Brugada Syndrome: ICD or not in asymptomatic or patients with "doubtful" syncope?

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Nantes

Case

- 22 years old man
- No medical history
- No familial history of SCD
- First syncope while seated during the lunch
- Few prodroma

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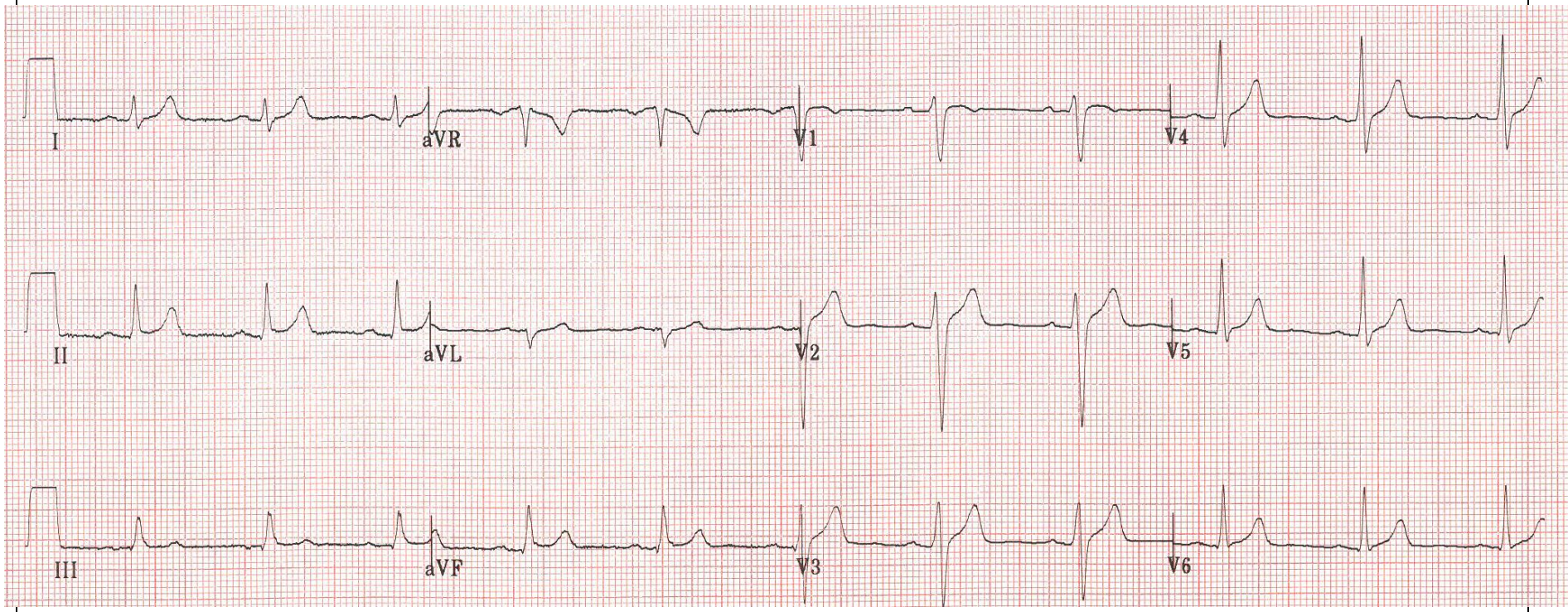
ECG



What exams do you propose?

- 1 Ajmaline challenge
- 2 head up tilt test
- 3 echocardiography
- 4 All the propositions
- 5 Nothing

Results of the exams

- Normal echocargiography
- Positive head up tilt test at 6 min
- Positive ajmaline challenge

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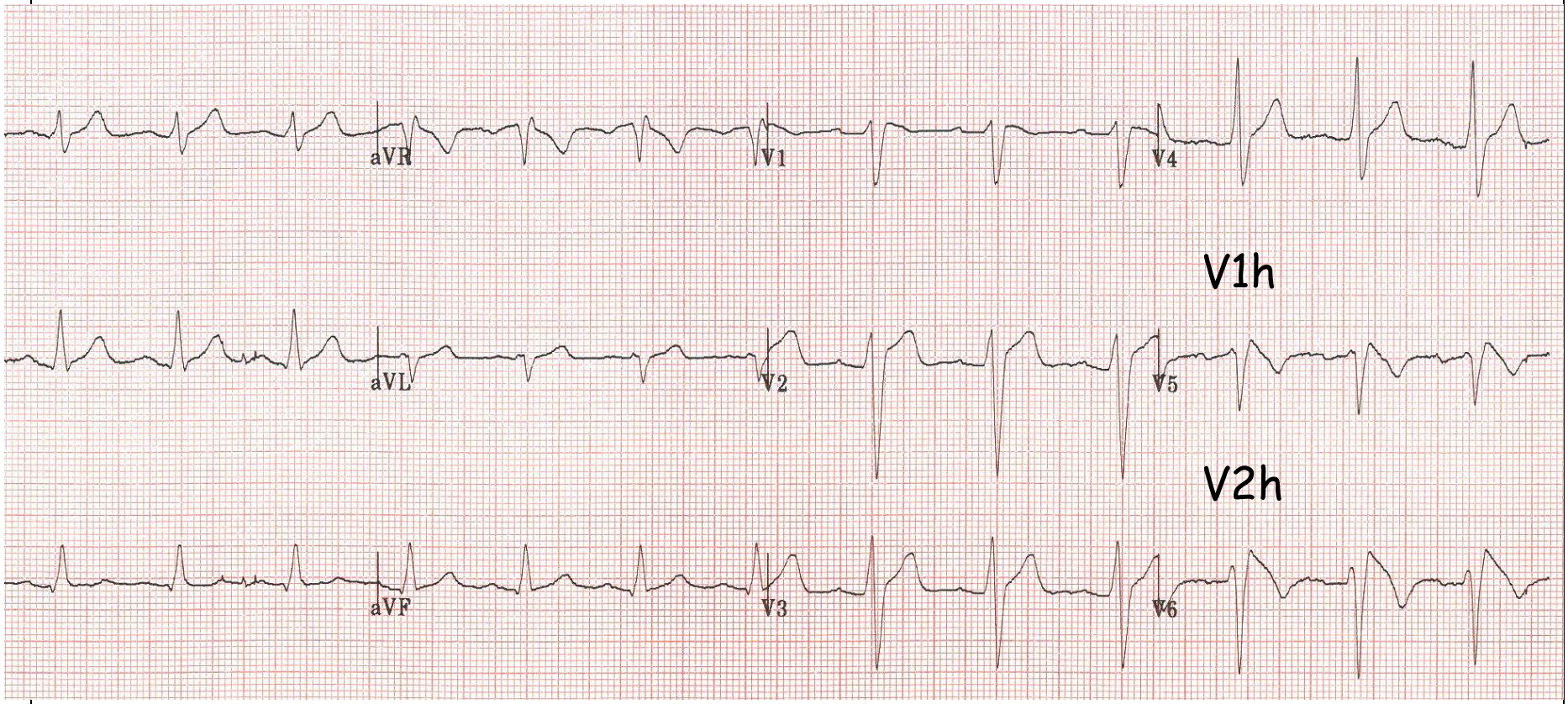
Ajmaline challenge



What is the proportion of patients affected by the Brugada syndrome presenting after syncope?

