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Guy's and St Thomas'

NHS Foundation Trust NHS

The role of imaging on risk substrate detection and risk stratification

Dr. Amedeo Chiribiri, MD, PhD

Head of CMR Service at Division of Imaging Sciences and Department of Cardiology
King's College London and Guy's and St. Thomas' Trust Foundation

Can imaging influence patient outcomes?

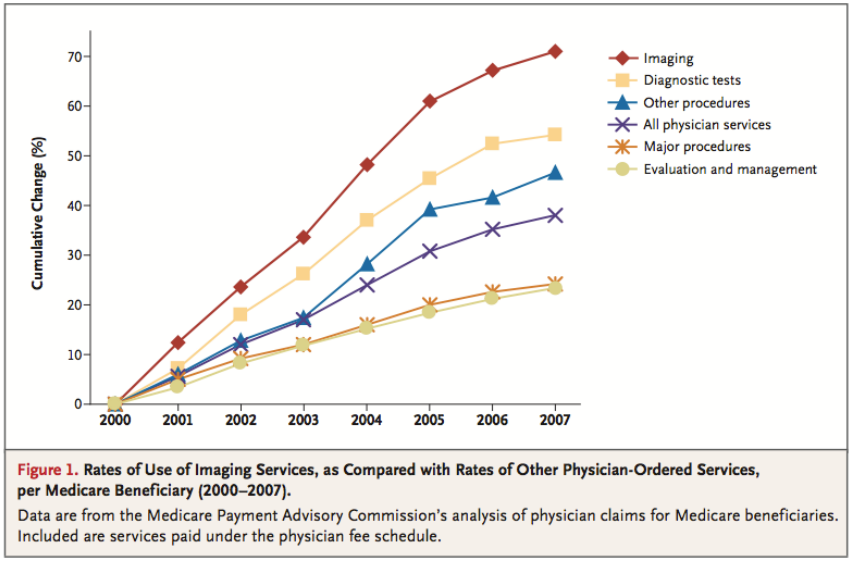
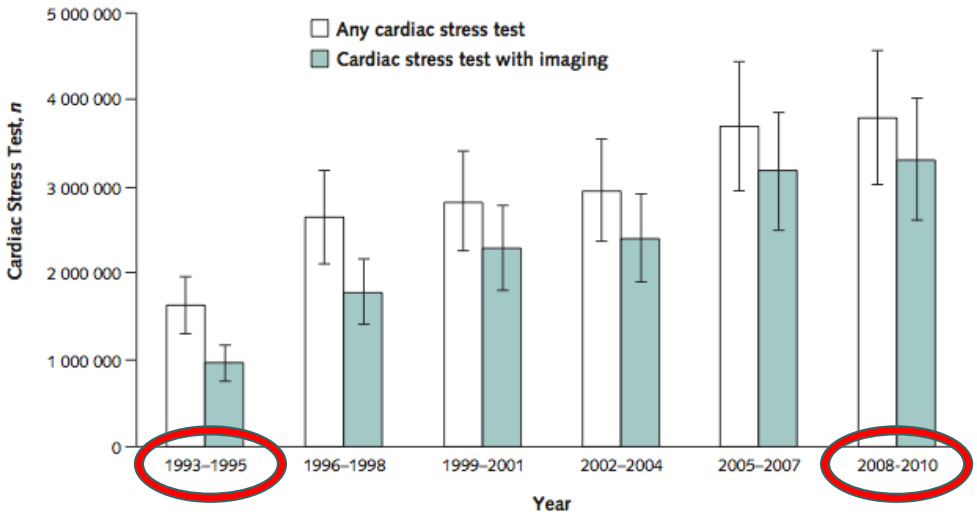


Figure 1. Rates of Use of Imaging Services, as Compared with Rates of Other Physician-Ordered Services, per Medicare Beneficiary (2000–2007).

Data are from the Medicare Payment Advisory Commission's analysis of physician claims for Medicare beneficiaries. Included are services paid under the physician fee schedule.

Iglehart, J. K. (2009). NEJM 360:1030-73



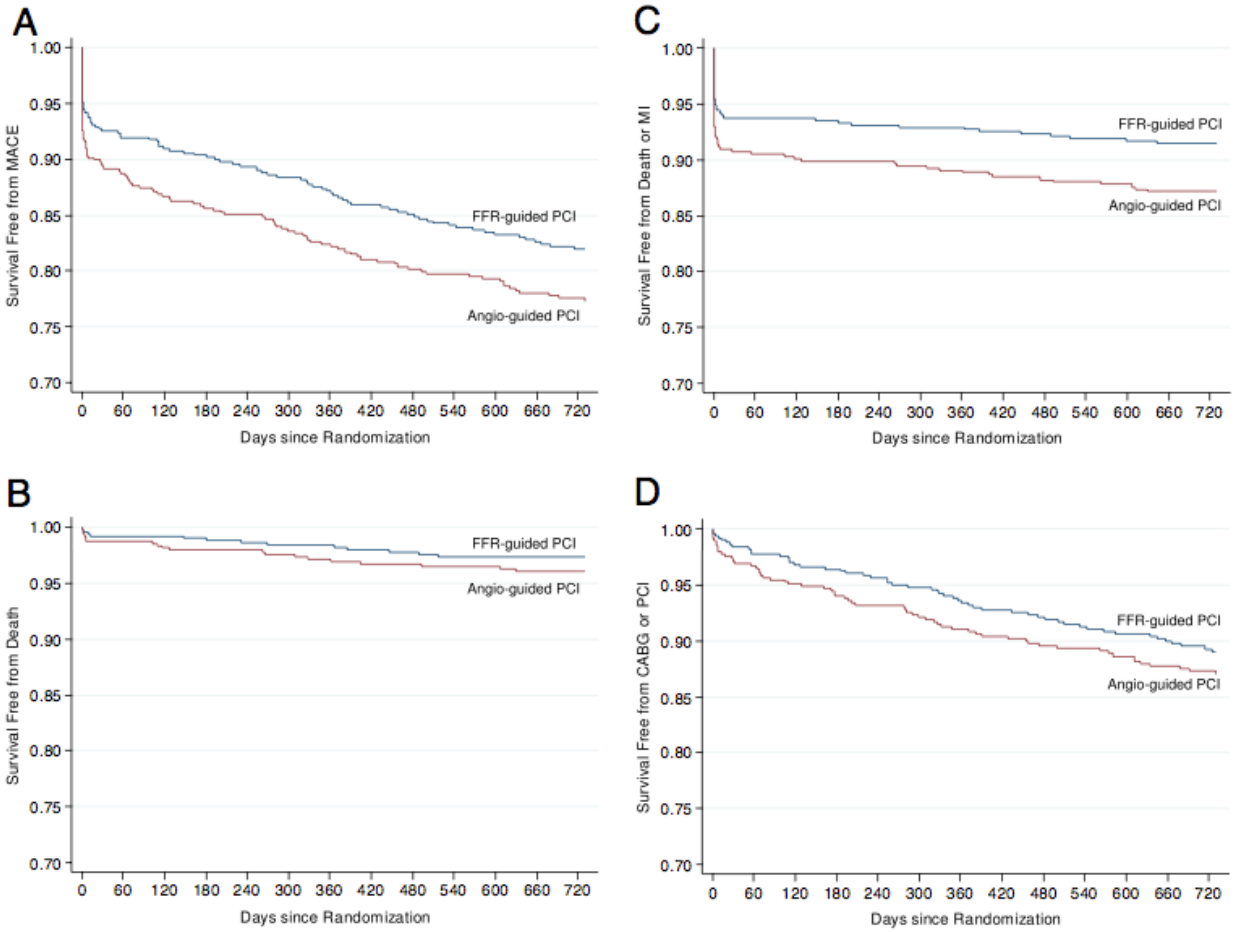
Ladapo, J. A., et al. *Annals of Internal Medicine*, *161*(7), 482–490.

Can imaging influence patient outcomes?

Diagnostic accuracy

Risk stratification

Can imaging influence patient outcomes?



Pijls, N et al. *JACC*, *56*(3), 177–184. doi:10.1016/j.jacc/2010.04.012

Can imaging influence patient outcomes?

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association

Criteria for Evaluation of Novel Markers of Cardiovascular Risk: A Scientific Statement From the American Heart Association

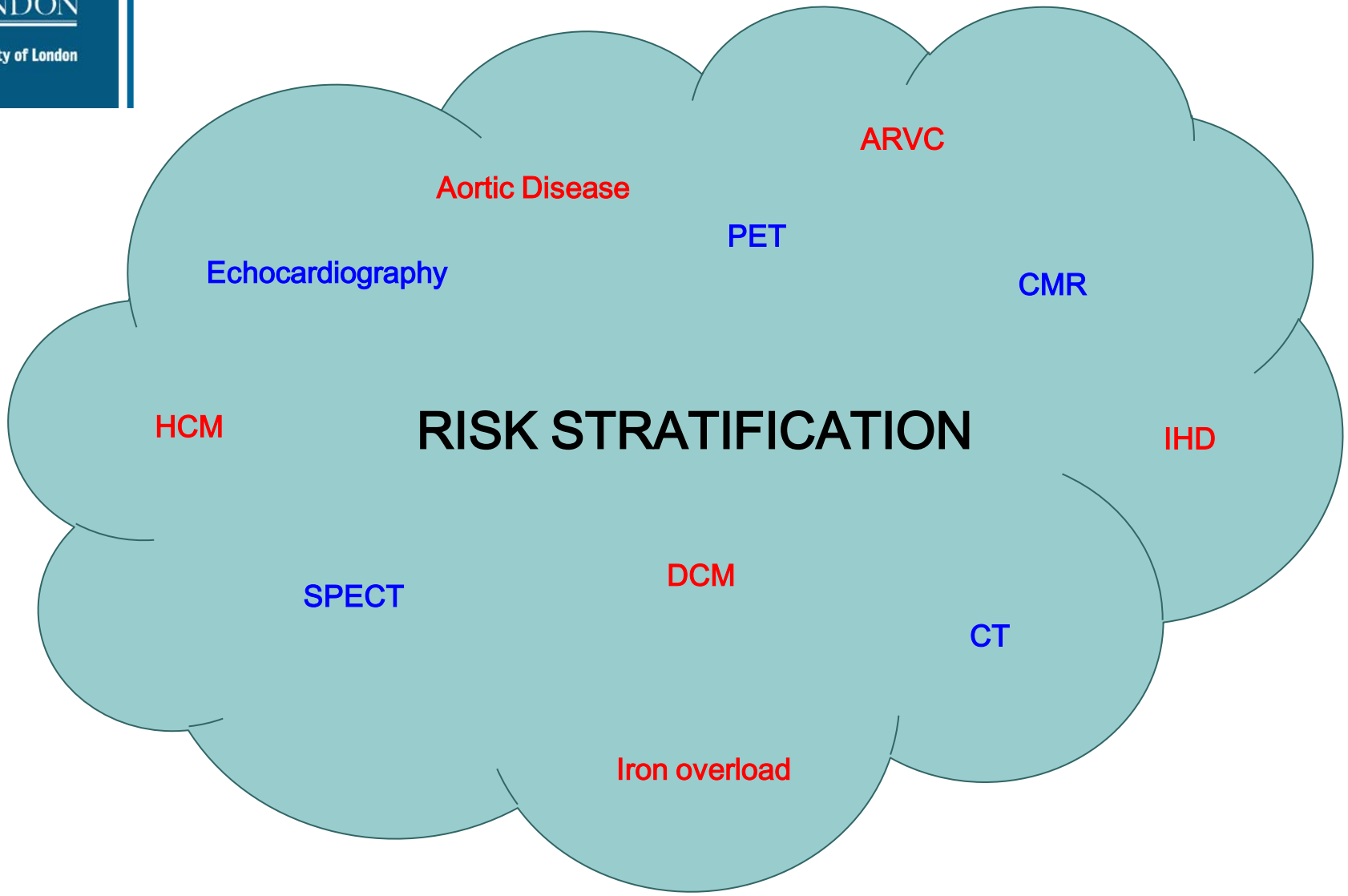
Mark A. Hlatky, Philip Greenland, Donna K. Arnett, Christie M. Ballantyne, Michael H. Criqui, Mitchell S.V. Elkind, Alan S. Go, Frank E. Harrell, Jr, Yuling Hong, Barbara V. Howard, Virginia J. Howard, Priscilla Y. Hsue, Christopher M. Kramer, Joseph P. McConnell, Sharon-Lise T. Normand, Christopher J. O'Donnell, Sidney C. Smith, Jr and Peter W.F. Wilson

Circulation, *119*(17), 2408–2416. doi:10.1161/CIRCULATIONAHA.109.192278

Can imaging influence patient outcomes?

Phases of evaluation of a novel risk marker.

1. Proof of concept—Do novel marker levels differ between subjects with and without outcome?
2. Prospective validation—Does the novel marker predict development of future outcomes in a prospective cohort or nested case-cohort/case-cohort study?
3. Incremental value—Does the novel marker add predictive information to established, standard risk markers?
4. Clinical utility—Does the novel risk marker change predicted risk sufficiently to change recommended therapy?
5. Clinical outcomes—Does use of the novel risk marker improve clinical outcomes, especially when tested in a randomized clinical trial?
6. Cost-effectiveness—Does use of the marker improve clinical outcomes sufficiently to justify the additional costs of testing and treatment?


