Sudden Death Risk Assessment in Hypertrophic Cardiomyopathy

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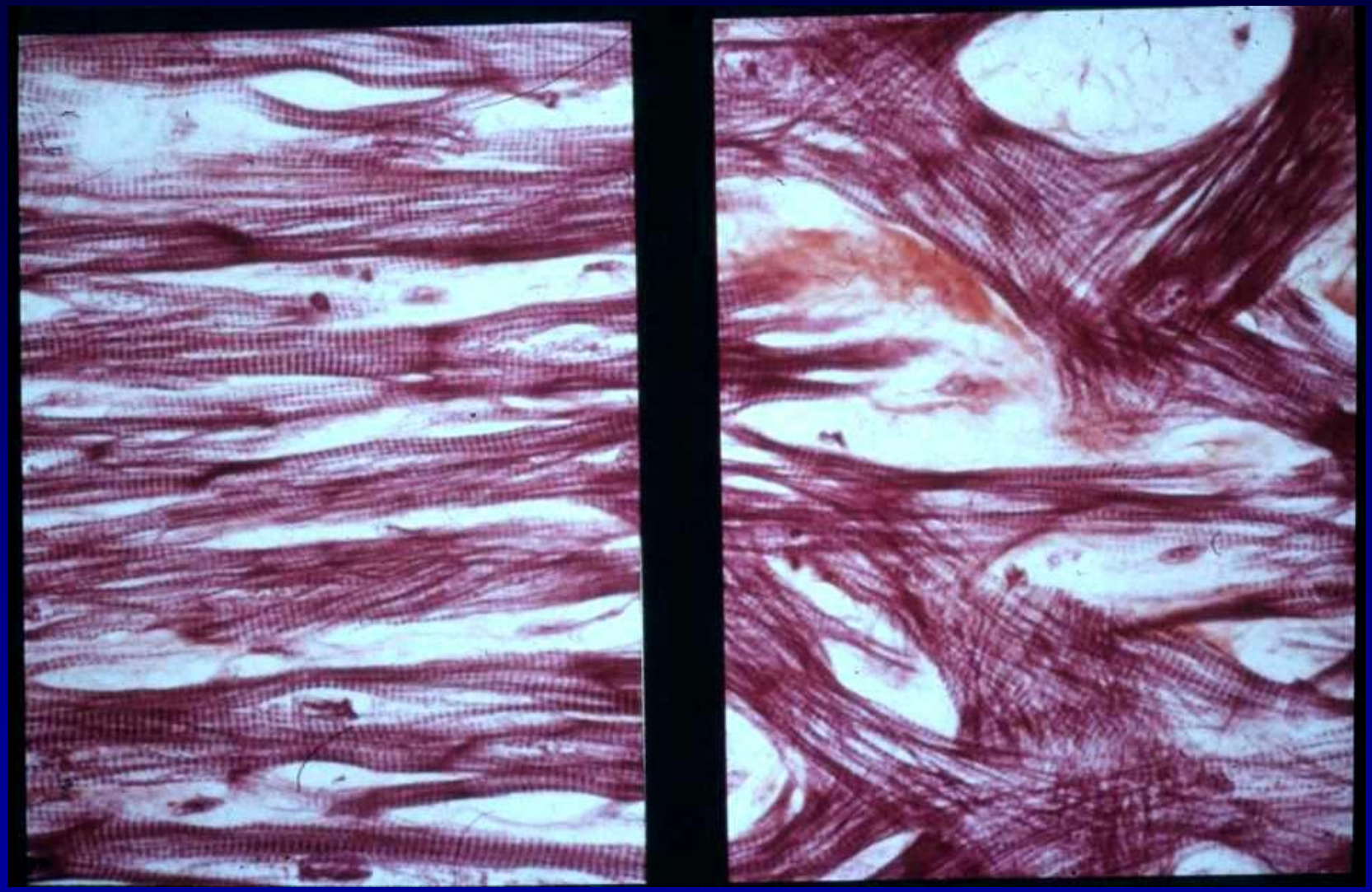
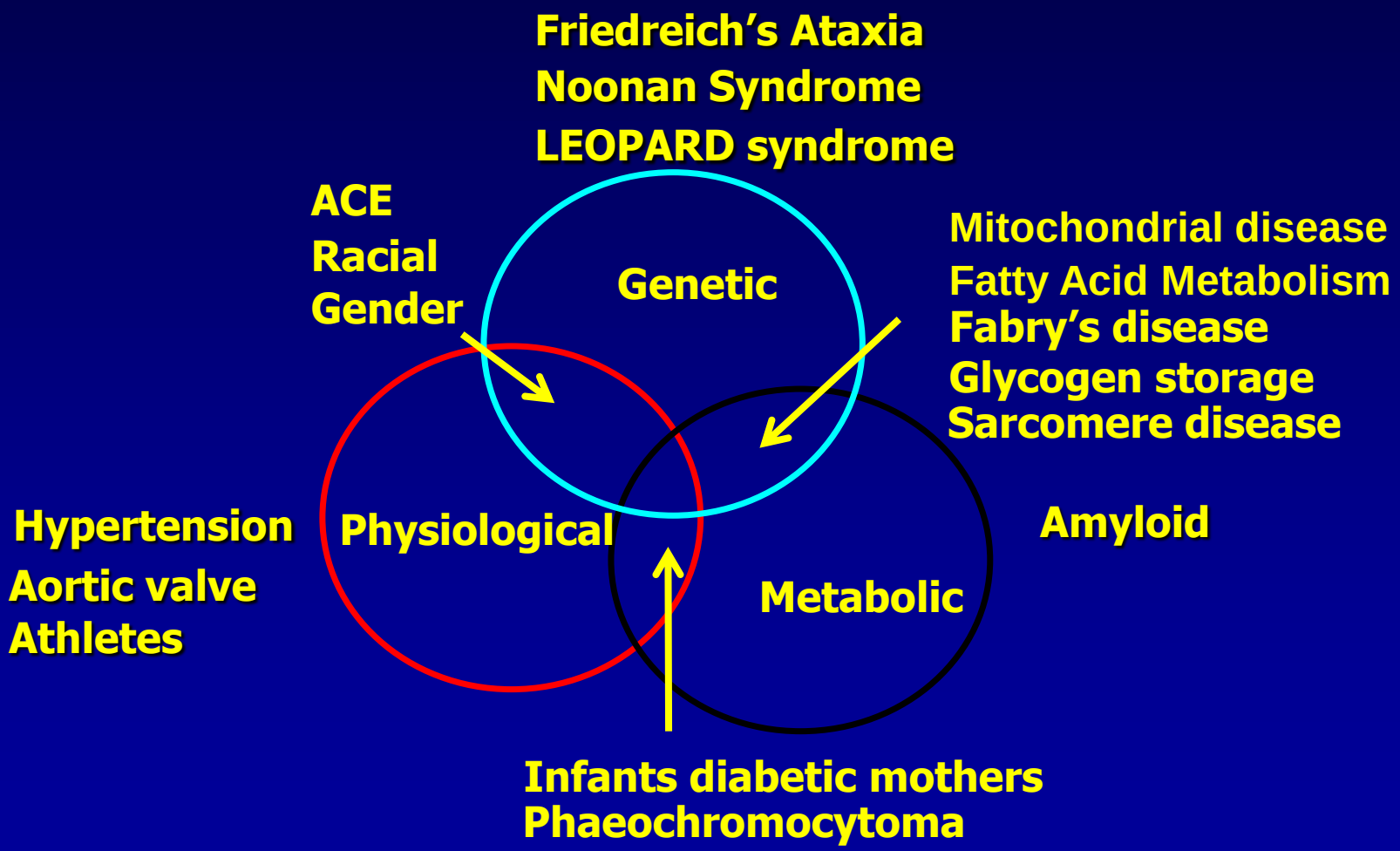
>3cm LVH

