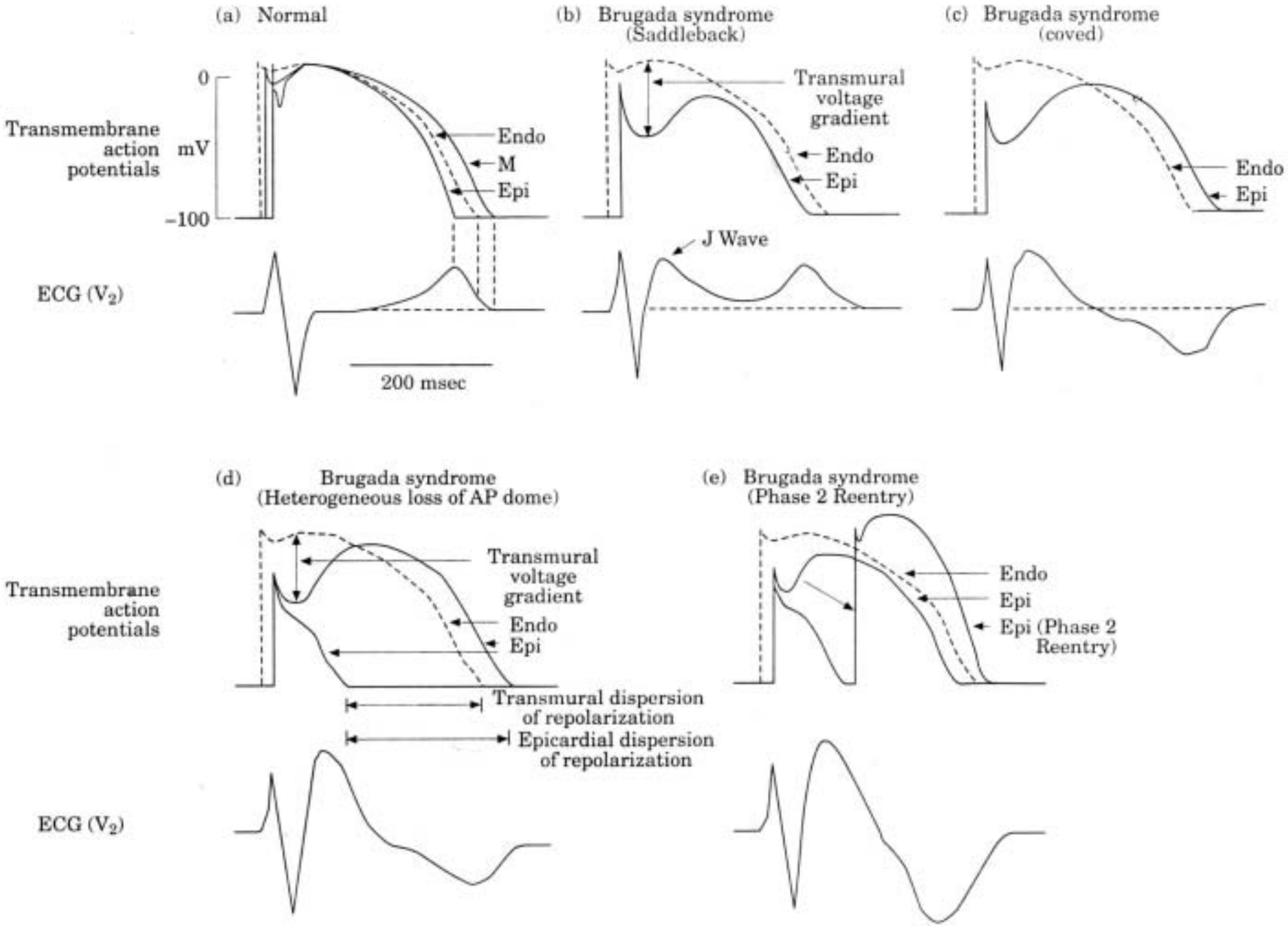


Journal of Electrocardiology 2004;;37

Patient Characteristics

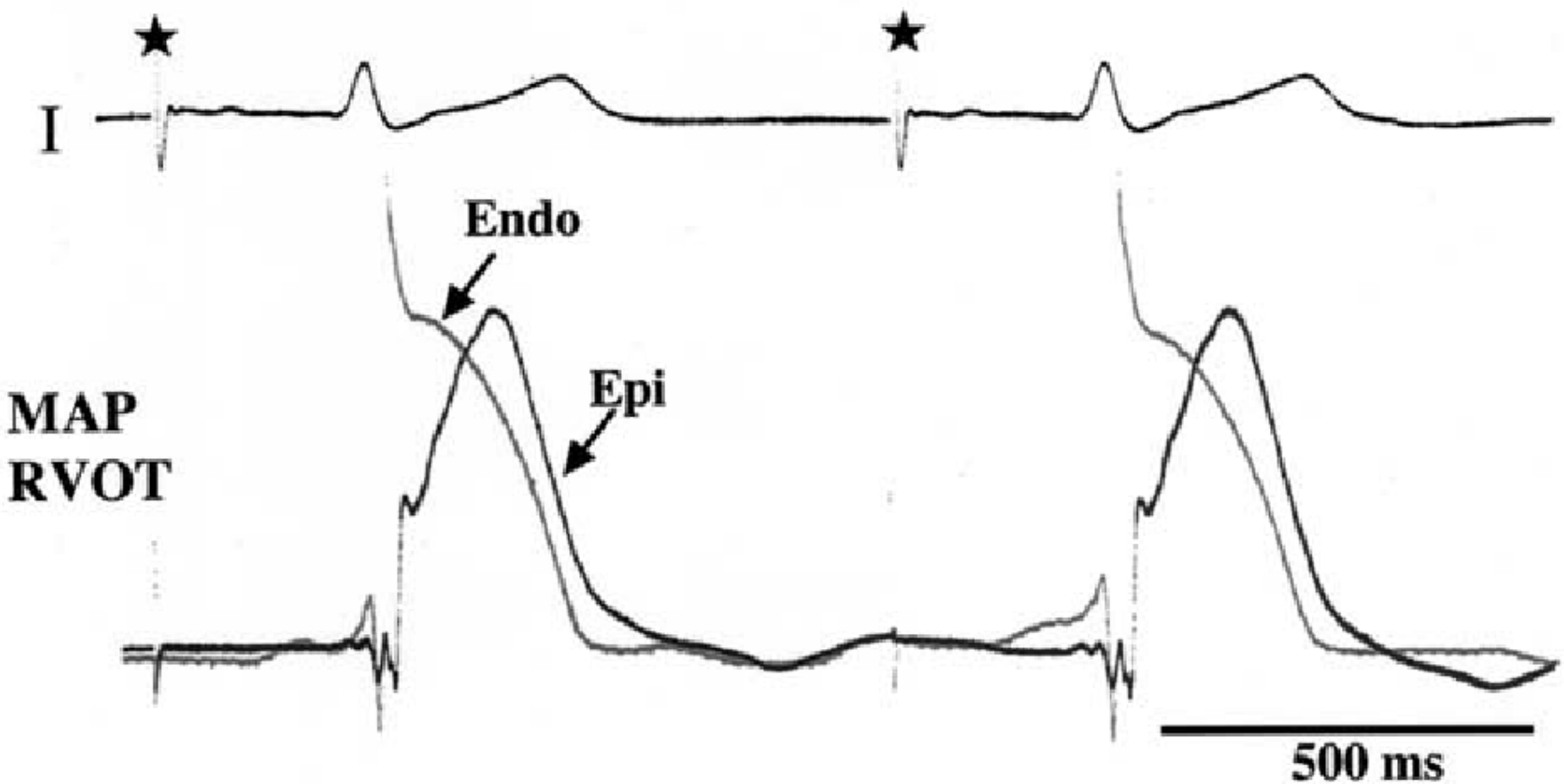
Prevalence	0.01 to 6.0 %
Male : Female ratio	8-10 : 1
VT/VF is bradycardia-dependent	Die during sleep
Age at the time of Dx or SCD	42 (2^{w} to 84^{yr})
Inheritance	Autosomal Dominant
Inducible polymorphic VT	70 - 80%
Prolonged HV interval	60% (65+20 ms)
Associated with atrial fibrillation	10 %

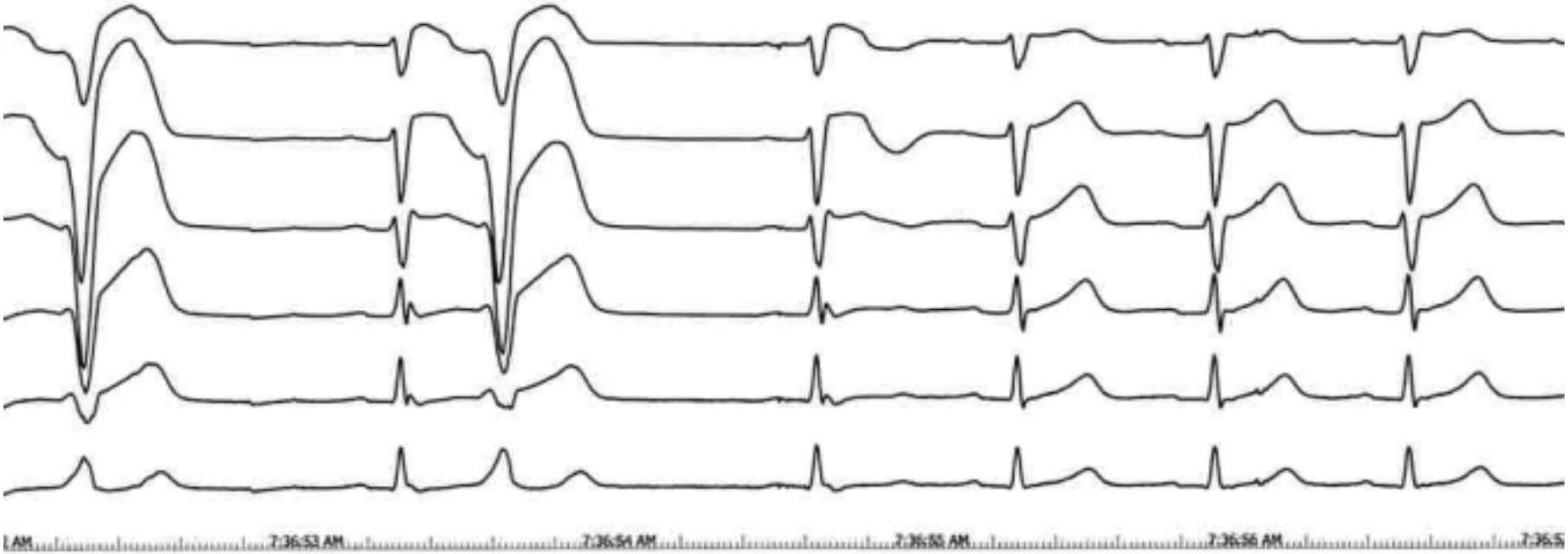

NaV1.5
INa
Plasma
membrane
KvLQT1/ MinK
IKs
L-type calcium
channel
SR
HERG/MiRP1
IKr
Calsequestrin
T-tubule
Ryanodine
receptor


