Brugada syndrome: tests and diagnosis.

Torino, 27 ottobre 2017

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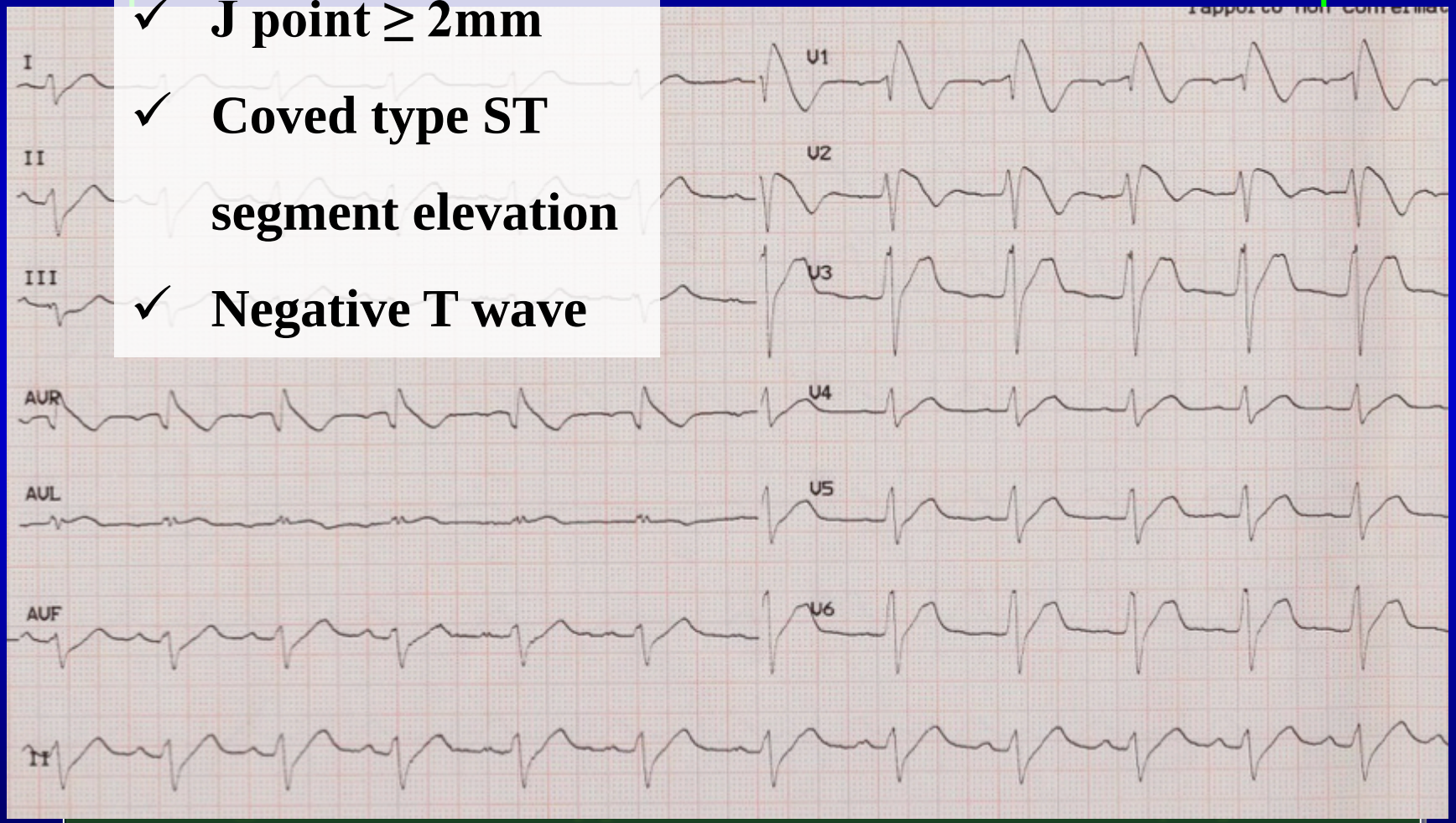
Brugada syndrome: diagnosis

- ✓ J point ≥ 2mm
- ✓ Coved type ST segment elevation
- ✓ Negative T wave



EPS
12L-HOLTER
F-UP
ABLATION
ICD
LOOP RECORDER
HIDROQUINIDINE

Brugada Piedmont Registry

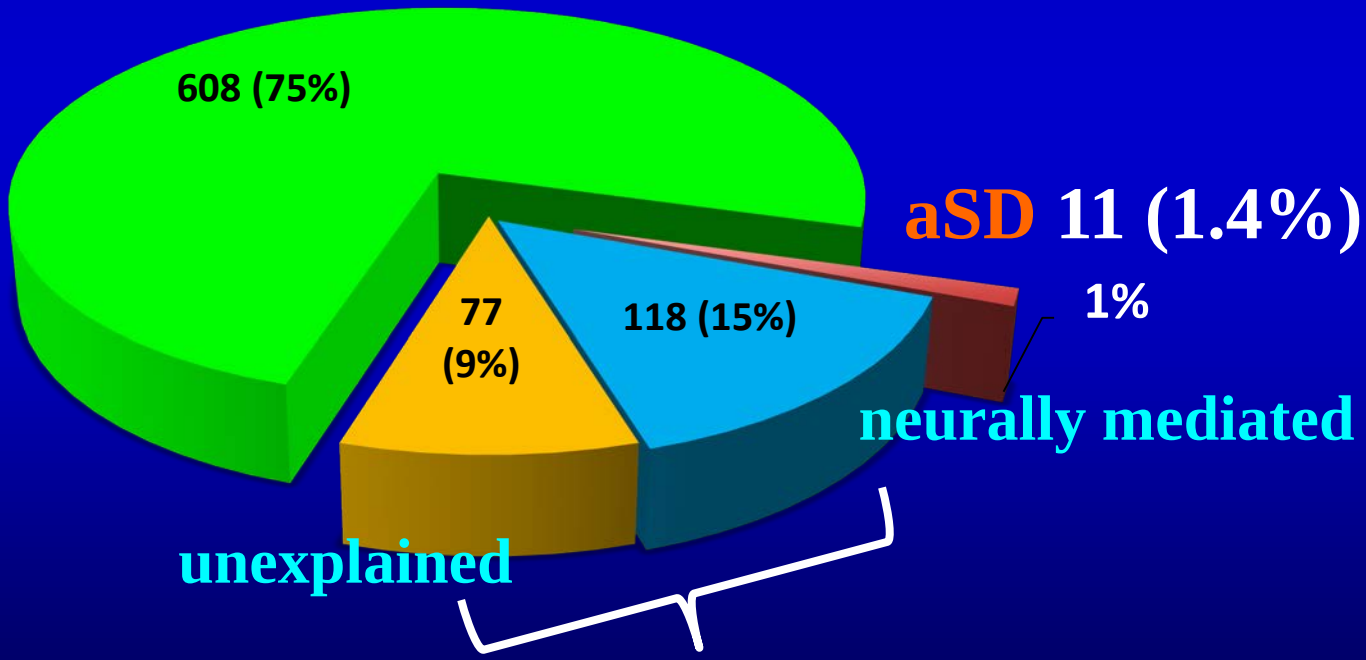
826 pts → 12 diagnosed after Sudden Death

total 814 pts

2001-2016

Symptoms at presentation

Asymptomatic 608



aSD 11 (1.4%)

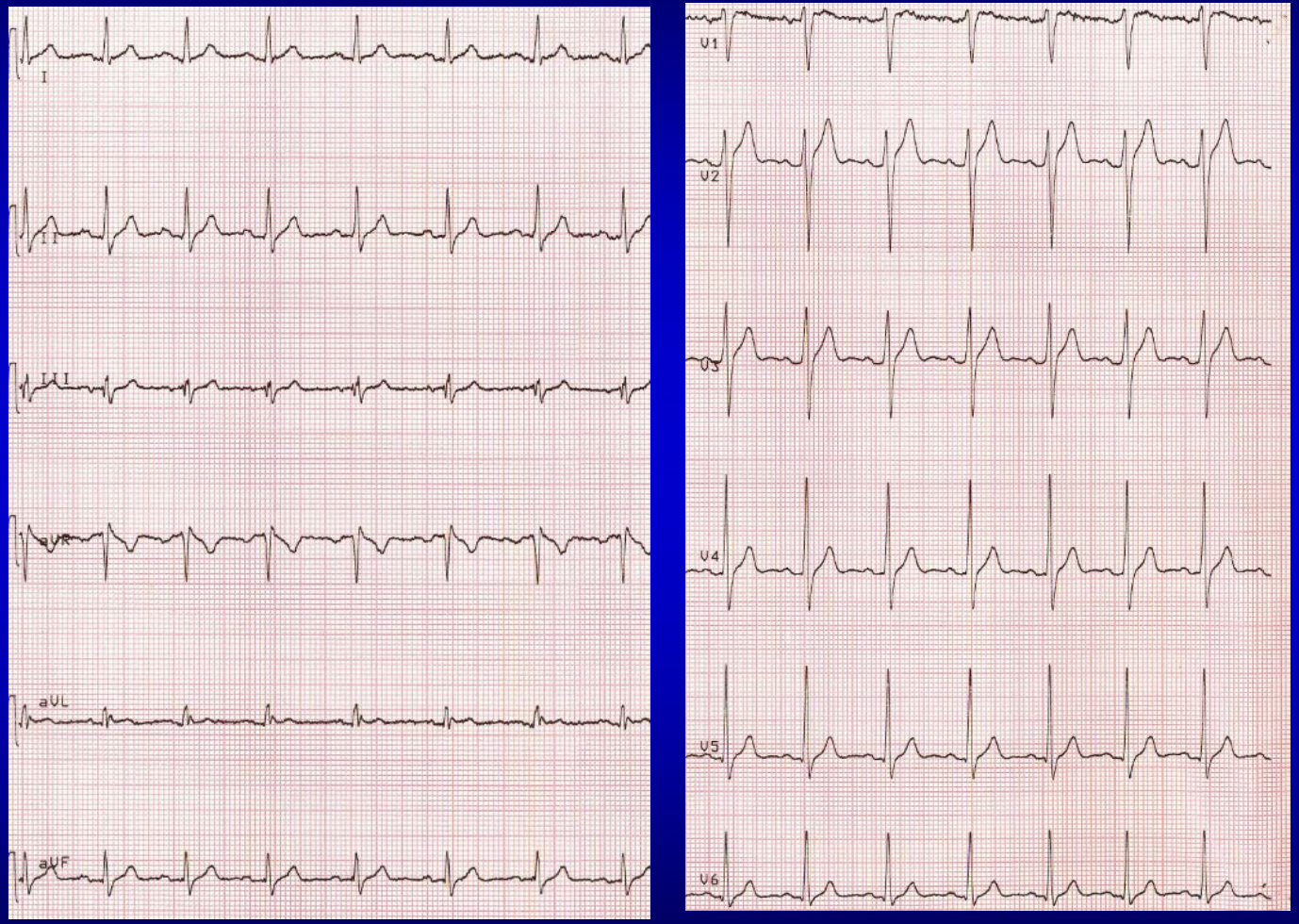
neurally mediated

unexplained

Syncope 195 (24%)

- Torino
- Asti
- Vercelli
- Orbassano
- Rivoli
- Cuneo
- Novara
- Savigliano

A 45 years old man: traumatic syncope, which occurred after awakening at 6.30 a.m, while he was in the bathroom, with doubtful prodromes

