

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

SERGIO BONGIOANNI

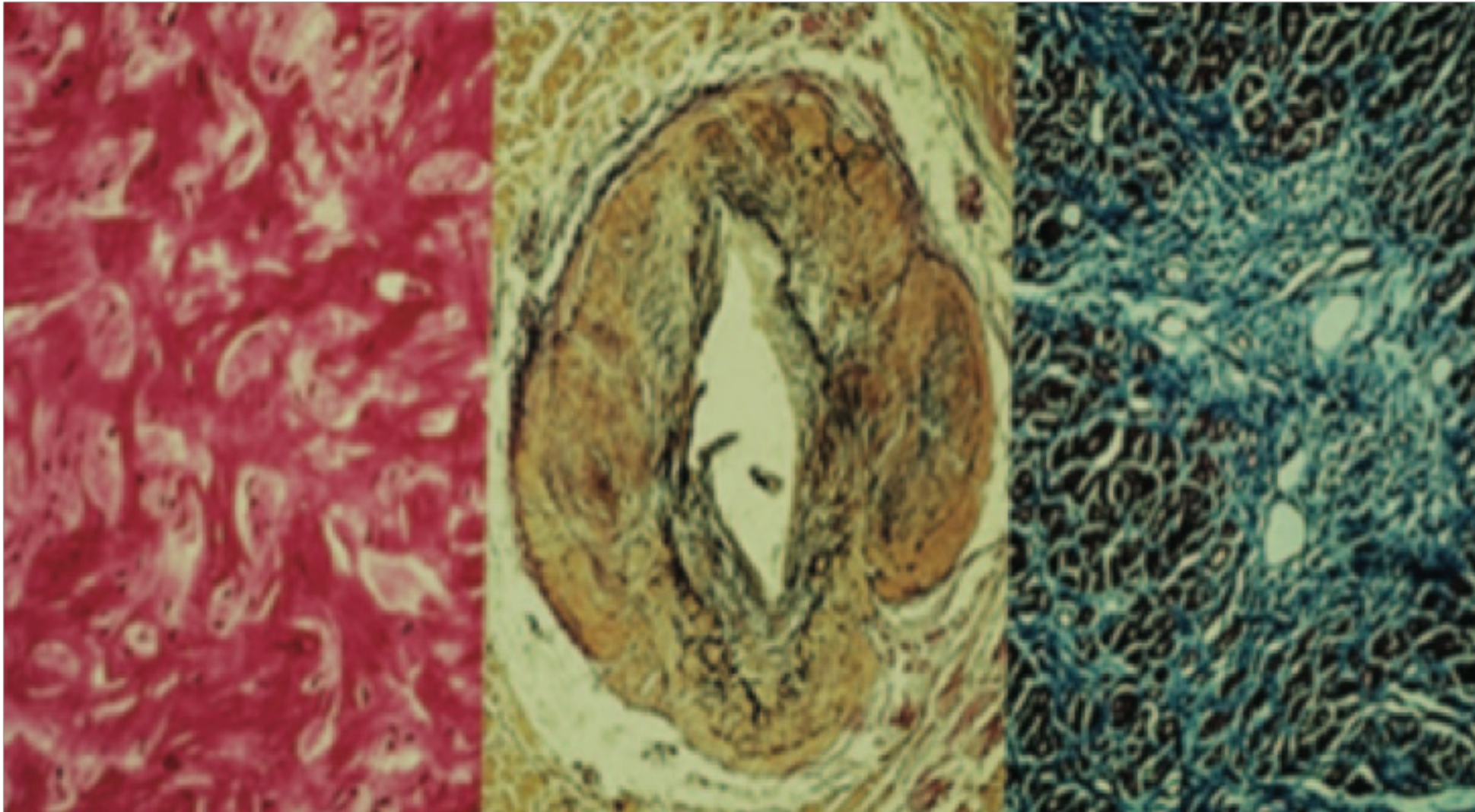
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Turin October 14, 2016



