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CMR in chronic ischemic heart disease

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European Society
of Cardiology

Conflict of Interest Statement



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None



ESC

cMR in chronic ischemic heart disease

Objectives



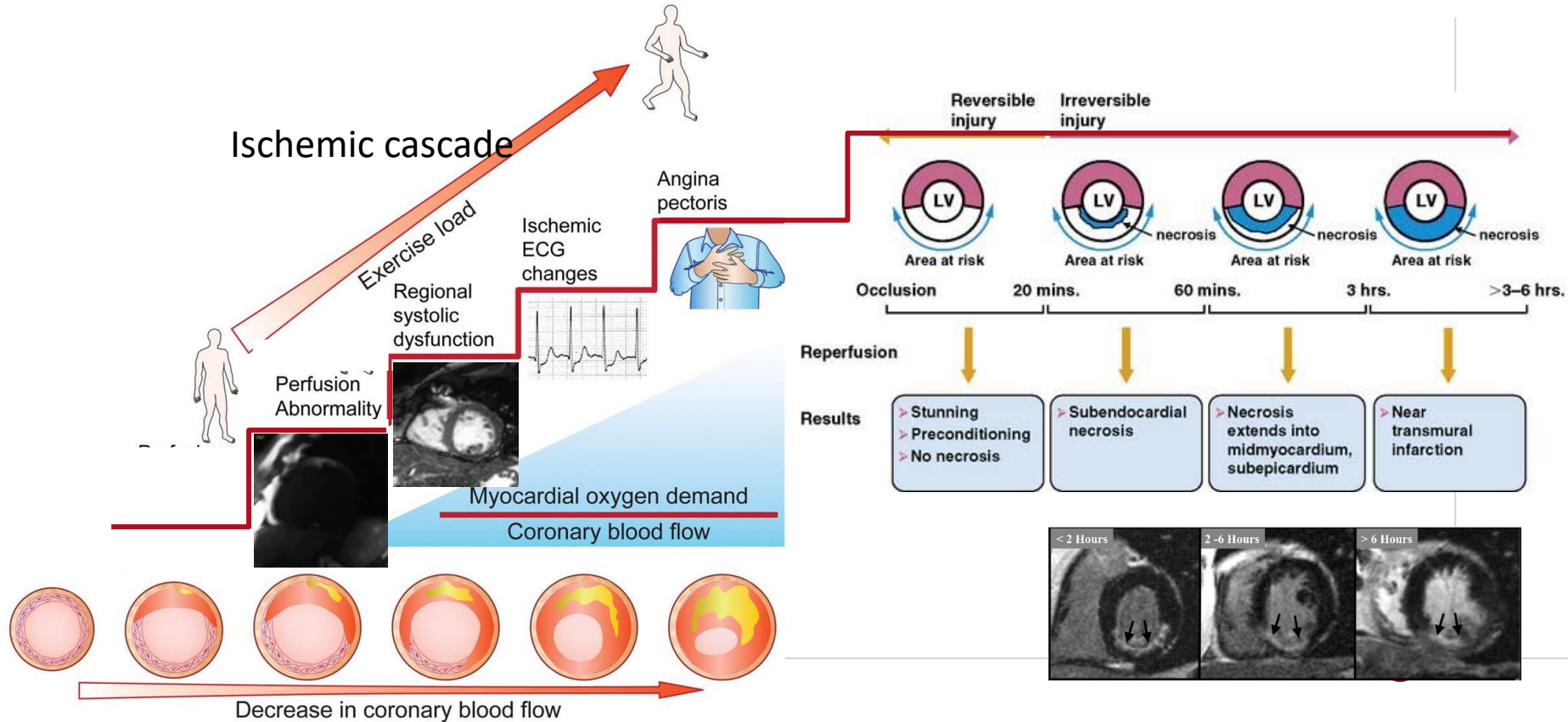
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- 1. Detection of myocardial ischemia**
2. Detection of myocardial viability and treatment selection
3. Prognostication

Pathophysiology of myocardial ischemia



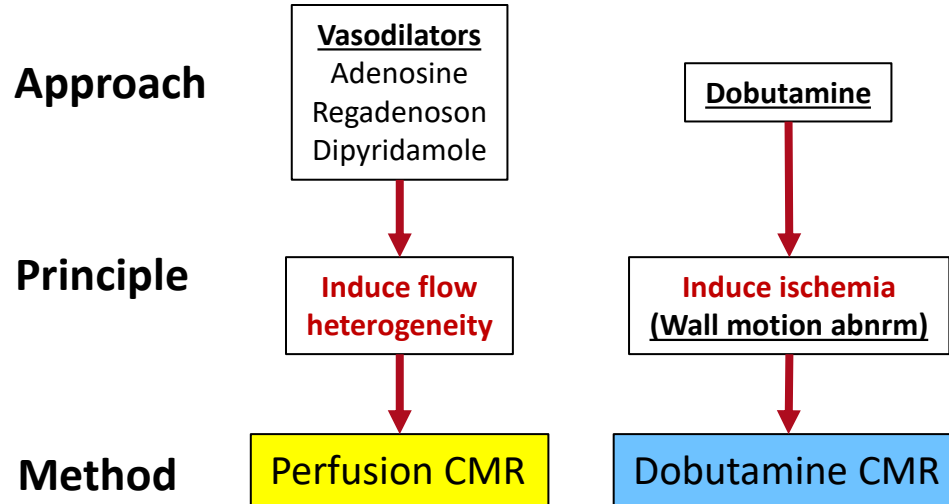
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Ischemia detection Methods



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Stress cMR Suite requirements

Staff required

- 1 physician, certified in BLS and ALS
- 1 nurse certified in BLS and ALS operating the stress protocol
- 1 technician for image acquisition

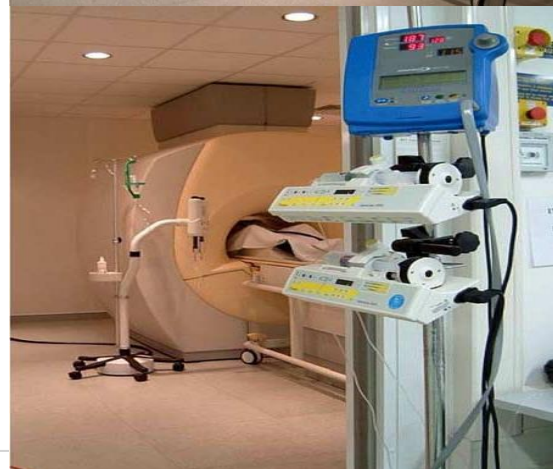
MR-compatible monitoring equipment in the scanner room (additional display outside the room)

- Continuous ECG monitoring
- Periodic BP monitoring
- Oxygen saturation monitoring (optional)

Infusion pumps outside the room with long lines

Crash cart with defibrillator, ECG and emergency drugs (adrenaline, lidocaine, amiodarone, atropine) outside of the room

Trained procedures for evacuation of the patient in case of side effects.



an Association of
vascular Imaging

Stress CMR

Patient preparation and setup



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Patient Instructions prior to test

Vasodilatory stress

Withhold caffeine-containing beverages, chocolate, and aminophylline/ theophylline for 24 hours

Dobutamine stress

beta-blockers and negatively chronotropic calcium antagonists should be stopped for at least 24–48 hours

Both tests:

nitrates should be stopped on the day of the study
All other medications, including oral hypoglycaemic agents, can be taken.

Patient Evaluation

- Evaluate for general contraindications to CMR: ie claustrophobia and non-MR-conditional metallic implants, devices, defibrillators (ICD), or pacemakers
- Evaluate patient history and characteristics
- Review renal function
- Evaluate contraindications to stress

Patient preparation

- 2 IV lines should be placed (for adenosine and Gd)
- Resting ECG performed prior to cMR
- Vital signs (ECG and blood pressure) need to be monitored continuously using a MR compatible monitoring system

Stress cMR

Contraindications



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Contraindication to any stress test

- Unstable angina pectoris or MI < 3 days
- High grade stenotic valvular disease

Contraindications to dobutamine cMR

- Ventricular or atrial Arrhythmias
- Hypertension (>160/100 mmHg)
- Glaucoma or prostate hypertrophy (contraindication to atropine injection)

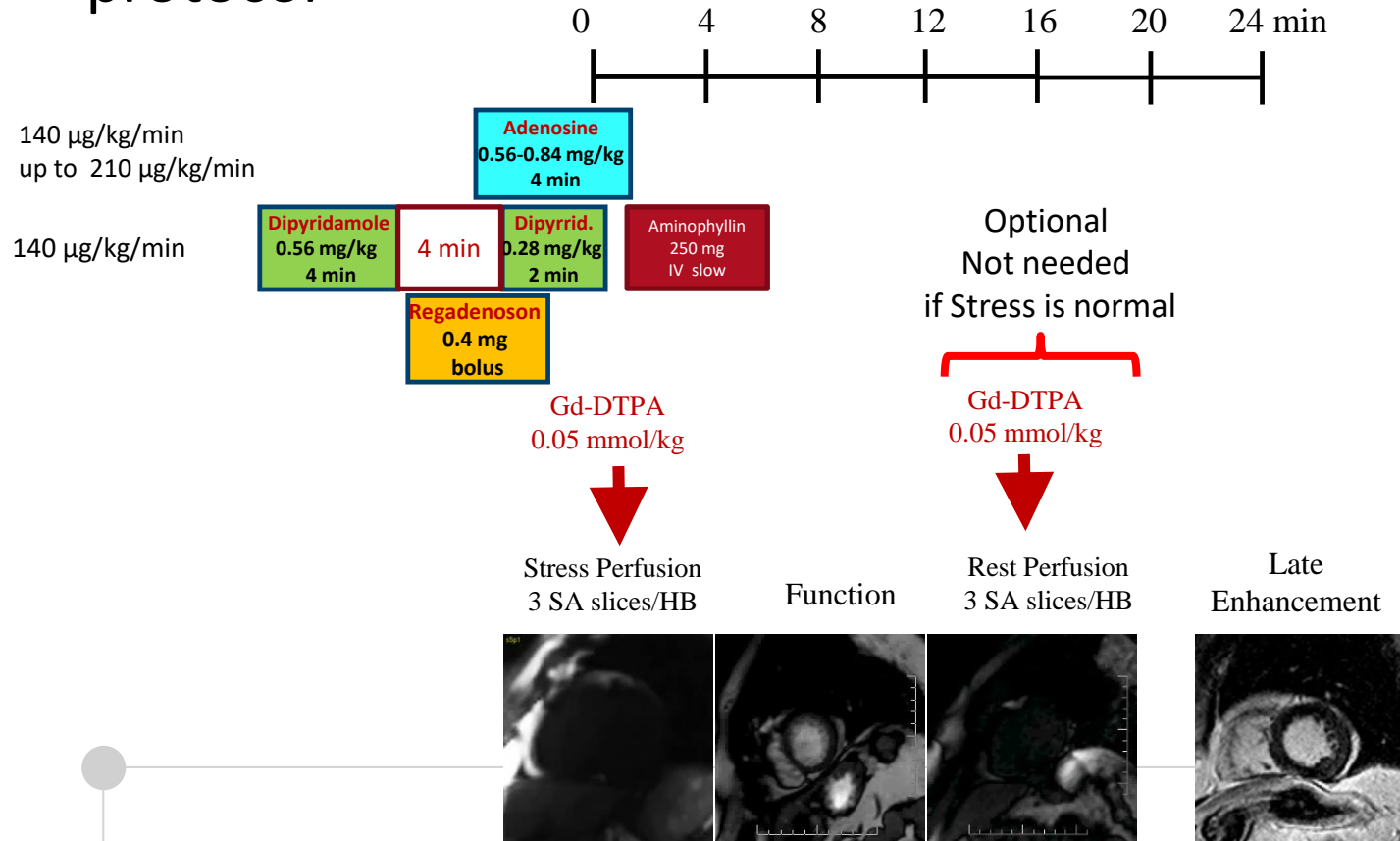
Contraindications to stress perfusion cMR

- Systolic blood pressure < 90 mmHg
- Asthma or severe COPD
- 2nd or 3rd degree AV block
- Atrial fibrillation / flutter
- Decompensated heart failure
- QT prolongation
- Sick sinus syndrome
- severe bilateral carotid stenosis

Stress perfusion protocol



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Selection of the drug



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Adenosine

direct action A2A (non selective)
shortest half life 5-10 sec
onset of action 30 sec

