Management of Syncope in Heart Failure

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University of Iowa

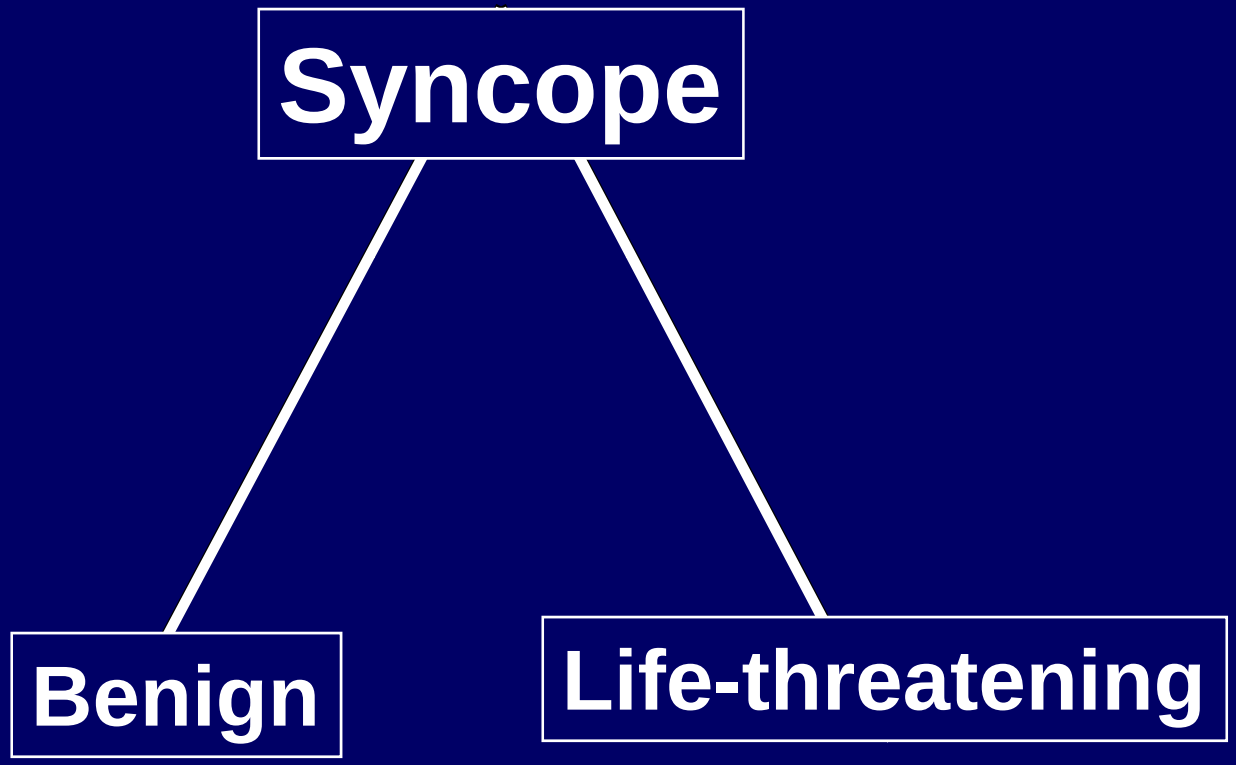
Syncope

- Transient loss of consciousness, with rapid, usually complete, recovery, with or without prodrome
- A common, non-specific, alarming, debilitating, symptom with diverse causes due to various conditions

Syncope – Observations

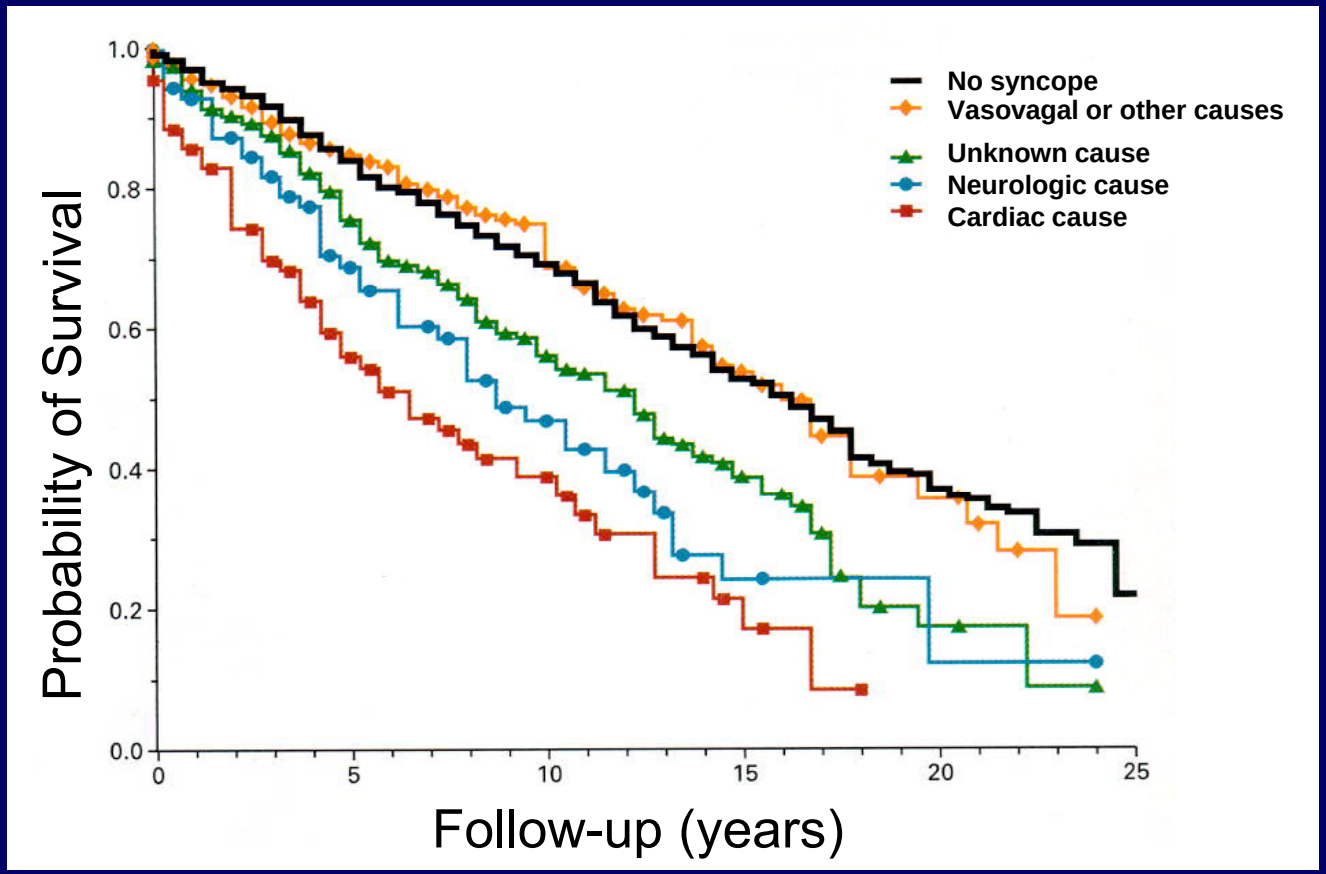
- Symptom – confusing
- Evaluation - no gold standard
- Diagnosis – suspect
- Natural history - uncertain
- Treatment – complex with several goals

The Challenge



Not the only challenge

Syncope - Outcomes



Cardiac diagnosis doubles the risk of death

Soteriades ES. N Engl J Med. 2002;347:878-885

Syncope in Heart Failure

- Syncope in 12-16% in FC III-IV CHF
- 1-year sudden death rate: 45% (syncope) vs 12% (no syncope) $p<0.00001$
- Cardiac cause in 48% but cause of syncope and EP results did not predict risk of death
- Syncope an independent risk factor

Middlekauff H. J Am Coll Cardiol. 1993;21:110-6
Stevenson W. J Am Coll Cardiol. 1996;28:1458-63

In Dilated Cardiomyopathy

- Syncope incurred higher risk of sudden death (5/16 vs. 1/34)[1]
- Syncope associated with greater risk of inducible arrhythmias[2]
- Syncope associated with similar rate of death but greater risk of sudden death[3]

[1]Tchou PJ. JACC 1991;17:196a; [2]Brembilla-Perrot. Am Heart J 1991;121:1124-1131
[3]Fruhwald FM. Cardiology 1996 87:177-180

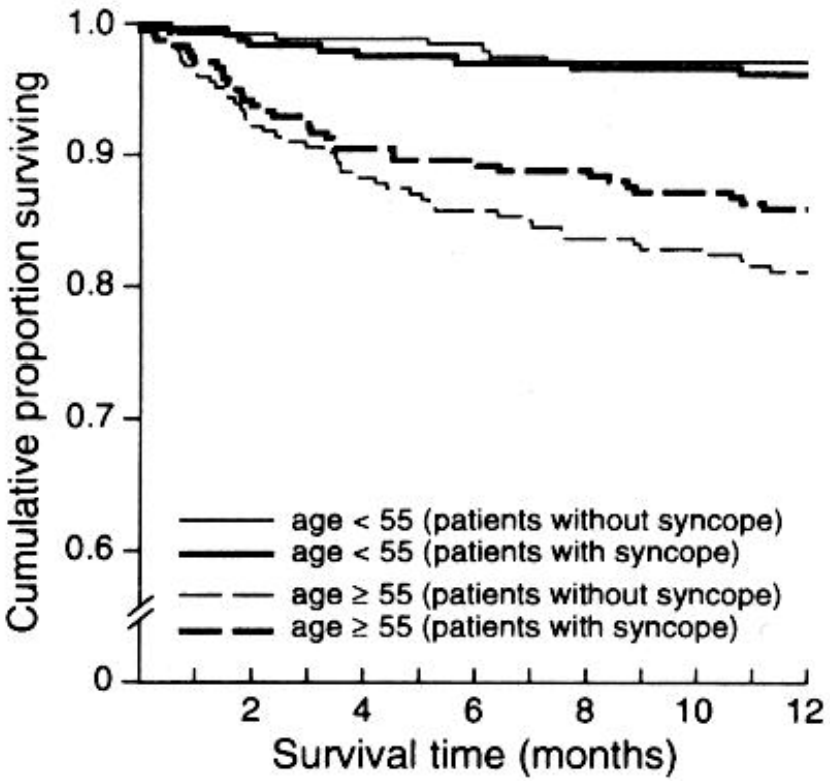
What Increases Risk of Death?