- 1 5%
- 2 15%
- 3 30%
- 4 50%

	Brugada et al. Circ 2002	Brugada et al. Circ 2003	Priori et al. Circ 2002	Eckardt et al. Circ 2005
No. (men)	334 (255)	547 (408)	200 (152)	212 (152)
Index (men)		294	130 (110)	165(132)
Aborted SCD	71	0	22	24
Syncope	73	124	34	65
Asymptomatic	190	423	144	123
Age at diagnosis, y	42±16	41±15	41±18	45±6
Brugada ECG pattern				
Spontaneous	234 (70%)	391 (71%)	90 of 176 (51%)	125 (59%)
After Class I	100 (30%)	156 (29%)	86 (49%)	87 (41%)
FH of SCD	180 of 334 (54%)	302 of 547 (55%)	26 of 130 (22%)	60 of 212 (28%)
Aborted SCD	23 (38%)	0	na	3 (13%)
Syncope	26 (39%)	na	na	16 (25%)
Asymptomatic	131 (72%)	na	na	41 (33%)
SCN5A				
Screened Index pts	na	na	130	136
Mutation	na	na	28 (22%)	32(24%)
EPS	252	408	86	186
Inducible	130 (52%)	163 (40%)	57 (66%)	93 (50%)
Aborted SCD	44 of 54 (83%)	na	18 (82%)	15 of 22 (68%)
Syncope	41 of 62 (68%)	na	na	40 of 65 (62%)
Asymptomatic	45 of 136 (33%)	na	na	38 of 98 (39%)
ICD	na	177 (32%)	Na	113 (53%)
Follow-up, months	33±39	24±33	34±44	40±50
Aborted SCD	54±54	na	na	83±66
Syncope	26±36	na	na	39±37
Asymptomatic	27±29	na	na	34±52

	Sudden cardiac death	Syncope	Asymptomatic
No.	62	313	654
Male (%)	55 (89%)	238 (76%)	452 (69%)
Age/yrs	43±14	46±14	44±14
Family history of SCD	6 (10%)	63 (20%)	195 (30%)
Spontaneous type 1 (%)	31 (50%)	169 (54%)	268 (41%)
EPS performed (%)	36(58%)	233 (74%)	369 (56%)
Inducible VT/VF	16 (44%)	109 (47%)	137 (37%)
Screened for *SCN5A* mutation	49 (79%)	203 (65%)	398 (60%)
SCN5A mutations	12 (24%)	53 (26%)	120 (30%)
Follow-up, months	55±43	39±28	35±25
Mean event rate per year (%)	7.7	1.87	0.5

Probst, Circ 2010

Is there a difference in the frequency of HUT between Brs patients and general population?

- 1 Brs=general population
- 2 Brs>general population
- 3 general population>Brs

Frequency of positive HUT

- General population: 10%
- Neurally mediated syncope: 67%
- Brs 35%
  - ✓Patients with documented VT/VF 50%
  - ✓Patients with syncope 26%
  - ✓Asymptomatic patients 31%

Yokokawa, JCE 2010

Complex relation between vagal tone and the Brugada syndrome

- Vagal tone is high in Brugada patients
- Vagal syncope are frequent in Brugada patients
- Vagal tone increase the ST segment elevation
  - ✓ ST segment elevation occurred in 70% of the Brs patients during positive HUT
- ST segment elevation and tachyarrhythmias more often occur during rest or sleep when the vagal tone is predominant
- Heart rate variability analysis revealed an increased vagal tone preceding VF episodes

Kasanuki H, Circ 1997; Yokokawa, JCE 2010

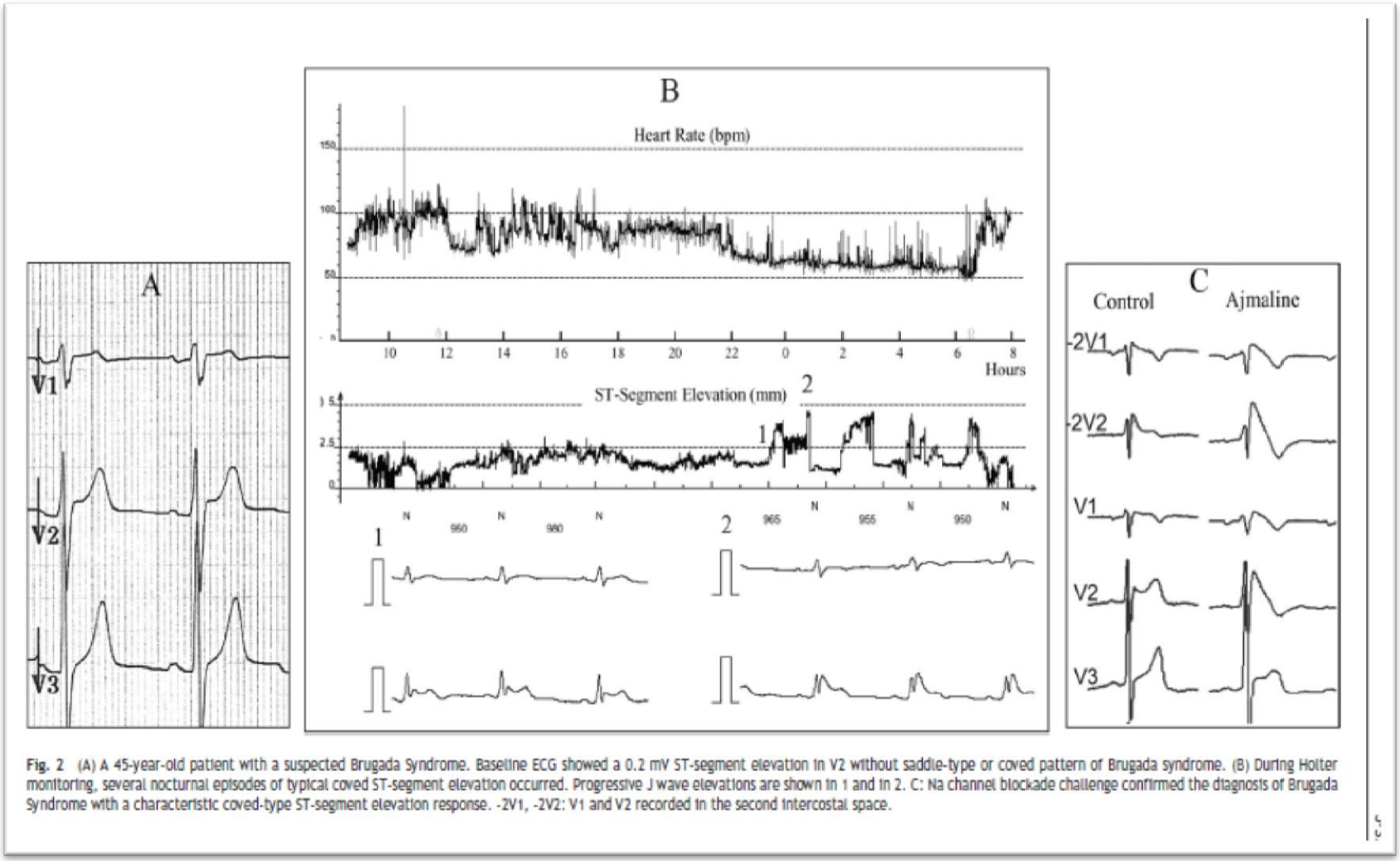
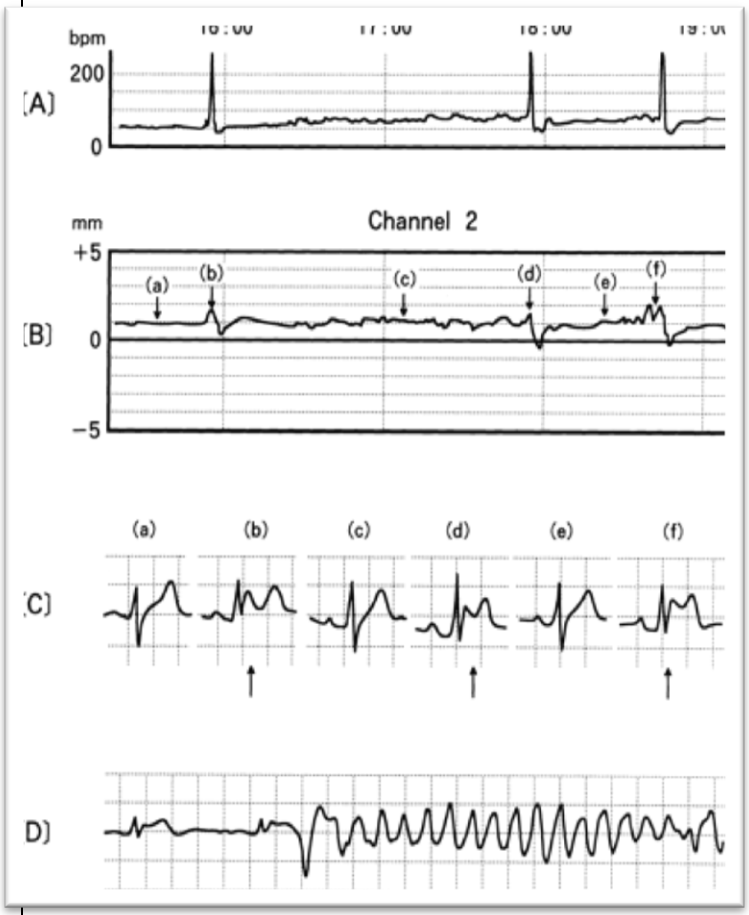


