The Role of Imaging for in the Diagnosis and Risk Stratification for Recovery

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The Role of CMR for in the Diagnosis and Risk Stratification for Recovery

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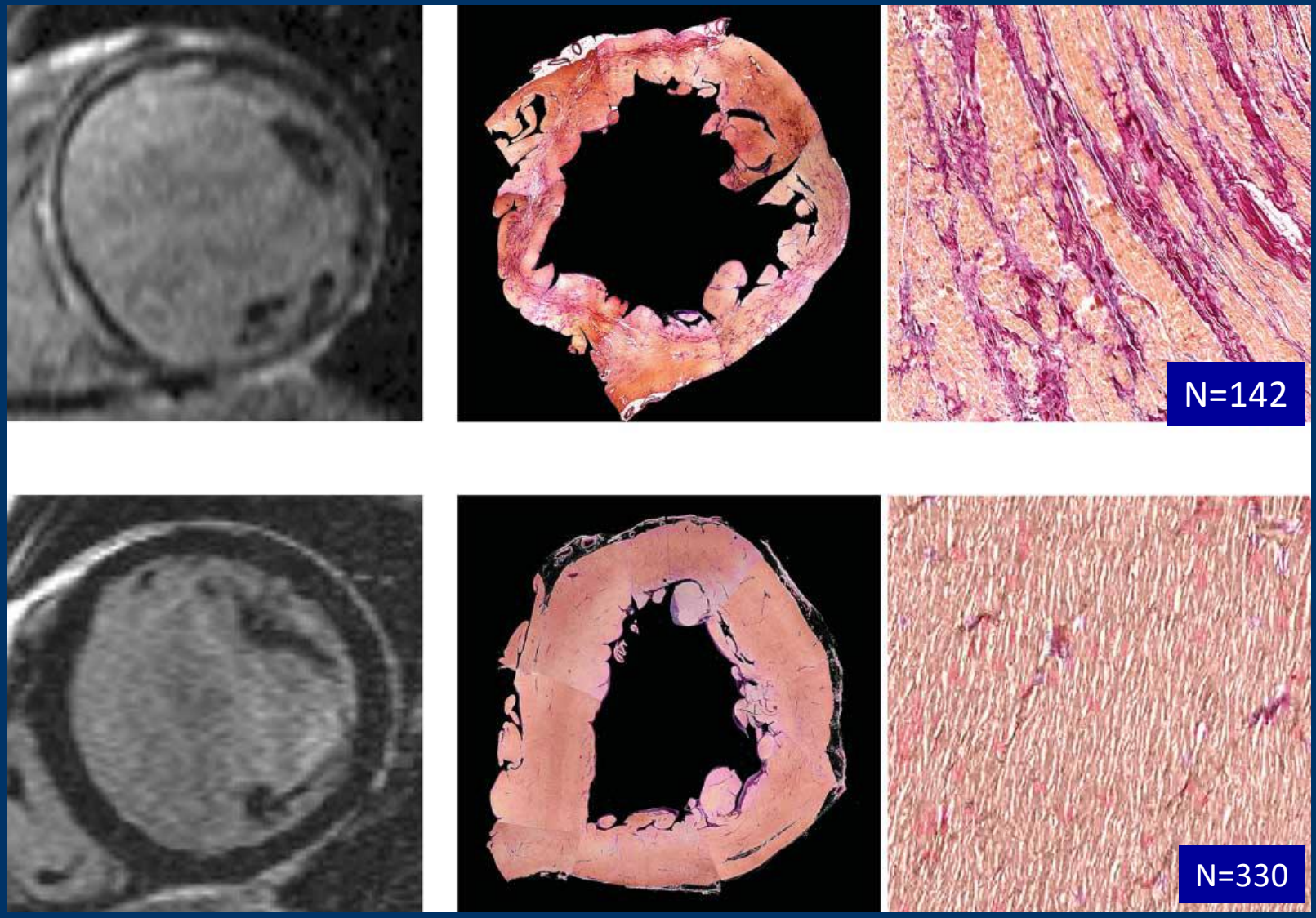
Agenda

- Idiopathic DCM
- Genetic CM
- Sarcoidosis
- Takotsubo
- Recovery

DCM

- Accurate and reproducible quantification of LVEF and LVEDVi
- Evidence of mid wall fibrosis with LGE
- Mapping parameters
- Detailed biomechanics features

