KSC 2015

Reasonable Incomplete Revascularization versus Complete Revascularization in Multivessel PCI (STEMI)

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Multivessel PCI for STEMI

	COR	LOE
Ischemic symptoms <12 h	I	A
Ischemic symptoms <12 h and contraindications to fibrinolytic therapy irrespective of time delay from FMC	I	B
Cardiogenic shock or acute severe HF irrespective of time delay from MI onset	I	B
Evidence of ongoing ischemia 12 to 24 h after symptom onset	IIa	B
PCI of a noninfarct artery at the time of primary PCI in patients without hemodynamic compromise	III: Harm	B

CLASS I

1. **PCI is indicated in a noninfarct artery at a time separate from primary PCI in patients who have spontaneous symptoms of myocardial ischemia. (*Level of Evidence: C*)**

CLASS IIa

1. **PCI is reasonable in a noninfarct artery at a time separate from primary PCI in patients with intermediate- or high-risk findings on noninvasive testing (216,232,233). (*Level of Evidence: B*)**

2013 ACC/AHA STEMI guideline

Primary PCI should be limited to the culprit vessel with the exception of cardiogenic shock and persistent ischaemia after PCI of the supposed culprit lesion.	IIa	B

2012 ESC STEMI guideline

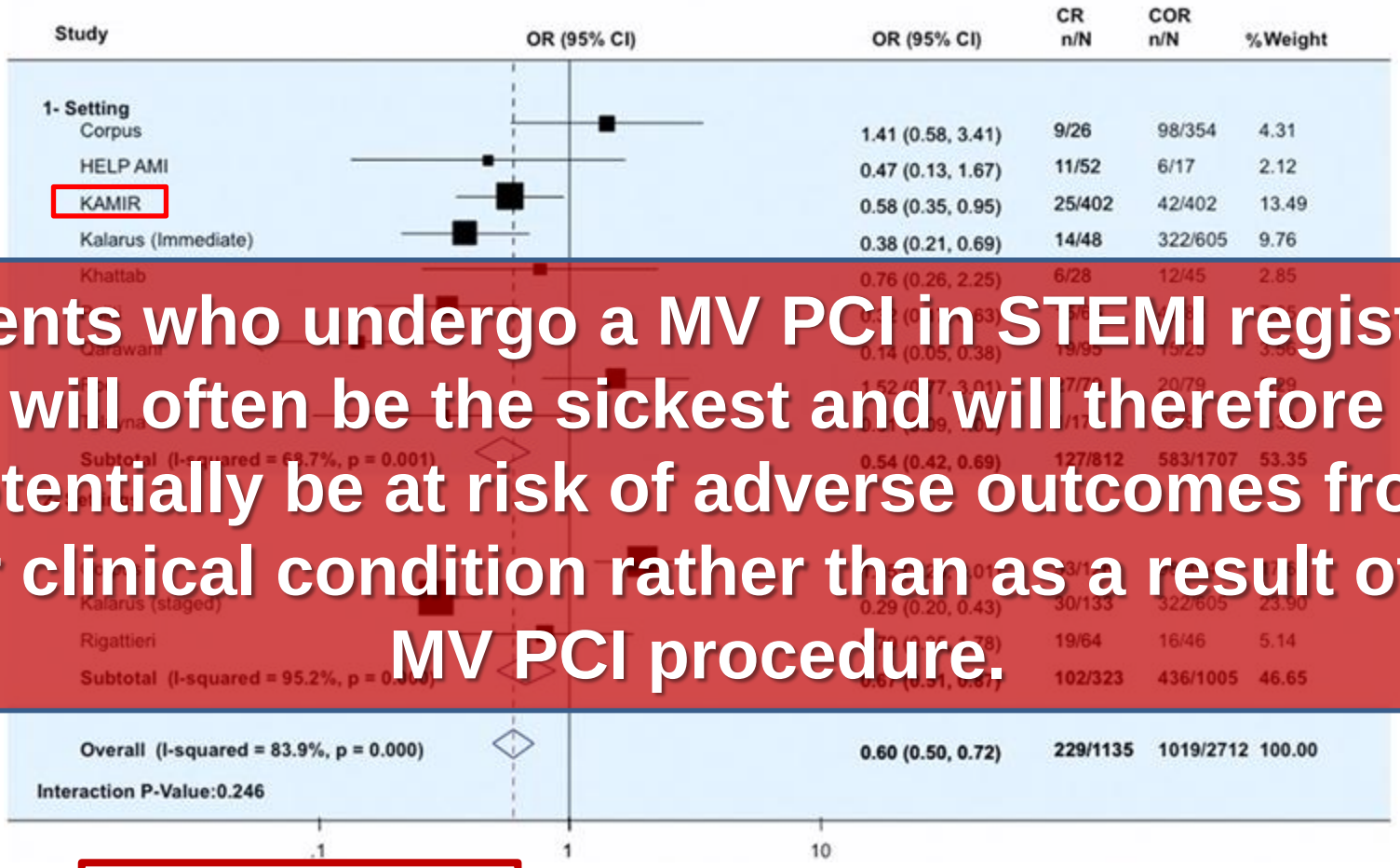
Incomplete Revascularization (IR)

- **Commonly defined as any non-revascularized vessel with >1.5 mm diameter and 50% to 100% stenosis**
- **Other registry studies have used a more stringent stenosis requirement of >70% severity**
- **Overall incidence: 50~70%**
- **More frequent in PCI patients (60%) than CABG populations (33%)**

SYNTAX Investigators. N Engl J Med 2009;360:9612-

Complete Revascularization (CR) vs. IR

Risks of long-term MACE



Patients who undergo a MV PCI in STEMI registries will often be the sickest and will therefore potentially be at risk of adverse outcomes from their clinical condition rather than as a result of the MV PCI procedure.

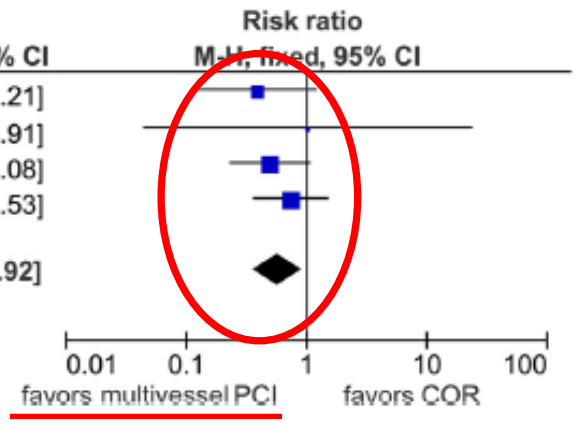
Bangalore S and The KAMIR Investigators. Am J Cardiol 2011;107:1300-10

CR vs. IR

Study or subgroup	multivessel PCI events	Total	COR events	Total	Weight	Risk ratio M-H, fixed, 95% CI
Culprit	4	150	10	146	23.7%	0.39 [0.12, 1.21]
HELP AMI	1	52	0	17	1.7%	1.02 [0.04, 23.91]
Politi	10	130	13	84	36.9%	0.50 [0.23, 1.08]
PRAMI	12	234	16	231	37.6%	0.74 [0.36, 1.53]
Total (95% CI)		**566**		**478**	**100.0%**	**0.57 [0.36, 0.92]**
Total events	27		39			

Heterogeneity: chi square = 1.18, df = 3 (p = 0.76); I^2 = 0%

Test for overall effect: Z = 2.32 (p = 0.02)

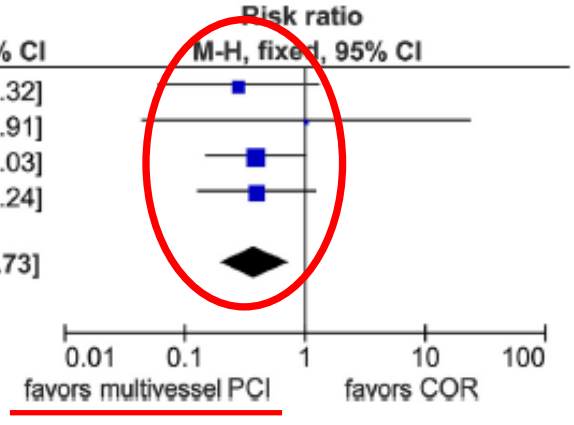


All-cause death

Study or subgroup	multivessel PCI events	Total	COR events	Total	Weight	Risk ratio M-H, fixed, 95% CI
Culprit	2	150	7	146	23.6%	0.28 [0.06, 1.32]
HELP AMI	1	52	0	17	2.5%	1.02 [0.04, 23.91]
Politi	6	130	10	84	40.4%	0.39 [0.15, 1.03]
PRAMI	4	234	10	231	33.5%	0.39 [0.13, 1.24]
Total (95% CI)		**566**		**478**	**100.0%**	**0.38 [0.20, 0.73]**
Total events	13		27			

Heterogeneity: chi square = 0.54, df = 3 (p = 0.91); I^2 = 0%

Test for overall effect: Z = 2.91 (p = 0.004)