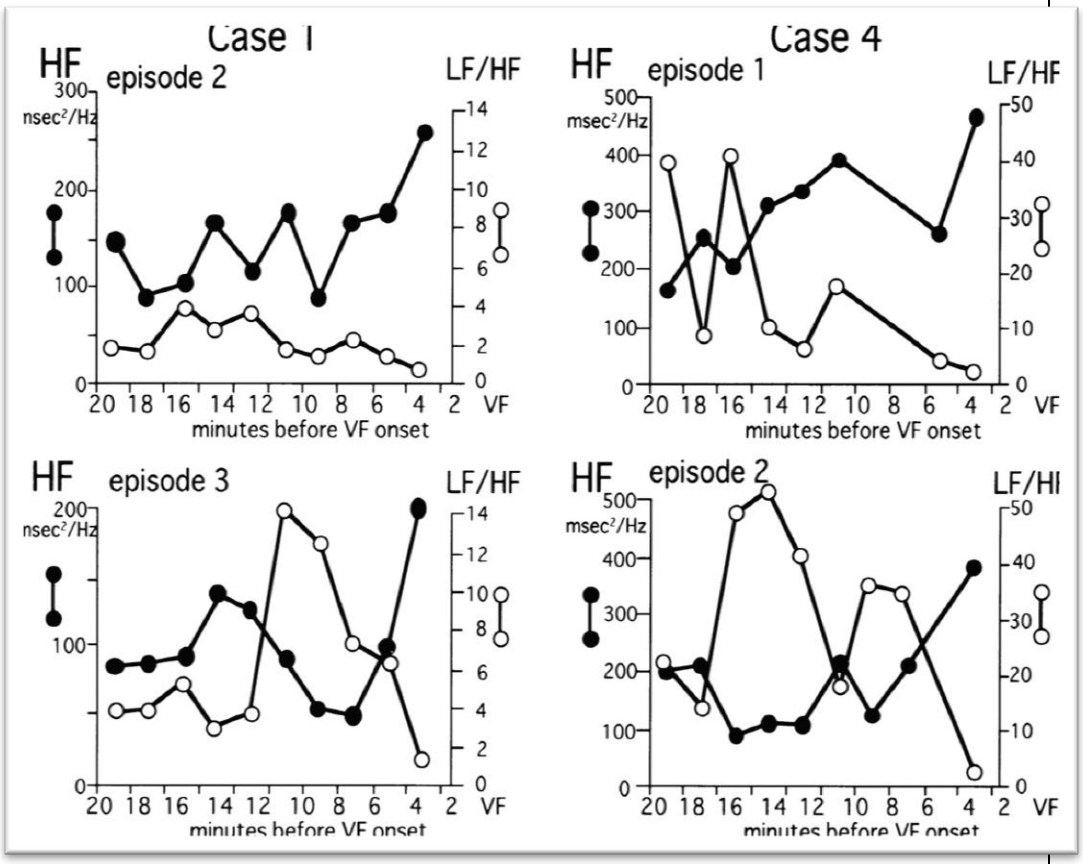
Fig. 2 (A) A 45-year-old patient with a suspected Brugada Syndrome. Baseline ECG showed a 0.2 mV ST-segment elevation in V2 without saddle-type or coved pattern of Brugada syndrome. (B) During Holter monitoring, several nocturnal episodes of typical coved ST-segment elevation occurred. Progressive J wave elevations are shown in 1 and in 2. C: Na channel blockade challenge confirmed the diagnosis of Brugada Syndrome with a characteristic coved-type ST-segment elevation response. -2V1, -2V2: V1 and V2 recorded in the second intercostal space.

Kasanuki H, Circ 1997

ST elevation just before all VF episodes



HRV just before VF episodes



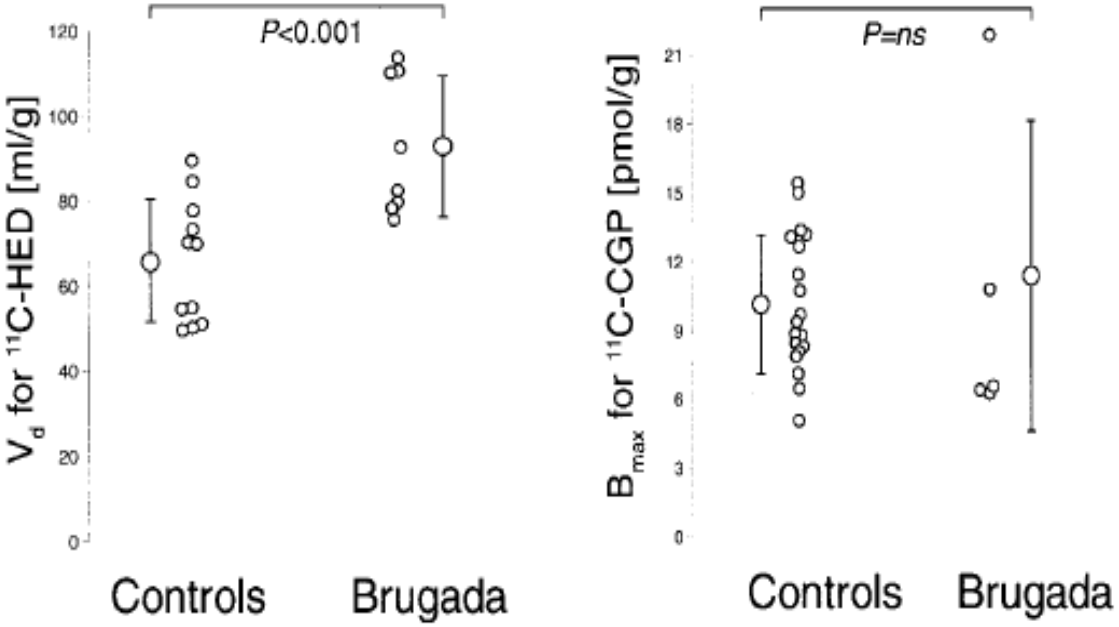
H Kasanuki, Circulation. 1997

Viskin, S. et al. Circulation 1998

Myocardial pre and postsynaptic sympathetic function assessed by the means of tomography positron emission

