Prognostic role of syncope in patients with Brugada Syndrome

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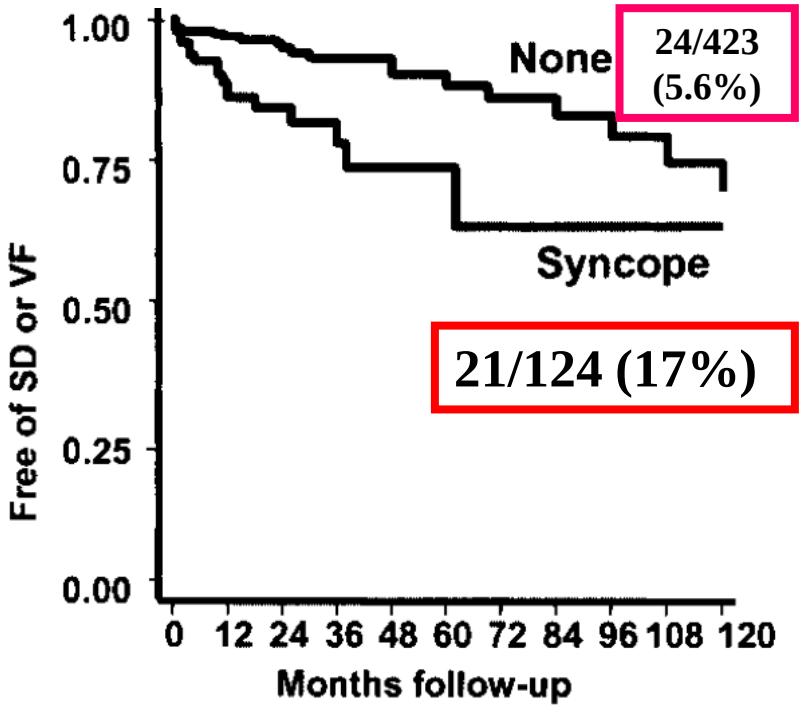
Syncope is a predictor of arrhythmic events

547 pts, mean f-up: 24±32 months

Probability of Sudden Death or Ventricular Fibrillation During Follow-up

	Multivariate Analysis		
	azard Ratio	95% CI	*P*
Inducible	5.88	2.0–16.7	0.0001
Noninducible	1	. . .	. . .
Syncope	2.50	1.2–5.3	0.017
No syncope	1	. . .	. . .

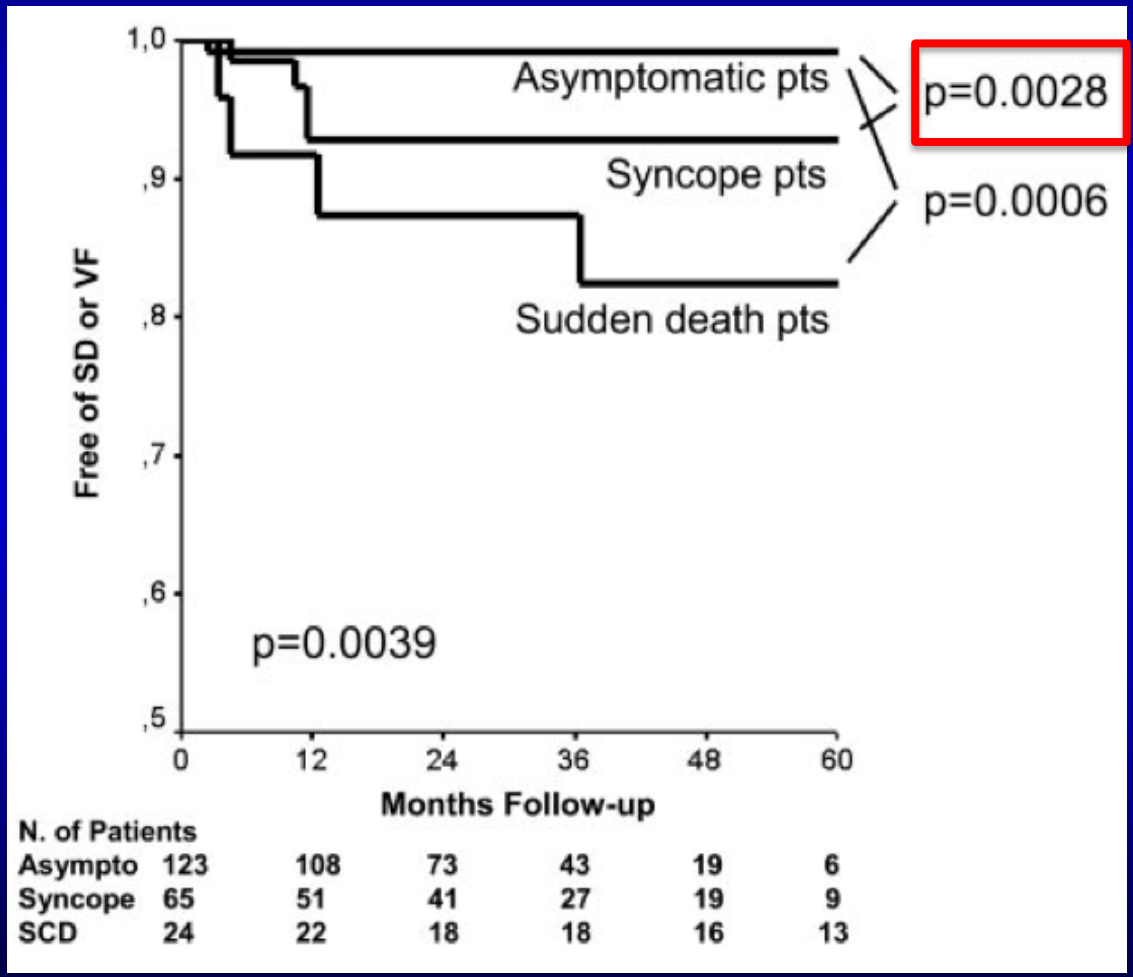


Multivariate analysis identified history of syncope as predictor of sudden death or ventricular fibrillation at f-up.

Brugada et al. Circulation 2003;108:3092-3096

Syncope is a predictor of arrhythmic events

212 pts, 40 months f-up, 4% arrhythmic events (overall incidence)



1/123 (1%) asymptomatic

4/65 (6%) syncope

Previous history of **syncope** was a predictor of adverse outcome

Eckardt et al. Circulation 2005;111:257-263

Clinical risk factors in individuals with Brugada ECG: a meta-analysis

19 prospective studies

1545 patients

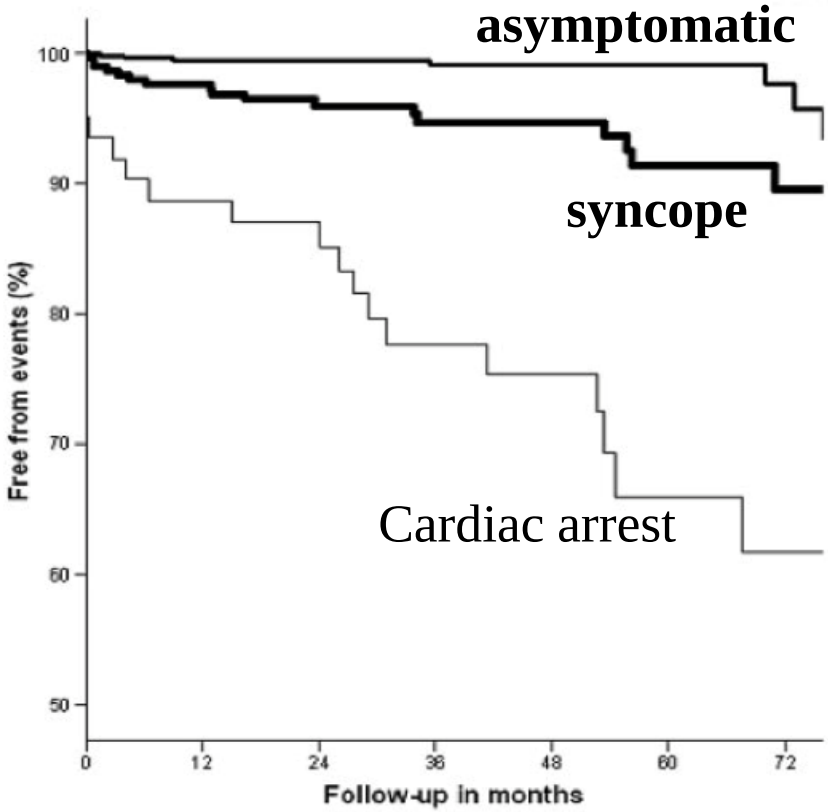
History of syncope or SD	RR = 3.51
Spontaneous type 1 ECG	RR = 4.65
Men (*vs* women)	RR = 3.47
Family history of SCD	RR = 1.04
SCN5A mutation	RR = 0.60
Inducible at EP study	RR = 1.88