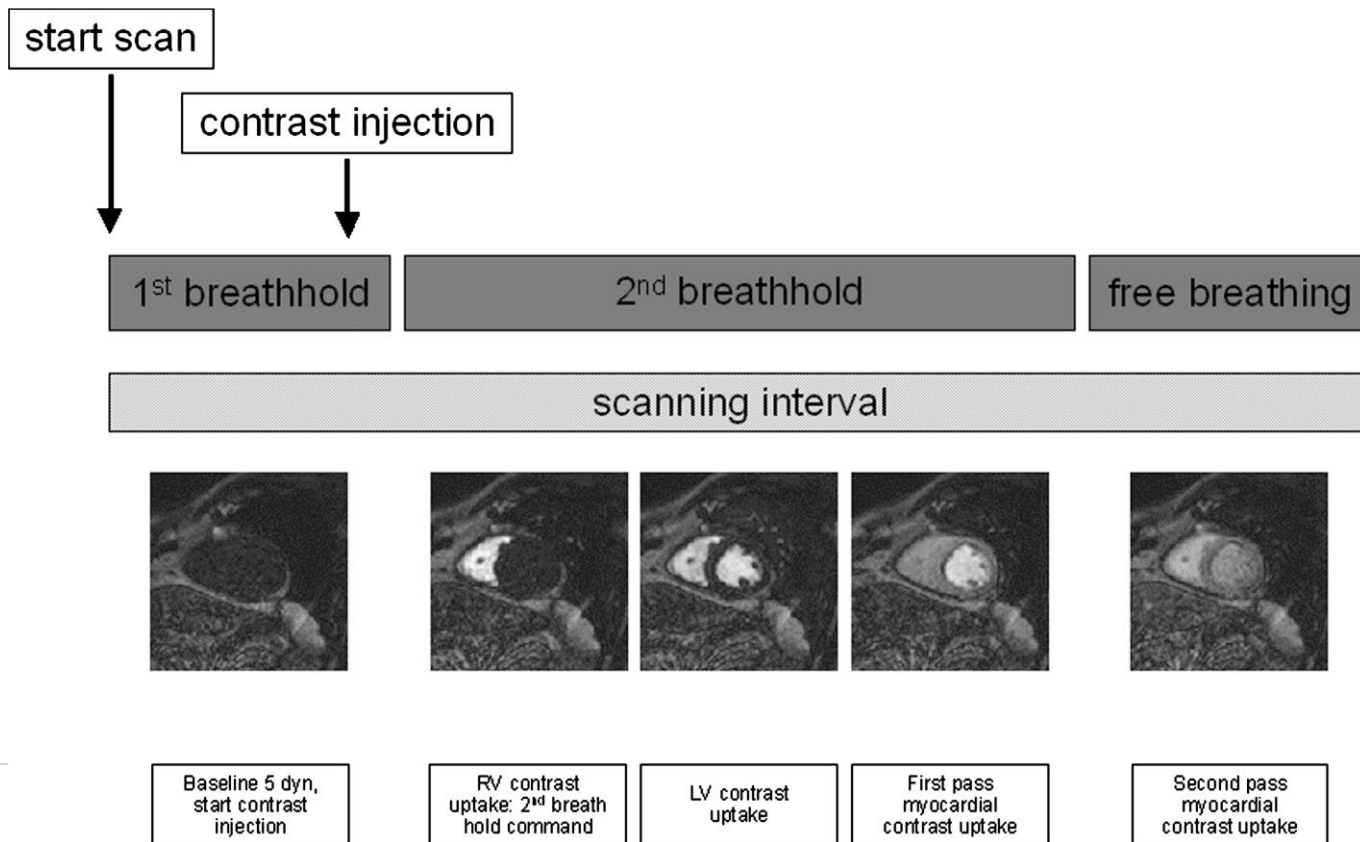
Dipyridamole

indirect drug (liberation of adenosine) through the liver
longest half life 30 min
antagonist: theophylline
cheapest drug

Regadenasone

direct action A2A selective (less bronchospasm)
easy administration bolus
half life 2 min

Patient instructions during test

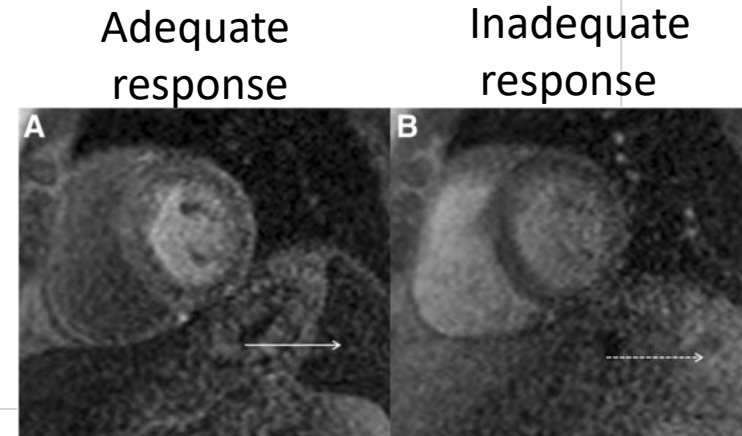
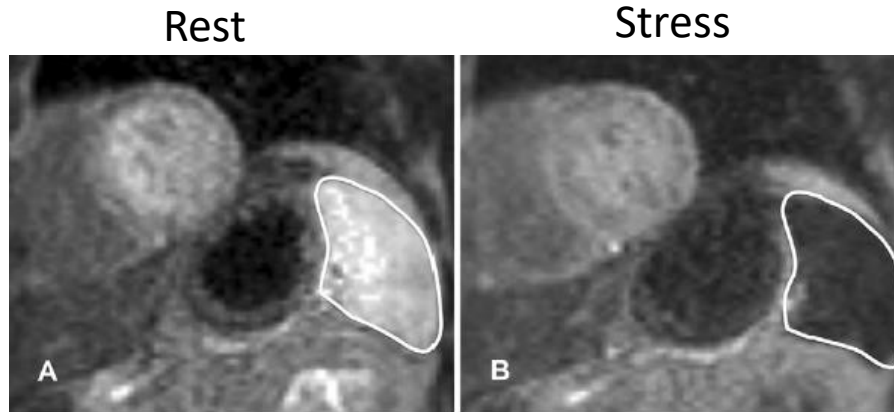


Evaluation of vasodilatory response

Hemodynamic response (increase of heart rate > 10 bpm or drop of BP > 10 mmHg)

Symptoms (heat)

Splenic Switch-off (specific to adenosine only, not dobutamine or regadenoson)



Indications for stopping the test



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- atrioventricular block or severe bradycardia
- complex cardiac arrhythmias,
- decrease in systolic blood pressure of >40 mmHg
- Patient request

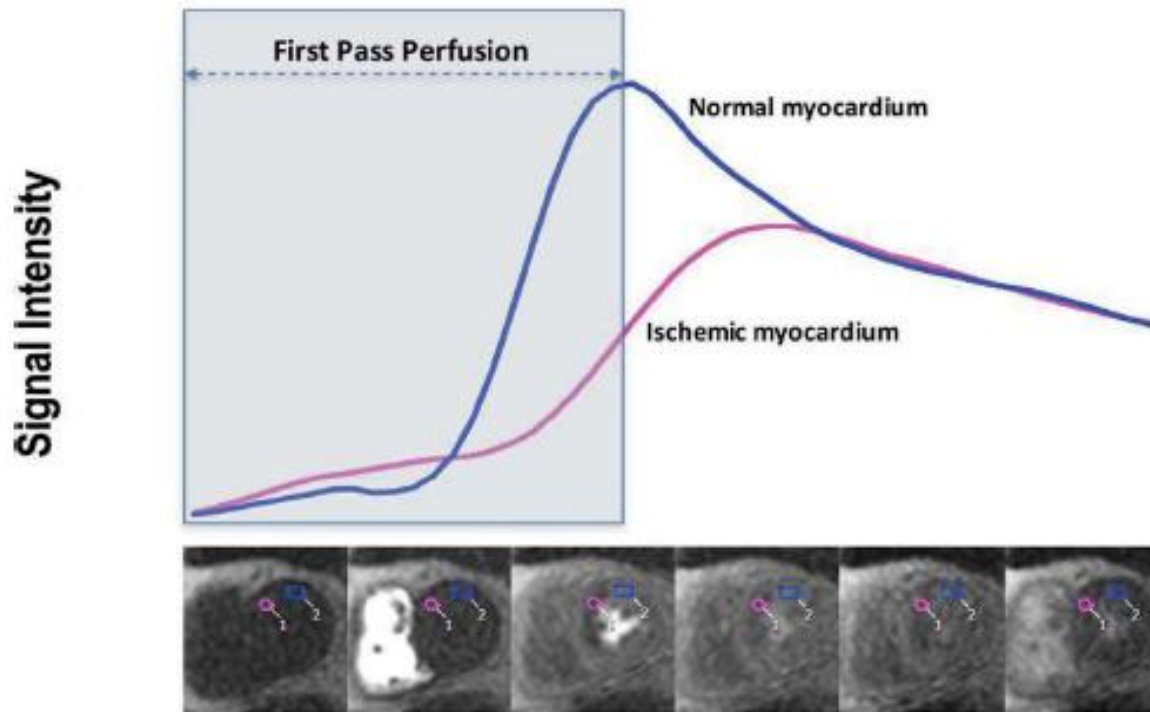
Perfusion Stress MR Safety and Complications



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	Dipyridamole N=11430	Adenosine N=351	Regadenoson N=728
Unstable Angina	2 (0.02%)	0	0
Acute pulmonary edema	2 (0.02%)	0	1 (0.1%)
VT	1 (0.01%)	0	0
AF	1 (0.01%)	0	0
AV block	0 (0%)	27 (8%)	0
Bronchospasm	0	0	1 (0.1%)
Asystole	1 (0.01%)	0	0
TIA	1 (0.01%)	0	0
Anaphylactic shock (Gd)	1 (0.01%)	0	0

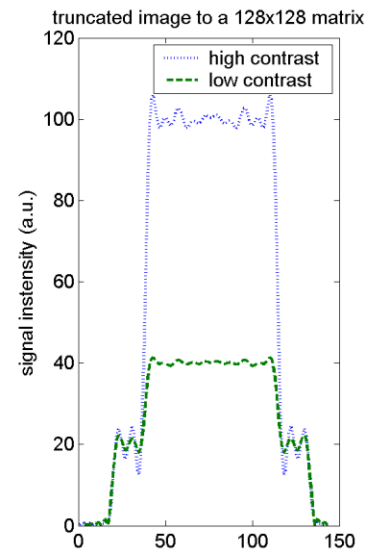
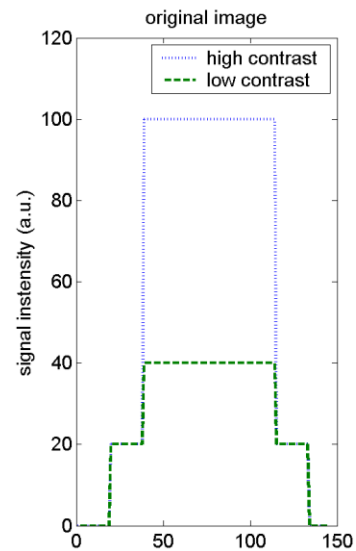
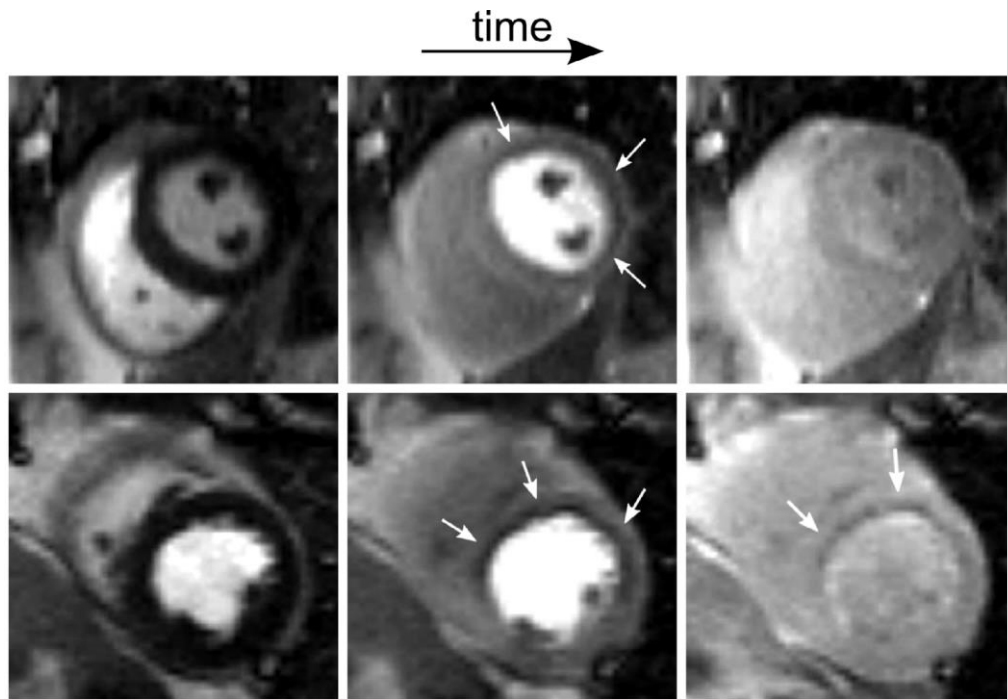
Stress perfusion interpretation