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Arrhythmogenic Substrate



SCD Risk Prediction algorithm/model

Increasing risk of VF

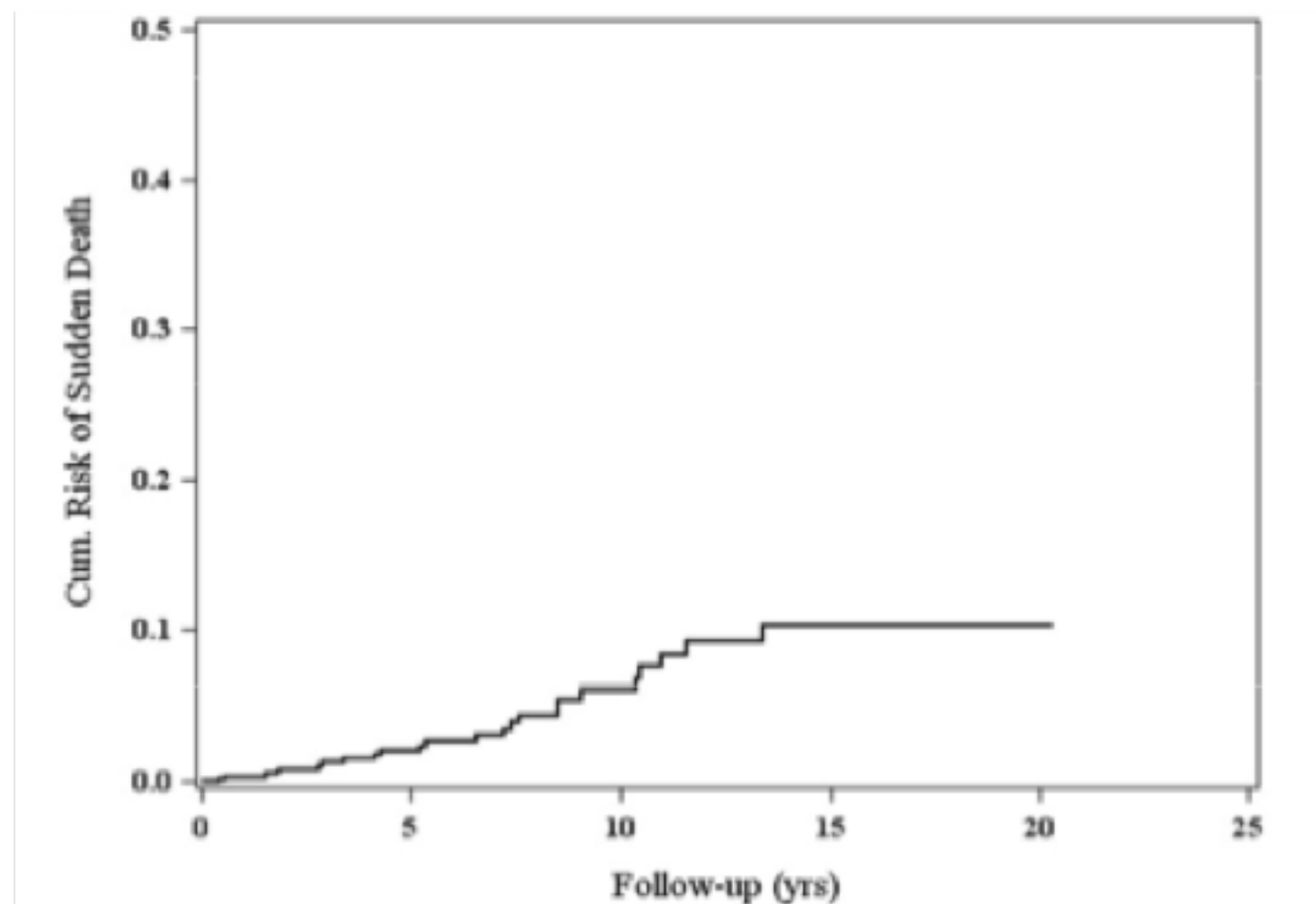
5 RF
4 RF
3 RF
2 RF
1 RF
No Risk Factor



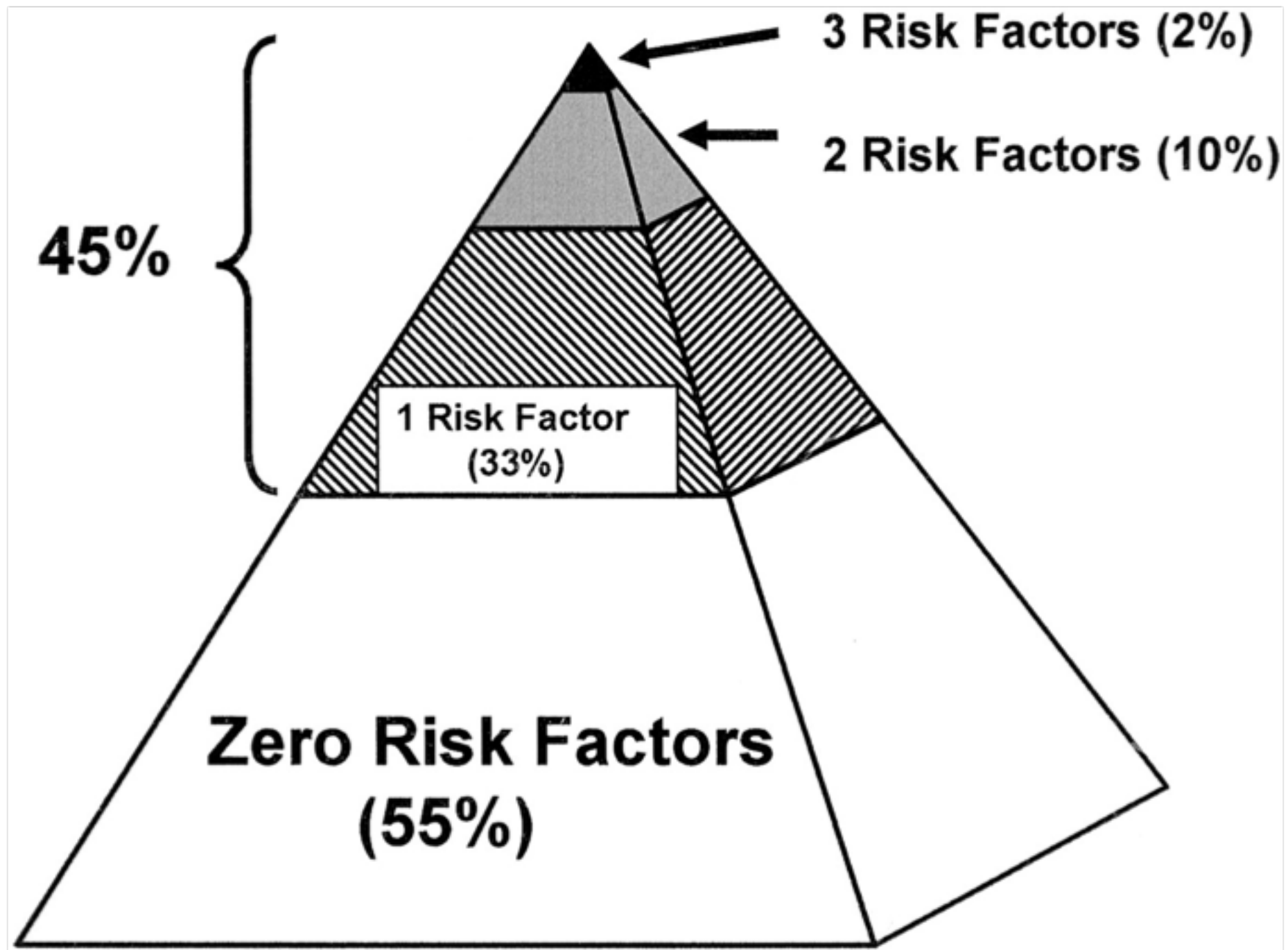
HCM Risk-SCD Calculator

Age	Years	Age at evaluation
Maximum LV wall thickness	mm	Trans thoracic 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 Bernoulli equation: $\text{Gradient} = 4V^2$, 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.
Risk of SCD at 5 years (%)		
Recommendations		
Reset		

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



1 event/year in every 150 pts



Cardiac Magnetic Resonance (CMR)

- Ventricular Mass, Volumes, EF
- Site and degree of Hypertrophy
- Absence of limitations from poor acoustic window

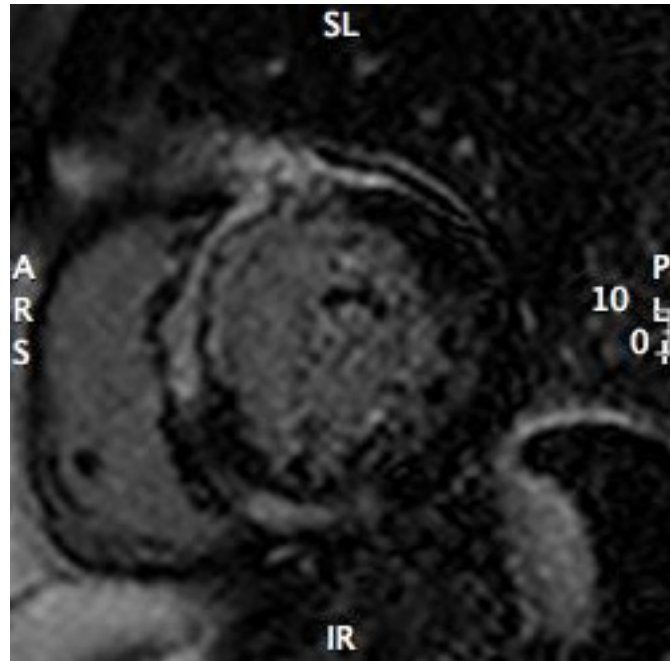
Ability of detect Myocardial Fibrosis
with Late Gadolinium Enhancement



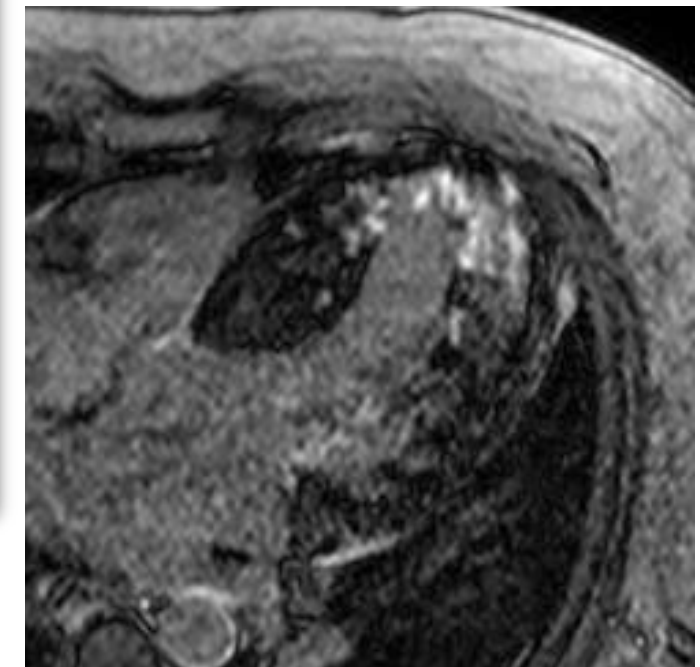
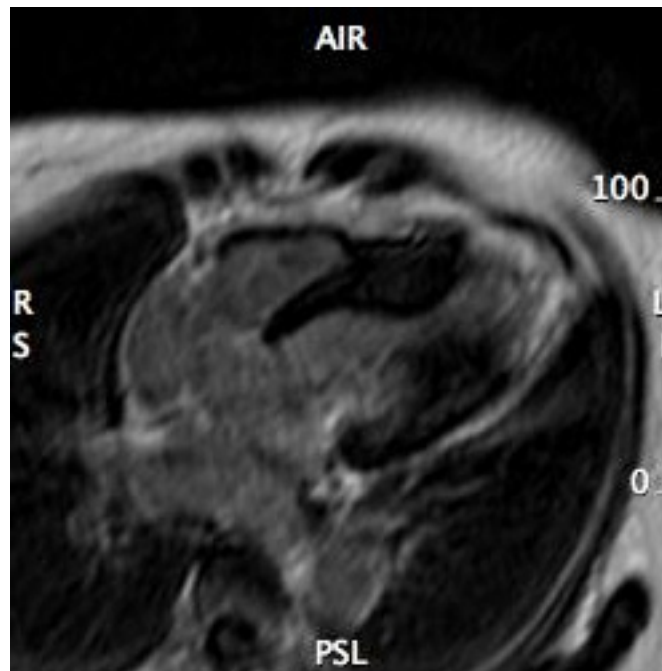
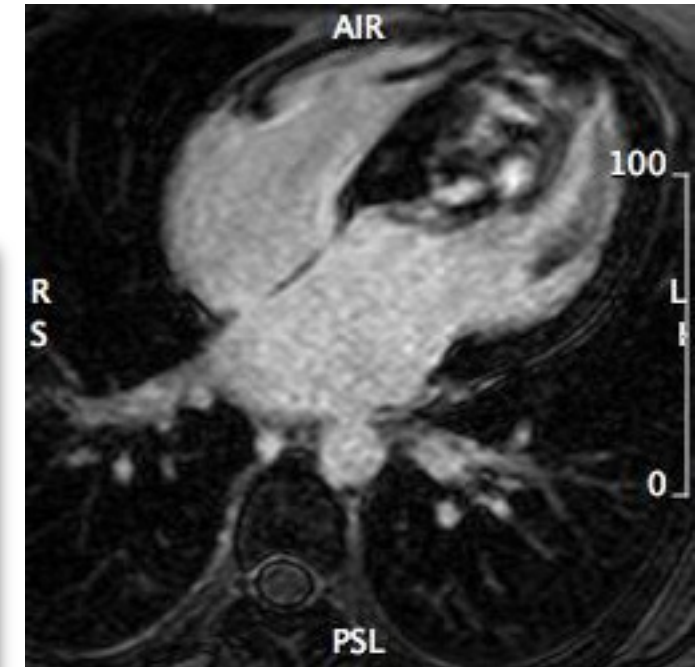
Fibrosis

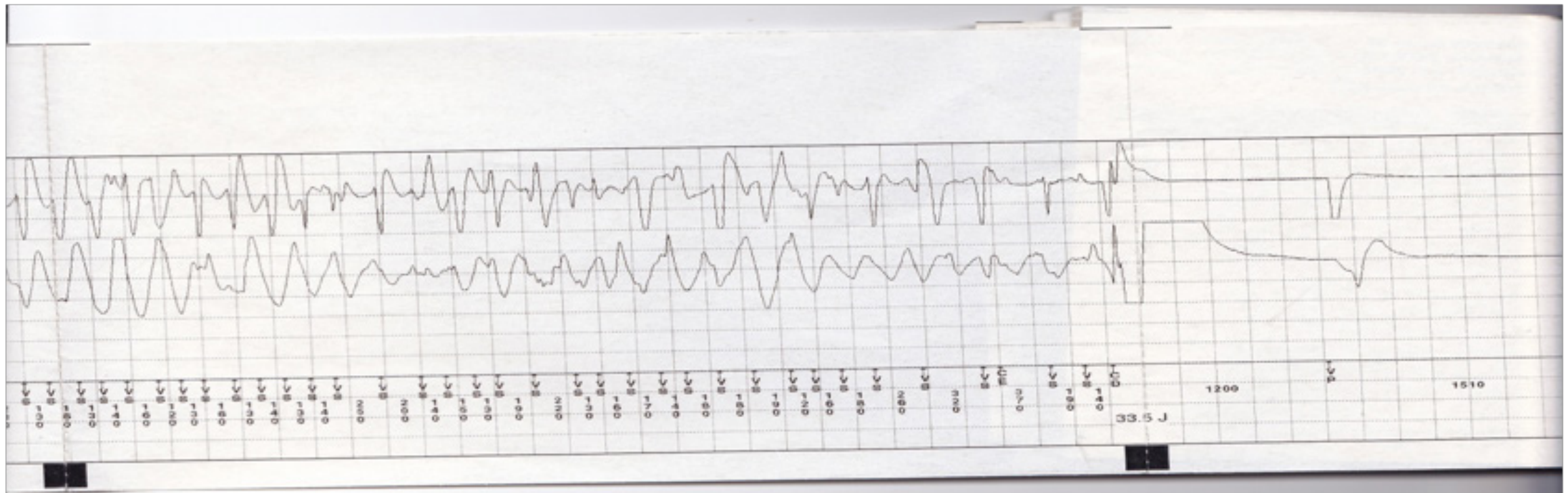
- Replacement Fibrosis
(Scarring)
- Interstitial Fibrosis