(except the study of Brugada et al, Circulation 2003)

Gehi AK et al. J Cardiovasc Electrophysiol 2006, 17:577-583

Syncope is a predictor of arrhythmic events

1029 pts, 32 months f-up, 5% arrhythmic events (overall incidence)



	0	12	24	36	48	60	72
group A	82	54	47	36	29	18	15
group B	313	244	192	148	99	73	49
group C	654	505	379	275	195	109	54

10/654 (1.5%) **0.5% per year**

19/313 (6%) **1.9% per year**

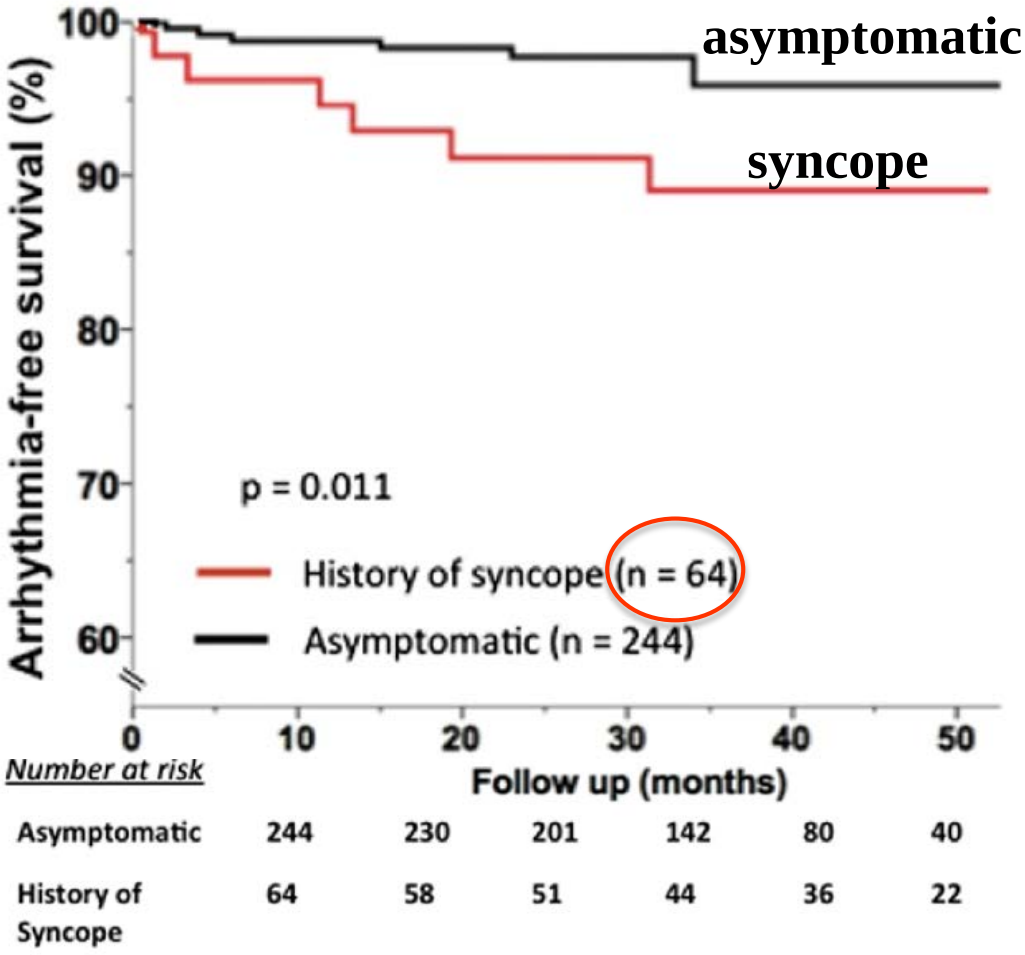
p=0.002
HR 3.4

Time to first event was shorter in the syncope group patients than in the asymptomatic

Probst et al. FINGER Registry, Circulation 2010; 121:635-643

Syncope is a predictor of arrhythmic events

308 pts, 34 months f-up, 4.5% arrhythmic events (overall incidence)



7/244 (2.9%)

7/64 (10.9%)

p=0.011

PRELUDE Registry, J Am Coll Cardiol 2012; 59:37–45

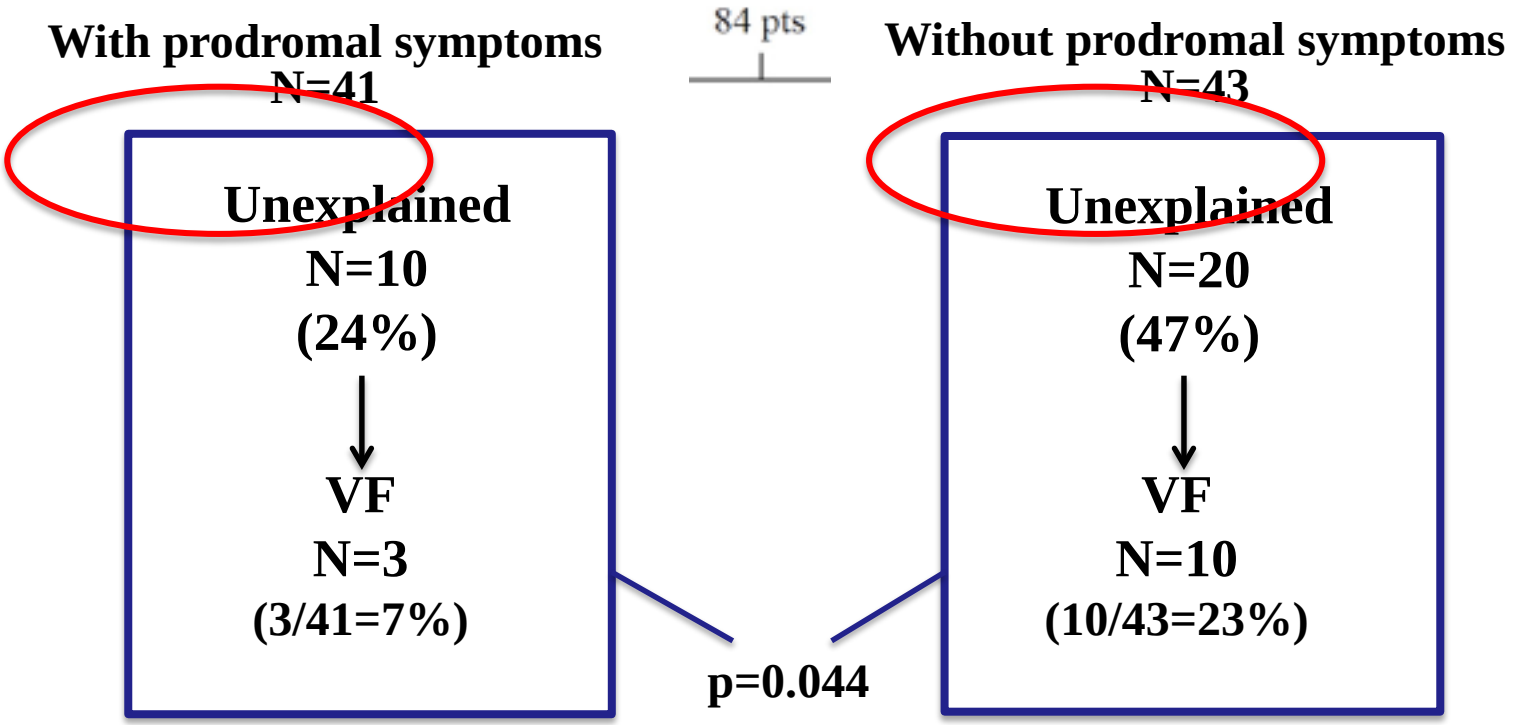
2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Recommendations	Class[a]	Level[b]	Ref.[c]
The following lifestyle changes are recommended in all patients with a diagnosis of Brugada syndrome: (a) Avoidance of drugs that may induce ST-segment elevation in right precordial leads (http://www.brugadadrugs.org) (b) Avoidance of excessive alcohol intake and large meals (c) Prompt treatment of any fever with antipyretic drugs.	I	C	This panel of experts
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	451
ICD implantation should be considered in patients with a spontaneous diagnostic type I ECG pattern and history of syncope.	IIa	C	451
Quinidine or isoproterenol should be considered in patients with Brugada syndrome to treat electrical storms.	IIa	C	453
Quinidine should be considered in patients who qualify for an ICD but present a contraindication or refuse it and in patients who require treatment for supraventricular arrhythmias.	IIa	C	454
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	120
Catheter ablation may be considered in patients with a history of electrical storms or repeated appropriate ICD shocks.	IIb	C	201, 455