Hypertrophic Cardiomyopathy

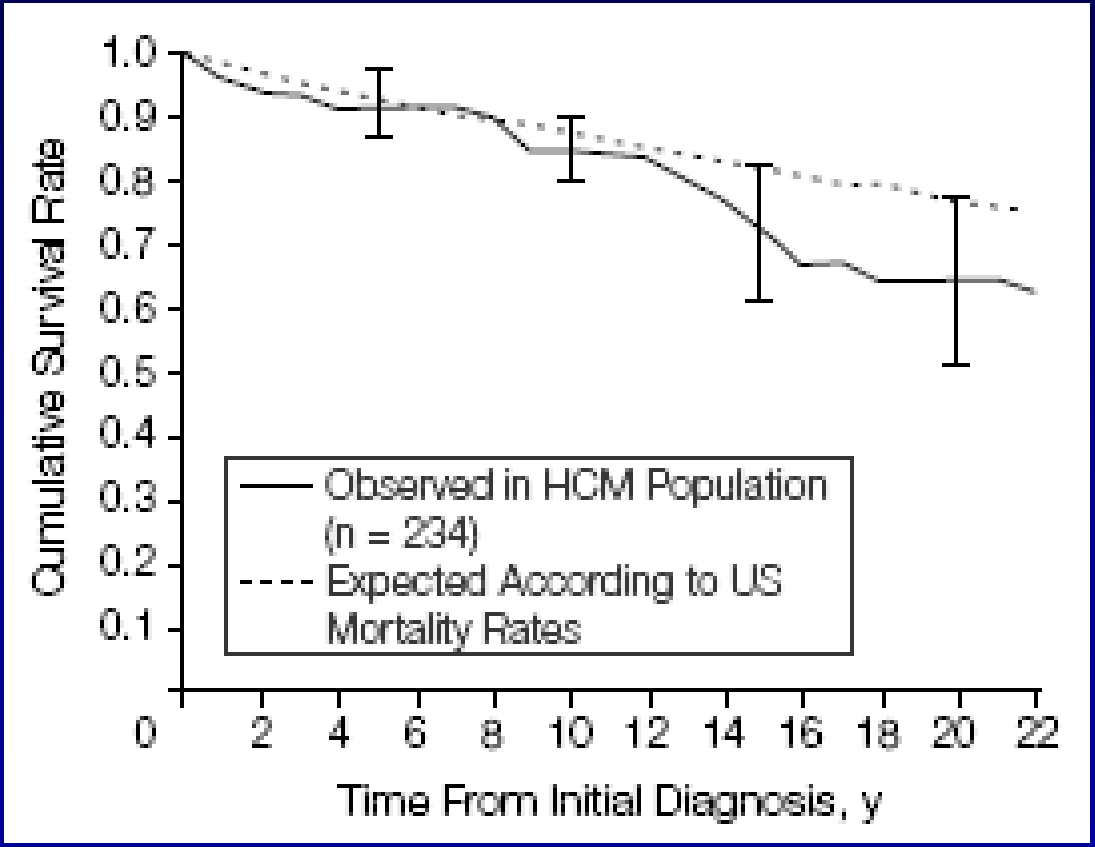


Pathological Dx - disarray

Causes of Left Ventricular Hypertrophy

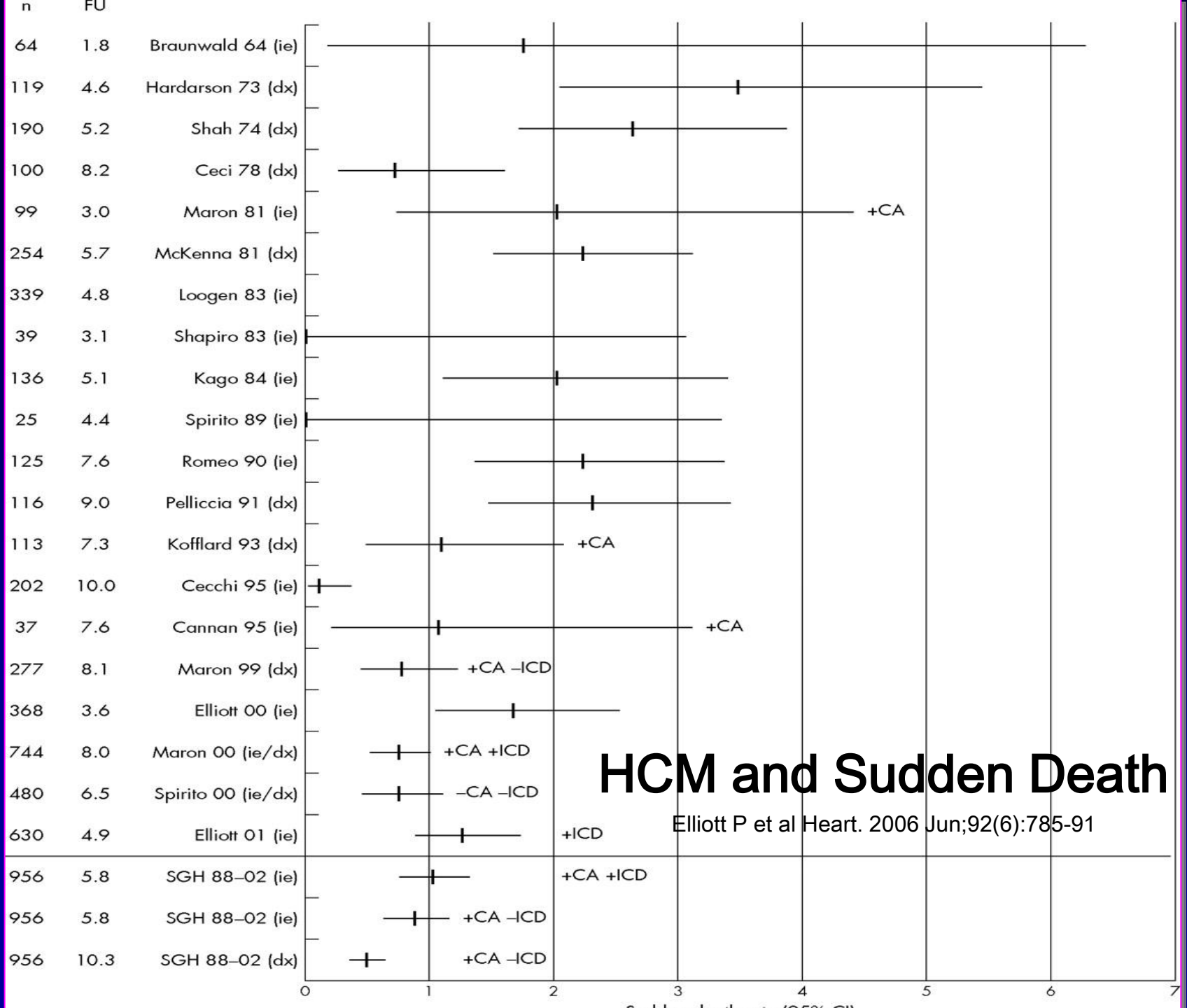


Cumulative survival after initial diagnostic evaluation among adults



Maron et al. JAMA 1999;282:650

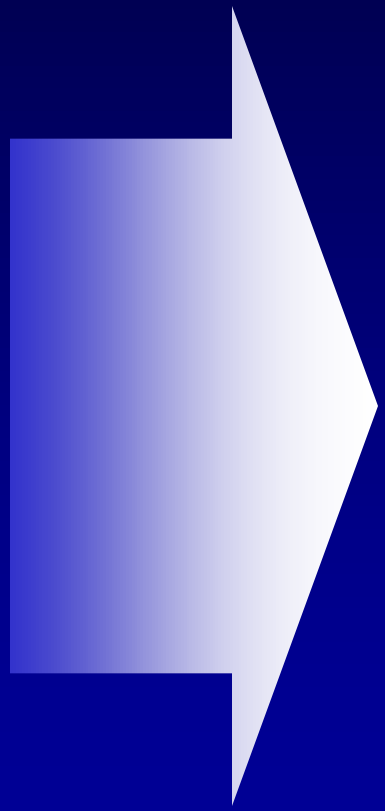
HCM and Sudden Death



Elliott P et al Heart. 2006 Jun;92(6):785-91

Risk Factors in HCM

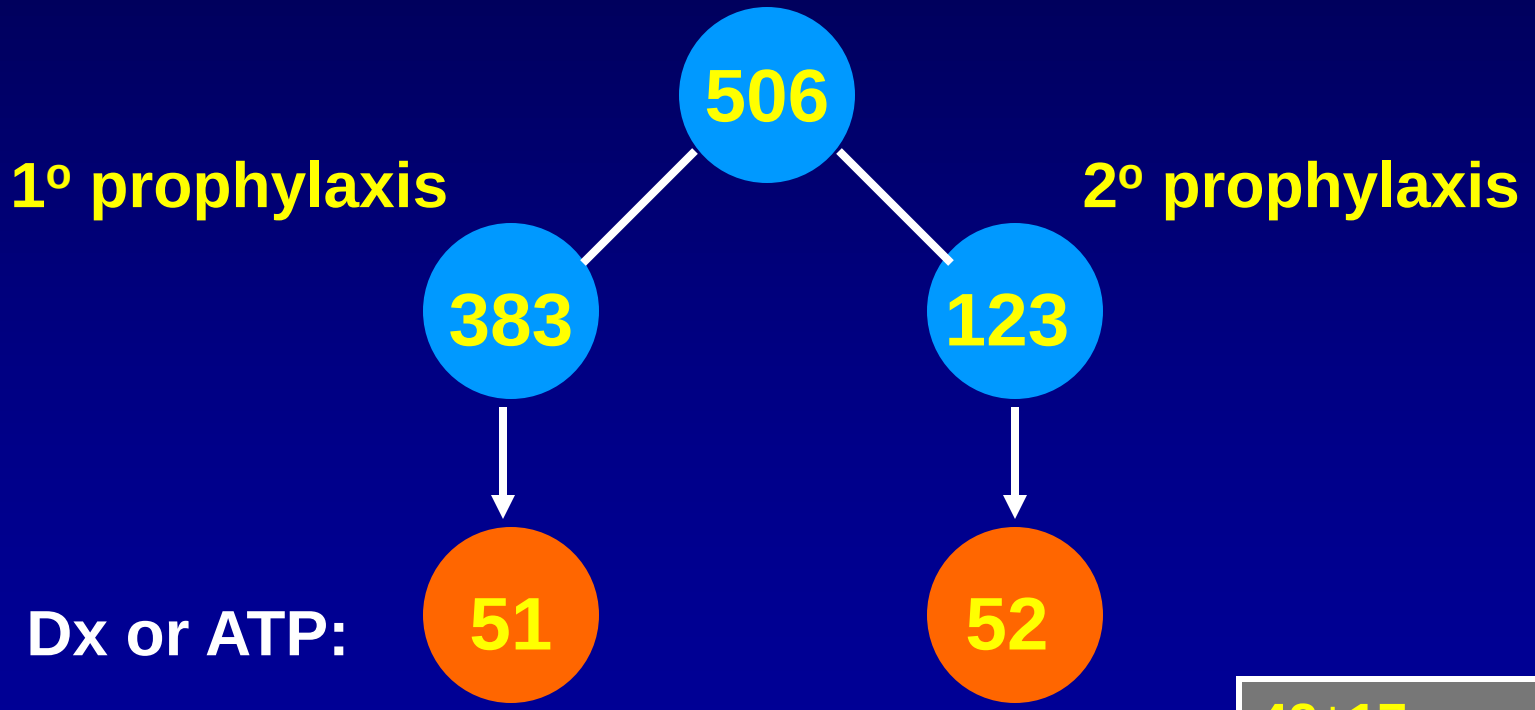
Youth
Genotype
Family history
Exercise capacity
Syncope
Severe LVH
Large gradient
Diastolic dysfunction
Abn exercise BP
Ischemia
Atrial fibrillation
Non-sustained VT
Inducible VT / VF
Fractionation