Abnormal Myocardial Presynaptic Norepinephrine Recycling in Patients With Brugada Syndrome

Peter Kies, MD; Thomas Wichter, MD, FESC; Michael Schäfers, MD, Matthias Paul, MD; Klaus P. Schäfers, PhD; Lars Eckardt, MD; Lars Stegger, MD; Eric Schulze-Bahr, MD; Ornella Rimoldi, MD; Günter Breithardt, MD, FESC; Otmar Schober, MD, PhD, FESC; Paolo G. Camici, MD, FESC, FRCP



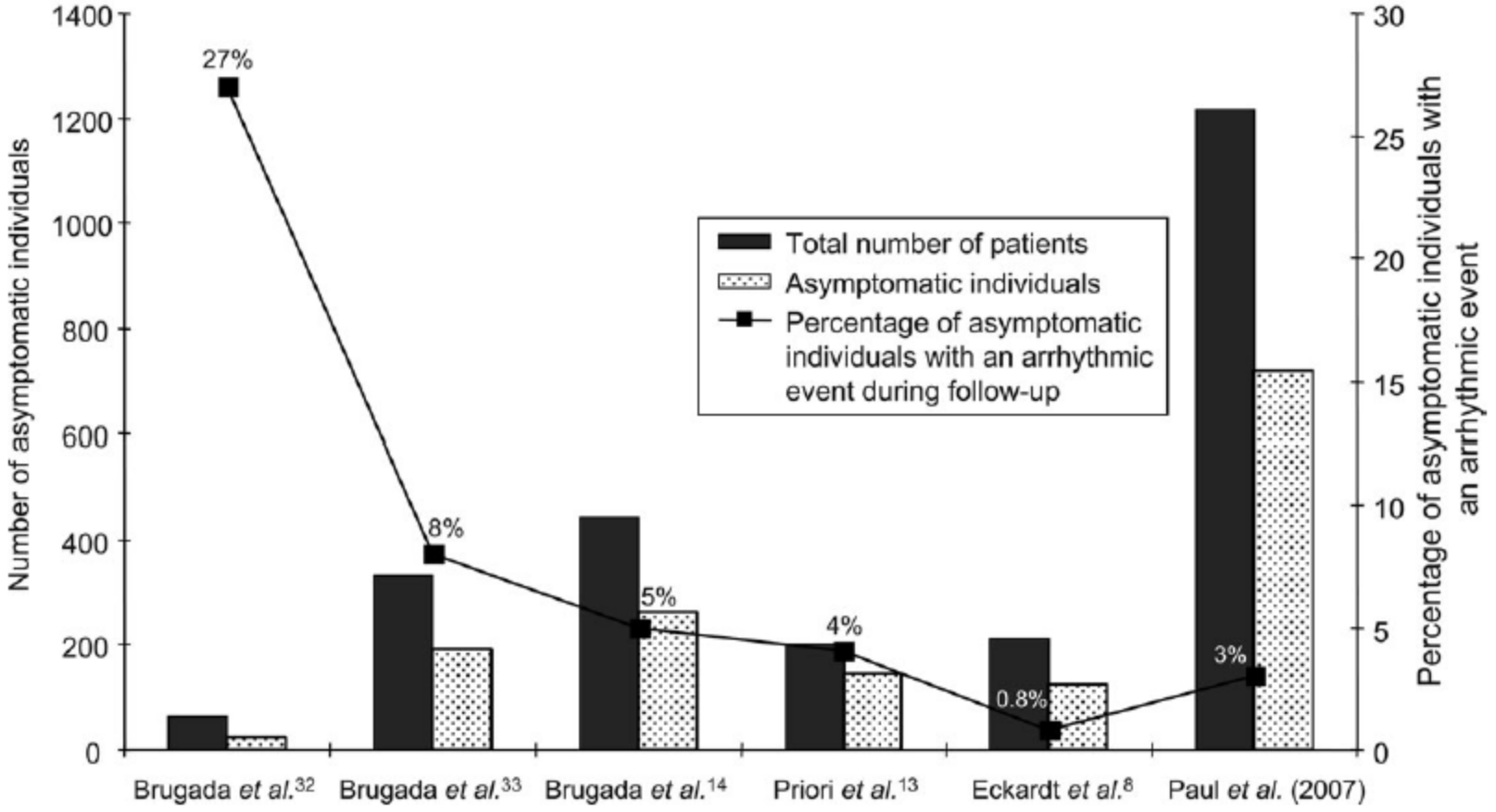
(*Circulation*. 2004;110:3017-3022.)

Figure 1. Increased presynaptic norepinephrine recycling (V_d of ^{11}C-HED, left) and preserved postsynaptic β-adrenoceptor density (B_{max} assessed by ^{11}C-CGP 12177; right) in Brugada patients compared with age-matched control subjects (individual values, mean±SD).

If you consider the syncope of arrhythmic origin what is the risk of arrhythmic event in the next 10 years for the patient?