(a) Normal
(b) Brugada syndrome (Saddleback)
(c) Brugada syndrome (coved)
Transmembrane action potentials
0
mV
−100
Endo
M
Epi
Transmural voltage gradient
Endo
Epi
Endo
Epi
J Wave
ECG (V2)
200 msec
(d) Brugada syndrome (Heterogeneous loss of AP dome)
(e) Brugada syndrome (Phase 2 Reentry)
Transmembrane action potentials
Transmural voltage gradient
Endo
Epi
Endo
Epi
Epi (Phase 2 Reentry)
Transmural dispersion of repolarization
Epicardial dispersion of repolarization
ECG (V2)

Monophasic action potential recording

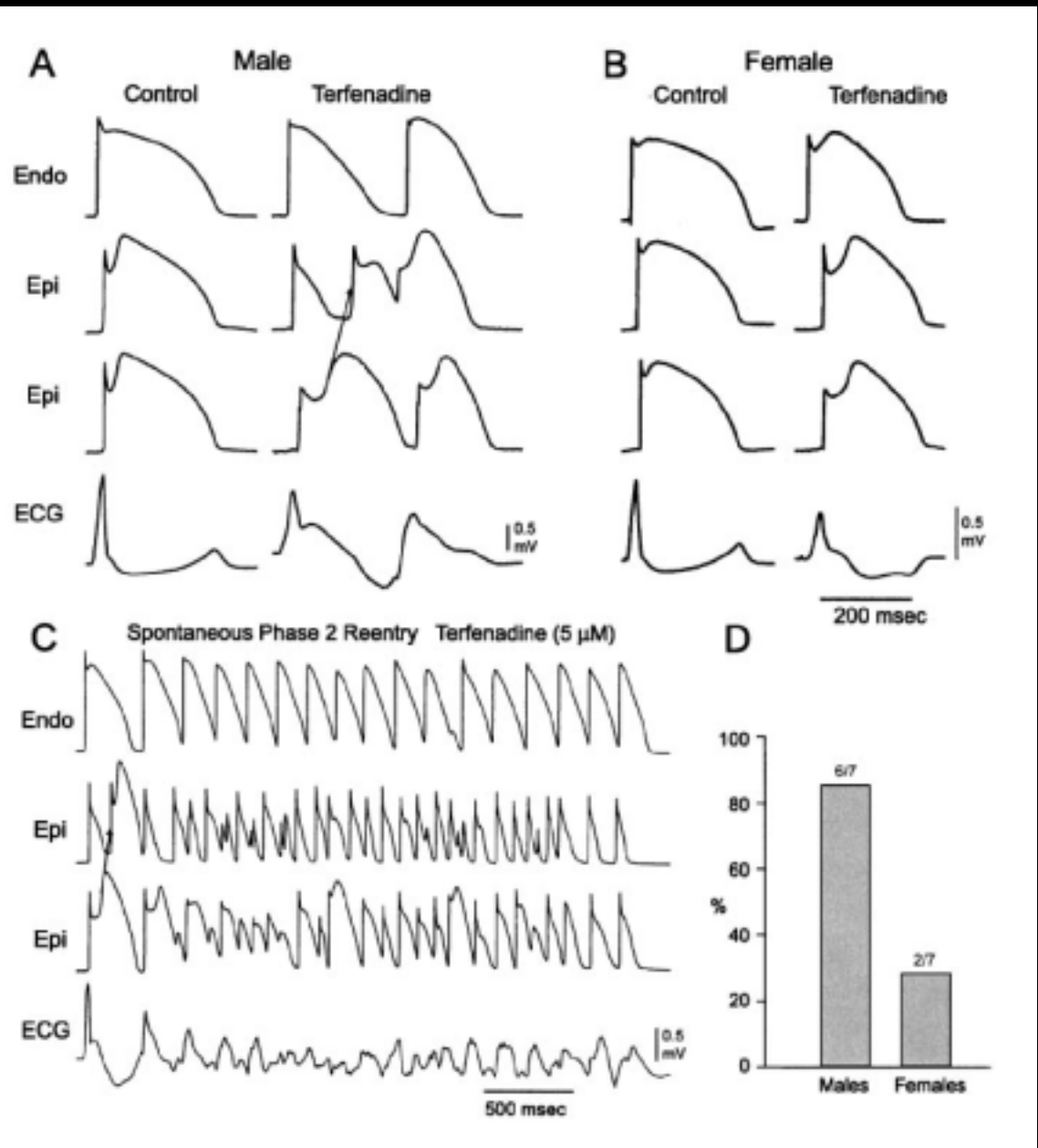
Nagase et al.,
JACC 2002;39:1992





5.1C

Ionic and Cellular Basis for the Predominance of the Brugada Syndrome Phenotype in Males

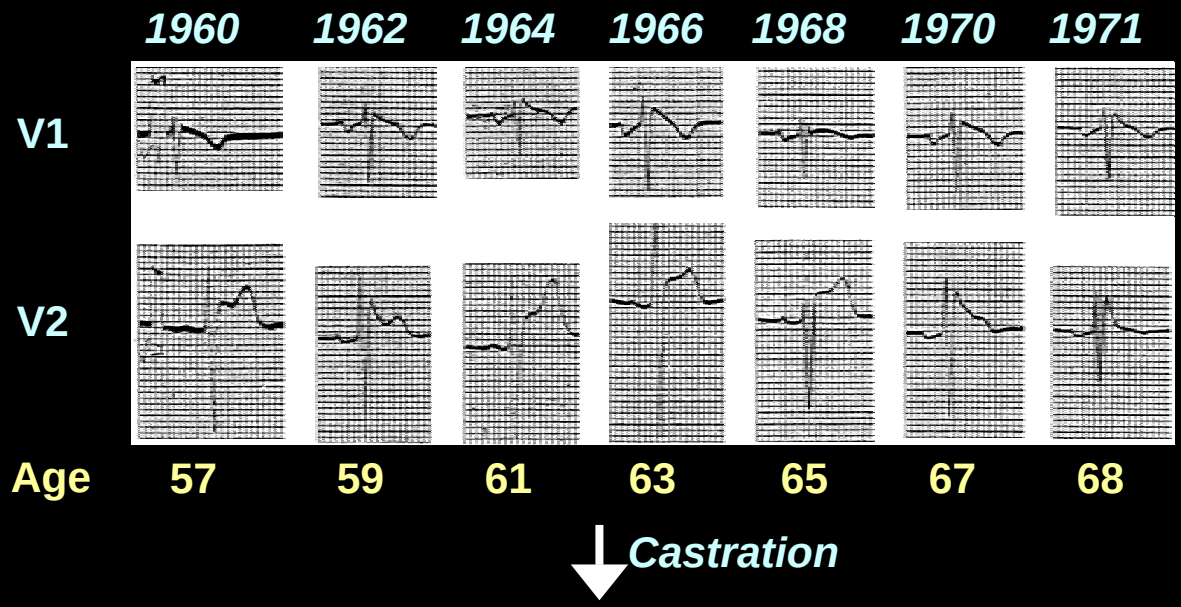


Male / Female ratio

8:1 ----- Non-Asian
10:1 ----- Asian

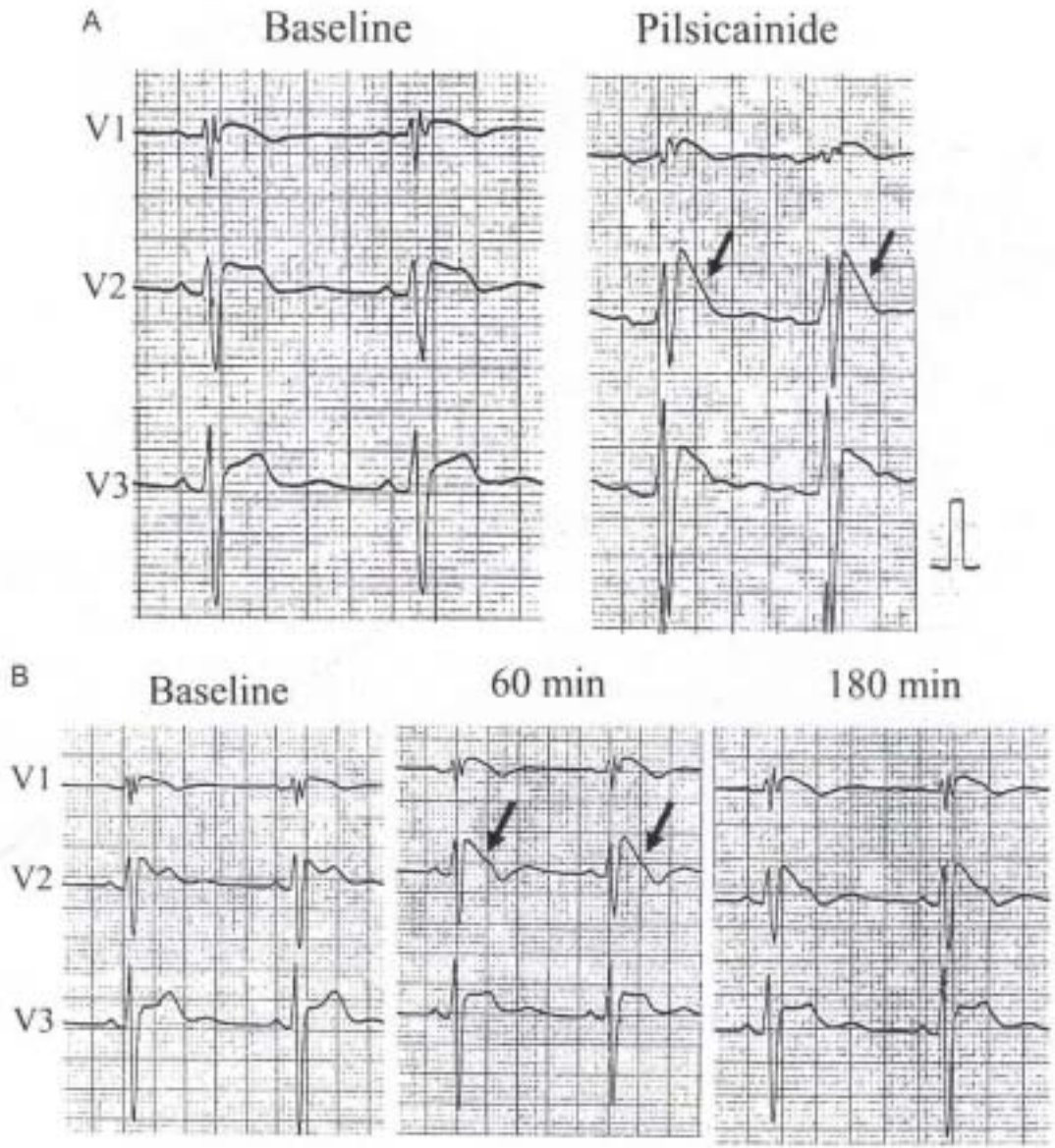
DiDiego et al.
***Circulation*. 2002;106:2004**