Family history
Syncope
Exercise BP
NSVT
LVH

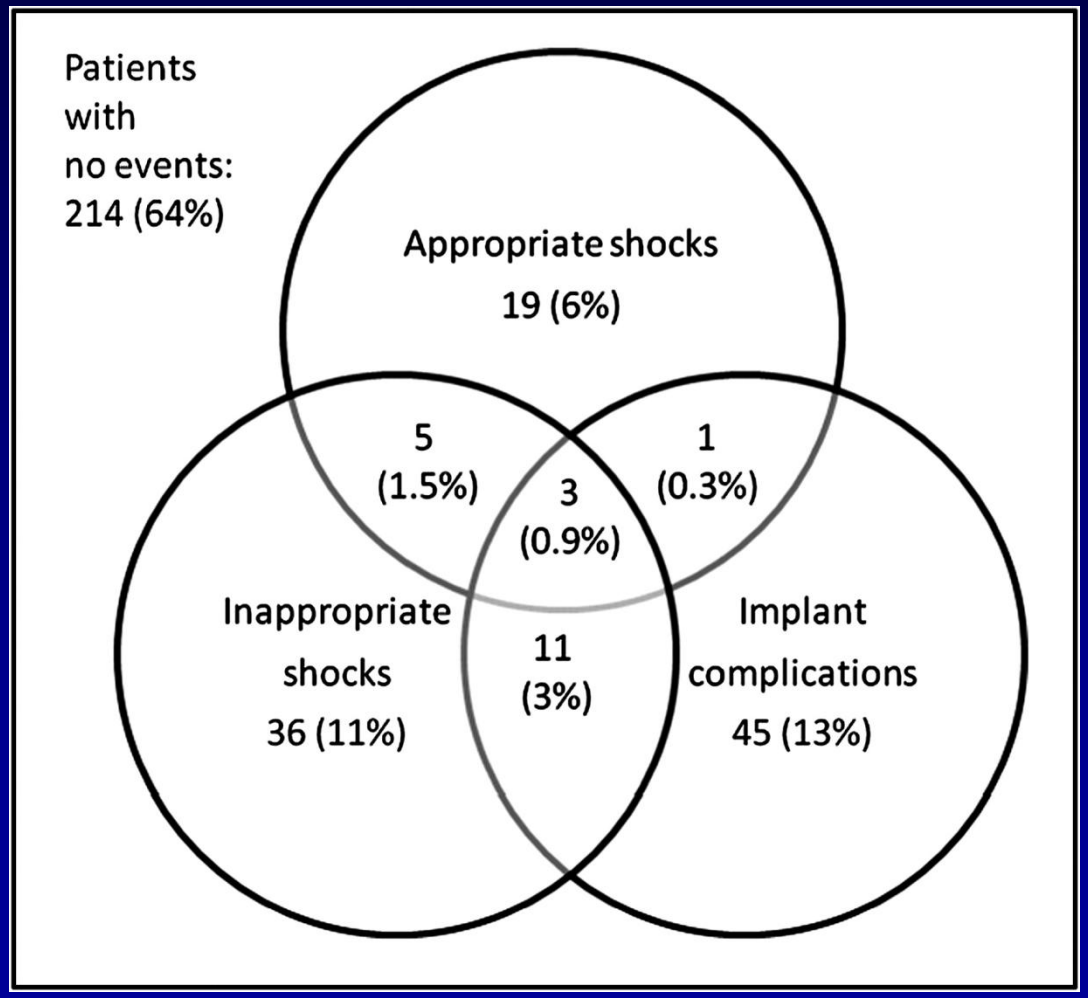
ICD in HCM

Maron B et al. JAMA 2007;298:405-12



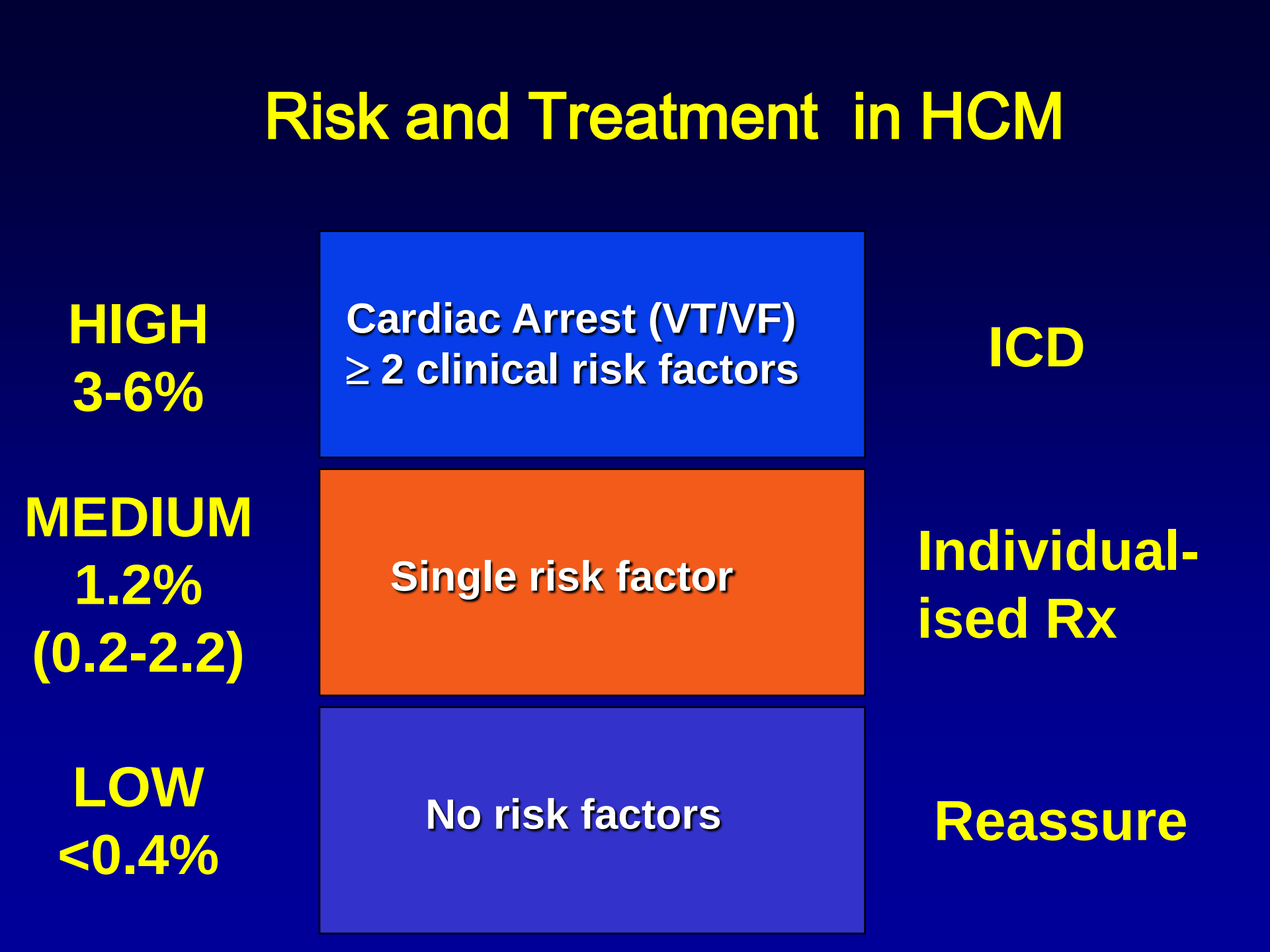
Inappropriate shocks 136 (27%)

ICD in HCM



O'Mahony et al, Heart 2012

Risk and Treatment in HCM



Limitations of current approach to risk stratification

Family Hx	- ? accuracy
	- ? denominator
Syncope	- 'unexplained'
LVH, Ex BP	- use of ROC cut off to define risk
	- accuracy of measurements
NSVT	- differentiation from aberrancy in pts with PAF

