The role of imaging in predicting and optimizing the benefit of CRT

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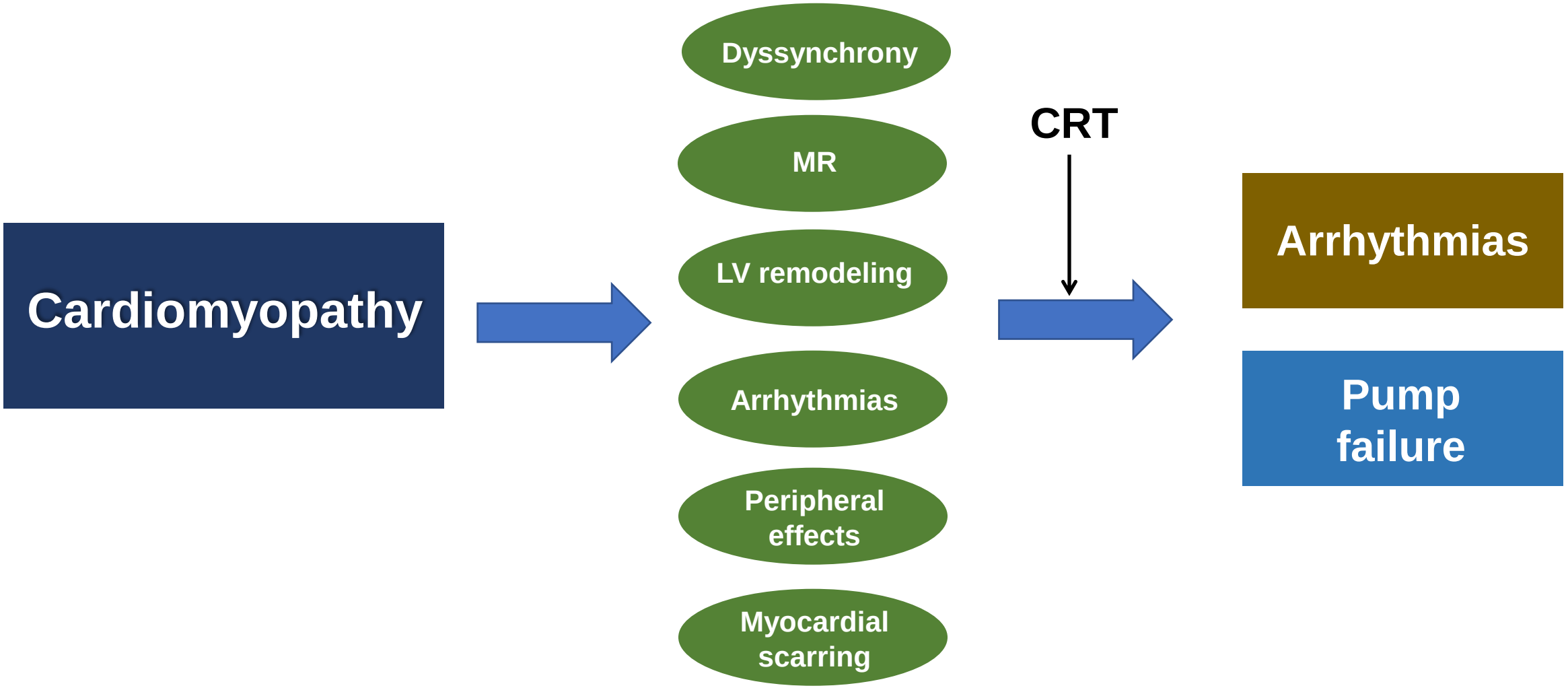
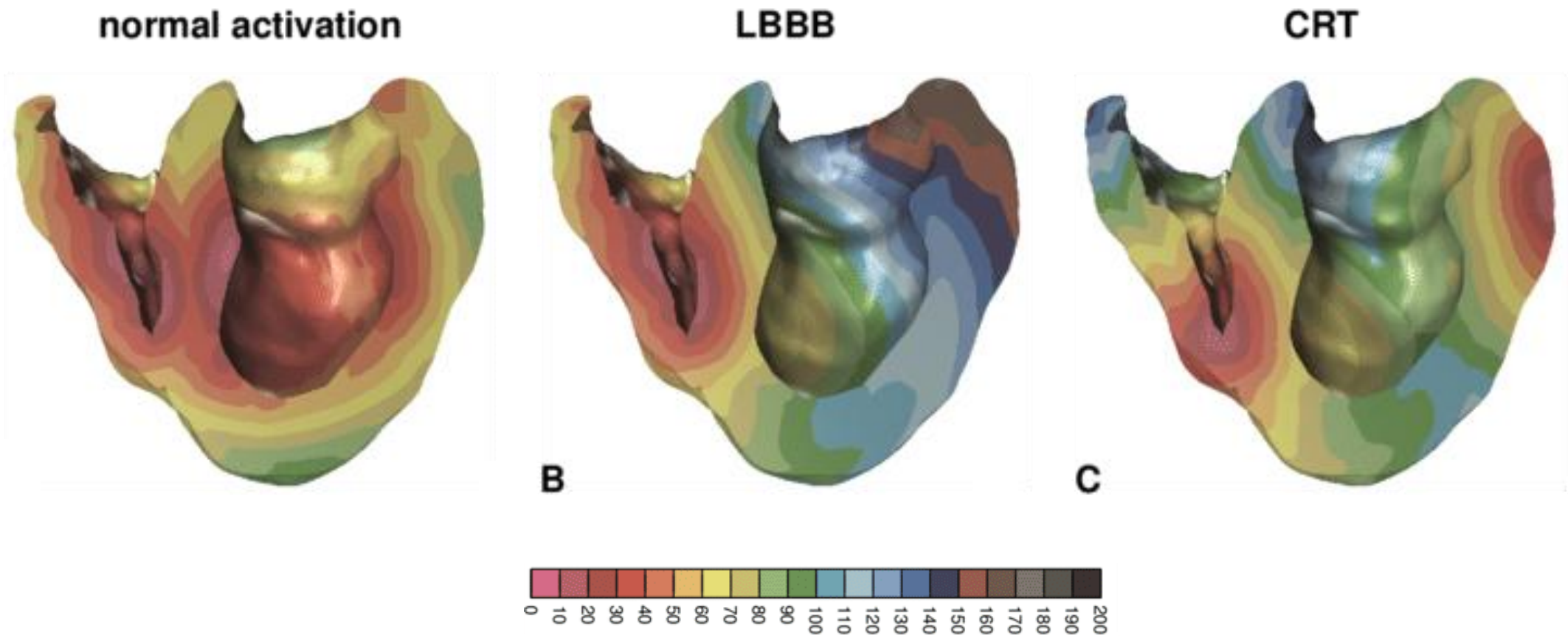
Benefit from CRT

BETTER RESPONSE	WORSE RESPONSE
• Female • NICM • LBBB • No LV scar • LV lead over LAS? • Q-LV guided LV?	• Male • ICM • Non-LBBB • AF • PHT • Valvular cardiomyopathy • Renal impairment • Lead over scar?

CRT ‘substrates’



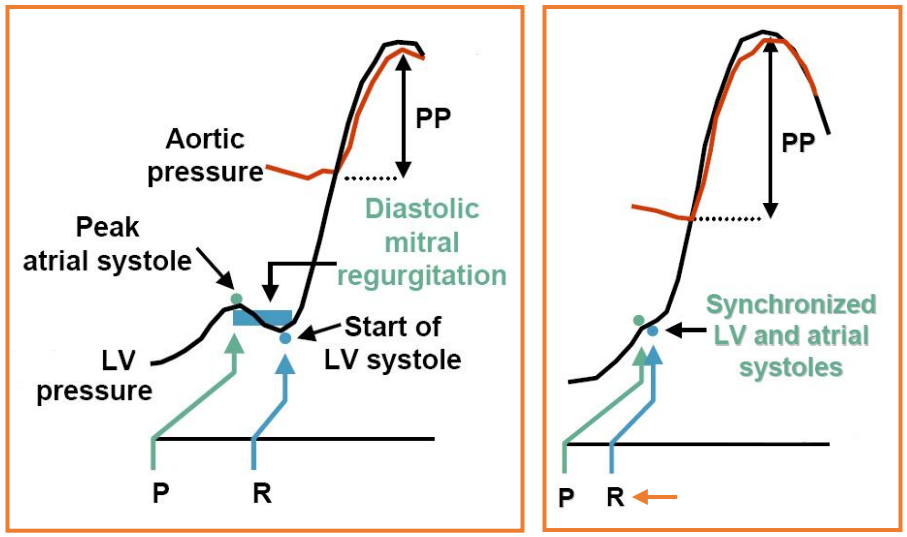
CRT: the paradigm



Potse M, et al. Europace 2012:Suppl. 5:v33-v39

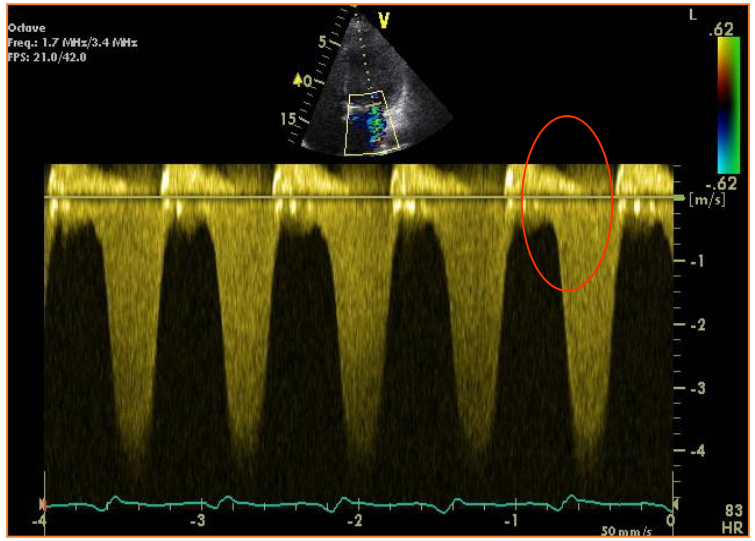
Echo

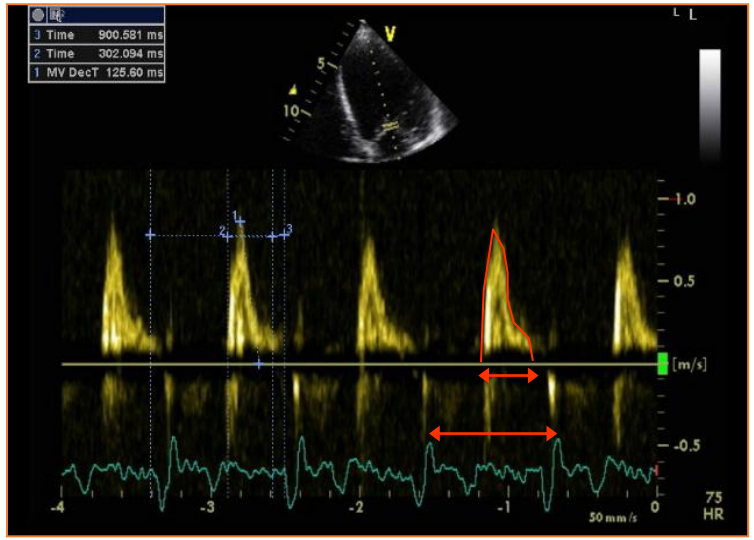
Optimisation: AV delay



Short AV delay

- Increase diastolic phase
- Pre-systolic MR ↓
- Optimise LV filling
- Stroke volume ↑

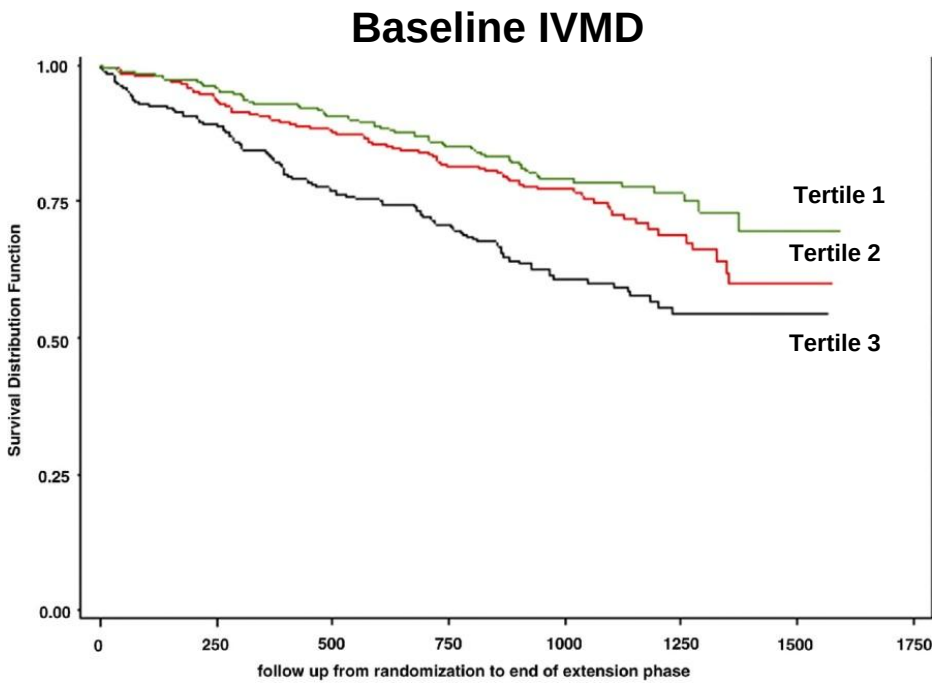




Auricchio A *et al* JACC 2002;39:1163

CARE-HF study: IVMD as a predictor of mortality ?

N=813 patients randomised to CRT or optimum medical treatment only
Model for predicting all-cause mortality included 15 pre-implant variables



Multivariate analysis:

As predictor of all-cause mortality:

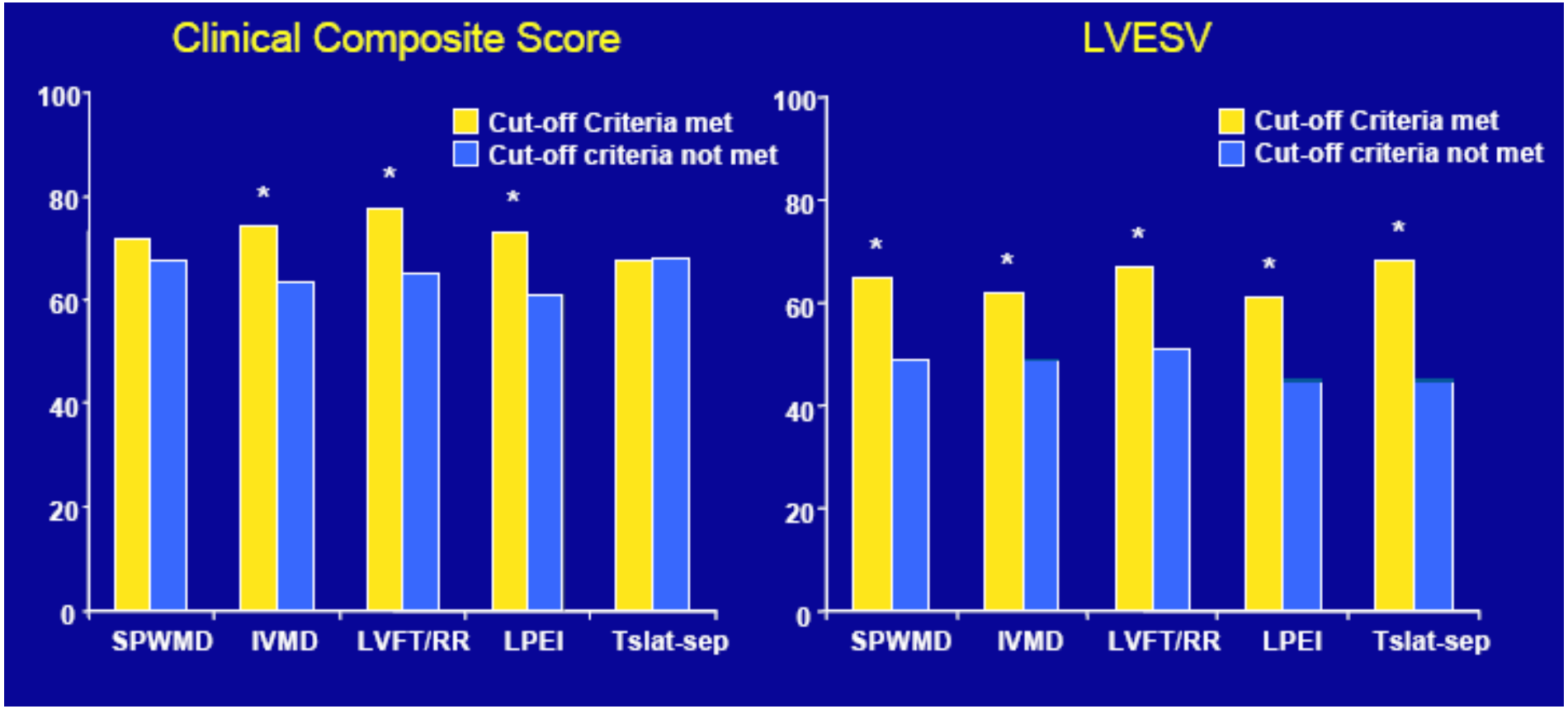
HR: 0.991 (95% CI: 0.986 -0.997)

No internal validation
No external validation
No Bayesian analysis

Conclusions: '... The effect of CRT on mortality cannot be usefully predicted using such information.'