Dark rim artifact



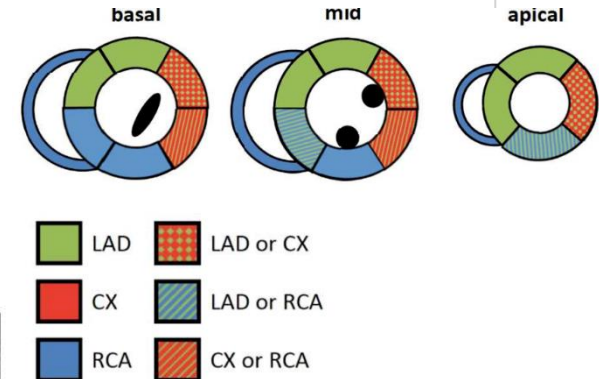
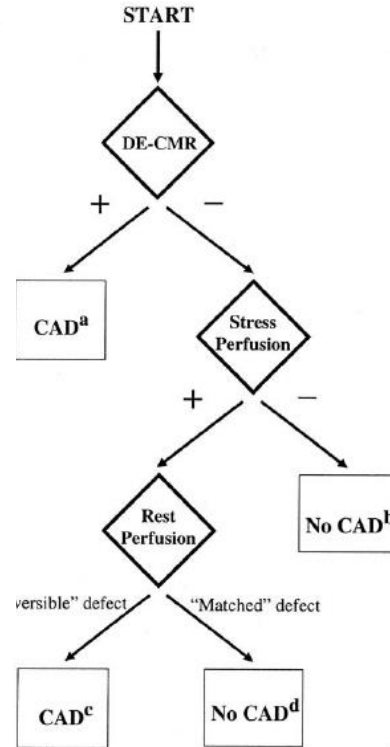
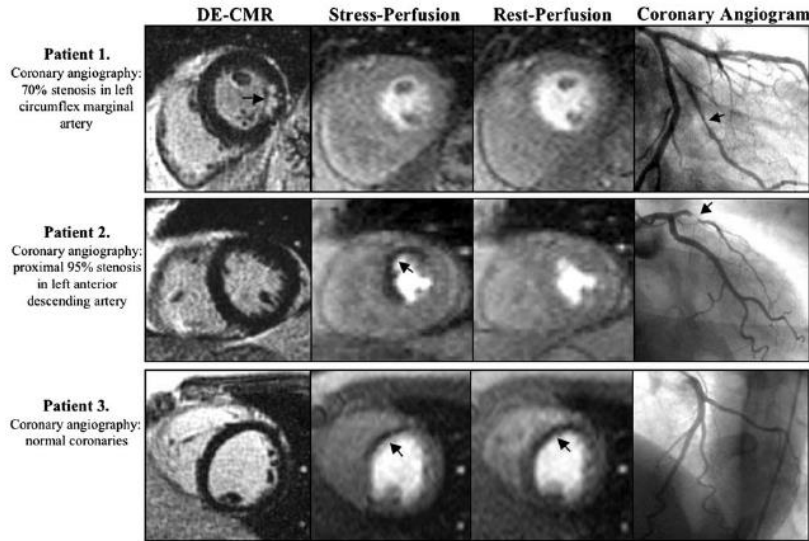
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Stress perfusion Interpretation



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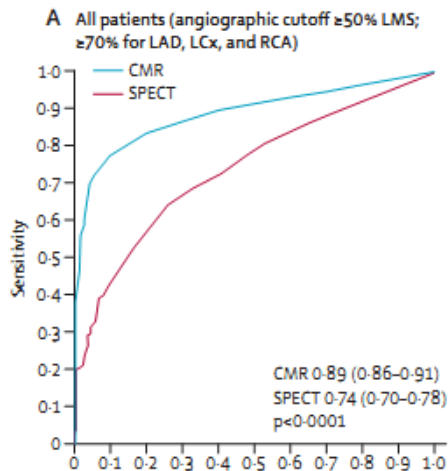


cMR for evaluation of ischemia

CE-MARC

cMR perfusion vs SPECT

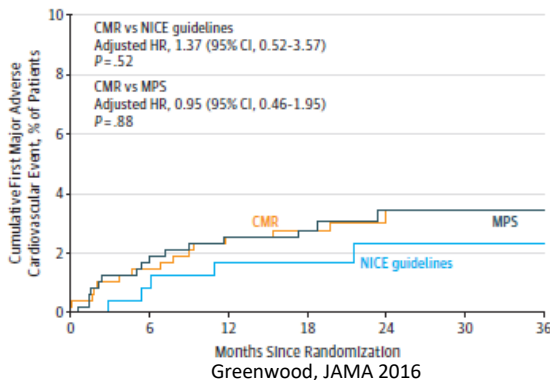
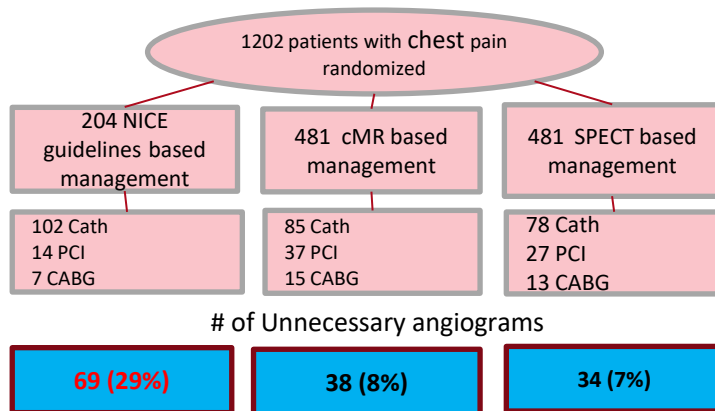
- **Two center trial:** 752 pts undergoing CAD
- **Adenosine stress-rest cMR vs ⁹⁹Tc MIBI SPECT**
- **Endpoint: CAD (70% by QCA)**



Greenwood, Lancet 2012 ;379(9814):453-60

CE-MARC II

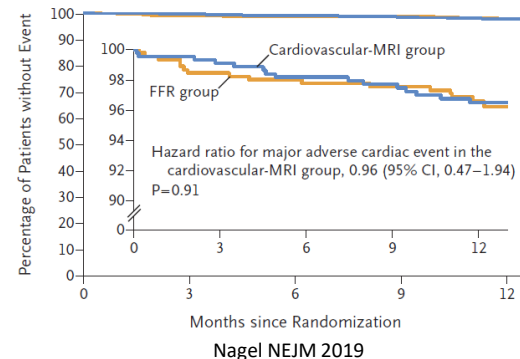
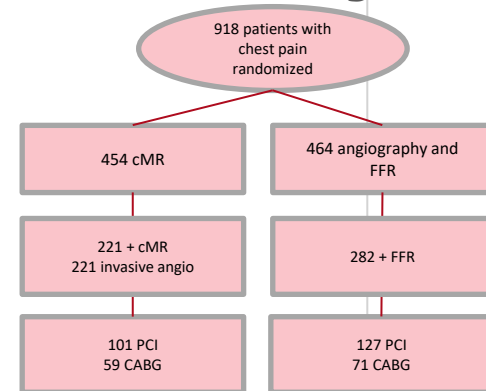
cMR vs NICE guided



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MR INFORM

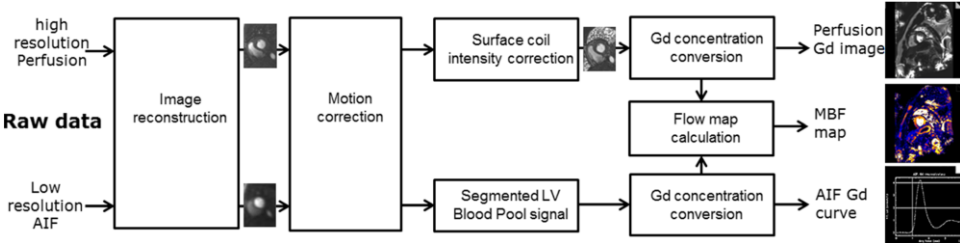
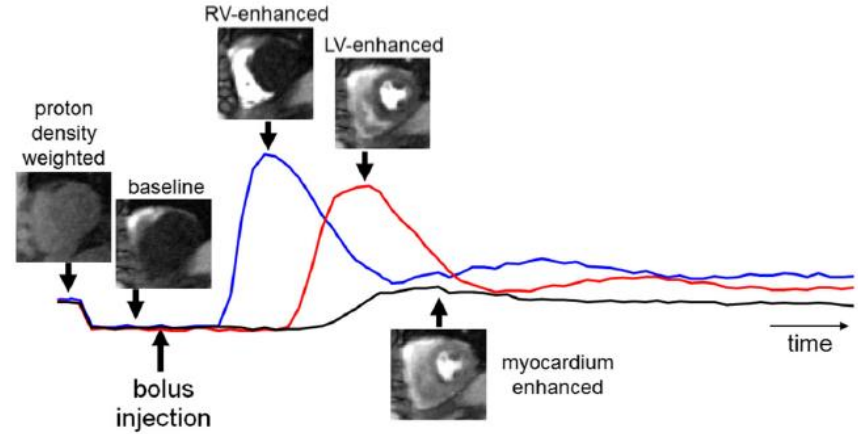
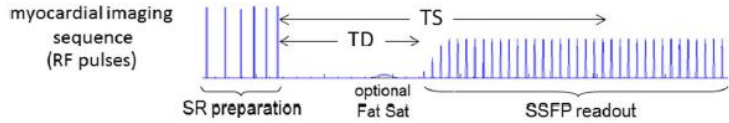
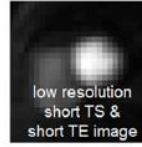
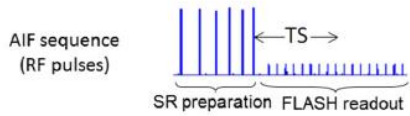
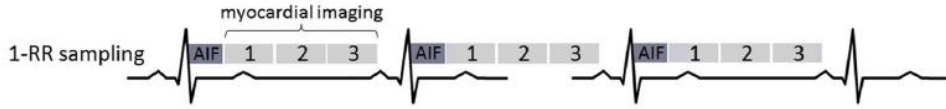
cMR vs FFR guided



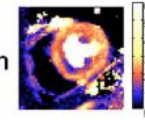
Quantitative stress perfusion



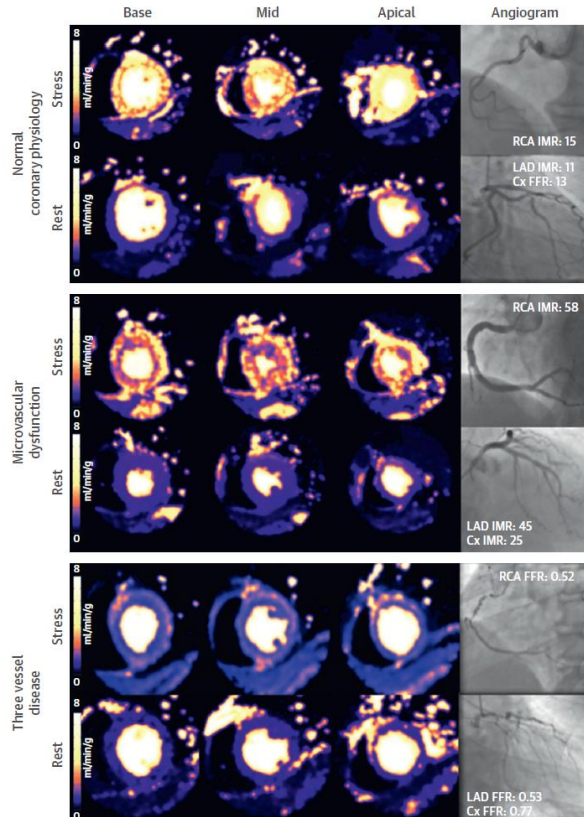
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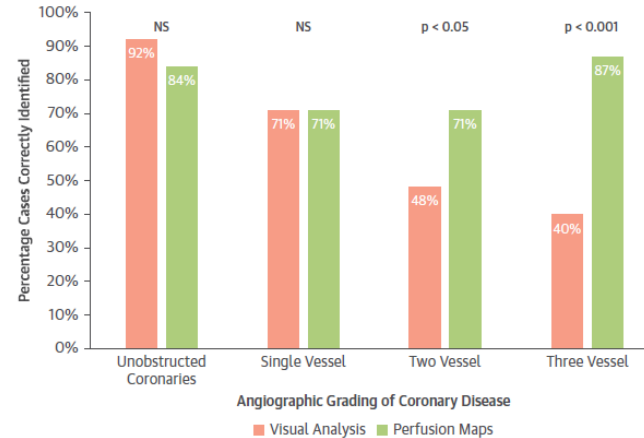
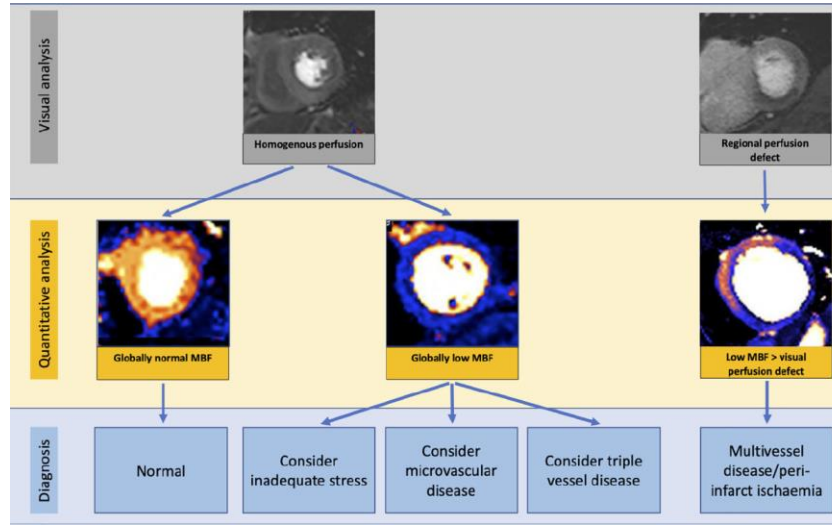
Quantitative
Myocardial Perfusion
Flow Map