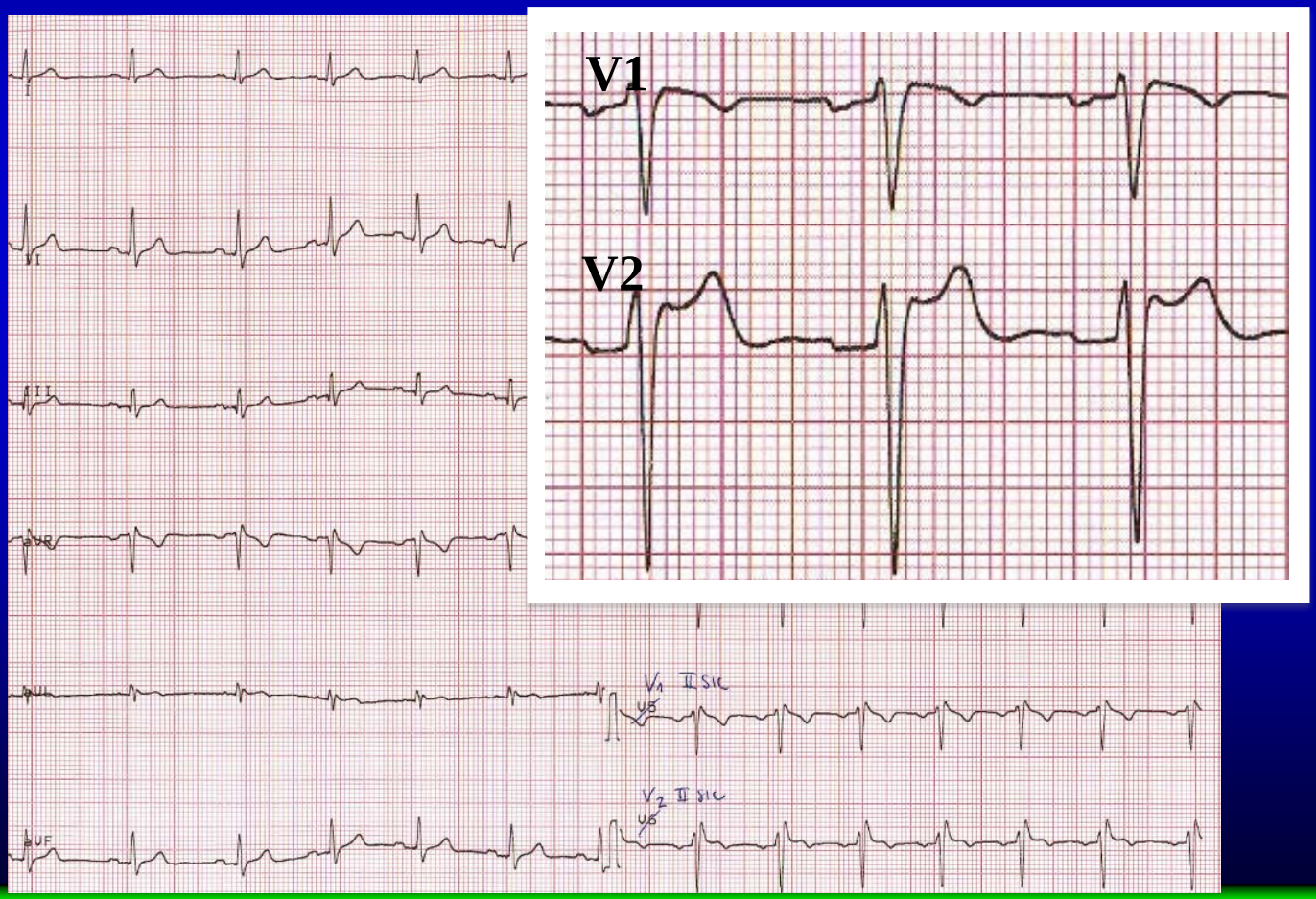


1st ECG: sinus rhythm, normal conduction, non-significant ST-T alterations

Head-up tilt test (HUTT)

Tilt test was negative but

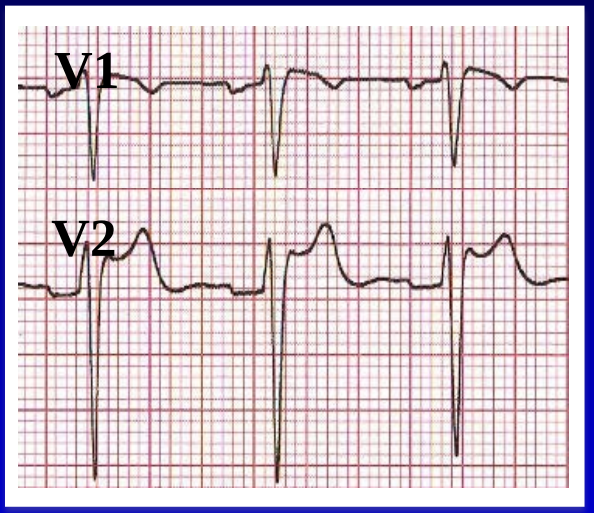
ST segment in V1-V2 with a type 2 Brugada pattern was recorded



Pt with syncope

+

suspect Brugada ECG (type 2)



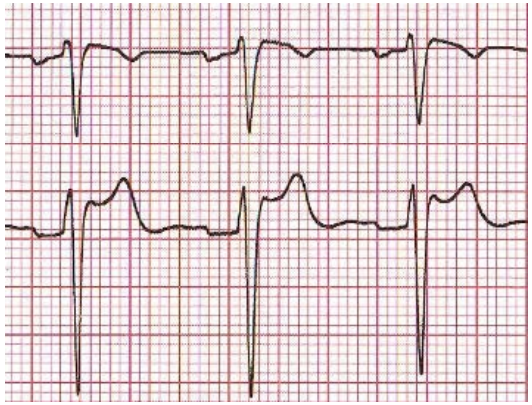
Which investigations are reasonable/recommended?

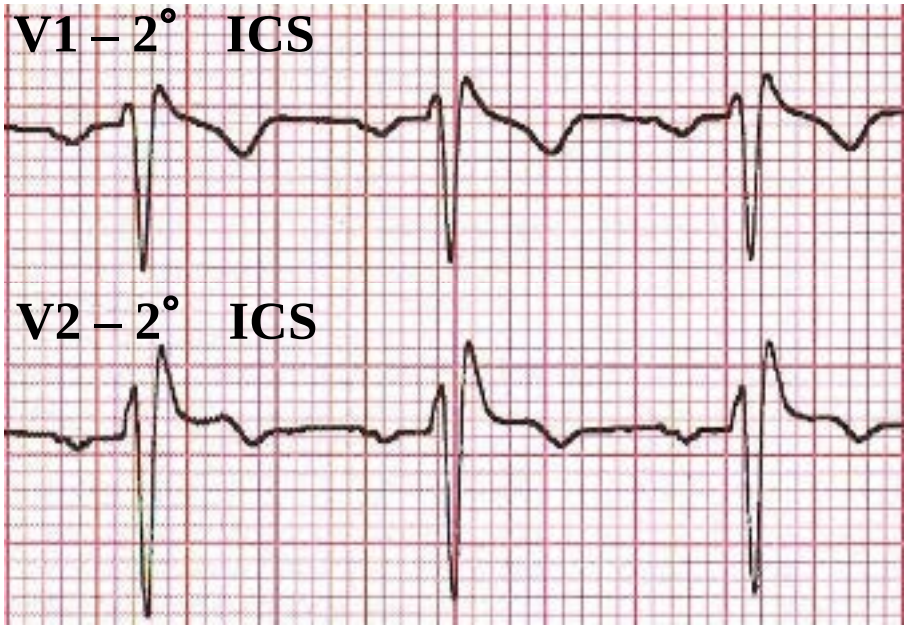
ECG with V1-V2 at 2nd and 3rd intercostal space (ICS)

ECG was recorded with V1-V2 at a higher intercostal space →

in this case it remained doubtful, still <u>not</u> diagnostic

ECG 4th ICS





Which investigations are reasonable/recommended?

Pt with syncope
+
suspect Brugada ECG pattern (type 2)

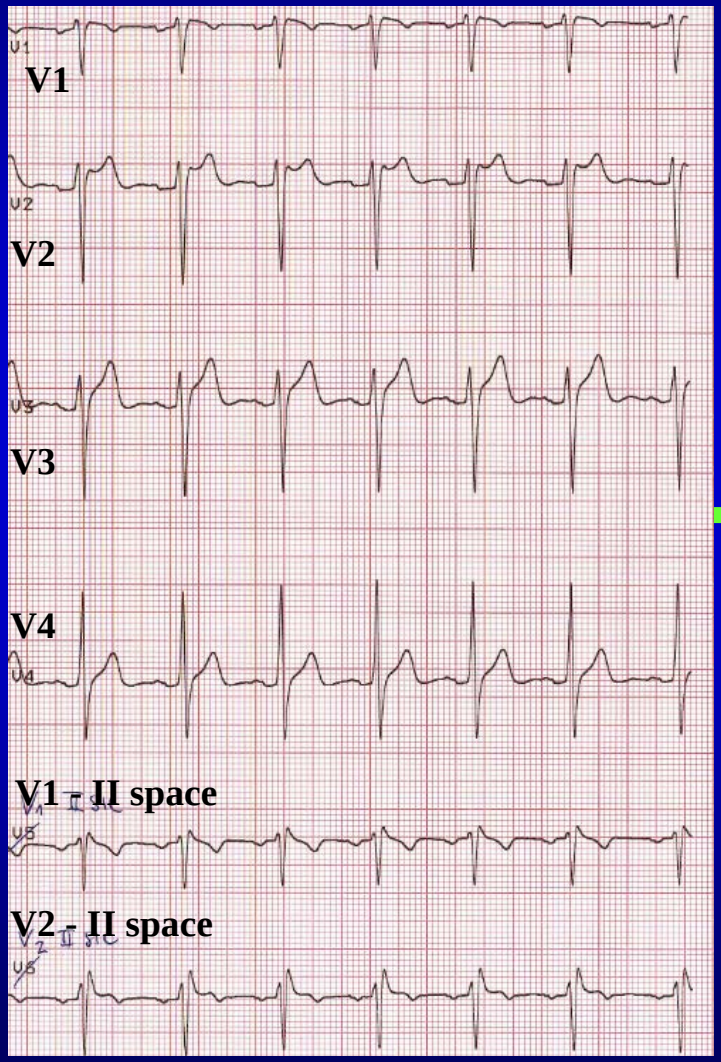
ECG with V1-V2 at 2^{nd} and 3^{rd} intercostal space

type 2 Brugada ECG

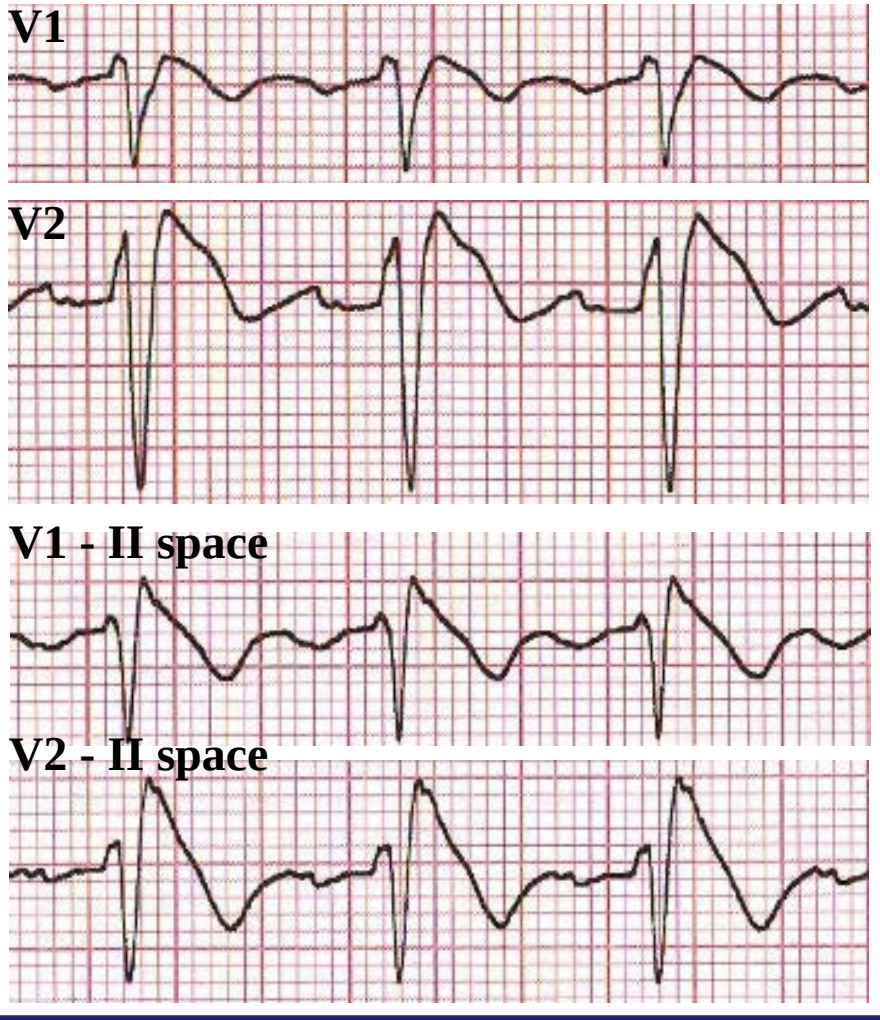
Drug challenge with sodium channel blockers

Pharmacological challenge with Na^+-channel blockers was performed…

Basal ECG



Ajmaline infusion (1mg/kg in 5 min)



Summary…

- ✓45 years old man
- ✓syncope of uncertain origin
- ✓Drug induced type 1 Brugada ECG pattern

What does literature report ?