ARVC
Aortic Disease
PET
Echocardiography
CMR
HCM
RISK STRATIFICATION
IHD
DCM
SPECT
CT
Iron overload

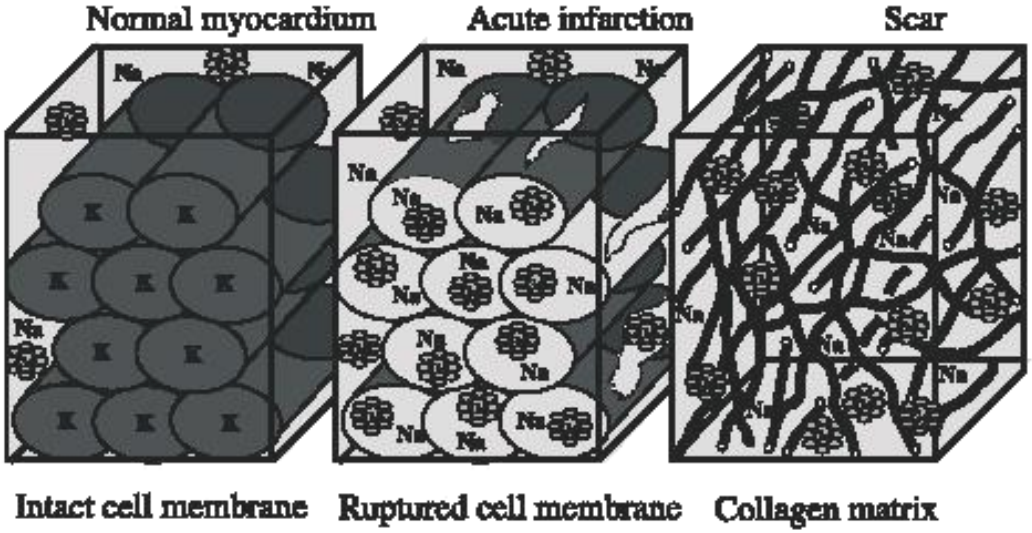
Advantages of CMR

- No radiation
- Good safety profile of cyclic Gd chelates
- Tissue characterization
  - Scar/fibrosis
  - Oedema
  - Iron
  - Fat

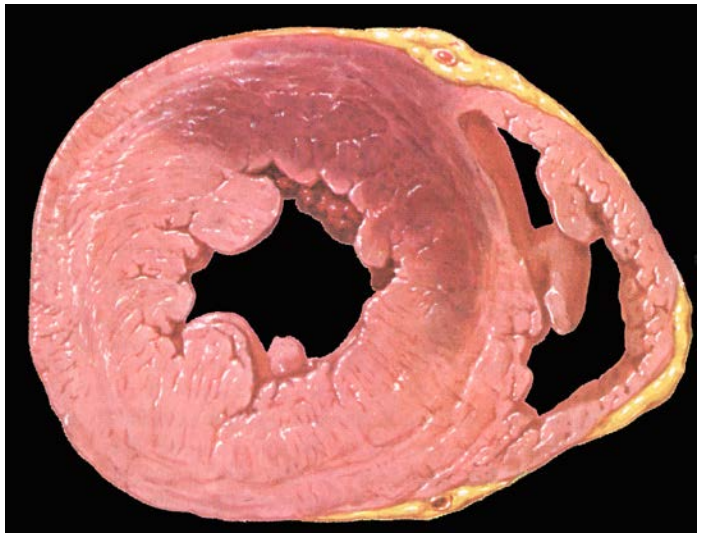
  - Perfusion and function in a single stop

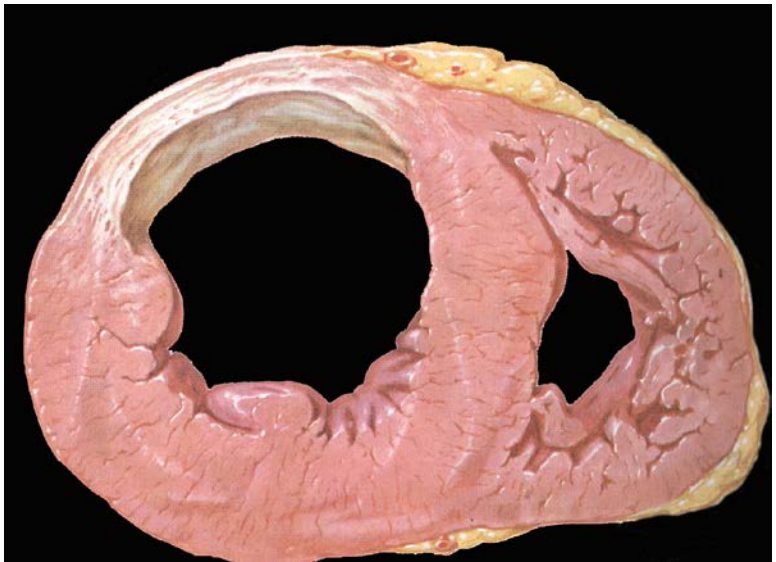
  - Interstitial fibrosis
  - Extracellular volume (ECV)
  - Microvascular obstruction/intramyocardial haemorrage

LATE GADOLINIUM ENHANCEMENT



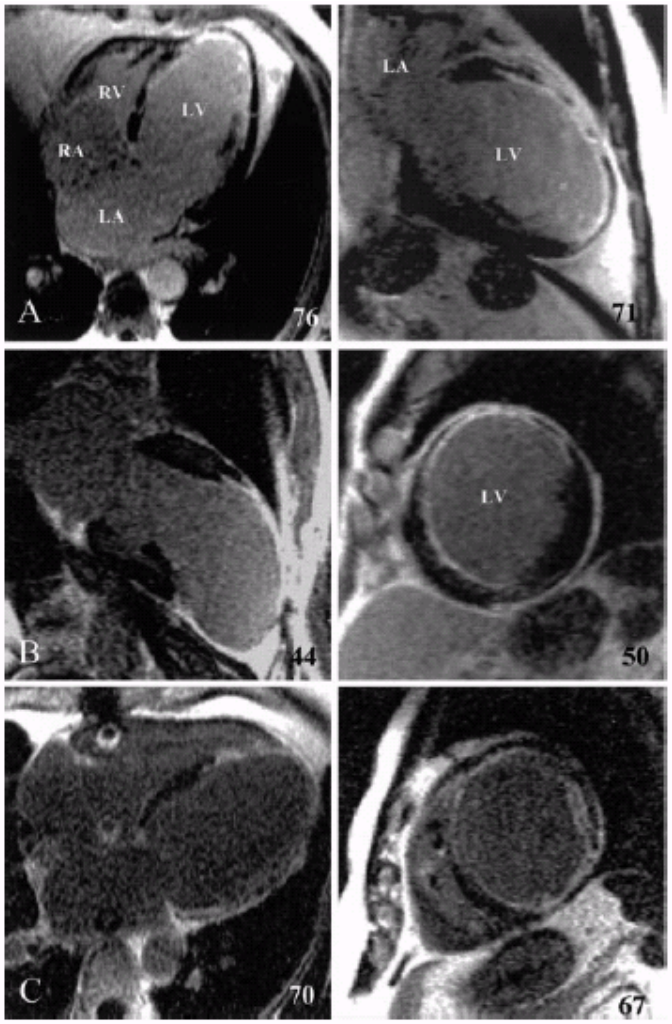
Mahrholdt: Eur H J 2002

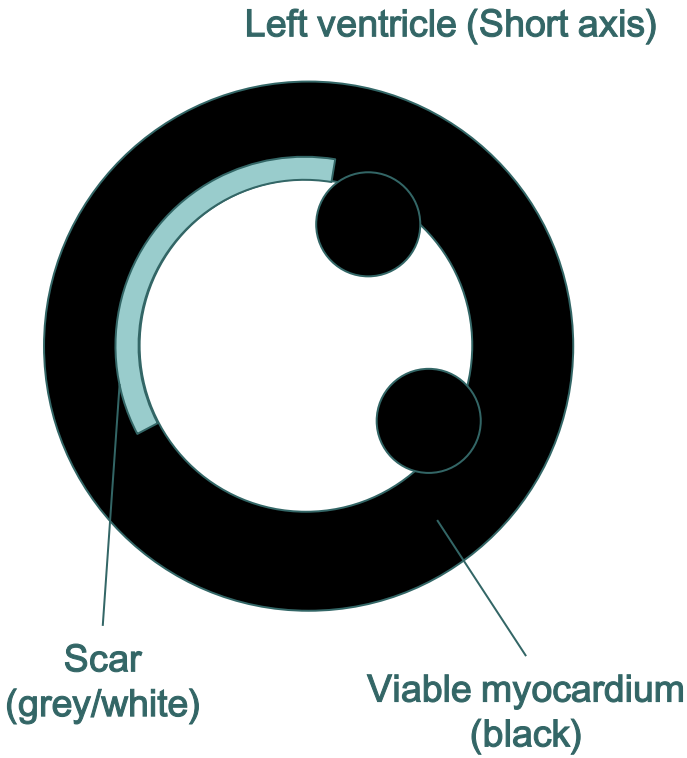




LATE GADOLINIUM ENHANCEMENT

IHD





McCrohon, Pennell et al. Circulation 2003

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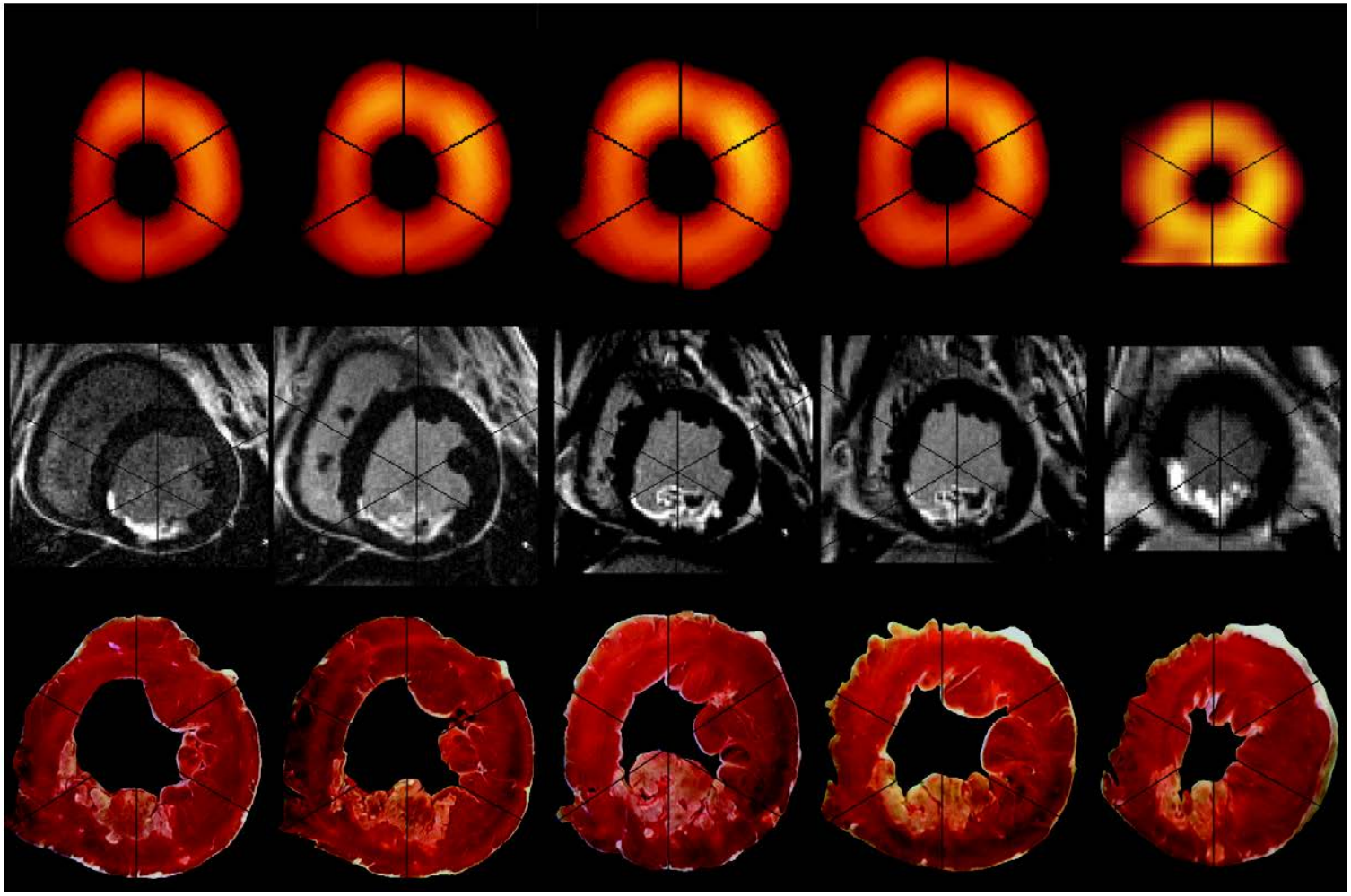
LATE GADOLINIUM ENHANCEMENT

SPECT

CMR

Histology



Wagner, et al; Lancet 2003

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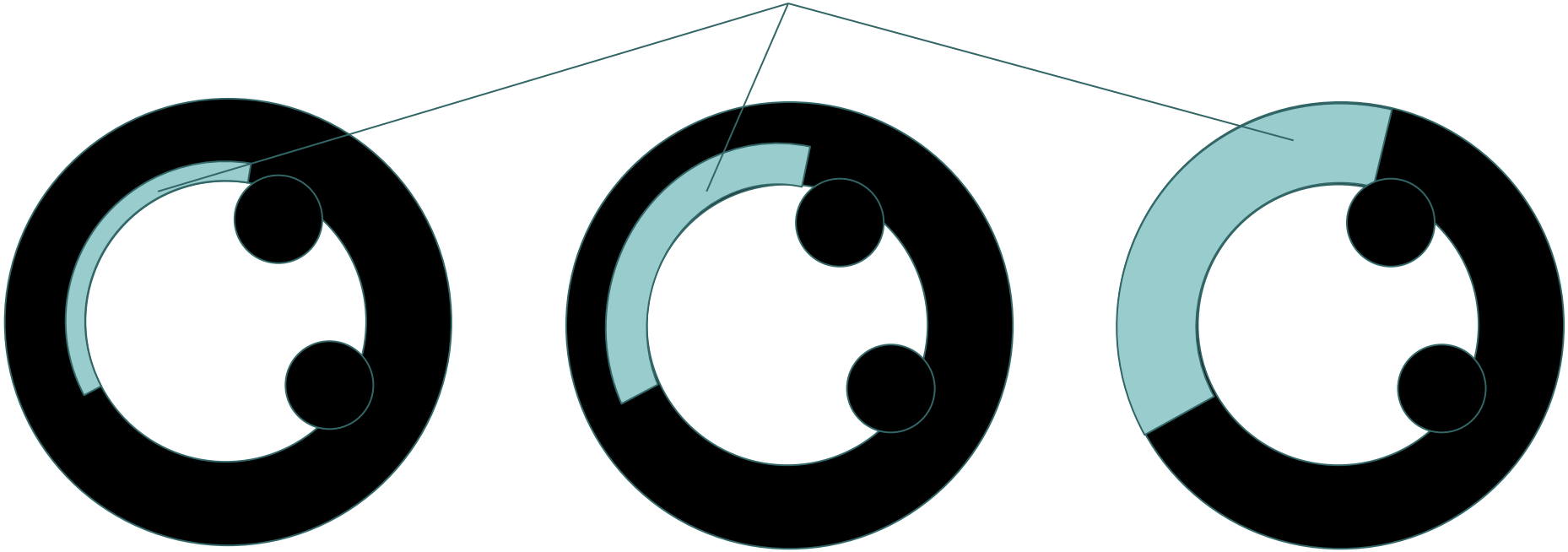
LATE GADOLINIUM ENHANCEMENT