Cleland, J. et al. J Am Coll Cardiol 2008;52:438-445

PROSPECT study: value of echo dyssynchrony



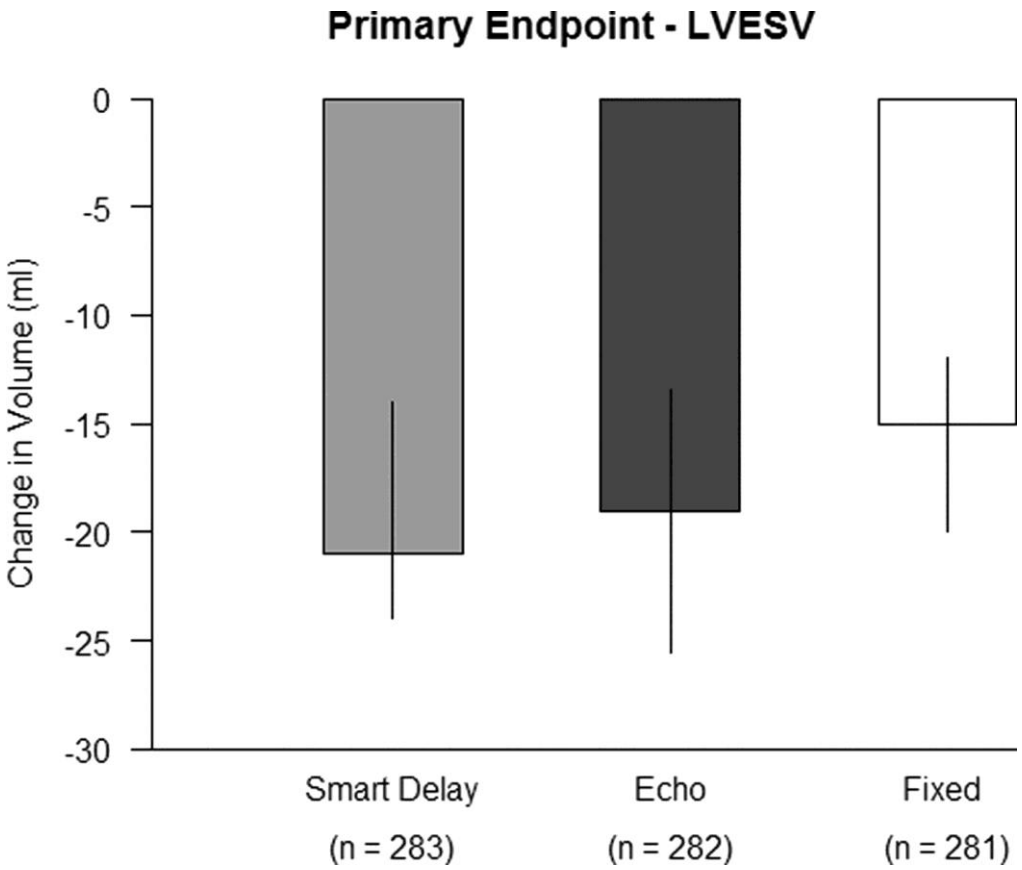
Measure	Yield (%)
SPWMD	72
IVMD	**92**
LVFT/RR	85
LPEI	95
Ts Lat-Se	67
Ts-SD	**50**

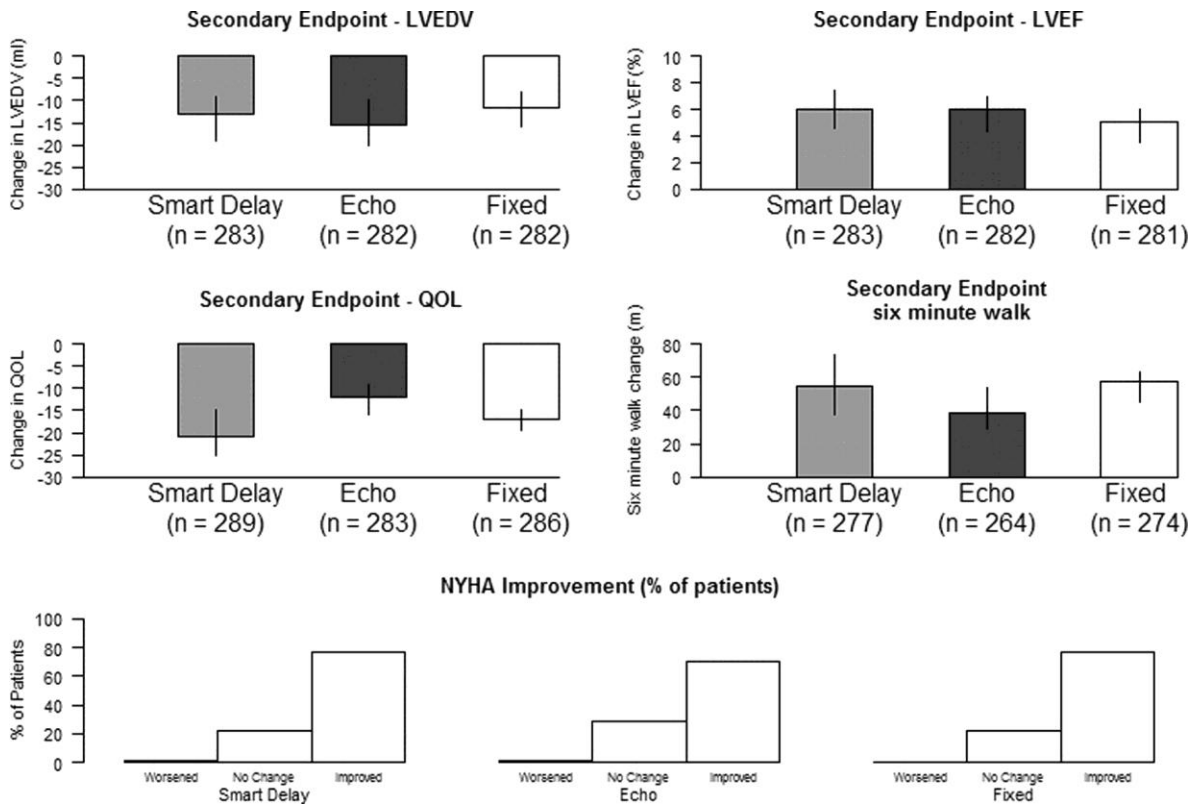
	CV (%)
Ts-SD	**33.7**
SPWMD	**72.1**

Chung E, et al. Circulation 2008;117:2608-16

AV optimisation

Comparison of echo and device-based optimisation with fixed approach

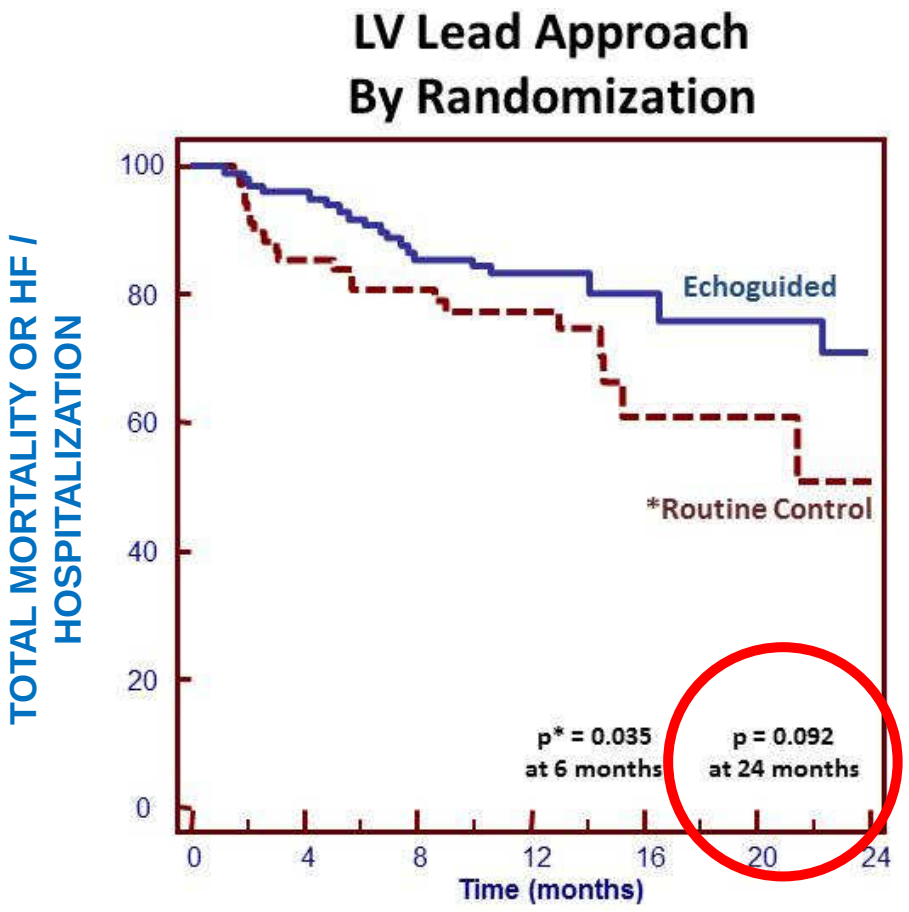




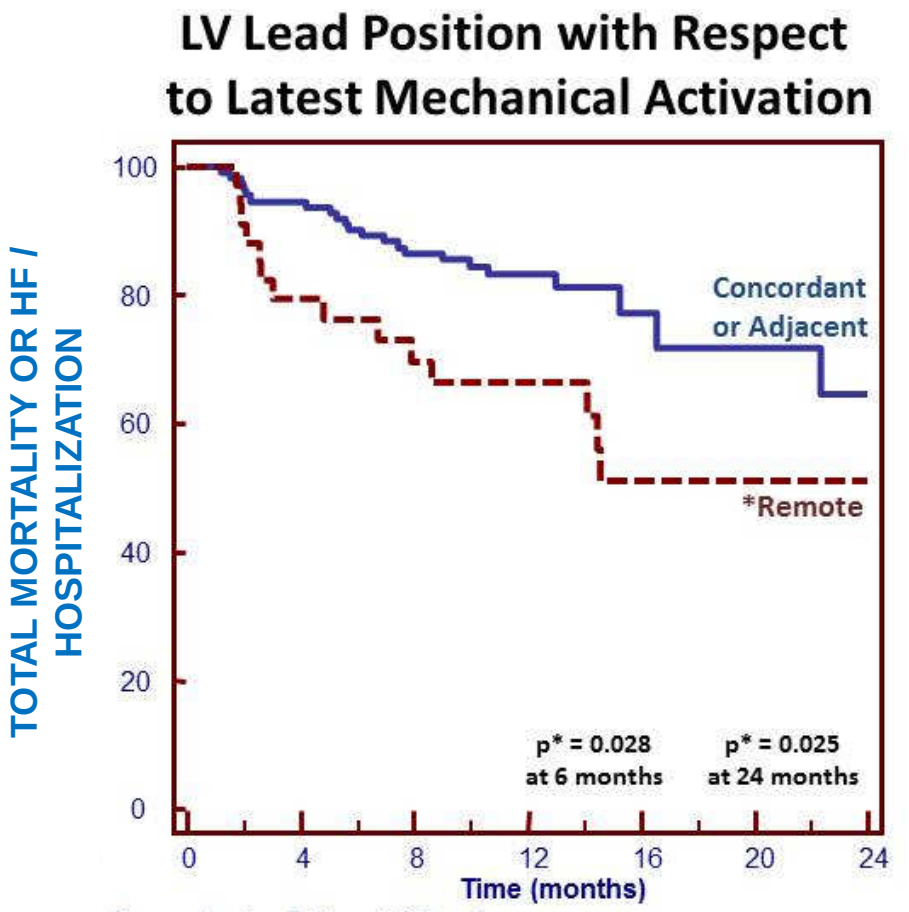
Ellenbogen K A et al. Circulation. 2010;122:2660-2668

STARTER: is echo guidance useful?

INTENTION-TO-TREAT



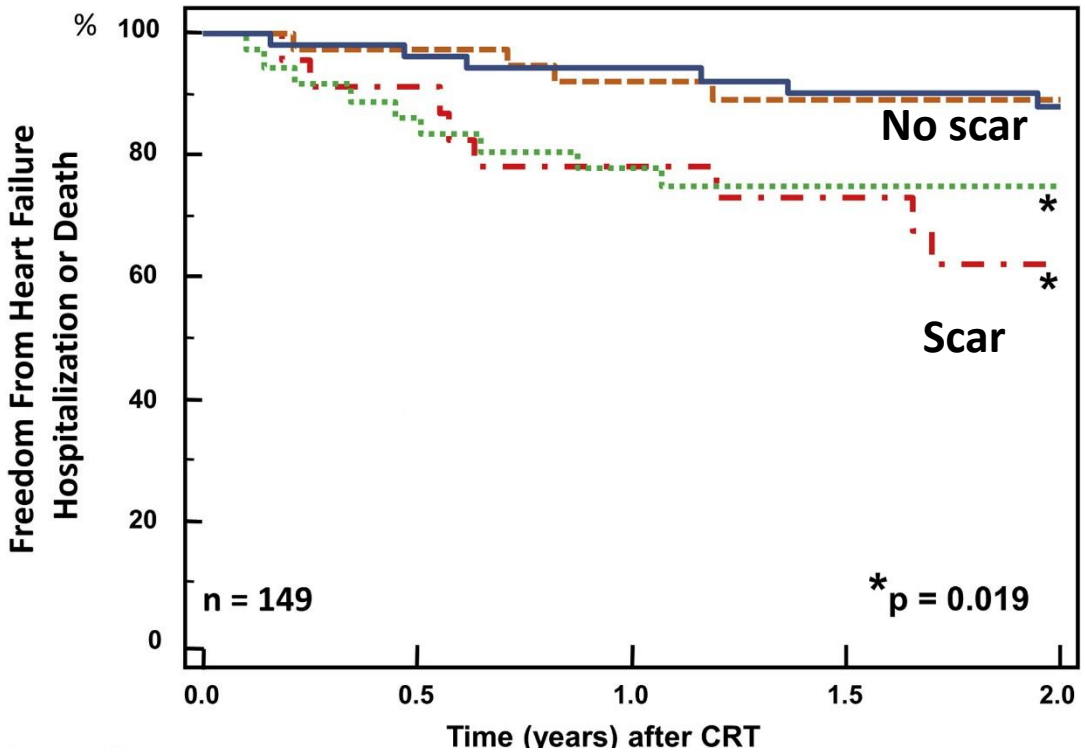
ON TREATMENT

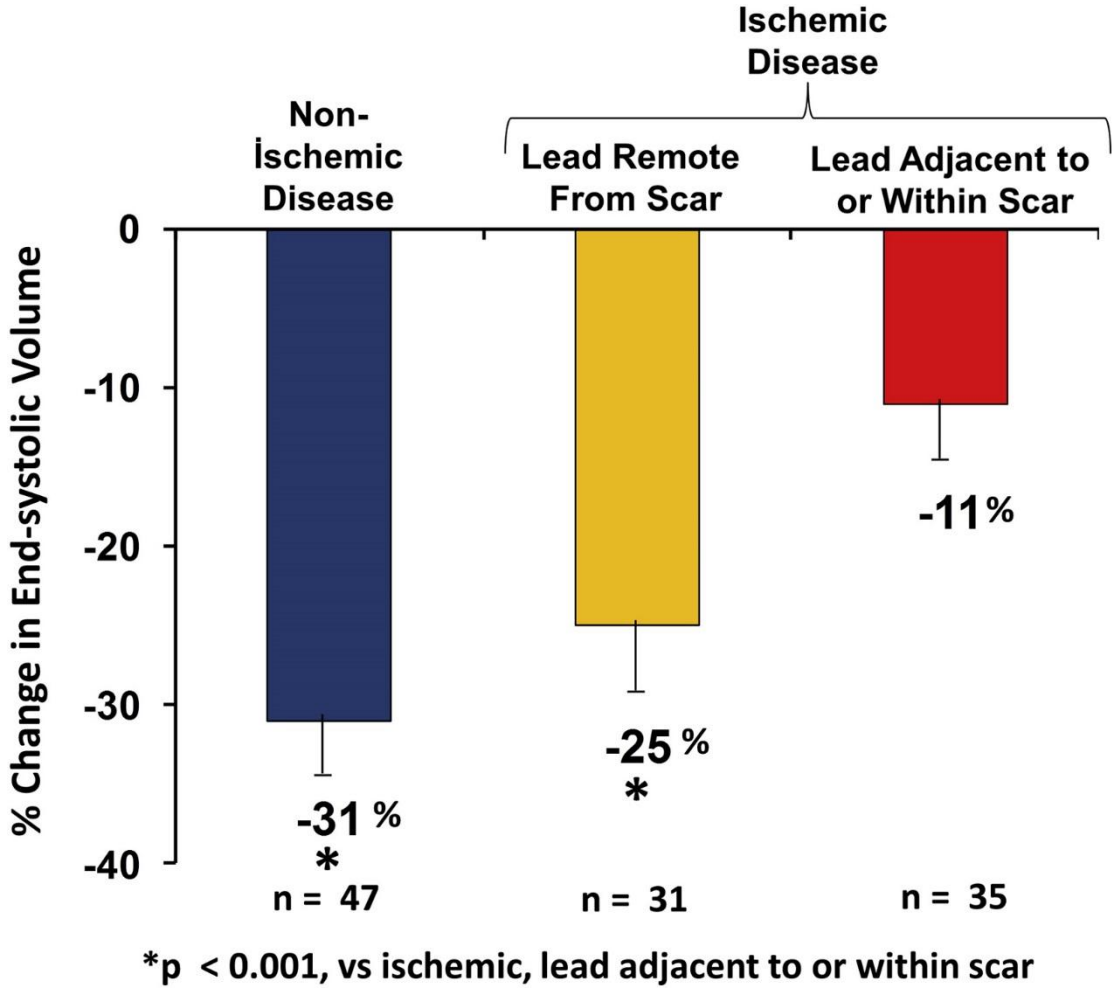


Headline: Targeted LV lead placement reduces HF hospitalizations or death compared to fluoroscopy-only lead placement

Saba S, et al. Circ HF 2013;6:427-34

STARTER: about late activation or scar?

