Hypertrophic Cardiomyopathy

New advances in clinical management and sudden death prevention

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2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy

The Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC)
European Heart Journal
doi:10.1093/eurheartj/ehu284

Guidelines are developed to aid the practitioner in pursuing the most appropriate healthcare response for the clinical circumstances of a specific patient

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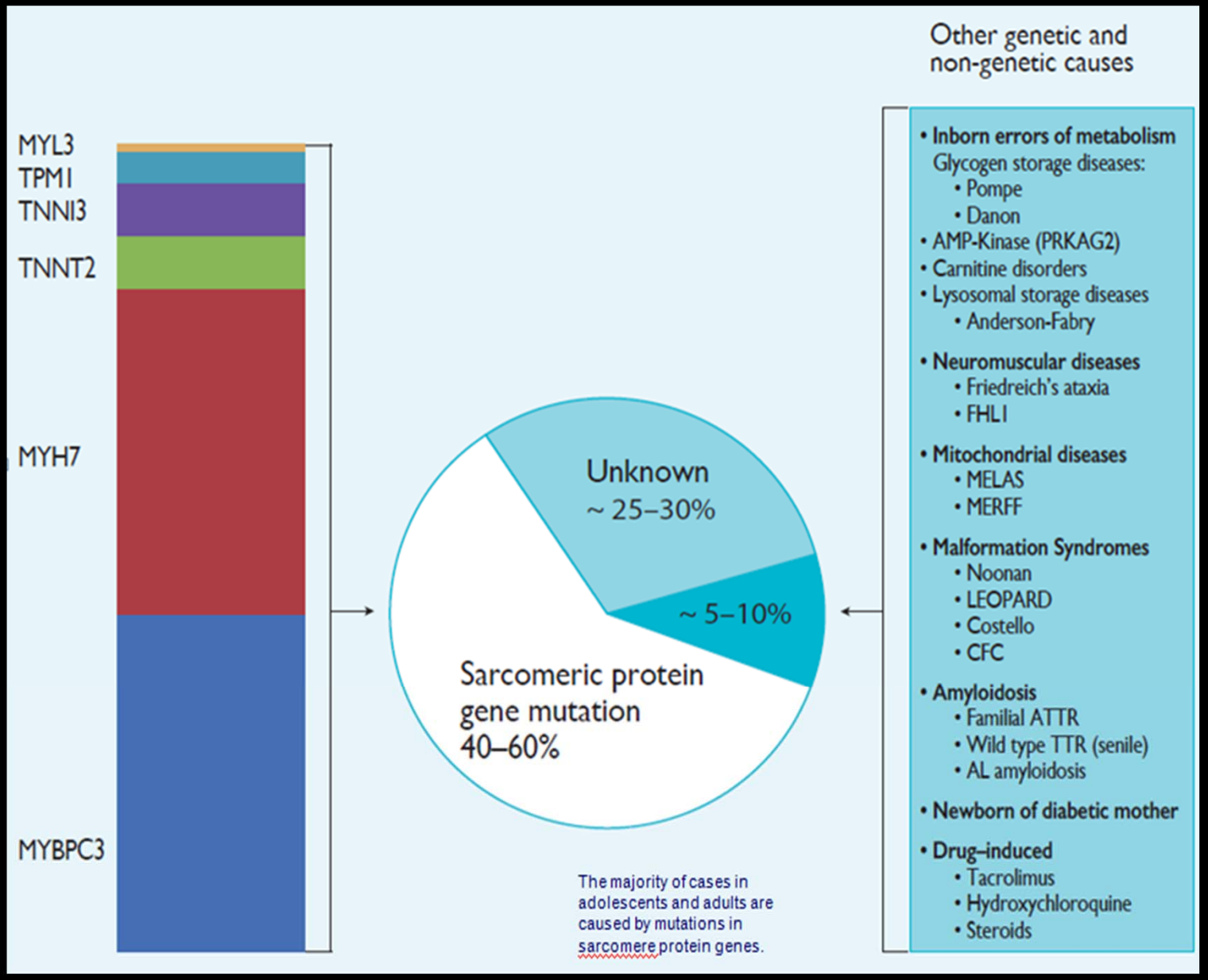
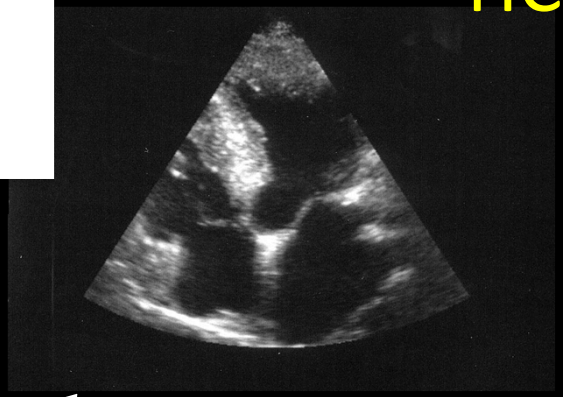


HCM in adults

Classification of the cardiomyopathies: a position statement from the european society of cardiology working group on myocardial and pericardial diseases

Perry Elliott, Bert Andersson, Eloisa Arbustini, Zofia Bilinska, Franco Cecchi, Philippe Charron, Olivier Dubourg, Uwe Kühl, Bernhard Maisch, William J. McKenna, Lorenzo Monserrat, Sabine Pankuweit, Claudio Rapezzi, Petar Seferovic, Luigi Tavazzi, and Andre Keren*

European Heart Journal (2008) **29**, 270–276



Amyloid

LV Non Compaction

LV wall tumor

Z-disc and Ca++ regul Mutations (2-5%)

Non-Sarcomeric HCM (5-10% ?)

Glycogen Storage disease

Danon

Metabolic Deficiency

Myofilament Protein Mutations

65 – 80 %

MYBPC3-MYH7-TNN2-TNNI3

22 Genes

> 1000 mutations

Mitochondrial Disease

Syndromic (RAS):

Noonan S.

Leopard S.

Freidreich Ataxia

SARCOMERIC HCM

LSD α-Galactosidase mut

Anderson-Fabry disease (~1%)

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The Italian registry for hypertrophic cardiomyopathy: A nationwide survey

Franco Cecchi, MD, Iacopo Olivotto, MD, Sandro Betocchi, MD, Claudio Rapezzi, MD, Maria Rosa Conte, MD, Gianfranco Sinagra, MD, Elisabetta Zachara, MD, Antonello Gavazzi, MD, Roberto Rordorf, MD, Gianfranco Carnemolla, MD, Maurizio Porcu, MD, Stefano Nistri, MD, Paolo Gruppillo, MD, and Simona Giampaoli, MD, on behalf of the participating centers *Rome and Florence, Italy*

Am Heart J 2005;150:947-54

1677 pts, 40 Italian centers
mean FU 9,7 yrs

Annual CV mortality 1% Sudden Death 0,3% Appropriate ICD discharge 0,3%

CV EVENTS

Atrial Fibrillation	22 %
ACS + MI	3.5 %
Sustained VT	3 %
Syncope	7 %
SA /AV-block	5 %
Others	4 %

Progression to FC II

Progression to FC III-IV/ Endstage HF

Sudden Death

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HCM : RISK STRATIFICATION FOR SUDDEN DEATH

