How agressively should we treat asymptomatic patients with Brugada syndrome

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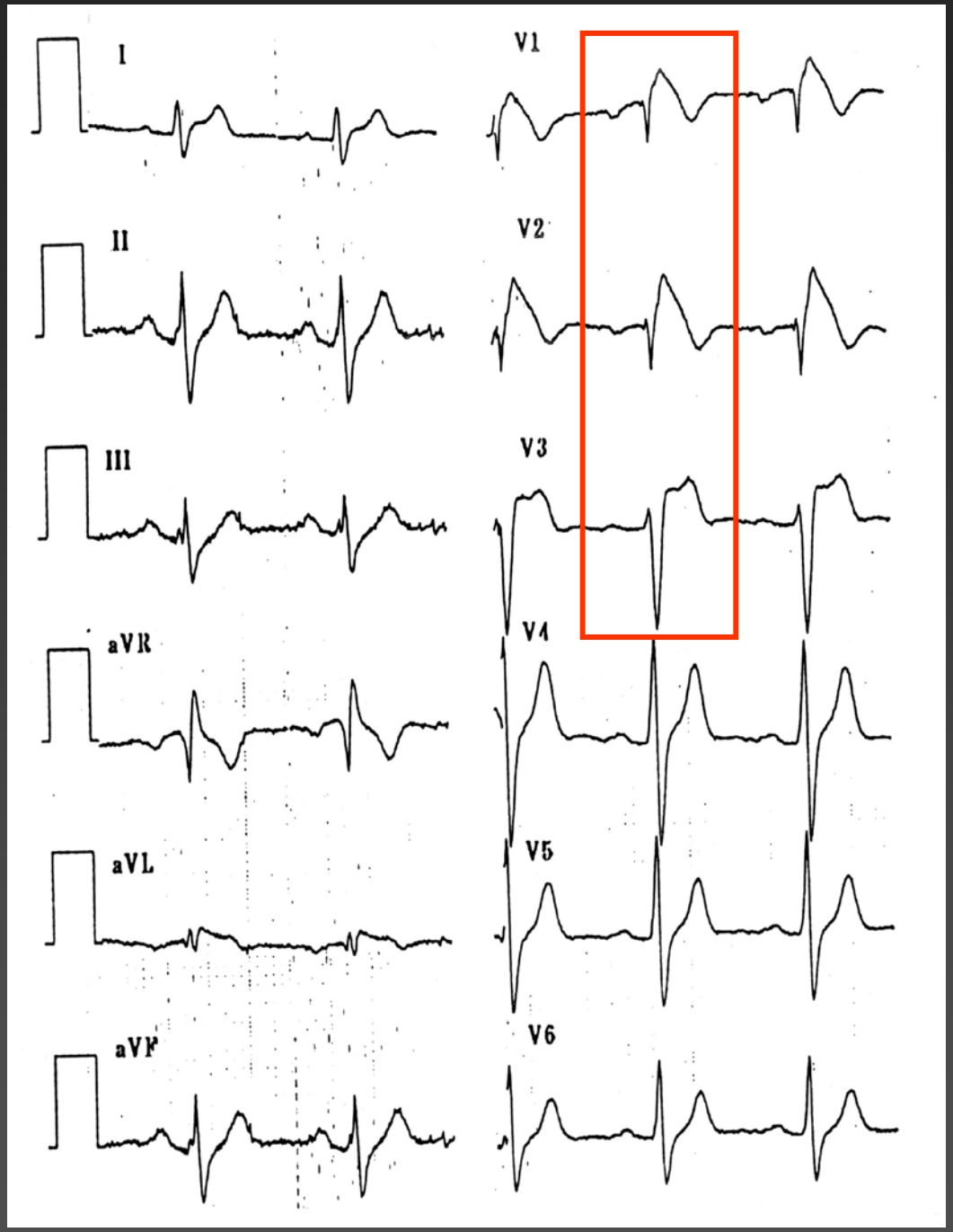
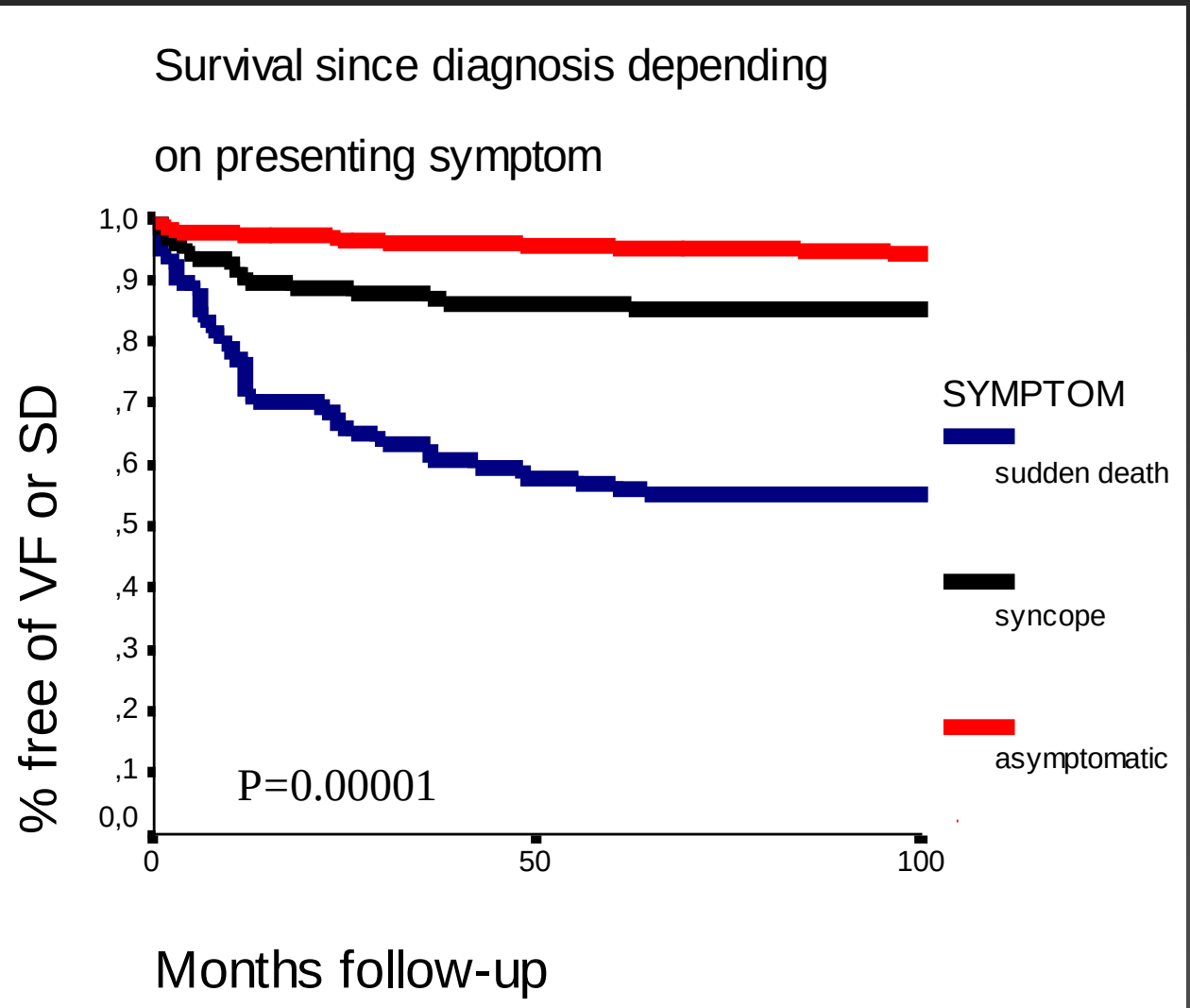
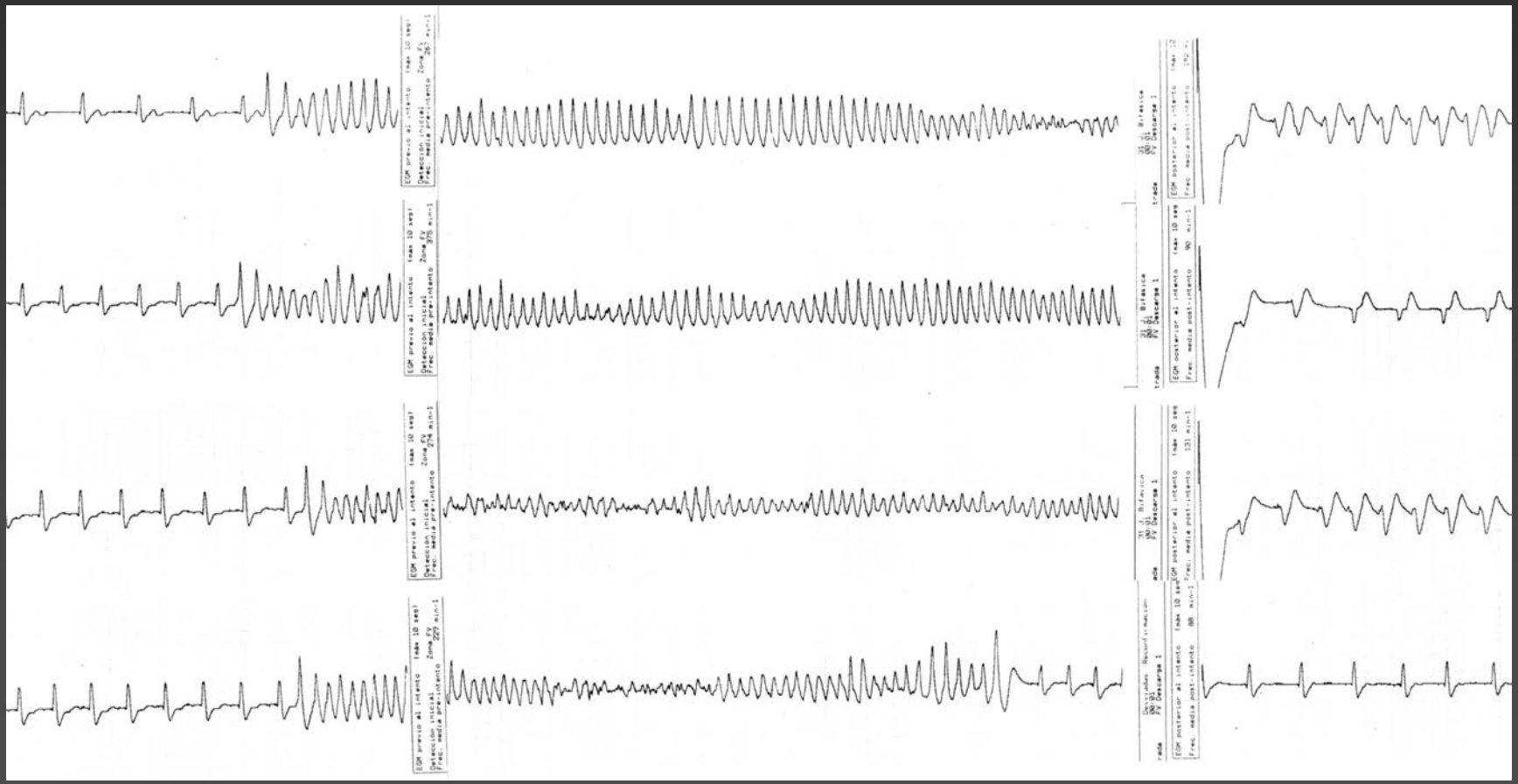
The ECG in Brugada syndrome

- Prolonged PR
- RBBB
- ST segment ↑

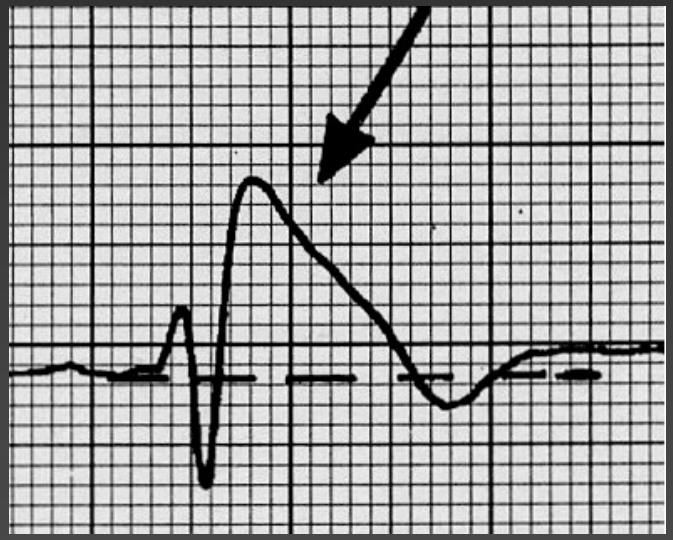



Survival since diagnosis depending
on presenting symptom
% free of VF or SD
1,0
,9
,8
,7
,6
,5
,4
,3
,2
,1
0,0
0
50
100
P=0.00001
SYMPTOM
sudden death
syncope
asymptomatic
Months follow-up

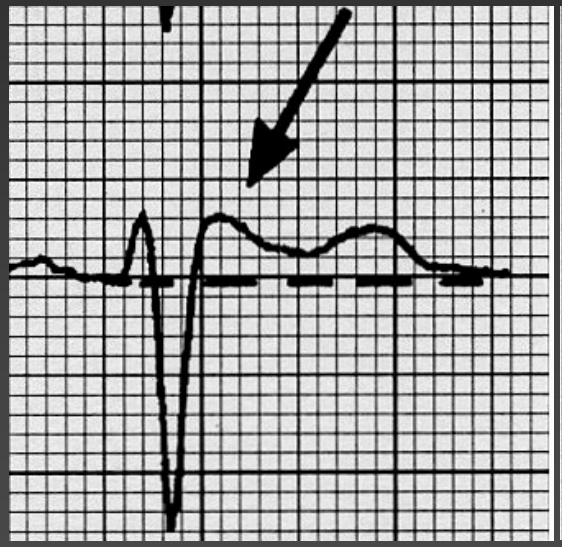
Appropriate ICD therapies

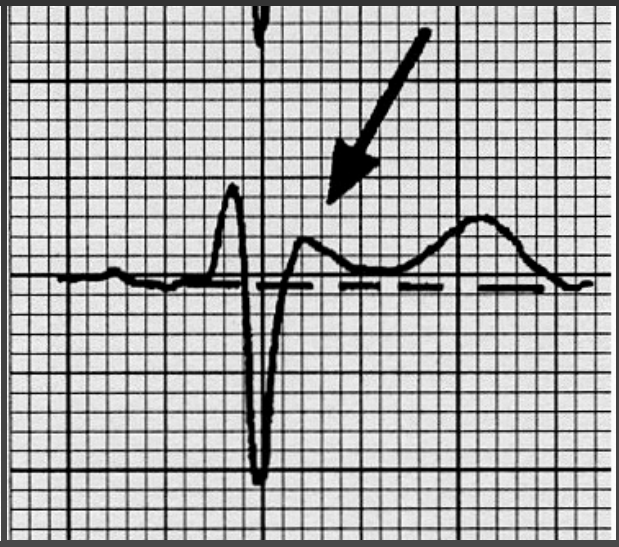


Type 1
"Coved"



Type 2 & 3
"Saddle back"





NON DIAGNOSTIC

Does an ST segment elevation always indicate Brugada syndrome?

