



Il ruolo della RM cardiaca nella stratificazione prognostica delle cardiomiopatie

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Cardiac Magnetic Resonance and Phenotype



Cardiac Magnetic Resonance is the optimal technique to assess the Phenotype of Cardiomyopathies and cardiac diseases.

- Morphological phenotype
- Functional phenotype
- Tissue phenotype :
 - fibrosis
 - edema
 - fat infiltration\metaplasia
 - calcific metaplasia
 - perfusion defects
 - amyloid-deposit
 - iron-overload
 - intracellular fat overload

with conventional T1w T2w LGE pulse sequence + T1- T2- T2* -ECV mapping

Late Gadolinium enhancement



Gd-based c.m. are not specific marker fibrosis!!!
LGE is secondary to all the causes that increase of Volume of Distribution of Gd

Normal interstitium



Fast wash-out®no LGE

Enlarged interstitium

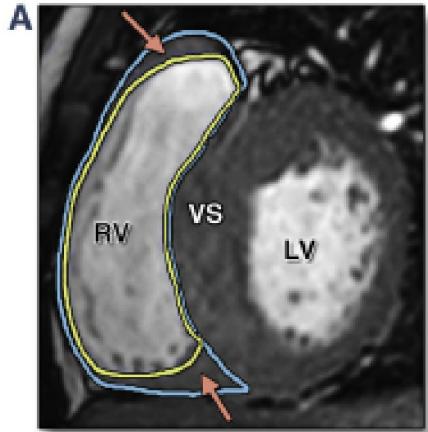


Slow wash-out® LGE

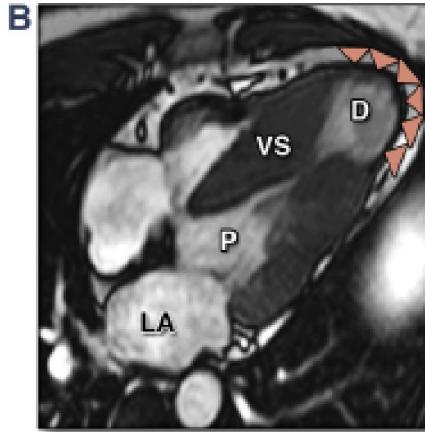
Different buckets
Same 'Holes'

Hypertrophic Cardiomyopathy: MRI and Phenotype

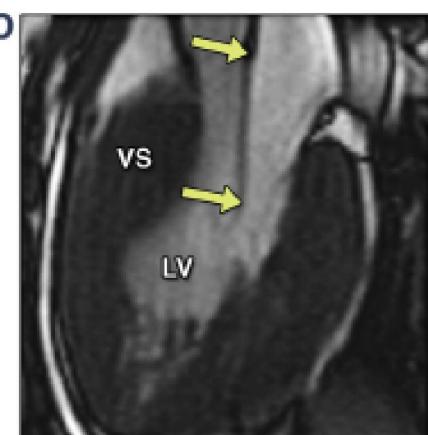
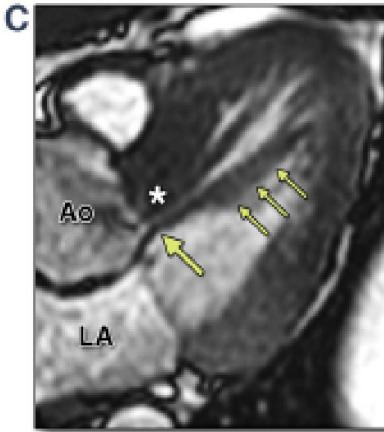
RV hypertrophy



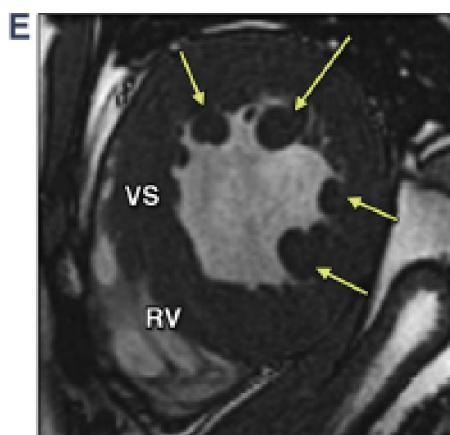
Apical Aneurysm



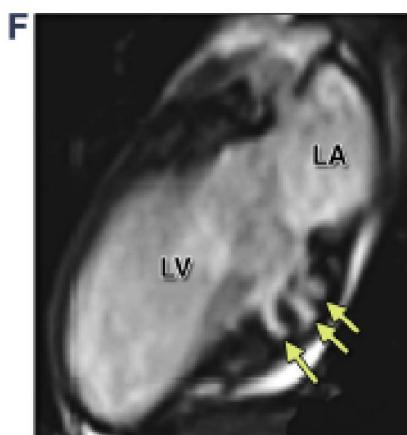
Sub-mitralic apparatus



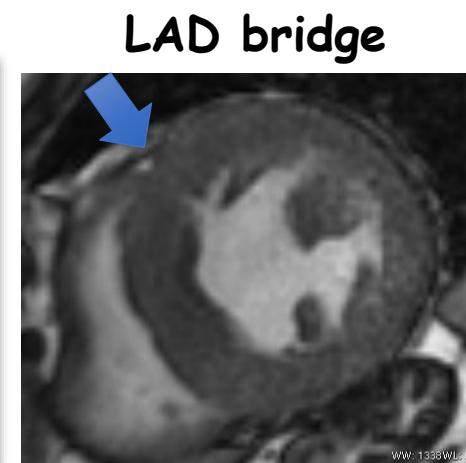
Elongated AML



Papillary muscle anomaly



Crypts



Prognostic role of apical aneurysm in HCM

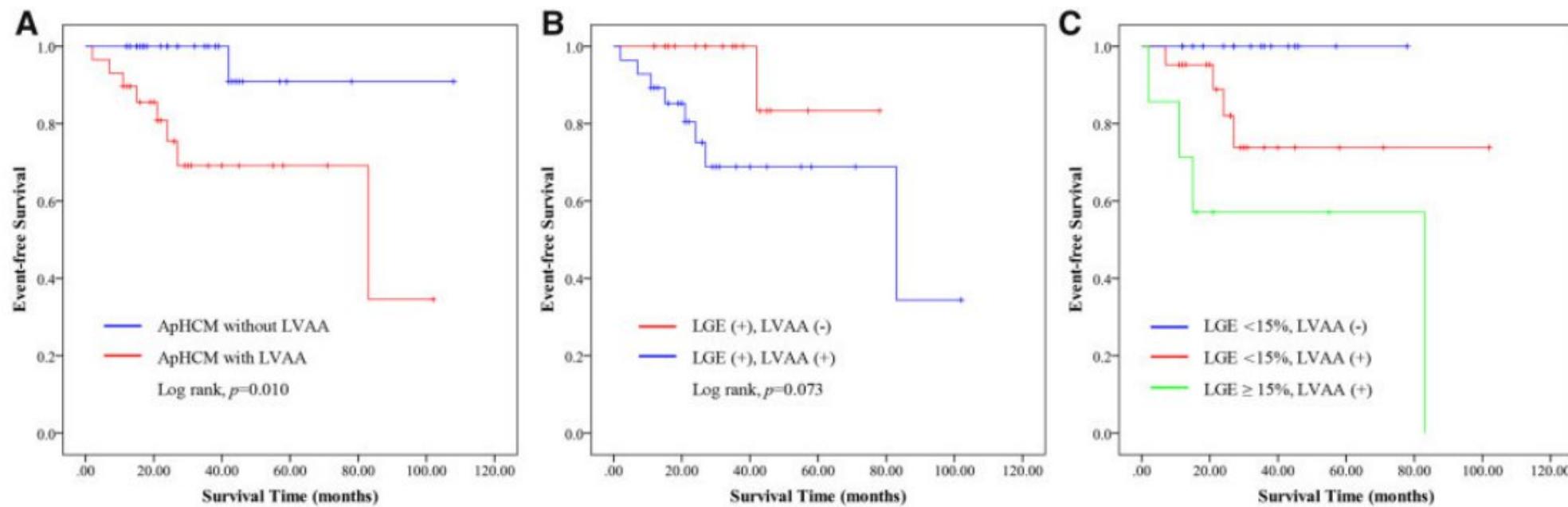
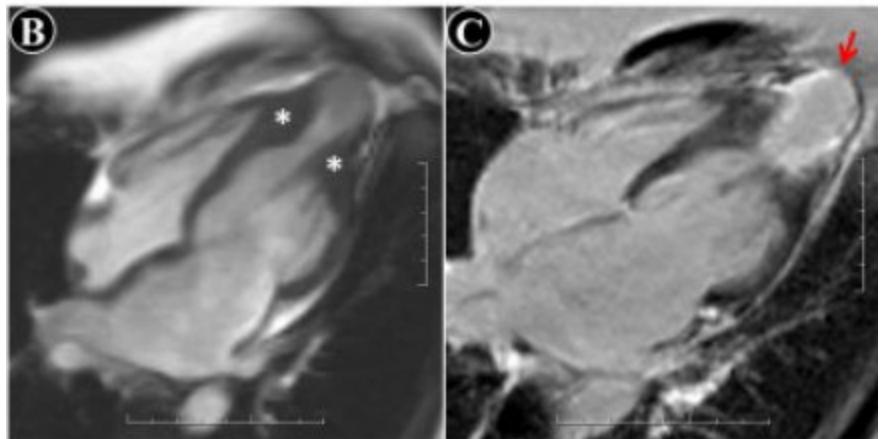


Figure 5 Survival analyses. (A) Kaplan–Meier curves for ApHCM patients with or without LVAA ($P = 0.010$). (B) Kaplan–Meier curves for LGE (+) patients with or without LVAA ($P = 0.073$). (C) Kaplan–Meier curves for patients with or without LVAA and LGE $\geq 15\%$ (blue vs. red, $P = 0.059$; blue vs. green, $P = 0.005$; and red vs. green, $P = 0.071$). ApHCM, apical hypertrophic cardiomyopathy; LVAA, left ventricular apical aneurysm; LGE, late gadolinium enhancement.

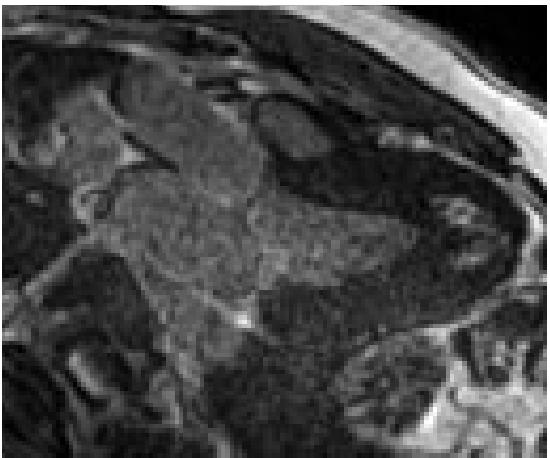


Hypertrophic Cardiomyopathy

Midwall LGE in hypertrophic segments

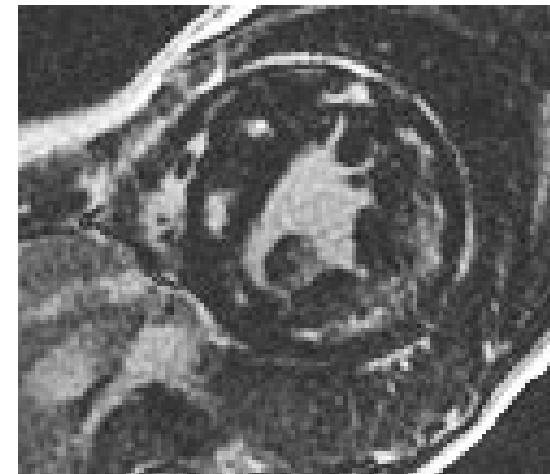


Septal



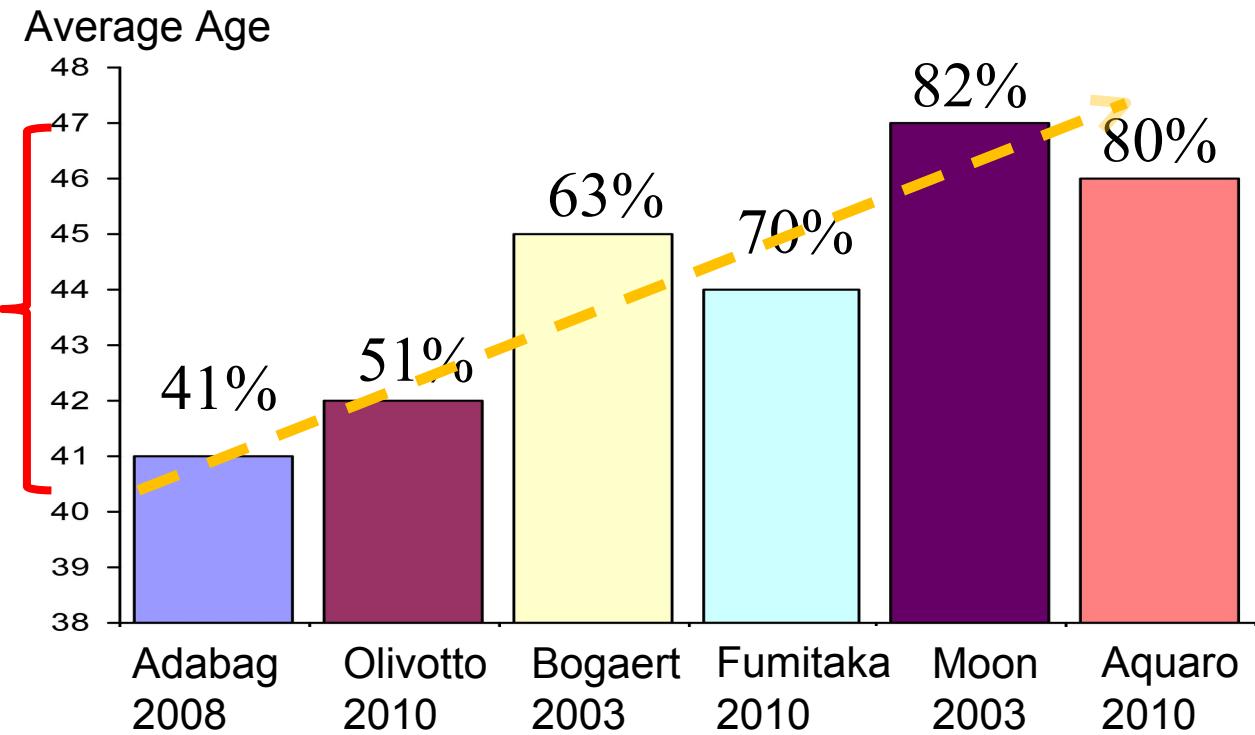
Apical

Diffuse





Late Enhancement in Hypertrophic Cardiomyopathy: Prognostic role of prevalence



A) Cardiac Death

Study	Odds Ratio(95% CI)	p-value
Bruder	8.00 (1.04-61.87)	0.046
O'Hanlon	5.00 (0.61-40.73)	0.133
Maron	0.54 (0.08-3.29)	0.503
Rubinshtain	10.33 (0.58-184.51)	0.112
Pooled	2.92 (1.01-8.42)	0.047

B) SCD/Aborted SCD

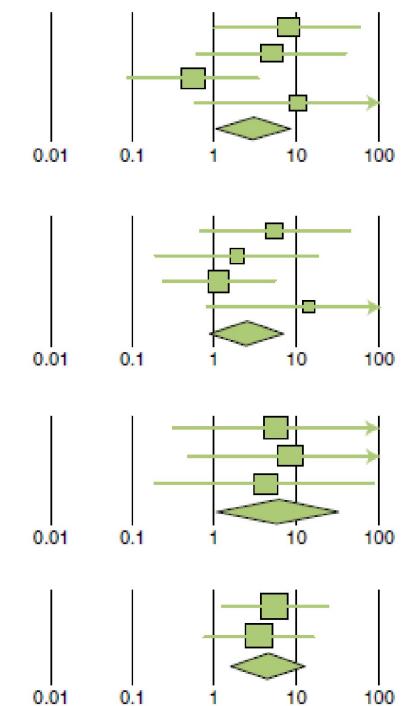
Study	Odds Ratio(95% CI)	p-value
Bruder	5.15 (0.65-41.00)	0.112
O'Hanlon	1.81 (0.19-17.64)	0.612
Maron	1.10 (0.24-5.03)	0.906
Rubinshtain	13.62 (0.78-237.55)	0.073
Pooled	2.39 (0.87-6.58)	0.091

C) HF Death

Study	Odds Ratio(95% CI)	p-value
Bruder	5.56 (0.30-101.90)	0.248
O'Hanlon	8.12 (0.45-146.04)	0.115
Rubinshtain	3.91 (0.19-81.83)	0.380
Pooled	5.68 (1.04-31.07)	0.045