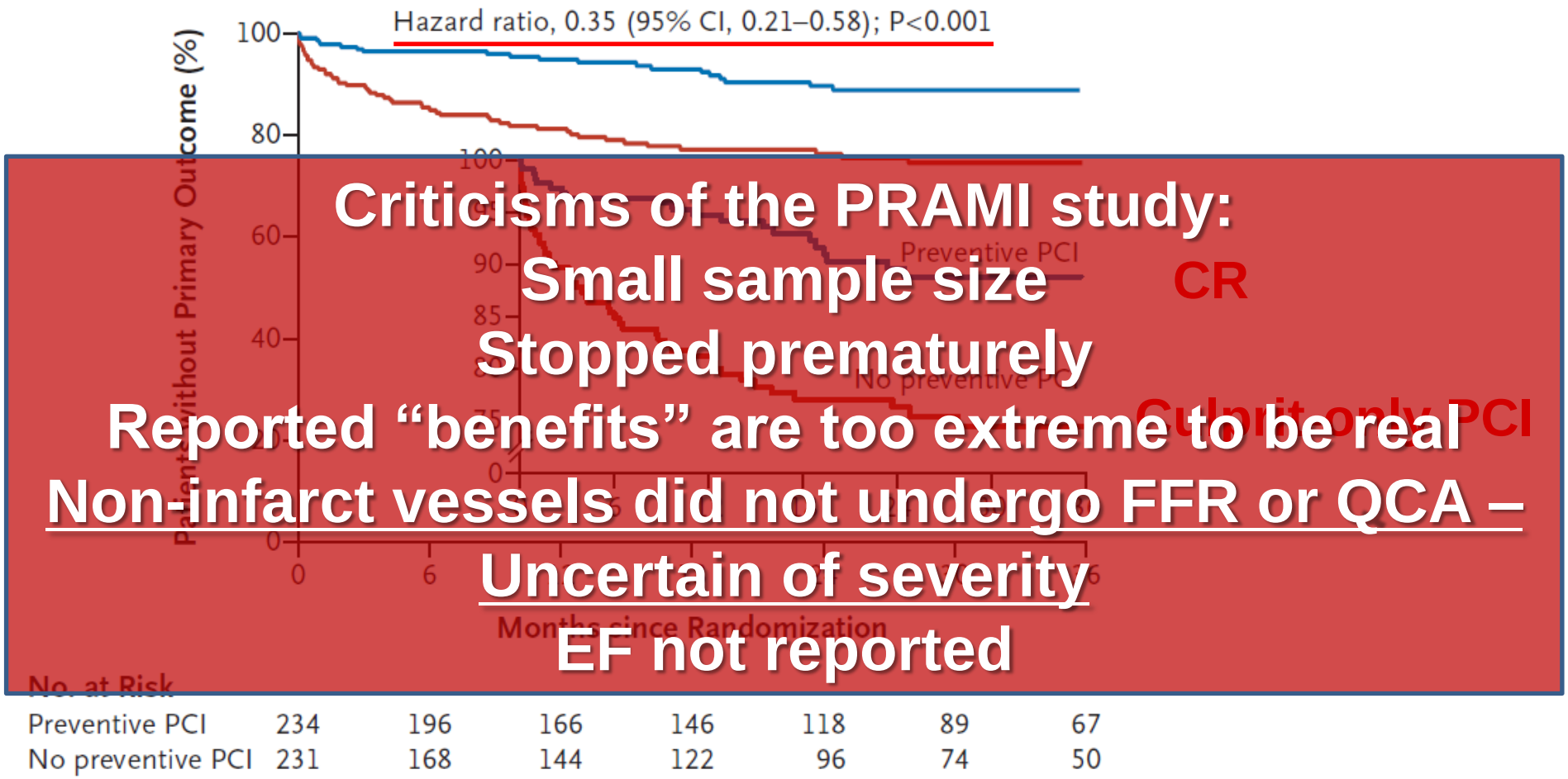


Cardiac death

Multivessel PCI also reduced risks of recurrent MI and future revascularization.

El-Hayek GE et al. Am J Cardiol 2015;115:1481-6

CR vs. IR



Criticisms of the PRAMI study:

Small sample size

Stopped prematurely

Reported "benefits" are too extreme to be real

Non-infarct vessels did not undergo FFR or QCA – Uncertain of severity

EF not reported

PRAMI Investigators. N Engl J Med 2013;369:1115-23

CR vs. IR

- **42% of enrolled patients were treated by non-culprit vessel intervention during primary PCI.**
- **There were *no* significant differences in long-term clinical outcome between MV PCI during the index procedure and staged PCI within 1 week.**
- **Delayed staged PCI more than 1 week was associated with worse clinical outcome.**

COREA Registry Data. Submitted

CR vs. IR

CNUH data

575 patients with STEMI and MVD
who underwent successful primary PCI
January 2006 to July 2009

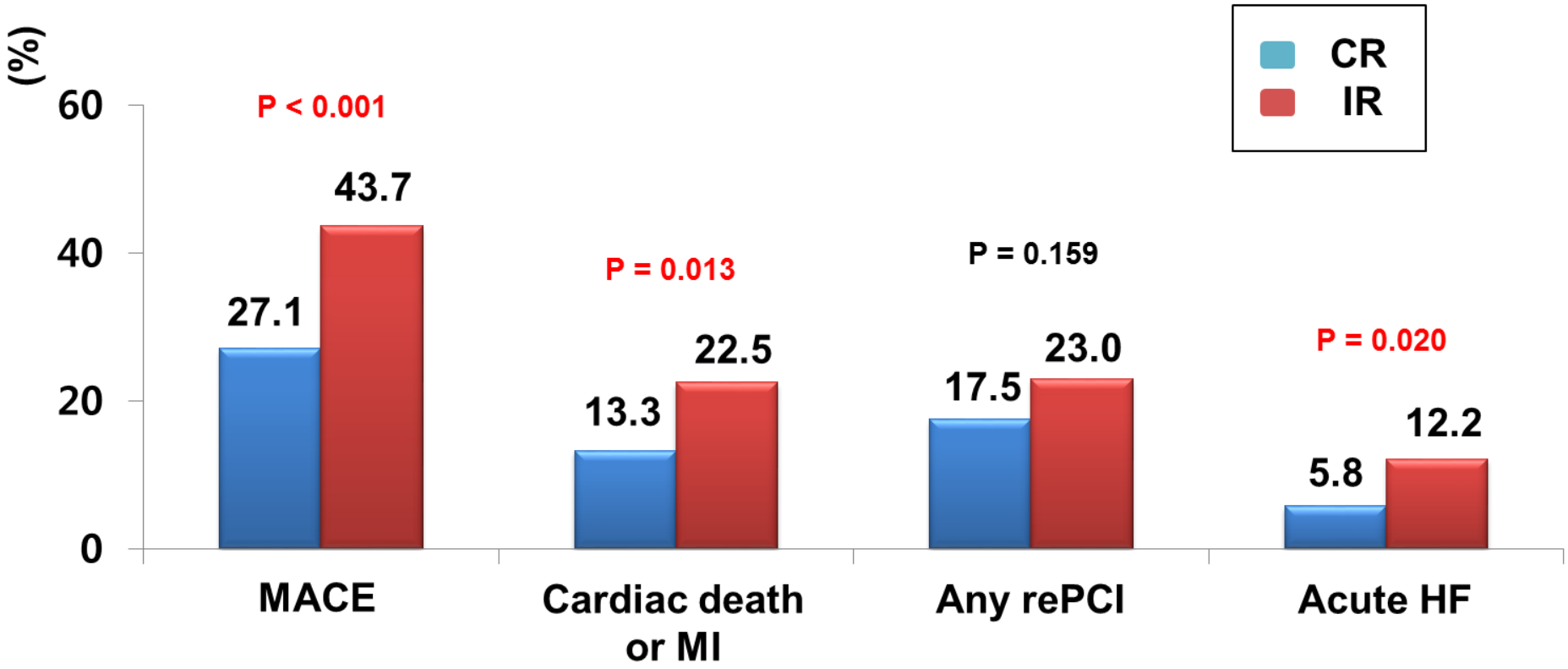
Exclusions (122 patients):
Cardiogenic shock
In-hospital death
Patients experienced CPR

CR (n = 240; 52.9%)

IR (n = 213; 47.1%)

CNUH data (unsubmitted). 2015 KSC

CR vs. IR



MACE: all-cause death, MI, and any revascularization

Median FU duration: 6.3 YRS (interquartile range – 3.7 to 7.7 YRS)

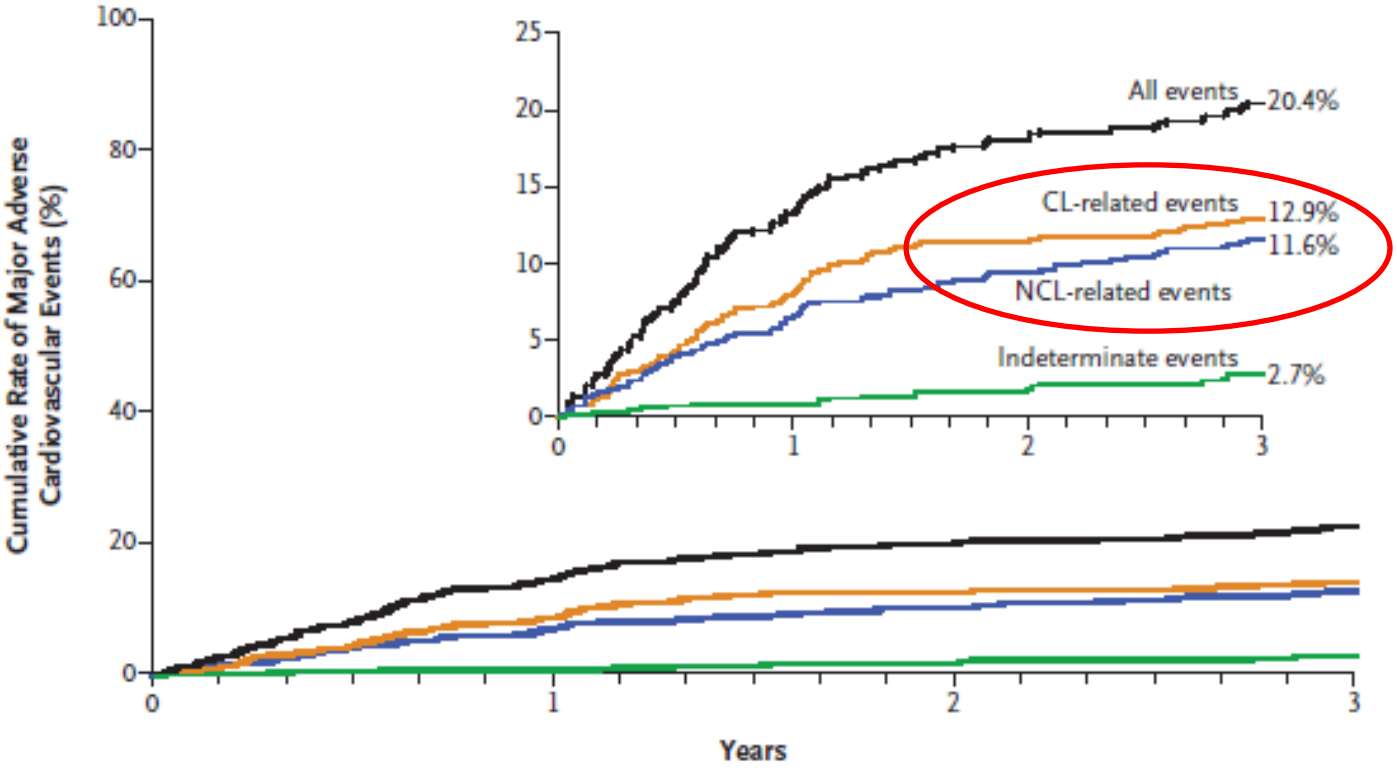
CNUH data (unsubmitted). 2015 KSC

Natural History of Non-IRA in ACS

IVUS study:

CL (culprit)
Treated lesions

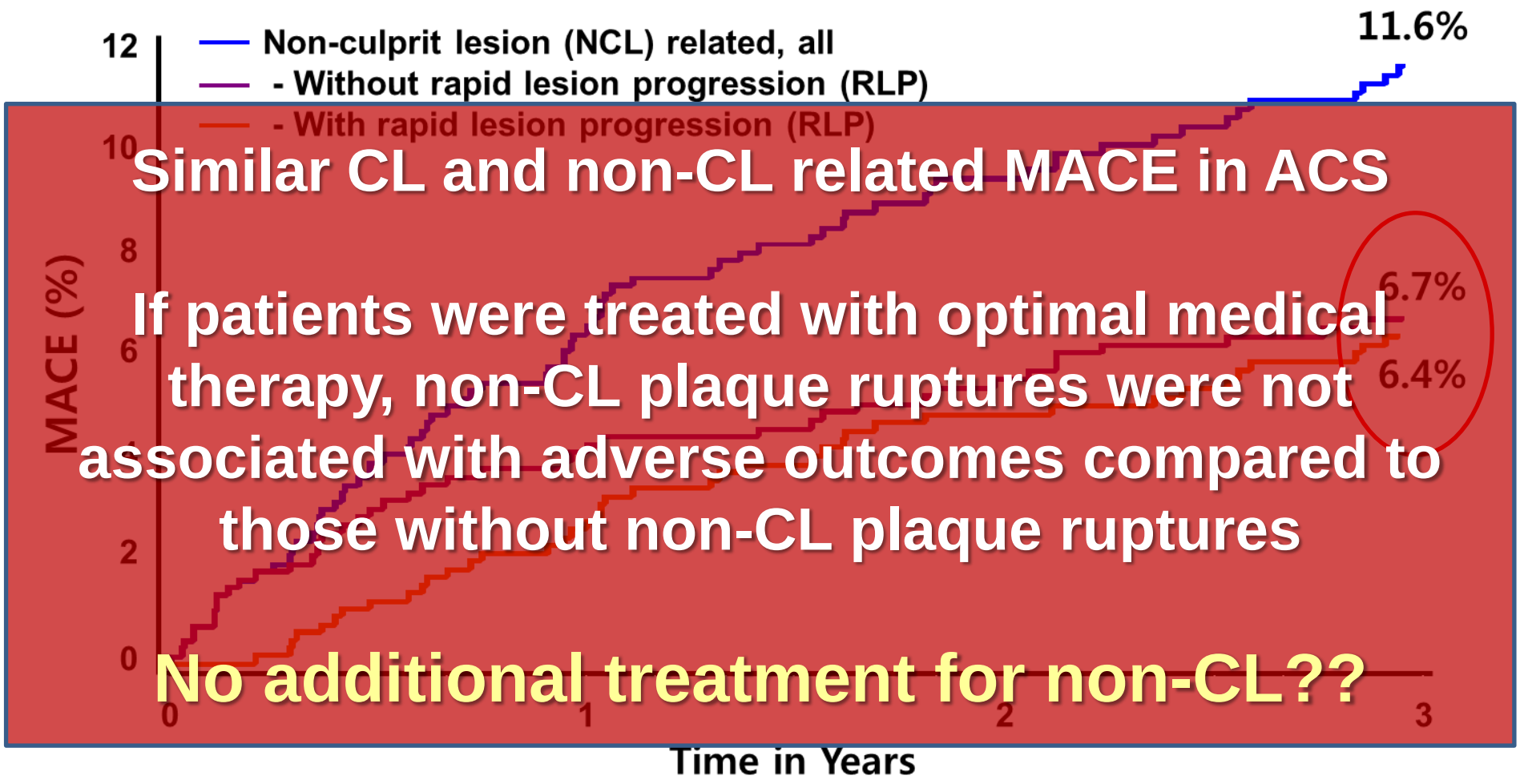
NCL (non-culprit)
Non-treated lesions
(included non-significant lesions)
30~70% stenosis



No. at Risk				
All patients	697	557	506	480
Patients with CL-related events	697	590	543	518
Patients with NCL-related events	697	595	553	521
Patients with indeterminate events	697	634	604	583

PROSPECT Investigators. N Engl J Med 2011;364:226-35

Natural History of Non-IRA in ACS



Similar CL and non-CL related MACE in ACS

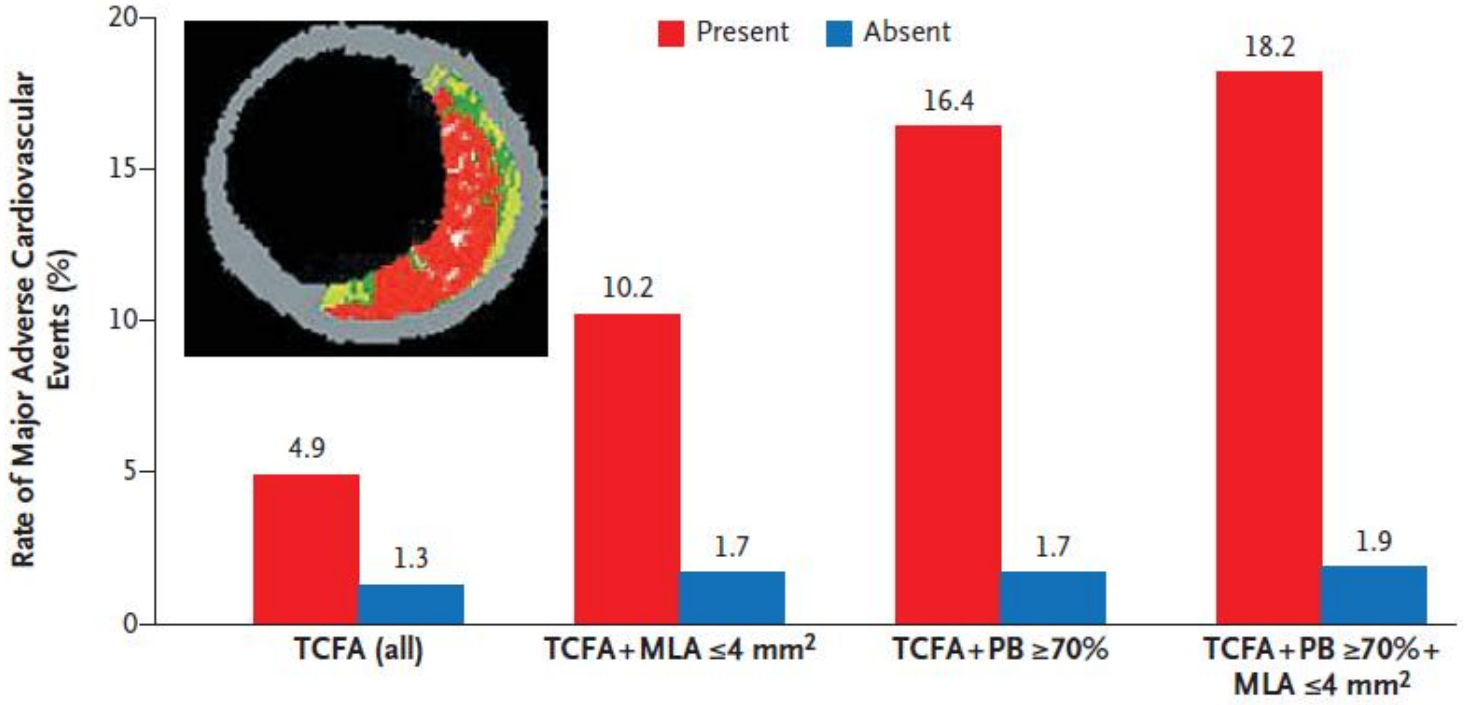
If patients were treated with optimal medical therapy, non-CL plaque ruptures were not associated with adverse outcomes compared to those without non-CL plaque ruptures

No additional treatment for non-CL??

PROSPECT Investigators. N Engl J Med 2011;364:226-35

Natural History of Non-IRA in ACS

Event rates according to presence of thin-cap fibroatheromas



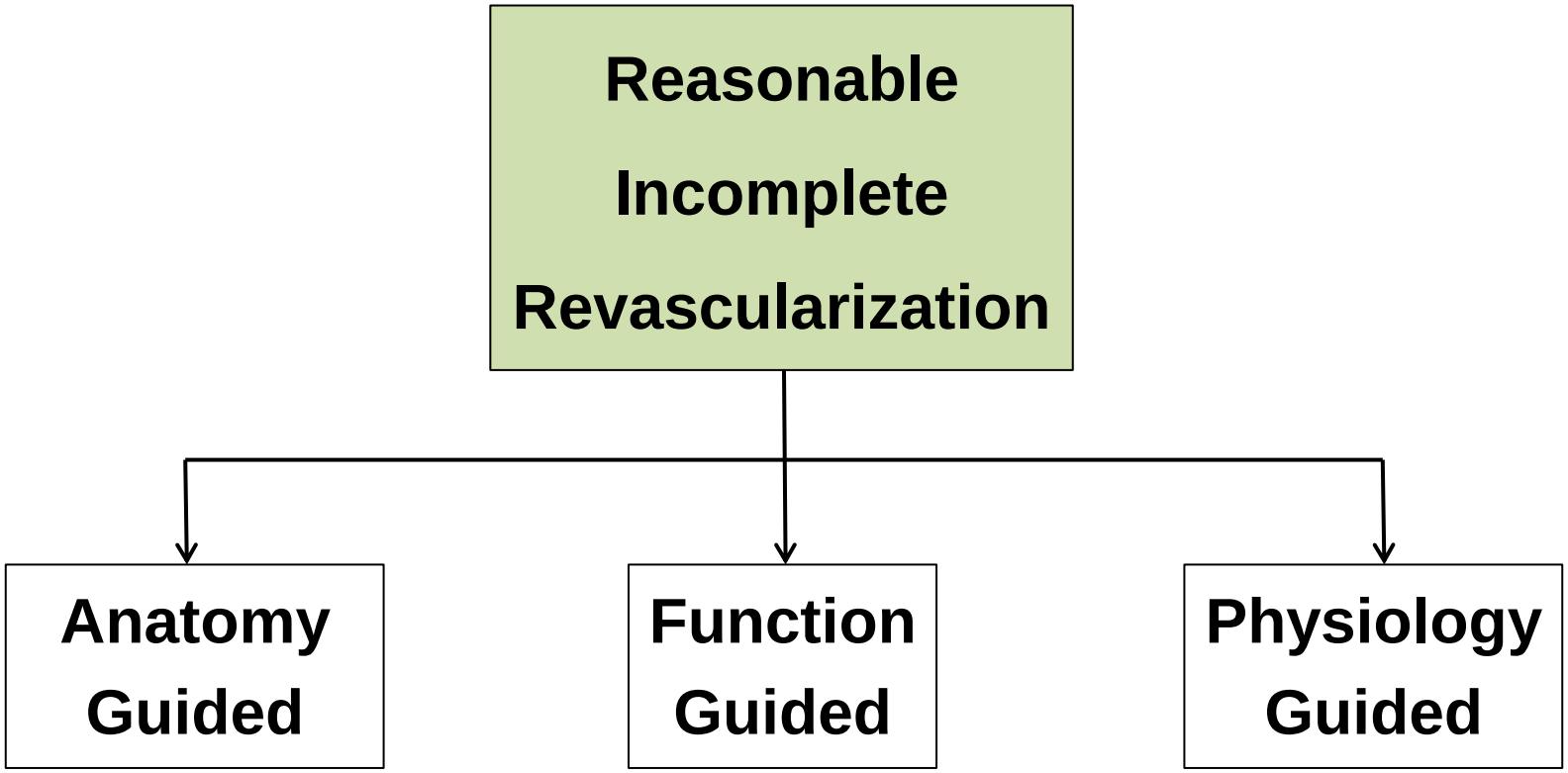
Lesion hazard ratio (95% CI)	3.90 (2.25–6.76)	6.55 (3.43–12.51)	10.83 (5.55–21.10)	11.05 (4.39–27.82)
P value	<0.001	<0.001	<0.001	<0.001
Prevalence (%)	46.7	15.9	10.1	4.2