Identification of high-risk syncope related to ventricular fibrillation in patients with Brugada syndrome

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



f-up 48 months

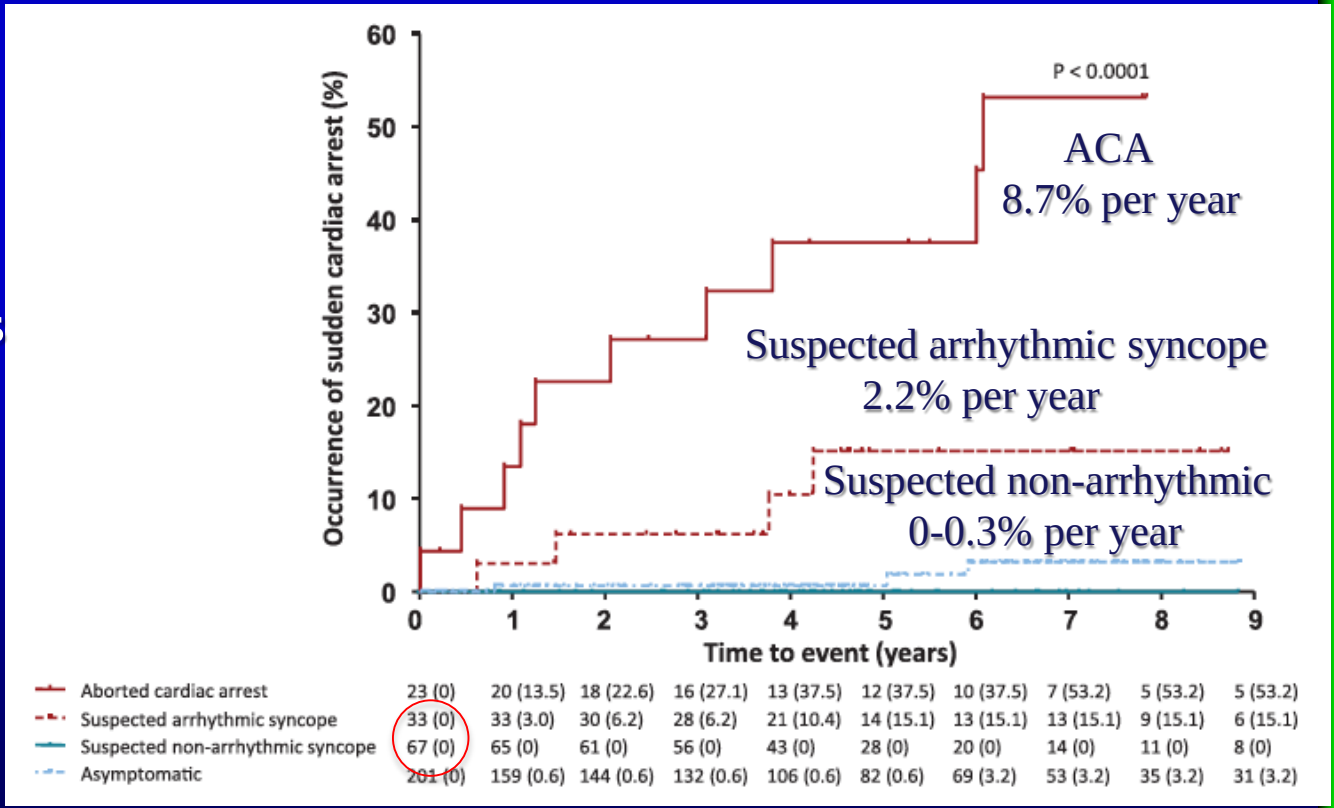
Syncope in Brugada syndrome: Prevalence, clinical significance, and clues from history taking to distinguish arrhythmic from nonarrhythmic causes

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
median f-up 54 months

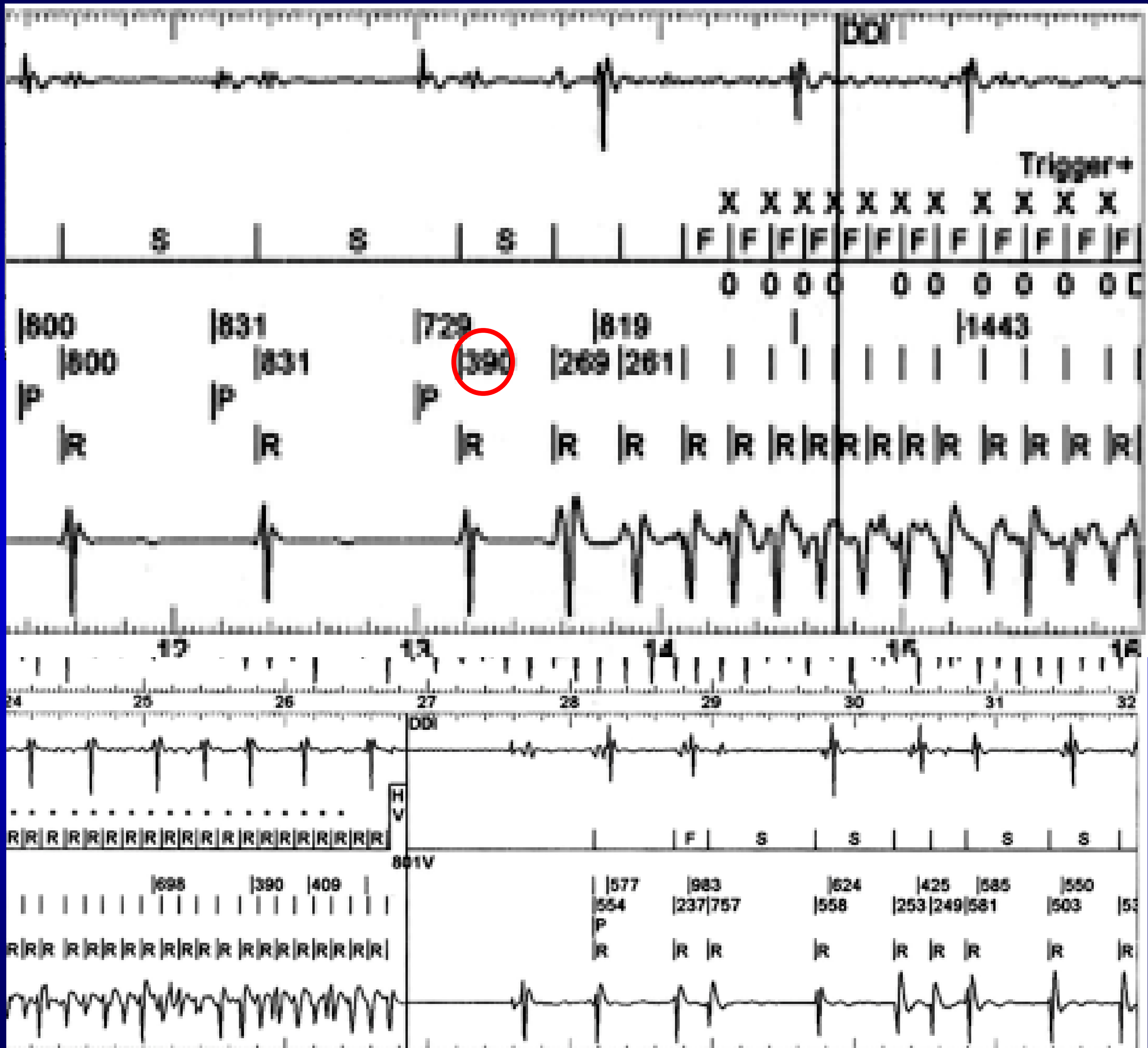


31 years-old man

- No family history of sudden death
- Syncope with brief prodromes whatching TV
- In the emergency room, syncope during ECG monitoring, with evidence of VF
- ECG: type 1 Brugada pattern
- ICD implant