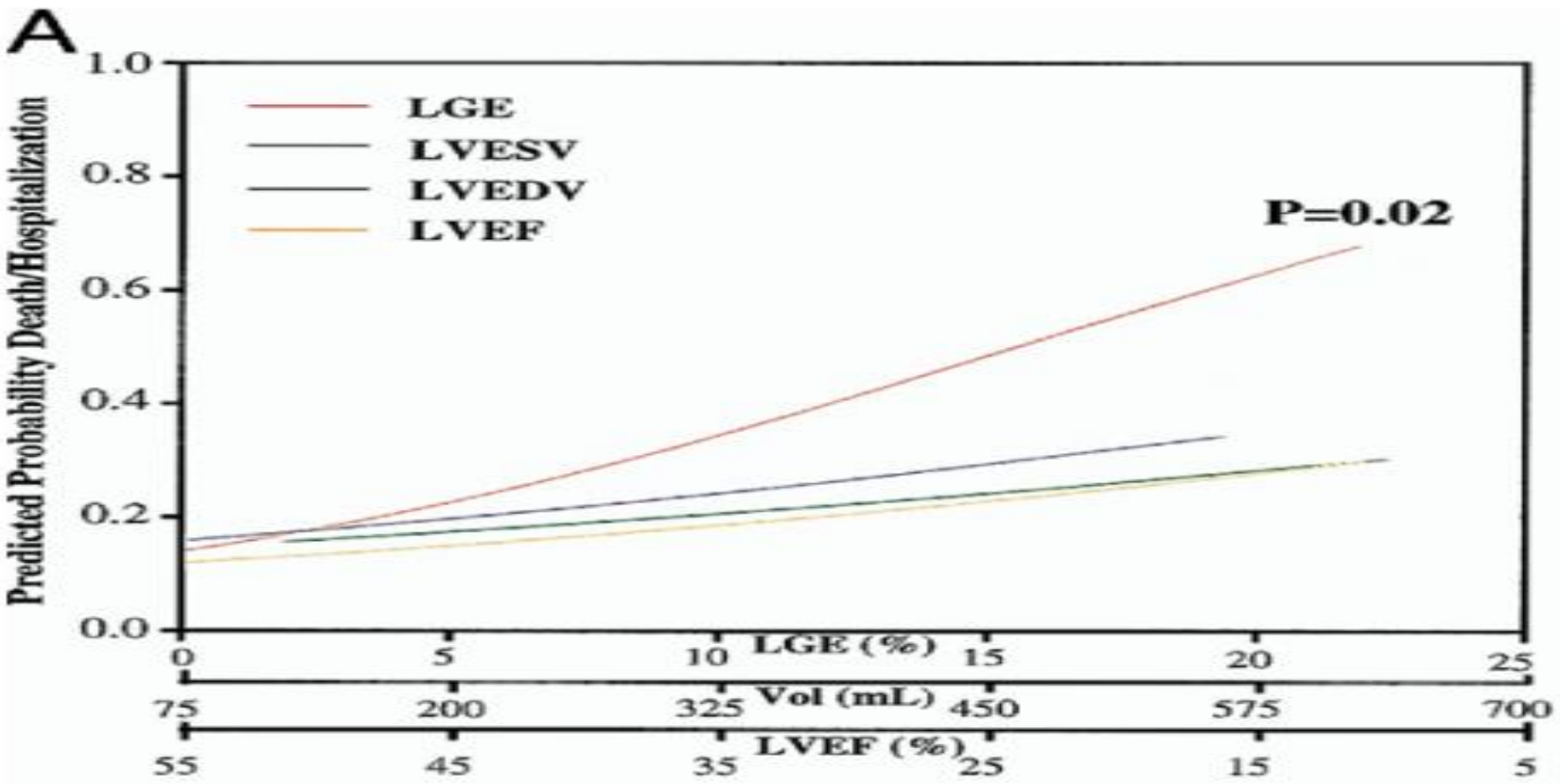
MRI Macroscopic findings Microscopy



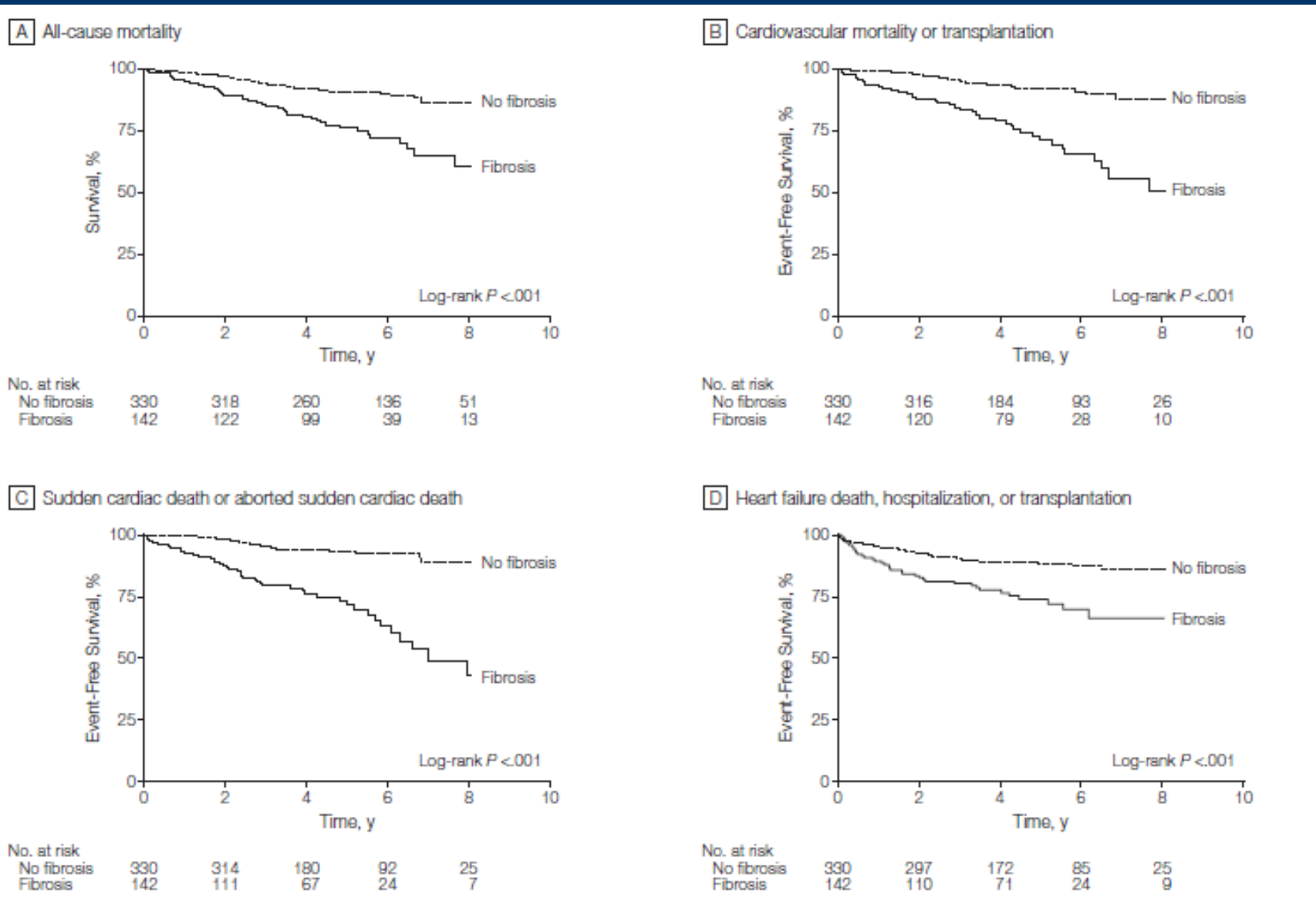
Gulati et al, JAMA 2013

Assomull *et al.*
Prognosis in DCM by CMR

JACC Vol. 48, No. 10, 2006
November 21, 2006:1977–85



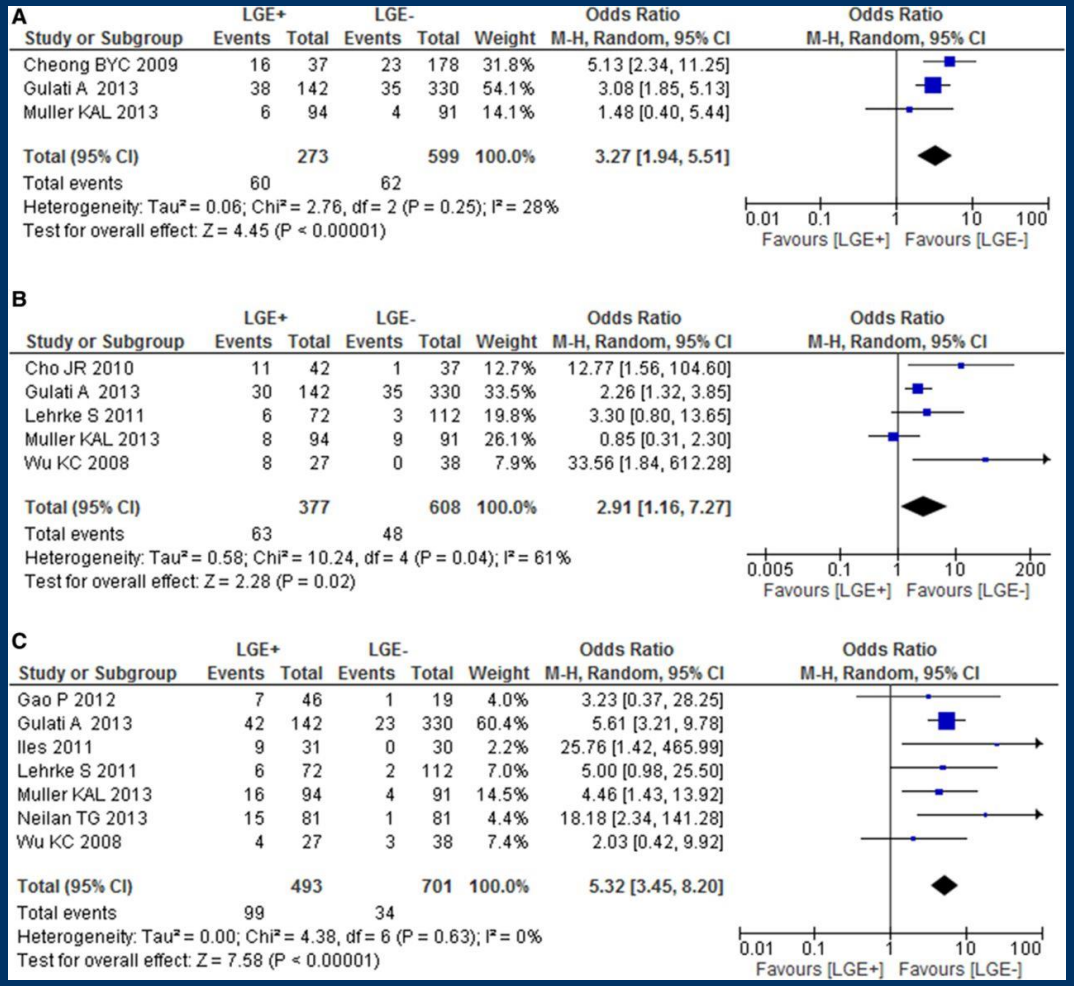
•Correlation between LGE and volumes and function



Gulati et al, JAMA 2013

Outcome	No. (%) of Patients by Presence of Midwall Fibrosis		Hazard Ratio (95% CI)	*P* Value[a]
	No (n = 330)	Yes (n = 142)		
Primary end point (all-cause mortality)	35 (10.6)	38 (26.8)	2.96 (1.87-4.69)	<.001
Principal secondary outcomes				
Cardiovascular mortality or cardiac transplantation	26 (7.9)	41 (28.9)	4.11 (2.51-6.72)	<.001
Cardiovascular death	24 (7.3)	34 (23.9)	3.88 (2.30-6.55)	<.001
Cardiac transplantation	2 (0.6)	7 (4.9)	8.63 (1.79-41.58)	.007
Arrhythmic secondary composite end point				
Sudden cardiac death or aborted sudden cardiac death[b]	23 (7.0)	42 (29.6)	5.24 (3.15-8.72)	<.001
Sudden cardiac death	11 (3.3)	15 (10.6)	3.81 (1.75-8.33)	.001
Aborted sudden cardiac death	12 (3.6)	29 (20.4)	6.93 (3.53-13.61)	<.001
Heart failure secondary composite end point				
Heart failure death, heart failure hospitalization, or cardiac transplantation[b]	37 (11.2)	36 (25.4)	2.49 (1.57-3.95)	<.001
Heart failure death	12 (3.6)	18 (12.7)	4.05 (1.95-8.41)	<.001
Heart failure hospitalization	35 (10.6)	30 (21.1)	2.21 (1.36-3.60)	.001
Device implantation				
Implantable cardioverter-defibrillator	21 (6.4)	30 (21.1)	3.80 (2.17-6.64)	<.001
Cardiac resynchronization therapy without defibrillator	24 (7.3)	10 (7.0)	1.03 (0.49-2.16)	.93
Cardiac resynchronization therapy with defibrillator	31 (9.4)	28 (19.7)	2.40 (1.44-4.01)	.001

Individual and Pooled Risk of CV Outcomes for LGE-CMR



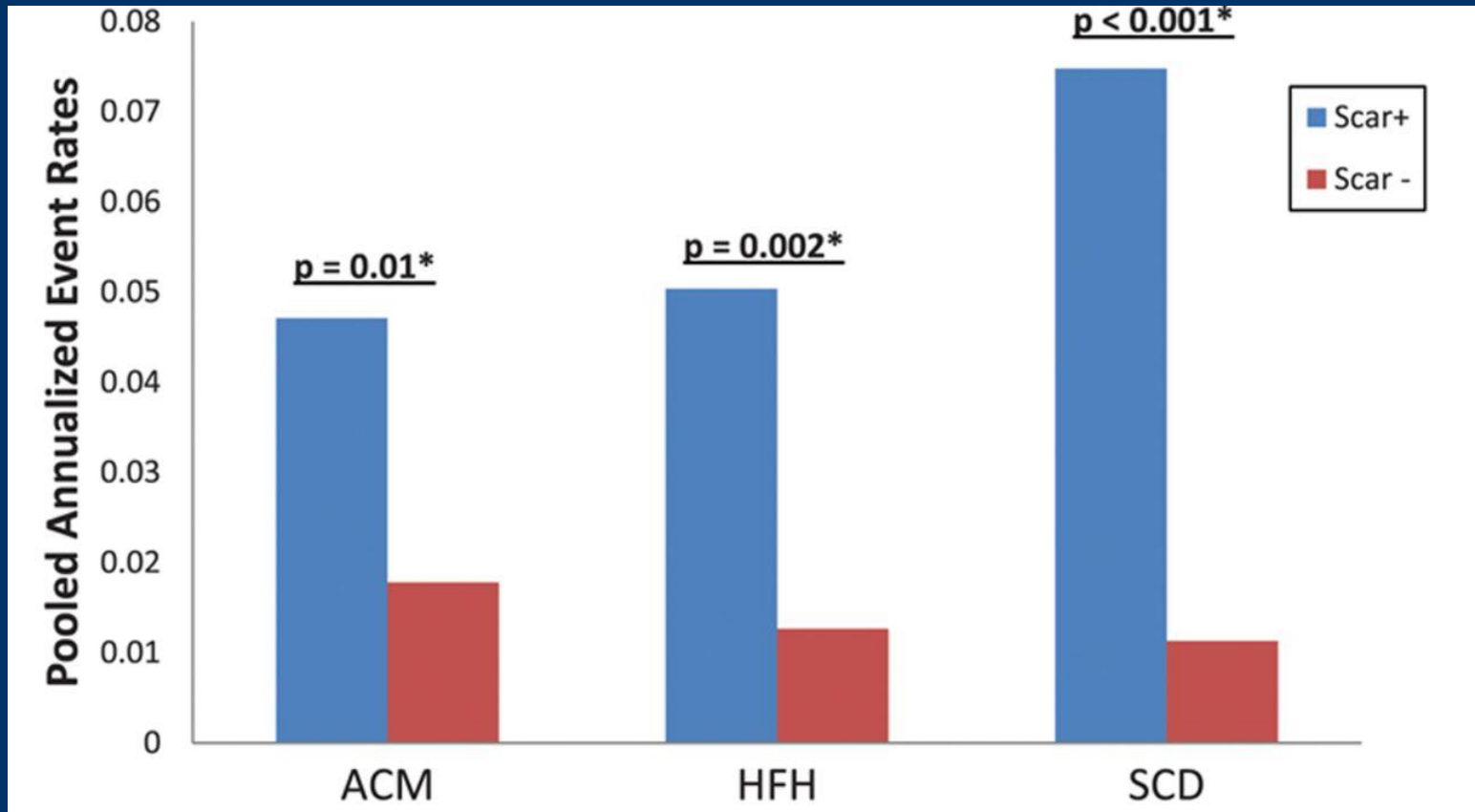
ACM

HFH

Composite EP

Kuruvilla S et al. Circ Cardiovasc Imaging. 2014

Annualized Event Rates of CV Outcomes Based on the Presence of LGE

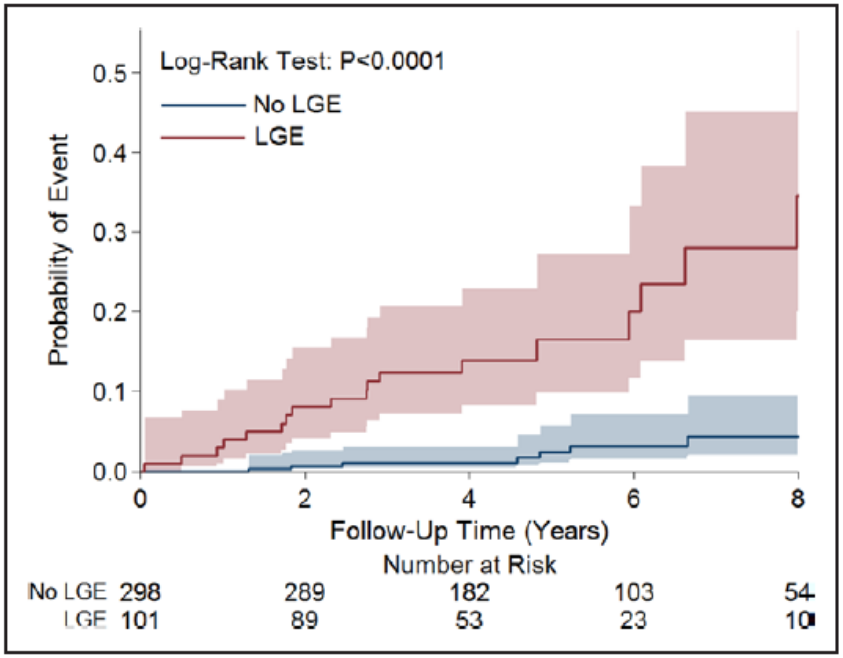


*p-values are for the significance of the annualized event rate difference between LGE+ and LGE- subjects.