What do guidelines recommend ?

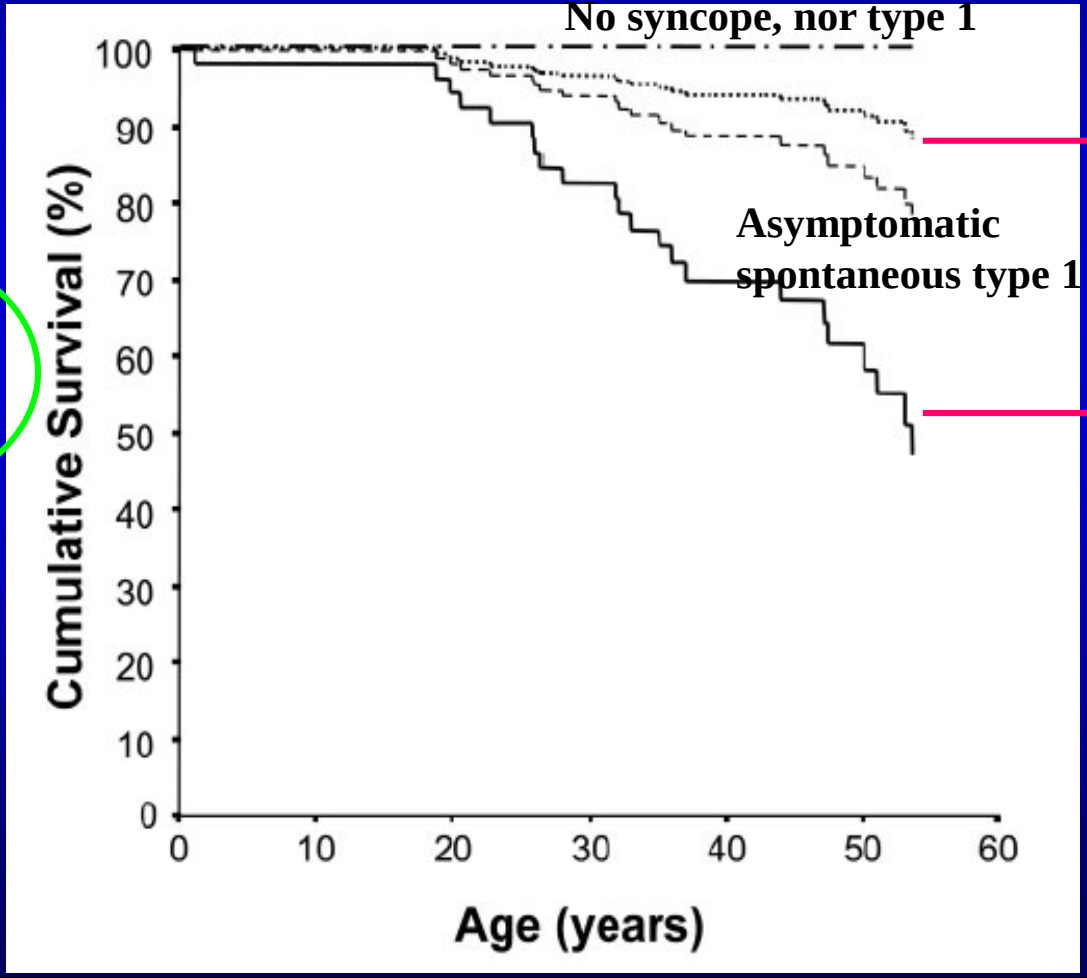
Natural History of Brugada Syndrome

Insights for Risk Stratification and Management

Silvia G. Priori, MD, PhD; Carlo Napolitano, MD, PhD; Maurizio Gasparini, MD; Carlo Pappone, MD; Paolo Della Bella, MD; Umberto Giordano, MD; Raffaella Bloise, MD; Carla Giustetto, MD; Roberto De Nardis, MD; Massimiliano Grillo, MD; Elena Ronchetti, PhD; Giovanna Faggiano, MD; Janni Nastoli, BS

Circulation 2002;105:1342

Italian Registry 200 pts



Syncope + induced type 1

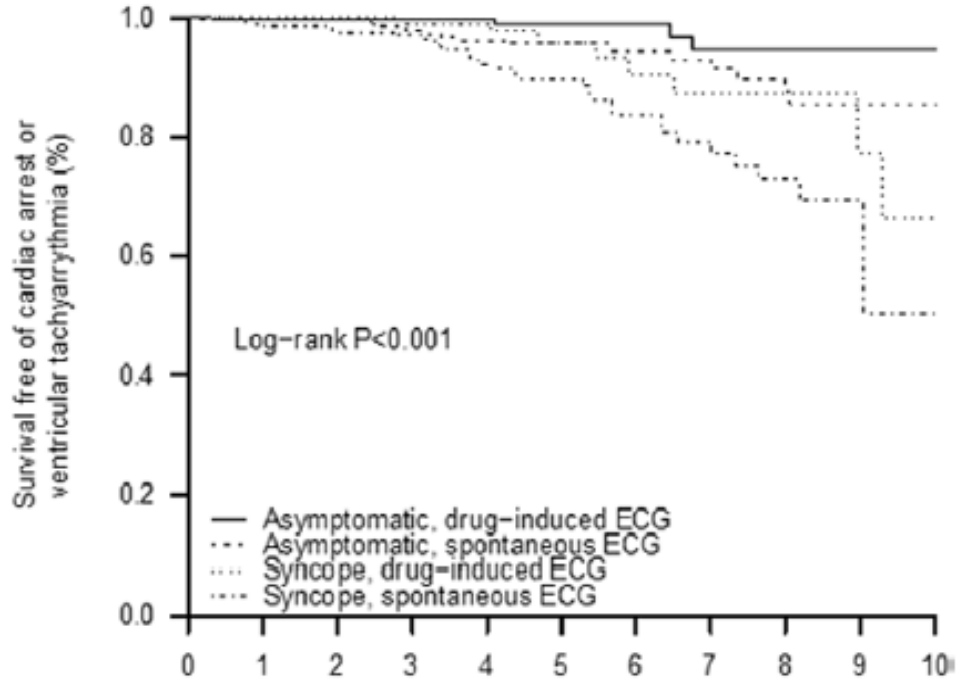
Syncope + spontaneous type 1

HR 6.4 for risk of cardiac arrest

Programmed Ventricular Stimulation for Risk Stratification in the Brugada Syndrome

A Pooled Analysis

Jakub Sroubek, MD, PhD; Vincent Probst, MD, PhD; Andrea Mazzanti, MD; Pietro Delise, MD; Jesus Castro Hevia, MD; Kimie Ohkubo, MD; Alessandro Zorzi, MD; Jean Champagne, MD; Anna Kostopoulou, MD; Xiaoyan Yin, PhD; Carlo Napolitano, MD, PhD; David J. Milan, MD; Arthur Wilde, MD; Frederic Sacher, MD, PhD; Martin Borggrefe, MD, PhD; Patrick T. Ellinor, MD, PhD; George Theodorakis, MD; Isabelle Nault, MD; Domenico Corrado, MD, PhD; Ichiro Watanabe, MD; Charles Antzelevitch, PhD; Giuseppe Allocca, MD; Silvia G. Priori, MD, PhD; Steven A. Lubitz, MD, MPH



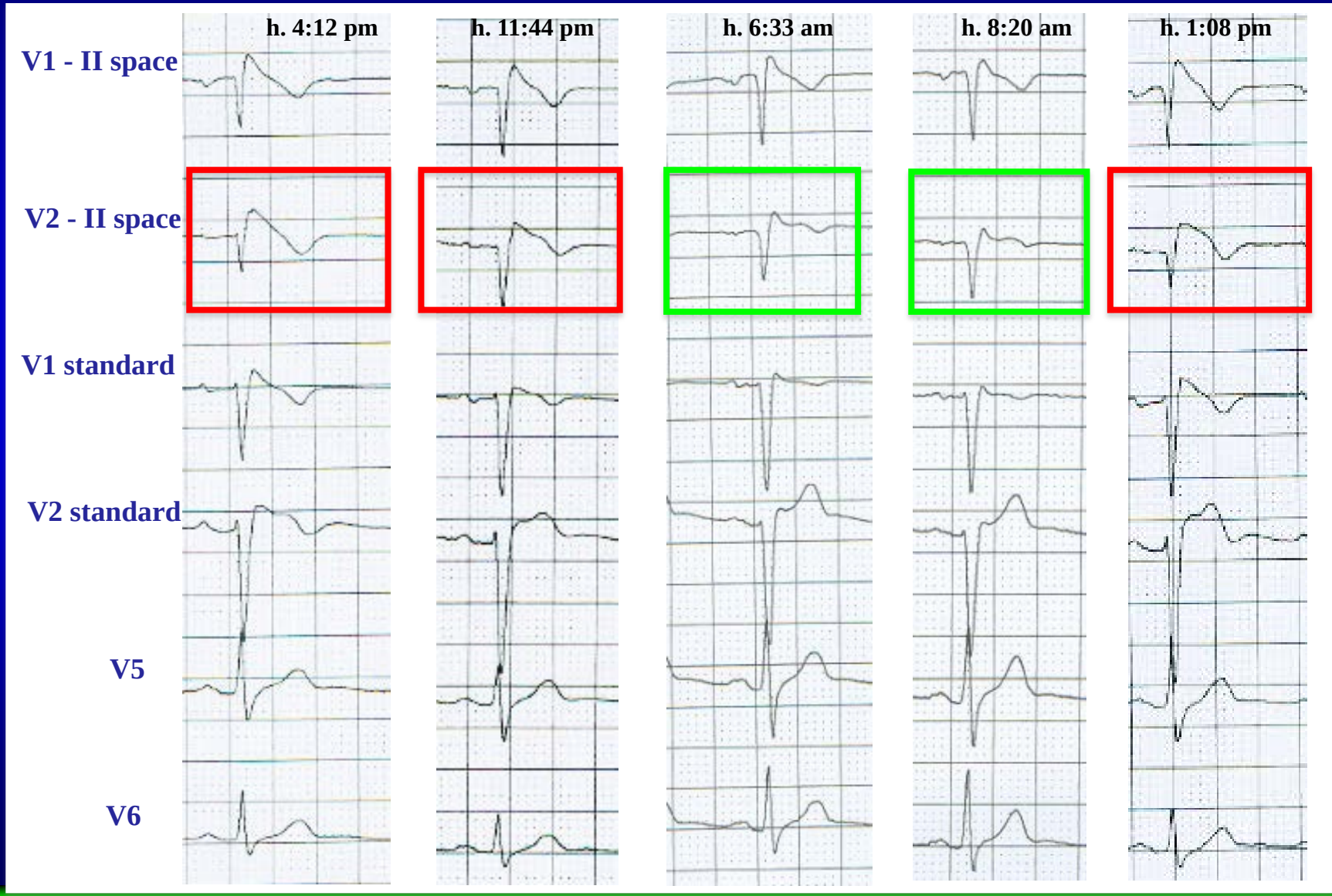
No. at risk

Asymptomatic, drug−induced ECG	442	390	295	217	145	93	56	35	24	13	8
Asymptomatic, spontaneous ECG	441	371	298	213	157	105	72	58	44	32	25
Syncope, drug−induced ECG	174	155	137	104	78	47	31	22	16	8	6
Syncope, spontaneous ECG	255	218	189	160	118	91	60	42	25	11	6

1312 patients from 14 prospective observational studies

Circulation 2016;133:622-630

12-lead 24-hour Holter monitoring:
intermittent spontaneous type 1 Brugada pattern



Summary…

- ✓45 years old man
- ✓syncope of uncertain origin
- ✓drug induced type 1 Brugada ECG pattern and
- ✓ spontaneous type 1 documented at f-up

What do guidelines recommend?

What does literature report?