2 years later…

- 3 episodes of pre-syncope after meals
- Once, after a heavy meal, pre-syncope → ICD intervention


DDI
Trigger+
|800
|800
|831
|831
|729
|390
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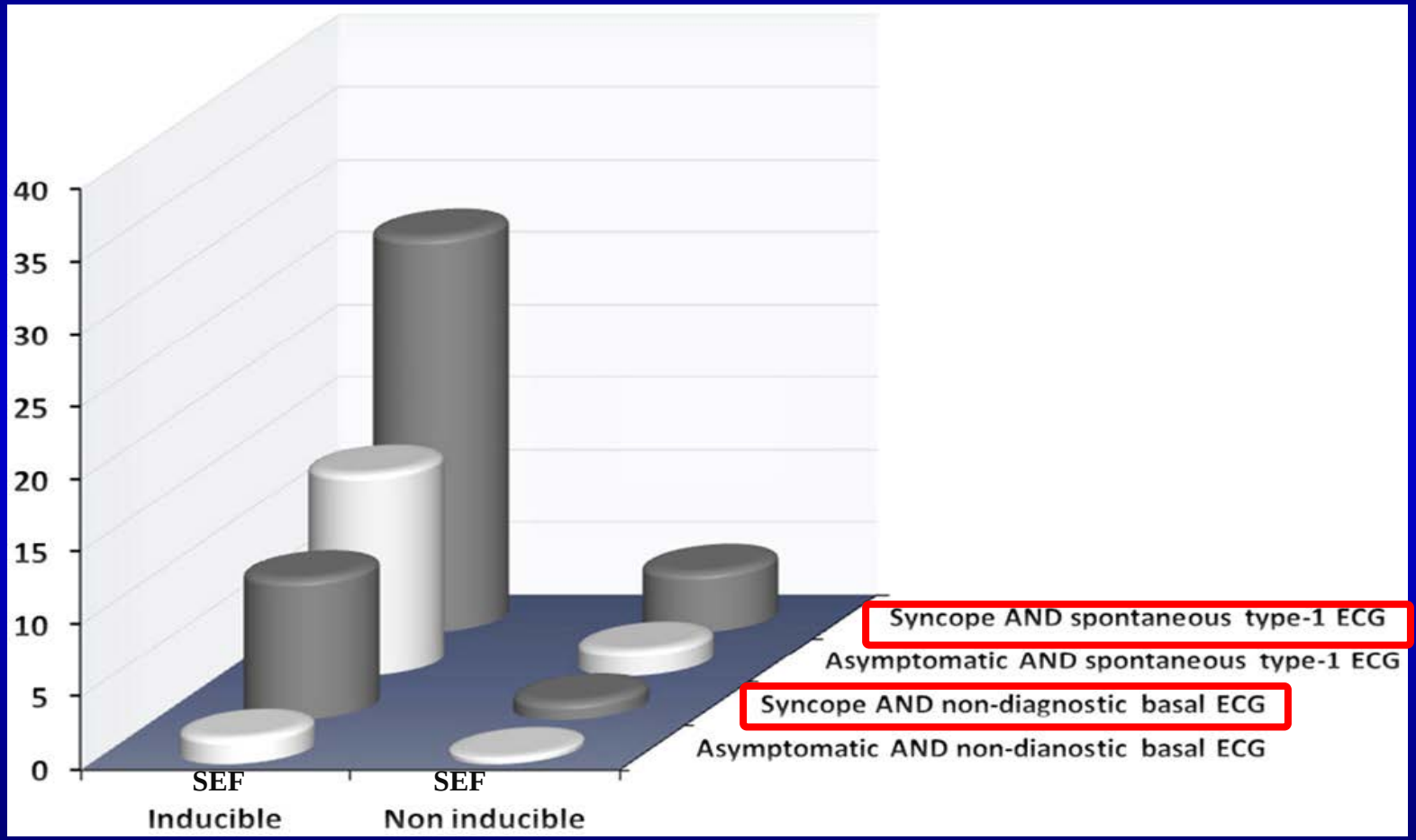
25
26
27
28
29
30
31
32
|698
|390
|409
|577
|554
|983
|237|757
|624
|558
|425
|585
|253|249|581
|550
|503

Role of EP-study in Brugada patients with syncope

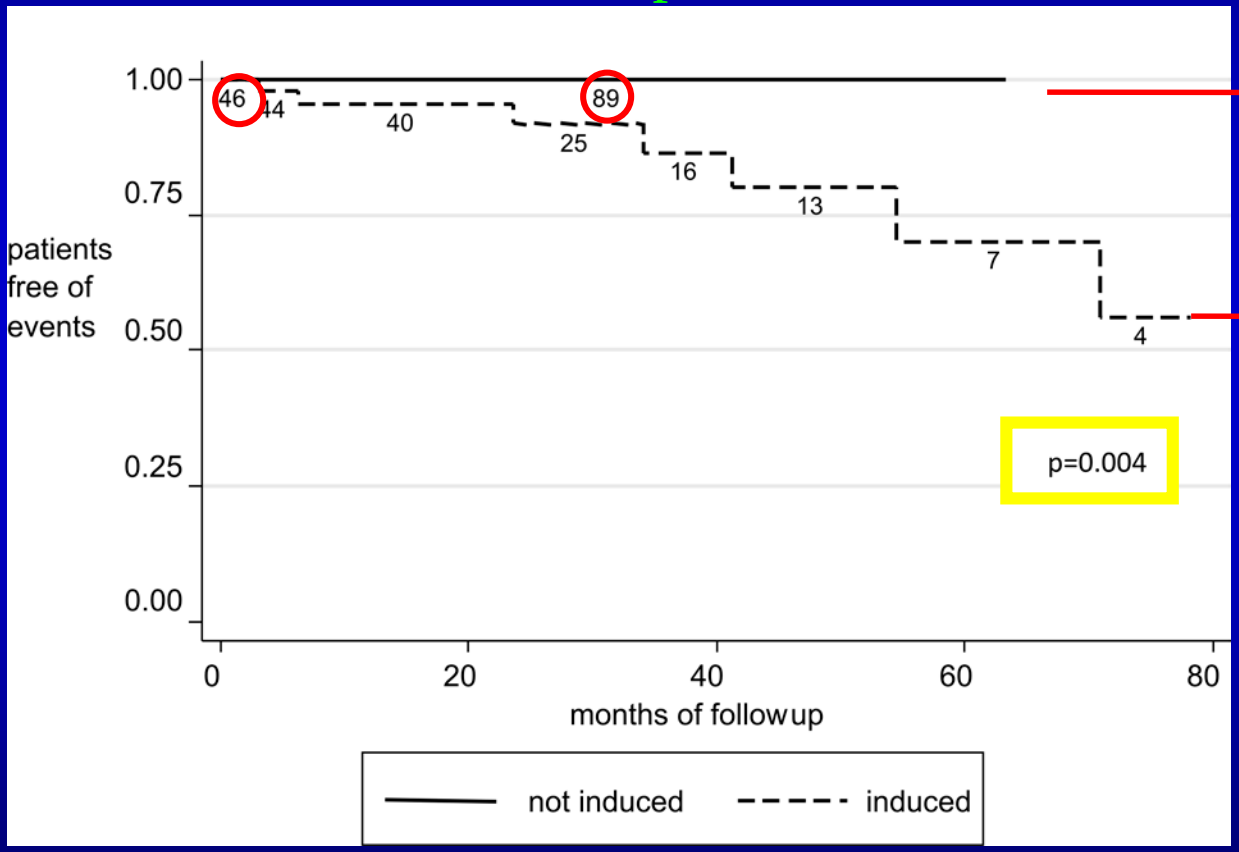


Benito, Brugada et al. Progress in Cardiovascular Diseases, 2008; 51

Role of EP-study in Brugada patients with syncope

135 pts undergoing EPS

mean f-up =30 ±21 months



0/ 89

7/ 46 (15%)

