

La sincope nel paziente con ECG Brugada-like

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

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^g Division of Cardiology, E. Agnelli Hospital, via Brigata Cagliari, 39, 10064 Pinerolo, TO, Italy

Brugada Piedmont Registry 2001-2014



825 consecutive Brugada patients

(mean age 45 ± 14 years; 78% males)

608 asymptomatic

11 SD

8 aSD

198
syncope

neurally-mediated syncope
118 (60%)

arrhythmic
syncope
4 (2%)

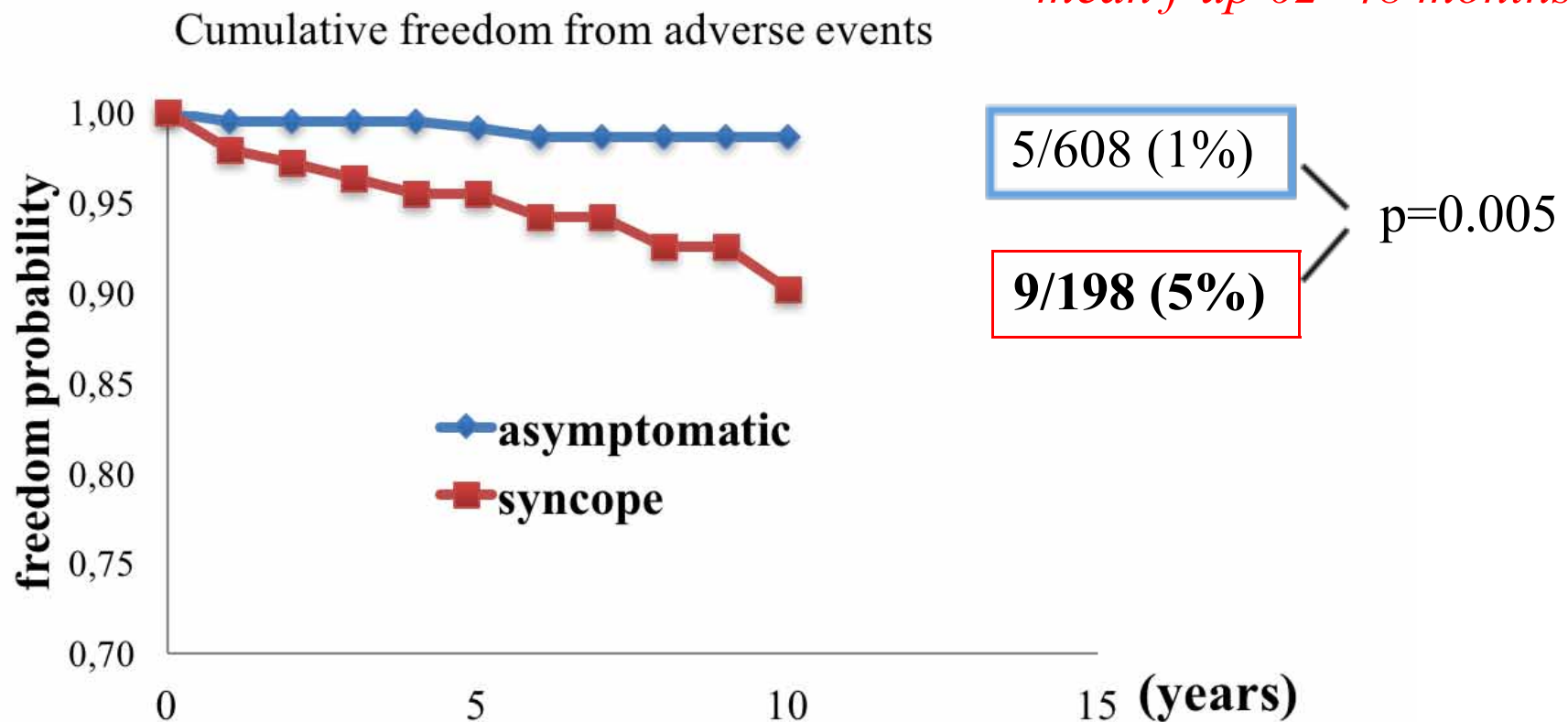
unexplained syncope
76 (38%)

Giustetto et al, Intern J Cardiol 2017, in press

Syncope is a predictor of arrhythmic events

825 patients from the Brugada Piedmont Registry (2001-2014)

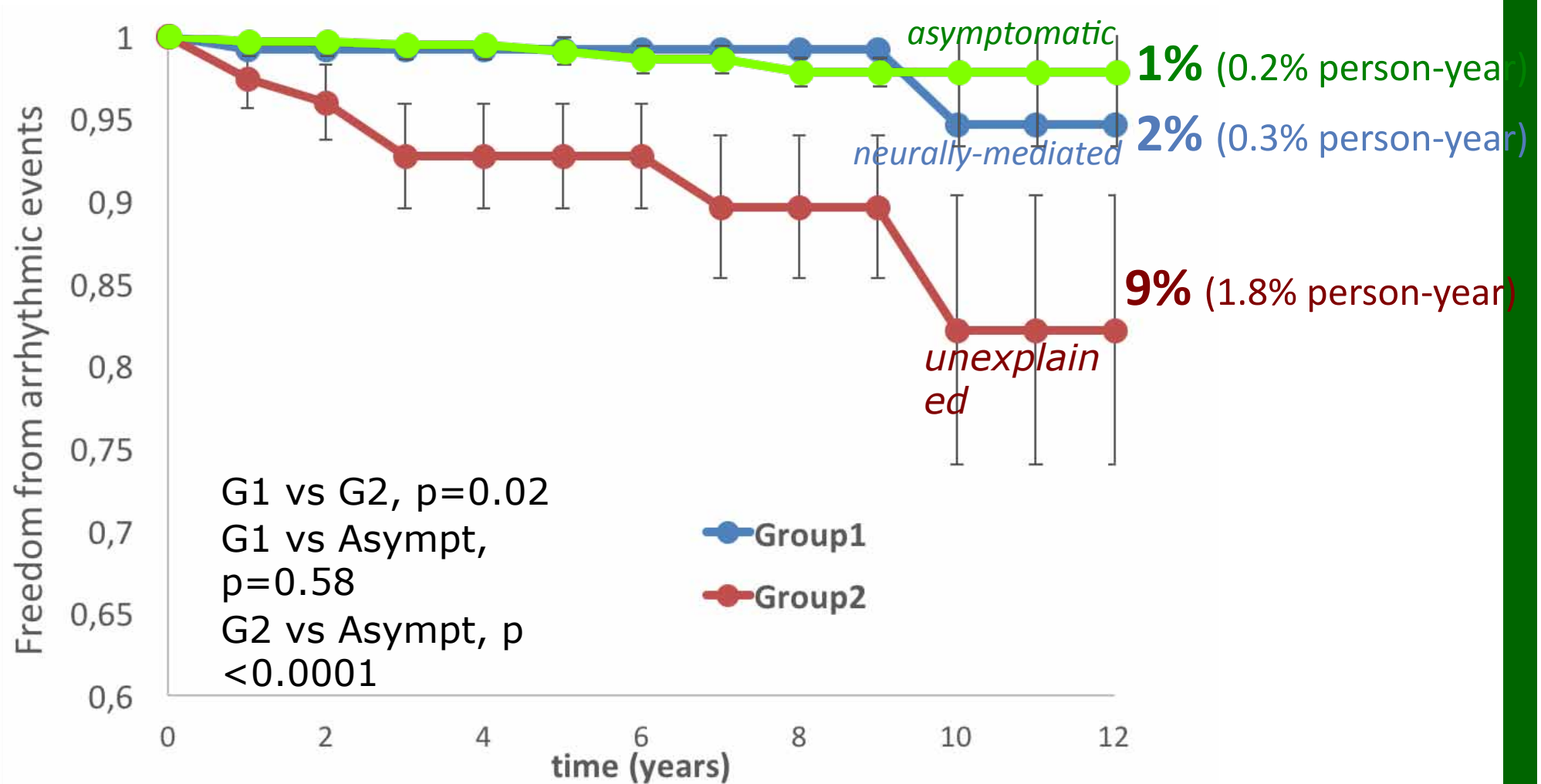
mean f-up 62±48 months



Asymptomatic	544	513	425	361	282	198	160	136	116	70
Syncope	141	135	122	110	91	74	62	56	51	39

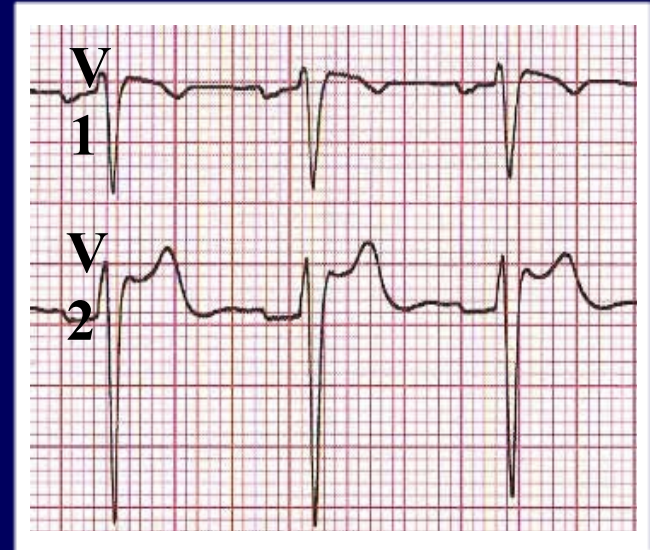
Arrhythmic events at follow-up

Mean follow-up of 62±48 months



G1	11	97	78	64	50	39	33	28	23	22	18
G2	87	68	59	49	42	37	30	26	19	12	9
Asymp	60	57	51	42	36	28	19	15	12	11	70
t	8	3	8	5	1	6	2	2	9	0	

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

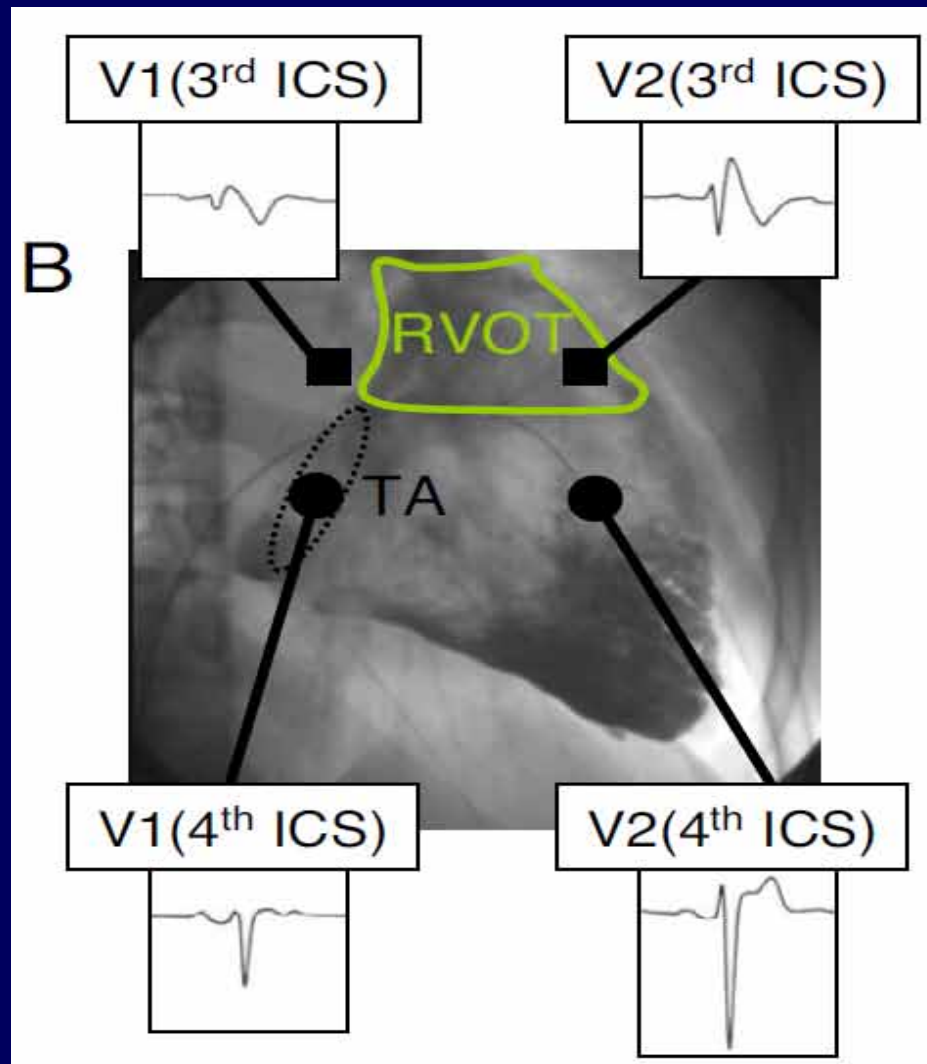


**Which investigations are
reasonable/recommended?**

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

Correlation between RVOT position and exploring electrodes

RVOT is the section of the myocardium where Ito is more represented and this area in the chest is variable between the 2nd and 4th ICS