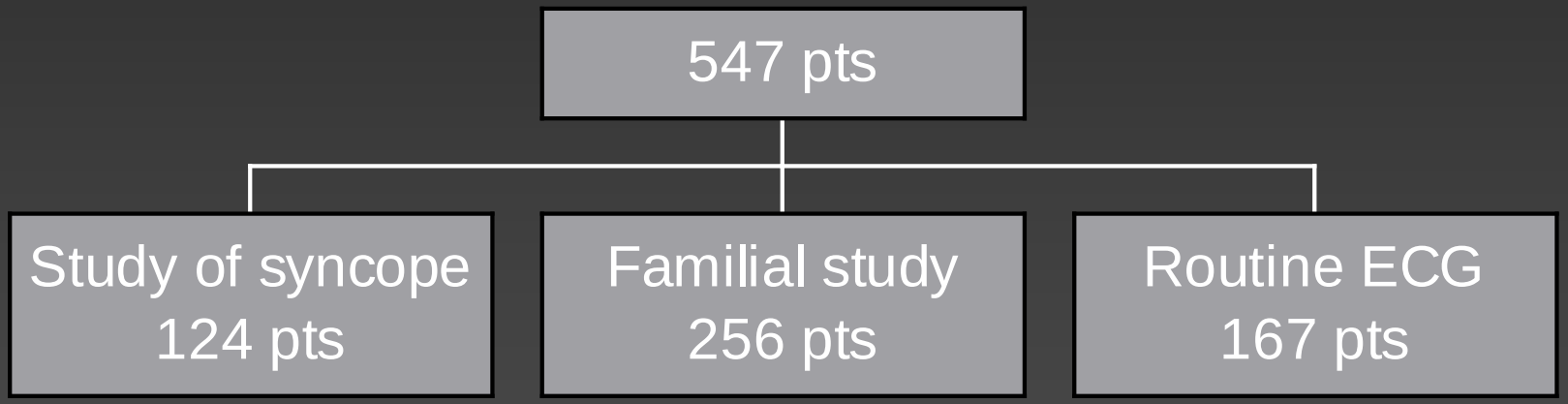
- Mediastinal tumour compressing RVOT
- Cocaine intoxication
- Acute myocardial infarction
- Acute myocarditis
- Right ventricular infarction
- Dissecting aortic aneurysm
- Various central and autonomic nervous system abnormalities
- Heterocyclic antidepressant overdose
- Duchenne muscular dystrophy
- Thiamine deficiency
- Hypercalcemia
- Hyperkalemia

Brugada syndrome in patients without previous cardiac arrest

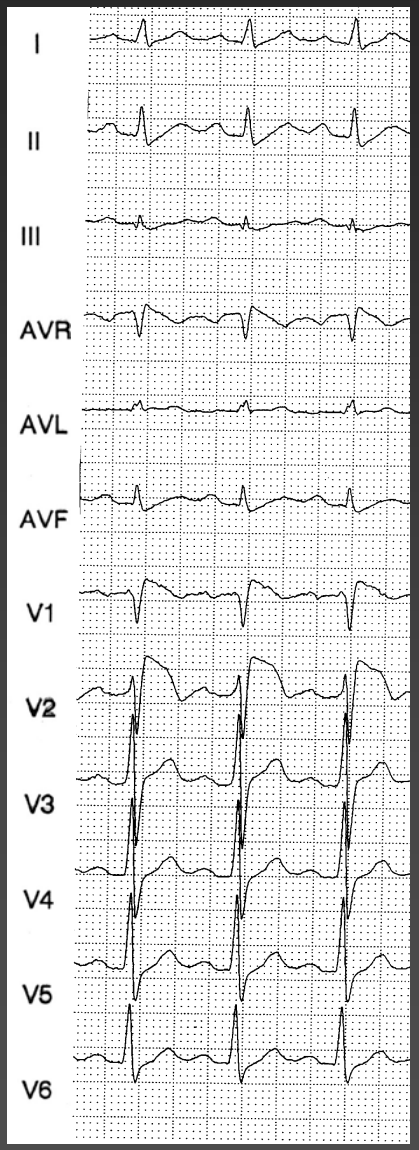
Patient characteristics

- 547 patients
- 408 males, 139 females
- Mean age at diagnosis: 41±15 years

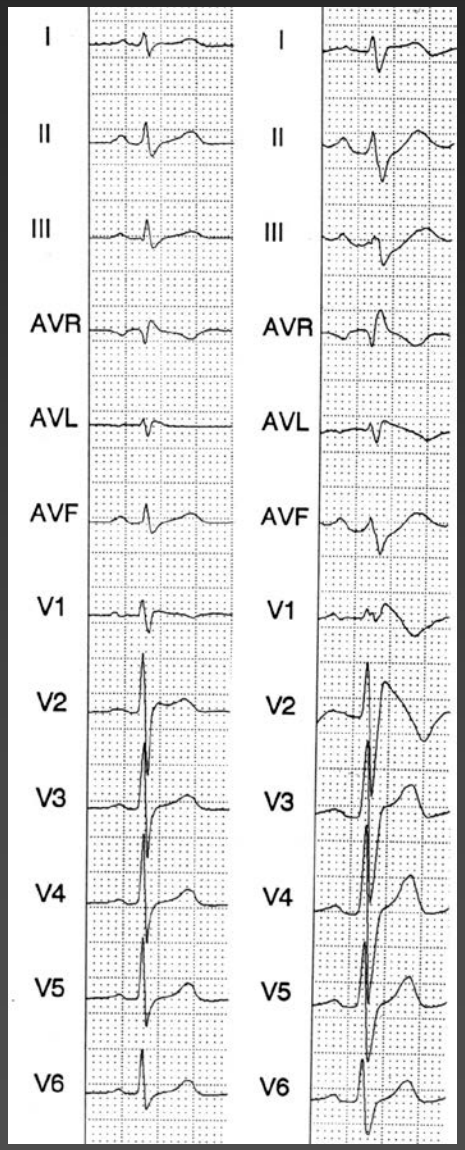
Diagnosis


547 pts
Study of syncope
124 pts
Familial study
256 pts
Routine ECG
167 pts

Basal abnormal ECG in 391

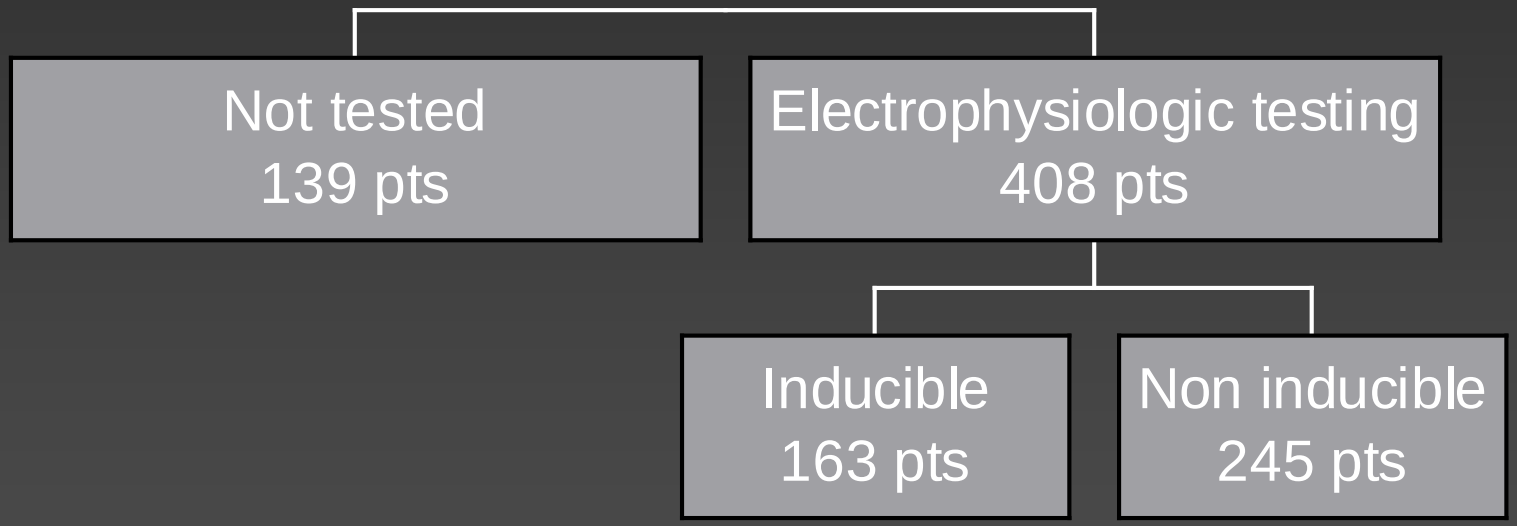


Class I AAD abnormal ECG in 156

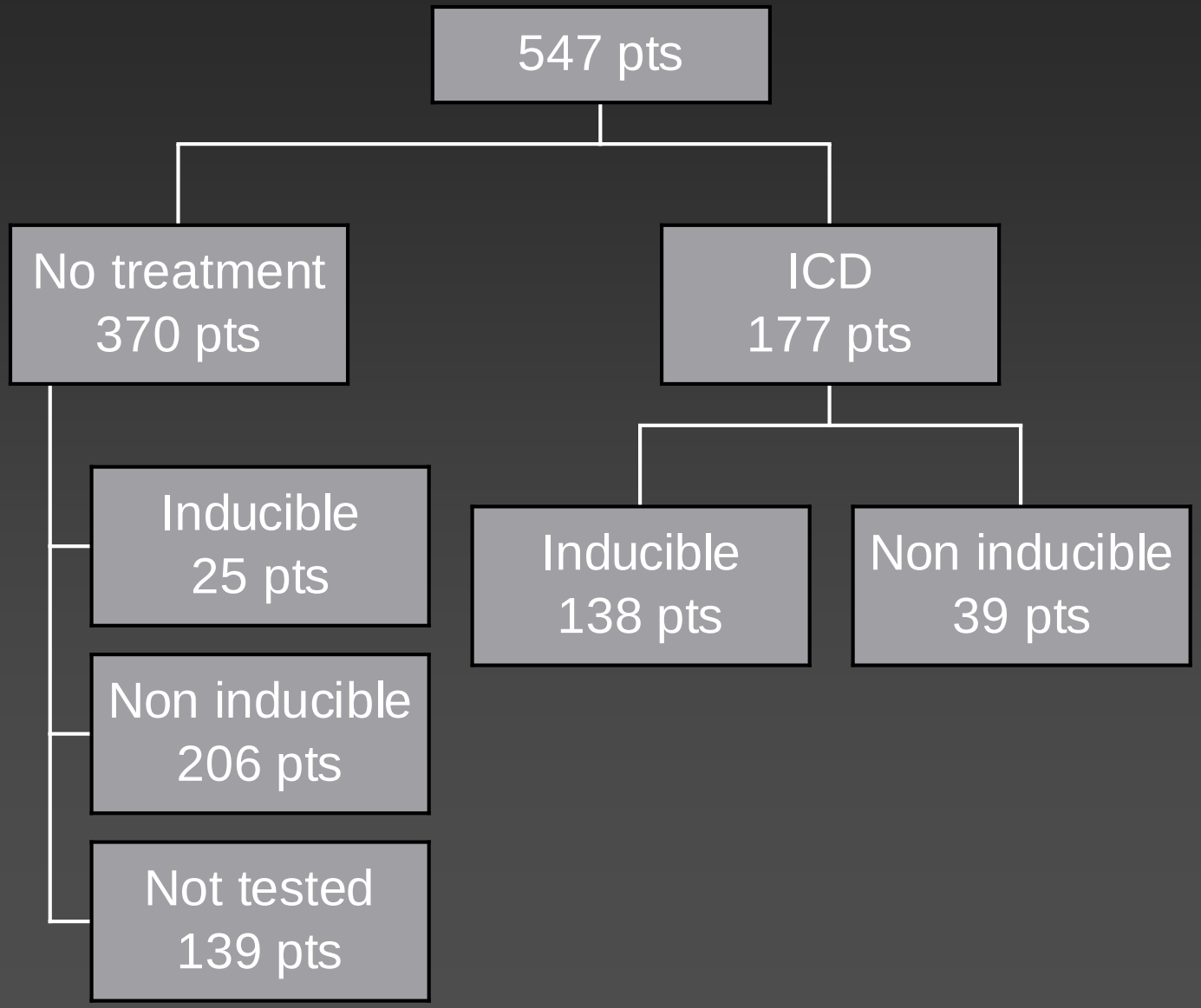


basal ajmaline

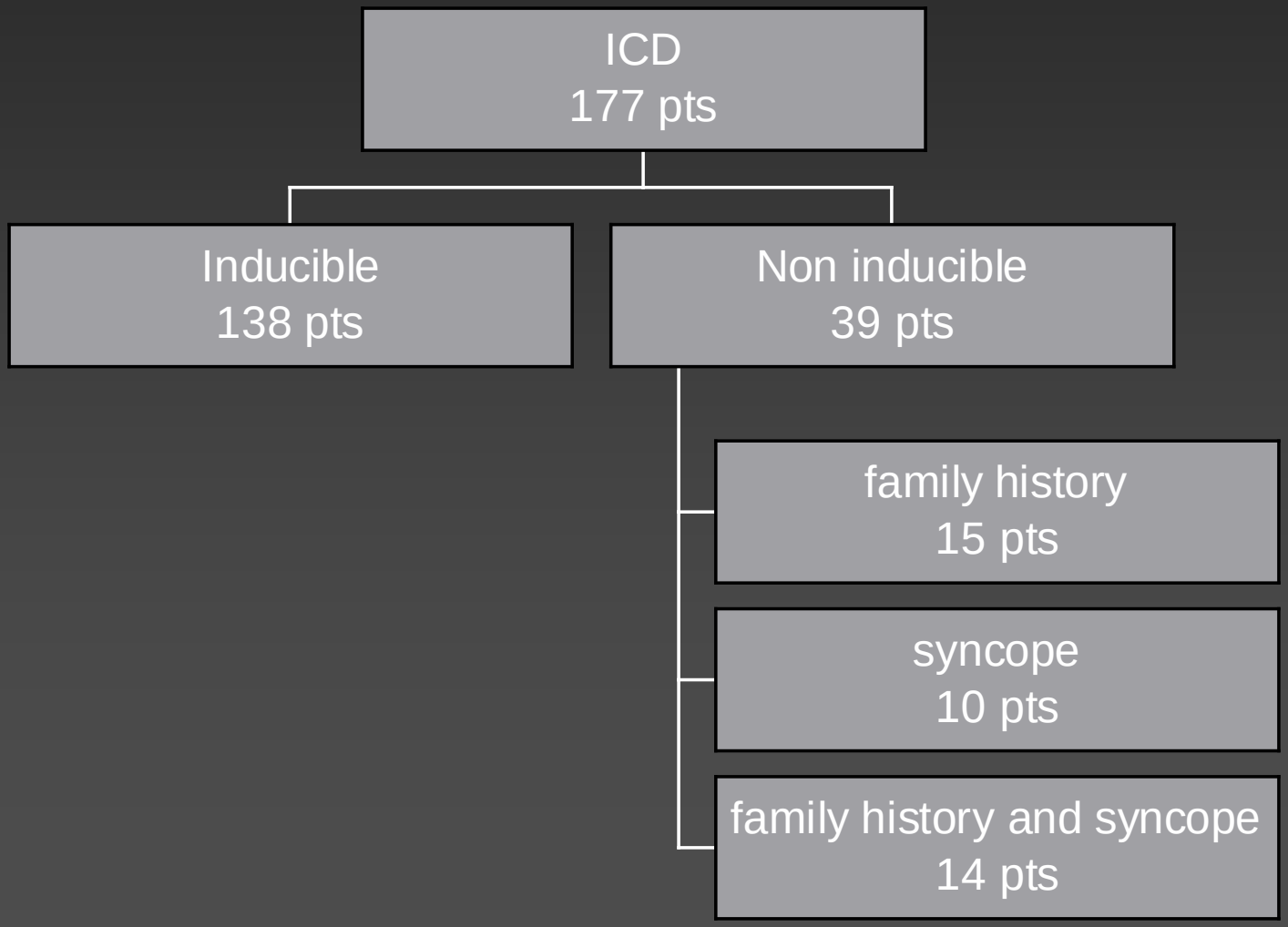
Results of EP study



Treatment


547 pts
No treatment
370 pts
ICD
177 pts
Inducible
25 pts
Non inducible
206 pts
Not tested
139 pts
Inducible
138 pts
Non inducible
39 pts