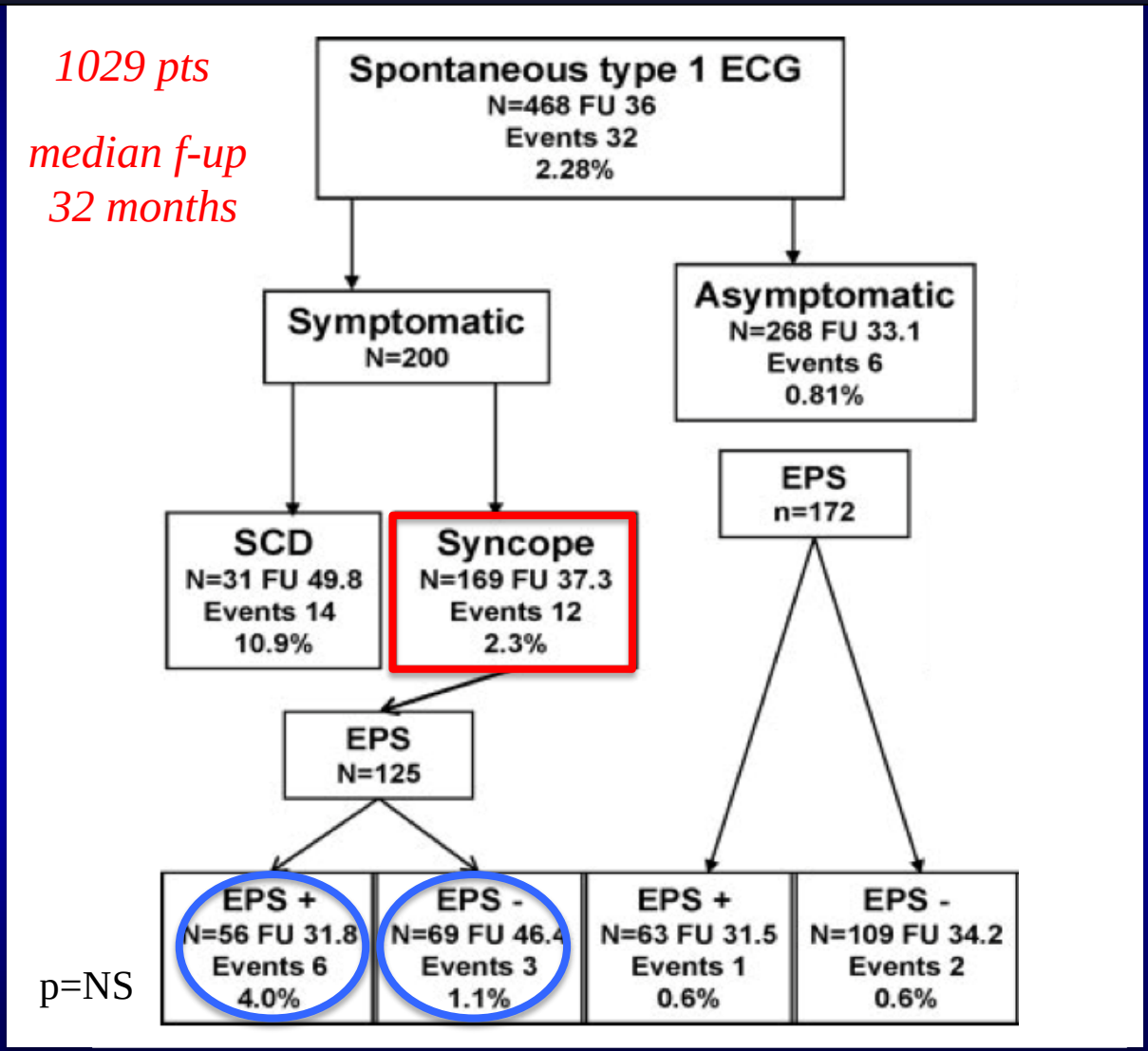
NO EVENTS IN PTS WITH NEGATIVE EPS

Giustetto, Gaita et al. Europace 2009; 11: 507-13

Role of EP-study in Brugada patients with syncope

1029 pts

median f-up 32 months



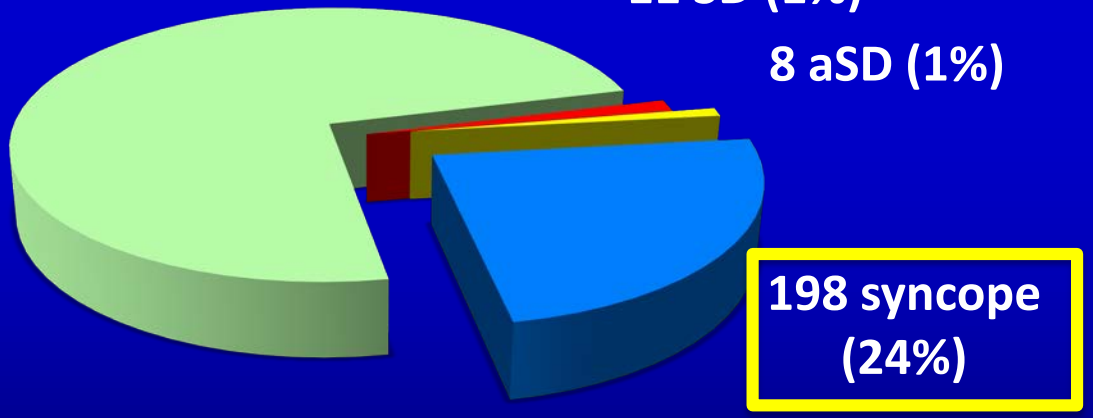
p=NS

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

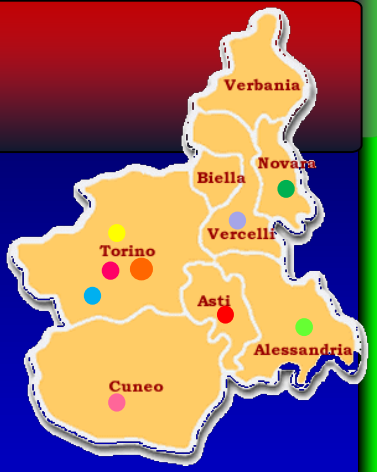
Brugada Piedmont Registry 2001-2014

825 consecutive Brugada patients

(mean age 45±14 years; 78% males)



Results



825 consecutive Brugada patients

(mean age 45±14 years; 78% males)

608 asymptomatic

11 SD

8 aSD

198 syncope

neurally-mediated syncope
118 (60%)

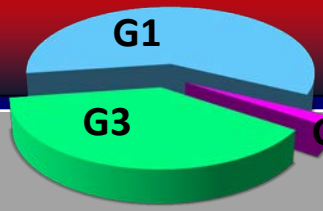
arrhythmic syncope
4 (2%)

unexplained syncope
76 (38%)

Results: syncopal features

	Group 1 n=118	Group 2 n=4	Group 3 n=76	G1 vs G2	G1 vs G3	G2 vs G3
Prodromes (nausea/vomiting, diaphoresis, pallor, flushing, dizziness, blurred vision, palpitations)	91%	25%	40%	**0.002**	**<0.001**	0.94
Fever	14%	0	16%	0.97	0.82	0.89
Standing / postural changes	63%	0	43%	**0.03**	**0.03**	0.38
After strong emotion/ trauma	14%	0	7%	0.97	0.20	0.60
After micturition, venipuncture, seeing blood, intense pain	40%	0	0	0.28	**<0.001**	0.48
After meal/drink	13%	50%	22%	0.20	0.12	0.51
During driving	1%	0	13%	0.99	**<0.001**	0.66
Incontinence	3%	0	8%	0.19	0.17	0.70
Agonal respiration	0	25%	4%	0.07	0.11	0.48
With trauma	8%	0	24%	0.75	**0.01**	0.62

Results: patients' features



	Group 1 n=118	Group 2 n=4	Group 3 n=76	G1 vs G2	G1 vs G3	G2 vs G3
Age at diagnosis (years)	45±13	50±17	44±14	0.46	0.61	0.41
Age at 1st syncope	33±16	47±19	36±15	0.13	0.19	0.22
Men	70%	75%	83	0.72	0.07	0.79
Spontaneous type 1 ECG	31%	100%	66%	**0.02**	**<0.001**	0.38
Recurrent syncope	54%	75%	21%	0.76	**<0.001**	0.07
Genetic test	36%	50%	54%	0.95	**0.02**	0.72
SCN5A/SCN1B mutation	36%	0	27%	0.78	0.53	0.99
PR interval (ms)	185±30	150±14	169±29	**0.02**	**<0.001**	0.20
Supraventricular arrhythmias	10%	25%	9%	0.90	0.98	0.86
Tilt test	23%	0	13%	0.64	0.14	0.99
Positive tilt test	44%		10%	-	0.12	-
EPS	60%	75%	74%	0.94	0.08	0.60
Positive EPS	34%	67%	45%	0.58	0.29	0.88
Hydroquinidine	10%	25%	13%	0.90	0.68	0.94
Loop recorder	11%	0	18%	0.90	0.22	0.79
ICD	19%	100%	57%	**<0.001**	**<0.001**	0.23
Documented NSVT	4%	0	16%	0.48	**0.02**	0.89
Mean follow-up (months)	58±46	106±151	67±42	0.07	0.17	0.14