ISCHAEMIC LAD SCAR



25% TRANSMURALITY

50% TRANSMURALITY

100% TRANSMURALITY

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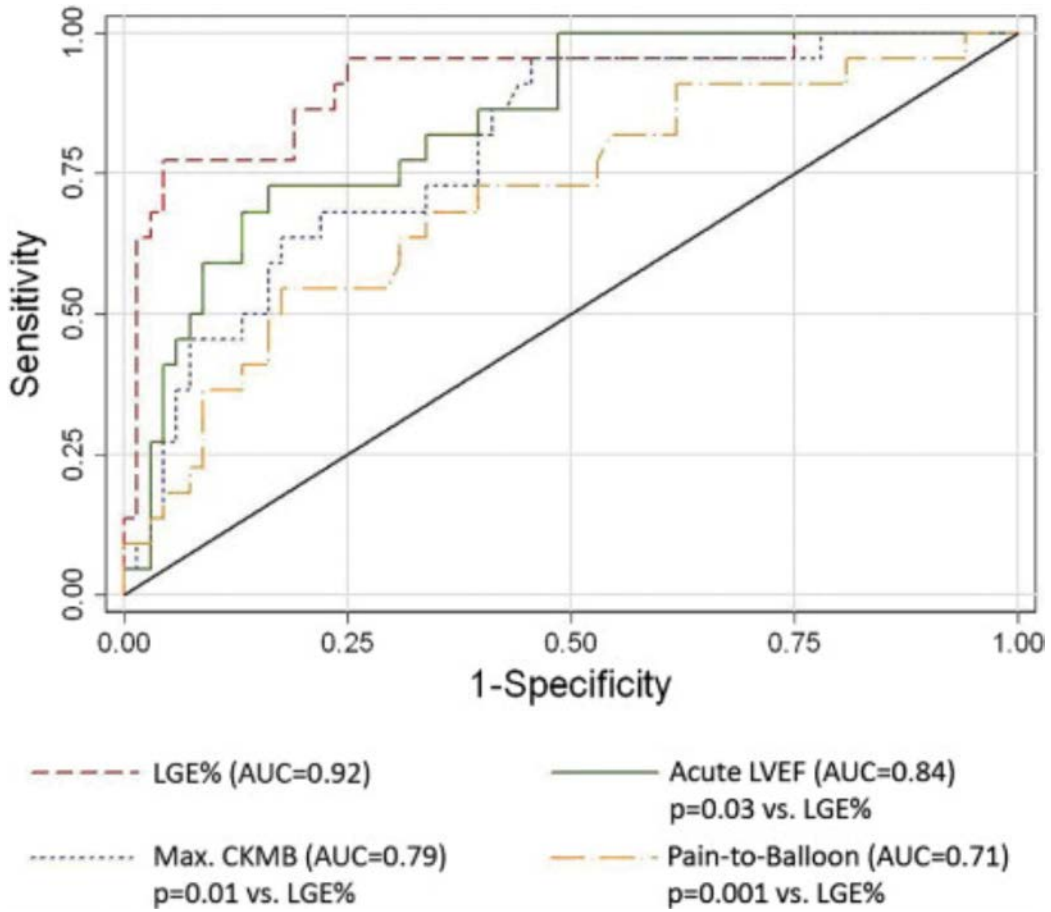
Predicting Late Myocardial Recovery and Outcomes in the Early Hours of ST-Segment Elevation Myocardial Infarction: Traditional Measures Compared With Microvascular Obstruction, Salvaged Myocardium, and Necrosis Characteristics by Cardiovascular Magnetic Resonance



J Am Coll Cardiol. 2010;55(22):2459-2469. doi:10.1016/j.jacc.2010.02.033

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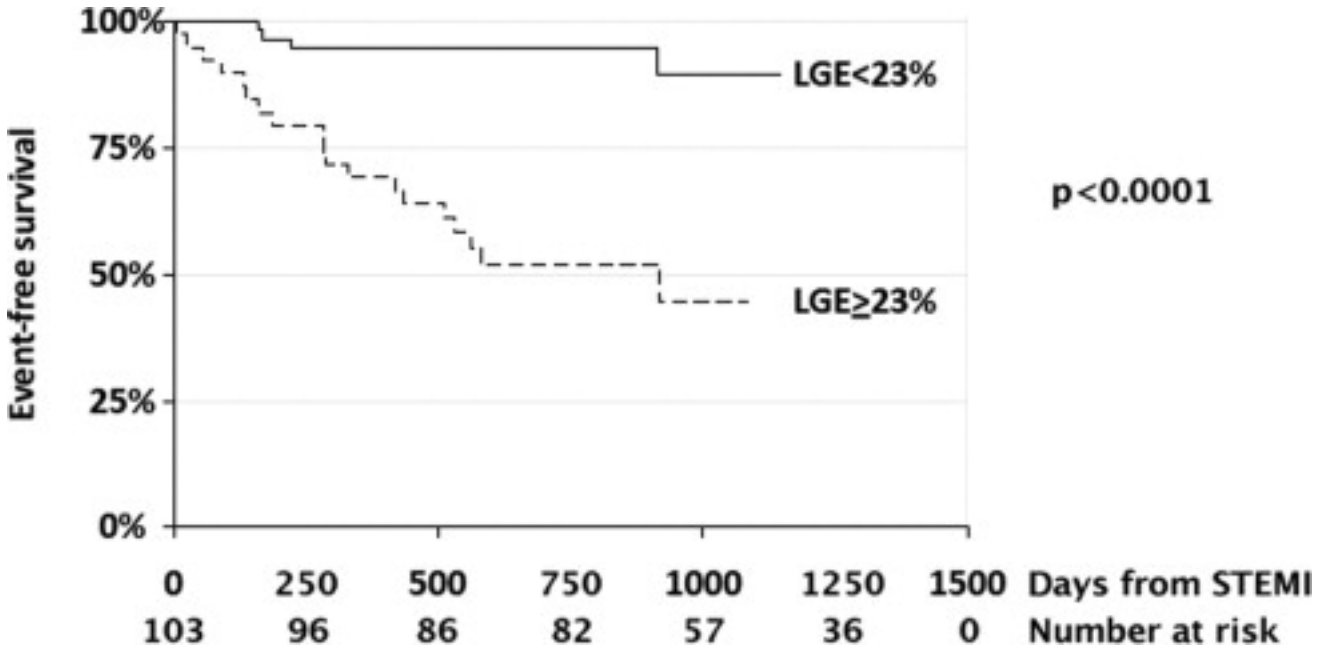
Predicting Late Myocardial Recovery and Outcomes in the Early Hours of ST-Segment Elevation Myocardial Infarction: Traditional Measures Compared With Microvascular Obstruction, Salvaged Myocardium, and Necrosis Characteristics by Cardiovascular Magnetic Resonance



Larose E, et al. J Am Coll Cardiol. 2010;55(22):2459-2469. doi:10.1016/j.jacc.2010.02.033

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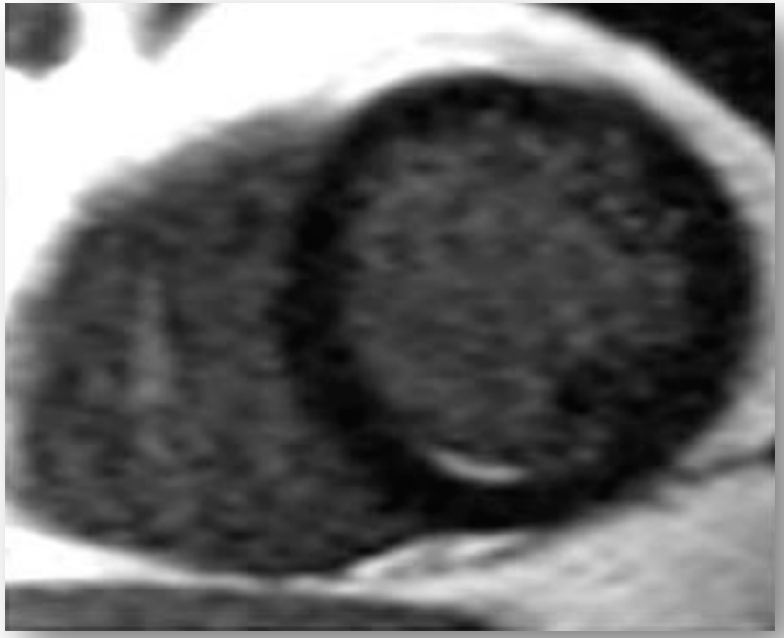
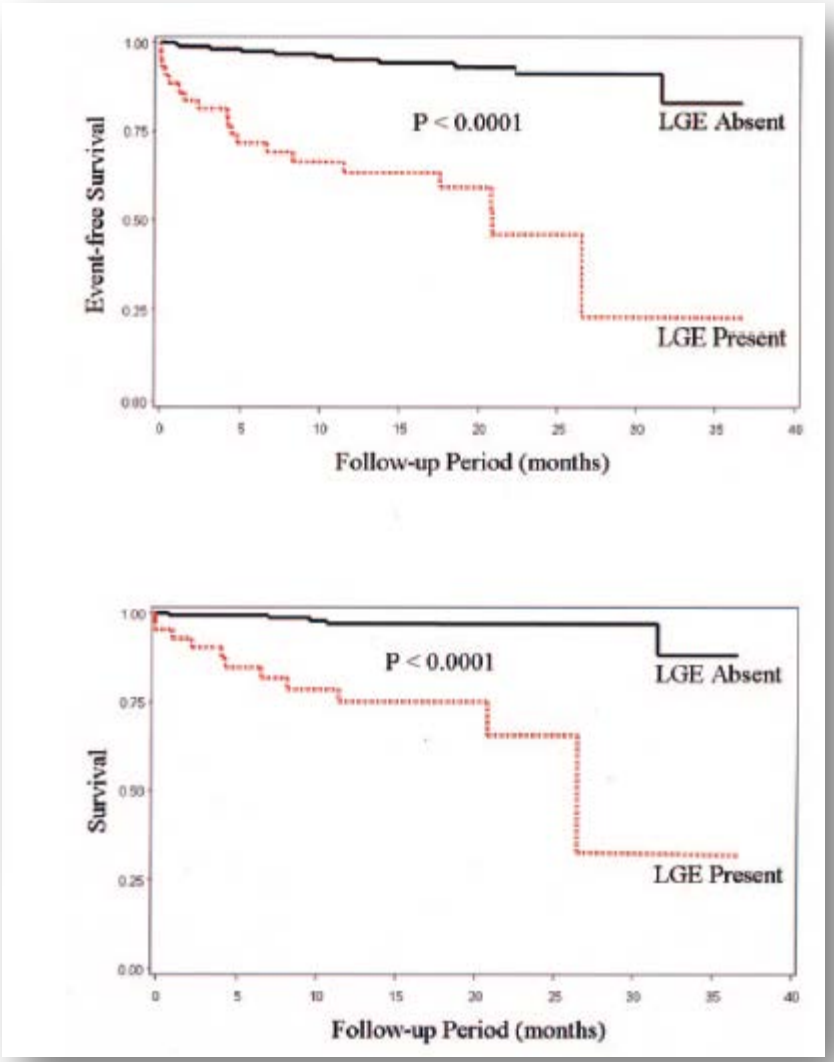
Impact of Unrecognized Myocardial Scar Detected by Cardiac Magnetic Resonance Imaging on Event-Free Survival in Patients Presenting With Signs or Symptoms of Coronary Artery Disease

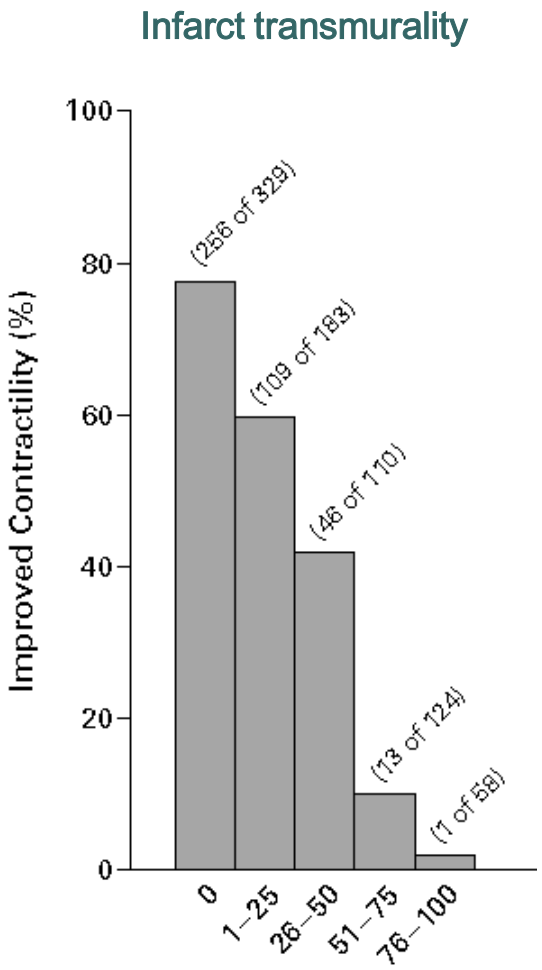
Raymond Y. Kwong, Anna K. Chan, Kenneth A. Brown, Carmen W. Chan, H. Glenn Reynolds, Sui Tsang and Roger B. Davis

Circulation 2006;113;2733-2743; originally published online Jun 5, 2006;

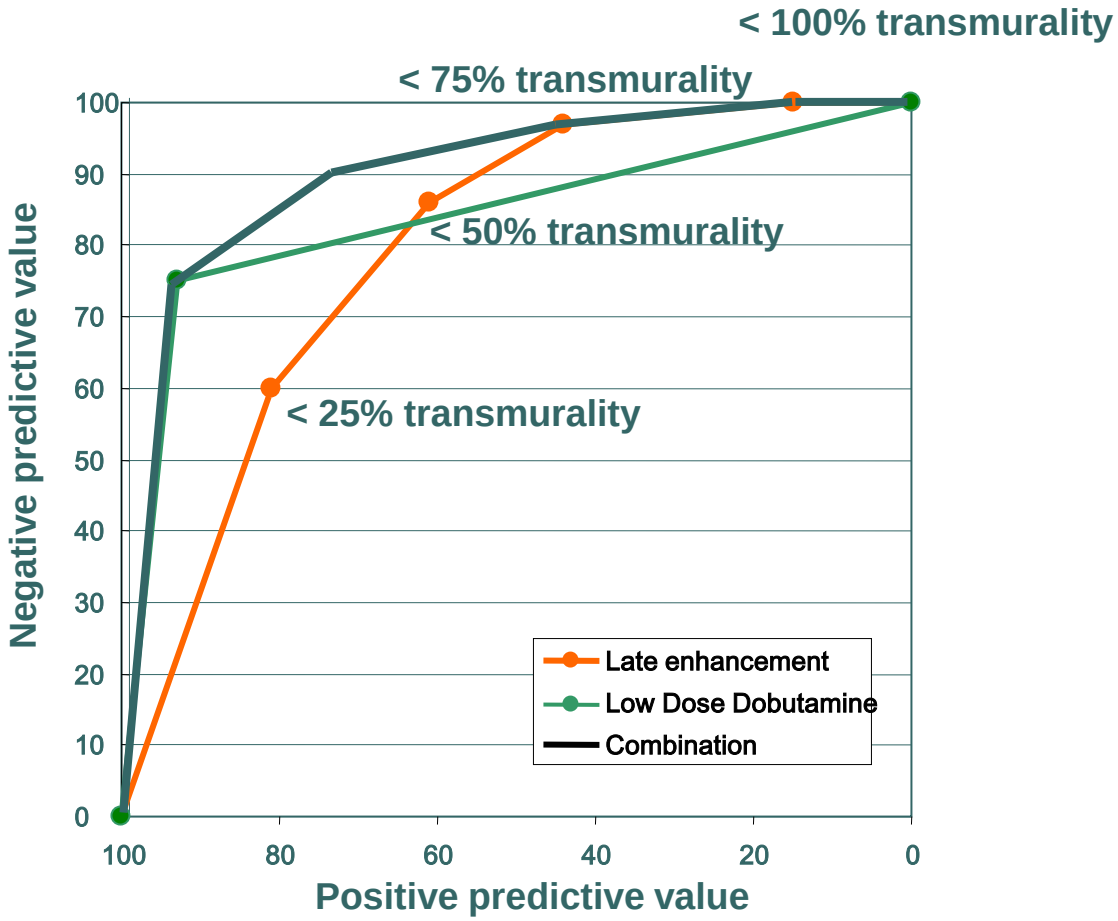




Prediction of functional recovery



Kim: NEJM 2000



Wellnhofer: Circulation 2004

STICH Trial: the end of imaging-guided revascularization?