Limited Data Zone

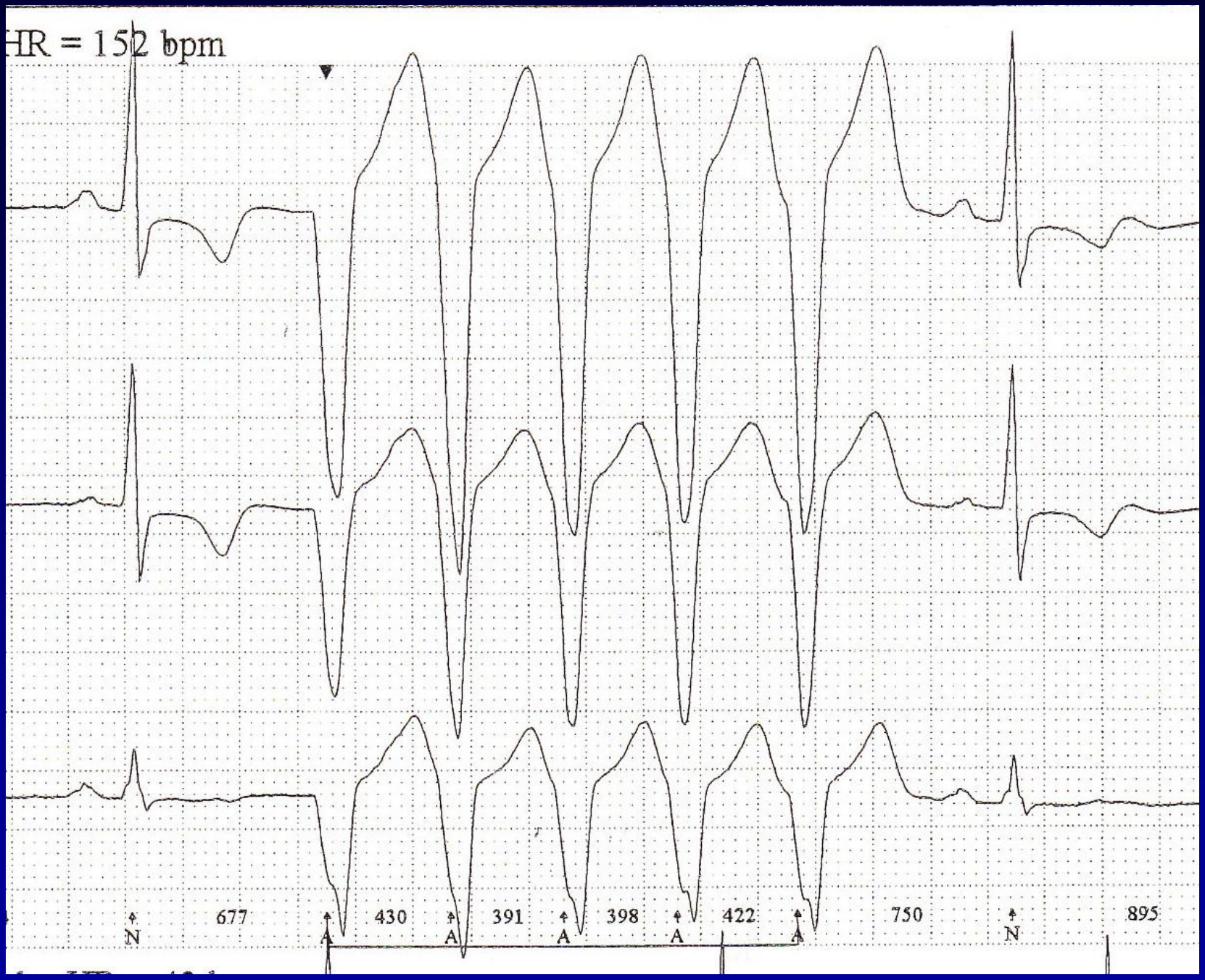
Single risk factor

- **Family history of sudden death**
  - **low positive predictive accuracy**
  - **high anxiety / legal risk**

  hypothesis
  risk is heterogeneous even within ‘malignant’ families

Plan: **risk stratify**

Rx: **low threshold for ICD**


HR = 152 bpm
N
677
A
430
A
391
A
398
A
422
A
750
N
895

Limited Data Zone

Single risk factor

- **Non sustained VT on 24hr ECG**
  age 15 – relative risk 6
  age 50 – relative risk 2

Monserrat, JACC 2003

Rx ICD in adolescent
No Rx, BB or amio in adult

Limited Data Zone

Single risk factor

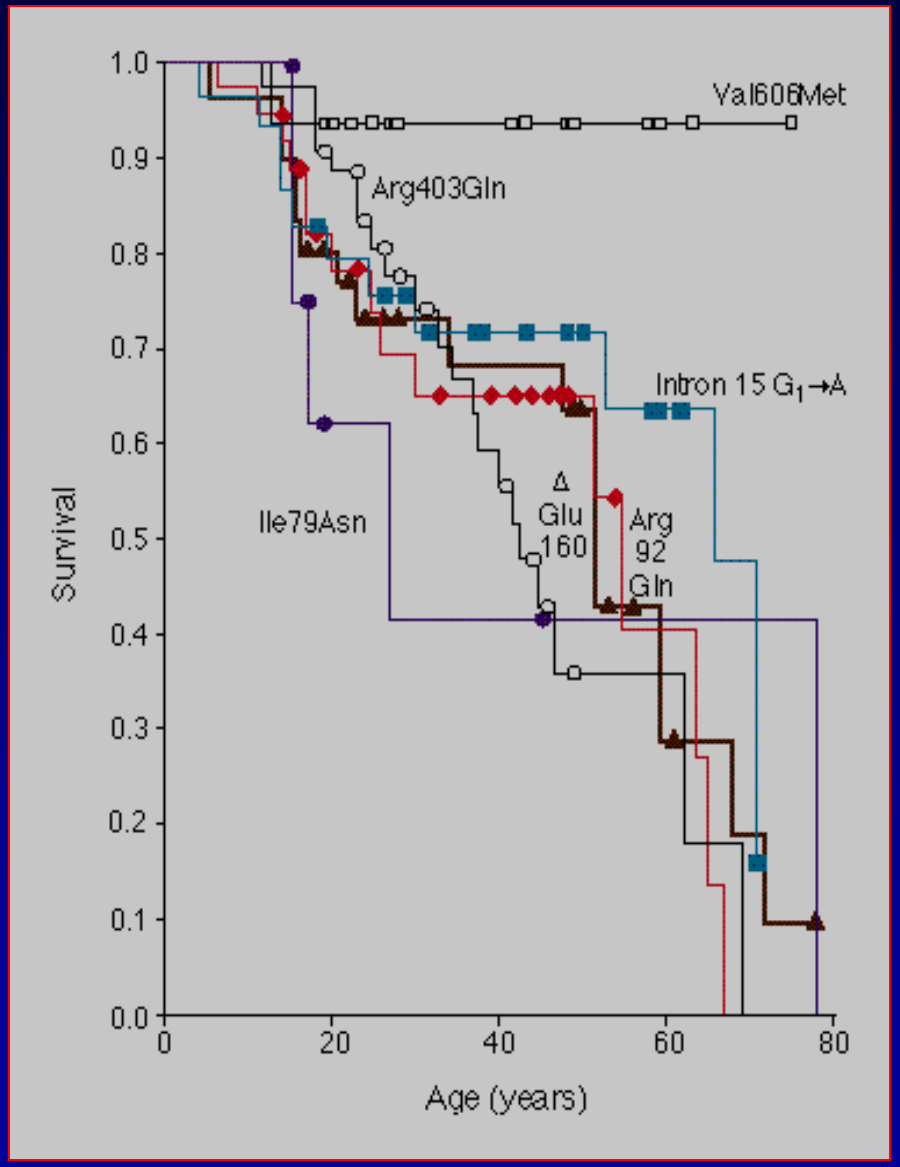
- **Abnormal exercise BP response**
  age 15 – relative risk 2 - 3
  age 50 – relative risk < 2

Plan: **define cause of Abn BP**
- obstruction
- ischemia } **Rx**
- MR
- abn vasc responses (Troponin T)

↓

Rx: consider ICD

Troponin T Mutations & Survival



Watkins et al, NEJM 1995;332:1058

Data Free Zone

Single risk factor

- **Asymptomatic severe LVOT obstruction VO2 >75% predicted**
- **Rx options: do nothing**
  diso + BB
  myectomy
  alcohol ablation
  ICD