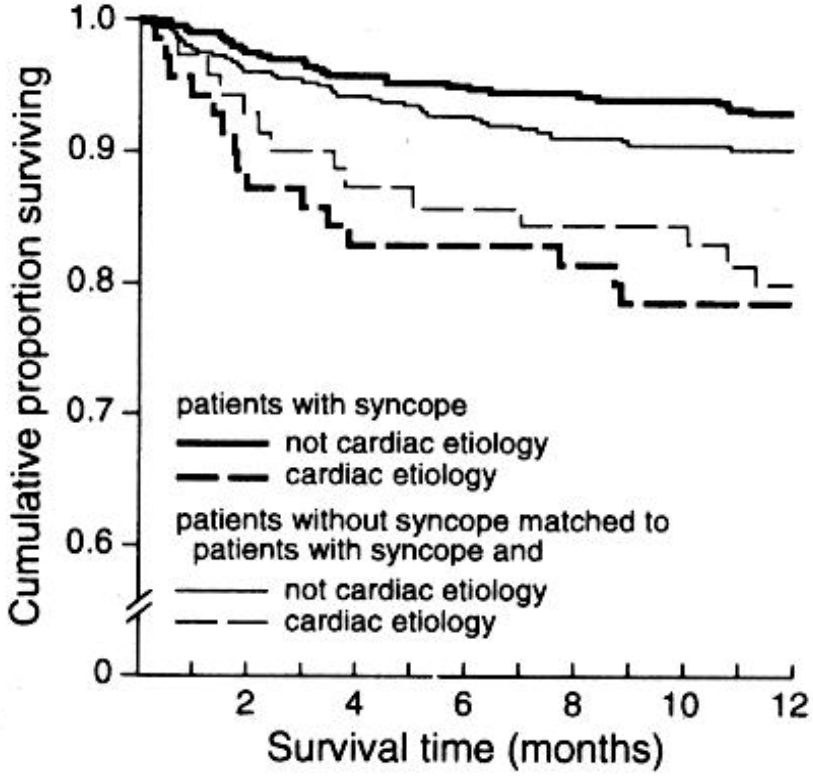
- Cardiomyopathy
- Heart failure symptoms
- Bundle branch block

- Does syncope increase risk independent of these factors?

Syncope

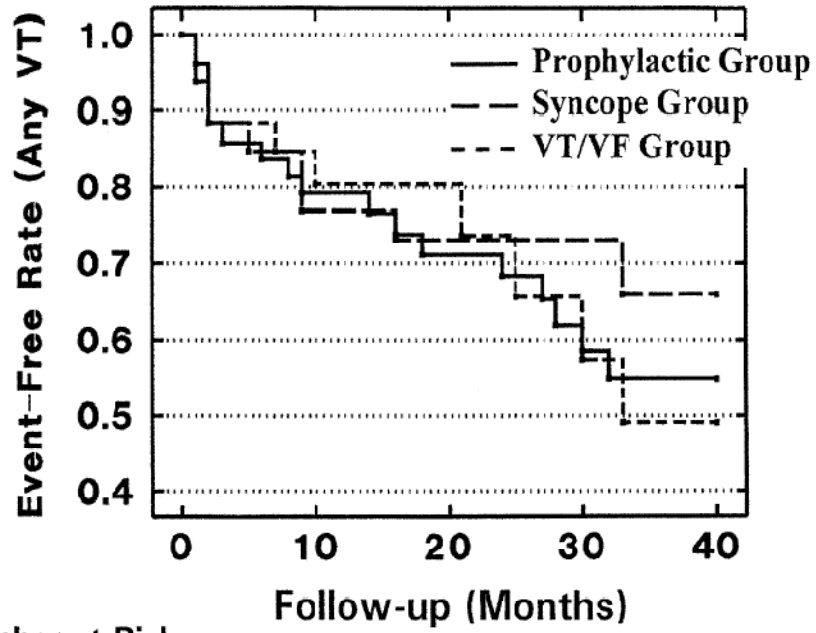
A Risk Factor for a Poor Outcome?



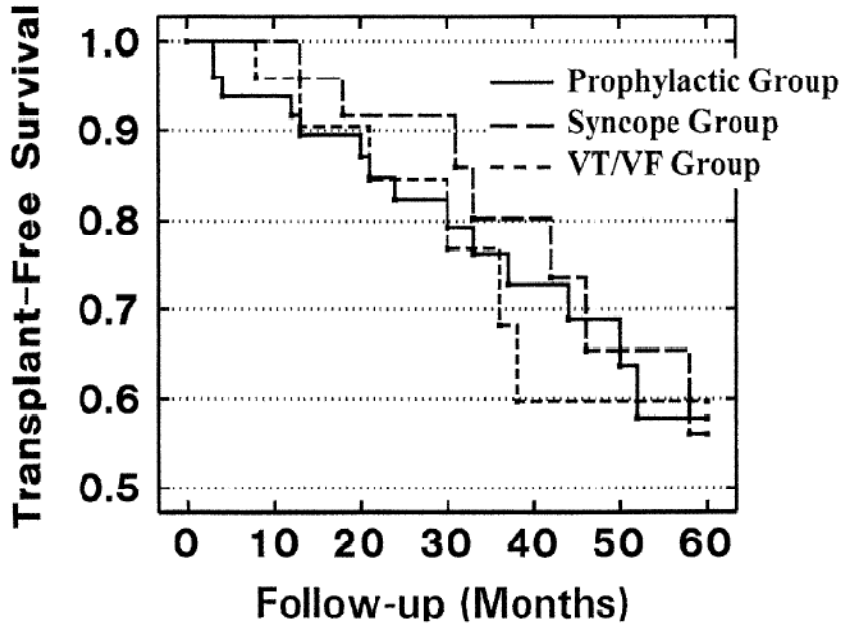


Kapoor WN, Hanusa BH. Am J Med 1996;100:646-55

Does Syncope Predict?



Number at Risk					
Prophyl. Group	49	35	26	18	12
Syncope Group	26	19	15	12	10
VT/VF Group	26	20	12	8	5



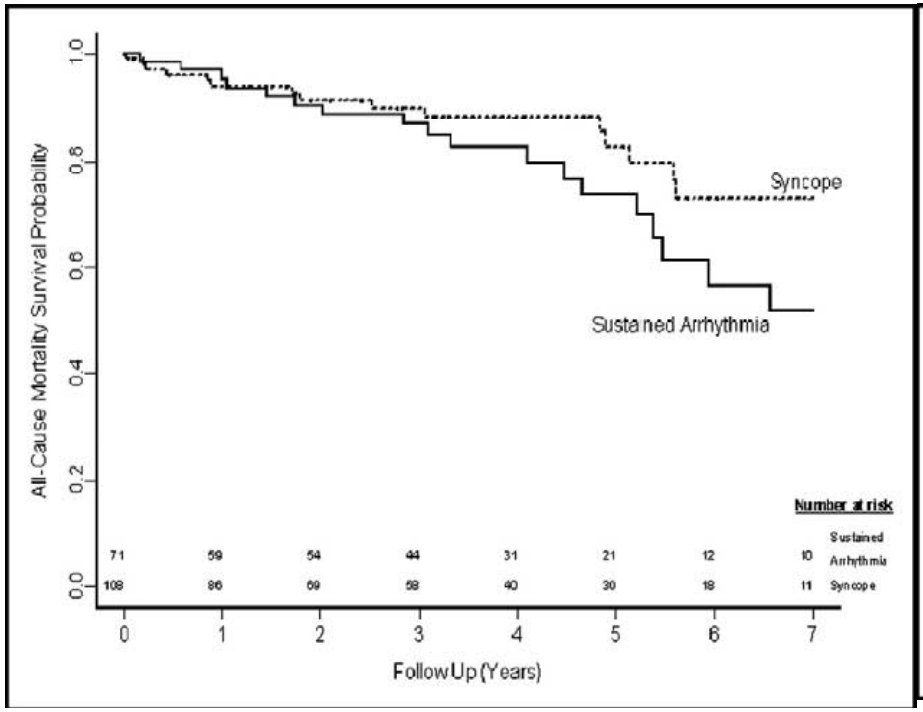
Number at Risk							
Prophyl. Group	49	44	38	27	20	13	7
Syncope Group	26	25	20	17	14	8	7
VT/VF Group	26	22	15	11	7	6	6