Kuruvilla S et al. Circ Cardiovasc Imaging. 2014;7:250-258

ORIGINAL RESEARCH ARTICLE

Association Between Midwall Late Gadolinium Enhancement and Sudden Cardiac Death in Patients With Dilated Cardiomyopathy and Mild and Moderate Left Ventricular Systolic Dysfunction



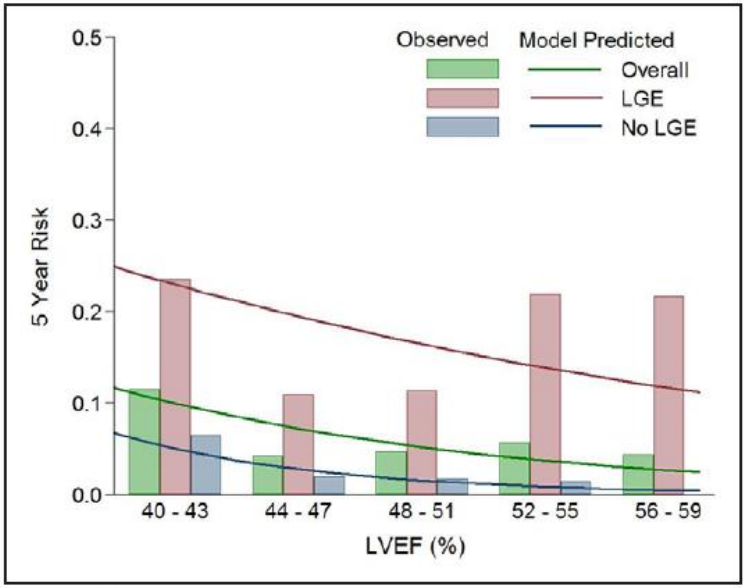


Figure 3. Five-year risk estimates of the primary end point.

Halliday, Circulation 2017

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 77, NO. 23, 2021

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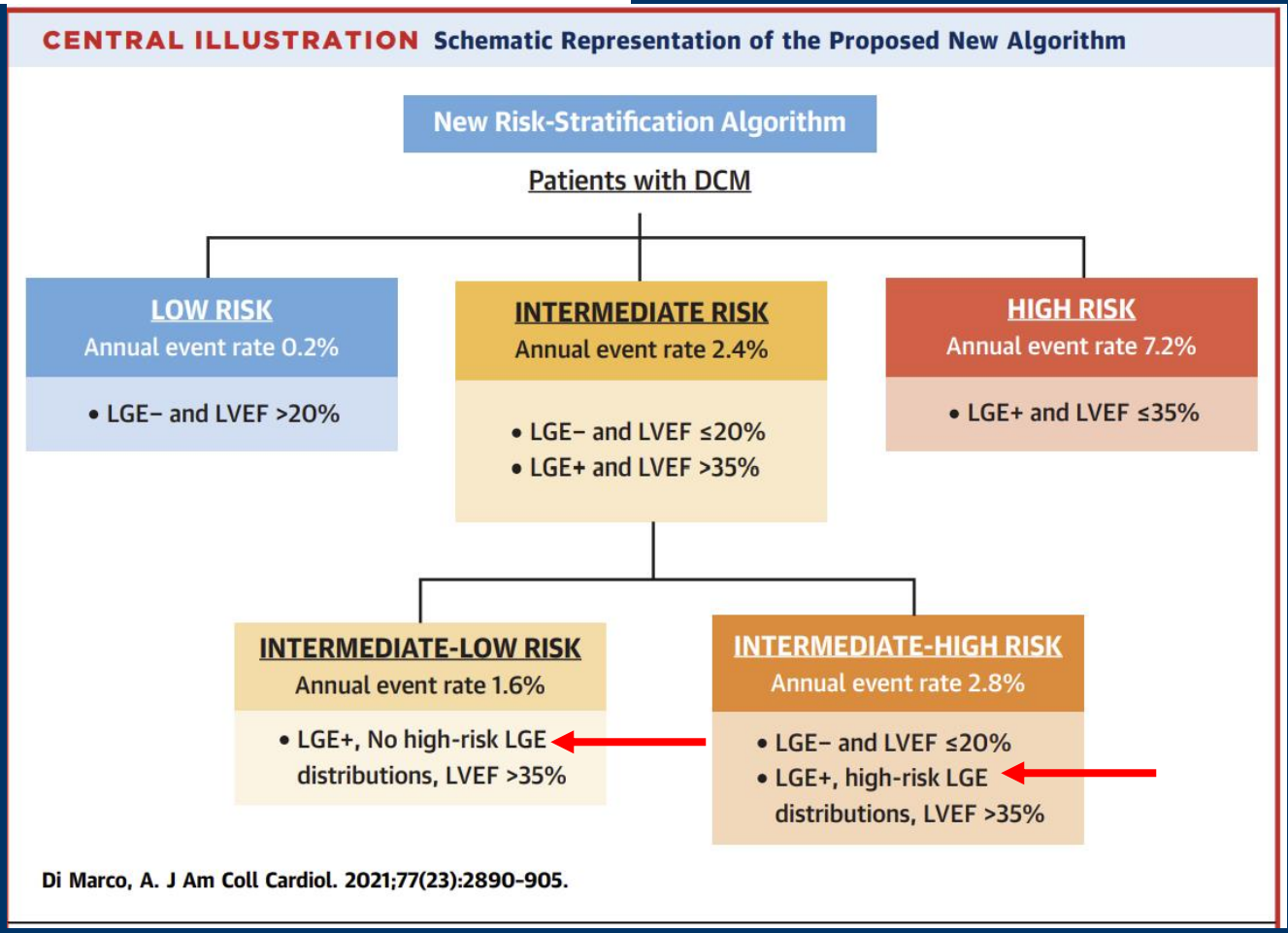
Improved Risk Stratification for Ventricular Arrhythmias and Sudden Death in Patients With Nonischemic Dilated Cardiomyopathy

1,165 patients with a median follow-up of 36 months

The presence of at least one of the following features was identified as high-risk LGE: epicardial LGE, transmural LGE combined septal and free-wall LGE

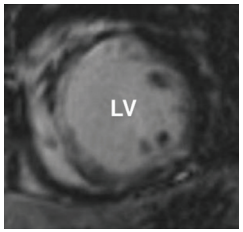
High-risk LGE was found in 222 cases (46% of all LGE+ patients)

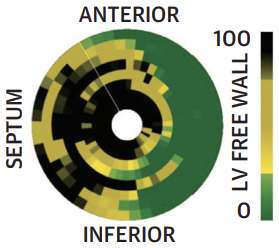


CENTRAL ILLUSTRATION Cardiac Magnetic Resonance to Predict Sudden Cardiac Death in Cardiac Implantable Device Implantation Recipients

Methods

Myocardial Fibrosis Present on Visual Assessment → Myocardial Fibrosis Quantification





After assessing myocardial fibrosis present on visual assessment (myocardial fibrosis shows up as white myocardium), total fibrosis mass and gray zone fibrosis mass were quantified. The difference between total fibrosis mass using the 5SD method and the 2SD method constitutes gray zone fibrosis using 5SD method mass.

Results

Risk Groups

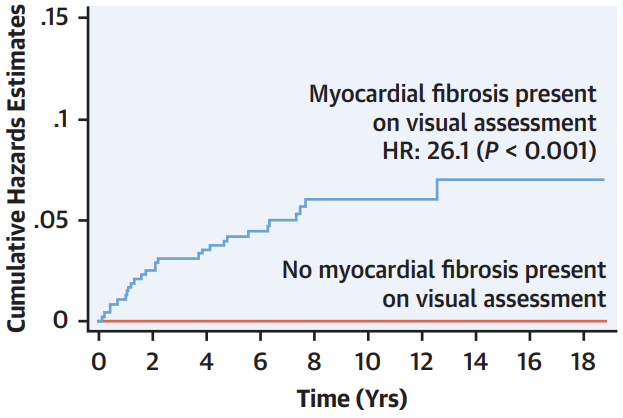
Cardiac implantable device implantation

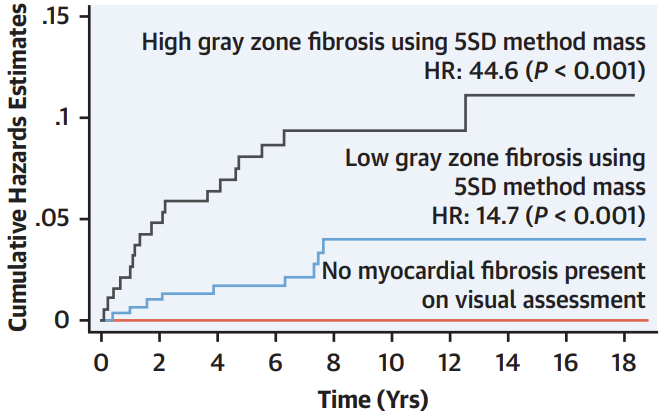
No myocardial fibrosis present on visual assessment	Myocardial fibrosis present on visual assessment and low gray zone fibrosis using 5SD method mass	Myocardial fibrosis present on visual assessment and high gray zone fibrosis using 5SD method mass
LOW RISK	INTERMEDIATE RISK	HIGH RISK

INCIDENCE RATES

SCD	0%	0.19%	1.01%
ARRHYTHMIC ENDPOINT	0.14%	1.22%	4.46%

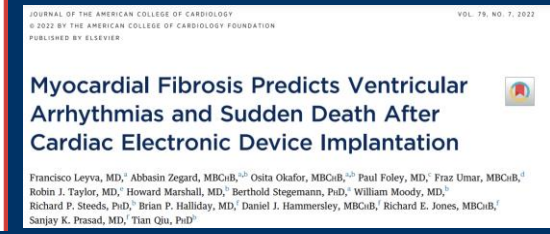
Sudden Cardiac Death





Leyva, F. et al. J Am Coll Cardiol. 2022;79(7):665-678.

0g, 0-17g, >17g


JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 79, NO. 7, 2022
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Myocardial Fibrosis Predicts Ventricular Arrhythmias and Sudden Death After Cardiac Electronic Device Implantation

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JACC: CARDIOVASCULAR IMAGING
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VOL. 9, NO. 1, 2016
ISSN 1936-878X/$36.00
http://dx.doi.org/10.1016/j.jcmg.2015.12.001

T1-Mapping and Outcome in Nonischemic Cardiomyopathy

All-Cause Mortality and Heart Failure

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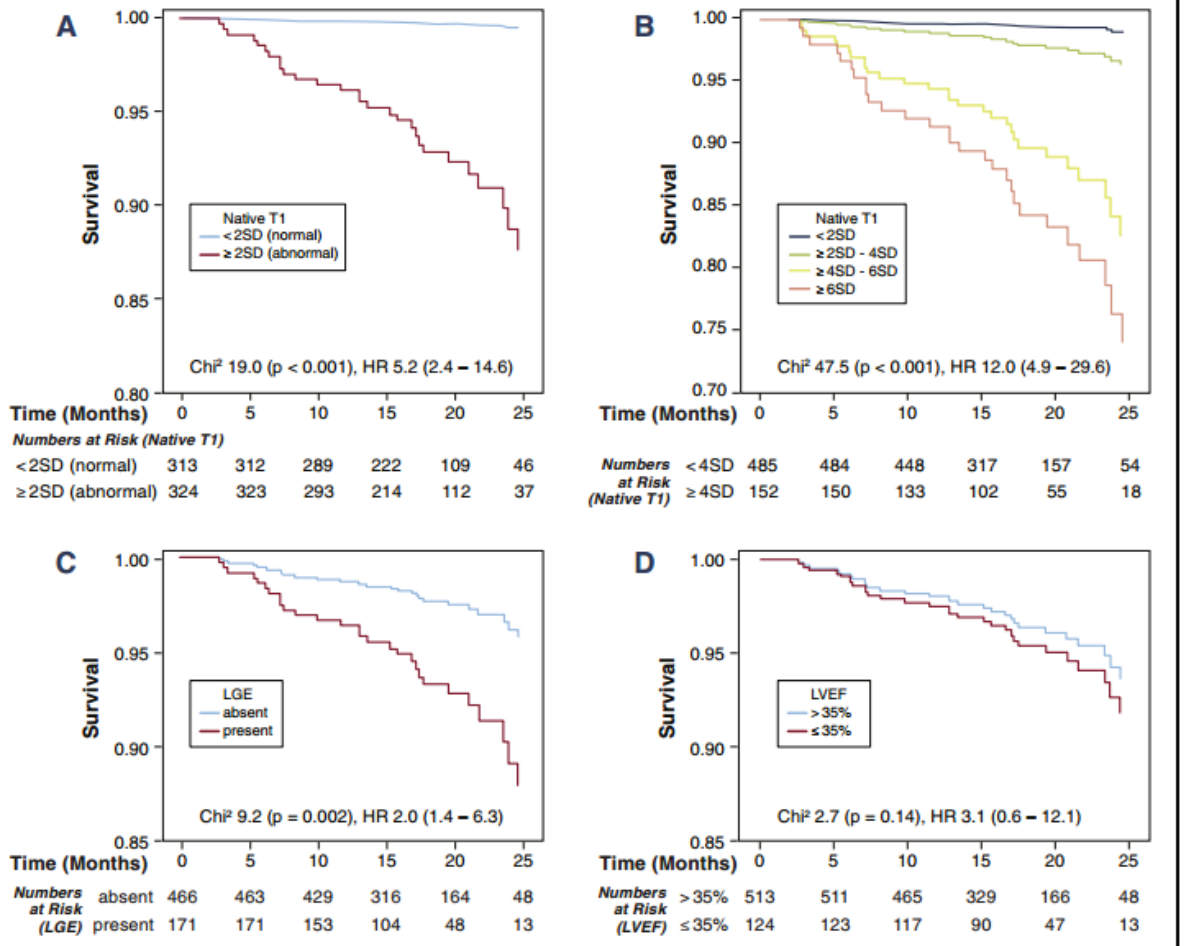
on behalf of the International T1 Multicentre CMR Outcome Study