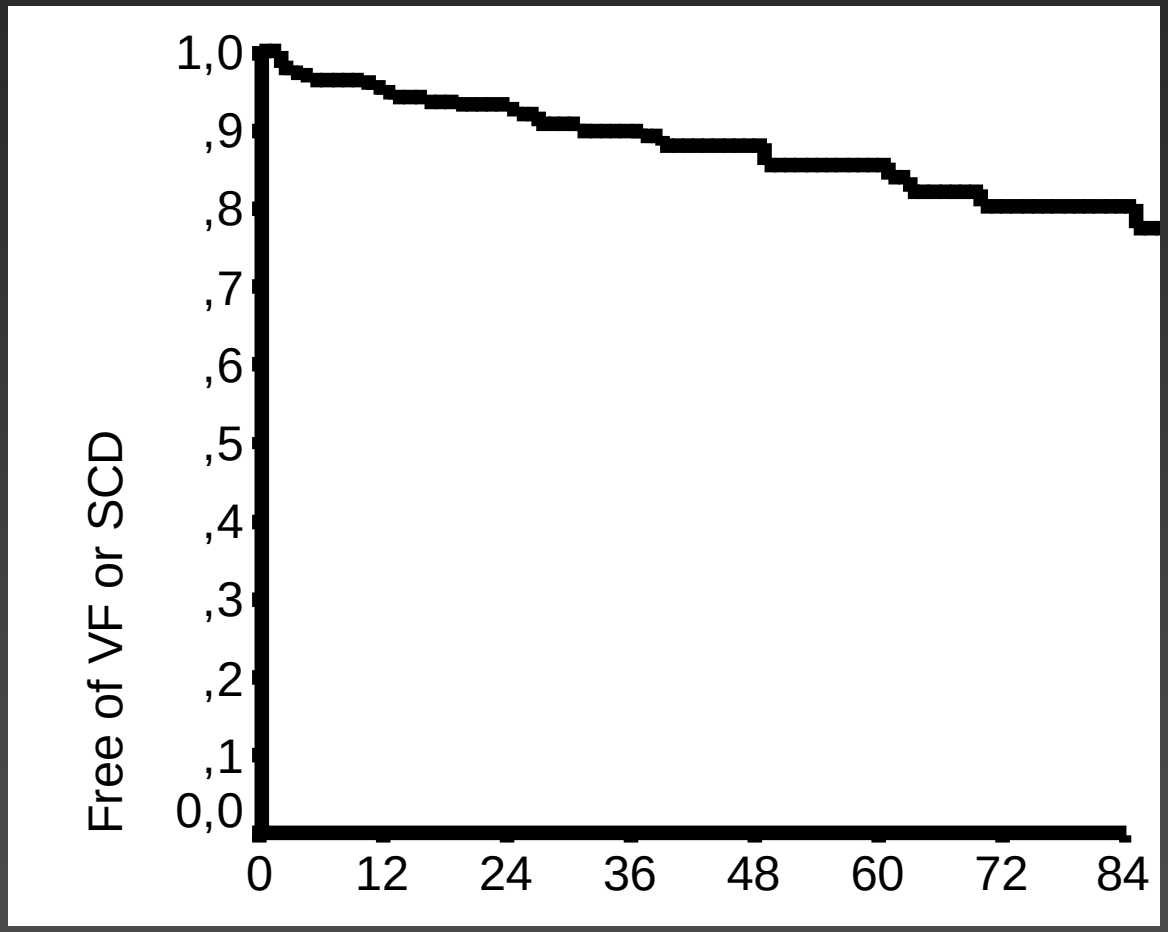
Treatment


ICD
177 pts
Inducible
138 pts
Non inducible
39 pts
family history
15 pts
syncope
10 pts
family history and syncope
14 pts

Follow-up

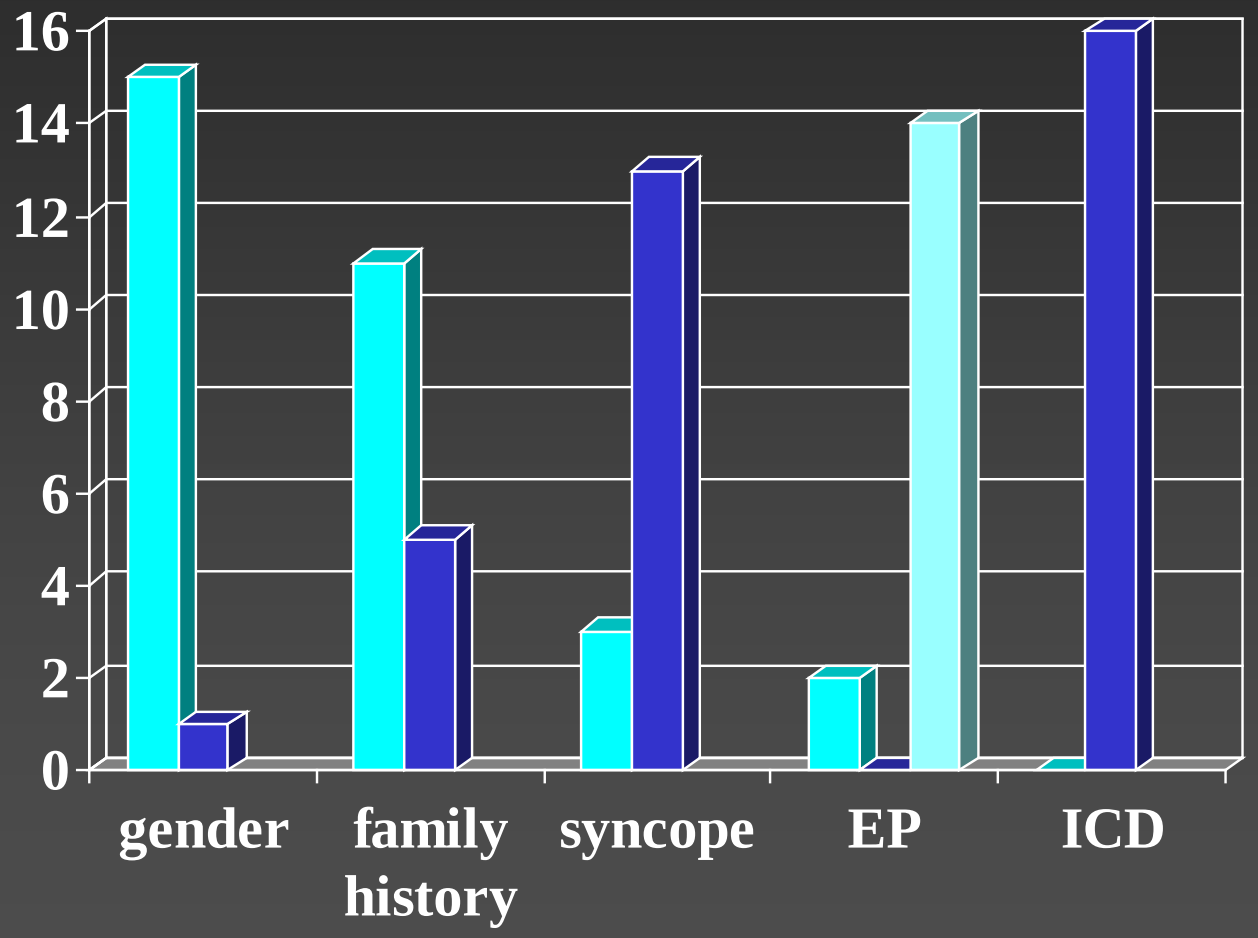
- Mean follow-up 36±31 months
- 45 patients (8%) had events
  - 16 SCD
  - 29 documented VF

