HYPERTROPHIC CARDIOMYOPATHY
RISK OF SUDDEN DEATH

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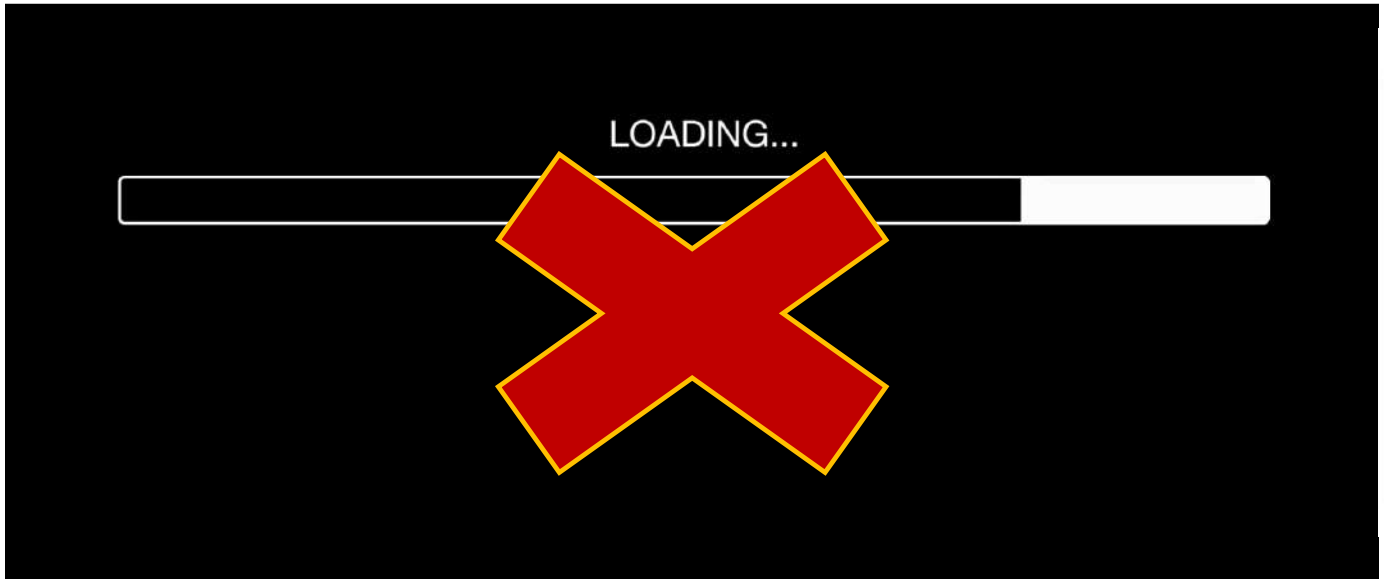
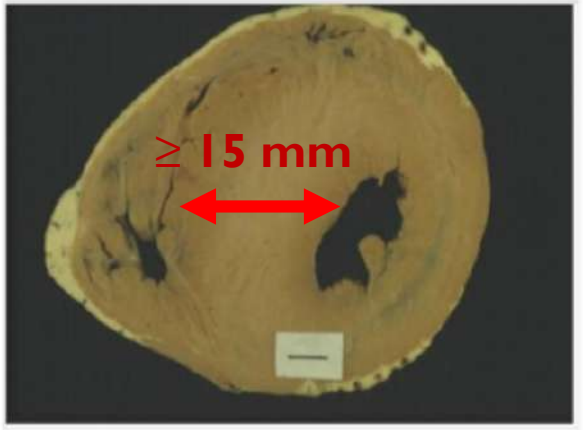
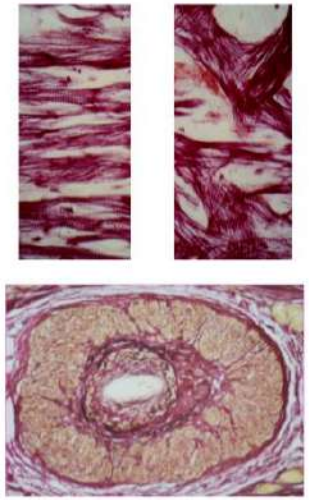
June 29th, 2019

HYPERTROPHIC CARDIOMYOPATHY

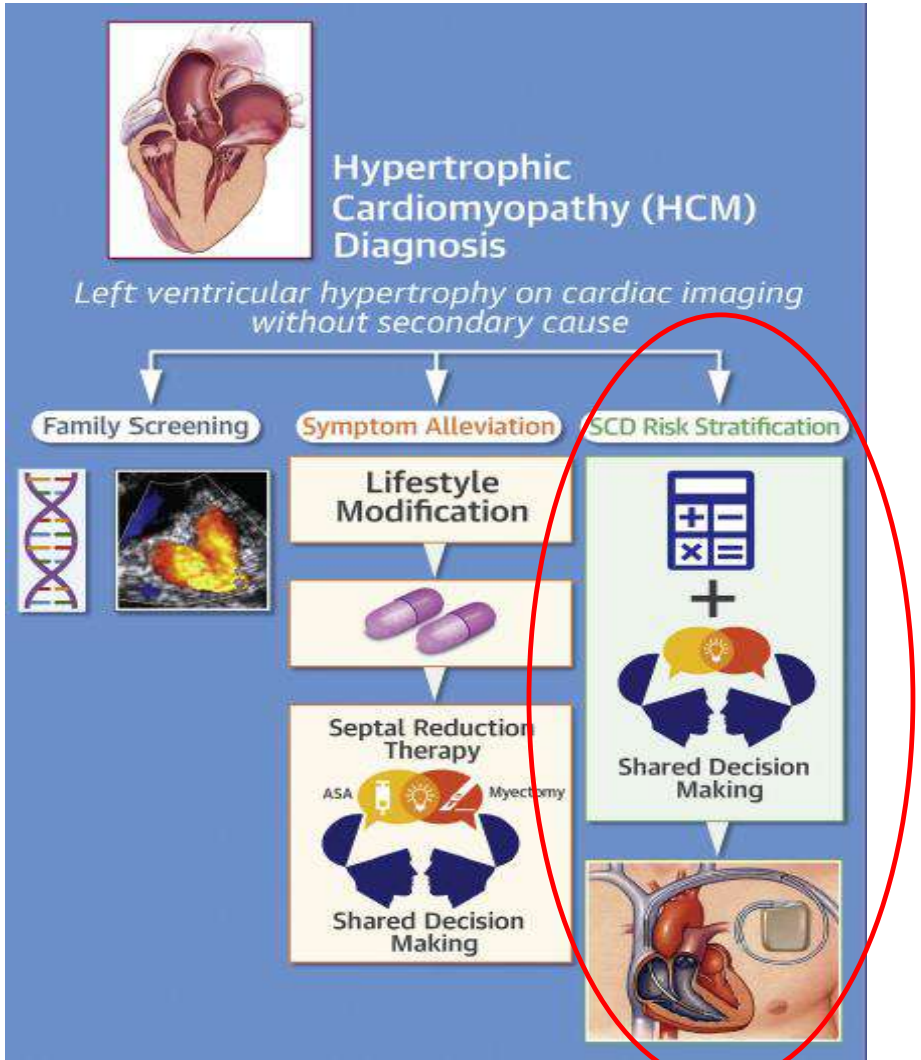
Hypertrophic cardiomyopathy (HCM) is defined by the presence of increased left ventricular (LV) wall thickness that is not solely explained by abnormal loading conditions.