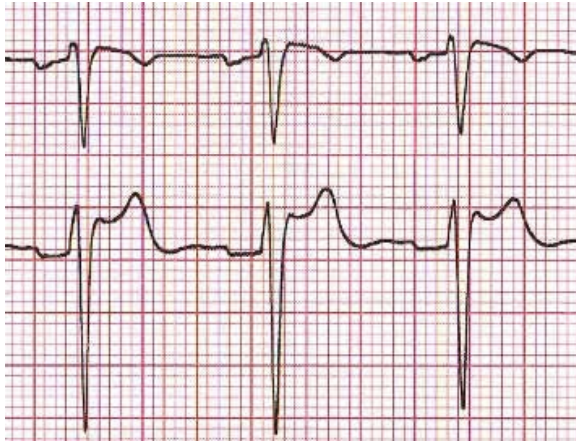


ICS= intercostal
space

Nagase et al, JACC 2010, 56

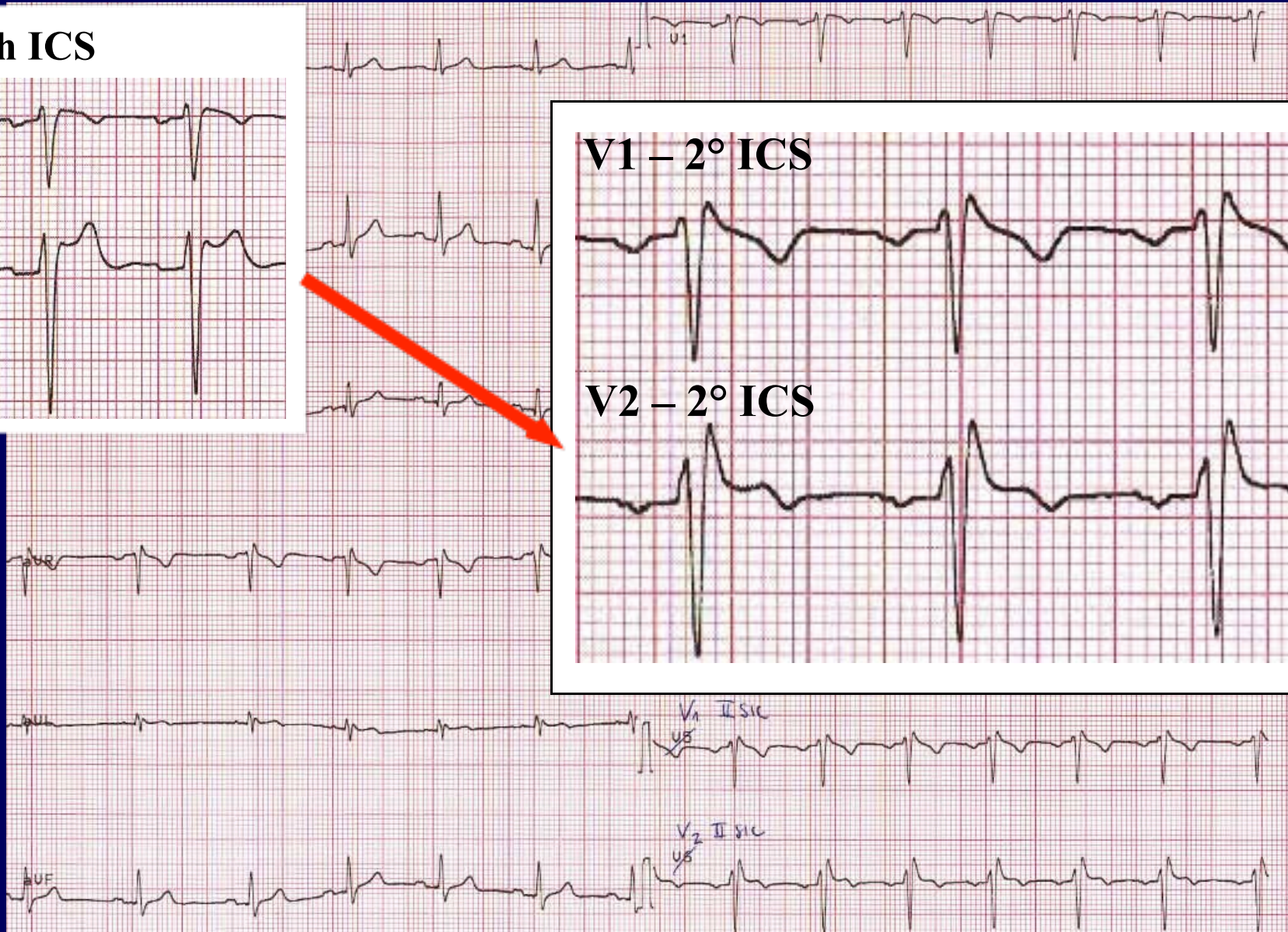
ECG was recorded with V1-V2 at a higher intercostal space →
in this case it remained doubtful, still not diagnostic

ECG 4th ICS



V1 – 2° ICS

V2 – 2° ICS



Which investigations are reasonable/recommended?

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

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

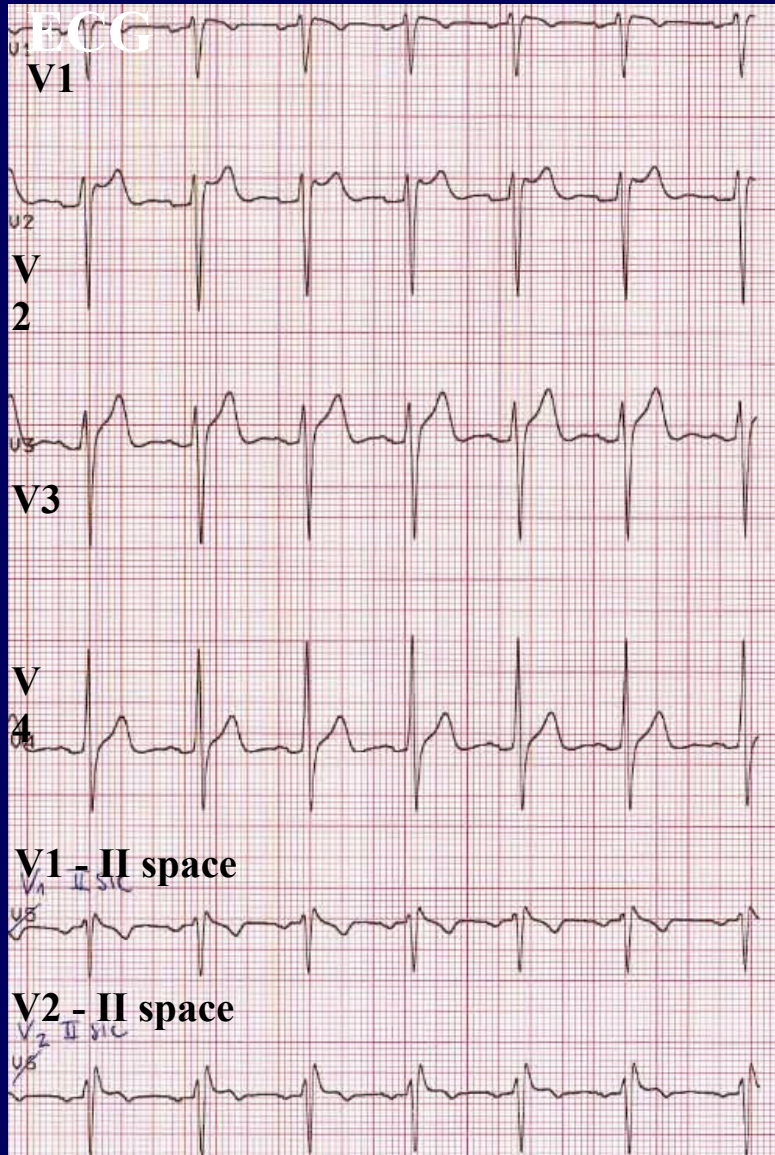
type 2 Brugada ECG

Drug challenge with
sodium channel
blockers

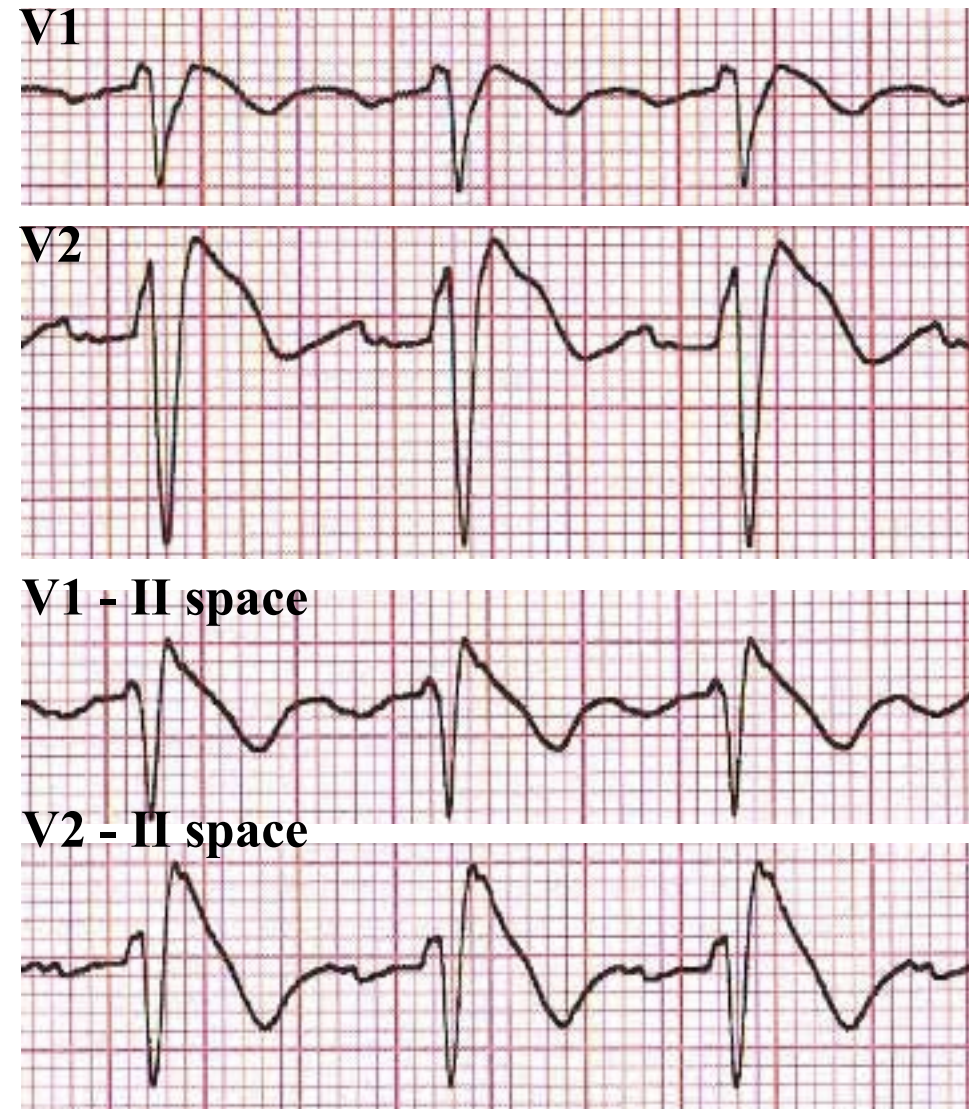


Pharmacological challenge with **Na⁺-channel blockers** was performed...

Basal



Ajmaline infusion (1mg/kg in 5 min)



Summary...

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



Which is the appropriate treatment for this patient ?

What does literature report ?

What do guidelines recommend ?