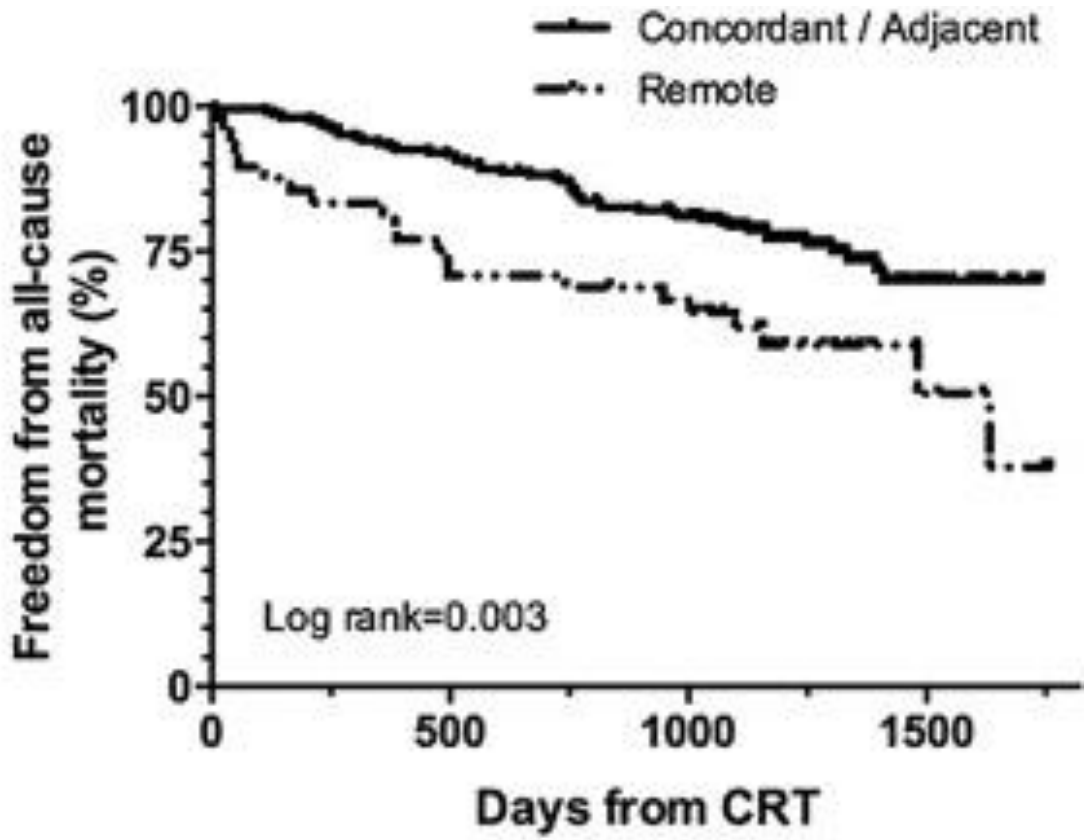


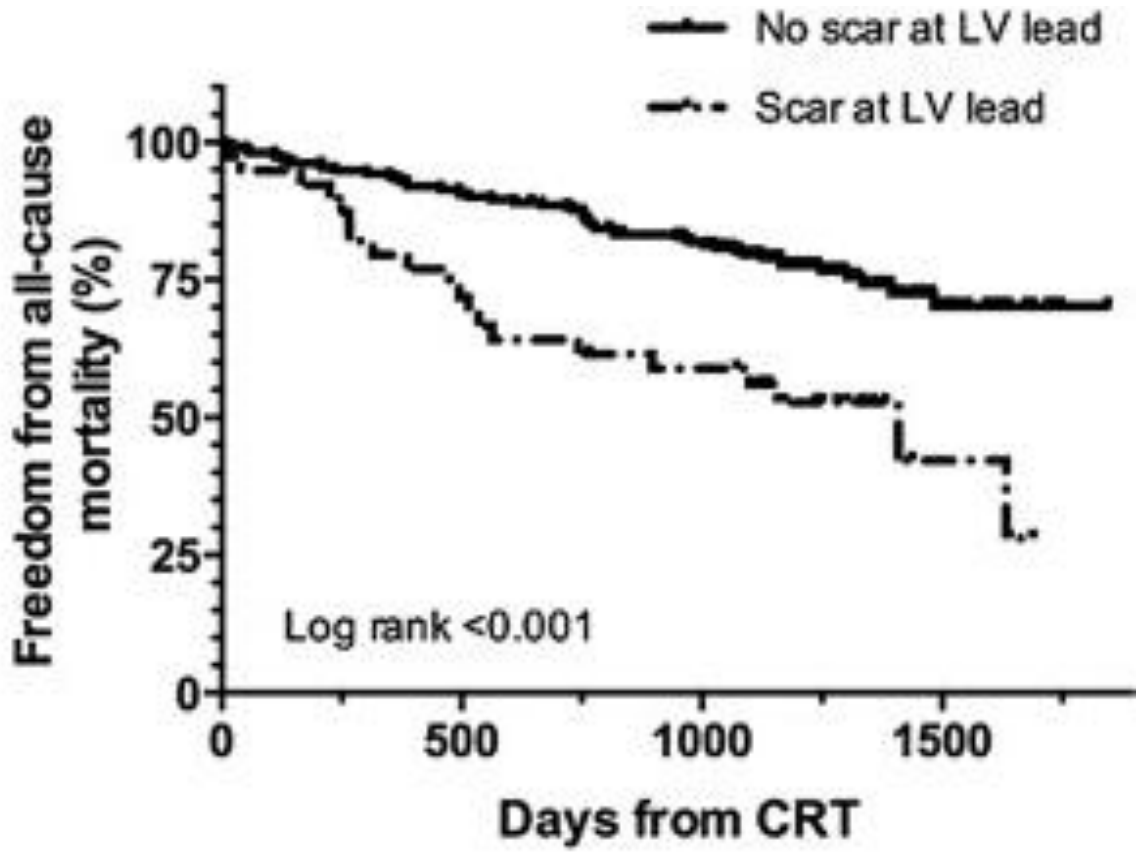


Speckle-tracking echo validated against scar assessed using MPI in 64 patients

Sade LE, et al. JASE 2014;27:648-65

TARGET: about late activation or scar?

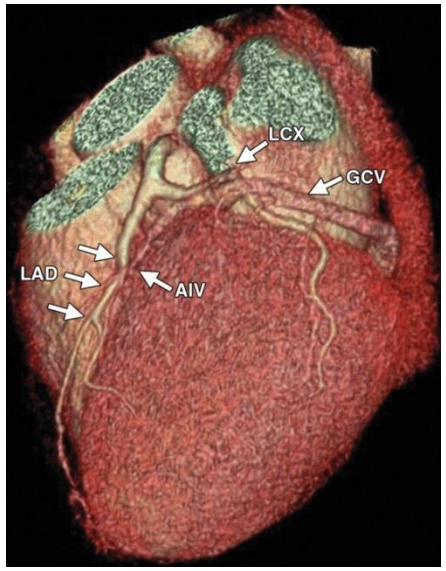


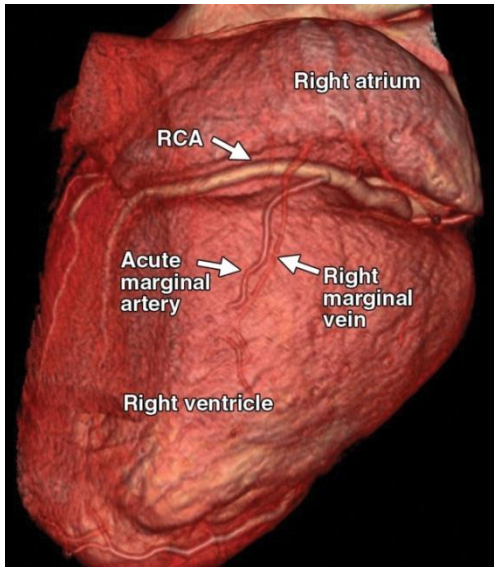


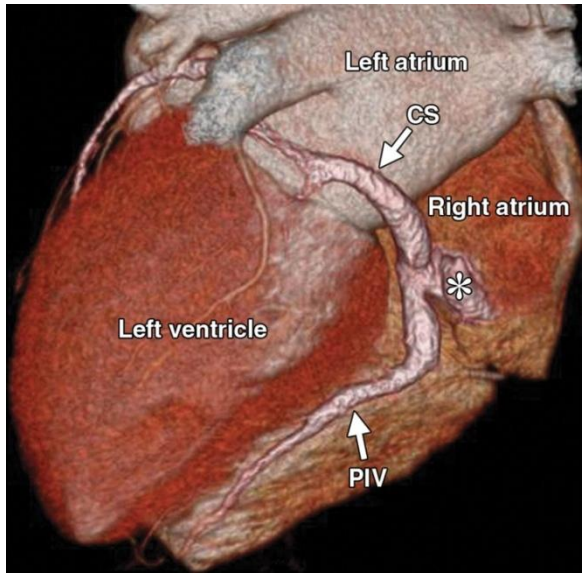
Kidd AC, et al. JACC HF2014;2:205-212

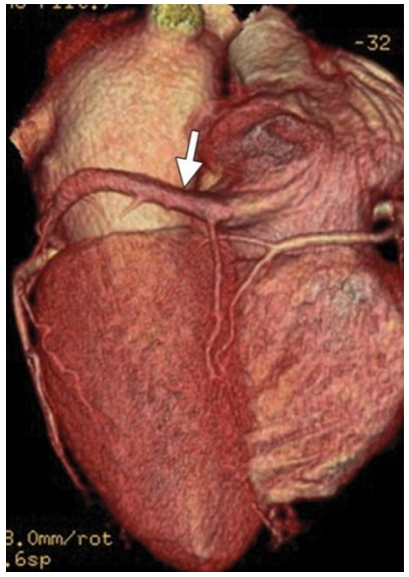
CT

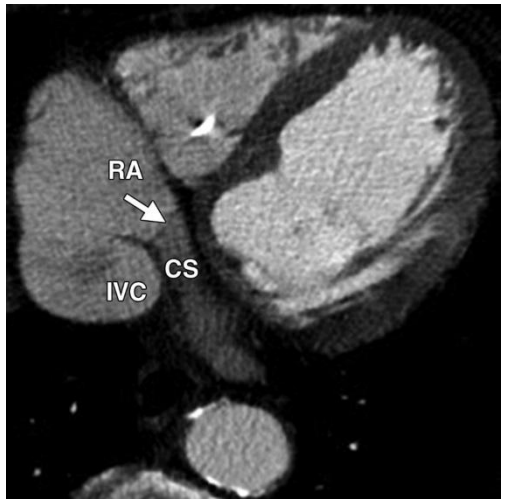
Cardiac CT venography

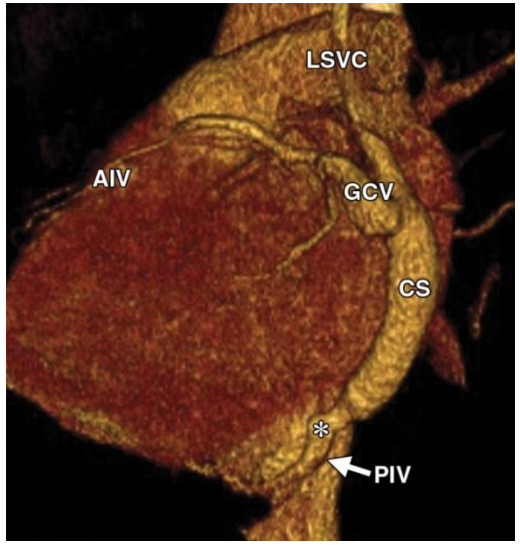








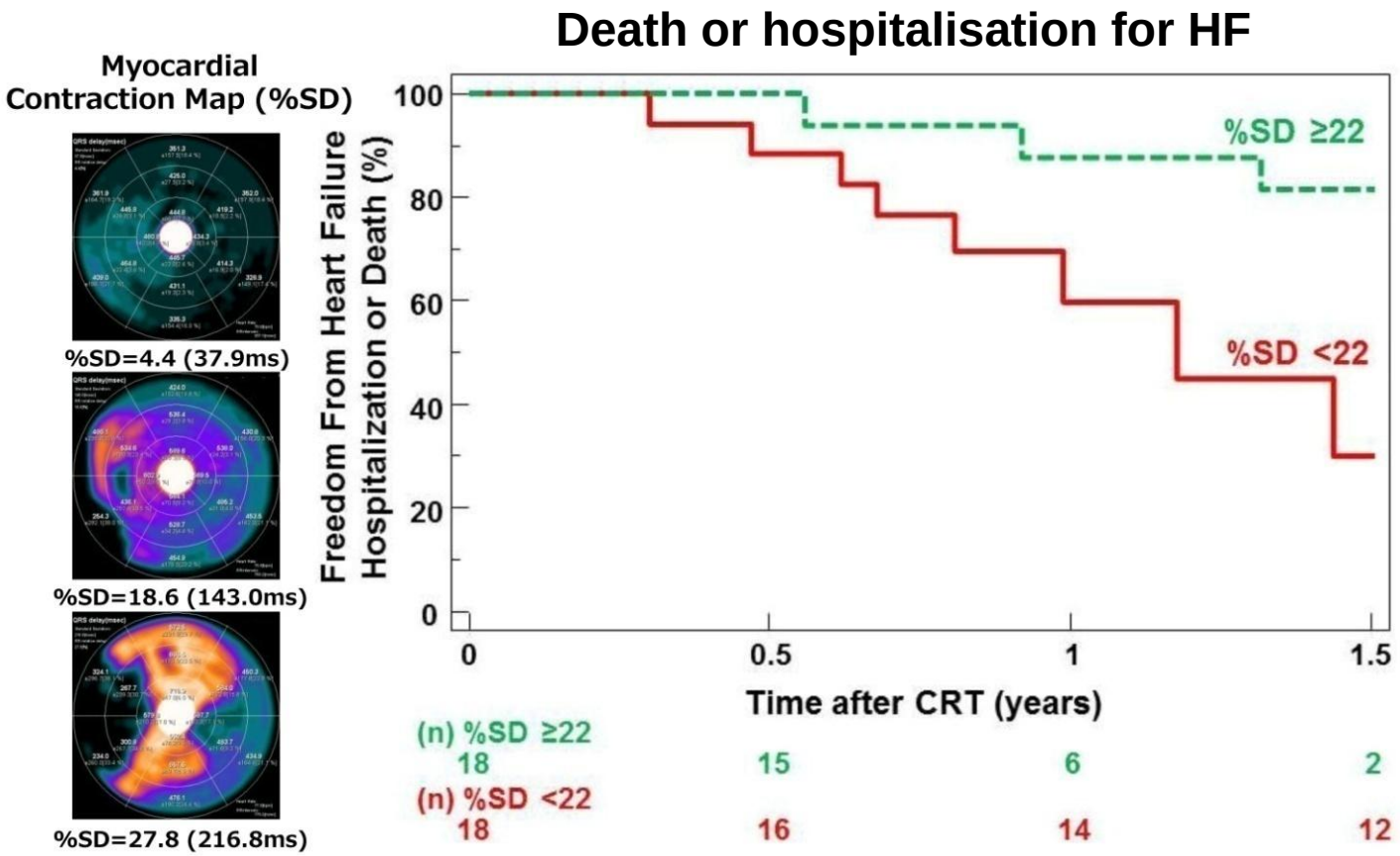




Shah S S et al. Radiographics 2012;32:991-1008

CT: dyssynchrony and outcome of CRT

N = 36 undergoing CRT
MDCT before CRT
Myocardial contraction map: SD modified by mean HF (%SD) as a global measure of dyssynchrony



Onishi T, et al. HRS 2013

CT for aetiology: comparison with CMR

N = 71
LVEF: 26%

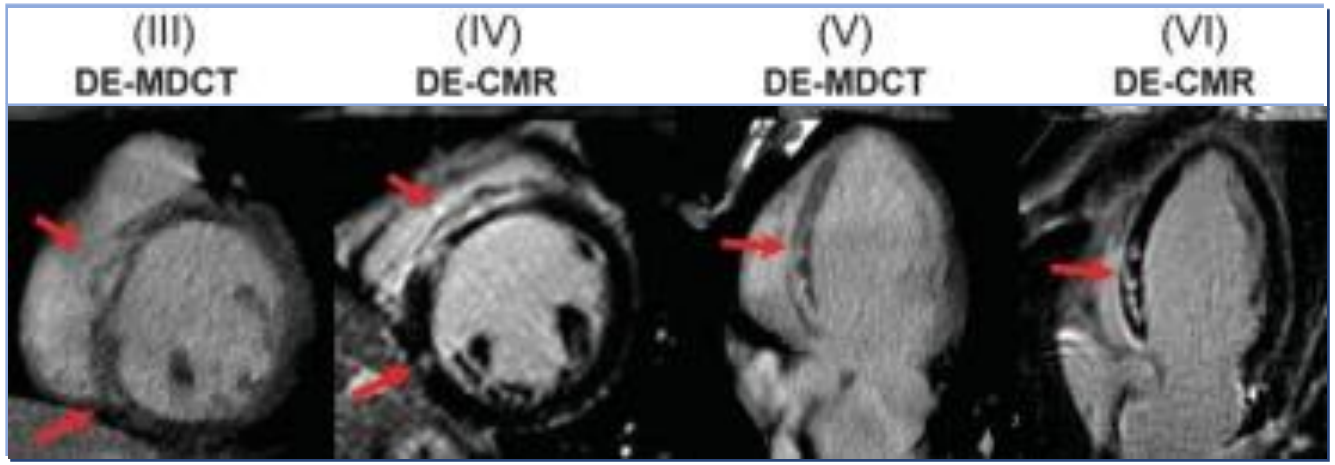
Coronary and LE-MDCT and LGE-CMR

CAD defined as transmural or subendocardial scars

Kappa: 0.89 (p<0.001)

Detection of CAD by MDCT:

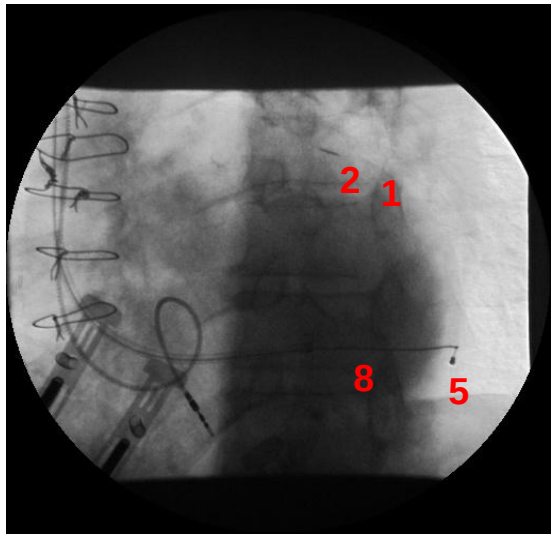
Sensitivity:	97%
Specificity:	94%
Accuracy:	87%

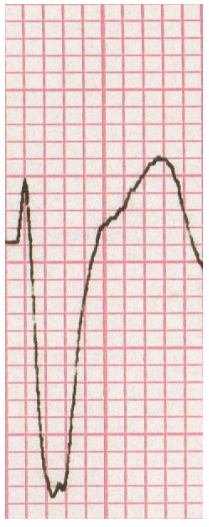
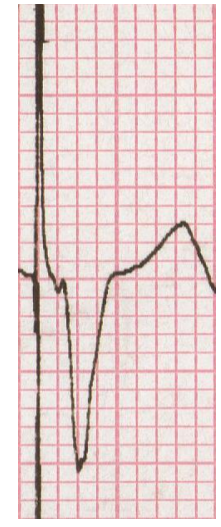
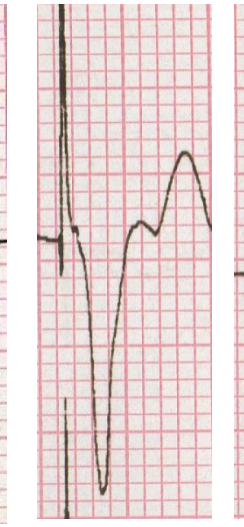
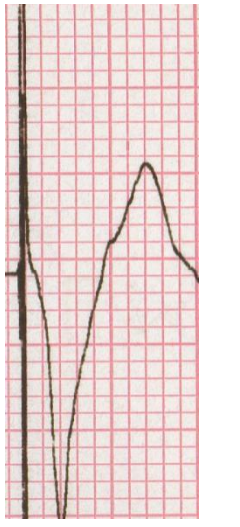