- Prospective observational multicenter longitudinal study in 637 consecutive patients with NIDCM (mean age 50 years [interquartile range: 37 to 76 years]; 395 males [62%])
- The primary endpoint was all-cause mortality. A composite of heart failure (HF) mortality and hospitalization was a secondary endpoint.
- Median follow-up period of 22 months

FIGURE 2 Kaplan-Meier Curves for CMR Parameters and All-Cause Mortality



(A) Native T1 (normal vs. abnormal myocardium, based on >2 standard deviations [SD] above the mean of the normal reference range) (17), **(B)** native T1 ranked by 2n-times SD (ranks of SD: <2, ≥2 to 4, ≥4 to 6, ≥6) (17), **(C)** late gadolinium enhancement present versus absent, and **(D)** left ventricular ejection fraction <35%. CMR = cardiac magnetic resonance.

In multivariable analyses, native T1 was the sole independent predictor of all-cause mortality and HF composite endpoints

Amyloidosis - DE, Native T1 or ECV?

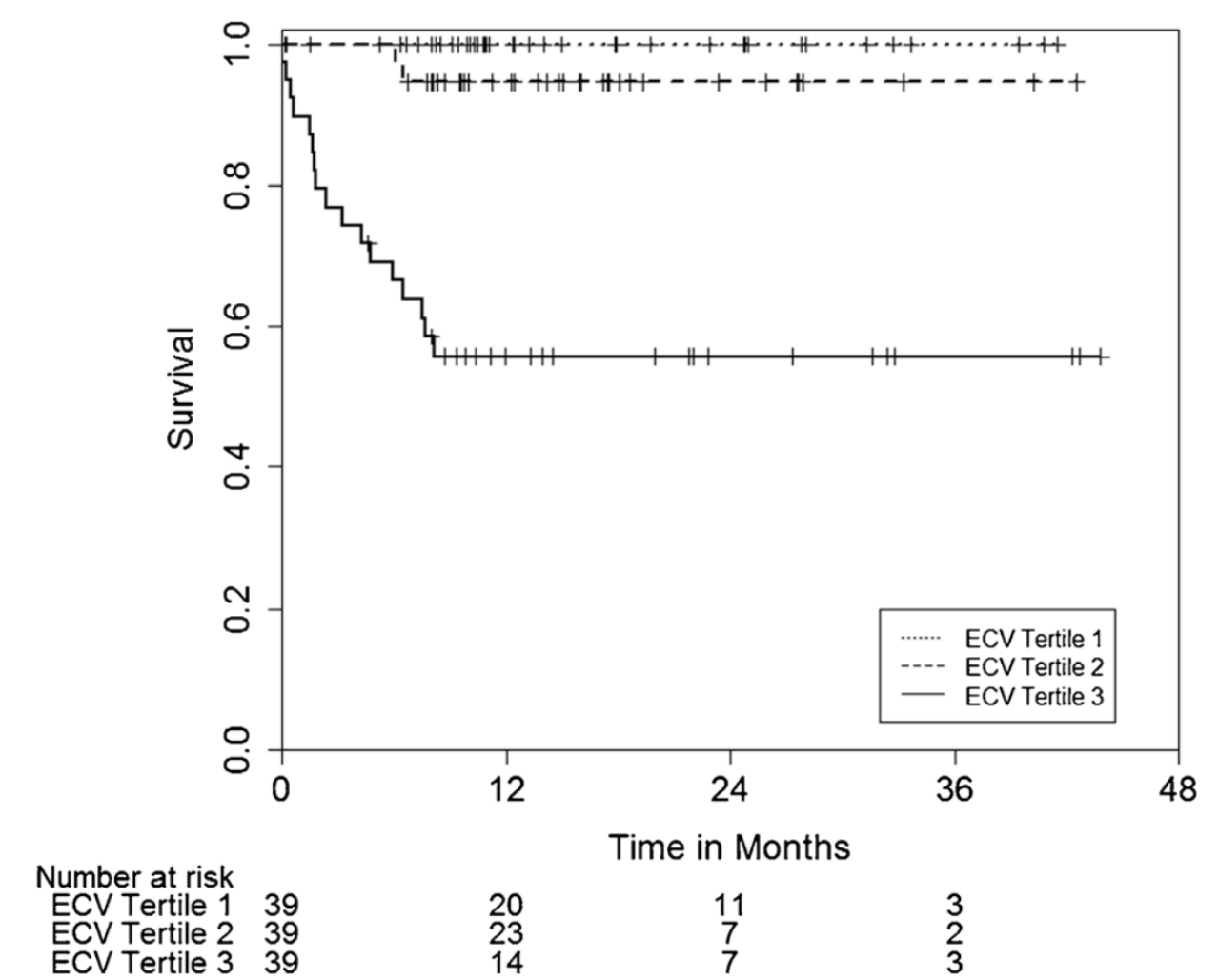
TABLE 4 Bivariate Pooled Diagnostic Performance

Modality	Studies	n	Sensitivity	Specificity	Odds Ratio
LGE	13	703	0.84 (0.74-0.90)	0.80 (0.68-0.88)	20.1 (9.1-44.1)
T1	4	1,321	0.89 (0.80-0.95)	0.80 (0.61-0.91)	34.6 (11.4-105.1)
ECV	6	1,369	0.93 (0.86-0.96)	0.87 (0.74-0.94)	84.6 (30.3-236.2)*

Pooled values are point estimates (95% confidence interval). *$p < 0.05$ vs. LGE.

ECV = extracellular volume mapping; LGE = late gadolinium enhancement; T1 = native T1 mapping.

DCM - ECV



Youn, Eur Rad 2017

Tissue tracking

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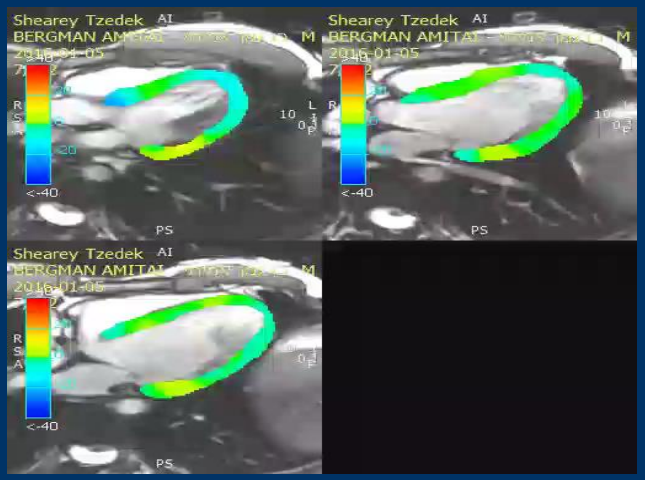
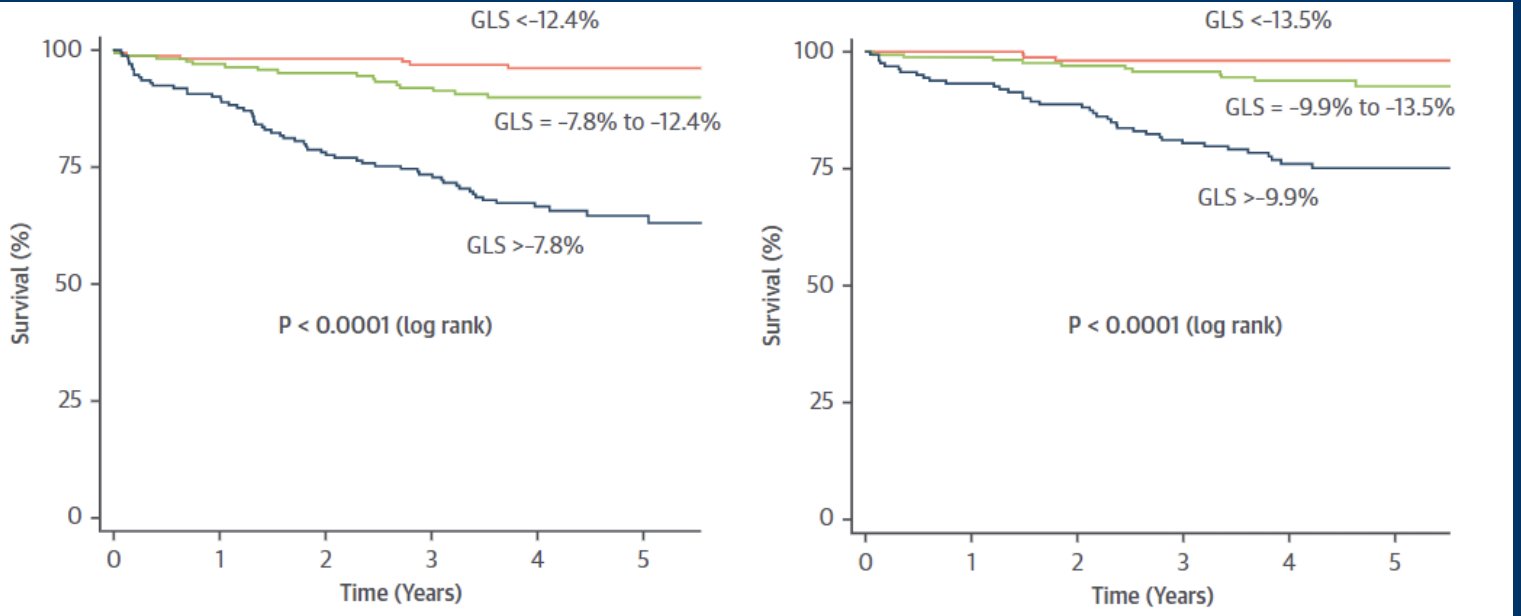
Feature-Tracking Global Longitudinal Strain Predicts Death in a Multicenter Population of Patients With Ischemic and Nonischemic Dilated Cardiomyopathy Incremental to Ejection Fraction and Late Gadolinium Enhancement

Simone Romano, MD,[a,b] Robert M. Judd, PhD,[c] Raymond J. Kim, MD,[c] Han W. Kim, MD,[c] Igor Klem, MD,[c]



- EF <50% and ischemic or nonischemic dilated cardiomyopathy
- 1,012 patients in this study, 133 died during median follow-up of 4.4 years.
- Each 1% worsening in GLS was associated with an HR 1.89 after adjustment for clinical and imaging risk factors including EF and LGE