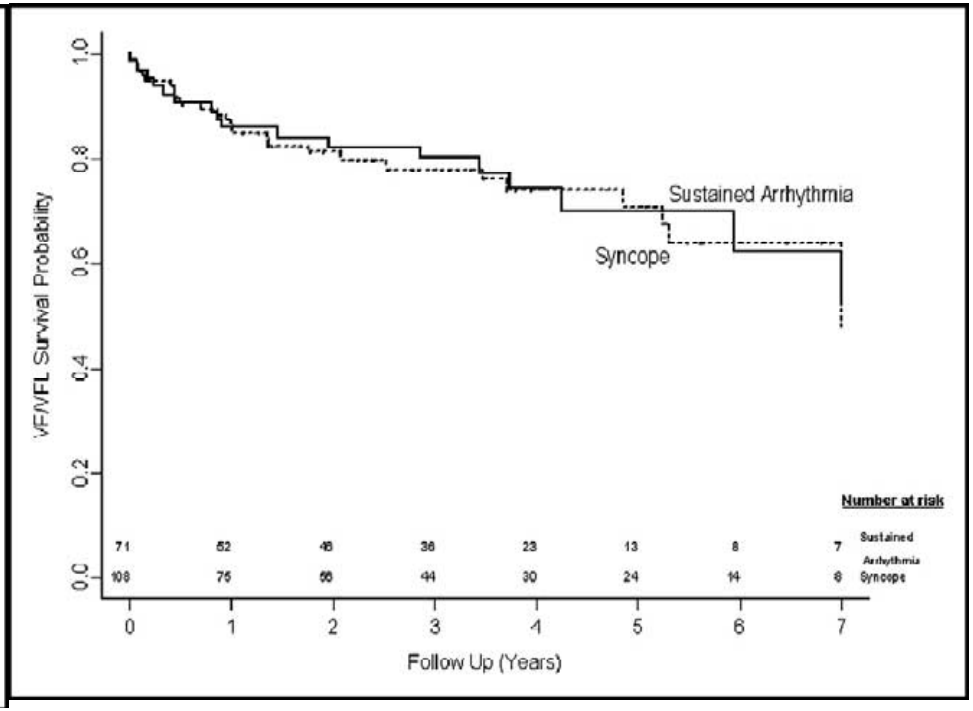
Dilated Cardiomyopathy
primary and secondary prevention ICDs - outcomes

Grimm W. J Am Coll Cardiol 2002;39:780 –7

Dilated Cardiomyopathy

A High Risk Group?

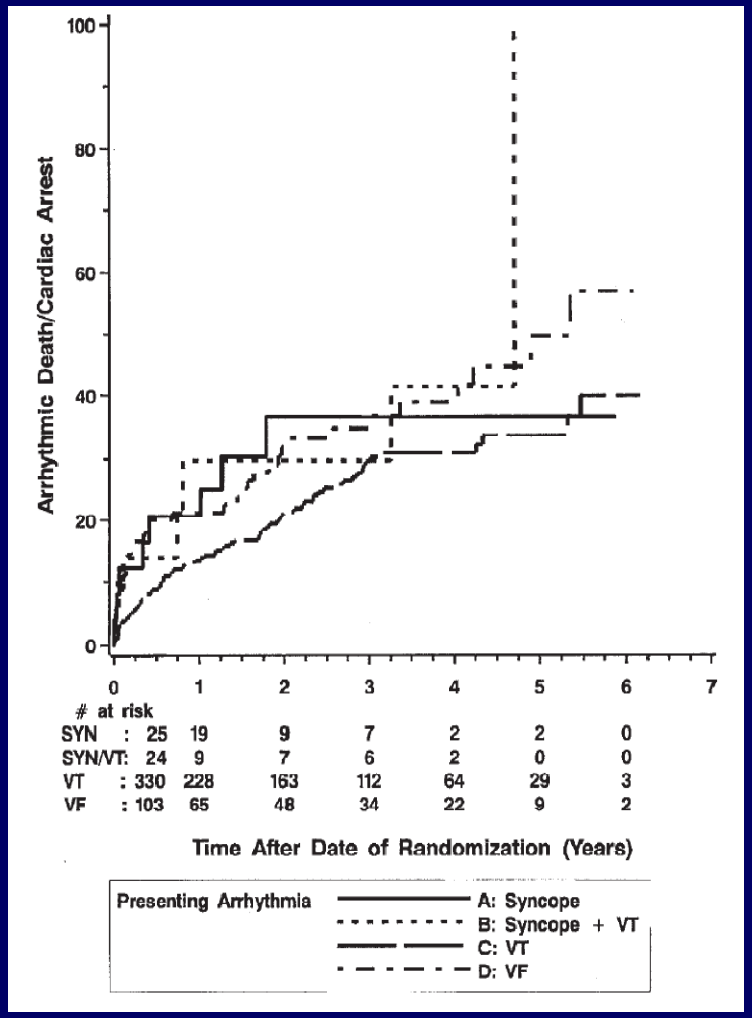


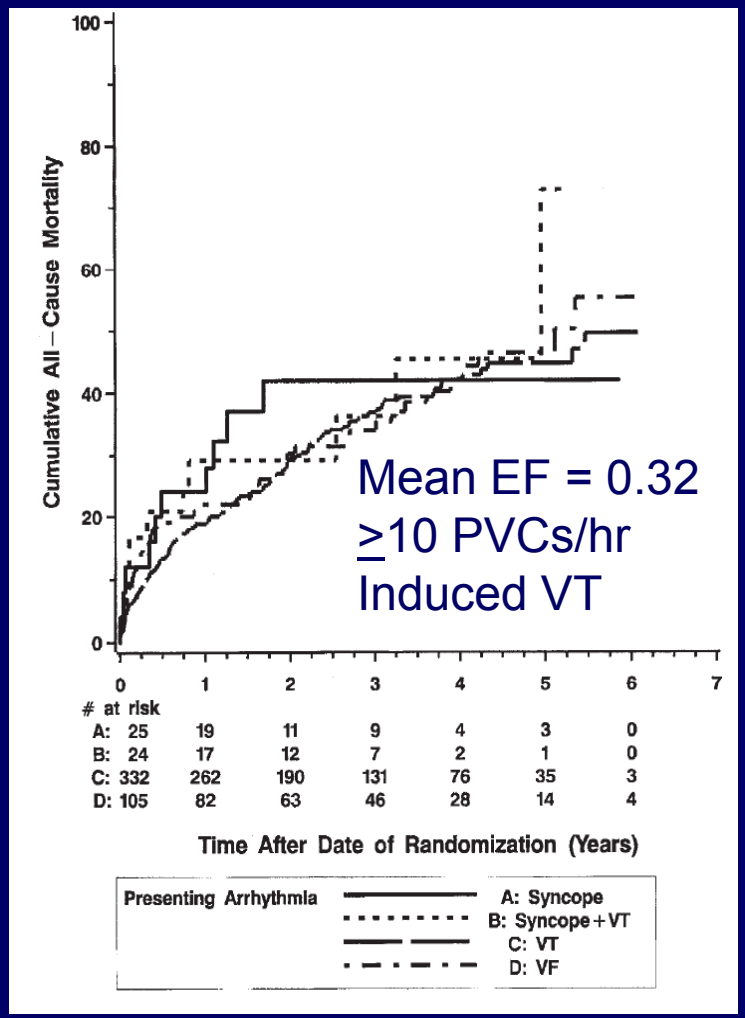


Conclusion: "Patients with DCMP presenting with syncope are a high-risk group, with event rates similar to patients with DCMP presenting with sustained arrhythmias and should be considered for ICD therapy".

Phang RS. Am J Cardiol 2006;97:416–420

Does Syncope Predict - ESVEM





Mean EF = 0.32
≥10 PVCs/hr
Induced VT

Olshansky B. Am Heart J 1999;137:878-86

Syncope in ESVEM

Covariate	Risk ratio (95% CI)	P value
Syncope*	1.27 (0.58, 2.79)	.544
VT with syncope	1.78 (0.81, 3.89)	.150
VF	1.38 (0.91, 2.09)	.126
VT alone	1.00	–
CAD	0.91 (0.52, 1.61)	.744
Average PVC/hour (log scale)	1.04 (0.90, 1.19)	.588
Utah center	0.80 (0.53, 1.22)	.307
EPS method	0.77 (0.53, 1.11)	.157
SAS class I	0.48 (0.29, 0.80)	.005
LVEF	0.97 (0.95, 0.99)	<.001