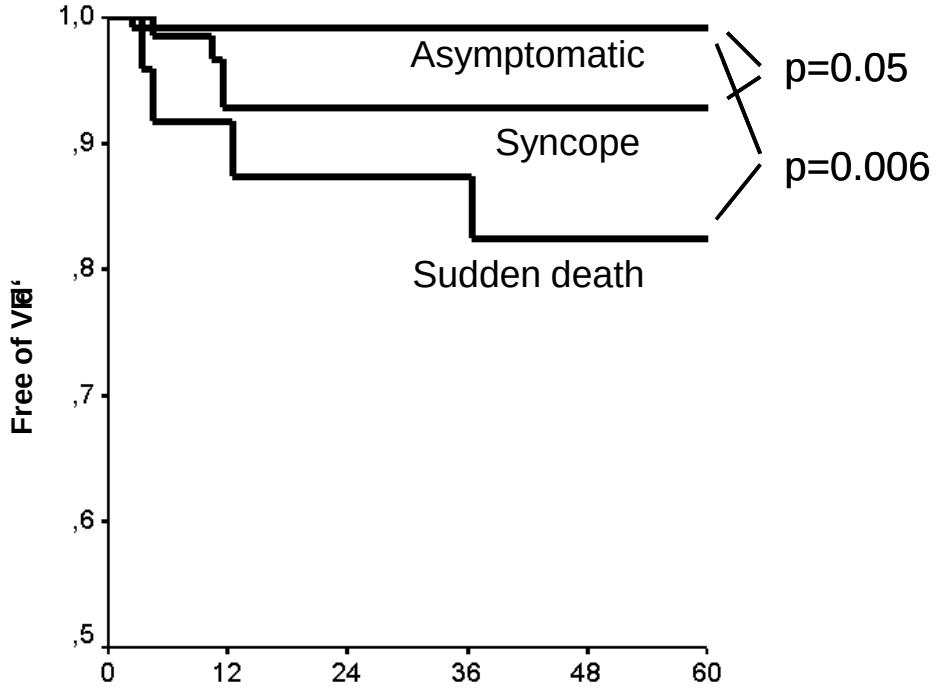
- 1 1%
- 2 5%
- 3 15%
- 4 30%
- 5 50%

Evaluation of the arrhythmic risk



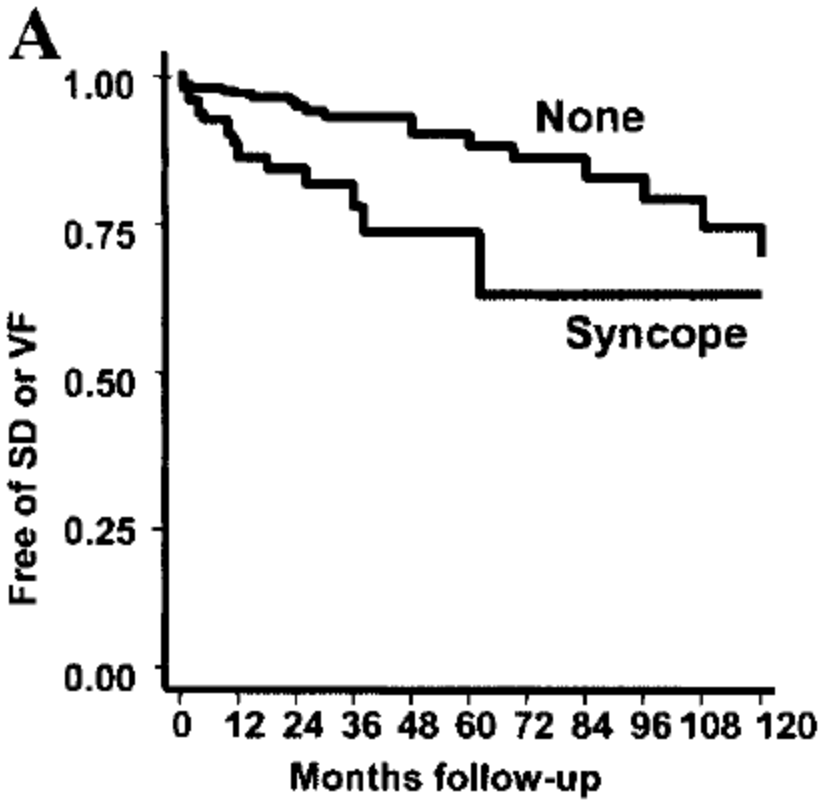
Paul, M EHJ, 2007

Prognostic regarding to the symptoms



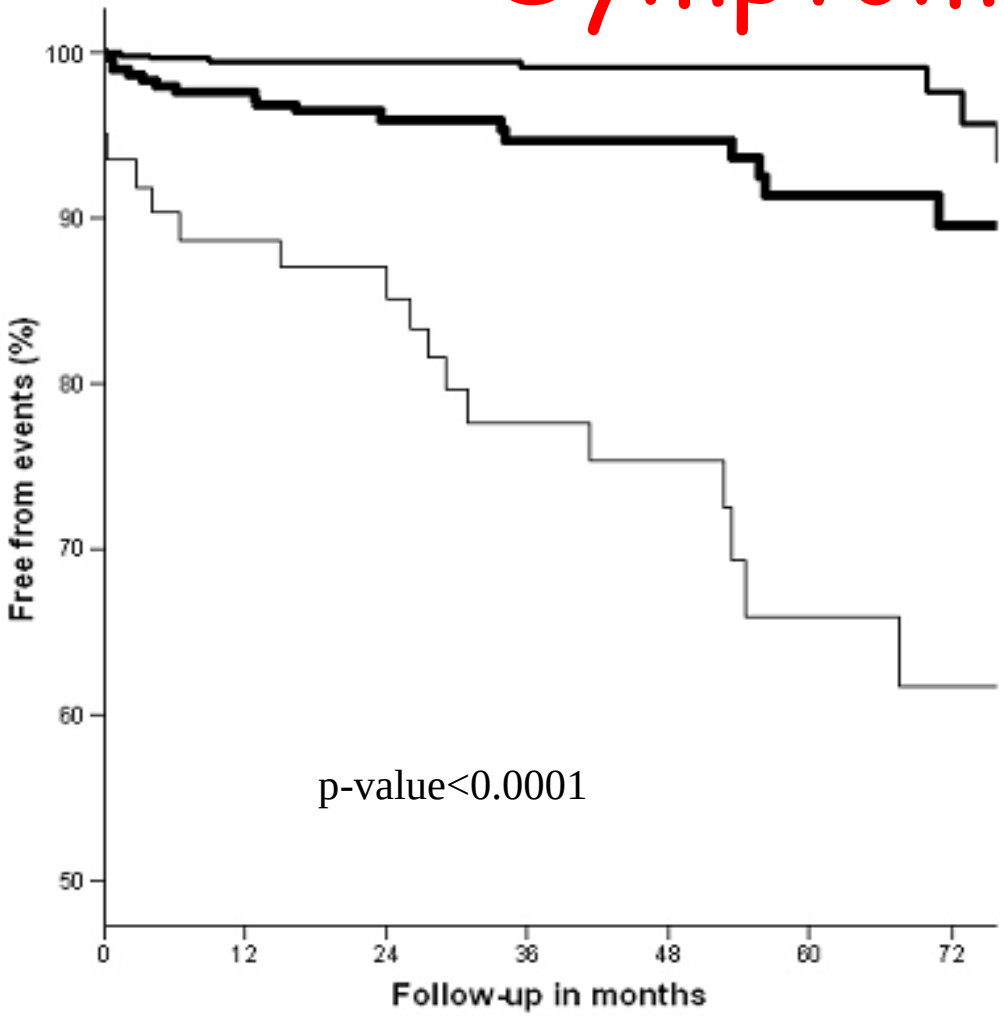
N. de Patients						
Asympto	123	108	73	43	19	6
Syncope	65	51	41	27	19	9
MS	24	22	18	18	16	13

Eckart, Circ 2005



Brugada J, Circ 2003

Symptoms



Asymptomatic (group C)

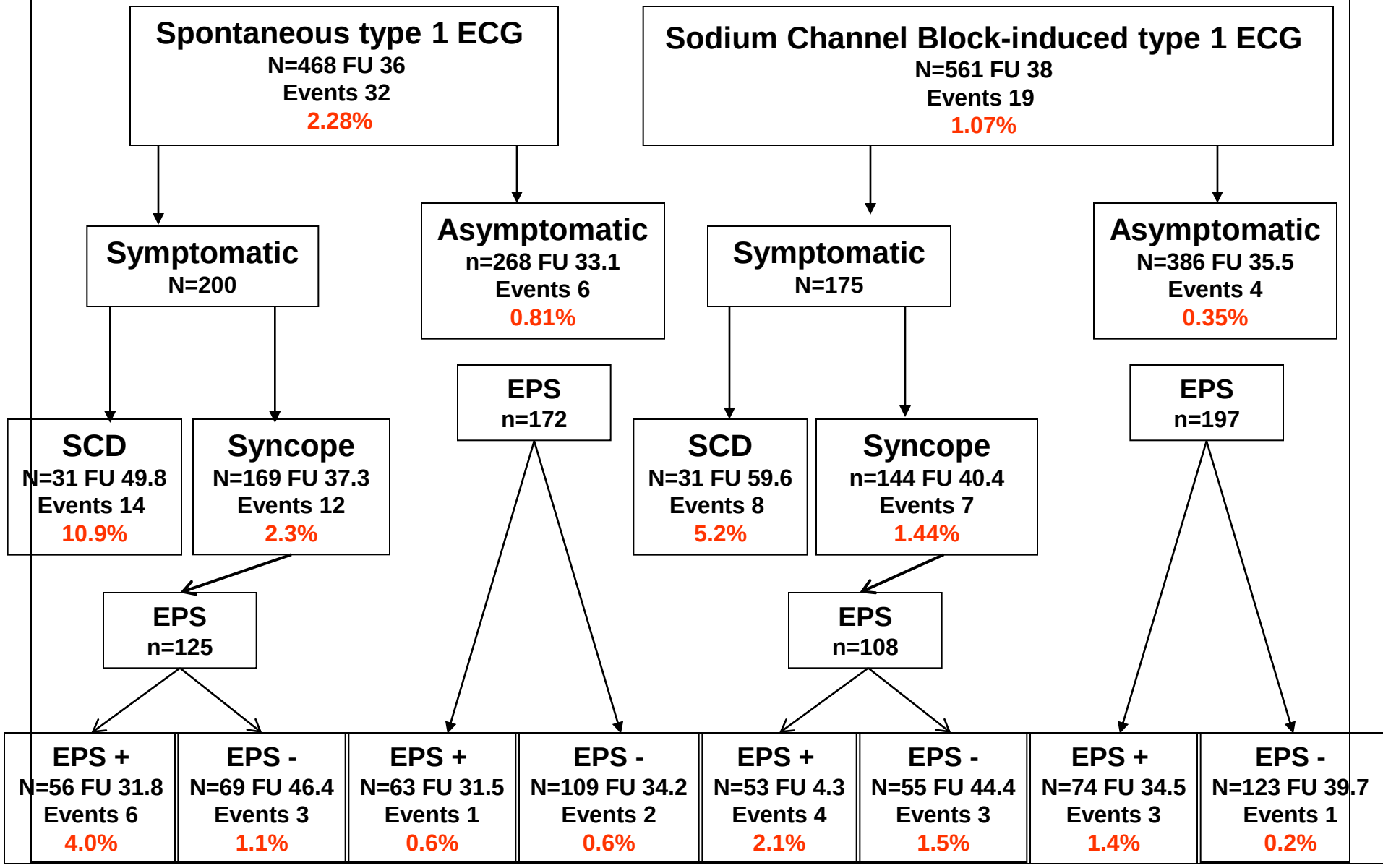
Syncope (group B)