Disappearance of ST Elevation in BS Patient after Orchiectomy



Matsuo K, et al., PACE, 2003;26:1551

Enhancement of ST elevation by glucose and insulin



Hiraoka et al., JCE 2003;14:243

Dynamic change of ST elevation in BS

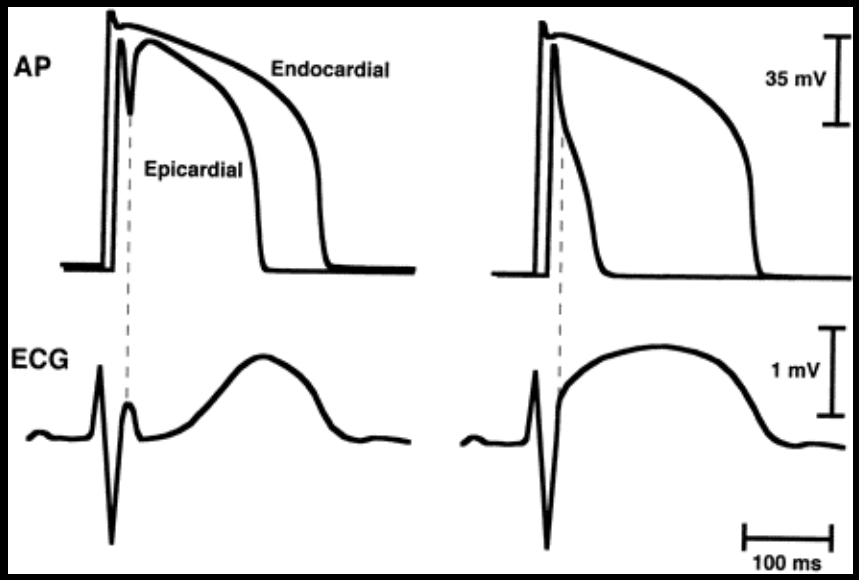
Electrolyte
Fever
Drugs (cocaine, TCA, flecainide)
Autonomic Nervous system
Glucose
Hormonal

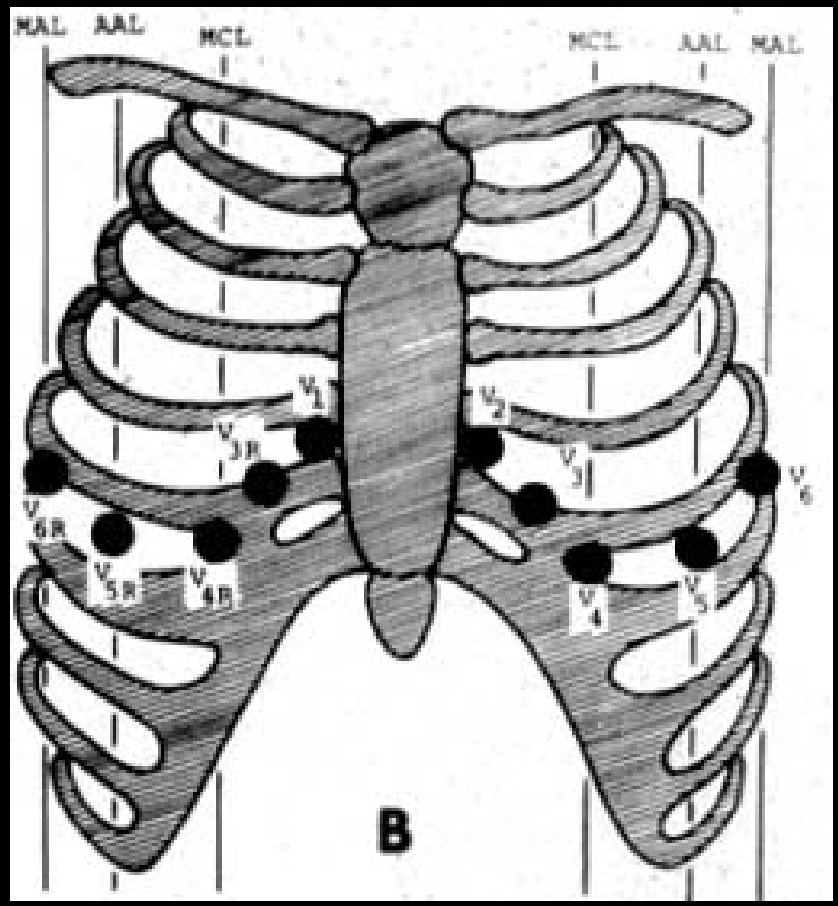
Laboratory tests

Echo, Treadmill
Thallium scan, MRI
CAG, Biopsy

SAECG
Class IC Provocation study
EP study

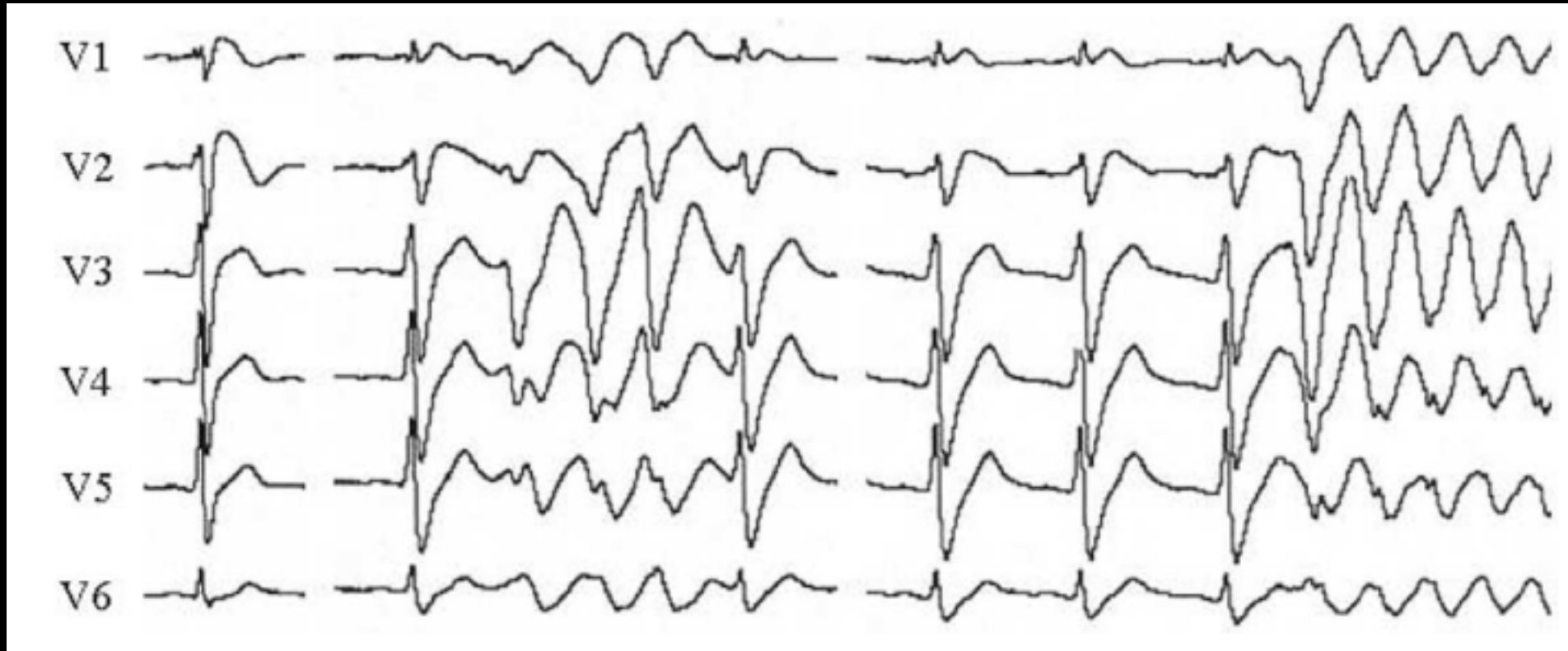
Provocation test





Flecainide	**2mg/Kg over 10 min**
Ajmaline	**1 mg/kg/5 min**
Procainamide	**10 mg/kg/10 min**

Provocation study : Induction of VT/VF



Rolf S, Eur Heart J. 2003;24:1104

Provocation study : Precautions

Standby : external defibrillator, intubation set
and drugs (atropine, isoproterenol)

Termination : Typical ECG change
PVC, VT, Sinus arrest
QRS prolongation >30%.
AV-block (Type II or III)

Patient and ECG supervision until normalization of ECG.