Late Gadolinium Enhancement



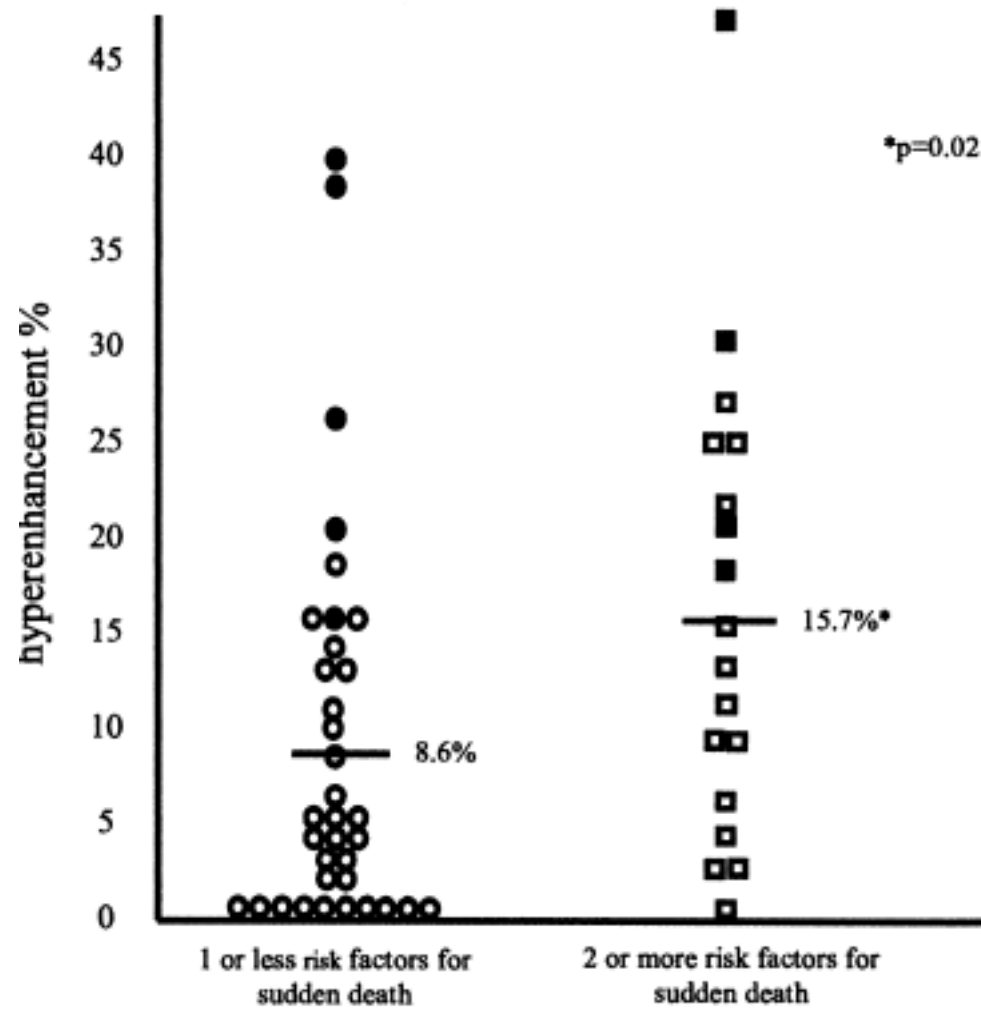
- 50 (30-80) % of HCM pts
- On average 10% LV volume
- Any location and distribution
- Midmyocardium LV septum (30%)



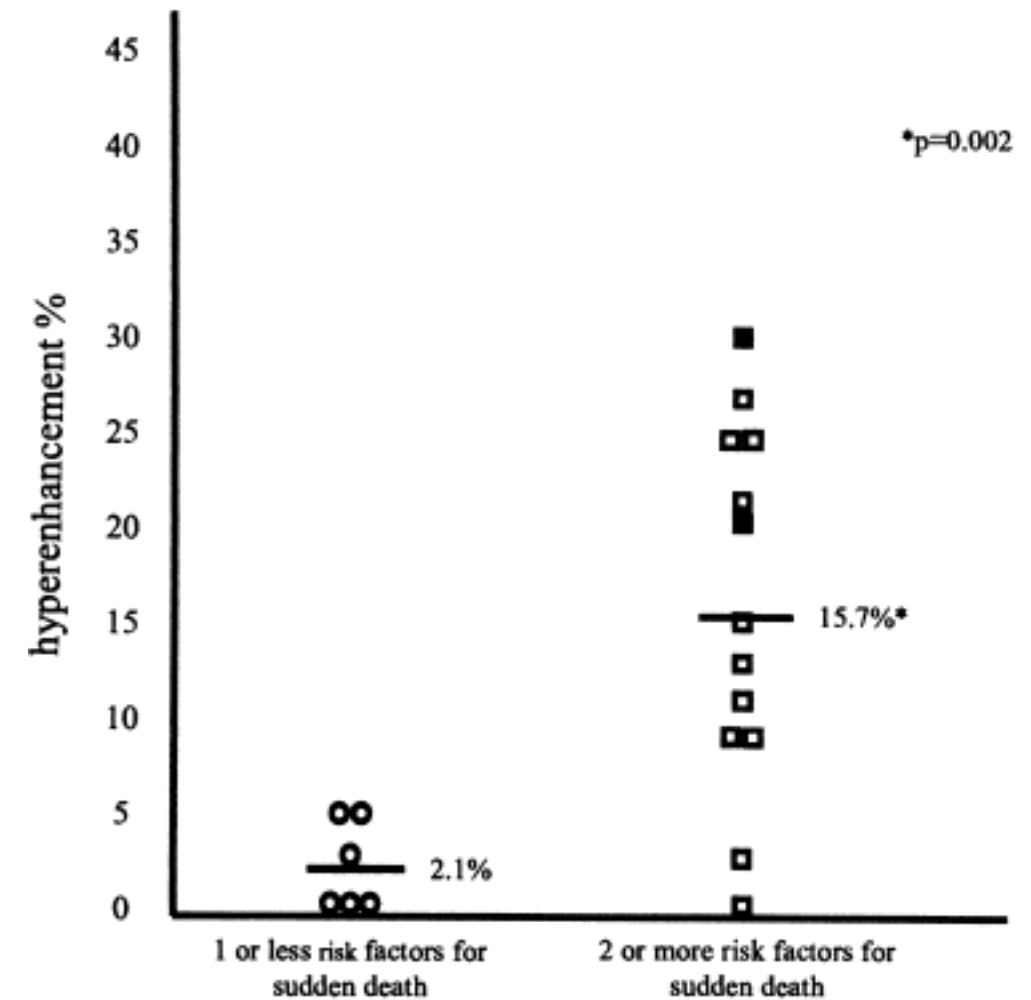


LGE and Prognosis

Toward Clinical Risk Assessment in Hypertrophic Cardiomyopathy With Gadolinium Cardiovascular Magnetic Resonance

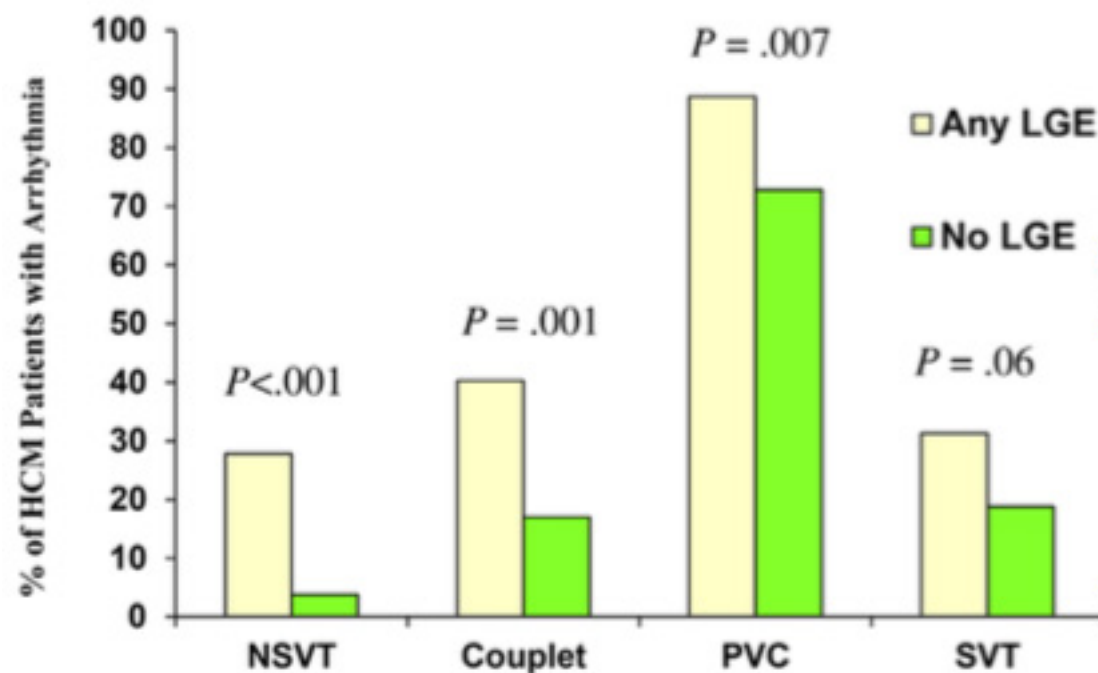


All patients n=53



Patients <40 yrs old n=19

Occurrence and Frequency of Arrhythmias in Hypertrophic Cardiomyopathy in Relation to Delayed Enhancement on Cardiovascular Magnetic Resonance