Olshansky B. Am Heart J 1999;137:878-86

Syncope Evaluation

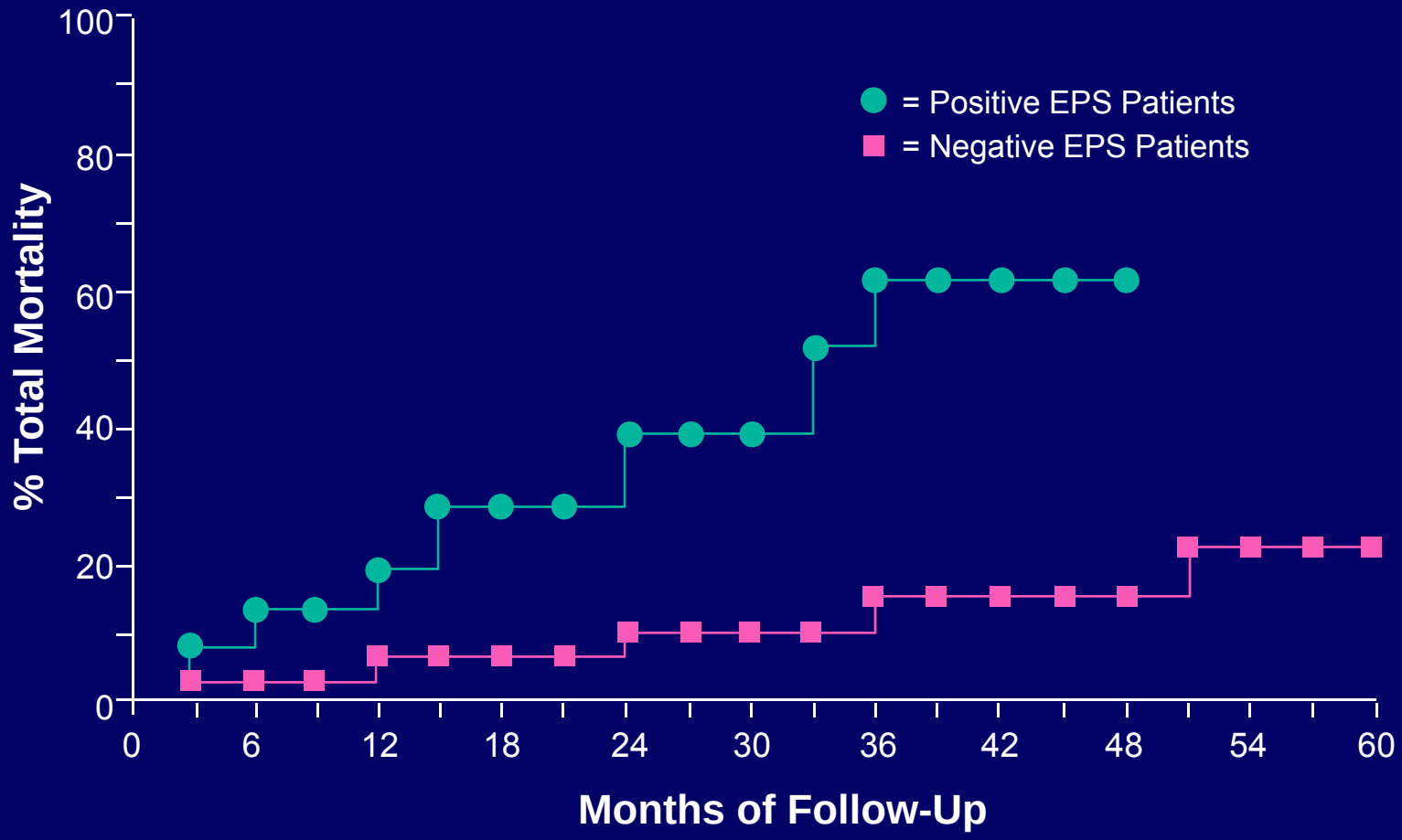
In Heart Failure

- History
- Physical
- Diagnostic tests

Diagnostic Tests

- Electrocardiogram
- Echocardiogram
- Monitor (external, implantable recorder)
- Treadmill
- Tilt table test (?)
- Electrophysiology test (?)
- T wave alternans (?)
- Signal averaged ECG (?)

EP Testing – Is There a Role?



Bass EB. Am J Cardiol 1988;62:1186-1191

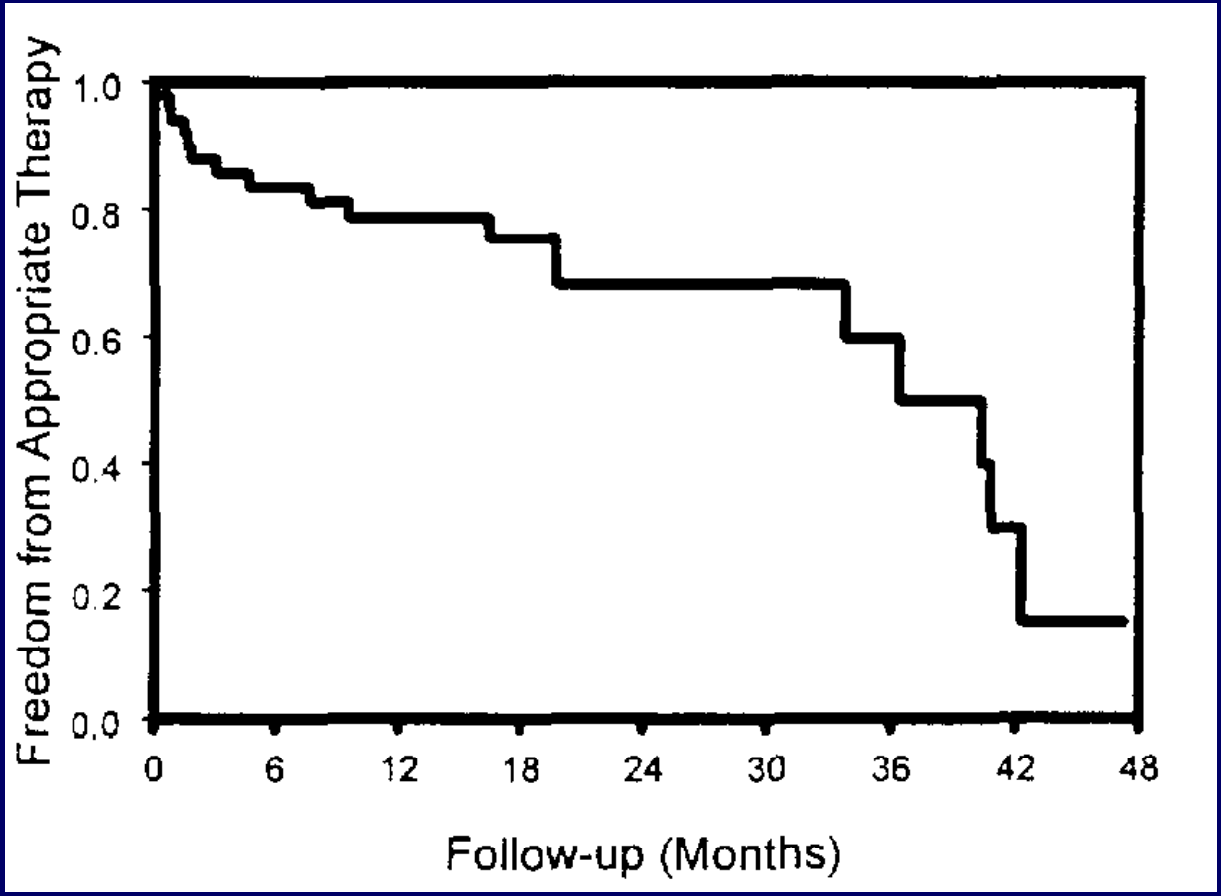
Does EP Testing Predict ICD Shocks in Syncope Patients?

- Inducible VT and EF ≤0.35 predicted appropriate ICD shocks in patients with syncope and structural heart disease.
- ->In these patients VT accounts for syncope.