De Waroux, et al. Eur Heart J 2008;29:2544-51

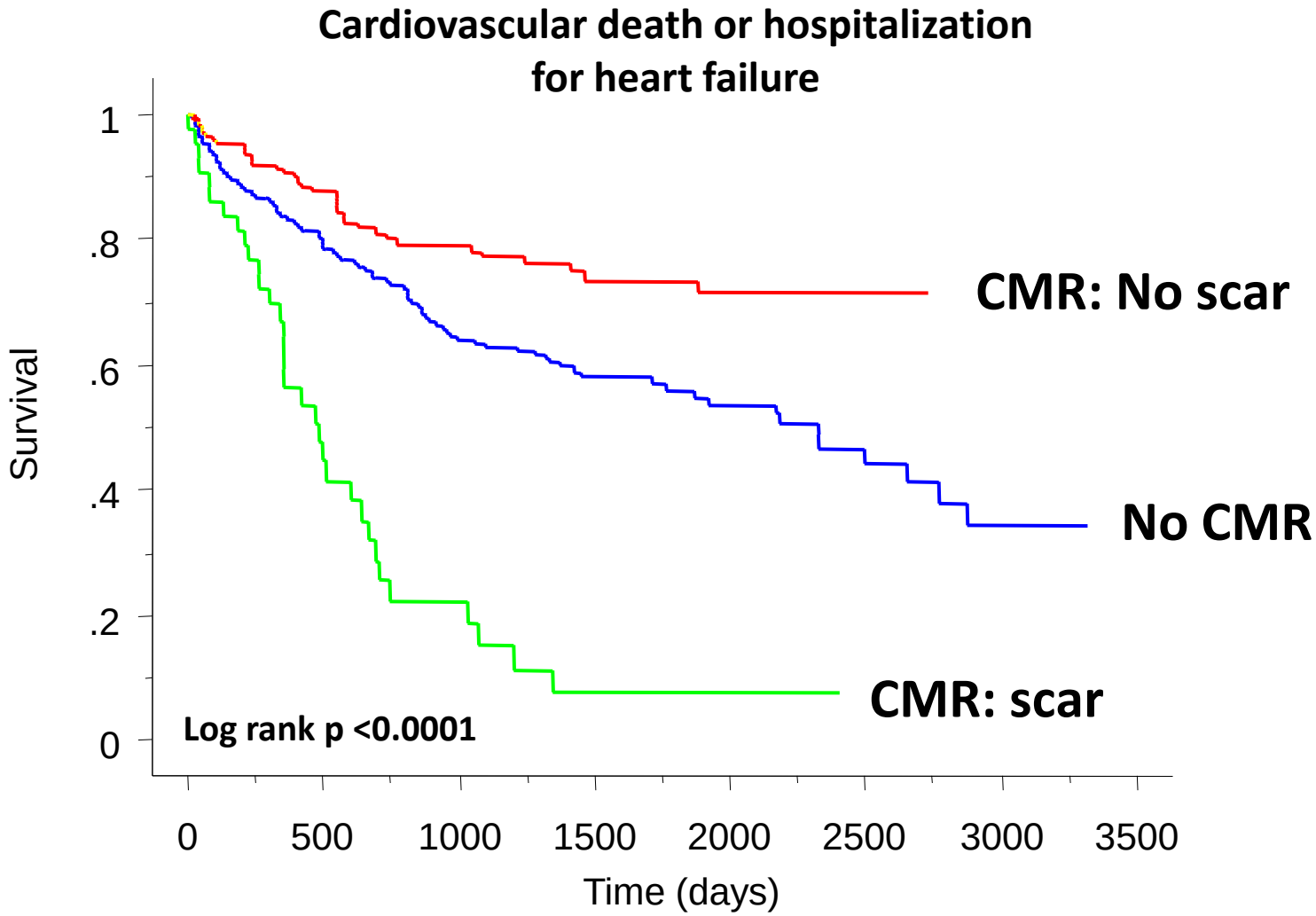
CMR

Scar and CRT



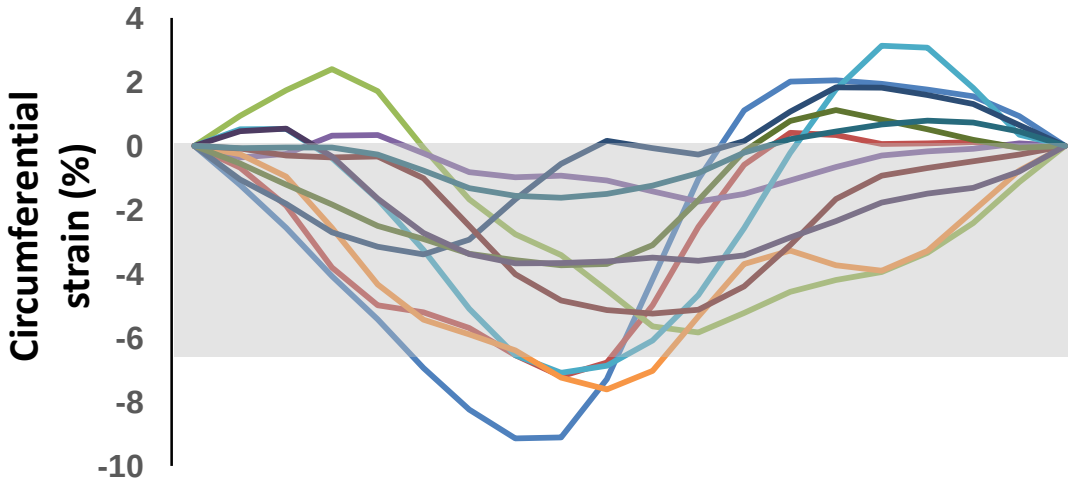
	Intrinsic	2	1	8	5
					
QRS (ms)	169	91	85	118	198
Threshold (V)		0.6	1.0	0.3	9.0
R wave (mV)		3.9	13.1	12.0	8.7

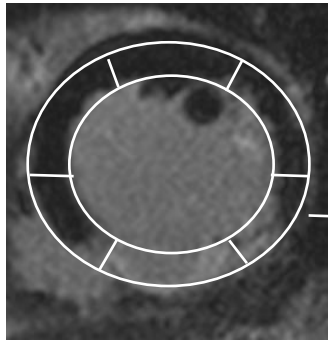
Role of CMR in LV lead deployment



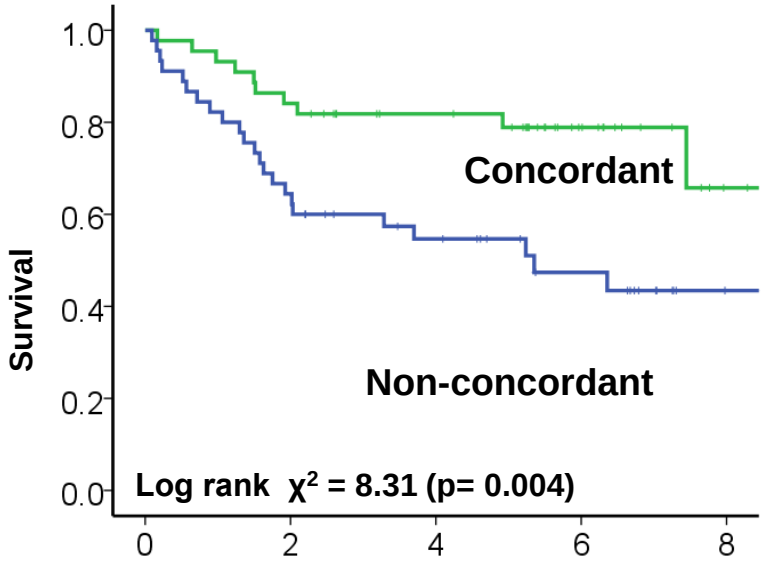
Leyva F et al. JCMR 2011

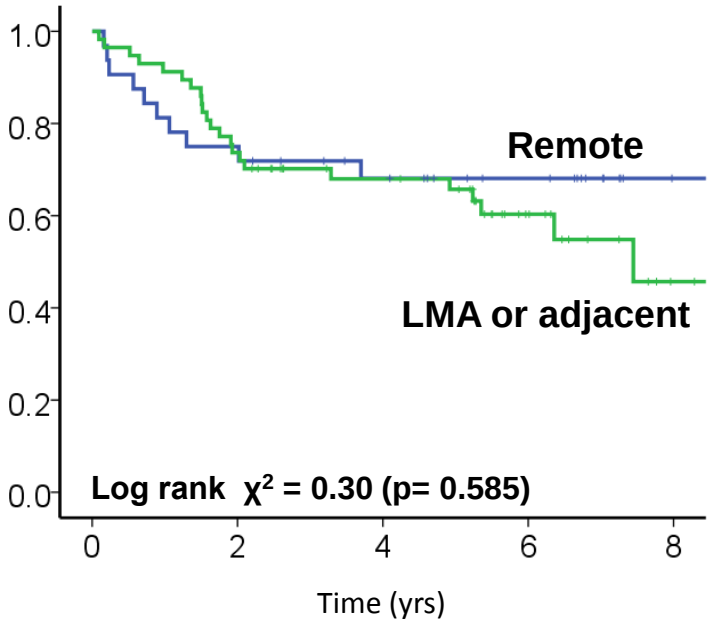
Feature tracking CMR: about late activation or scar?

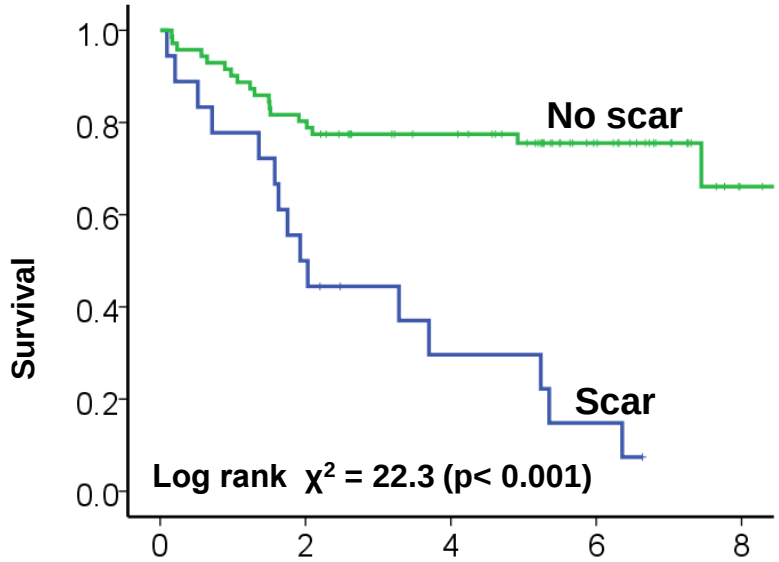




CARDIAC MORTALITY OR HF HOSPITALIZATIONS

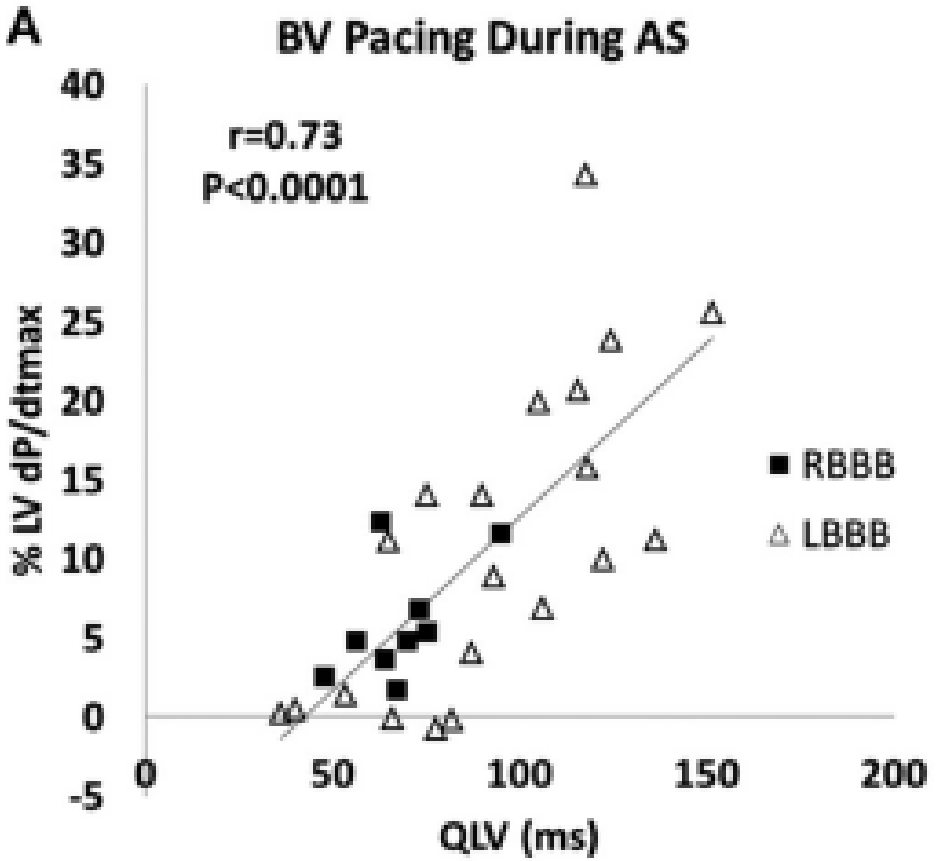






Taylor R, et al. HRJ 2015

The Effect of Left Ventricular Electrical Delay on the Acute Hemodynamic Response with Cardiac Resynchronization Therapy



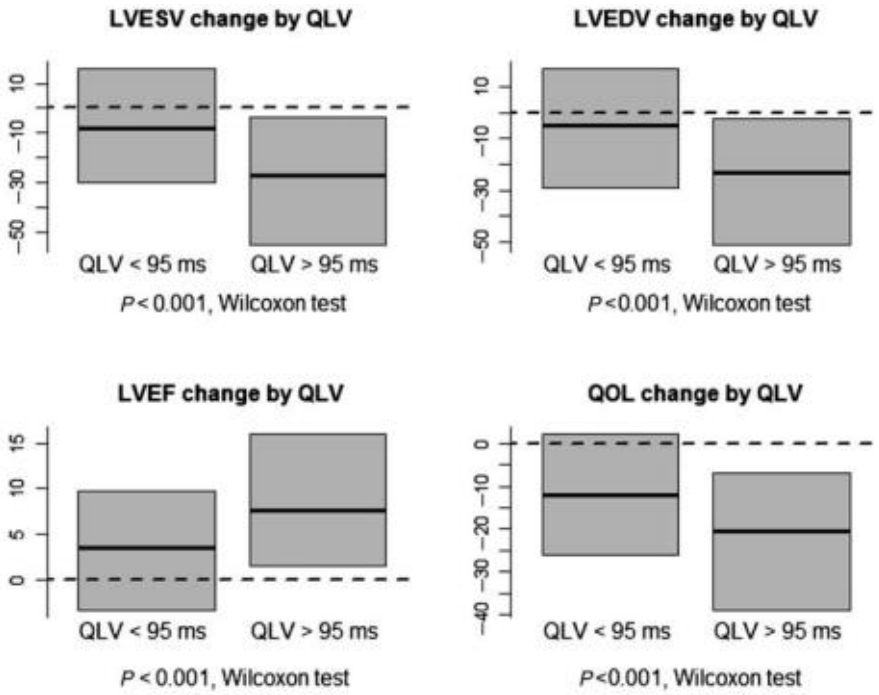
Clinical implications: …the QLV interval helps identify favorable LV pacing sites. Thus, it seems reasonable to consider measuring QLV at the time of LV lead implantation

But:

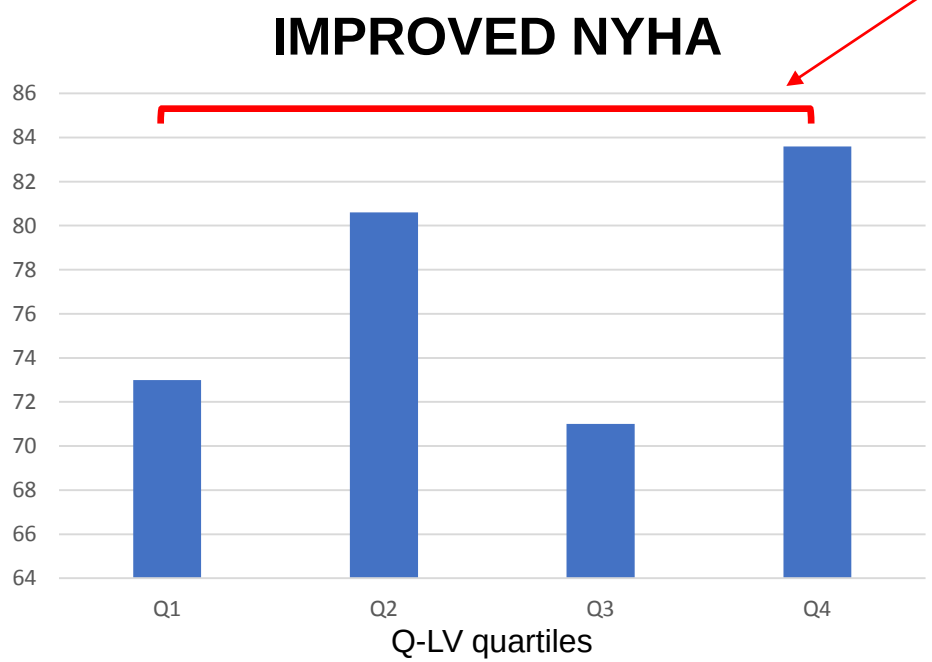
- Q-LV range is at group level, not at individual patient level
- Intention to treat has not been tested