Which Brugada patients to treat: Guidelines

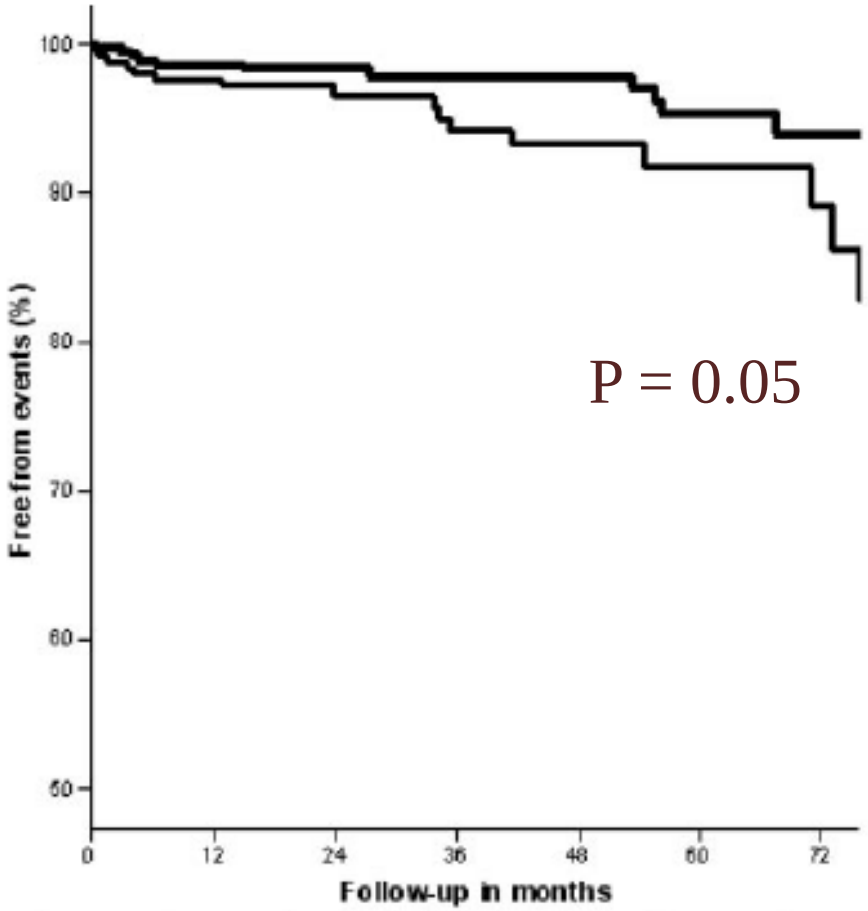
2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

EUROPEAN SOCIETY OF CARDIOLOGY®

2015

ICD implantation should be considered in patients with a spontaneous diagnostic type I ECG pattern and history of syncope.	**IIa**	C
ICD implantation may be considered in patients with a diagnosis of Brugada syndrome who develop VF during PVS with two or three extrastimuli at two sites.	**IIb**	C

Role of EP-study in Brugada pts (overall population)

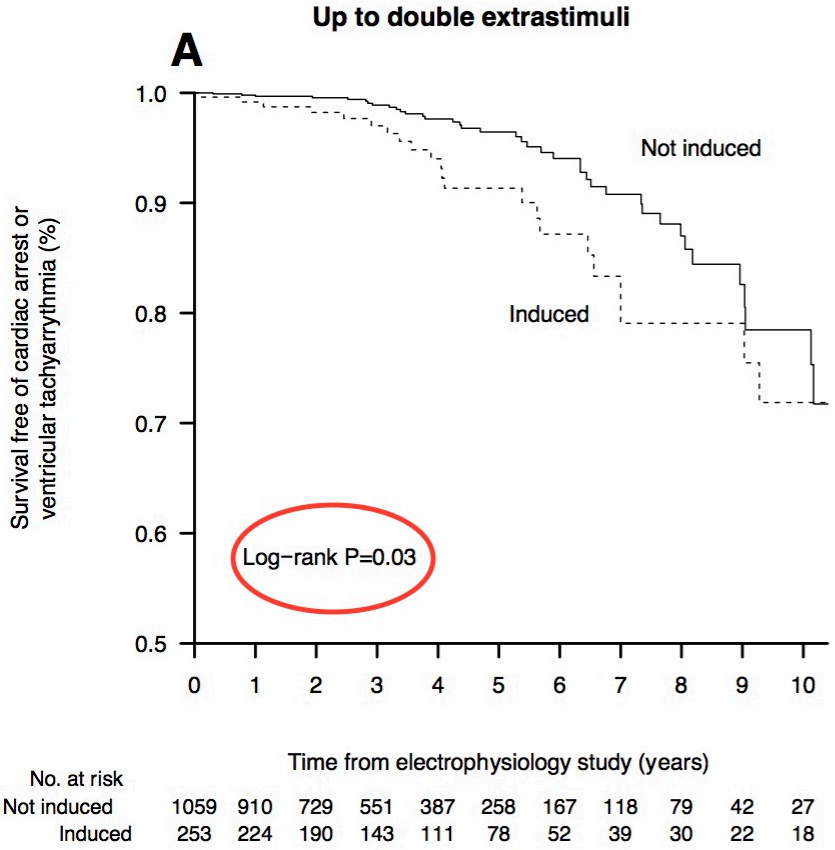


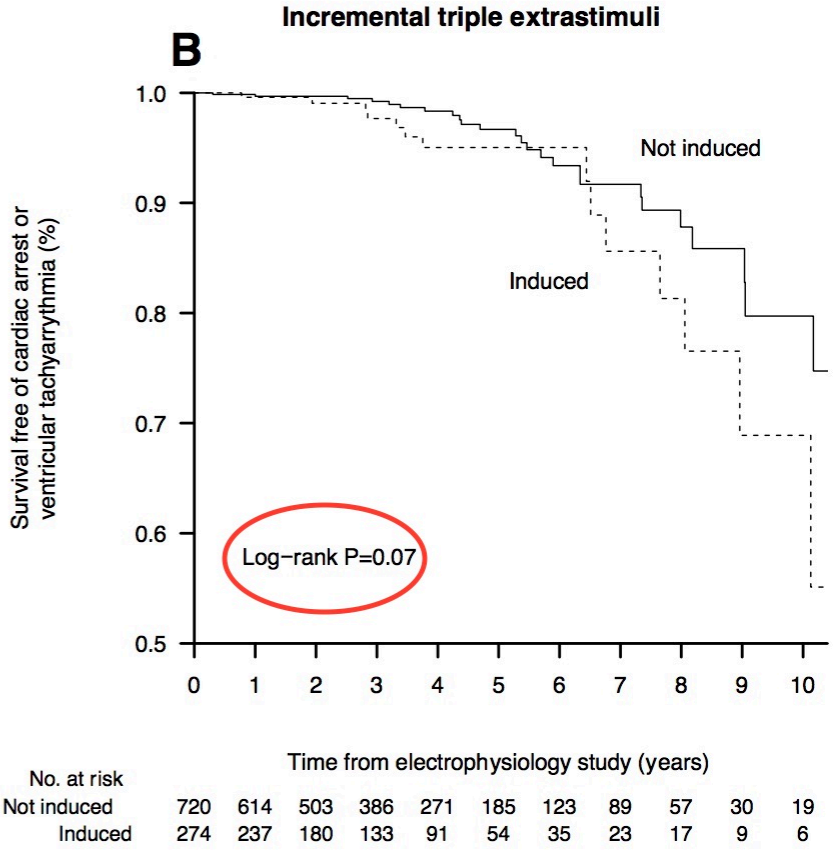
	0	12	24	36	48	60	72
negative	376	301	237	187	136	94	59
positive	262	212	161	113	81	52	34

Probst et al, FINGER Registry, Circulation 2010;121: 635

Programmed Ventricular Stimulation for Risk Stratification in the Brugada Syndrome

A Pooled Analysis





Sroubek J et al. Circulation 2016;133:622-630

Annual incidence of cardiac arrest among 1312 individuals included in the analysis

	Spontaneous Type 1 ECG Pattern	Drug-Induced Type 1 ECG Pattern
Syncope at presentation		
Events, n/person-y	34/1056	10/693
Overall	3.22 (2.23–4.50)	1.44 (0.69–2.65)
Induced arrhythmia	5.60 (2.98–9.58)	1.96 (0.40–5.73)
No induced arrhythmia	2.55 (1.58–3.89)	1.29 (0.52–2.67)
Asymptomatic at presentation		
Events, n/person-y	17/1630	4/1506
Overall	1.04 (0.61–1.67)	0.27 (0.07–0.68)
Induced arrhythmia	1.70 (0.73–3.35)	0.45 (0.01–2.49)
No induced arrhythmia	0.78 (0.36–1.47)	0.23 (0.05–0.68)

Incidence rates expressed as annual percentages, (95% confidence intervals). Induced arrhythmia defined as that occurring with single or double extrastimuli.

Sroubek J et al. Circulation 2016;133:622-630

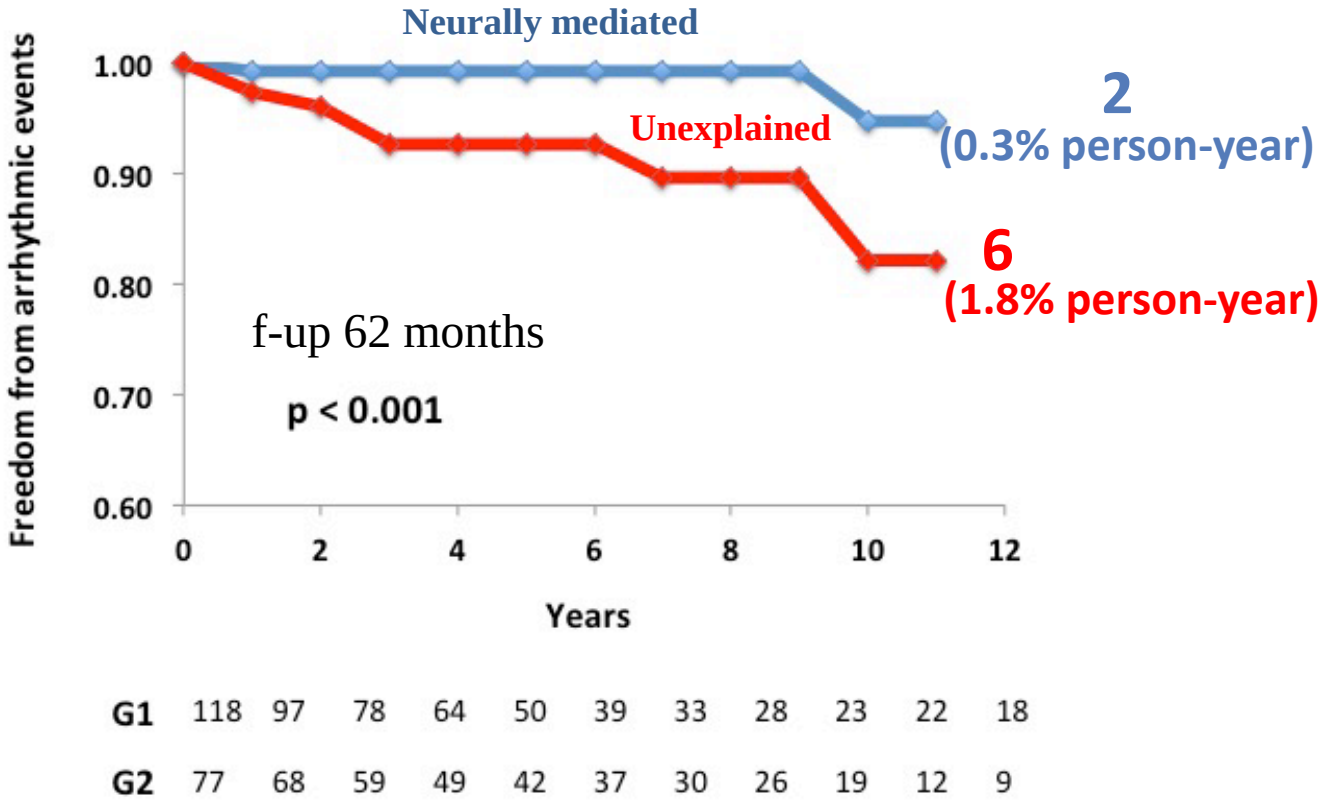
Etiological diagnosis, prognostic significance and role of electrophysiological study in patients with Brugada ECG and syncope☆