VF or SCD during follow-up

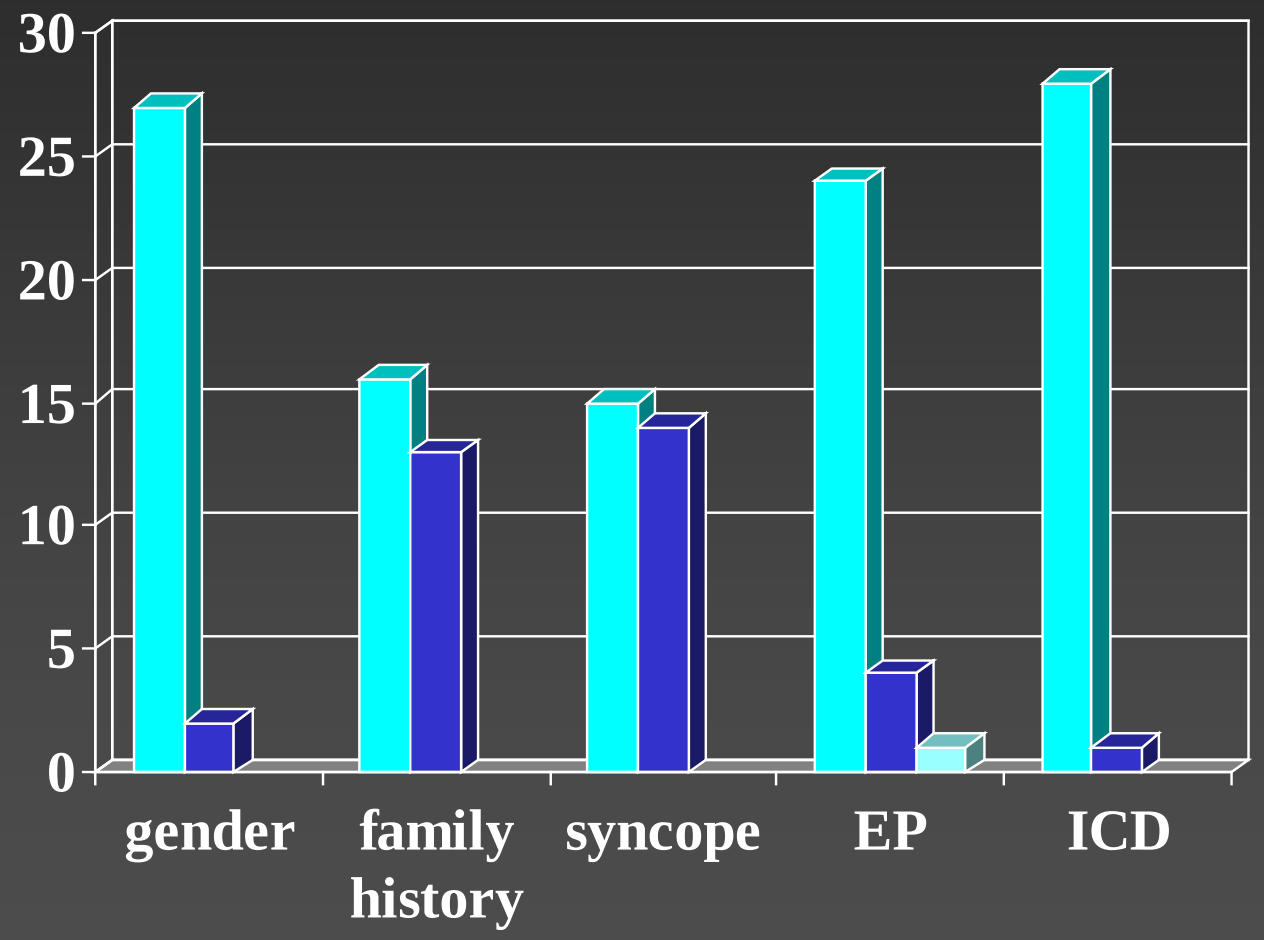


n	**547**	**329**	**179**	**106**	**78**	**53**	**42**	**33**

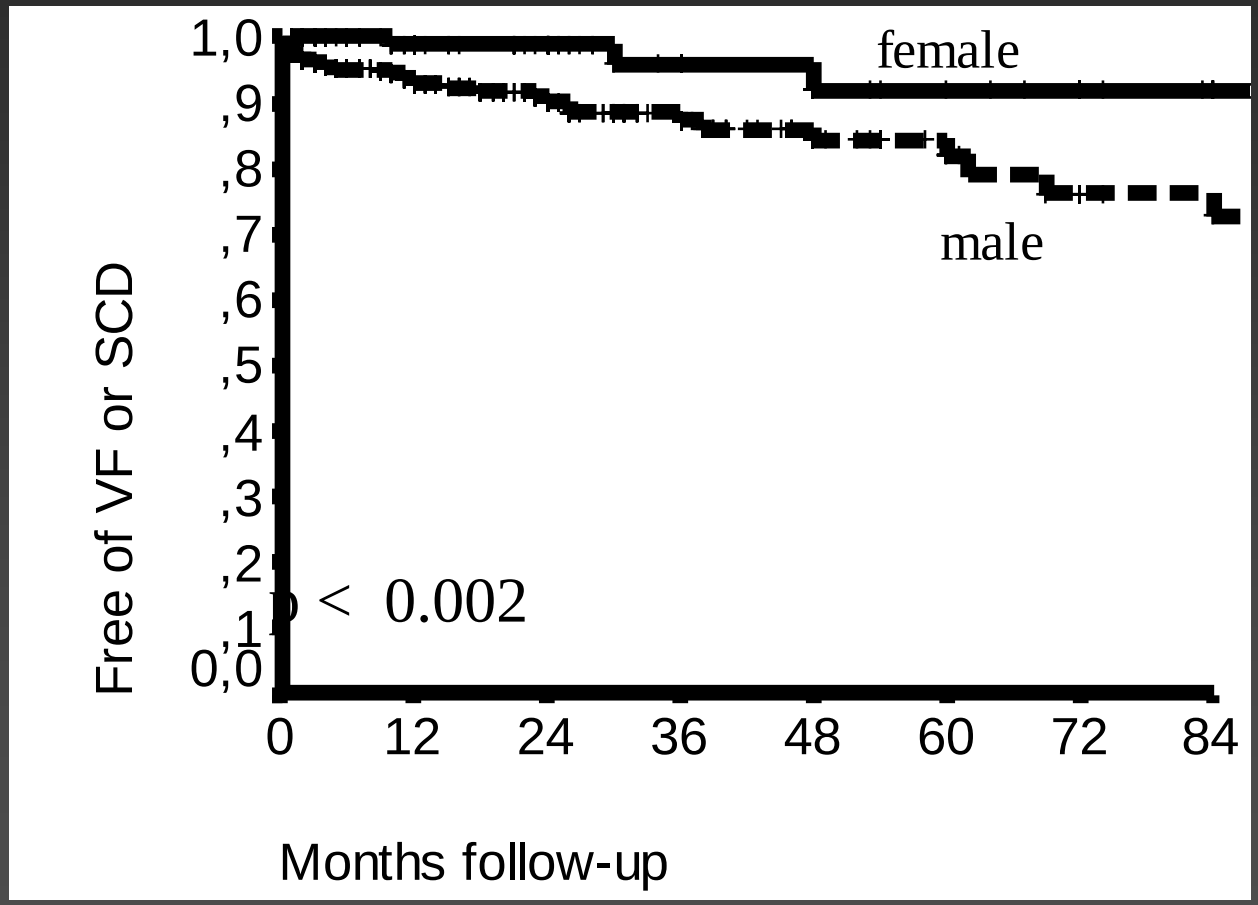
Sudden cardiac death, n=16



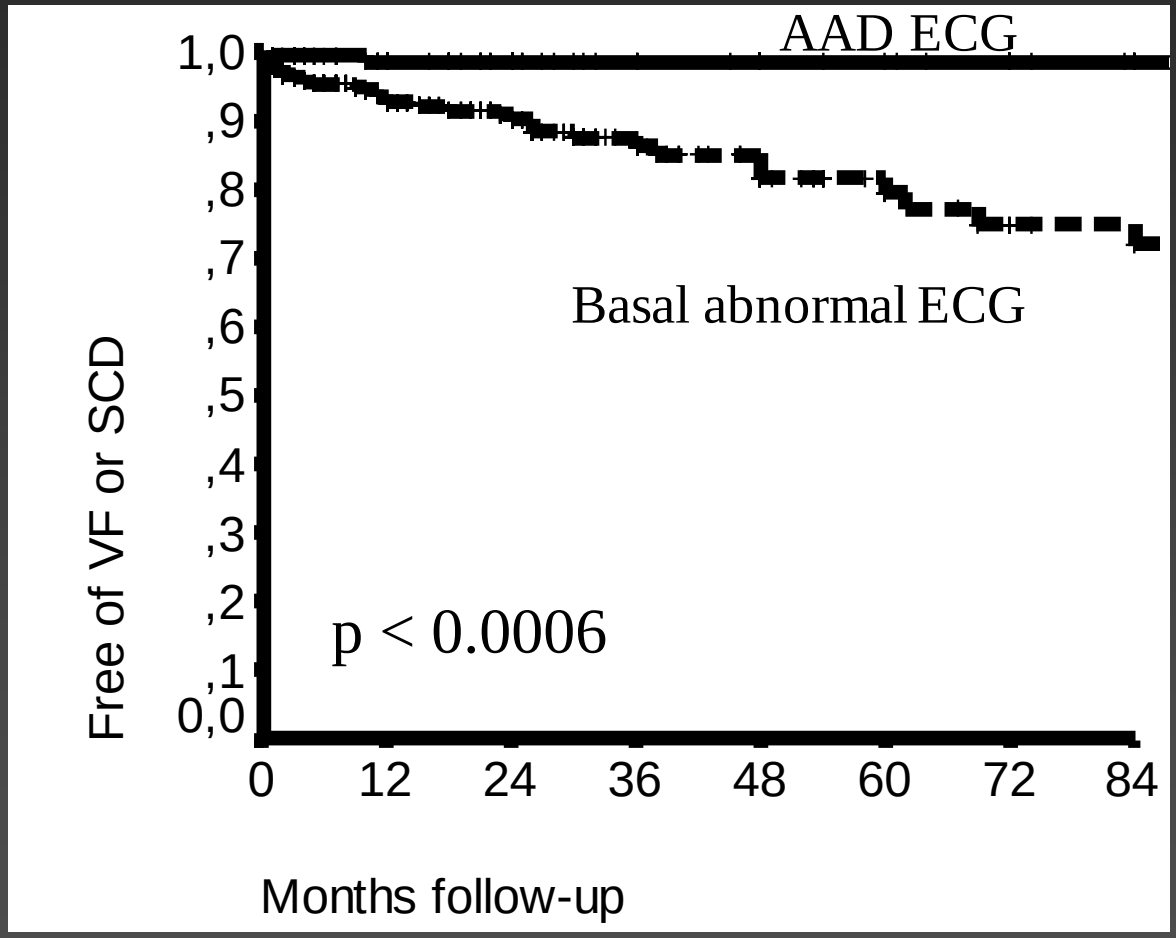
Documented VF, n=29



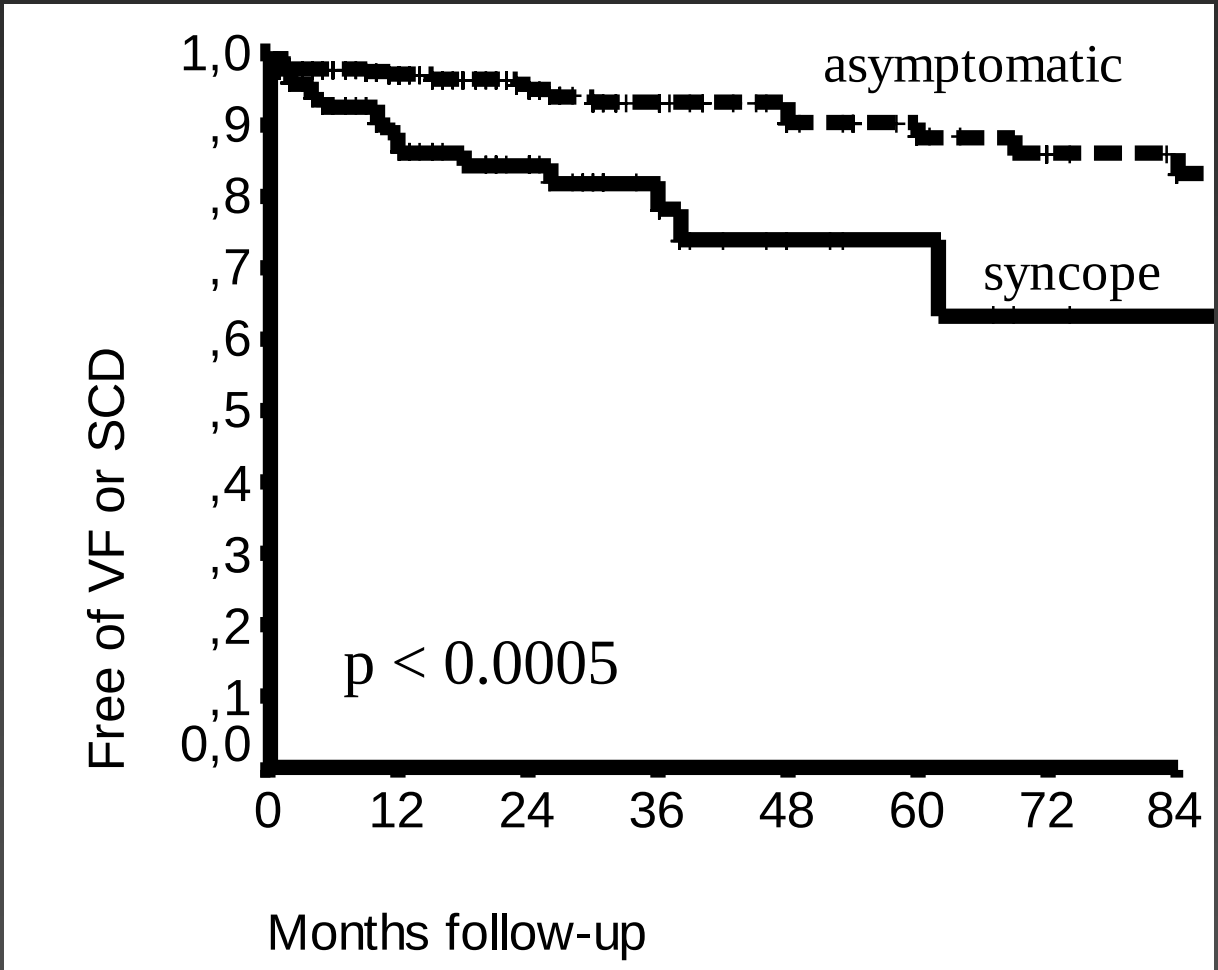
VF or SCD during follow-up depending on gender



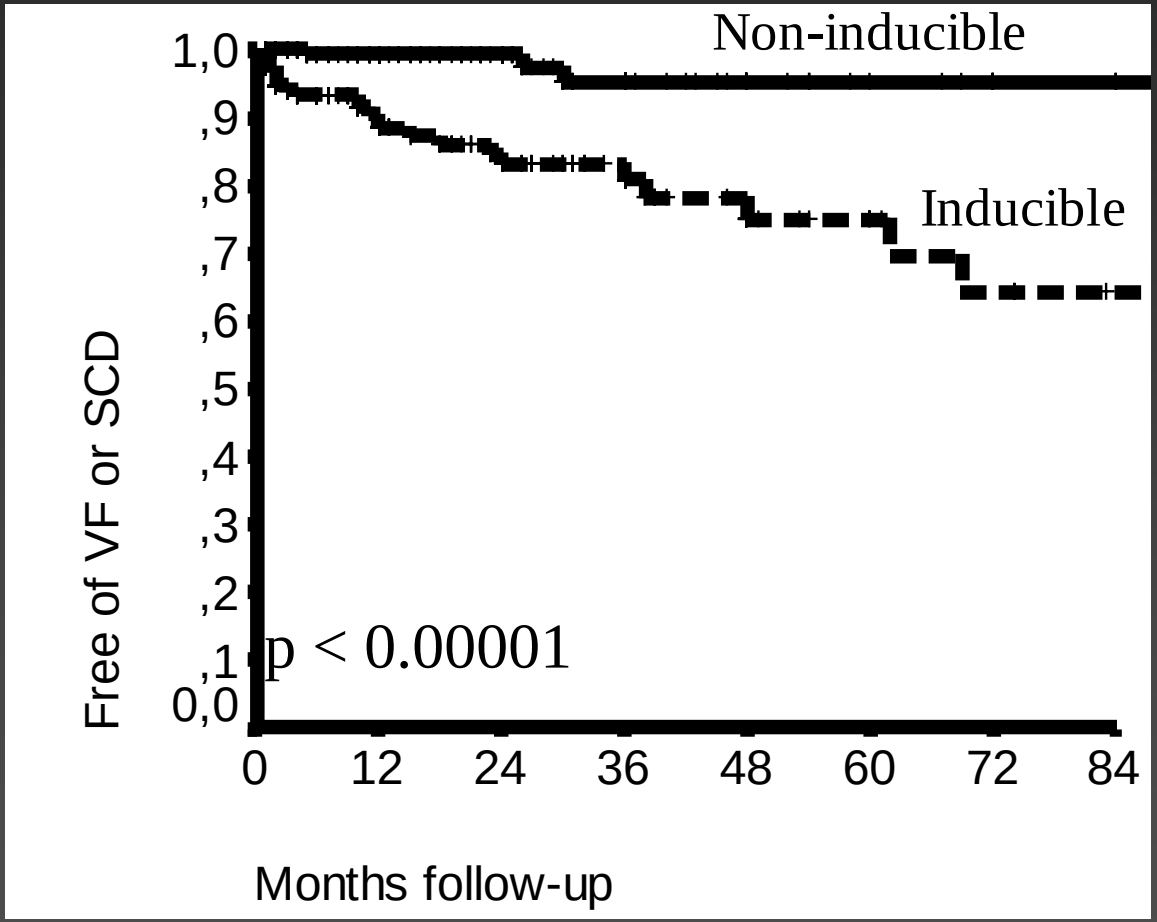
VF or SCD during follow-up depending on ECG



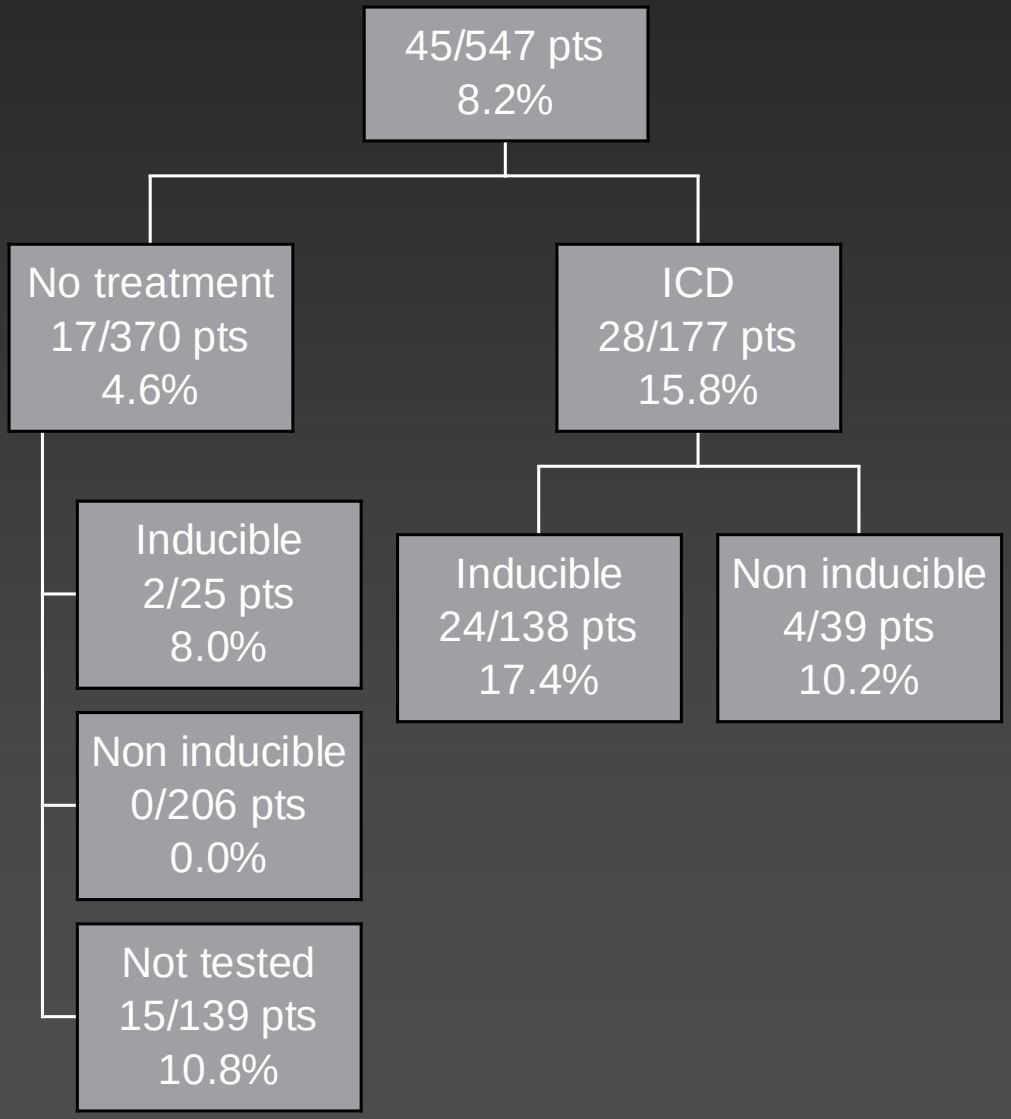
VF or SCD during follow-up depending on symptoms