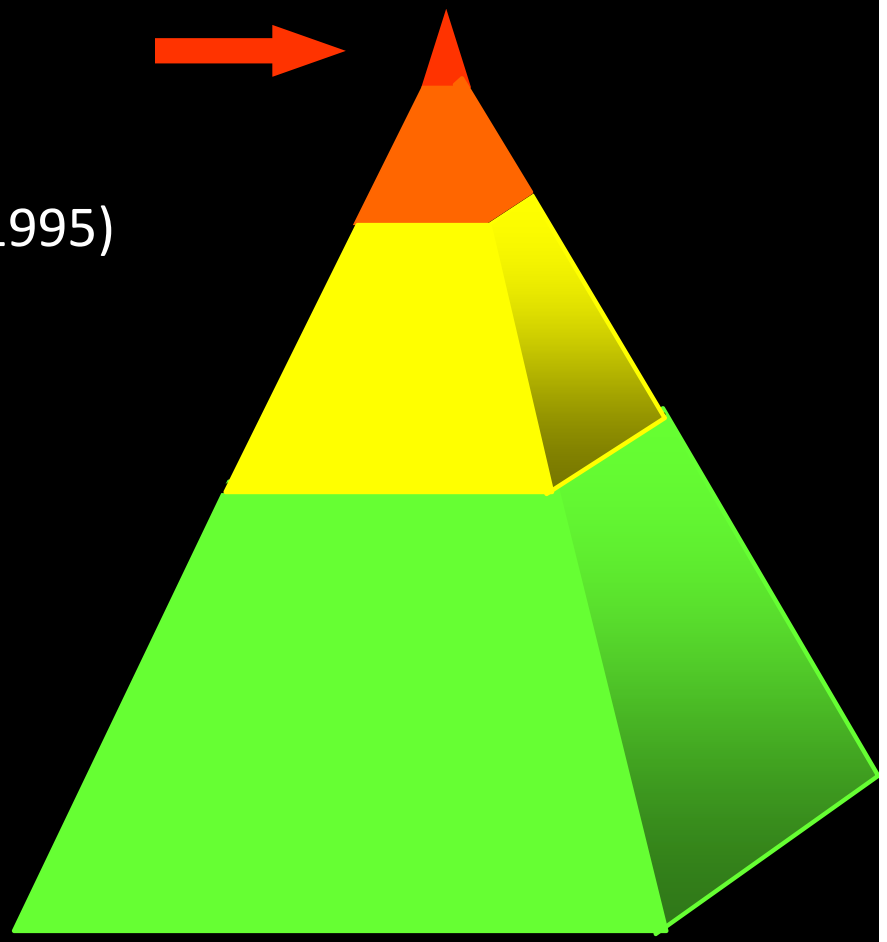
ANNUAL RISK OF SUDDEN DEATH : < 1% (range 0 - 10%)

10% CMI END-STAGE (stage IV)

7% CARDIAC ARREST SURVIVOR (1989-1995)

1,4% CARDIAC ARREST SURVIVOR (2010)

0%



LIMITATIONS OF CLASSICAL RISK FACTORS
(ICD Guidelines for HCM 2003 & 2011)

RISK FACTOR	Sensitivity	Specificity	PPV	NPV
Family history of SD	42	79	28	88
Max LV thickness > 30 mm	26	88	13	95
Non sustained VT (ECG D)	69	80	22	97
Abnormal pressure response at exercise test age < 45	75	66	15	97
Syncope	29	83	25	86

Elliot P, W.McKenna, 2003

Level of evidence C

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]

Heart 2013;**99**:534–541.

- PPV remains low even in the presence of multiple risk factors
- The aggregation of risk factors is associated with increased risk of SCD

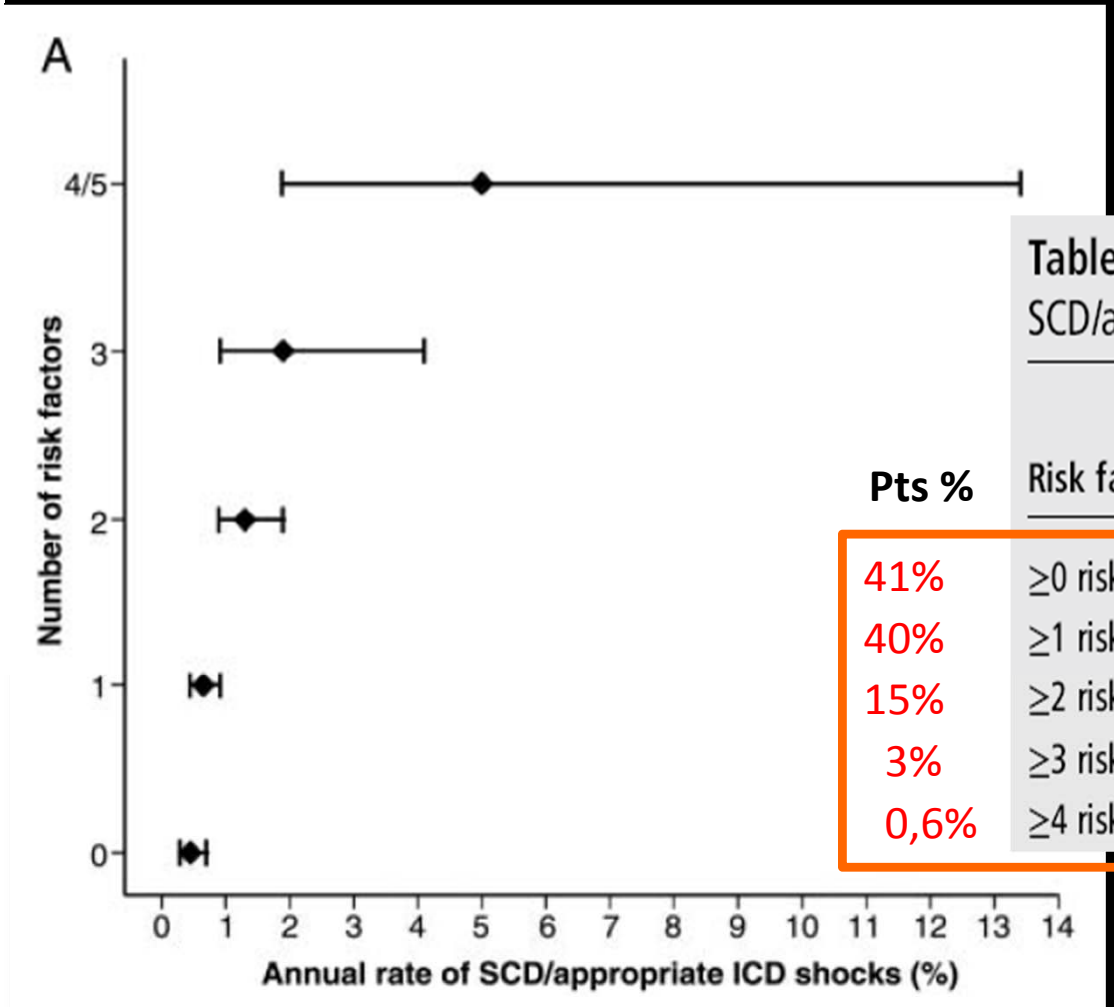


Table 4 The PPV and NPV of accumulating major risk factors and SCD/appropriate ICD discharge

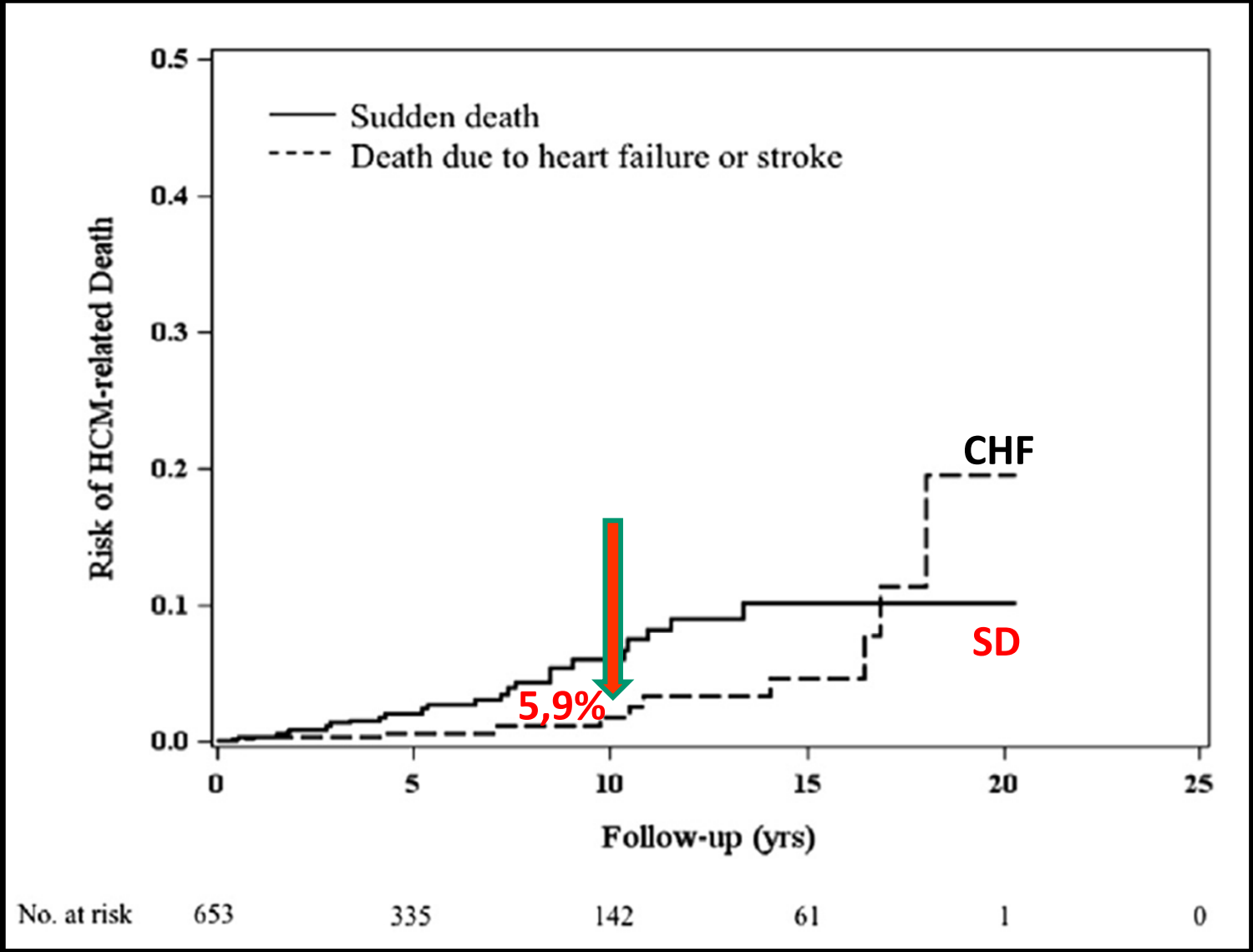
Pts %	Risk factor profile	At 1 year PPV%	At 1 year NPV%	At 5 years PPV%	At 5 years NPV%
41%	≥0 risk factors*	5.5	NA	5.5	NA
40%	≥1 risk factors	8.9	95.1	9.0	95.3
15%	≥2 risk factors	22.4	90.5	23.3	90.7
3%	≥3 risk factors	54.2	84.5	52.1	84.0
0,6%	≥4 risk factors	88.4	61.5	87.7	61.1