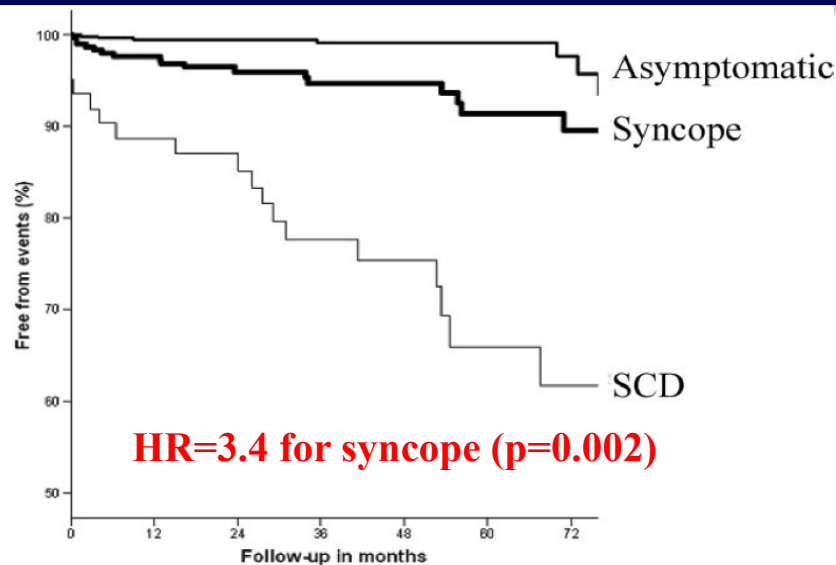
Long-Term Prognosis of Patients Diagnosed With Brugada Syndrome. Results From the FINGER Brugada Syndrome Registry

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

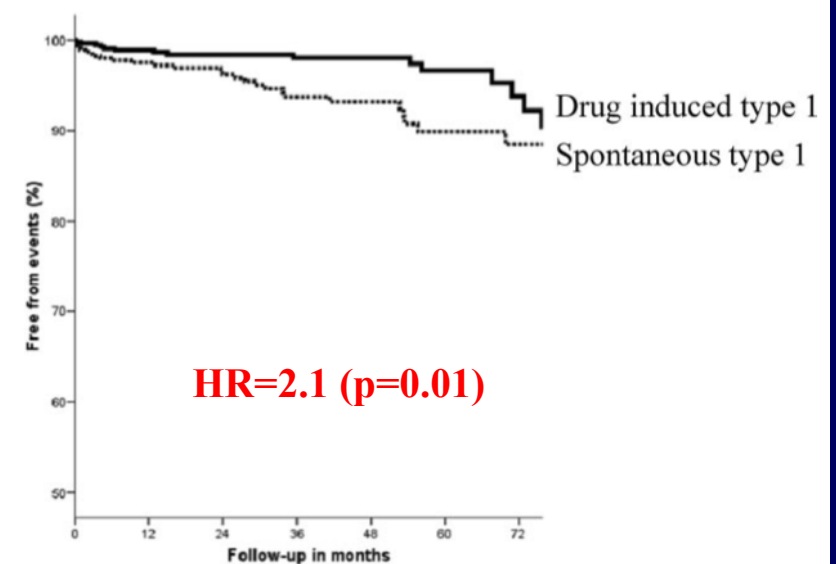
Circulation 2010;121: 635

Symptoms and spontaneous type 1 ECG were predictors of arrhythmic events

1029 pz - median f-up 32 months



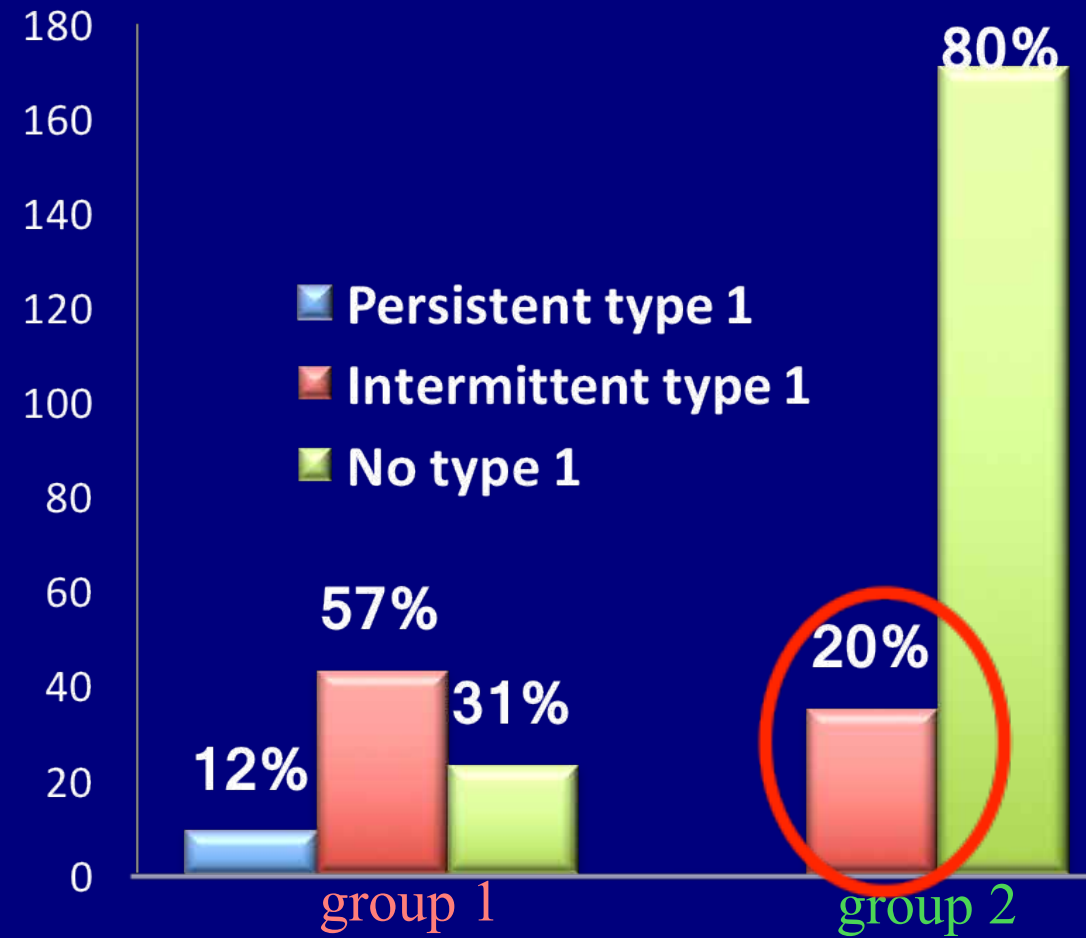
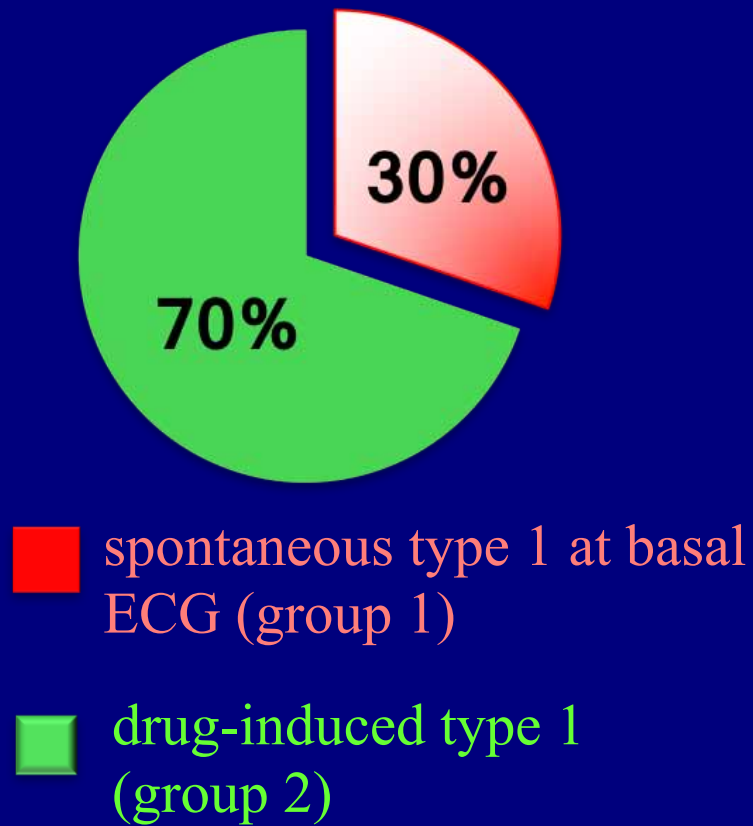
	0	12	24	36	48	60	72
group A	62	54	47	36	29	18	15
group B	313	244	192	148	99	73	49
group C	654	505	379	275	195	109	54



	0	12	24	36	48	60	72
type1	468	350	269	200	135	88	58
no type 1	561	453	349	259	188	112	60

Brugada Piedmont Registry 684 patients

12 Lead - 24 hour Holter
251 patients



Summary...

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



Which is the appropriate treatment for this patient?

What do guidelines recommend?

What does literature report?

2015 ESC GUIDELINES

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

The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC)

ICD implantation is recommended in patients with a diagnosis of Brugada syndrome who

- (a) Are survivors of an aborted cardiac arrest and/or
- (b) Have documented spontaneous sustained VT.

I

C

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

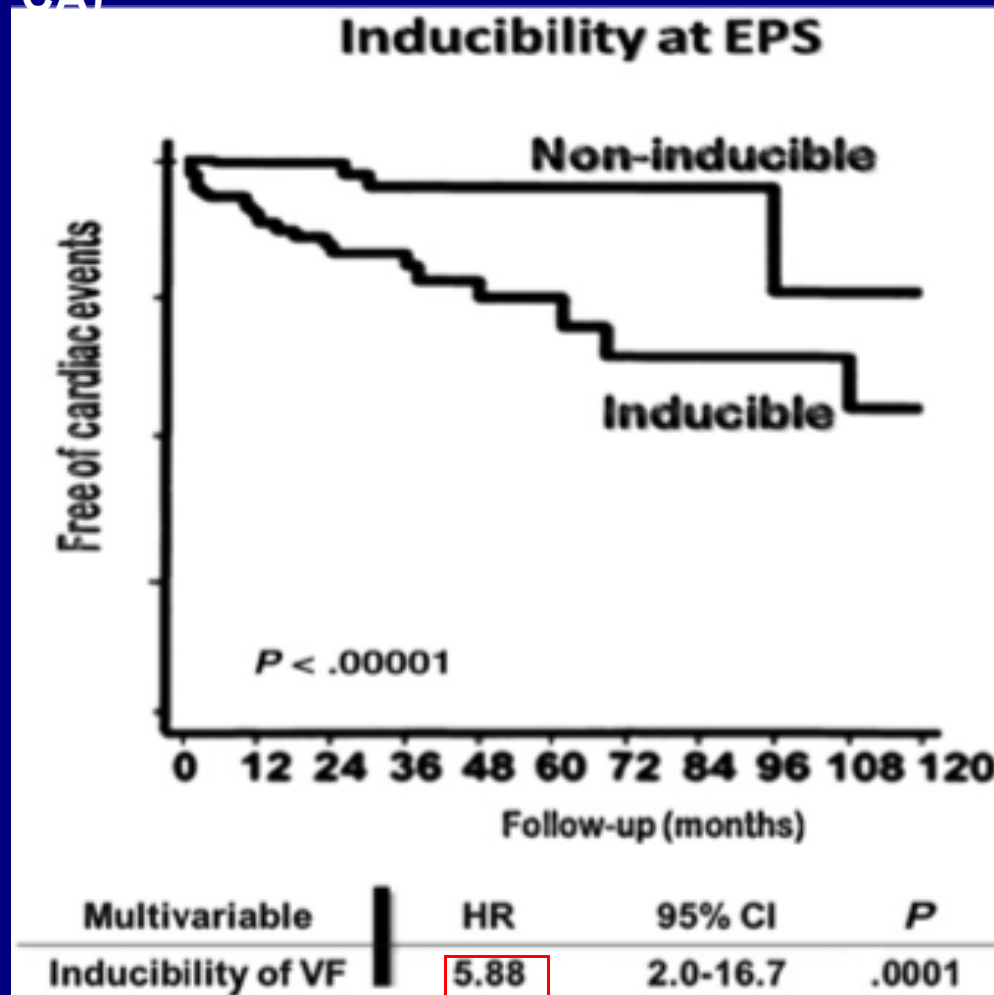
Arrhythmic events (SD or documented VF) during follow-up depending on inducibility of VF at the EP study.