PROSPECT Investigators. N Engl J Med 2011;364:226-35

Reasons Against Multivessel PCI

- **The acute phase of STEMI is a highly unstable condition: not an ideal situation to perform PCI of a stable stenosis**
- **The acute phase of STEMI is an extremely prothrombotic and inflammatory milieu: contributes to the potentially higher risk of additional PCI**
- **Some degree of diffuse coronary spasm is frequently present in the acute phase of STEMI: may lead to overestimation of stenosis severity in non-IRA**
- **Risk of contrast-induced nephropathy**
- **No evidence for myocardial ischemia in non-IRA**

The Concept of Reasonable IR



- Very small vessels
- Only 1 epicardial vessel revascularized
- Jailed asymptomatic side branches

- Non-viable myocardium
- Less than 5% residual ischemic territory expected
- Small territory of ischemia

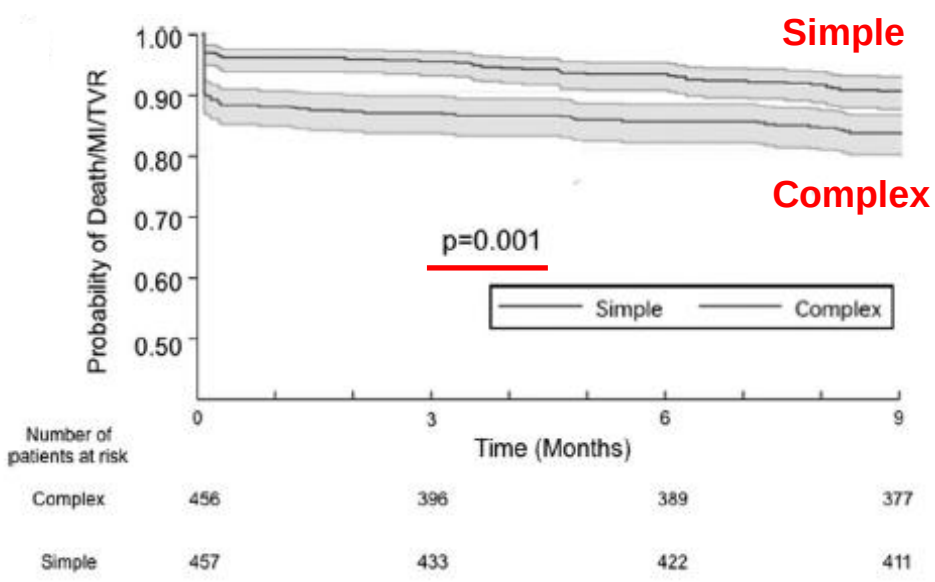
- Fractional Flow Reserve > 0.80

Dauerman HL. Circulation 2011;123:2337-40

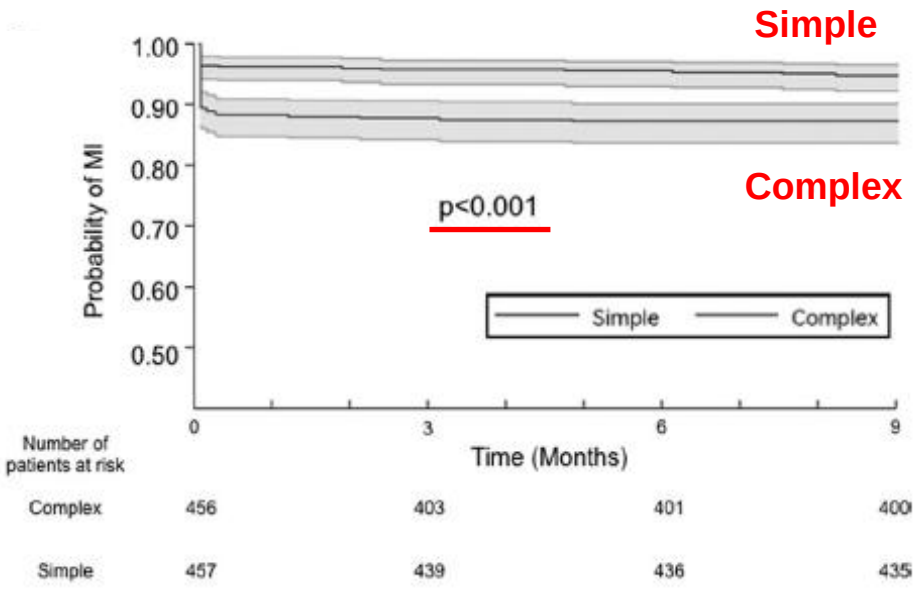
Reasonable IR: Anatomy-Guided

Patient-level data of two large RCTs: The NORDIC I and BBC ONE Provisional single vs. complex stenting in bifurcation lesions

Death, MI or TVR



MI



Behan et al. Circ Cardiovasc Interv 2011;4:57-64

Reasonable IR: Anatomy-Guided

Patient-level data of two large RCTs: The NORDIC I and BBC ONE
Risk of primary endpoint for complex stenting in subgroups

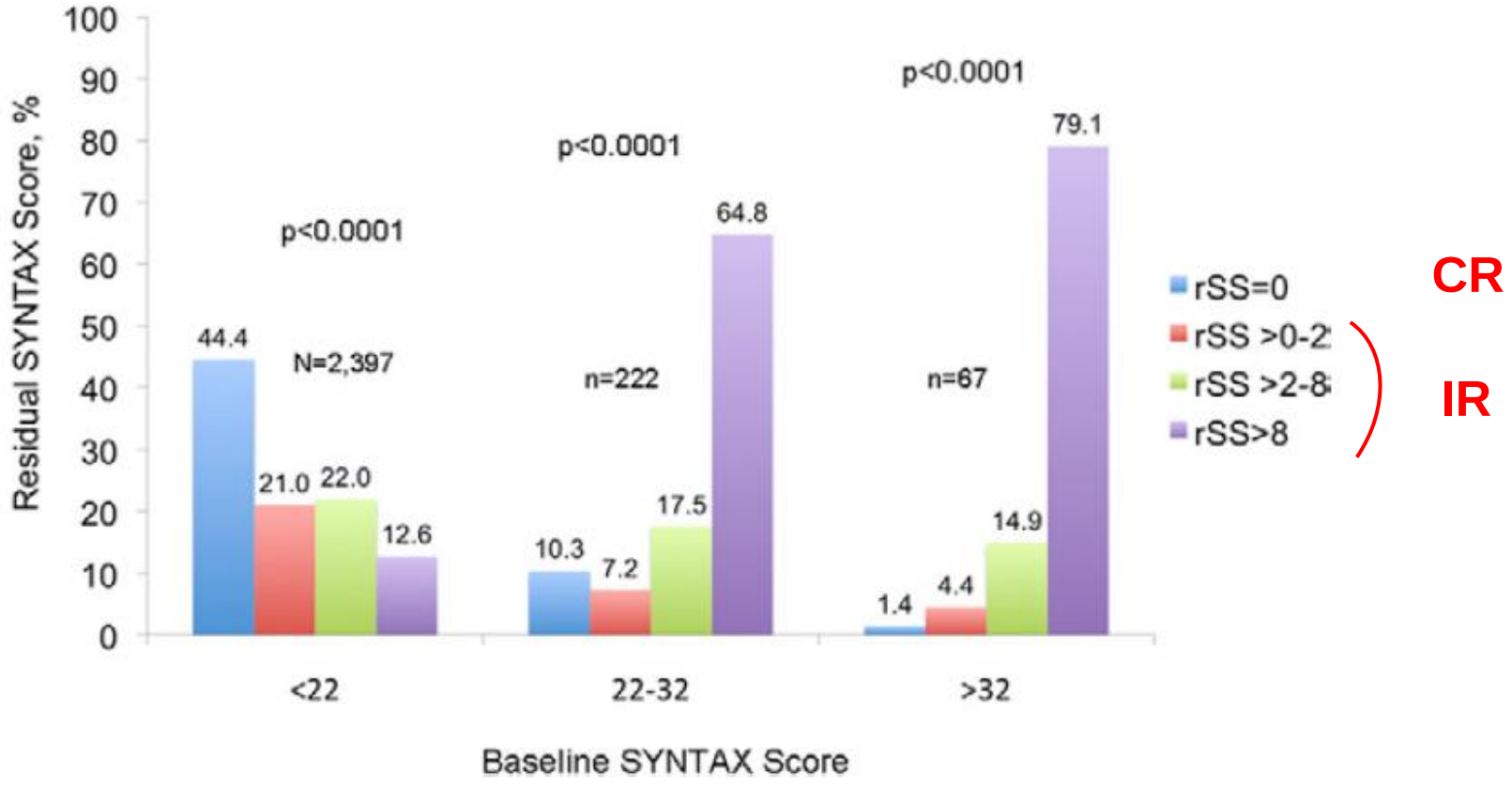
	Odds ratio and 95% CI
True bifurcation (n = 657)	1.90 (1.22-2.94)
Angle > 60-70° (n = 217)	1.67 (0.78-3.62)
SB diameter ≥ 2.75 mm (n = 291)	2.42 (1.22-4.80)
SB lesion length > 5 mm (n = 464)	1.71 (1.05-2.77)
SB diameter ≥ 2.75 mm / length > 5mm (n = 137)	1.84 (0.68-4.97)
Total (n = 913)	1.84 (1.28-2.66)

Simple one-stenting (IR for coronary bifurcation) is associated with lower rates of clinical outcomes.