Risk of Sudden Death and Outcome in Patients With Hypertrophic Cardiomyopathy With Benign Presentation and Without Risk Factors

Paolo Spirito, MD[a,*], Camillo Autore, MD[b], Francesco Formisano, MD[a], Gabriele Egidy Assenza, MD[b], Elena Biagini, MD[c], Tammy S. Haas, RN[d], Sergio Bongioanni, MD[e], Christopher Semsarian, MD[f], Emmanuela Devoto, MD[a], Beatrice Musumeci, MD[b], Francesco Lai, MD[c], Laura Yeates, BSc[f], Maria Rosa Conte, MD[e], Claudio Rapezzi, MD[c], Luca Boni, MD[g], and Barry J. Maron, MD[d]

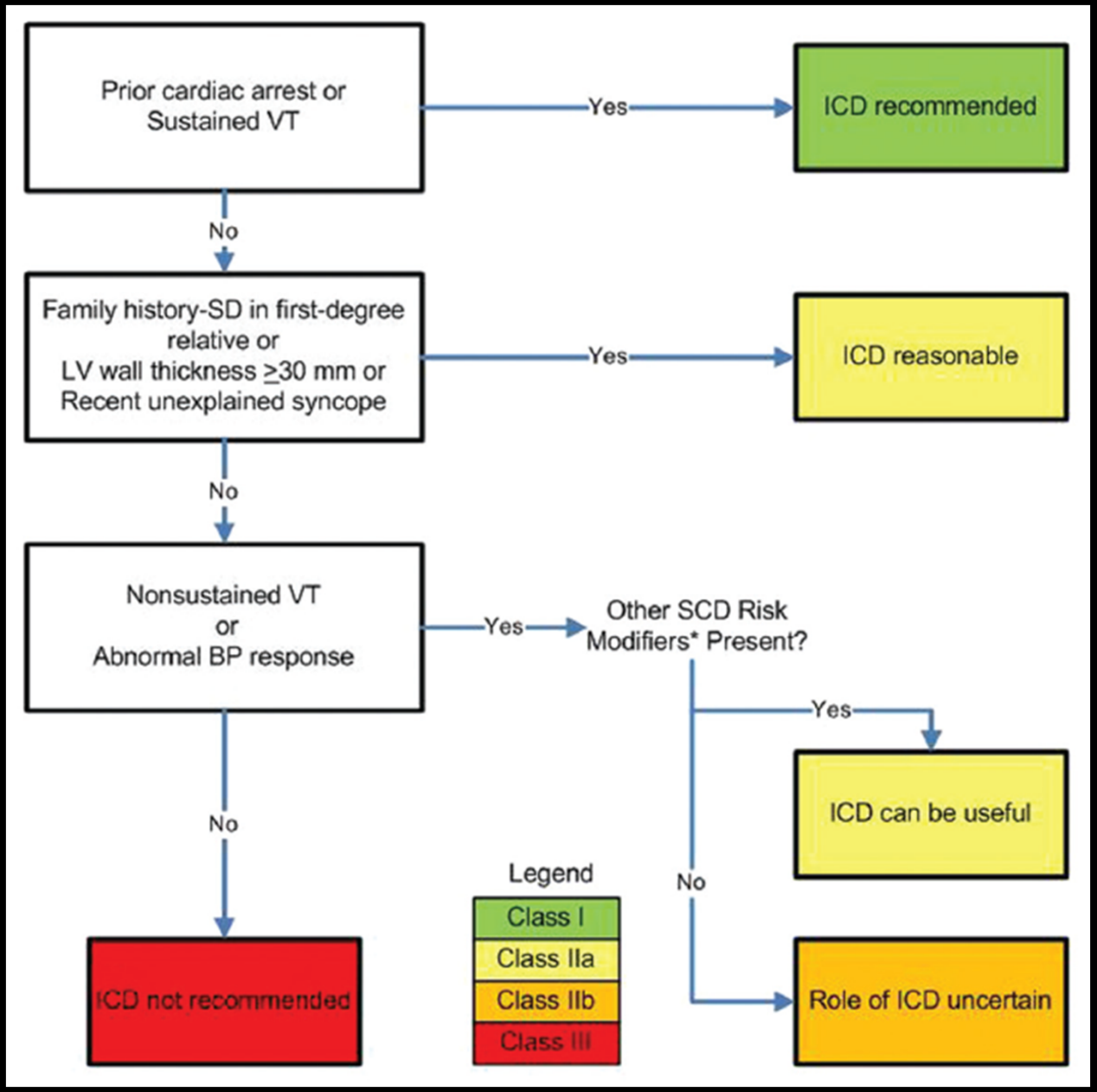
Am J Cardiol 2014;113:1550–1555

…..these results underscore the need for a more accurate assessment of the sudden death risk in patients with HC



2011 ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy

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



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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