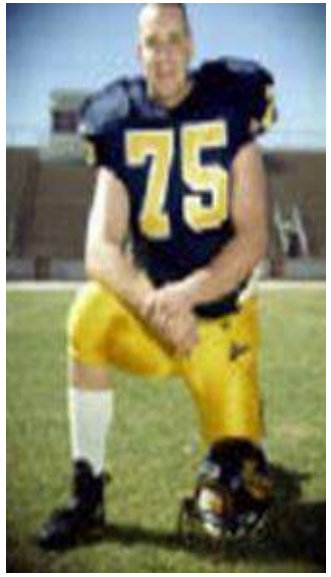


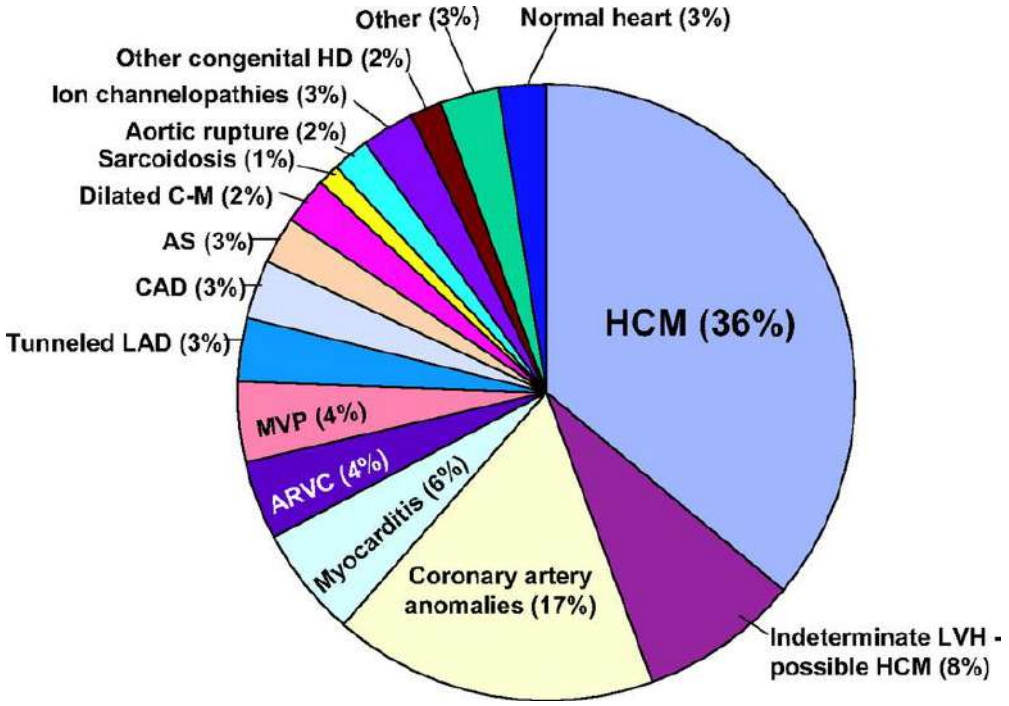
HYPERTROPHIC CARDIOMYOPATHY



HCM – RISK OF SUDDEN DEATH

- Cardiac hereditary disease more comun (1: 500)
- Main cause of SCD in athletes





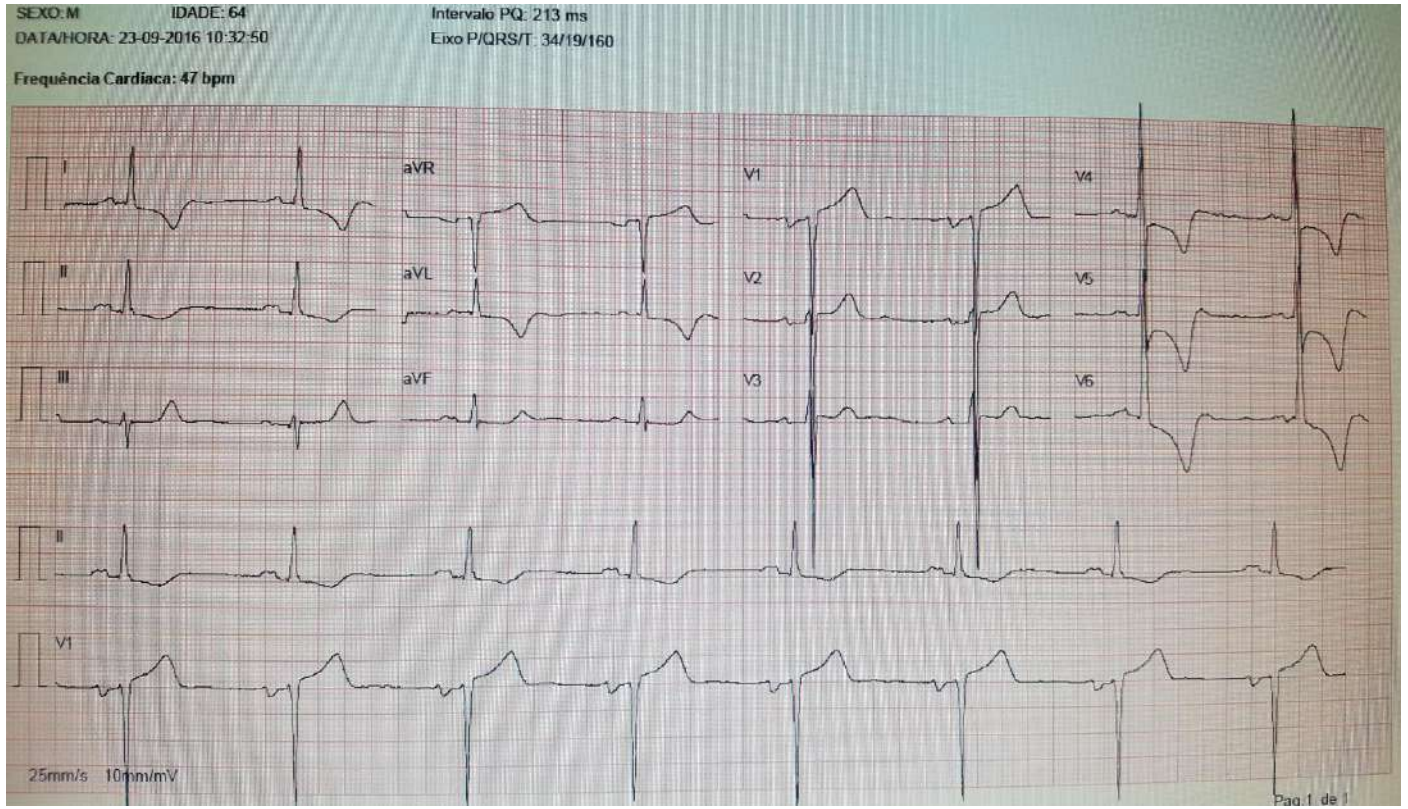
HCM – RISK OF SUDDEN DEATH

♂, 64 yo

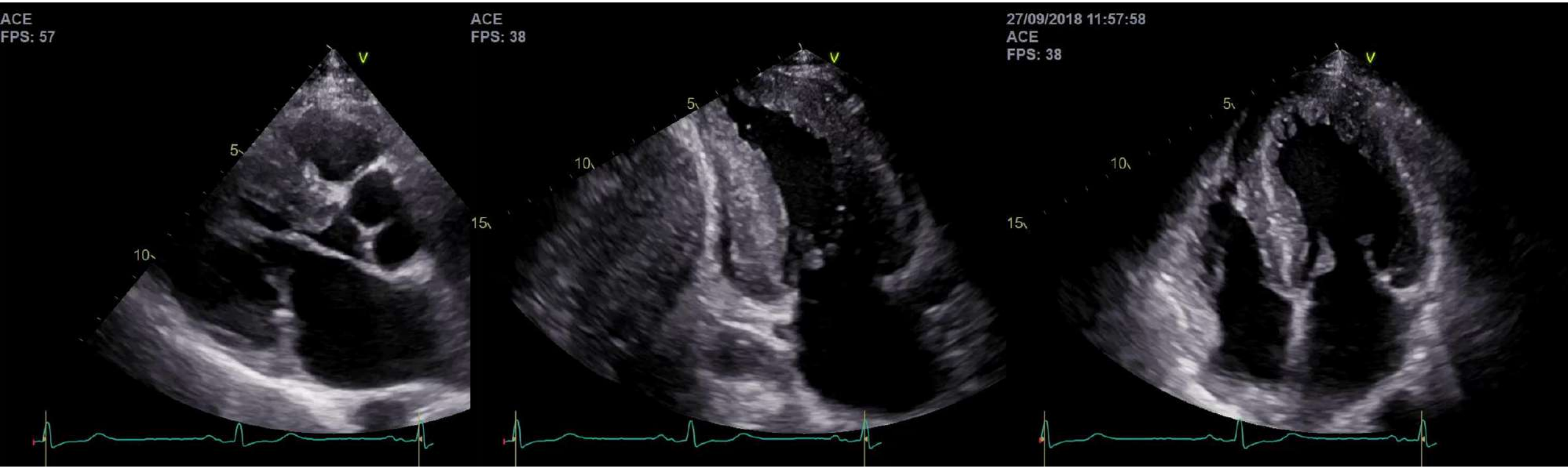
Cardiac arrest

Ventricular fibrillation

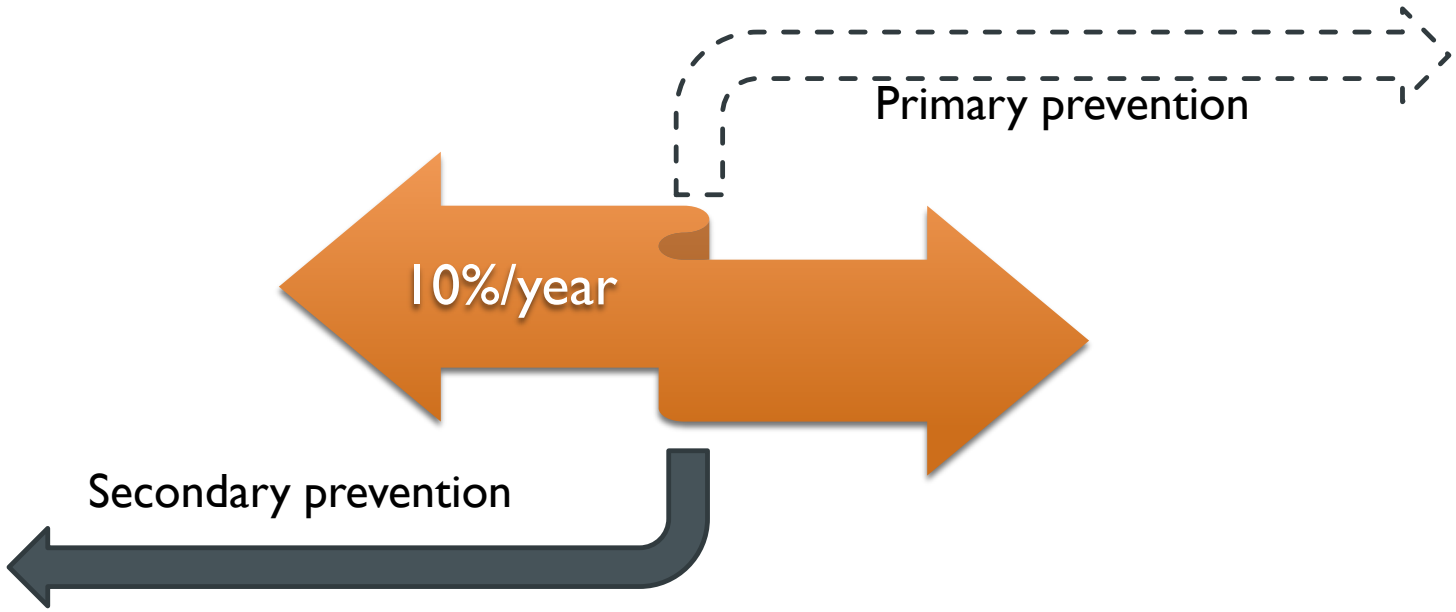
ECG after ROSC



HCM – RISK OF SUDDEN DEATH



HCM – RISK OF SUDDEN DEATH



ICD implantation is recommended in patients who have survived a cardiac arrest due to VT or VF, or who have spontaneous sustained VT causing syncope or haemodynamic compromise, and have a life expectancy of >1 year.	I	B