Militianu A. J Cardiovasc Electrophysiol 1997;10:1087-97

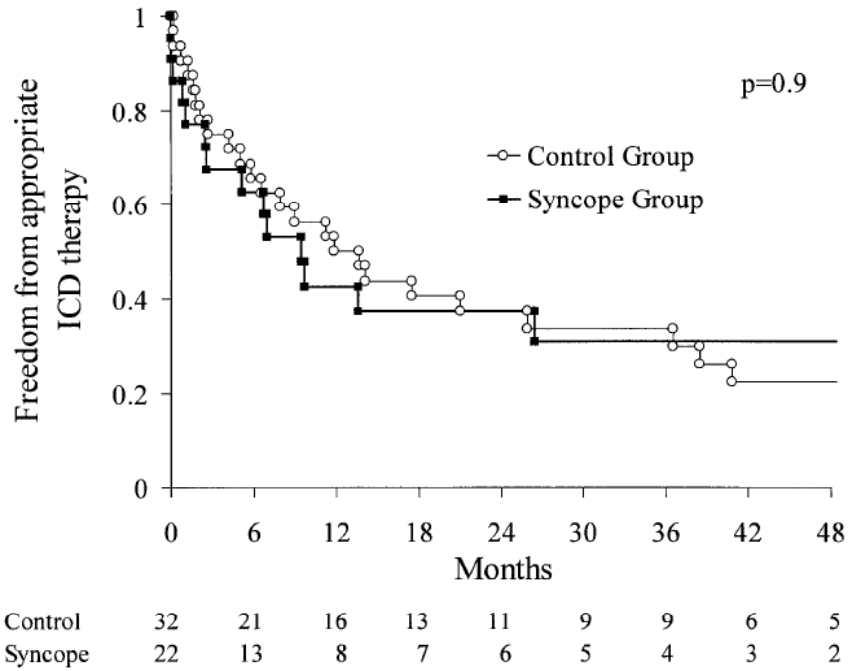
Syncope and Inducible VT/VF

ICDs Implanted for VT/VF



Link M. J Am Coll Cardiol 1997; 29:370-5

ICD Therapy – Syncope with Induced VT vs. Spontaneous VT



Clinical Characteristics*

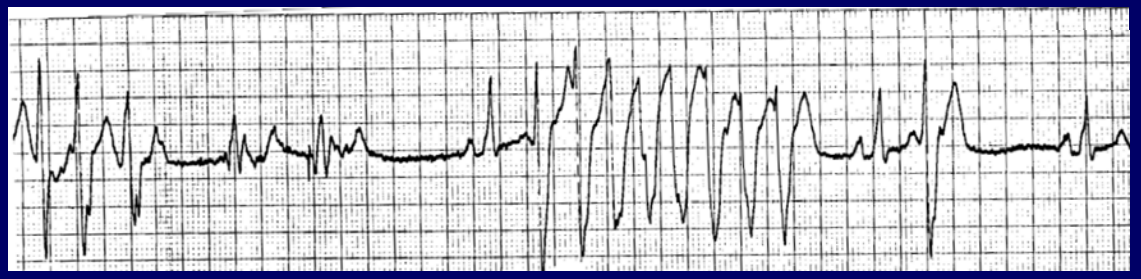
	Syncope (n = 22)	Control (n = 32)	p Value
Age, yrs ± SEM	69 ± 2	66 ± 1	0.11
Male	18 (82)	25 (78)	1.00
LV ejection fraction, % ± SEM	30 ± 3	29 ± 2	0.73
Nonsustained VT	11 (50)	8 (25)	0.08
Underlying heart disease			
Coronary artery disease	19 (86)	28 (88)	1.00
Myocardial infarction	12 (55)	24 (75)	0.15
Segmental LV dysfunction	17 (77)	26 (81)	0.74
LV aneurysm	2 (9)	8 (25)	0.17
3-vessel disease	8 (36)	14 (44)	0.78
CABG	7 (32)	15 (47)	0.40
Dilated cardiomyopathy	2 (9)	2 (6)	1.00
Other	1 (5)	2 (6)	1.00
Congestive heart failure	14 (64)	11 (34)	0.052
NYHA class III/IV	6 (27)	4 (13)	0.29
Hypertension	11 (50)	11 (34)	0.28
Diabetes mellitus	7 (32)	4 (13)	0.10
Bundle branch block	10 (45)	8 (25)	0.15

*Values are number of subjects (%) with characteristic unless otherwise stated.
LV = left ventricle; CABG = coronary artery bypass grafting; NYHA = New York Heart Association functional classification.

Andrews NP. J Am Coll Cardiol 1999;34:2023-30

77 yo Driver Collapses Drives into the River

- Echo - LV ejection fraction 0.25.
- Cardiac cath: 2 vessel CAD cannot be fixed. No acute ischemia
- Monitor ->

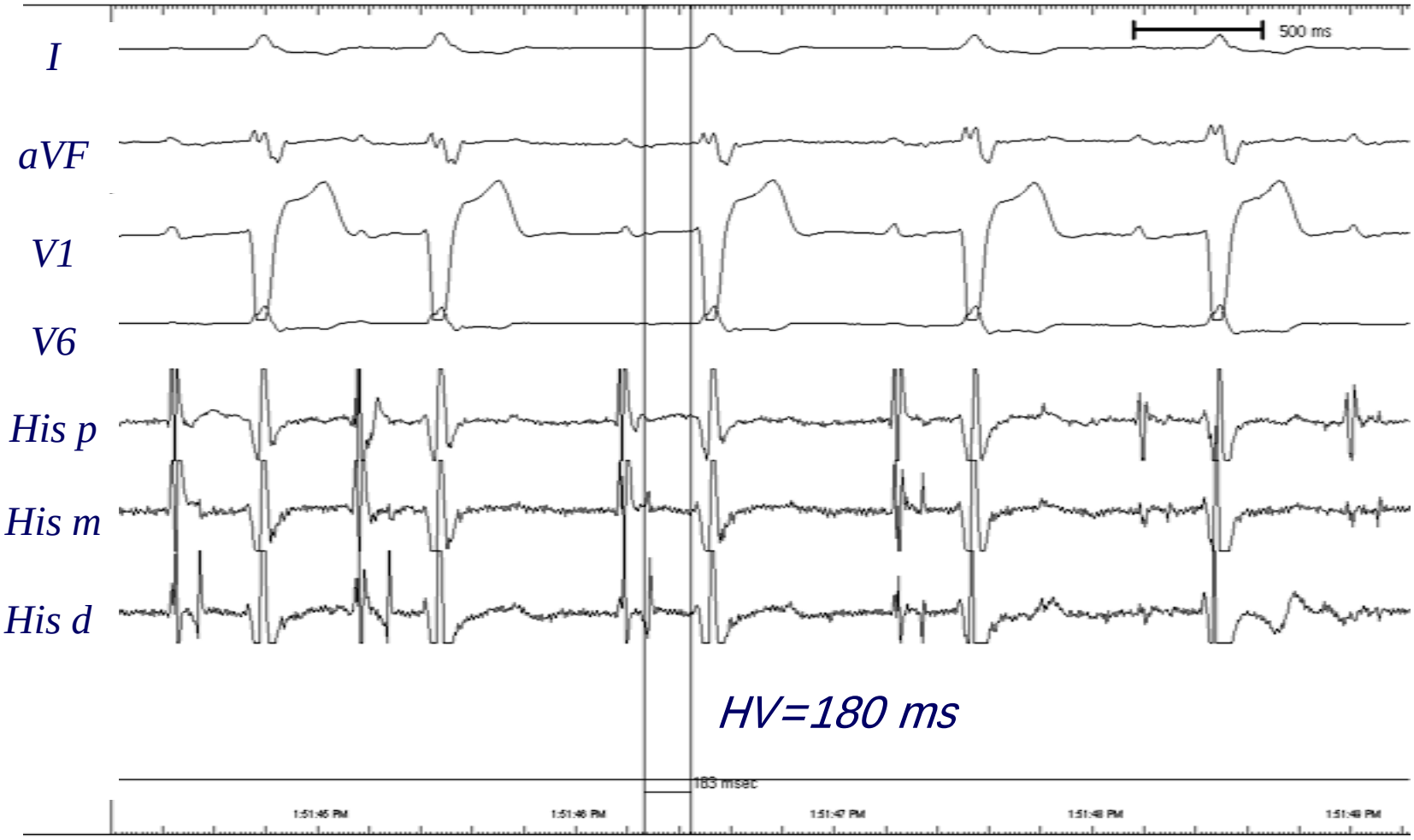


- Do you do an EP study?

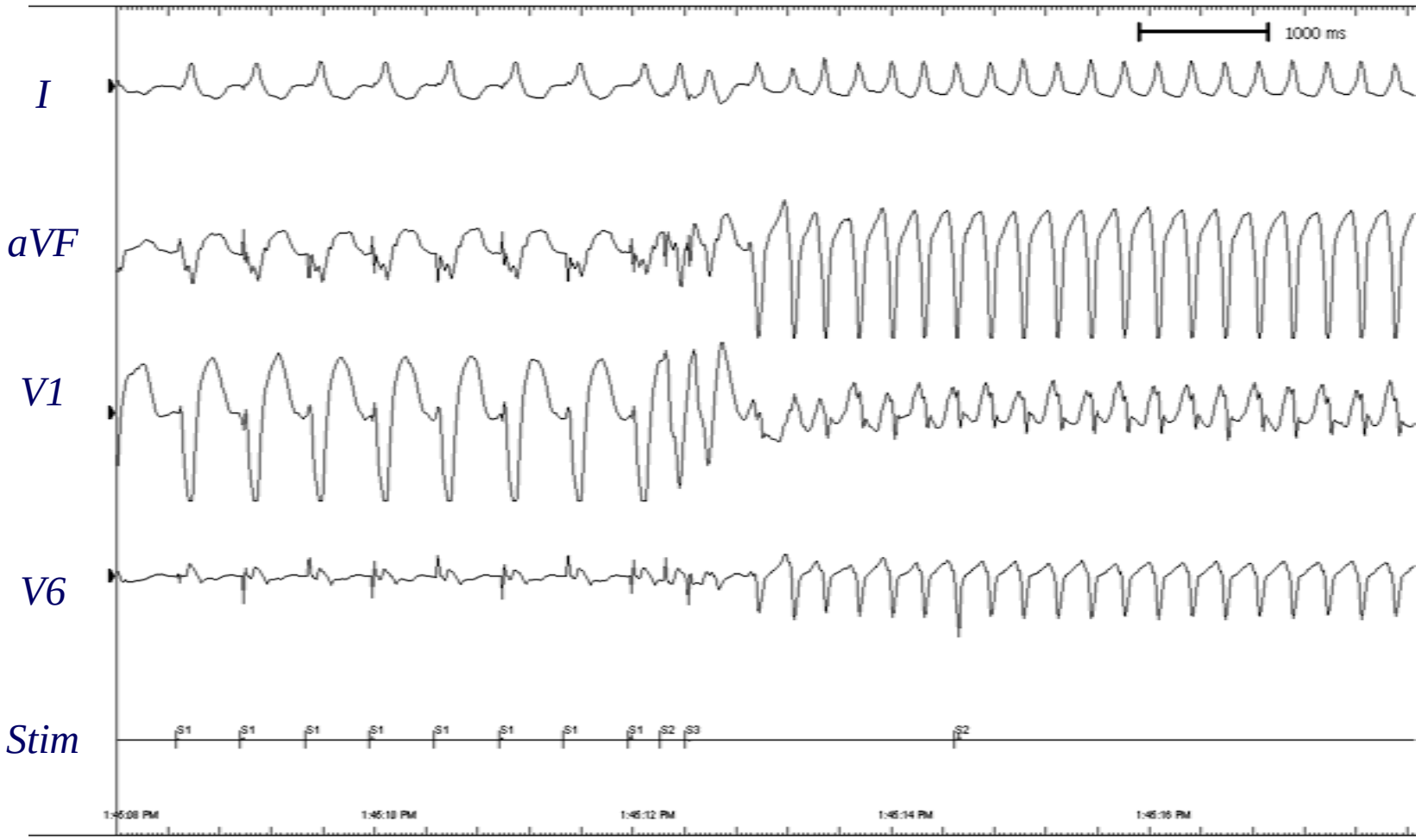
49 yo Male - Cardiomyopathy

- Recurrent syncope
- Left ventricular ejection fraction = 0.38
- Left bundle branch block
- Do you do an EP study?