* 심전도 기록 전극을 하나 혹은 두 늑간 위에서도 기록

Rolf S, Eur Heart J. 2003;24:1104

Response to electrical stimulation

1. Inducibility of VF in BS : 60-80 %
   cf. Inducibility of VF in structurally normal heart : 6-9 %

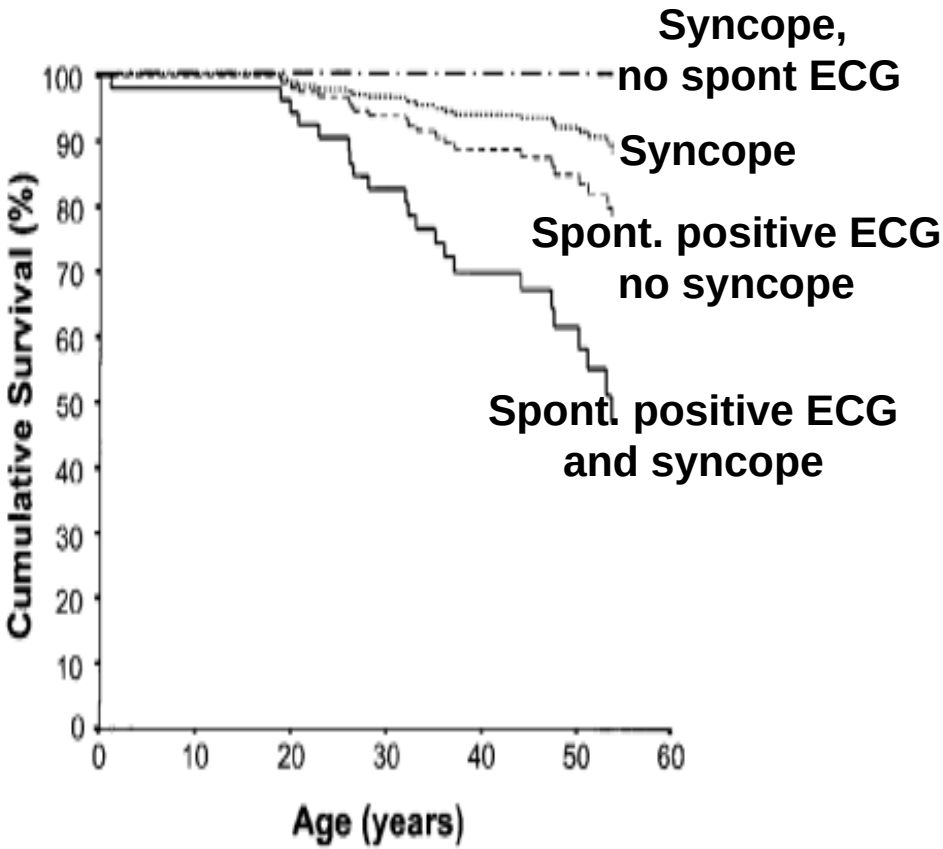
2. Dose response relationship
   asymptomatic : 33%
   syncope : 63%
   SCD survivor : 83%