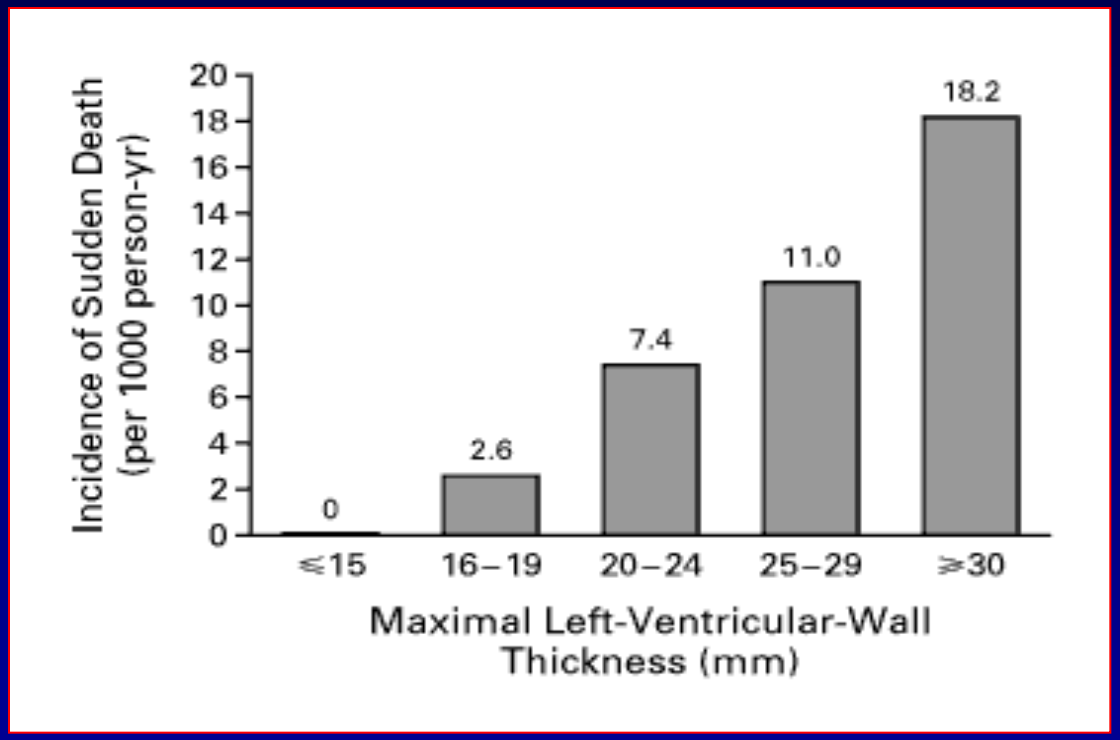
Limited Data Zone

Single risk factor

- **≥ 3cm LVH**
  - **age 15**
  - **age 50**

Spirito P, NEJM 2000
Elliott PM, Lancet 2001

LVH and Sudden Death

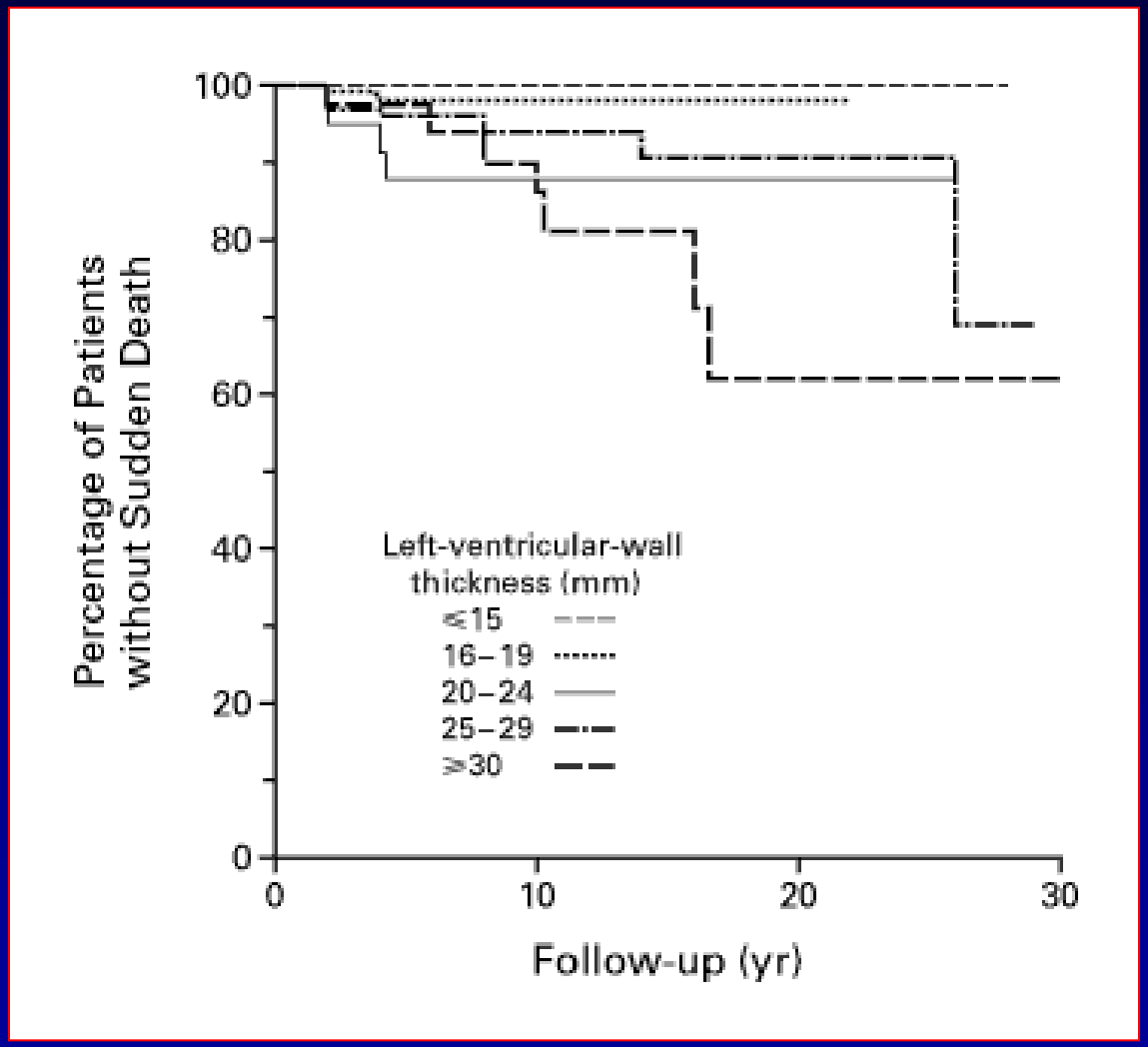


N=480

PPA=16% for ≥30 mm

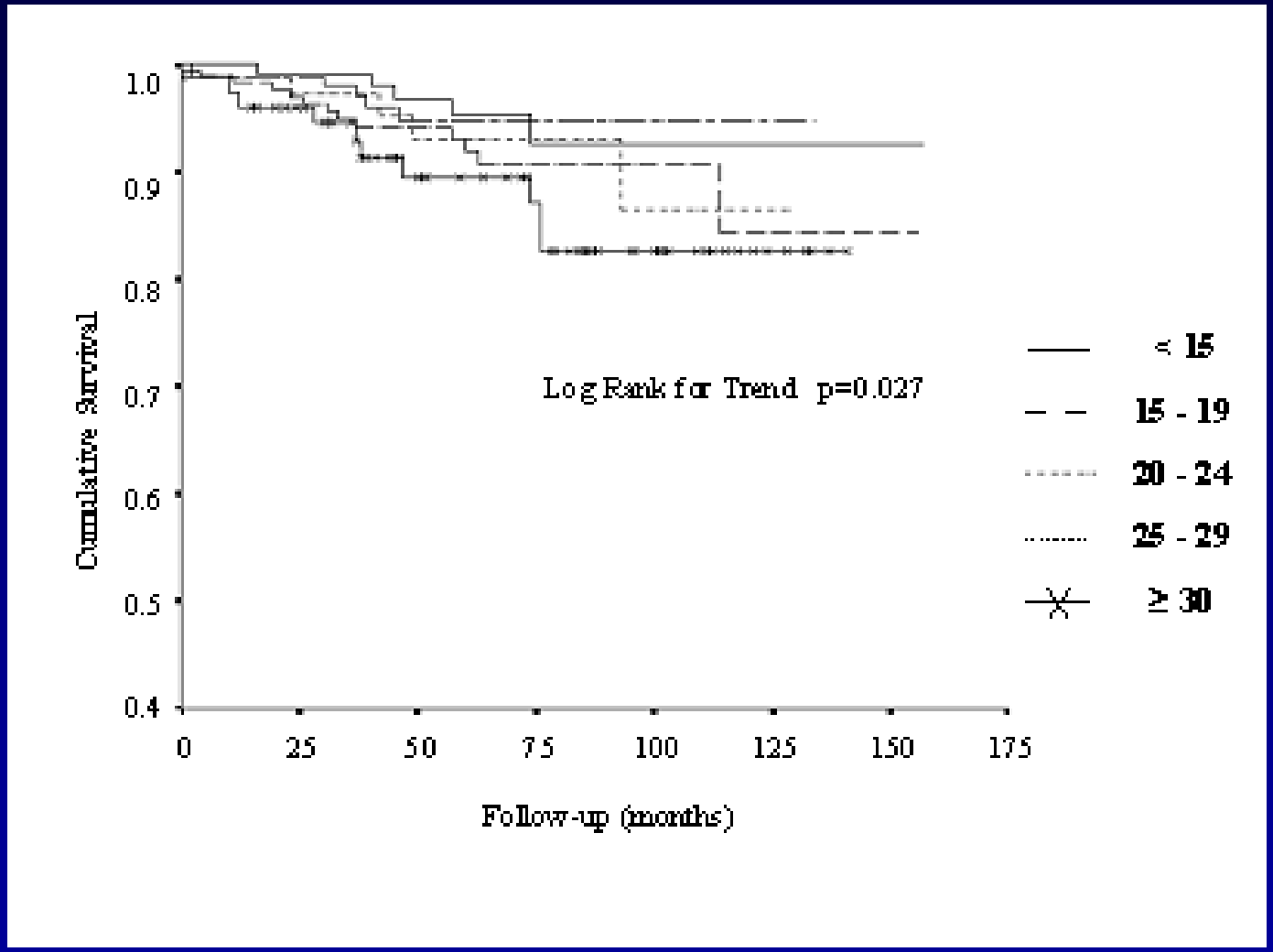
Spirito P et al. NEJM 2000;342:1778

LVH and Sudden Death



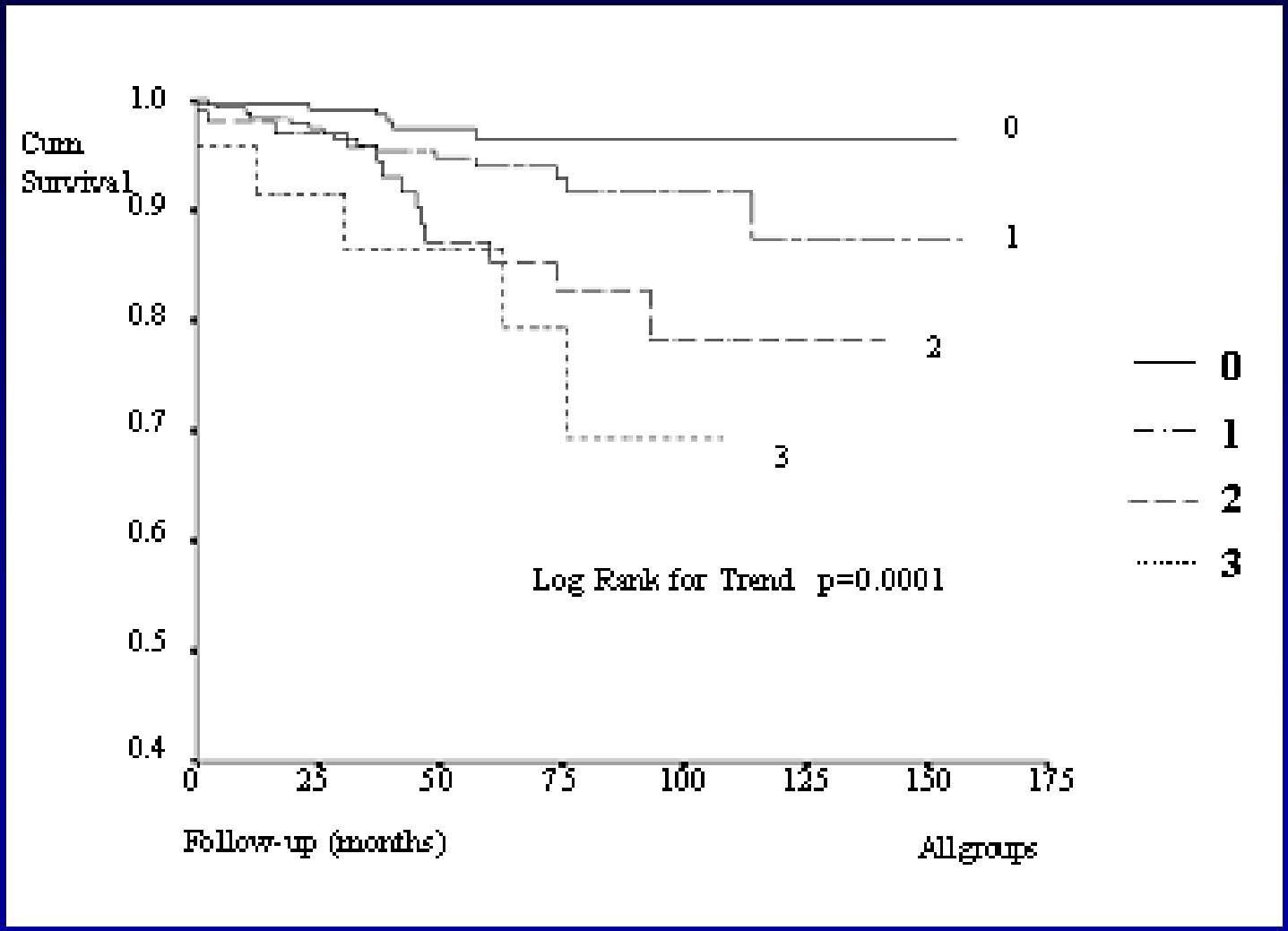
Spirito P et al. NEJM 2000;342:1778

LVH and Sudden Death



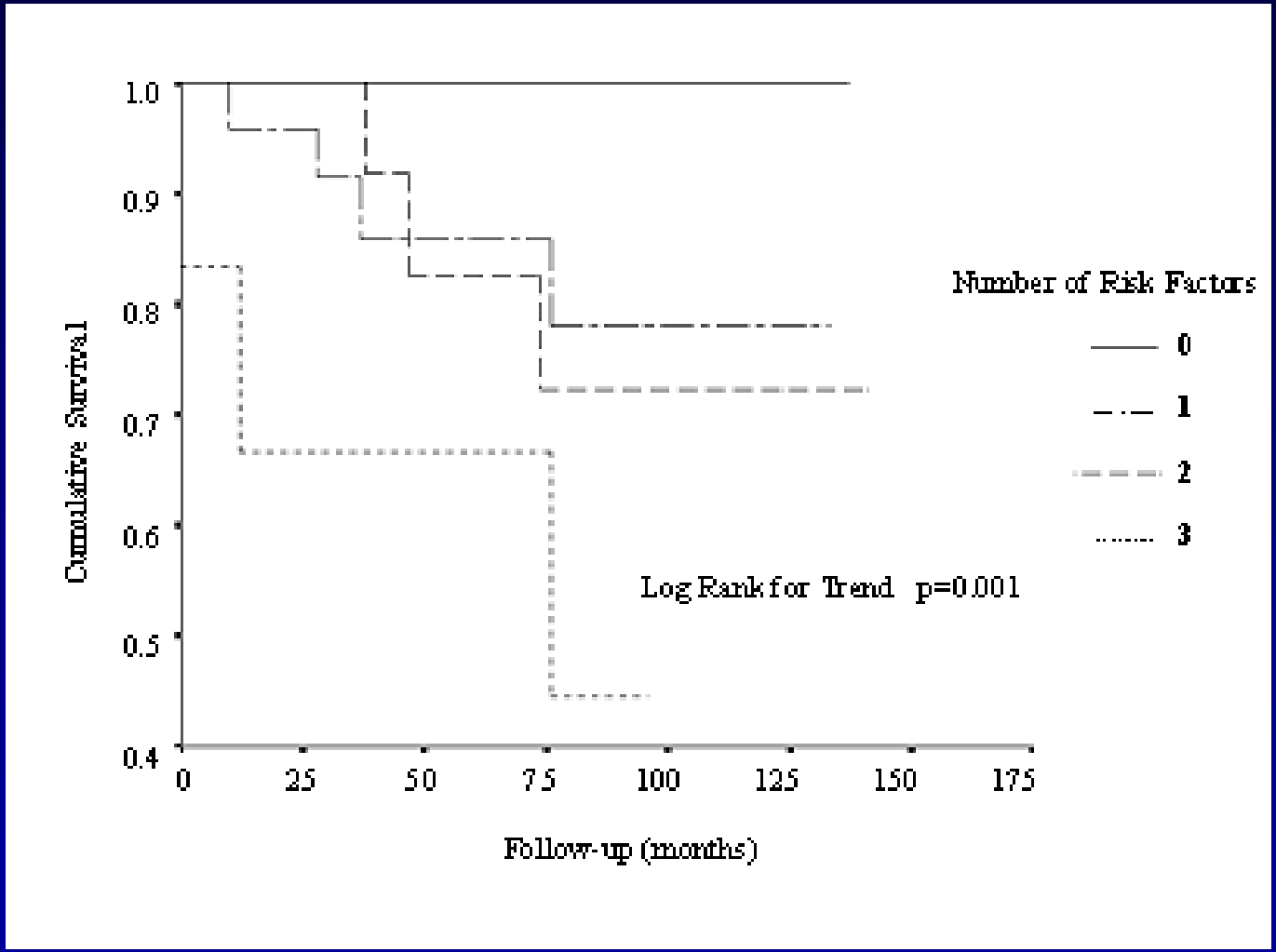
Elliott PM et al. Lancet 2001;357:420-4

Risk Factors & Sudden Death



Elliott PM et al. Lancet 2001;357:420-4

Risk Factors & Sudden Death in Severe LVH (≥ 3cm)



Elliott PM et al. Lancet 2001;357:420-4

SCD Risk Predictors in HCM

Predictor variable	SCD risk prediction model	
	Hazard Ratio (95% Confidence Interval)	**p**
Age (years)	0.98 (0.97, 0.99)	0.001
Maximal wall thickness (mm)	1.17 (1.01, 1.37)	0.042
Maximal wall thickness^2 (mm^2)	0.997 (0.99, 1.0003)	0.078
Left atrial diameter (mm)	1.03 (1.01, 1.05)	0.006
LV outflow gradient (mmHg)	1.004 (1.001, 1.01)	0.021