Very Long HV Interval



Ventricular Tachycardia



Typical Day in the Hospital

- 55 yo male, found on street, dazed possibly passed out
- He has history of exertional dyspnea but no prior cardiac history
- Physical exam – S_3 gallop
- EKG – left bundle branch block

Typical Day in the Hospital

- 55 yo male, found on street, dazed
- EKG – left bundle branch block
- Echo - ejection fraction = 0.35
- Cardiac catheterization – no lesions
- Electrophysiology test – negative

Typical Day in the Hospital

Unexplained syncope – now what?

- 55 yo male, found on street, dazed
- EKG – left bundle branch block
- Echo - ejection fraction = 0.35
- Cardiac catheterization – no lesions
- Electrophysiology test – negative

Role of Programmed Ventricular Stimulation and Implantable Cardioverter Defibrillators in Patients with Idiopathic Dilated Cardiomyopathy and Syncope

EMMANOUIL S. BRILAKIS, WIN K. SHEN, STEPHEN C. HAMMILL, DAVID O. HODGE, ROBERT F. REA, NANCY Y. LEXVOLD, and PAUL A. FRIEDMAN

From the Department of Internal Medicine, Division of Cardiovascular Diseases, Mayo Clinic and Mayo Foundation, Rochester, Minnesota

BRILAKIS, E.S., ET AL.: Role of Programmed Ventricular Stimulation and Implantable Cardioverter Defibrillators in Patients with Idiopathic Dilated Cardiomyopathy and Syncope. *The aim of this study was to evaluate the role of programmed ventricular stimulation and ICDs in patients with idiopathic dilated cardiomyopathy and syncope. Between 1990 and 1998, 54 (mean age 67 ± 11 years, 76% men) patients presented with idiopathic dilated cardiomyopathy and syncope. An electrophysiological study was done in 37 of the 54 patients: 10 had inducible sustained monomorphic ventricular tachycardia, 12 had conduction system disease or neurocardiogenic syncope, and 15 had a normal study. Overall, 17 patients received an ICD, 15 patients received a pacemaker, and 22 patients received no device. Nine of the 15 patients with a negative electrophysiological study eventually received an ICD: 3 because they were considered high risk and 6 because of recurrent syncope or presyncope. In the 17 patients who received an ICD, incidence of appropriate shocks at 1 and 3 years was 47% and 74%, respectively, in the inducible sustained monomorphic ventricular tachycardia group, and 40% and 40%, respectively, in the group without inducible sustained monomorphic ventricular tachycardia (P = 0.29, log-rank test). In conclusion, programmed ventricular stimulation is not useful in risk stratification of patients with idiopathic dilated cardiomyopathy and syncope and may delay necessary ICD implantation. (PACE 2001; 24:1623–1630)*

Cardiomyopathy and Syncope

An ICD is Indicated!

- 14 syncope patients, negative EPS vs. 19 cardiac arrest survivors. ICDs placed.
- "Appropriate" shocks: 7/14 syncope (f/u 24 mos) and 8/19 arrest patients (f/u 45 mos)
- Mortality high both groups (28% v. 32%)

- What does syncope have to do with it?
- Does an ICD help?

Knight B. J Am Coll Cardiol. 1999;33:1964-70

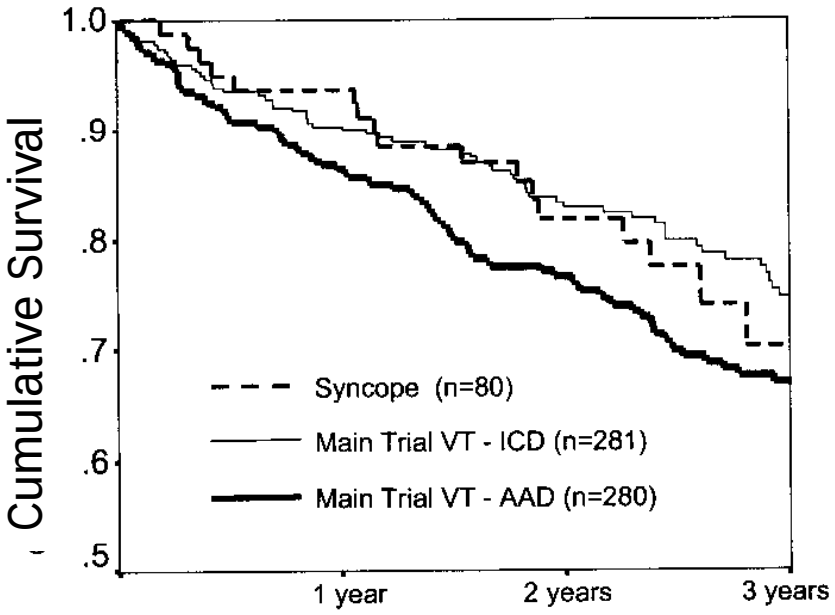
Syncope and Cardiomyopathy

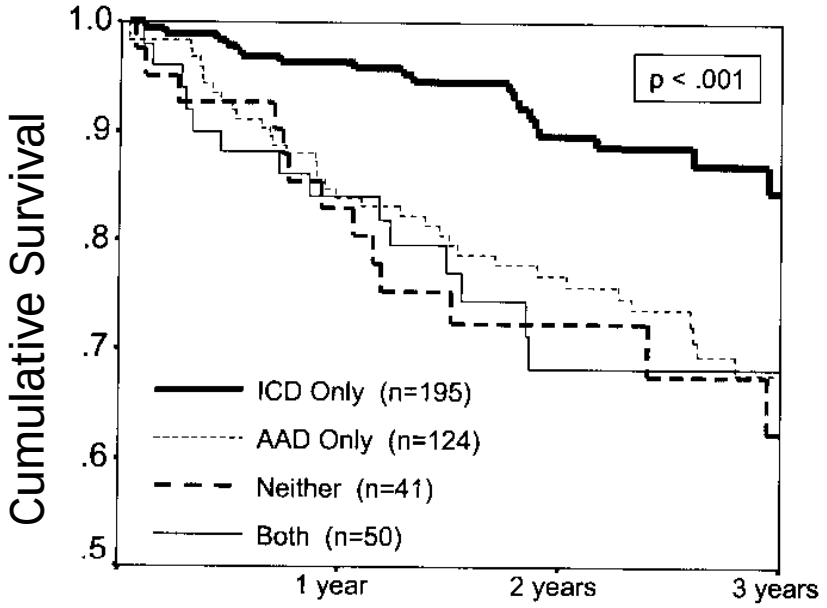
The EP Test is Negative

- **Blinded, matched, case-control analysis of 51 with unexplained syncope, cardiomyopathy and negative EPS (19 ICD vs. 32 “conventional”).**
- **14 death/cardiac arrest in 44±20 mos. 2 ICD vs. 12 “conventional”. HR 0.18, 95% CI 0.04,0.85, *P*=0.04.**
- **Appropriate ICD shocks in 26% at 2 years.**
- **->ICDs improve outcome of patients with unexplained syncope, ischemic or nonischemic cardiomyopathy and negative EPS**

Lindsey B. Heart Rhythm 2005;2:367-373

AVID Substudy and Registry





The Substudy

The Registry

Steinberg J. J Cardiovasc Electrophysiol 2001;12:996-1001

ICD Indications - Syncope

- **Class I** - Syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced at EP study when drug therapy is ineffective, not tolerated, or not preferred. **(Level of evidence: B)**
- **Class IIb -** Syncope in patients with advanced structural heart disease in which thorough invasive and noninvasive investigation has failed to define a cause. **(Level of evidence: C)**

Gregoratos G. Circulation 2002;106:2145-2161

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ACC/AHA/ESC PRACTICE GUIDELINES—EXECUTIVE SUMMARY

ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death—Executive Summary

- **<u>Class IIa Indication</u> – "ICD can be beneficial for patients with unexplained syncope, significant LV dysfunction and nonischemic dilated cardiomyopathy who are receiving chronic optimal medical therapy. . . *(Level of Evidence: C)"***

. . . .without an EP test

Syncope Predicts Outcomes in CHF

	Dead	CV Death
HR (95% CI)	1.41 (1.13, 1.76)	1.55 (1.19, 2.02)
p value	0.002	0.001

Syncope did not predict sudden death

Syncope predicts ICD shocks
HR = 2.91 (CI 1.89, 4.47) p = 0.001

16% had syncope after enrollment

Olshansky B. J Am Coll Cardiol. in press. 2008

Syncope in SCD-HeFT

Mortality Independent of Treatment

Syncope - year 1	Amiodarone	Placebo	ICD
Yes	15.1%	17.0%	17.1%
No	11.2%	12.6%	8.6%
HR (95% CI)	1.33 (0.91, 1.96)	1.52 (1.04, 2.21)	1.72 (1.16, 2.56)

No difference between arms (p=0.64)