VF or SCD during follow-up depending on inducibility



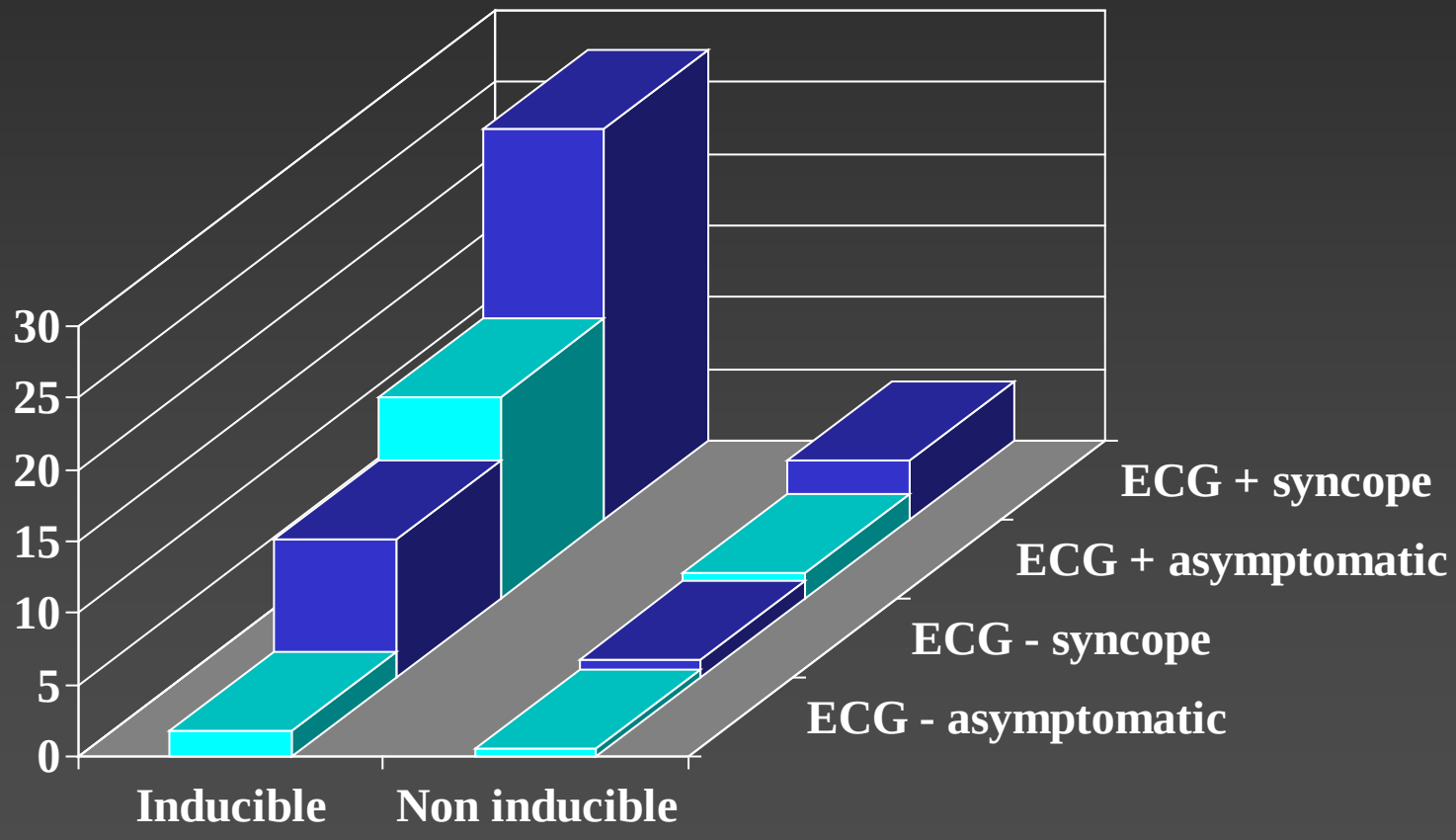
Treatment


45/547 pts
8.2%
No treatment
17/370 pts
4.6%
ICD
28/177 pts
15.8%
Inducible
2/25 pts
8.0%
Non inducible
0/206 pts
0.0%
Not tested
15/139 pts
10.8%
Inducible
24/138 pts
17.4%
Non inducible
4/39 pts
10.2%

Multivariate analysis

	Hazard ratio	95% CI	p
Inducible	5.88	2.0-16.7	0.0001
Syncope	2.51	1.2-5.3	0.017
Basal ECG	2.86	0.7-12.3	0.103

Logistic regression analysis. Probability of SD or VF after the diagnosis in patients without previous SD



Long Term follow-up

N = 361 patients

Mean age = 44.5 ±16 years

285 male (78.9%) and 76 female (21.1%)

58% asyntomatics, 19% syncope, 22% SD

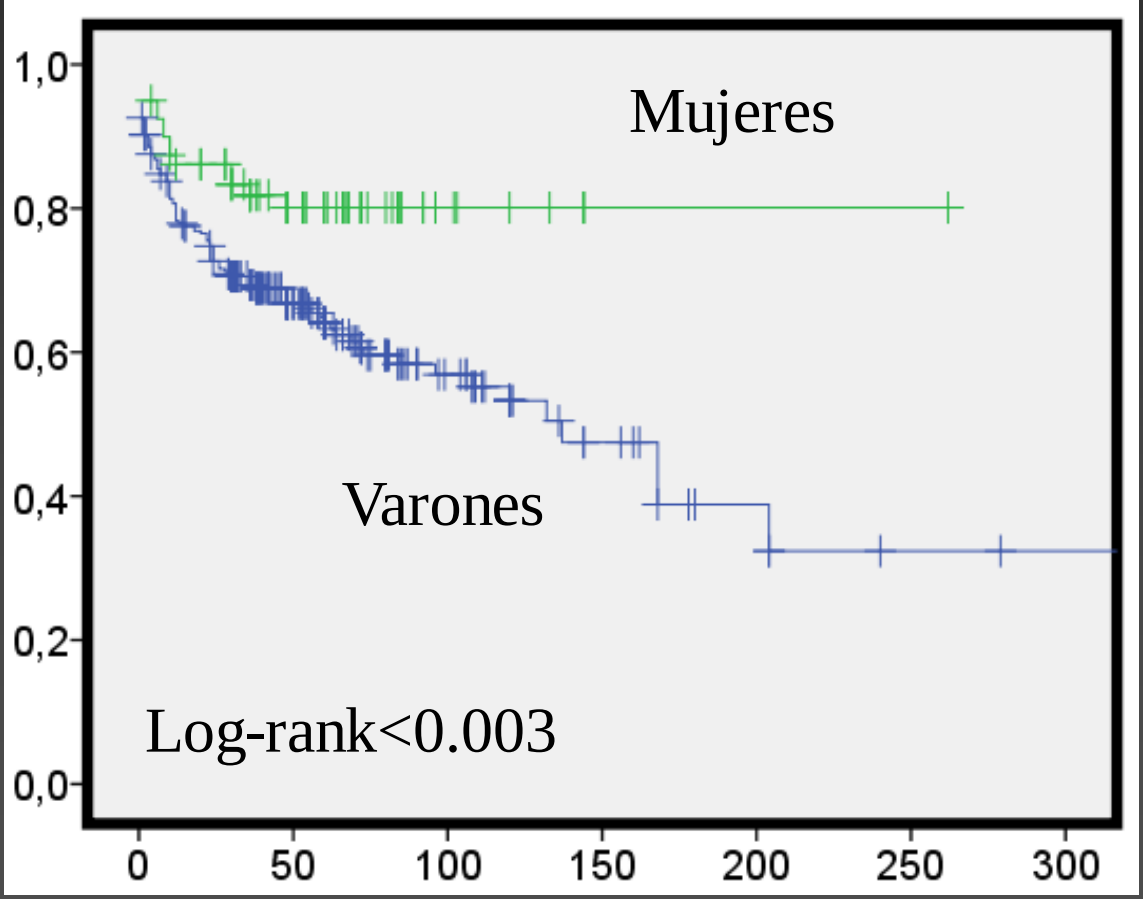
ECG basal diagnostic in 288 patients (80%) and in

73 patients (20%) with Class I drug

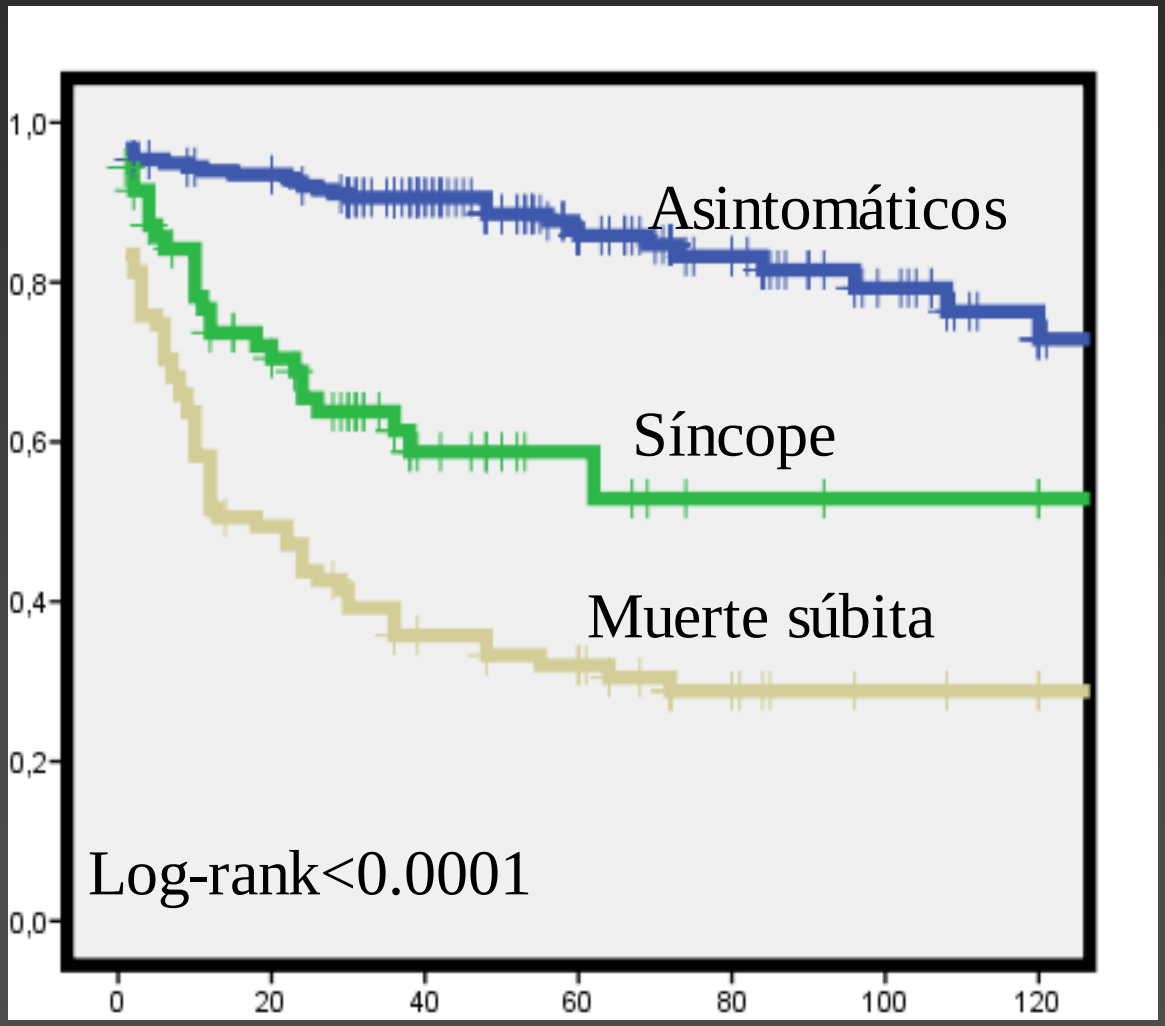
Follow-up

- ICD in 188 patients (52%)
- During a follow-up of 65 ± 46 months, 116 patients (32%) had major events (SD or documented VF).

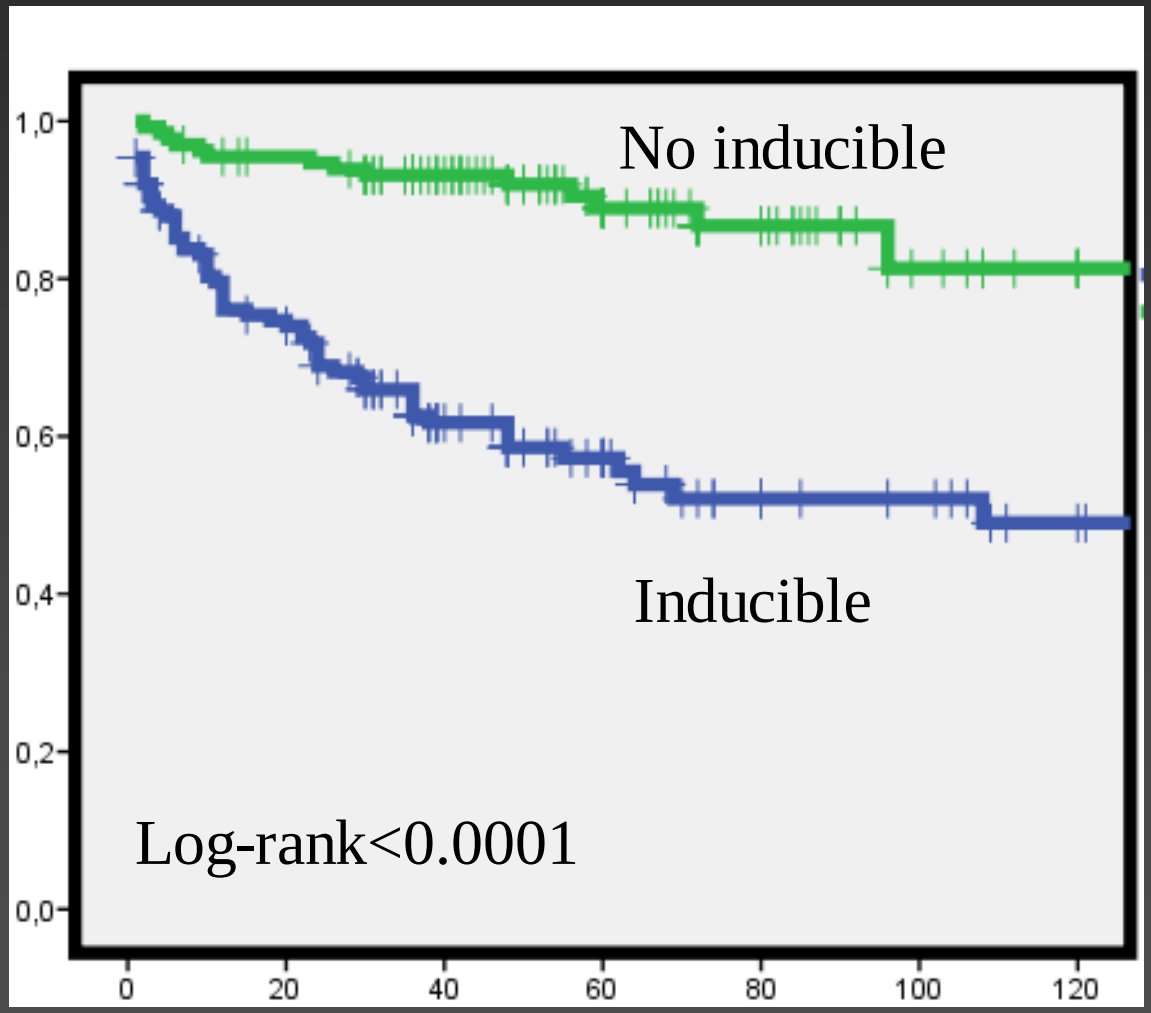
Major events (SD or VF) depending on gender



Major events (SD or VF) depending on previous symptoms



Major events (SD or VF) depending on inducibility



Multivariate analysis

Variable	HR	95% IC	P
Male	2,13	1,2-3,9	0,01
Syncope	3,77	2,2-6,3	< 0,001
SD	5,28	3,3-8,4	< 0,001
Inducibility	2,73	1,5-4,9	0,001

I am 28 years old, male. I was a very healthy individual.

I was on my duty about 10 p.m. I was talking on the phone when suddenly had lost my consciousness and hit the ground.