124 → syncope (23%)

547 pts 253 → family members (60%)

(no previous spontaneous ecg pattern CA)

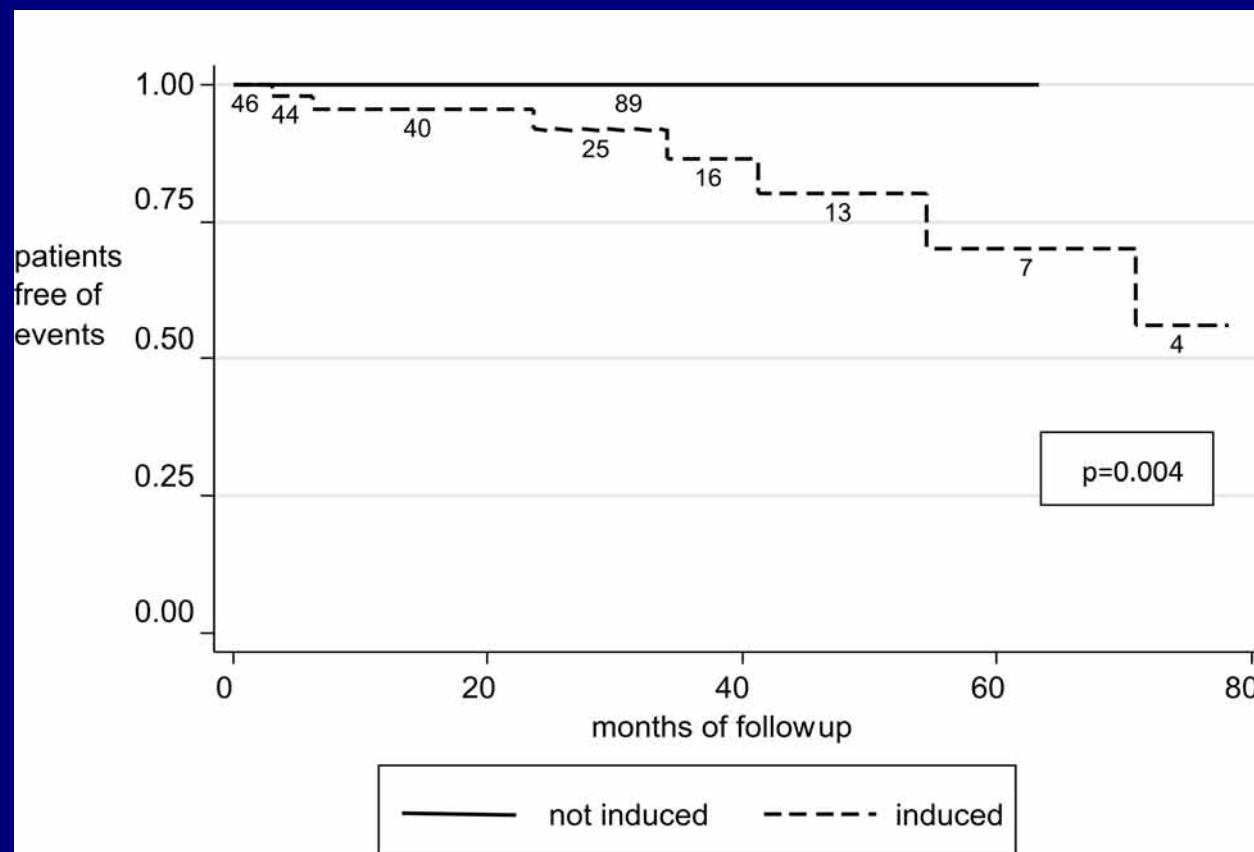
Mean f-up
24±32 m



Brugada *Circulation* 2003;108;3092-3096

Risk stratification of the patients with Brugada type electrocardiogram: a community-based prospective study

Carla Giustetto^{1*}, Stefano Drago¹, Pier Giuseppe Demarchi², Paola Dalmasso³, Francesca Bianchi⁴, Andrea Sibona Masi⁵, Paula Carvalho⁶, Eraldo Occhetta⁷, Guido Rossetti⁸, Riccardo Riccardi⁴, Roberta Bertona⁹, Fiorenzo Gaita¹,



0/ 89

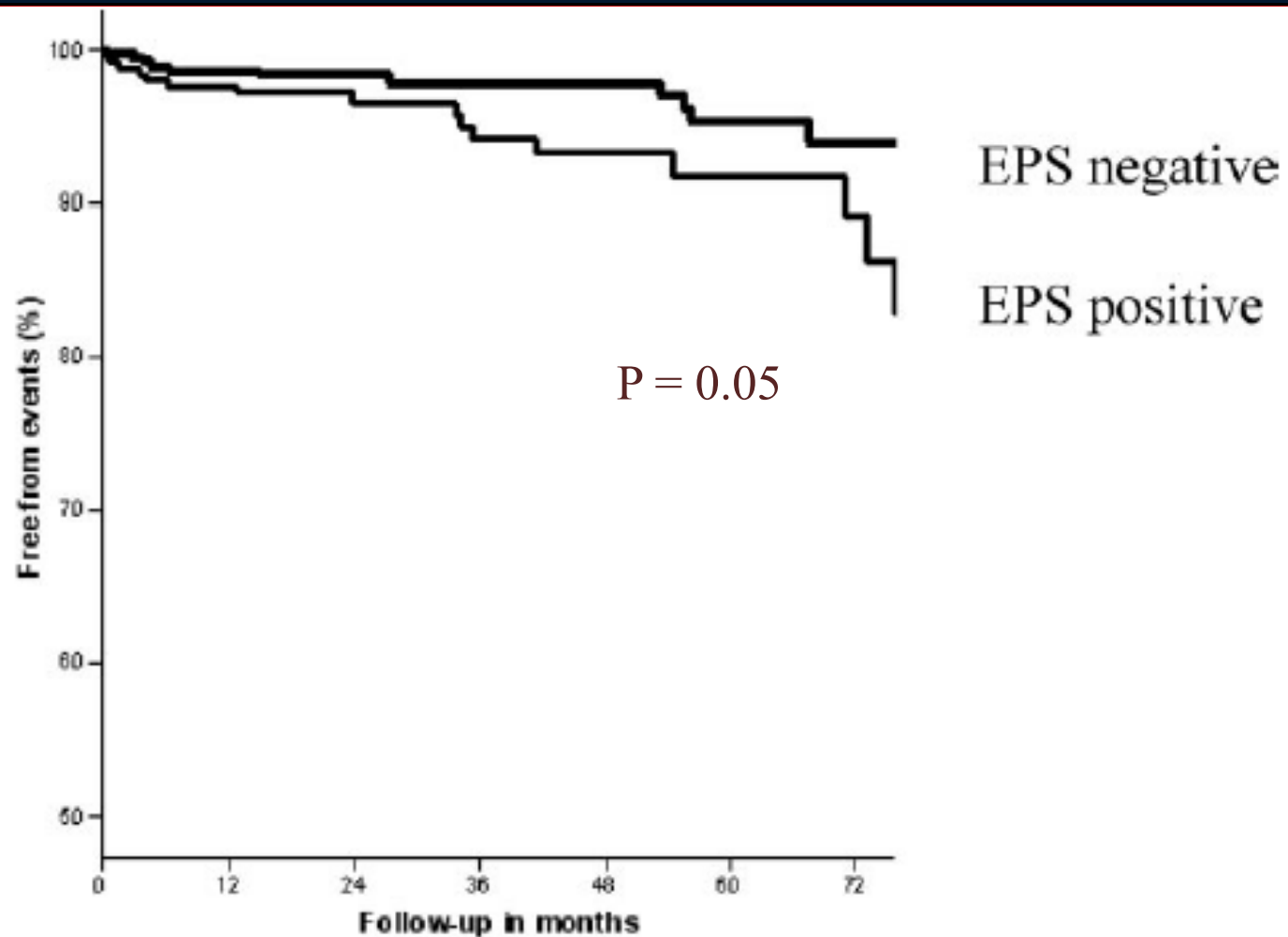
7/ 46 (15%)

135 patients

Follow-up: 30±21 mesi

Europace (2009) **11**, 507–513

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

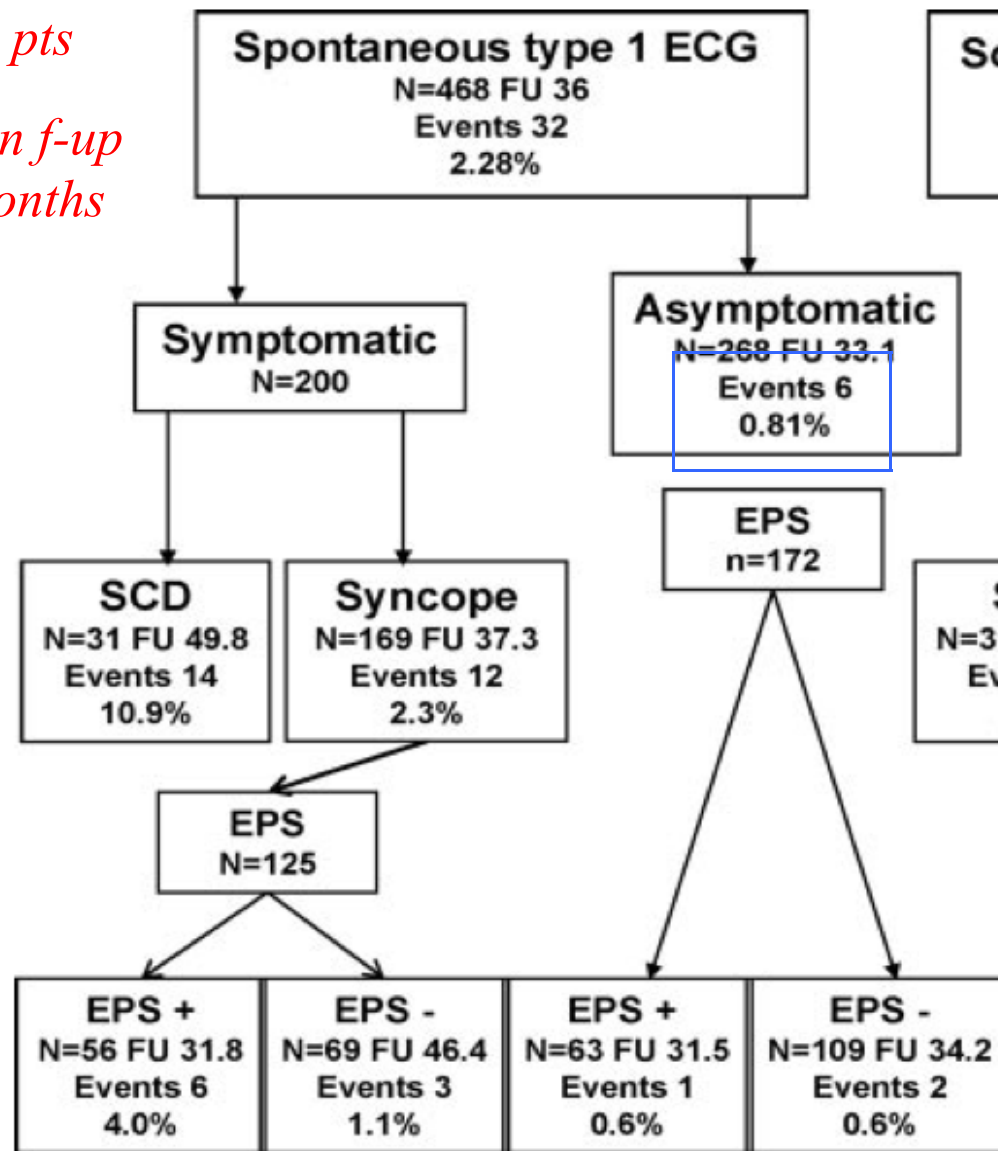


	0	12	24	36	48	60	72
negative	376	301	237	187	136	94	59
positive	262	212	161	113	81	52	34