HCM – RISK OF SUDDEN DEATH

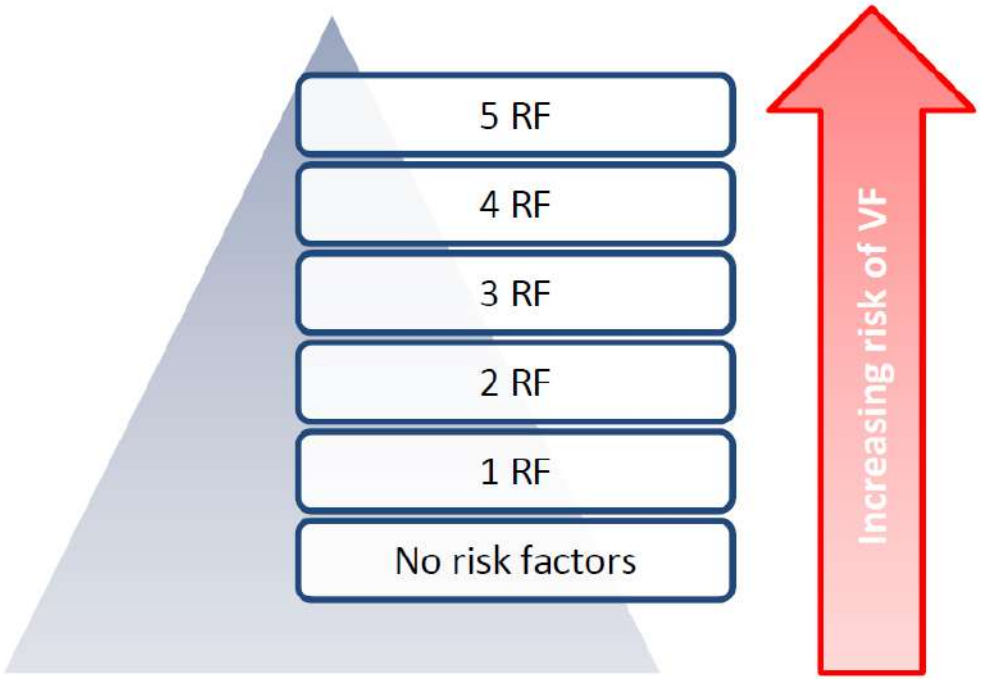
- Mores factors → higher risk
- ICD in primary prevention if: ≥ 2 risk factors

Journal of the American College of Cardiology
© 2003 by the American College of Cardiology Foundation and the European Society of Cardiology
Published by Elsevier Inc.
Vol. 42, No. 9, 2003
ISSN 0735-1097/03/$30.00
doi:10.1016/S0735-1097(03)00941-0

ACC/ESC EXPERT CONSENSUS DOCUMENT

American College of Cardiology/
European Society of Cardiology Clinical Expert
Consensus Document on Hypertrophic Cardiomyopathy

A Report of the American College of Cardiology Foundation
Task Force on Clinical Expert Consensus Documents and the
European Society of Cardiology Committee for Practice Guidelines

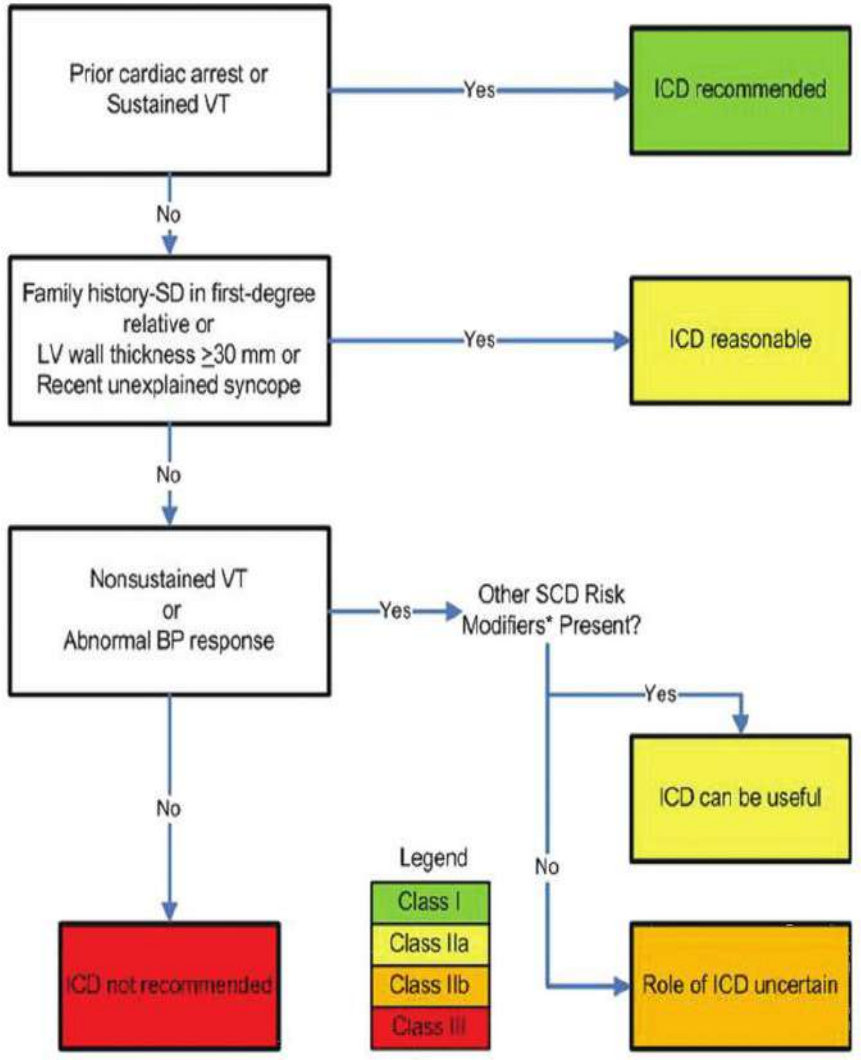


Family history of premature sudden death
Unexplained syncope
LV thickness greater than or equal to 30 mm
Abnormal exercise blood pressure
Nonsustained ventricular tachycardia (Holter)

HCM – RISK OF SUDDEN DEATH

2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: Executive summary

A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines



LVOTO
Late Gad
Apical Aneurysm
Compound mutations

HCM – RISK OF SUDDEN DEATH

ORIGINAL ARTICLE

A validation study of the 2003 American College of Cardiology/European Society of Cardiology and 2011 American College of Cardiology Foundation/American Heart Association risk stratification and treatment algorithms for sudden cardiac death in patients with hypertrophic cardiomyopathy

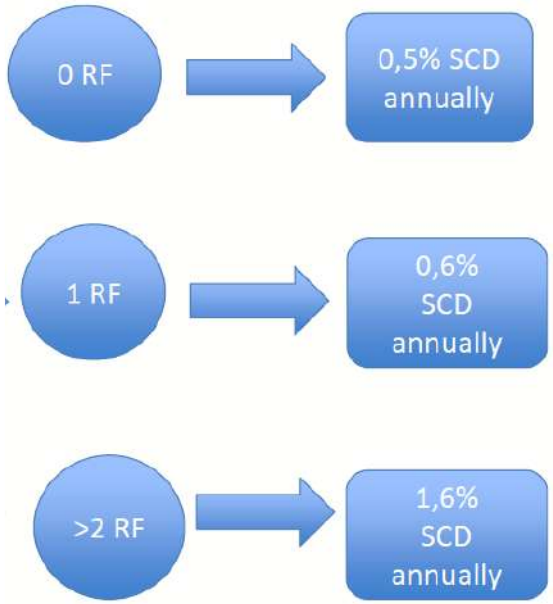
Constantinos O'Mahony,[1,2] Maite Tome-Esteban,[1] Pier D Lambiase,[1] Antonios Pantazis,[1] Shaughan Dickie,[1] William J McKenna,[1] Perry M Elliott[1]

Table 3 SCD/appropriate ICD shock in patients with a single risk factor

Risk factor	Number of patients*	Years of follow-up, median (IQR)	Number of events	Annual rate of SCD/ICD discharge (%)	5-Year cumulative incidence of SCD/ICD discharge	10-Year cumulative incidence of SCD/ICD discharge
Syncope	122 (19%)	6.4 (3.7–9.8)	4 (3%)	0.5% (95% CI 0.2 to 1.2)	4% (95% CI 1.5 to 10.4)	4% (95% CI 1.5 to 10.4)‡
Severe LVH	39 (6%)	8.7 (6.9–14.3)	2 (5%)	0.5% (95% CI 0.1 to 2.1)	0%†	5.9% (95% CI 0.9 to 35.0)
NSVT	157 (25%)	6.6 (4.2–9.6)	10 (6%)	0.9% (95% CI 0.4 to 1.7)	3.6% (95% CI 1.5 to 8.6)	9.6% (95% CI 4.7 to 18.9)
ABPRE	52 (8%)	9.3 (5.4–12.5)	2 (4%)	0.4% (95% CI 0.1 to 1.6)	2.0% (95% CI 0.3 to 13.1)	5.7% (95% CI 1.4 to 22.1)
FHSCD	266 (42%)	6.4 (4.2–10.2)	13 (5%)	0.7% (95% CI 0.4 to 11.5)	3.3% (95% CI 1.7 to 6.5)	7.1% (95% CI 3.8 to 13.0)

*A total of 636 patients had a single risk factor in isolation; this [illegible] the denominator for the percentage provided in the parentheses.
†The first SCD/appropriate ICD shock occurred after 8 years of follow-up.
‡In those with unexplained syncope, no SCD/appropriate ICD shock occurred after 5 years.
ABPRE, abnormal systolic blood pressure response to exercise; FHSCD, family history of SCD; ICD, implantable cardioverter defibrillator; LVH, left ventricular hypertrophy; NSVT, non-sustained ventricular tachycardia; SCD, sudden cardiac death.