Behan et al. Circ Cardiovasc Interv 2011;4:57-64

Reasonable IR: Anatomy-Guided

Quantification of untreated non-IRA after PCI
Residual SYNTAX score (rSS) after PCI: *In the ACUITY trial*
Moderate to high-risk ACS patients



Genereux et al. J Am Coll Cardiol 2012;59:2165-74

Reasonable IR: Anatomy-Guided

Quantification of untreated non-IRA after PCI

Residual SYNTAX score (rSS) after PCI: *In the ACUITY trial*

Moderate to high-risk ACS patients

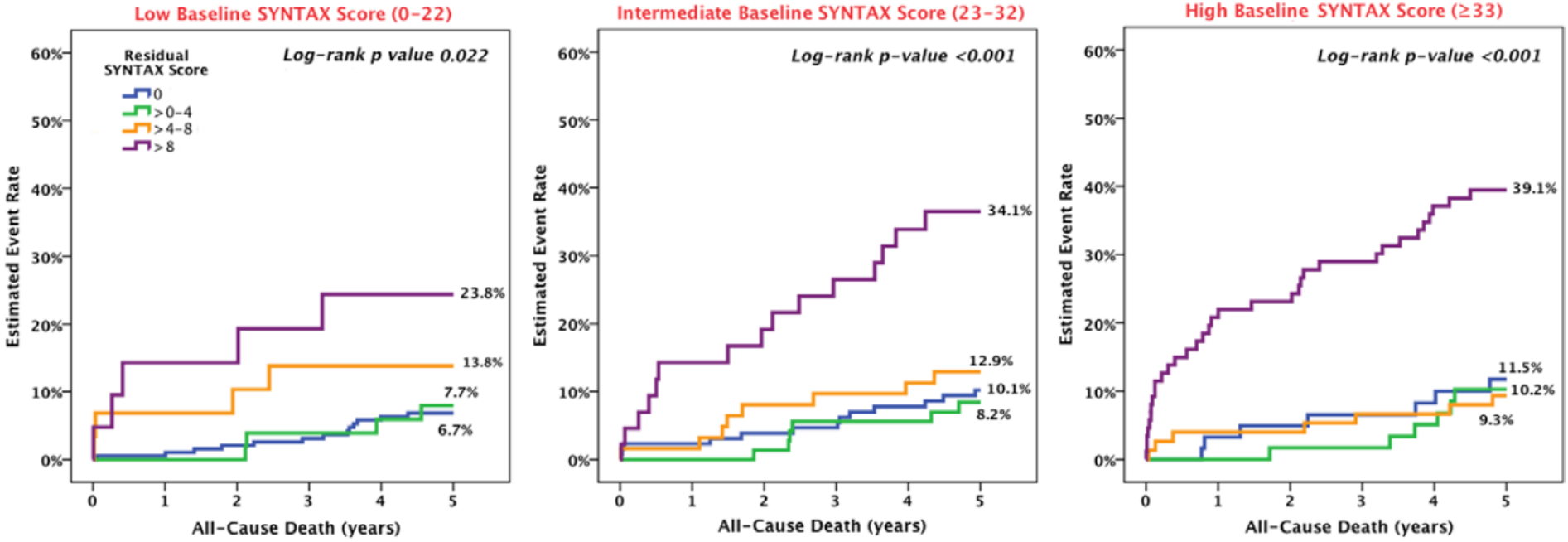
	HR (95% CI)	P value
All-cause death	1.05 (1.03-1.08)	<0.001
Cardiac death	1.06 (1.03-1.10)	<0.001
Myocardial infarction	1.02 (1.01-1.04)	0.003
Ischemia-driven repeat PCI	1.04 (1.02-1.05)	<0.001

One-year clinical outcomes for rSS

Genereux et al. J Am Coll Cardiol 2012;59:2165-74

Reasonable IR: Anatomy-Guided

Quantification of untreated non-IRA after PCI
Residual SYNTAX score: *In the SYNTAX trial*

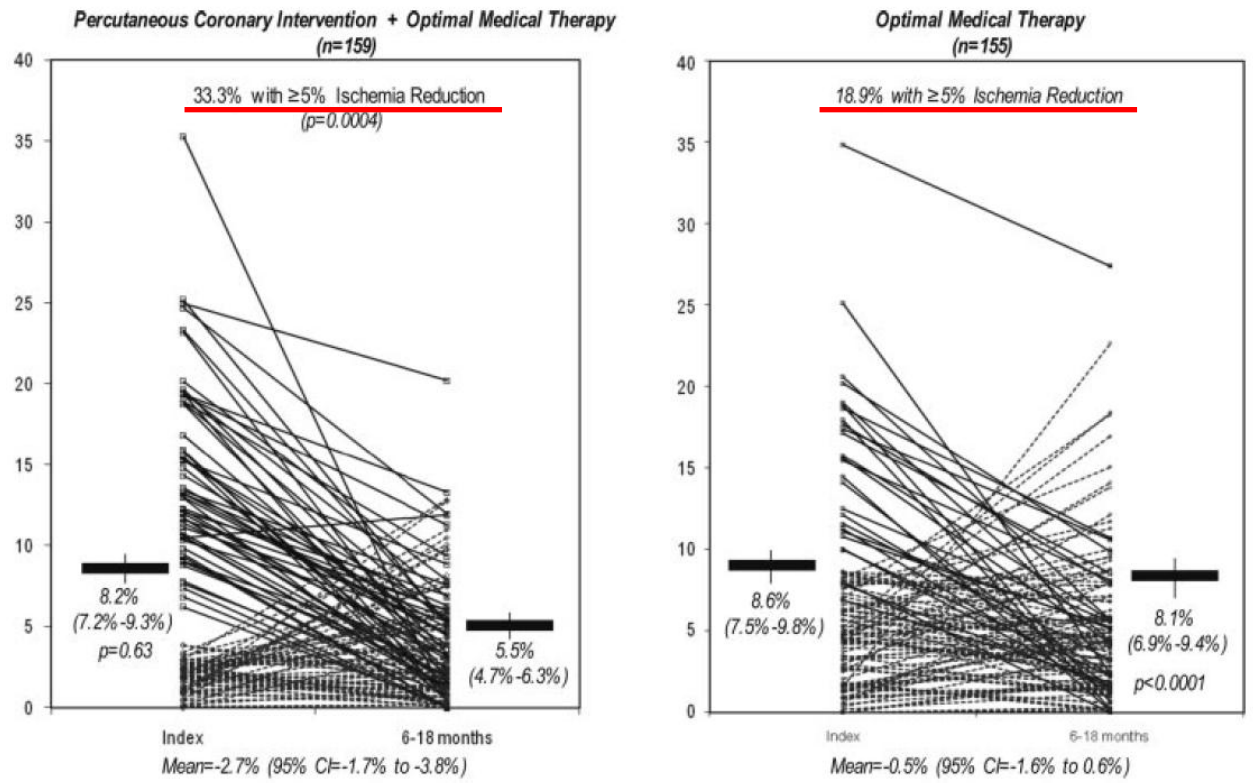


The rSS (especially, rSS >8) is a powerful indicator of 5-year morality in the SYNTAX trial.

Farooq et al. Circulation 2013;128:141-51

Reasonable IR: Function-Guided

OMT vs. OMT+PCI to reduce ischemic burden
The COURAGE nuclear substudy

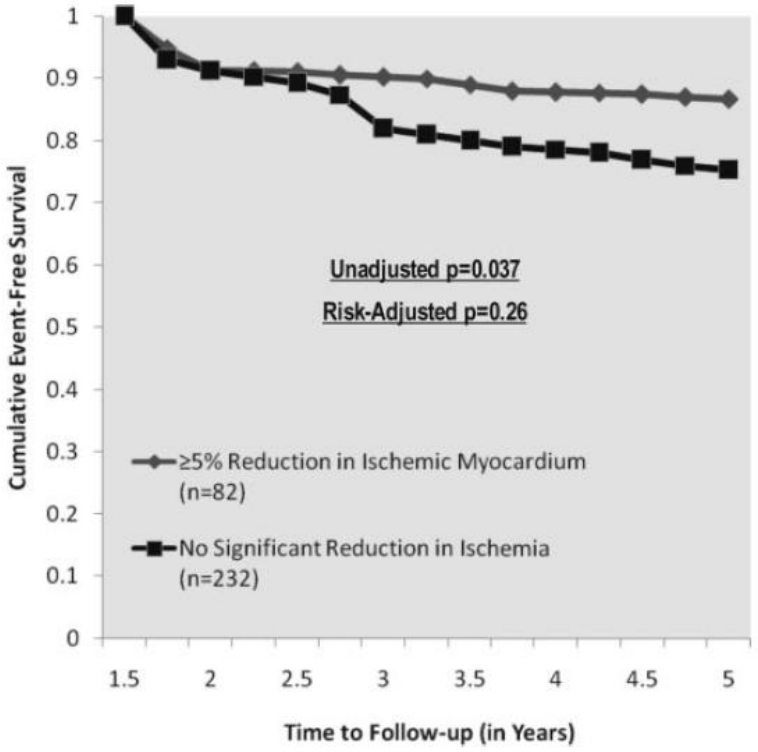


Serial M-SPECT (pretreatment and after 6-18 months)

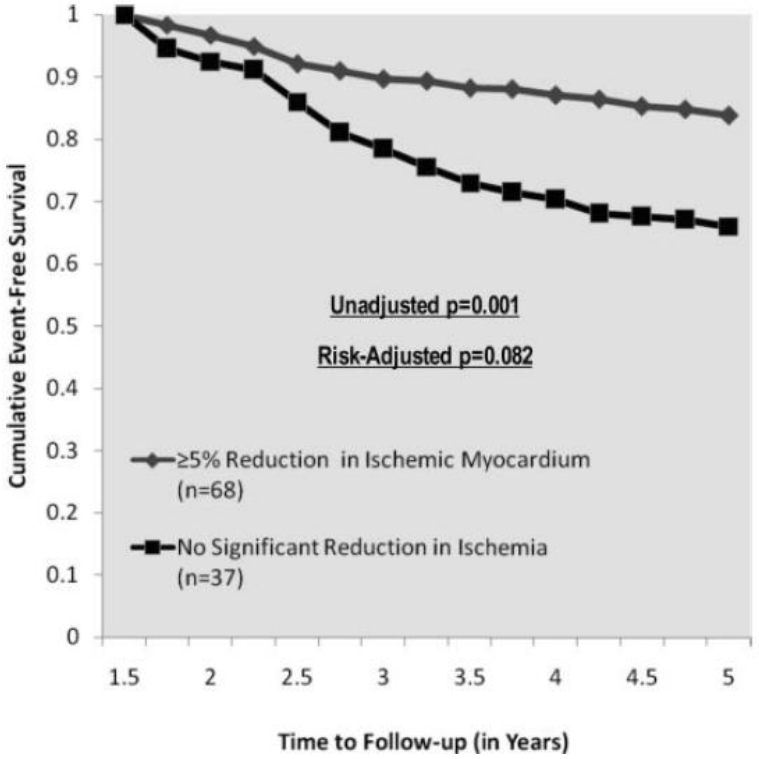
Shaw et al. Circulation 2008;117:1283-91

Reasonable IR: Function-Guided

OMT vs. OMT+PCI to reduce ischemic burden
The COURAGE nuclear substudy



Overall population



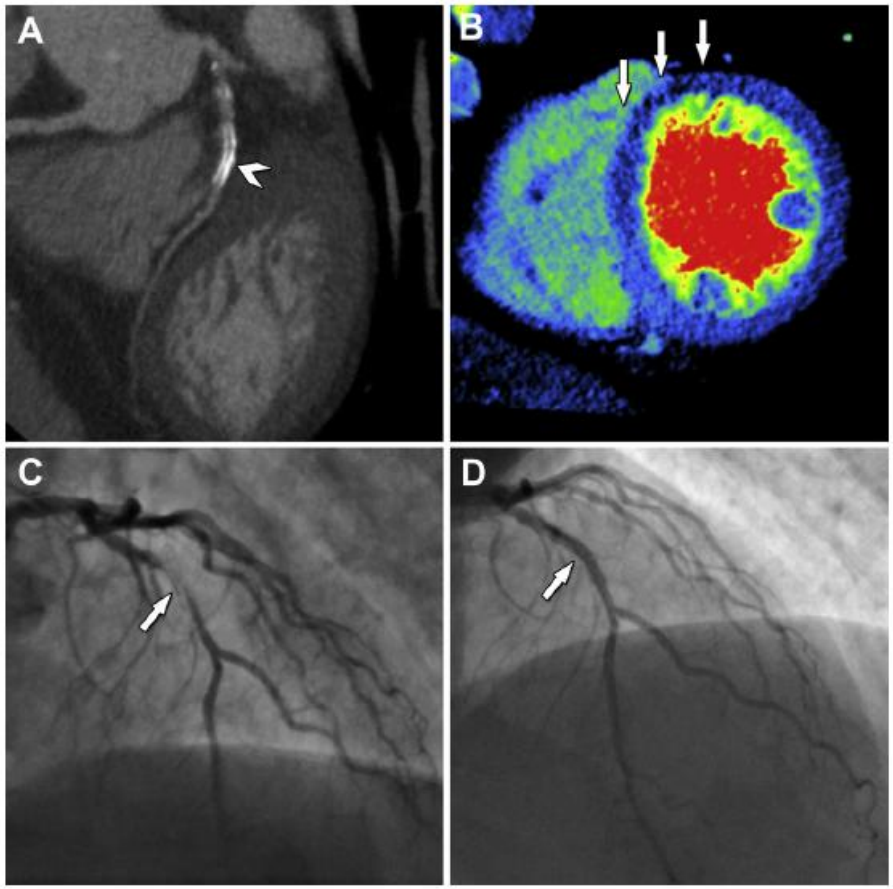
Moderate to severe pretreatment ischemia