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

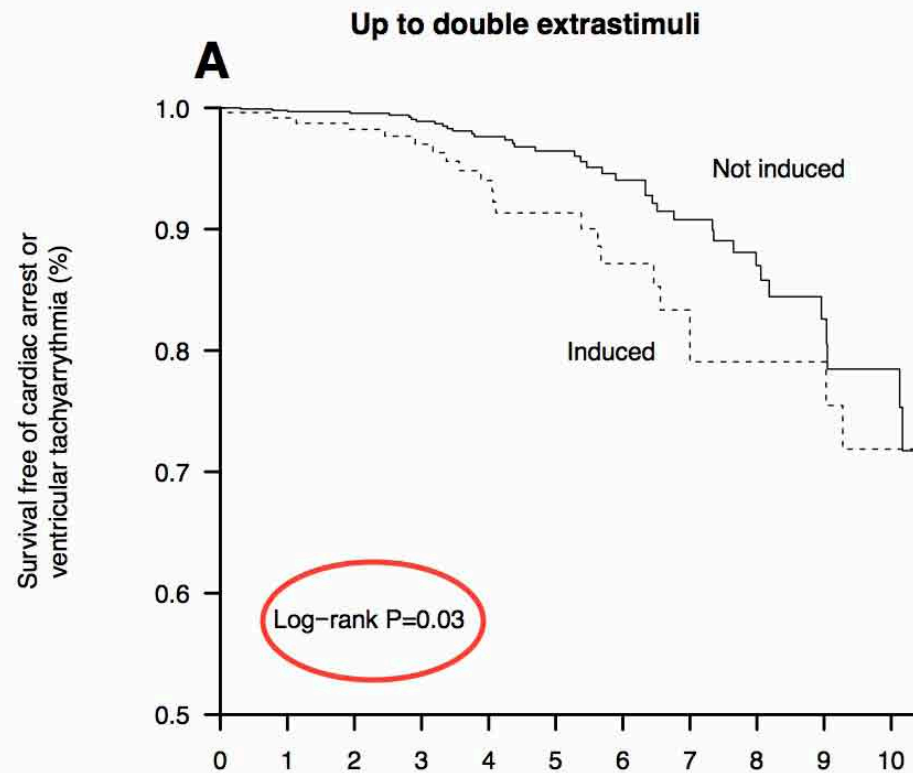
Role of EP-study in Brugada patients with syncope

1029 pts
median f-up
32 months

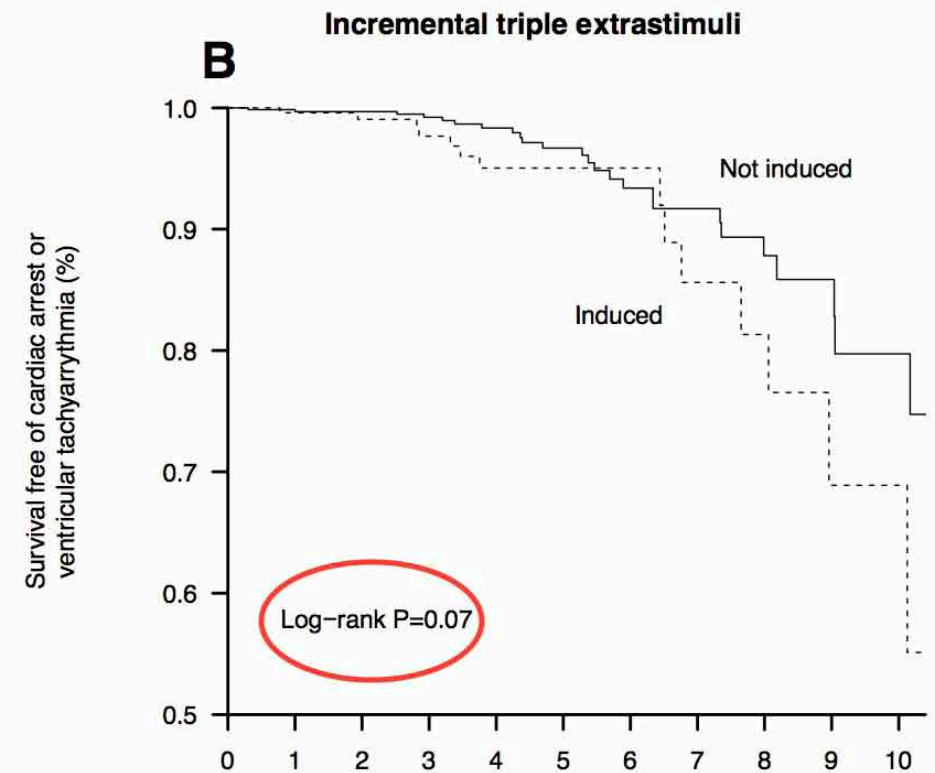


Programmed Ventricular Stimulation for Risk Stratification in the Brugada Syndrome

A Pooled Analysis



No. at risk	Time from electrophysiology study (years)	0	1	2	3	4	5	6	7	8	9	10
Not induced	1059	910	729	551	387	258	167	118	79	42	27	
Induced	253	224	190	143	111	78	52	39	30	22	18	

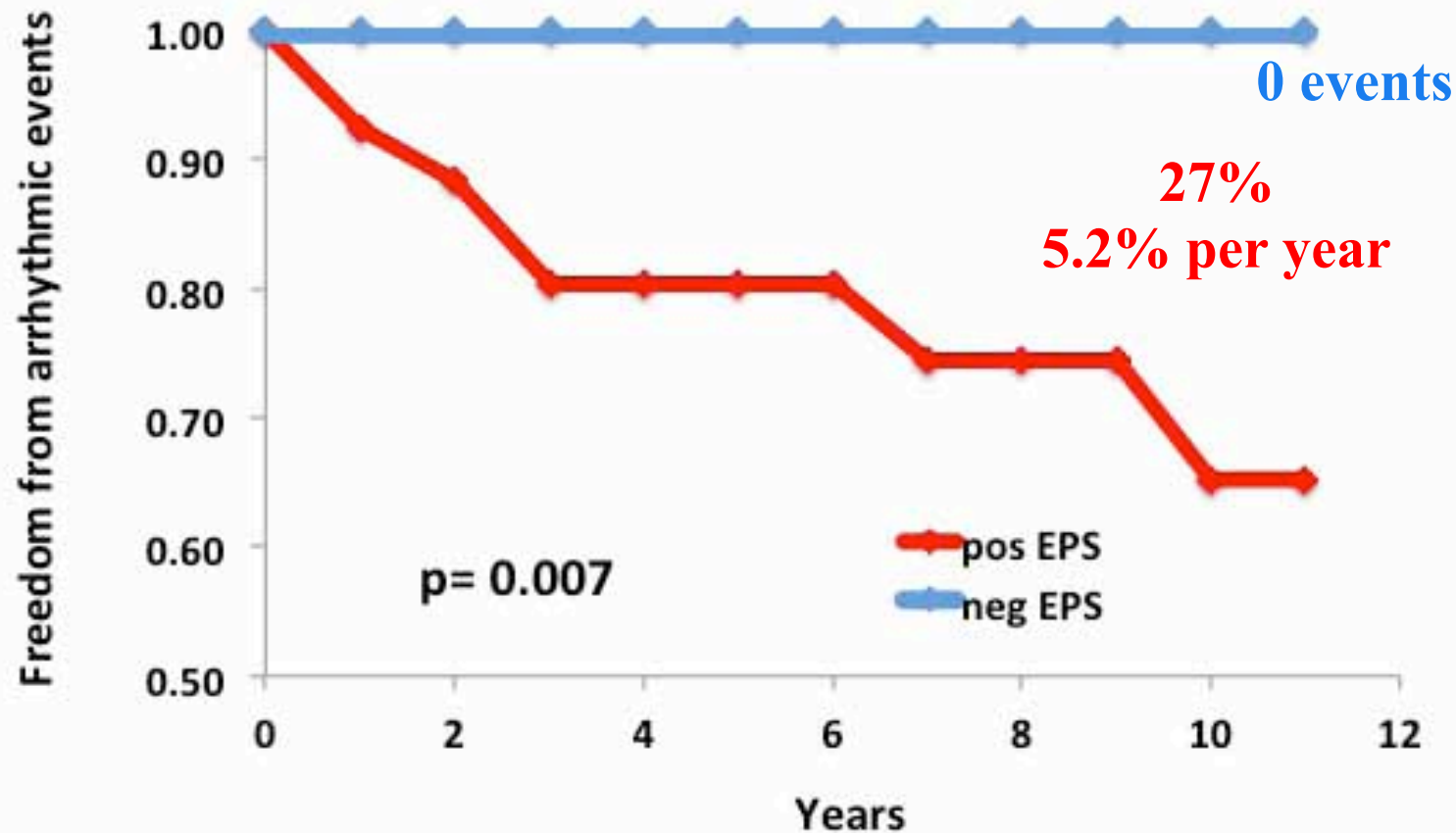


No. at risk	Time from electrophysiology study (years)	0	1	2	3	4	5	6	7	8	9	10
Not induced	720	614	503	386	271	185	123	89	57	30	19	
Induced	274	237	180	133	91	54	35	23	17	9	6	

Table 2. Annual Incidence Rates of Cardiac Arrest or Ventricular Tachyarrhythmia 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)

Role of EPS in pts with UNEXPLAINED SYNCOPE



Giustetto et al, Intern J Cardiol 2017, in press

Spontaneous type 1 ECG

N= 97 Events 7 (7%)
1.4 per 100 person-year

Unexplained syncope

N= 51

Events 6 (12%)
2.3 per 100 person-year

EPS done
N= 39 (76%)

EPS not done
N= 12 (24%)

ICD +
N= 7

ICD -
N= 5

Events
0

Events
0

EPS +
N= 21 (53%)

EPS -
N= 18 (47%)

ICD +
N= 21

ICD -
N= 0

ICD +
N= 5

ICD -
N= 13

Events
6 (29%)

Events
-

Events
0

Events
0

Syncope of uncertain origin + Brugada ECG

Electrophysiologic study (EPS)

pos

neg

ICD in primary prevention

follow-up with implantable loop recorder



Will ablation change our therapeutic approach?

Prevention of Ventricular Fibrillation Episodes in Brugada Syndrome by Catheter Ablation Over the Anterior Right Ventricular Outflow Tract Epicardium

Koonlawee Nademanee, MD; Gumpanart Veerakul, MD; Pakorn Chandanamattha, MD;
Lertlak Chaothawee, MD; Aekarach Ariyachaipanich, MD; Kriengkrai Jirasirojanakorn, MD;
Khanchit Likittanasombat, MD; Kiertijai Bhuripanyo, MD; Tachapong Ngarmukos, MD

Circulation 2011, 123: 1270-79

Brugada Syndrome Phenotype Elimination by Epicardial Substrate Ablation

Josep Brugada, MD*; Carlo Pappone, MD, PhD*; Antonio Berruezo, MD, PhD;
Gabriele Vicedomini, MD; Francesco Manguso, MD, PhD; Giuseppe Ciconte, MD;
Luigi Giannelli, MD; Vincenzo Santinelli, MD

Circ Arrhythm Electrophysiol 2015

**efficacy/complications balance,
arrhythmic risk in the different pts**

Patients selection

9 patients

ICD carriers

Arrhythmic storm

2-6 shock previous month

Lertlak Chaothawee, MD; Aekarach Ariyachaipanich, MD; Kriengkrai Jirasirojanakorn, MD;
Khanchit Likittanasombat, MD; Kiertijai Bhuripanyo, MD; Tachapong Ngarmukos, MD