SCD (group A)

	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

Probst, Circ 2010

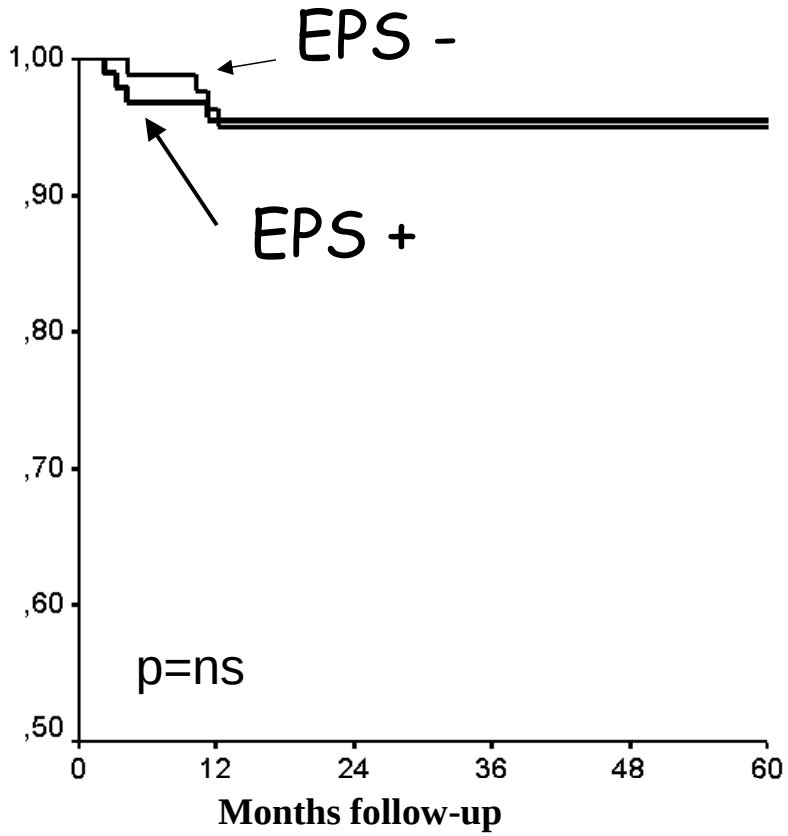
Mean rate of event per year and per patient



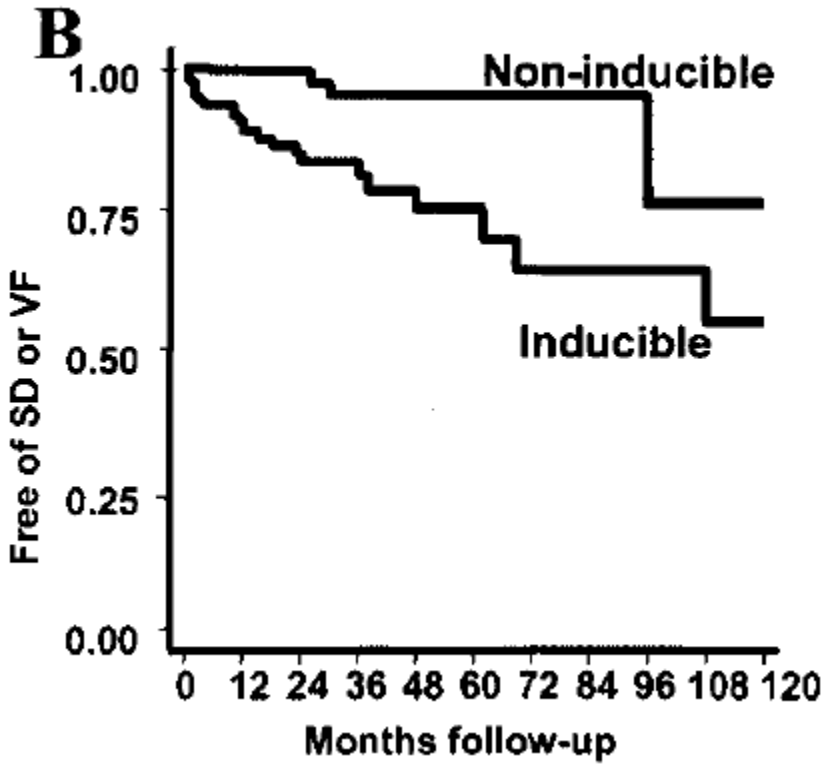
Do you plan to perform an EPS to this patient?

