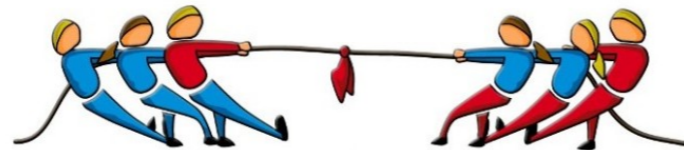


IAM EN MALALTIA MULTIVÀS TRACTAR-HO TOT O NO AGUT O DIFERIT

TRACTAR ALTRES LESIONS QUE LA RESPONSABLE EN LA FASE AGUDA APORTA AVANTATGES

- PART I -



Oriol Rodríguez Leor
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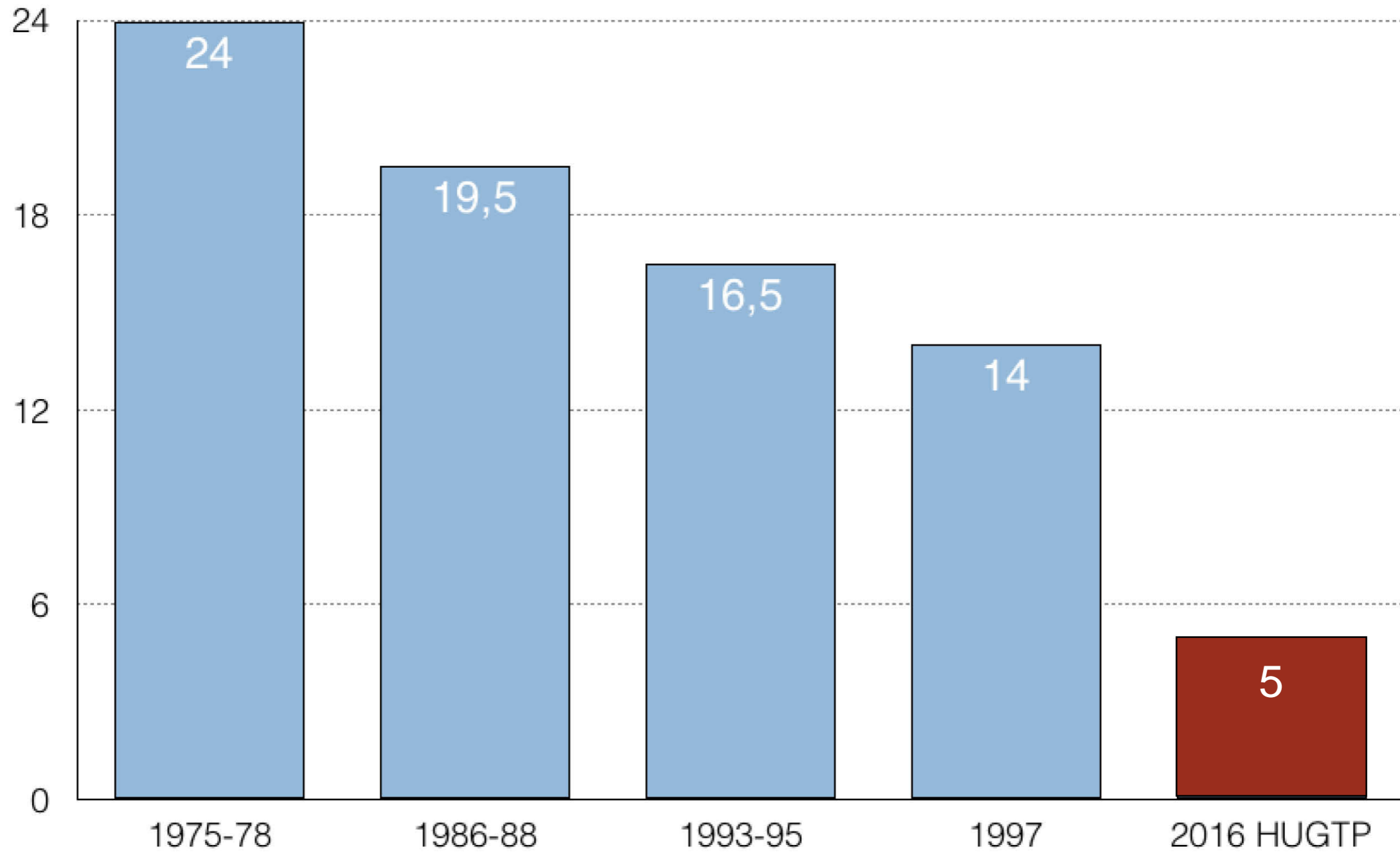