Carla Giustetto [a,*,1], Natascia Cerrato [a,1], Enrico Ruffino [a], Elena Gribaudo [a], Chiara Scrocco [a], Lorella Barbonaglia [b], Francesca Bianchi [c], Miriam Bortnik [d], Guido Rossetti [e], Paula Carvalho [f], Riccardo Riccardi [g], Davide Castagno [a], Matteo Anselmino [a], Laura Bergamasco [a], Fiorenzo Gaita [a]

Int. J. of Cardiology2017; 241:188–193

Arrhythmic events in neurally mediated syncope versus unexplained

118 neurally-mediated *vs* 77 unexplained syncope



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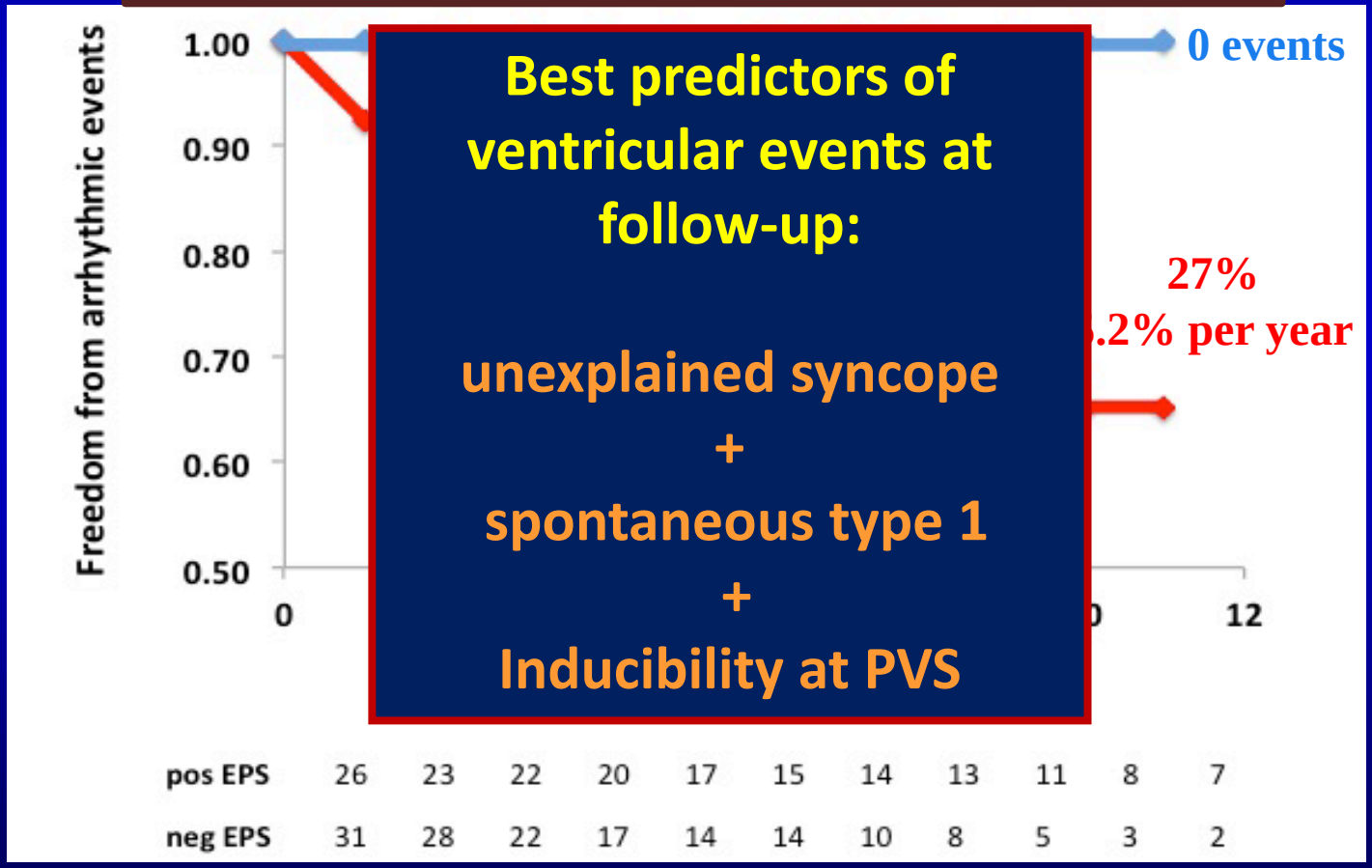
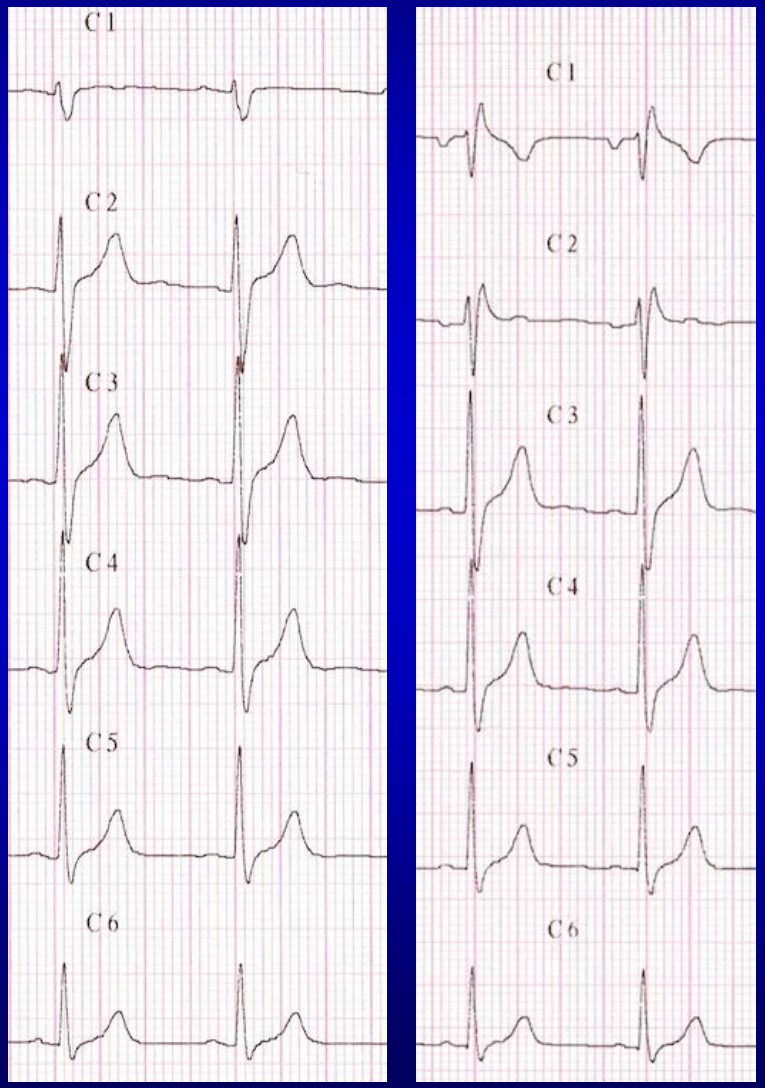
Int. J. of Cardiology2017; 241:188–193

Role of PVS in unexplained syncope



19 years old man, asymptomatic for syncope, no history of SD.

ECG for sport eligibility: suspicious for Brugada pattern



What should we do?

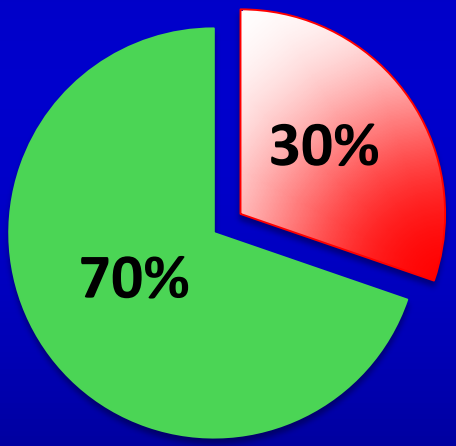
Prevalence of Type 1 Brugada Electrocardiographic Pattern Evaluated by Twelve-Lead Twenty-Four-Hour Holter Monitoring

Am J Cardiol 2015; 115: 52-56

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]

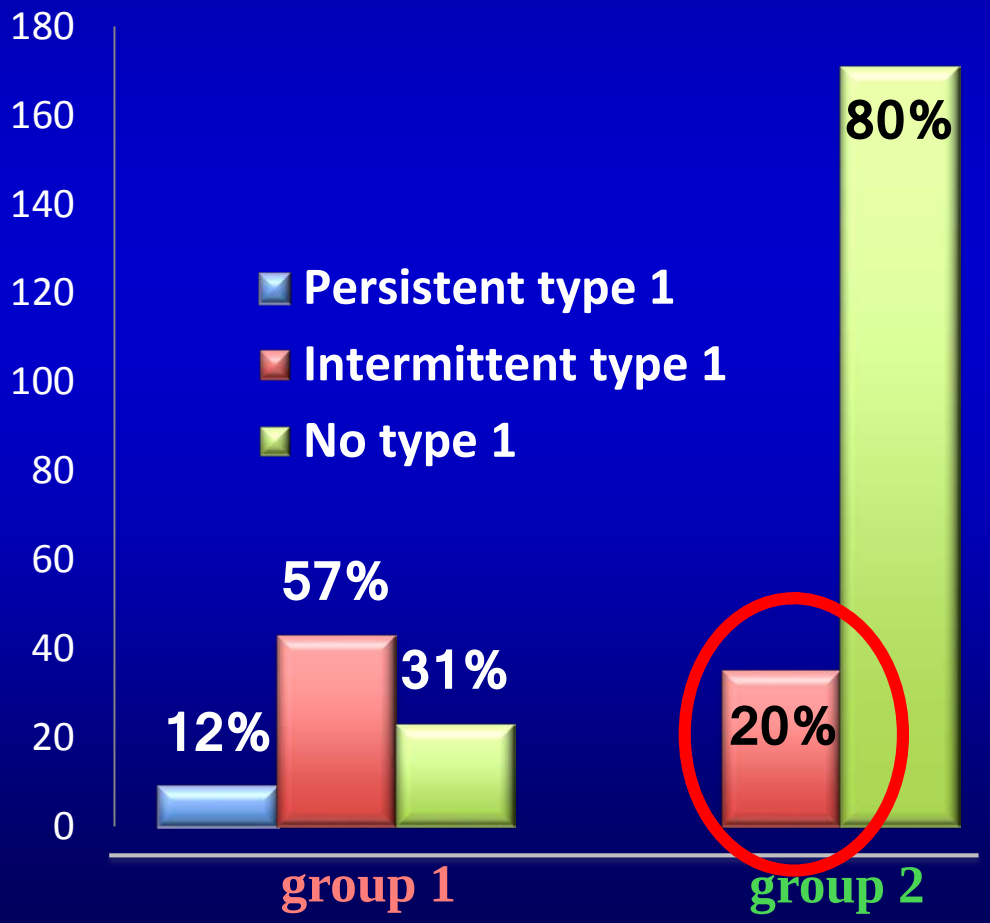
Brugada Piedmont Registry **684 patients**