- **Limitations**



- Binary variables

HCM – RISK STRATIFICATION

European Heart Journal
doi:10.1093/eurheartj/eht439

FASTTRACK CLINICAL RESEARCH

A novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCM Risk-SCD)

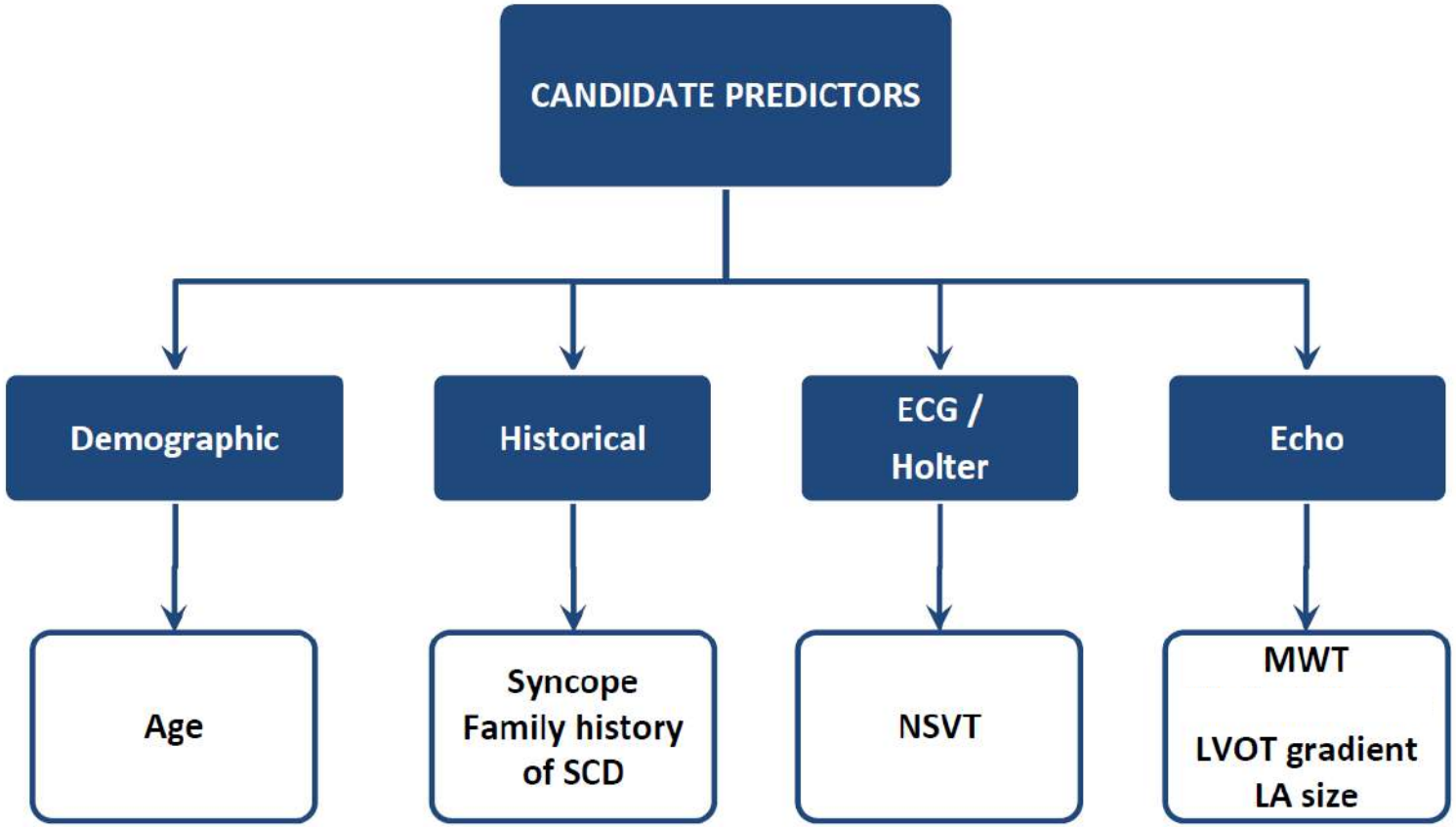
Constantinos O'Mahony[1], Fatima Jichi[2], Menelaos Pavlou[8], Lorenzo Monserrat[3], Aristides Anastasakis[4], Claudio Rapezzi[5], Elena Biagini[5], Juan Ramon Gimeno[6], Giuseppe Limongelli[7], William J. McKenna[1], Rumana Z. Omar[2,8] and Perry M. Elliott[1]*, for the Hypertrophic Cardiomyopathy Outcomes Investigators

$$\hat{P}_{SCD\ at\ 5\ years} = 1 - S_0(t)^{\exp(\text{Prognostic Index})}$$

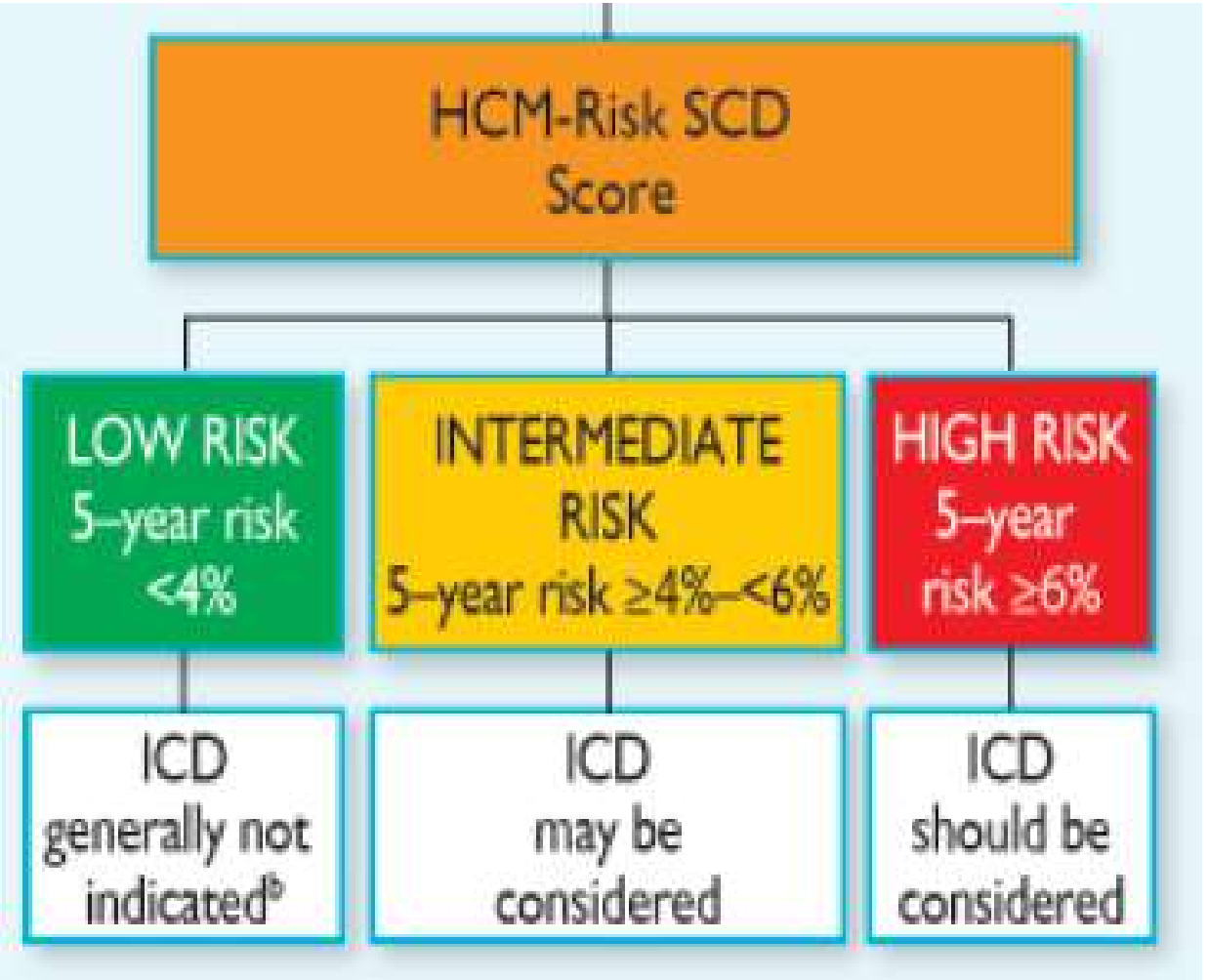
Mathematical functions that mimic natural processes

Eur Heart J 2014

HCM – RISK OF SUDDEN DEATH



HCM – RISK OF SUDDEN DEATH



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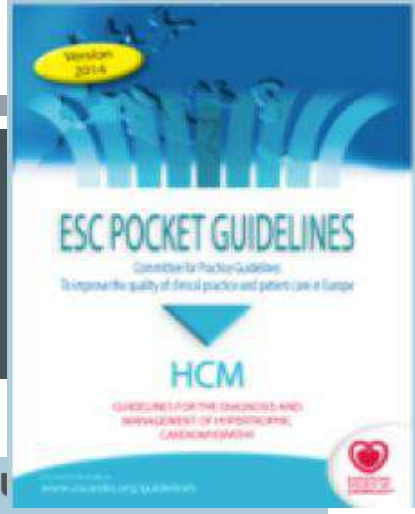

HCM Risk-SCD Calculator

Age	55 **Years**	*Age at evaluation*	
Maximum LV wall thi-ckness	20 **mm**	*Transthoracic Echocardiographic measurement*	
Left atrial size	40 **mm**	*Left atrial diameter determined by M-Mode or 2D echocardiography plane at time of evaluation*	
Max LVOT gradient	40 **mmHg**	*The maximum LV outflow gradient determined at rest and with Vals (irrespective of concurrent medical treatment) using pulsed and cor the apical three and five chamber views. Peak outflow tract gradien using the modified Bernouilli equation: Gradient= 4V², where V is t velocity*	
Family History of SCD	◉ No ○ Yes	*History of sudden cardiac death in 1 or more first degree relatives u SCD in a first degree relative with confirmed HCM at any age (post*	
Non-sustained VT	◉ No ○ Yes	*3 consecutive ventricular beats at a rate of 120 beats per minute ar monitoring (minimum duration 24 hours) at or prior to evaluation.*	
Unexplained syncope	○ No ◉ Yes	*History of unexplained syncope at or prior to evaluation.*	