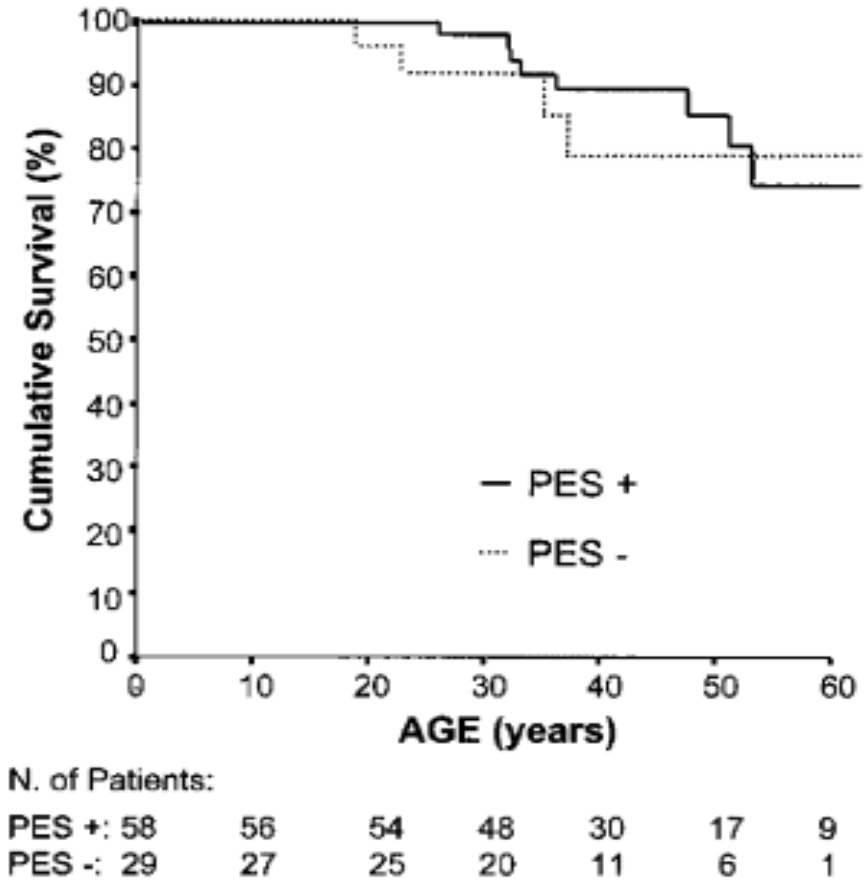
3. SN, SP, PPV, NPP

Role of EP study in Risk Stratification

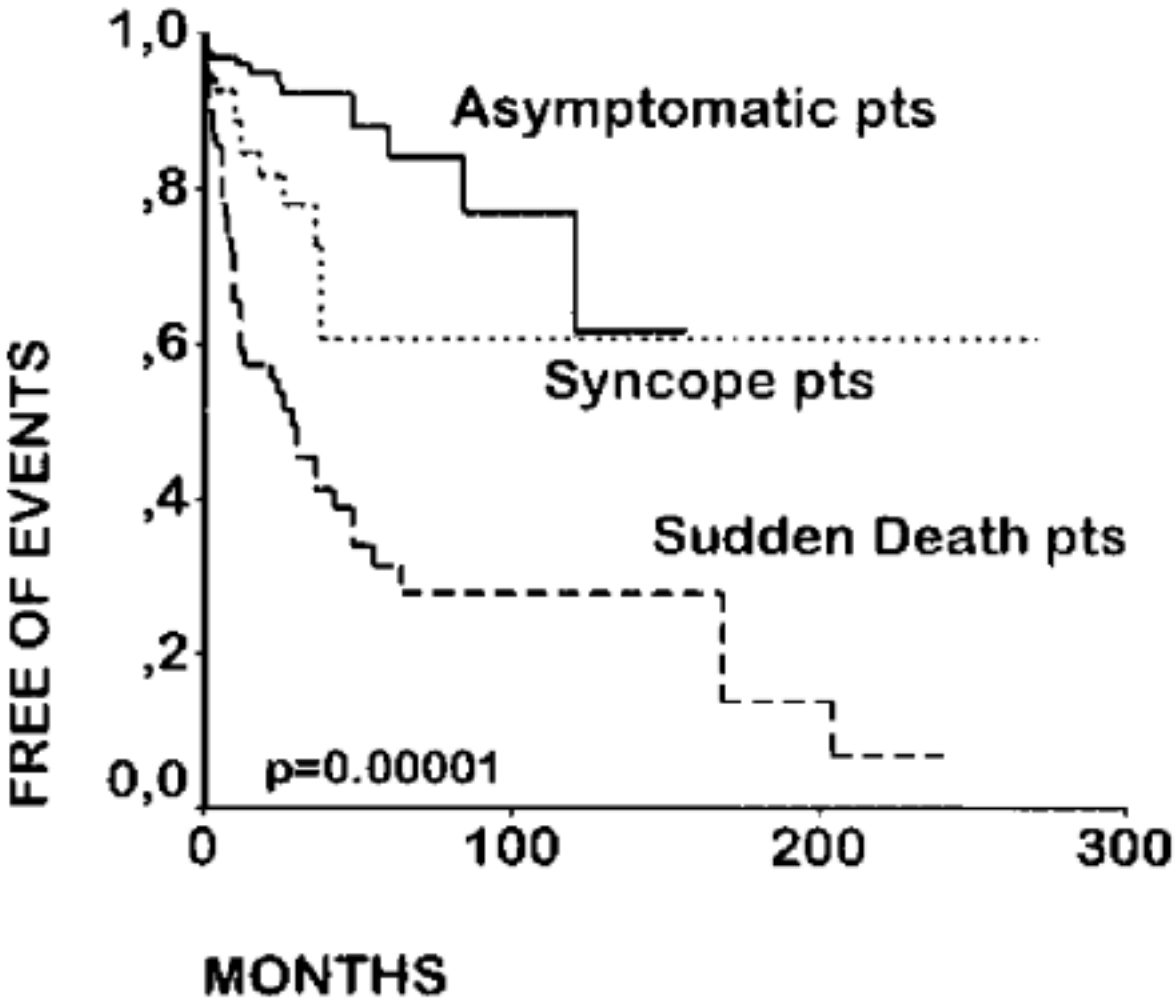
QTd, TWA
SAECG

Symptom
ECG change – spontaneous vs drug-induced
EP study

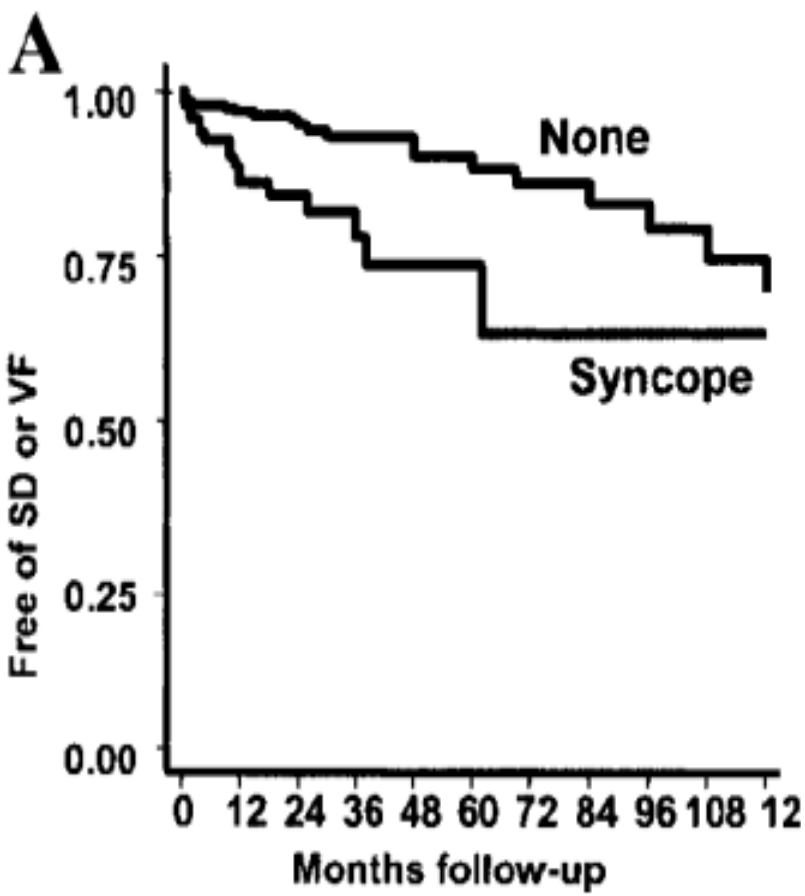


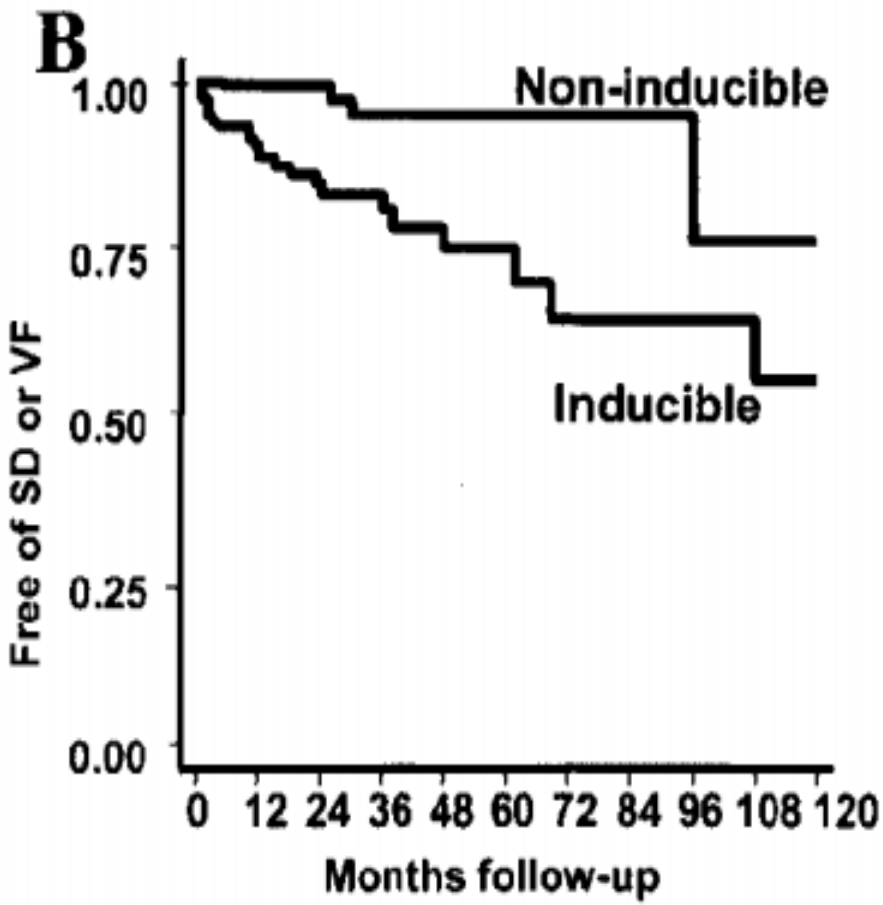


Priori et al., Circulation 2002:105, 1342



Brugada et al.,
Circulation. 2002;105:73





Brugada et al,
Circulation 2003;108:3092

Therapy

Devices

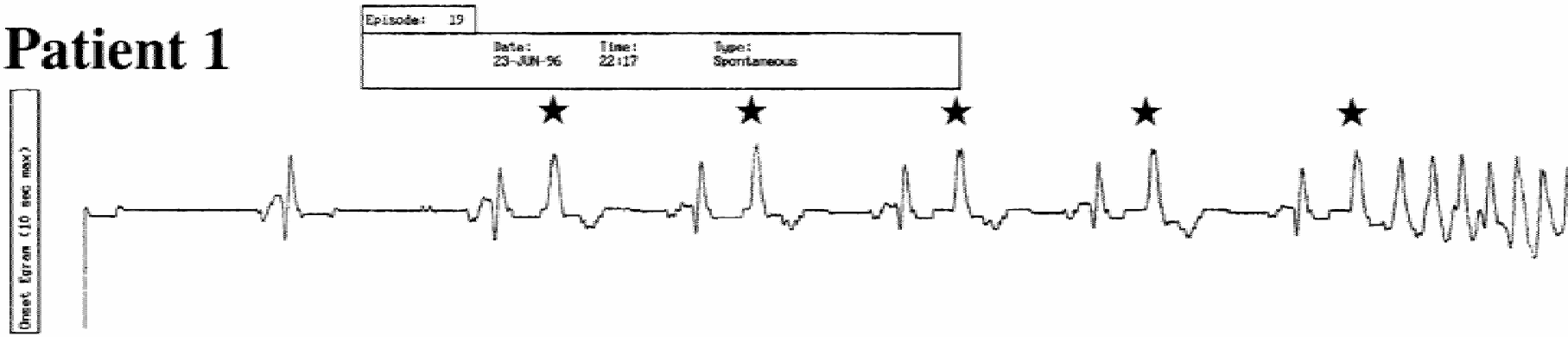
- ***ICD***
- **RF ablation**
- **Pacemaker**

Pharmacologic

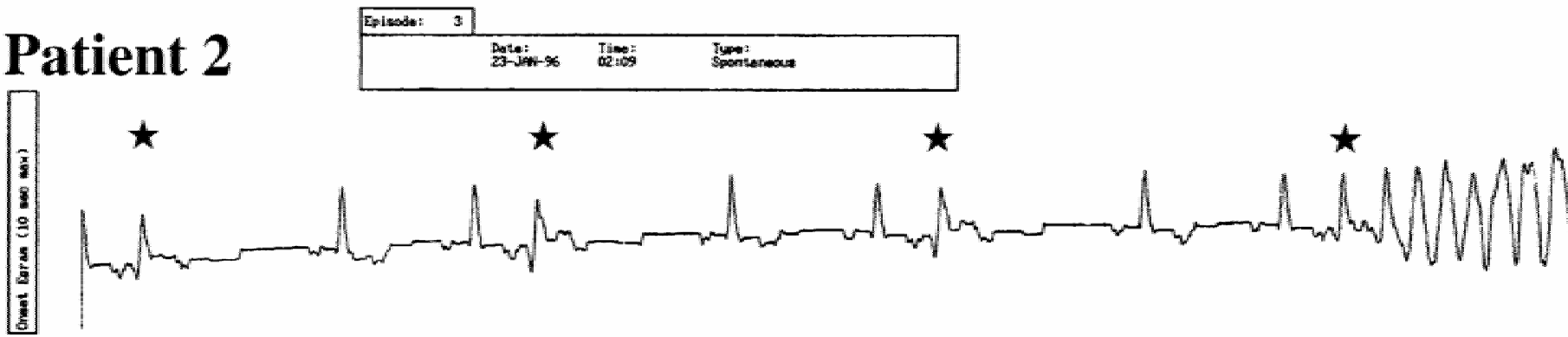
- **Beta-adrenergic agonists :*isoproterenol***
- **Phosphodiesterase Inhibitors :*cilostazol***
- **Amiodarone, beta-blockers : not helpful**
- **Class IC antiarrhythmics : flecainide, propafenone - CIx**
- **Class IA antiarrhythmics : procainamide, disopyramide - CIx**