12 Lead - 24 hour Holter
251 patients

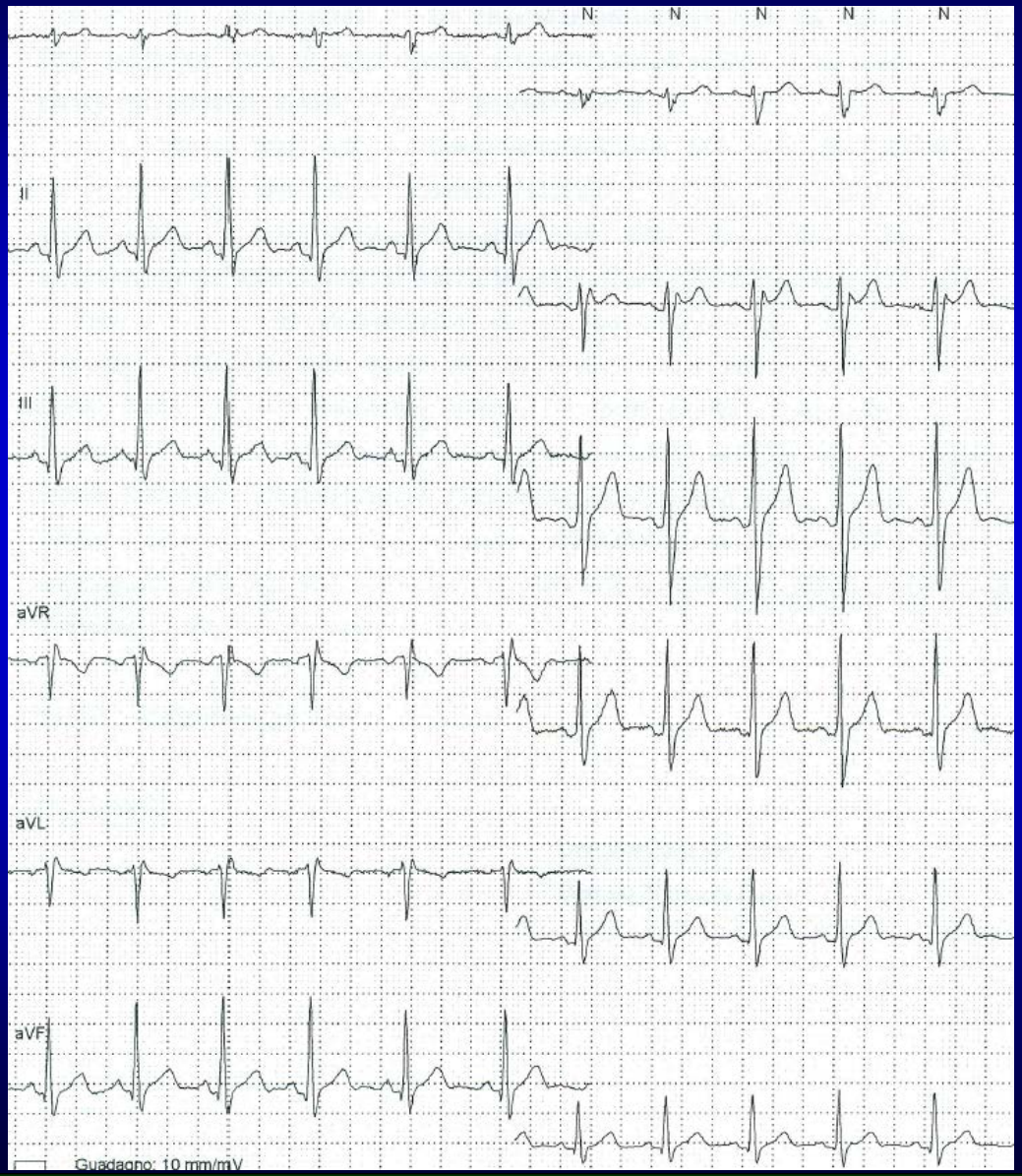


spontaneous type 1 at basal ECG (group 1)

drug-induced type 1 (group 2)

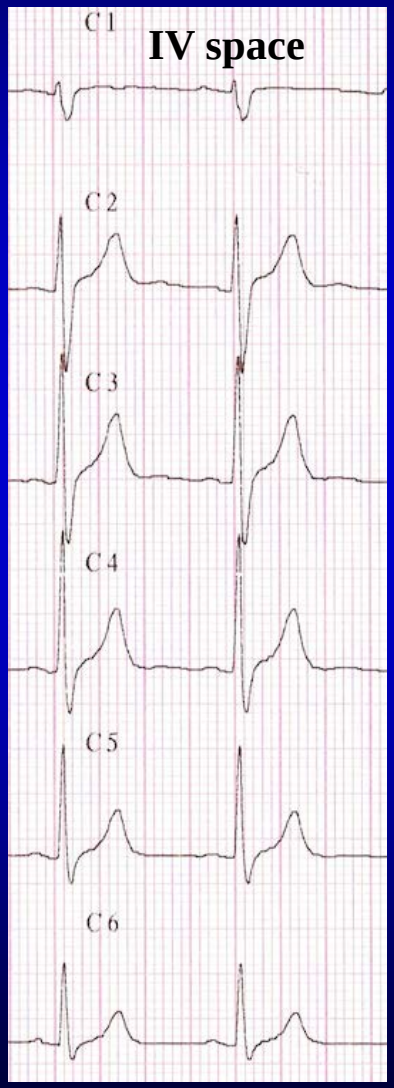


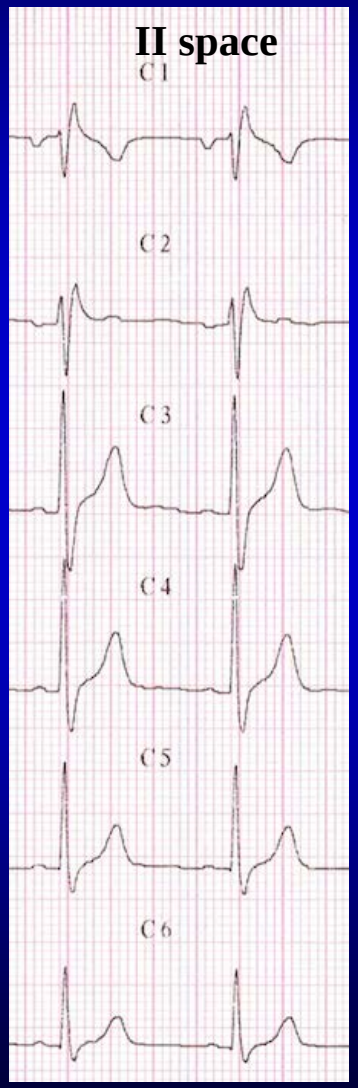
12-lead Holter ECG: NO spontaneous type 1



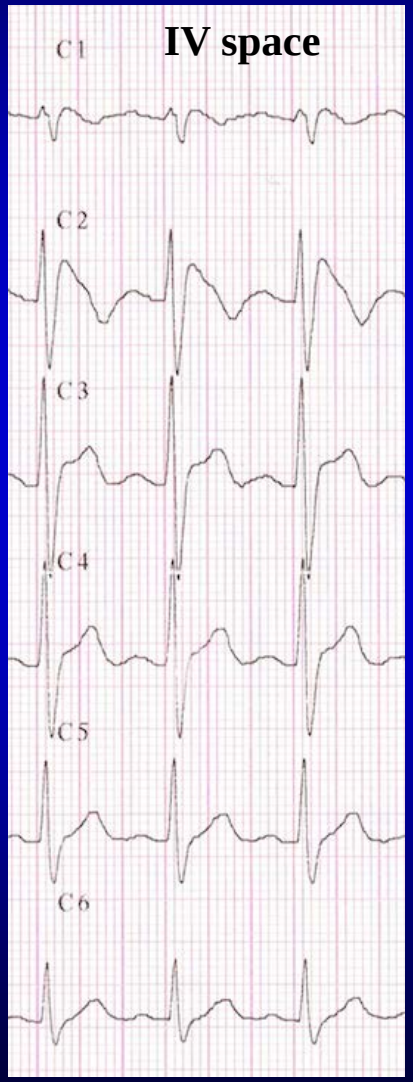
Asymptomatic 19 years old pt evaluated for sport eligibility