Risk of SCD at 5 years (%):	3.76
ESC recommendation:	ICD generally not indicated **

HCM Risk-SCD Calcu

Age	20 **Years**	*Age at evaluation*	
Maximum LV wall thi-ckness	20 **mm**	*Transthoracic Echocardiographic measurement*	
Left atrial size	40 **mm**	*Left atrial diameter determined by M-Mode or 2D echocardiograph plane at time of evaluation*	
Max LVOT gradient	40 **mmHg**	*The maximum LV outflow gradient determined at rest and with Va (irrespective of concurrent medical treatment) using pulsed and co the apical three and five chamber views. Peak outflow tract gradie using the modified Bernouilli equation: Gradient= 4V², where V is velocity*	
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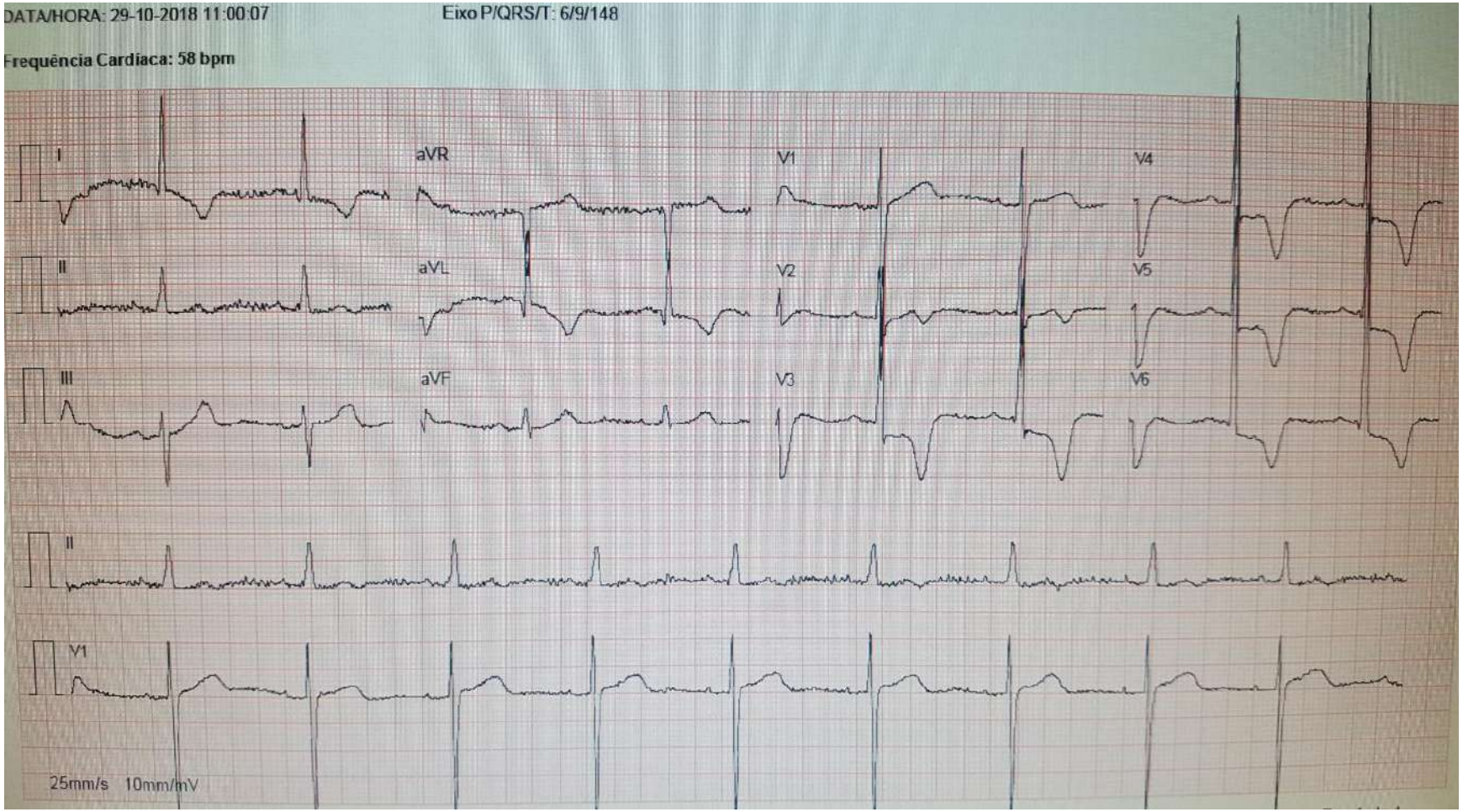
Unexplained syncope	○ No ◉ Yes	*History of unexplained syncope at or prior to evaluation.*	

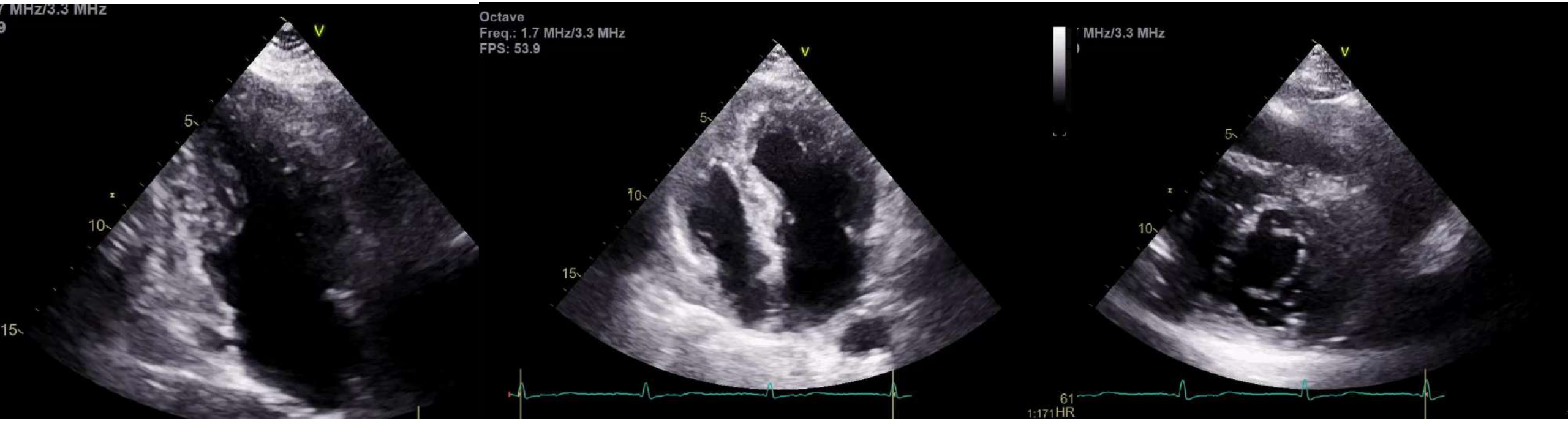
Risk of SCD at 5 years (%):	6.94
ESC recommendation:	ICD should be considered