Quantitative Stress Perfusion



Kotecha JACC Im 2019



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Sharrack EHJCVI 2022

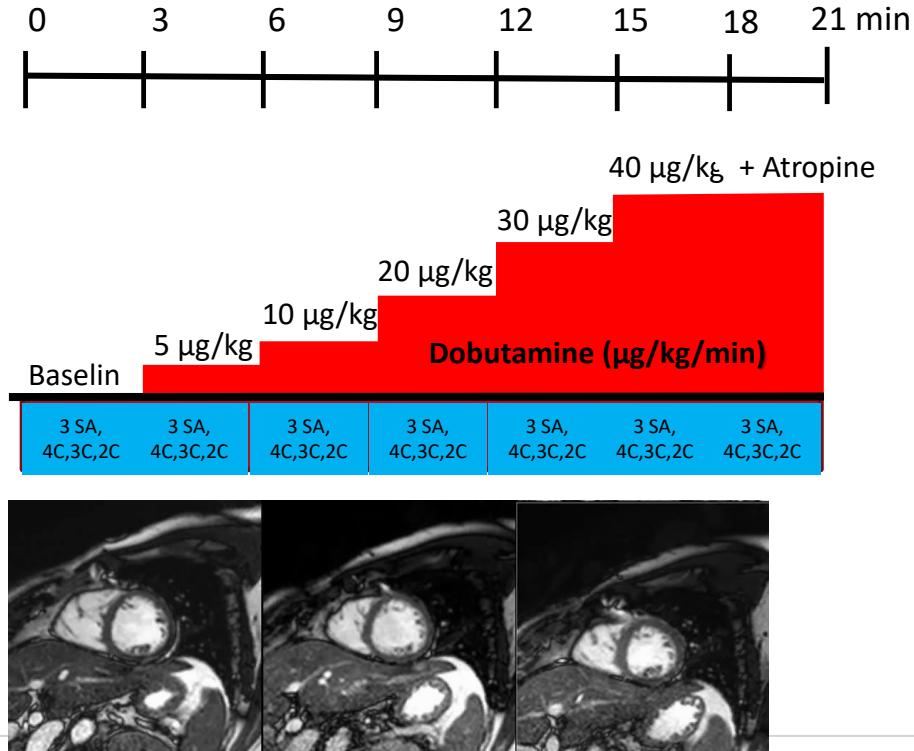


Kotecha JACC Im 2020

Dobutamine stress MR Protocol



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Indications for stopping the test



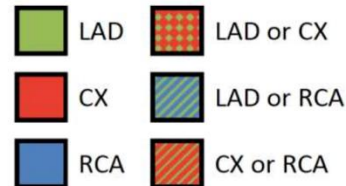
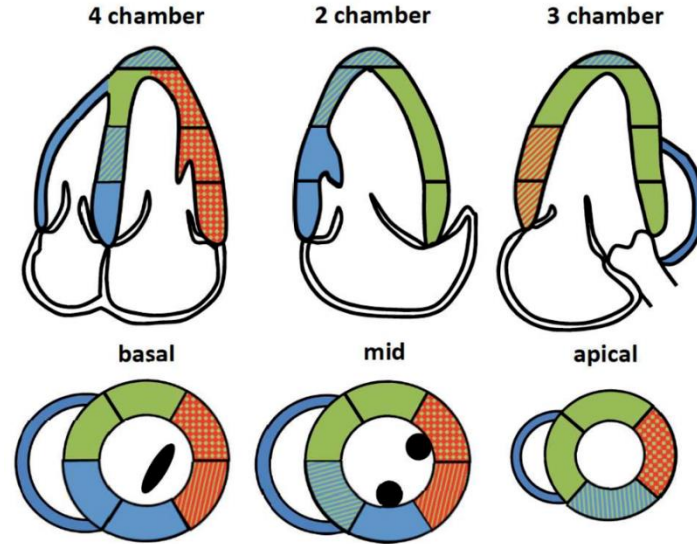
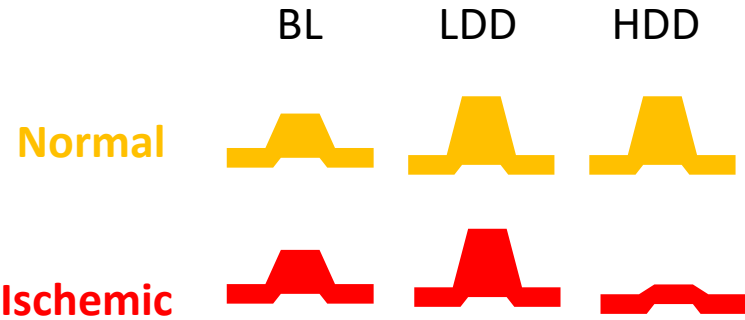
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- Reaching 85% of the maximal predicted HR
men: $(220 - \text{age})$, women $(210 - \text{age})$
- intolerable chest pain or dyspnea
- complex ventricular or atrial arrhythmias,
- decrease in systolic blood pressure of >40 mmHg
- hypertension $>240/120$ mmHg
- new or worsening WMA in >1 territories
- Patient request

Dobutamine stress imaging Interpretation



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Dobutamine stress MR Complications



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(1000 pts)

	n
Severe chest pain	10 (1%)
Severe dyspnea	10 (1%)
Nausea	4 (0.4%)
Urinary urgency	1 (0.1%)
HTA (>240/120 mmHg)	5 (0.5%)
↘ SBP (>40 mmHg)	3 (0.3%)
V premature Beats	8 (0.8%)
Paroxysmal AF	5 (0.5%)



Dobutamine stress MR Accuracy



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		Prevalence					
	# of pts	of CAD	Sensitivity	Specificity	PPV	NPV	Accuracy
Nagel (Circulation 1999)	172	63%	86%	86%	91%	78%	86%
Hundley (Circulation 1999)	41	73%	83%	83%	97%	45%	83%
Schalla (Radiology 2002)	22	73%	81/88%	83%	93%	63/71%	82/86%
Wahl (Radiology 2004)	160	74%	85%	78%	92%	64%	83%
Paetch (Circulation 2004)	79	67%	89%	81%	90%	78%	86%
Jahnke (Radiology 2006)	40	70%	89%	83%	93%	77%	88%
All	514	69%	86%	83%	92%	71%	85%

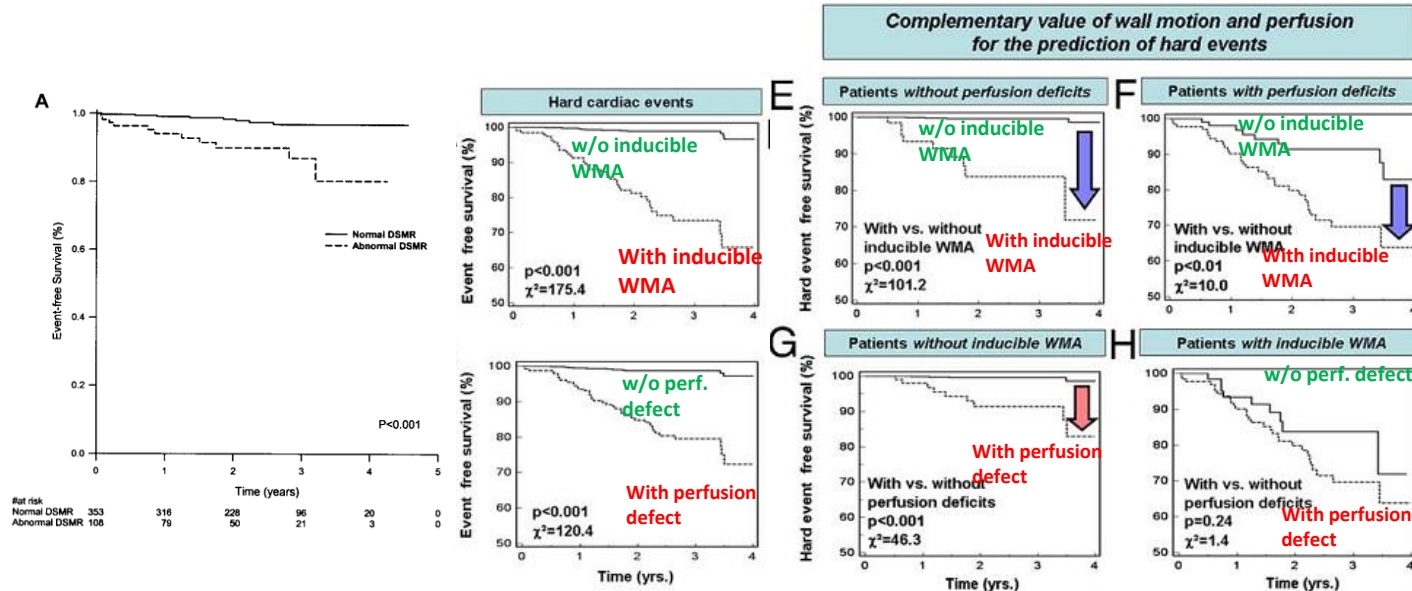
Dobutamine and perfusion MR

Prognostic value



513 pts

1493 pts, undergoing perfusion-DSE MR

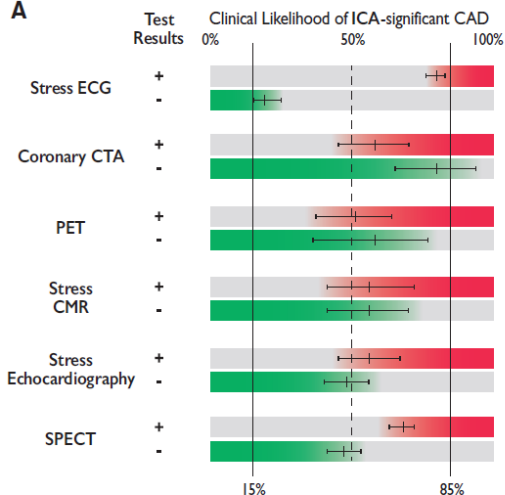


Use of cMR in chronic CAD Guidelines



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A



ANY

Use of diagnostic imaging tests in the initial diagnostic management of symptomatic patients with suspected CAD

Non-invasive functional imaging for myocardial ischaemia or coronary CTA is recommended as the initial test for diagnosing CAD in symptomatic patients in whom obstructive CAD cannot be excluded by clinical assessment alone.

I **B**

Resting echocardiography and CMR in the initial diagnostic management of patients with suspected CAD

A resting transthoracic echocardiogram is recommended in all patients for:

- Exclusion of alternative causes of angina;
- Identification of regional wall motion abnormalities suggestive of CAD;
- Measurement of LVEF for risk-stratification purposes;
- Evaluation of diastolic function.

I **B**

CMR may be considered in patients with an inconclusive echocardiographic test.