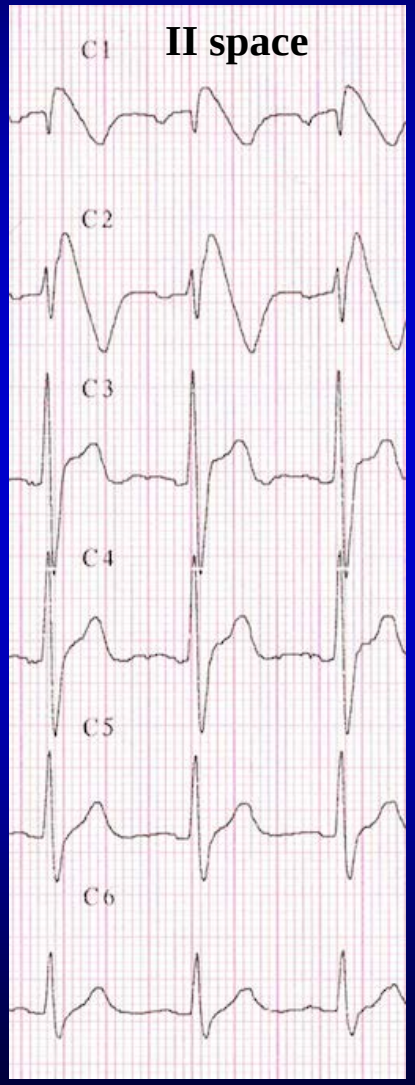
Basal ECG





Positive ajmaline test

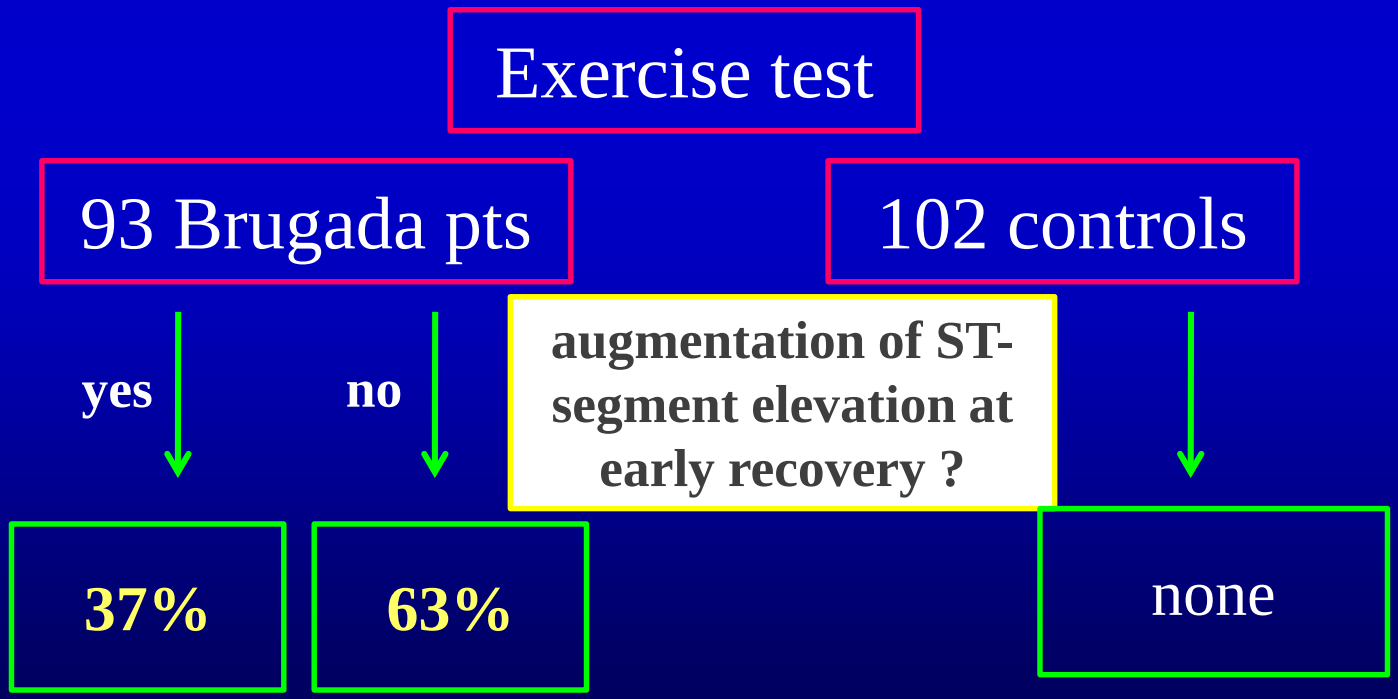


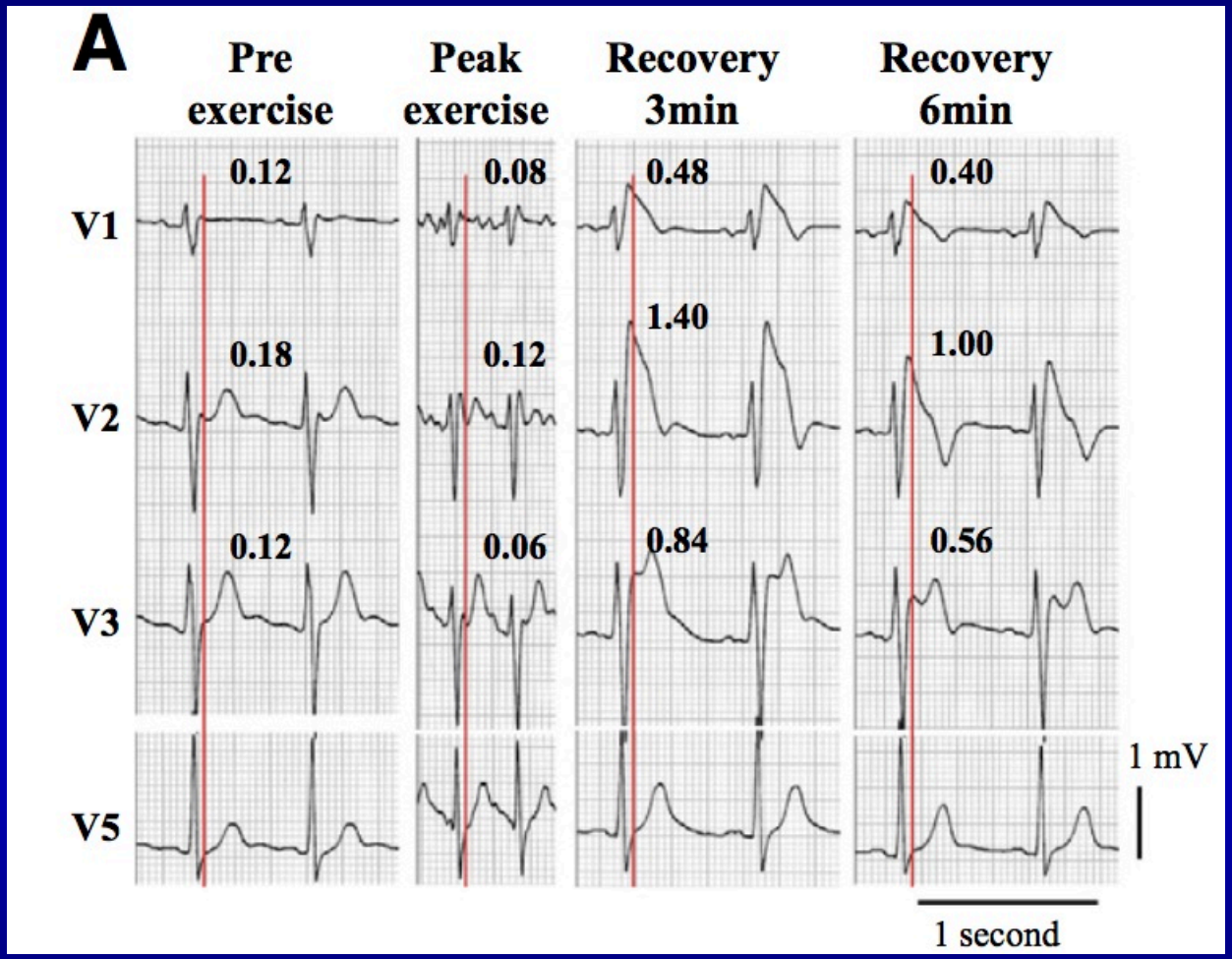


Augmented ST-Segment Elevation During Recovery From Exercise Predicts Cardiac Events in Patients With Brugada Syndrome

Hisaki Makimoto, MD,* Eiichiro Nakagawa, MD, PHD,† Hiroshi Takaki, MD, PHD,* Yuko Yamada MD,* Hideo Okamura, MD,* Takashi Noda, MD, PHD,* Kazuhiro Satomi, MD, PHD,* Kazuhiro Suyama, MD, PHD,* Naohiko Aihara, MD,* Takashi Kurita, MD, PHD,‡ Shiro Kamakura, MD, PHD,* Wataru Shimizu, MD, PHD*

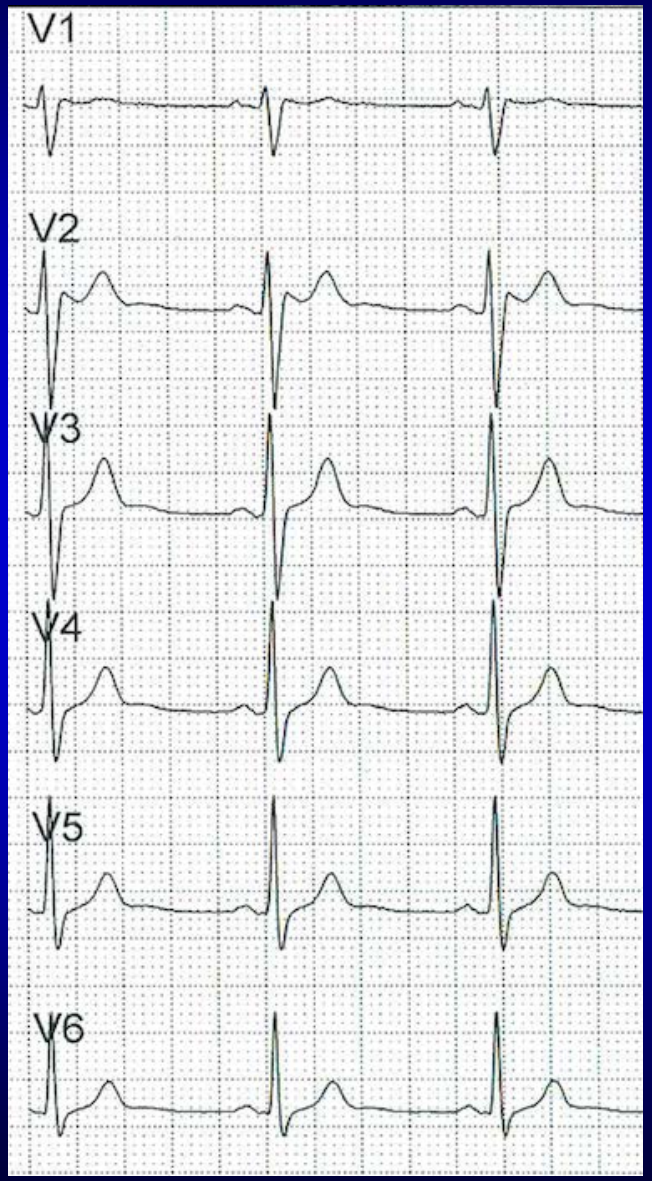
J Am Coll Cardiol **2010**;56:1576–84



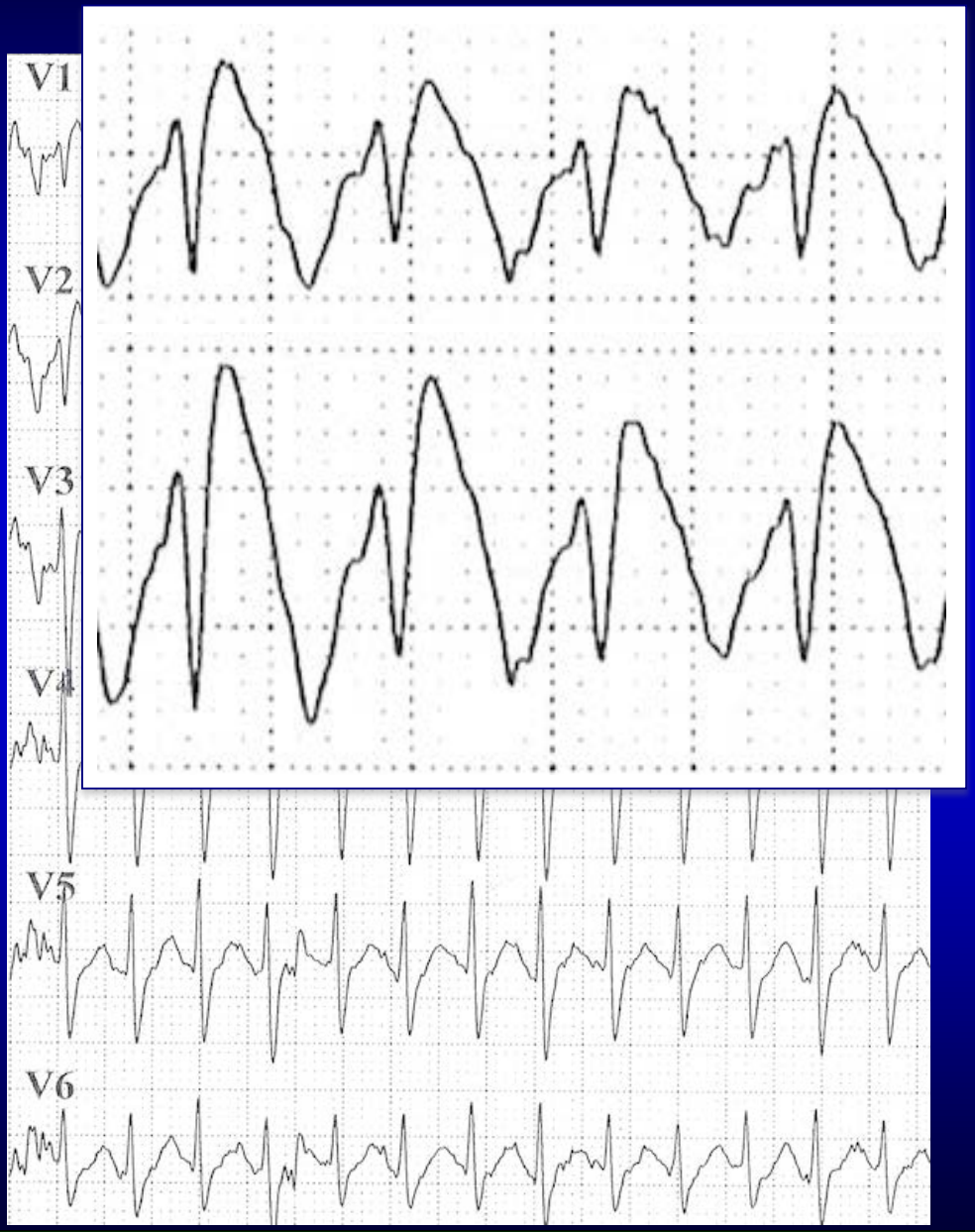


Makimoto, J Am Coll Cardiol 2010;56:1576–84

pre-exercise test



Peak exercise



Which investigations are reasonable/recommended?

Asymptomatic pt
+
suspect Brugada ECG pattern (type 2)

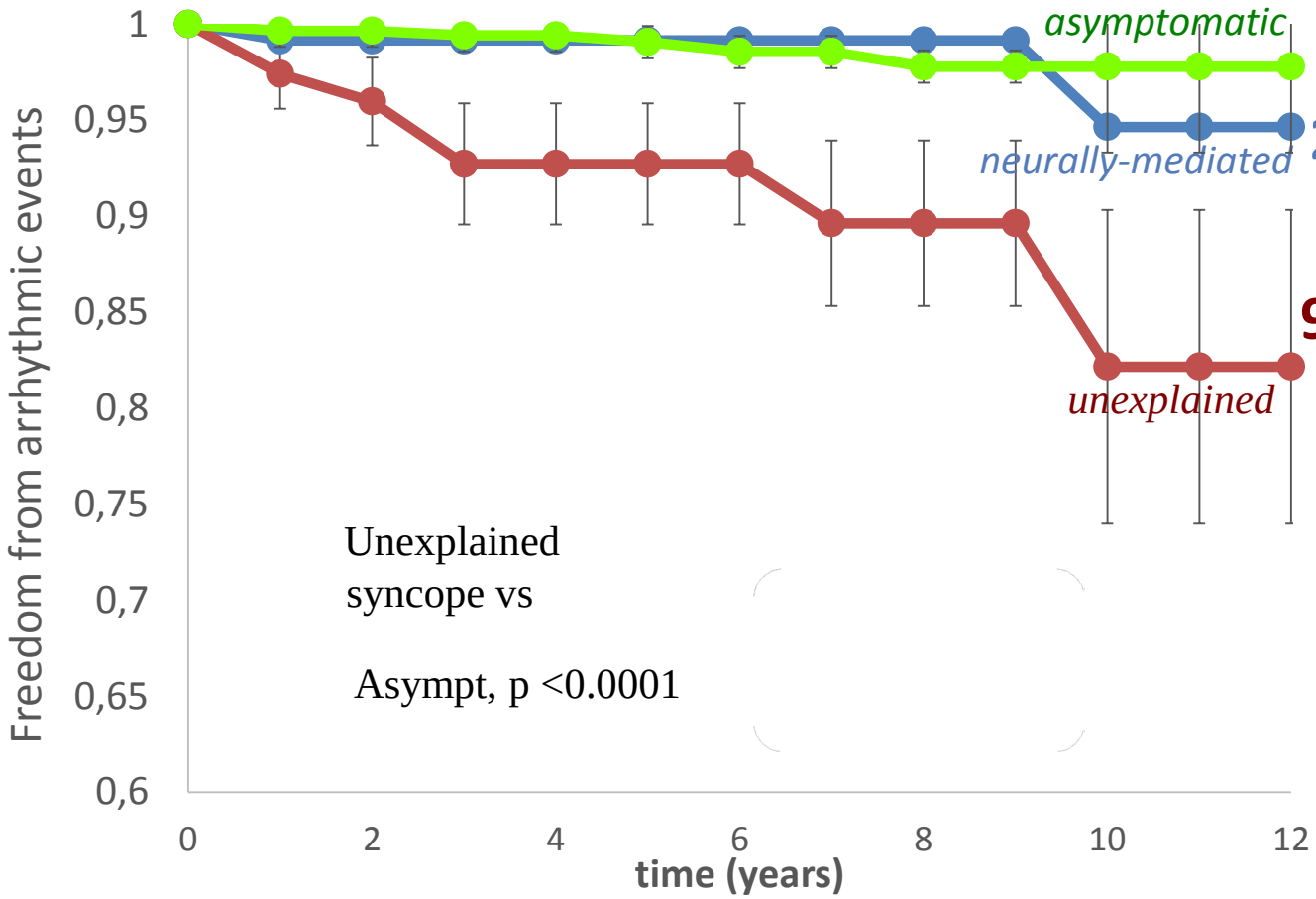
Negative 12-lead-Holter monitoring

Type 1 Brugada ECG at exercise test

programmed ventricular stimulation

Brugada Registry of the Piedmont region: arrhythmic events at follow-up

Mean follow-up of 62±48 months



G1	118	97	78	64	50	39	33	28	23	22	18
G2	77	68	59	49	42	37	30	26	19	12	9
Asympt	608	573	518	425	361	286	192	152	129	110	70