Gold MR, et al. JCE 2014;25:624-630

Q-LV and LVRR



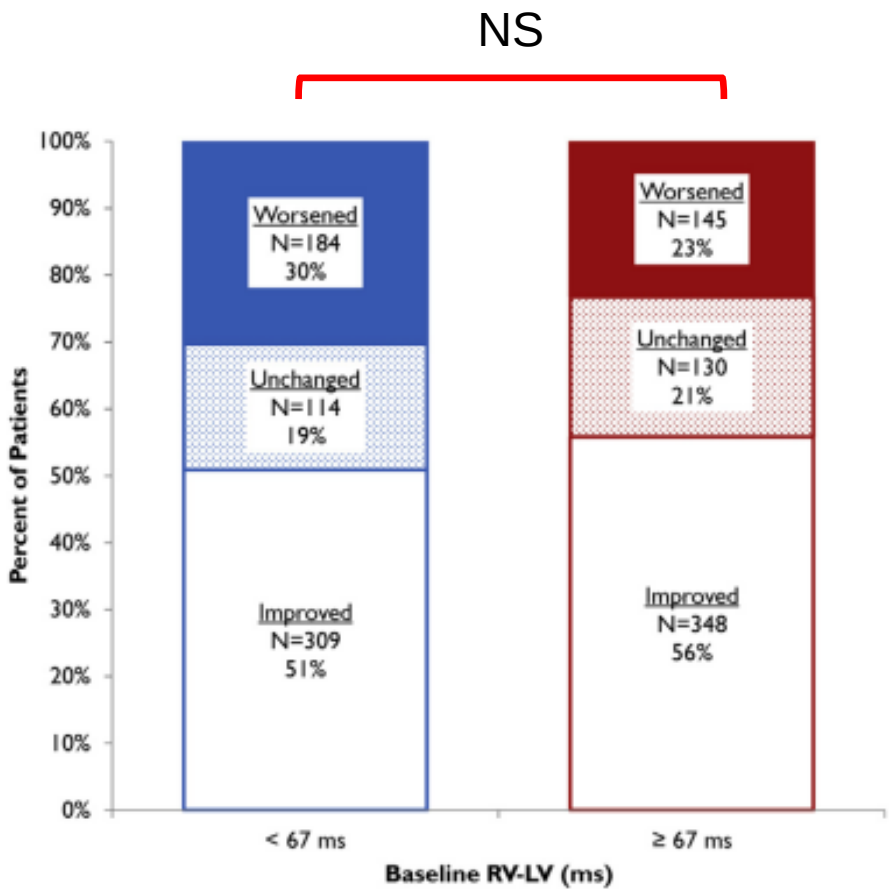
	QLV quartiles						
	Q1: 0–70 ms (%)	Q2: 70–95 ms (%)	Q3: 95–120 ms (%)	Q4: 120–195 ms (%)	Total (%)	Overall *P*-value	Q4 vs. Q1 *P*-value
Patients with HF events	15 (12.1)	7 (7.1)	7 (6.4)	6 (6.3)	35 (8.2)	0.37	0.17
NYHA							
Improved	89 (73.0)	79 (80.6)	76 (71.0)	77 (83.7)	321 (76.6)	0.04	0.04
No change	33 (27.1)	16 (16.3)	30 (28.0)	14 (15.2)	93 (22.2)		
Worsened	0 (0.0)	3 (3.1)	1 (0.9)	1 (1.1)	5 (1.2)		
Six minute walk delta	52 ± 118	68 ± 91	50 ± 104	70 ± 93	59 ± 103	0.36	0.13



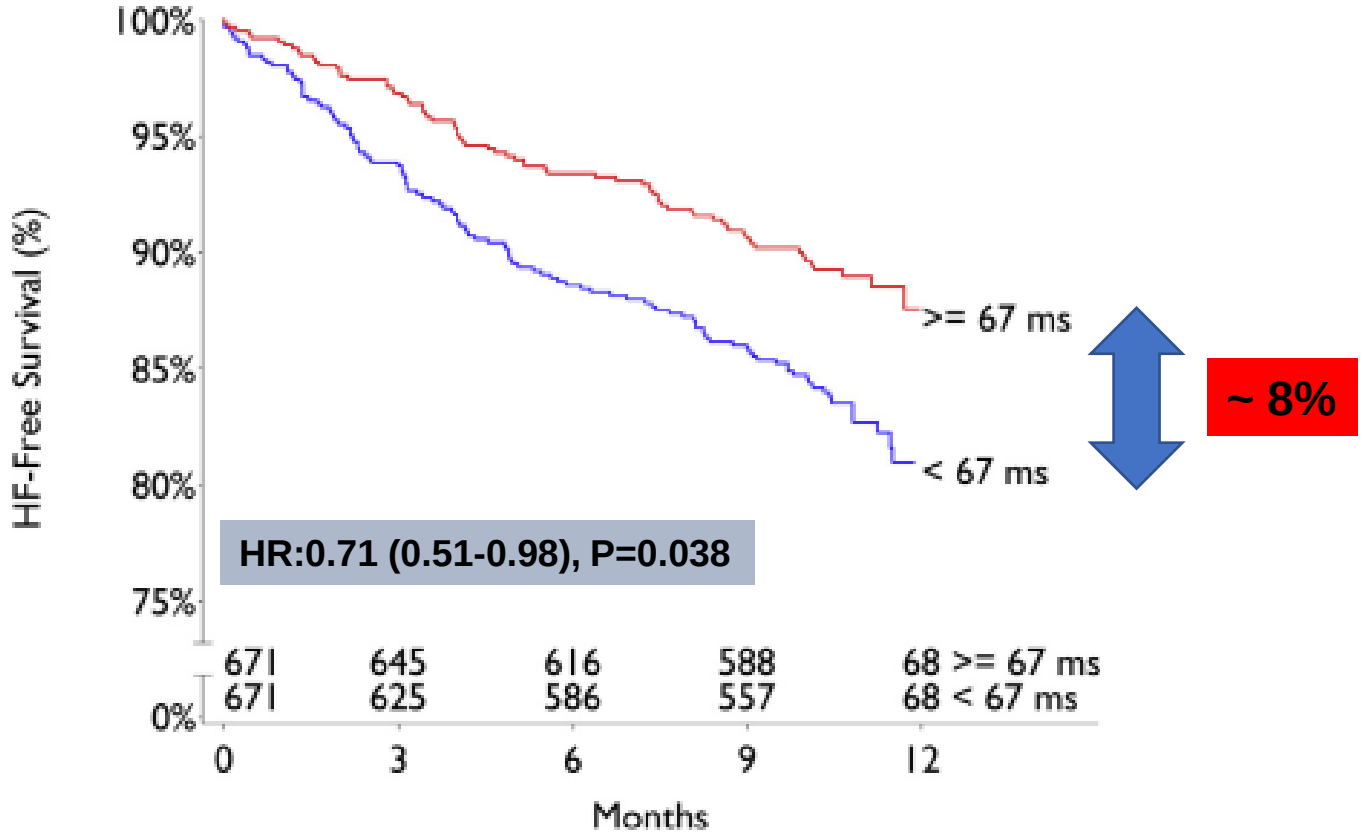
Gold MR, et al. Eur Heart J 2011;32:2516-2524

Interventricular delay and outcomes after CRT: PEGASUS study

COMPOSITE CLINICAL SCORE



HF-FREE SURVIVAL



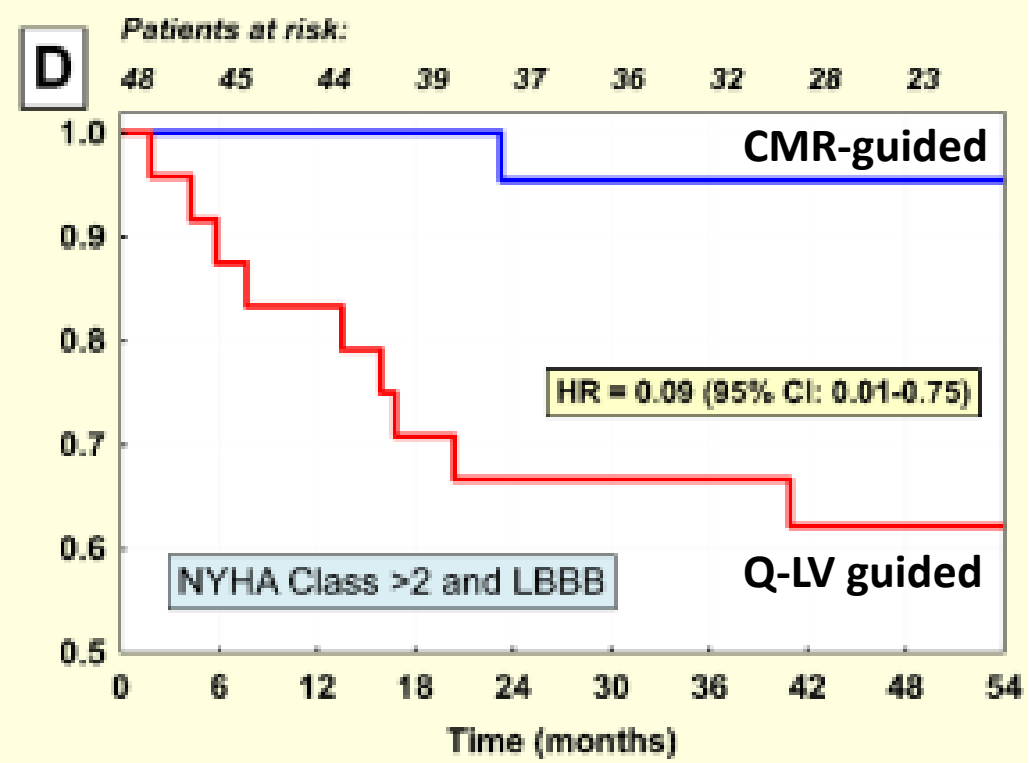
Maximising IV delay was not pre-specified: intention to treat not tested

Gold MR, et al. Heart Rhythm 2017;14:1748-1755

CMR vs Q-LV guided CRT: the CMR-CRT study

N=99 patients
Randomized to CMR or Q-LV guidance

CARDIOVASCULAR DEATH OR HF HOSPITALIZATION



Kočková R, et al. Int J Cardiol. 2018;270:325-330

Gold MR, et al. Heart Rhythm 2017;14:1748-1755

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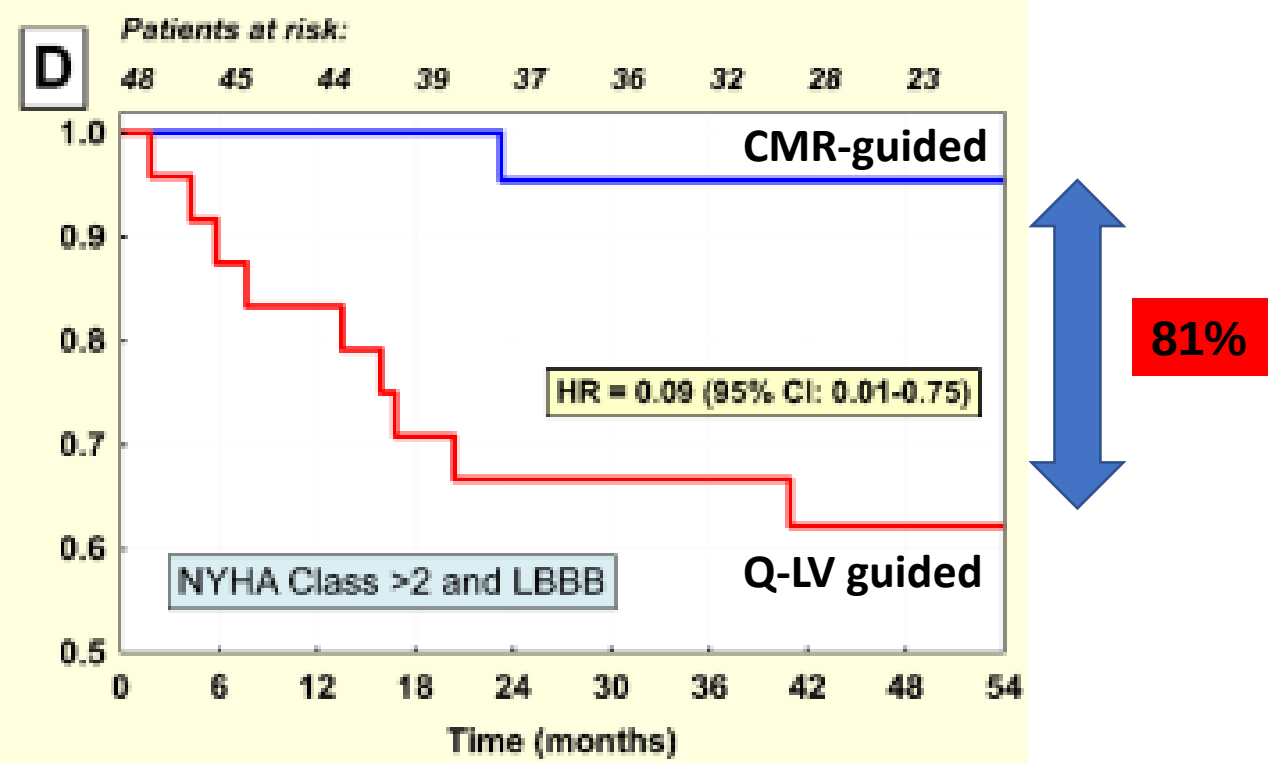

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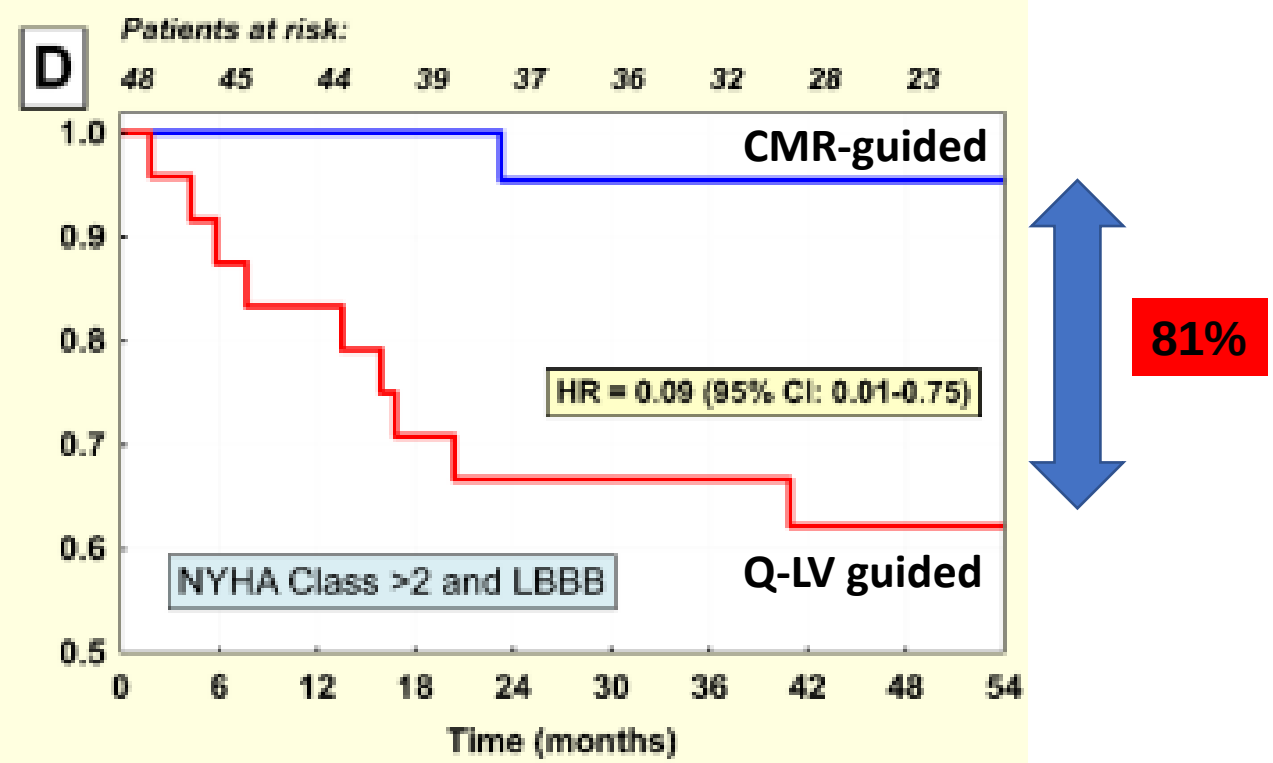
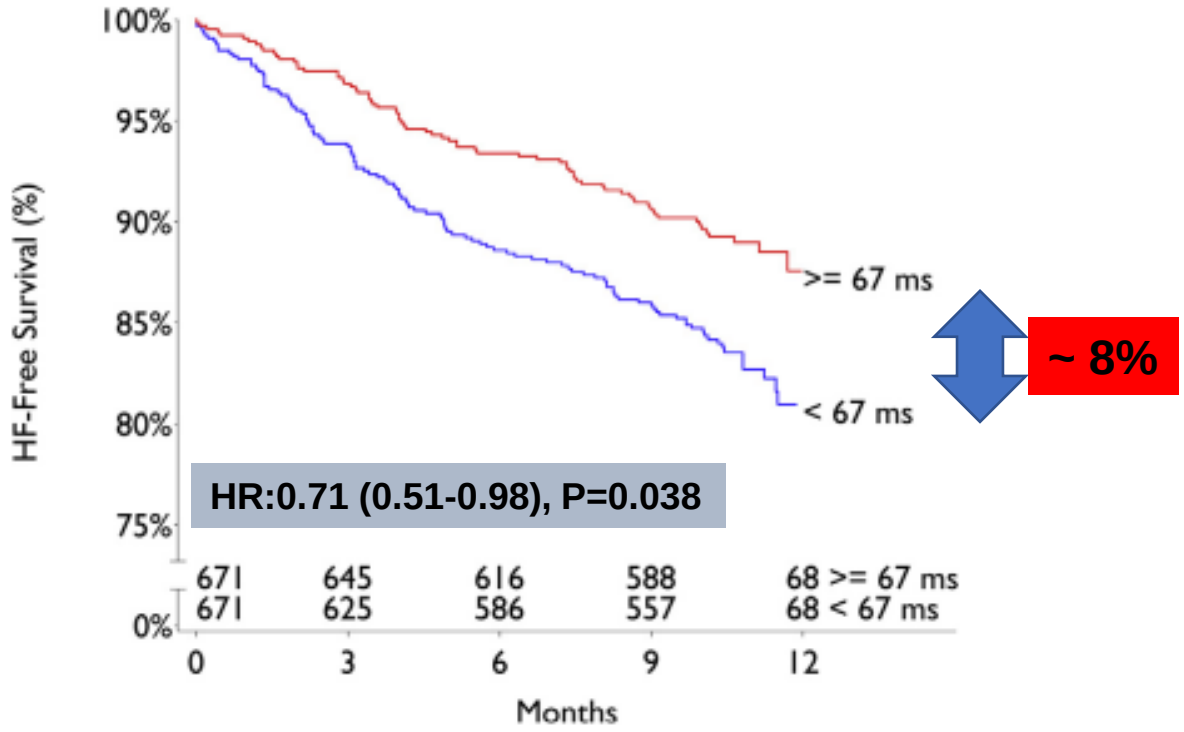
PEGASUS study