quinidine

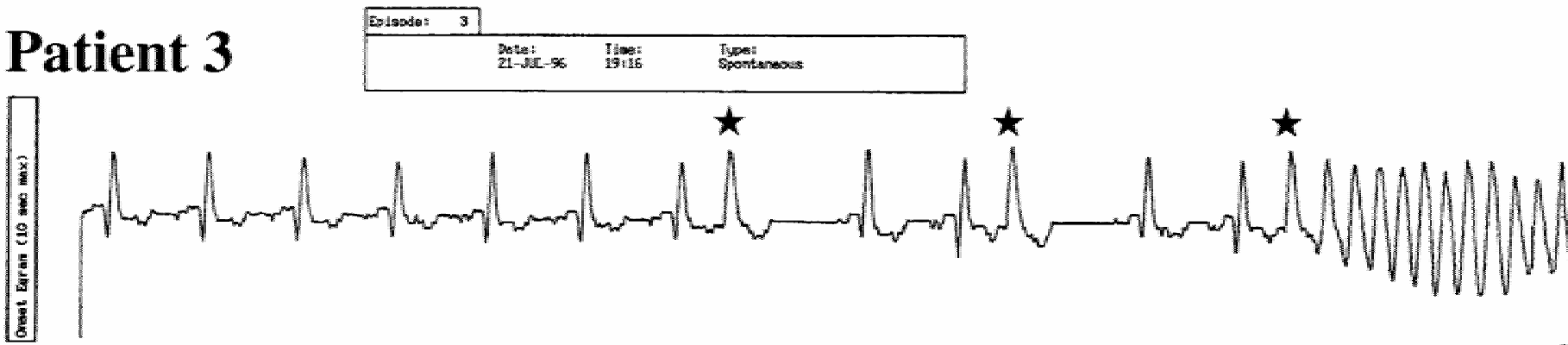
Patient 1



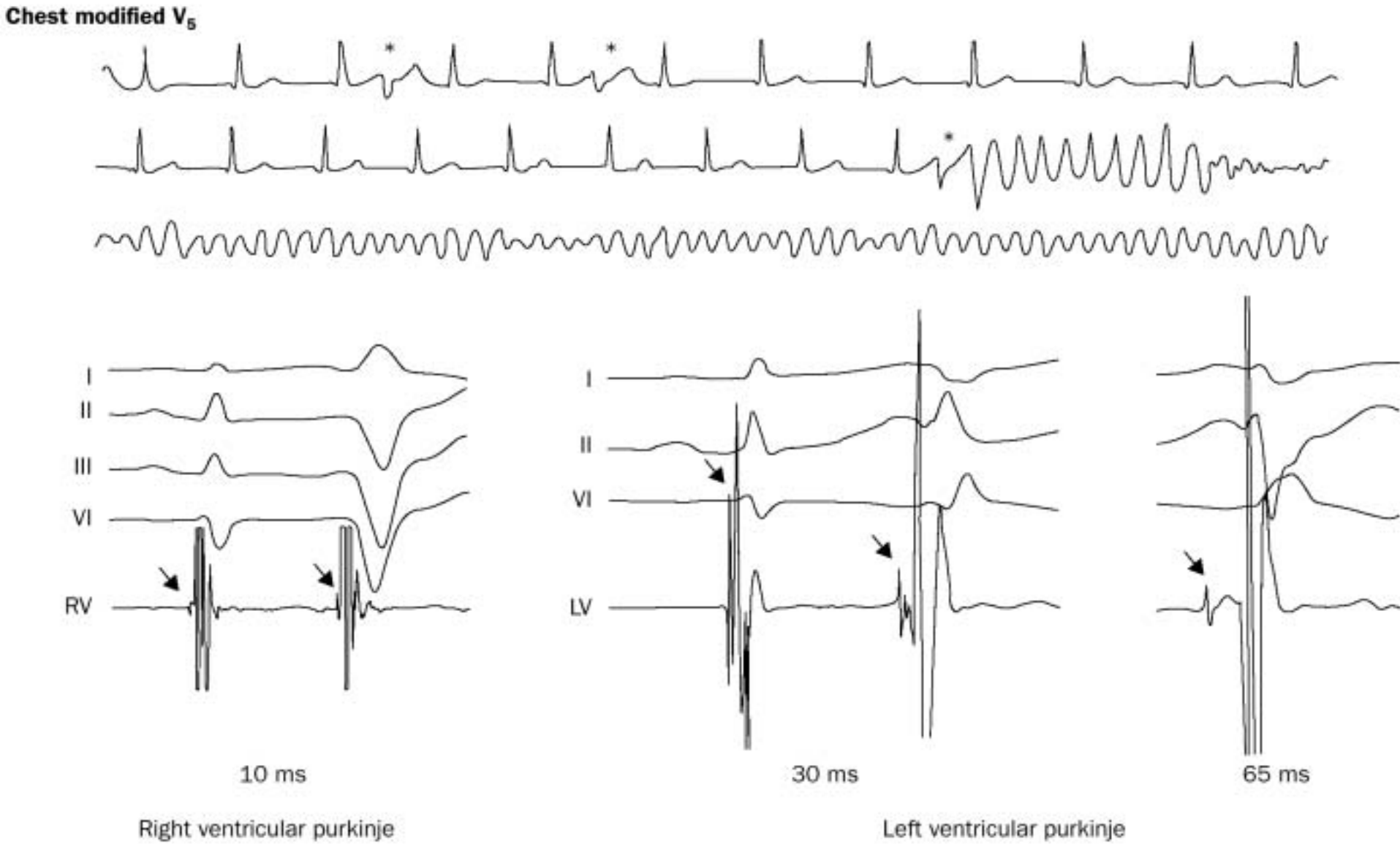
Patient 2



Patient 3

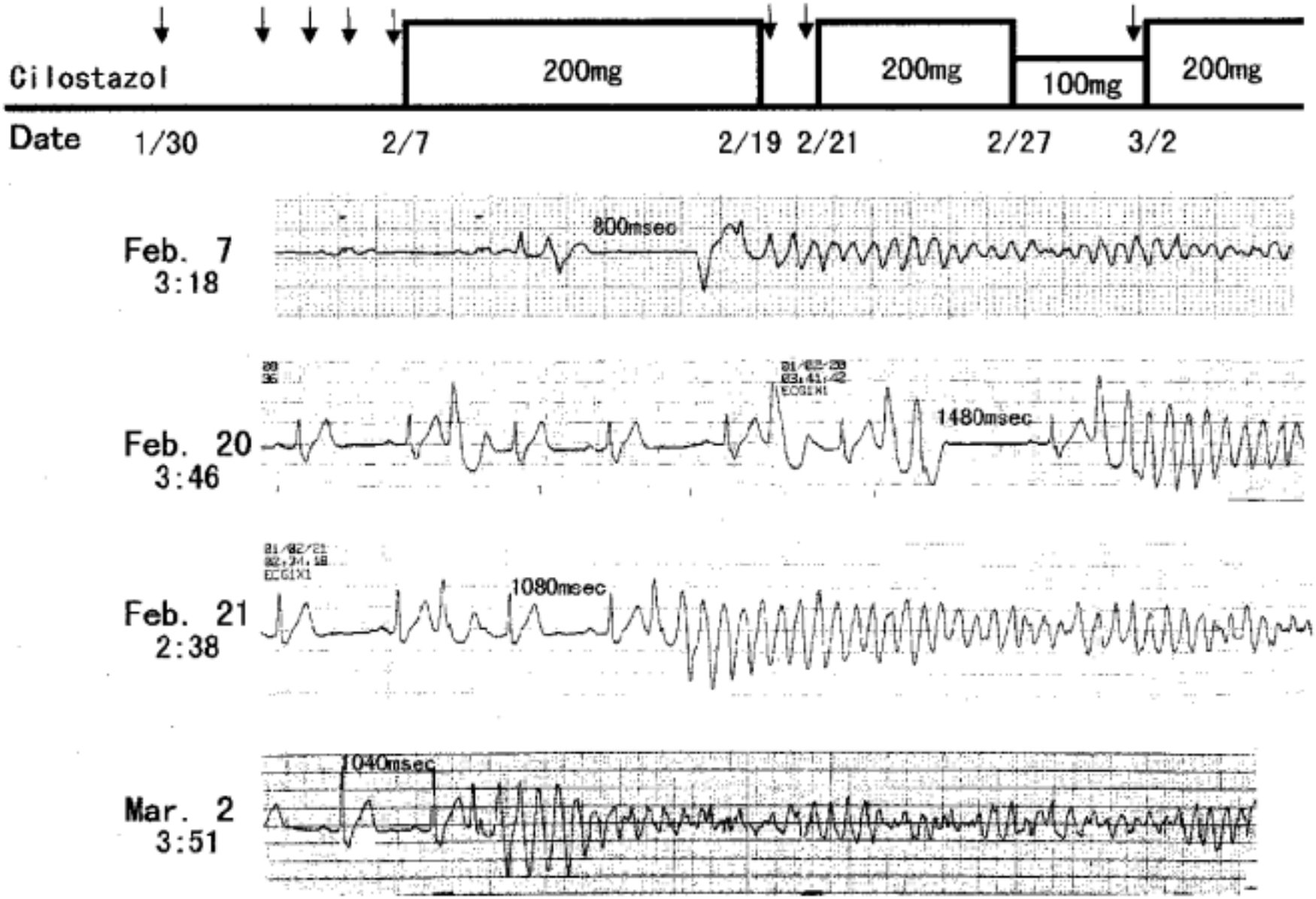


RF catheter ablation of initiating foci in idiopathic VF

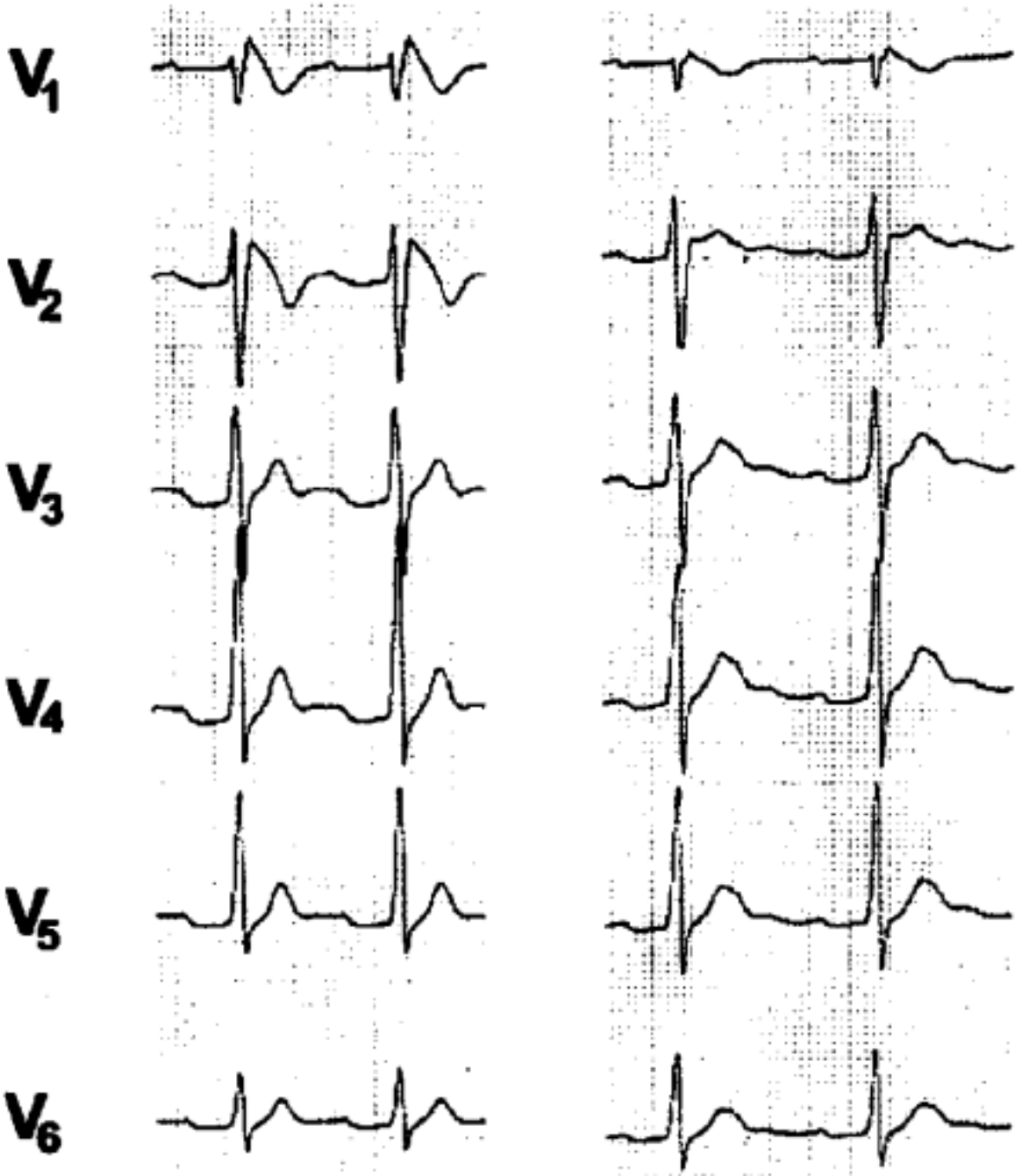


Pharmacologic suppression

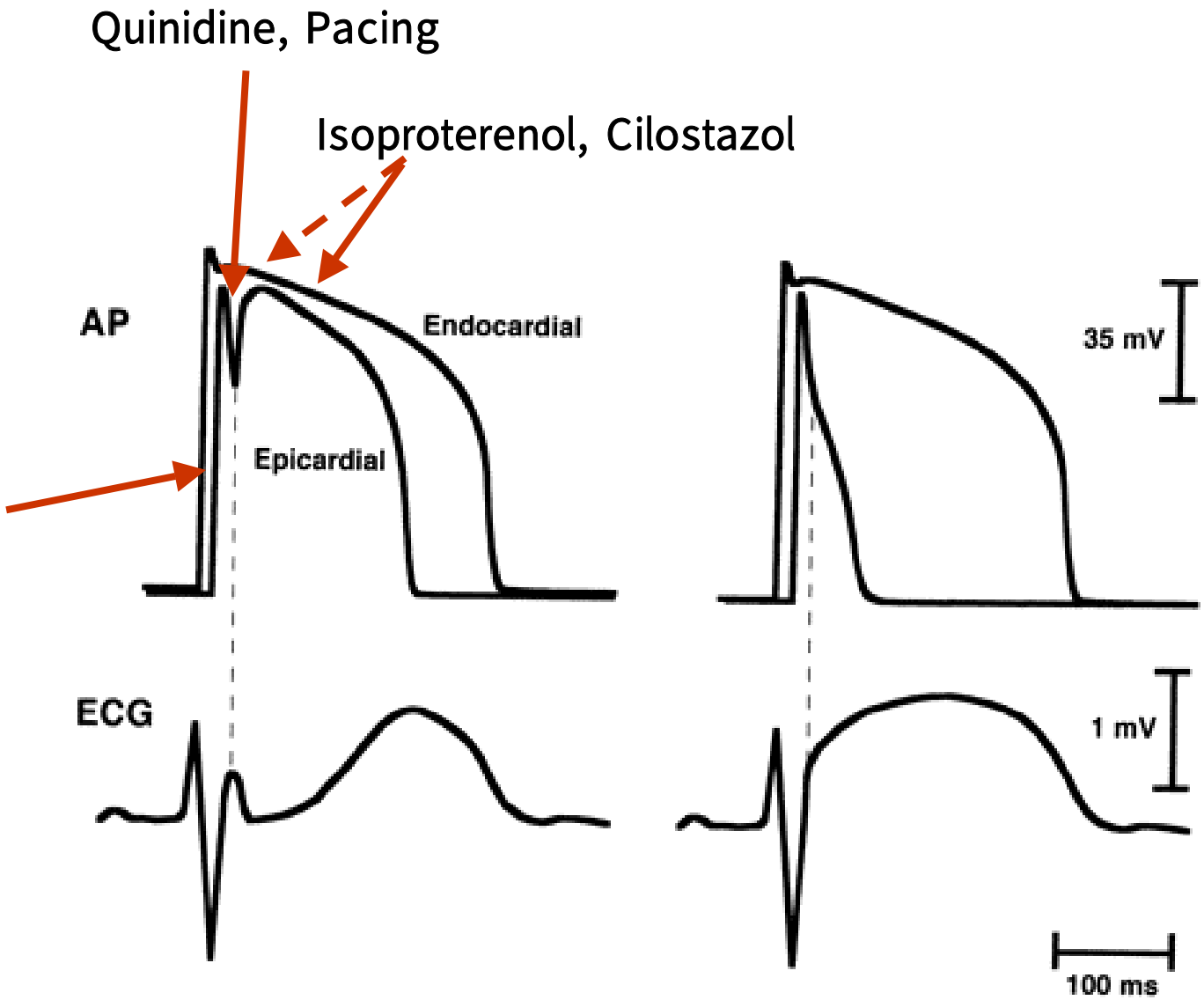
Isoproterenol
Quinidine
Cilostazol



Tsuchiya et al.,
JCE 2002;13: 698



Alings et al.
PACE 2001;24:1420


Quinidine, Pacing
Isoproterenol, Cilostazol
AP
Endocardial
Epicardial
35 mV
ECG
1 mV