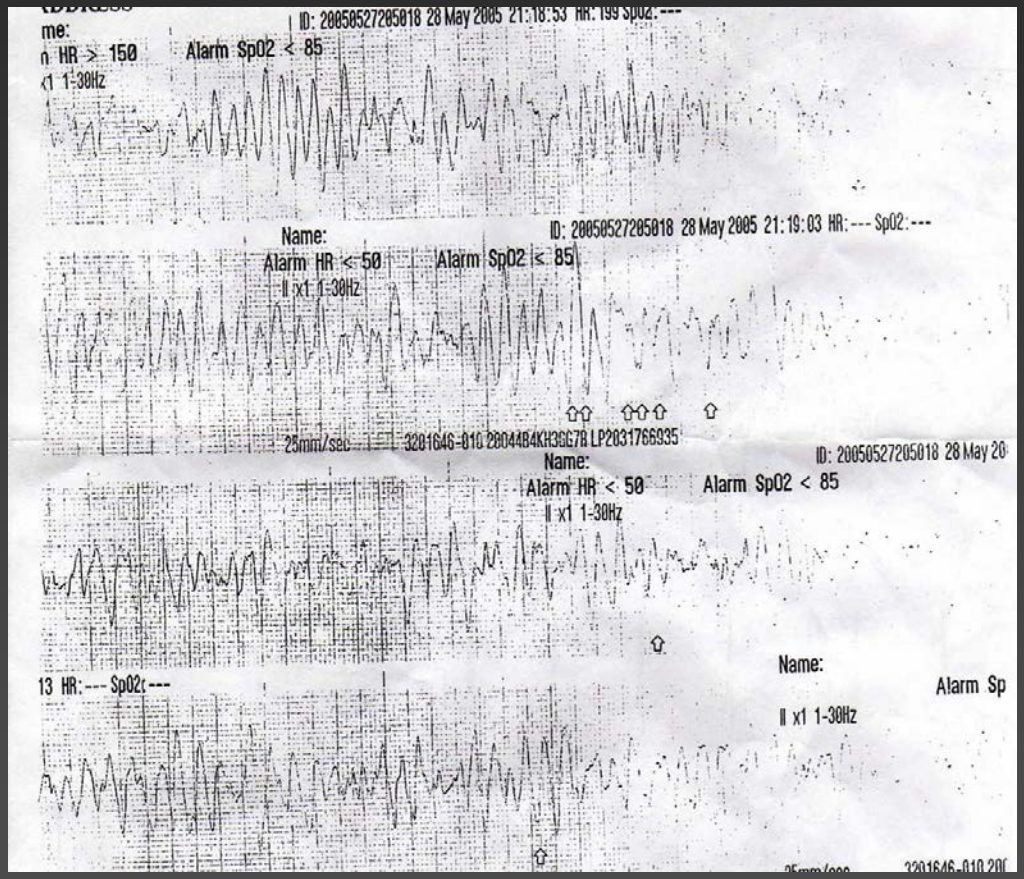
Luckily, I was seen by my co-resident …

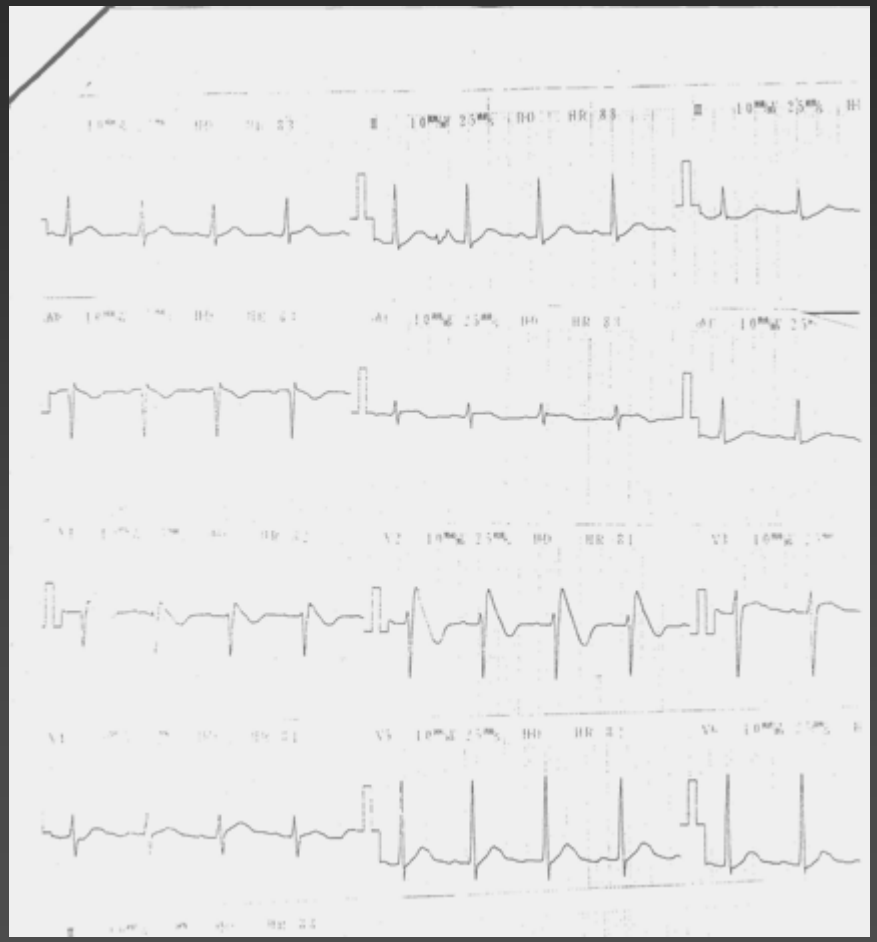
He immediately hooked me to a cardiac monitor.

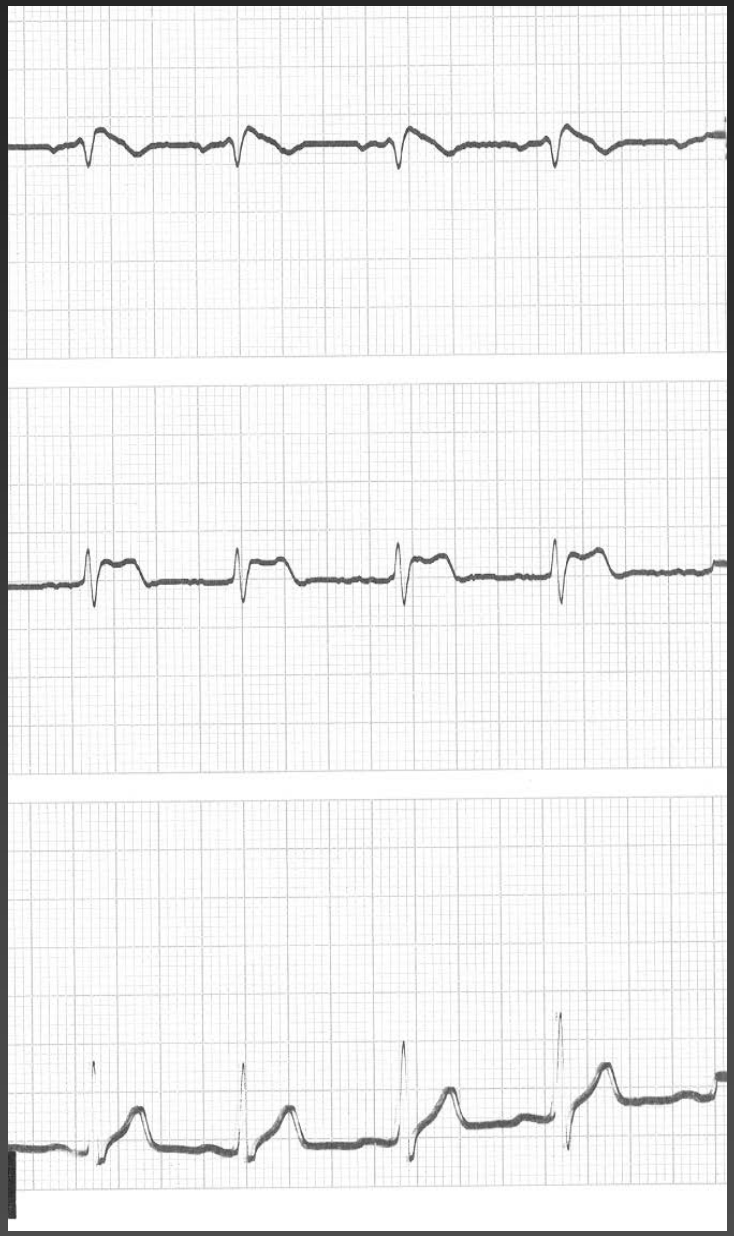
When I got my consciousness, I could not remember what happened….

Can you confirm the diagnosis and tell me the steps I need to follow to protect my family.

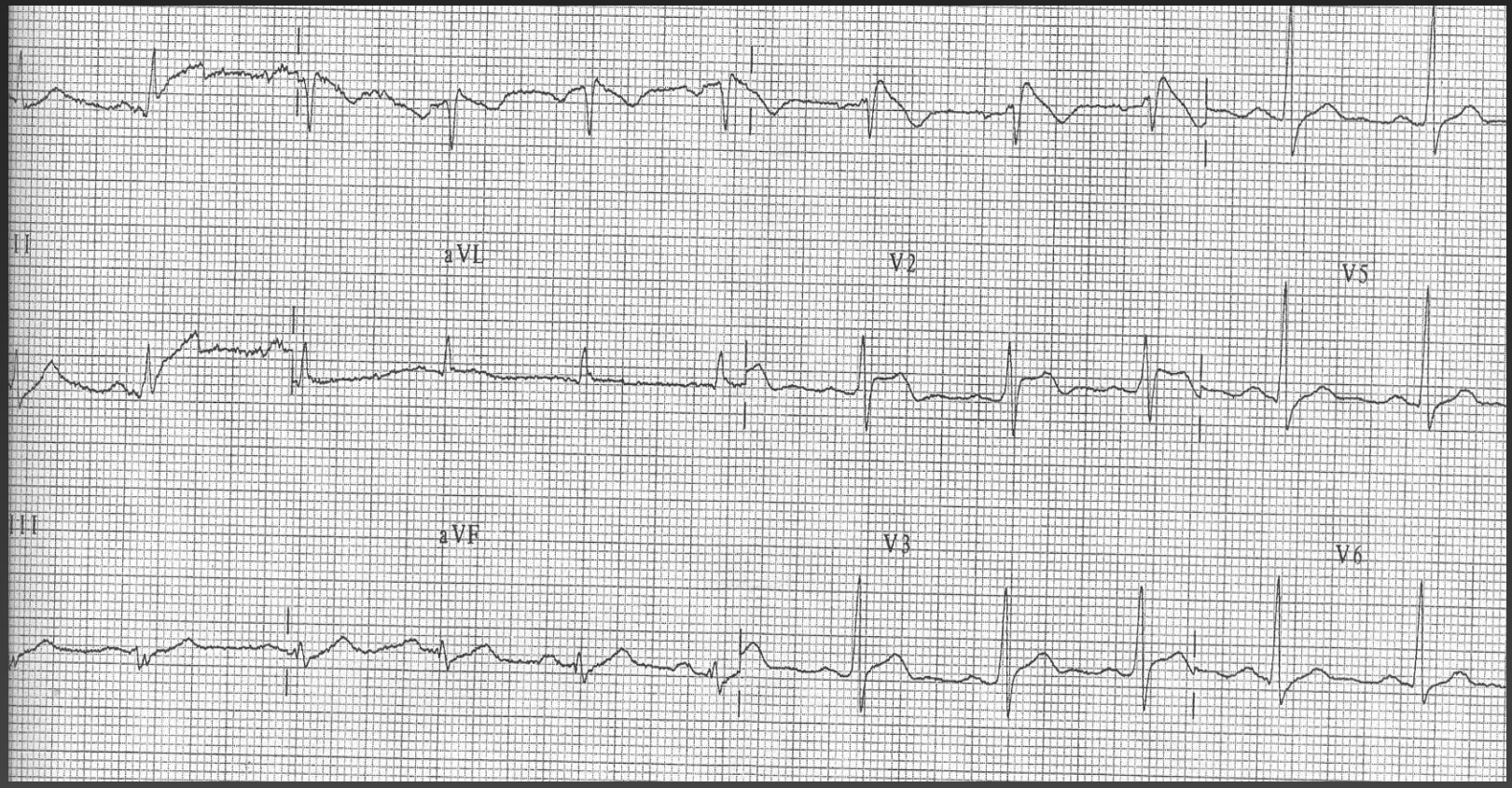
Cardiac arrest







34 years old male, asymptomatic, no family history, routine ECG, january 2004



ECG June 2004, asymptomatic, Echocardio normal, Holter normal, stress test normal. EPS advised, refused by the patient

August 2004: sudden arrhythmic death at 1 a.m., VF when EMS arrives

Necropsy: normal heart, normal coronary arteries. No other cause for sudden death: probably arrhythmic

Brugada syndrome: asymptomatic, sporadic cases

- 167 pts with a diagnostic abnormal ECG, and:
  - No previous symptoms
  - No family history of SCD or Brugada syndrome

Brugada syndrome: asymptomatic, sporadic cases - characteristics

- 137 males, 30 females
- Mean age 44±12 years old
- Basal abnormal ECG in 154 pts, after AAD in 13 pts
- EP testing done in 125 pts, not done in 43 pts
  - Inducible 36/125 pts (29%)

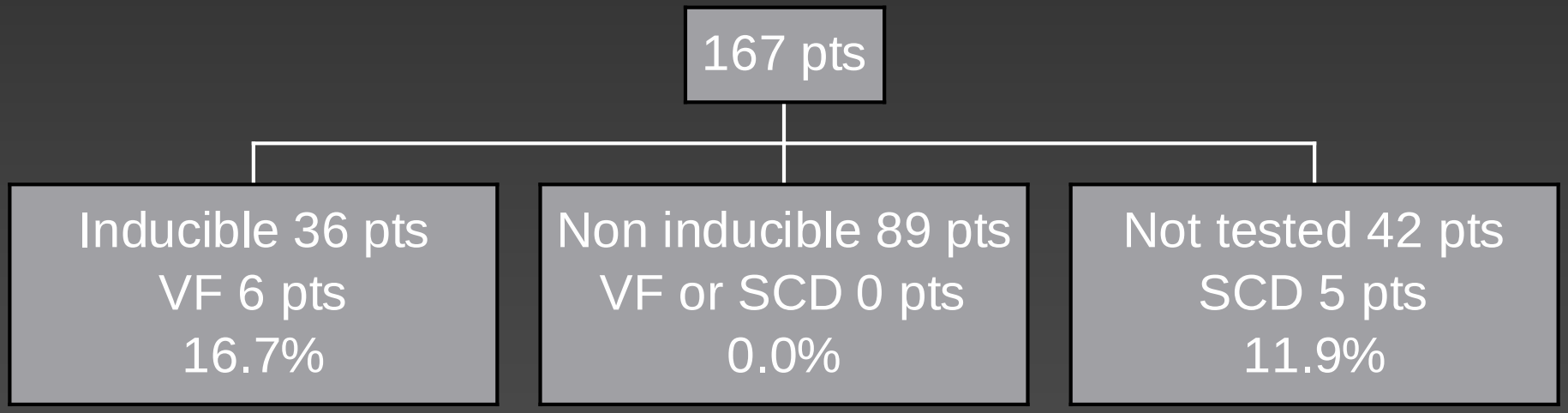
Brugada syndrome: asymptomatic, sporadic cases - treatment