CARDIOVASCULAR DEATH OR HF HOSPITALIZATION



81%

HF-FREE SURVIVAL



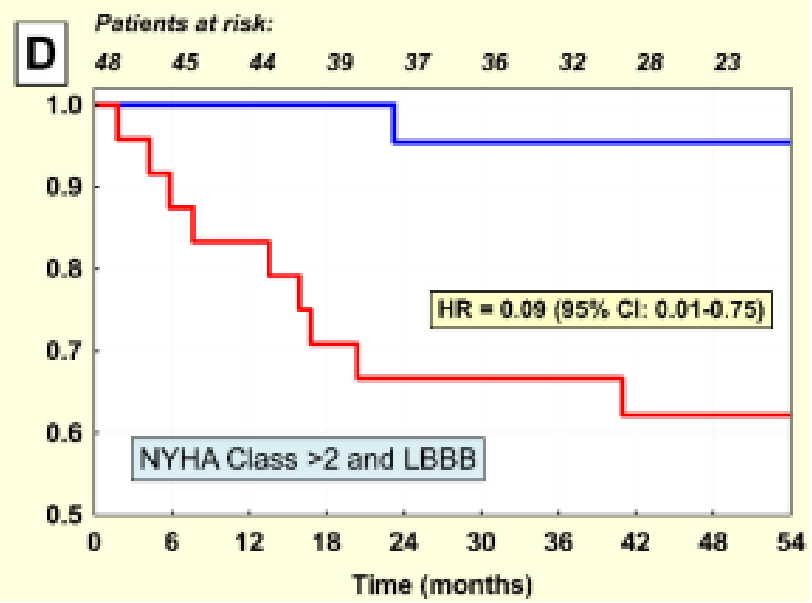
~ 8%

Kočková R, et al. Int J Cardiol. 2018;270:325-330

Gold MR, et al. Heart Rhythm 2017;14:1748-1755

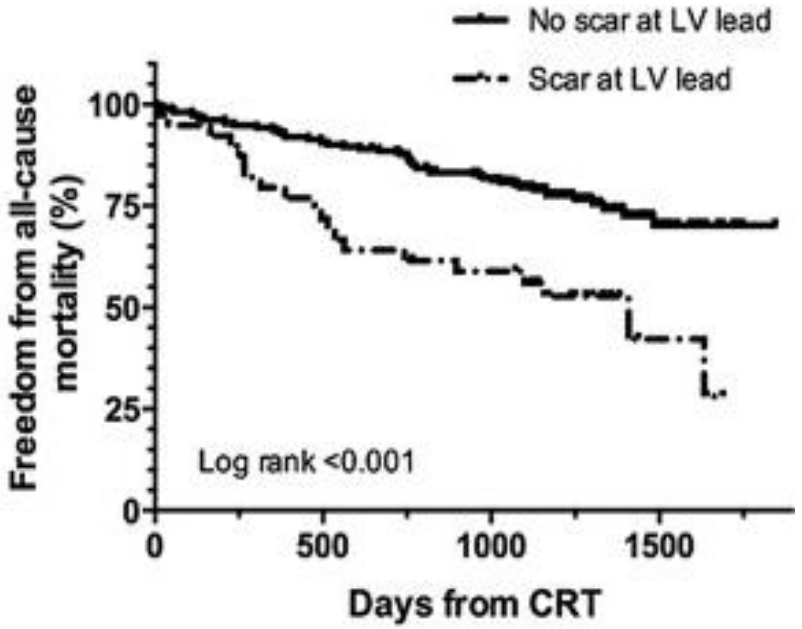
Scar vs no-scar on LV lead tip

CMR-CRT



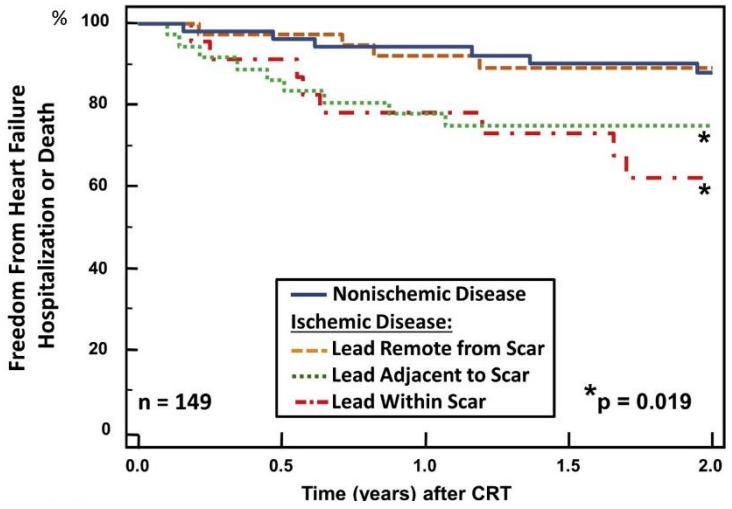
Kočková R, et al. Int J Cardiol. 2018;270:325-330

TARGET: STE



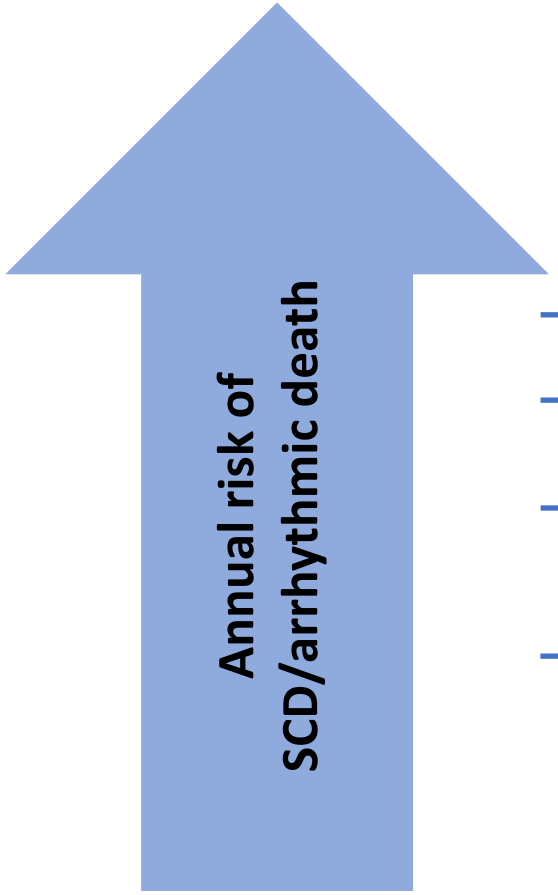
Kidd AC, et al. JACC HF2014;2:205-212

STARTER: STE



Sade LE, et al. JASE 2014;27:648-65

CRT-D vs CRT-P: what is 'high risk' of SCD?



2.6% **MADIT**

2.2% **SCD-HeFT**

2.1% **MADIT-II**

1.2% **HCM: ICD indicated**
(2014 ESC)

0 %

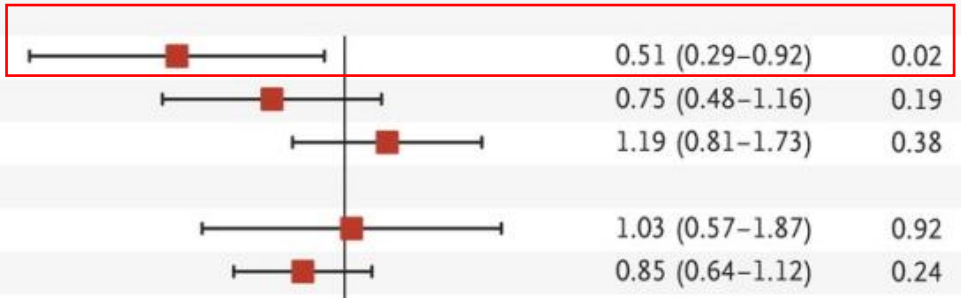
Figures for ICD trials relate to control group

DANISH

Outcome	ICD Group† (N=556)	Control Group† (N=560)	Hazard Ratio (95% CI)	P Value
	no. of patients/total no. (%)			
Death from any cause	120 (21.6)	131 (23.4)	0.87 (0.68–1.12)	0.28
Cardiovascular death	77 (13.8)	95 (17.0)	0.77 (0.57–1.05)	0.10
Sudden cardiac death	24 (4.3)	46 (8.2)	0.50 (0.31–0.82)	0.005
Other cardiovascular death	53 (9.5)	49 (8.8)	1.03 (0.70–1.52)	0.89

50%

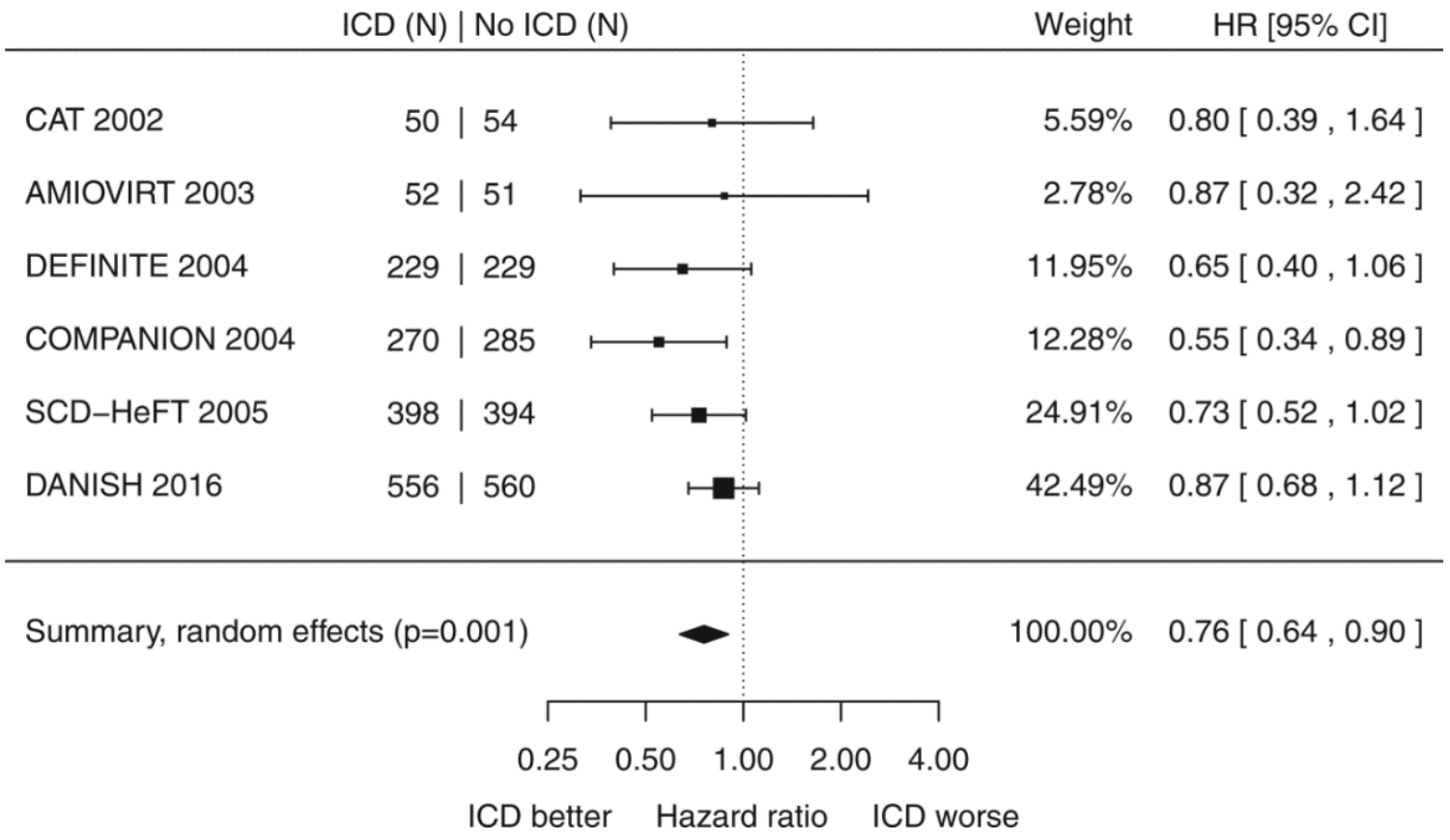
Subgroup	ICD Group	Control Group	Hazard Ratio (95% CI)	P Value	P Value for Interaction
	no. of events/total no.				
Age					0.009
<59 yr	17/167	34/181	0.51 (0.29–0.92)	0.02	
≥59 to <68 yr	36/173	50/202	0.75 (0.48–1.16)	0.19	
≥68 yr	67/216	47/177	1.19 (0.81–1.73)	0.38	
Sex					0.66
Female	22/151	23/156	1.03 (0.57–1.87)	0.92	
Male	98/405	108/404	0.85 (0.64–1.12)	0.24	