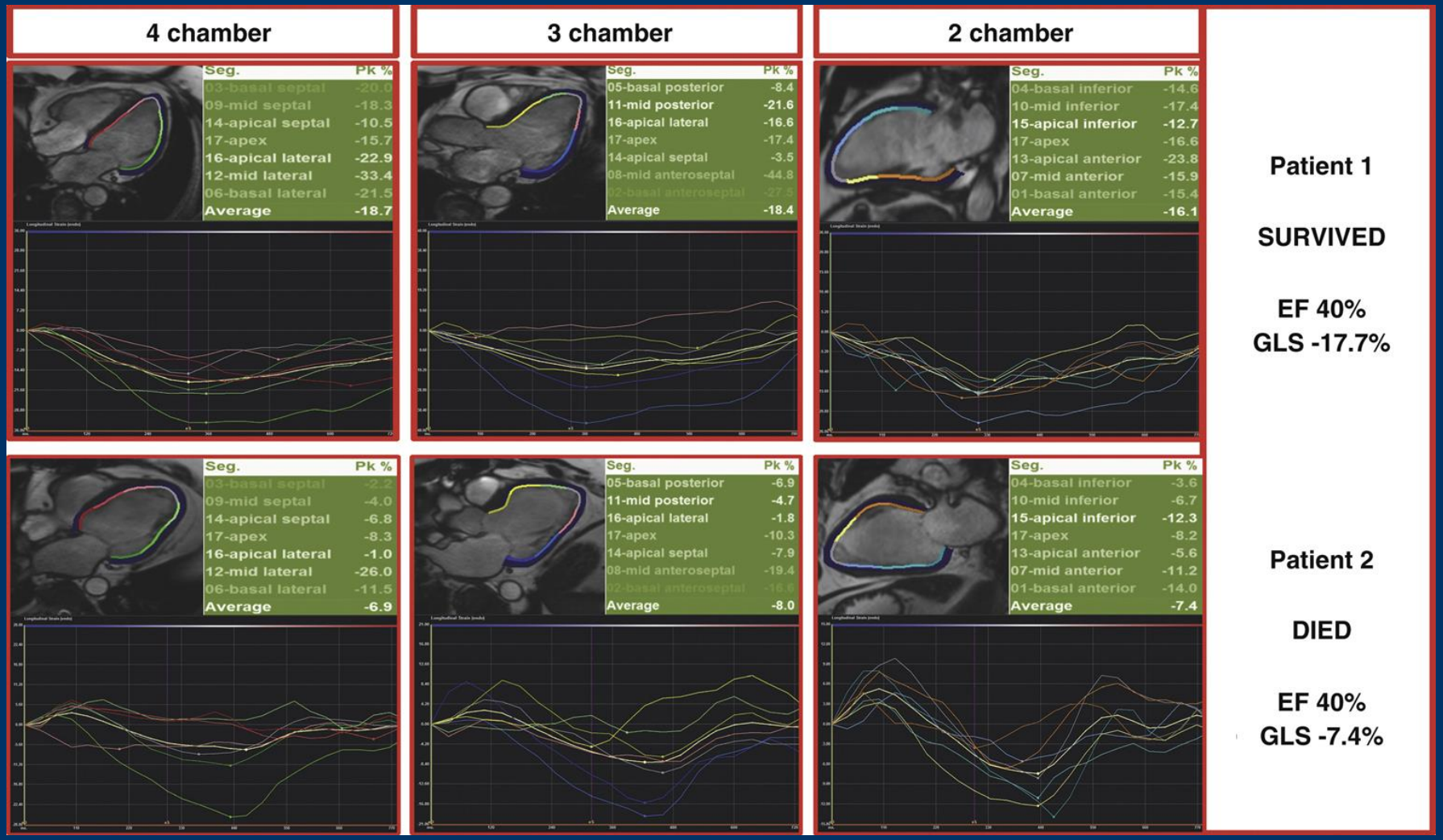
Ischemic cardiomyopathy **(left)** and nonischemic dilated cardiomyopathy **(right)** patients are stratified by tertiles of global longitudinal strain (GLS).

TABLE 4 Multivariable Models of Mortality With GLS Adjusted to Univariate Clinical and Imaging Predictors (at p ≤ 0.20) for Patients With Nonischemic Dilated Cardiomyopathy

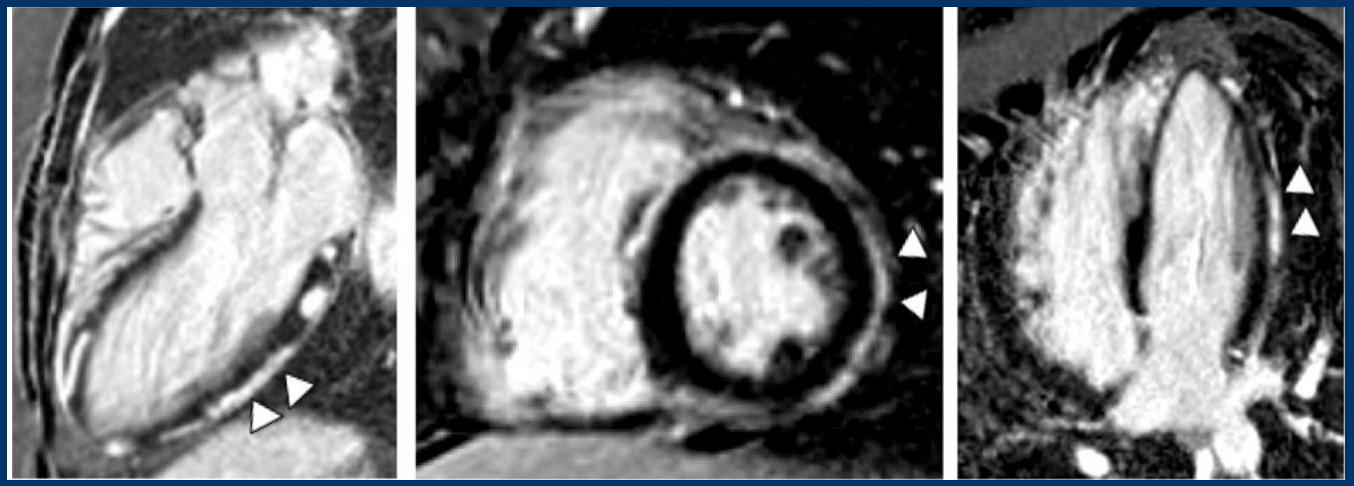
	Univariable		Multivariable Using LGE extent		Multivariable Using LGE presence	
	Hazard Ratio (95% CI)	p Value	Hazard Ratio (95% CI)	p Value	Hazard Ratio (95% CI)	p Value
Age	1.024 (1.008–1.041)	0.004	1.003 (0.985–1.022)	0.717	1.002 (0.984–1.021)	0.791
Diabetes	1.779 (0.996–3.175)	0.061	1.107 (0.588–2.086)	0.752	0.955 (0.510–1.789)	0.885
LVEDV index	1.012 (1.002–1.022)	0.048	0.998 (0.993–1.003)	0.376	0.997 (0.992–1.002)	0.283
GLS	1.402 (1.299–1.513)	<0.001	2.101 (1.546–2.854)	<0.001	2.135 (1.564–2.913)	<0.001
LGE present	2.514 (1.249–3.715)	0.007	–	–	1.914 (1.092–3.355)	0.023
LGE extent	1.057 (1.030–1.085)	<0.001	1.044 (1.015–1.073)	0.002	–	–
LVEF	0.978 (0.958–0.997)	0.020	0.981 (0.927–1.039)	0.511	0.981 (0.926–1.040)	0.525

Abbreviations as in Tables 1 and 2.

Tissue Tracking



Fibrotic and Inflammatory Form of Cardiomyopathy



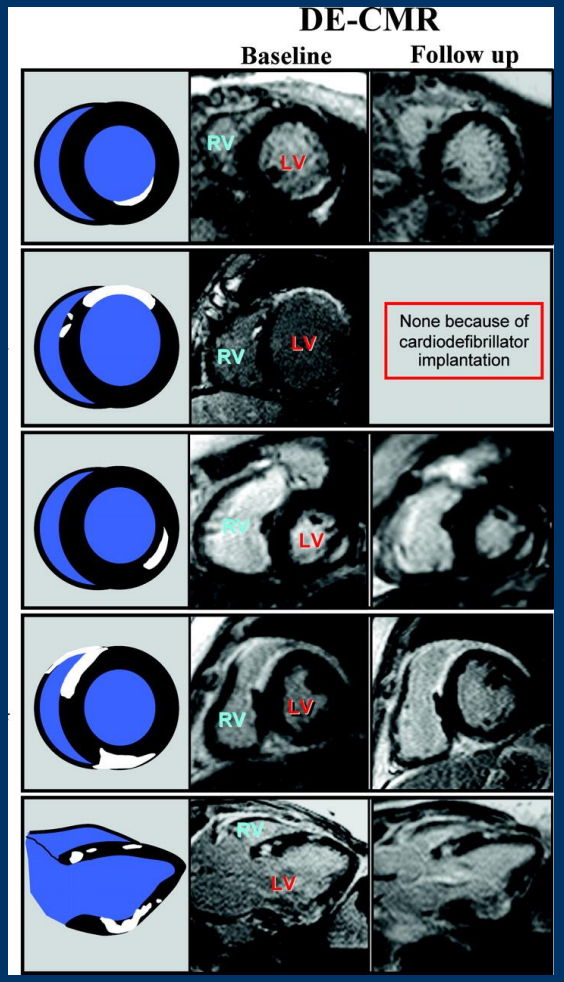
Desmoplakin DSP Cardiomyopathy

- Extent >10%
- Subepicardial in the inferior segment with extension to the midmyocardium in the septum in some cases / Circumferential LGE with a primarily subepicardial distribution is also present
- Relapse

Smith, Circulation 2020

Sarcoidosis

- Recently more data
- LGE is the key finding



Circulation

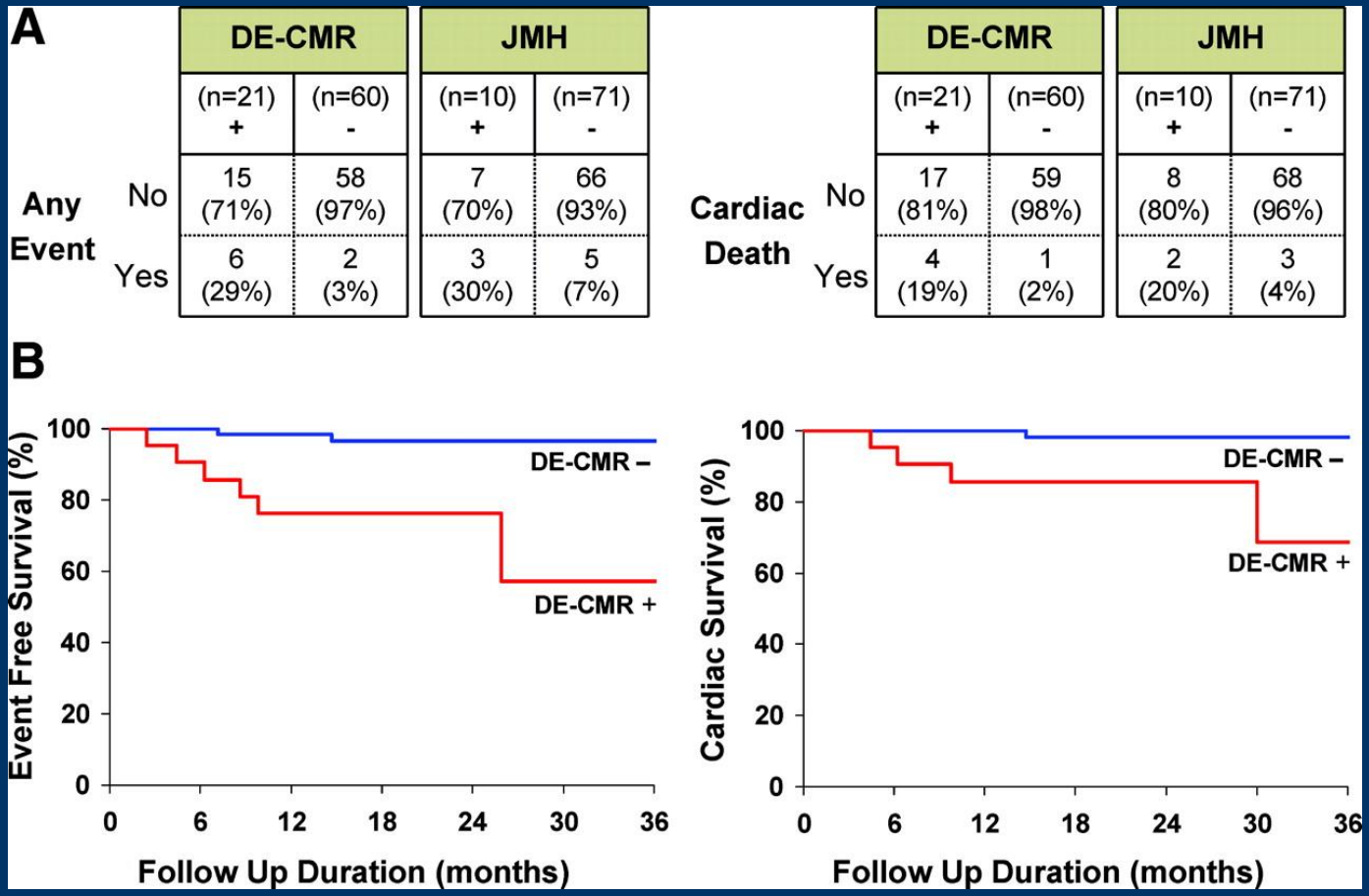
ORIGINAL RESEARCH ARTICLE

Incidence of Sudden Cardiac Death and Life-Threatening Arrhythmias in Clinically Manifest Cardiac Sarcoidosis With and Without Current Indications for an Implantable Cardioverter Defibrillator