Shaw et al. Circulation 2008;117:1283-91

Reasonable IR: Function-Guided

Coronary CT angiogram combined with CT perfusion scan : 75-Year-Old man with LAD ISR

Non-diagnostic CTA because of metallic stent artifact



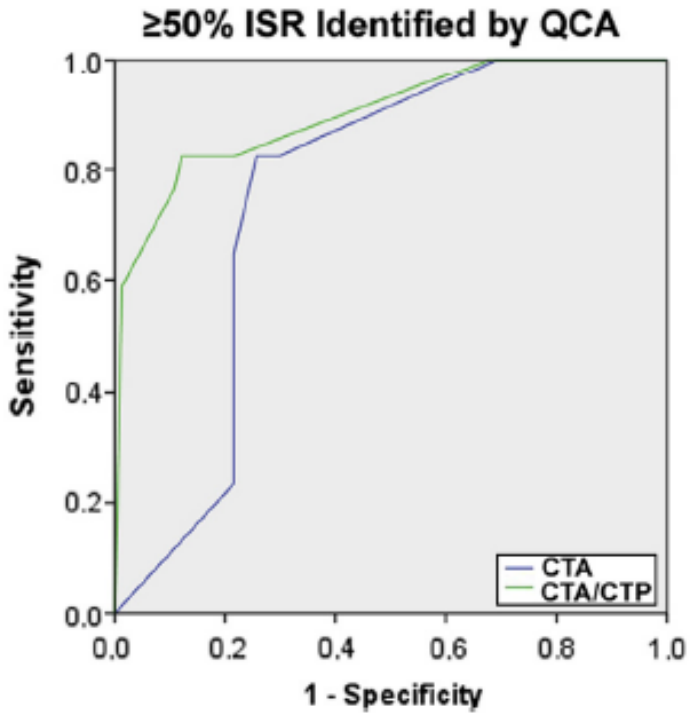
CTP: Stress-induced anteroseptal ischemia

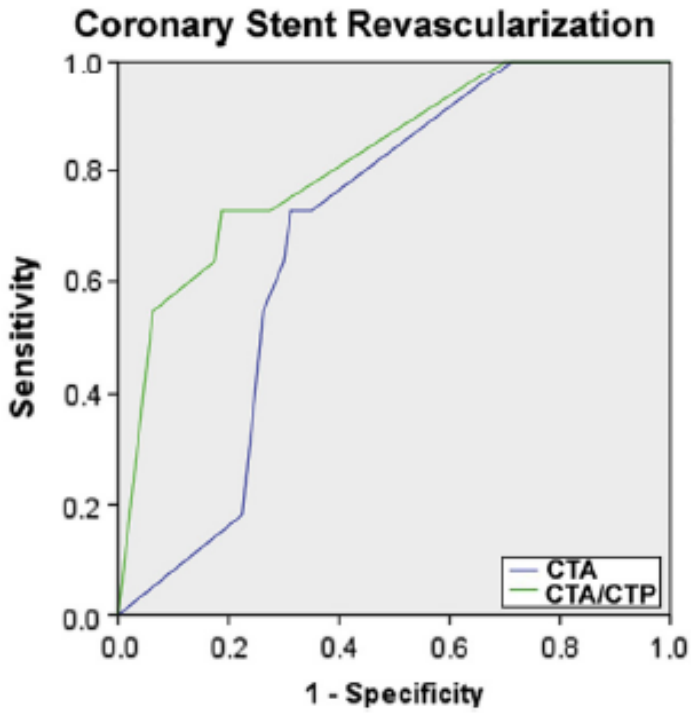
CAG confirmed severe ISR in LAD

Rief et al. J Am Coll Cardiol 2013;62:1476-85

Reasonable IR: Function-Guided

Coronary CT angiogram combined with CT perfusion scan

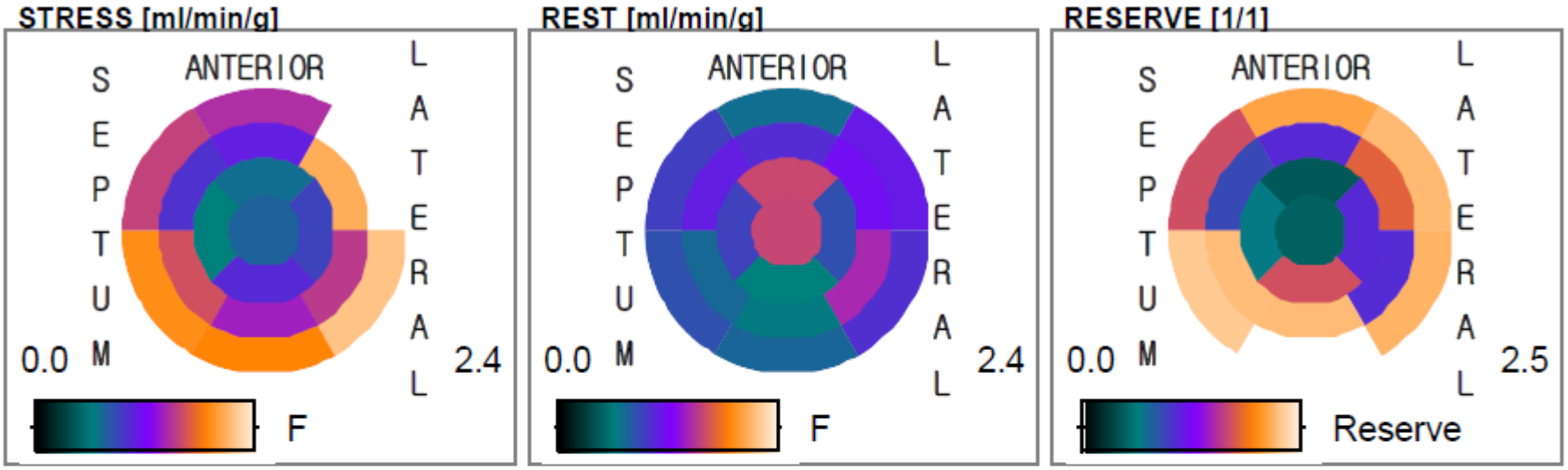


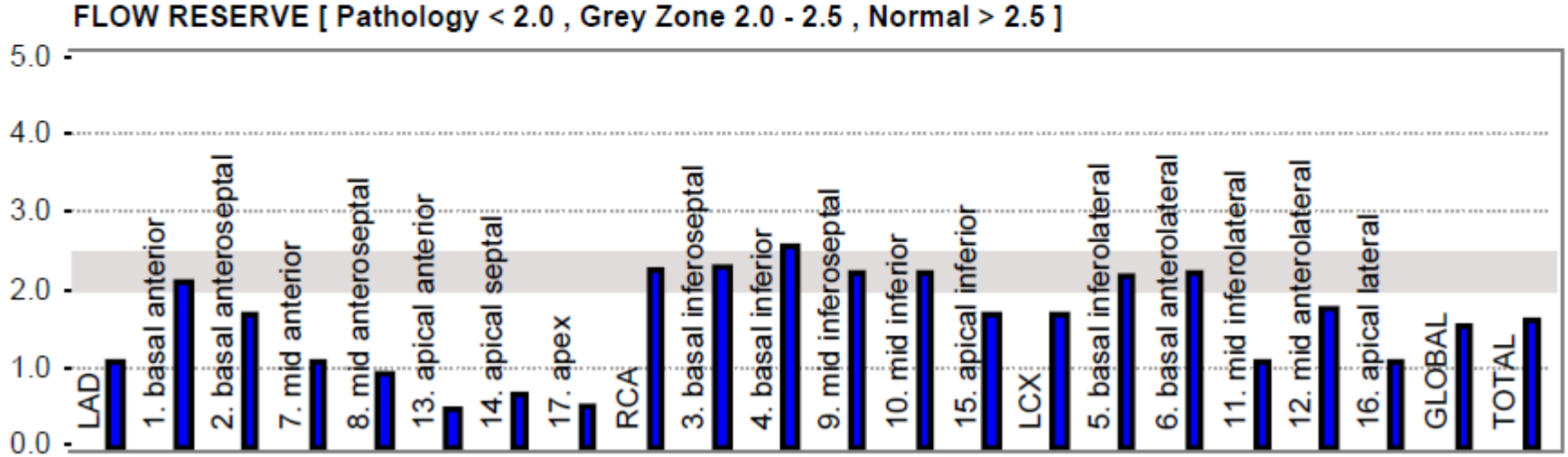


CTA combined with CT perfusion scan improves diagnosis of CAD and ISR compared with CTA alone

Rief et al. J Am Coll Cardiol 2013;62:1476-85

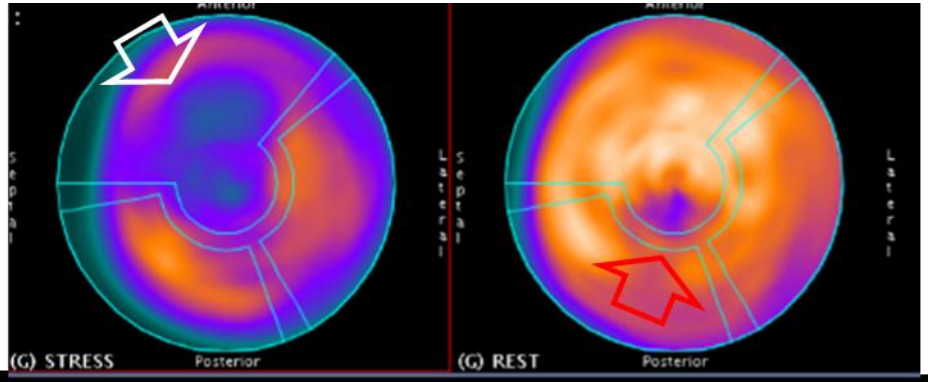
Ammonia PET/CT (Investigating in CNUH)