D) All Cause Mortality

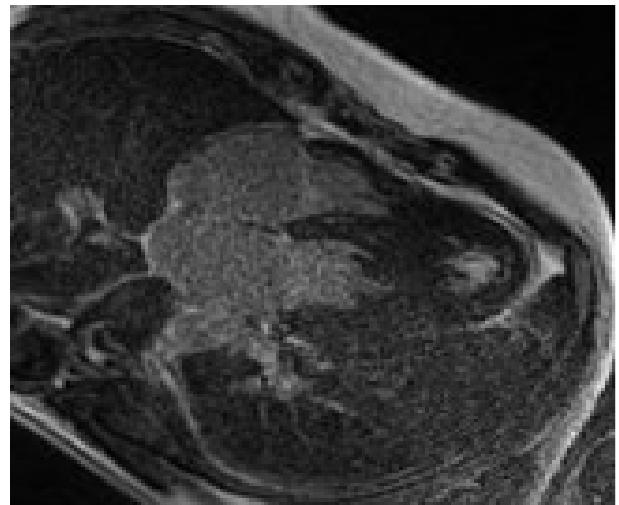
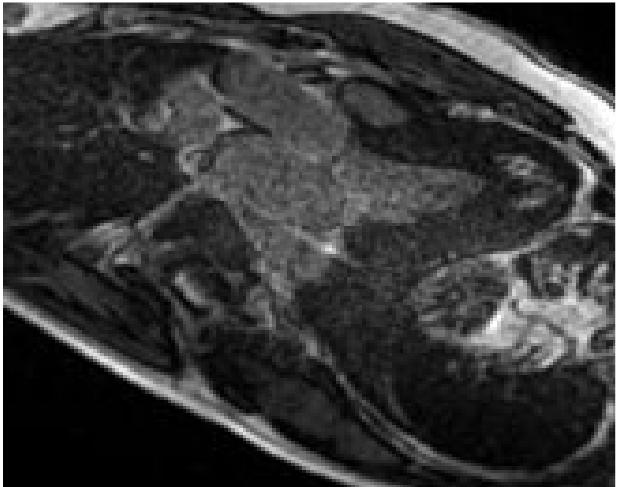
Study	Odds Ratio(95% CI)	p-value
Bruder	5.47 (1.24-24.08)	0.025
Rubinshtain	3.58 (0.76-16.78)	0.106
Pooled	4.46 (1.53-13.01)	0.006



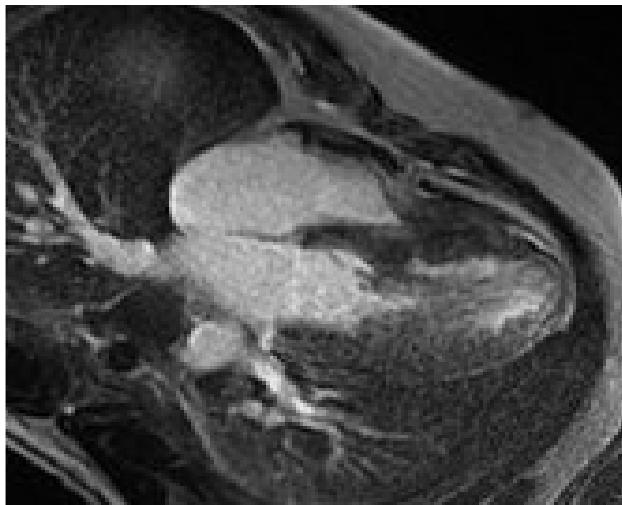
Late enhancement was evidenced in 51-80% HCM patients

Green, JACC imaging 2012

Late Enhancement in Hypertrophic Cardiomyopathy: Prognostic role of extent



B.E. 32y 2008



B.E. 34y 2010

In 3 years:

LGE prevalence in 80% \pm 95% of HCM

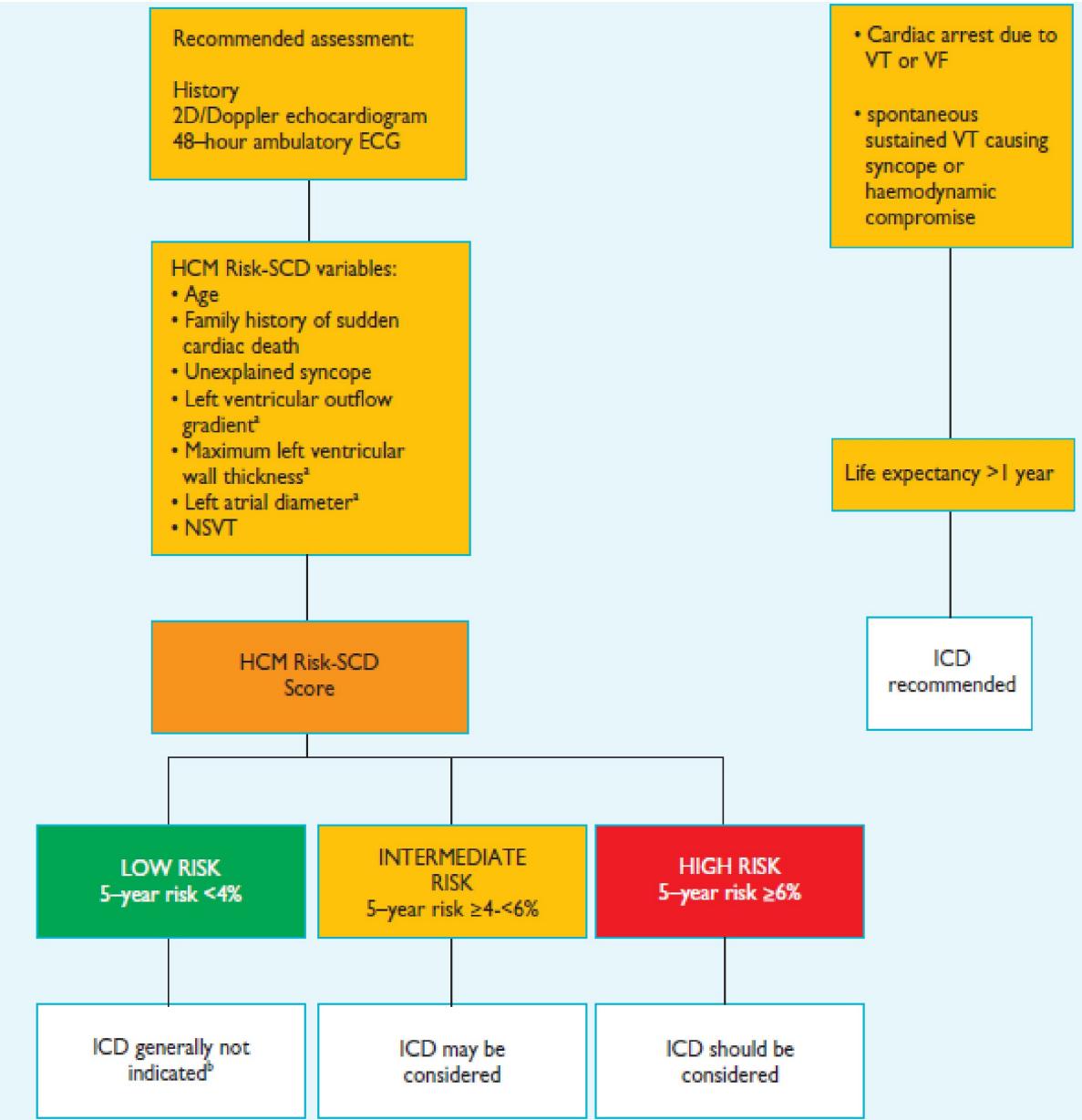
LGE extent from 13 \pm 16 \pm 25 \pm 30 grams

The HCM Risk-SCD formula is as follows:

$$\text{Probability}_{\text{SCD}} \text{ at 5 years} = 1 - 0.998^{\exp(\text{Prognostic index})}$$

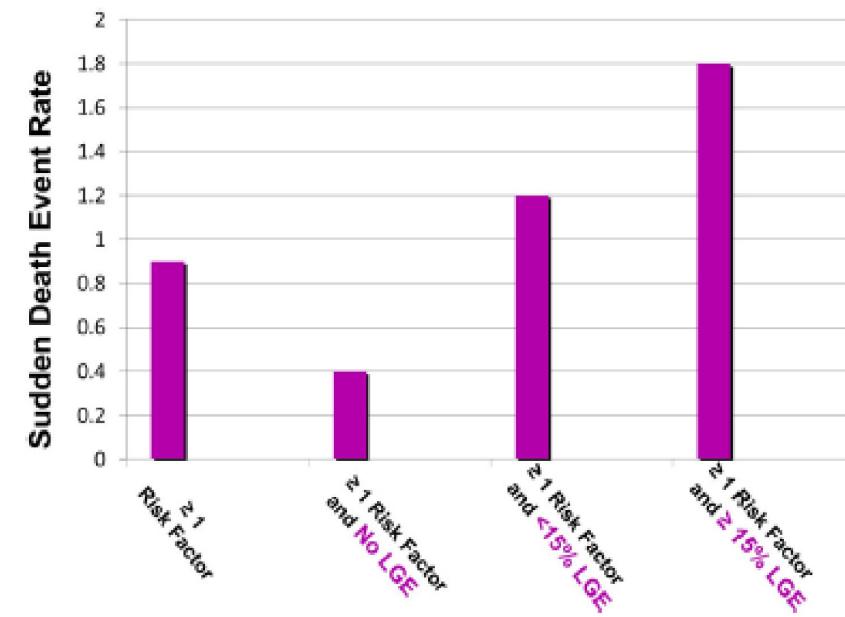
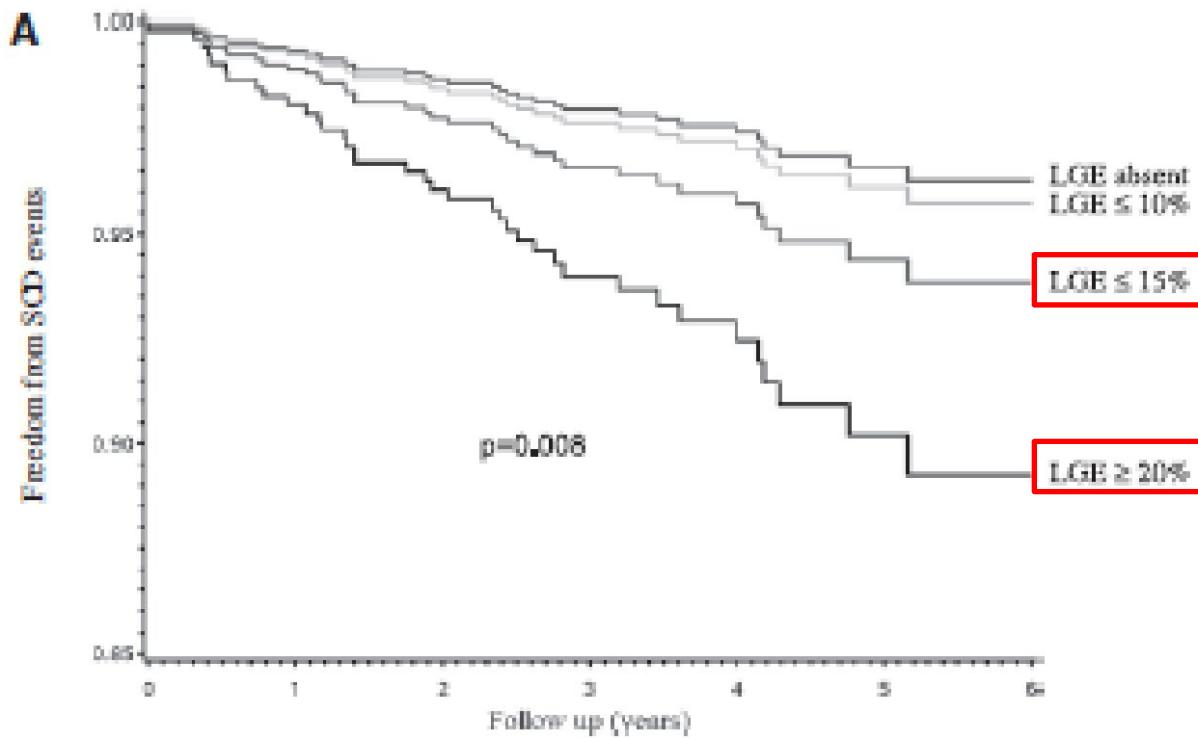
where Prognostic index = $[0.15939858 \times \text{maximal wall thickness (mm)}] - [0.00294271 \times \text{maximal wall thickness}^2 (\text{mm}^2)] + [0.0259082 \times \text{left atrial diameter (mm)}] + [0.00446131 \times \text{maximal (rest/Valsalva) left ventricular outflow tract gradient (mm Hg)}] + [0.4583082 \times \text{family history SCD}] + [0.82639195 \times \text{NSVT}] + [0.71650361 \times \text{unexplained syncope}] - [0.01799934 \times \text{age at clinical evaluation (years)}]$.

O'Mahony, Eur Heart J 2014





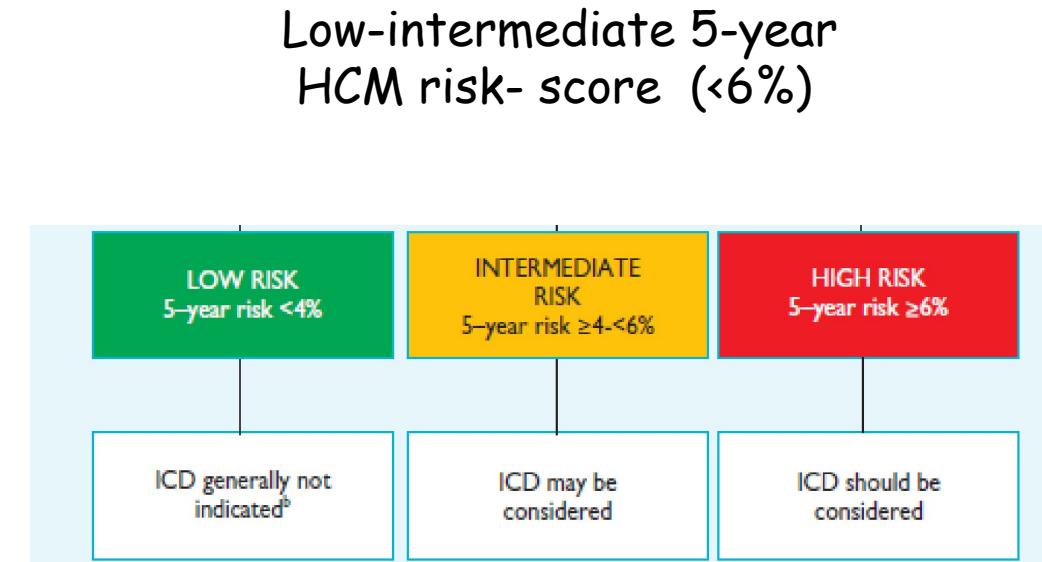
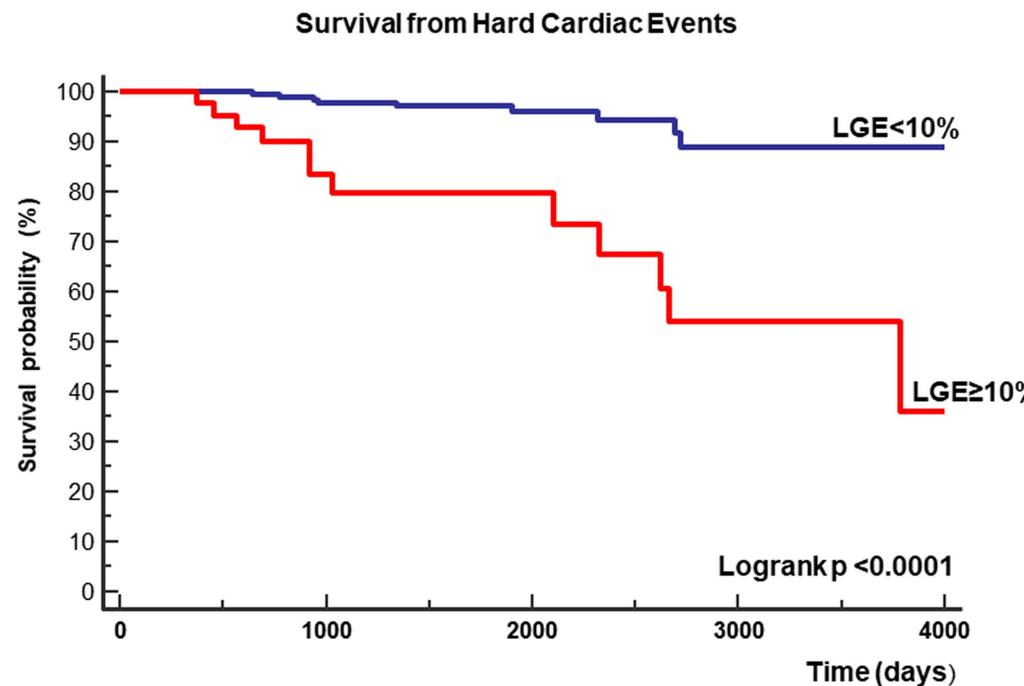
Late Enhancement in Hypertrophic Cardiomyopathy: Prognostic role of extent