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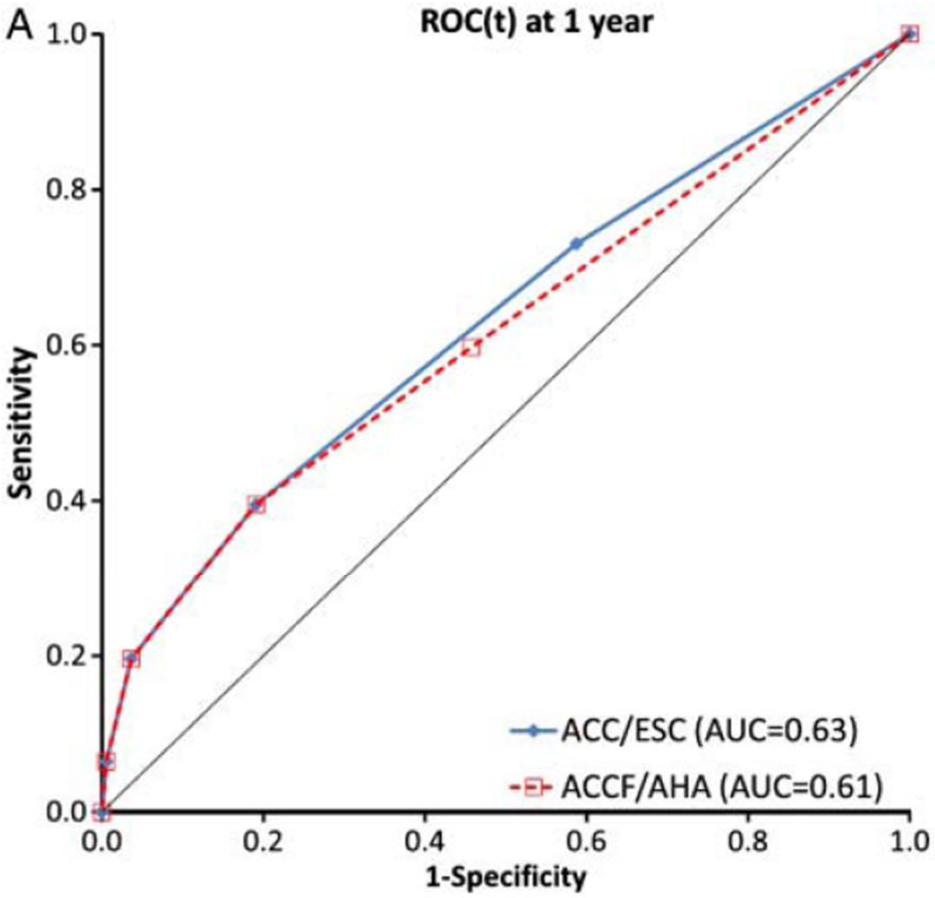
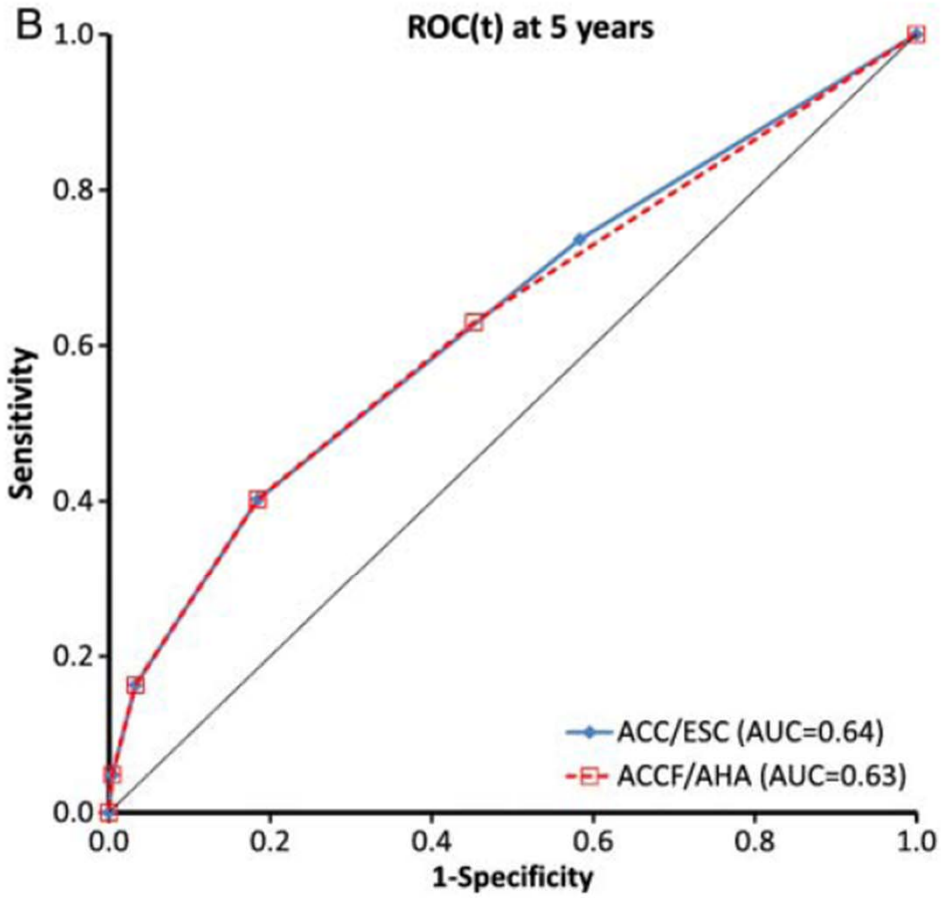
Heart 2013;**99**:534–541.





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

European Heart Journal 2014

Multicenter study (6) 3675 pts

Age > 16 yrs at diagnosis

Predictor variable	SCD risk prediction model	
	Hazard ratio (95% confidence interval)	*P*-value
Age (years)	0.98 (0.97, 0.99)	0.001
Maximal wall thickness (mm)	1.17 (1.01, 1.37)	0.042
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

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Risk of SCD at 5 years (%):

HCM Risk-SCD should not be used in:

Paediatric patients (<16 years)
Elite/competitive athletes
HCM associated with metabolic diseases (e.g. Anderson-Fabry disease), and syndromes (e.g. Noonan syndrome).
Patients with a previous history of aborted SCD or sustained ventricular arrhythmia who should be treated with an ICD for secondary prevention.

Caution should be exercised when assessing the SCD in patients following invasive reduction in left ventricular outflow tract obstruction with myectomy or alcohol septal ablation.

Pending further studies, HCM-RISK should be used cautiously in patients with a maximum left ventricular wall thickness ≥35 mm.

HCM = hypertrophic cardiomyopathy; LV = left ventricular; LVOT = left ventricular outflow tract; NSVT = non-sustained ventricular tachycardia; SCD = sudden cardiac death; VT = ventricular tachycardia

http://www.doc2do.com/hcm/webHCM.html

HCM Risk-SCD Calculator

Age	Years	*Age at evaluation*
Maximum LV wall thickness	mm	*Transthoracic Echocardiographic measurement*
Left atrial size	mm	*Left atrial diameter determined by M-Mode or 2D echocardiography in the parasternal long axis plane at time of evaluation*
Max LVOT gradient	mmHg	*The maximum LV outflow gradient determined at rest and with Valsalva provocation (irrespective of concurrent medical treatment) using pulsed and continuous wave Doppler from the apical three and five chamber views. Peak outflow tract gradients should be determined using the modified Bernouilli equation: Gradient= $4V^2$, where V is the peak aortic outflow velocity*
Family History of SCD	○ No ○ Yes	*History of sudden cardiac death in 1 or more first degree relatives under 40 years of age or SCD in a first degree relative with confirmed HCM at any age (post or ante-mortem diagnosis).*
Non-sustained VT	○ No ○ Yes	*3 consecutive ventricular beats at a rate of 120 beats per minute and <30s in duration on Holter monitoring (minimum duration 24 hours) at or prior to evaluation.*
Unexplained syncope	○ No ○ Yes	*History of unexplained syncope at or prior to evaluation.*

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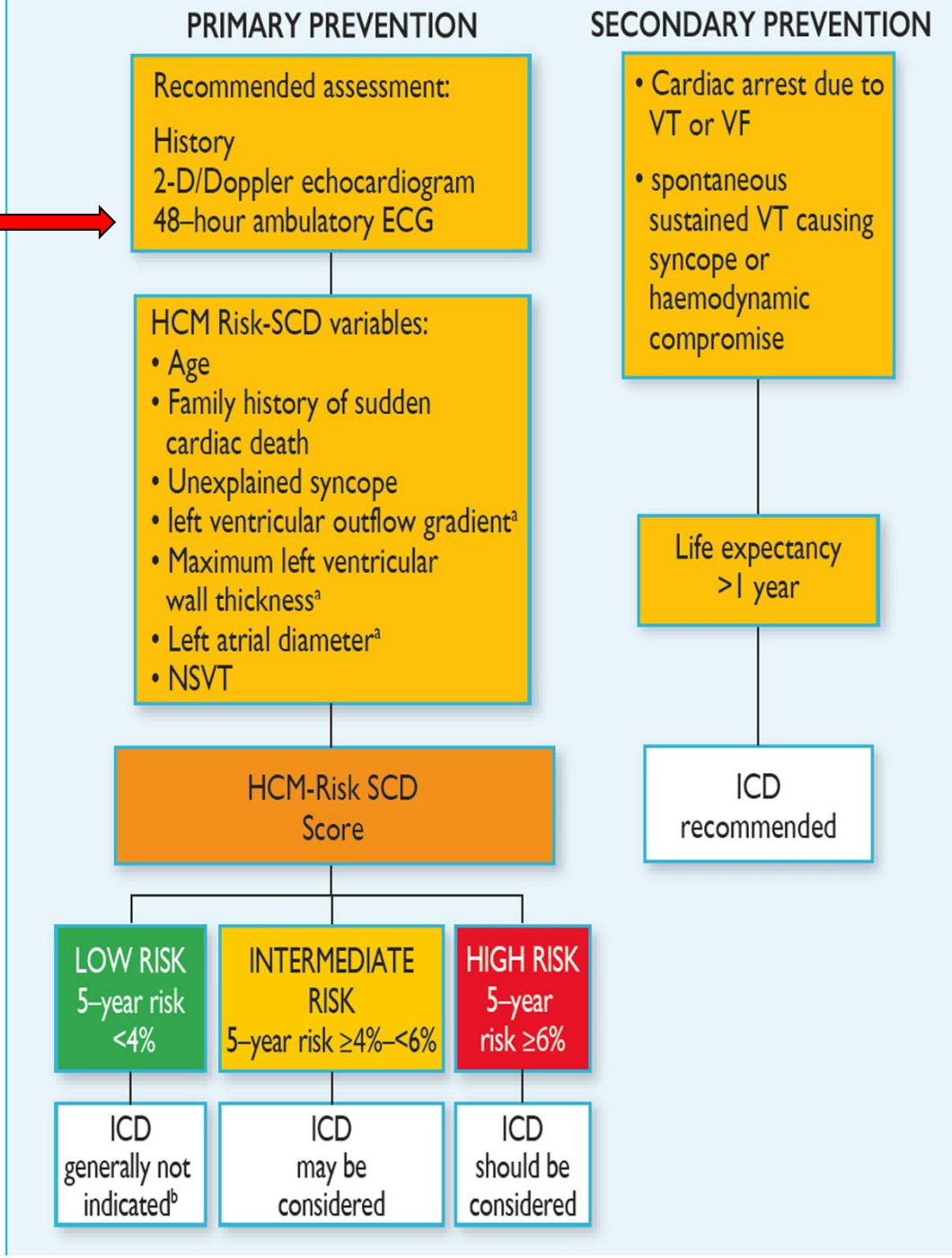
Prevention of Sudden Cardiac Death