Results: follow-up

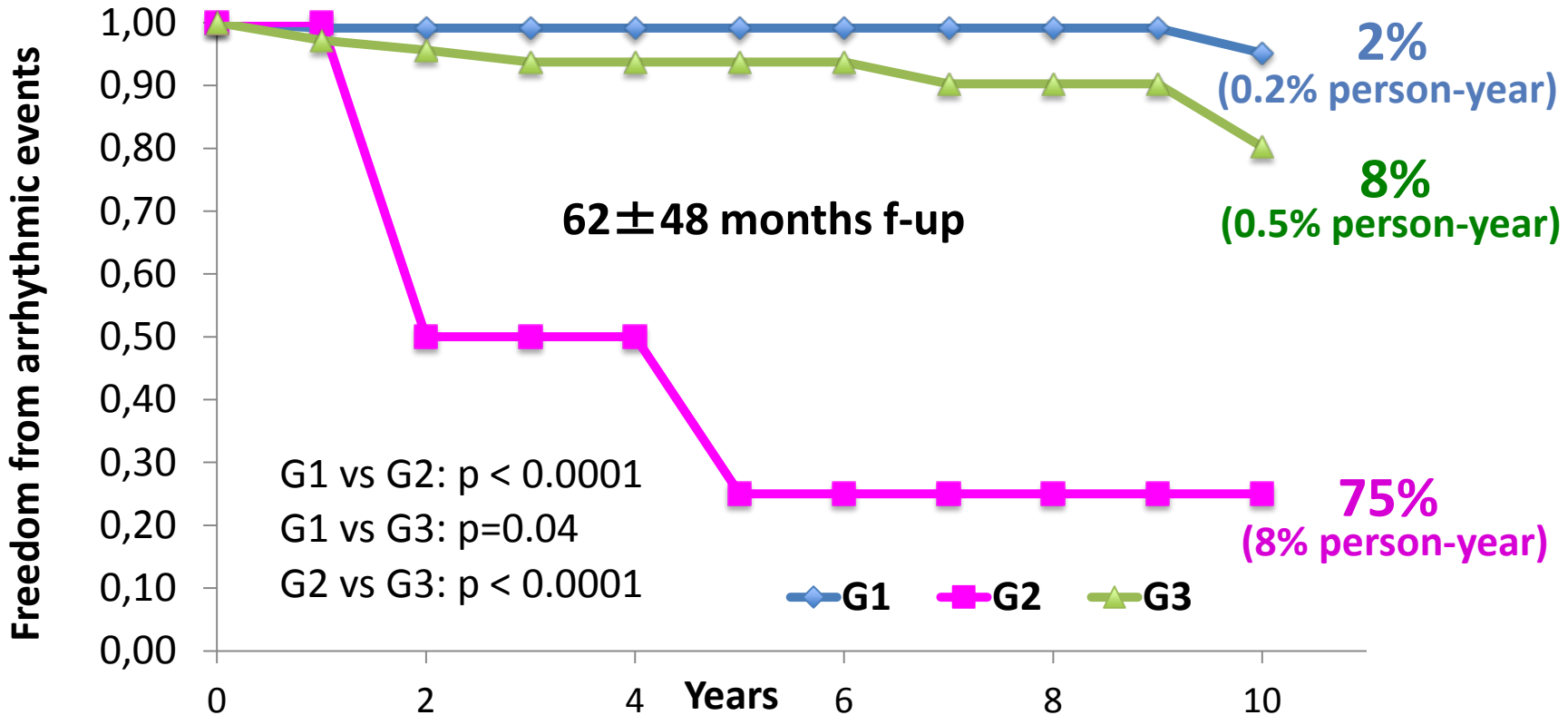
Mean follow-up of 62±48 months

11 arrhythmic events
(6%, 1 per 100 person-year)

in the overall population, all in patients with ICD

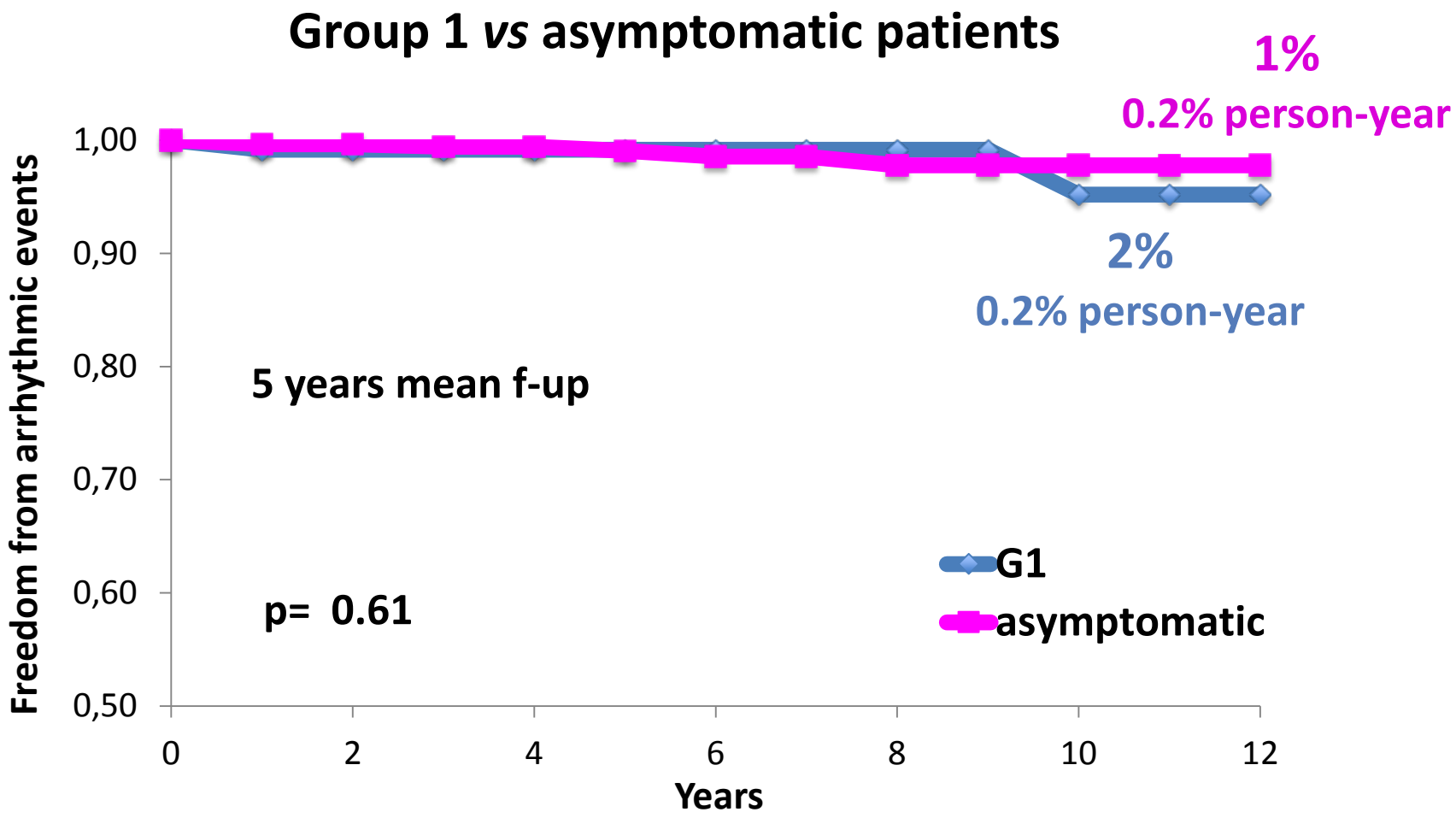
Results: arrhythmic events at follow-up

118 neurally-mediated (G1) *vs* 4 arrhythmic (G2) *vs* 76 unexplained (G3) syncope