Family History SCD	1.58 (1.18, 2.13)	0.002
NSVT	2.29 (1.64, 3.18)	<0.001
Unexplained syncope	2.05 (1.48, 2.82)	<0.001

O'Mahony et al, Eur Heart J. 2013 Oct 14. [Epub ahead of print]

Absolute Risk Assessment in HCM

Age and NSVT

	Pt characteristic
Age	**17**
MWT	23
LA	44
LVOTO	64
FHSCD	0
NSVT	1
Syncope	0
PI	3.99
Survival	0.897431905
SCD at 5y	**10.25680946**

	Pt characteristic
Age	**58**
MWT	23
LA	44
LVOTO	64
FHSCD	0
NSVT	1
Syncope	0
PI	3.252
Survival	0.94957981
SCD at 5y	**5.042018989**

Age and LVH

	Pt characteristic
Age	50
MWT	**23**
LA	44
LVOTO	64
FHSCD	0
NSVT	0
Syncope	0
PI	2.57
Survival	0.974181337
SCD at 5y	**2.581866337**

	Pt characteristic
Age	50
MWT	**33**
LA	44
LVOTO	64
FHSCD	0
NSVT	0
Syncope	0
PI	2.48
Survival	0.976377052
SCD at 5y	**2.362294786**

	Pt characteristic
Age	**17**
MWT	33
LA	44
LVOTO	64
FHSCD	0
NSVT	0
Syncope	0
PI	3.074
Survival	0.957624251
SCD at 5y	**4.237574868**

$$\hat{P}_{SCD\,at\,5\,years} = 1 - 0.998^{\exp(\text{Prognostic Index})}$$

O'Mahony et al, Eur Heart J. 2013 Oct 14. [Epub ahead of print]