Recommendations for ICD in each risk category take into account not only the absolute statistical risk, but also the age and general health of the patient, socio-economic factors and the psychological impact of therapy.

Figure 7 Flow chart for ICD implantation.

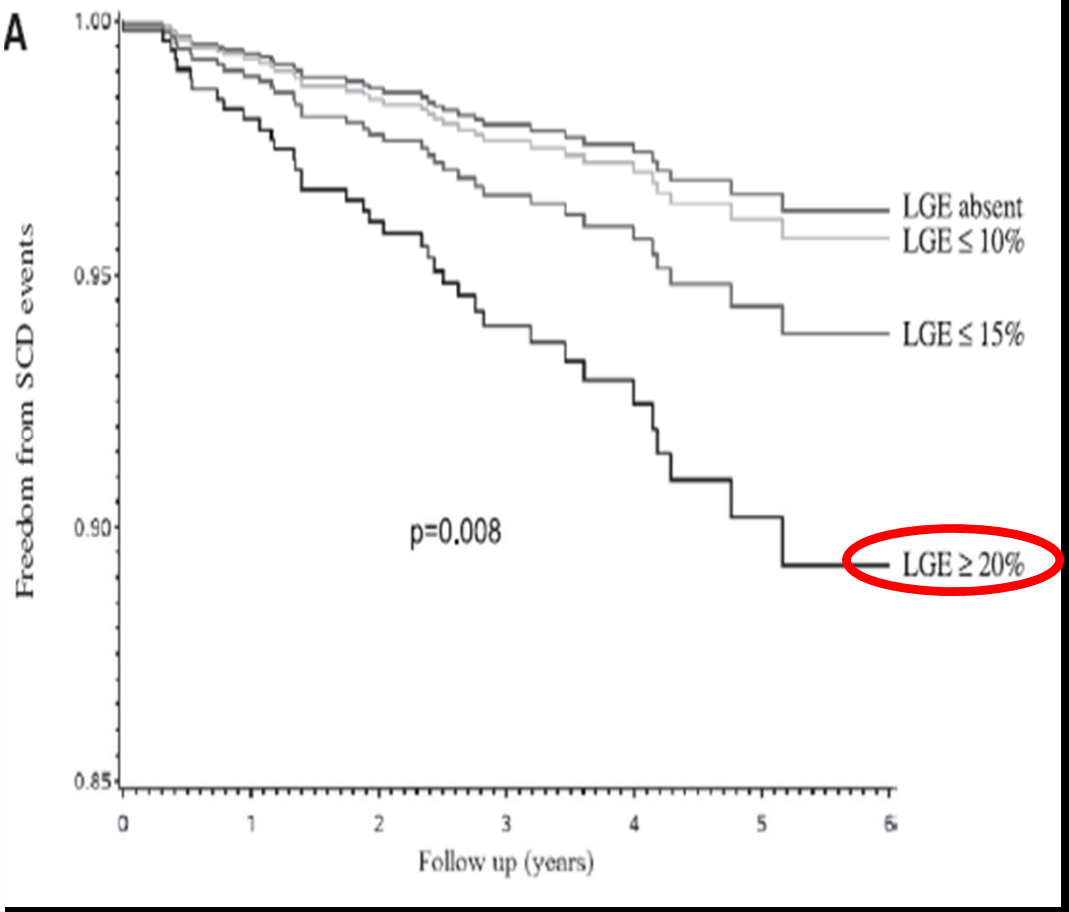


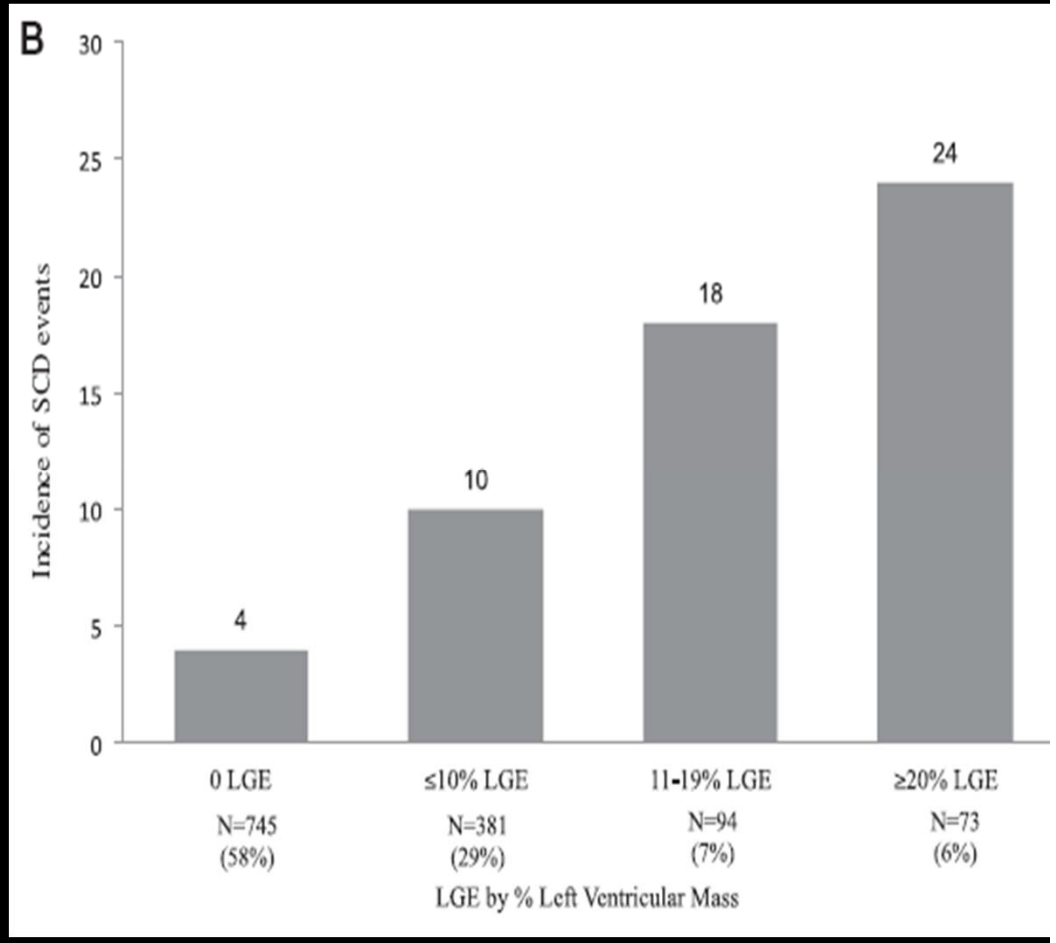
Prognostic Value of Quantitative Contrast-Enhanced Cardiovascular Magnetic Resonance for the Evaluation of Sudden Death Risk in Patients With Hypertrophic Cardiomyopathy

Raymond H. Chan, MD, MPH; Barry J. Maron, MD; Iacopo Olivotto, MD; Michael J. Pencina, PhD; Gabriele Egidy Assenza, MD; Tammy Haas, RN; John R. Lesser, MD; Christiane Gruner, MD; Andrew M. Crean, MD; Harry Rakowski, MD; James E. Udelson, MD; Ethan Rowin, MD; Massimo Lombardi, MD; Franco Cecchi, MD; Benedetta Tomberli, MD; Paolo Spirito, MD; Francesco Formisano, MD; Elena Biagini, MD; Claudio Rapezzi, MD; Carlo Nicola De Cecco, MD; Camillo Autore, MD; E. Francis Cook, PhD; Susie N. Hong, MD; C. Michael Gibson, MD, MS; Warren J. Manning, MD; Evan Appelbaum, MD; Martin S. Maron, MD