HCM – RISK OF SUDDEN DEATH

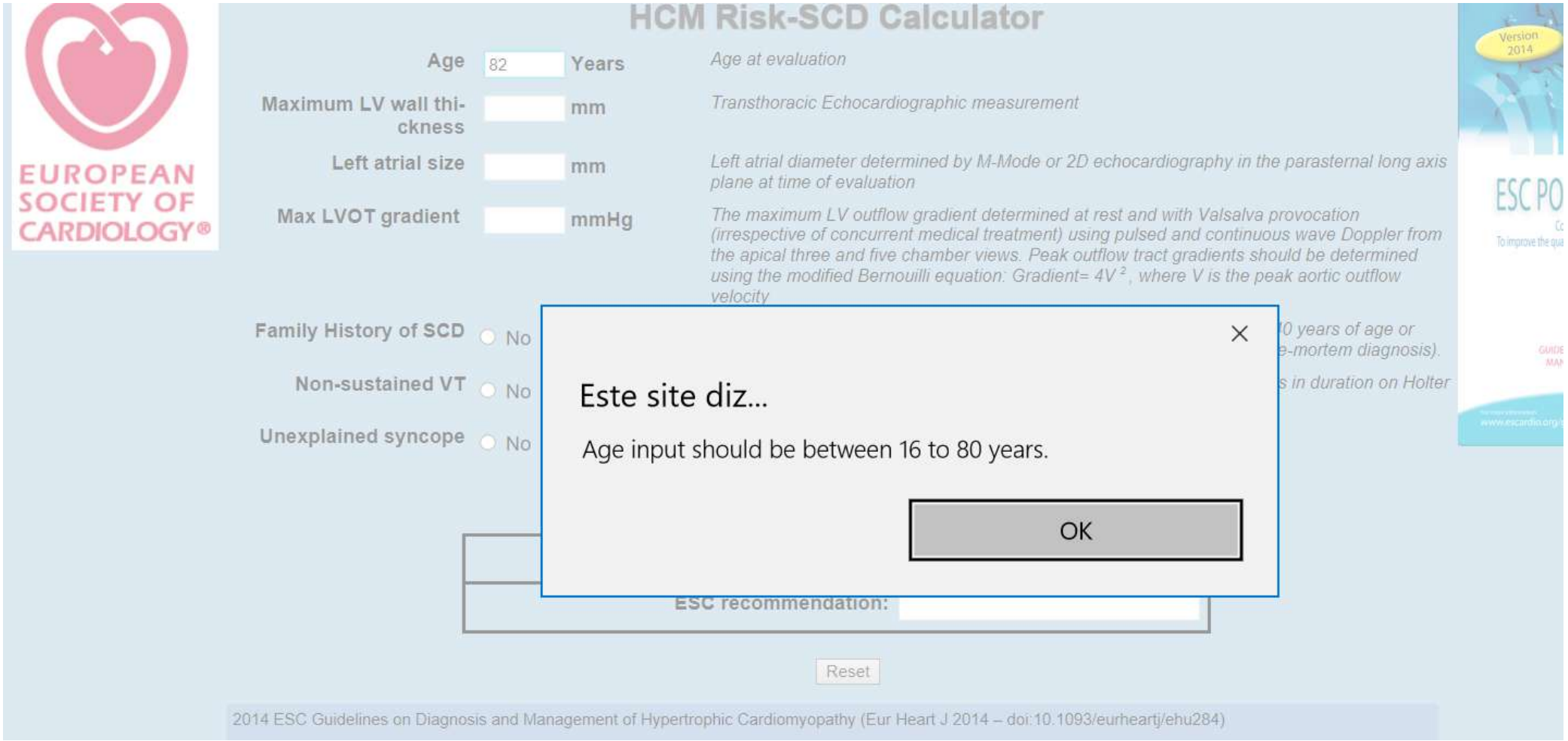
- 82 yo, ♀
- Syncope



HCM – RISK OF SUDDEN DEATH



HCM – RISK OF SUDDEN DEATH



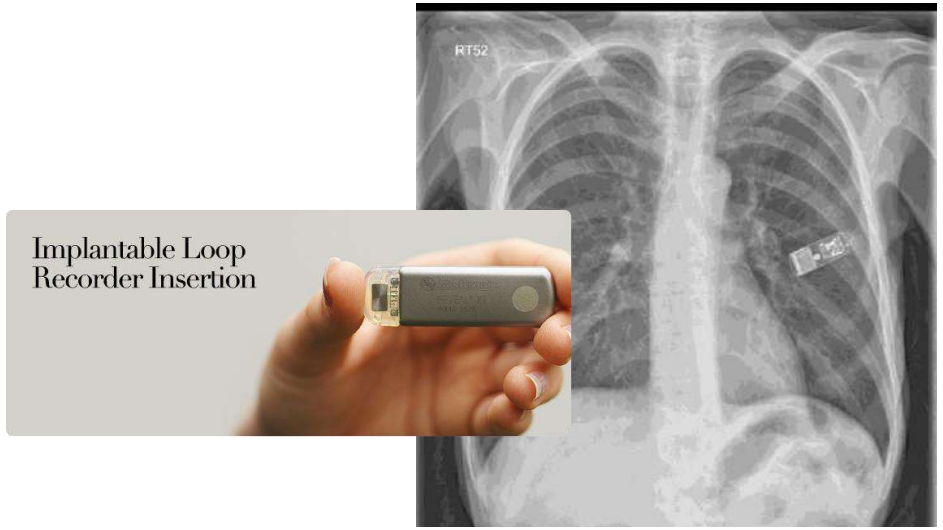
HCM – RISK OF SUDDEN DEATH

EUROPEAN SOCIETY OF CARDIOLOGY®

HCM Risk-SCD Calculator

Age	80	**Years**	*Age at evaluation*
Maximum LV wall thickness	21	**mm**	*Transthoracic Echocardiographic measurement*
Left atrial size	45	**mm**	*Left atrial diameter determined by M-Mode or 2D echocardiograp plane at time of evaluation*
Max LVOT gradient	25	**mmHg**	*The maximum LV outflow gradient determined at rest and with Va (irrespective of concurrent medical treatment) using pulsed and c the apical three and five chamber views. Peak outflow tract gradie using the modified Bernouilli equation: Gradient= 4V², where V is velocity*
Family History of SCD	◉ No ○ Yes		*History of sudden cardiac death in 1 or more first degree relatives SCD in a first degree relative with confirmed HCM at any age (po*
Non-sustained VT	◉ No ○ Yes		*3 consecutive ventricular beats at a rate of 120 beats per minute monitoring (minimum duration 24 hours) at or prior to evaluation.*
Unexplained syncope	○ No ◉ Yes		*History of unexplained syncope at or prior to evaluation.*

Risk of SCD at 5 years (%):	2.67
ESC recommendation:	ICD generally not indicated **



4. Implantable loop recorder in risk stratification

- ILRs have a potential role in identifying the correlation between symptoms and suspected ventricular tachyarrhythmia in selected high-risk patients affected by Brugada ECG pattern, long or short QT, hypertrophic cardiomyopathy, and arrhythmogenic right ventricular dysplasia.

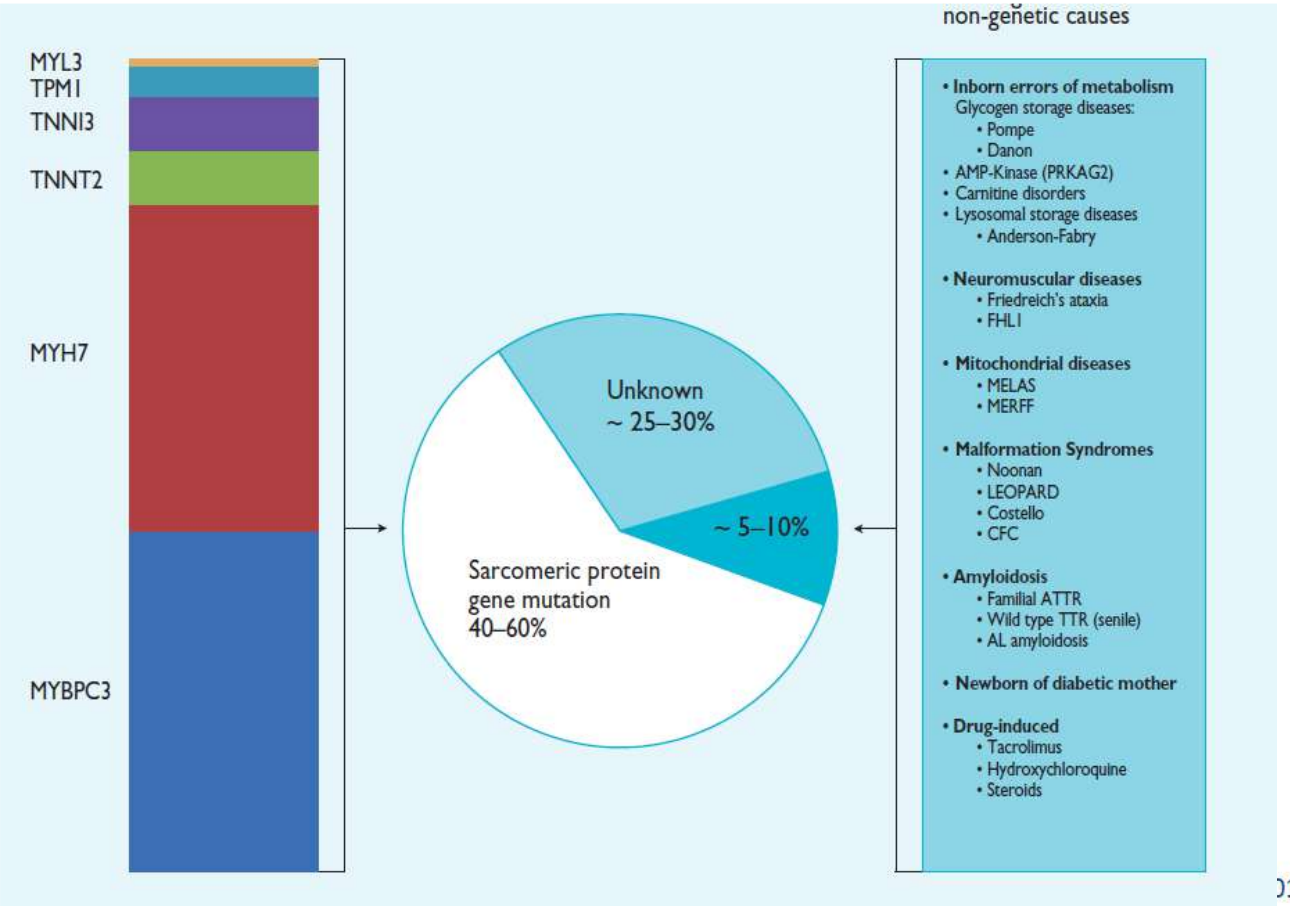
HCM – RISK OF SUDDEN DEATH

Limitations:

- Age: < 16 and > 80 yo
- Athletes
- After myectomy
- After alcohol septal ablation
- Individuals with metabolic/infiltrative diseases

(e.g. Anderson-Fabry disease)

- Syndromes (e.g. Noonan syndrome).