24 yr old university student

Dx age 6, asymptomatic

Family history - negative HCM or SD

MyBPC mutation

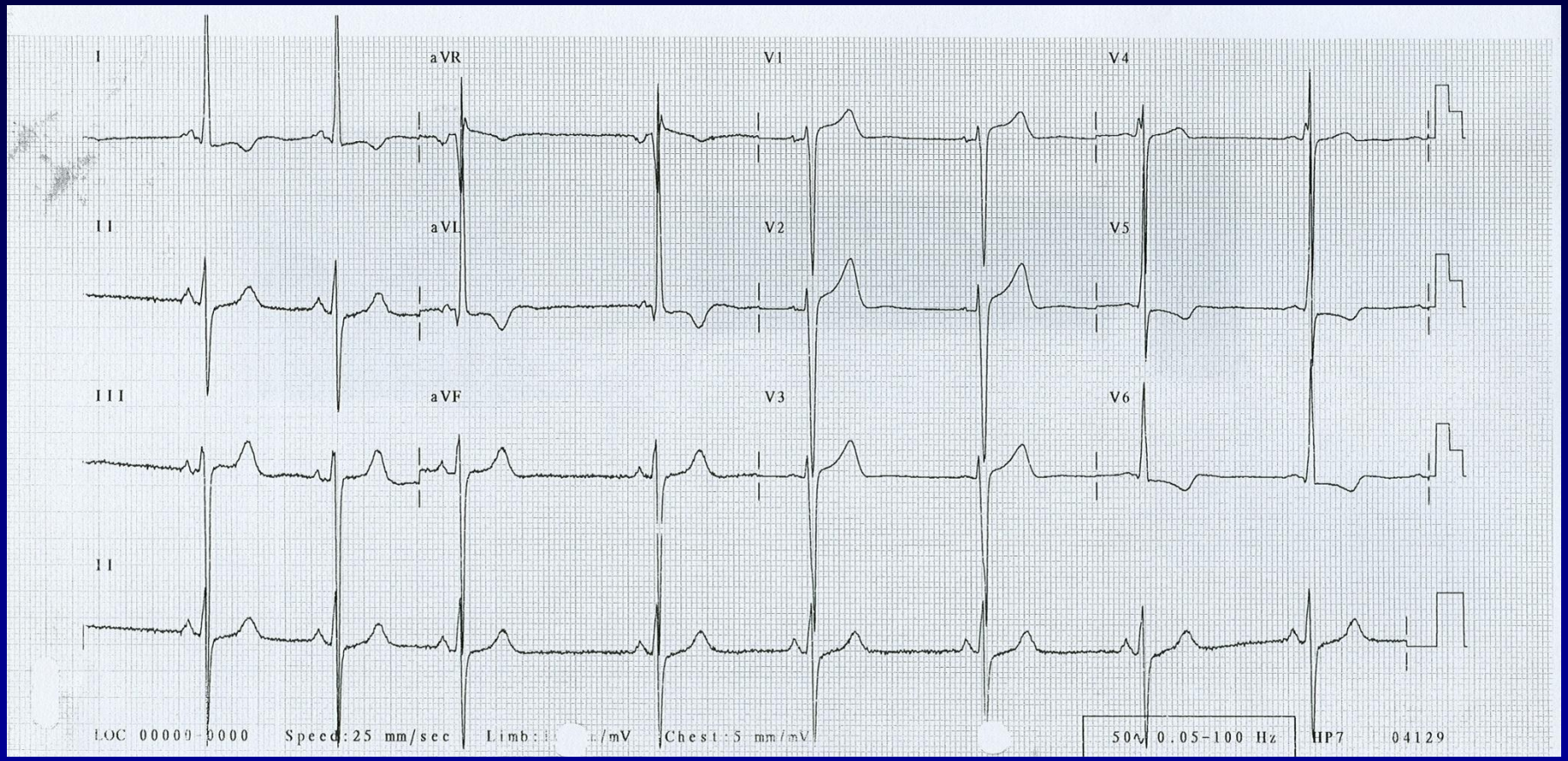
Echo **3 – 4 cm LVH**
diastolic dysfunction
LVOT obstruction
20 – 40 mmHg diso + BB
50 – 70 mmHg amio

VO2 **80% predicted**

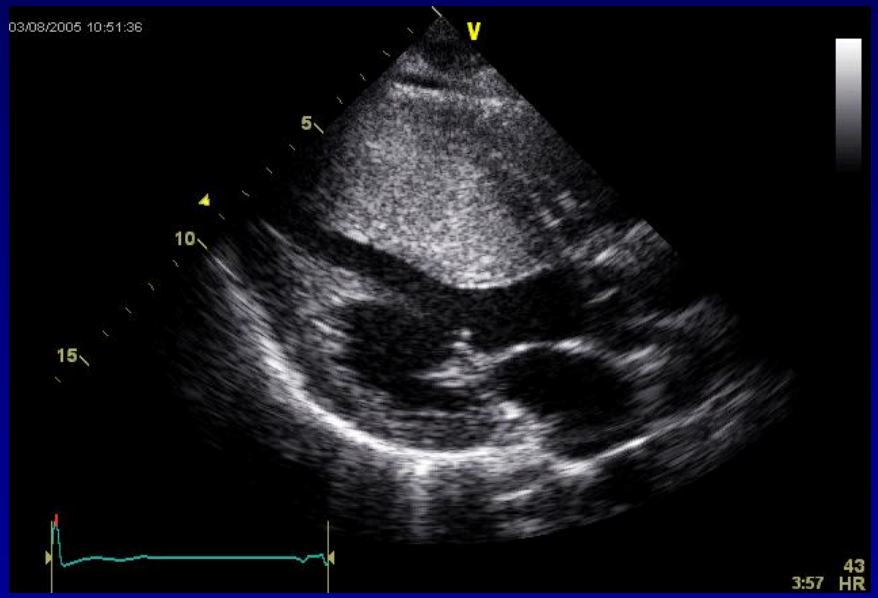
BP response **normal (110 → 160 mmHg)**

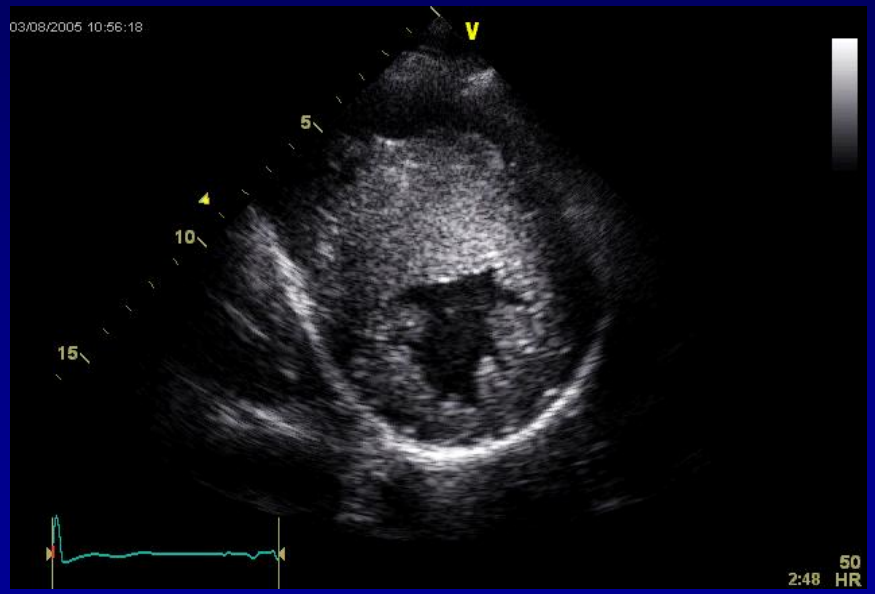
24 hr ECG – no arrhythmia

Age 19


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
Speed:25 mm/sec
Chest:5 mm/mV
0.05-100 Hz
HP7
04129

>3cm LVH


03/08/2005 10:51:36
V
5
10
15
43
3:57 HR


03/08/2005 10:56:18
V
5
10
15
50
2:48 HR

Data Free Zone

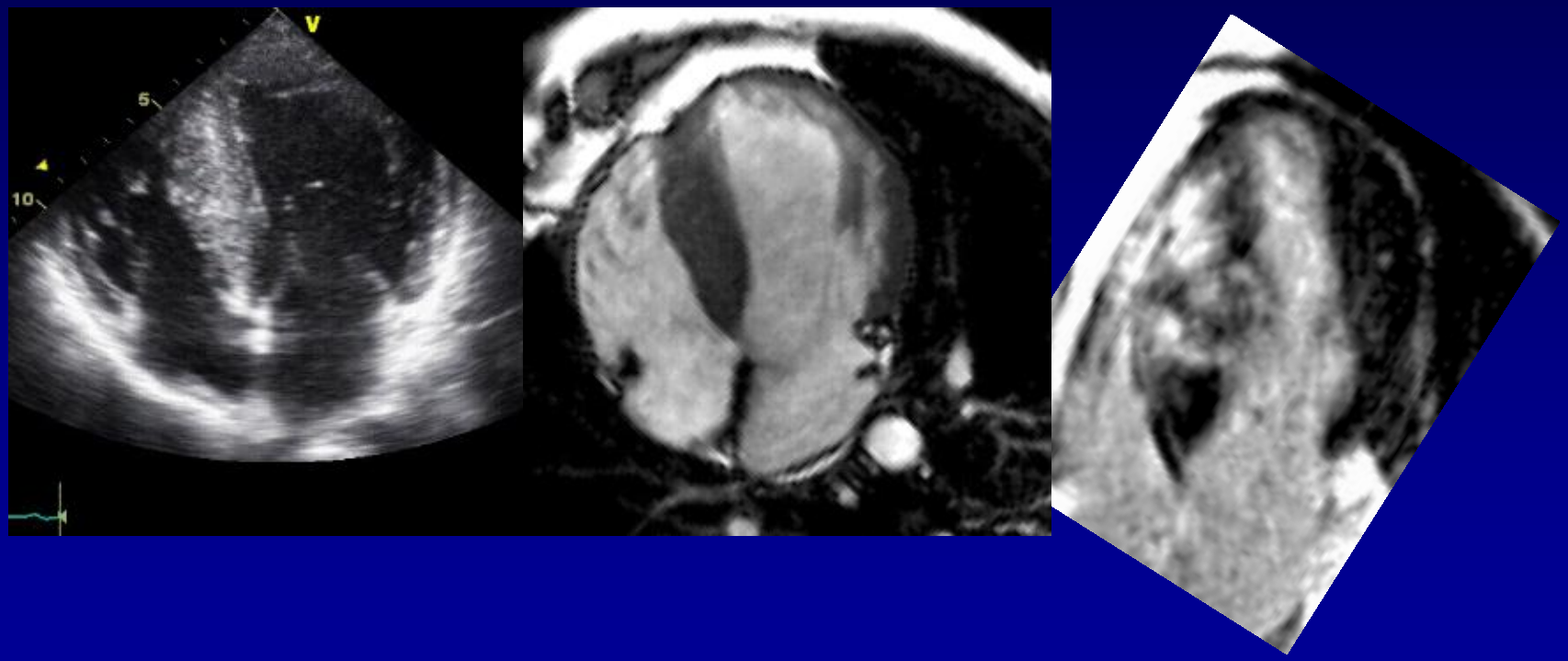
- 3cm ASH + obstruction (30-70mmHg)