Hanna-Kaisa Nordenswan, MD; Pauli Pöyhönen, MD; Jukka Lehtonen, MD; Kaj Ekström, MD; Valtteri Uusitalo, MD, PhD; Meri Niemelä, MD; Tapani Vihinen, MD; Kari Kaikkonen, MD; Petri Haataja, MD; Tuomas Kerola, MD; Tuomas T. Rissanen, MD; Aleksi Alatalo, MD; Päivi Pietilä-Effati, MD; Markku Kupari, MD

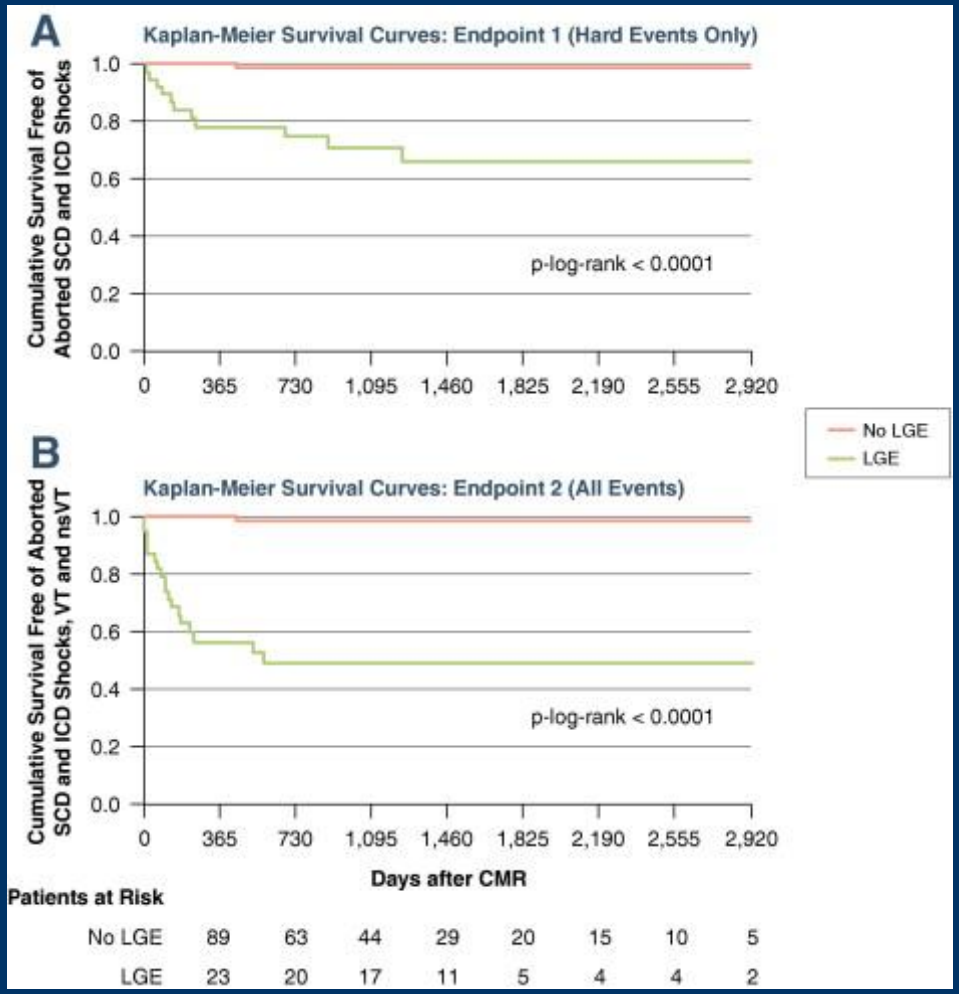
Patel M R et al. Circulation. 2009;120:1969-1977

Events According to LGE and JMH Status



Patel M R et al. Circulation. 2009;120:1969-1977

Events According to LGE



N=155, 39 (25.5%) LGE+

LGE (+) yields a Cox HR of:

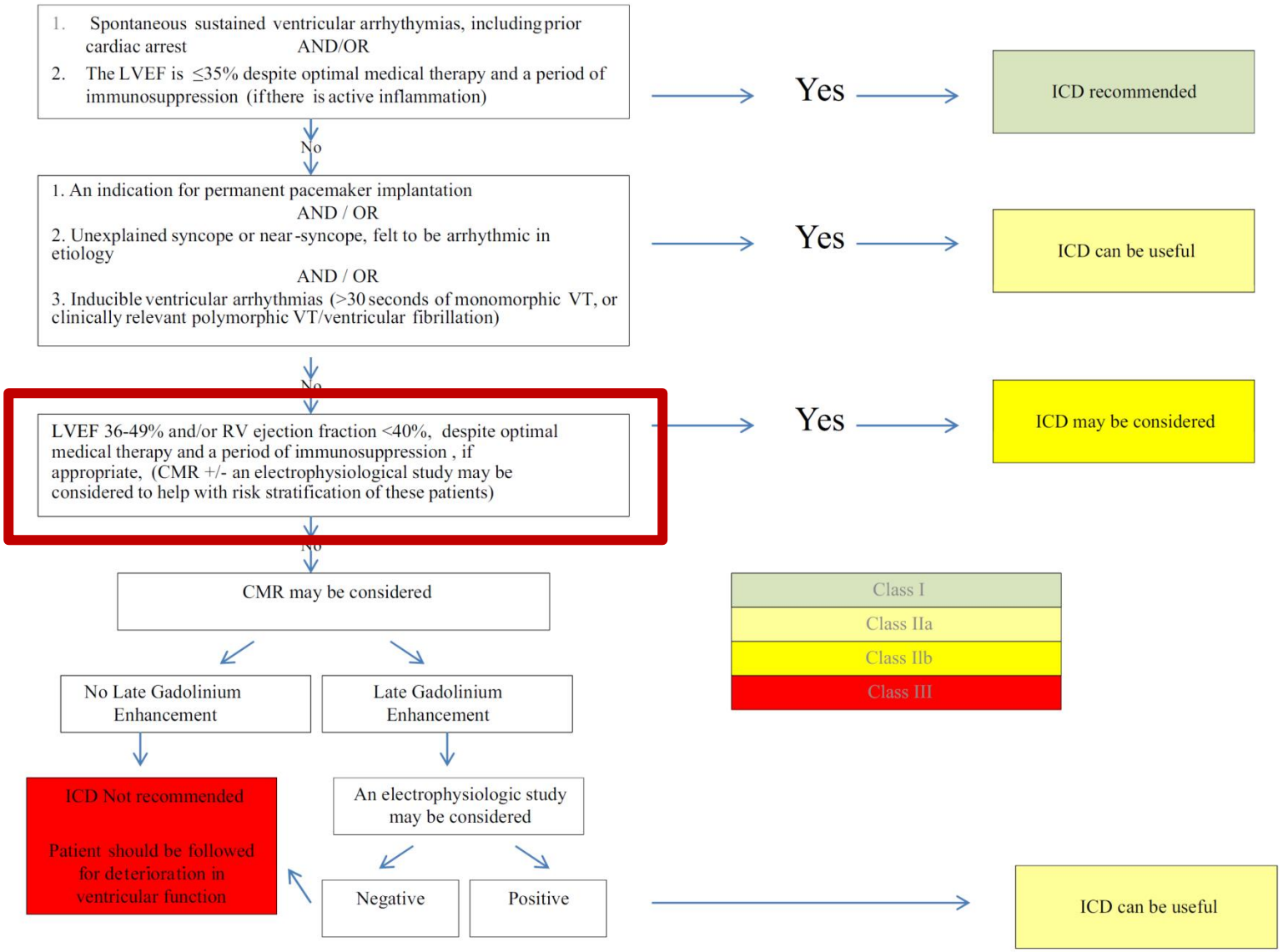
- 31.6 for death, aborted SCD, or appropriate ICD discharge
- 33.9 for any event.
- This is superior to functional or clinical parameters such as LVEFLV EDV or NYHA

Greulich et al. *JCCC CVI*, 2013

HRS Expert Consensus Statement on the Diagnosis and Management of Arrhythmias Associated With Cardiac Sarcoidosis

Heart Rhythm 2014

The writing group acknowledges the need for additional data from large multicenter studies or registries; however, despite the limitations of the current data, there was consensus that CMR for the purpose of sudden death risk stratification may be considered in patients with CS. In particular, CMR may be considered in patients with chronic LVEF >35%. The writing group suggests that CMR be performed and interpreted at centers with experience in CMR imaging and LGE interpretation in CS. The utilization of standardized CMR protocols published by the Society of Cardiovascular Magnetic Resonance[93] is advised to maximize the utility of CMR in patients with suspected CS.