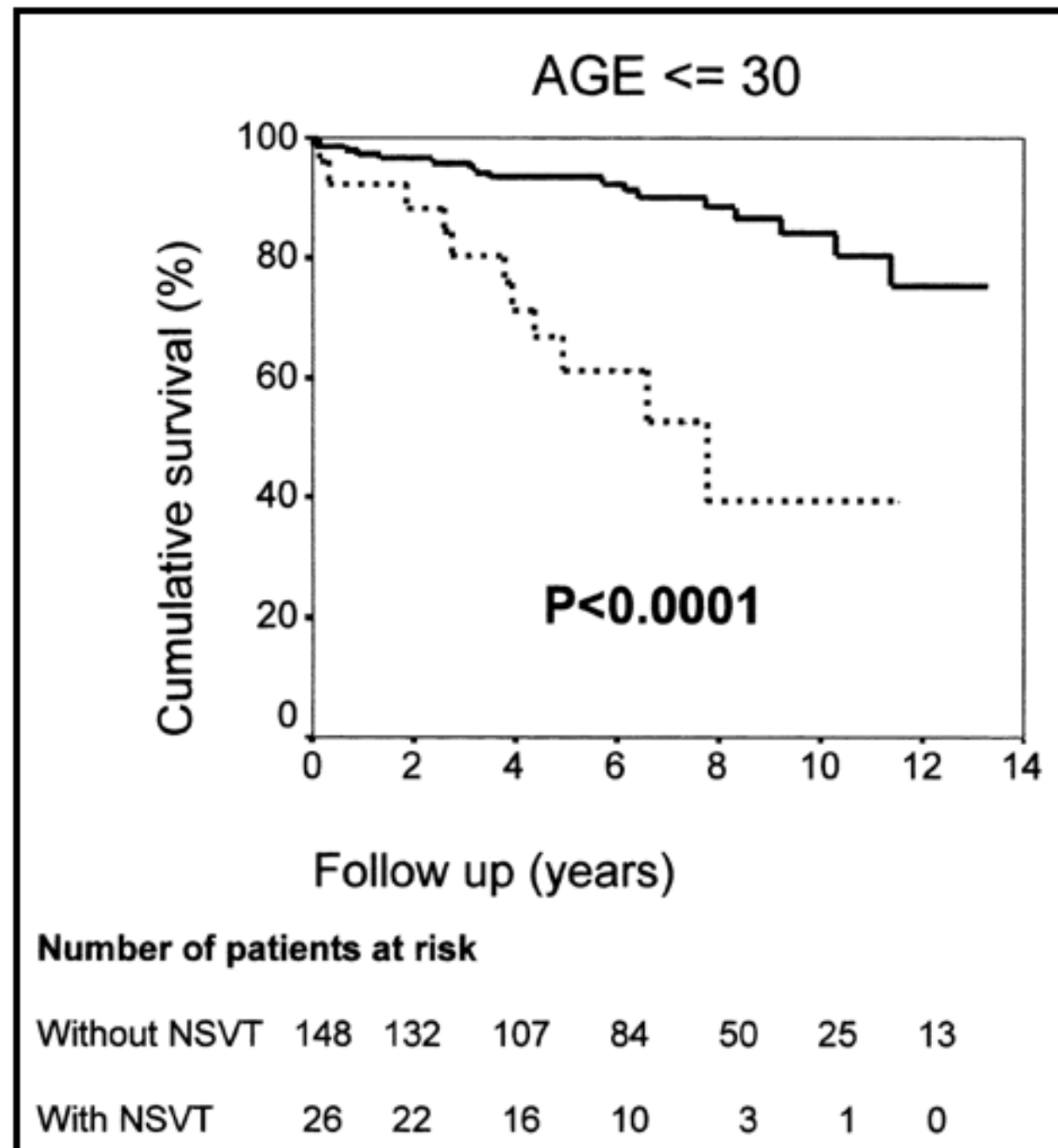
Late gadolinium enhancement on cardiac magnetic resonance and phenotypic expression in hypertrophic cardiomyopathy

Table III. Clinical and CMR findings according to tertiles of LGE

	1st tertile of LGE (n = 41)	2nd tertile of LGE (n = 42)	3rd tertile of LGE (n = 41)	P
Male gender (%)	27 (65%)	24 (57%)	35 (85%)	.05
Family history of sudden death	10 (24%)	13 (30%)	13 (30%)	.46
Unexplained syncope	3 (7%)	2 (4%)	6 (14%)	.13
Abnormal exercise pressure response	5 (12%)	1 (2%)	2 (4%)	.16
Nonsustained ventricular tachycardia	2 (4%)	5 (11%)	13 (30%)	.001
Atrial fibrillation	3 (7%)	7 (16%)	7 (17%)	.19
Wall thickness >30 mm (echo)	1 (2%)	3 (7%)	5 (12%)	.09
LV outflow gradient (echo)	10 (24%)	19 (45%)	16 (39%)	.16
Maximum LV wall thickness (CMR)	18.5 ± 5.0	21.3 ± 6.3	23.0 ± 6.0	.002
LV mass (CMR)	93 ± 48.07	92 ± 34.71	115 ± 41.62	.02
Left atrium dilation (CMR)	13 (30%)	16 (38%)	22 (53%)	.04
Ejection fraction <50% (CMR)	2 (4%)	2 (4%)	7 (17%)	.02
Telediastolic volume (mL/m ²) (CMR)	74.6 ± 11.7	74.8 ± 11.4	83.0 ± 13.8	.1
Telesystolic volume (mL/m ²) (CMR)	27.3 ± 7.5	29.4 ± 6.5	34.5 ± 9.5	.04
Perfusion alterations (CMR)	3 (7%)	7 (16%)	17 (41%)	<.01

Non-sustained ventricular tachycardia in hypertrophic cardiomyopathy

an independent marker of sudden death risk in young patients



Monserat et al. J Am Coll Cardiol 2003

Prognostic Value of Late Gadolinium Enhancement in Clinical Outcomes for Hypertrophic Cardiomyopathy

First Author (Ref. #)	Year	Inclusion	Exclusion	Primary Endpoints
Maron (18)	2008	HCM patients presenting to Tufts Medical Center and Minneapolis Heart Institute Foundation	Significant atherosclerotic CAD (>50% stenosis in 1 major artery); no patients with prior myectomy	Occurrence of heart failure symptoms, LV systolic dysfunction, adverse cardiovascular events
Rubinshtein (17)	2010	HCM patients who underwent CE-MRI at Mayo Clinic	Previous septal myectomy or ablation; MRI performed without IV gadolinium	HCM genes status, severity of symptoms, degree of ventricular ectopy on Holter ECG, subsequent SCD, appropriate ICD therapies
O'Hanlon (16)	2010	HCM patients referred for CMR at Royal Brompton Hospital	Significant CAD (>50% stenosis), previous myocardial infarction, prior gradient reduction therapy	Cardiovascular death, unplanned cardiovascular admission, sustained VT/VF, appropriate ICD discharge
Bruder (15)	2010	Patients with known or suspected HCM presenting to Essen and Stuttgart for workup	CAD, aortic stenosis, amyloidosis, hypertension, prior septal ablation or myectomy	All-cause mortality, cardiac mortality

Green et al. J Am Coll Cardiol Img 2012

2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy

“On balance, the extent of LGE on CMR has some utility in predicting cardiovascular mortality, but current data do not support the use of LGE in prediction of SCD risk.”

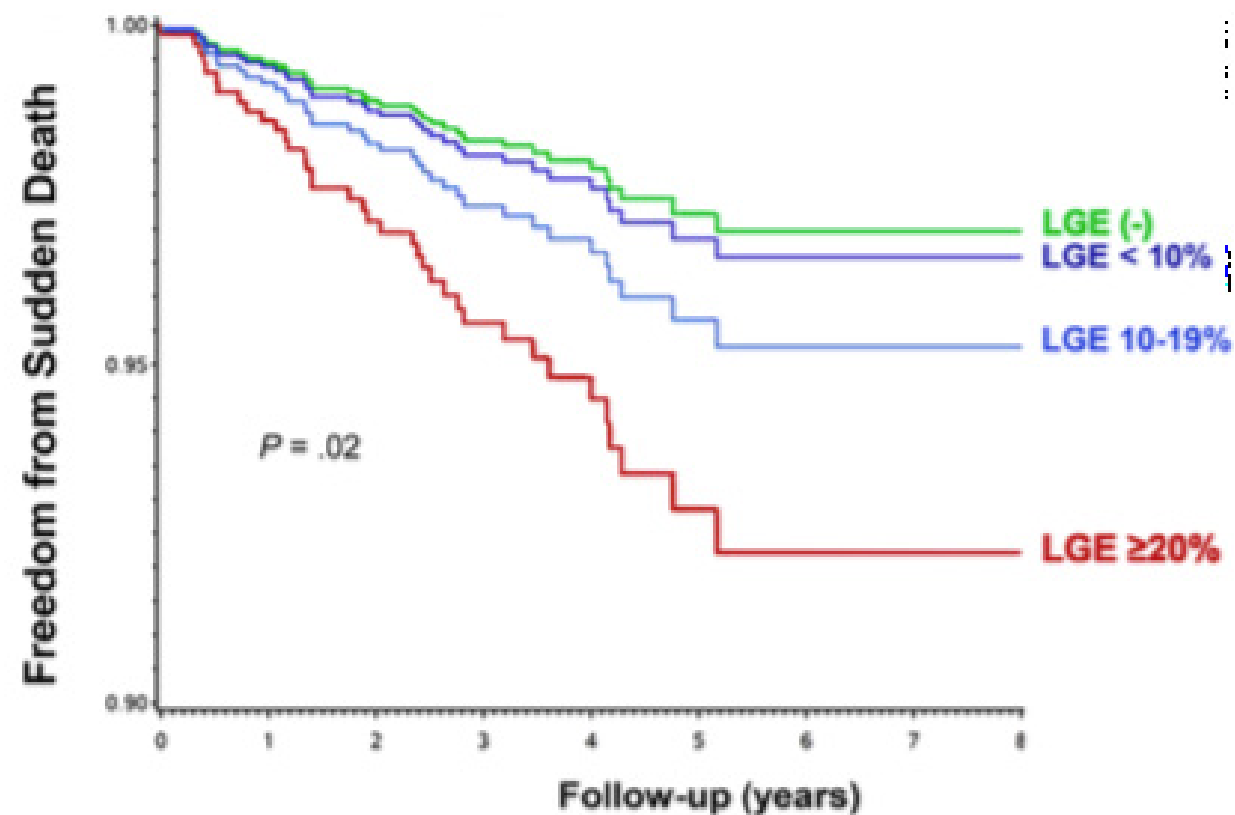
Role of late gadolinium enhancement cardiovascular magnetic resonance in the risk stratification of hypertrophic cardiomyopathy