Rx options:	no treatment
	ICD
	gradient reduction
	gradient reduction + ICD
Additional:	MRI (late enhancement)
tests	exercise echo (obstruction)
Rx:	myectomy (07/07)

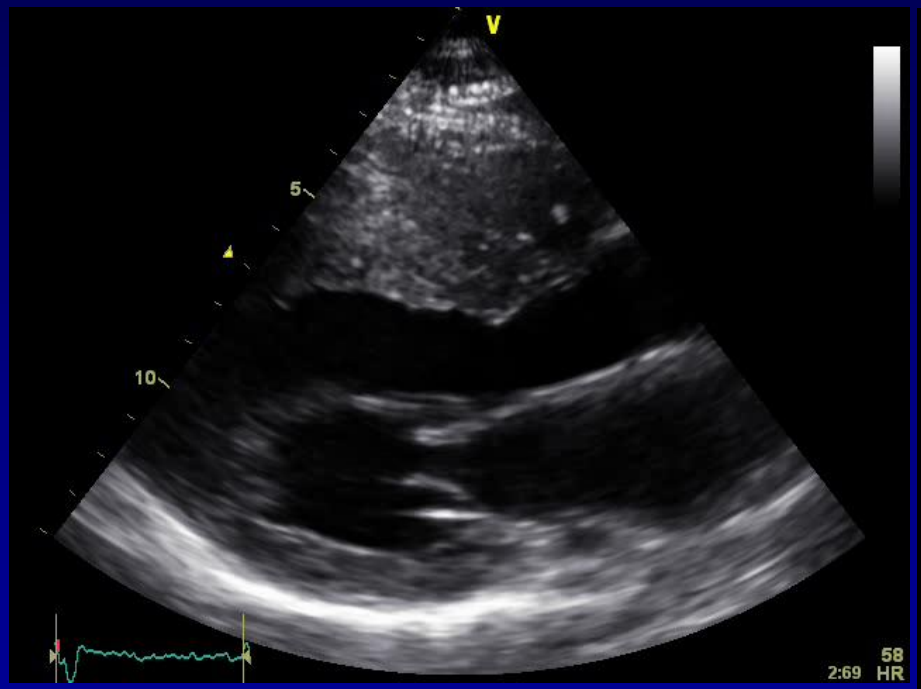
Absolute Risk Assessment in HCM

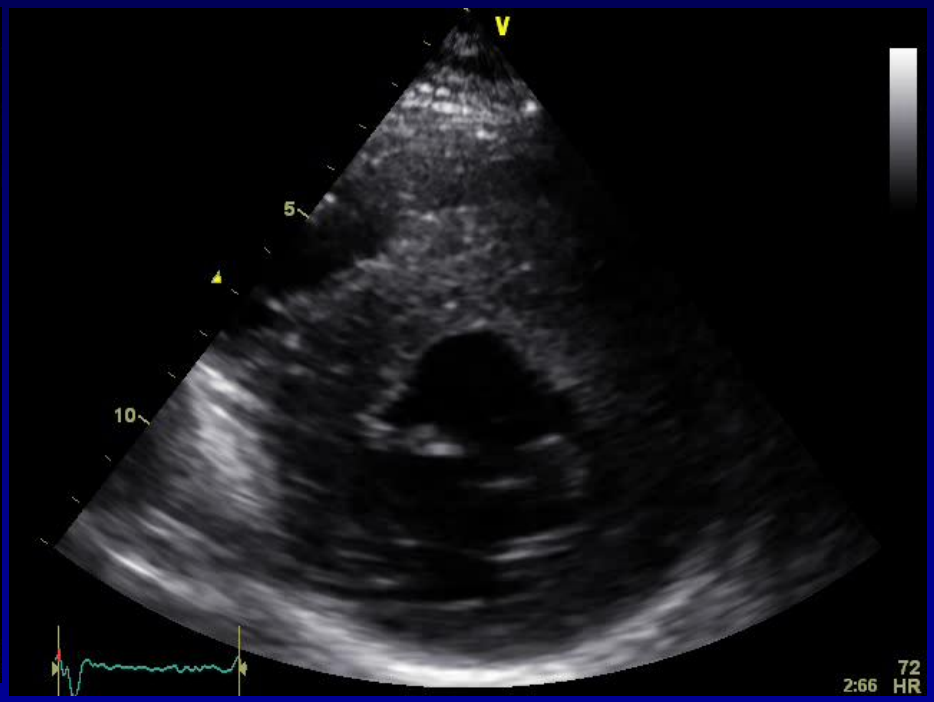
	Pt characteristics
Age	24
MWT	35
LA	40
LVOTO	50
FHSCD	0
NSVT	0
Syncope	0
PI	**2.698**
Survival	0.970708
SCD at 5y	**2.929216**

CMR – late enhancement

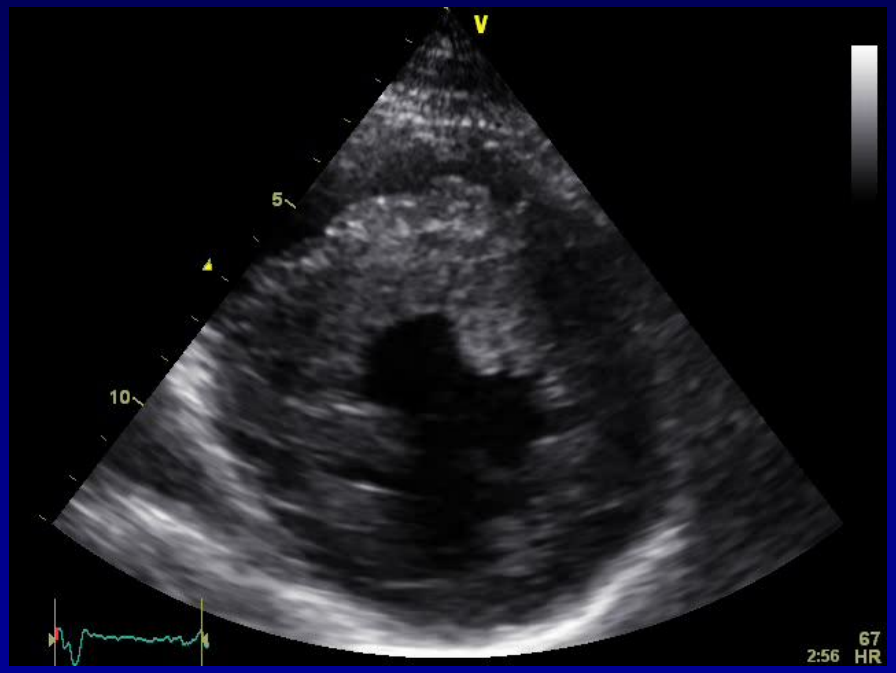


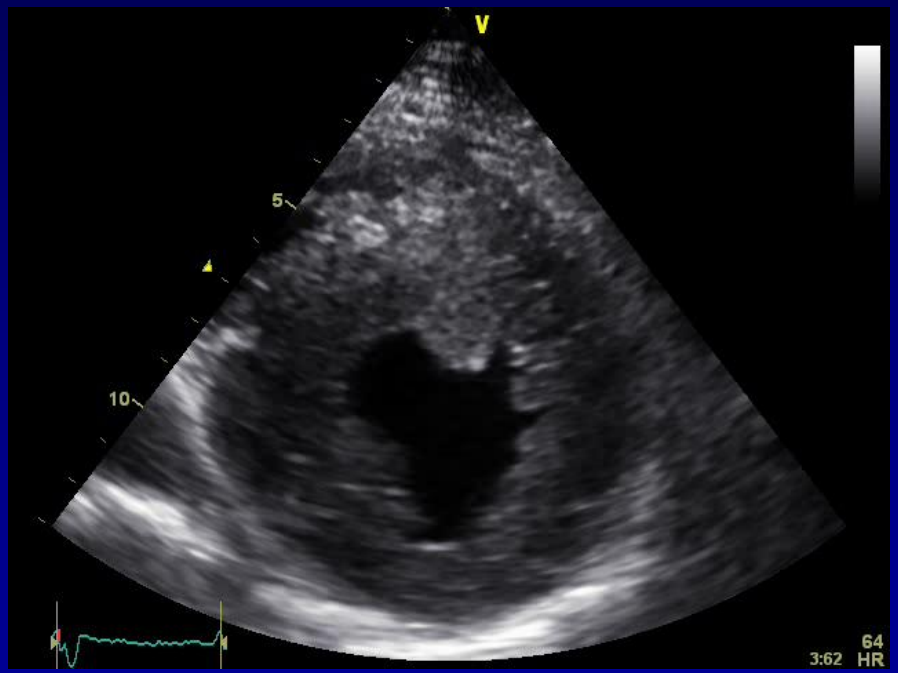
Post myectomy





Post myectomy





Summary

Risk assessment

- **the absence of RF accurately identifies the low risk cohort**
- **multiple RF accurately identifies the high risk cohort**
- **the presence of a single risk factor identifies individuals at increased risk who warrant careful consideration for ICD**
- **the ability to establish absolute rather than relative risk should improve sudden death prevention**