Circulation 2014

Extent of LGE (> 6 SD above the mean) is an additional risk factor in pts considered at low risk

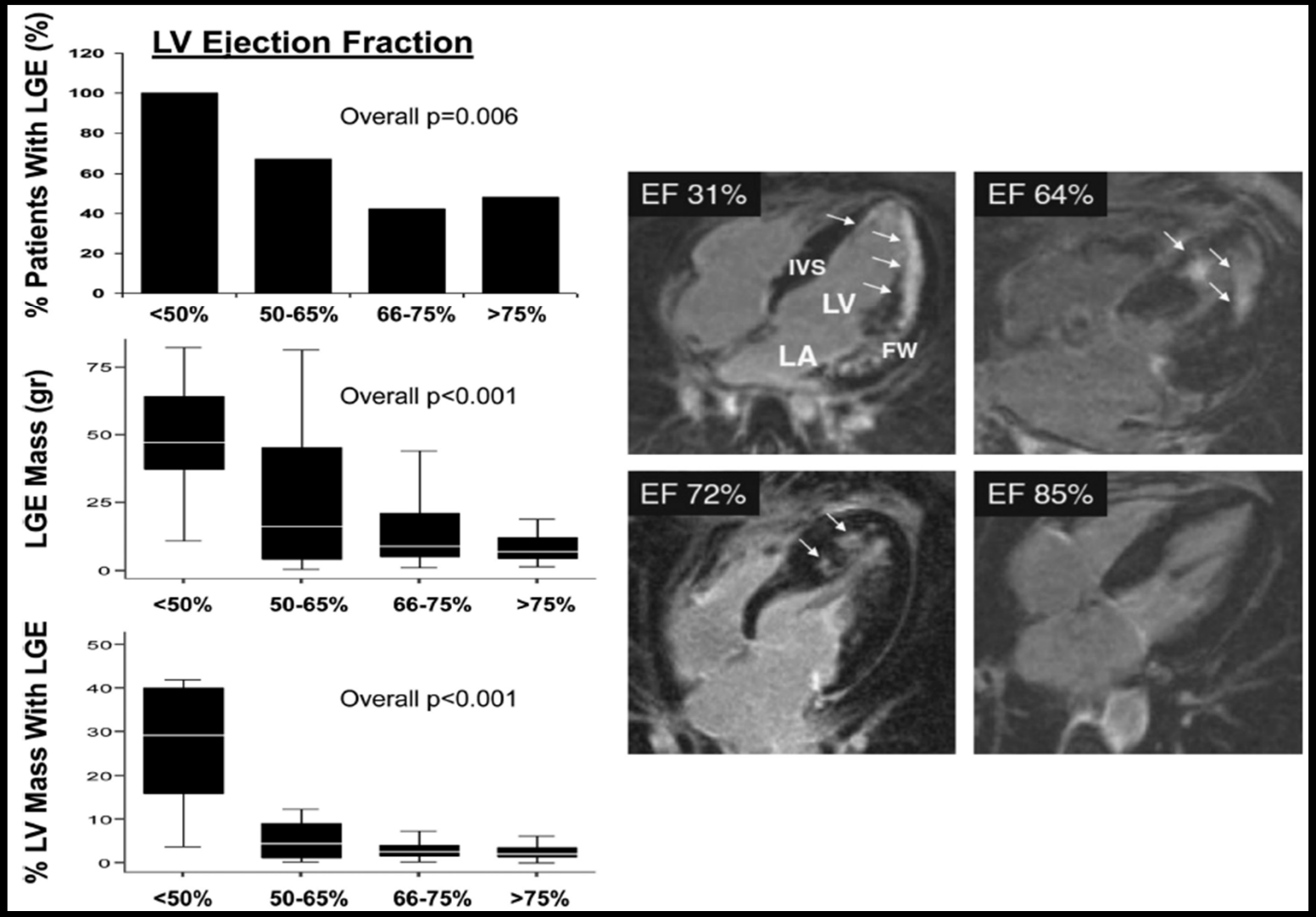




Patterns of Disease Progression in Hypertrophic Cardiomyopathy
An Individualized Approach to Clinical Staging

Iacopo Olivotto, MD; Franco Cecchi, MD; Corrado Poggesi, MD; Magdi H. Yacoub, MD, FRS
Circ Heart Fail. 2012;5:535-546

LGE extension + LVEF <60% are markers of disease progression



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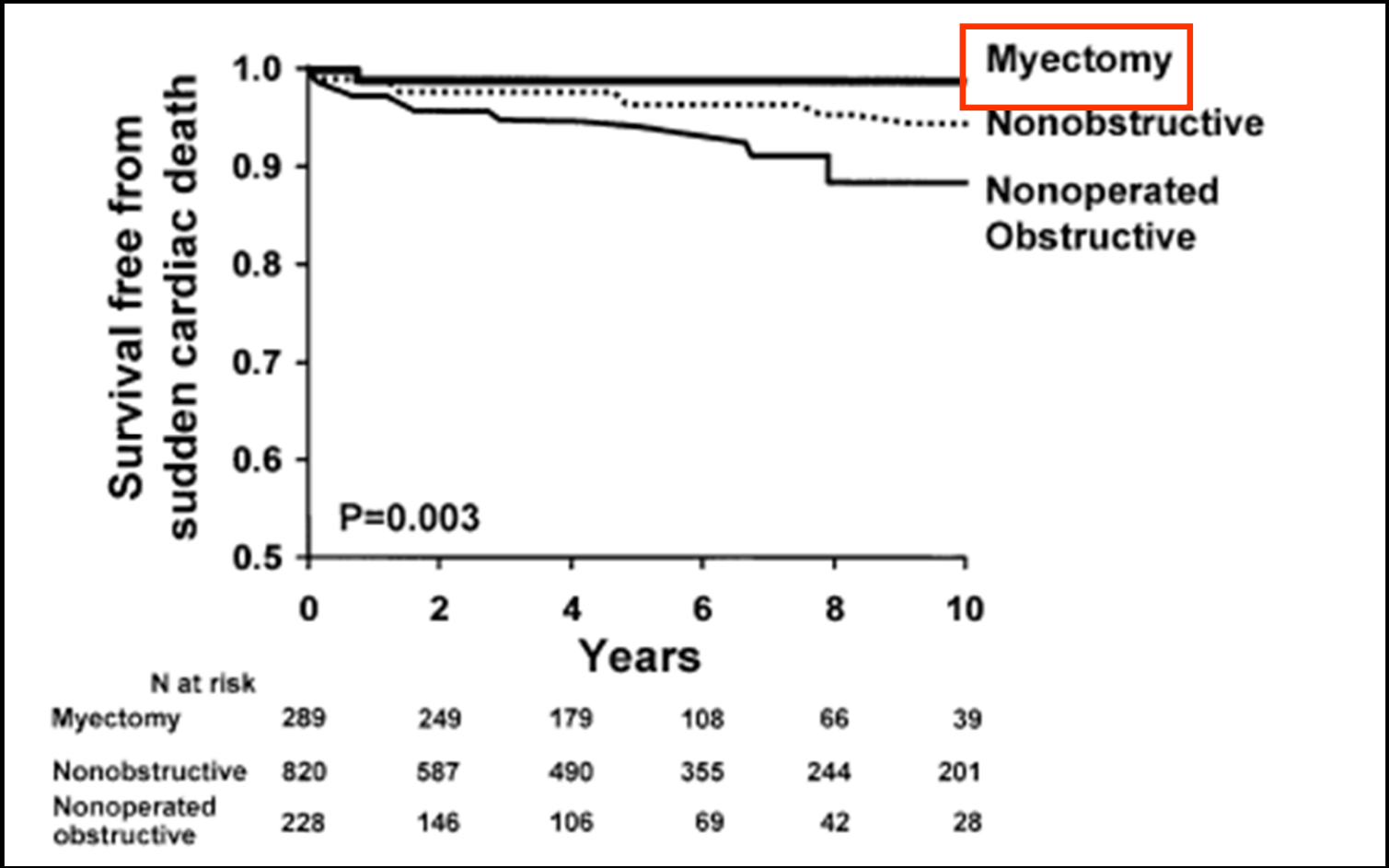
RISK STRATIFICATION: risk factors modifications