Analyses of the predictors of sudden cardiac death or aborted sudden cardiac death

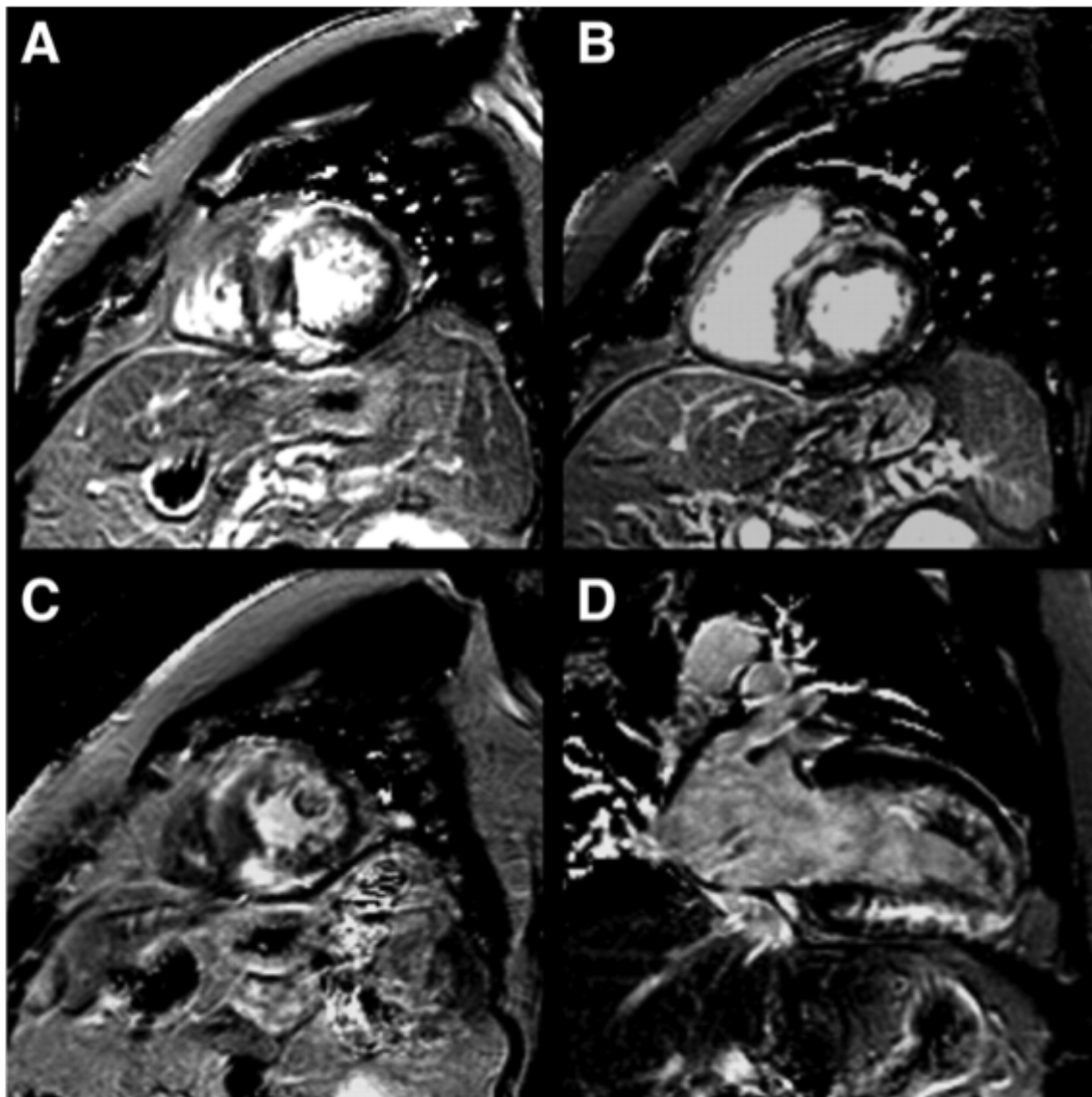
Univariable Analysis	Hazard ratio	95% CI		p Value
Male	1.42	0.52	3.84	0.493
New York Heart Association functional class	1.02	0.54	1.93	0.951
Sustained ventricular tachycardia/fibrillation	7.76	1.79	33.57	0.006
Family history of sudden cardiac death	0.75	0.17	3.21	0.698
LV wall thickness ≥ 30 mm	1.62	0.38	6.98	0.516
LV outflow tract obstruction ≥ 30 mm Hg	0.50	0.17	1.47	0.207
Non-sustained ventricular tachycardia	1.71	0.40	7.38	0.472
Unexplained syncope	0.84	0.19	3.59	0.809
Number of risk factors	1.00	0.55	1.80	0.995
Maximum LV end-diastolic wall thickness (mm)	1.01	0.93	1.09	0.845
Indexed LV end-diastolic volume (per 10 ml/m ²)	1.17	0.89	1.54	0.257
Indexed LV end-systolic volume (per 10 ml/m ²)	1.88	1.45	2.45	<0.001
LV EF (%)	0.92	0.89	0.95	<0.001
LV mass index (per 10 g/m ²)	1.07	0.99	1.17	0.104
Presence of fibrosis	2.69	0.91	7.97	0.073
Amount of fibrosis (per 5% of LV mass)	1.24	1.06	1.45	0.007
Multivariable analysis				
Presence of fibrosis as a candidate				
LV EF (%)	0.92	0.89	0.95	<0.001
Presence of fibrosis	2.98	0.66	13.44	0.155
Amount of fibrosis as a candidate				
LV EF (%)	0.92	0.89	0.95	<0.001
Amount of fibrosis (per 5% of LV mass)	1.10	0.92	1.31	0.299

Ismail et al. Heart 2014; 100

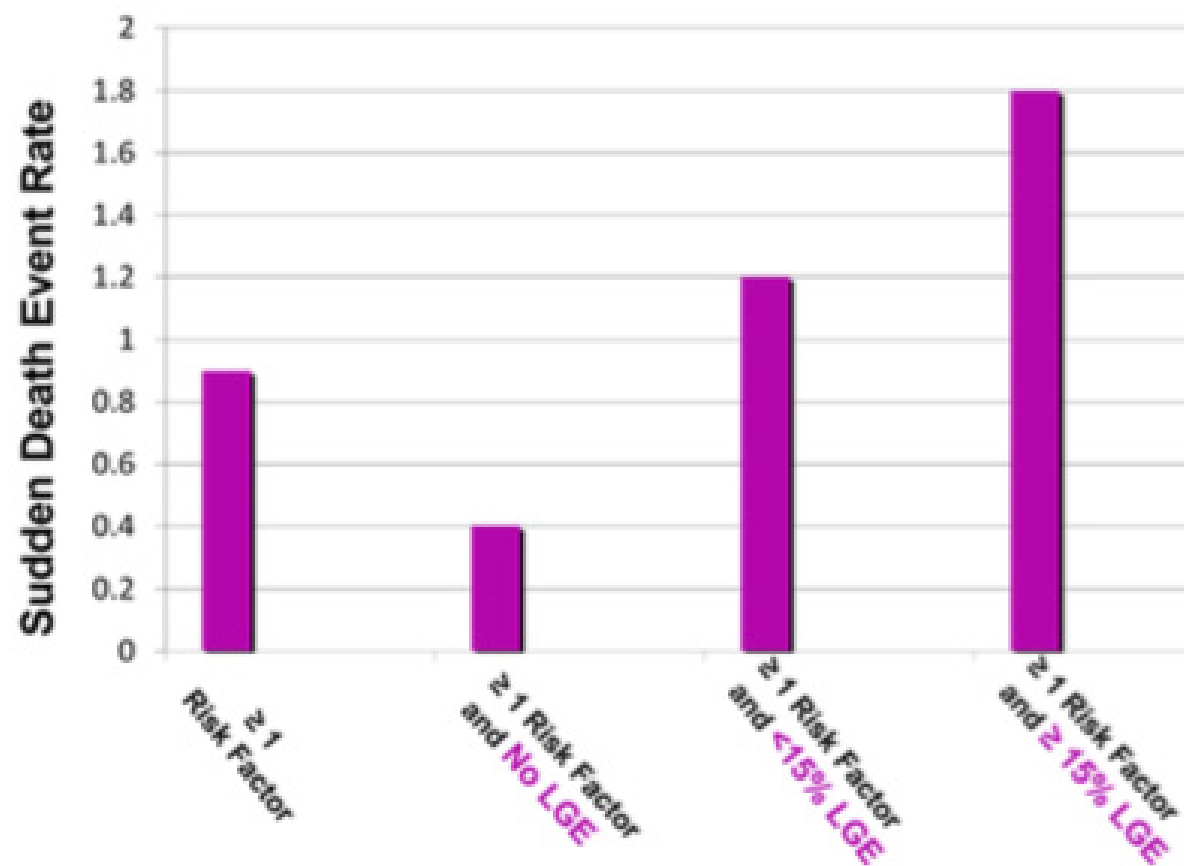
Prognostic Value of Quantitative Contrast-Enhanced Cardiovascular Magnetic Resonance for the Evaluation of Sudden Death Risk in Patients With Hypertrophic Cardiomyopathy