IIb **C**



cMR in chronic ischemic heart disease

Objectives



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1. Detection of myocardial ischemia
- 2. Detection of myocardial viability and treatment selection**
3. Prognostication

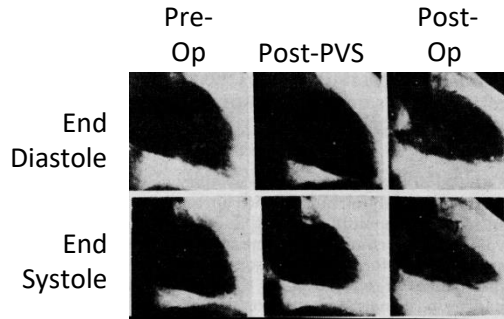
Concept and pathophysiology of myocardial viability



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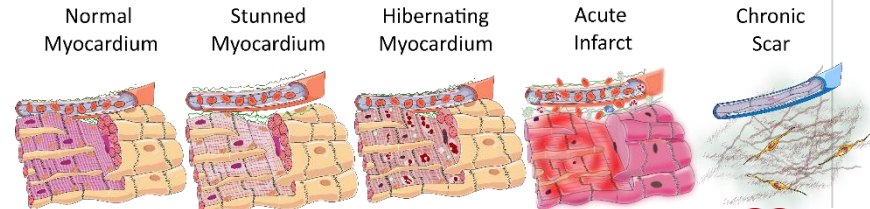
Concept of myocardial viability

The concept of “*myocardial viability*” was established in the early ‘70s following the clinical observation that chronically dysfunctional myocardium in stable coronary artery disease, may sometimes partially or completely recover contraction following coronary revascularization



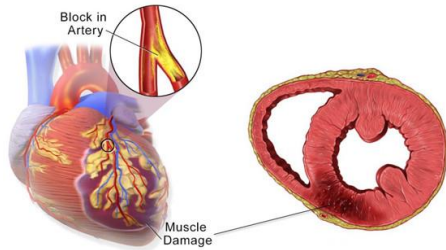
Pathophysiology of dysfunction in CAD

- acute/chronic necrosis and replacement fibrosis **Irreversible**
 - Acute ischemia
 - Post ischemic / chronic stunning
 - Chronic hibernation
- } **Possibly reversible when revascularized**
- Other confounding / coexisting diseases
 - tethering/remodelling
 - Electromechanical dyssynchrony
 - Other cardiomyocyte diseases (inflammation/metabolic)**Uncertain**

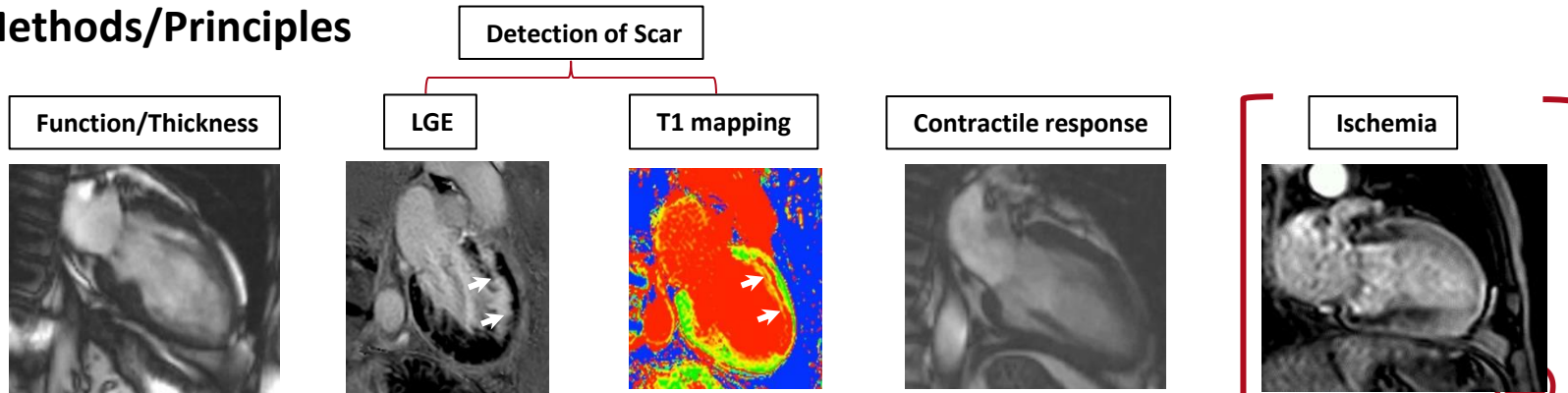


cMR aims and methods for detection of myocardial viability

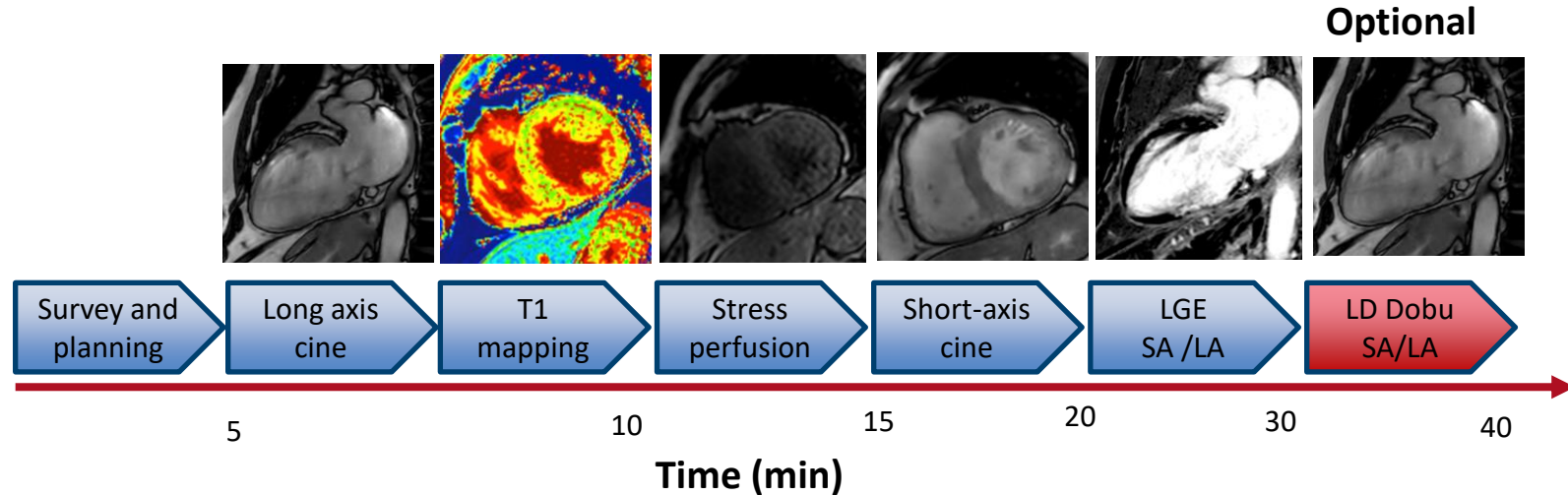
- **Aims:** Myocardial viability imaging aims at evaluating status of dysfunctional myocardium in territories sustained by severe chronic coronary disease.



- **Methods/Principles**

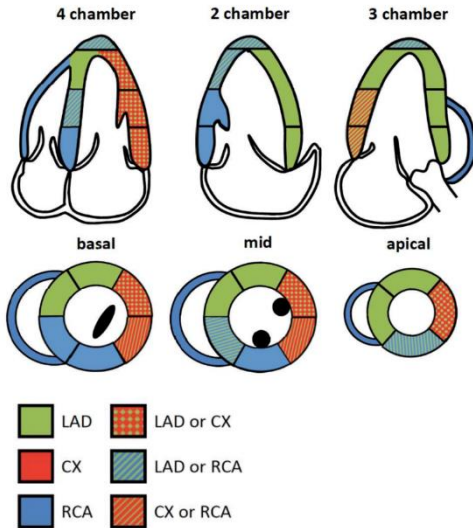
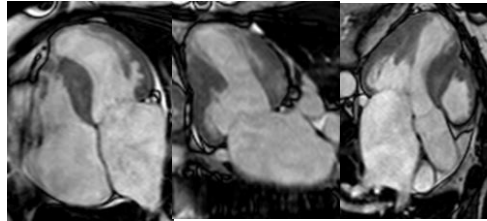


cMR protocol for evaluation of patients with chronic CAD.

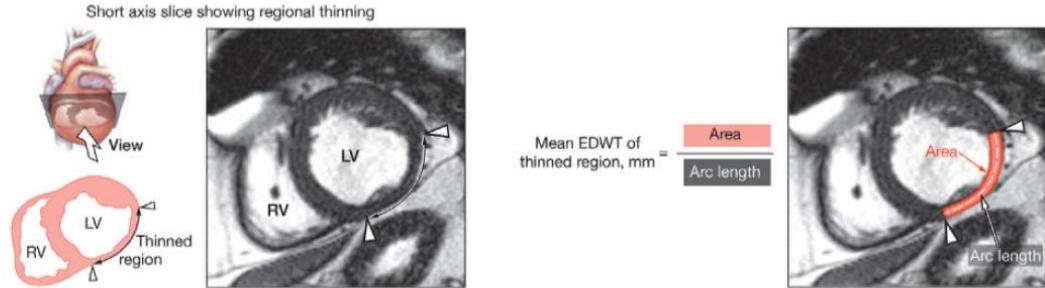


Modified after Morton EHJ (2010) 31, 2209–2216

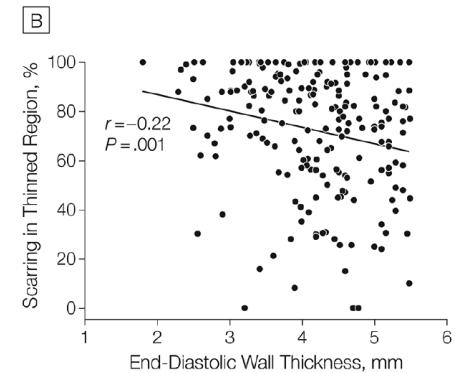
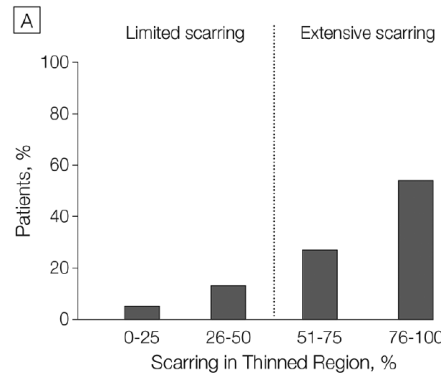
Evaluation of wall thickening / thickness



A Cine-MR analysis of regional left ventricular (LV) end-diastolic wall thickness (EDWT)



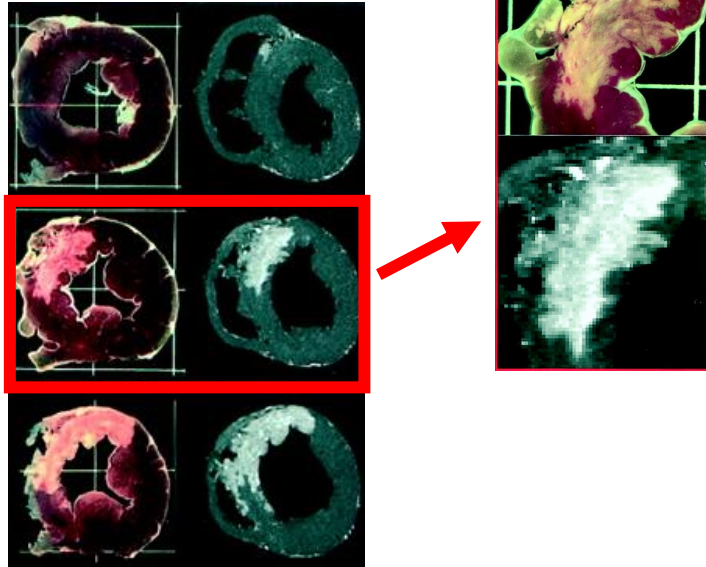
Regional thinning was defined as the sector in which LV end-diastolic wall thickness (EDWT) was ≤ 5.5 mm on the end-diastolic cine frame for each short axis slice. RV indicates right ventricle.