N =1,212

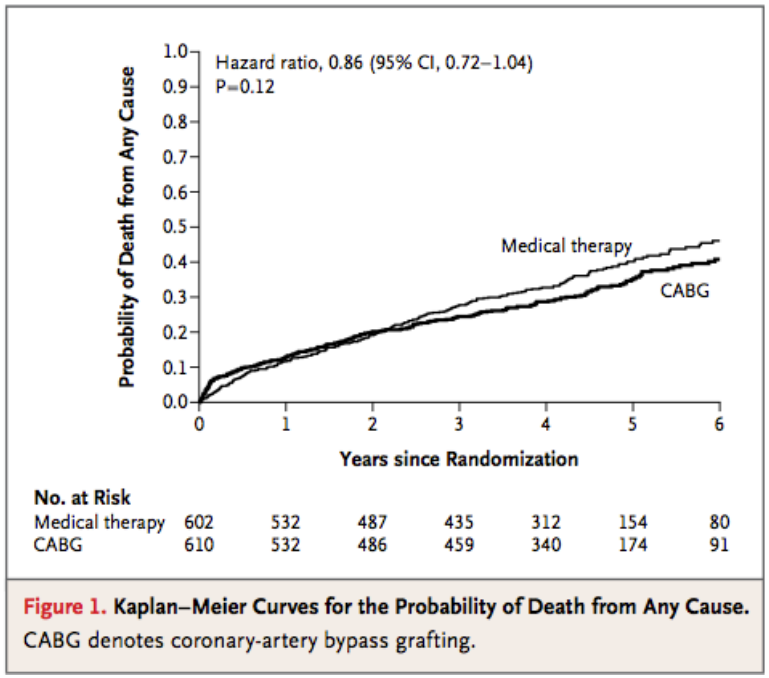
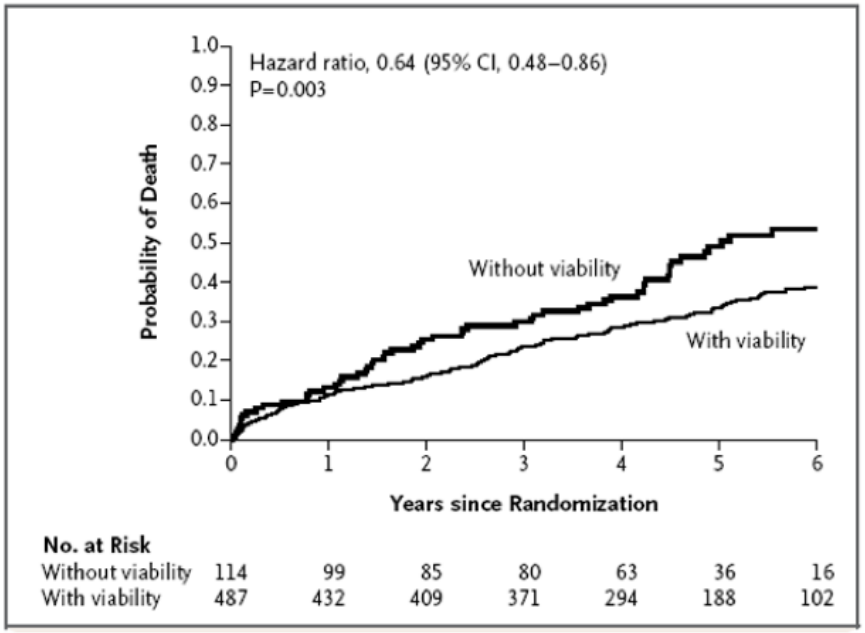


Figure 1. Kaplan–Meier Curves for the Probability of Death from Any Cause.
CABG denotes coronary-artery bypass grafting.

Velazquez, E. J. et al NEJM doi:10.7326/M13-1380

N =601



0.64 (95%CI: 0.48 - 0.86); P = 0.003 → P=0.21 after adjusting for baseline variables

Bonow, R. O., et al. *N*EJM, *364*(17), 1617–1625.

STICH Trial: the end of imaging-guided revascularization?

- SPECT → presence of ≥11 viable segments (≥65% of the entire left ventricle). When ≥7 segments were nonviable (≥41% of the left ventricle), the patient was considered to have insufficient mass of viable myocardium.

- ECHO-STRESS → 5 or more segments with abnormal resting systolic function but manifesting contractile reserve during dobutamine administration.

Bonow, R. O., et al. *N*EJM, *364*(17), 1617–1625.

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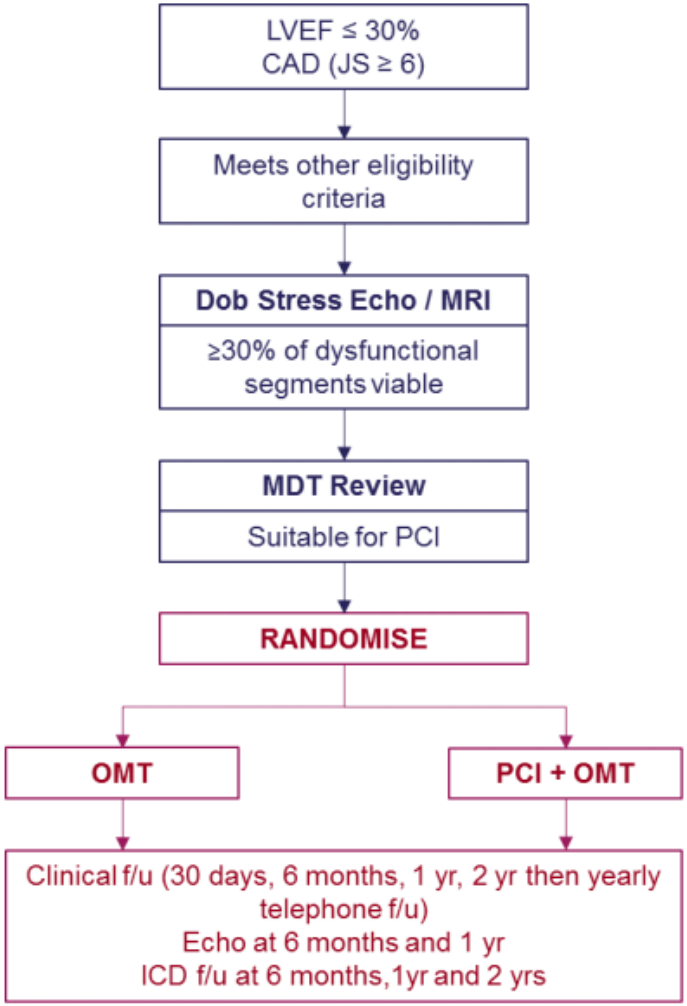
REVIVED

REVascularisation for Ischaemic Ventricular Dysfunction

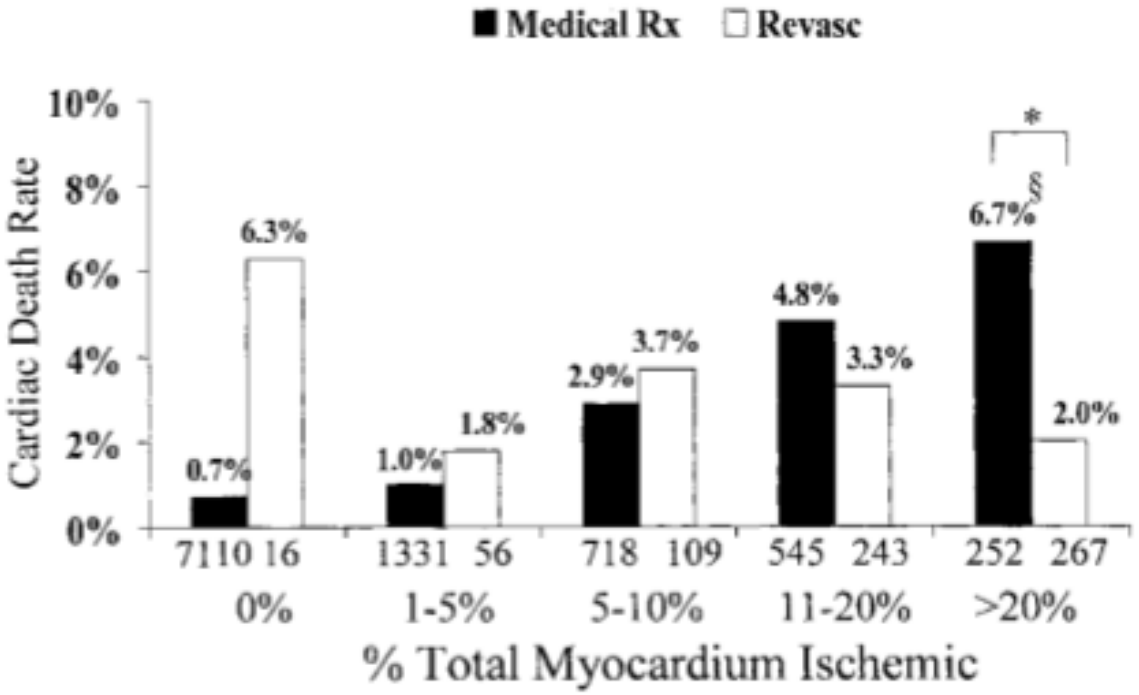


Primary Endpoint

All-cause death or hospitalisation due to heart failure over the duration of the trial (1 – 60 months)

http://revived.lshtm.ac.uk/files/2013/11/REVIVED-BCIS2_Protocol_V5_21_October_2013.pdf

Perfusion - SPECT



Hachamovitch, R. *Circulation 2003*, *107*(23), 2900–2907.

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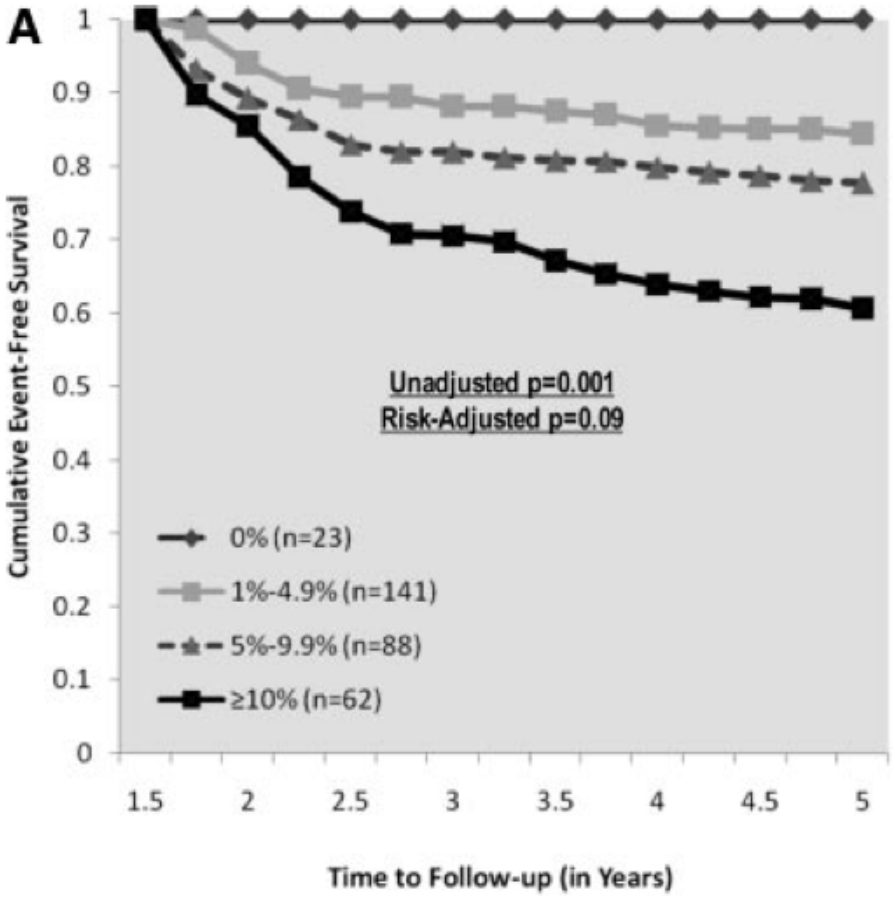
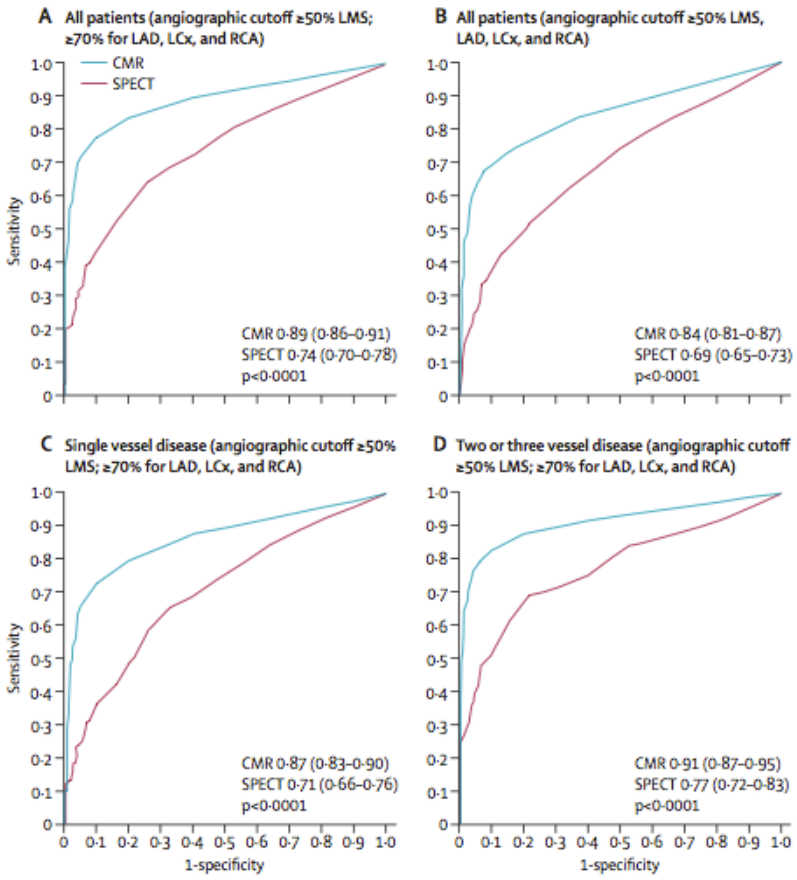
Perfusion - SPECT