- 1 Yes
- 2 No
- 3 I don't know perhaps

Prognostic regarding to the EPS



Eckart, Circ 2005



Brugada J, Circ 2003

EPS in Brugada patients after aborted SCD

FINGER Brugada registry:
1029 patients

↓

62 patients included after SCD

↓

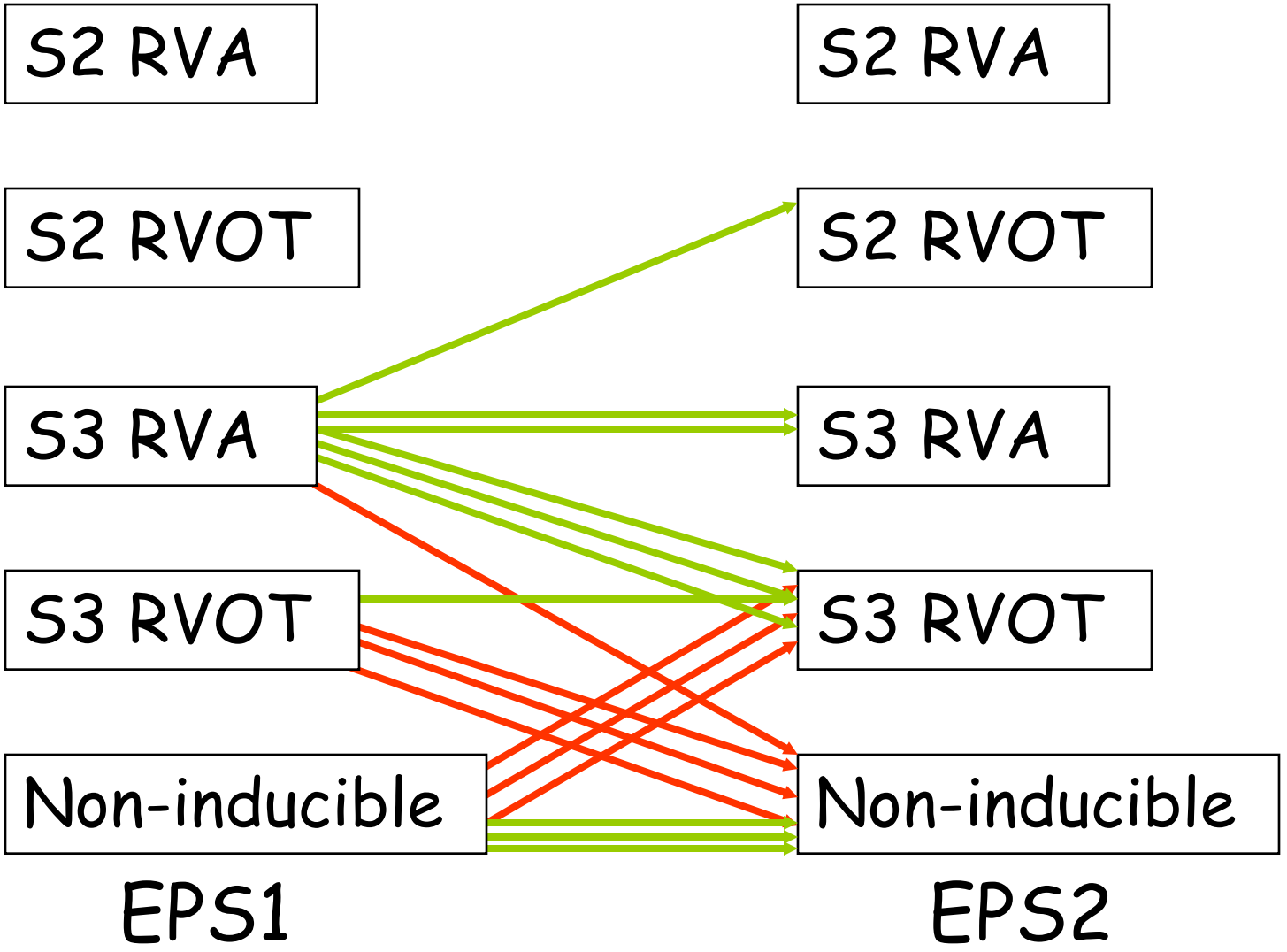
36 patients underwent an EPS

↙ ↘

16 positive EPS (45%)

20 negative EPS (55%)

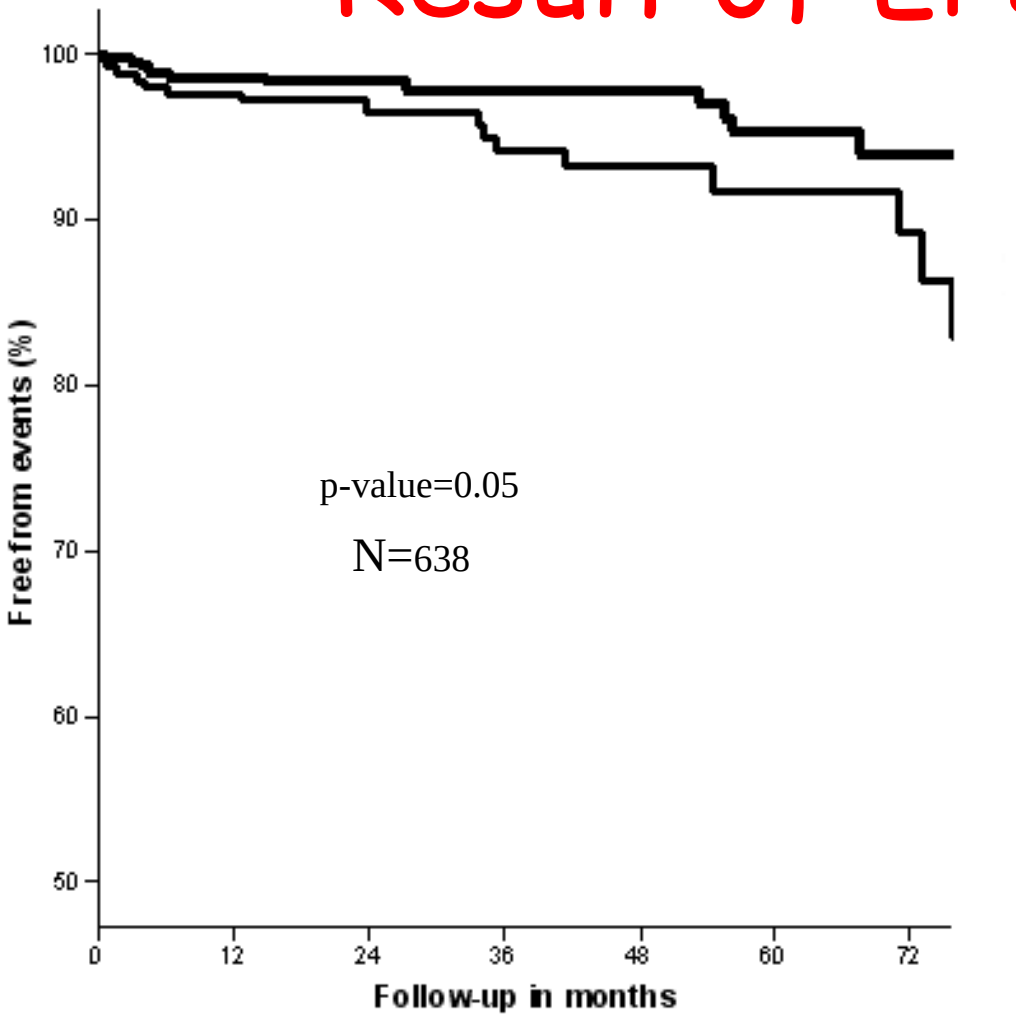
Reproducibility of the EPS in 17 patients



Reproducibility of 59%

Gasparini, JCE, 2002

Result of EPS



EPS negative

EPS positive

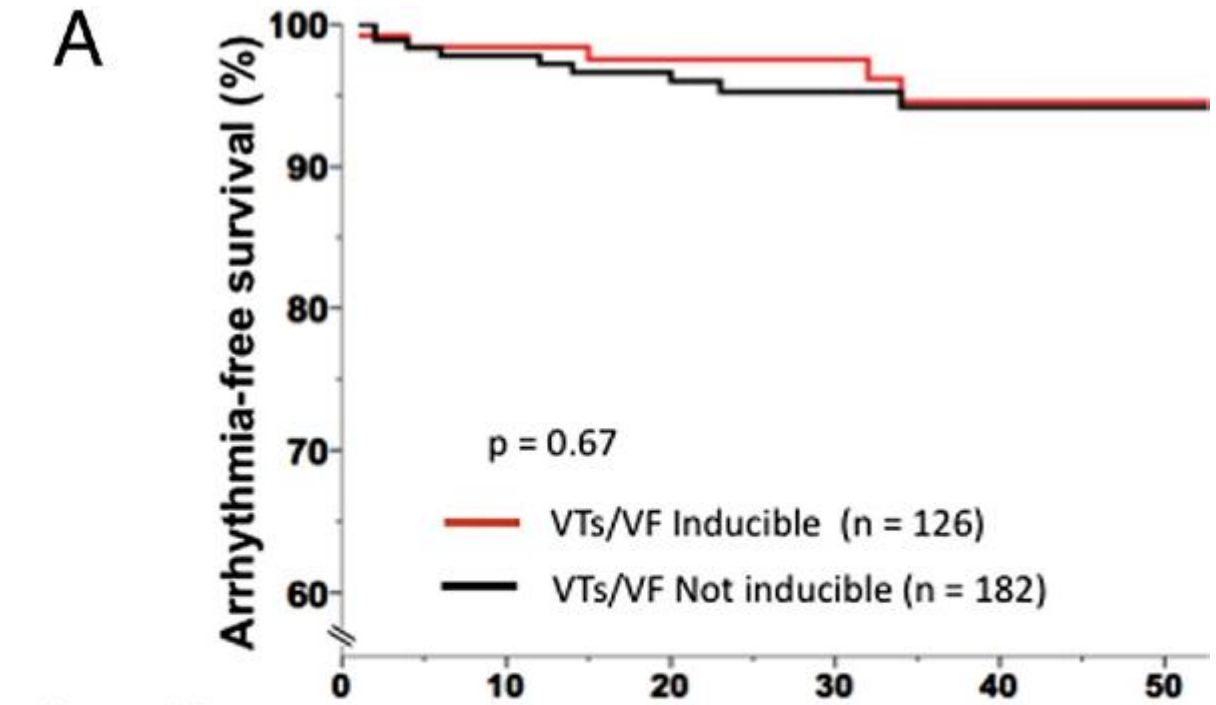
	0	12	24	36	48	60	72
negative	376	301	237	187	136	94	59
positive	262	212	161	113	81	52	34

