

ECG and Channelopathies

PLACE 2022



Prof. Fiorenzo Gaita

University of Turin

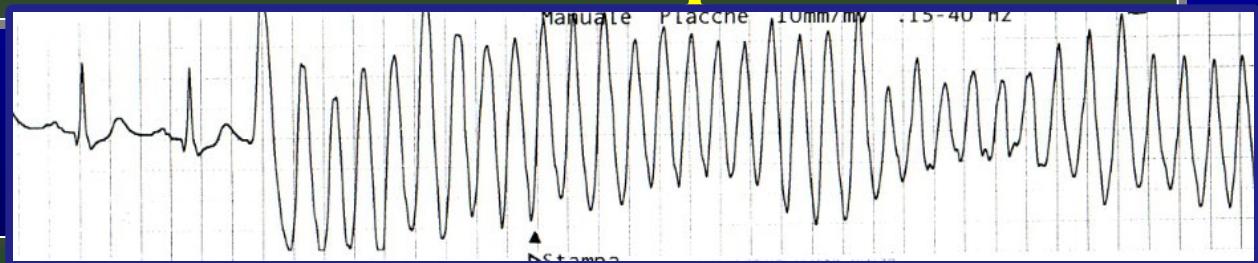


NO DISCLOSURES FOR THIS PRESENTATION

Channelopathies: what do they have in common?

Hereditary arrhythmogenic diseases

- Young subjects
- Absence of cardiac structural diseases
- Increased risk of ventricular arrhythmias that cause syncope or sudden death, often at first presentation.

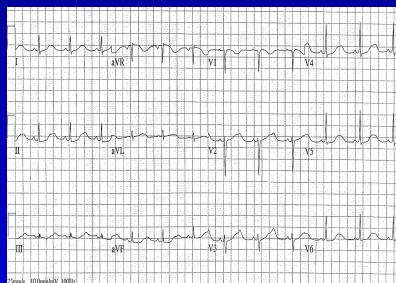


- Electrocardiographic diagnosis

Channelopathies

Long QT
(Romano 1963-Ward 1964)

0.2-0.4 : 1.000



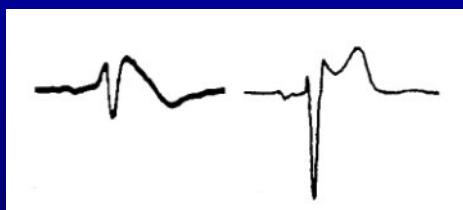
Polymorphic adrenergic ventricular tachycardia (Coumel 1978)

< 0.1 : 1.000



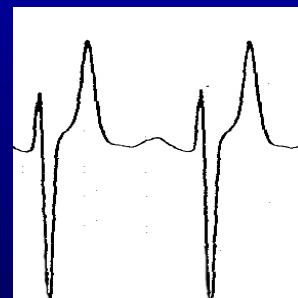
ST elevation V₁-V₃
(Martini-Brugada 1991)

0.5-7 : 1.000



Short QT
(Gaita-Giustetto-Borggrefe 2003)

< 0.1 : 1.000

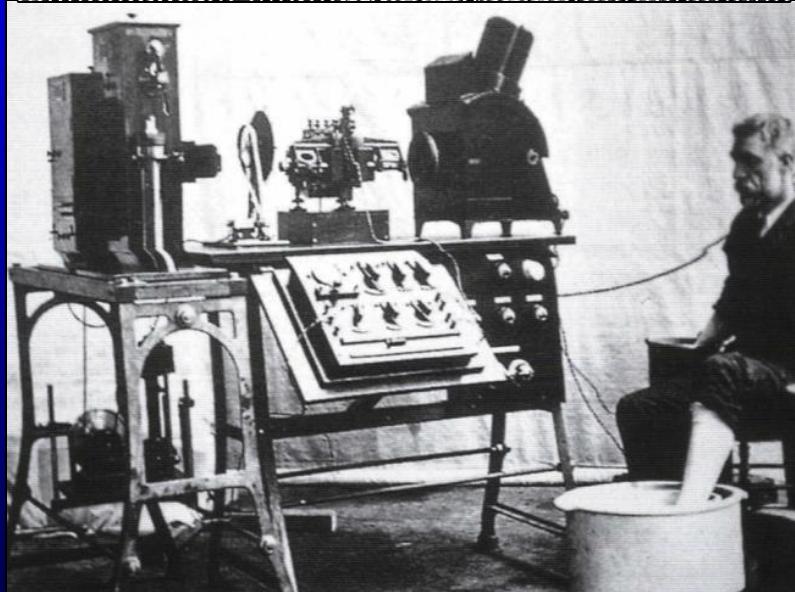
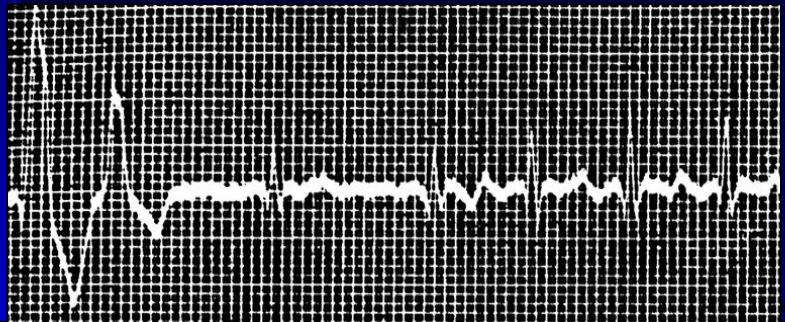


Early repolarization
(Haïssaguerre-Rosso 2008)

10-100 : 1.000



Roles of ECG in Long QT, Short QT, Brugada, Early Repolarization



➤ Diagnosis

➤ Risk stratification

➤ Evaluation of therapy

Nadolol: HR 0.38; Other BB: HR 0.76

5-year risk of LAE
off therapy (R)

Percentage (%)
of patients

R > 6%

7%

3% < R ≤ 6%

20%

1% < R ≤ 3%

31%

R ≤ 1%

42%

LQT2 QTc > 520 ms

LQT3 QTc > 510 ms

LQT1 QTc > 530 ms

LQT2 QTc 471 - 520 ms

LQT3 QTc 461 - 510 ms

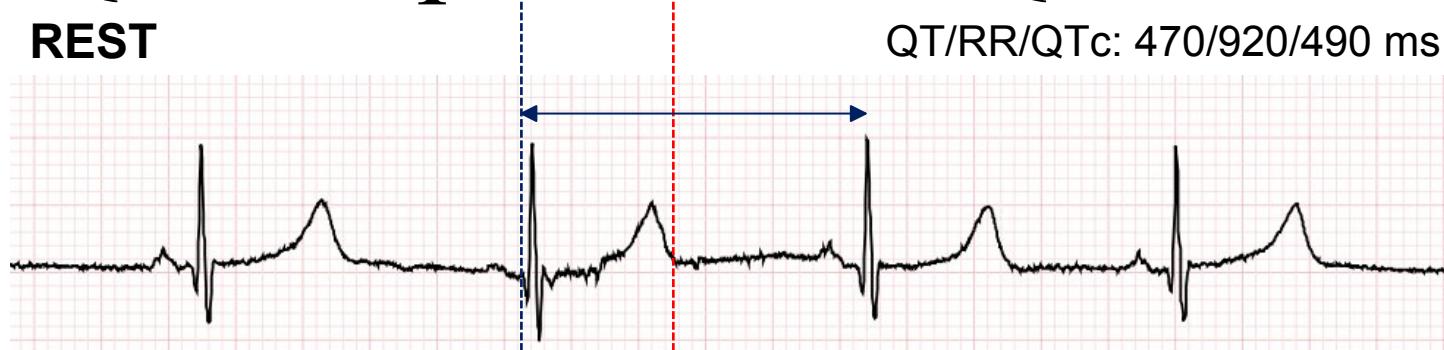
LQT1 QTc 461 - 530 ms

LQT2 QTc 461 - 470 ms

All genotypes QTc ≤ 460 ms

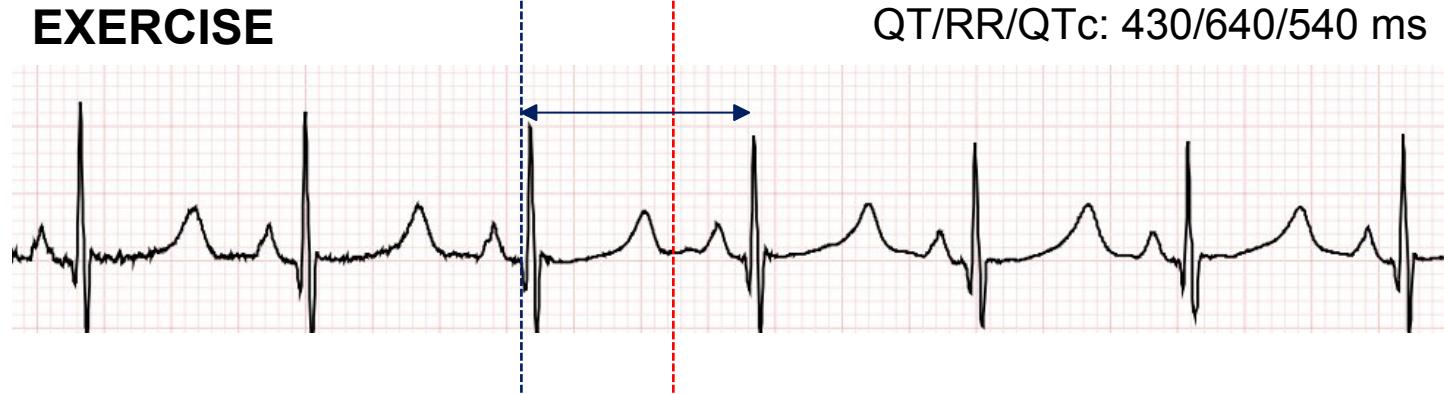
ECG and Genotype in LQTS: Poor QT Adaptation in LQT1

REST



QT/RR/QTc: 470/920/490 ms

EXERCISE



QT/RR/QTc: 430/640/540 ms

A.B.
Male
KCNQ1 (p.R190W)

A. Mazzanti

ECG and Genotype in LQTS: Normal QT Adaptation in LQT2

REST

QT/RR/QTc: 540/960/550 ms



EXERCISE

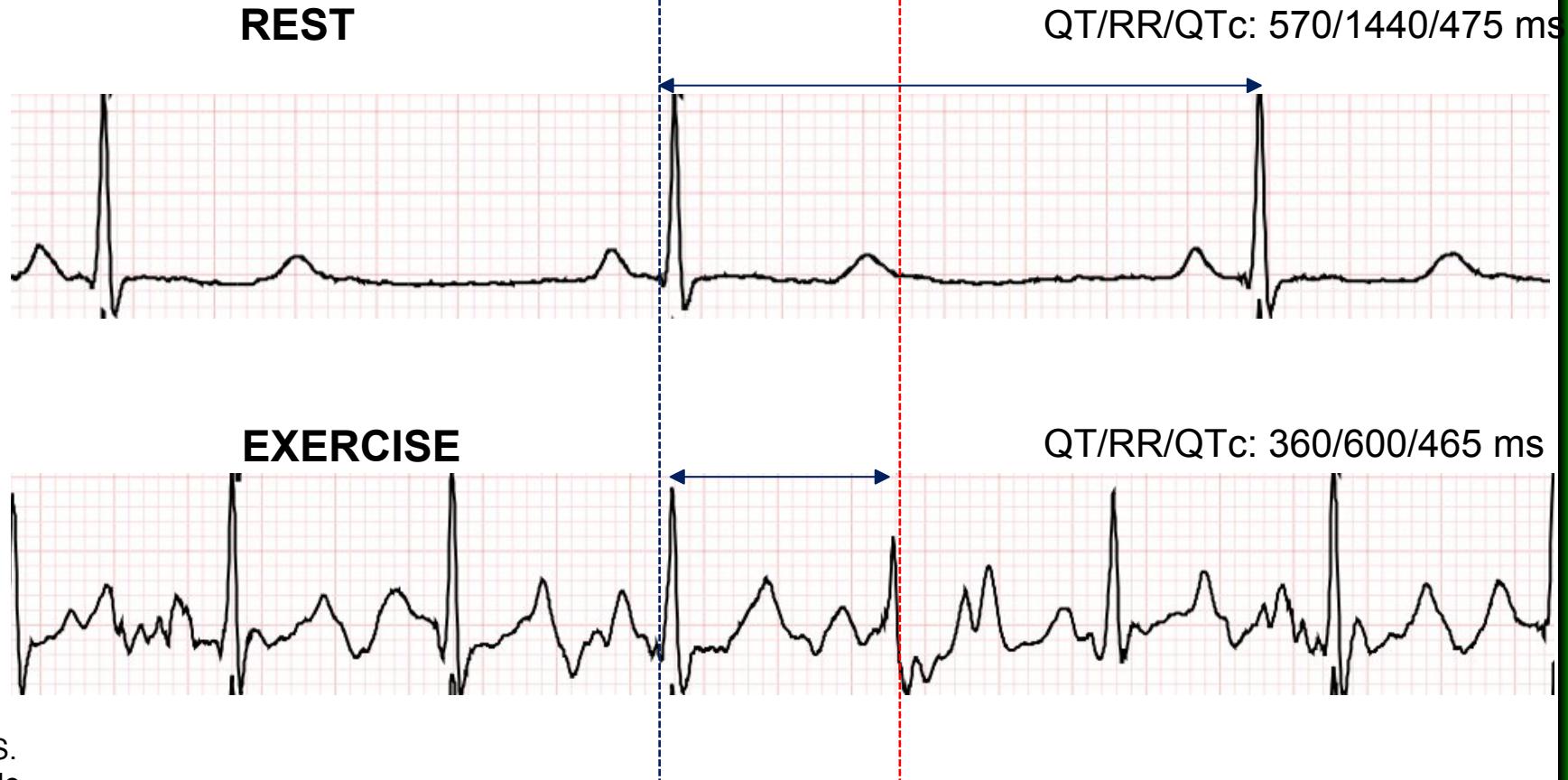
QT/RR/QTc: 450/800/503 ms



A.F.
Male
KCNH2 (p.R1014X)

A. Mazzanti

ECG and Genotype in LQTS: Normal QT Adaptation in LQT3

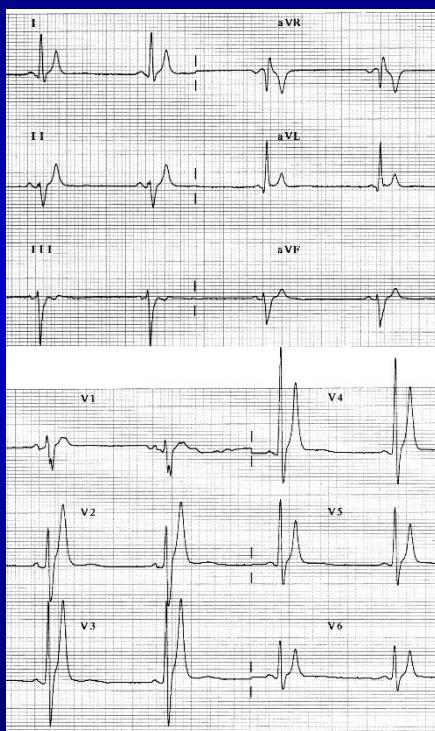


M.S.
Male
SCN5A (p.E1784K)

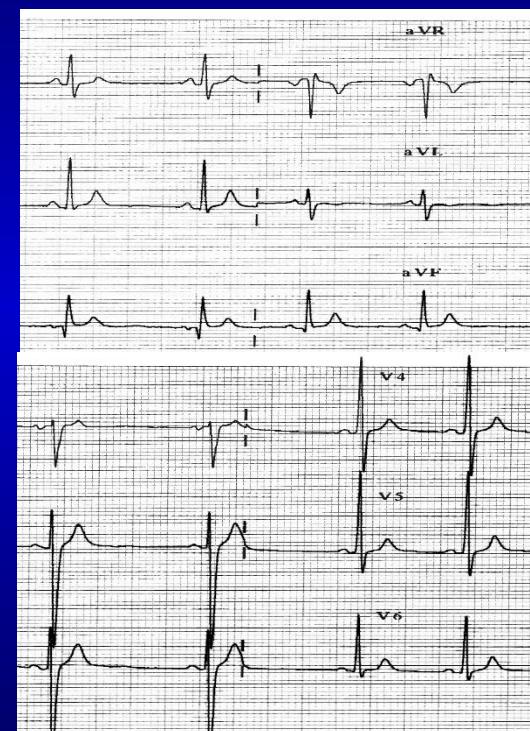
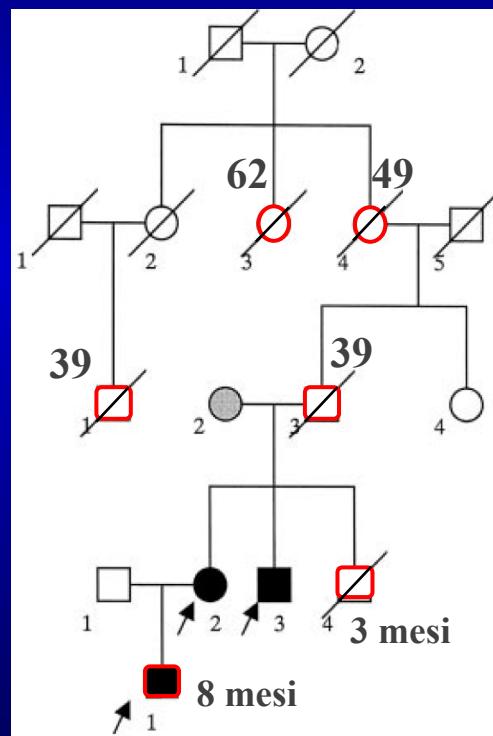
Short QT Syndrome : A Familial Cause of Sudden Death

Fiorenzo Gaita, Carla Giustetto, Francesca Bianchi, Christian Wolpert, Rainer Schimpf,
Riccardo Riccardi, Stefano Grossi, Elena Richiardi and Martin Borggrefe

(Circulation. 2003;108:965-970.)