Nademanee et al. Circulation 2011

14 patients

ICD carriers

Syncope 10 patients, 70%
Positive EP study 100%

ICD intervention
7 patients, 50%

Gabriele Vicedomini, MD; Francesco
Luigi Giannelli, M

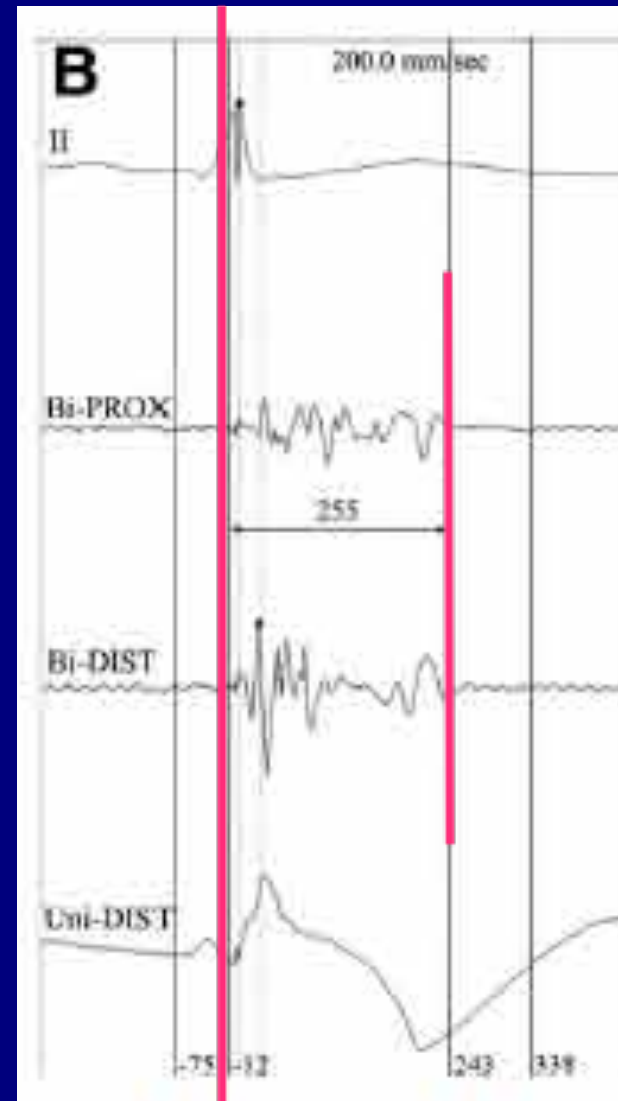
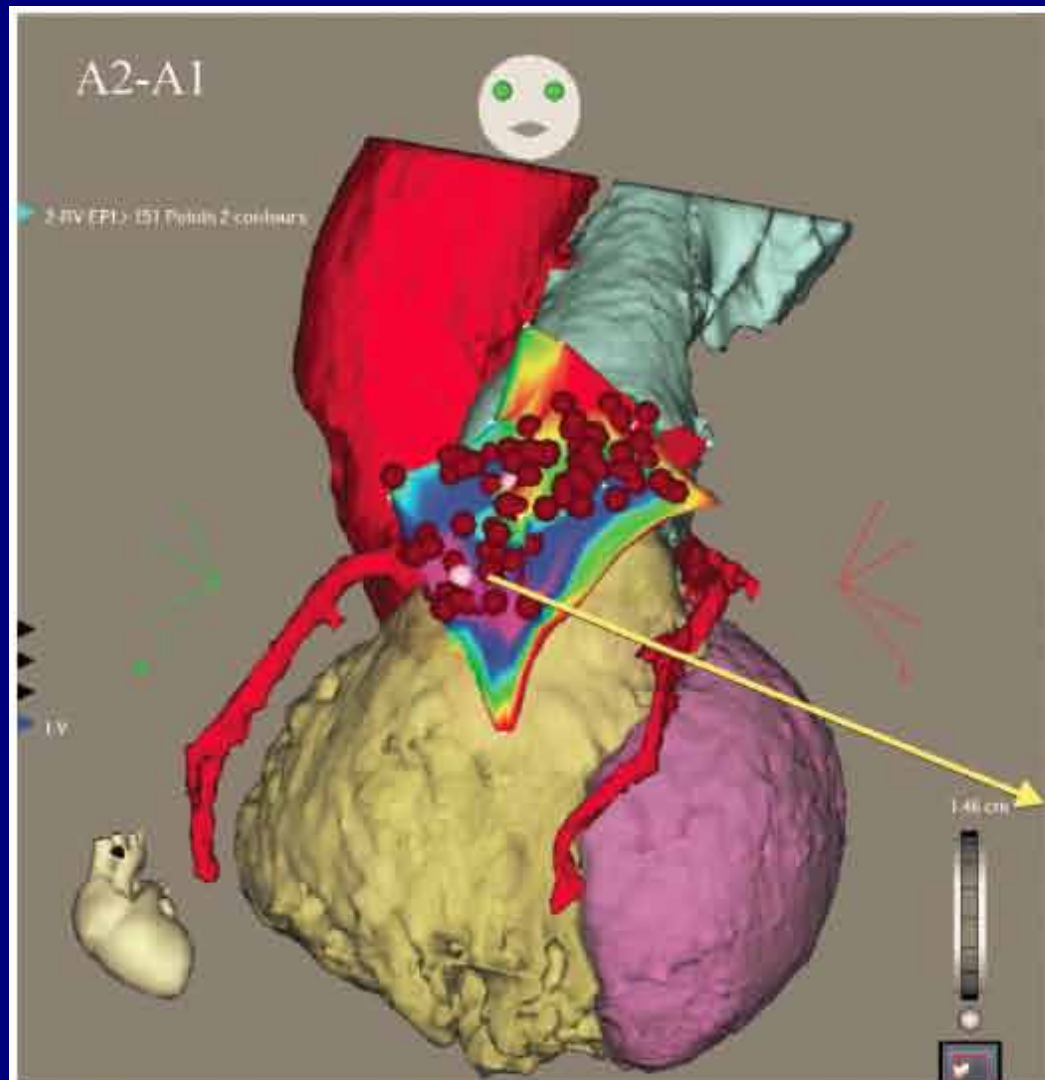
Brugada et al. Circ Arrhythm Electrophysiol 2015

9 Brugada
ICD patients

*2-6 shock previous
month*

RVOT mapping,
endo and
epicardial

Low and
fractionated
potentials



14 Brugada patients

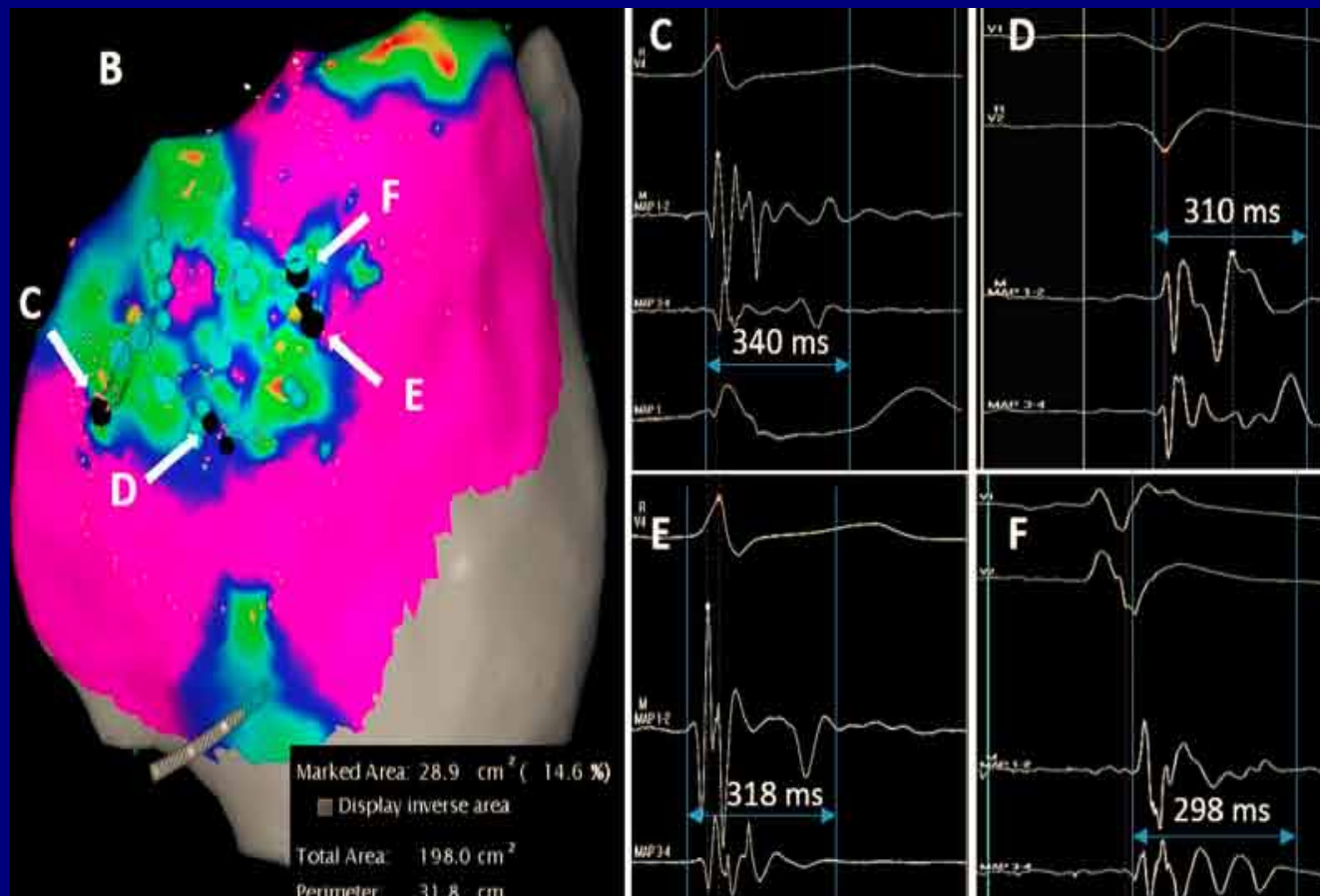
Pattern
spontaneous or
inducible

Positive
EP study

ICD carriers

Endocardial and epicardial mapping

Repeated after **flecainide infusion**



RVOT areas of low
and fractionated
potentials

Area dimension
**increased after
flecainide**

17.6 cm² → 28.5 cm²

Pappone-Brugada registry update

135 patients

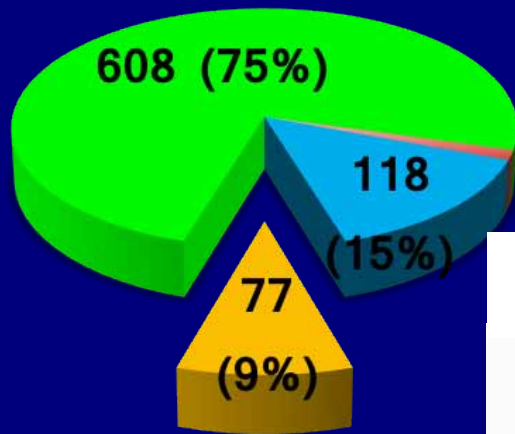
Aborted sudden death

Syncope

Asymptomatic

Asymptomatic →

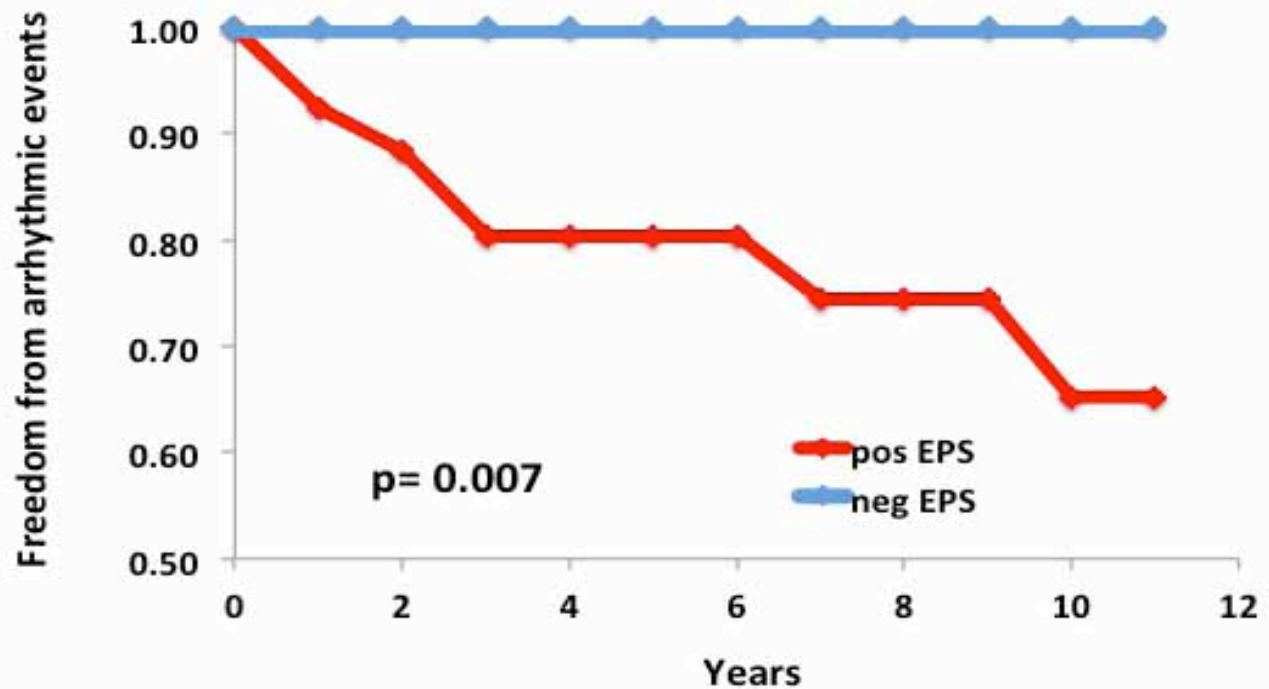
A lot of pts but with a very low arrhythmic risk