Prognostic Role of Late Gadolinium Enhancement in Patients With Hypertrophic Cardiomyopathy and Low-to-Intermediate Sudden Cardiac Death Risk Score



Giancarlo Todiere, MD, PhD^a, Cinzia Nugara, MD^{b,c}, Giovanni Gentile, MD^d, Francesco Negri, MD^e, Francesco Bianco, MD, MD^{b,f}, Calogero Falletta, MD^d, Giuseppina Novo, MD, PhD^b, Gianluca Di Bella, MD, PhD^g, Raffaele De Caterina, MD, PhD^f, Elisabetta Zachara, MD^h, Federica Re, MD^h, Francesco Clemenza, MD^d, Gianfranco Sinagra, MD, PhD^e, Michele Emdin, MD, PhD^{a,i}, and Giovanni Donato Aquaro, MD^{a,*}

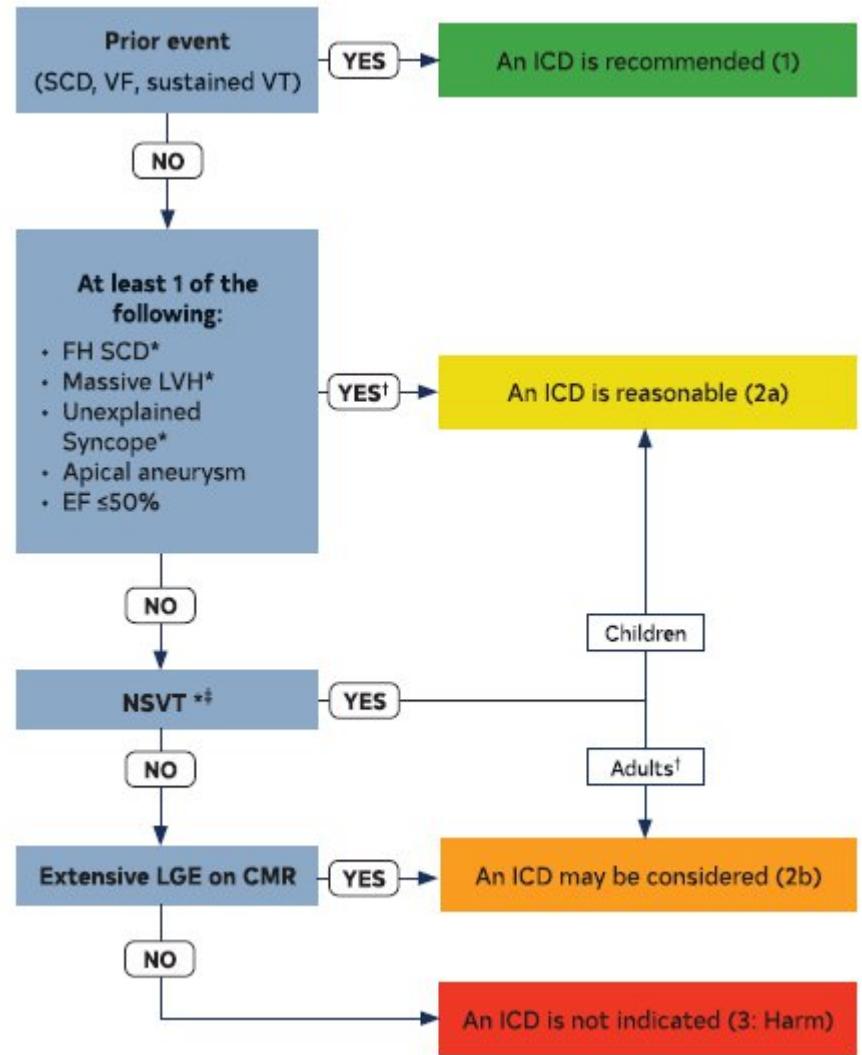
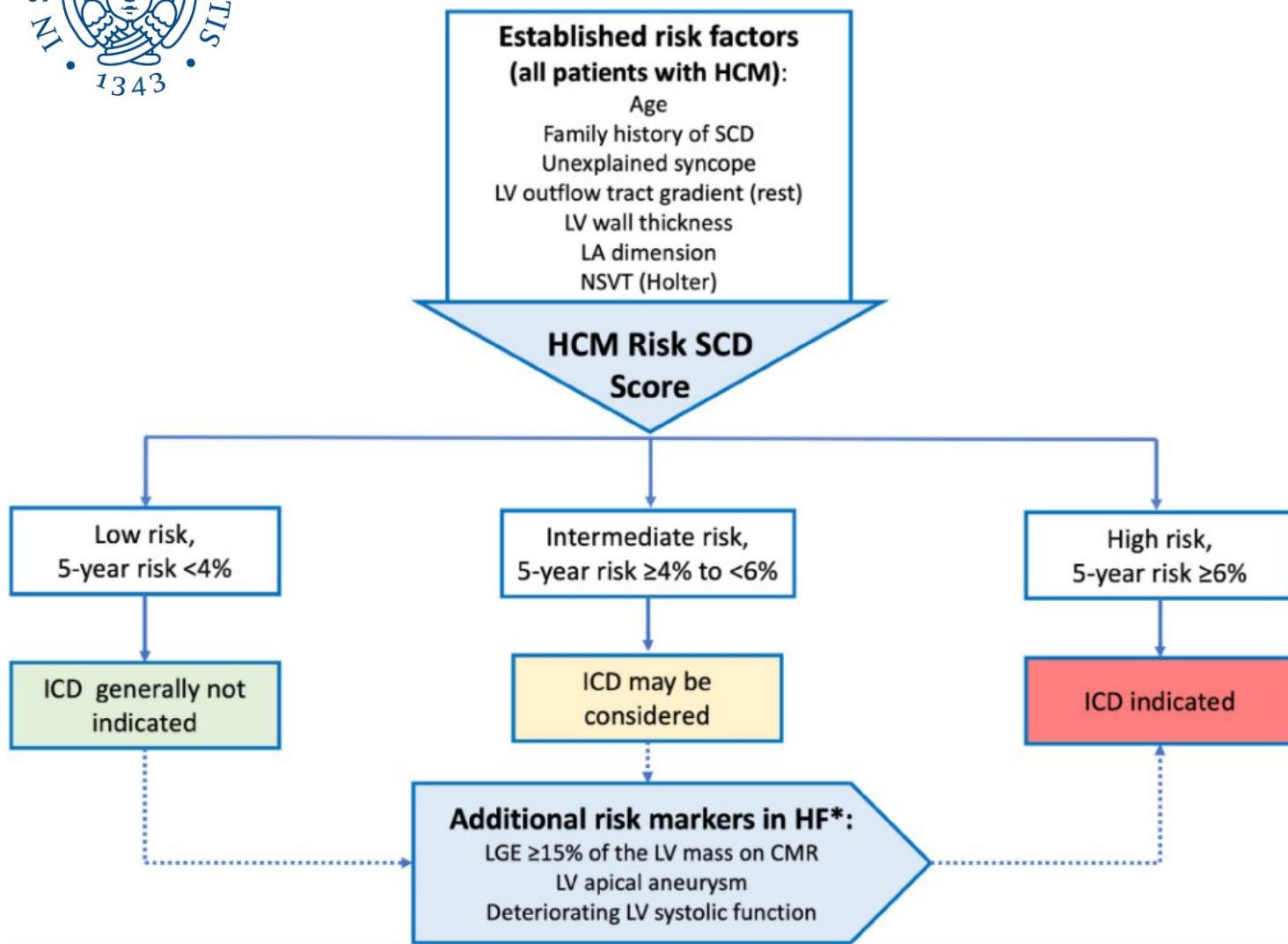


Number at risk

LGE<10%: 261 164 69 27 6

LGE≥10%: 70 22 14 3 2

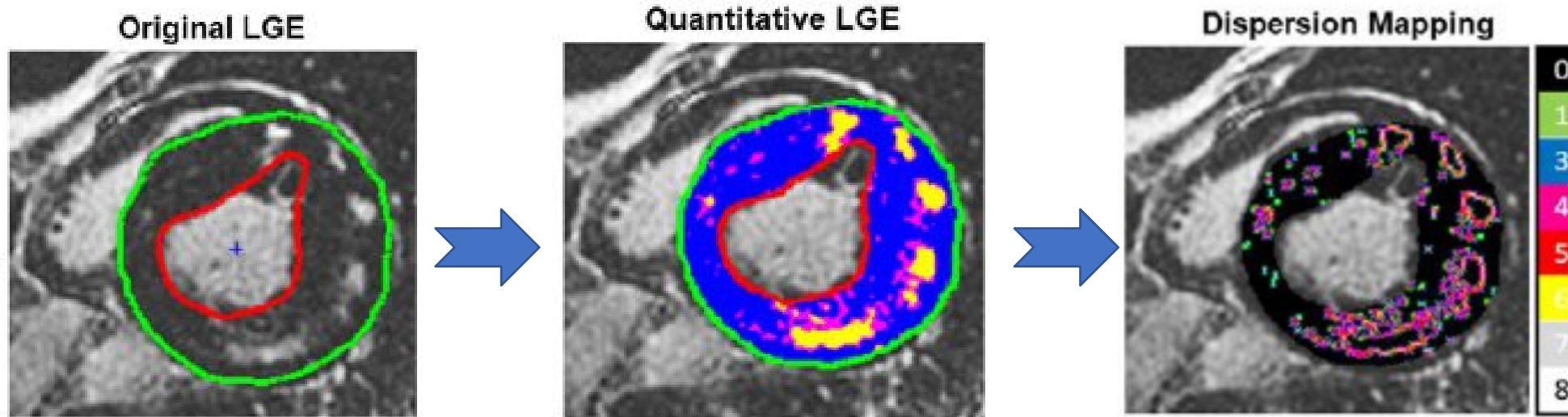
Prognostic role of extent!



AHA/ACC guidelines 2020

Radiomics in post processing: second order metrics

LGE Dispersion Mapping: 3 intensities mode



Dispersion score 0 Dispersion score 2 Dispersion score 5

1	2	3
4	A	5
6	7	8

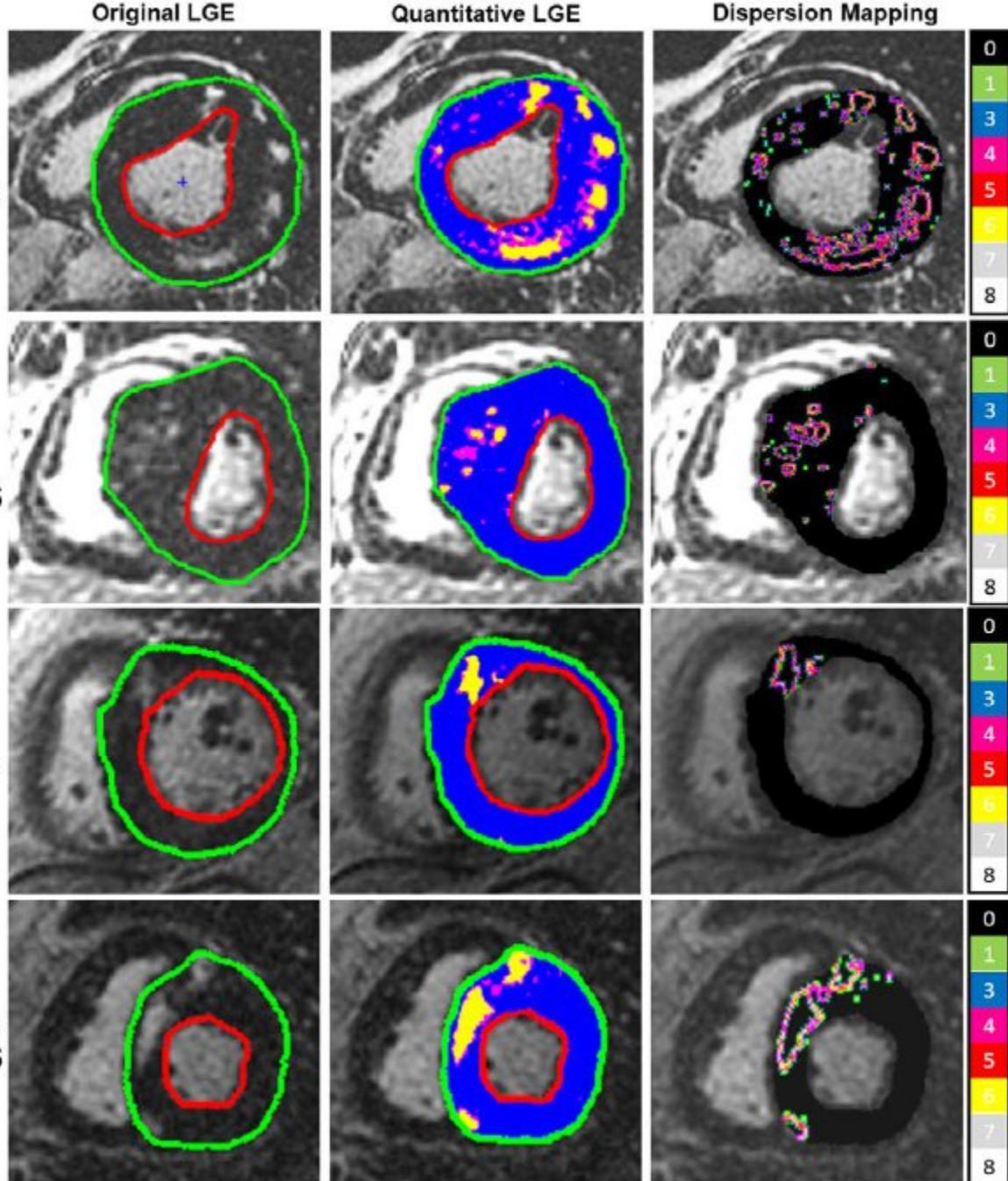
1	2	3
4	B	5
6	7	8

1	2	3
4	C	5
6	7	8

1	2	3
4	D	5
6	7	8

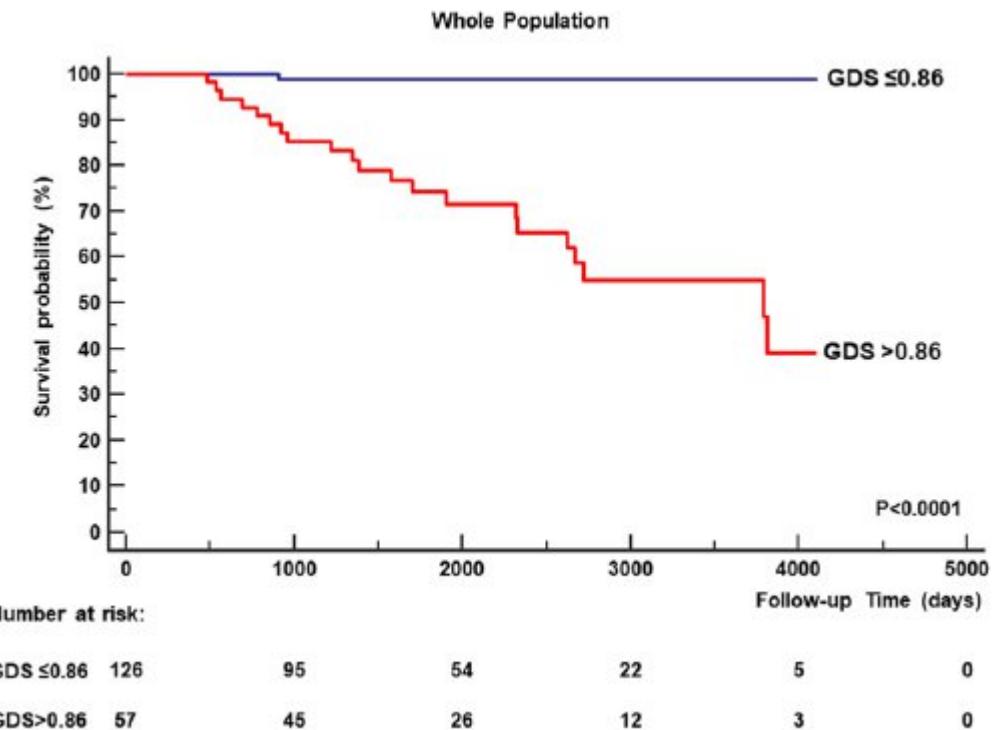
1	2	3
4	E	5
6	7	8

1	2	3
4	F	5
6	7	8



Late Gadolinium Enhancement–Dispersion Mapping

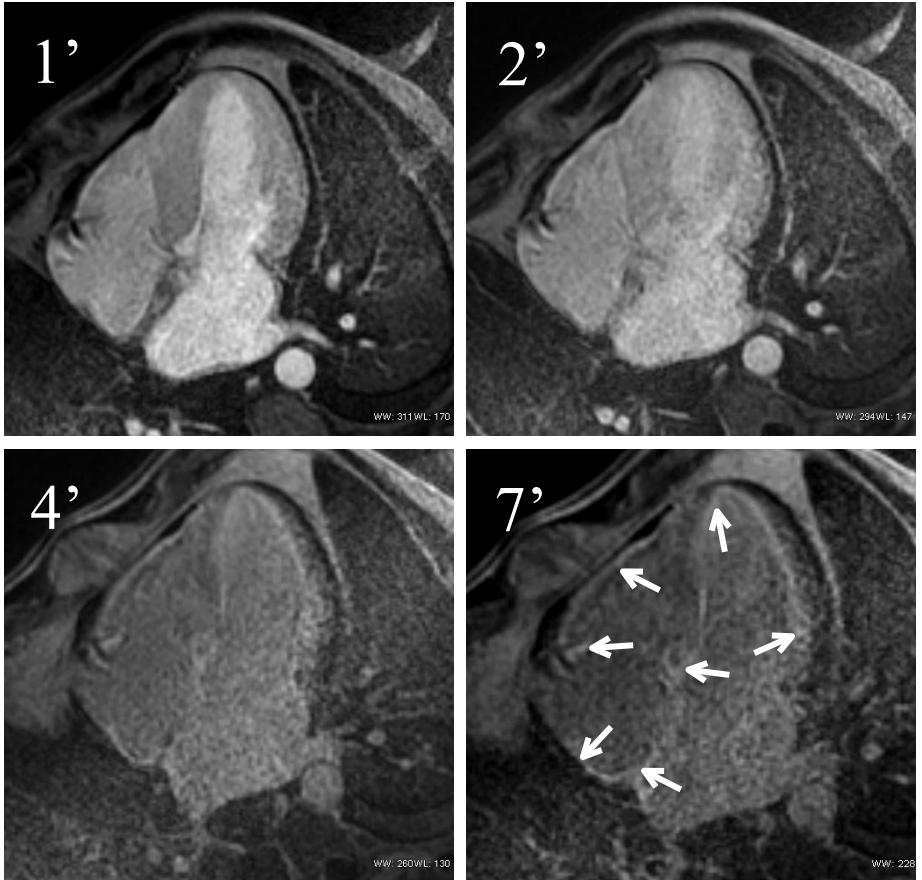
A New Magnetic Resonance Imaging Technique to Assess Prognosis in Patients With Hypertrophic Cardiomyopathy and Low-Intermediate 5-Year Risk of Sudden Death



Prognostic role of LGE Dispersion!