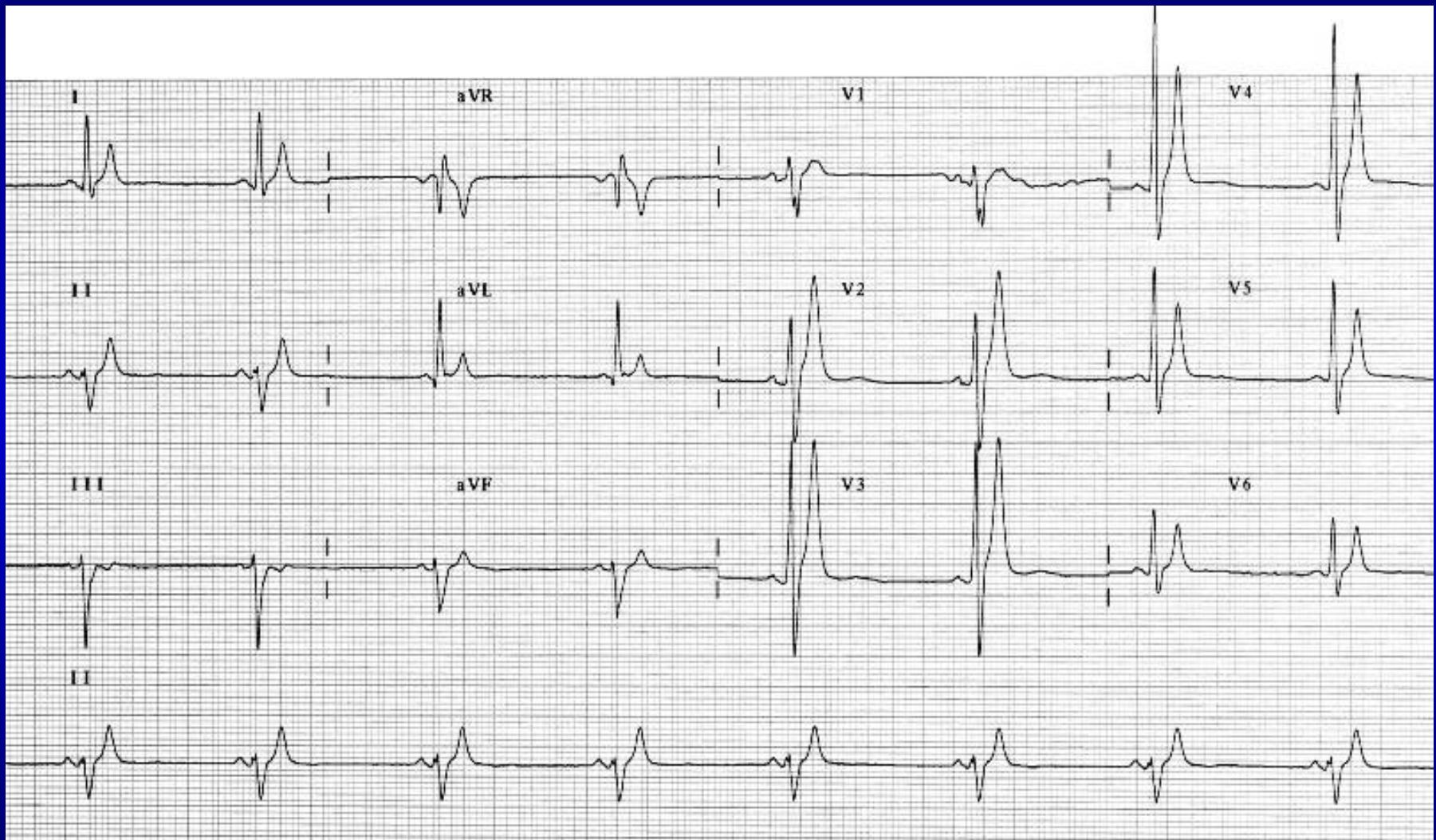
Onda T alta, appuntita, simmetrica



Onda T normale

Cardiopalmo, FA, sincope QT \leq 280/QTc \leq 300 Arresto cardiaco rianimato

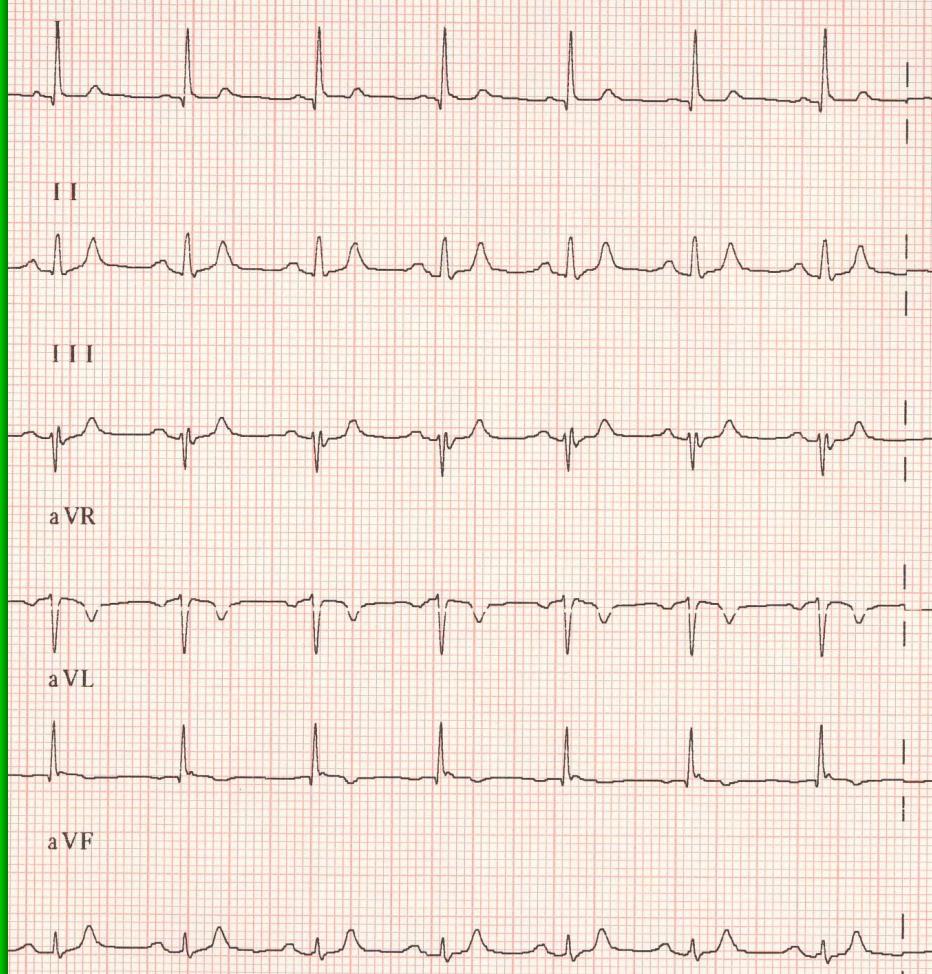
SHORT QT



Onde T strette, alte e appuntite

QT 280 ms QTc 260 ms

QT breve: ECG appearance



QT 270 ms; QTc 320 ms

C2



C3



270 ms

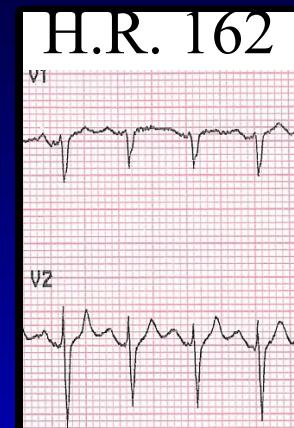
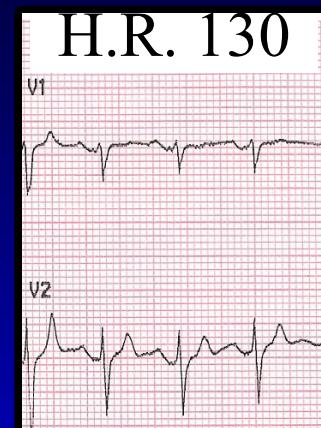
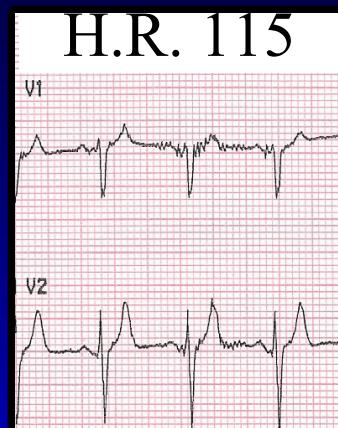
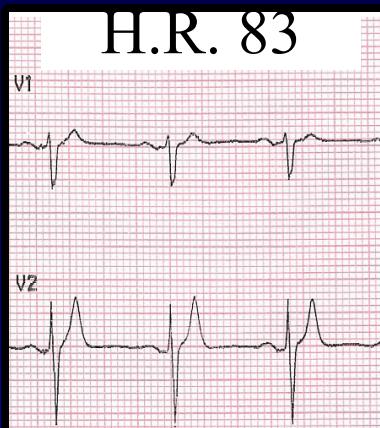
C4