Køber L, et al. N Engl J Med 2016

Metanalysis including DANISH

N=3128 patients without IHD

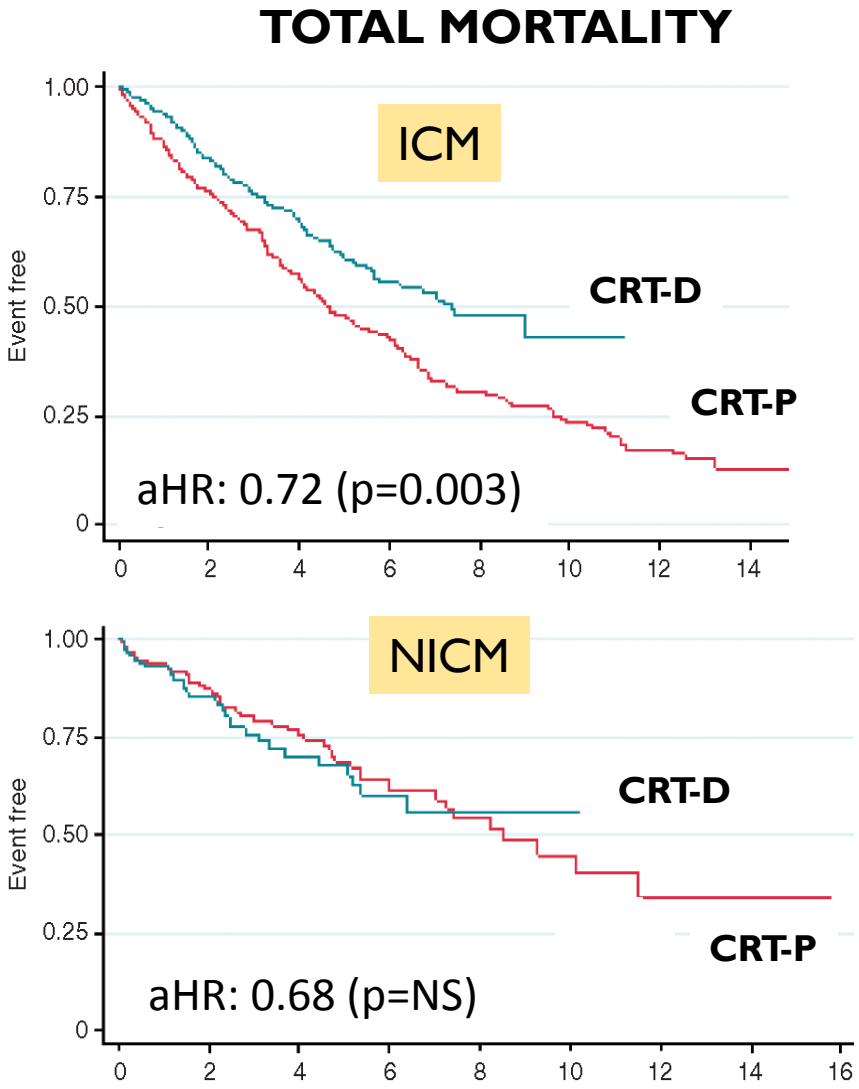


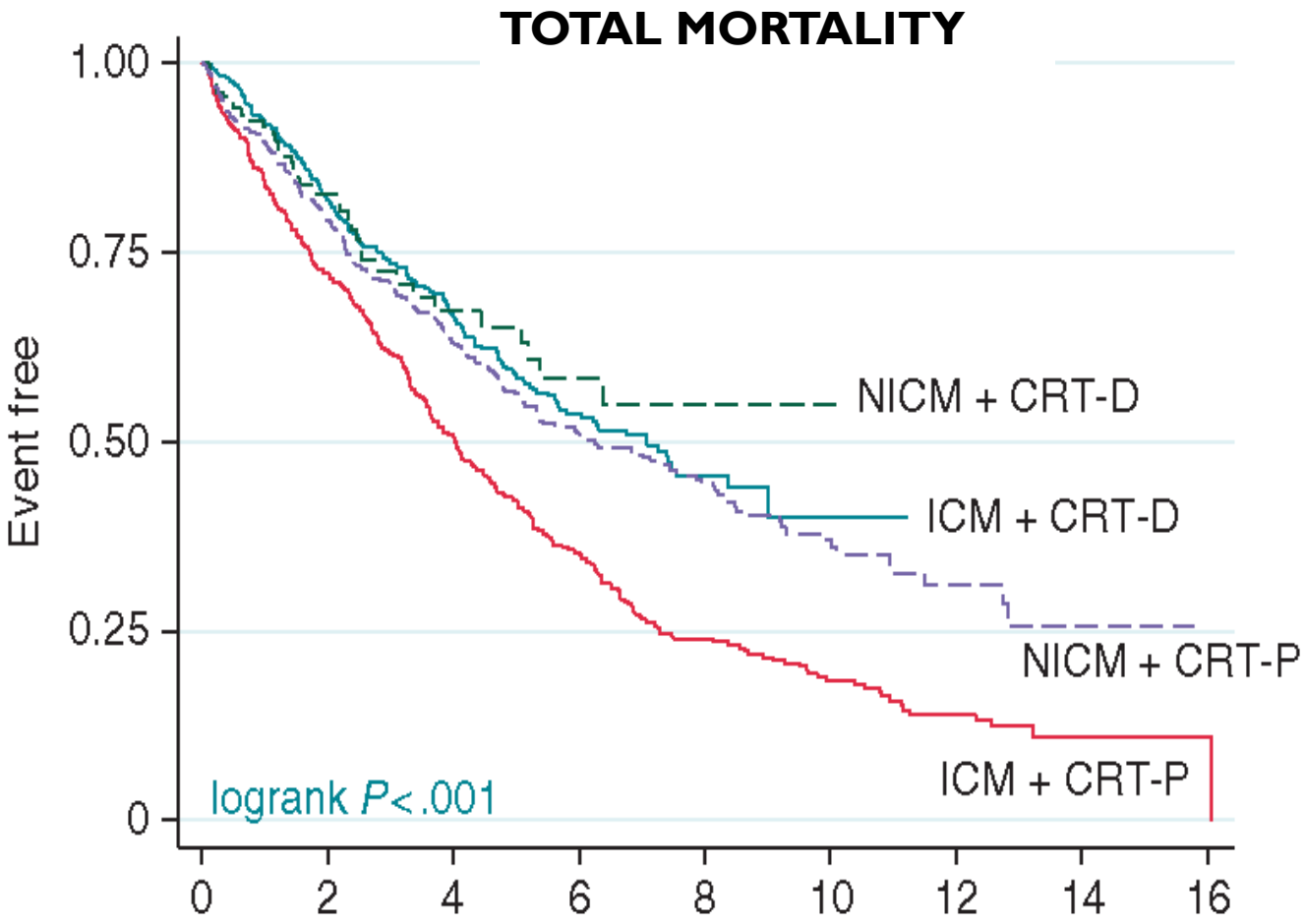
ICD therapy reduced mortality by 24%

Shun-Shin MJ, et al. Eur Heart J 2017;38:1738-1746

CRT-D vs CRT-D in the UK

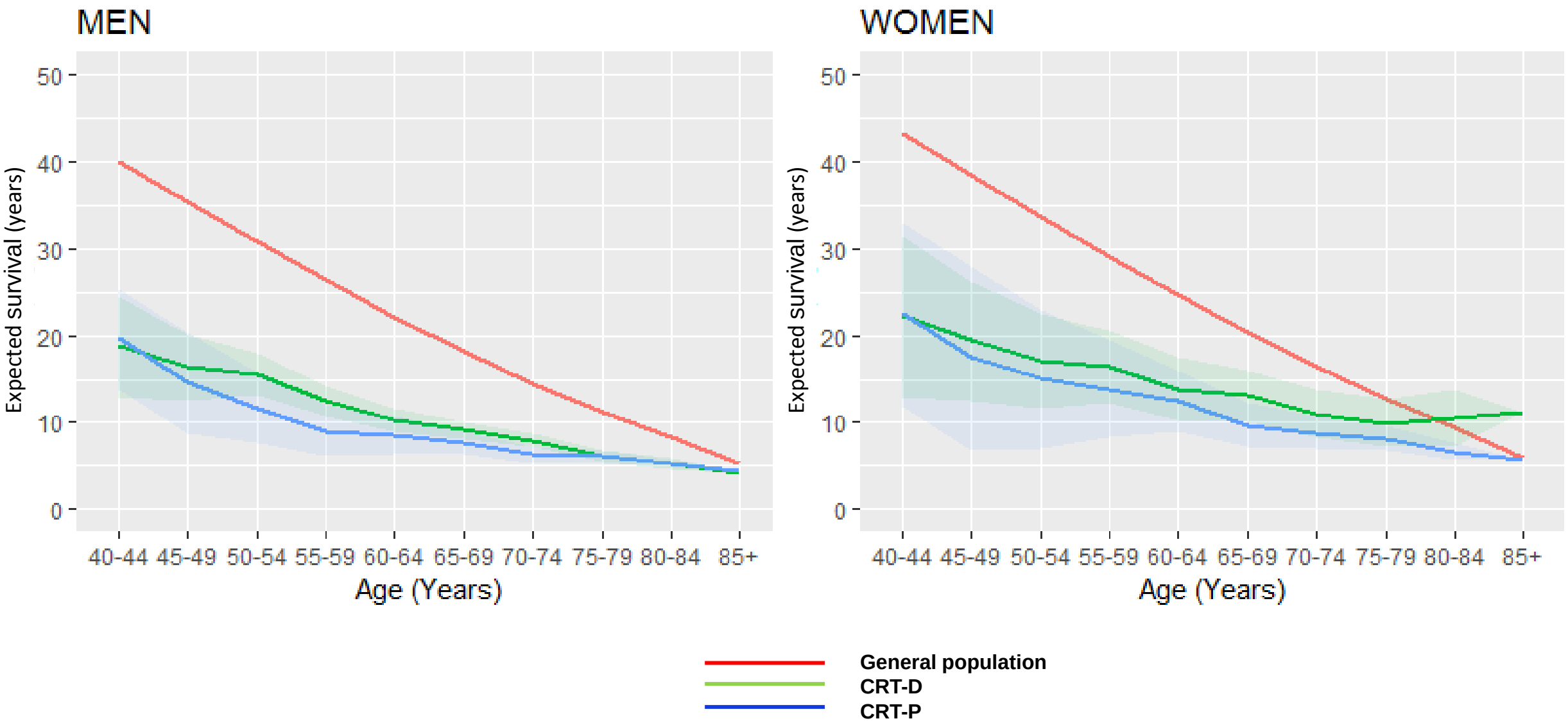
Single-centre: CRT-D=551, CRT-P=999





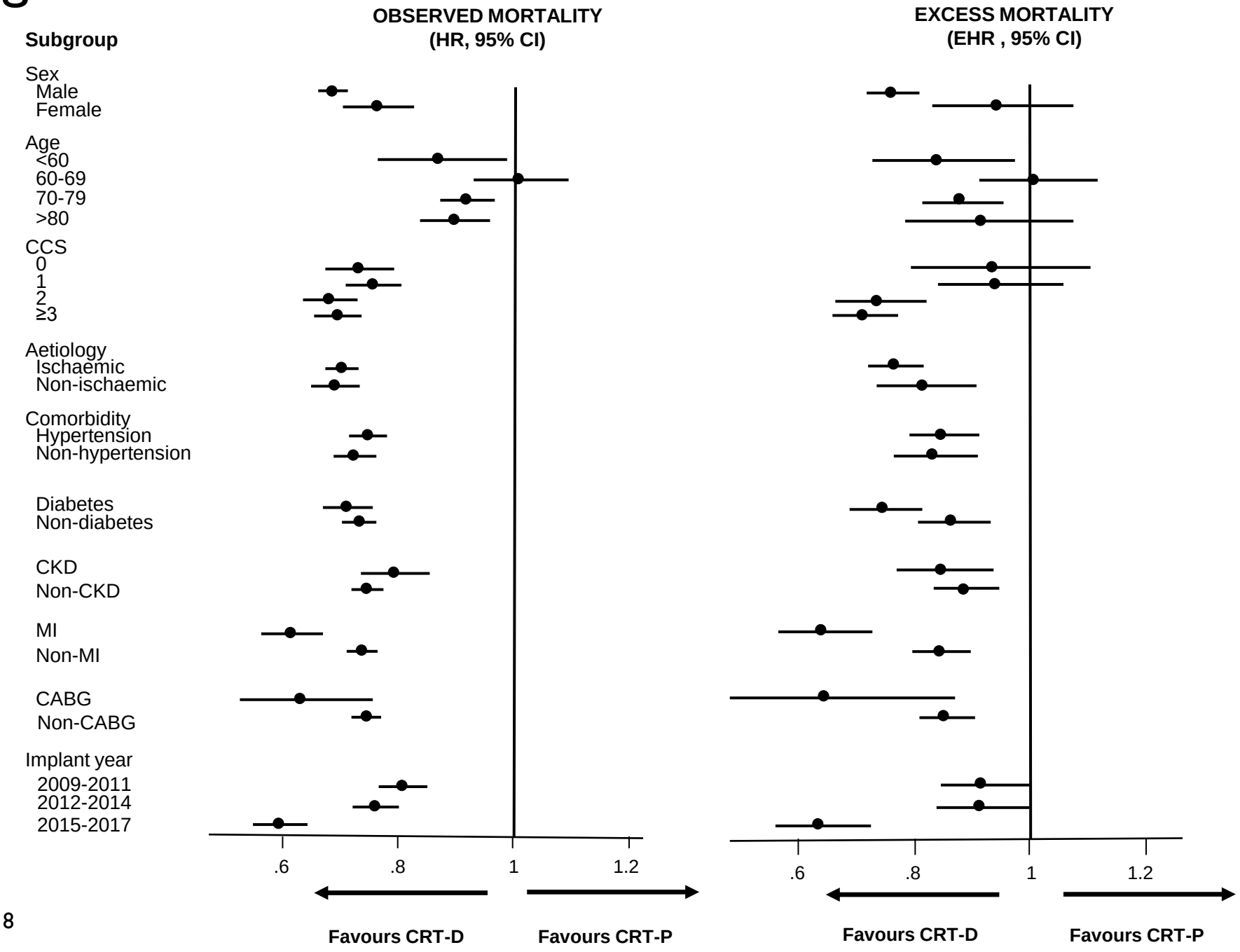
Leyva F, et al. EP Europace 2018:20:1804–1812

CRT in England: 2009-2017



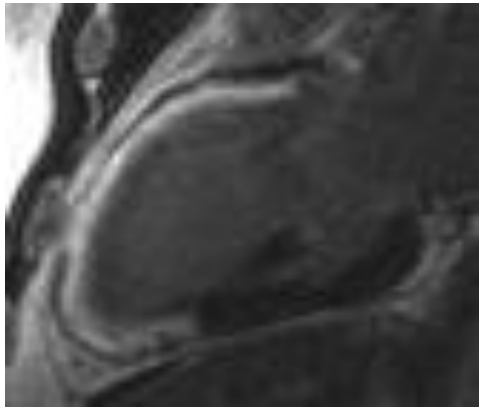
Leyva F, et al. Europace 2018

CRT in England: 2009-2017

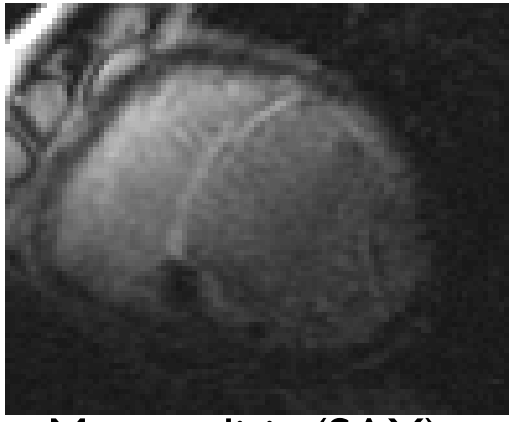


Leyva F, et al. Europace 2018

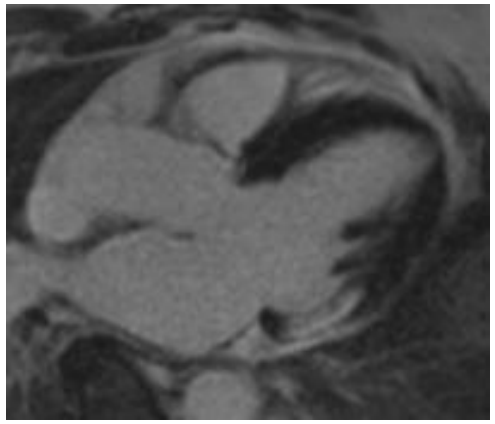
LAD infarct



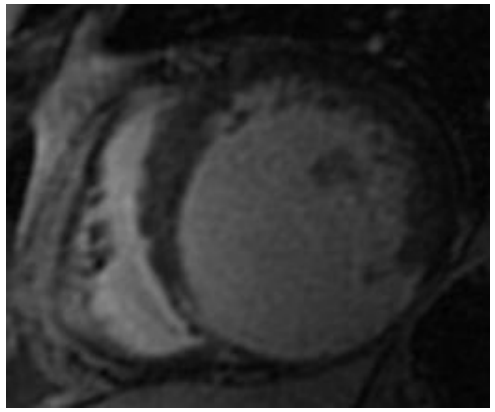
LAD and Cx infarct



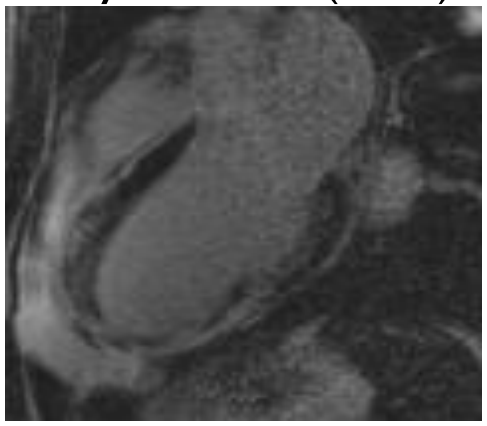
Cx infarct



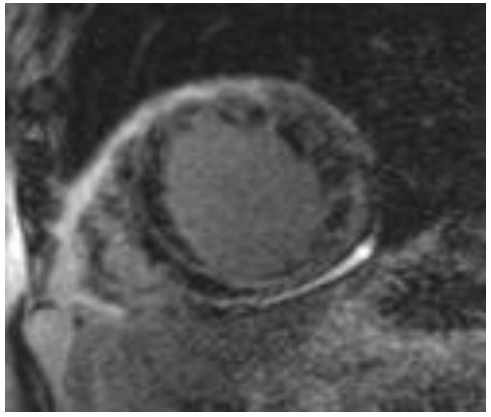
RCA infarct



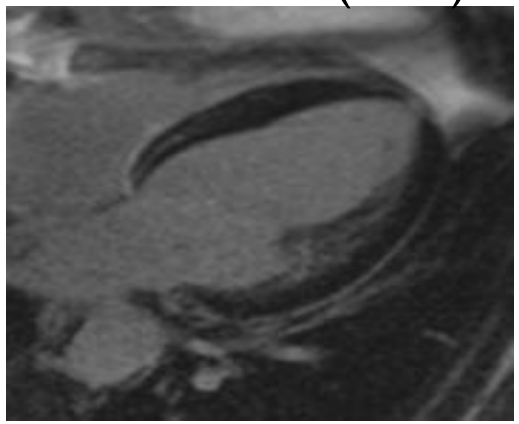
Myocarditis (LAX)



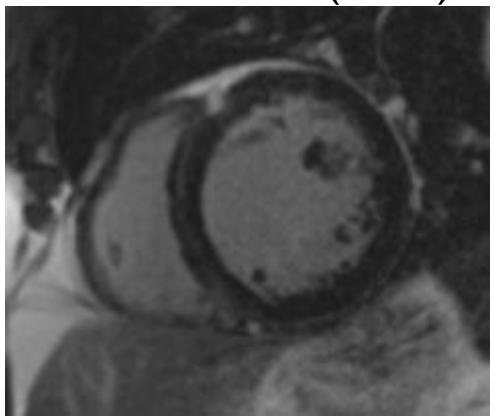
Myocarditis (SAX)



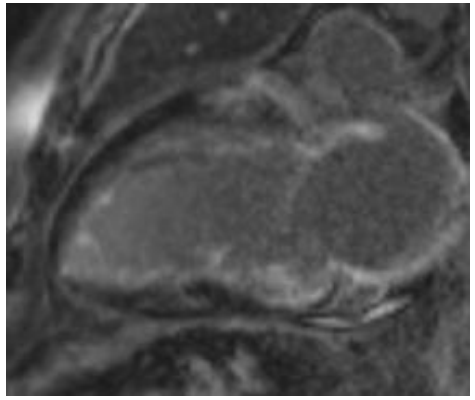
DCM+MWF (LAX)



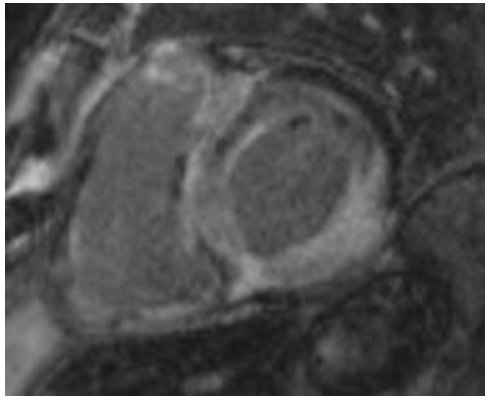
DCM+MWF (SAX)



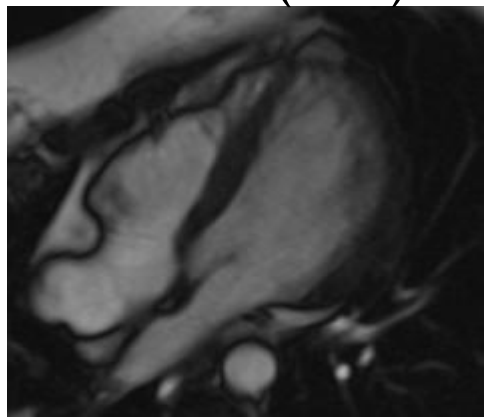
Amyloid (LAX)



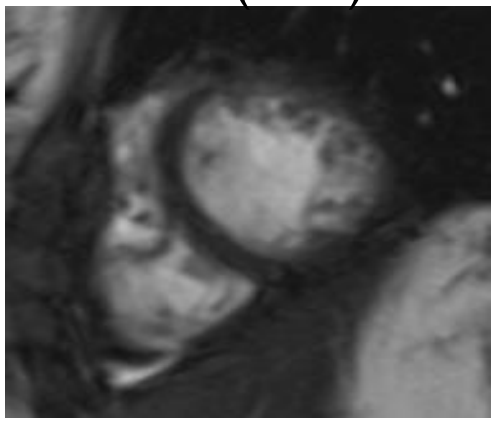
Amyloid (SAX)



LVNC? (LAX)