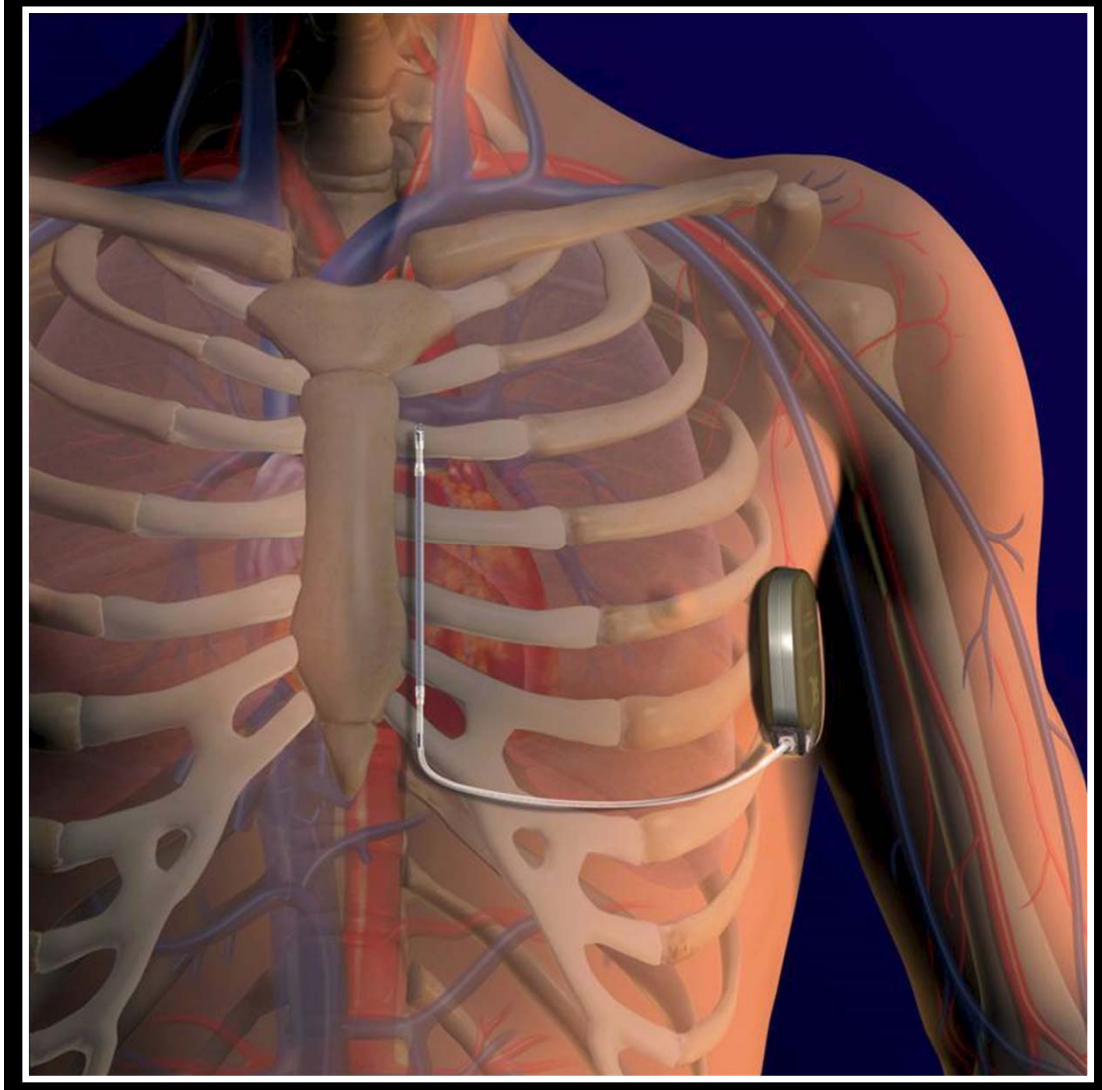
SURVIVAL FREE OF SUDDEN DEATH

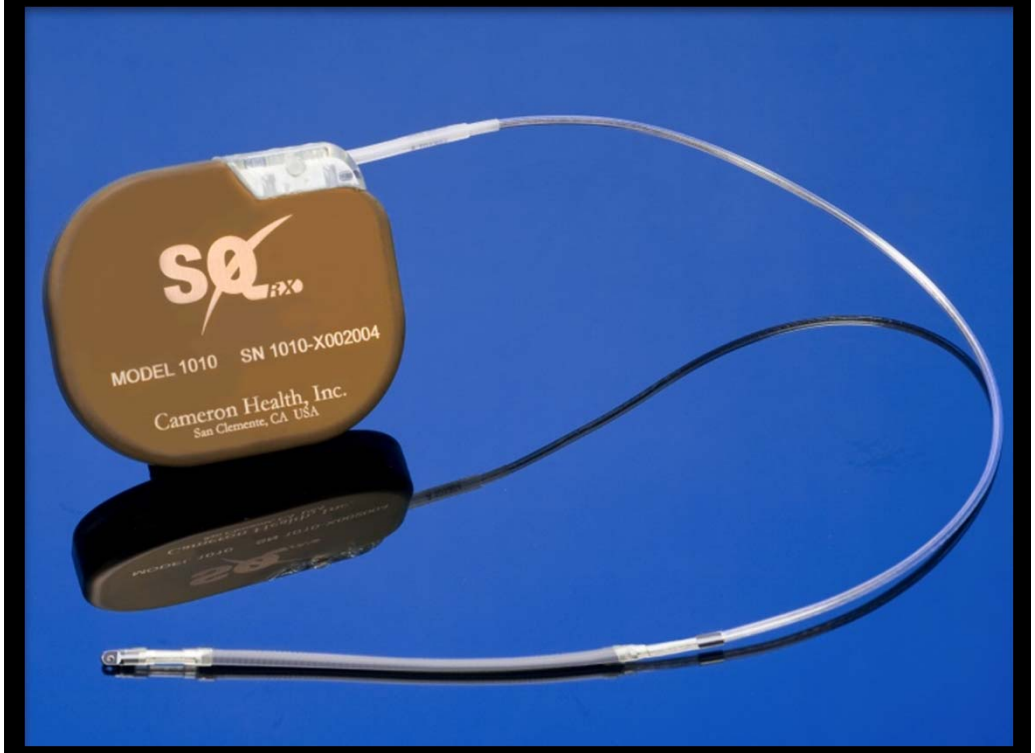
(Rochester Mayo Clinic, versus Minneapolis + Florence)



Ommen S, Maron BJ, Olivotto I et al, JACC 2005

SUBCUTANEOUS ICD





S-ICD for SD PREVENTION in pts with HCM

It may :

- improve LONG TERM RISK/BENEFIT RATIO + QOL
- increase acceptance by children and adolescents
- avoid lead fracture and sepsis
- reduce implant complications and
- inappropriate discharges due to SV arrhythmias

HEART RHYTHM CONGRESS 2014 AB06-06 - Combined Analysis of Subcutaneous ICD Outcomes in Hypertrophic Cardiomyopathy Patients from the EFFORTLESS Registry & IDE Study Lambiase P. et al.

96 HCM pts

Conclusions: This pooled analysis shows the S-ICD has equivalent conversion efficacy, appropriate rhythm discrimination & therapy in HCM vs non-HCM pts- demonstrating satisfactory early performance in the HCM population

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Recommendations on practical aspects of implantable cardioverter defibrillator therapy

Recommendations	Class[a]	Level[b]	Ref.[c]
Prior to ICD implantation, patients should be counselled on the risk of inappropriate shocks, implant complications and the social, occupational, and driving implications of the device.	I	C	219,327
ß-Blockers and/or amiodarone are recommended in patients with an ICD, who have symptomatic ventricular arrhythmias or recurrent shocks despite optimal treatment and device re-programming.	I	C	219,403
Electrophysiological study is recommended in patients with ICDs and inappropriate shocks due to regular supraventricular tachycardias, to identify and treat any ablatable arrhythmia substrate.	I	C	403
A subcutaneous ICD lead system (S-ICD™) may be considered in HCM patients who do not have an indication for pacing.	IIb	C	407