C5



SQT1 (F, 31 years), stress test

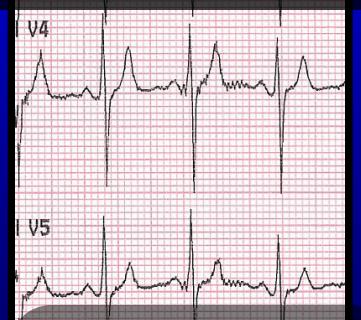


QT interval is so short that it can shorten
very fewly with HR increasing



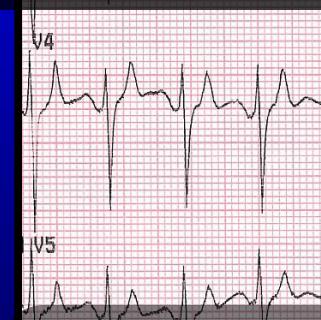
QT 240ms

QTc 282ms



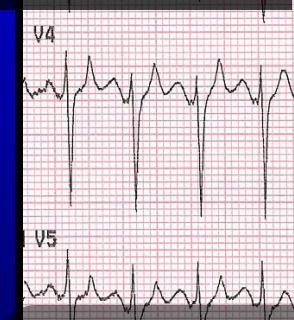
QT 235ms

QTc 325ms



QT 235ms

QTc 346ms



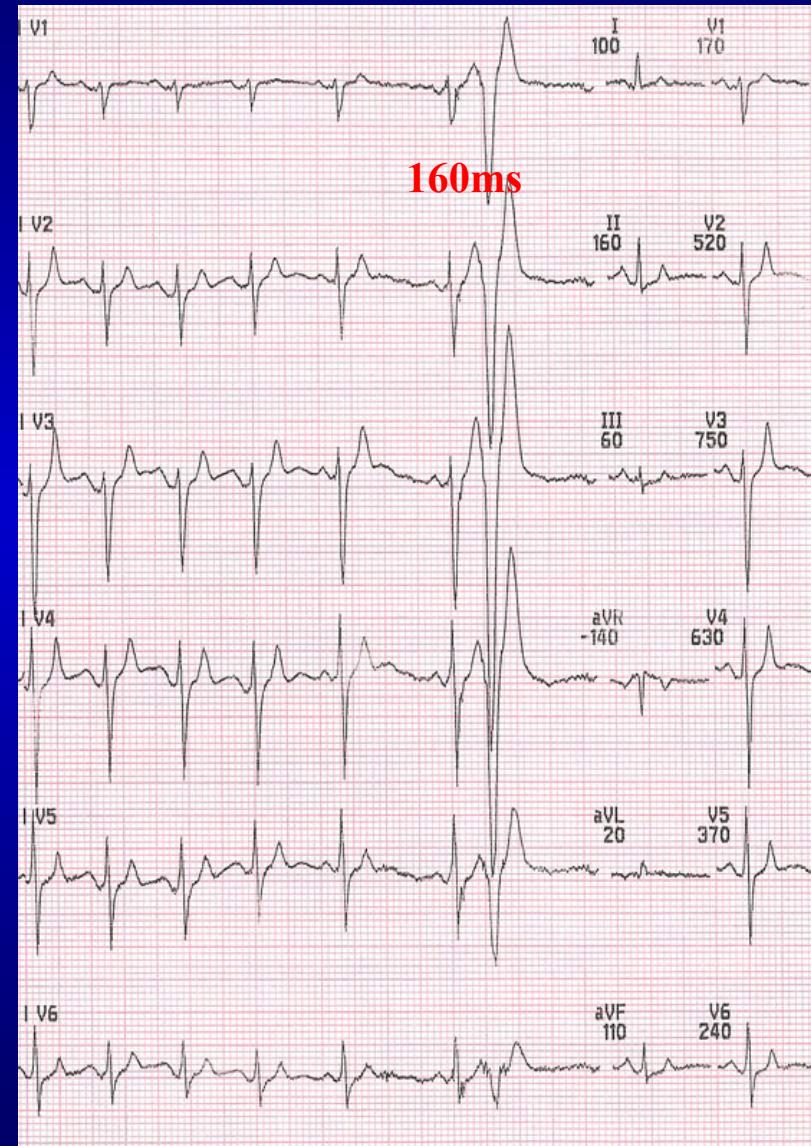
QT 220ms

QTc 360ms

Ventricular ectopic beats with short coupling

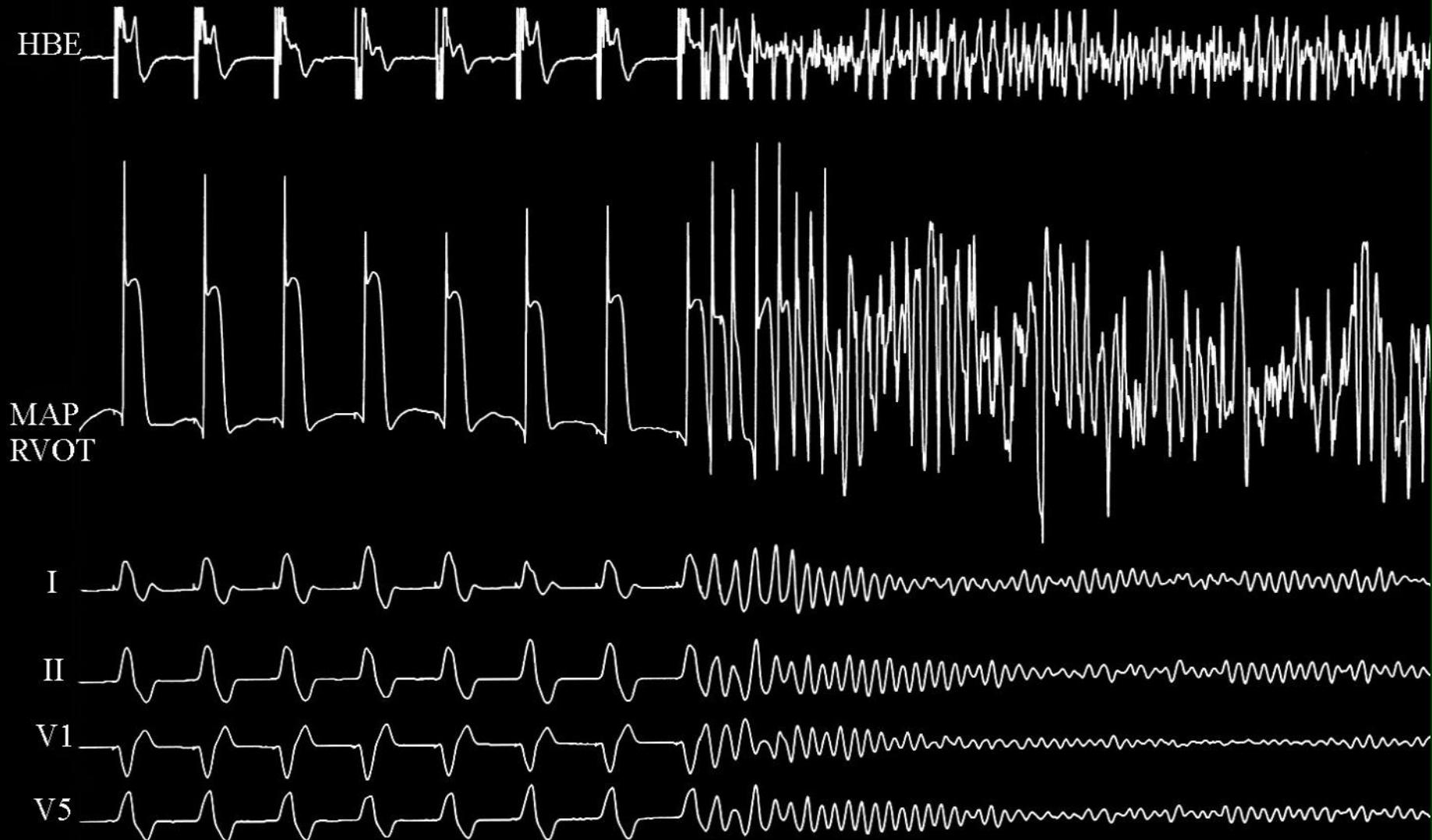


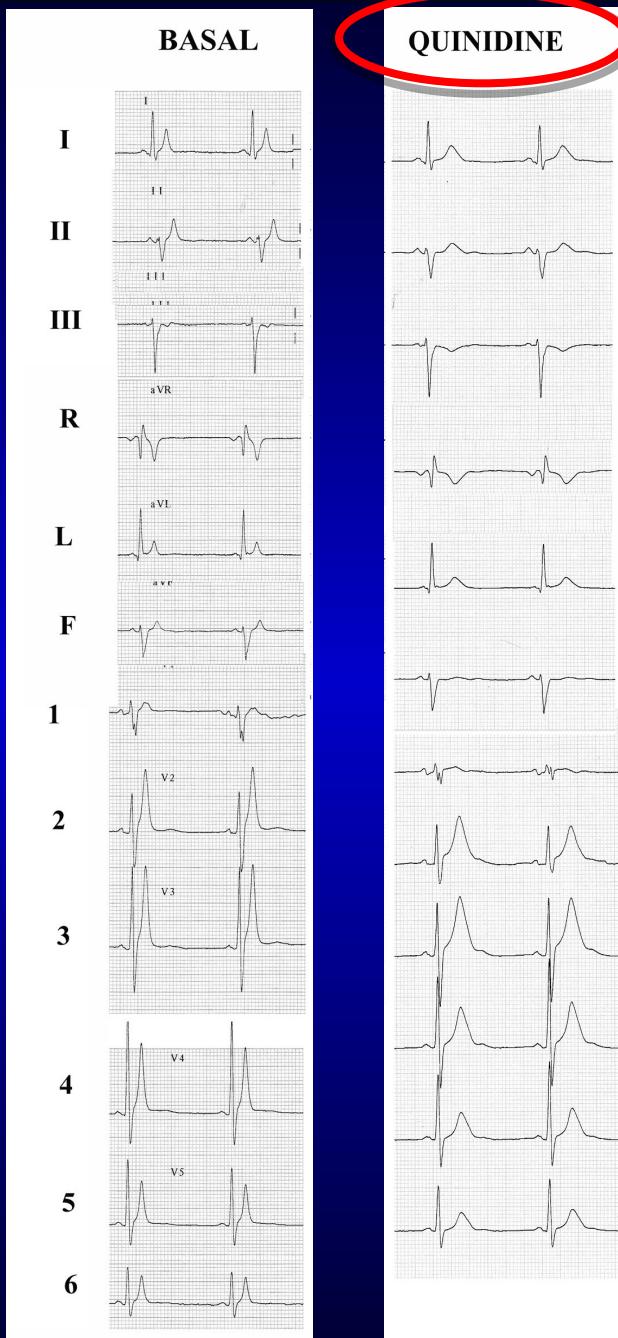
220ms



160ms

Ventricular fibrillation induced by electrocatheter positioning





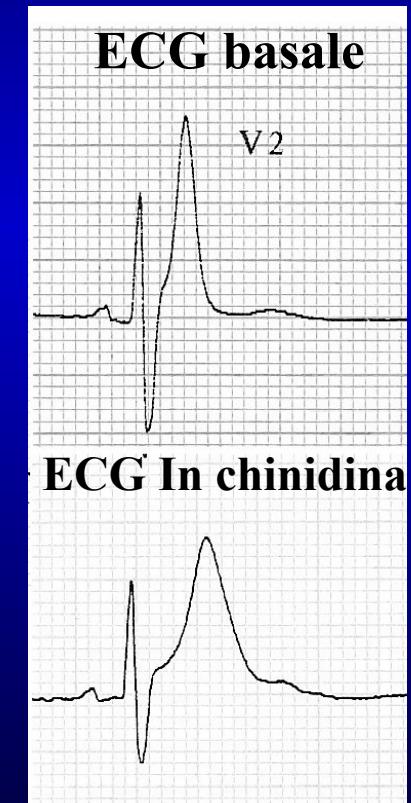
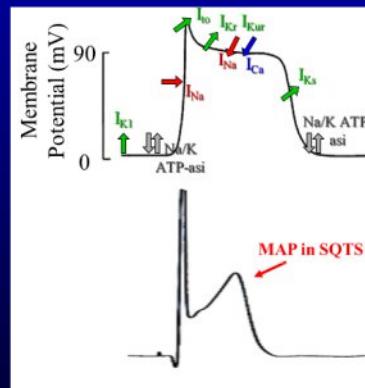
Short QT Syndrome: Pharmacological Treatment

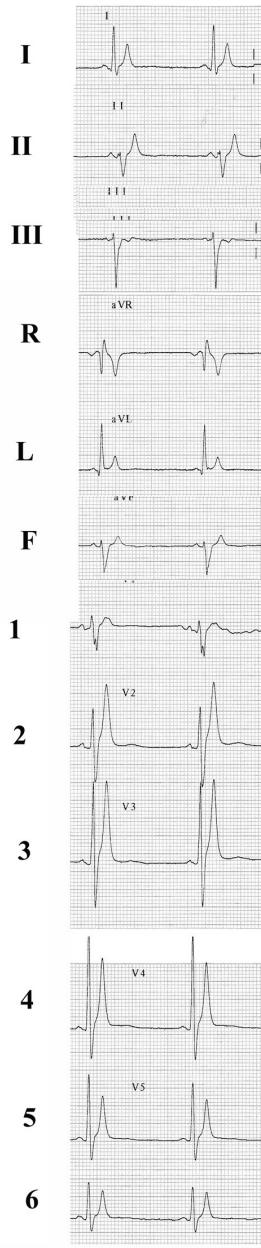
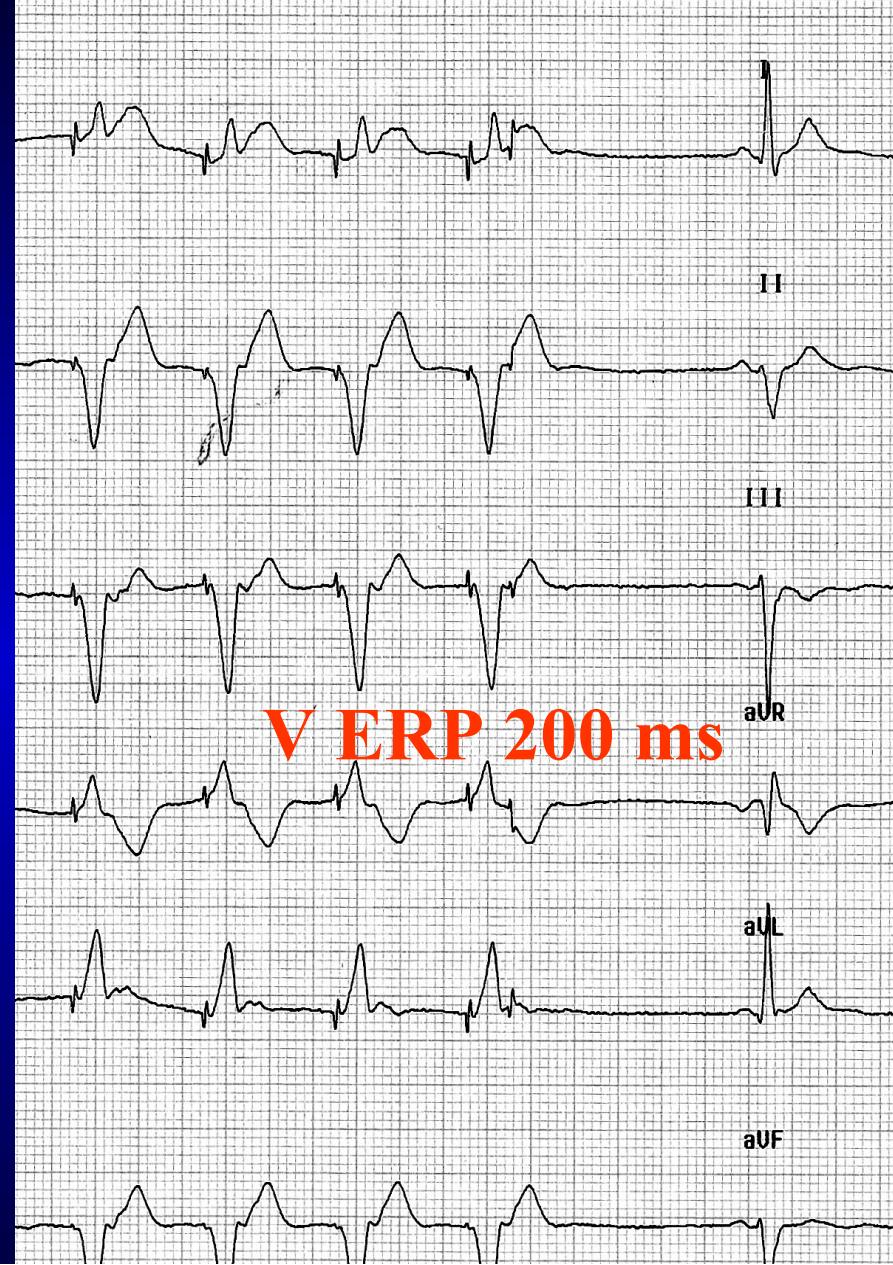
F. Gaita, MD; C. Giustetto, MD; F. Bianchi, MD; R. Schimpf, MD; M. Haissaguerre; MD, L. Calò, MD; R. Brugada, MD; C. Antzelevitch, PhD; M. Borggrefe, MD; C. Wolpert, MD.

J Am Coll Cardiol 2004; 43: 1494-99

blocca I_{Na+} , I_{Kr} ,
 I_{K1} , I_{to} , I_{K-ATP} , I_{Ks}

QT 440 ms
 QTc 390 ms



BASAL**QUINIDINE**

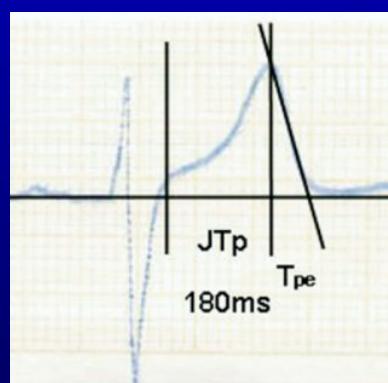
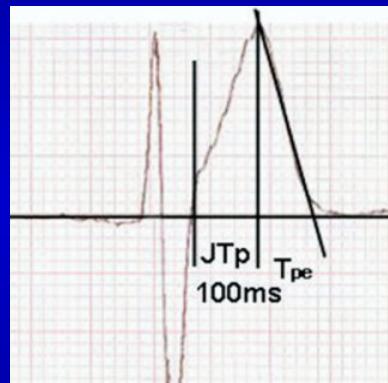
F.Gaita et al. J Am Coll Cardiol 2004; 43: 1494-

Differences in twelve-lead electrocardiogram between symptomatic and asymptomatic subjects with short QT interval

Olli Anttonen, MD,* M. Juhani Junntila, MD,† Philippe Maury, MD,§ Rainer Schimpf, MD,‡
 Christian Wolpert, MD,‡ Martin Borggrefe, MD,‡ Carla Giustetto, MD,¶ Fiorenzo Gaita, MD,¶
 Frederic Sacher, MD,** Michel Haïssaguerre, MD,** Pascal Sbragia, MD,|| Ramon Brugada, MD,††
 Heikki V. Huikuri, MD†

SQTS QTc 317ms
 JT_p 100 ms

Heart Rhythm 2009;6:267–271

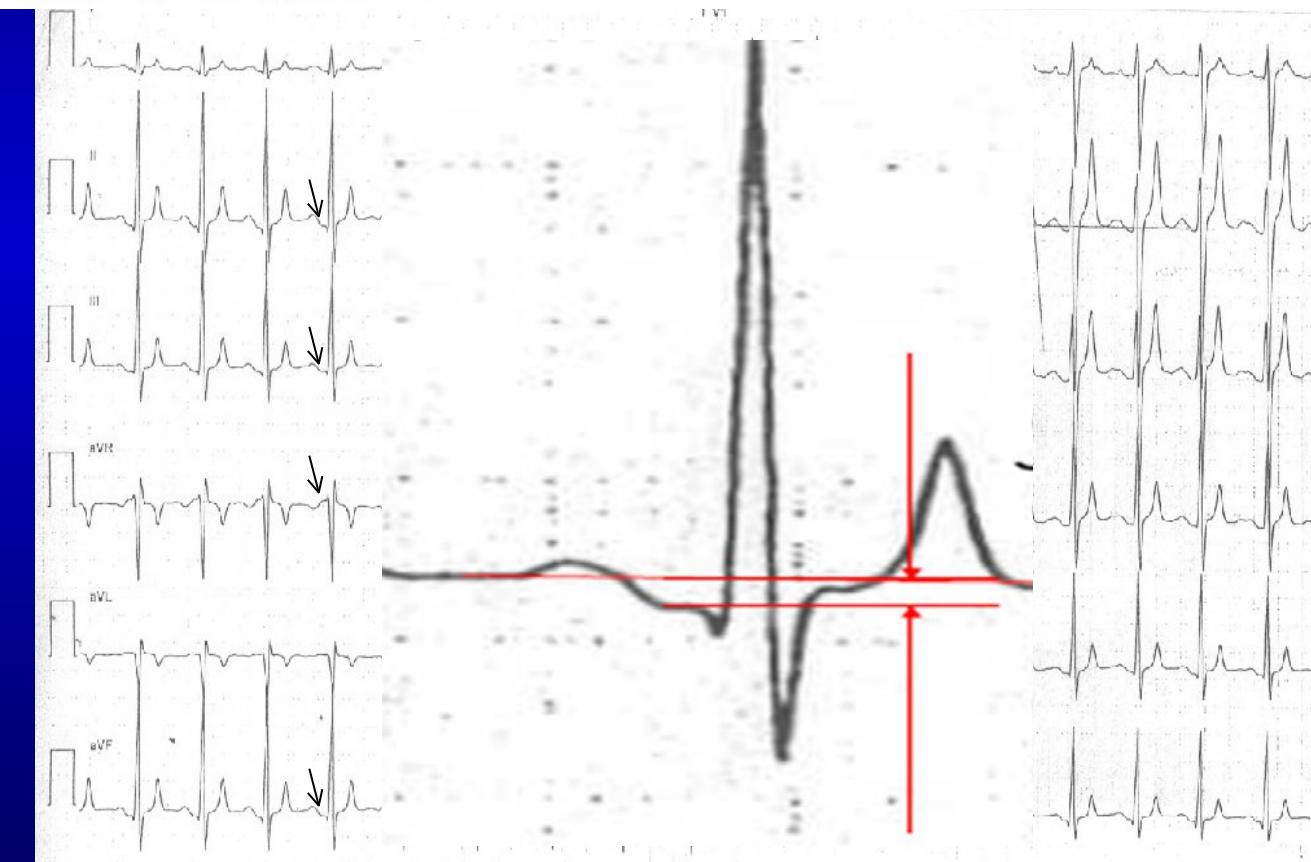


	SQTS patients (n = 10)	Subjects with short QTc (n = 12)	Subjects with normal QTc (n = 20)	P value (variance)
Heart rate (bpm) Mean ± SD	74 ± 9*	51 ± 8‡	66 ± 9	<.001
Median	75	52	66	
Range	59–86	36–65	47–81	
QTc (ms) Mean ± SD	317 ± 27†	314 ± 14‡	405 ± 28	<.001
Median	322	317	409	
Range	263–349	293–337	347–454	
T-wave amplitude (mV) Mean ± SD	1.2 ± 0.5††	1.1 ± 0.5‡‡	0.6 ± 0.3	<.001
Median	1.1	1.1	0.6	
Range	0.7–1.9	0.3–1.7	0.1–1.3	
Jpoint-Tpeak (ms) Mean ± SD	101 ± 18*†	184 ± 27	203 ± 33	<.001
Median	100	180	200	
Range	80–120	150–240	160–280	
Jpoint-Tpeak c (ms) Mean ± SD	112 ± 19*†	168 ± 17‡	211 ± 28	<.001
Median	108	170	210	
Range	87–140	136–191	157–268	
Jpoint-Tend (ms) Mean ± SD	189 ± 22*†	268 ± 31	294 ± 34	<.001
Median	190	260	285	
Range	160–220	230–340	230–360	
Jpoint-Tend c (ms) Mean ± SD	198 ± 20*†	260 ± 25‡‡	298 ± 30	<.001
Median	196	256	30	
Range	167–232	233–318	229–356	

PQ segment depression in patients with short QT syndrome:

A novel marker for diaanosisina short QT svndrome?