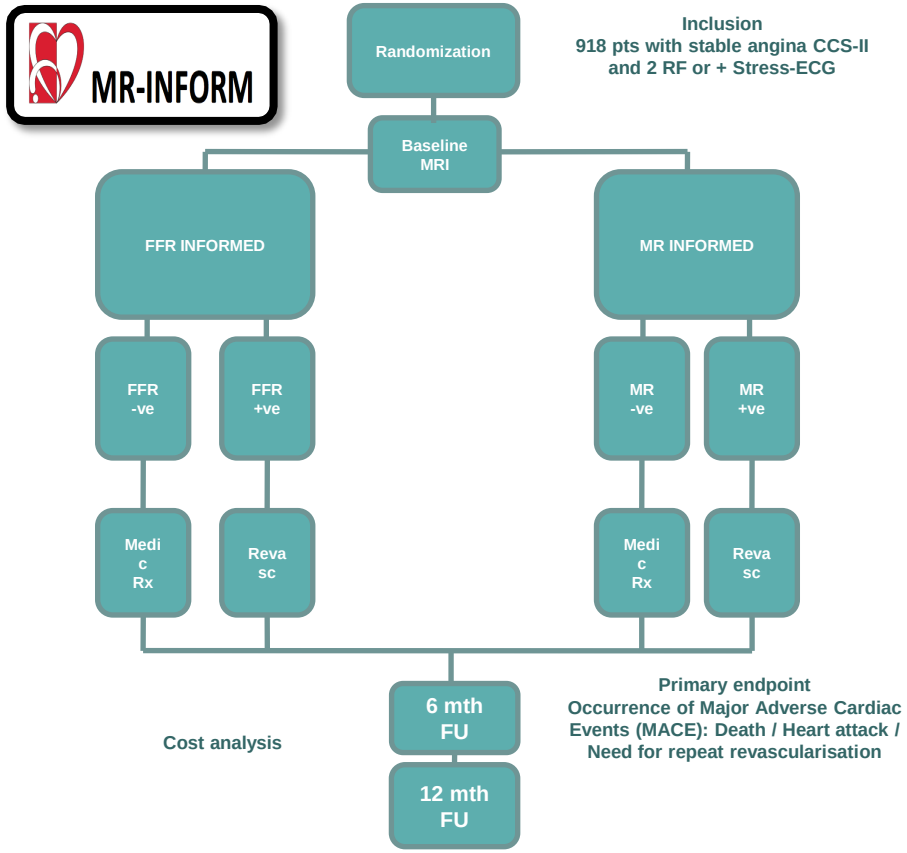


Perfusion - CMR

DIAGNOSTIC ACCURACY – CE-MARC trial



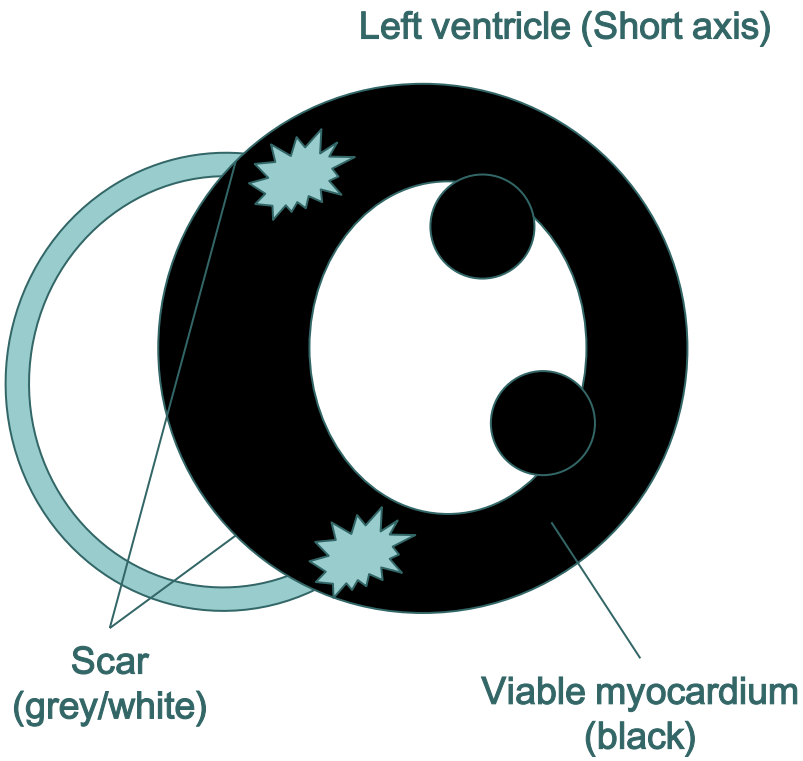
PATIENTS' MANAGEMENT – MR-INFORM study



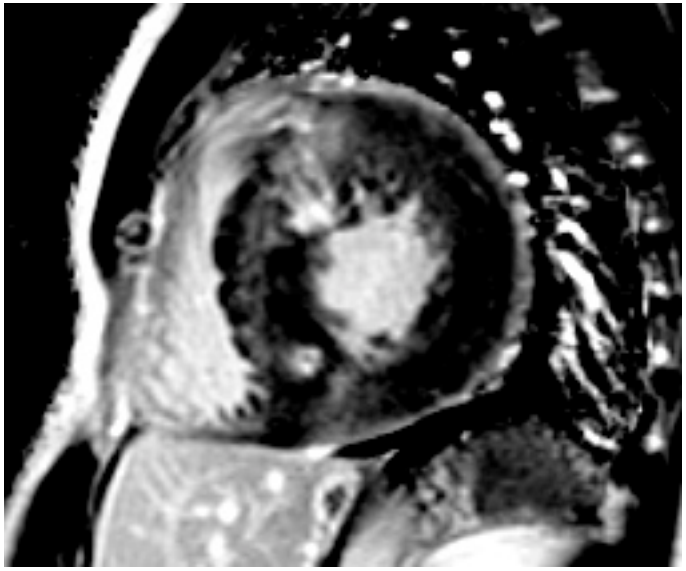
Greenwood J et al. CE-MARC trial. *The Lancet*, *379*(9814), 453–460.

Hussain, S. et al JCMR, *14*(1), 65.

LATE GADOLINIUM ENHANCEMENT

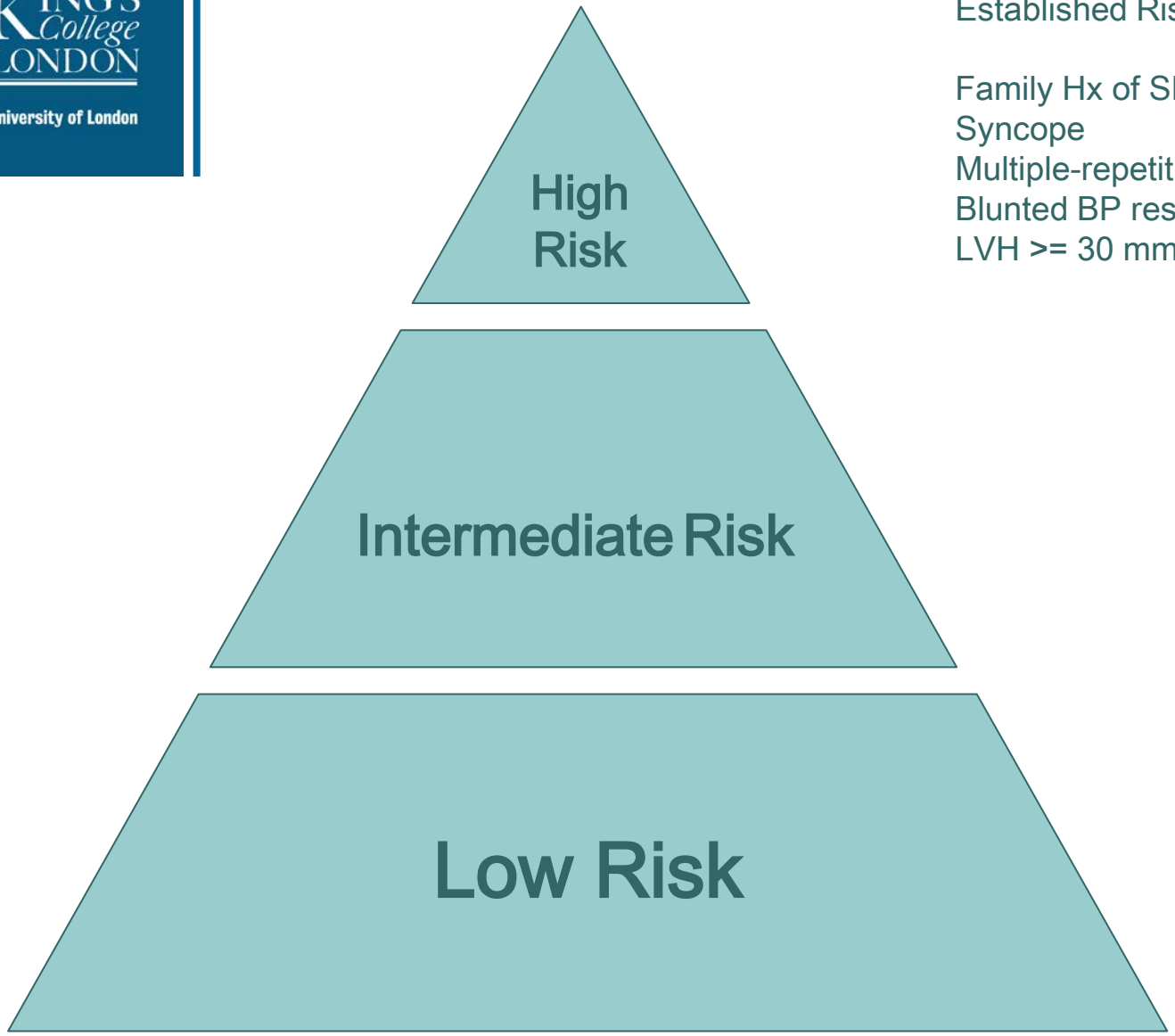


HCM



50-70% of patients
Associated with degree of HT and NSVT
Predicts clinical events

Published studies underpowered to detect association with SCD

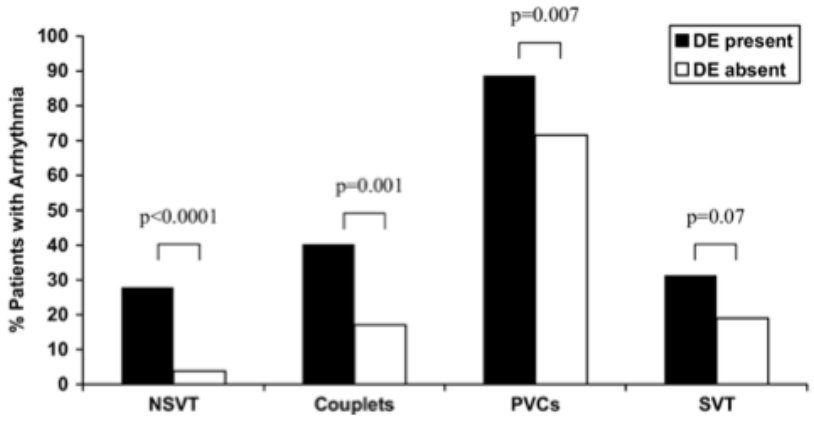


Established Risk Markers → ICD

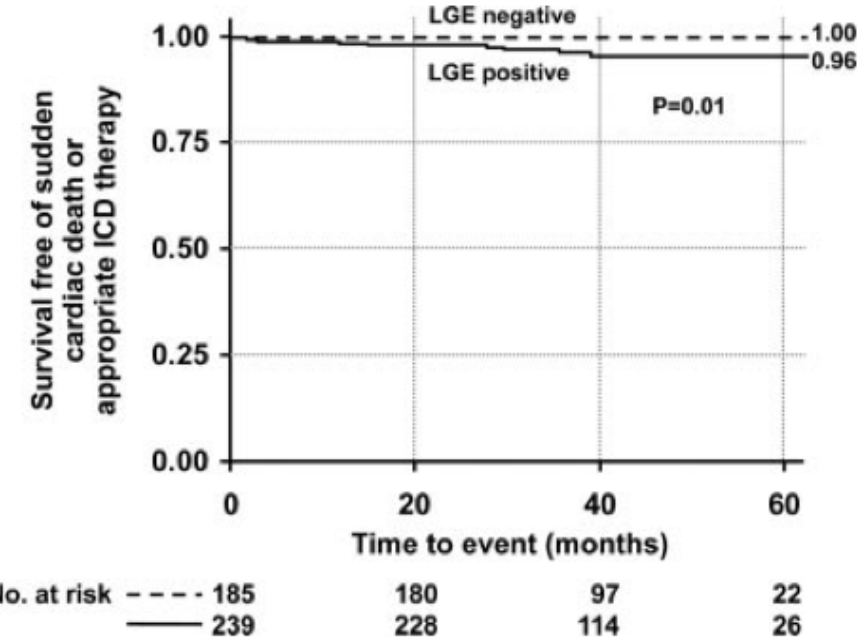
Family Hx of SD
Syncope
Multiple-repetitive NSVT
Blunted BP response on exercise
LVH >= 30 mm

"No risk factor patients"

Holter NSVT and LGE



7x RISK

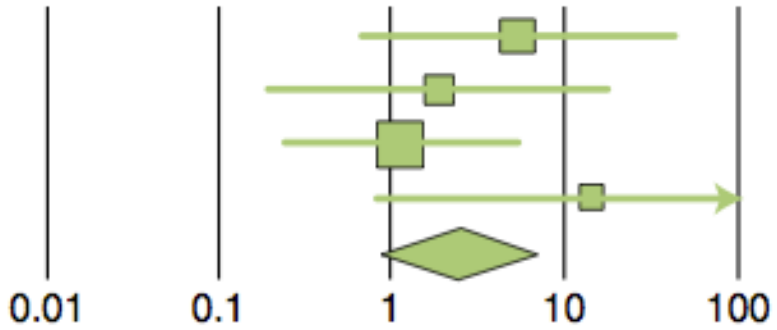


Adabag, A. S.et al. *JACC*, *51*(14), 1369–1374.