Olshansky B. J Am Coll Cardiol. in press. 2008

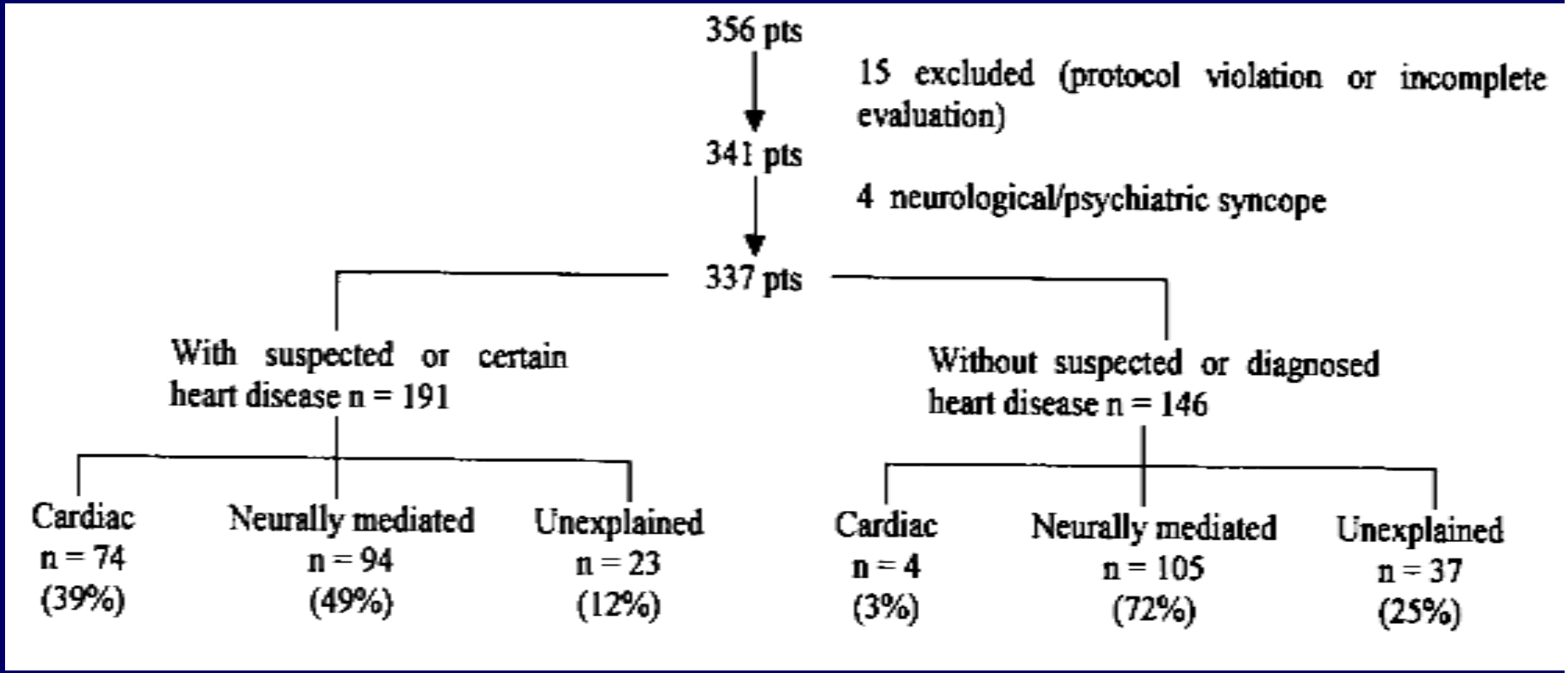
Presumed Causes for Syncope

458 episodes in 356 patients

• Orthostatic hypotension	65
• Ventricular tachycardia	44
• Drug induced hypotension	38
• Vasomotor	33
• Cardiac arrest (CPR given)	24
• Drug induced arrhythmia	2
• Seizures	7
• Other	159
• Unknown	86

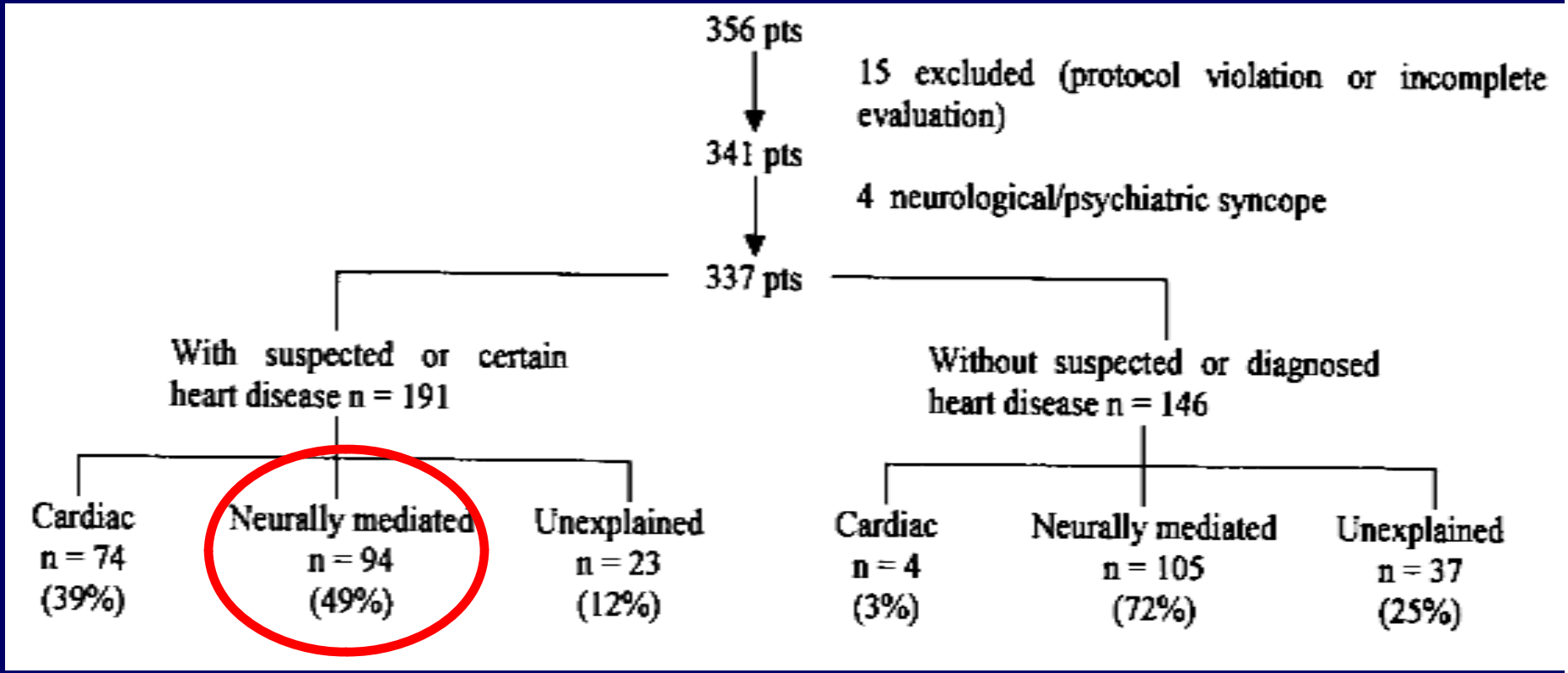
Olshansky B. J Am Coll Cardiol. in press. 2008

Cause of Syncope



Alboni P. J Am Coll Cardiol. 2001;37:1921

Cause of Syncope



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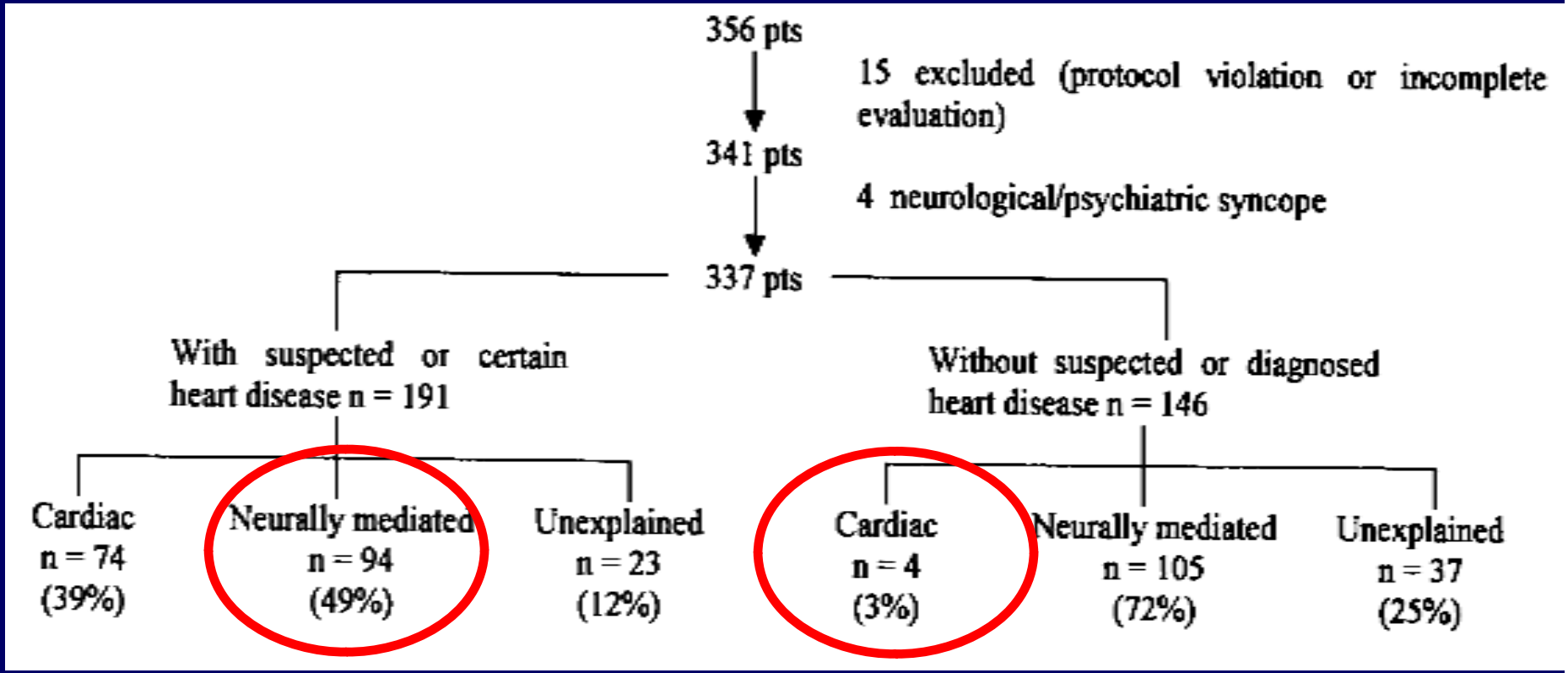