G1	118	107	87	68	51	40	34	29	26	25
G2	4	4	2	2	2	1	1	1	1	1
G3	76	71	62	51	46	39	31	27	20	13

Results: arrhythmic events at follow-up



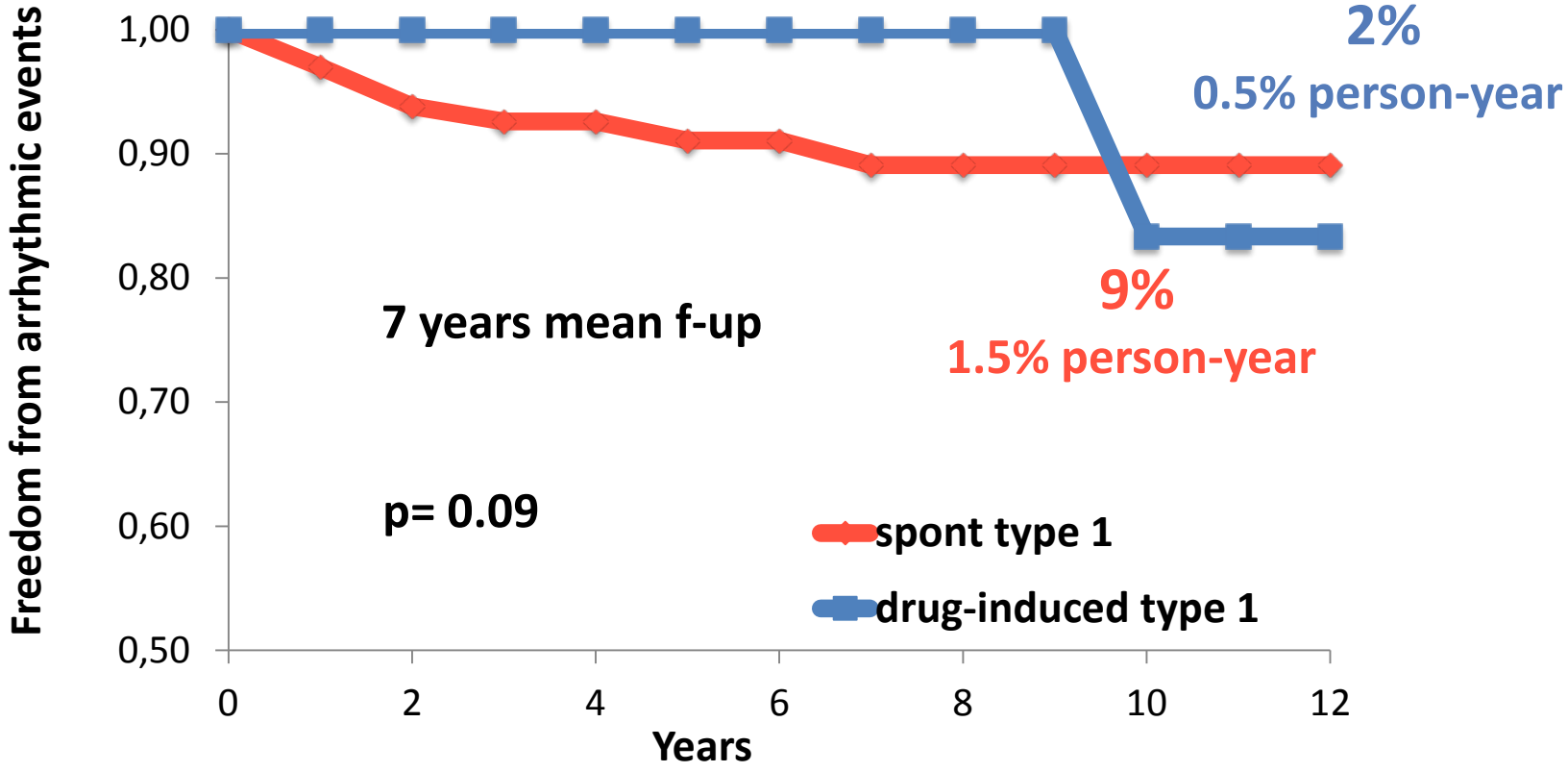
G1	118	107	87	68	51	40	34	29	26	25	18	13
Asympt	608	518	425	361	286	192	152	129	110	70	51	36

51 years-old man

- No family history of sudden death
- History of recurrent syncope after meals
- Spontaneous type 1 Brugada pattern at ECG
- Positive carotid sinus massage
- VF induced at EP study, ICD implant
- After 4 months he had recurrence of syncope after meal and the ICD documentedVF interrupted by shock.