100 ms

Therapy

Devices

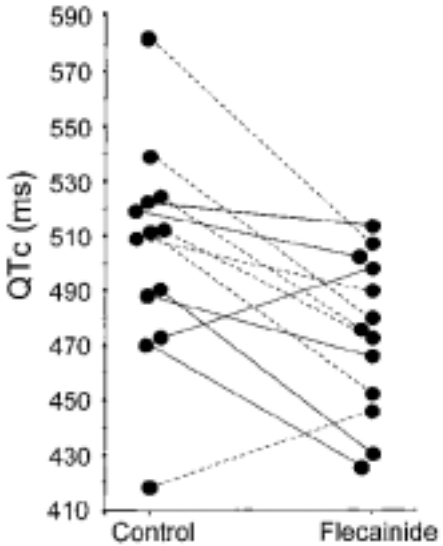
- ***ICD***
- **RF ablation ?**
- **Pacemaker ?**

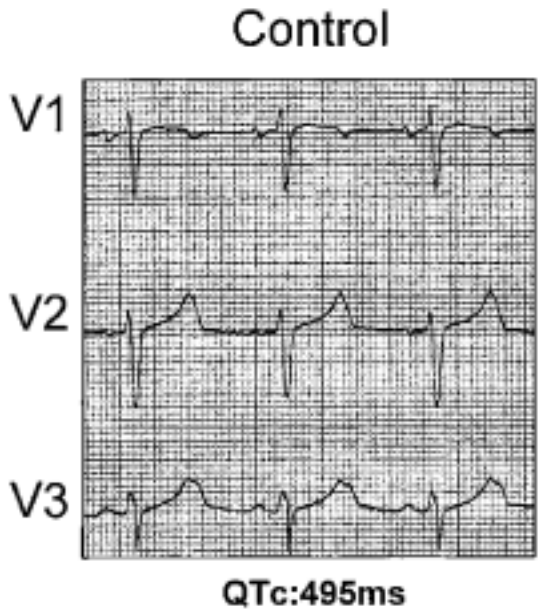
Pharmacologic

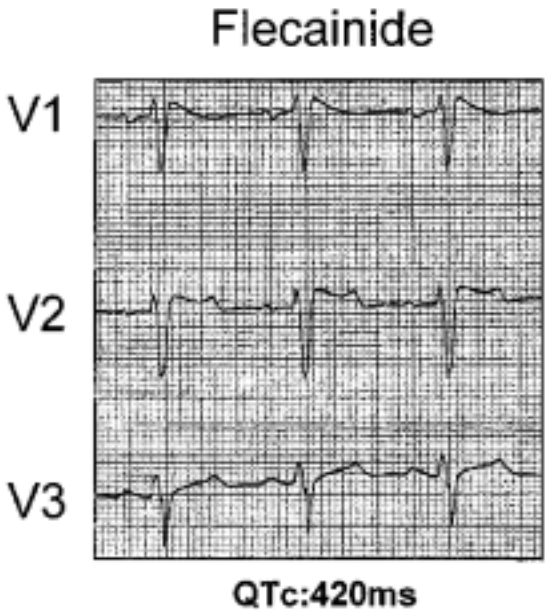
- **Beta-adrenergic agonists :*isoproterenol***
- **Phosphodiesterase Inhibitors :*cilostazol***
- **Amiodarone, beta-blockers : not helpful**
- **Class IC antiarrhythmics : flecainide, propafenone - CIx**
- **Class IA antiarrhythmics : procainamide, disopyramide - CIx**

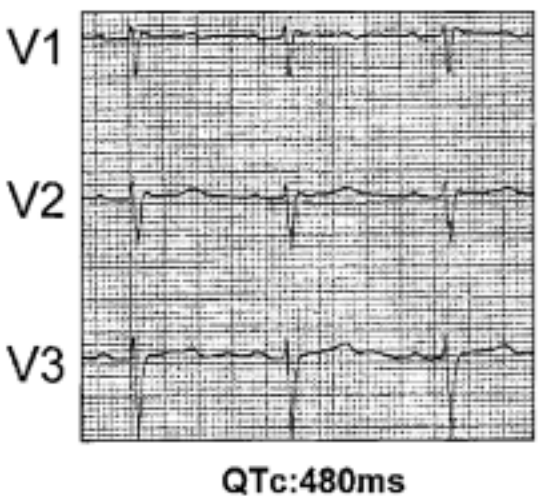
quinidine ?