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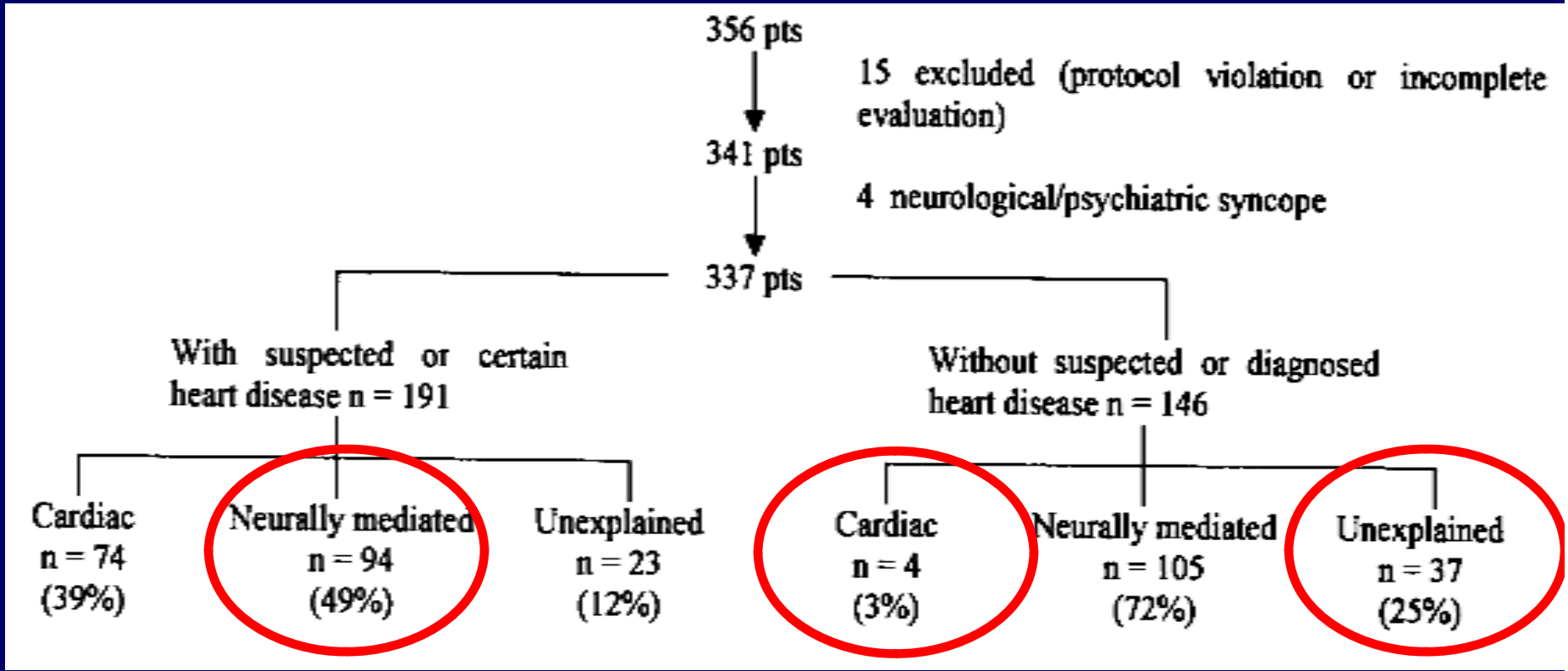
Cause of Syncope



Alboni P. J Am Coll Cardiol. 2001;37:1921

Neurocardiogenic Mechanisms of Unexplained Syncope in Idiopathic Dilated Cardiomyopathy

Efthimios G. Livanis, MD[a], Anna Kostopoulou, MD[a,*], George N. Theodorakis, MD[a], Nikolitsa Aggelopoulou, MD[a], Stamatis Adamopoulos, MD, PhD[a], Dimitrios Degiannis, MD[b], and Dimitrios Th. Kremastinos, MD, PhD[c]

Syncope in patients with advanced heart failure is a sign of poor prognosis. The cause of syncope in patients with dilated cardiomyopathy (DC) is not fully recognized and may remain elusive even after standardized evaluation. The purpose of the present study was to examine the implication of neurally mediated mechanisms in the pathophysiology of syncopal episodes in patients with DC. Twenty-six patients (21 men, 5 women; mean age 59 ± 2 years, range 38 to 79) with DC and left ventricular ejection fractions ≤40% were included in the study. Thirteen patients with unexplained syncope or presyncope and a control group of 13 patients without unexplained syncope underwent head-up tilt tests with clomipramine challenge. The 2 groups were matched with regard to age, gender, and left ventricular ejection fractions, and there were no major differences in terms of medication. Heart rate variability analysis and plethysmography of forearm flow were performed during the tilt tests. Blood samples were also drawn for catecholamine measurements. In the group with histories of unexplained syncope, the head-up tilt test results were positive in 11 patients (84.6%). Sympathetic and parasympathetic heart rate indexes were markedly stimulated, while catecholamine concentrations and blood flow changes indicated sympathetic withdrawal during tilting. In the control group, the head-up tilt test results were negative in 12 patients (92.3%). In conclusion, neurally mediated mechanisms seem to be implicated in the pathophysiology of syncope in patients with DC and should therefore be considered in the differential diagnosis of syncopal episodes of unexplained origin. © 2007 Elsevier Inc. All rights reserved. (Am J Cardiol 2007;99:558–562)

Reasons a Syncope Patient with an ICD May Still Pass Out

- Spontaneous VT treated by the ICD
- Untreated, undetected (e.g., below rate cut-off), recurrent, provoked (by ICD) or nonsustained VT
- Lead or device malfunction or programming issue
- Another arrhythmia (brady or tachy)
- Syncope due to another cause

78 yo Male Recurrent Syncope

- Dilated cardiomyopathy. LVEF = 0.32, LBBB and NYHA FC II. ICD implanted.
- Recurrent syncope despite ICD.
- EP study ->poorly tolerated SVT below programmed ICD detection interval.
- SVT ablation stopped syncope.

Syncope in Heart Failure

Restrictions

- No commercial driving
- If cause is identified and treated – no restriction
- For most restriction from standard driving for 6 months. Justified?

Before the ICD - What to Do?

- With prophylactic ICD use, tendency is to become lax regarding patient evaluation.
- Standard evaluation rules still apply.
- Evaluate potential responsible conditions. An ICD might not be enough.

85 yo Male – A Falling Episode

- He maybe passed out or just tripped on the rug. He is brought in for evaluation
- Procardia/Dyazide
- Px - orthostatic hypotension
- LVEF = 0.30. He has a LBBB

85 yo Male – A Falling Episode

- He maybe passed out or just tripped on the rug. He is brought in for evaluation
- Procardia/Dyazide
- Px - orthostatic hypotension
- LVEF = 0.30. He has a LBBB

  What if the EF is 0.40?

85 yo Male – A Falling Episode

- He maybe passed out or just tripped on the rug. He is brought in for evaluation
- Procardia/Dyazide
- Px - orthostatic hypotension
- LVEF = 0.30. He has a LBBB

  What if the EF is 0.40?

What if the EP test shows inducible polymorphic VT?

Elderly Male with “Syncope”

- Evaluated by several internists for AM collapse in his breakfast
- Moderate LV dysfunction. Monitoring negative. He is demented.
- He takes phenobarbital, xanax, acetaminophen with codeine and forgets how much he takes

Elderly Male with “Syncope”

- Evaluated by several internists for AM collapse in his breakfast
- Moderate LV dysfunction. Monitoring negative. He is demented.
- He takes phenobarbital, xanax, acetaminophen with codeine and forgets how much he takes

ICDs are not always the answer

Syncope in Heart Failure

- Evaluate causes for syncope
- Treat heart failure aggressively
- Treat to
  - prevent sudden and total mortality
  - reduce risk of recurrent syncope

Conclusion

- Syncope in heart failure, not always due to VT, indicates risk of death.
- ICDs reduce risk of arrhythmic death in high-risk syncope patients and have a key role in management.
- Identification of which patient benefits from an ICD can be complex and requires careful clinical assessment.