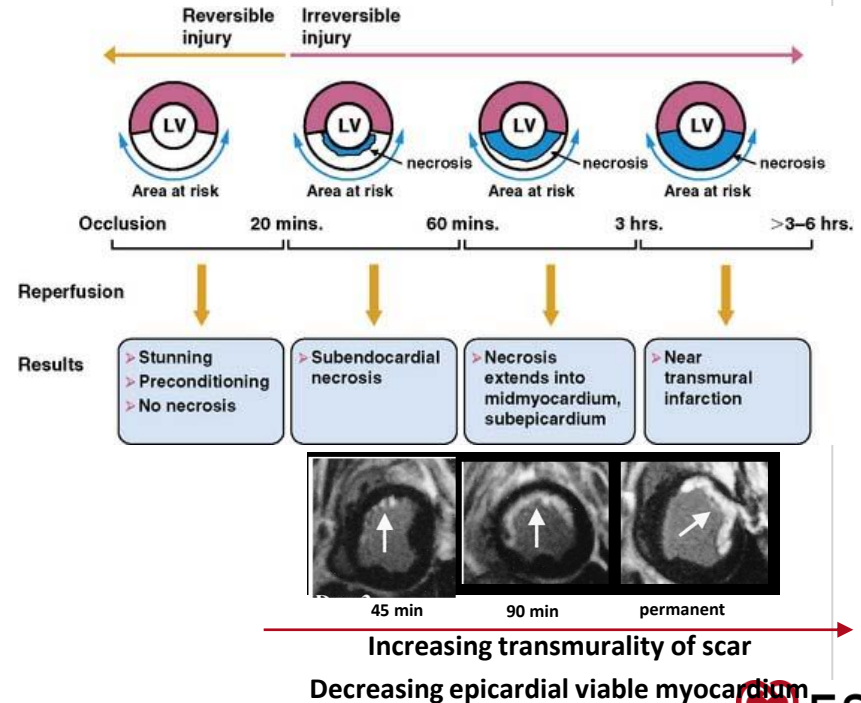
LGE evaluation of viability: Detection of scar = non viable myocardium



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Wavefront phenomenon of necrosis



Kim et al. Circulation. 1999;100:1992

Hildenbrand et al. Circulation. 2000;102:1678-1683

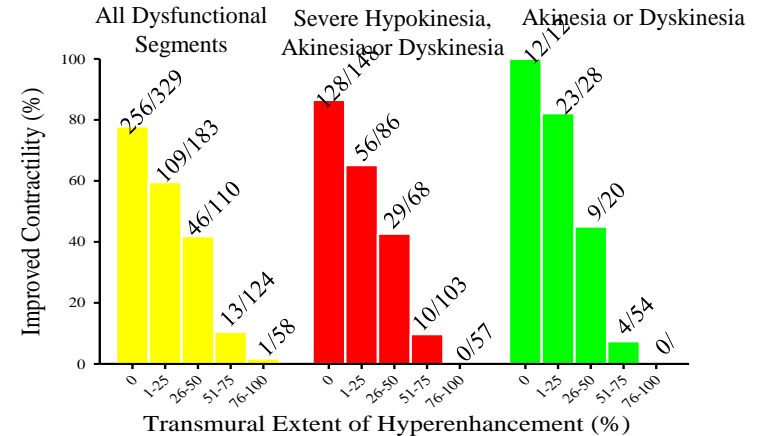
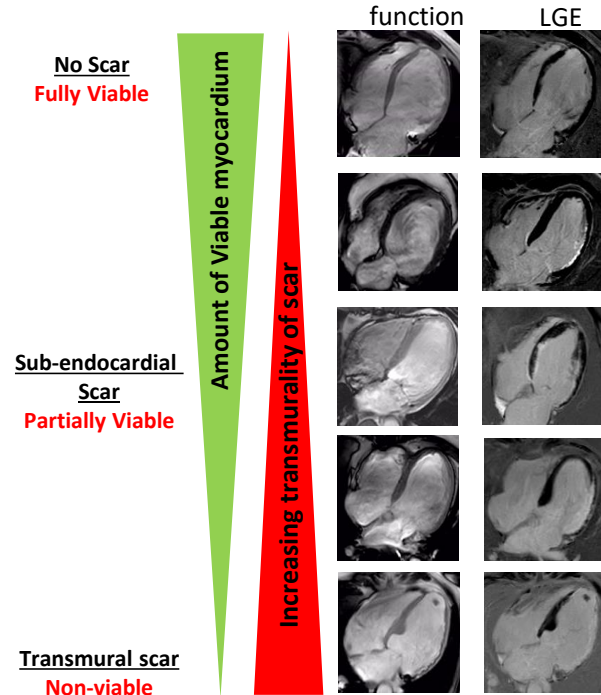


Principles of Detection of Viability by LGE

Transmurality of scar



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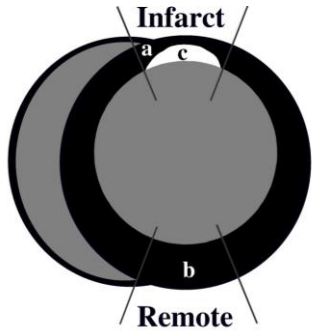
Kim *NEJM* 2001; 343(20):1445-53

- **Non viable:** Scars with transmurality >50%
- **Viable** no or less transmurality of scar in dysfunctional myocardium is considered viable myocardium.
- **LGE has high specificity for predicting absence of recovery** but **sensitivity may be limited** particularly in scars with intermediate transmurality (25–75%).

Methods of evaluating viable / nonviable myocardium



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Quantification of
regional viability
(% viability)

Direct: $\frac{a}{a+c}$
Transmurality of LGE

Indirect: $\frac{a}{b}$

Thickness of unenhanced rim

SEGMENTAL MYOCARDIAL VIABILITY

DELAYED MYOCARDIAL ENHANCEMENT



- Absent
- < 25% of the segment area
- < 50% of the segment area
- > 50% of the segment area
- > 75% of the segment area

POTENTIAL OF CONTRACTILE RECOVERY

- ■ ■ Segmental viability present
- ■ Segmental viability absent

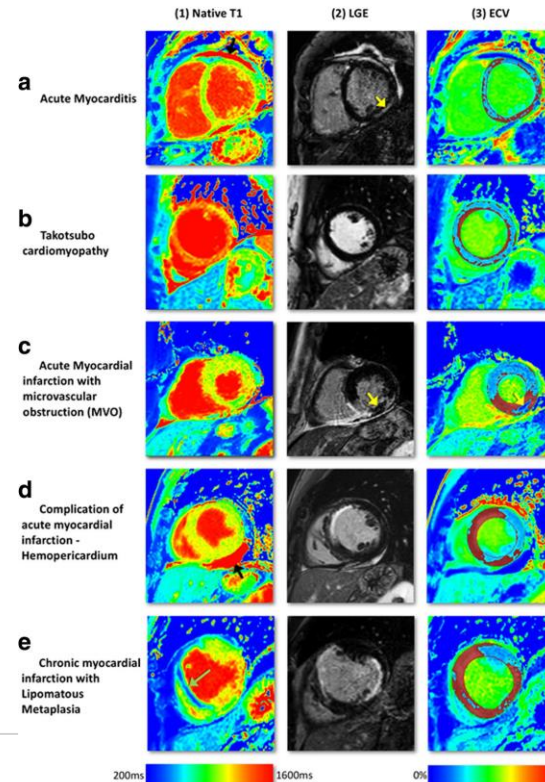
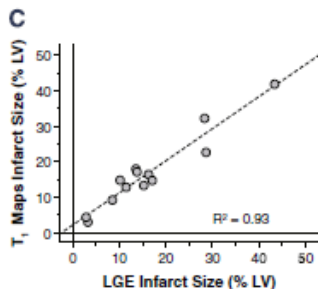
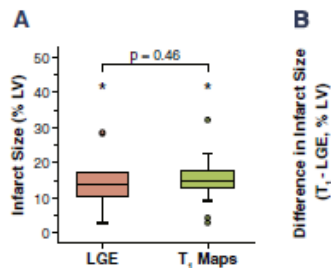
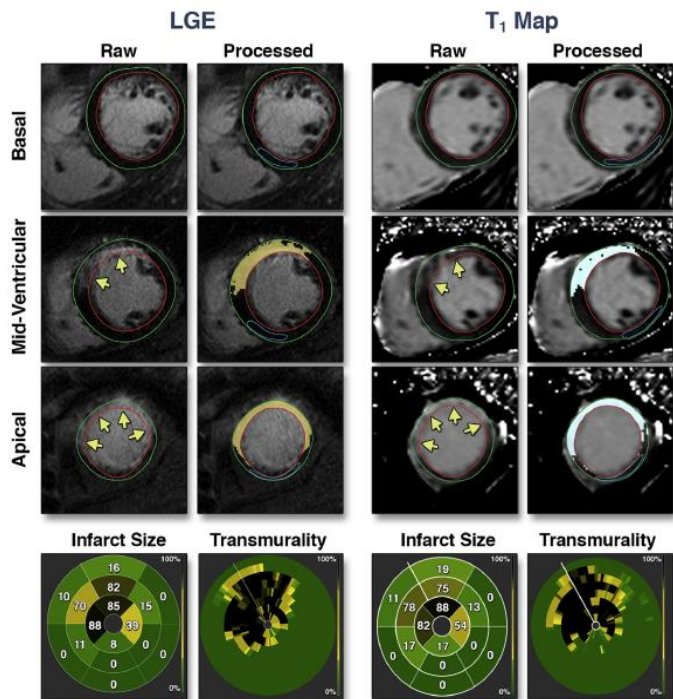
Native T1 mapping for viability?

native T1 increases occurs in scar but is non-specific of fibrosis / scar

However post contrast ECV imaging yields similar information as LGE



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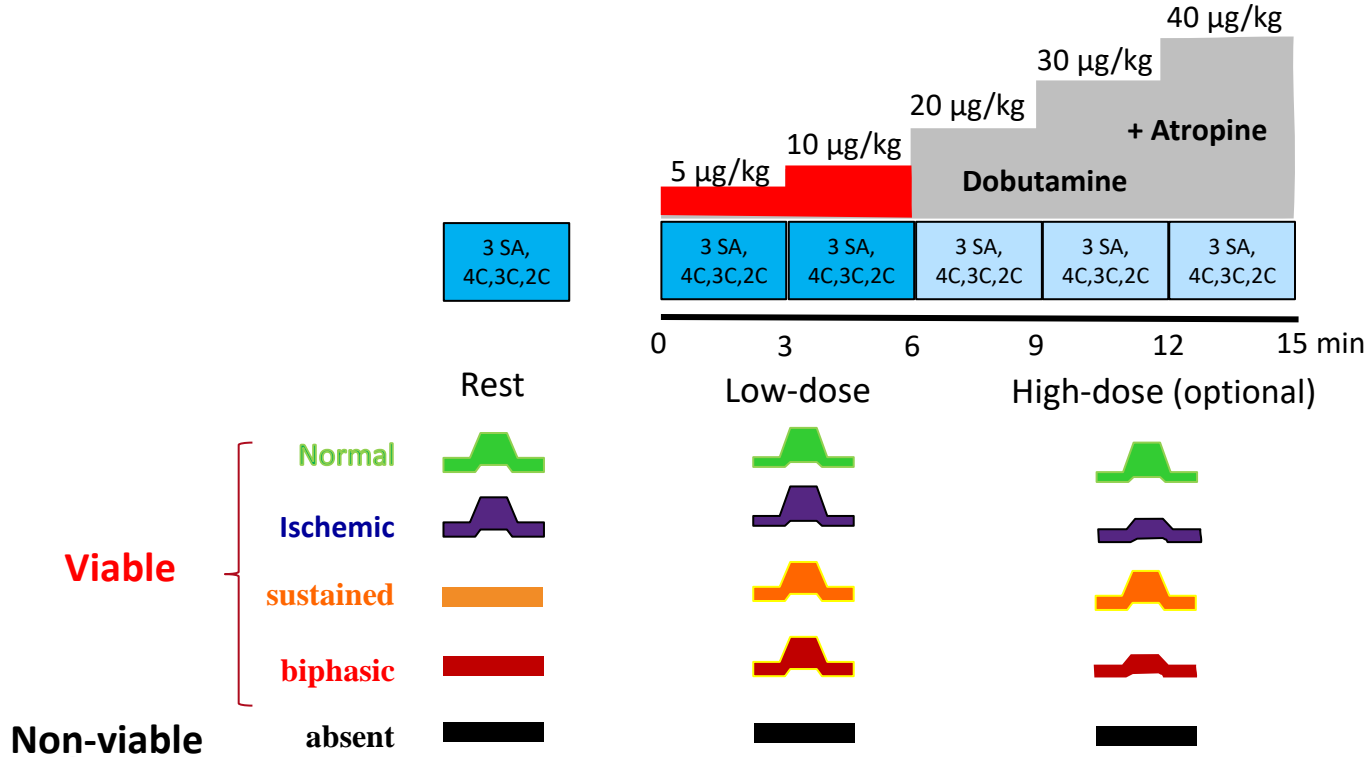