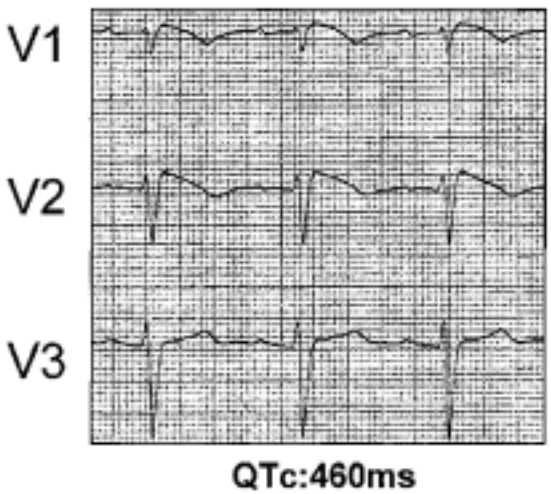
Elusive link between LQTS3 and BS



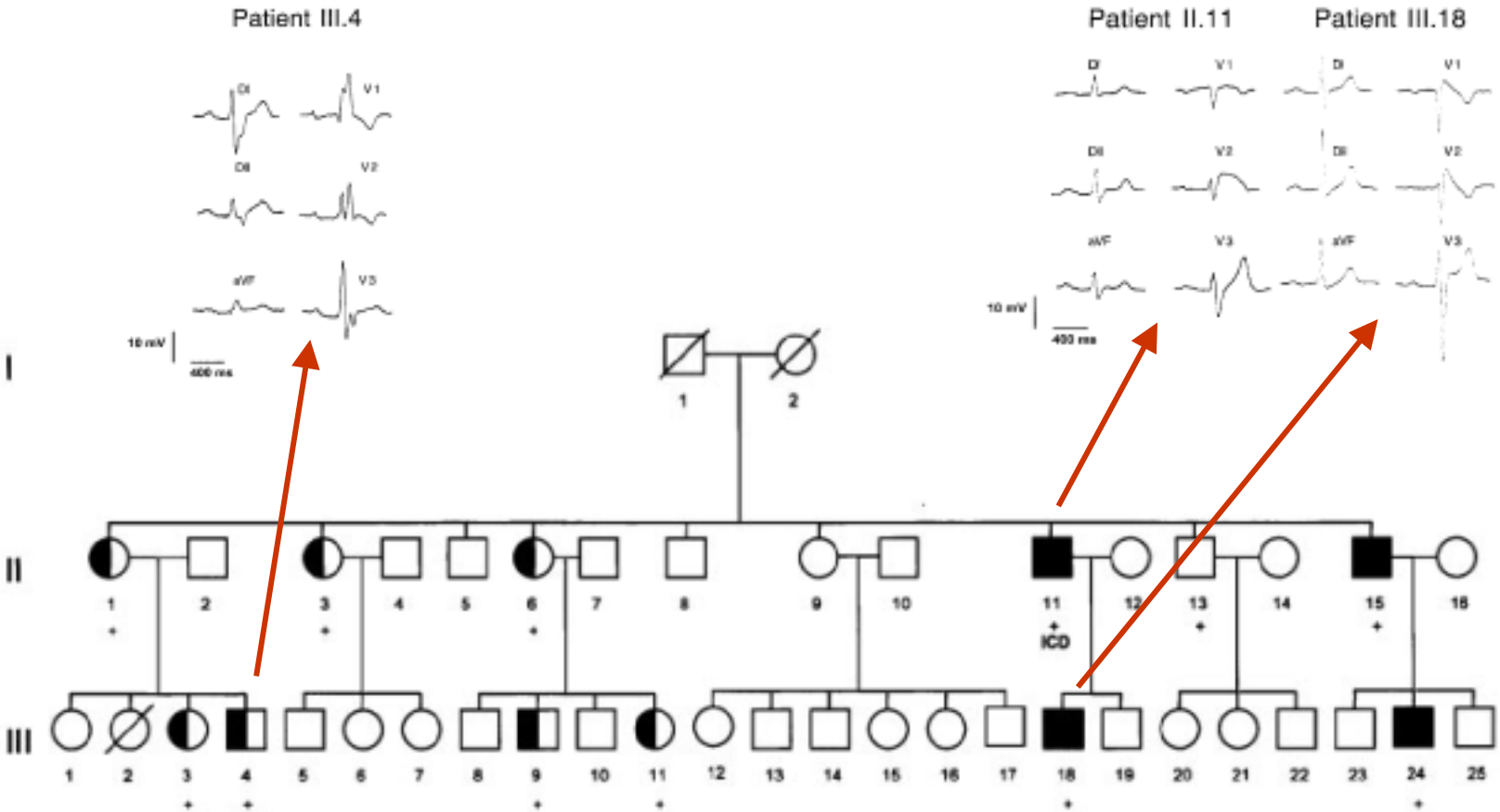








Priori, et al., Circulation. 2000;102:945-947

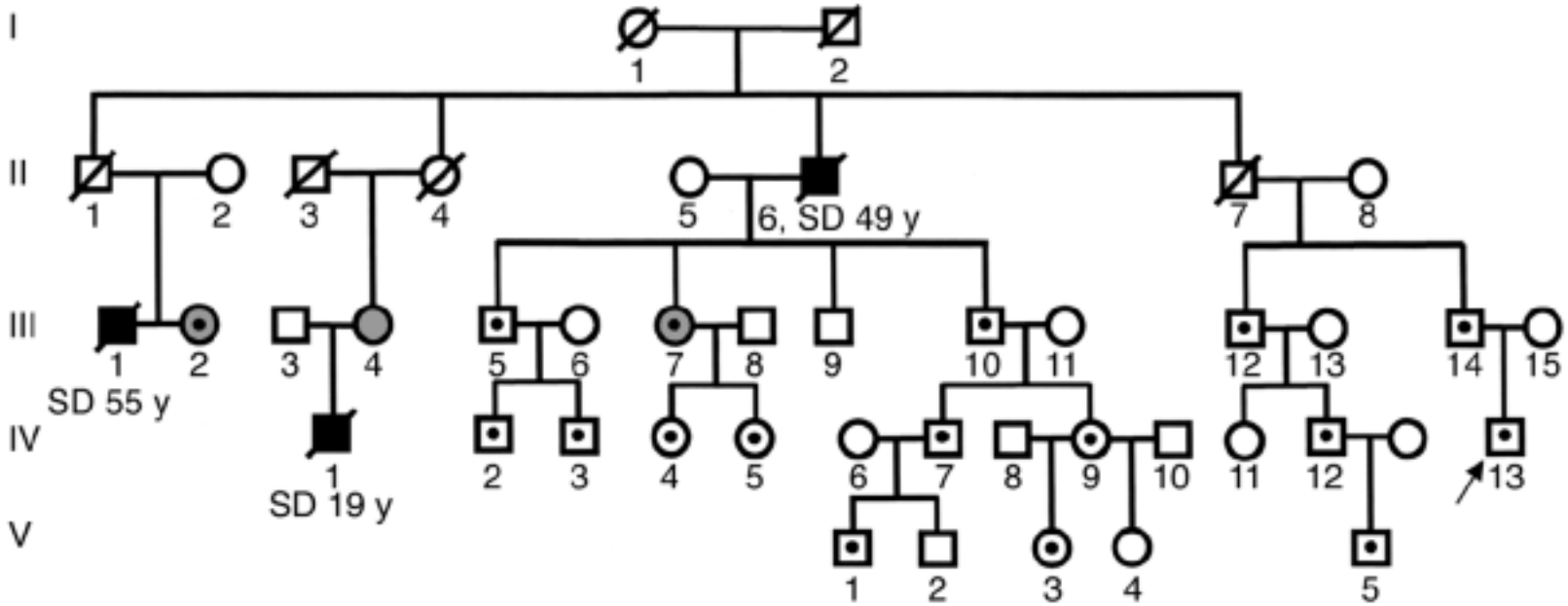


45 family members

13 carrying the G1406R *SCN5A* mutation

4 Brugada Syndrome

7 Isolated cardiac conduction defects

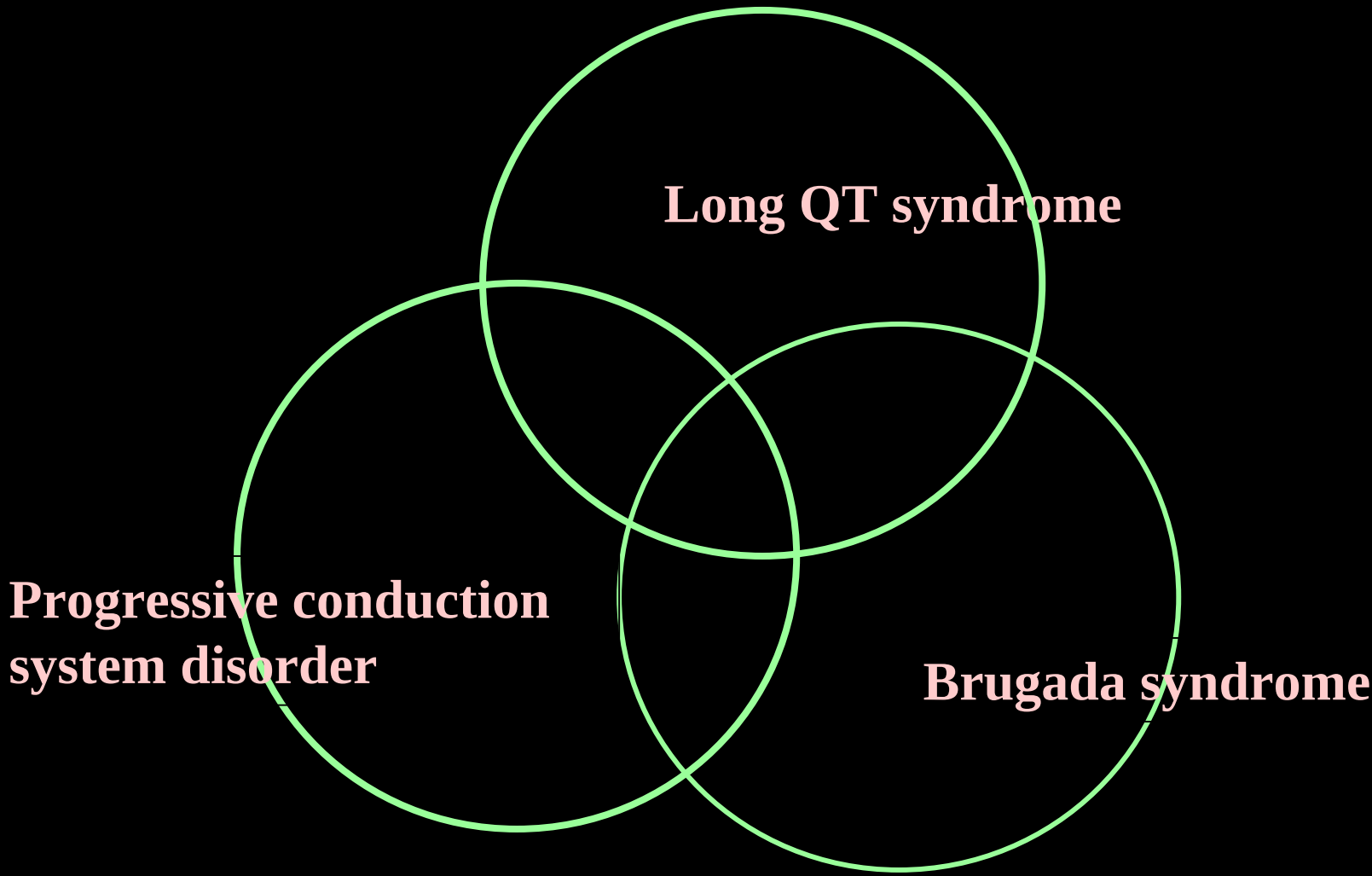


Gene carrier	QTc (ms)	LP	ST elevation*	CB	Flecainide	Syncope
III-5	450	–	+	–	+	–
III-10	486	NA	–	–	NA	+
III-12	490	+	+	–	–	–
III-14	475	+	+	+	NA	+
IV-2	465	–	+	+**	+	+
IV-3	510	+	+	+	+	–
IV-4	470	–	+	+**	+	+
IV-5	475	+	+	+**	+	–
IV-7	495	+	+	+	+	+
IV-9	495	–	+	–	+	–
IV-12	470	–	–	+**	–	–
IV-13 (pb)	500	NA	–	–	NA	–
V-1	490	NA	–	–	NA	–
V-3	460	–	–	+**	NA	–
V-5	490	–	–	+	NA	+

Gene carrier

No clinical data

Grant et al,
J Clin Invest


Long QT syndrome
Progressive conduction system disorder
Brugada syndrome