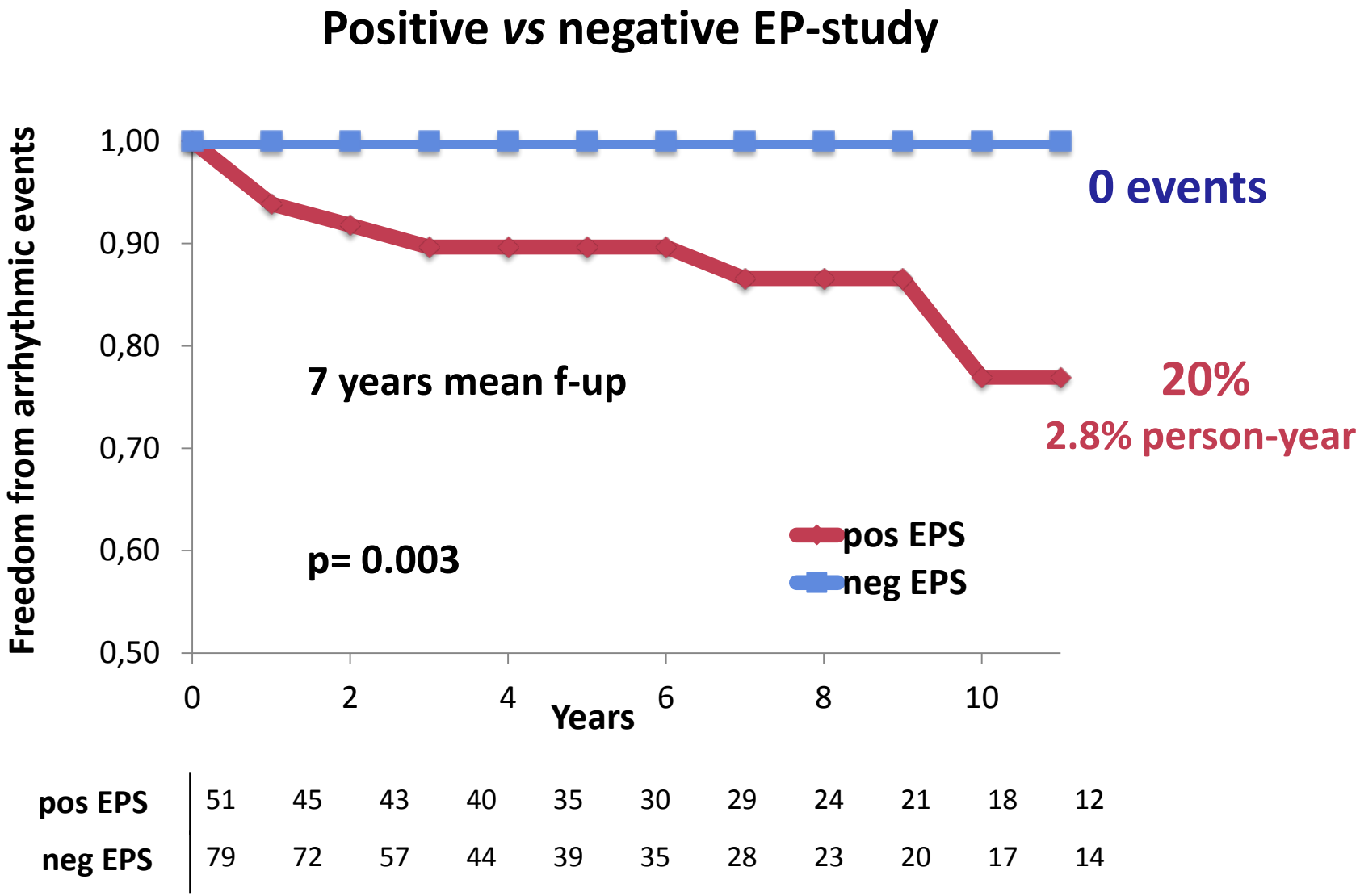
Results: arrhythmic events at follow-up

Spontaneous *vs* drug-induced type 1 ECG

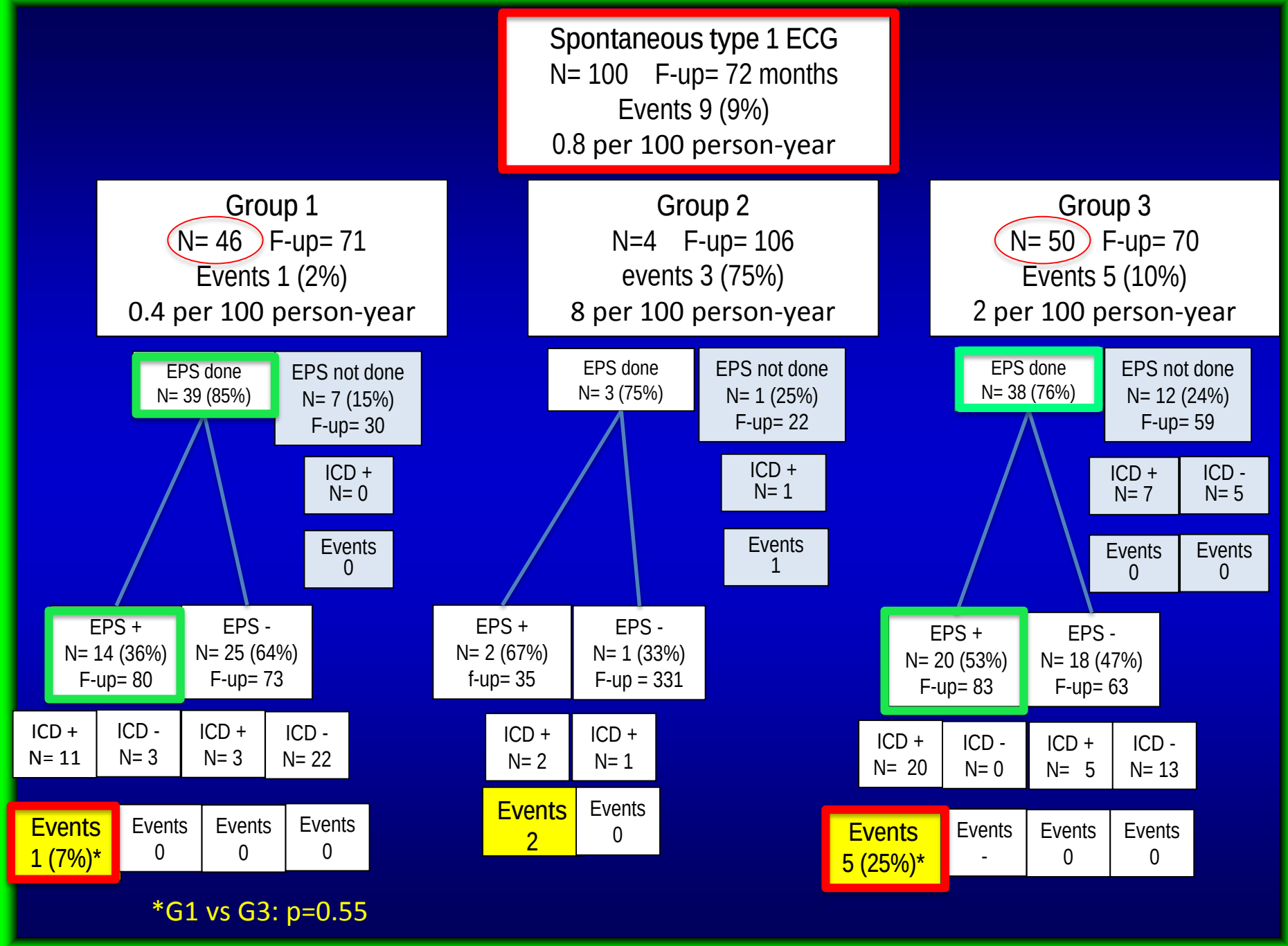


spont type 1	100	92	77	65	60	52	46	40	33	28	23	17
drug-induced	98	90	75	58	41	30	22	18	15	12	6	4

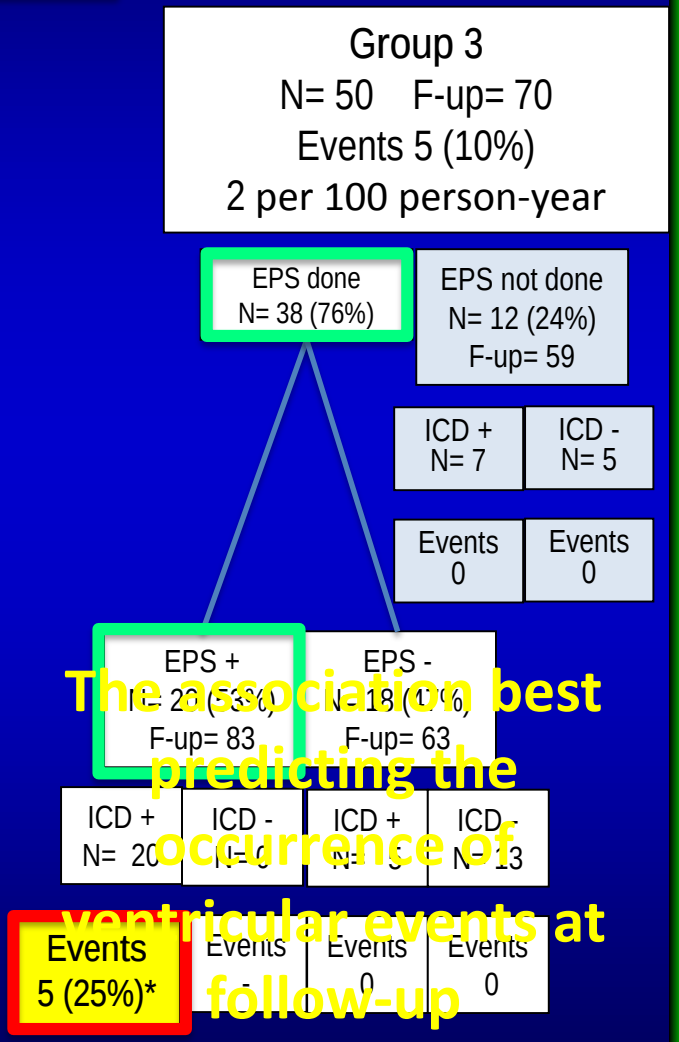
Results: electrophysiological (EP) study



pos EPS	51	45	43	40	35	30	29	24	21	18	12
neg EPS	79	72	57	44	39	35	28	23	20	17	14


Spontaneous type 1 ECG
N= 100 F-up= 72 months
Events 9 (9%)
0.8 per 100 person-year
Group 1
N= 46 F-up= 71
Events 1 (2%)
0.4 per 100 person-year
EPS done
N= 39 (85%)
EPS not done
N= 7 (15%)
F-up= 30
ICD +
N= 0
Events
0
EPS +
N= 14 (36%)
F-up= 80
EPS -
N= 25 (64%)
F-up= 73
ICD +
N= 11
ICD -
N= 3
ICD +
N= 3
ICD -
N= 22
Events
1 (7%)*
Events
0
Events
0
Events
0
Group 2
N=4 F-up= 106
events 3 (75%)
8 per 100 person-year
EPS done
N= 3 (75%)
EPS not done
N= 1 (25%)
F-up= 22
ICD +
N= 1
Events
1
EPS +
N= 2 (67%)
f-up= 35
EPS -
N= 1 (33%)
F-up = 331
ICD +
N= 2
ICD +
N= 1
Events
2
Events
0
Group 3
N= 50 F-up= 70
Events 5 (10%)
2 per 100 person-year
EPS done
N= 38 (76%)
EPS not done
N= 12 (24%)
F-up= 59
ICD +
N= 7
ICD -
N= 5
Events
0
Events
0
EPS +
N= 20 (53%)
F-up= 83
EPS -
N= 18 (47%)
F-up= 63
ICD +
N= 20
ICD -
N= 0
ICD +
N= 5
ICD -
N= 13
Events
5 (25%)*
Events
-
Events
0
Events
0
*G1 vs G3: p=0.55

Spontaneous type 1 ECG
N= 100 F-up= 72 months
Events 9 (9%)
0.8 per 100 person-year



The association best predicting the occurrence of ventricular events at follow-up

Therapeutic management and conclusions

***Probably non-arrhythmic* syncope :**
Good prognosis, similar to asymptomatic subjects

Spontaneous type 1 ECG

EPS +

EPS -

hydroquinidine

+

loop recorder

follow-up

***Unexplained* syncope:**
positive EPS is the main predictor of arrhythmic events

EPS +

EPS -

loop recorder