1. Spontaneous sustained ventricular arrhythymias, including prior cardiac arrest AND/OR
2. The LVEF is ≤35% despite optimal medical therapy and a period of immunosuppression (if there is active inflammation)
Yes
ICD recommended
No
1. An indication for permanent pacemaker implantation
AND / OR
2. Unexplained syncope or near-syncope, felt to be arrhythmic in etiology
AND / OR
3. Inducible ventricular arrhythmias (>30 seconds of monomorphic VT, or clinically relevant polymorphic VT/ventricular fibrillation)
Yes
ICD can be useful
No
LVEF 36-49% and/or RV ejection fraction <40%, despite optimal medical therapy and a period of immunosuppression , if appropriate, (CMR +/- an electrophysiological study may be considered to help with risk stratification of these patients)
Yes
ICD may be considered
No
CMR may be considered
Class I
Class IIa
Class IIb
Class III
No Late Gadolinium Enhancement
Late Gadolinium Enhancement
ICD Not recommended
Patient should be followed for deterioration in ventricular function
An electrophysiologic study may be considered
Negative
Positive
ICD can be useful

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ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

ESC Clinical Practice Guidelines

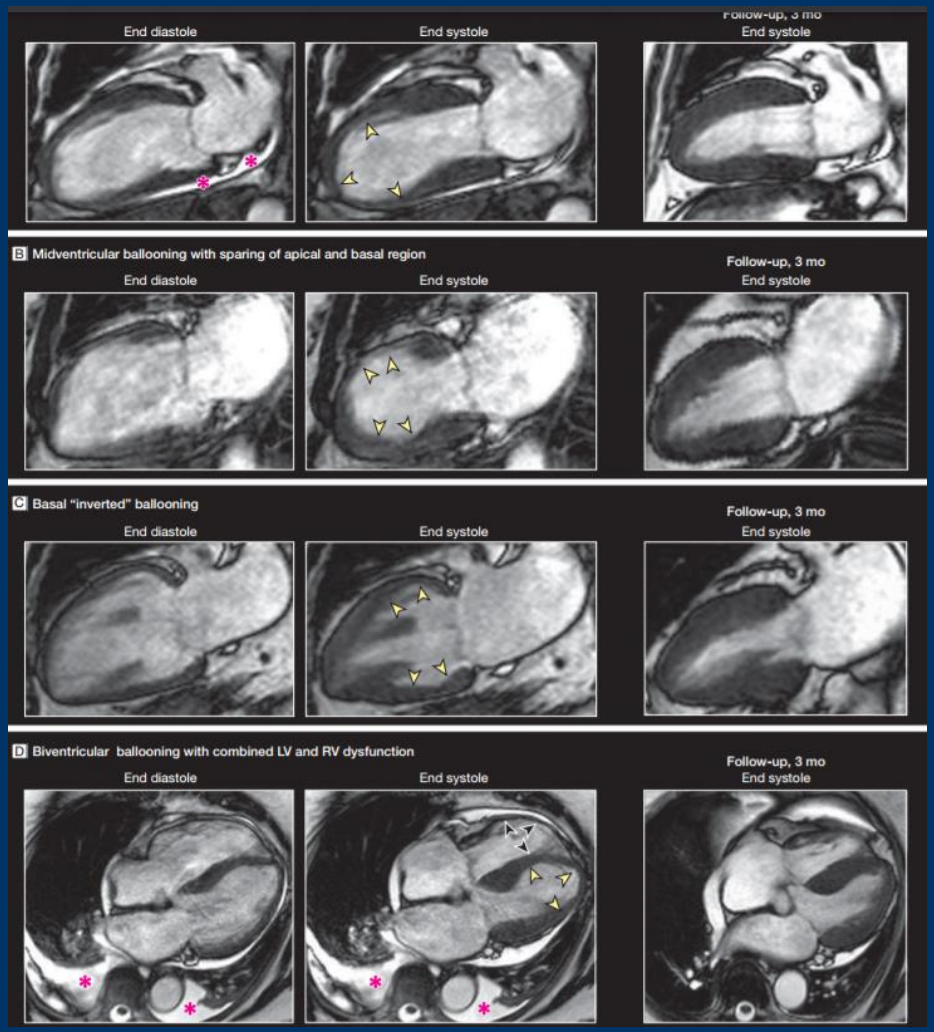
26 Aug 2022

In patients with cardiac sarcoidosis who have an LVEF >35% but significant LGE at CMR after resolution of acute inflammation, ICD implantation should be considered.	**IIa**
In patients with cardiac sarcoidosis who have an LVEF 35–50% and minor LGE at CMR, after resolution of acute inflammation, PES for risk stratification should be considered.	**IIa**

Significant >8% 2SD, Smedema et al. ESC Heart Fail. 2018

Significant - RV involvement, Velangi et al. JACC Img. 2020

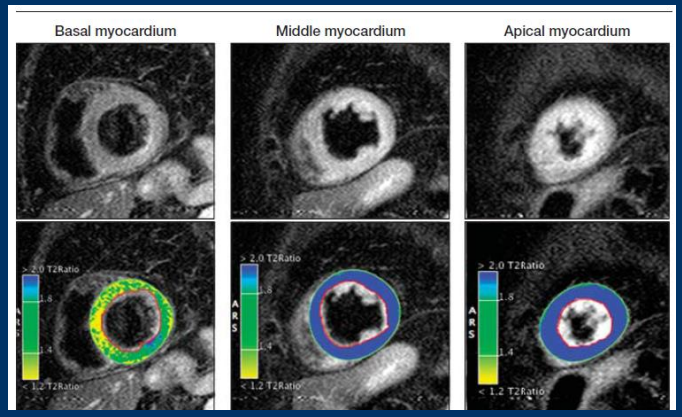
Takotsubo CMP

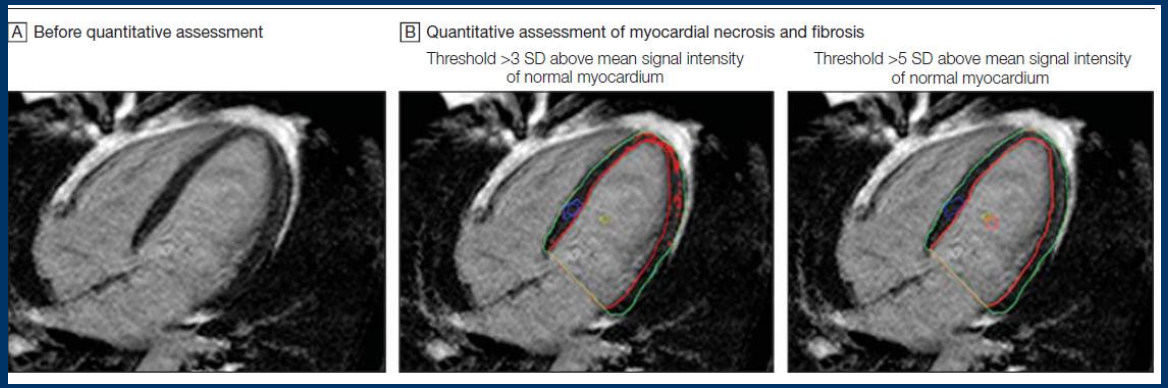


Characteristics	Baseline (n = 239)
Ballooning pattern, No. (%)	
Apical	197 (82)
Midventricular	40 (17)
Basal	2 (1)
Biventricular	81 (34)

JAMA, July 20, 2011—Vol 306, No. 3

Tissue Characterization



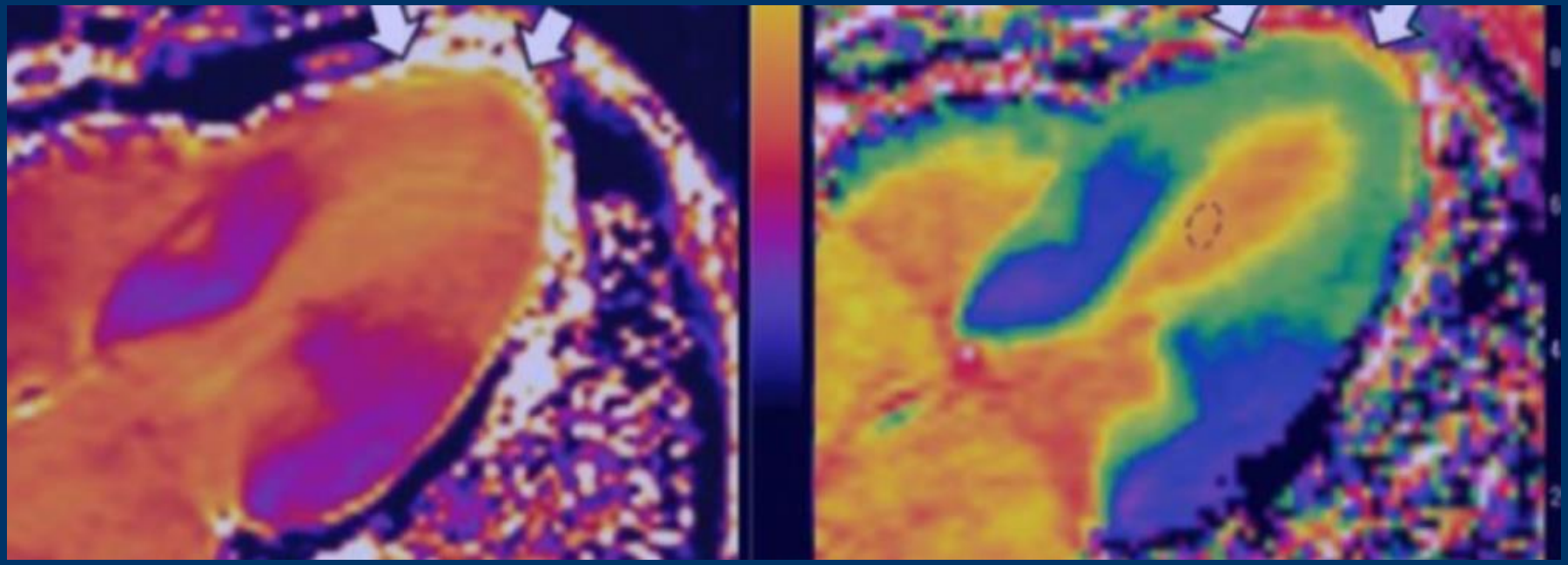


↑ TnT, no Δ EF, EDV ESV from LGE(-)

Characteristics	Baseline (n = 199)	Baseline With No Follow-up (n = 60)	Baseline With Follow-up (n = 139)	Follow-up (n = 139)
Focal edema, No. (%)[b]	162 (81)	45 (75)	117 (84)	2 (1)
Elevated T2 SI ratio, No. (%)[b]	169 (85)	49 (82)	120 (86)	4 (3)
T2 SI ratio, mean (SD) [95% CI] (cutoff level, ≥1.9)	2.3 (0.5) [2.2.-2.4]	2.3 (0.5) [2.1-2.4]	2.4 (0.5) [2.3-2.5]	1.7 (0.3) [1.6-1.8]
Elevated EGE ratio, No. (%)[c]	114 (70)	28 (72)	86 (69)	6 (5)
EGE ratio, mean (SD) [95% CI] (cutoff level, ≥4)	5.5 (3.1) [5.0-6.1]	5.2 (2.7) [4.4-6.0]	5.8 (3.3) [5.0-6.5]	3.3 (1.3) [2.9-3.6]
Elevated EGE ratio and T2 SI ratio, No. (%)[c]	110 (67)	27 (69)	83 (66)	2 (2)
Any LGE, No. (%)[d]	22 (9)	1 (1)	21 (13)	1 (1)
LGE >5 SD, No. (%)[d]	0	0	0	0