Extensive Myocardial Fibrosis in a Patient With Hypertrophic Cardiomyopathy and Ventricular Tachycardia Without Traditional High-Risk Features



LGE “Amount” Improves Risk Stratification

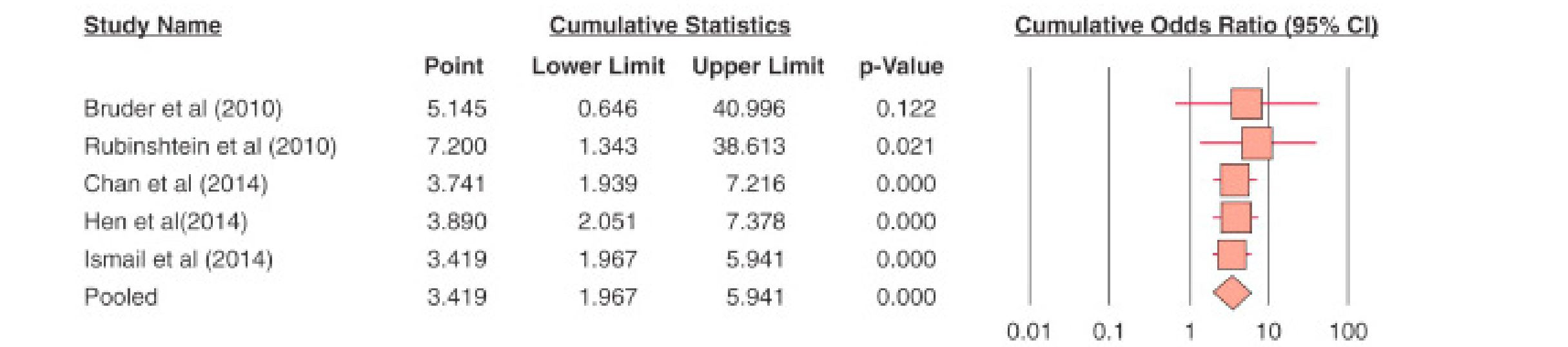


Prognostic Value of LGE-CMR in HCM

A Meta-Analysis

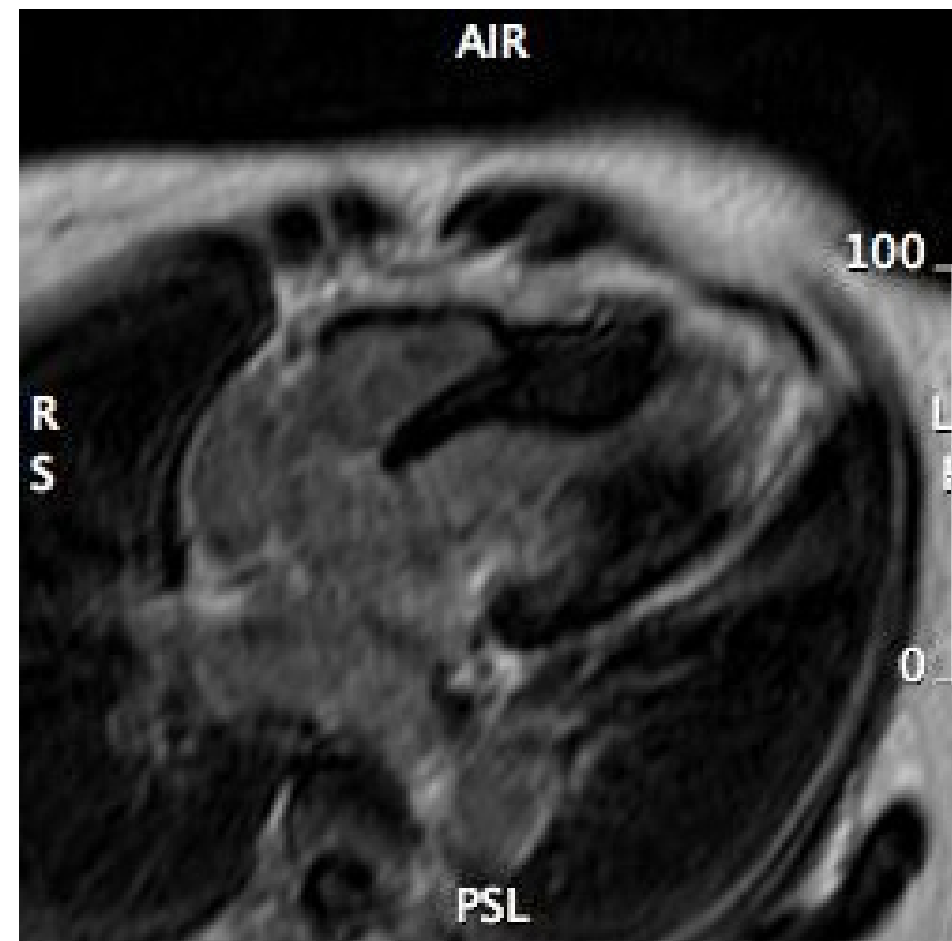
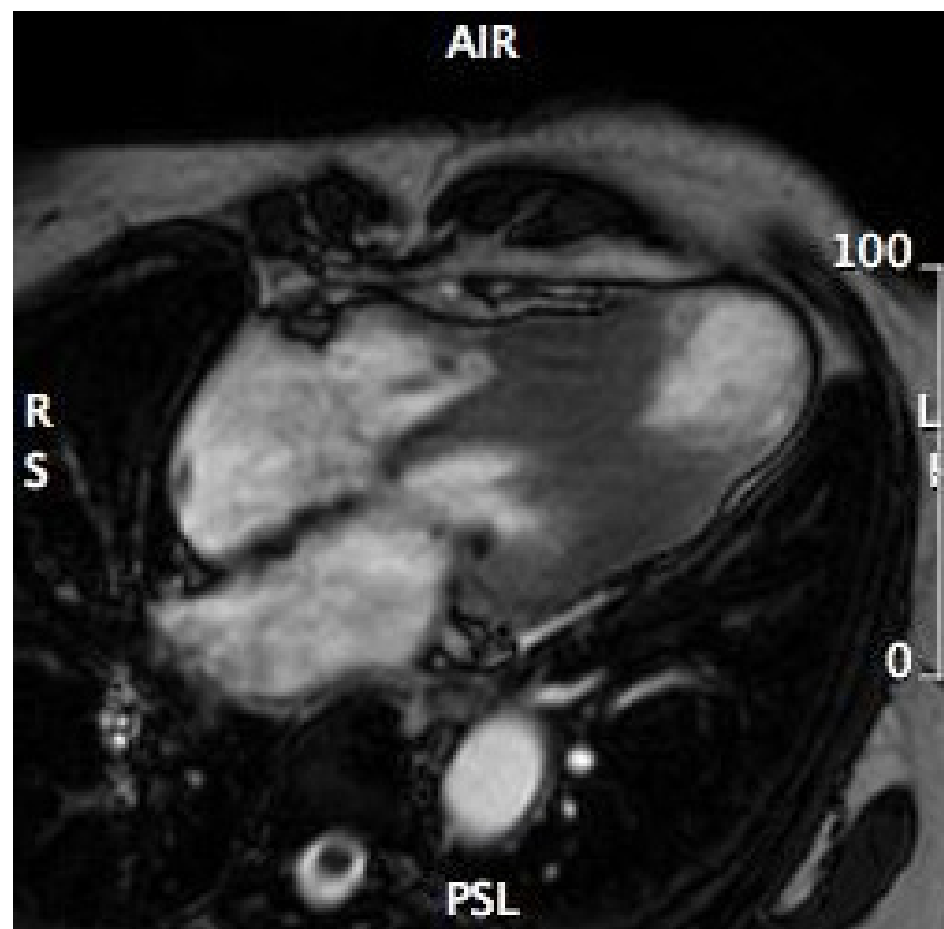
TABLE 1 Characteristics of Studies Complying With PRISMA Guidelines

First Author (Ref. #)	Patients Enrolled	Mean Follow-Up Time, Months	Design	Field Strength	Scar Assessment by LGE	Population Included
Bruder et al. (19)	220	36.3	Prospective, single center	1.5-T	Visual assessment of LGE by 2 reviewers	Patients with known or suspected HCM who underwent CMR
Rubinshtein et al. (20)	424	43	Retrospective, single center	1.5-T	Visual assessment of LGE by 2 reviewers	Patients with HCM who underwent ce-MRI
Chan et al. (11)	1293	40.2	Prospective, multiple center	1.5-T	Visual assessment of LGE by 2 reviewers	Patients with HCM who underwent CMR
Hen et al. (12)	345	21.8	Retrospective, single center	1.5-T	Visual assessment of LGE by 3 reviewers	Patients with HCM who underwent CMR
Ismail et al. (13)	711	42.6	Prospective, single center	1.5-T	NR	Consecutive patients with HCM referred for CMR