Cardiac Amyloidosis

Late gadolinium enhancement: diagnostic role



- Diffuse subendocardial enhancement
- early darkening of LV cavity
-
- Abnormal myocardial nulling
- septal subepicardial enhancement
- atrial and RV wall enhancement

Prevalence of LGE Pattern in
cardiac amyloidosis

Specificity 100%
Sensitivity 85%

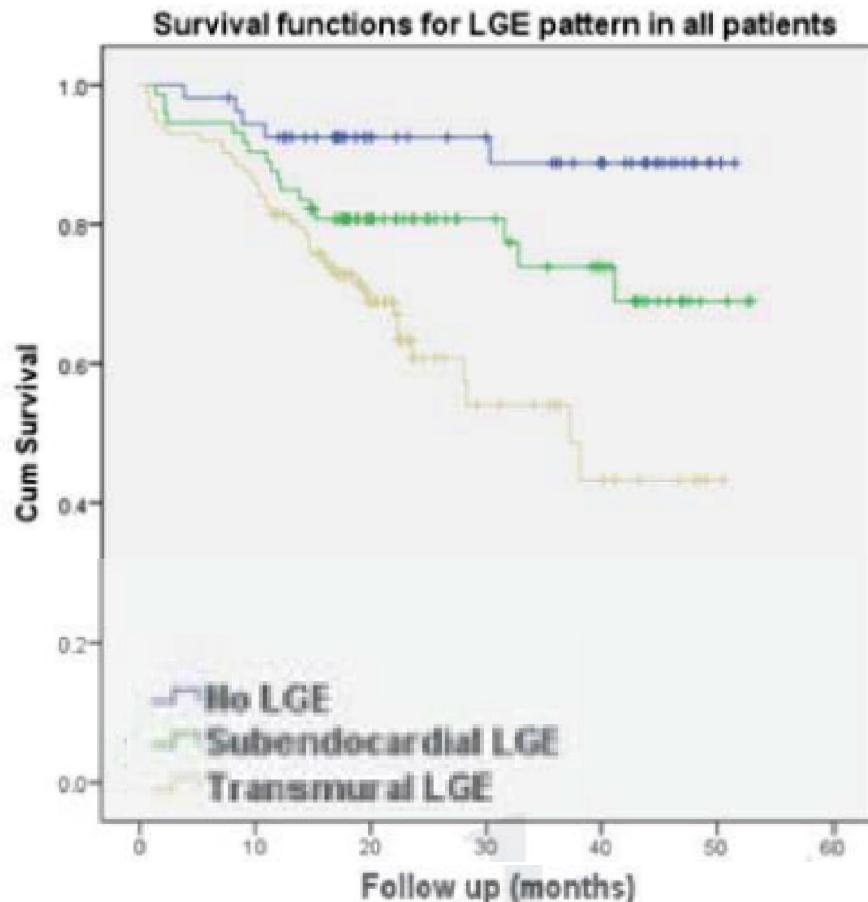


Cardiac Amyloidosis: CMR

Late gadolinium enhancement

119 with systemic AL amyloid, only 7 confirmed cardiac involvement by EMB

122 ATTR amyloidosis, DPD-SPECT in % unknown



	All patients n=250	AL patients [∞]		ATTR patients	
	No LGE n=37	Subendocardial LGE n=42	Transmural LGE n=30	No LGE n=17	Subendocardial LGE n=31
LV mass, g	203±77	140±45	170±60	204±56 [†]	109±25
LV mass _i , g/m ²	108±39	78±29	88±28	108±25 [†]	61±12
Maximal IVS, mm	15±4	11±2	14±3	16±3	10±2
EDV, mL	125±30	118±29	123±32	114±28	119±25
EDV _i , mL/m ²	67±16	64±17	65±16	61±16	67±12
ESV, mL	52±27	35±18	42±22	50±21*	38±19
ESV _i , mL/m ²	27±14	18±11	22±12	27±12*	21±9
SV, mL	74±20	83±20	81±21	64±17 [†]	81±16
SV _i , mL/m ²	39±10	45±9	43±11	35±9 [†]	46±8
LVEF, %	60±14	72±9	67±12	57±11 [†]	69±11
LA area, cm ²	27±7	23±6	25±6	26±5*	22±3
LA area _i , cm ² /m ²	15±3	13±4	13±3	14±2	12±2
RA area, cm ²	25±8	21±5	22±6	24±7	20±3
RA area _i , cm ² /m ²	13±4	12±3	12±3	13±3	11±2
MAPSE, mm	9±4	12±4	9±4	6±3 [†]	14±2
TAPSE, mm	15±6	21±3	17±5	12±5 [†]	23±3
Precontrast T1, ms	1082±75	993±46	1100±58	1150±68 [†]	968±41
ECV, %	0.50±0.12	0.31±0.04	0.47±0.06	0.58±0.07 [†]	0.29±0.04

Pts with negative LGE:
normal LV wall thickness, no ecg signs, normal BNP, no troponin elevation

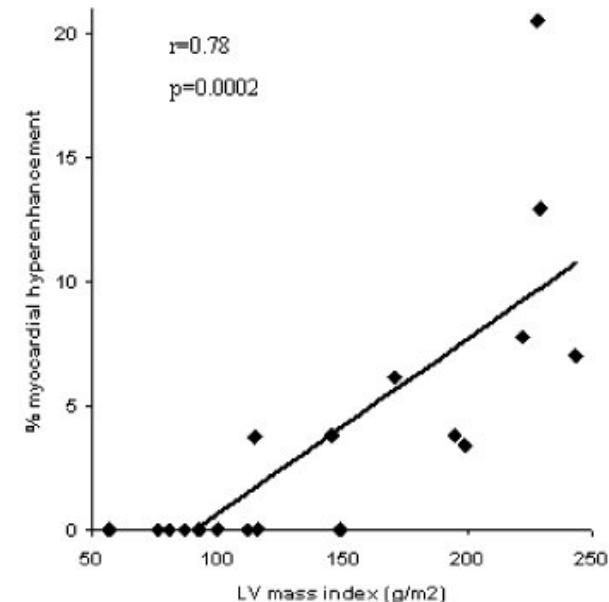
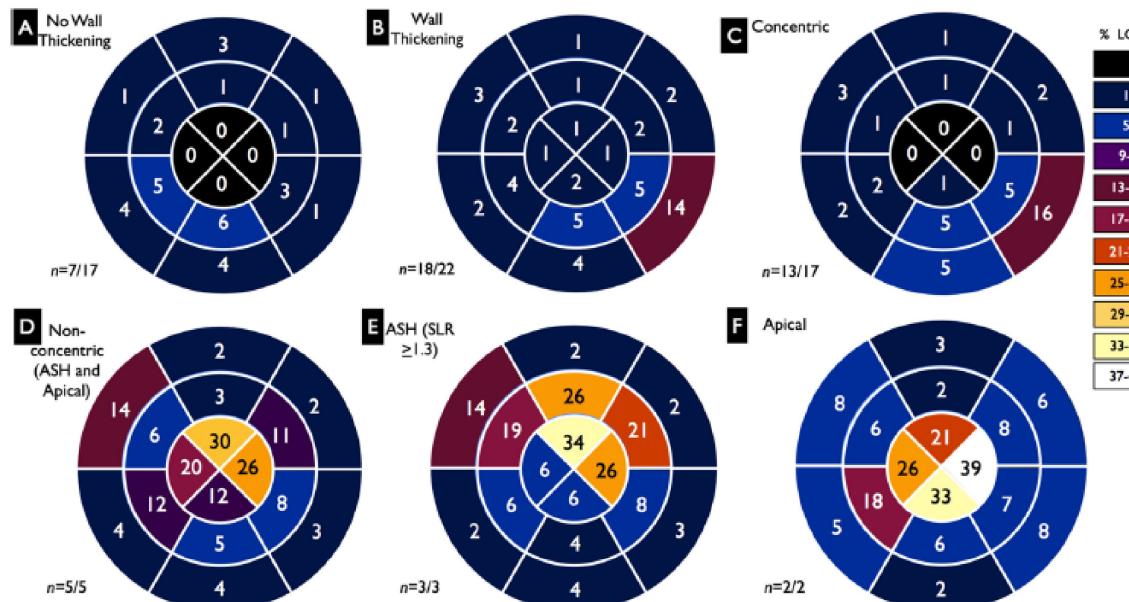


Pattern of LGE in Fabry disease

Intracellular
Globotriaosylceramide
overload
(NO LGE)

Myocytes
necrosis

LGE
(late manifestation)

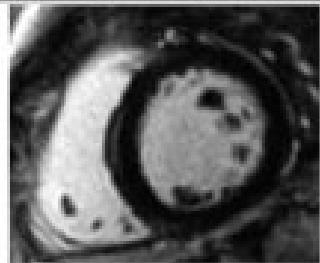


Deva et al. Journal of Cardiovascular Magnetic Resonance (2016) 18:14

Moon, Eur Heart J, 2003

LGE and Enzyme-Replacement Therapy in Fabry disease

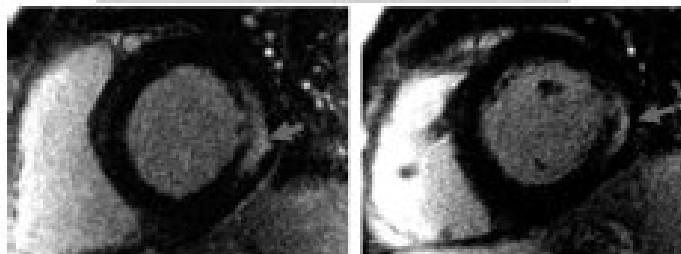
Patient: "No Fibrosis"



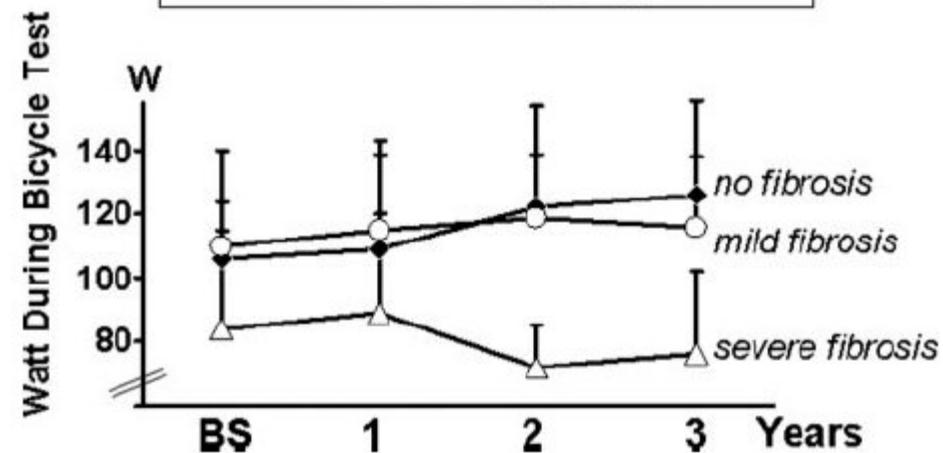
Patient: "Mild Fibrosis"



Patient: "Severe Fibrosis"



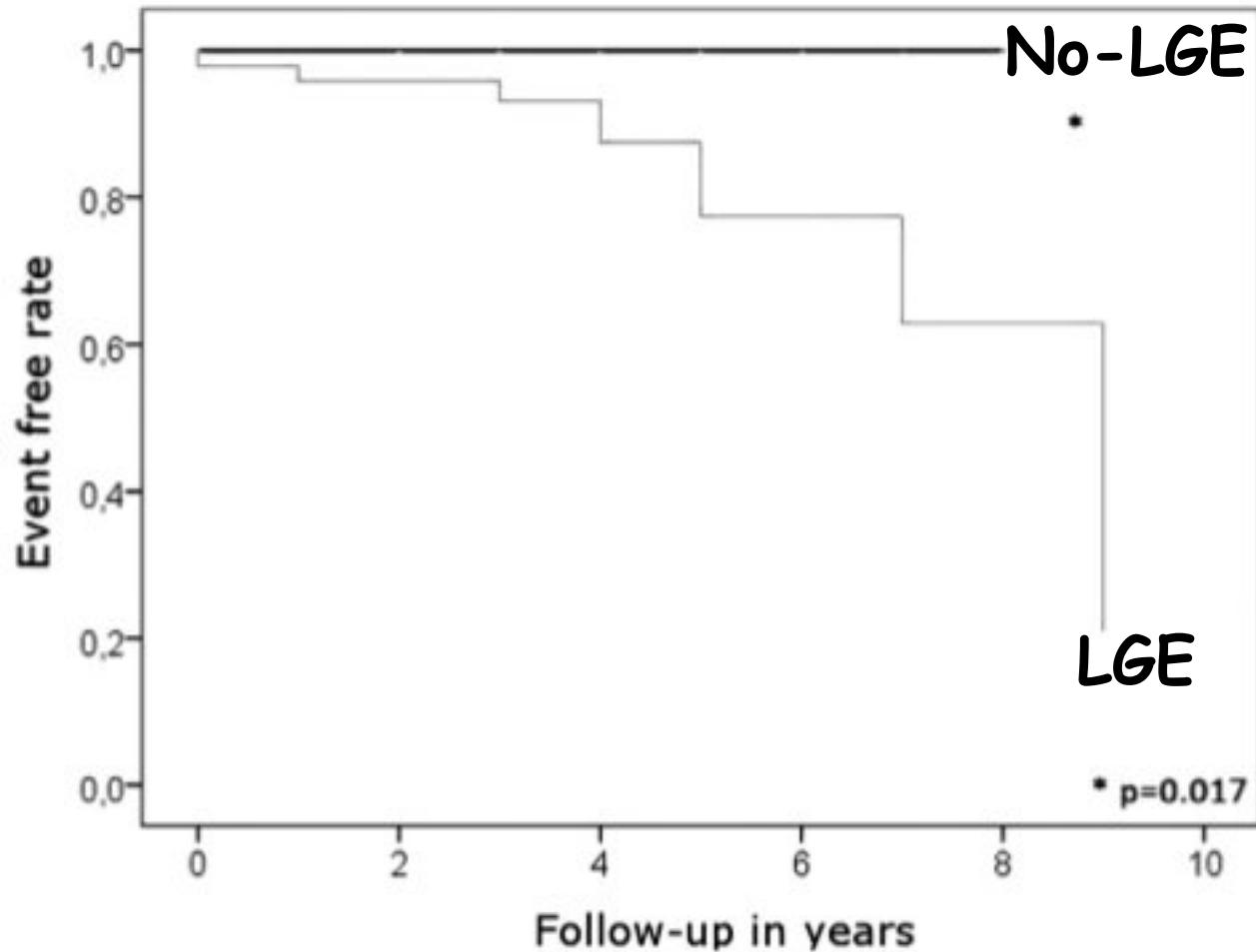
Exercise Capacity



	Fibrosis	Baseline	1 Year	2 Years	3 Years	P
LVEDD	No	48±4	49±4	49±6	49±4	0.89*
	Mild	49±5	48±5	47±5	48±6	0.99†
	Severe	51±12	49±5	47±3	49±6	0.69†
PWT, mm	No	13.0±1.2	11.7±1.6	11.3±1.8	11.5±1.6	<0.01*
	Mild	14.4±2.2	13.1±2.4	13.3±2.4	12.9±1.8	0.21†
	Severe	14.7±2.7	13.3±2.3	13.4±2.5	12.8±2.3	0.17†
Septum, mm	No	13.5±1.4	12.1±1.0	11.9±1.2	12.0±1.4	<0.01*
	Mild	14.4±1.8	13.3±1.9	13.4±1.9	13.4±1.4	0.20†
	Severe	14.9±3.0	14.3±2.7	14.3±2.6	14.1±2.0	0.01†
LV mass, g	No	238±42	213±46	201±65	202±46	<0.01*
	Mild	275±62	244±60	234±47	244±65	0.31†
	Severe	303±84	255±58	246±70	247±45	0.24†