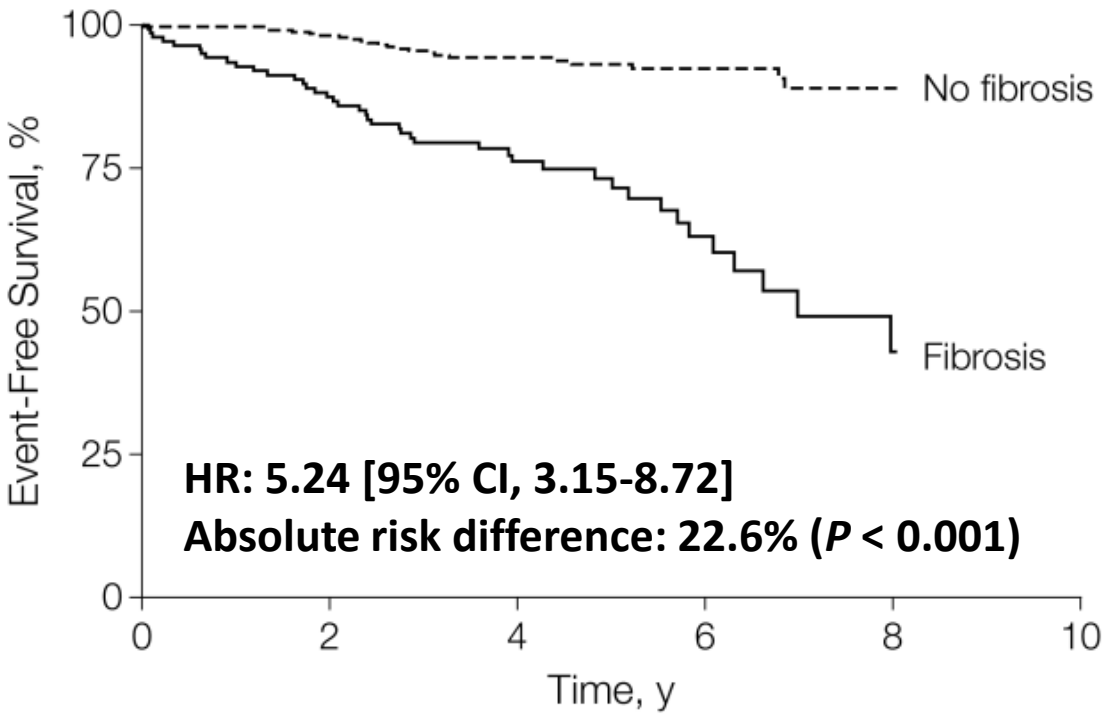
LVNC? (SAX)

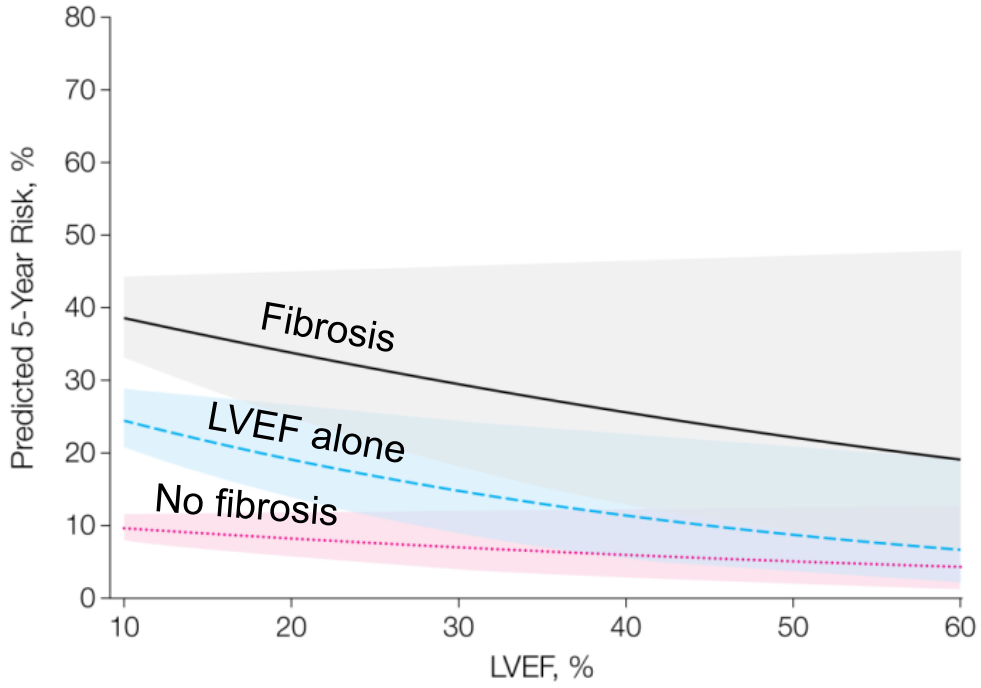


SCD in NICM: effect of scar

472 patients with NICM

SCD OR ABORTED SCD





Shaded areas represent 95% CIs.

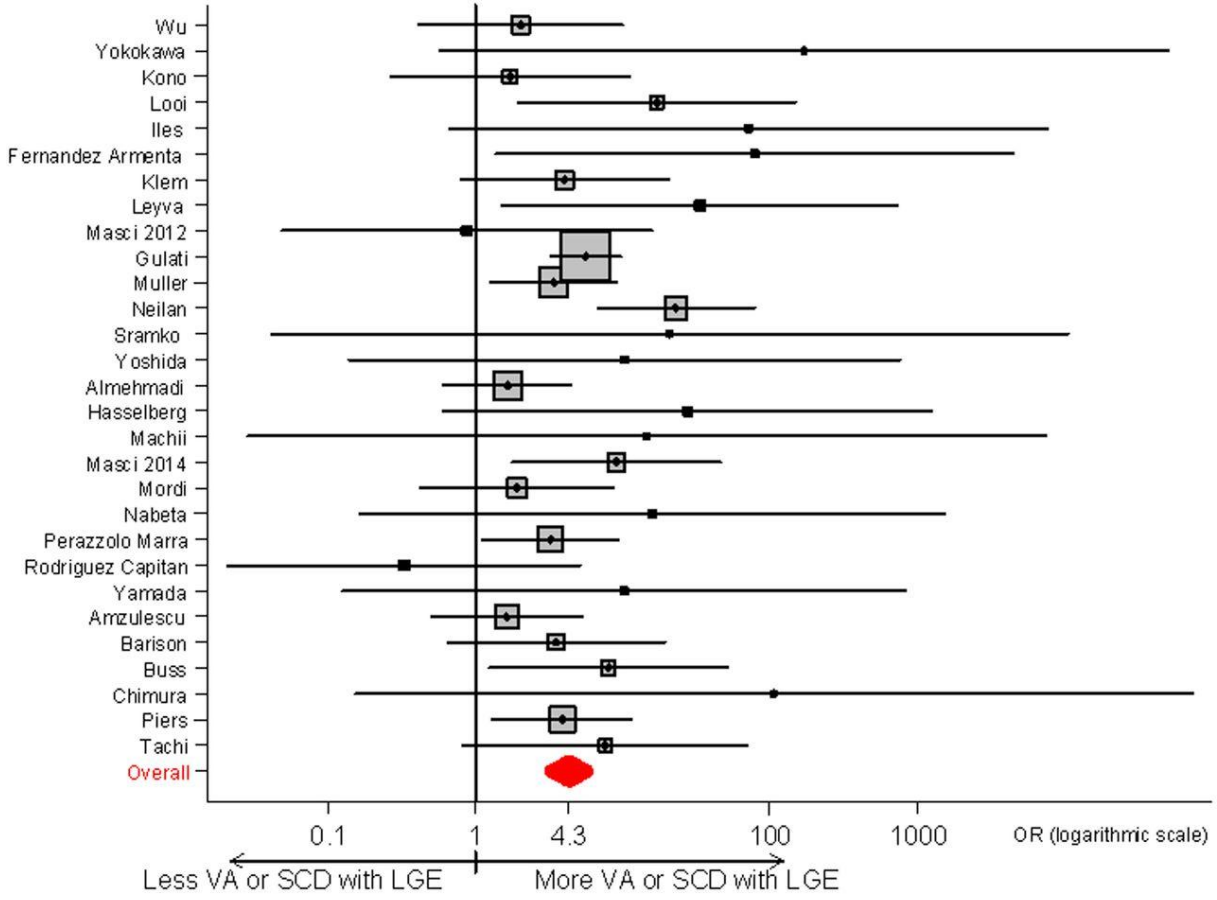
No cut-off of scar burden predicted outcome

Heuristic approach just as good

Gulati et al. JAMA. 2013;309(9):896-908

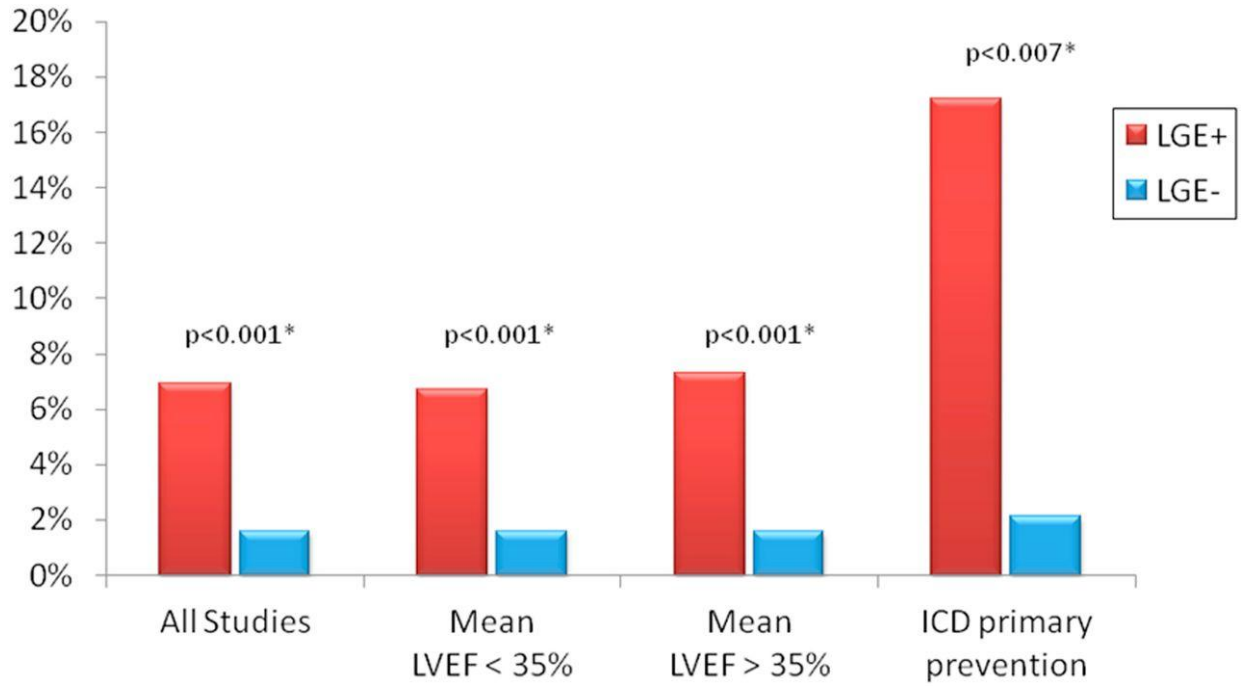
Scar and arrhythmias in NICM

SCD, sustained VT or appropriate ICD



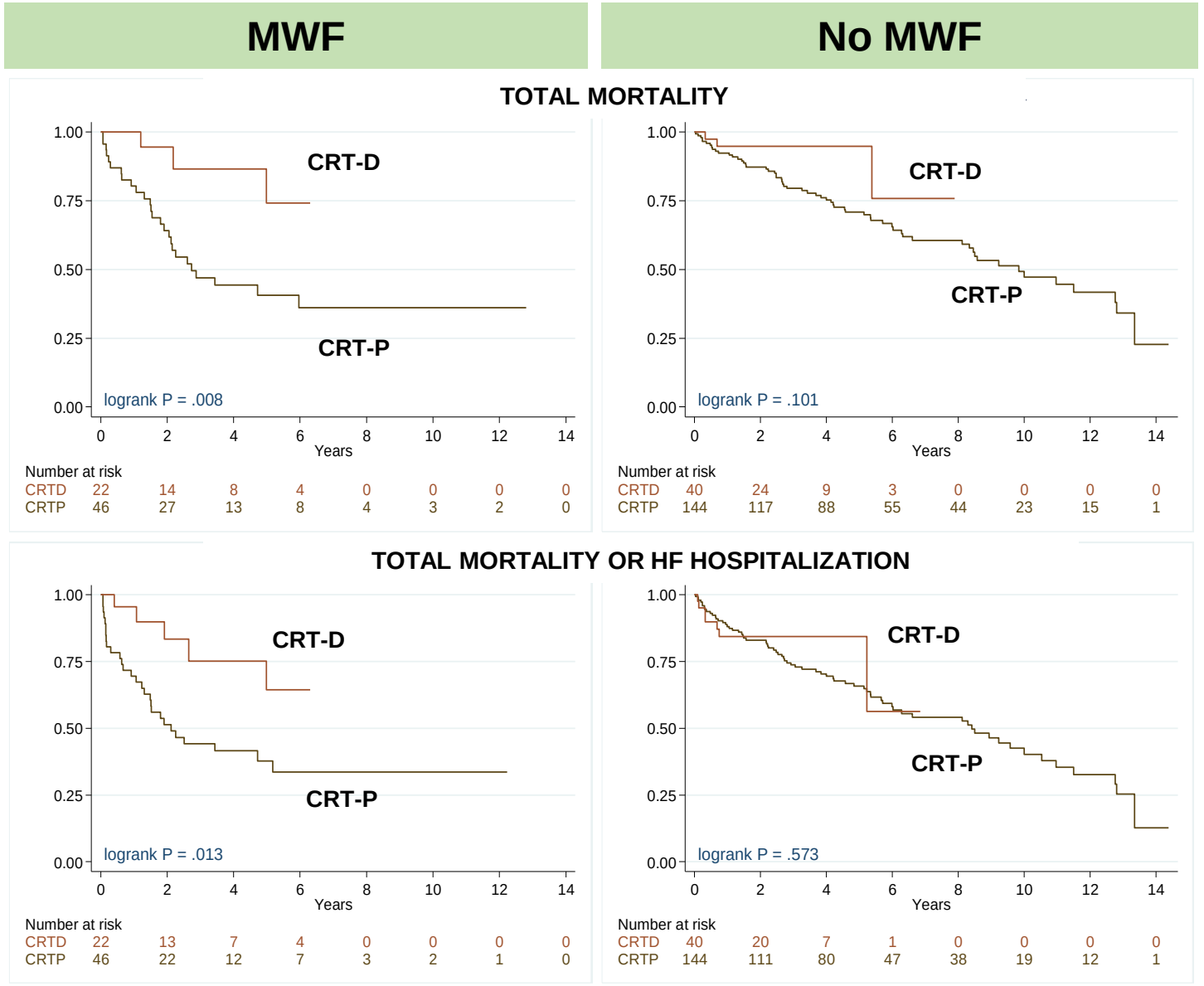
2,948 patients from 29 studies

Annual Rate of the Arrhythmic Endpoint



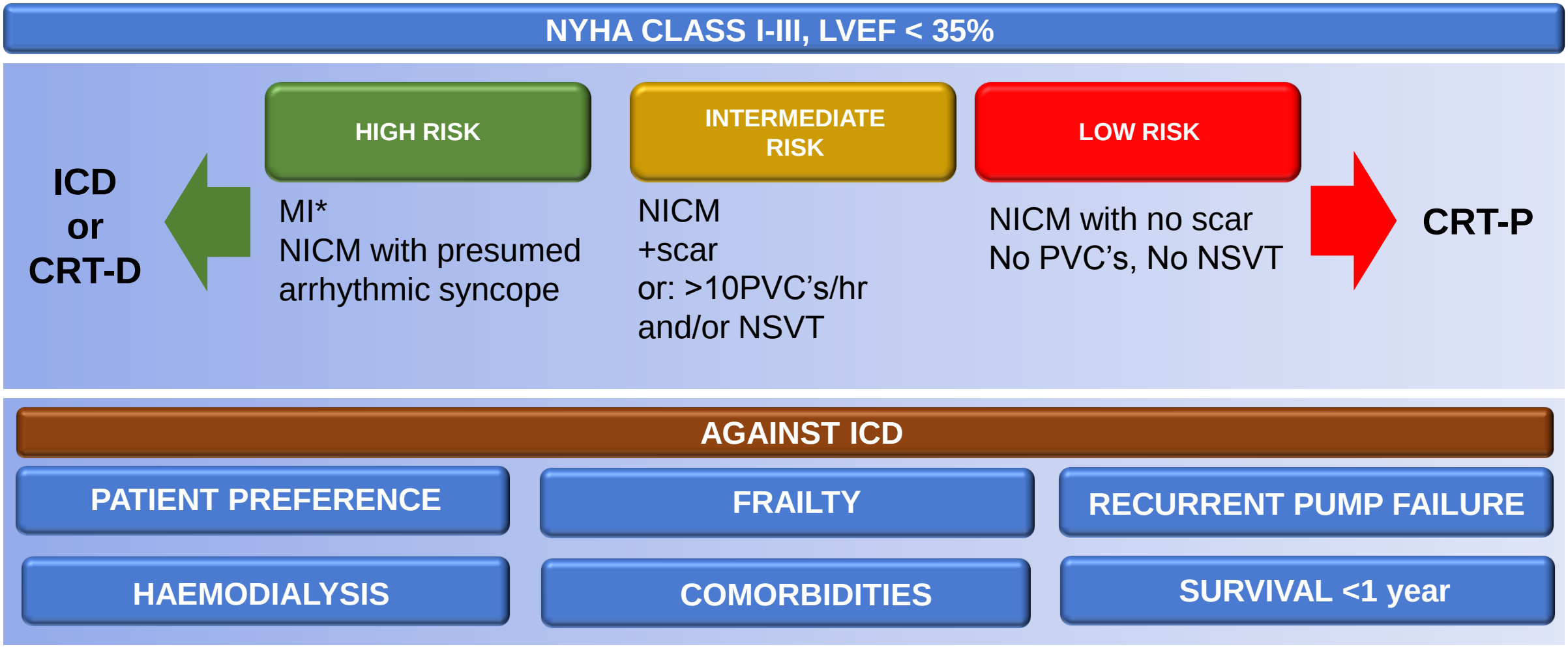
Di Marco A, et al. JACCHF 2017;5:28-38

CRT-D and CRT-P in NICM with scar



Leyva F, et al. JACC 2017

CRT-D or CRT-P: considerations



Conclusions

- No role for echo dyssynchrony in patient selection
- Questionable role for echo in optimization
- Late activation paradigm: sounds good but there is no firm clinical evidence
- Scar paradigm: also sounds good - treatment effect is higher
- Quadripolar leads change everything