Rubinshtein, R., etal. *Circulation HF*, *3*(1), 51–58.

LGE and SCD events

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
Rubinshtein	13.62 (0.78-237.55)	0.073
Pooled	2.39 (0.87-6.58)	0.091

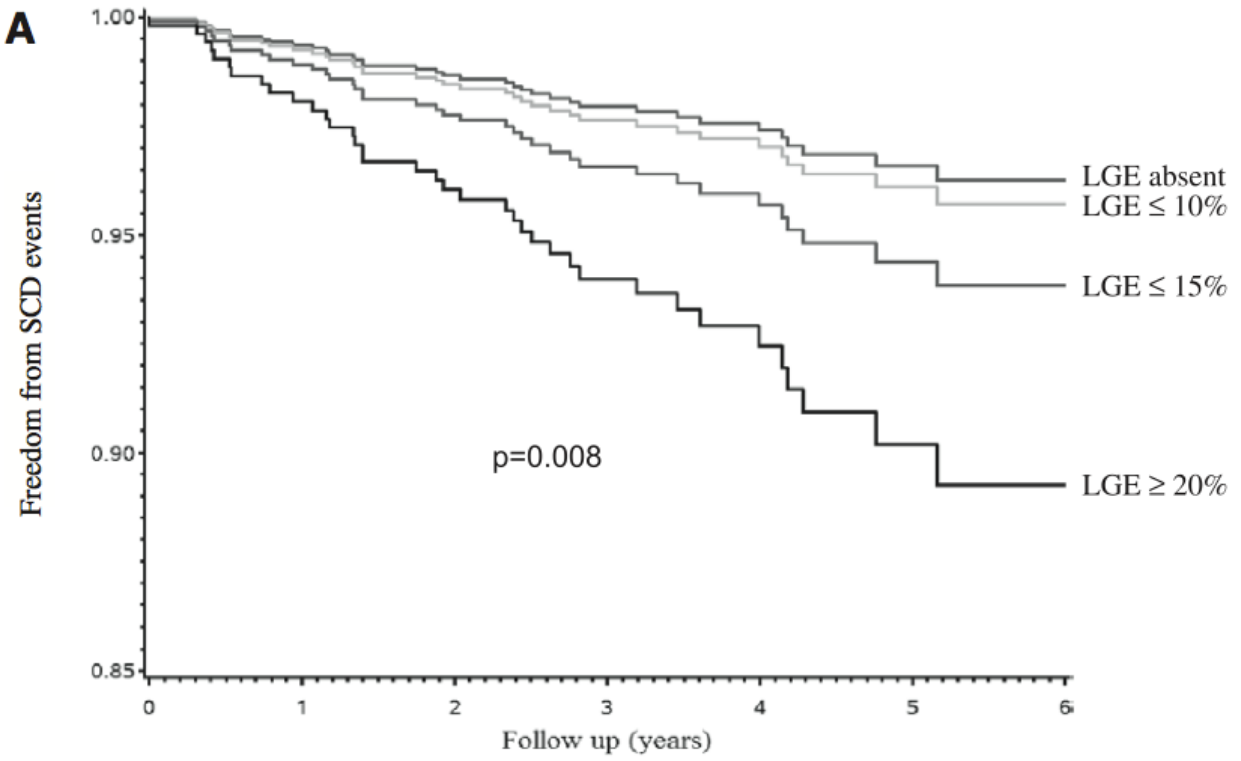


Green, J. J.et al. *JACC CV Imaging*, *5*(4), 370–377.

Presence of LGE is NOT ENOUGH to manage HCM patients… it is too common!

Chiribiri, A., Conte, M. R., Gaita, F.
JACC 57(12), 1402; author reply 1402–3.

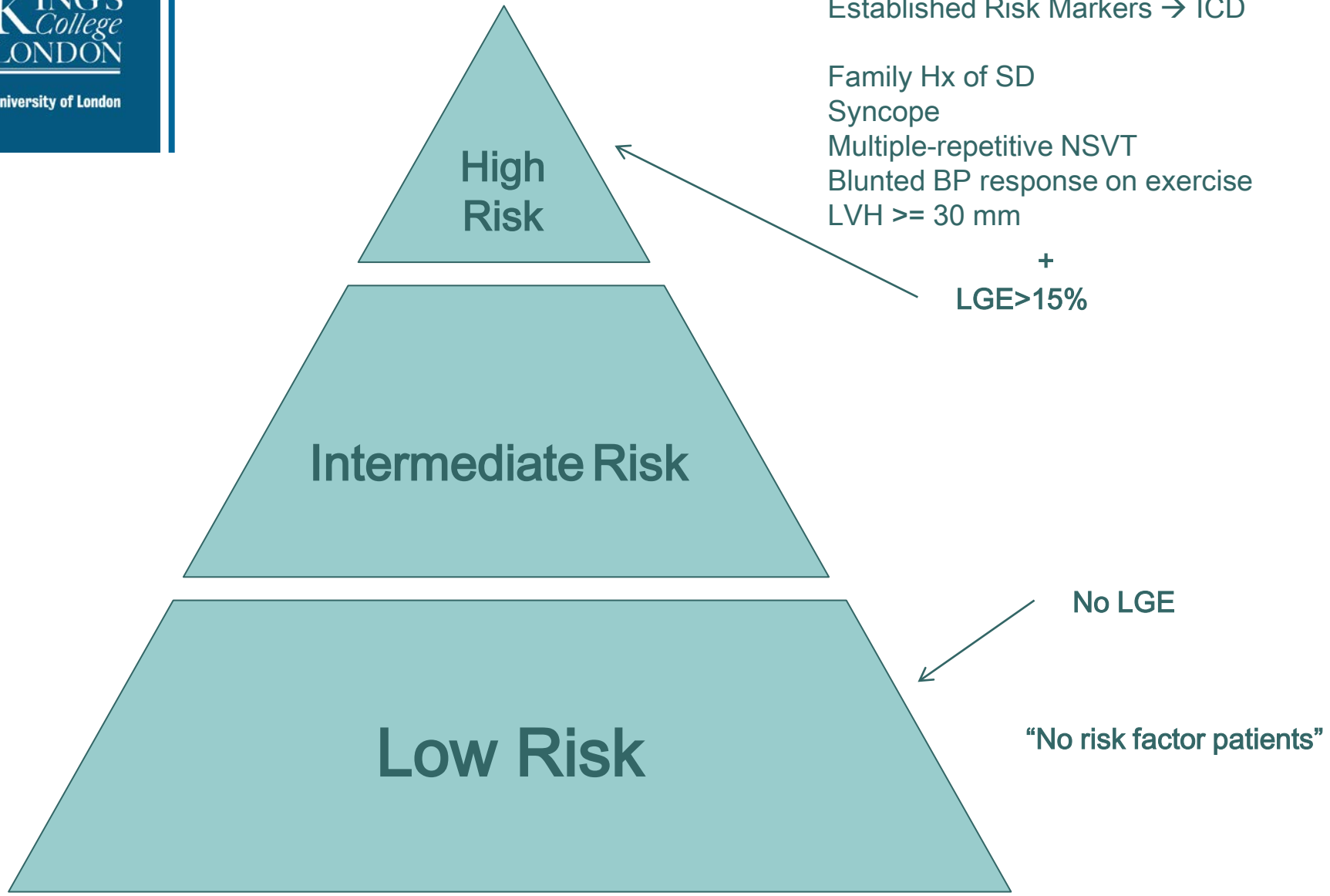
LGE and SCD events



Chan, R. H.et al *Circulation*, *130*(6), 484–495.

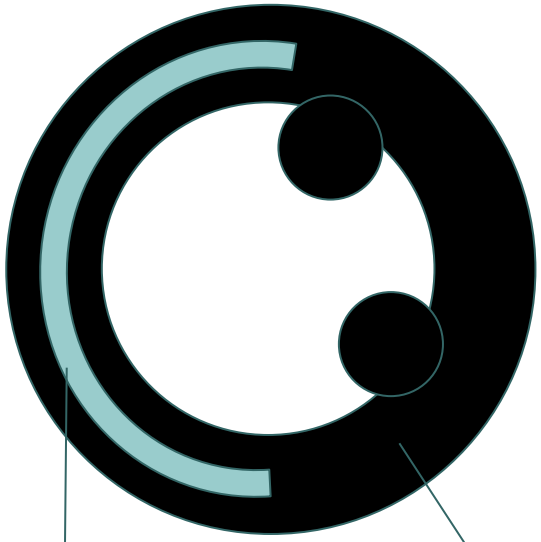
LGE and SCD events

%LGE	Adjusted HR Point Estimate*	95% CI	Estimated 5-y SCD event rate (%)	95% CI
0	1.0	…	3.0	1.4–4.6
1	1.05	1.02–1.08	3.2	1.5–4.8
5	1.29	1.11–1.49	3.8	2.0–5.7
10	1.66	1.24–2.23	4.9	2.6–7.3
15	2.14	1.38–3.32	6.3	3.1–9.4
20	2.76	1.54–4.95	8.1	3.4–12.5
25	3.56	1.71–7.38	10.3	3.5–16.6
30	4.58	1.91–11.01	13.0	3.0–22.1
40	7.61	2.36–24.5	20.7	0–37.6


High Risk
Intermediate Risk
Low Risk
Established Risk Markers → ICD
Family Hx of SD
Syncope
Multiple-repetitive NSVT
Blunted BP response on exercise
LVH >= 30 mm
+
LGE>15%
No LGE
"No risk factor patients"

LATE GADOLINIUM ENHANCEMENT

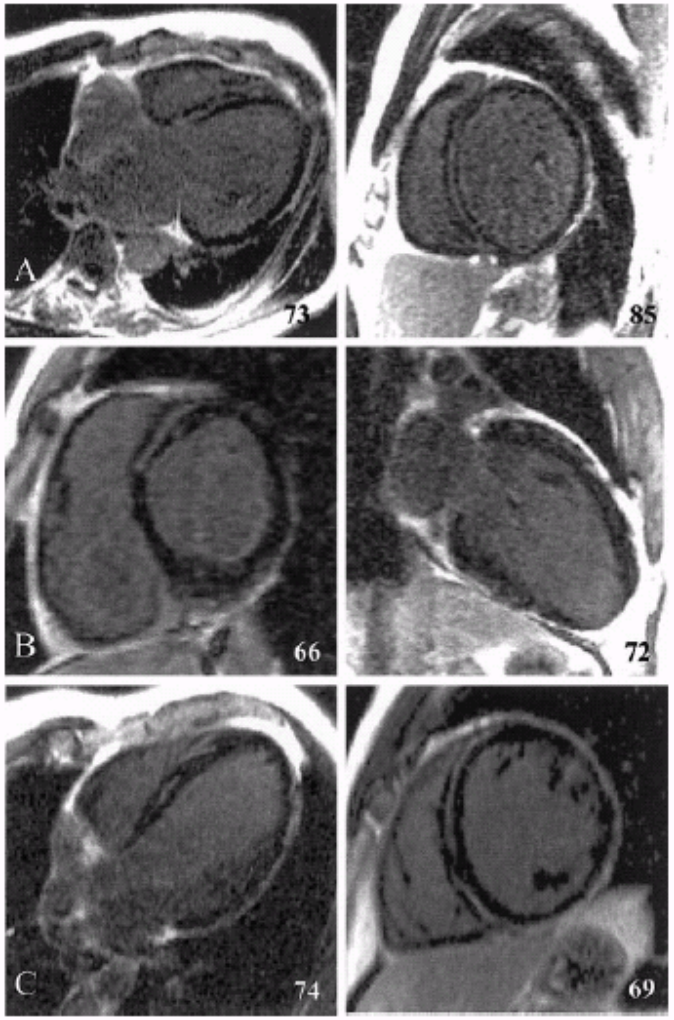
Left ventricle (Short axis)



Scar
(grey/white)

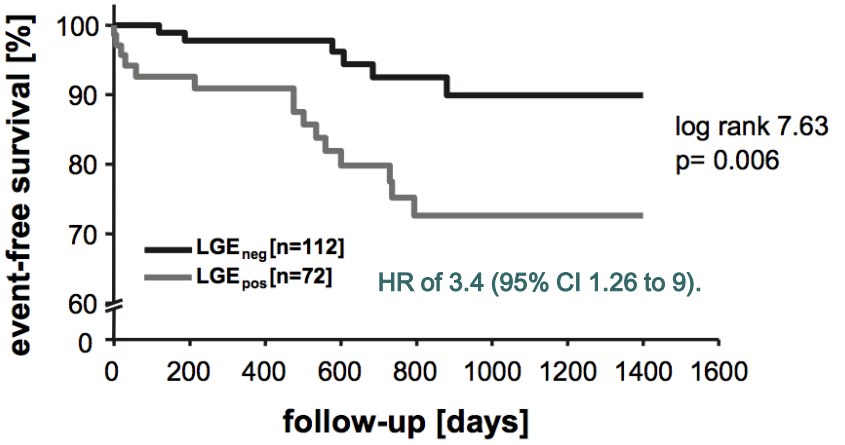
Viable myocardium
(black)