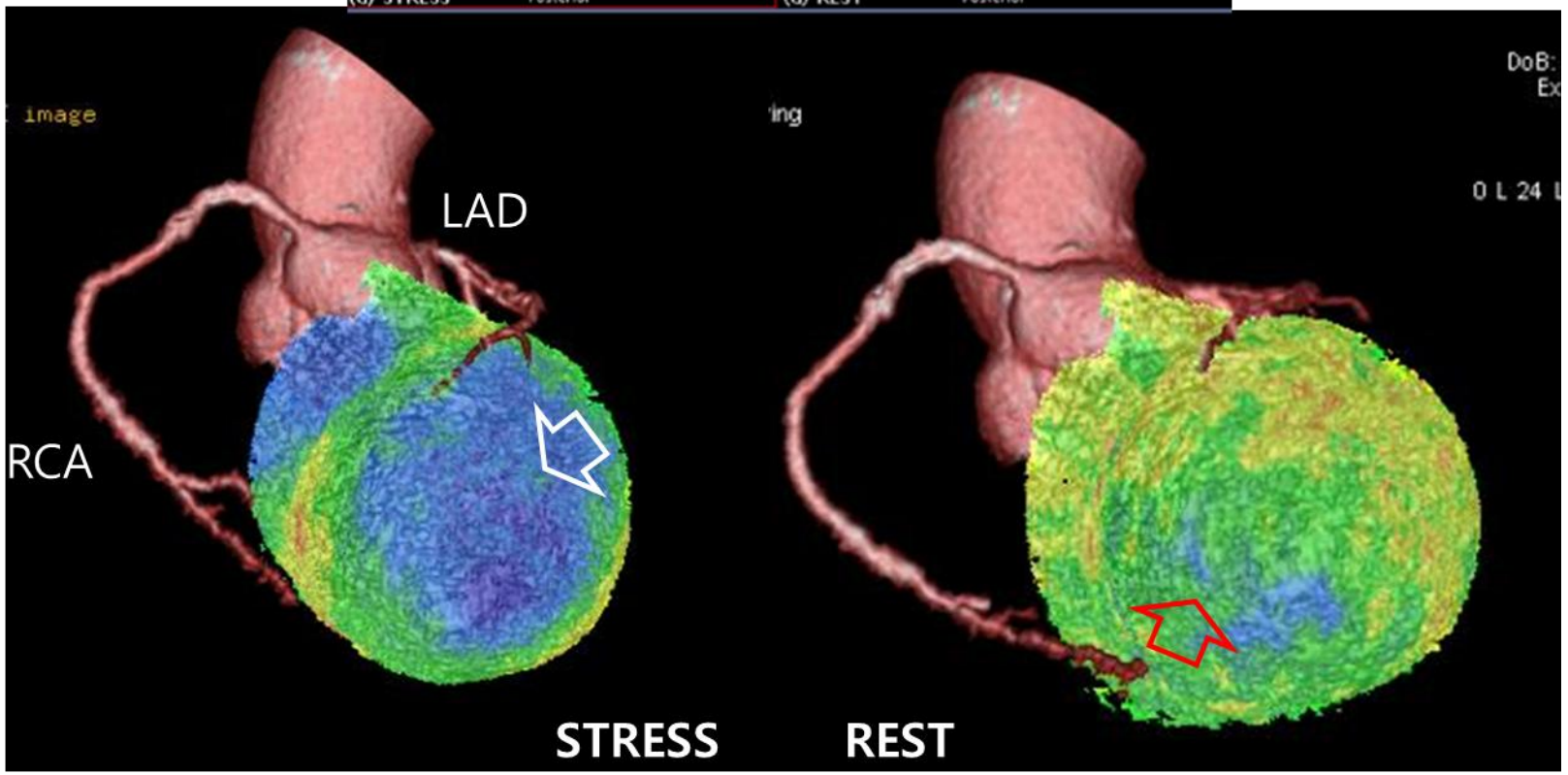




CNUH. Int J Cardiol 2014;174:e81-3.

Ammonia PET/CT (Investigating in CNUH)





Ammonia PET/CT (Investigating in CNUH)

- **Reconstruction of 3-D imaging**
- **Low radiation dose**

  : Compared to SPECT
- **Measure rest or stress perfusion of each vessel, flow reserve**

Reasonable IR: Physiology-Guided

Do not believe visual estimation: visual-functional mismatch

Journal of the American College of Cardiology

Volume 55, Issue 25, 22 June 2010, Pages 2816–2821

Clinical Research

Angiographic Versus Functional Severity of Coronary Artery Stenoses in the FAME Study : Fractional Flow Reserve Versus Angiography in Multivessel Evaluation

Pim A.L. Tonino, MD, William F. Fearon, MD, Bernard De Bruyne, MD, PhD, Keith G. Oldroyd, MD, Massoud A. Leesar, MD, Peter N. Ver Lee, MD, Philip A. MacCarthy, MD, PhD, Marcel van't Veer, MSc, PhD, Nico H.J. Pijls, MD, PhD

Lesion Characteristics per Category of Angiographic Stenosis Severity

	% Stenosis by Angiography		
	50% to 70% (n = 620, 47%)	71% to 90% (n = 513, 39%)	91% to 99% (n = 96, 15%)
FFR >0.80	402 (65)	104 (20)	7 (4)
FFR ≤0.80	218 (35)	409 (80)	189 (96)
Mean FFR for all lesions	0.81 ± 0.12	0.67 ± 0.15	0.52 ± 0.15
Mean FFR >0.80	0.89 ± 0.05	0.87 ± 0.05	0.87 ± 0.04
Mean FFR ≤0.80	0.68 ± 0.10	0.62 ± 0.13	0.51 ± 0.13

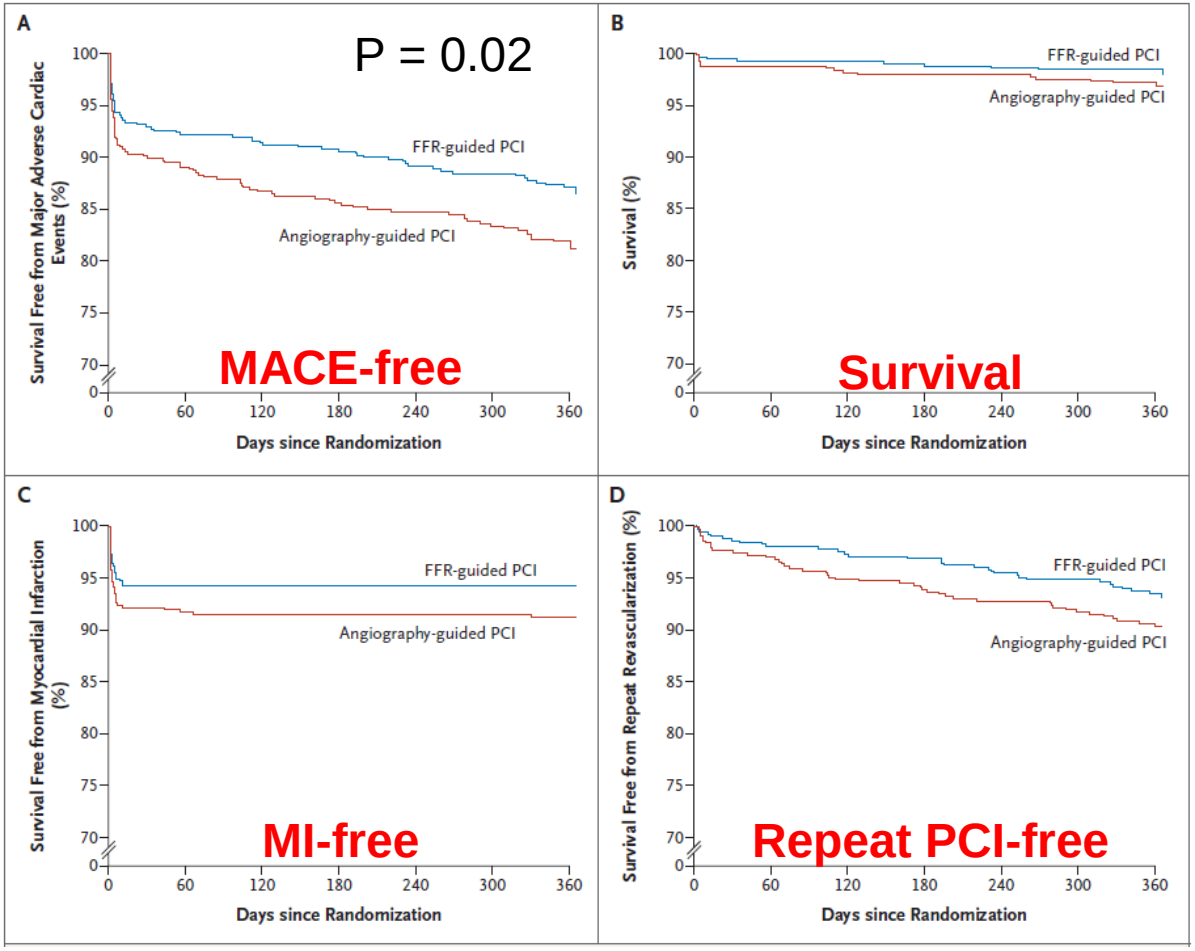
Values are n (%) or mean ± SD.

Angiographically severe lesions may be functionally insignificant if only a small myocardial mass is at risk.