Kali JACC Img 2015;8:1019-30

Haaf JCMR 2016

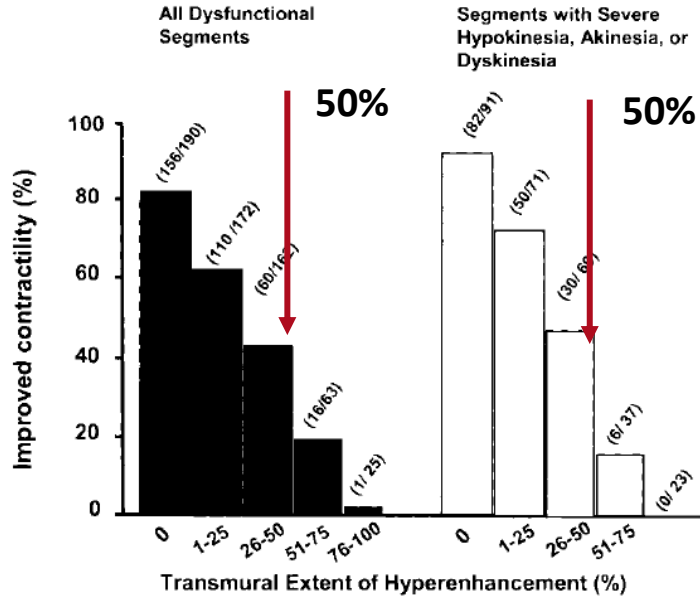
ESC

Dobutamine stress test MRI for viability



Outcomes of CMR viability

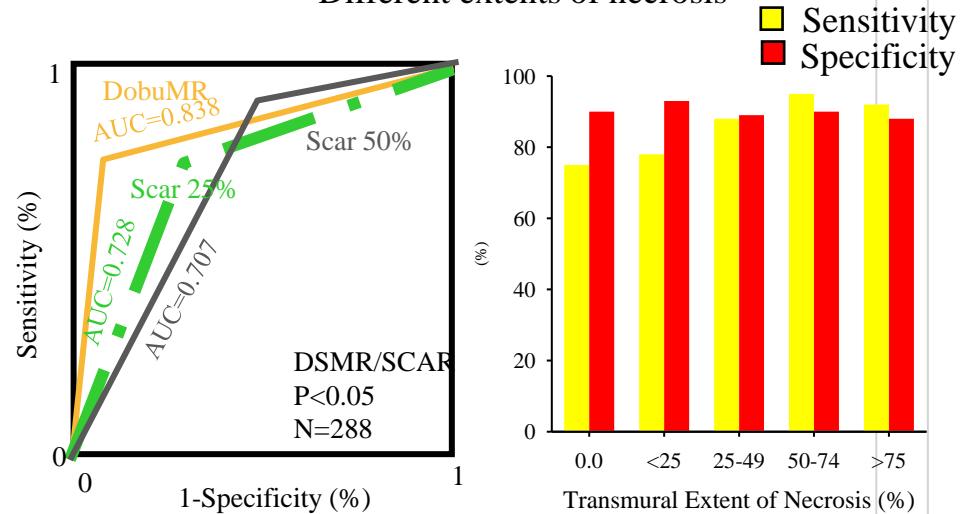
LGE



Selvanayagam *Circulation*. 2004;110:1535-1541

LD Dobutamine cMR

Dobu MR: Sensitivity/Specificity in Different extents of necrosis



Weinhofer *Circulation* 2004 ;109:2172-2174

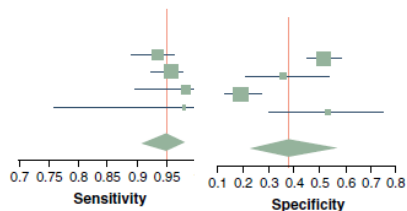
Prediction of functional recovery: metanalysis



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Wall thickness

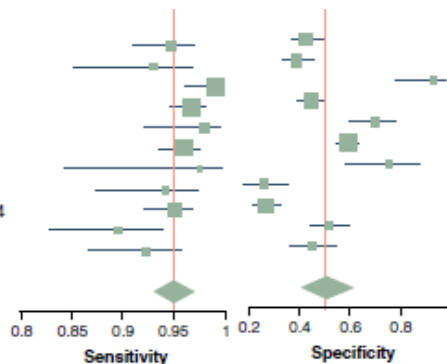
C
EDWT Studies
Baer 1998
Gutberlet 2005
Klow 1997
Schmidt 2004



Sens 96% Sens 38%

LGE

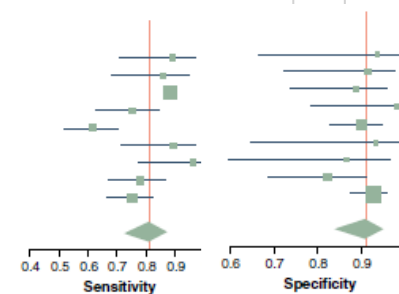
DE Studies
Becker 2008
Bordarenko 2007
Gutberlet 2005
Kim 2000
Kuhl 2006
Pegg 2010
Sandstede 2000
Schwartzman 2003
Selvanayagam 2004
Wellnhofer 2004
Wu 2007



Sens 95% Spec 51%

Dobutamine Echo

LDD Studies
Baer 1998
Baer 2000
Gutberlet 2005
Lauerma 2000
Sandstede 1999
Sayad 1998
Schmidt 2004
Van Hoe 2004
Wellnhofer 2004



Sens 81% Spec 91%

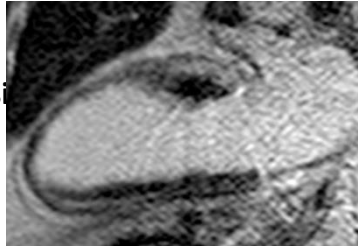
Romero JACC Im 2012;5:494-508



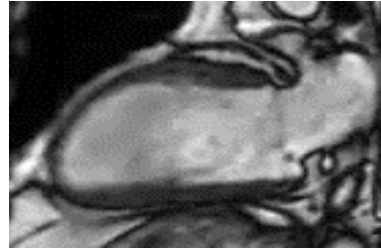
Clinical example

Viable

68 yo male
Acute ant MI
Critical LAD stenosis

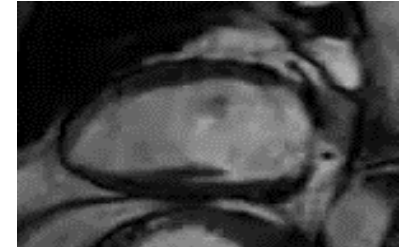


Baseline



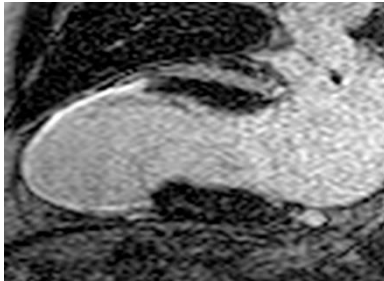
PCI
LAD

4mo post revasc.

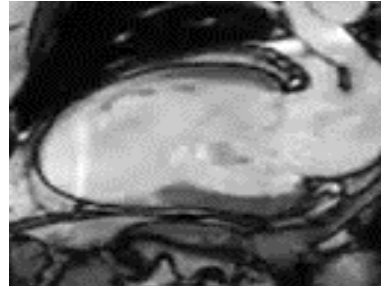


Non-Viable

58 yo male
Acute ant MI
3 vx disease

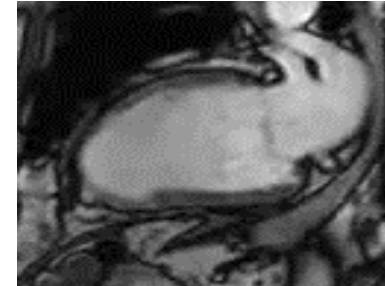


Baseline



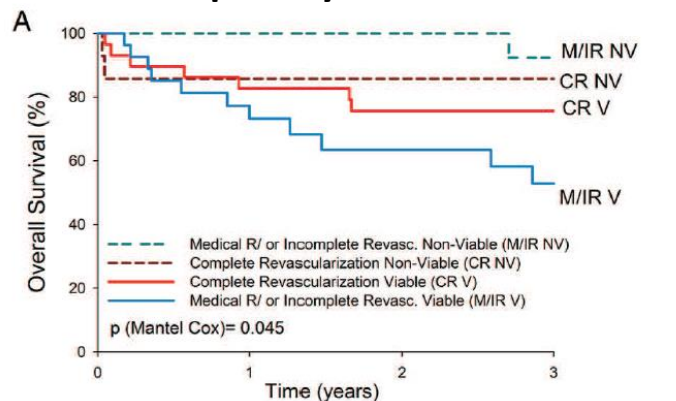
CABG

7mo post revasc.



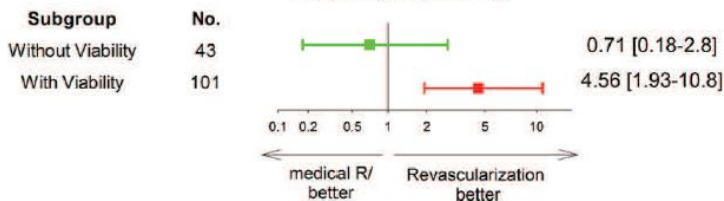
Prognostic value of viability by LGE vs revascularization

Propensity score matched



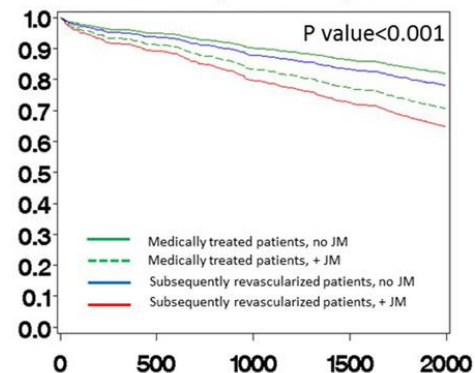
	0	1	2	3
M/IR NV	16	16	13	11
CR NV	14	12	12	10
CR V	29	24	18	12
M/IR V	77	14	12	10

Hazard Ratio [95% CI]



Gerber JACC 2012;59:825-35)

Survival Based on Treatment and Presence of Jeopardized Myocardium



Day	0	500	1000	1500	2000
Medically Treated no JM	169	138	108	83	60
Medically Treated + JM	126	111	92	77	51
Revascularized no JM	76	62	52	48	33
Revascularized + JM	260	235	199	179	131



Kwon J Am Heart Assoc. 2018;7 :e009394

Indications / Algorithm for use of (any) viability imaging



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Stich trial did not demonstrate benefit of Viability testing in CAD

ESC guidelines
Chronic CAD

Non-invasive stress imaging (CMR, stress echocardiography, SPECT, PET) may be considered for the assessment of myocardial ischaemia and viability in patients with HF and CAD (considered suitable for coronary revascularization) before the decision on revascularization.

IIb

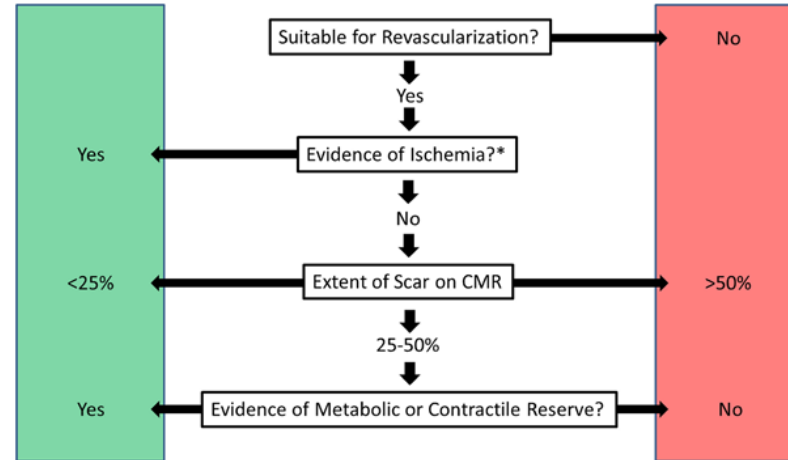
B

HOWEVER STICH DID NOT USE CMR

Knuuti 2019 ESC Guidelines for the diagnosis and management of chronic CAD Eur Heart J (2019)