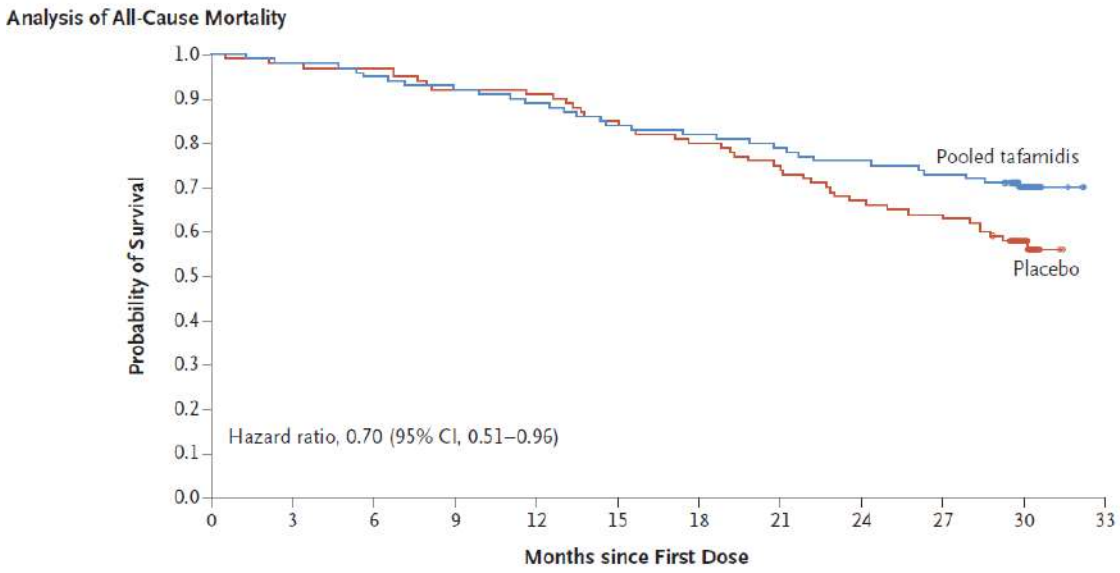
HCM – RISK OF SUDDEN DEATH

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy

Mathew S. Maurer, M.D., Jeffrey H. Schwartz, Ph.D., Balarama Gundapaneni, M.S., Perry M. Elliott, M.D., Giampaolo Merlini, M.D., Ph.D., Marcia Waddington-Cruz, M.D., Arnt V. Kristen, M.D., Martha Grogan, M.D., Ronald Witteles, M.D., Thibaud Damy, M.D., Ph.D., Brian M. Drachman, M.D., Sanjiv J. Shah, M.D., Mazen Hanna, M.D., Daniel P. Judge, M.D., Alexandra I. Barsdorf, Ph.D., Peter Huber, R.Ph., Terrell A. Patterson, Ph.D., Steven Riley, Pharm.D., Ph.D., Jennifer Schumacher, Ph.D., Michelle Stewart, Ph.D., Marla B. Sultan, M.D., M.B.A., and Claudio Rapezzi, M.D., for the ATTR-ACT Study Investigators*



HCM – RISK OF SUDDEN DEATH

Validation:

HCM Risck SCD

C-Index 0,70 (95% CI: 0,68 – 0,72)

ACC/ACCF (2011)

C-Index 0,54 (95% CI: 0,51 – 0,56)

Same as CHA2DS2-VASc

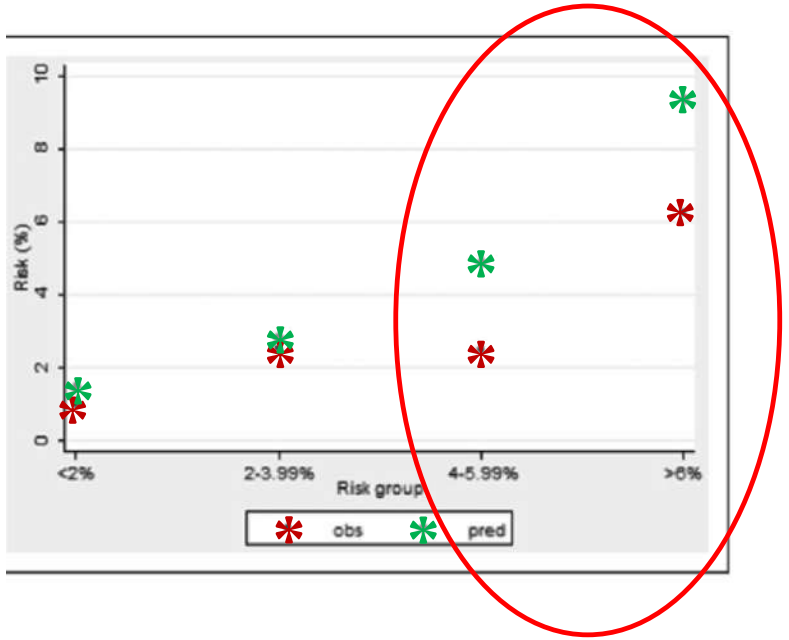
HCM – RISK OF SUDDEN DEATH

Circulation

ORIGINAL RESEARCH ARTICLE

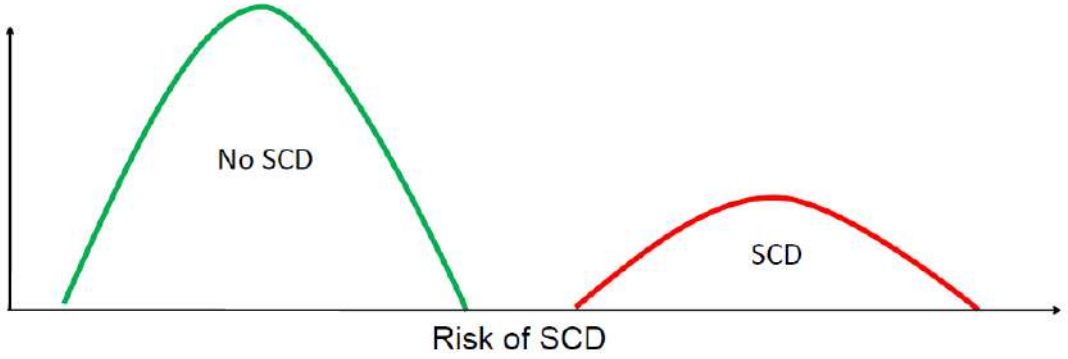
International External Validation Study of the 2014 European Society of Cardiology Guidelines on Sudden Cardiac Death Prevention in Hypertrophic Cardiomyopathy (EVIDENCE-HCM)

- 3703 patients
- 2% SCD during 5 y/follow-up



Circulation. 2018;137:1015–1023.

HCM – RISK OF SUDDEN DEATH



- "Ideal" World

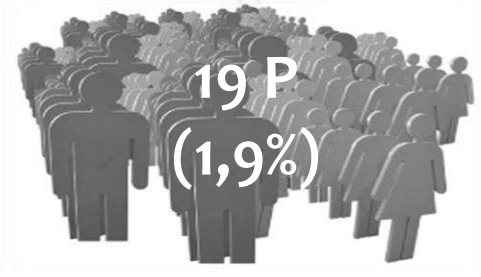
HCM – RISK OF SUDDEN DEATH

Develop a new Portuguese risk prediction score for sudden cardiac death

The Portuguese Registry of Hypertrophic Cardiomyopathy (PRo-HCM)
Enrollment period April 2013 – April 2015

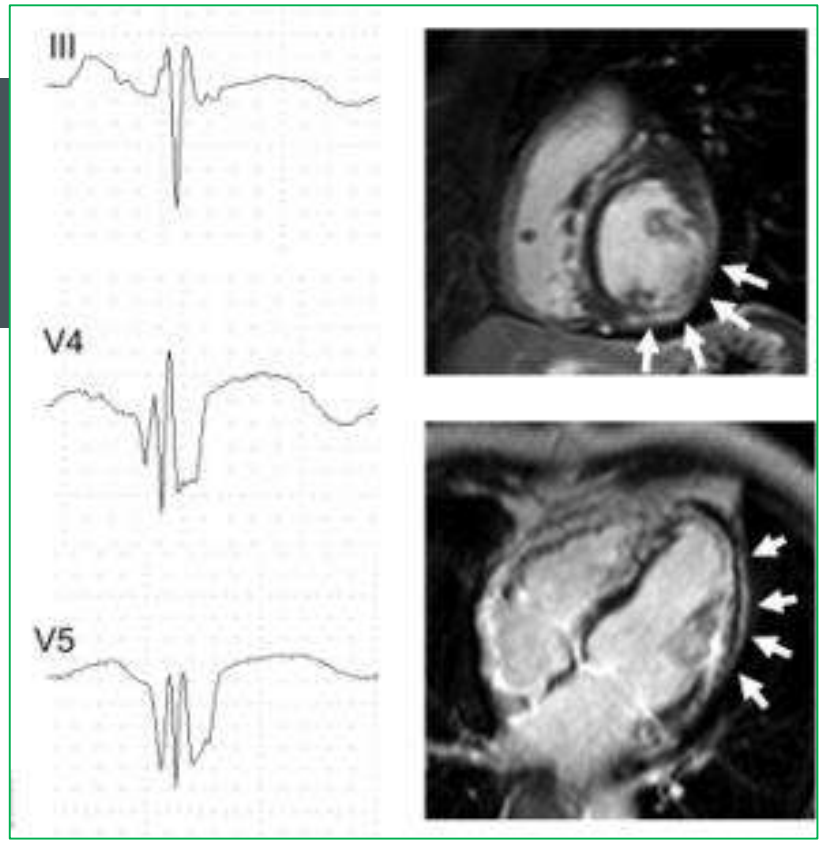
1022 HCM

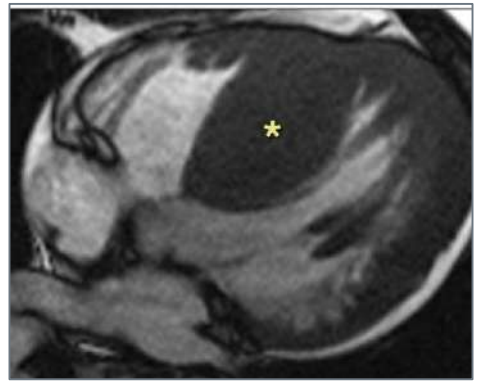
Endpoint:
Sudden Cardiac Death / Appropriate ICD shock
Follow-up period median of 5 years



HCM – RISK OF SUDDEN DEATH

Cox proportional hazards model	B	HR	(95% CI)		p-value
Unexplained **S**yncope	1,28	3,601	1,288	10,063	0,015
Signs of **H**eart failure	1,66	5,276	1,816	15,330	0,002
IVS ≥ 19mm	1,31	3,715	1,190	11,595	0,024
Fragmen**t**ed QRS (ECG)	1,29	3,631	1,150	11,464	0,028