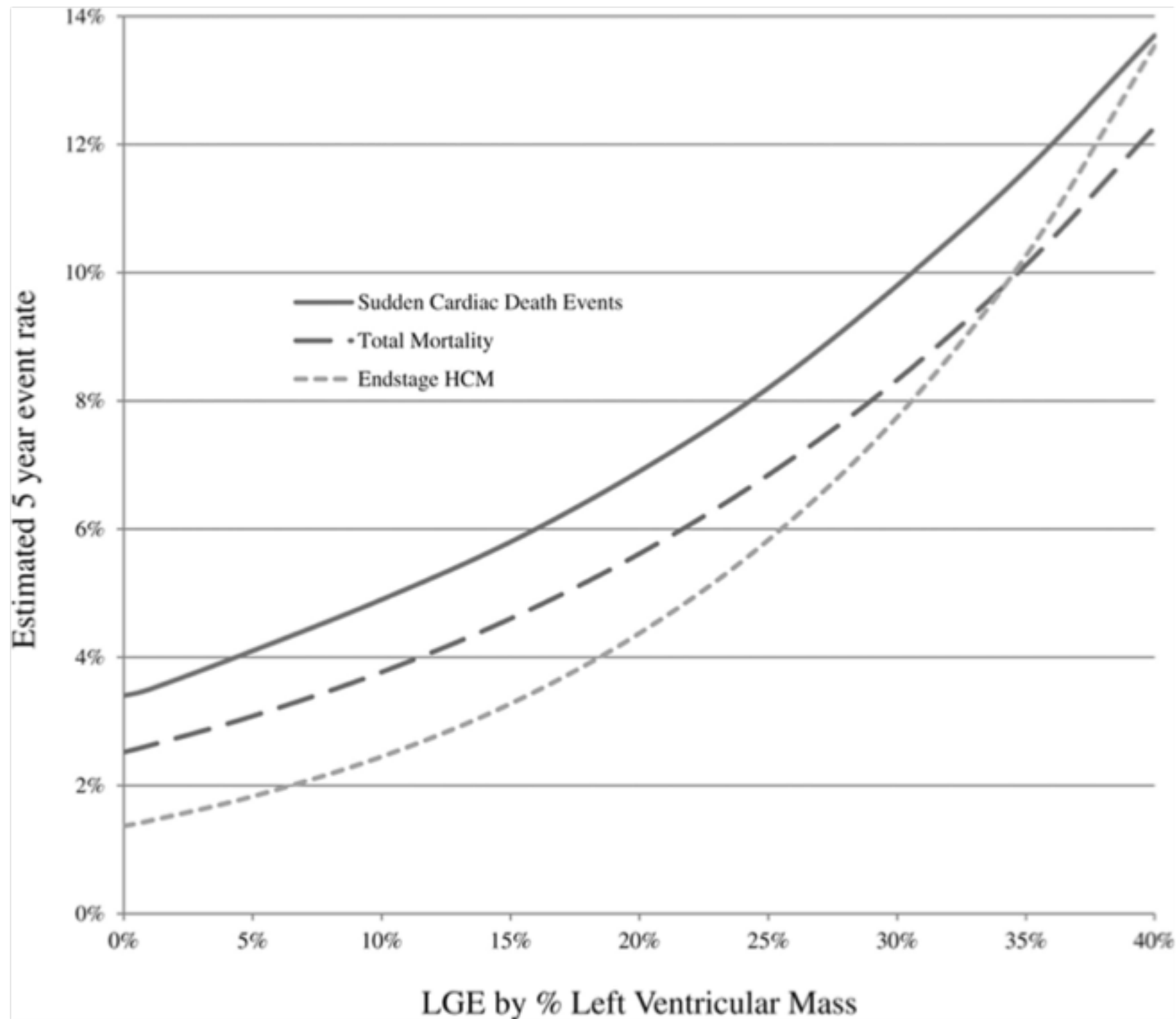


Cumulative analysis of SCD

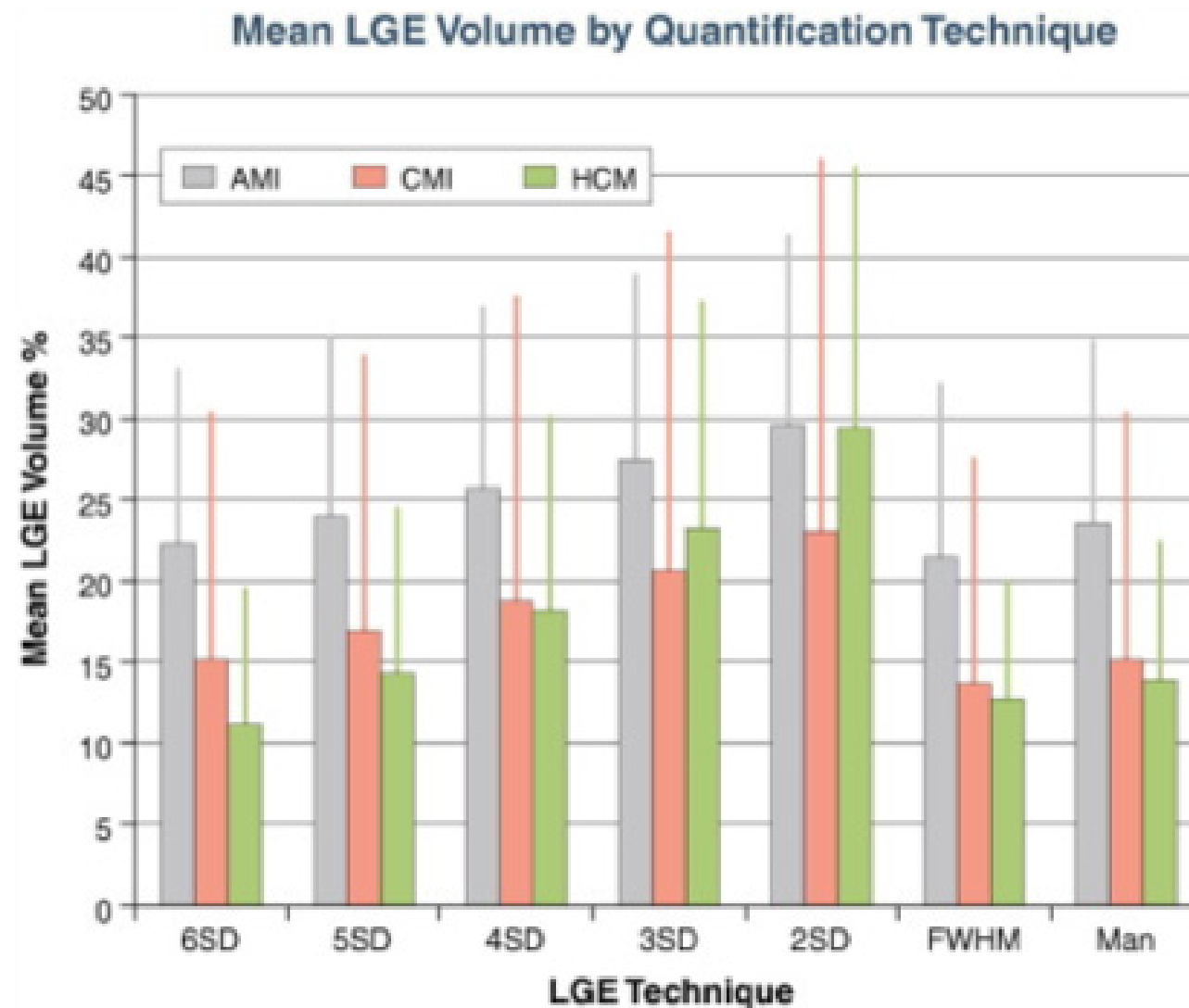
Left Ventricular Apical Aneurysms



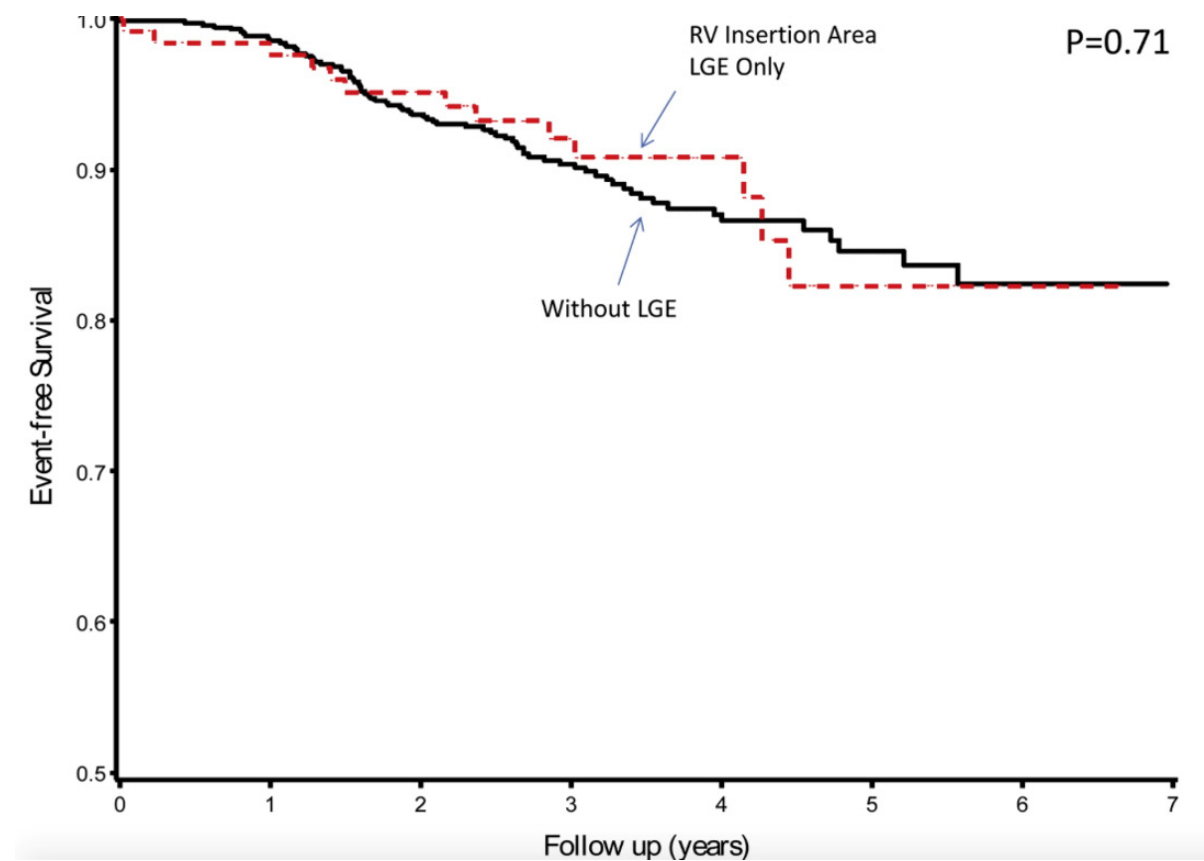
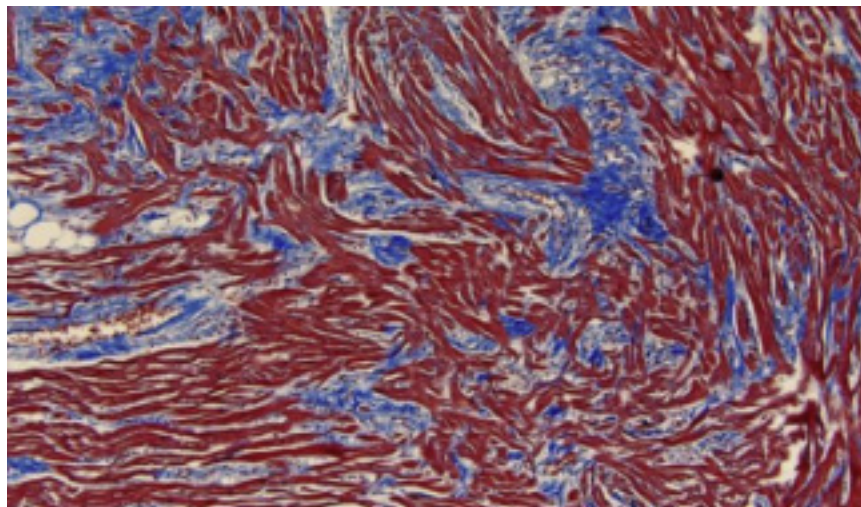
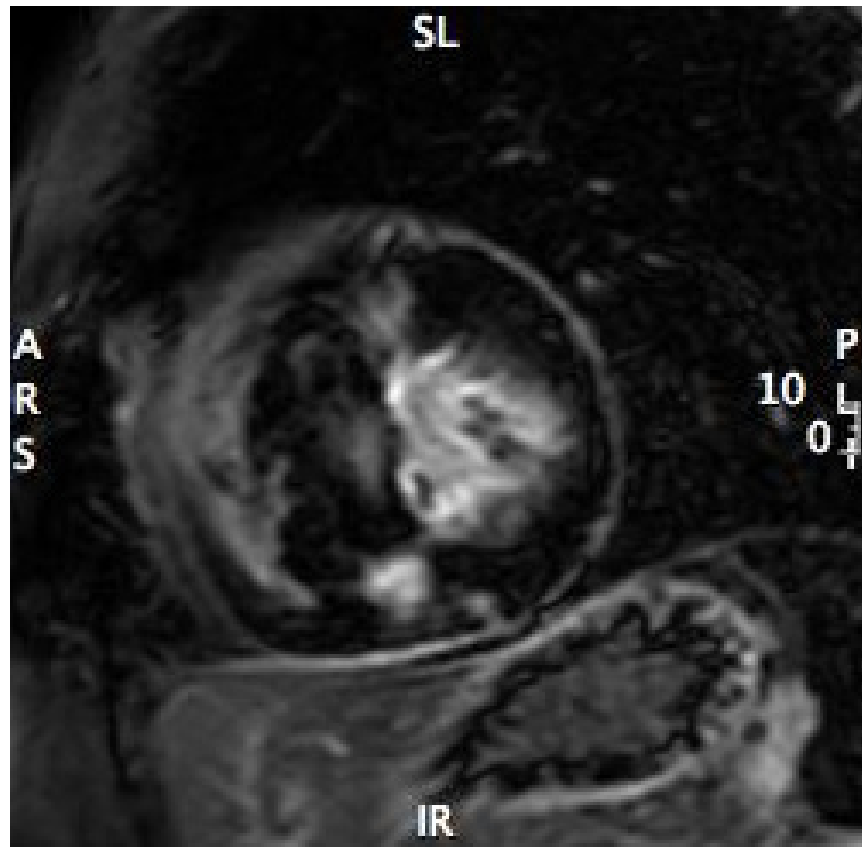
LGE and Endstage HCM



Evaluation of Techniques for the Quantification of Scar of Differing Etiology Using CMR

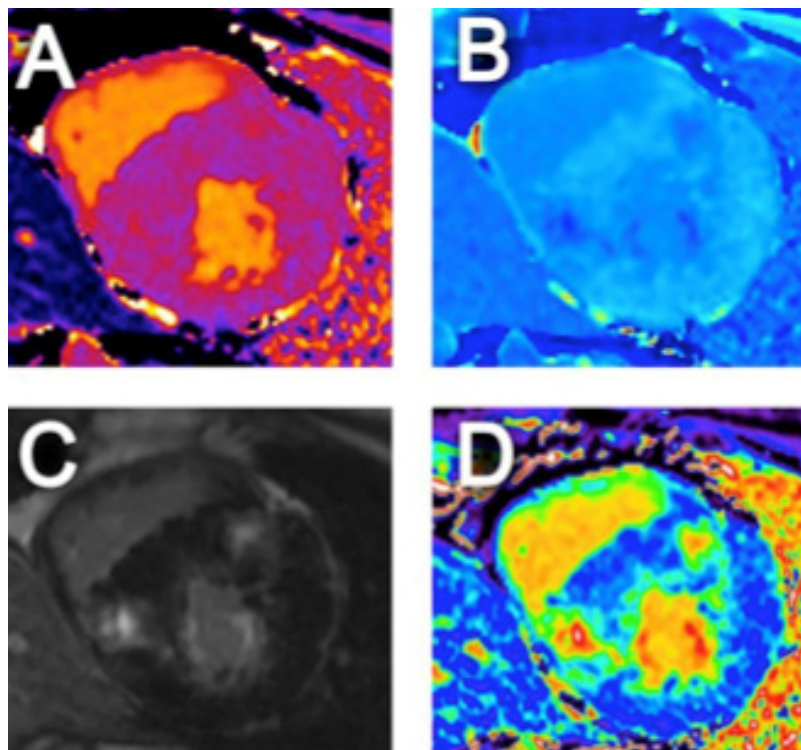
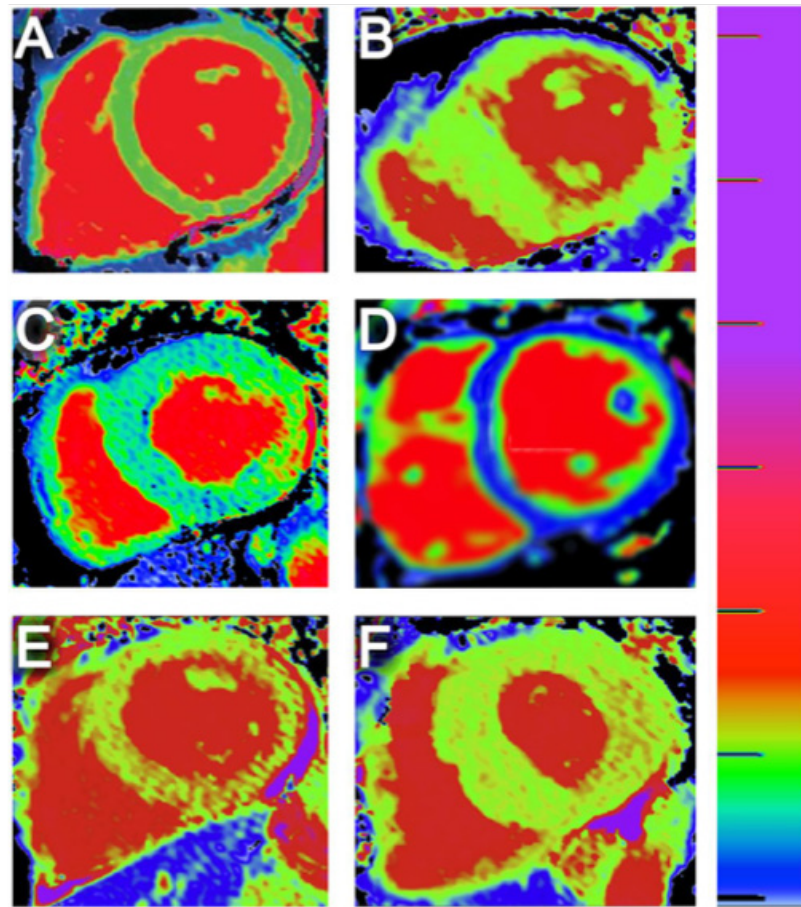


What Lies Behind the Bright Light of LGE ?



Chan et al. Am J Cardiol Coll 2015;116

T1 mapping



- Native (noncontrast T1)
- Extracellular Volume Fraction (ECV)

- Early recognition (Gen+/Phen-)
- Differential diagnosis
- Disease progression
- Prognostic Information (?)

LGE-CMR for SCD Risk Evaluation in HCM

- Relevant additional prognostic informations
- Better appreciation of the “risk status”
- Helpful in decision making (selection ICD candidates)
- Role in routine assessment as part of risk stratification

Thank you!

OVERALL CMR FINDINGS

Patients, N = 124

Any late enhancement (%), n = 96 (77%)

Late enhancement in the interventricular septum (%), n = 62 (50%)

Late enhancement in the apex (%), n = 23 (19%)

Late enhancement in the inferior wall (%), n = 22 (18%)

Late enhancement in the anterolateral wall (%), n = 13 (11%)

Maximum LV wall thickness (mm), 21 ± 6

LV mass (mg/m²), 100 ± 43

Left atrium dilatation (area >20 cm²), n = 51 (41%)

Ejection fraction, 59 ± 7.9

Ejection fraction <50%, n = 11 (8%)

End diastolic volume (mL/m²), 79 ± 20

End systolic volume (mL/m²), 31 ± 9

Perfusion defects, n = 27 (22%)