Erol Tülämen, MD, *† Carla Giustetto, MD, ‡ Christian Wolpert, MD, § Philippe Maury, MD, ||
Olli Anttonen, MD, ¶ Vincent Probst, MD, # Jean-Jacques Blanc, MD, ** Pascal Sbragia, MD, ††
Chiara Scrocco, MD, ‡ Boris Rudic, MD, *† Christian Veltmann, MD, *† Yaxun Sun, MD, ‡‡
Fiorenzo Gaita, MD, ‡ Charles Antzelevitch, PhD, FFRS, §§ Martin Borggrefe, MD, PhD, *†
Rainer Schimpf, MD *†

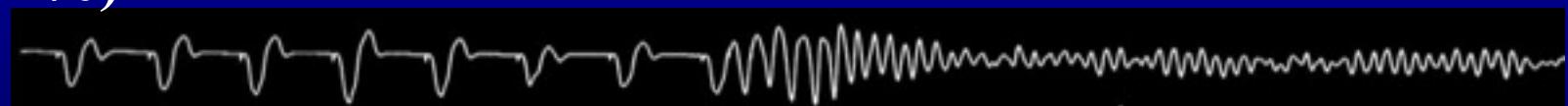
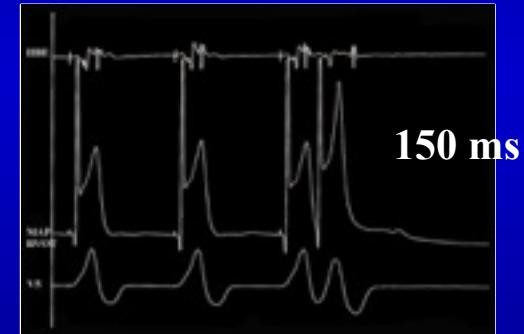


64 SQTS pts

PQ interval depression
>0.5 mm in 52 of them
(81%) and in 24%
of the control group

NO DIFFERENCES between symptomatic and asymptomatic SQTS patients regarding:

- ECG parameters (QT, QTc, J-T peak...)
- Gender, family history of SQTS or SD
- Presence of genetic mutations
- Ventricular effective refractory periods (mean: 158 ± 15 ms vs 148 ± 18 ms; p 0.21)
- inducibility of VF at EP-study (sensitivity 37%)



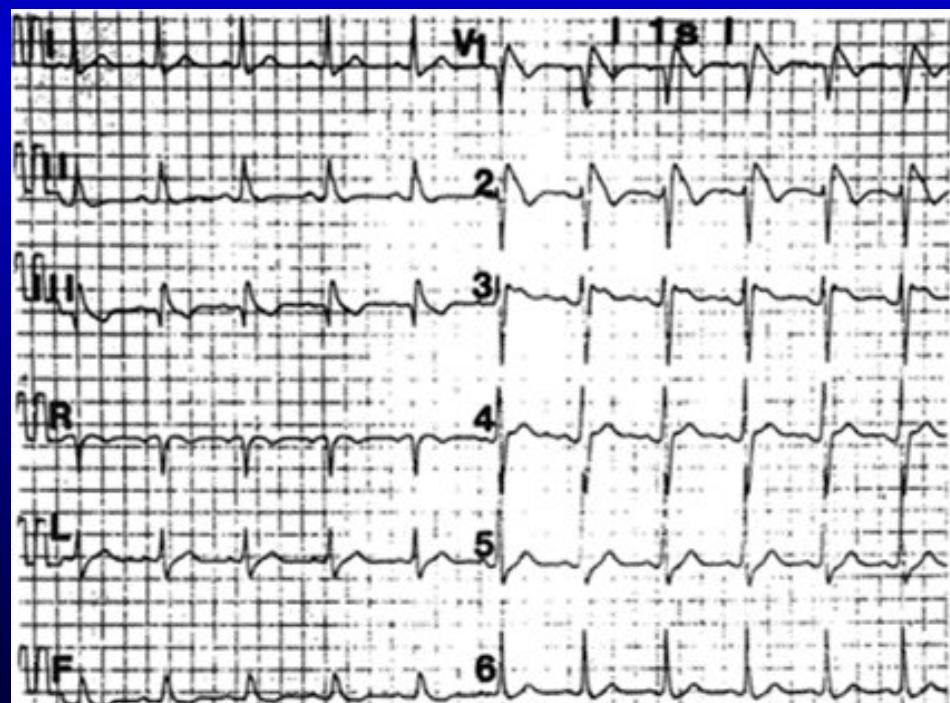
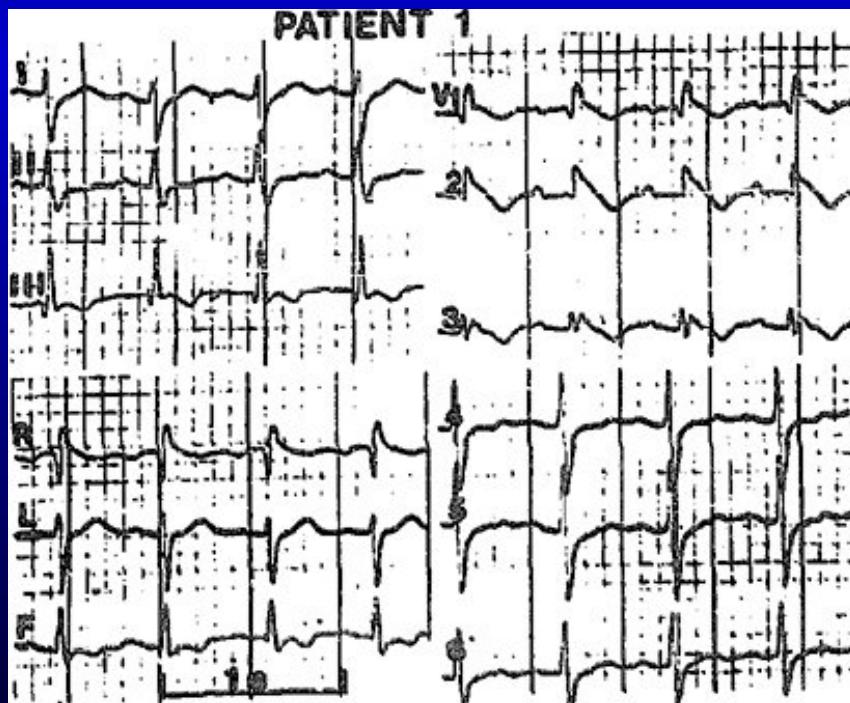
Right Bundle Branch Block, Persistent ST Segment Elevation and Sudden Cardiac Death: A Distinct Clinical and Electrocardiographic Syndrome

A Multicenter Report

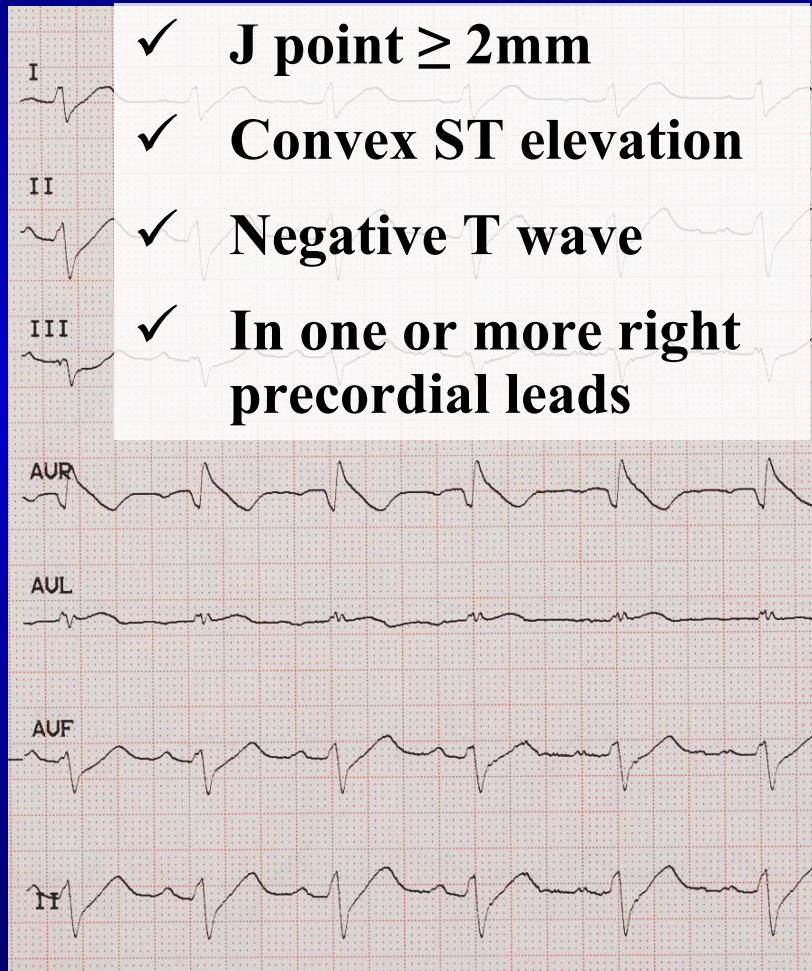
PEDRO BRUGADA, MD, JOSEP BRUGADA, MD*†

1992

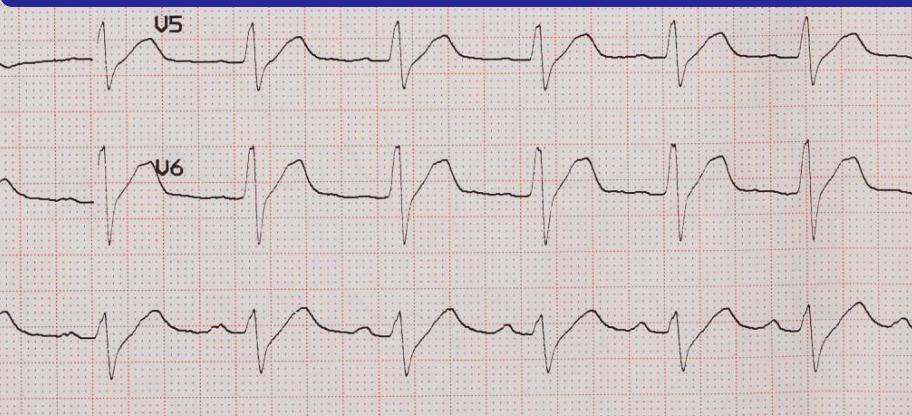
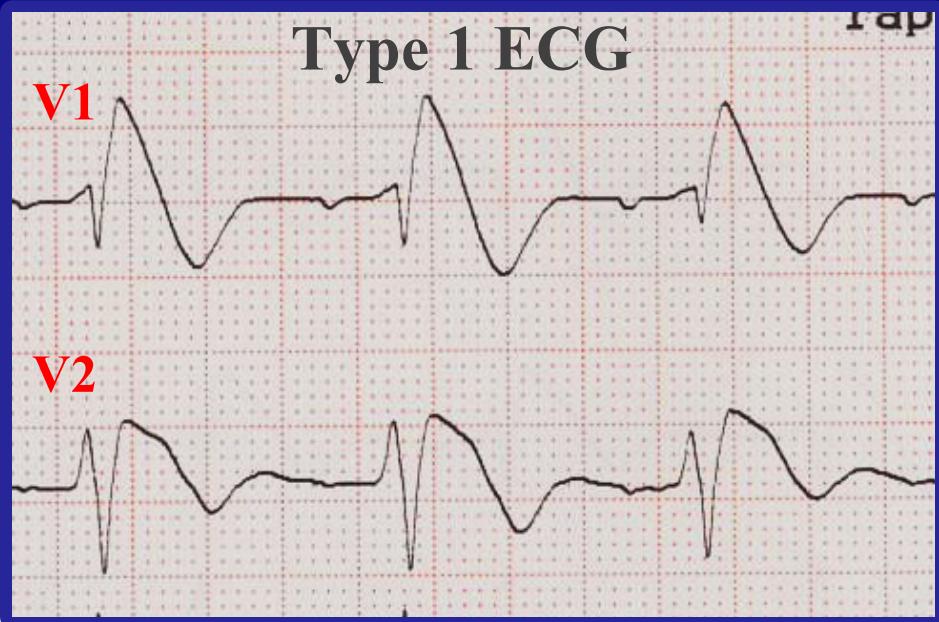
Aalst, Belgium and Barcelona, Spain



Brugada syndrome: type 1 pattern = diagnostic



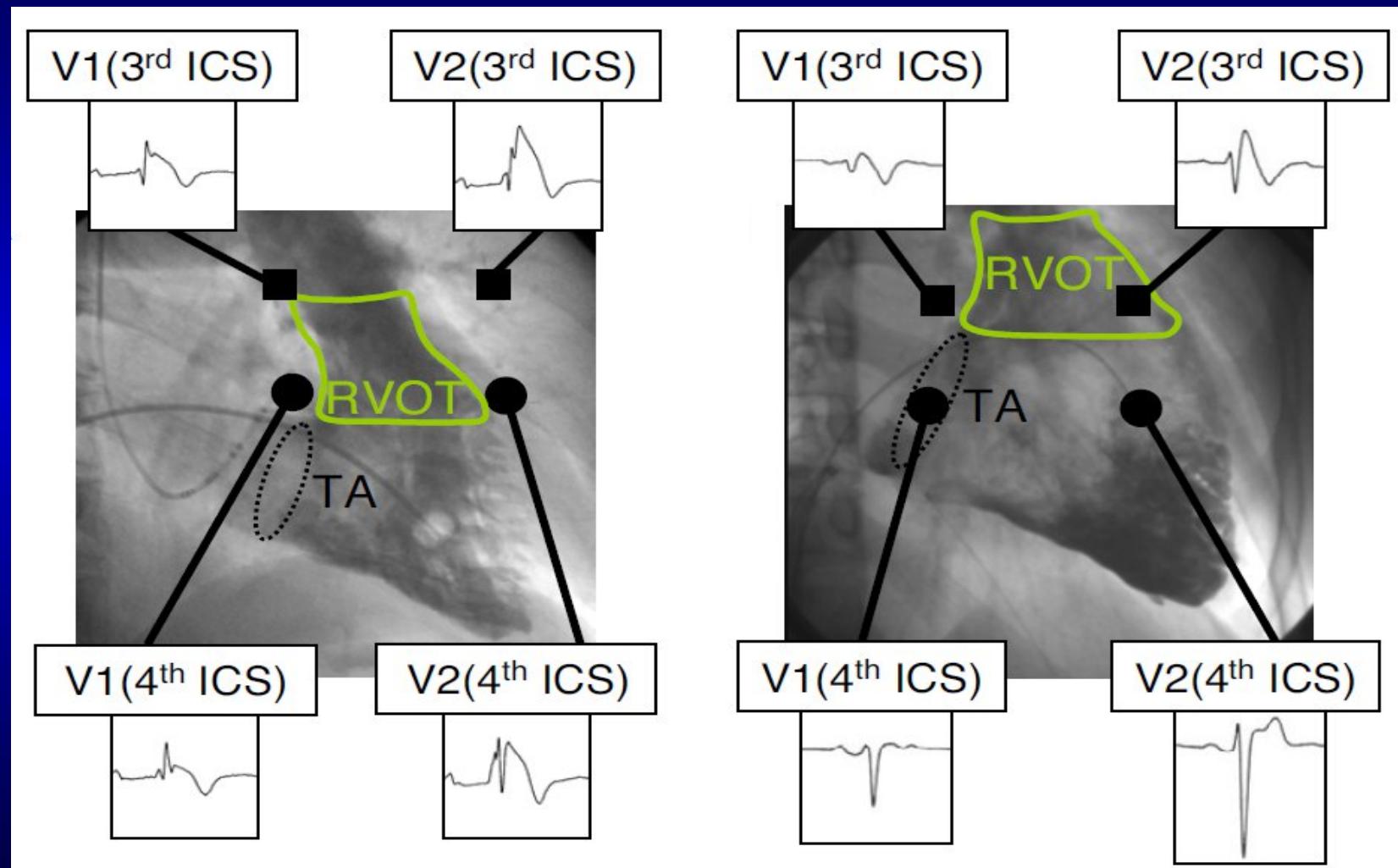
- ✓ J point \geq 2mm
- ✓ Convex ST elevation
- ✓ Negative T wave
- ✓ In one or more right precordial leads



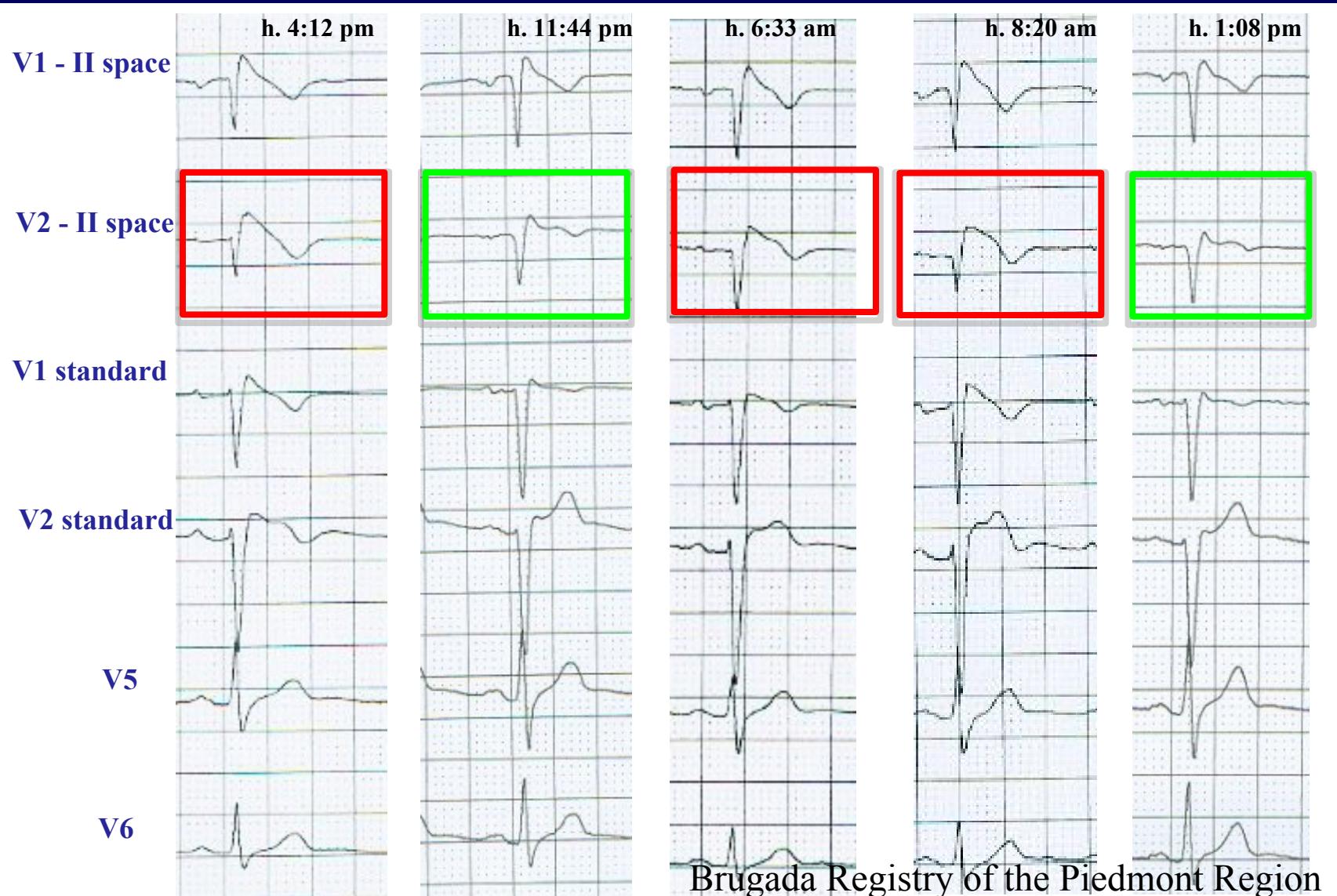
Brugada syndrome: suspicious patterns



Correlazione tra posizione del tratto di efflusso dal Vdx (RVOT) ed elettrodi esploranti