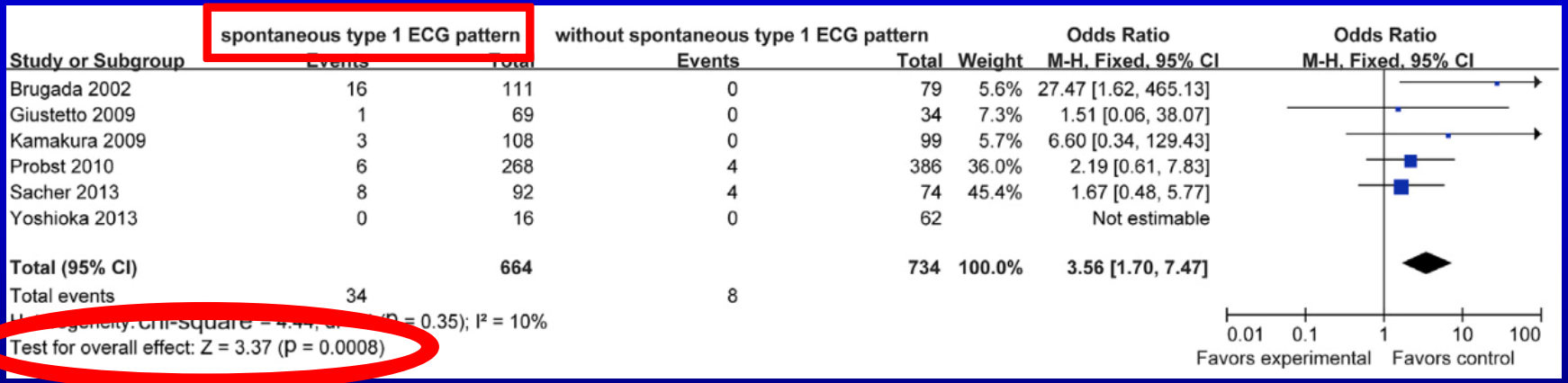
Meta-Analysis on Risk Stratification of Asymptomatic Individuals With the Brugada Phenotype

Konstantinos P. Letsas, MD[a,*], Tong Liu, MD, PhD[b], Qingmiao Shao, MD[b], Panagiotis Korantzopoulos, MD, PhD[c], Georgios Giannopoulos, MD[d], Konstantinos Vlachos, MD[a], Stamatis Georgopoulos, MD[a], Athanasios Trikas, MD[e], Michael Efremidis, MD[a], Spyridon Deftereos, MD[d], and Antonios Sideris, MD[a]

Am J Cardiol 2015;116:98e103

14 prospective observational studies
mean f-up 20 - 77 months

3,536 asymptomatic subjects (2,820 men) → 1,398 with spontaneous type 1 ECG



Study or Subgroup	spontaneous type 1 ECG pattern Events	Total	without spontaneous type 1 ECG pattern Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Brugada 2002	16	111	0	79	5.6%	27.47 [1.62, 465.13]
Giustetto 2009	1	69	0	34	7.3%	1.51 [0.06, 38.07]
Kamakura 2009	3	108	0	99	5.7%	6.60 [0.34, 129.43]
Probst 2010	6	268	4	386	36.0%	2.19 [0.61, 7.83]
Sacher 2013	8	92	4	74	45.4%	1.67 [0.48, 5.77]
Yoshioka 2013	0	16	0	62		Not estimable
Total (95% CI)		**664**		**734**	**100.0%**	**3.56 [1.70, 7.47]**
Total events	34		8			

Test for overall effect: Z = 3.37 (P = 0.0008)

Asymptomatic pts with spontaneous type 1 ECG exhibit an increased risk of arrhythmic events

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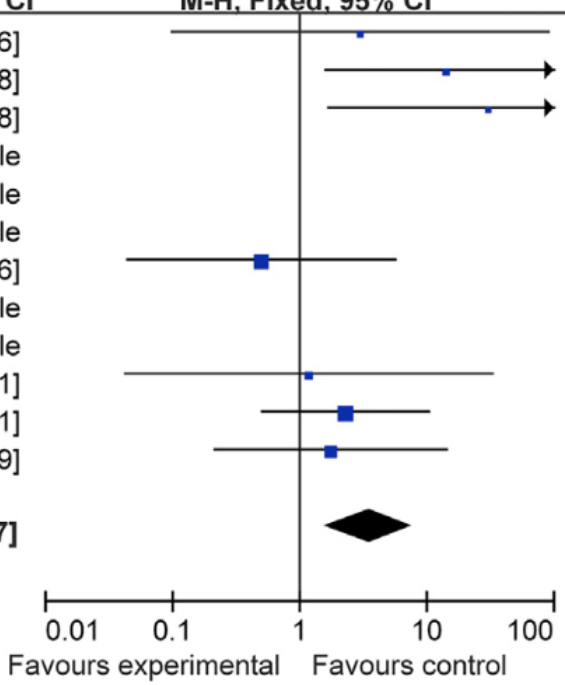
Am J Cardiol 2015;116:98e103

Study or Subgroup	Inducible VT Events	Total	Non-inducible VT Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Ajiro 2005	1	6	0	5	5.6%	3.00 [0.10, 90.96]
Brugada 2005	5	36	1	89	6.6%	14.19 [1.60, 126.28]
Delise 2011	6	50	0	104	3.8%	30.53 [1.68, 553.58]
Furushima 2005	0	8	0	1		Not estimable
Gasparini 2002	0	9	0	3		Not estimable
Giustetto 2009	0	17	0	64		Not estimable
Kamakura 2009	1	61	2	62	25.8%	0.50 [0.04, 5.66]
Mok 2004	0	3	0	8		Not estimable
Morita 2003	0	12	0	24		Not estimable
Ohkubo 2007	1	17	0	6	8.7%	1.18 [0.04, 32.91]
Probst 2010	4	137	3	232	28.6%	2.30 [0.51, 10.41]
Sacher 2013	11	130	1	20	21.0%	1.76 [0.21, 14.39]
Total (95% CI)		**486**		**618**	**100.0%**	**3.51 [1.60, 7.67]**
Total events	29		7			

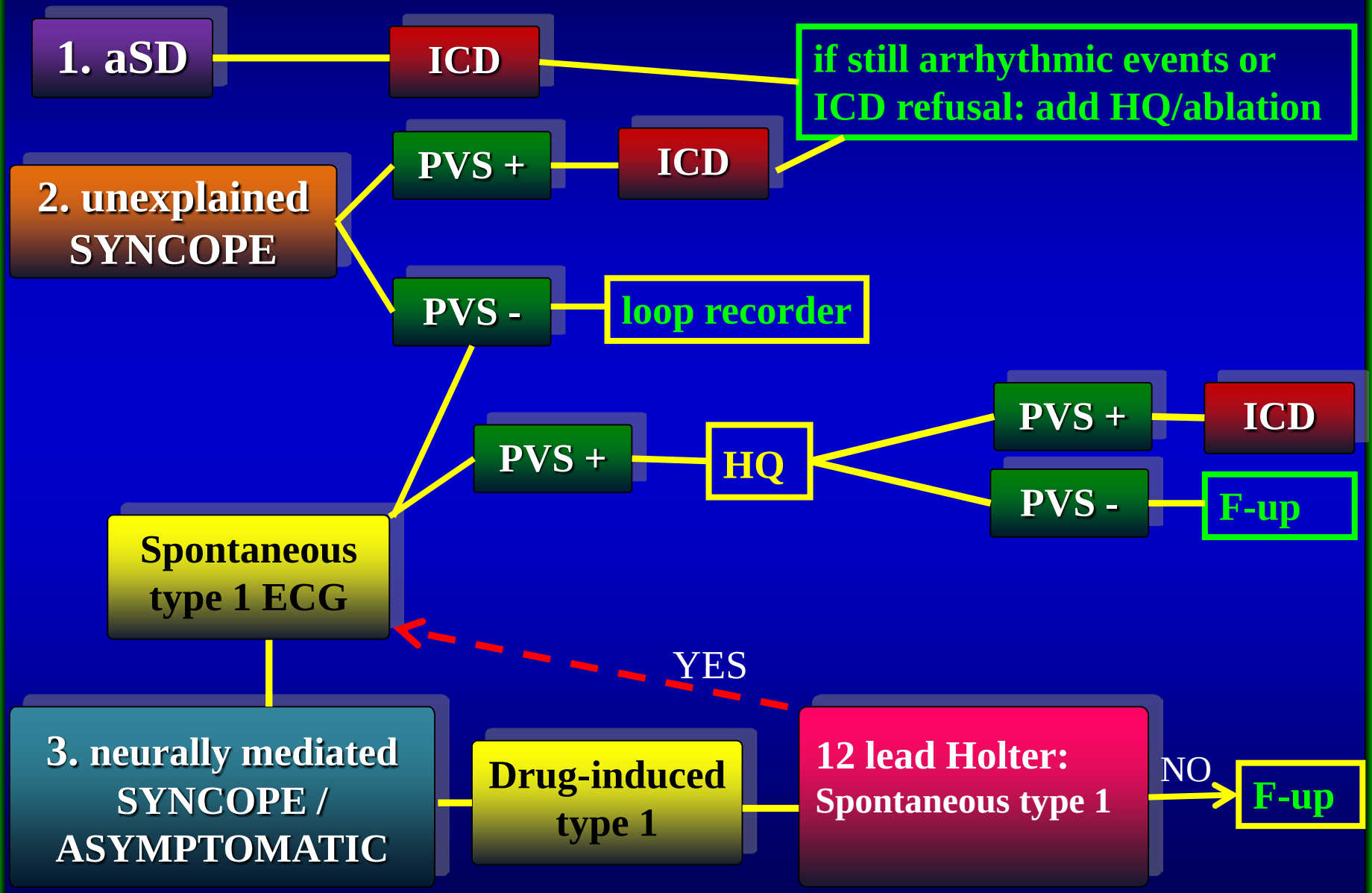
Heterogeneity: df = 6 (P = 0.29); I^2 = 18%

Test for overall effect: Z = 3.14 (P = 0.002)



Inducible ventricular arrhythmias at PVS were predictive of arrhythmic events

In summary:


1. aSD
ICD
if still arrhythmic events or ICD refusal: add HQ/ablation
2. unexplained SYNCOPE
PVS +
ICD
PVS -
loop recorder
PVS +
HQ
PVS +
ICD
PVS -
F-up
Spontaneous type 1 ECG
YES
3. neurally mediated SYNCOPE / ASYMPTOMATIC
Drug-induced type 1
12 lead Holter: Spontaneous type 1
NO
F-up

Thank you for your attention!