Asymptomatic patients Multivariate analysis

- Spontaneous type-1 ECG (p=0.26)
- Male gender (p=0.35)
- Results of EPS in 369 patients (p=0.83)
  - ✓No predictive value

- ICD implantation (p=0.01) was found as predictor of arrhythmic events.

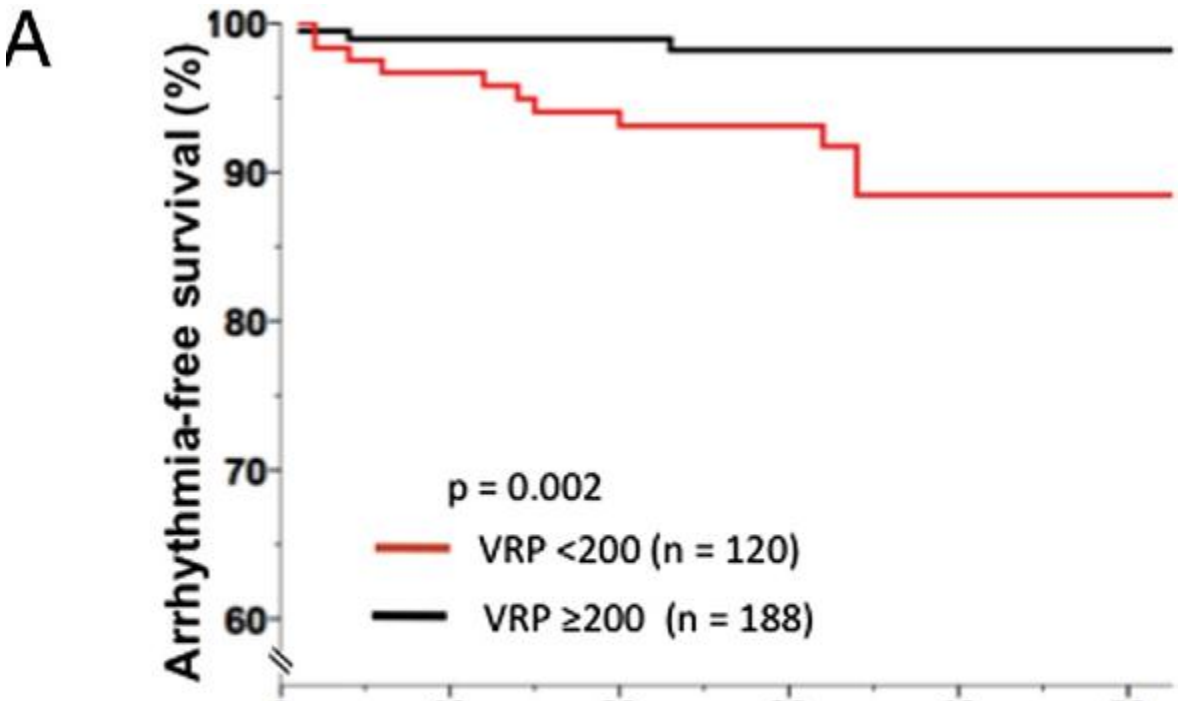
Results of the PRELUDE study



umber at risk

Not inducible	182	172	153	111	71	37
Inducible	126	116	100	77	46	25

Results of the PRELUDE study



umber at ris

VRP ≥200	188	178	152	110	73	38
VRP<200	120	113	101	74	43	23

Results of the PRELUDE study

	p Value	HR	Lower	Upper
Independent effects				
Inducibility	0.559	0.721	0.241	2.159
Spontaneous type 1 and syncope	0.001	6.406	2.211	18.558
Inducibility	0.835	0.890	0.298	2.661
Ventricular refractory period	0.008	5.666	1.578	20.346
Inducibility	0.972	1.020	0.337	3.091
QRS-fragmentation	0.000	8.898	3.040	26.038
Backward elimination—likelihood ratio				
Step 1				
Spontaneous type 1 and syncope	0.012	4.198	1.378	12.788
QRS-fragmentation	0.007	4.928	1.540	15.776
Ventricular refractory period	0.045	3.908	1.030	14.824
Inducibility	0.959	1.030	0.336	3.155
Step 2				
Spontaneous type 1 and syncope	0.011	4.205	1.382	12.791
QRS-fragmentation	0.007	4.902	1.560	15.402
Ventricular refractory period	0.045	3.903	1.030	14.786

Do you plan to implant an ICD to this patient?

- 1 Yes
- 2 No
- 3 I don't know

ICD in Brugada syndrome

- 220 patients (34 ±27 month)
  - ✓24 (12%) high defibrillation threshold
  - ✓53 (27%) high stimulation threshold
  - ✓29 (15%) low R wave amplitude.
- Annual rate of appropriated shock in asymptomatic patients 1,5 %
- Annual rate of inappropriated shock 3.75%

Sacher F, Circulation 2006.

Table 2 Results of the 36-item short-form health survey in the 3 groups

		Physical functioning	Physical role	Bodily pain	General health	Vitality	Social functioning	Emotional role	Mental health
G1—ICD symptomatic patients	*n*	61	60	60	60	59	61	60	59
	Mean	82.17	67.59	77.14	58.96	52.68	80.84	72.92	56.76
	SD	17.83	32.35	26.75	23.95	24.10	24.31	36.04	24.31
G2—ICD asymptomatic patients	*n*	77	74	74	77	76	77	72	74
	Mean	88.15	74.92	76.23	63.94	54.40	83.36	73.96	62.99
	SD	13.52	27.59	25.88	23.96	19.92	20.22	32.35	21.88
G3—No ICD asymptomatic patients	*n*	52	51	52	51	52	51	51	52
	Mean	87.24	72.66	83.28	66.09	58.05	81.50	71.81	60.13
	SD	17.58	34.55	23.49	20.57	20.60	24.01	36.98	24.19
P value		0.081	0.39	0.27	0.24	0.41	0.79	0.94	0.31

ICD, implantable cardioverter defibrillator; *n*, number of patients; SD, standard deviation.

Probst V, Europace 2011.

Conclusion

- Syncope in Brugada syndrome patients is always a difficult situation
- Determination of the syncope origin is often (always?) difficult
- Particular attention has to be paid for these patients role of ILR?
- Risk benefit ratio of ICD has to be discuss