- 36 pts received an ICD
  - 28 inducible
  - 8 non inducible

Brugada syndrome: asymptomatic, sporadic cases - follow-up

- Follow-up 28±42 months
  - 5 SCD
  - 6 documented VF

Arrhythmic events depending on EP study



PATIENTS AT RISK ACCORDING TO GENDER

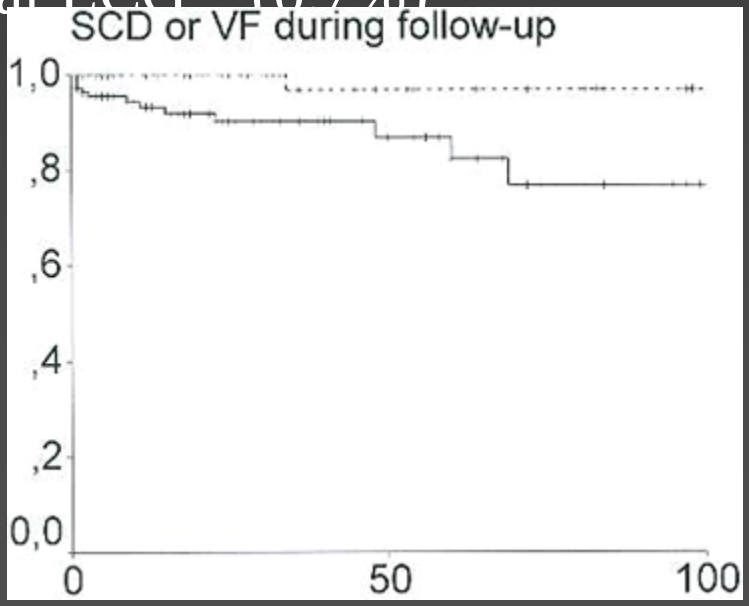
	MALE POPULATION			FEMALE POPULATION		
	No events (n=241)	Events (n=31)	p	No events (n=109)	Events (n=3)	p
Symptoms (%)	46 (19)	20 (64)	<0.001	16 (15)	1 (33)	NS
Spont Type-1 ECG	105 (43)	21 (67)	0.01	23 (21)	2 (67)	NS
PR interval (ms)	175 ± 30	178 ± 40	NS	173 ± 32	240 ± 62	0.001
QRS duration (ms)	107 ± 17	110 ± 18	NS	97 ± 16	130 ± 62	NS
QTc interval (ms)	421 ± 48	432 ± 42	NS	420 ± 49	486 ± 47	0.06
ST elevation	3.6 ± 2	3 ± 1	NS	2.4 ± 1	3.2 ± 1	NS
Induc. of VF (%)	64/232 (28)	20/27 (74)	<0.001	10/89 (11)	1/2 (50)	NS
HV interval (ms)	48 ± 10	46 ± 7	NS	46 ± 8	60 ± 11	0.02

Family members

- 267 asymptomatic individuals with familial forms
  - 136 with a basal abnormal ECG
  - 131 diagnosed after ajmaline-flecainide test
  - 64 inducible, 122 non inducible, 81 not tested
  - 65 ICD, 202 no treatment

Family members
Follow-up

- 16/267 (6%) individuals had an event (33±31 months)
- 9 sudden cardiac death, 7 VF documented by ICD
  - 15/136 with basal ECG + (11%)
  - 1/131 with basal ECG – (0.7%)



Events during follow-up vs inducibility

	VF	SCD	No event	Total
Inducible	7	1	56	64
Non inducible	0	1	121	122
Not done	0	7	74	81
Total	7	9	251	267

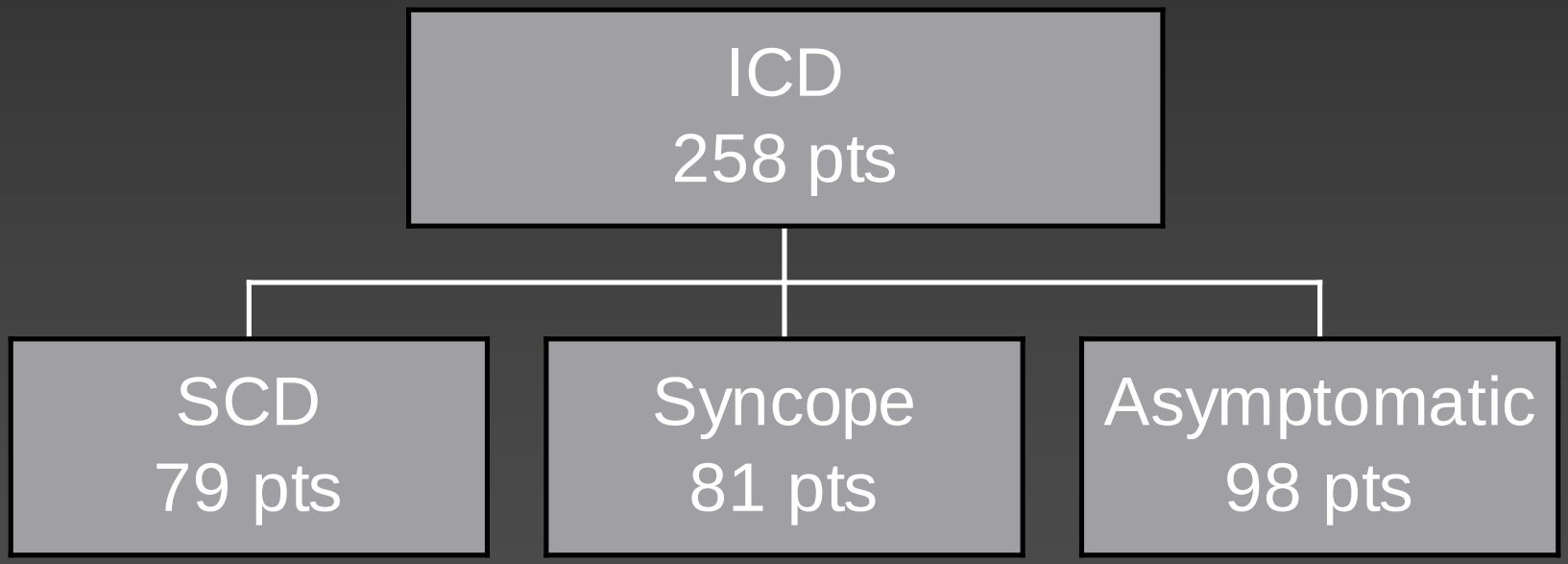
How to screen family members

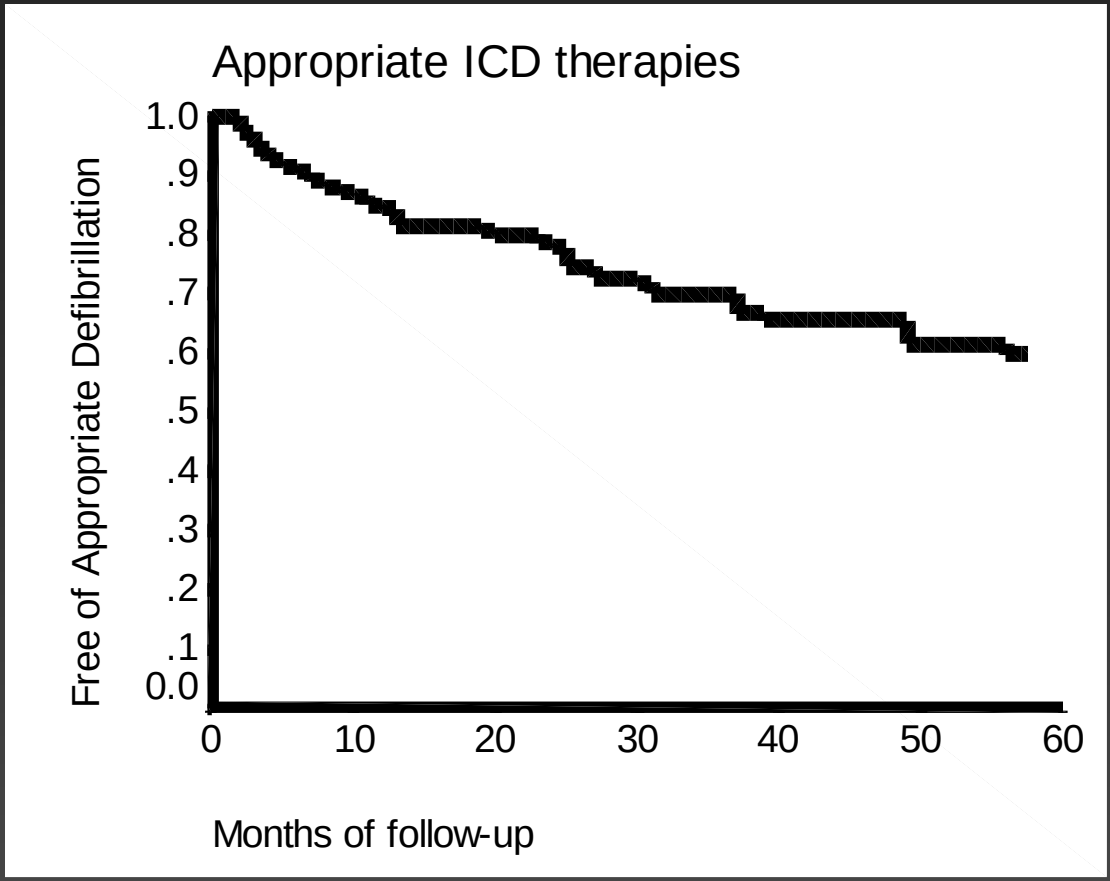
- Familial forms are usual in Brugada syndrome
- ECG is the tool for diagnosis
- Class I AAD test is very useful in identifying carriers of the disease

How to screen family members

- Asymptomatic family members with a basal normal ECG have a good prognosis
  - Ajmaline test should be done only for diagnostic purposes
- Asymptomatic family members with a basal abnormal ECG should be tested using PES
  - If non inducible they have a good prognosis
  - If inducible they should be protected

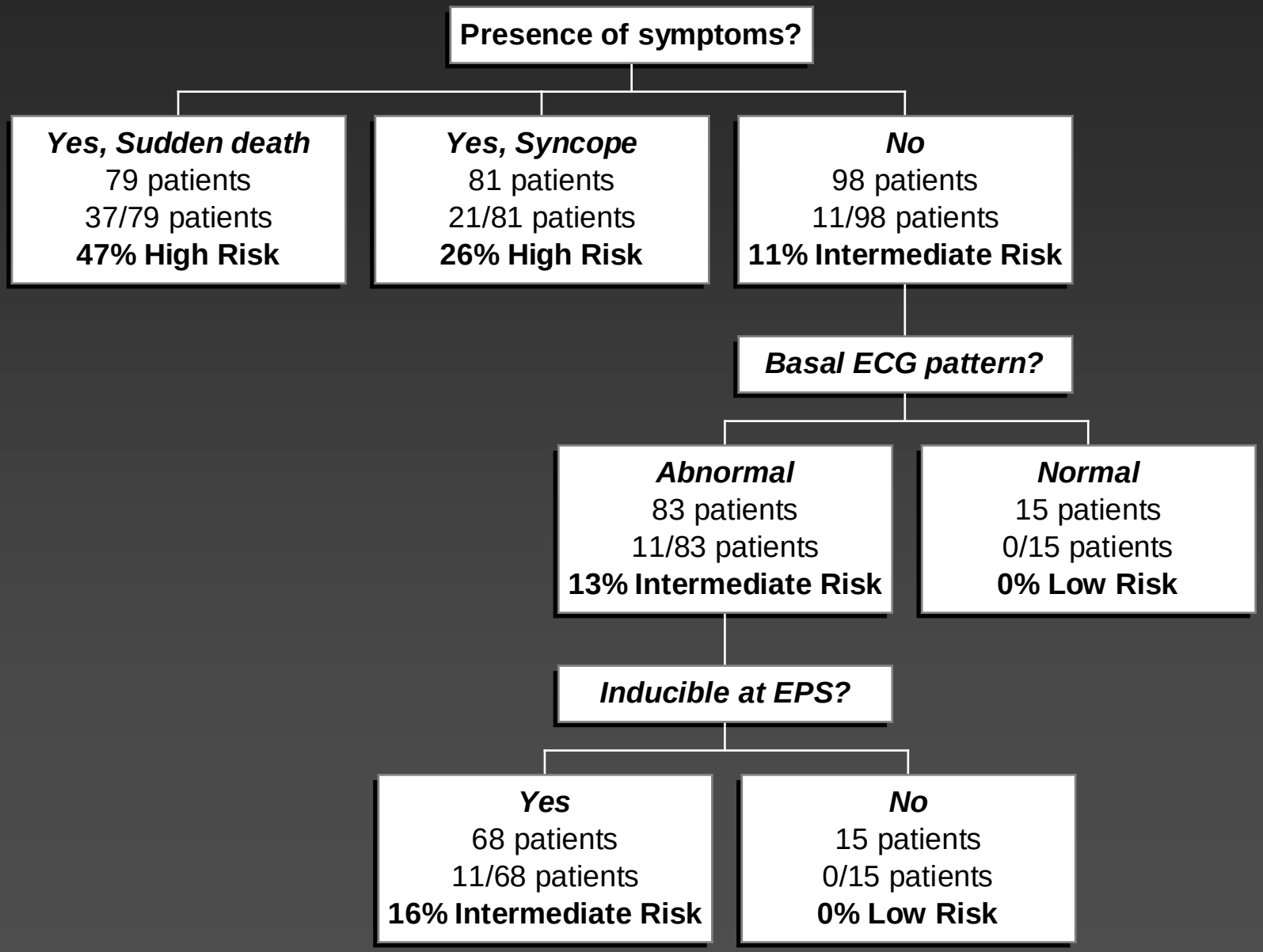
Patients with ICD





Months	0	12	24	36	48	60
Patients	258	154	101	66	50	35
VF events	0	39	9	8	4	1
Events (%)	0	19	26	34	39	41

Risk stratification in pts with Brugada syndrome and an ICD



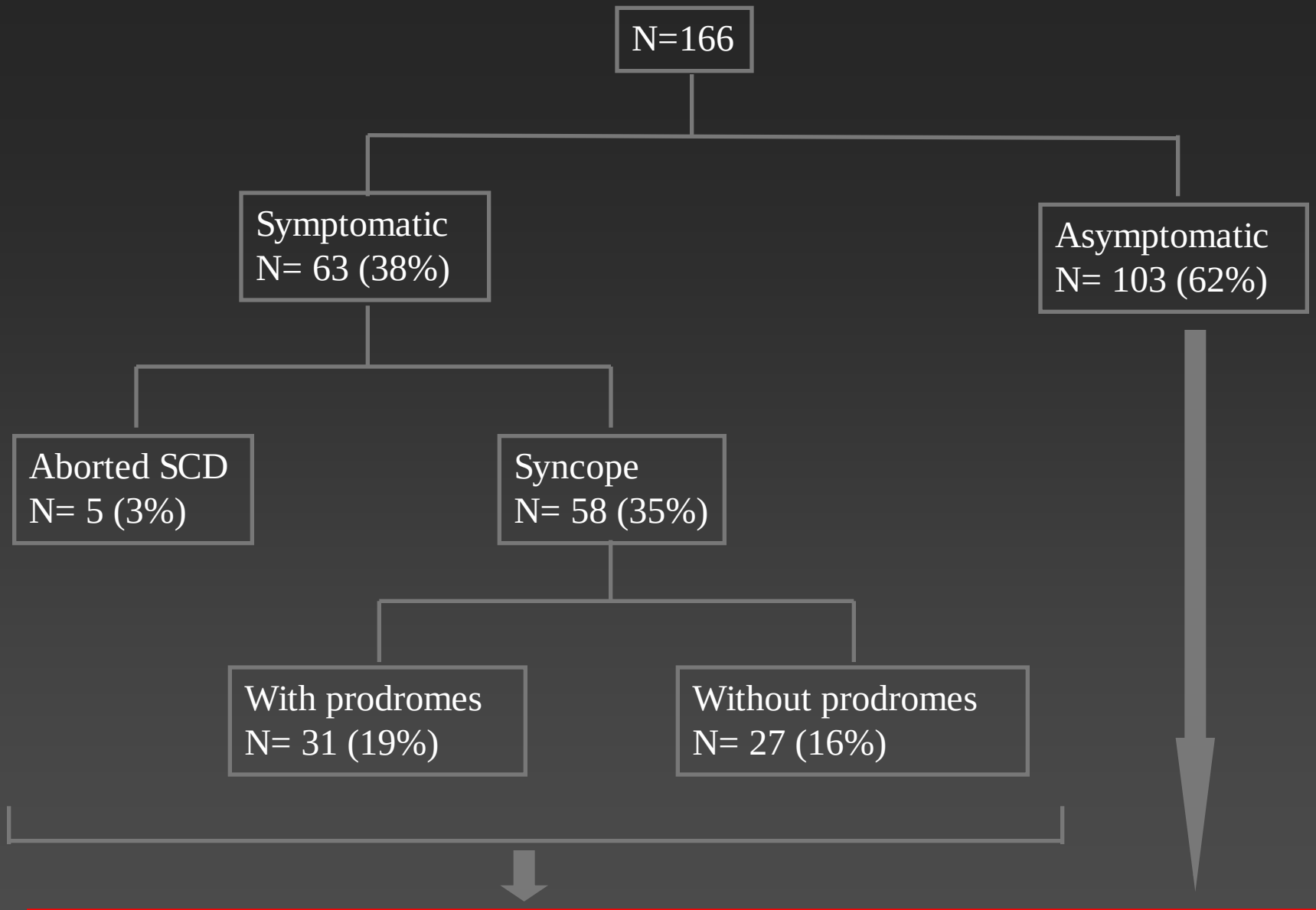
Europace (2009) 11, 507–513
doi:10.1093/europace/eup006