Torino et al. J Am Coll Cardiol 2010;55:2816-21

Reasonable IR: Physiology-Guided

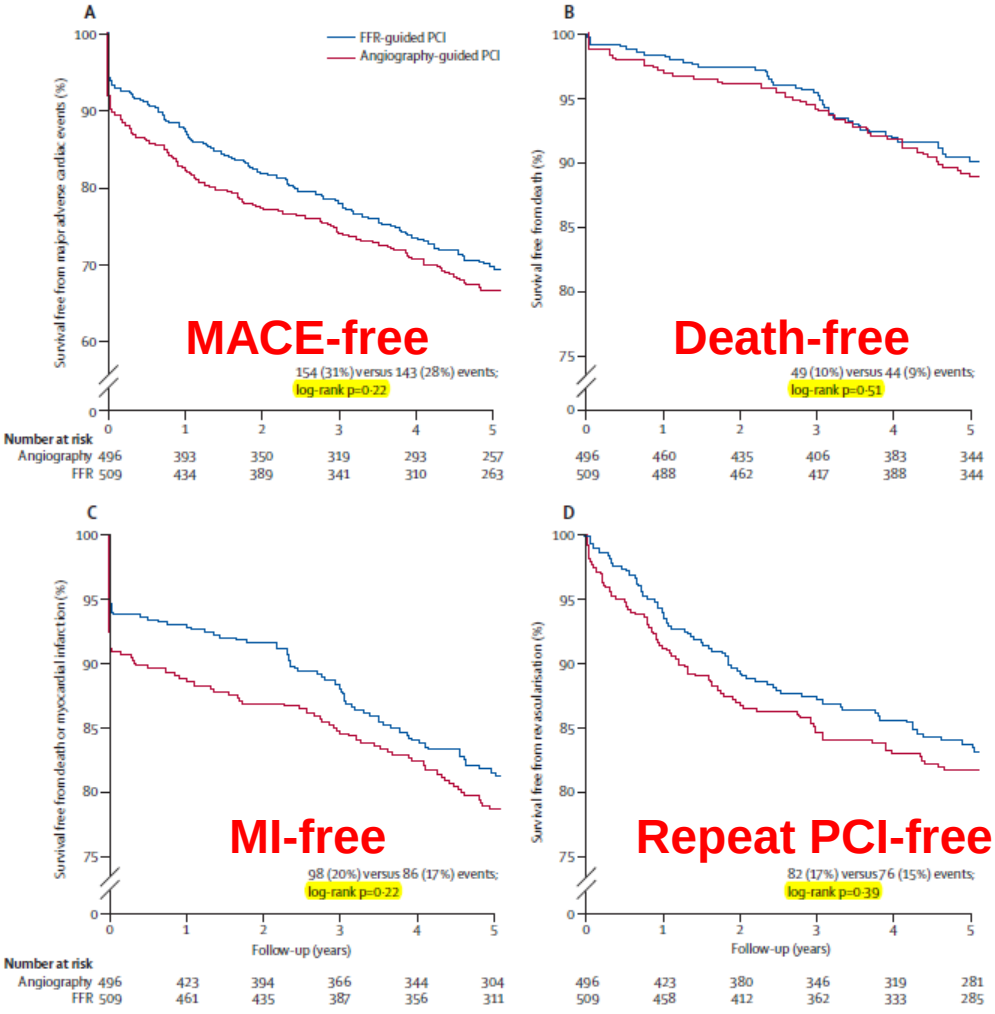
1005 patients with MVD
Randomization to angio- vs. FFR-guided PCI



FAME Investigators. N Engl J Med 2009;360:213-24

Reasonable IR: Physiology-Guided

The FAME trial: 5-year FU outcomes



Similar incidence of events in both groups beyond 2-years.

The benefits of FFR-guided PCI occurs mainly during the first 2 years.

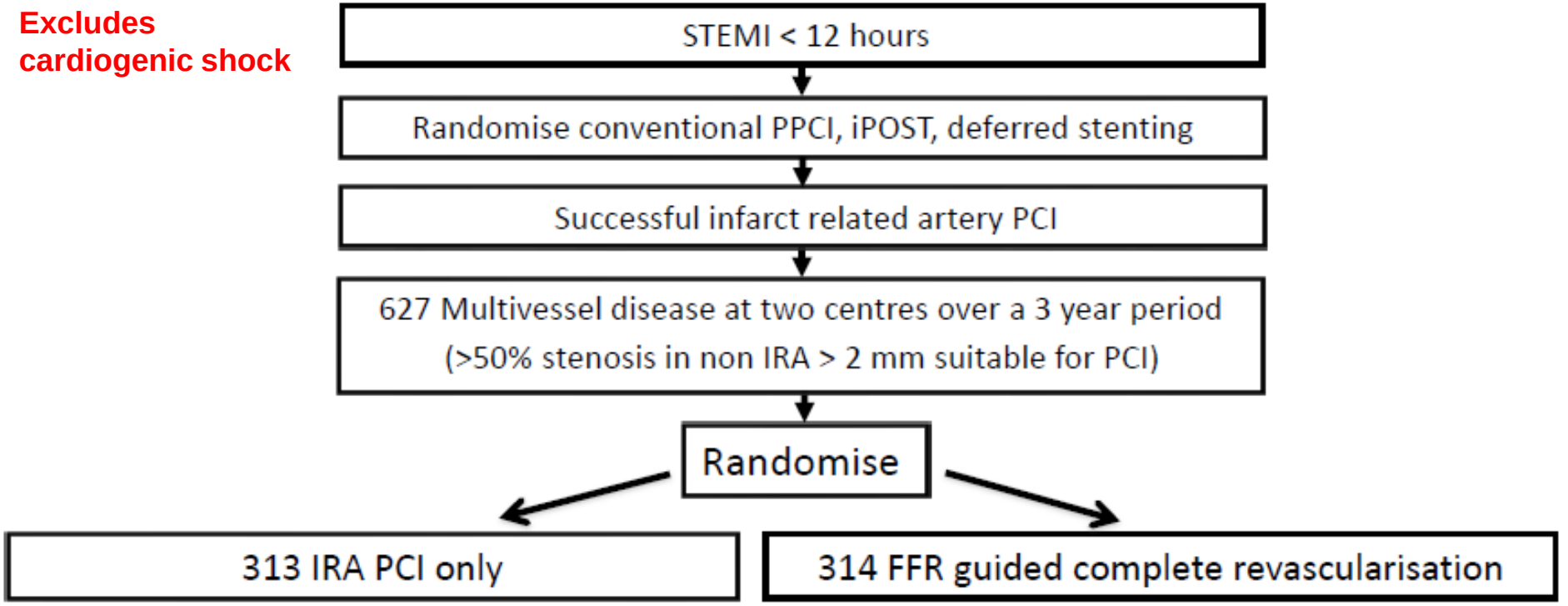
The results confirm the long-term safety of FFR-guided PCI in patients with MVD.

FAME Investigators. Lancet 2015, in press

Reasonable IR: Physiology-Guided

DANAMI3-PRIMULTI Trial (STEMI with MVD)

Excludes cardiogenic shock



Staged PCI within index admission:
> 50% diameter stenosis and FFR <0.80
or
> 90% diameter stenosis

Engstrom et al. Lancet 2015;386:665-71

Reasonable IR: Physiology-Guided

DANAMI3-PRIMULTI Trial: 27-month outcomes

	IRA only (n = 313)	Complete revascularisation (n = 314)	HR [95% CI]	p
Primary endpoint	68 (22%)	40 (13%)	0·56 [0·38 – 0·83]	0·004
All-cause death	11 (4%)	15 (5%)	1·4 [0·63 – 3·0]	0·43
Nonfatal MI	16 (5%)	15 (5%)	0·94 [0·47 – 1·9]	0·87
Ischaemia-driven revascularisation*	52 (17%)	17 (5%)	0·31 [0·18 – 0·53]	<0·001
Secondary endpoints				
Cardiac death	9 (3%)	5 (2%)	0·56 [0·19 – 1·7]	0·29
Cardiac death or nonfatal MI	25 (8%)	20 (6%)	0·80 [0·45 – 1·45]	0·47
Urgent PCI	18 (6%)	7 (2%)	0·38 [0·16 – 0·92]	0·03
Non-urgent PCI	27 (9%)	8 (3%)	0·29 [0·13 – 0·63]	0·002

* PCI or CABG

CR guided by FFR significantly reduced the risk of repeat revascularization compared to culprit-only PCI in STEMI patients with MVD.

Engstrom et al. Lancet 2015;386:665-71

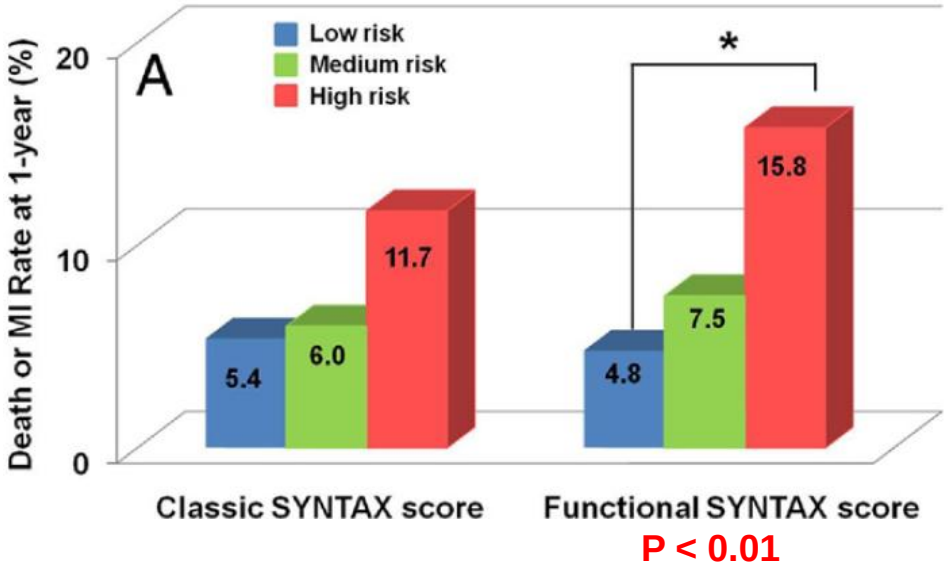
Reasonable IR: Physiology-Guided

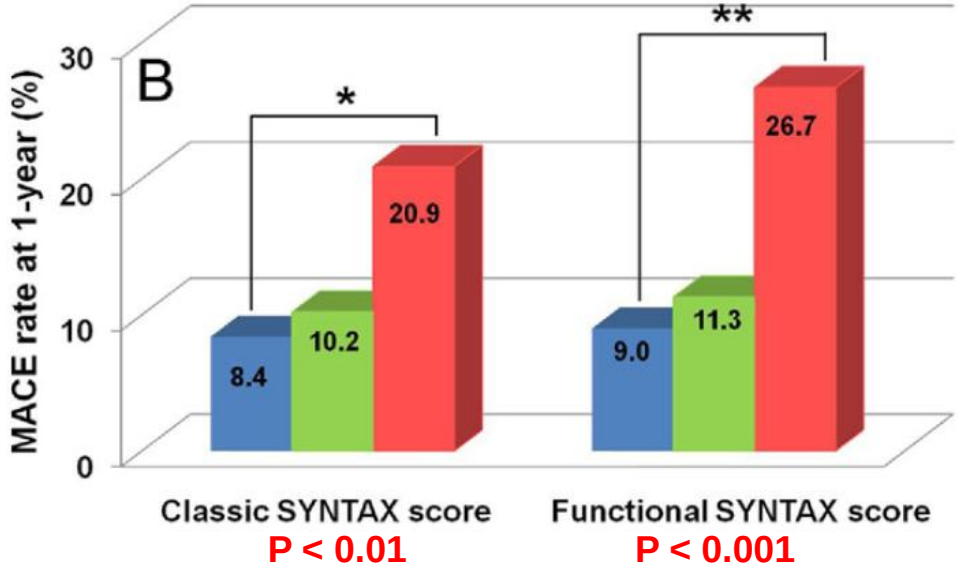
Functional supplementation of existing risk-stratification tools

Analysis of patients who enrolled in the FAME study

Functional SYNTAX score:

counts only lesions with significance based on FFR





Nam et al. J Am Coll Cardiol 2011;58:1211-8

Conclusions

- **Recent evidences support CR in patients with MVD (even STEMI patients) as possible.**
- **However, unnecessary revascularization can be avoided with use of function, invasive coronary imaging or physiology-based studies such as myocardial perfusion scan, IVUS or FFR in coronary lesion with moderate severity.**