Non sustained VT, sustained VT, sudden cardiac death

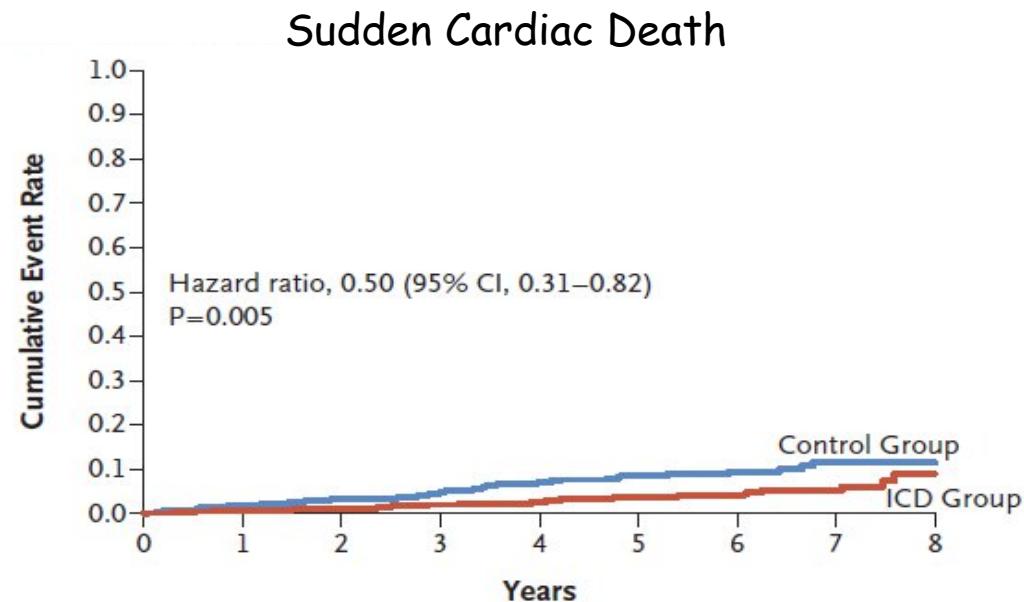
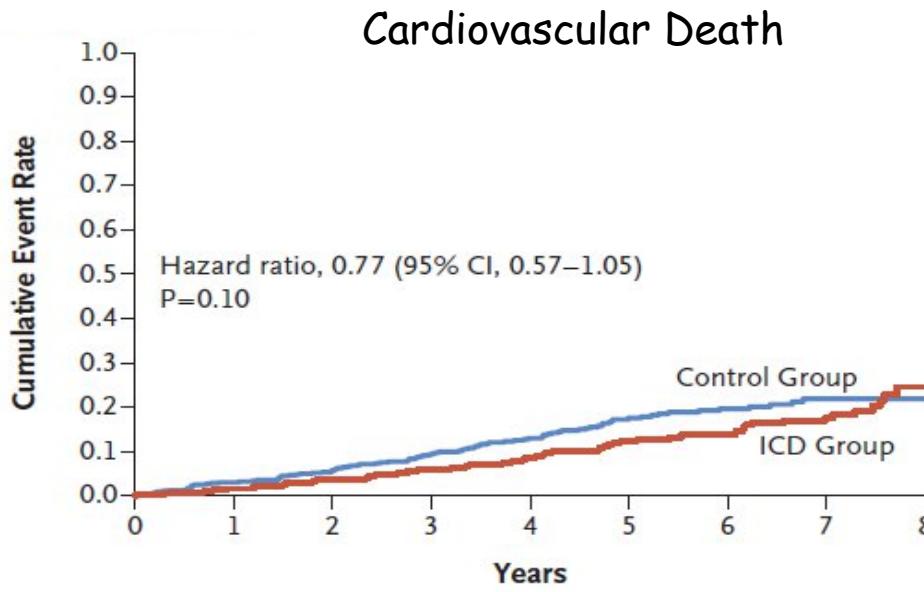


Annual increase in LGE was:
0.9±0.6% in patients with MVAs
0.2± 0.3% in patients without MVAs
($p <0.001$).

Non Ischemic Dilated Cardiomyopathy: LV dysfunction and Dilation



MADIT I&II trials: EF<35% \oplus ICD implantation



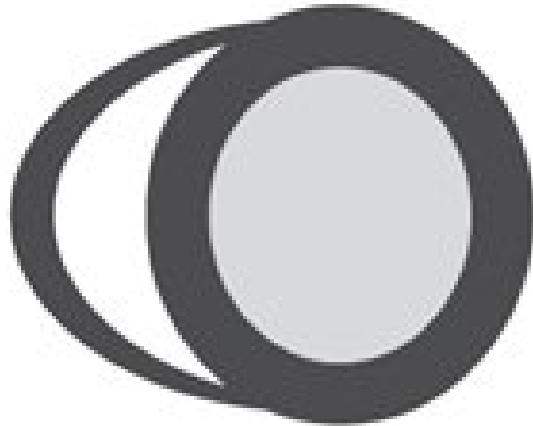
LVEF \leq 35%

ICD does not improve survival in pts di DCM

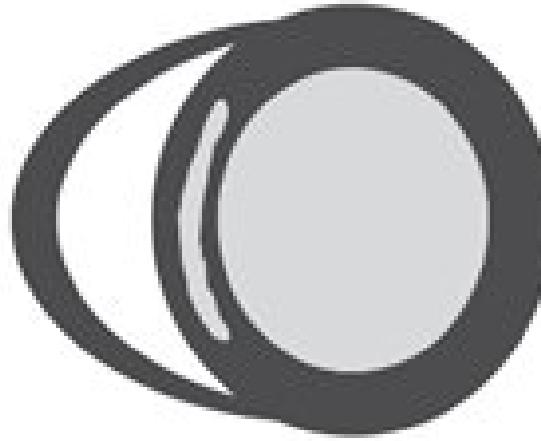


LGE in Dilated Cardiomyopathy

No LGE: 65-75%



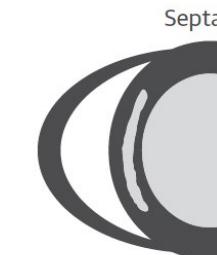
Non ischemic LGE: 25-35%



Ischemic LGE: 0-5%

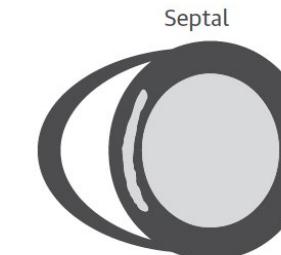


LGE location



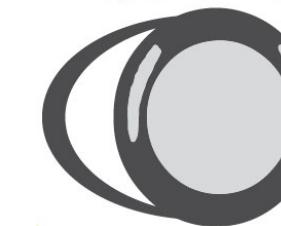
Septal

47%



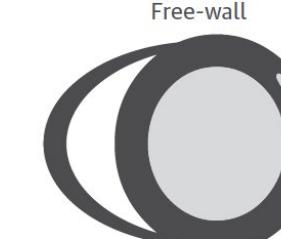
Focal

8%



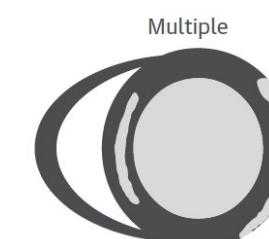
Septal and free-wall

39%



Free-wall

14%



Multiple

23%

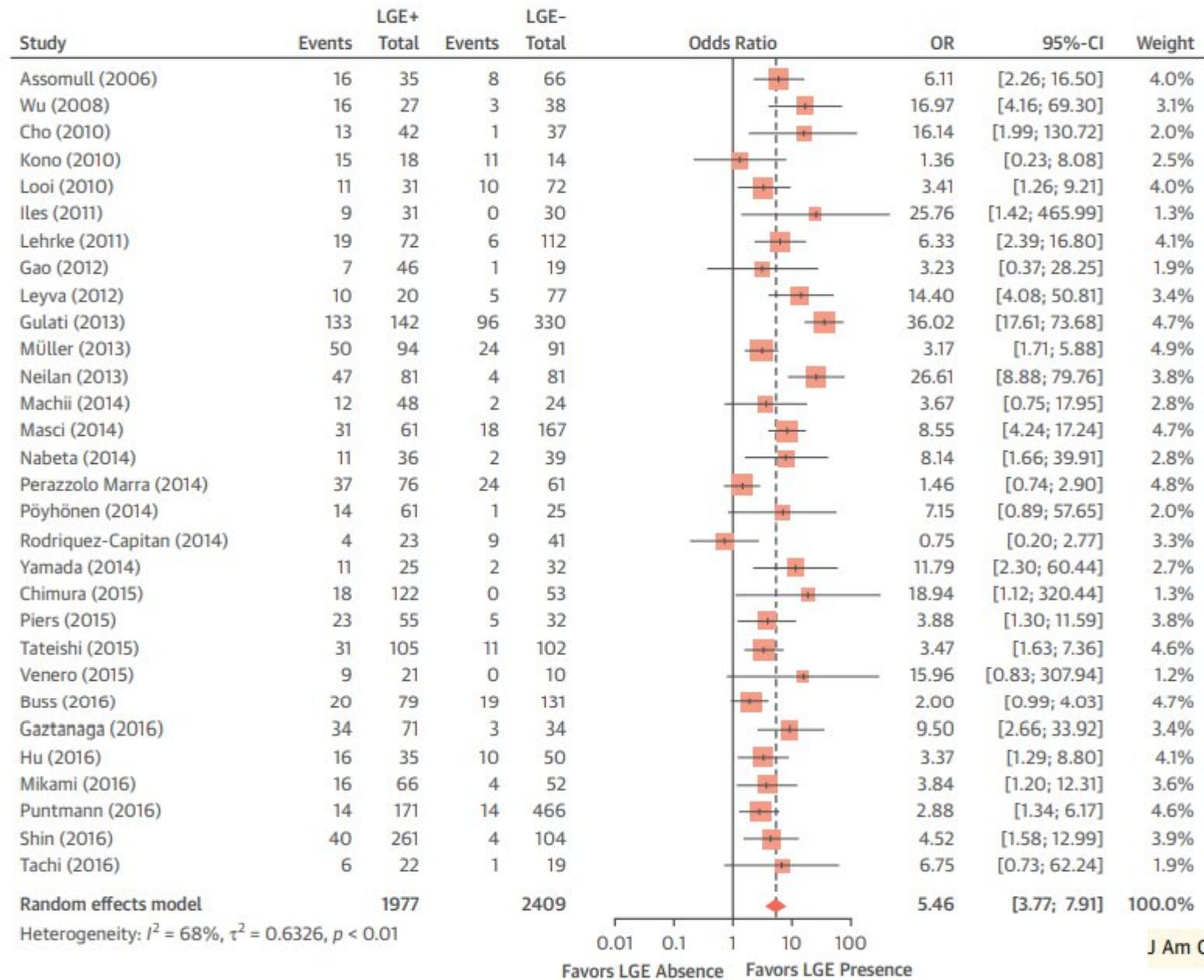


MAJOR CARDIOVASCULAR EVENTS

The Prognostic Value of Late Gadolinium-Enhanced Cardiac Magnetic Resonance Imaging in Nonischemic Dilated Cardiomyopathy

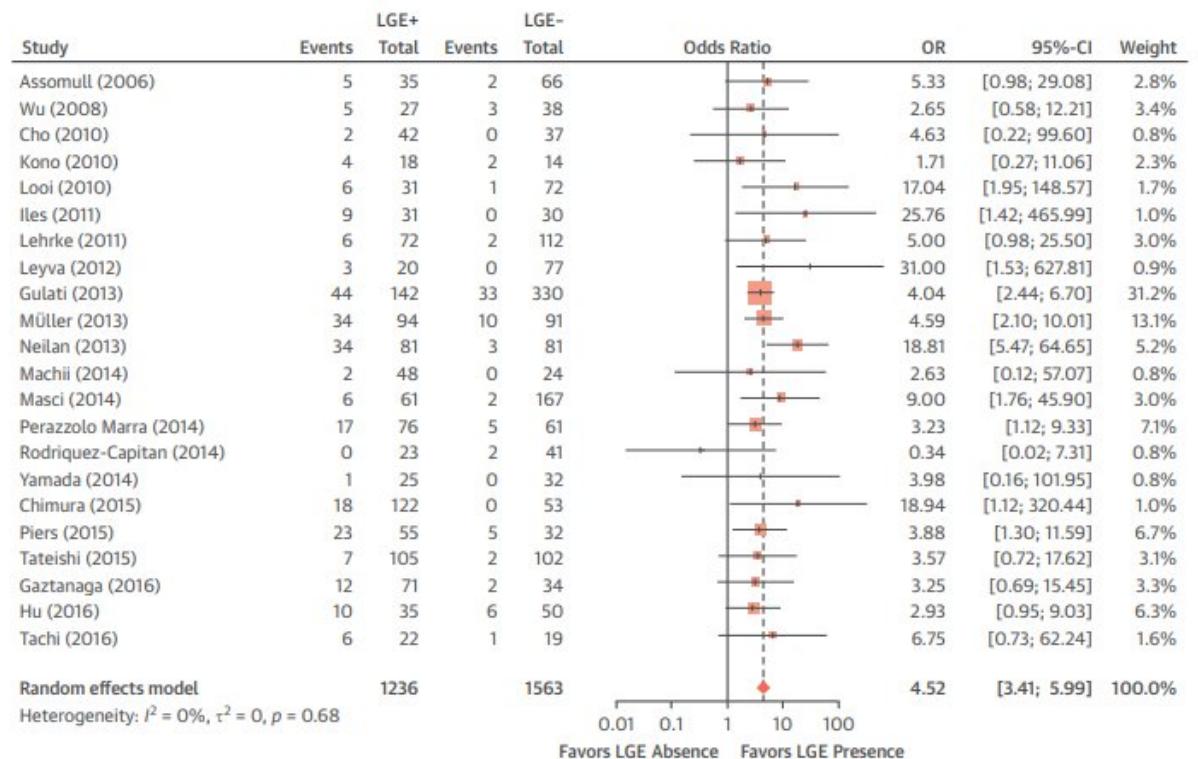
Marthe A.J. Becker, MD,^{a,b} Jan H. Cornel, MD, PhD,^a Peter M. van de Ven, PhD,^b Albert C. van Rossum, MD, PhD,^b Cornelis P. Allaart, MD, PhD,^b Tjeerd Germans, MD, PhD^{a,b}

**Prognostic role of LGE presence:
OR 5.46**



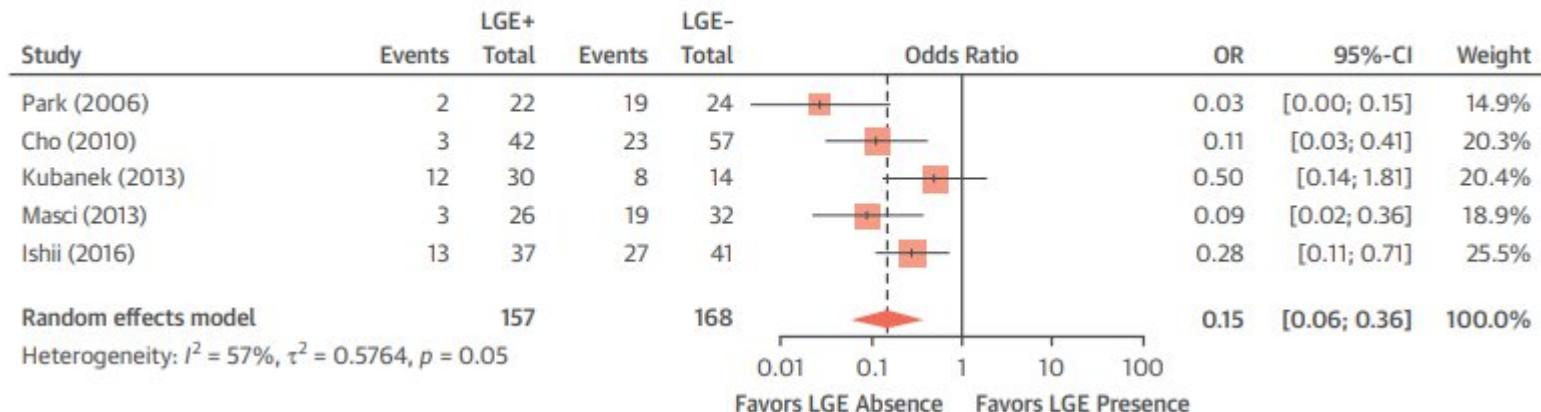


VENTRICULAR TACHYARRHYTHMIC EVENTS



Prognostic role of
LGE presence:
OR 4.5

REVERSE REMODELLING



LGE
OR 0.15



Prognostic role of LGE presence in mild-moderate dysfunction

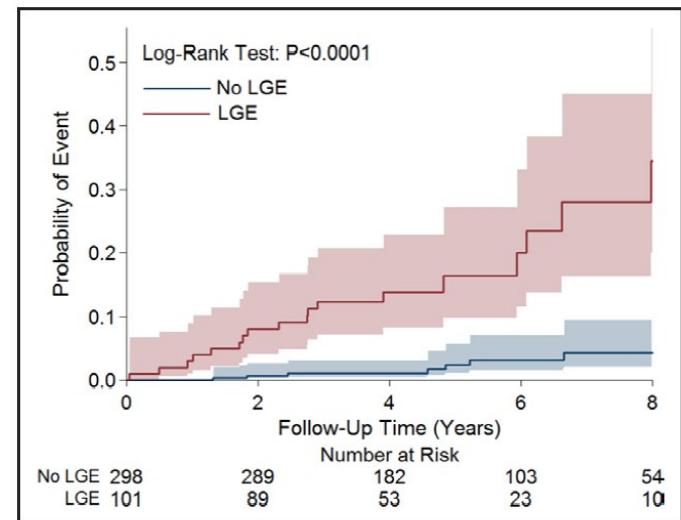


Figure 2. Primary end point survival analysis.
Kaplan-Meier curve of the time to first event for the primary end point by presence (red line) or absence (blue line) of midwall late gadolinium enhancement (LGE).