AHA:
Unanswered question

AHA Scientific statement Algorithm for chronic ischemic dysfunction

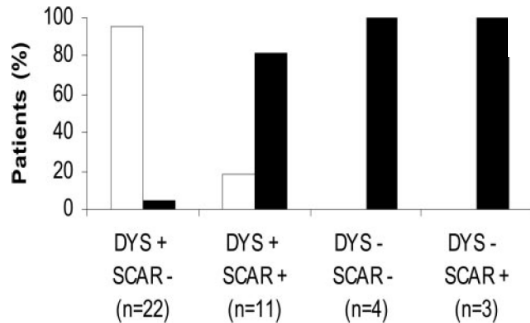
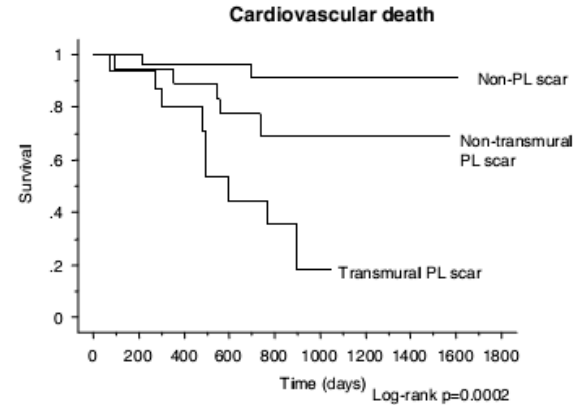
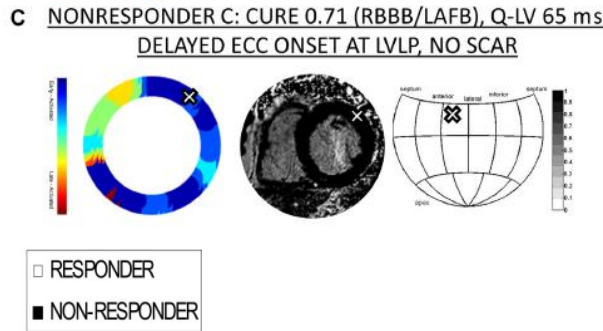
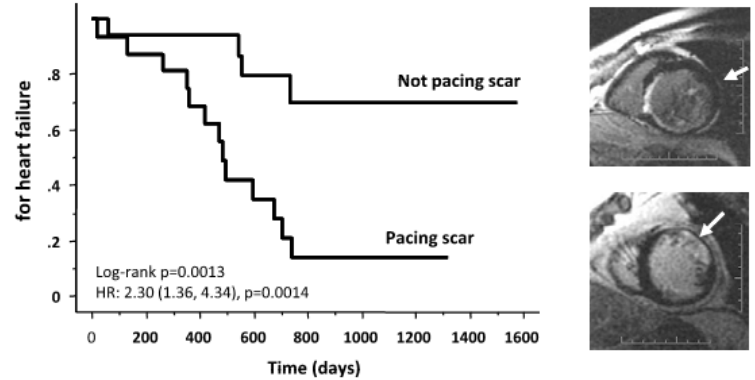
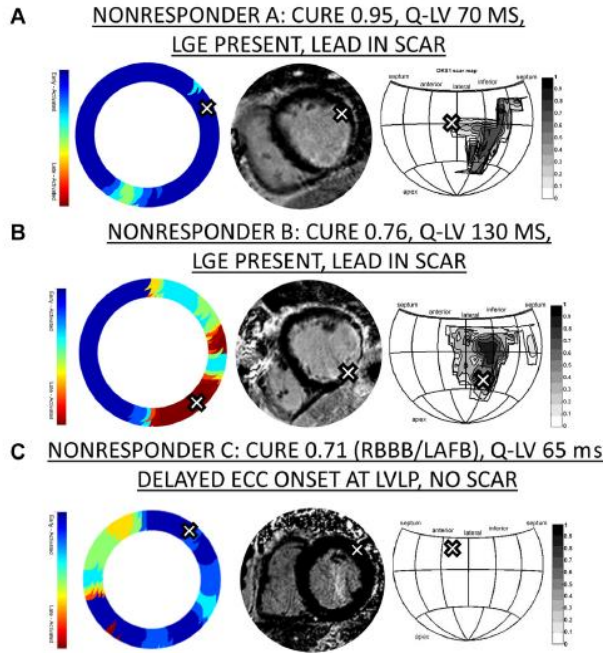
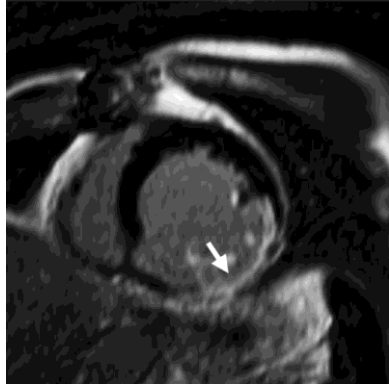


Garcia Circulation 2020
REVASCULARIZATION



CMR 2.2 - Ischemic heart disease – evaluation of viability

CRT response



cMR in chronic ischemic heart disease

Objectives



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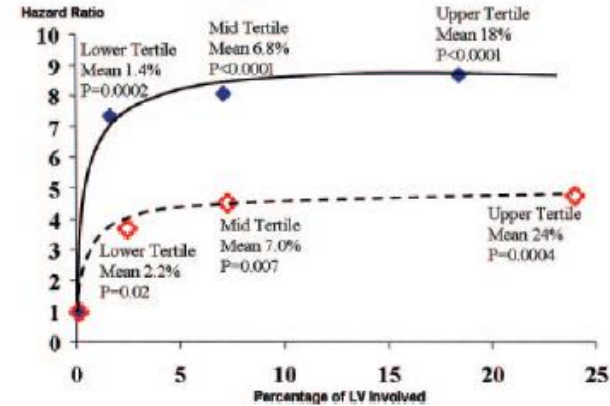
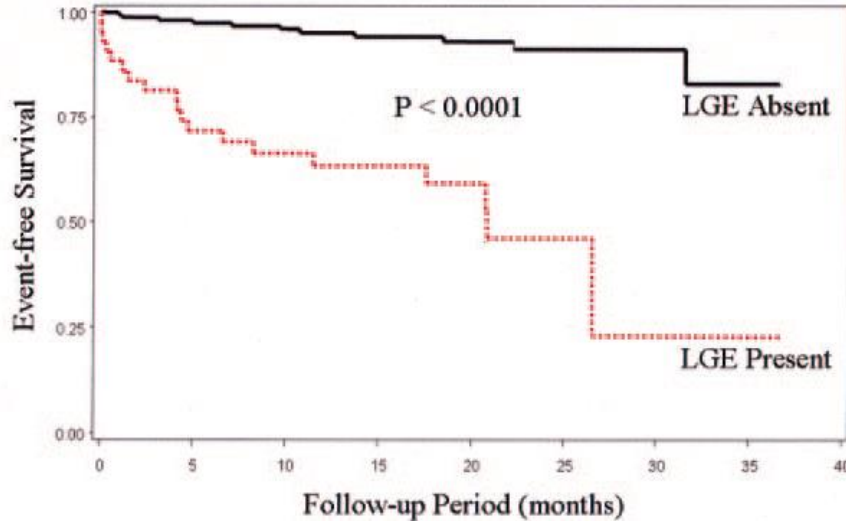
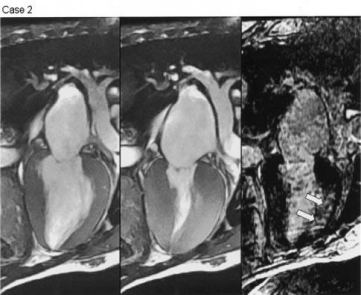
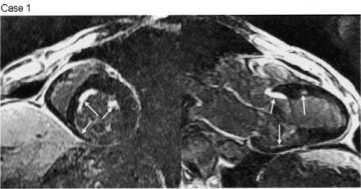
- 1.** Detection of myocardial ischemia
- 2.** Detection of myocardial viability and treatment selection
- 3.** Prognostication

Prognostic value of unrecognized scar in CAD



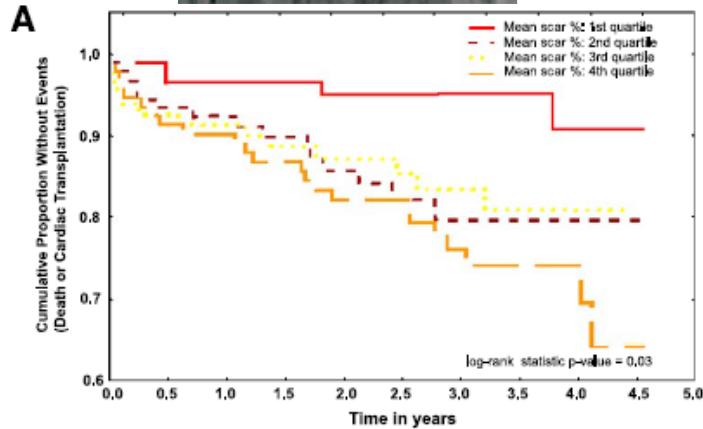
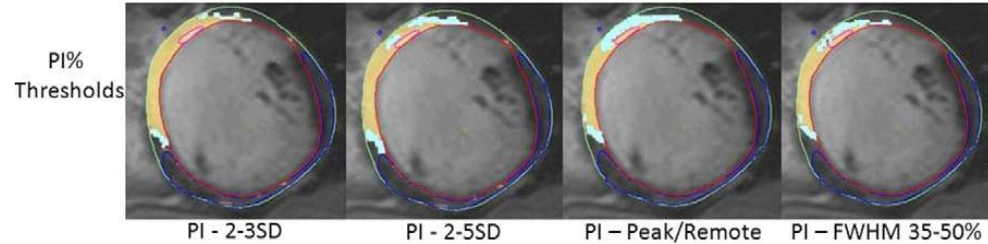
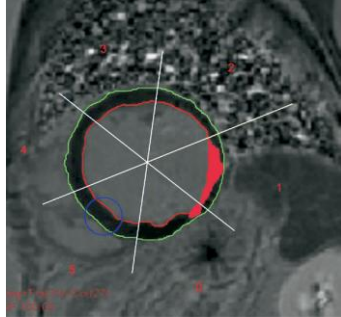
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195 pts with signs or symptoms of CAD without known MI



ESC

Prognostic value of LGE extent and heterogeneity in chronic CAD

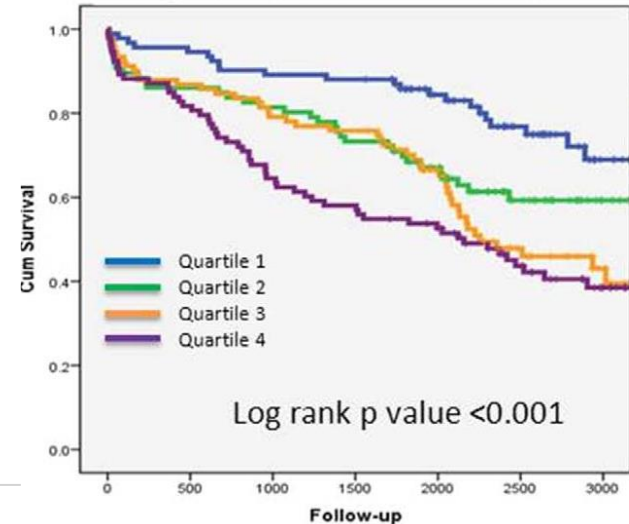


Number of patients at risk of events

1st Quartile	82	80	73	60	53	41	27	17	5	0
2nd Quartile	85	78	71	55	39	30	23	15	2	0
3rd Quartile	75	70	63	57	46	37	26	16	0	0
4th Quartile	84	82	75	67	60	42	24	16	2	0

Kwon JACC Img 2009;2:34-44

Unadjusted Survival based on TMS% \geq 3SD



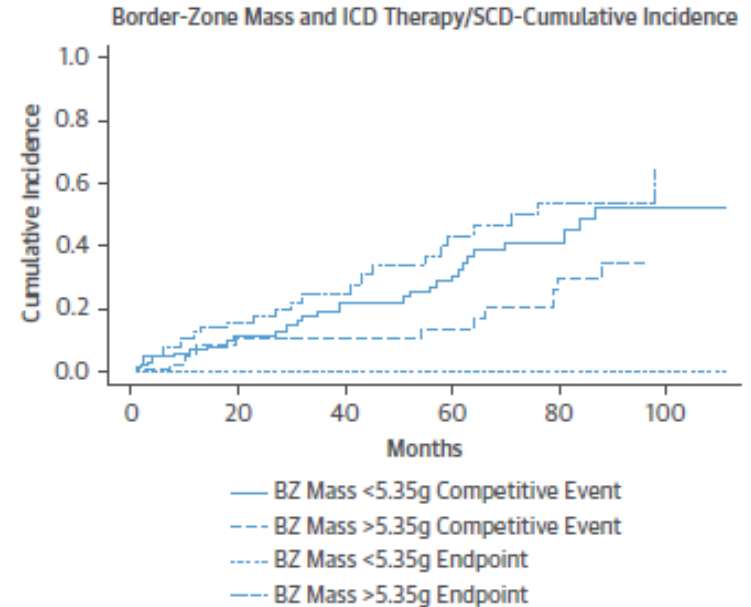
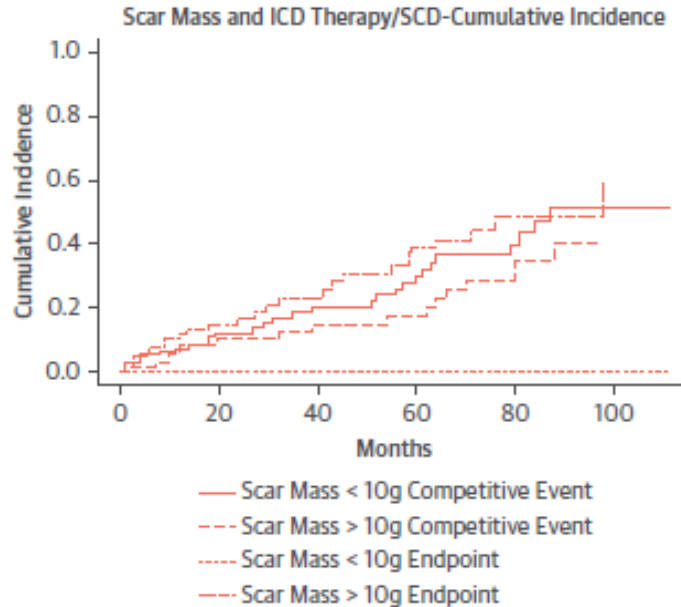
Kwon *Circ CV Im* 2014;7:796-804

Prognostic value for ICD discharge in patients with CRT-D



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217 patients with CRT



Conclusion



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cMR allows

- 1) To identify ischemia in symptomatic patients and detect chronic coronary artery disease either using perfusion stress or high dose dobutamine imaging**
- 2) To detect myocardial viability using LGE, low dose dobutamine, and potentially using native T1 mapping**
- 3) To define prognosis by LGE, T1 mapping in chronic coronary artery disease.**