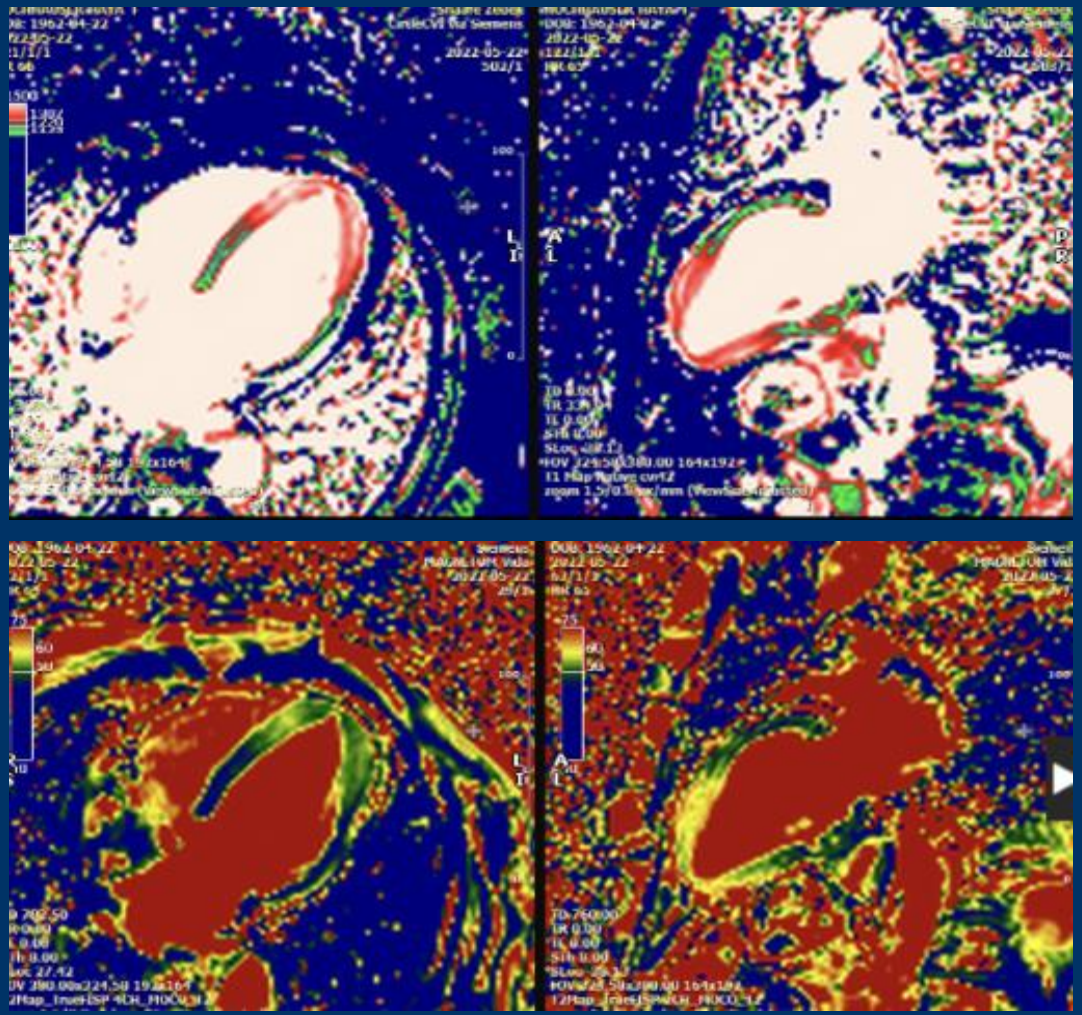
JAMA, July 20, 2011—Vol 306, No. 3

Native T1 / ECV



Aikawa, *European Heart Journal - Cardiovascular Imaging*, Volume 2019

Native T1/ T2

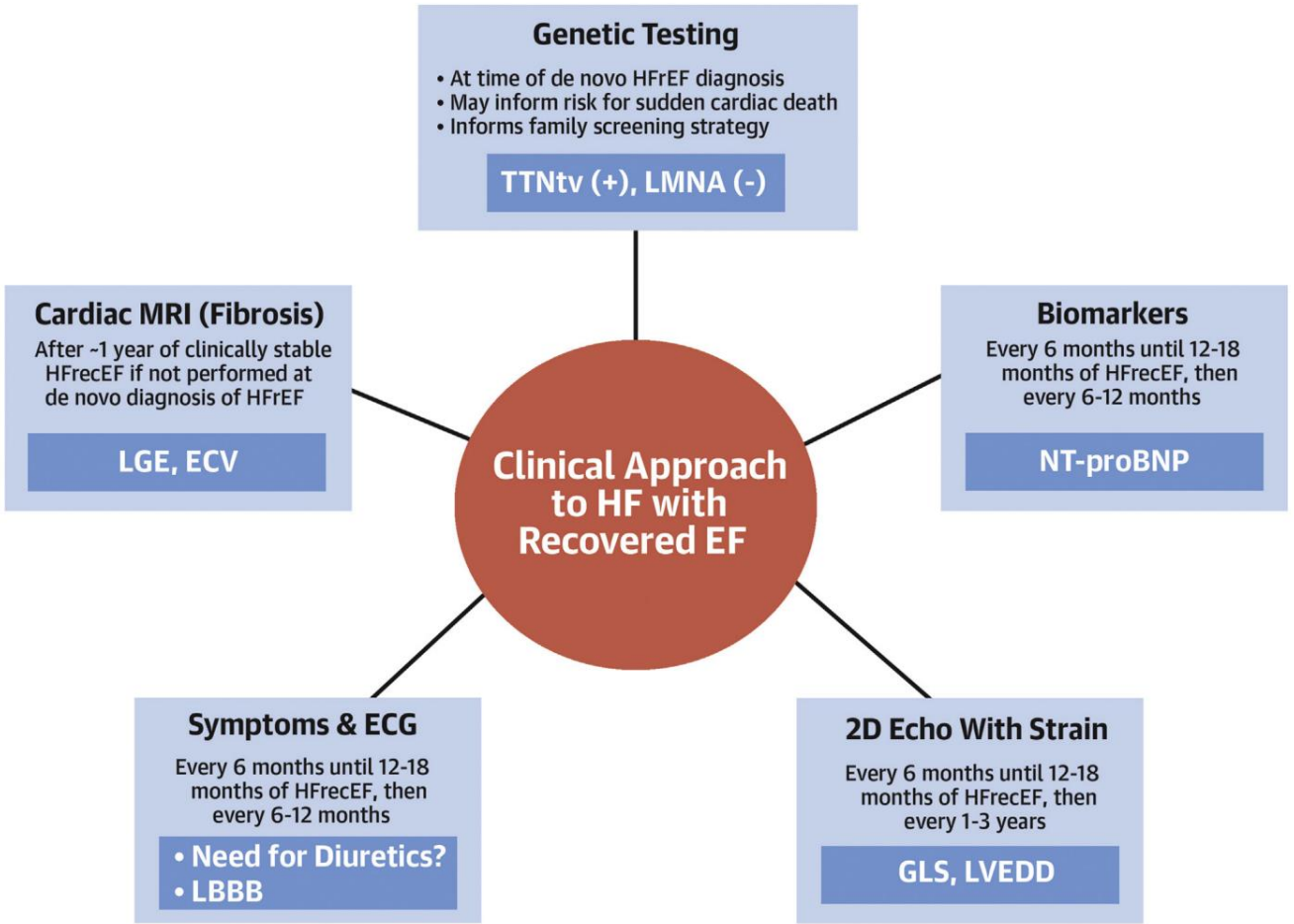


- Lasts for at least 3 month
- The number of segments with elevated native T1 correlates with prolonged LV wall motion recovery time

SZMC Pt. 2022

Aikawa, EHJ CVI 2019, Vermes, IJC 2020

CENTRAL ILLUSTRATION Clinical Assessment of Patients With Recovered Left Ventricular Ejection Fraction



Remaining Gaps and Research Targets

- Clinical trials of maintaining remission from HF
- Natural history of HFrecEF
- Biology of HFrecEF

Wilcox, J.E. et al. J Am Coll Cardiol. 2020;76(6):719-34.

JACC: HEART FAILURE
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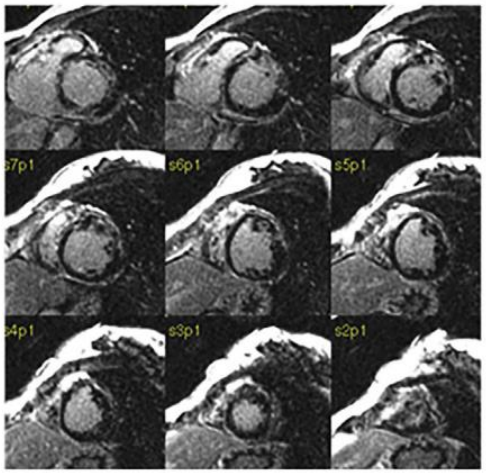
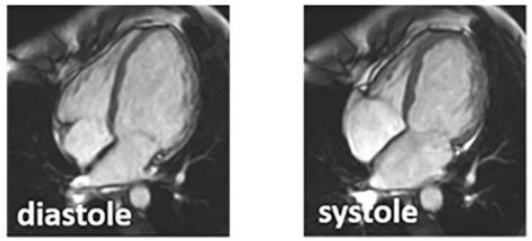
PUBLISHED BY ELSEVIER
VOL. 7, NO. 9, 2019

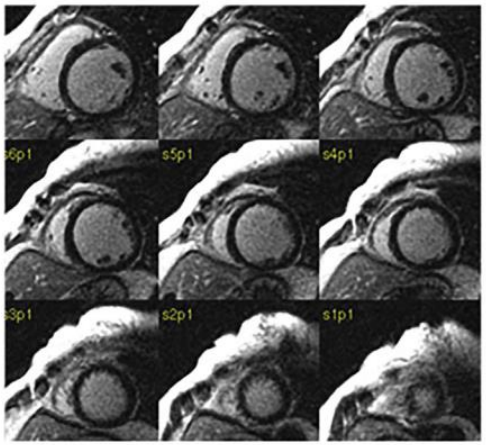
STATE-OF-THE-ART REVIEW

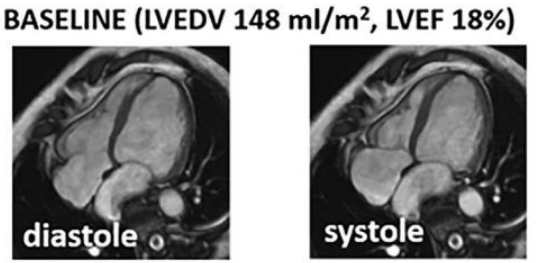
Imaging, Biomarker, and Clinical Predictors of Cardiac Remodeling in Heart Failure With Reduced Ejection Fraction

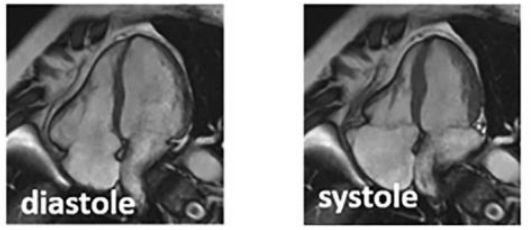
Alberto Aimo, MD,[a,*] Hanna K. Gaggin, MD, MPH,[c,d,*] Andrea Barison, MD, PhD,[a,b] Michele Emdin, MD, PhD,[a,b]











2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Table 5 Causes of heart failure, common modes of presentation and specific investigations

Cause	Examples of presentations	Specific investigations
CAD	Myocardial infarction Angina or "angina-equivalent" Arrhythmias	Invasive coronary angiography CT coronary angiography Imaging stress tests (echo, nuclear, CMR)
Hypertension	Heart failure with preserved systolic function Malignant hypertension/acute pulmonary oedema	24 h ambulatory BP Plasma metanephrines, renal artery imaging Renin and aldosterone
Valve disease	Primary valve disease e.g., aortic stenosis Secondary valve disease, e.g. functional regurgitation Congenital valve disease	Echo – transoesophageal/stress
Arrhythmias	Atrial tachyarrhythmias Ventricular arrhythmias	Ambulatory ECG recording Electrophysiology study, if indicated
CMPs	All Dilated Hypertrophic Restrictive ARVC Peripartum Takotsubo syndrome Toxins: alcohol, cocaine, iron, copper	CMR, genetic testing Right and left heart catheterization CMR, angiography Trace elements, toxicology, LFTs, GGT
Congenital heart disease	Congenitally corrected/repaired transposition of great arteries Shunt lesions Repaired tetralogy of Fallot Ebstein's anomaly	CMR
Infective	Viral myocarditis Chagas disease HIV Lyme disease	CMR, EMB Serology
Drug-induced	Anthracyclines Trastuzumab VEGF inhibitors Immune checkpoint inhibitors Proteasome inhibitors RAF+MEK inhibitors	
Infiltrative	Amyloid Sarcoidosis Neoplastic	Serum electrophoresis and serum free light chains, Bence Jones protein, bone scintigraphy, CMR, CT-PET, EMB Serum ACE, CMR, FDG-PET, chest CT, EMB CMR, EMB
Storage disorders	Haemochromatosis Fabry disease Glycogen storage diseases	Iron studies, genetics, CMR (T2* imaging), EMB α-galactosidase A, genetics, CMR (T1 mapping)
Endomyocardial disease	Radiotherapy Endomyocardial fibrosis/eosinophilia Carcinoid	CMR EMB 24 h urine 5-HIAA
Pericardial disease	Calcification Infiltrative	Chest CT, CMR, right and left heart catheterization

Recommendations	Class[a]	Level[b]
CMR		
CMR is recommended for the assessment of myocardial structure and function in those with poor echocardiogram acoustic windows.	I	C
CMR is recommended for the characterization of myocardial tissue in suspected infiltrative disease, Fabry disease, inflammatory disease (myocarditis), LV non-compaction, amyloid, sarcoidosis, iron overload/haemochromatosis.	I	C
CMR with LGE should be considered in DCM to distinguish between ischaemic and non-ischaemic myocardial damage.	IIa	C


Thank you