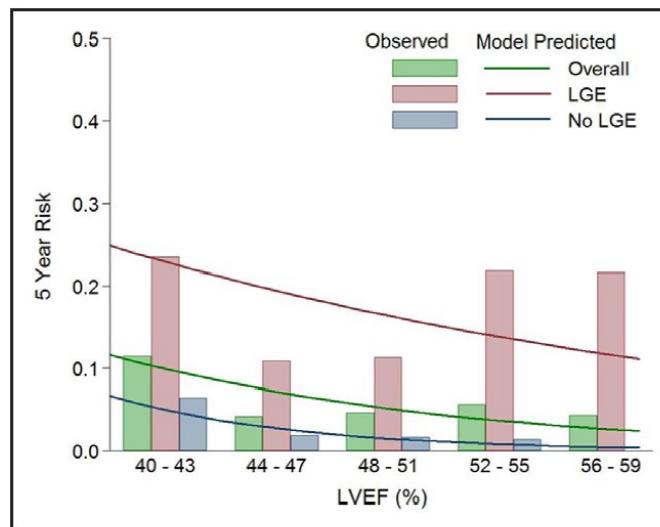


Figure 3. Five-year risk estimates of the primary end point.

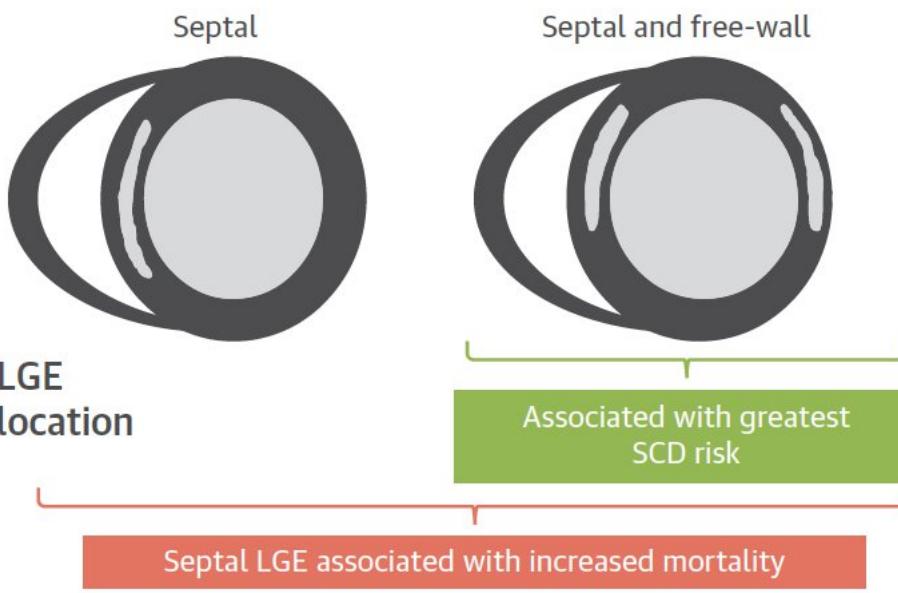
Five-year risk estimates for primary end point based on LVEF alone (green line) and midwall LGE status in addition to LVEF (red line, presence of LGE; blue line, absence of LGE). LGE indicates late gadolinium enhancement; and LVEF, left ventricular ejection fraction.

Table 2. Univariable and Multivariable Analyses for the Primary End Point

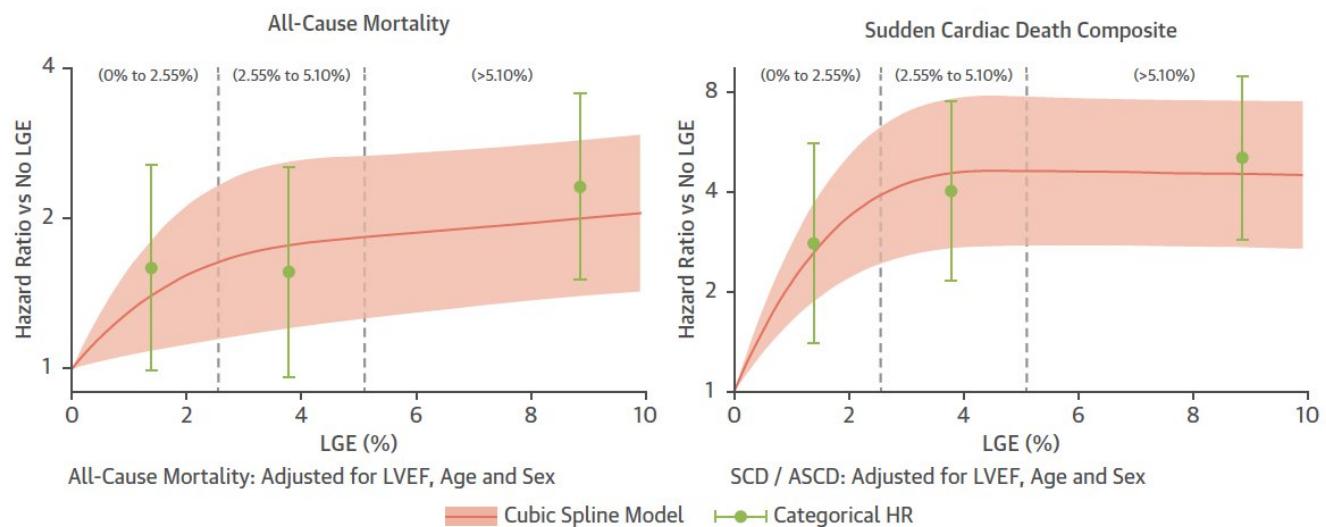
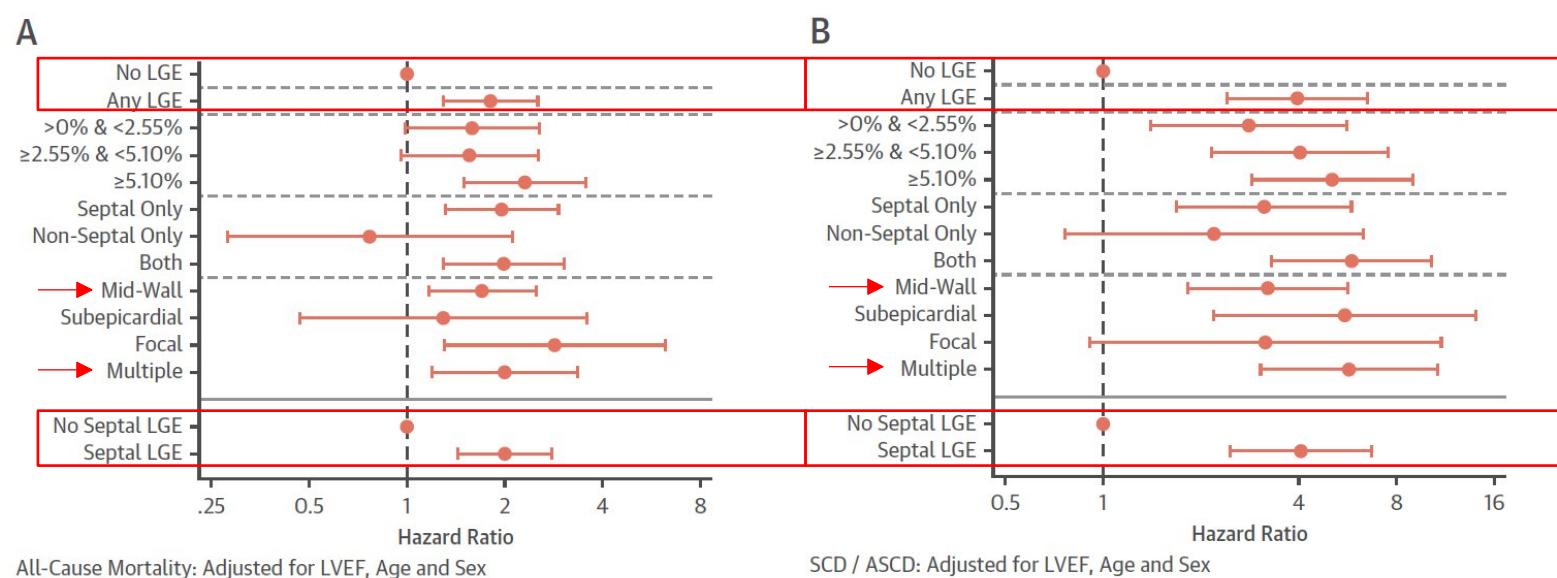
Outcome	LGE Status	Events n (%)	Univariable		Multivariable*	
			HR (95% CI)	P Value	HR (95% CI)	P Value
SCD or Aborted SCD	LGE-	7 (2.3)	9.2 (3.9, 21.8)	<0.0001	9.3 (3.9, 22.3)	<0.0001
	LGE+	18 (17.8)				
SCD	LGE-	6 (2.0)	4.9 (1.8, 13.5)	0.002	4.8 (1.7, 13.8)	0.003
	LGE+	9 (8.9)				
Aborted SCD	LGE-	1 (0.3)	34.8 (4.6, 266.6)	<0.0001	35.9 (4.8, 271.4)	<0.001
	LGE+	10 (9.9)				

399 DCM Patients with LVEF $\geq 40\%$
median-LVEF: 50% [IQR 46%-54%]
LGE+: 25.3%
median-FUP: 4.6Y
Primary endpoint: SCD/aborted-SCD

Prognostic role of LGE pattern: Midwall septal LGE



874 DCM Patients
mean-FUP: 4.9Y [IQR 3.5-7]
Primary endpoint: all-cause mortality
Secondary endpoint: SCD/aborted-SCD

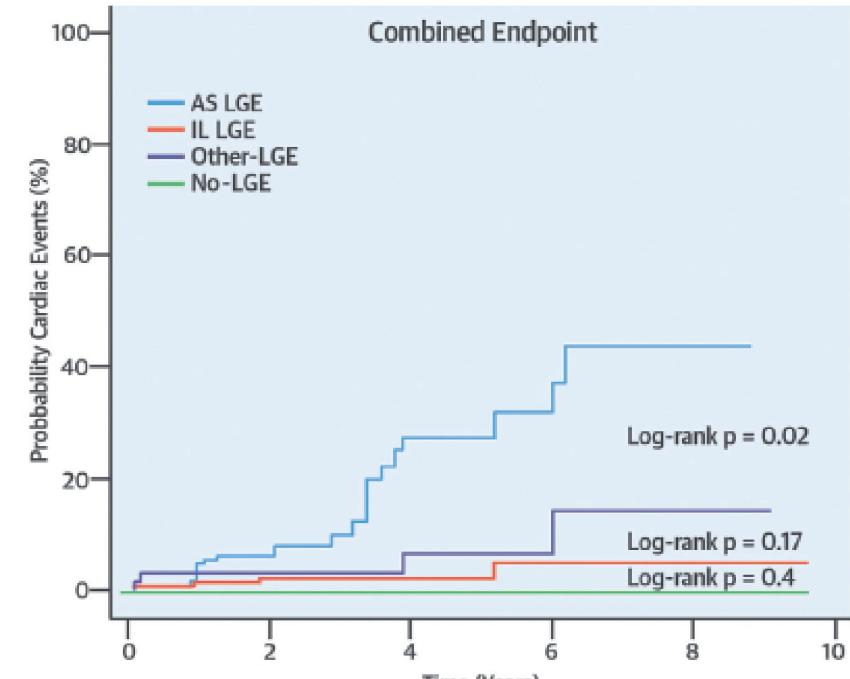
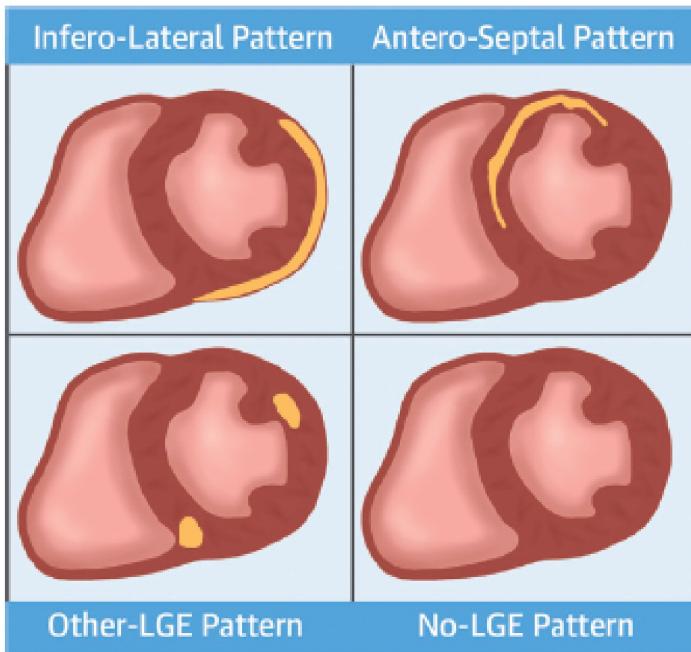


Cardiac MR With Late Gadolinium Enhancement in Acute Myocarditis With Preserved Systolic Function



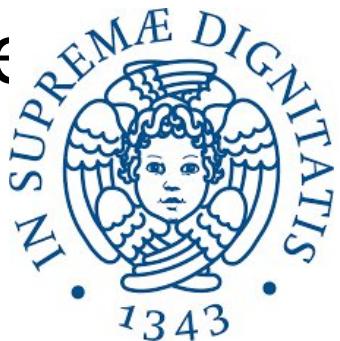
ITAMY Study

386 pts with Acute Myocarditis and preserved EF

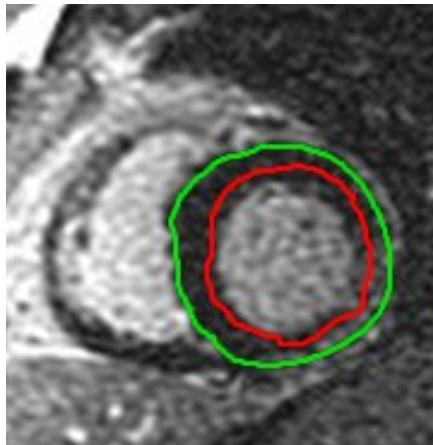


Prognostic role of
LGE pattern:
Midwall septal LGE

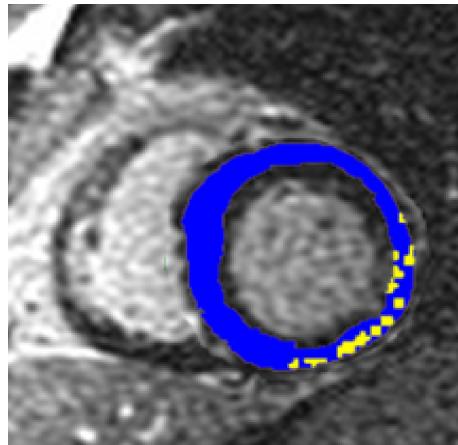
LGE Dispersion Mapping in DCM: 2 intensities mode