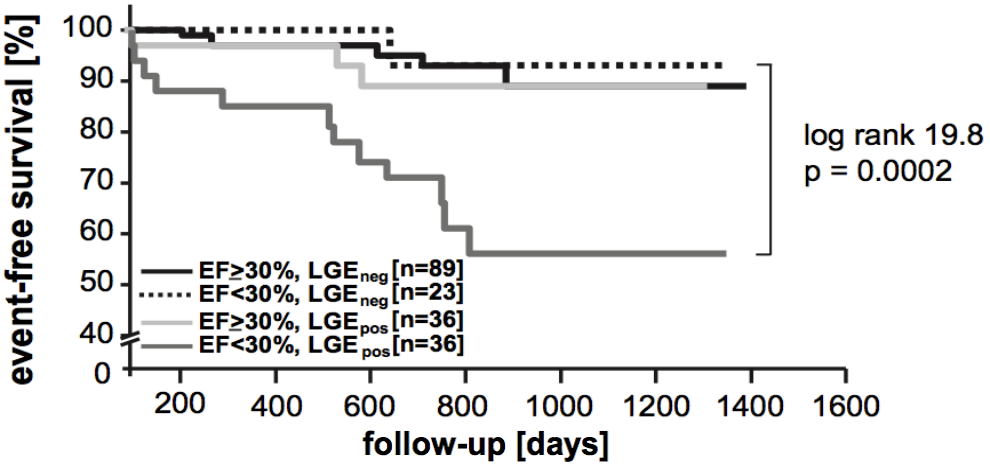
Dilated CMP

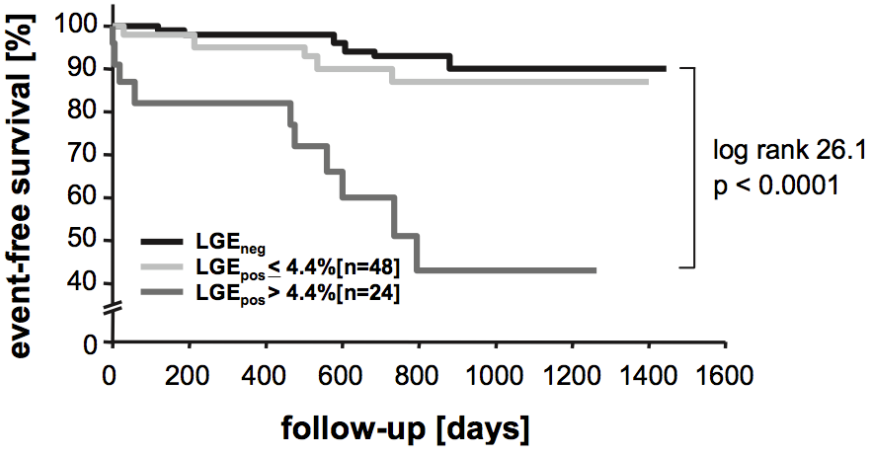


McCrohon, Pennell et al. Circulation 2003

LGE and event-free survival







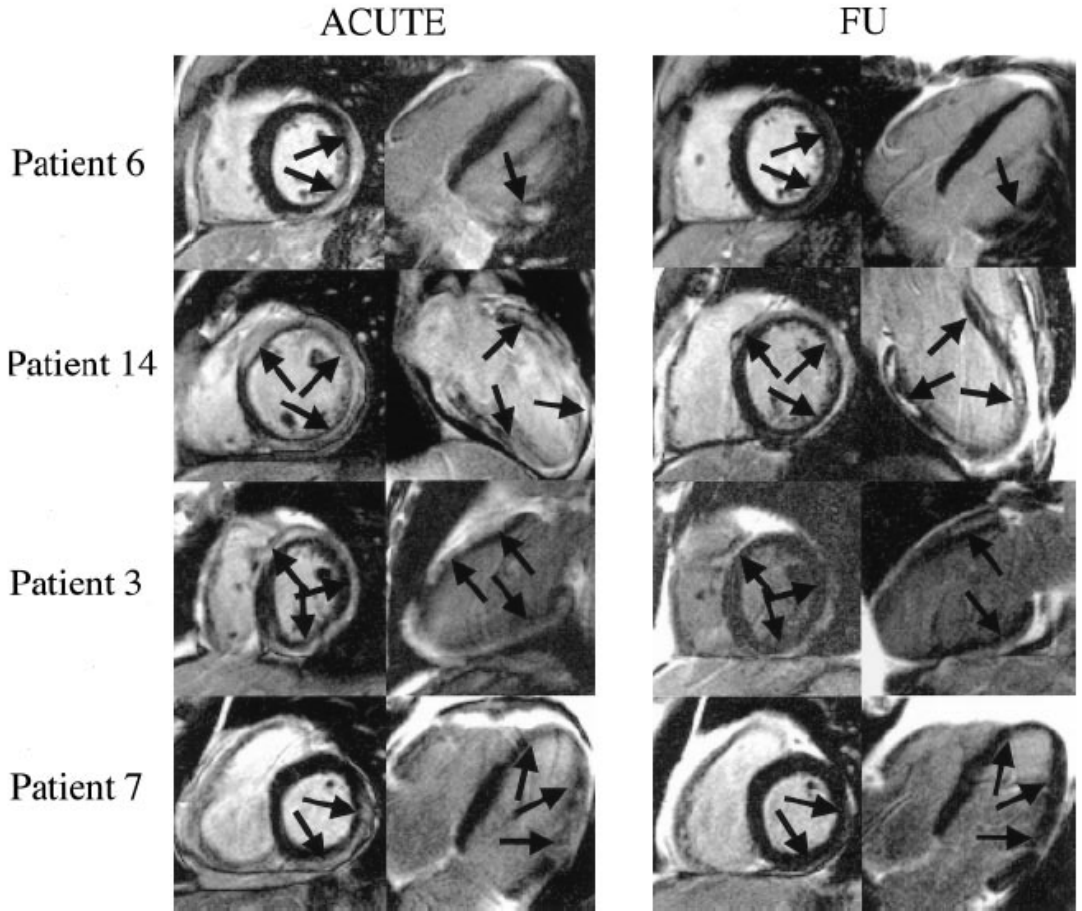
Lehrke, S., et al. *Heart 2011*, *97*(9), 727–732.

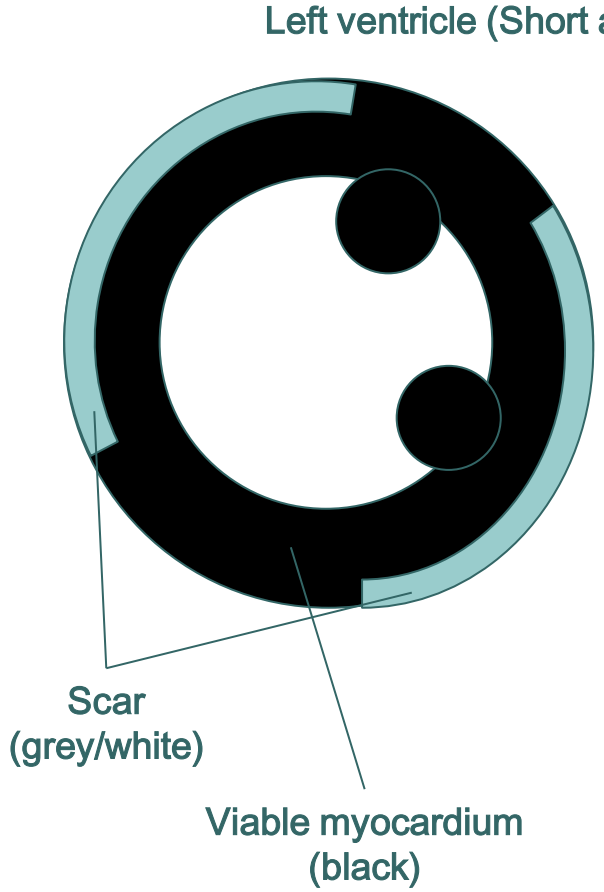
LATE GADOLINIUM ENHANCEMENT

Cardiovascular Magnetic Resonance Assessment of Human Myocarditis

A Comparison to Histology and Molecular Pathology

Heiko Mahrholdt, MD; Christine Goedecke, MD; Anja Wagner, MD; Gabriel Meinhardt, MD; Anasthasios Athanasiadis, MD; Holger Vogelsberg, MD; Peter Fritz, MD; Karin Klingel, MD; Reinhard Kandolf, MD; Udo Sechtem, MD





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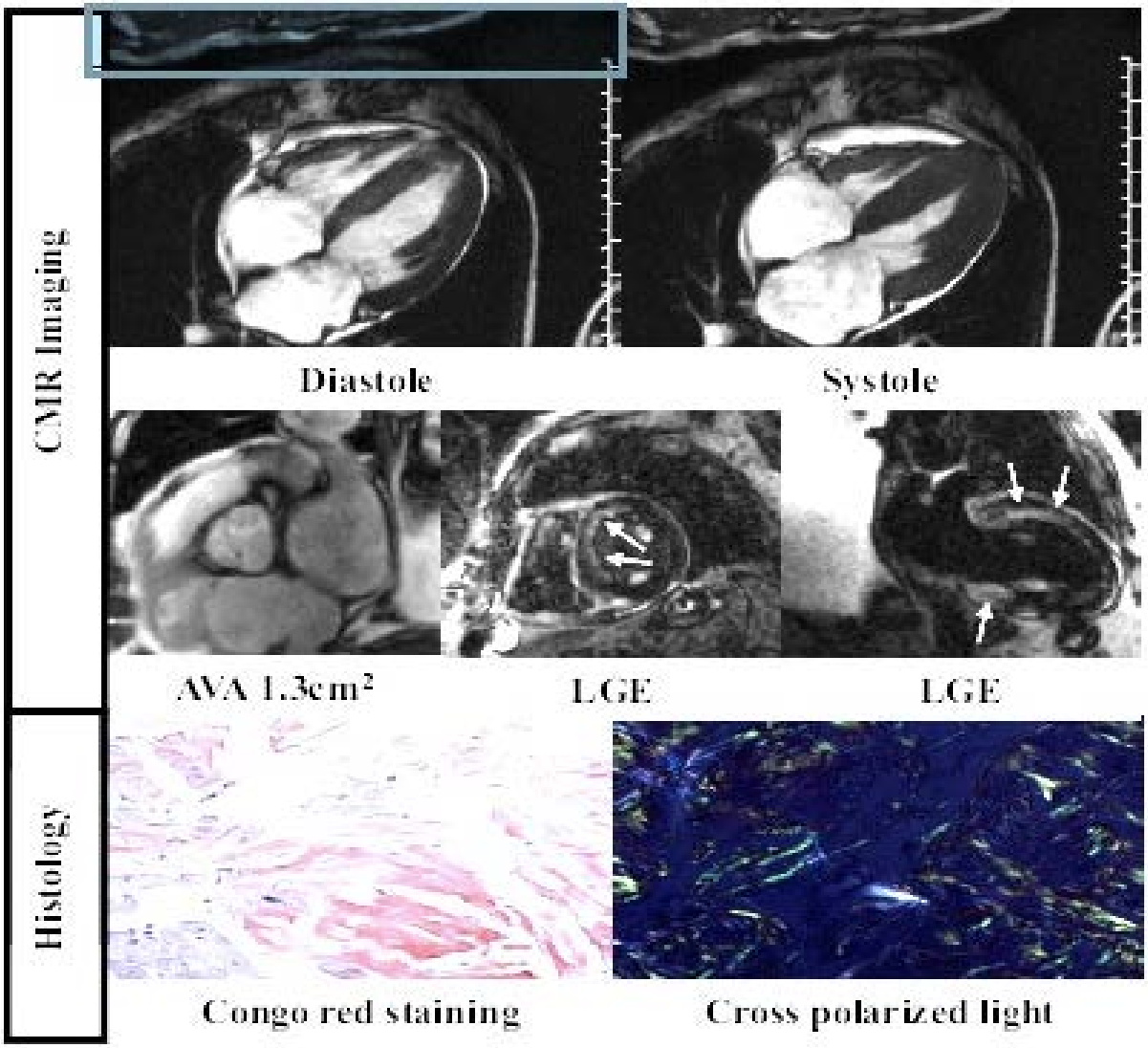
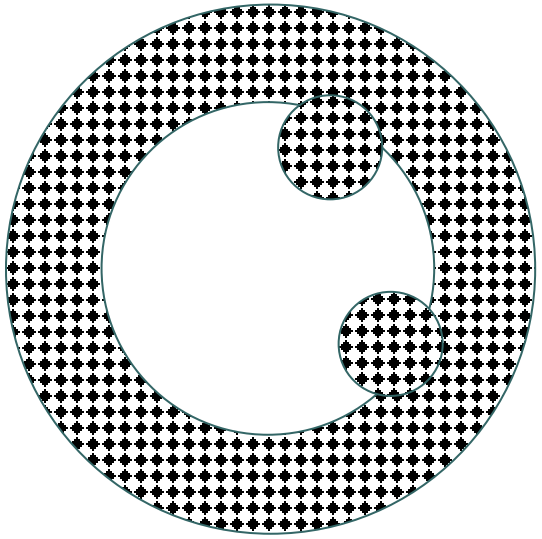
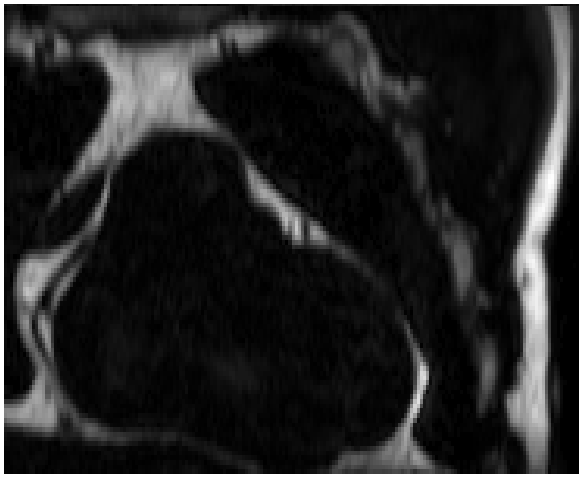
LATE GADOLINIUM ENHANCEMENT



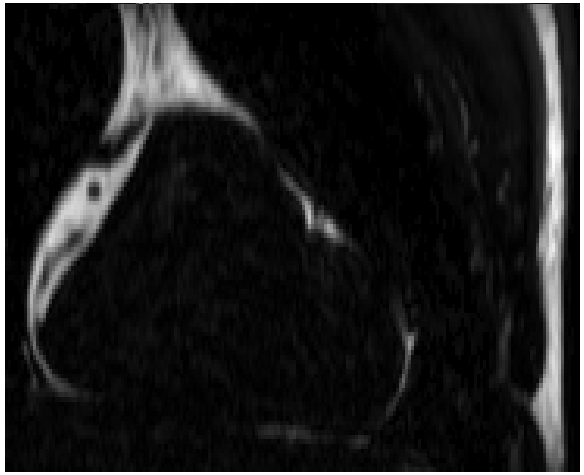


FAT IMAGING

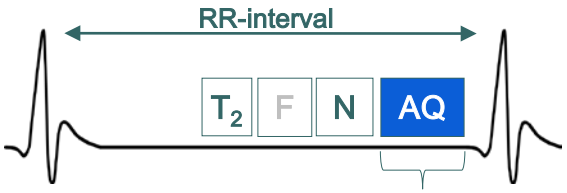
WATER IMAGING



FAT IMAGING



DIXON METHOD – selective water or fat imaging



Images courtesy of Peter KOKEN

FAT IMAGING - ARVC

Criteria for diagnosis of right ventricular dysplasia

I Global and/or regional dysfunction and structural alterations[17–23] *

MAJOR
Severe dilatation and reduction of right ventricular ejection fraction with no (or only mild) LV impairment
Localised right ventricular aneurysms (akinetic or dyskinetic areas with diastolic bulging)
Severe segmental dilatation of the right ventricle