aSD →

high arrhythmic risk, but few pts

SYNCOPE and positive EPS



pos EPS	26	23	22	20	17	15	14	13	11	8	7
neg EPS	31	28	22	17	14	14	10	8	5	3	2

PROPOSAL OF MULTICENTRIC RANDOMIZED STUDY

Study protocol

**Unexplained syncope
Positive EPS**



90 pts



RF Ablation

45 pts

Follow-up

45 pts

**estimated
sample size:**

**each arm
3-year f-up**

...2020

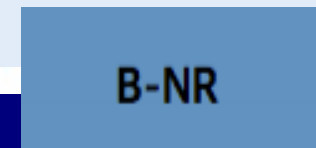


2020 ACC/AHA/HRS Guideline for the Management of Adult Patients With Brugada Syndrome

Substrate catheter ablation for Symptomatic Brugada patient



Substrate catheter ablation for Asymptomatic Brugada patient

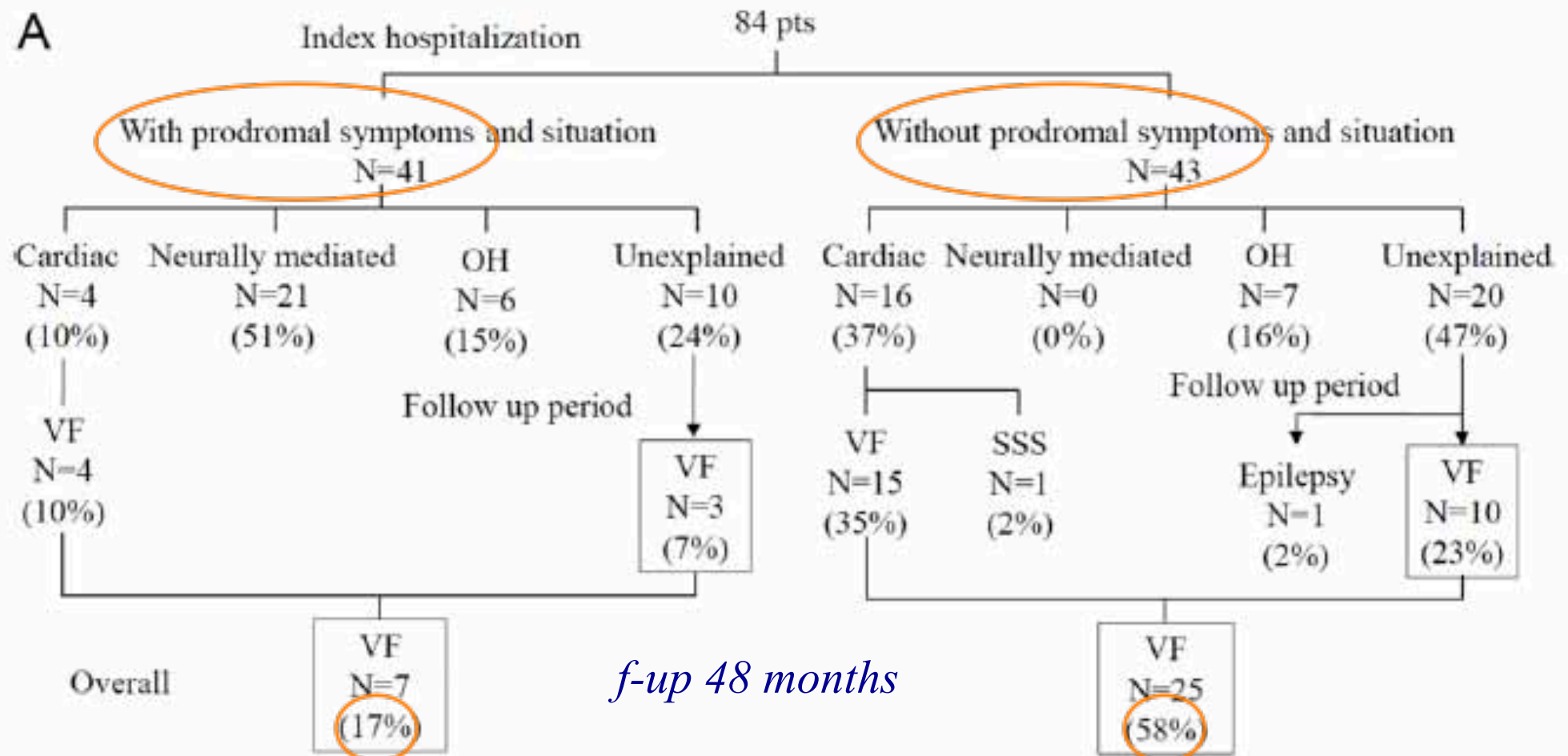


Thank you for your attention



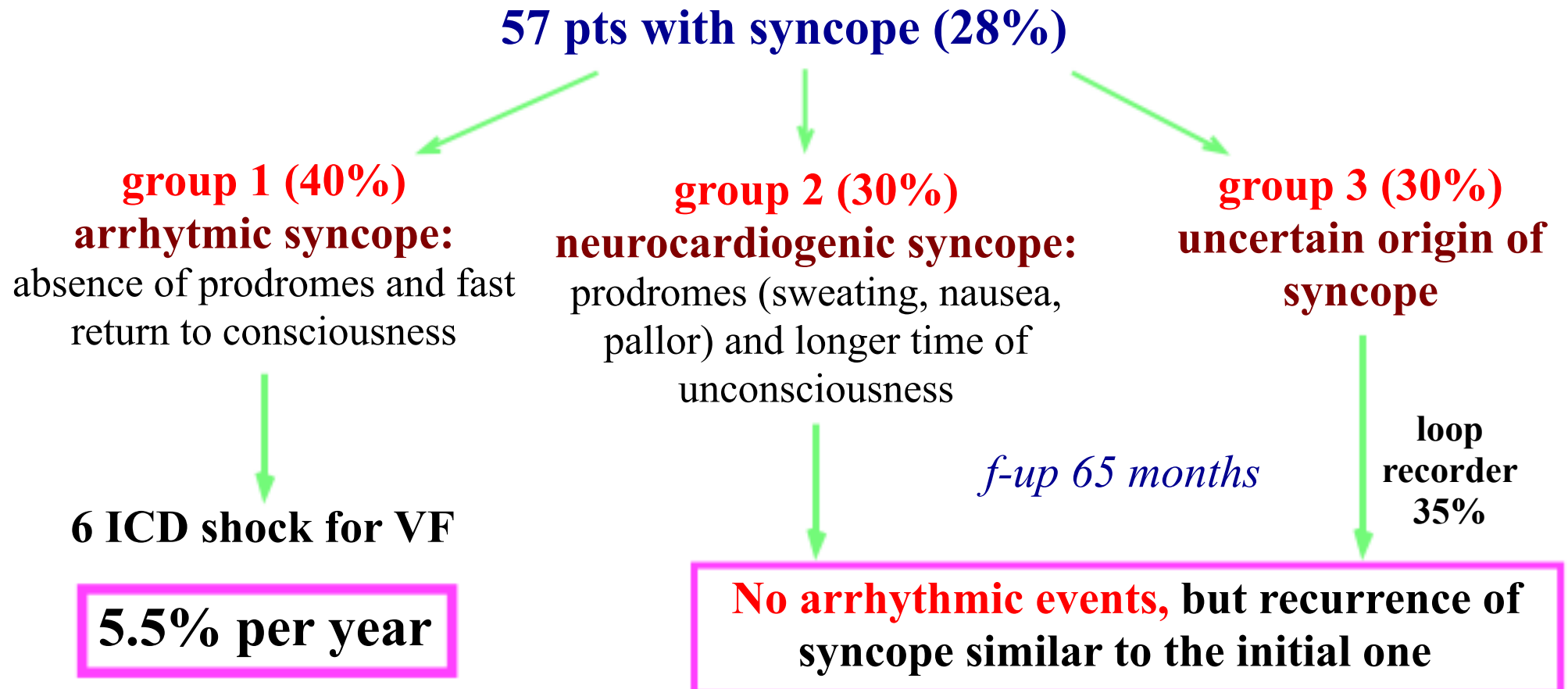
Yutaka Take, MD,* Hiroshi Morita, MD,*[†] Norihisa Toh, MD,* Nobuhiro Nishii, MD,*
Satoshi Nagase, MD,* Kazufumi Nakamura, MD,* Kengo F. Kusano, MD,* Tohru Ohe, MD, FHRS,[†]
Hiroshi Ito, MD*
Heart Rhythm 2012;9:752–759

Yutaka Take, MD,* Hiroshi Morita, MD,*[†] Norihisa Toh, MD,* Nobuhiro Nishii, MD,*
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Hiroshi Ito, MD* Heart Rhythm 2012;9:752–759



Syncope in Brugada syndrome patients: Prevalence, characteristics, and outcome

Sacher F, et al, Heart Rhythm 2012; 9:1272–1279



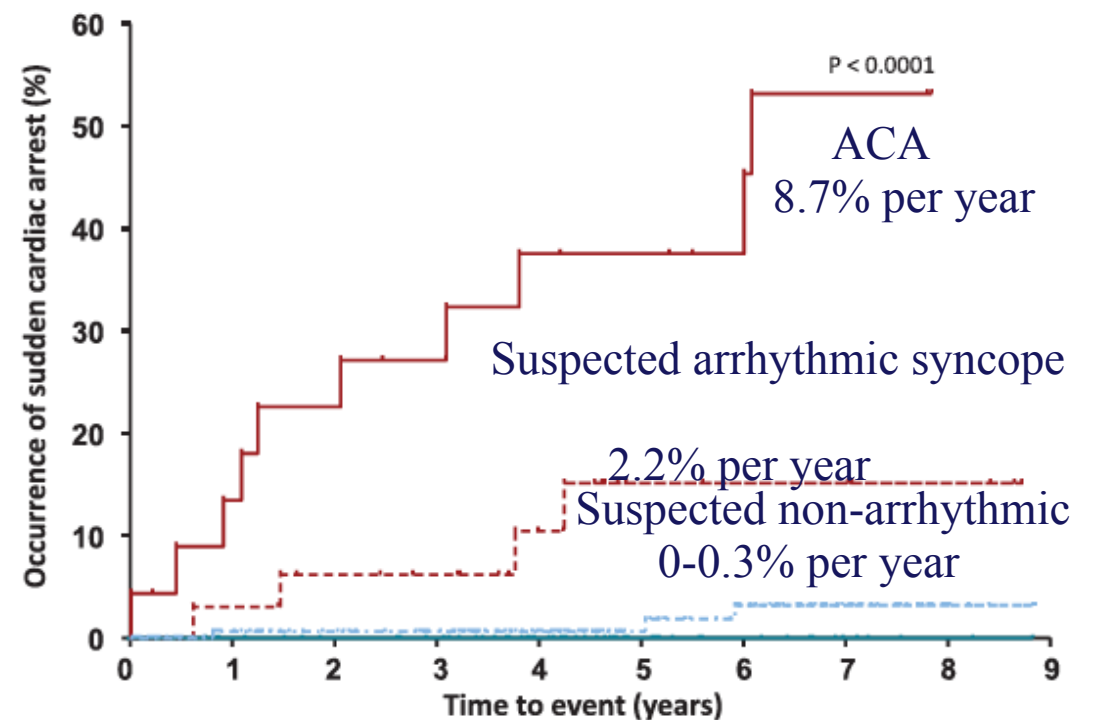
Syncope in Brugada syndrome: Prevalence, clinical significance, and clues from history taking to distinguish arrhythmic from nonarrhythmic causes ^e ^{CP}

Louise R.A. Olde Nordkamp, MD, ^{*} Arja S. Vink, MD, ^{*} Arthur A.M. Wilde, MD, PhD, ^{*} Freek J. de Lange, MD, PhD, ^{*} Jonas S.S.G. de Jong, MD, ^{*} Wouter Wieling, MD, PhD, [†] Nynke van Dijk, MD, PhD, [‡] Hanno L. Tan, MD, PhD ^{*}