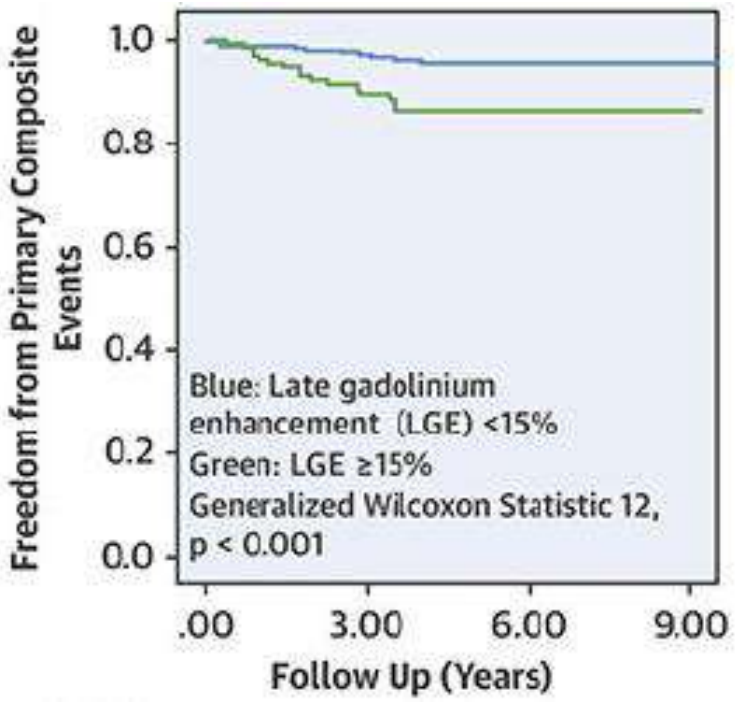




SHIFT model: C-index 0.81 (95% CI: 0.77 - 0.83)

ESC model: C-index 0.77 (95% CI: 0.73 - 0.81)

CARDIAC MAGNETIC RESONANCE



	Log-Likelihood Ratios and Chi-Square	p Value	Categorical NRI (95% CI)	p Value
A: Nonobstructive Group				
ESC risk score	−159.06			
ESC risk score + LGE cutoff 15%	−154.4 (chi-square 9)	0.002	0.56 (0.27-0.84)	<0.001
B: Obstructive Group				
ESC risk score	−227.85			
ESC risk score + LGE cutoff 15%	−219.14 (chi-square 17)	<0.001	0.34 (0.05-0.63)	0.02
ESC risk score + LGE cutoff 15% + myectomy	−215.14 (chi-square 8)	0.005	0.31 (0.10-0.51)	0.003
C: Myectomy Group*				
ESC risk score	−82.36			
ESC risk score + LGE cutoff 15%	−79.3 (chi-square 6)	0.01	0.48 (0.05-0.91)	0.02

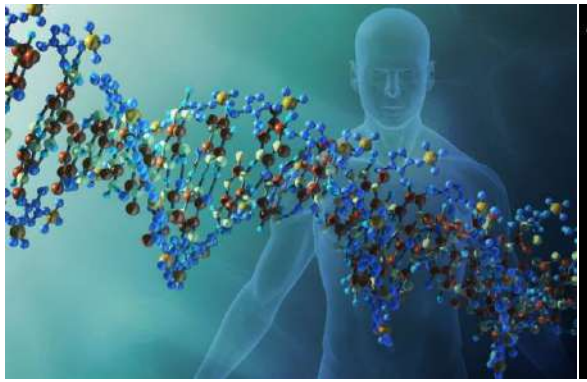
CONCLUSIONS In low-/intermediate-risk adult patients with HCM (obstructive, myectomy, and nonobstructive subgroups) with preserved systolic function, %LGE was significantly associated with a higher rate of composite endpoint, providing incremental prognostic utility. (J Am Coll Cardiol 2018;72:857-70)

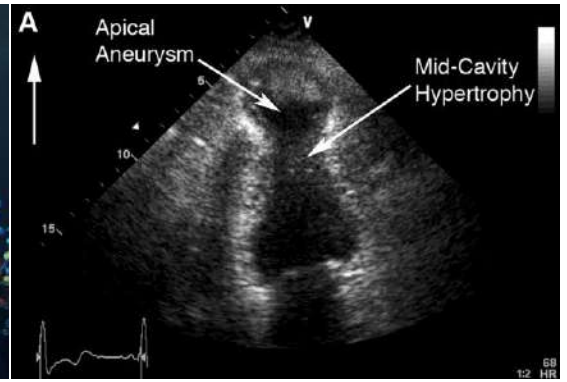
HCM – RISK OF SUDDEN DEATH

Intermediate / low risk?

Higher Arrhythmic Risk:

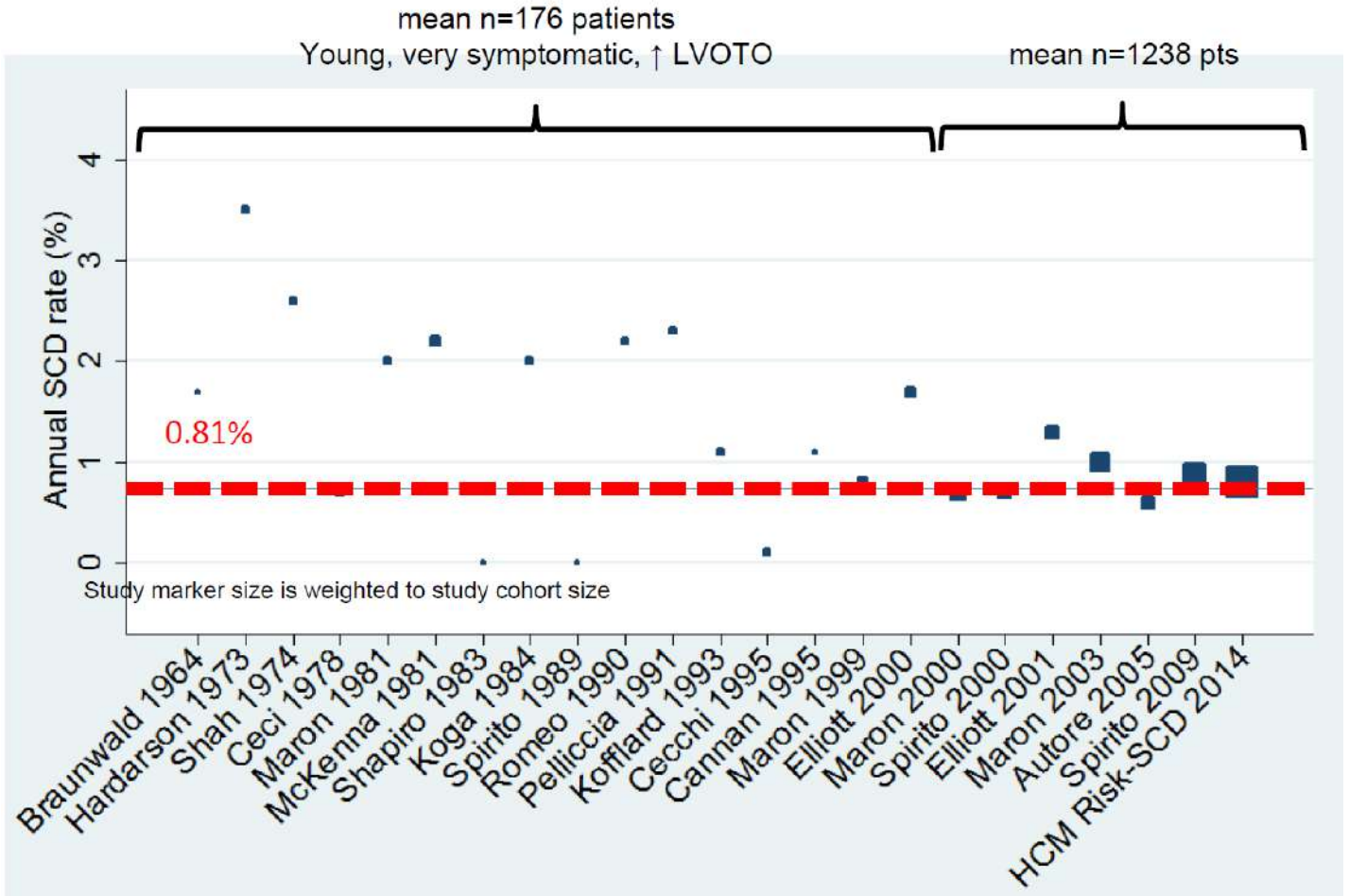
- LGE
- Apical Aneurism| LVEF < 50%
- NSVT during exercise
- Abnormal BP during exercise ⇒ LVOTO (fail ↑ SBP > 20mmHg or ↓ > 20mmHg)
- Genetic → double sarcomeric mutation





HCM – RISK OF SUDDEN DEATH

- SCD incidence < 1% / y



HCM – RISK OF SUDDEN DEATH

Survival and mortality outcome in 1,902 patients with HC, stratified according to age at presentation

Age at Presentation (years)	No. Patients	Survived	Mortality		
			All Deaths	Died Non-HC	Died HC
<30	474	452 (95%)	22 (5%)	4/22 (18%)	18/22 (82%)
30-59	1000	918 (92%)	82 (8%)	42/82 (51%)	40/82 (49%)
≥60	428	283 (66%)	145 (34%)	132/145 (92%)	13/145 (8%)
Totals	1902	1653 (87%)*	249 (13%)	178/249 (72%)	71/249 (28%)

Maron BJ, Rowin EJ, Casey SA, Garberich RF, Maron MS. What do patients with hypertrophic cardiomyopathy die from? Am J Cardiol 2016;117: 434–5.

Exercise	• Patients with HCM should avoid competitive sports activities, but should maintain a healthy lifestyle • Advice on recreational activities should be tailored to symptoms and the risk of disease-related complications including sudden cardiac death

TAKE HOME MESSAGE

- Clinical history (family, syncope, etc)
- Accurate investigation
- Tailored decision
- Encouragement of healthy lifestyle

HYPERTROPHIC CARDIOMYOPATHY
RISK OF SUDDEN DEATH

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June 29th, 2019