Intermittent spontaneous type 1 Brugada pattern at 12-lead 24-hour Holter monitoring

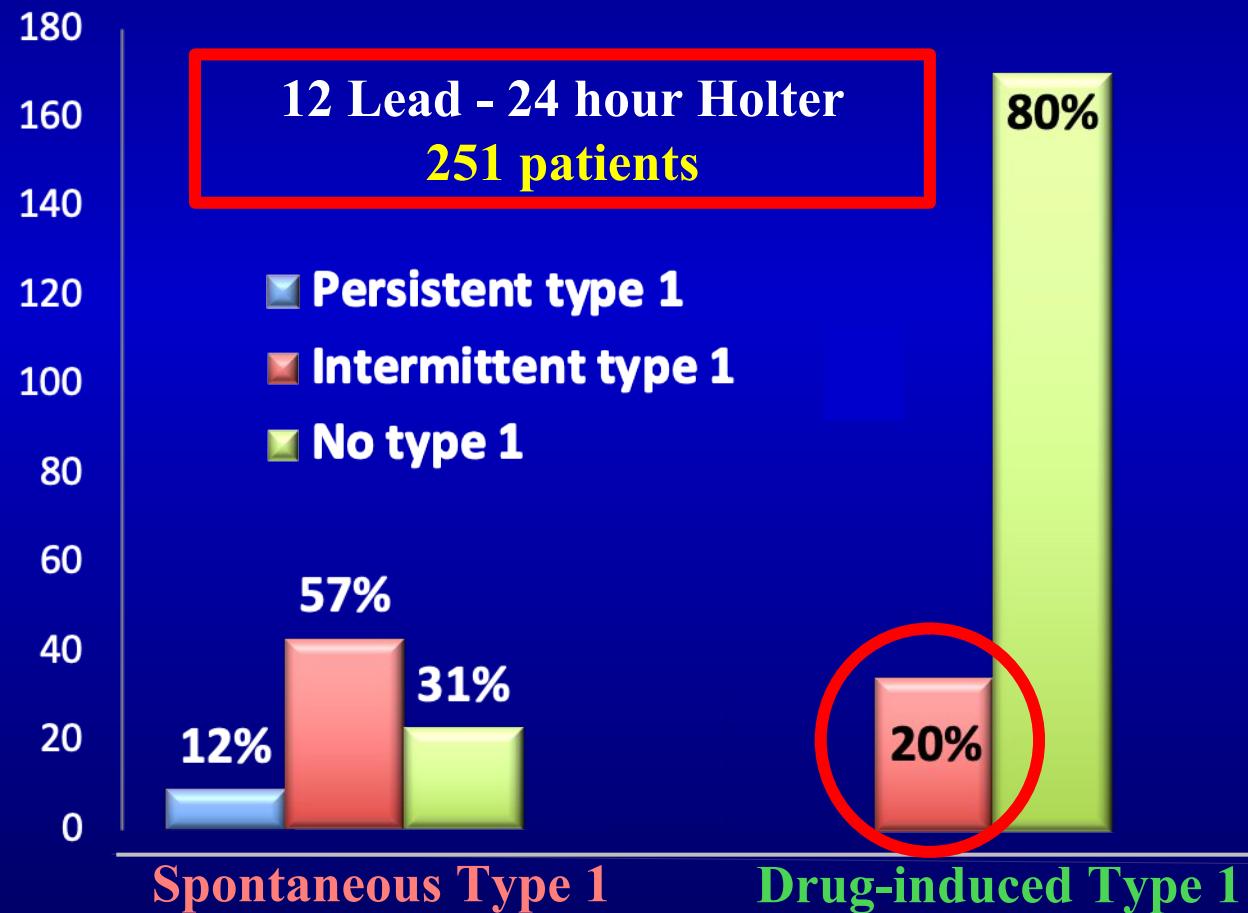


Prevalence of Type 1 Brugada Electrocardiographic Pattern Evaluated by Twelve-Lead Twenty-Four-Hour Holter Monitoring



Natascia Cerrato, MD^a, Carla Giustetto, MD^{a,*}, Elena Gribaudo, MD^a, Elena Richiardi, MD^b,
Lorella Barbonaglia, MD^c, Chiara Scrocco, MD^a, Domenica Zema, MD^a, and Fiorenzo Gaita, MD^a

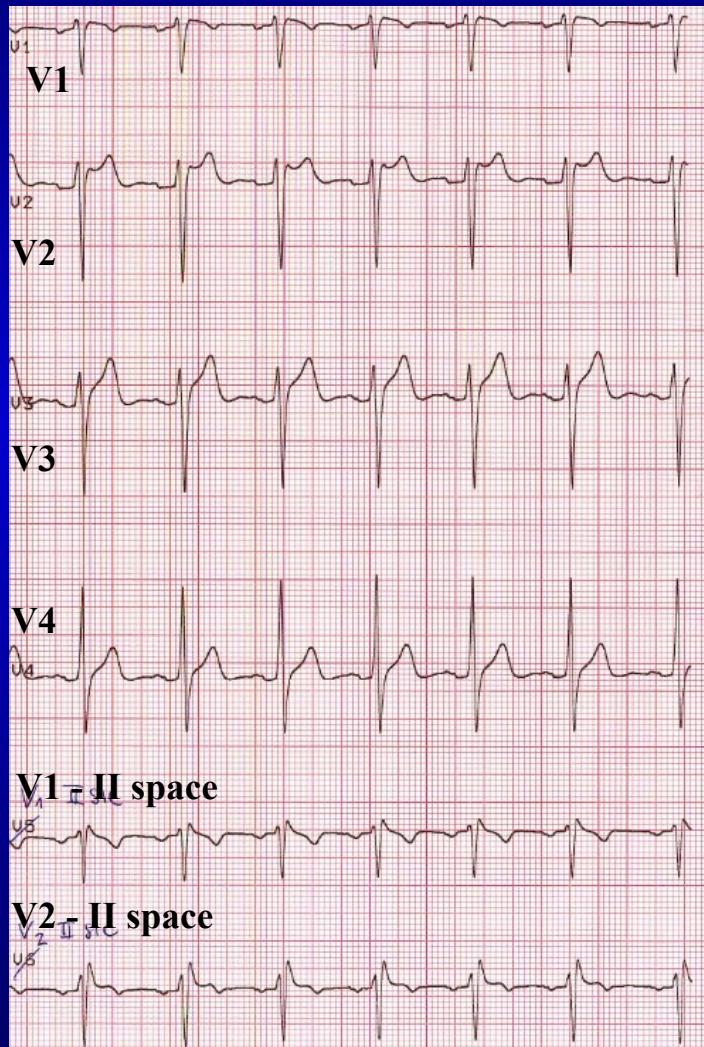
Am J Cardiol 2015; 115:



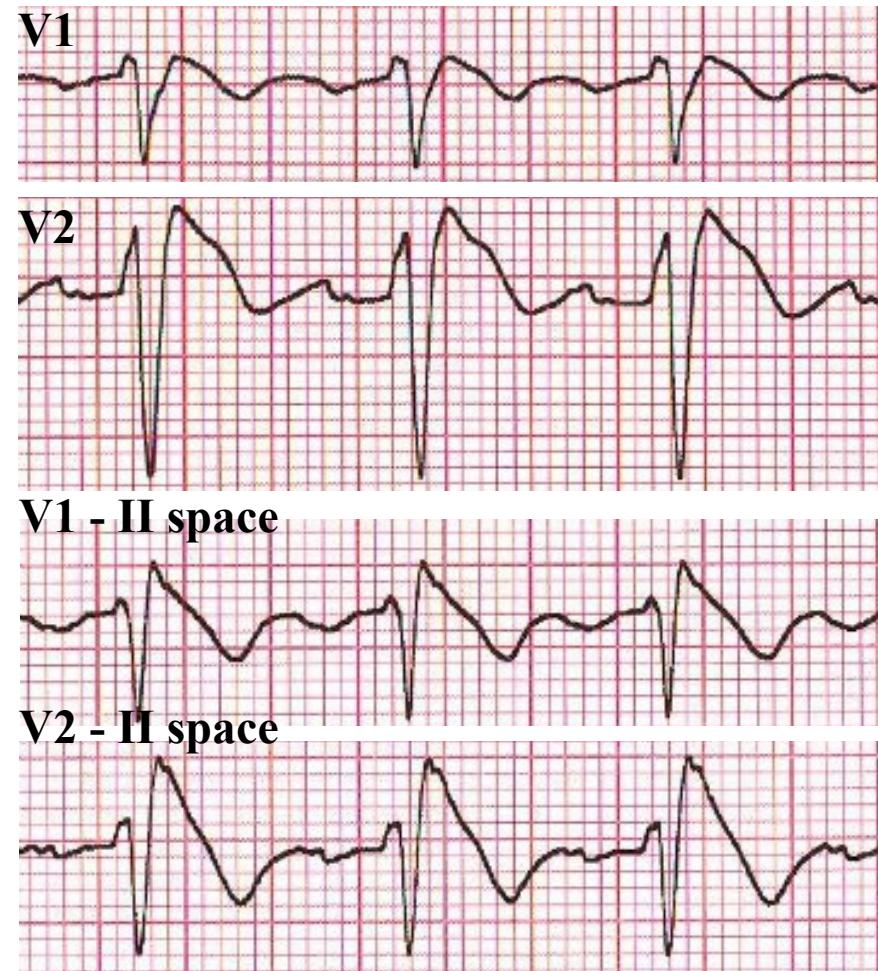
Drug challenge with Na^+ channel blockers

(ajmaline 1 mg/kg IV over 5 -10 min or flecainide 2 mg/kg IV over 10 min)

Basal ECG



Ajmaline infusion (1mg/kg in 5 min)



ECG markers of risk in Brugada patients

Clinical risk factors for arrhythmic events

Most patients with arrhythmic events are between 20 and 65 years old

	Probst et al. (1029 pts)	Sieira et al. (343 pts)
Aborted sudden death	HR= 12.4, p<0.001	HR= 10.9, p<0.01
History of <u>syncope</u>	HR = 3.4, p=0.002	HR = 3.7, p<0.01
<u>Spontaneous type 1 ECG</u>	HR = 1.8, p=0.04	HR = 2.7, p<0.01
EP-Study	HR= 1.9, p=0.05	HR = 4.7, p<0.01
Male gender	NS	HR = 2.7, p=0.02
SCN5A mutations	NS	-

aSD, syncope and spontaneous type 1 ECG pattern are known as significant risk factors

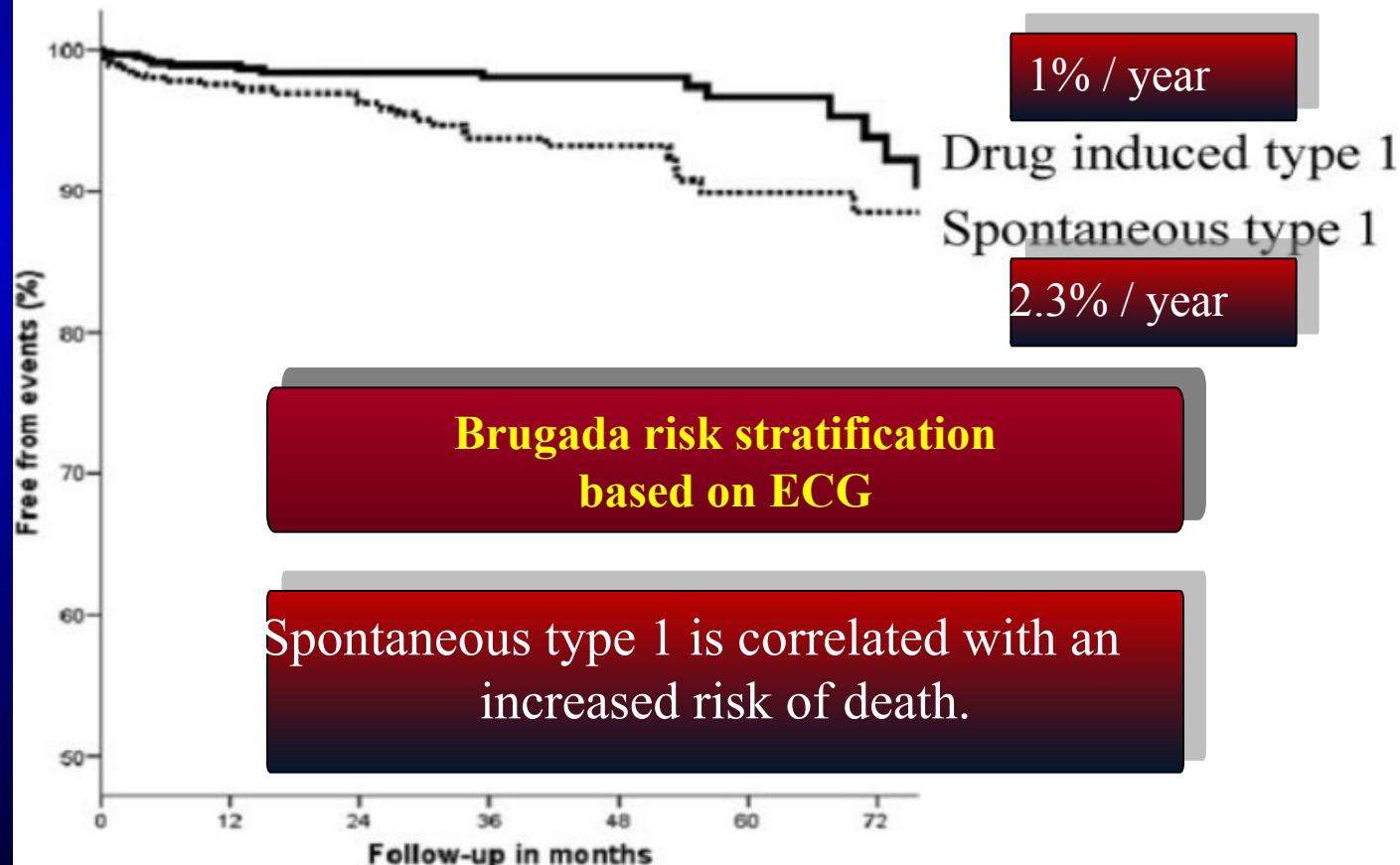
Long-Term Prognosis of Patients Diagnosed With Brugada Syndrome