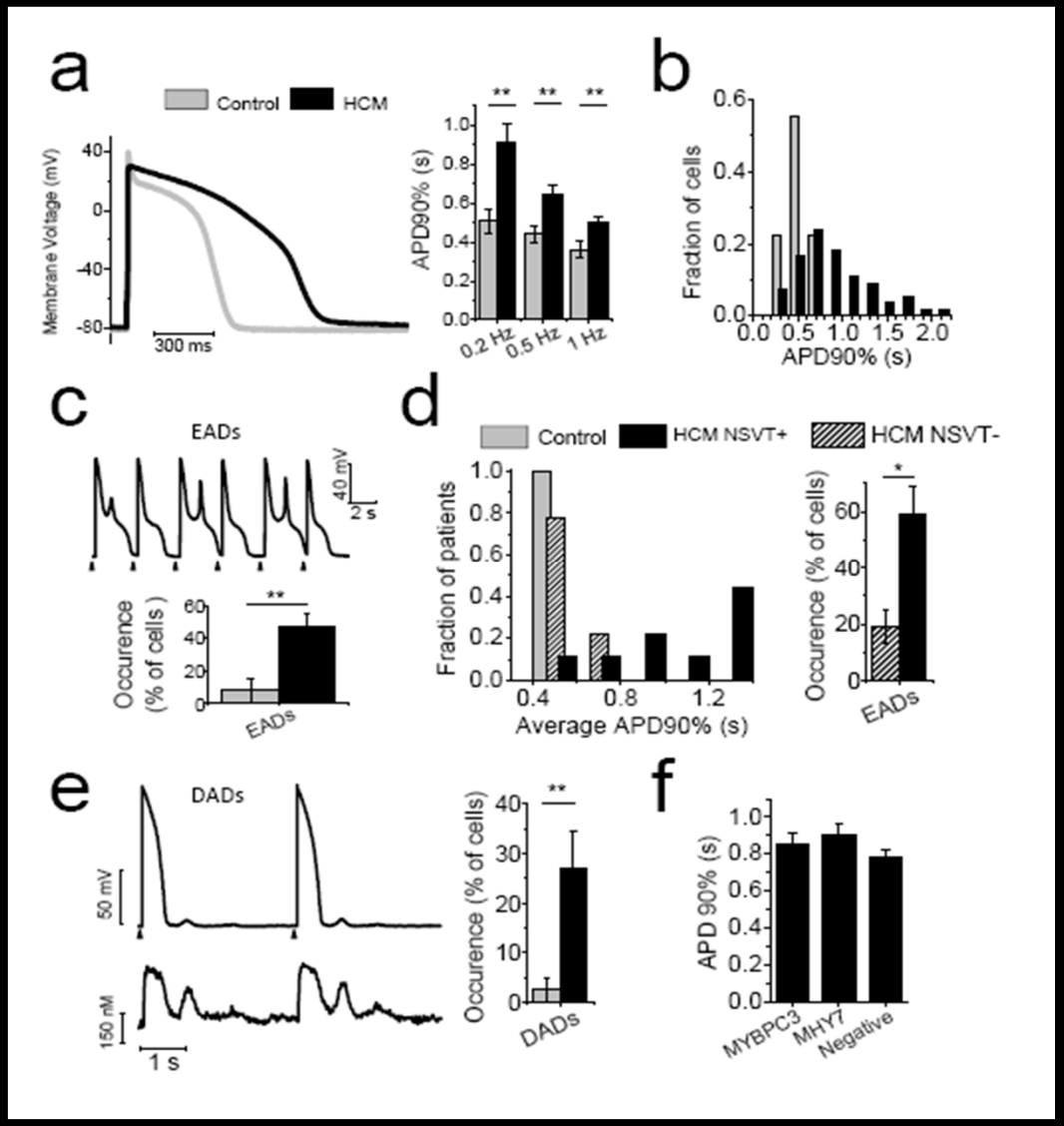
New areas of Clinical research and options

HCM: RANOLAZINE EFFECTS ON CARDIOMYOCITES

Late Sodium Current Inhibition Reverses Electromechanical Dysfunction in Human Hypertrophic Cardiomyopathy

Coppini R et al.

Circulation. 2013;127:575-584,

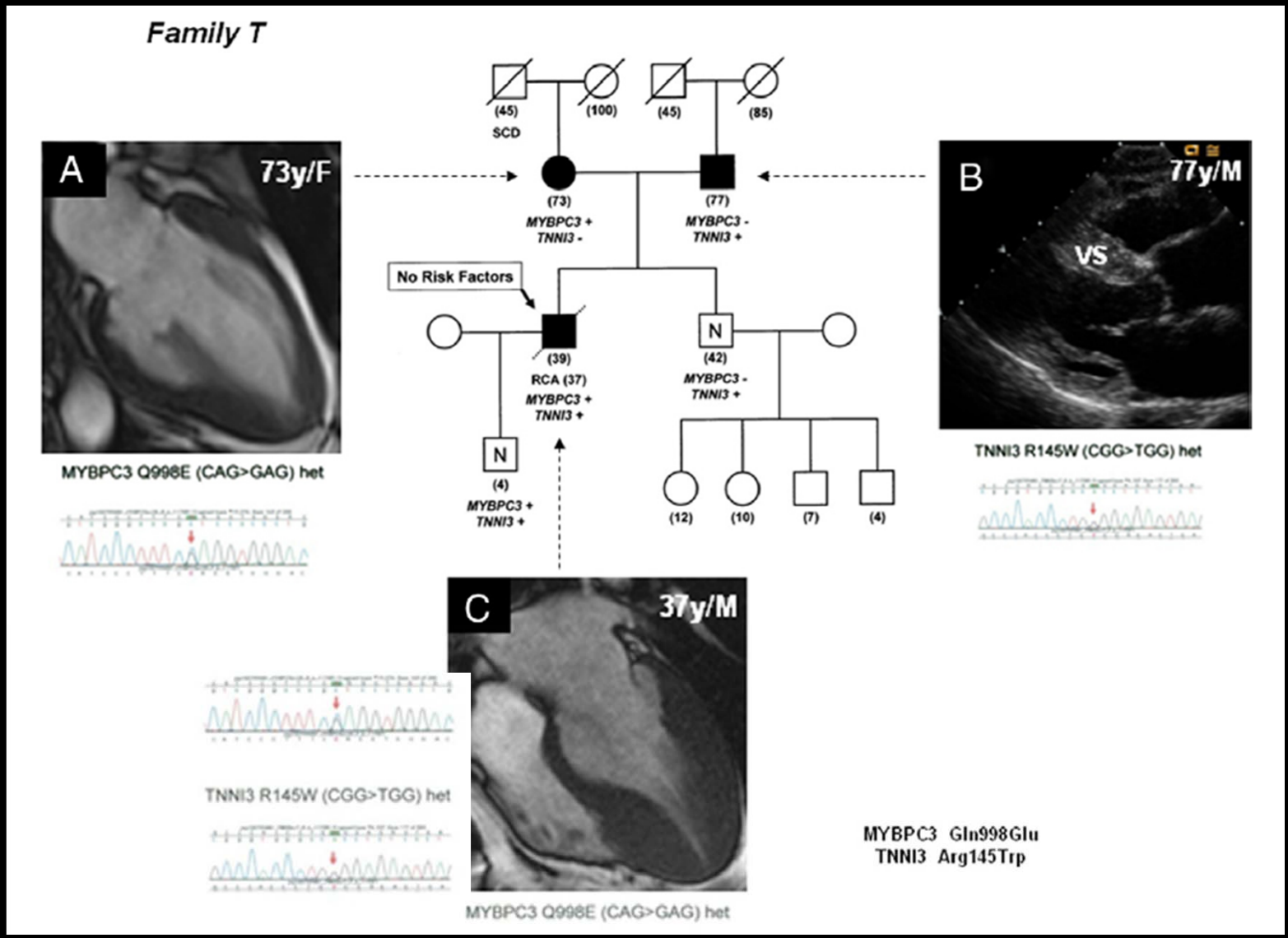


The reappraisal of complex GENE MUTATIONS

Double or compound sarcomere mutations in hypertrophic cardiomyopathy: A potential link to sudden death in the absence of conventional risk factors

Barry J. Maron, MD,* Martin S. Maron, MD,† Christopher Semsarian, MB, BS, PhD‡

Heart Rhythm 2012;9:57–63



Thanks !!

I. OLIVOTTO, B. TOMBERLI

NURSING	K.Baldini, S.Fantini
GENETICS	F. Torricelli, F. Girolami
CMR	L.Rega, S.Pradella
PET	R. Sciagrà
ALCOHOL SA	D. Antoniucci
CARDIAC SURGERY	M.Yacoub, PL.Stefano, G.Popoff, P. Ferrazzi
ISTOPATHOLOGY	G. D'Amati, O.Leone
ELECTROPHYSIOLOGY	L. Padeletti, P.Pieragnoli, G.Ricciardi, F.Gaita, MG Bongiorni
PHYSIOLOGY	C. Poggesi, C.Ferrantini, R. Coppini
NEUROLOGY	W.Borsini
NEPHROLOGY	L.Cirami
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