MINOR
Mild global right ventricular dilatation and/or ejection fraction reduction with normal left ventricle
Mild segmental dilatation of the right ventricle
Regional right ventricular hypokinesia

II Tissue characterisation of walls

MAJOR
Fibrofatty replacement of myocardium on endomyocardial biopsy

III Repolarisation abnormalities

MINOR
Inverted T waves in right precordial leads (V2 and V3) (people aged more than 12 yr; in absence of right bundle branch block)

IV Depolarisation/conduction abnormalities

MAJOR
Epsilon waves or localised prolongation (>110 ms) of the QRS complex in right precordial leads (V1–V3)

MINOR
Late potentials (signal averaged ECG)

V Arrhythmias

MINOR
Left bundle branch block type ventricular tachycardia (sustained and non-sustained) (ECG, Holter, exercise testing).
Frequent ventricular extrasystoles (more than 1000/24 h) (Holter)

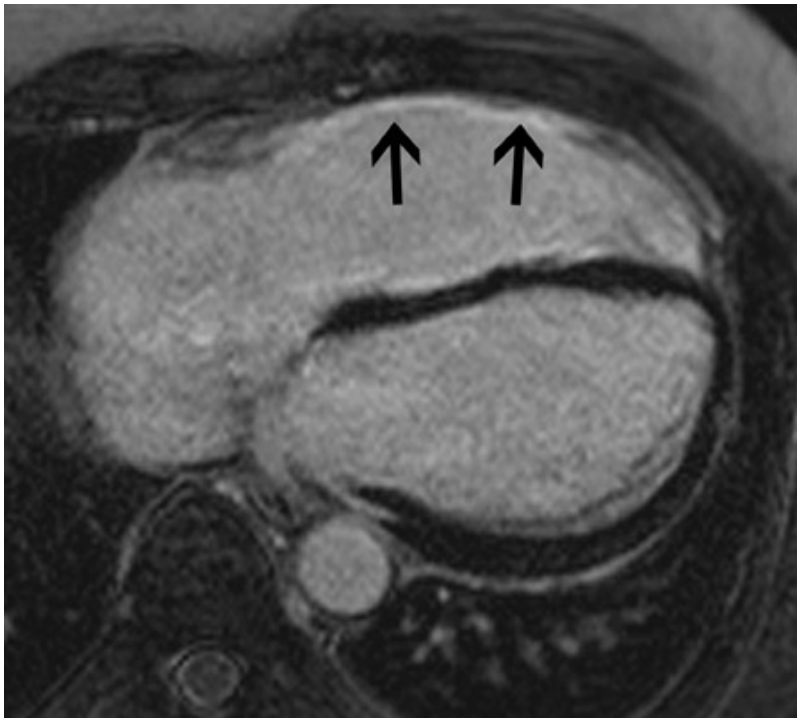
VI Family history

MAJOR
Familial disease confirmed at necropsy or surgery

MINOR
Familial history of premature sudden death (<35 yr) due to suspected right ventricular dysplasia.
Familial history (clinical diagnosis based on present criteria)

*Detected by echocardiography, angiography, magnetic resonance imaging, or radionuclide scintigraphy. ECG, electrocardiogram; LV, left ventricle.

McKenna, Br Heart J 1994



~~FAT~~ IMAGING - ARVC

Table 1. Comparison of Original and Revised Task Force Criteria

Original Task Force Criteria	Revised Task Force Criteria
I. Global or regional dysfunction and structural alterations*	
Major	
• Severe dilatation and reduction of RV ejection fraction with no (or only mild) LV impairment • Localized RV aneurysms (akinetic or dyskinetic areas with diastolic bulging) • Severe segmental dilatation of the RV	**By 2D echo:** • Regional RV akinesia, dyskinesia, or aneurysm • *and* 1 of the following (end diastole): — PLAX RVOT ≥32 mm (corrected for body size [PLAX/BSA] ≥19 mm/m^2) — PSAX RVOT ≥36 mm (corrected for body size [PSAX/BSA] ≥21 mm/m^2) — *or* fractional area change ≤33% **By MRI:** • Regional RV akinesia or dyskinesia or dyssynchronous RV contraction • *and* 1 of the following: — Ratio of RV end-diastolic volume to BSA ≥110 mL/m^2 (male) or ≥100 mL/m^2 (female) — *or* RV ejection fraction ≤40% **By RV angiography:** • Regional RV akinesia, dyskinesia, or aneurysm
Minor	
• Mild global RV dilatation and/or ejection fraction reduction with normal LV • Mild segmental dilatation of the RV • Regional RV hypokinesia	**By 2D echo:** • Regional RV akinesia or dyskinesia • *and* 1 of the following (end diastole): — PLAX RVOT ≥29 to <32 mm (corrected for body size [PLAX/BSA] ≥16 to <19 mm/m^2) — PSAX RVOT ≥32 to <36 mm (corrected for body size [PSAX/BSA] ≥18 to <21 mm/m^2) — *or* fractional area change >33% to ≤40% **By MRI:** • Regional RV akinesia or dyskinesia or dyssynchronous RV contraction • *and* 1 of the following: — Ratio of RV end-diastolic volume to BSA ≥100 to <110 mL/m^2 (male) or ≥90 to <100 mL/m^2 (female) — *or* RV ejection fraction >40% to ≤45%

Marcus, Circulation 2010

Conclusions

- Focus is moving from diagnostic accuracy to risk prediction and improved patients' management
- Studies made difficult by large populations and long follow up required
- LGE can be used in risk prediction and to plan patients' treatment in IHD and HCM

ADVANCES IN CARDIAC ARRHYTHMIAS
and
GREAT INNOVATIONS IN CARDIOLOGY

XXVI Giornate Cardiologiche Torinesi

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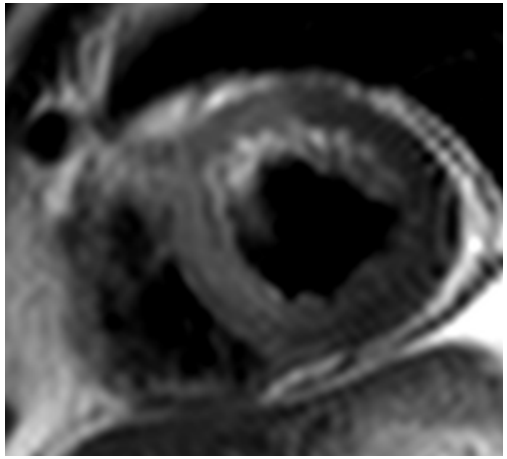
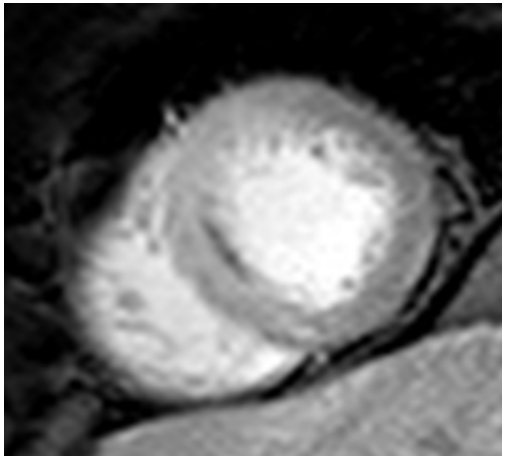
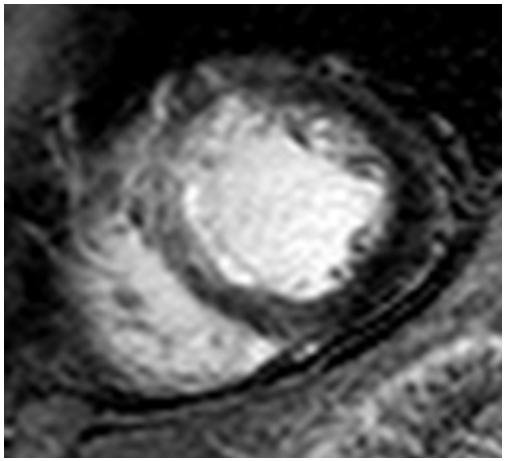
T2 IMAGING - AMI



T2-TSE



Early Viability



Late Viability

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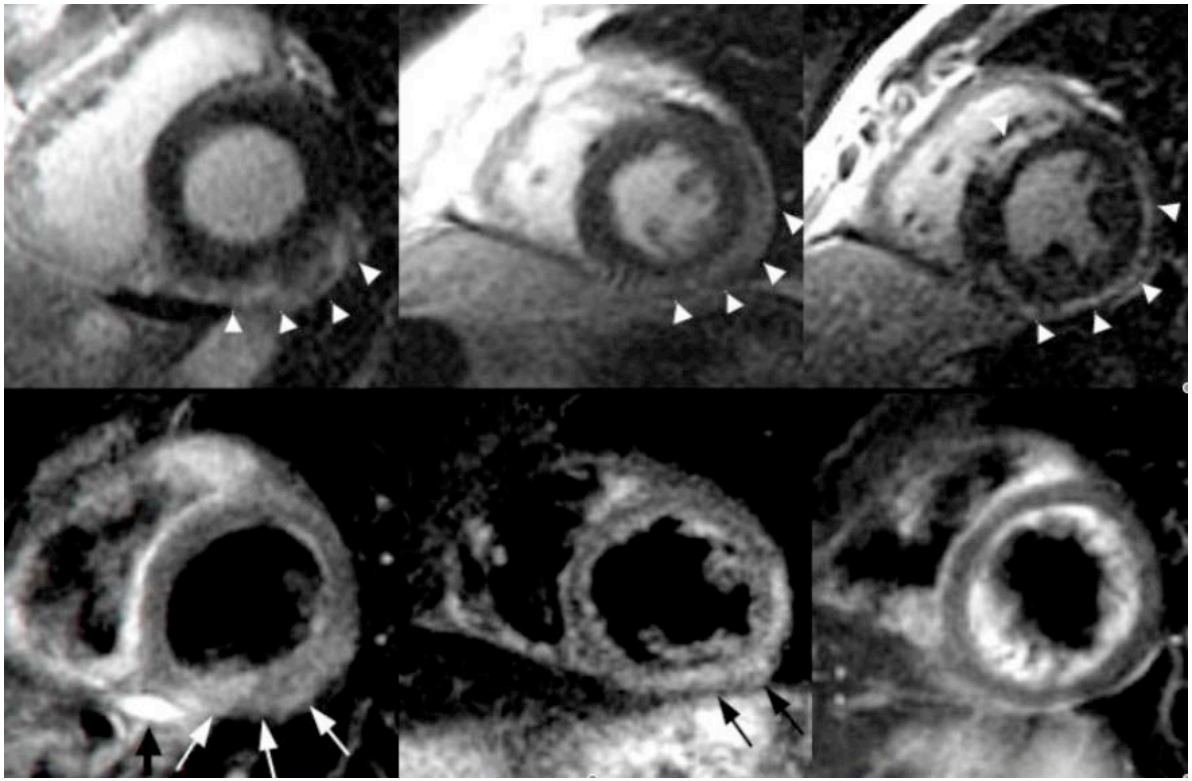
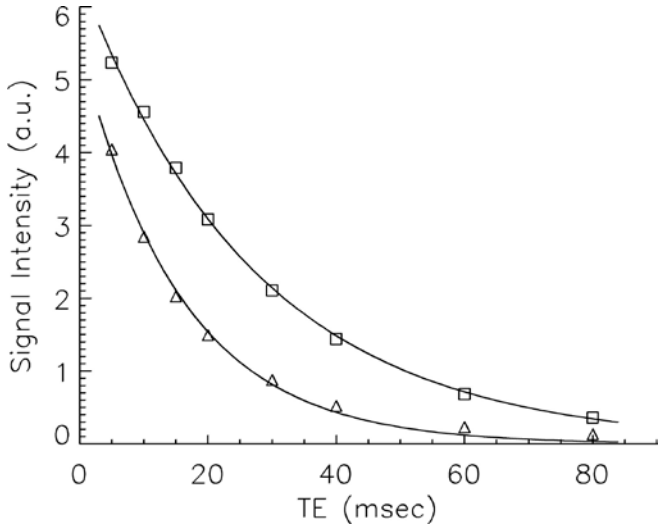
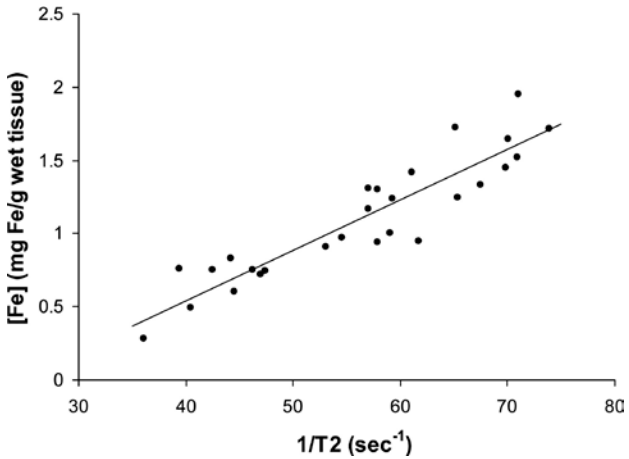
T2 IMAGING - MYOCARDITIS



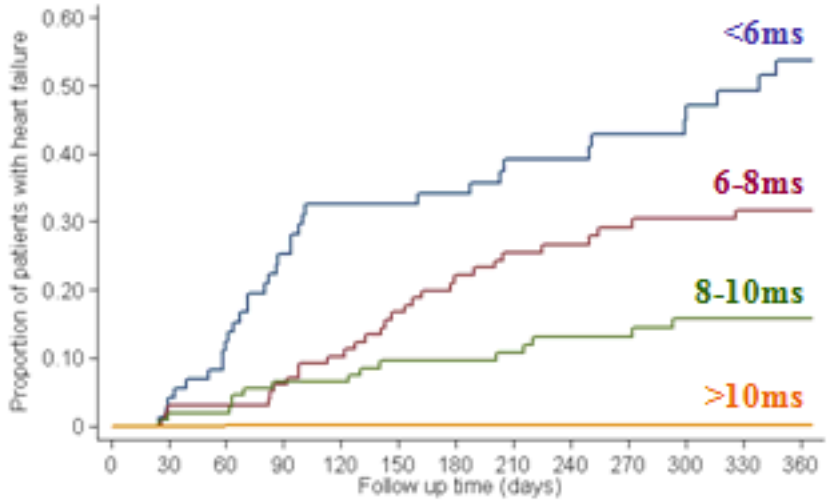
Abdel-Aty et al. JACC 2005

IRON DEPOSITION – T2*





Wang Z J et al. Radiology 2005;234:749-755



Kirk P, et al. Circulation 2009