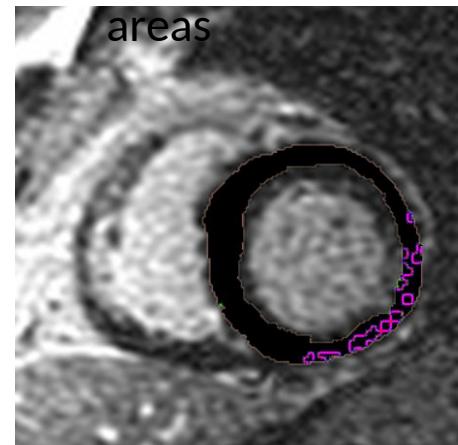
Low LGE areas



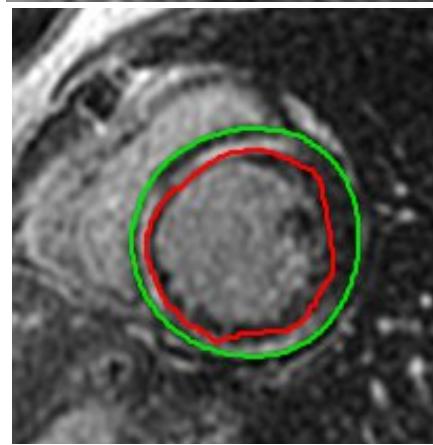
Quantitative LGE: 5%



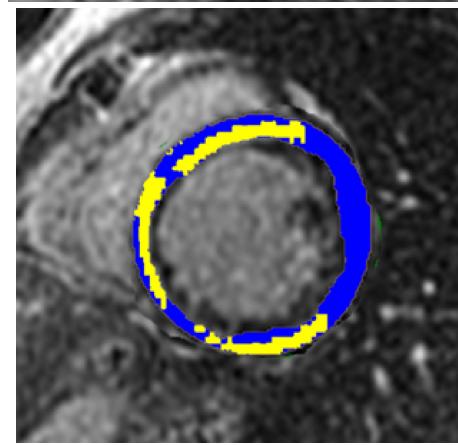
High GDS areas



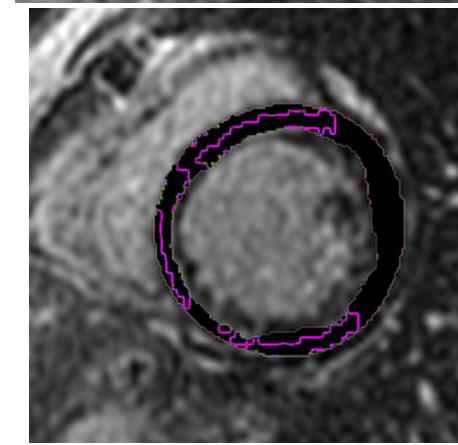
High LGE areas



Quantitative LGE:
20%



Low GDS areas



④ Cardiac Arrest during FU

④ No event during FU

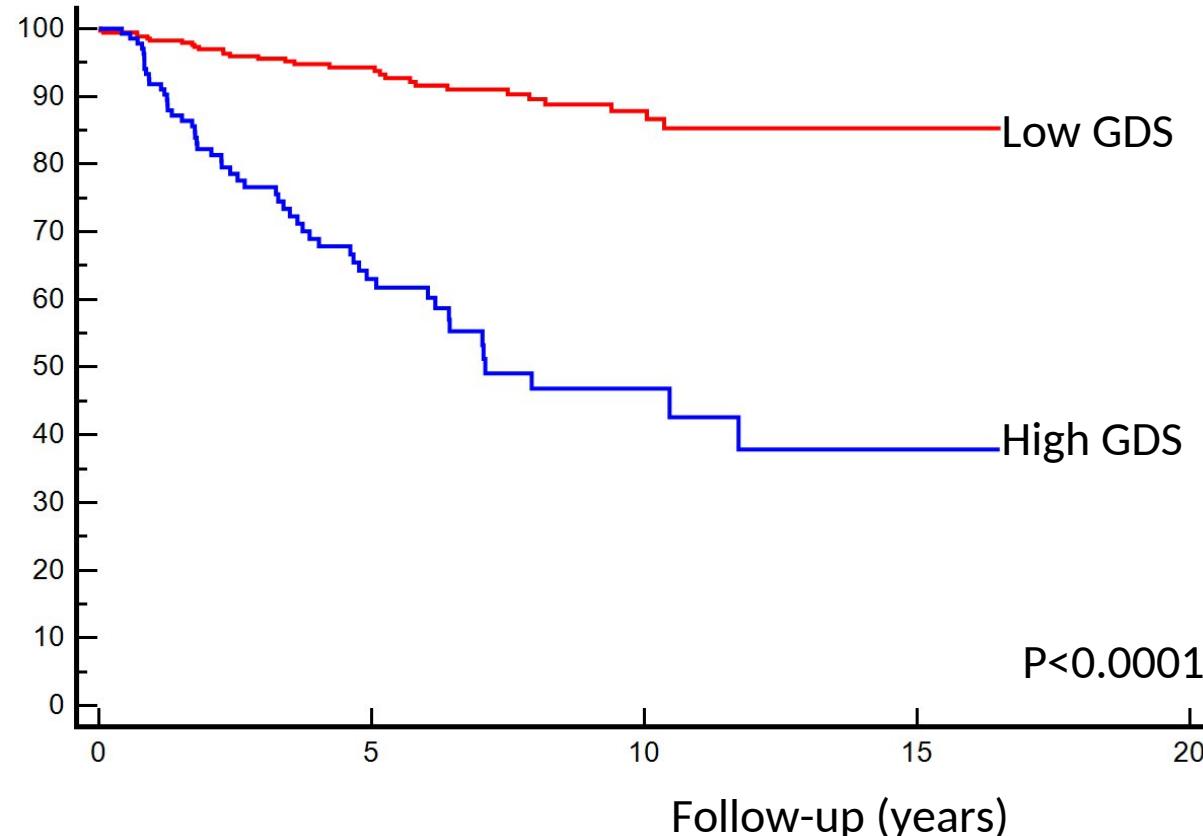
LGE Dispersion Mapping in DCM

510 pts with DCM



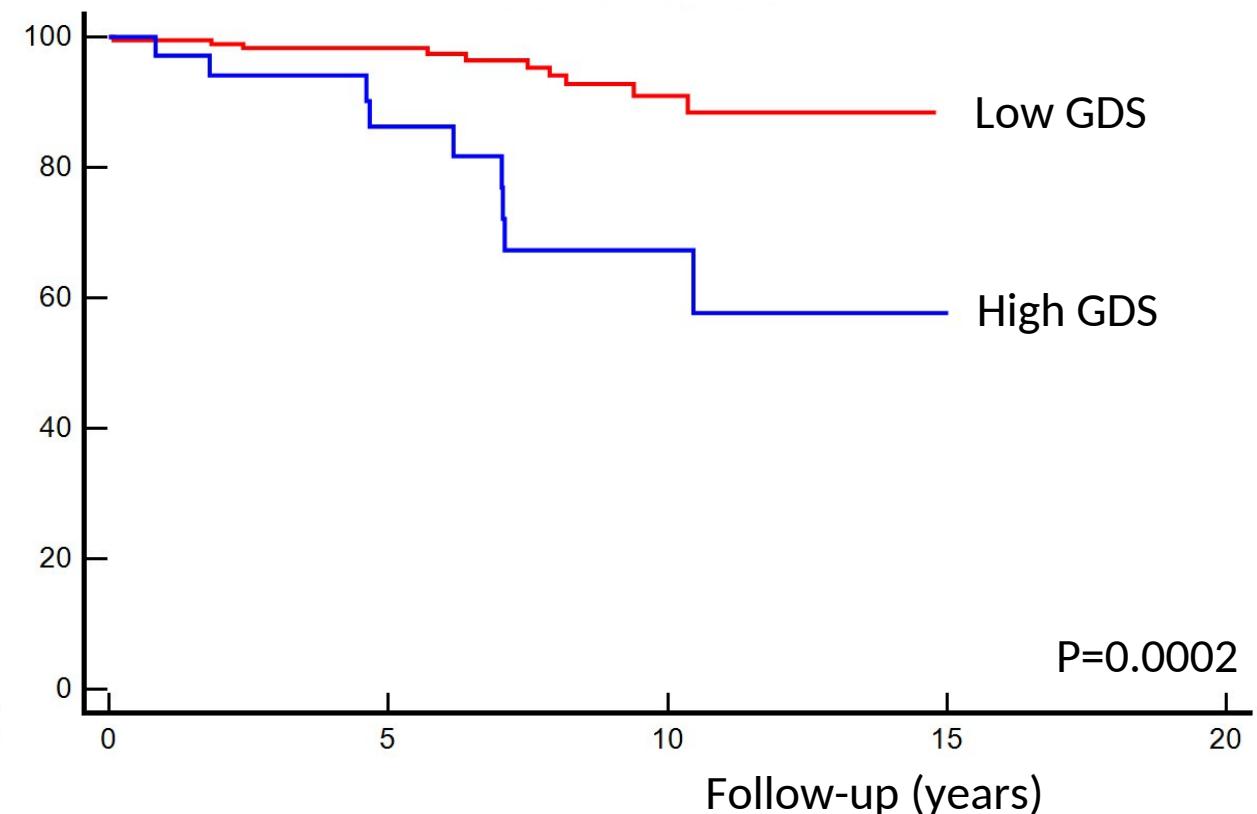
Whole population

Combined Endpoint (SCD, ICD intervention, Cardiac arrest)



DCM with EF>35%

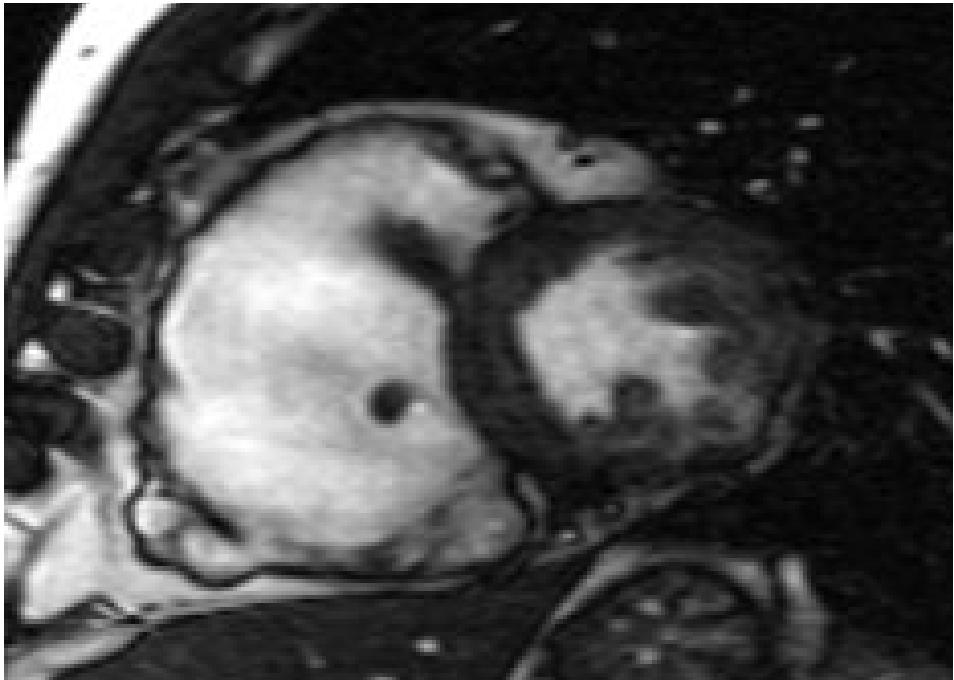
Combined Endpoint (SCD, ICD intervention, Cardiac arrest)



MRI IN ARVC



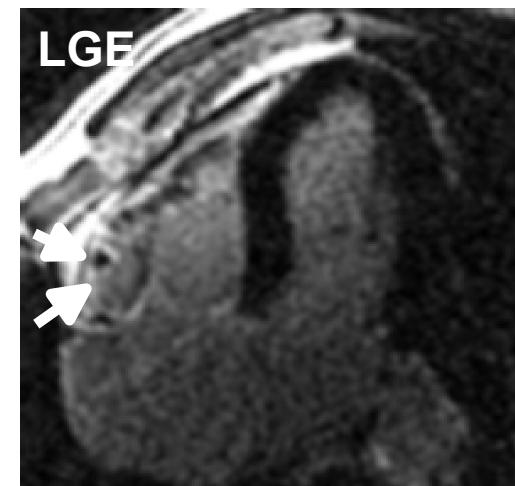
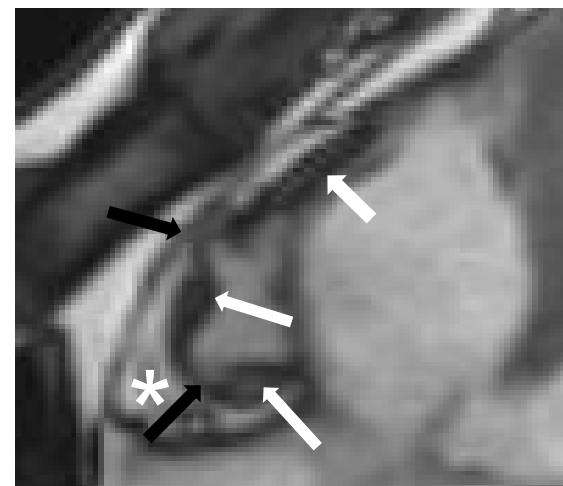
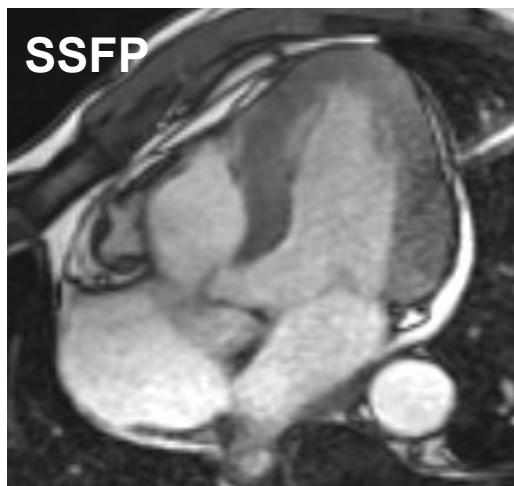
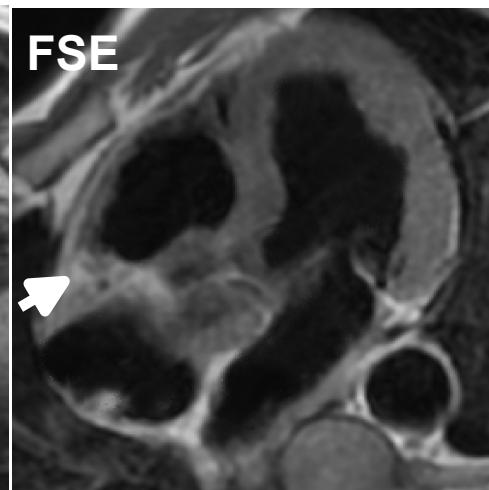
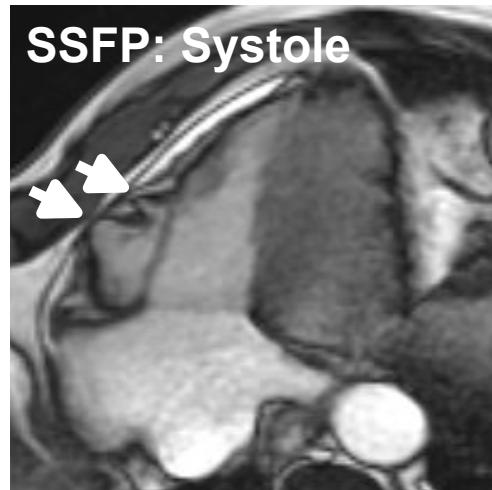
Lone RV involvement with RV dysfunction/RV dilation