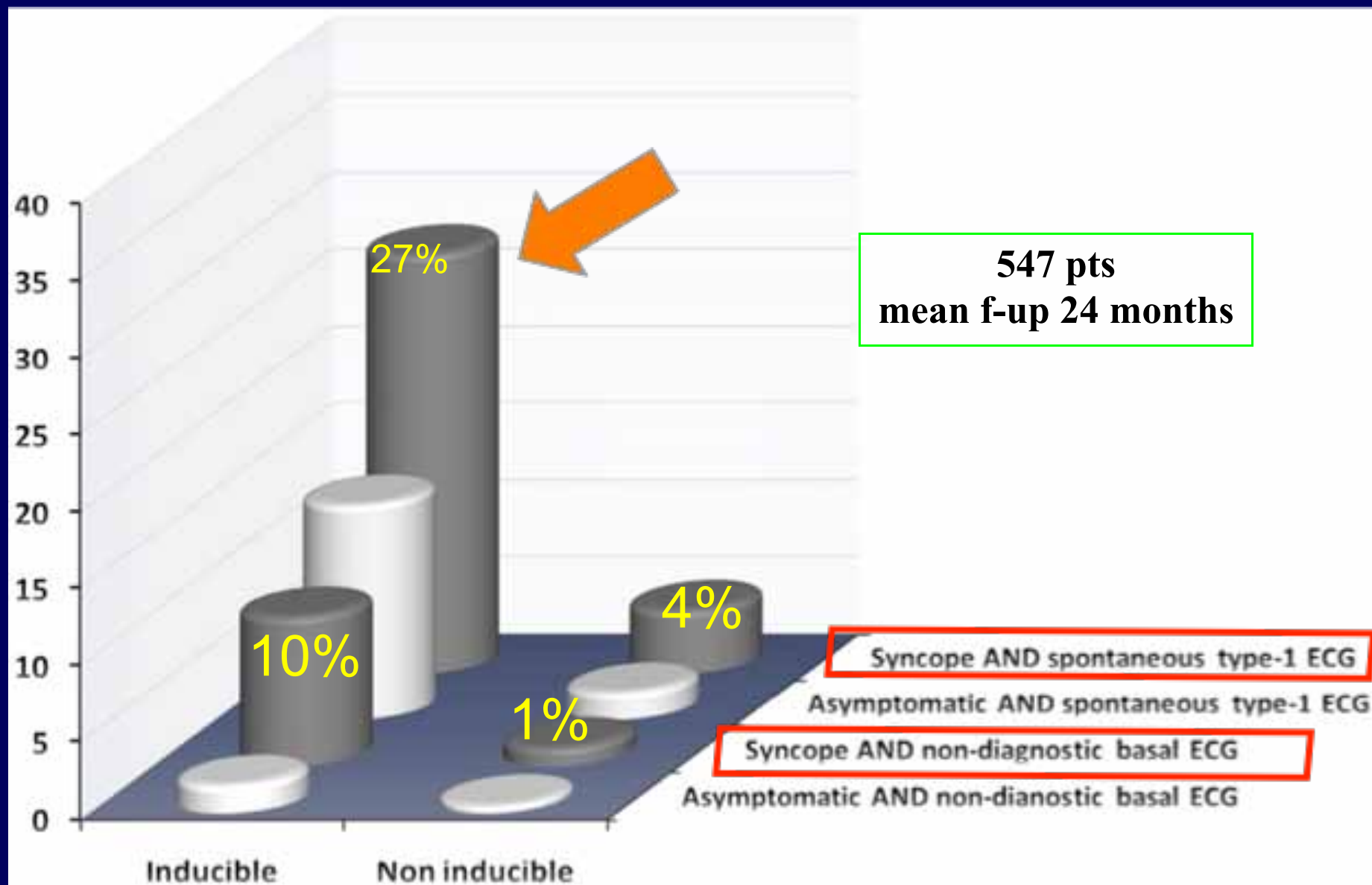
Heart Rhythm 2015;12:367–375

Occurrence of cardiac arrest during follow-up

342 pts, 100 with syncope
median f-up 54 months



Aborted cardiac arrest	23 (0)	20 (13.5)	18 (22.6)	16 (27.1)	13 (37.5)	12 (37.5)	10 (37.5)	7 (53.2)	5 (53.2)	5 (53.2)
Suspected arrhythmic syncope	33 (0)	33 (3.0)	30 (6.2)	28 (6.2)	21 (10.4)	14 (15.1)	13 (15.1)	13 (15.1)	9 (15.1)	6 (15.1)
Suspected non-arrhythmic syncope	67 (0)	65 (0)	61 (0)	56 (0)	43 (0)	28 (0)	20 (0)	14 (0)	11 (0)	8 (0)
Asymptomatic	201 (0)	159 (0.6)	144 (0.6)	132 (0.6)	106 (0.6)	82 (0.6)	69 (3.2)	53 (3.2)	35 (3.2)	31 (3.2)

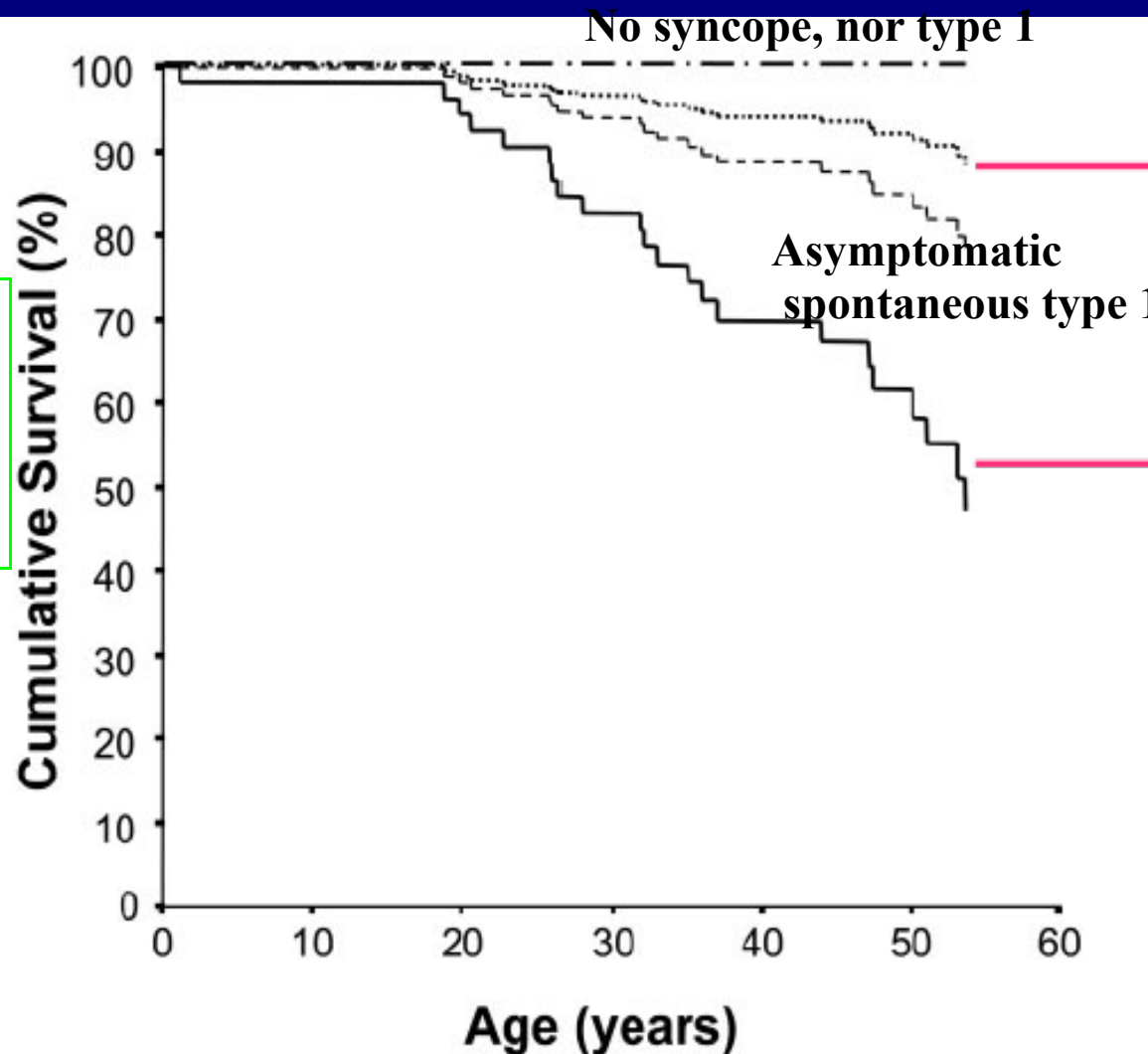


Natural History of Brugada Syndrome

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

Italian
Registry
200 pts



Circulation 2002;105:1342

Syncope +
induced type 1

Syncope +
spontaneous
type 1

**HR 6.4 for risk
of cardiac arrest**

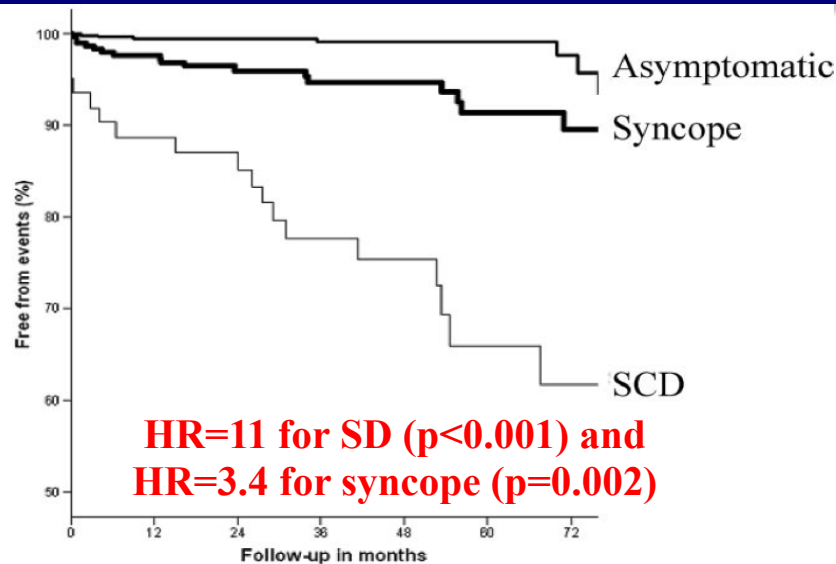
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V. Probst, C. Veltmann, L. Eckardt, P. G. Meregalli, F. Gaita, H. L. Tan, D. Babuty, F. Sacher, C. Giustetto, E. Schulze-Bahr, M. Borggrefe, M. Haissaguerre, P. Mabo, H. Le Marec, C. Wolpert and A. A.M. Wilde

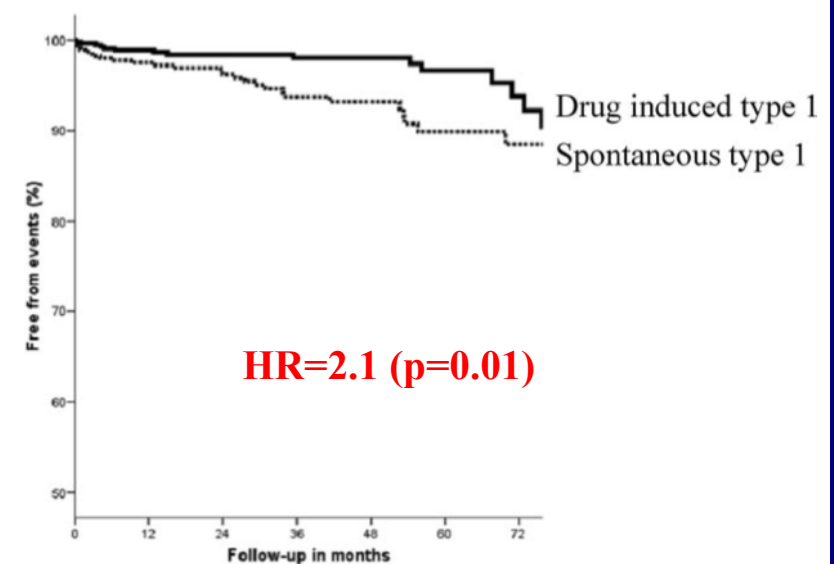
Circulation 2010;121: 635

Symptoms and spontaneous type 1 ECG were predictors of arrhythmic events

1029 pz - median f-up 32 months



	0	12	24	36	48	60	72
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	0	12	24	36	48	60	72
type1	468	350	269	200	135	88	58
no type 1	561	453	349	259	188	112	60

How we treat Brugada patients

1. aSD

ICD

if still arrhythmic events: add HQ

2. unexplained
SYNCOPE

EPS +

ICD

EPS -

Follow-up/loop recorder +/- HQ

Spontaneous
type 1 ECG

EPS +

HQ

EPS +

ICD

EPS -

F-up

3. neurally mediated
SYNCOPE /
ASYMPTOMATIC

Drug-induced
type 1

12 lead Holter:
Spontaneous type 1

NO

F-up

yes