1029 pts

Results From the FINGER Brugada Syndrome Registry

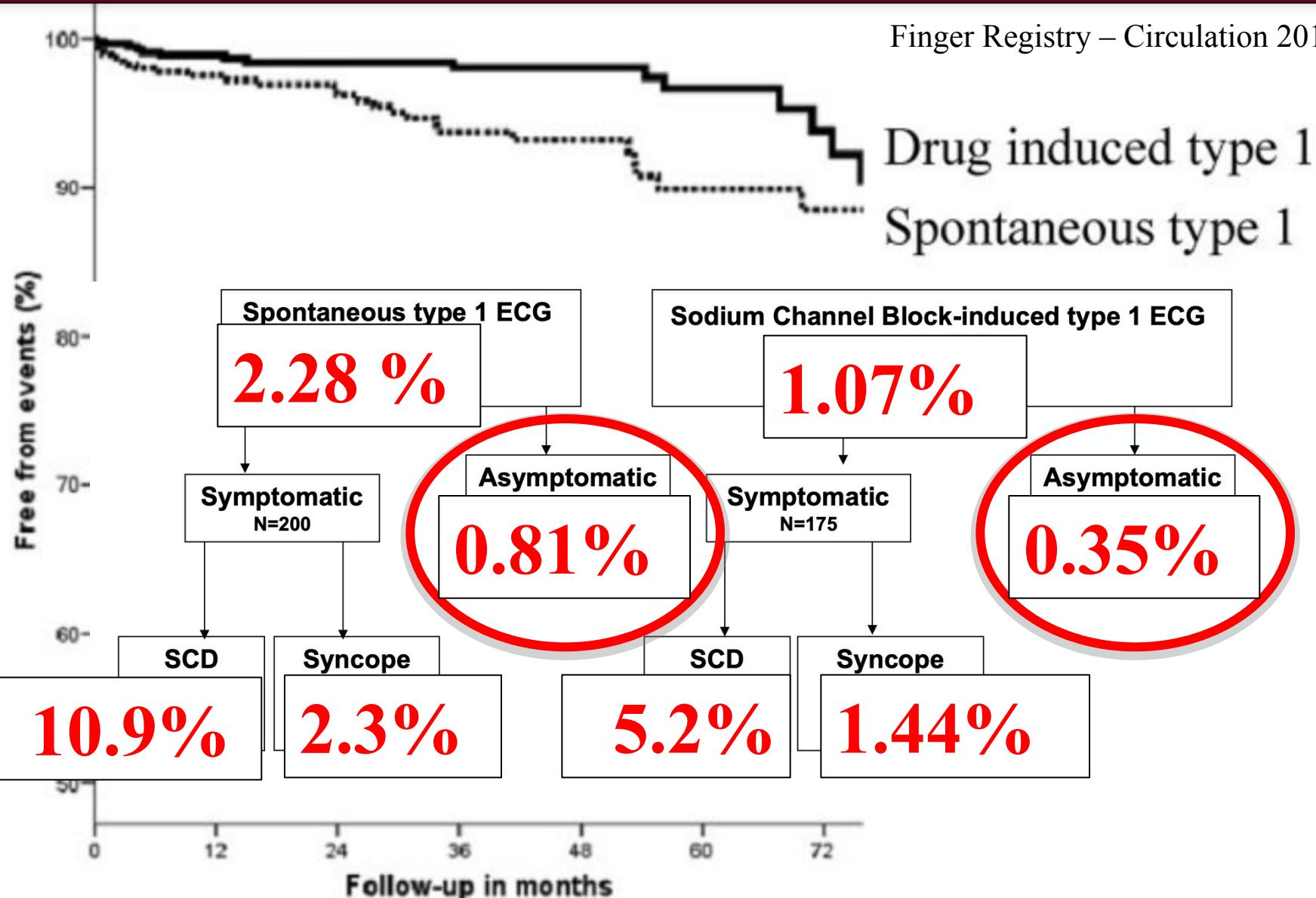
mean f-up 3 years

V. Probst, MD, PhD, C. Veltmann, MD, L. Eckardt, MD, P.G. Meregalli, MD, F. Gaita, MD, H.L. Tan, MD, PhD, D. Babuty, MD, PhD, F. Sacher, MD, C. Giustetto, MD, E. Schulze-Bahr, MD, PhD, M. Borggrefe, MD, PhD, M. Haissaguerre, MD, P. Mabo, MD, PhD, H. Le Marec, MD, PhD, C. Wolpert, MD, PhD, and A.A.M. Wilde, MD, PhD Circulation 2010



Brugada risk stratification
ECG & SYMPTOMS BASED

Finger Registry – Circulation 2010



ECG markers of risk in asymptomatic Brugada patients

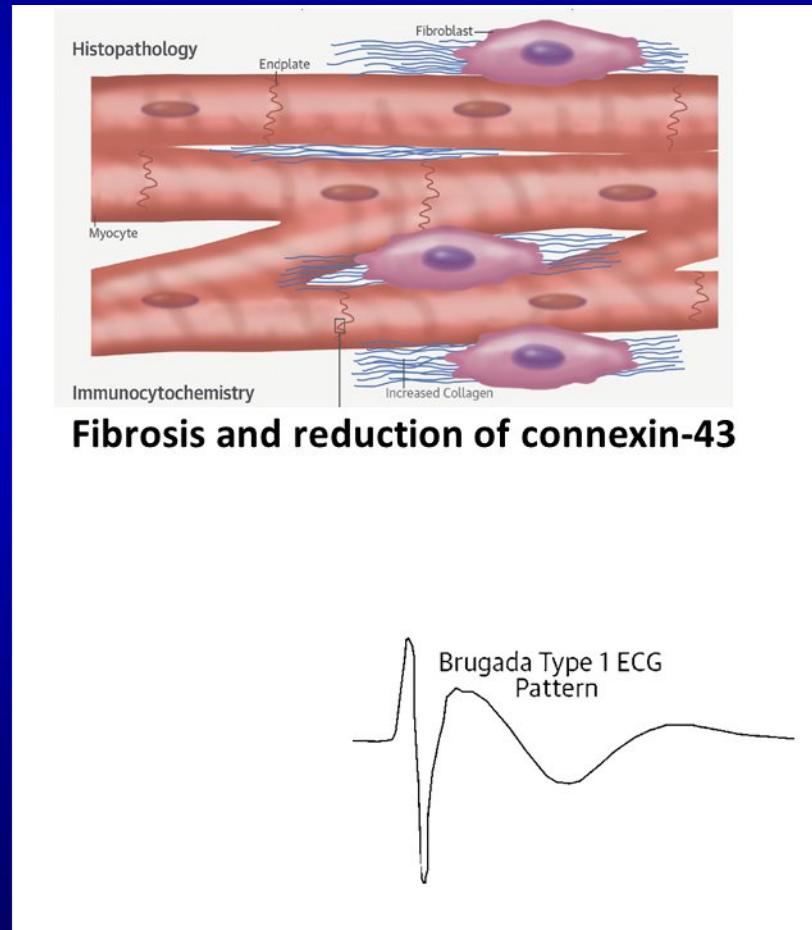
ECG variables associated with arrhythmic events

Signs of conduction delay

fragmented QRS

S wave in lead I

QRS duration

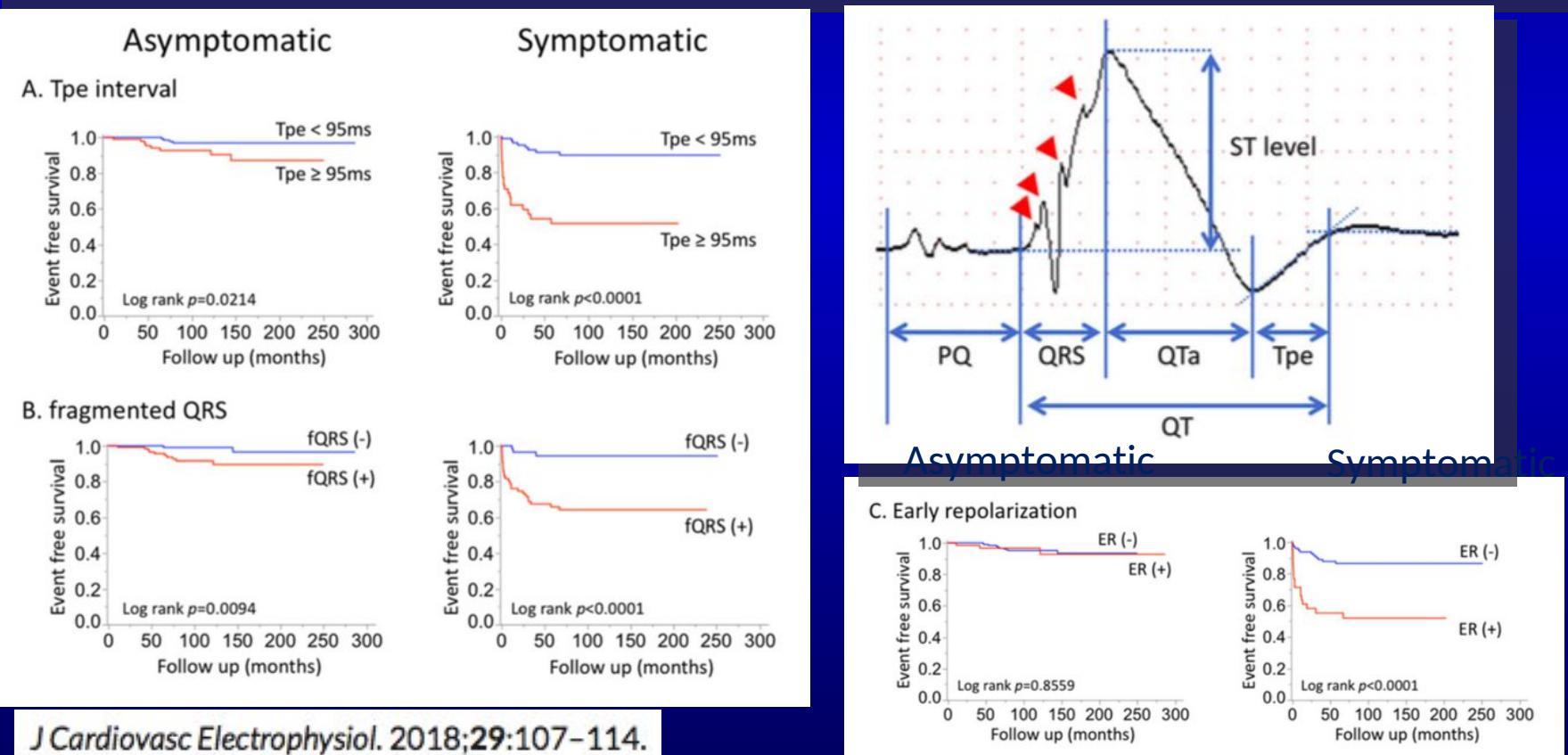


Identification of electrocardiographic risk markers for the initial and recurrent episodes of ventricular fibrillation in patients with Brugada syndrome

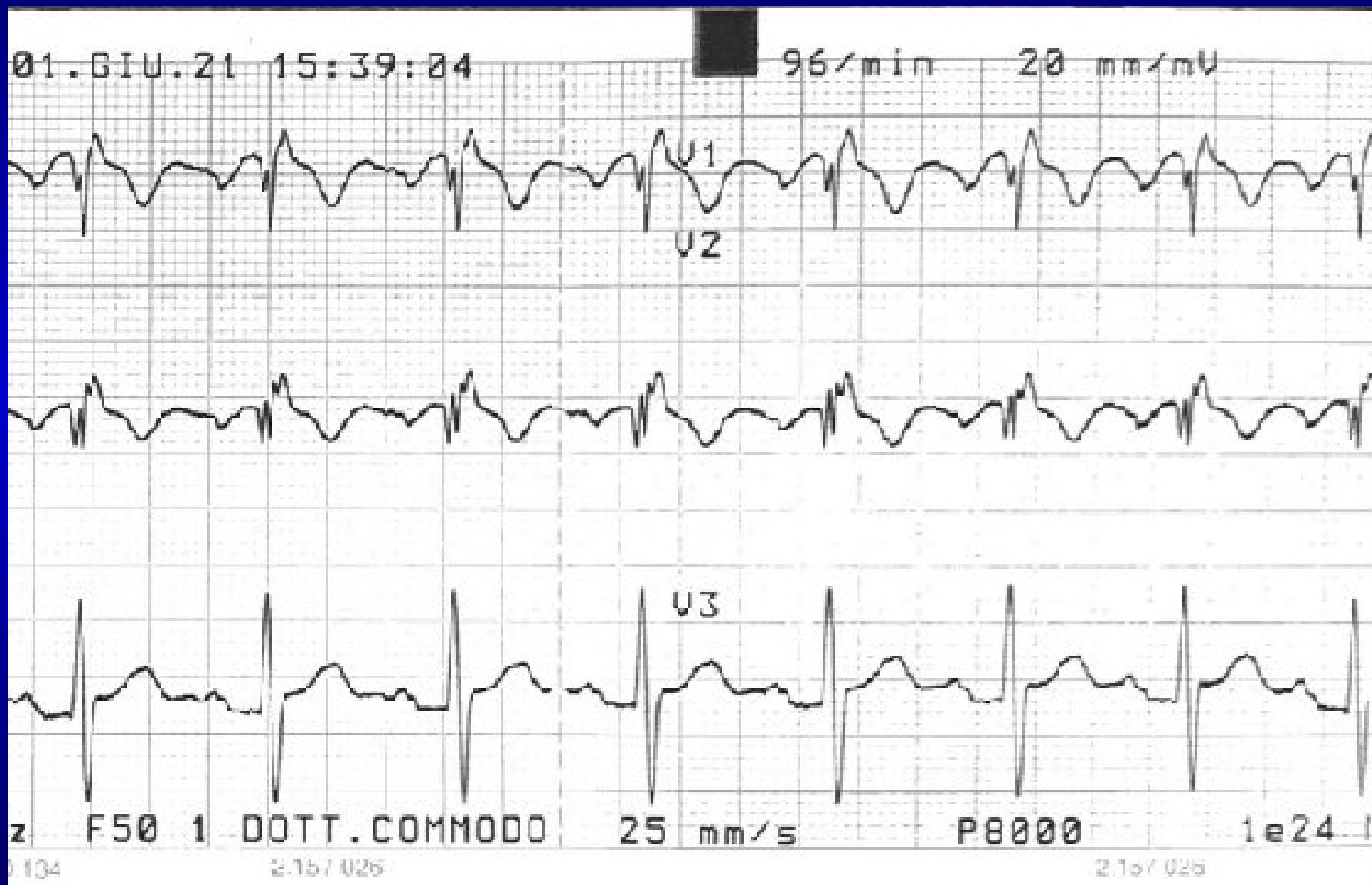
Abstract

Introduction: New onset of ventricular fibrillation (VF) in asymptomatic patients with Brugada-type ECG is not frequent, but it cannot be negligible. Risk markers for predicting VF are usu-

Nobuhiro Nishii MD, PhD¹ | Kazufumi Nakamura MD, PhD² | Hiroshi Ito MD, PhD²



Brugada and QRS fragmentation

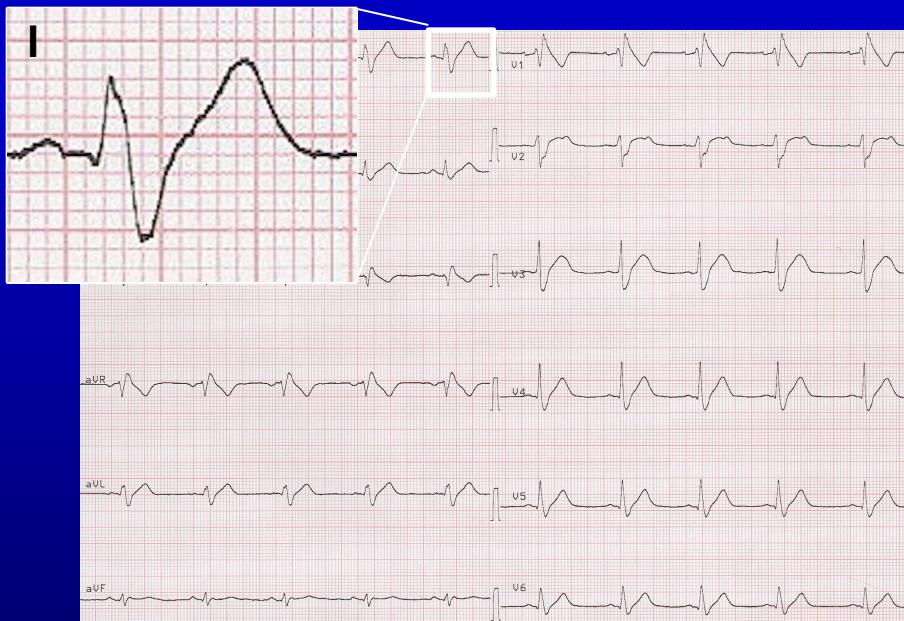


A New Electrocardiographic Marker of Sudden Death in Brugada Syndrome

The S-Wave in Lead I

Leonardo Calò, MD,^a Carla Giustetto, MD,^b Annamaria Martino, MD,^a Luigi Sciarra, MD,^a Natascia Cerrato, MD,^b Marta Marziali, MD,^a Jessica Rauzino, MD,^c Giulia Carlino, MD,^d Ermengildo de Ruvo, MD,^a Federico Guerra, MD,^e Marco Rebecchi, MD,^a Chiara Lanzillo, MD, PhD,^a Matteo Anselmino, MD,^b Antonio Castro, MD,^f Federico Turreni, MD,^f Maria Penco, MD,^d Massimo Volpe, MD,^c Alessandro Capucci, MD,^e Fiorenzo Gaita, MD^b

347 patients all with spontaneous type 1 ECG; mean follow-up 48 months



S-wave in lead I:

- ³ 0.1 mV (amplitude)
- ³ 40 ms (duration)
- ³ 1 mm² (area)

S-wave was present in all but 1 of those who had VF/SCD (96.9%)... but also in 59% of the remaining population

Ventricular conduction delay as marker of risk in Brugada Syndrome.
Results from the analysis of clinical and electrocardiographic features of a
large cohort of patients^{☆,☆☆}

Carla Giustetto ^{a,*1}, Giulia Nangeroni ^{a,1}, Natasia Cerrato ^{a,1}, Boris Rudic ^{b,c}, Erol Tülämen ^{b,c}, Elena Gribaudo ^a,
Daniela Francesca Giachino ^d, Lorella Barbonaglia ^e, Lorenza Michela Biava ^a, Paula Carvalho ^f,
Laura Bergamasco ^a, Martin Borggrefe ^{b,c}, Fiorenzo Gaita ^a

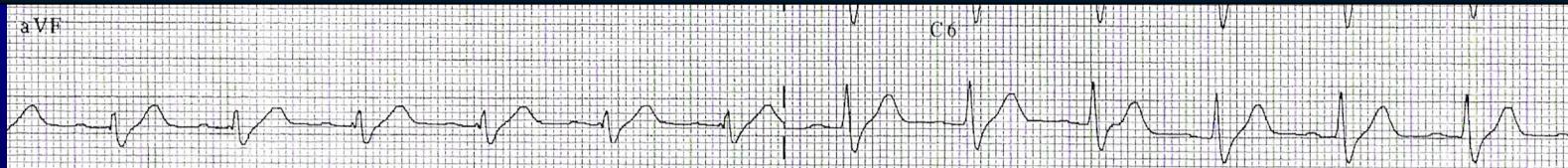
We analyzed ECG of 614 Brugada pts



The arrhythmic risk is related not only to the symptoms at presentation, but also to the presence of a ventricular conduction delay:

QRS duration ≥ 110 ms

S wave duration ≥ 40 ms



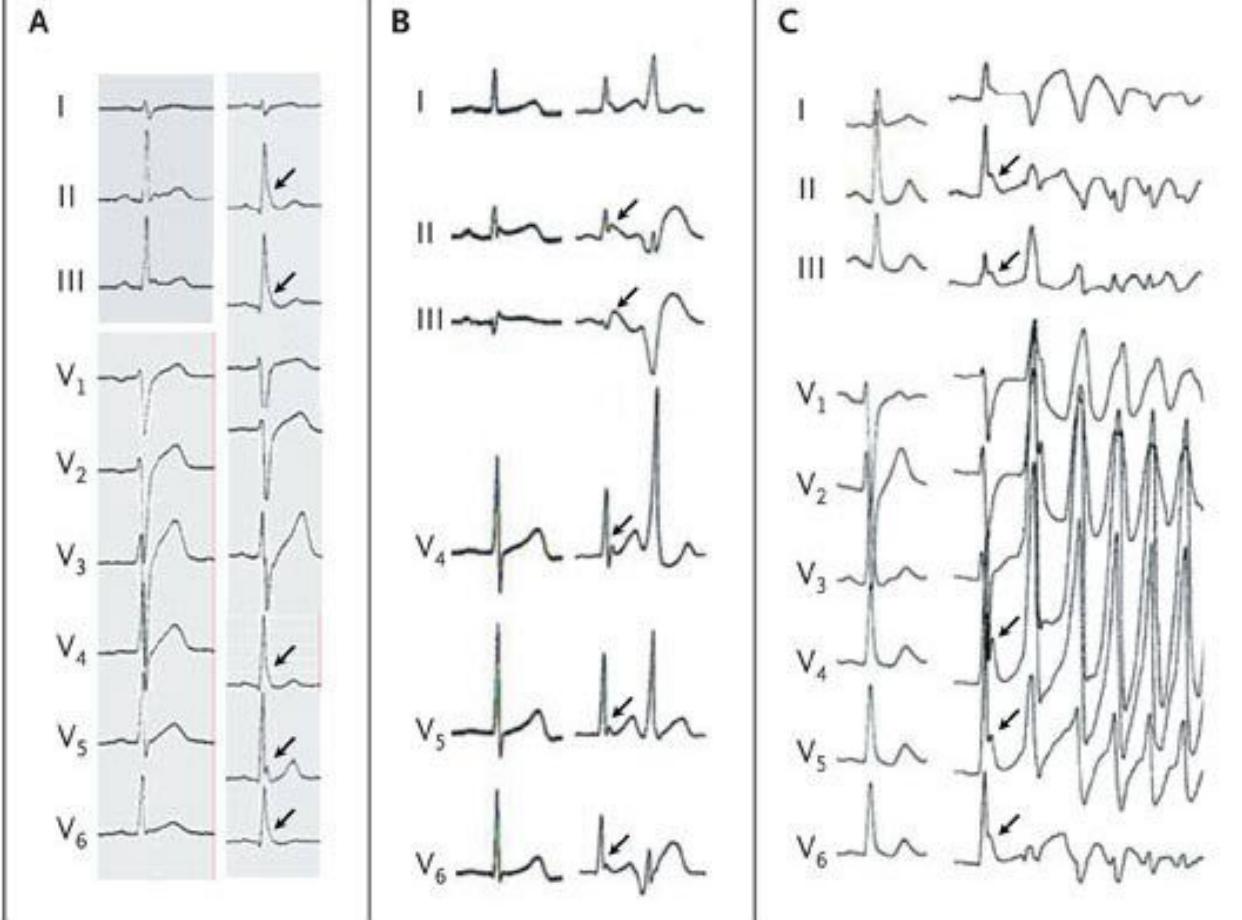


The NEW ENGLAND
JOURNAL of MEDICINE

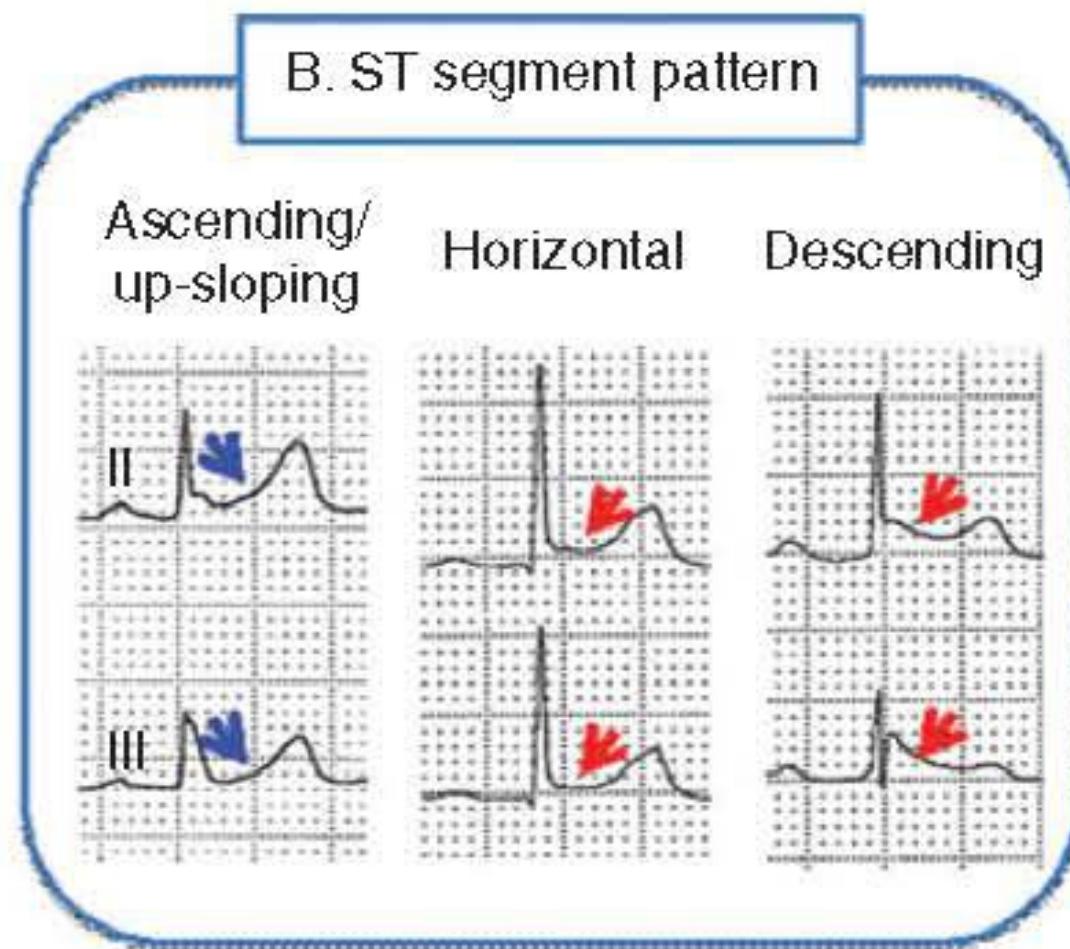
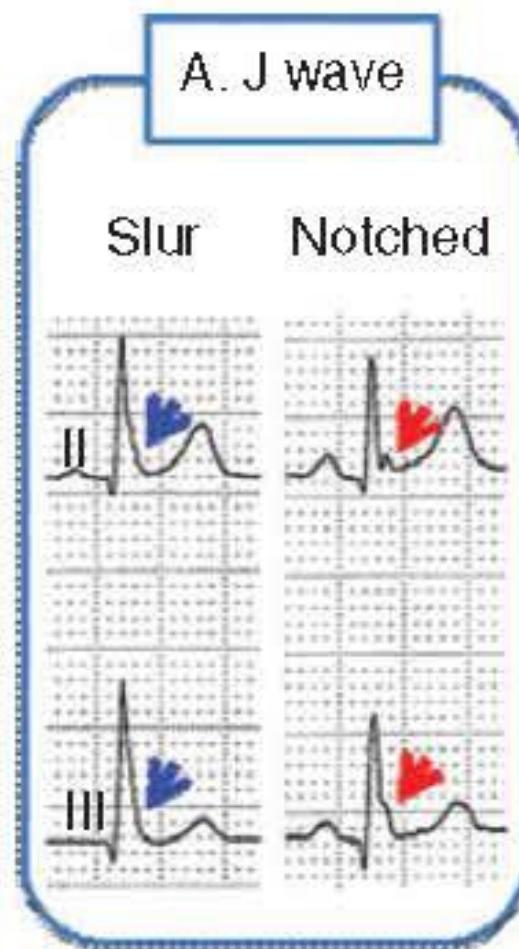
Sudden Cardiac Arrest Associated with Early Repolarization

• Michel Haïssaguerre, M.D., Nicolas Derval, M.D., Frédéric Sacher, M.D.,

• Laurence Isen, M.D., Isabel Deisenhofer, M.D., Luc de Rovira, M.D., Jean-Luc Pasquiat, M.D.

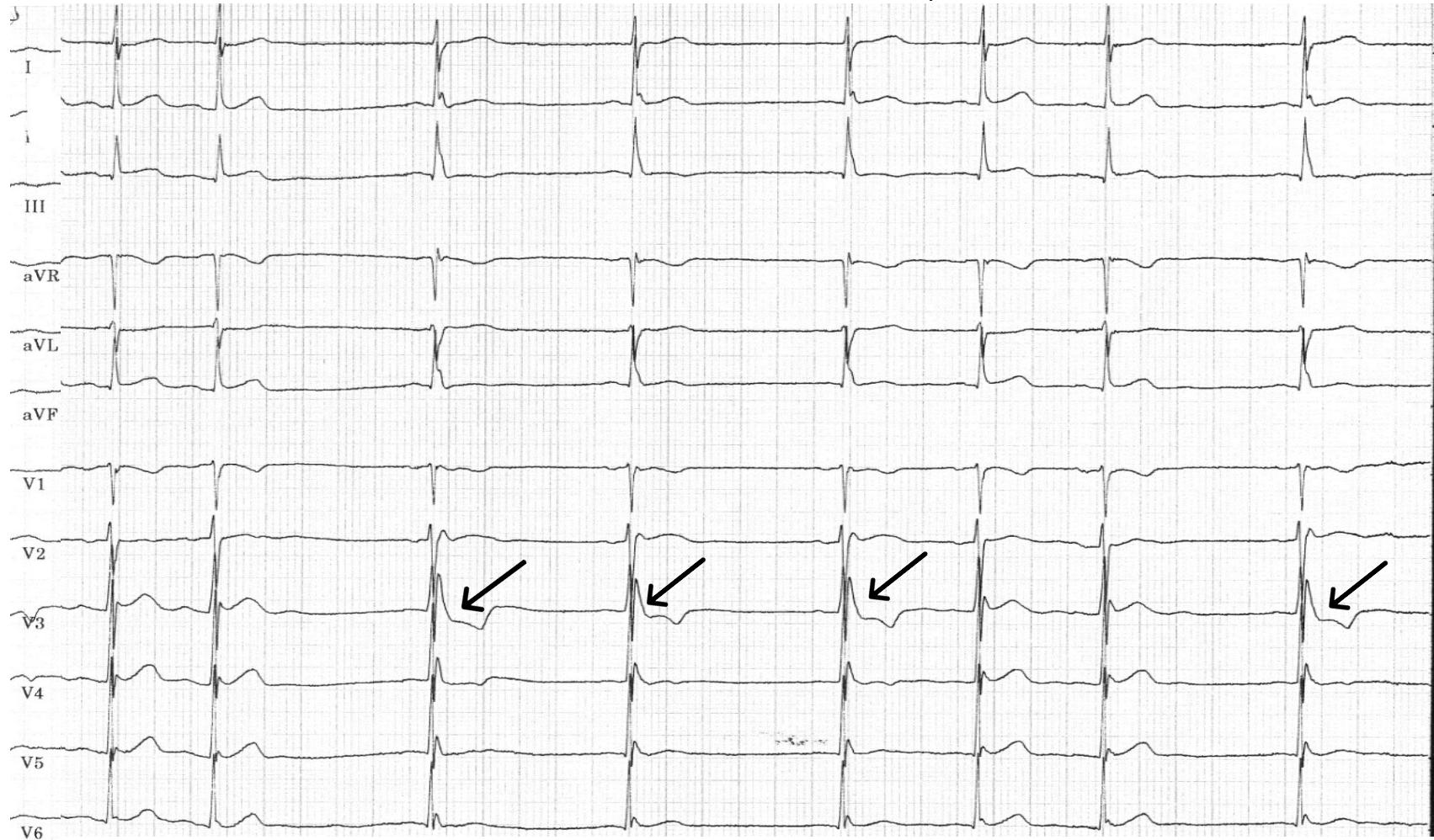


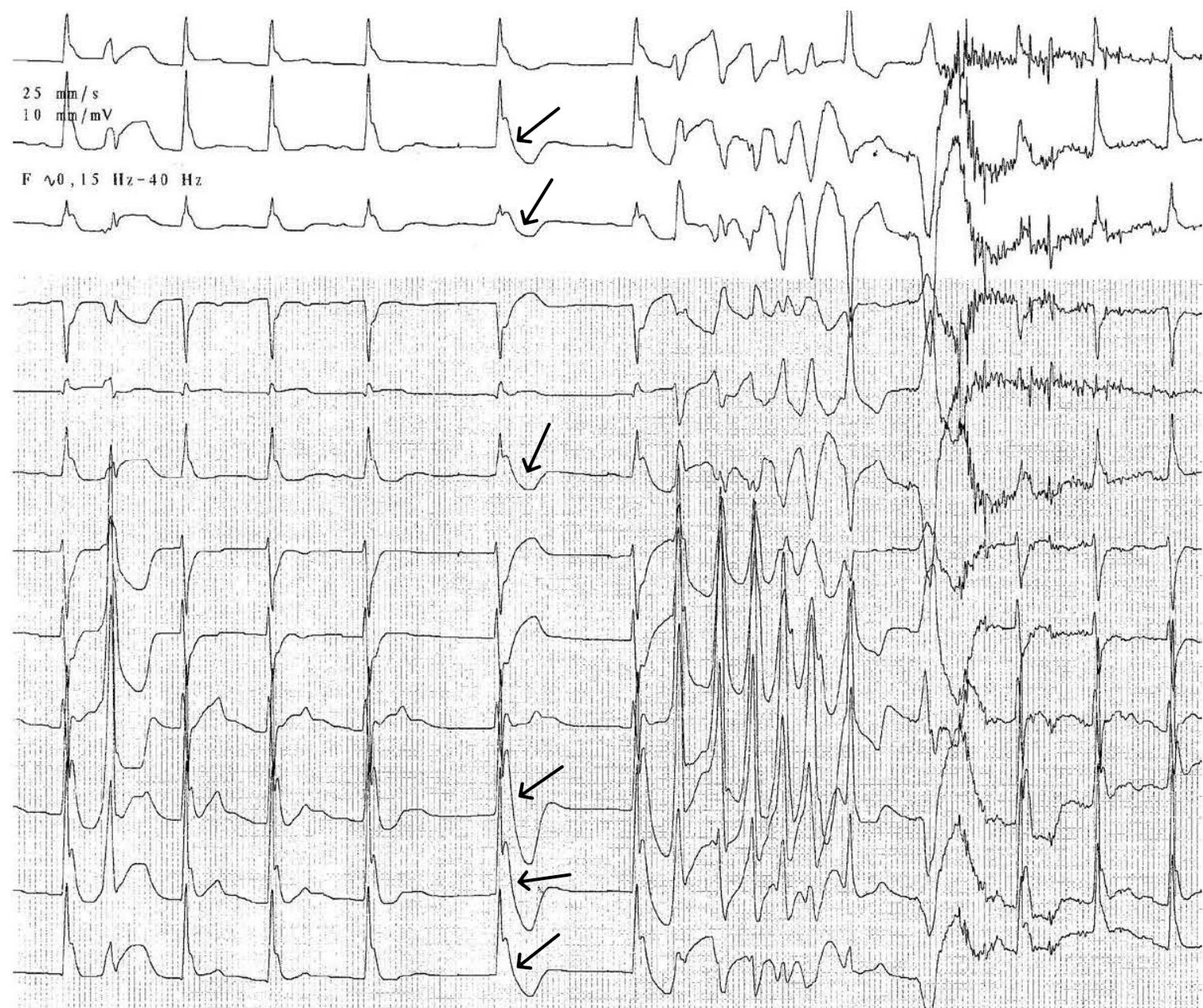
J-Wave syndromes expert consensus conference report: Emerging concepts and gaps in knowledge