CLINICAL RESEARCH
Brugada Syndrome

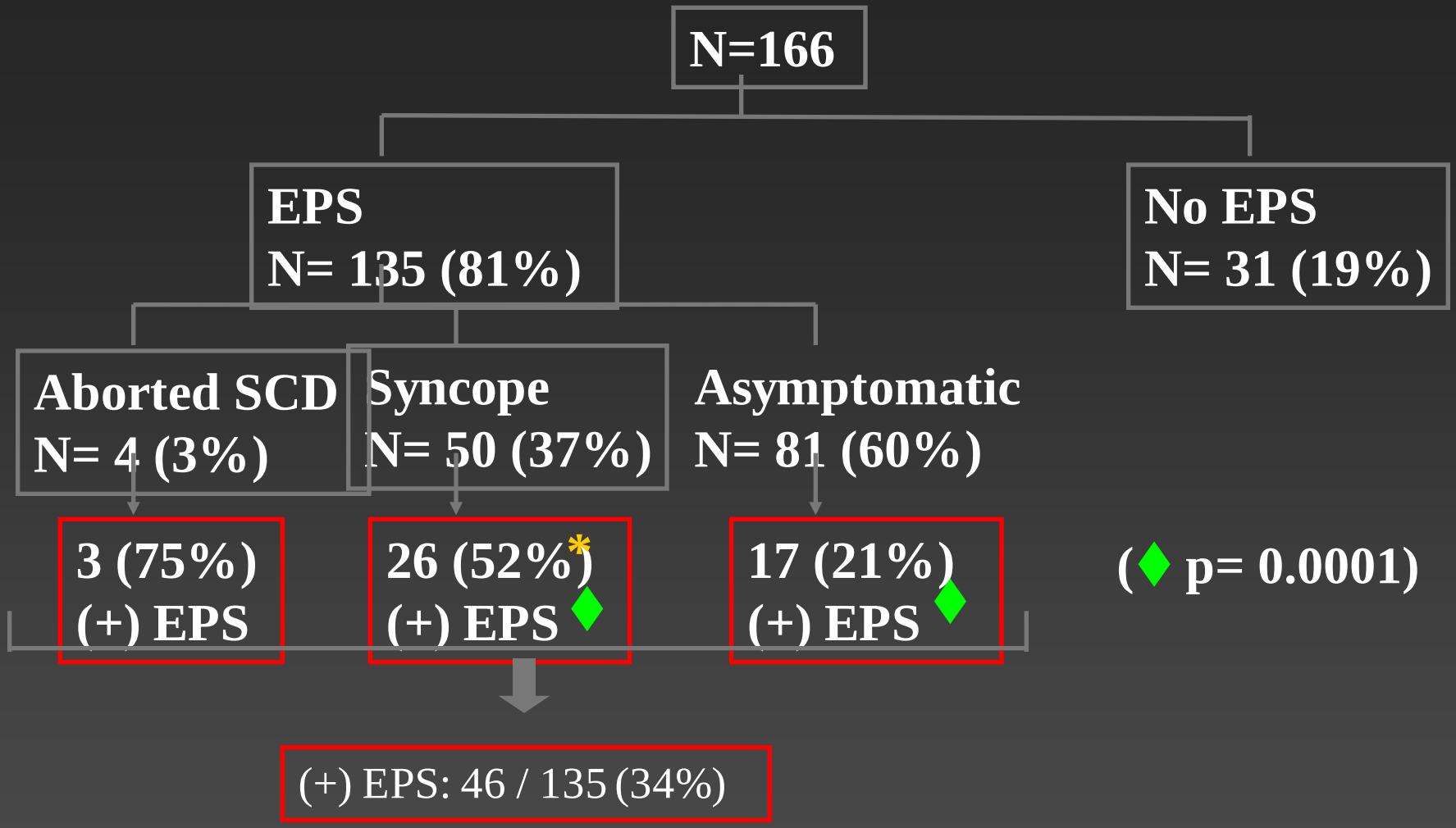
Risk stratification of the patients with Brugada type electrocardiogram: a community-based prospective study

Carla Giustetto[1]*, Stefano Drago[1], Pier Giuseppe Demarchi[2], Paola Dalmasso[3], Francesca Bianchi[4], Andrea Sibona Masi[5], Paula Carvalho[6], Eraldo Occhetta[7], Guido Rossetti[8], Riccardo Riccardi[4], Roberta Bertona[9], and Fiorenzo Gaita[1] on behalf of the Italian Association of Arrhythmology and Cardiostimulation (AIAC)—Piedmont Section

- 166 consecutive BS patients
- 138 ♂ (83%)
- Mean age at diagnosis: 45 ± 14 years
- Family history SCD: (+) in 39 (23%)
- Family history BS: (+) in 24 (14%)
- Basal ECG:
  - 72 (43%) Type 1
  - 38 (23%) Type 2
  - 56 (34%) Type 3
- Genotype: Done in 66 (40%)
  Results available in 48
  10/48 SCN5A (+) (21%)



Giustetto C et al. Europace (2009) 11,507-513.

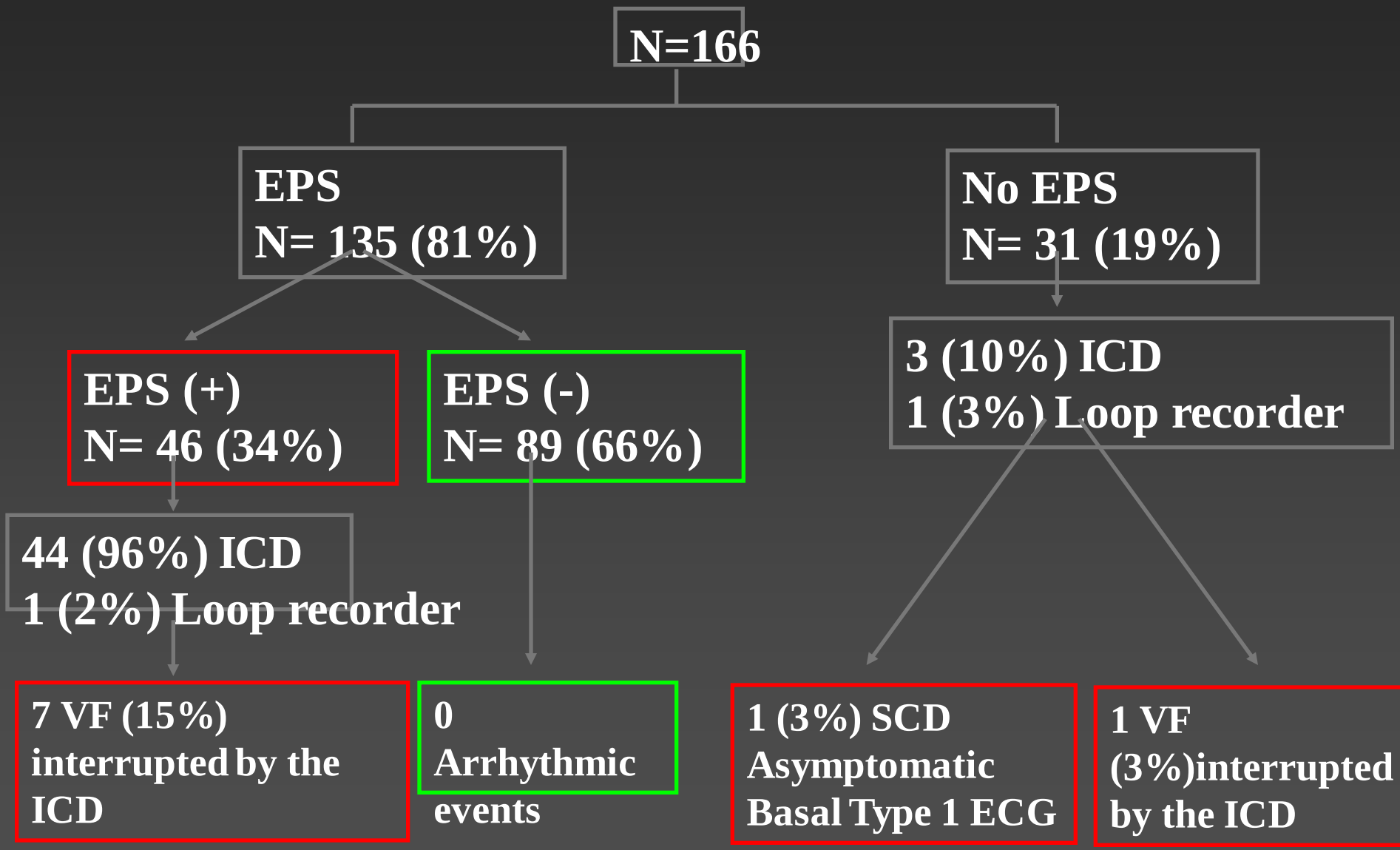


Syncope (OR=4.24; p=0.001)

♂ (OR= 11.1; p= 0.02)

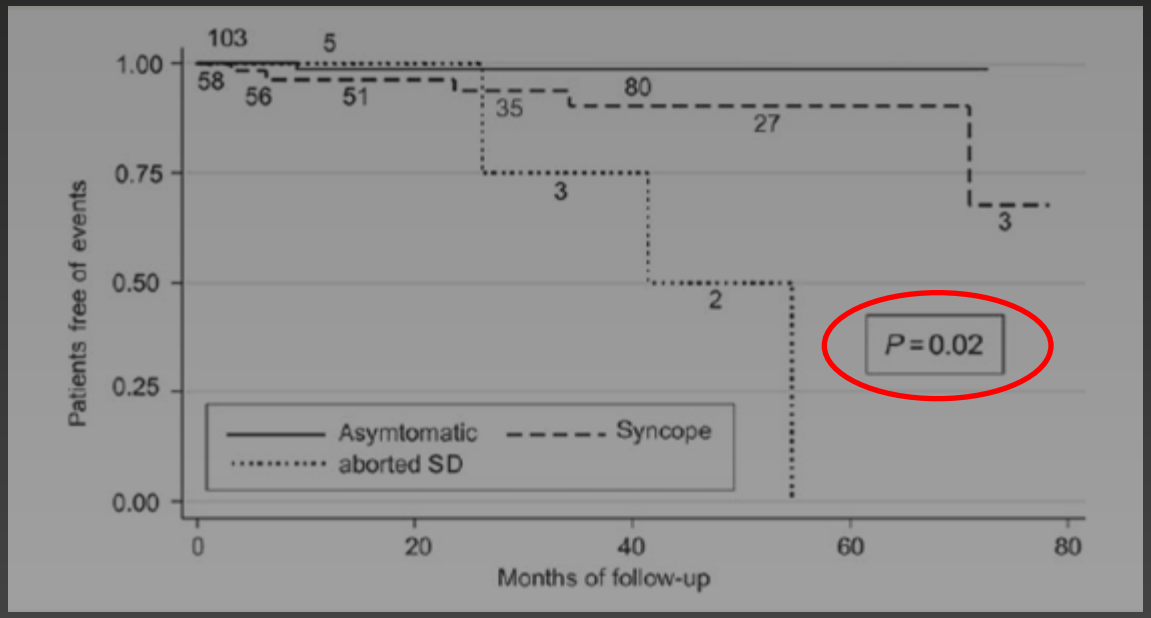
Giustetto C et al. Europace (2009) 11,507-513.

FOLLOW-UP: 30 ± 21 months



Giustetto C et al. Europace (2009) 11,507-513.

EVENTS IN THE FOLLOW-UP (HISTORY OF SYMPTOMS)



History of symptoms

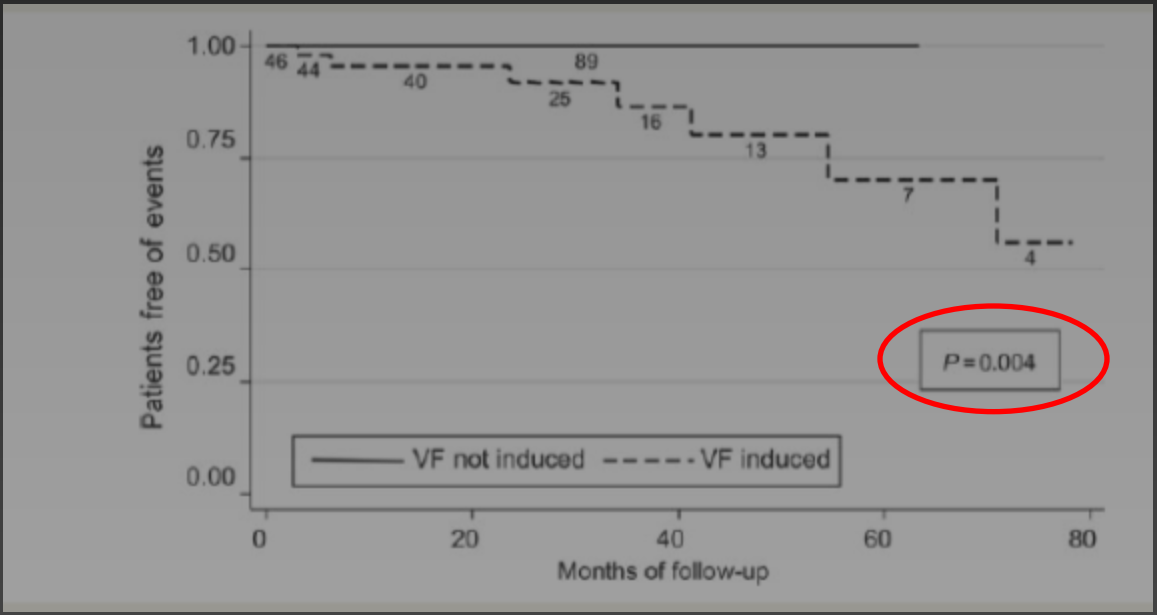
• SCD	3/5	(60%)
• Syncope *	5/58	(8.6%)
• Asymptomatic (Basal type 1 ECG)	1/103	(1%)

p= 0.02

Giustetto C et al. Europace (2009) 11,507-513.

* No difference according to prodromes

EVENTS IN THE FOLLOW-UP (EPS RESULTS)



Inducibility (EPS)

- EPS (-) 0/89 (0%)
- EPS (+) 7/46 (15%)

p= 0.004

Giustetto C et al. Europace (2009) 11,507-513.

CONCLUSIONS

- Clinical presentation is the most important parameter in risk stratification of BS patients
- Programmed electrical stimulation seems valuable, particulary in patients with previous syncope

Giustetto C et al. Europace (2009) 11,507-513.

Conclusions

- Asymptomatic pts with an spontaneous ECG diagnostic of Brugada syndrome should be studied using PES
  - Inducible pts should receive an ICD
  - Non inducible pts do not seem to benefit from the ICD
- An ICD is not indicated in asymptomatic pts with a diagnostic ECG seen only after class I AAD