MRI IN ARVC



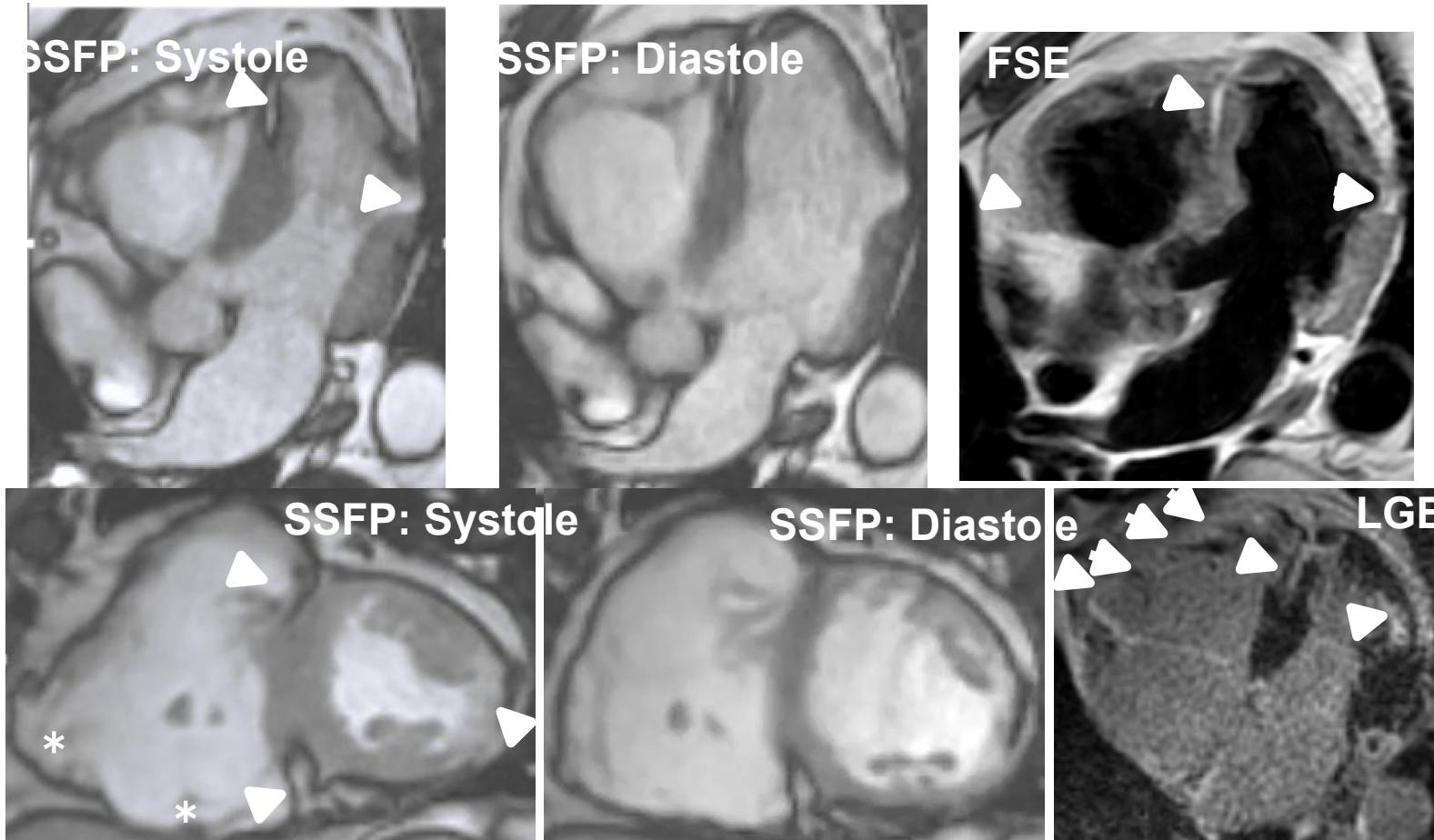
Lone RV involvement without RV dysfunction/dilation



MRI IN ARVC



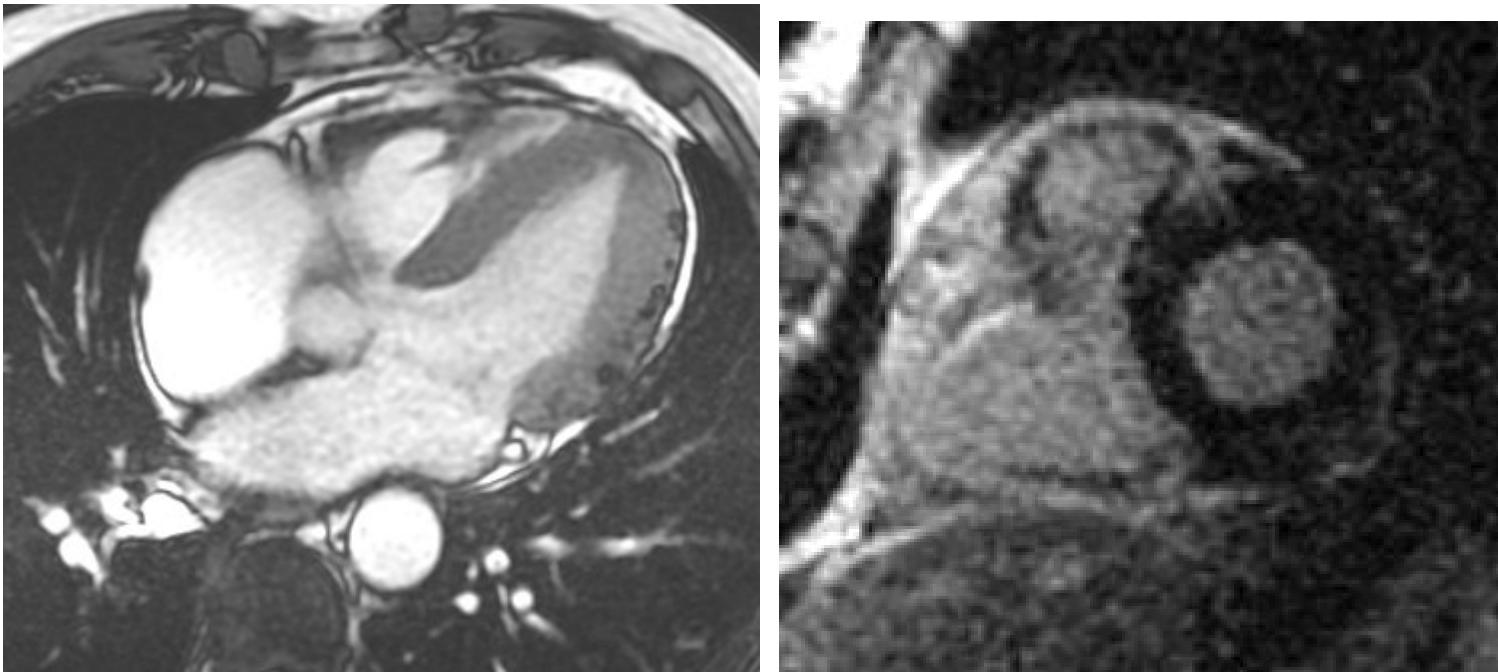
Biventricular involvement with fibrous-fatty infiltration, Wall motion abnormalities of RV walls



MRI IN ARVC



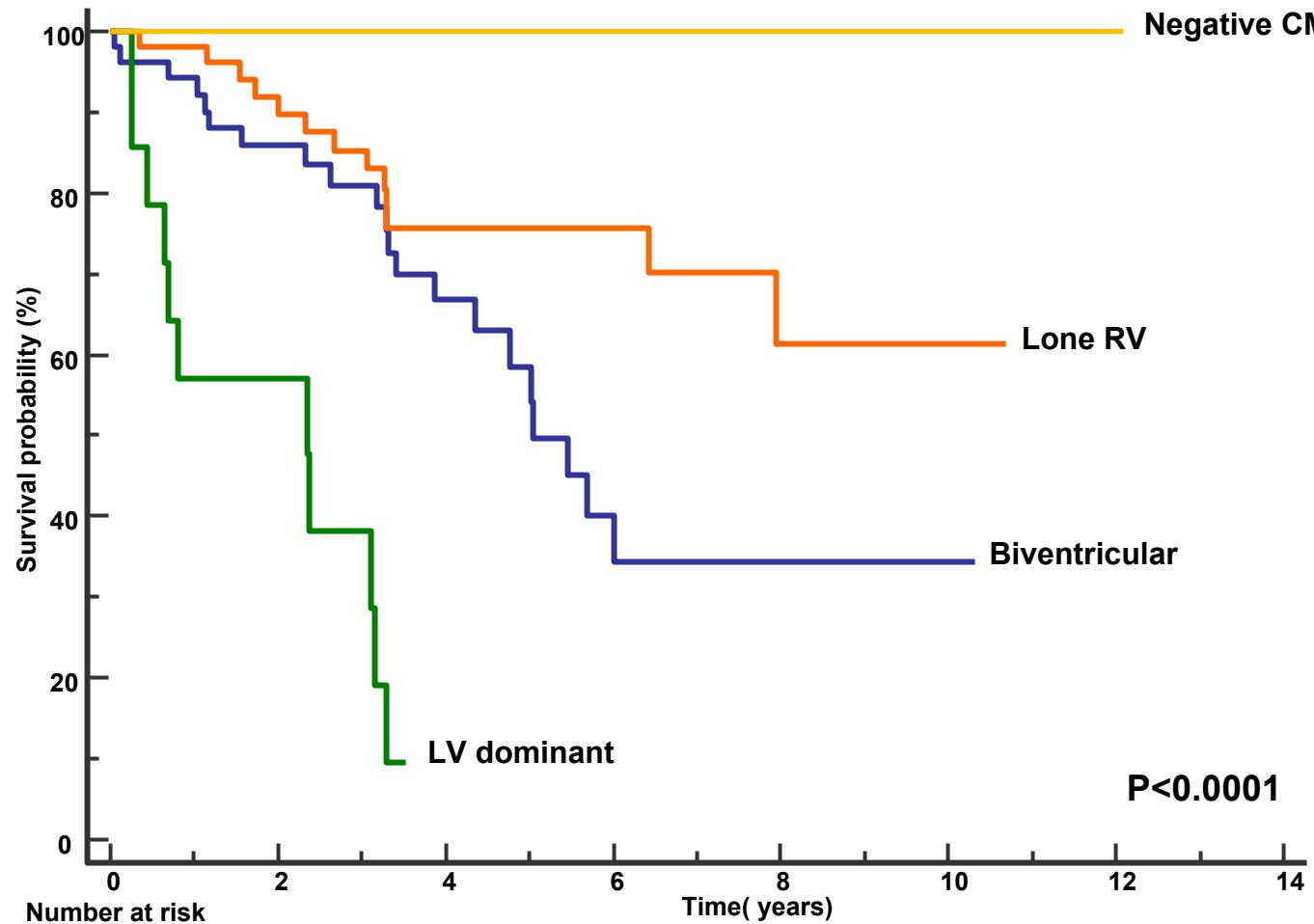
LV dominant/LV lone involvement with fibrous-fatty infiltration and/or
Wall motion abnormalities



Prognostic Value of
Magnetic Resonance Phenotype in
Patients With Arrhythmogenic
Right Ventricular Cardiomyopathy

MULTICENTER STUDY: 140 pts with definite ARVC/D at CMR

Combined Endpoint
(SCD, aborted cardiac arrest, appropriate ICD intervention)



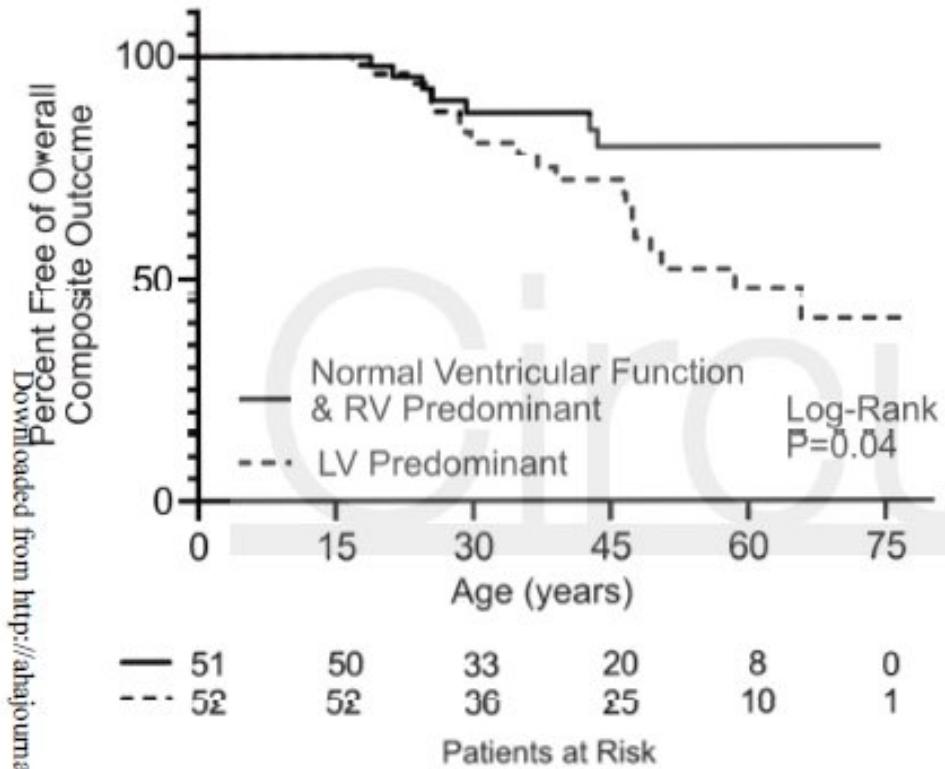
	0	2	4	6	8	10	12	14
Biventricular	55	37	22	7	5	1	0	0
LV dominant	16	6	0	0	0	0	0	0
Lone RV	54	43	25	14	7	2	0	0
Negative CMR	15	12	8	4	1	1	1	0

Prognostic role of LV
LGE presence

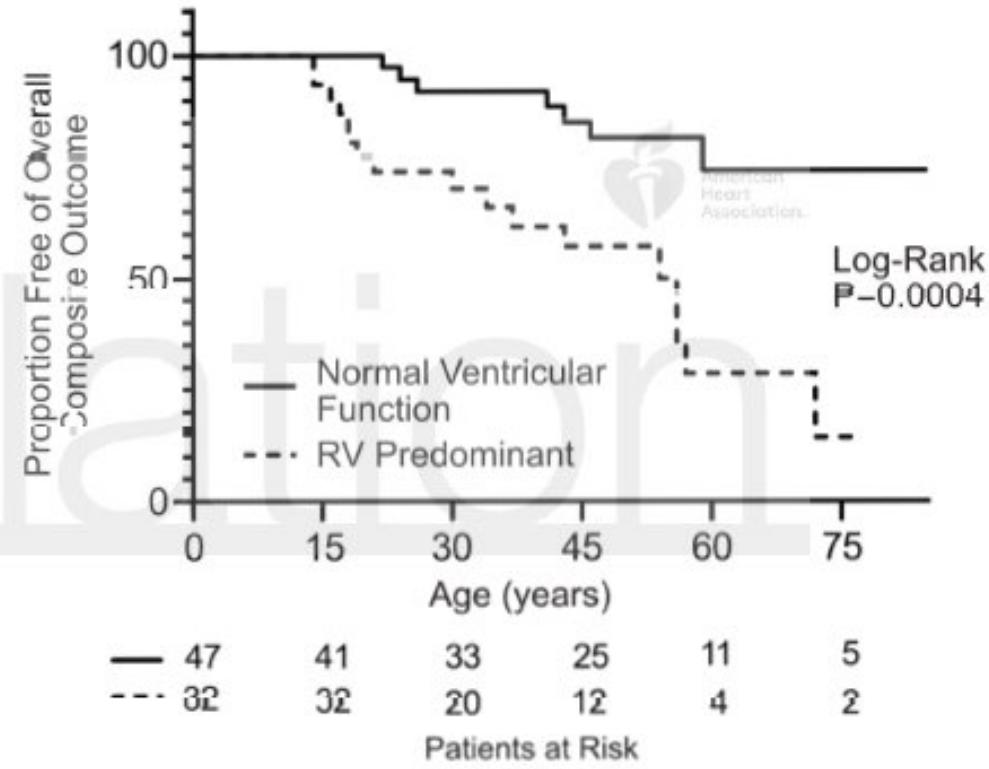
Desmoplakin Cardiomyopathy, a Fibrotic and Inflammatory Form of Cardiomyopathy Distinct from Typical Dilated or Arrhythmogenic Right



A.



B.



Prognostic role of LV LGE presence

DSP $\textcircled{P} 60\%$ LV involvement
PKP2 $\textcircled{P} 0\%$ LV involvement

Conclusions



LGE is an important prognosticator in cardiac diseases

Its prognostic role depends on pattern of distribution
and extent with different weight in different cardiac
conditions

Prognostic role of LGE in different Cardiac Diseases



- 1) Presence\absence of LGE: \oplus **DCM, Fabry, ARVC**
- 2) Pattern of distribution of LGE \oplus **DCM (midwall septal), Amyloidosis (transmural), Myocarditis (midwall septal),**
- 3) Extent of LGE \oplus **HCM (>15%), IHD**
- 4) Evolution of LGE \oplus **HCM (LGE-rate)**

Conclusions



LGE is an important prognosticator in cardiac diseases

Its prognostic role depends on pattern of distribution and extent with different weight in different cardiac conditions

In all the cardiac diseases, LGE has a great negative predictive value (NPV) for predicting cardiac events

The prognostic weight of LGE is greater in EF-preserved conditions or in those with low-moderate dysfunction