Most specific sign :
Dynamicity of J wave with bradycardia

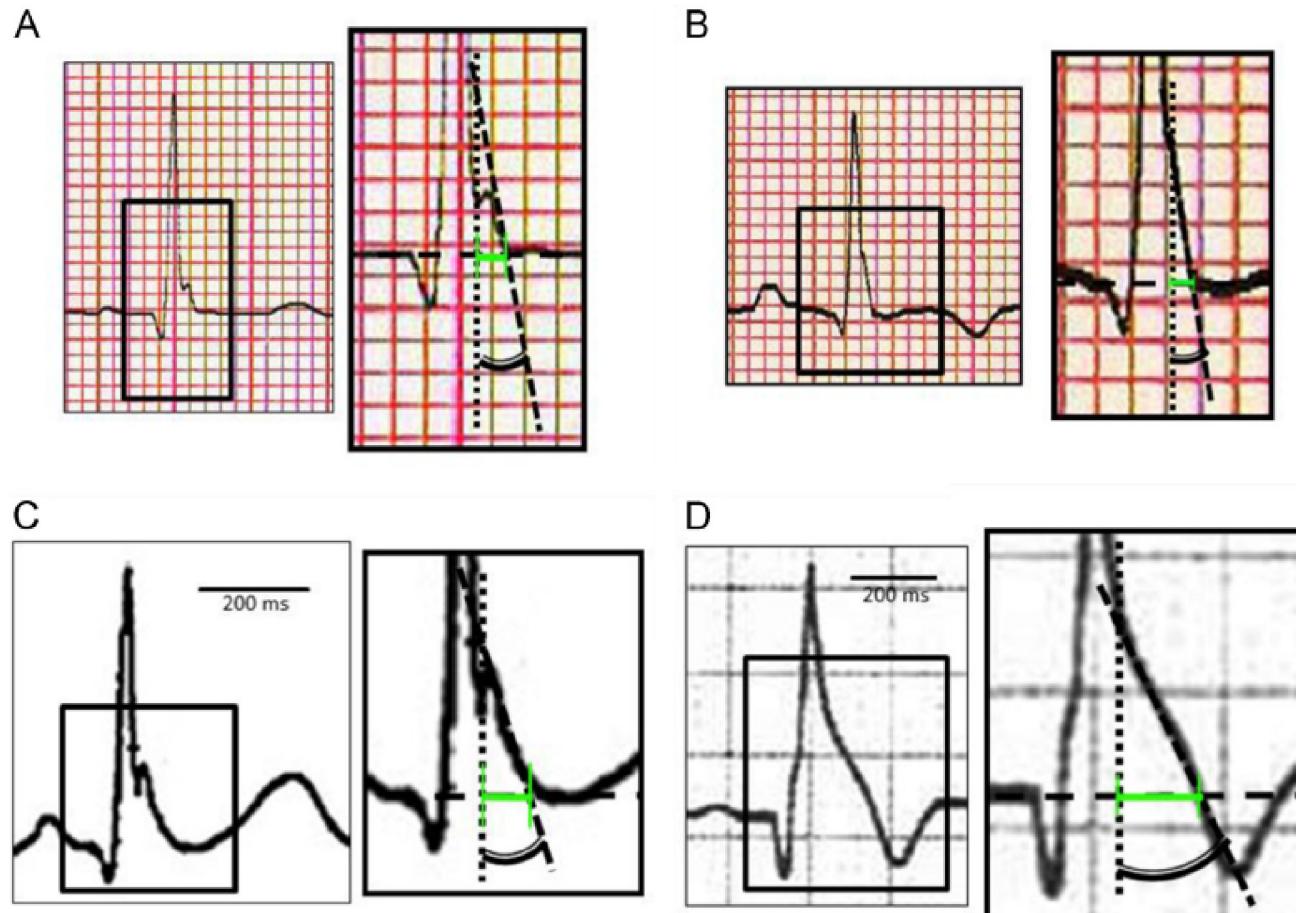
F. E. 15 yrs





J-wave duration and slope as potential tools to discriminate between benign and malignant early repolarization

Yvonne Cristoforetti, MD, * Luigi Biasco, MD, *† Carla Giustetto, MD, * Ole De Backer, MD, PhD, ‡
Davide Castagno, MD, * Piero Astegiano, MD, § Gianpasquale Ganzit, MD, §
Carlo Gabriele Gribaudo, MD, § Marco Moccetti, MD, † Fiorenzo Gaita, MD *

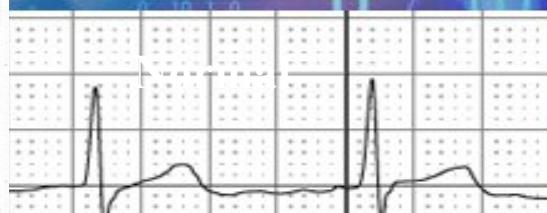


BASAL

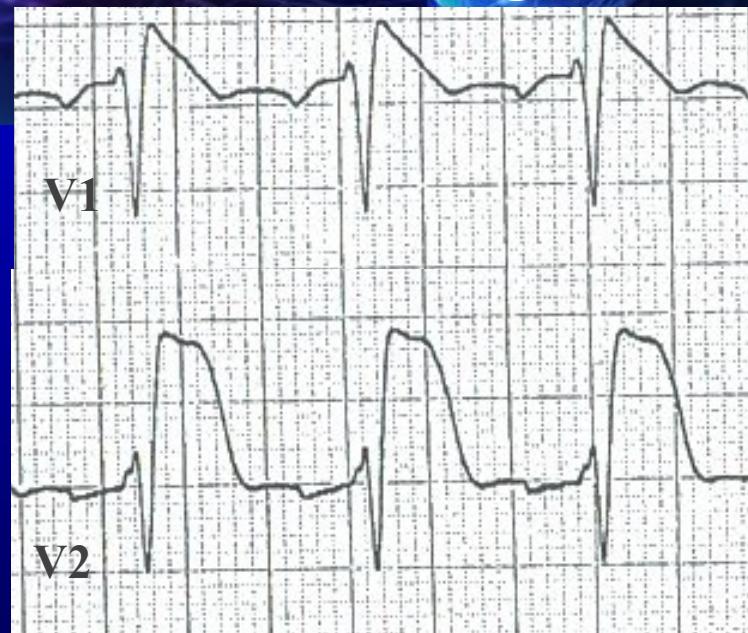


Artificial Intelligence and Channelopathies

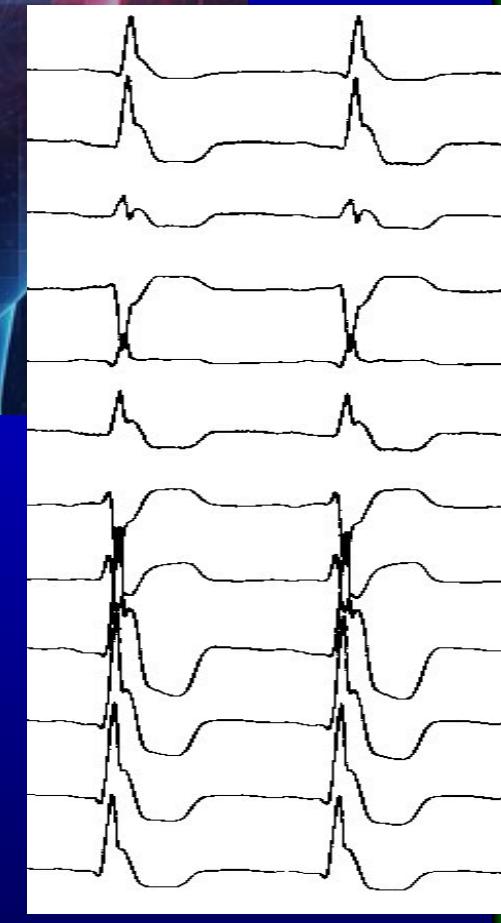
Short QT



Brugada



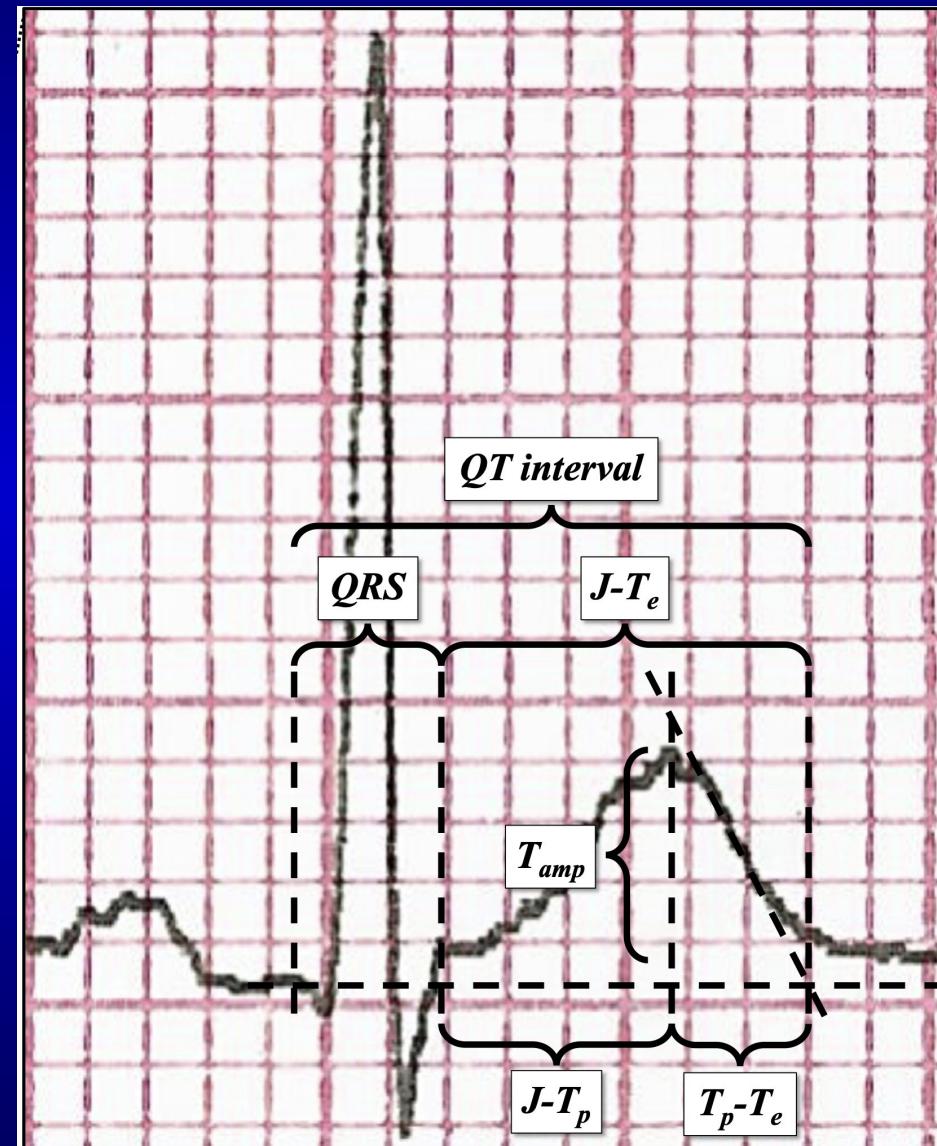
J WAVE



ECG feature and Short QT Syndrome

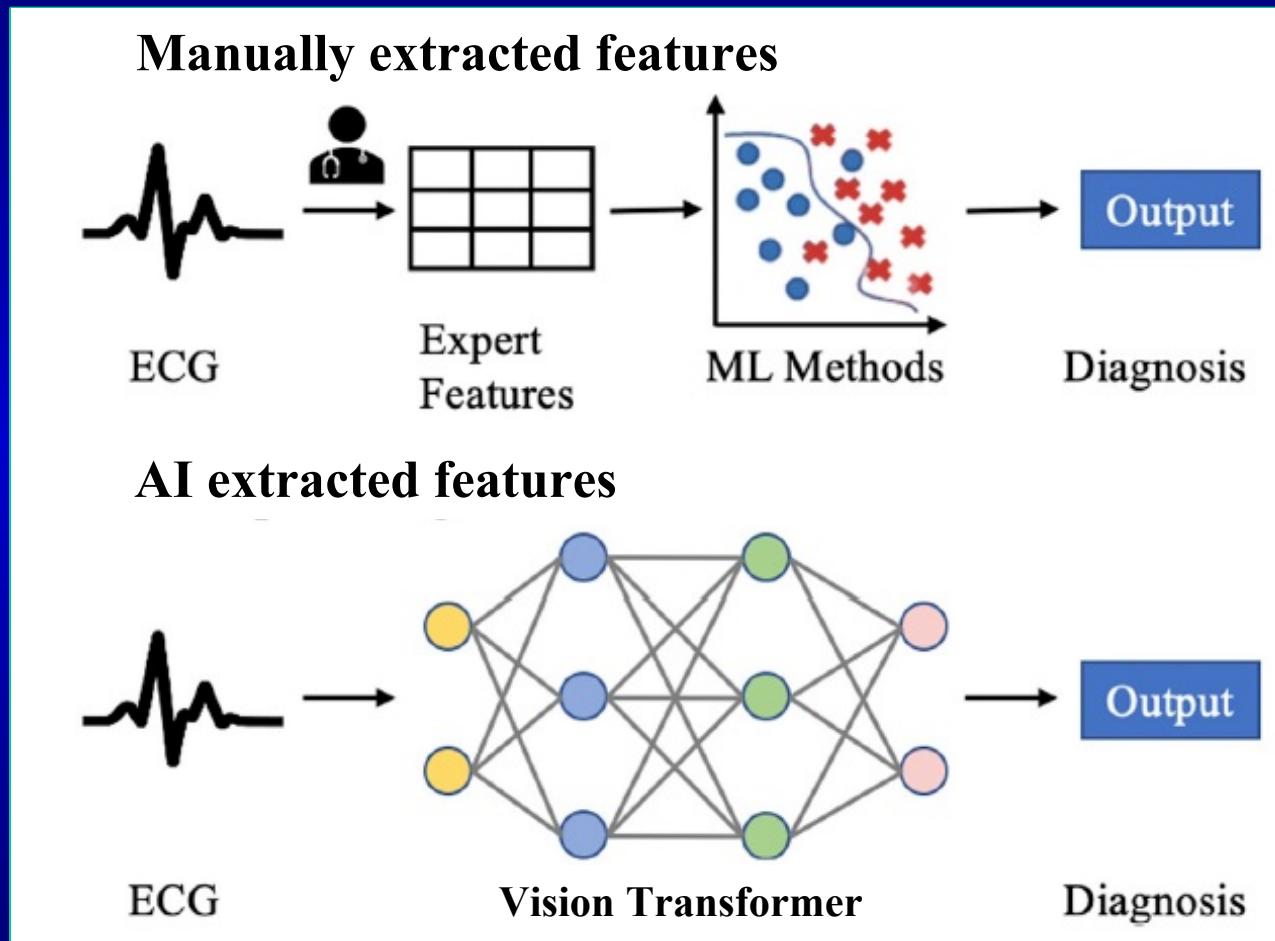
Feature (Measured)
RR (ms)
QT (ms)
QRS (ms)
J-T _p (ms)
T _p -T _e (ms)
J-T _e (ms)
T _{amp} (mV)

Feature (calculated)
QTc (ms)
QTp (ms)
cJ-T _p (ms)
cT _p -T _e (ms)
cJ-T _e (ms)
QT/QTp



Short QT syndrome & Artificial Intelligence

Firstly, AI was trained with data from 86 pts...



...the model was then validated on a cohort of 15 pts

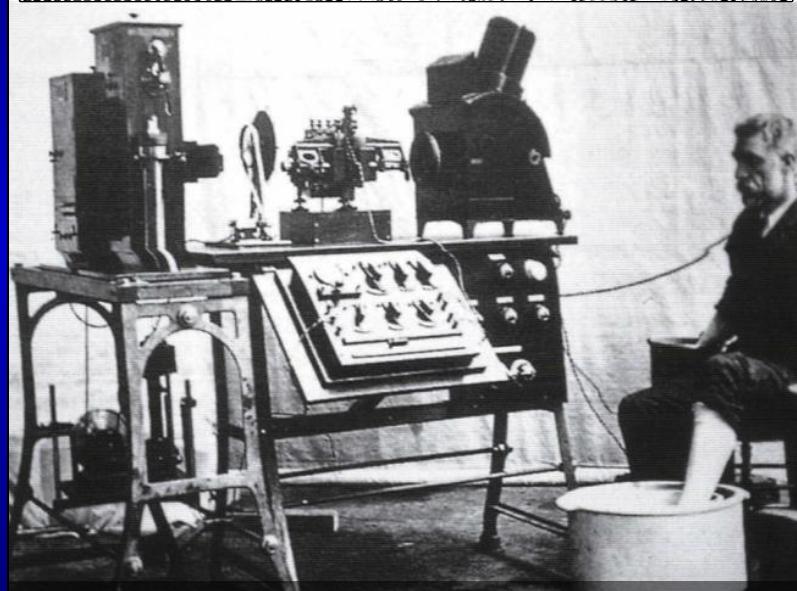
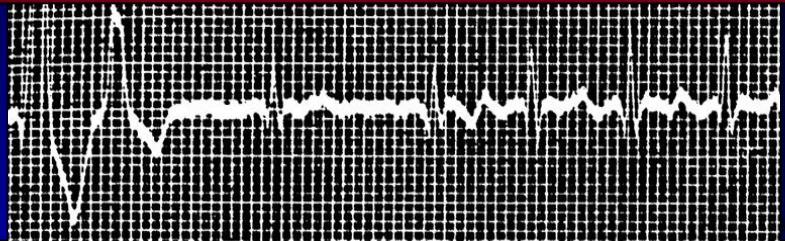
Short QT: performance of the two approaches

Metric	ML	ViT
Sensitivity	63.6 %	100.0 %
Specificity	85.0 %	93.3 %
PPV	70.0 %	80.0 %
NPV	81.0 %	100.0 %

NVP 100% = no risk of event, if algorithm predicts “no event”

Preliminary data

**At 120 years from its discovery, ECG remains crucial
in cardiologic diagnostic process.**



**Artificial intelligence will allow us to acquire new
informations hidden in the ECG that until today we
were not able to see**