germanstriashospital



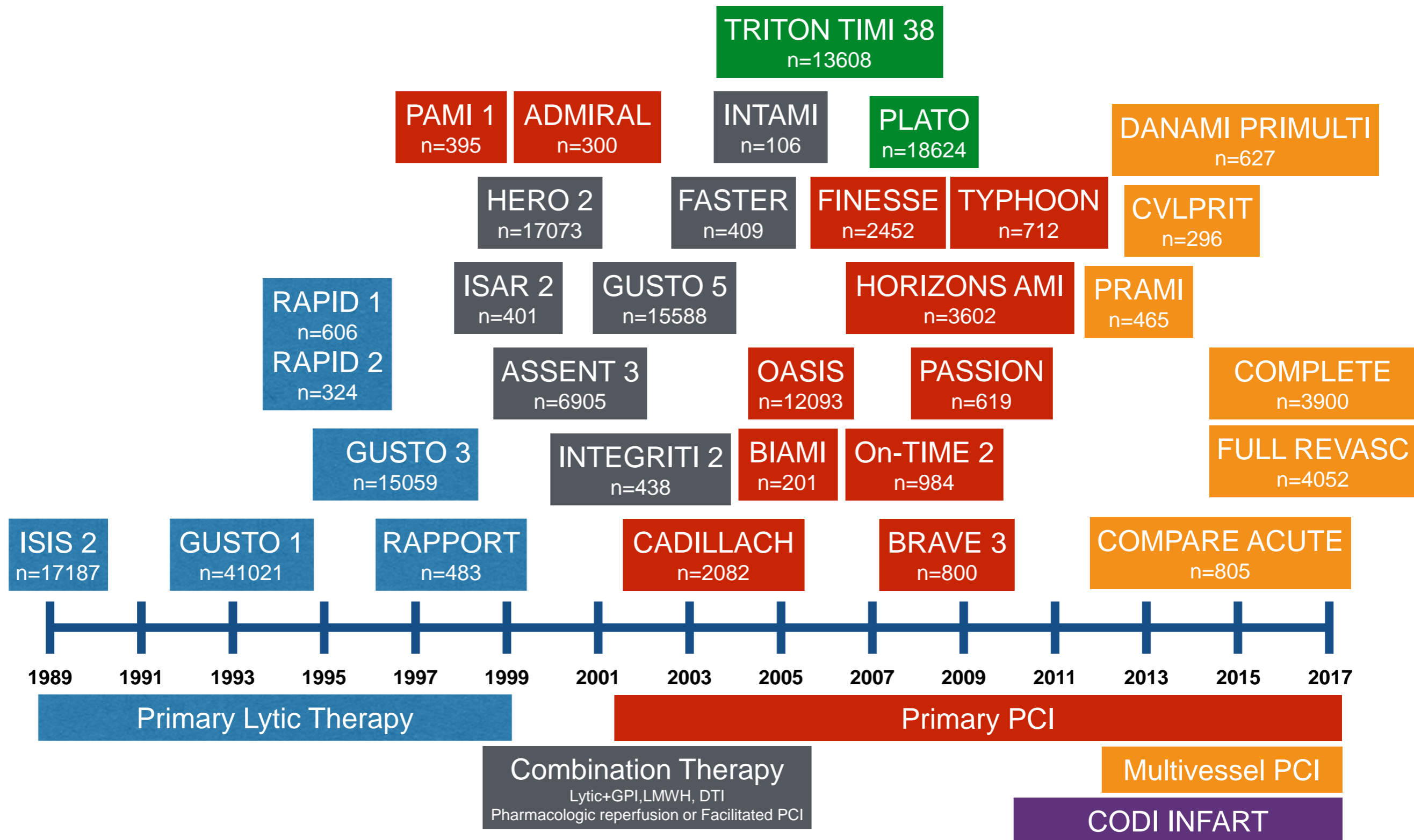
In-Hospital Mortality Evolution in STEMI

70s  2017



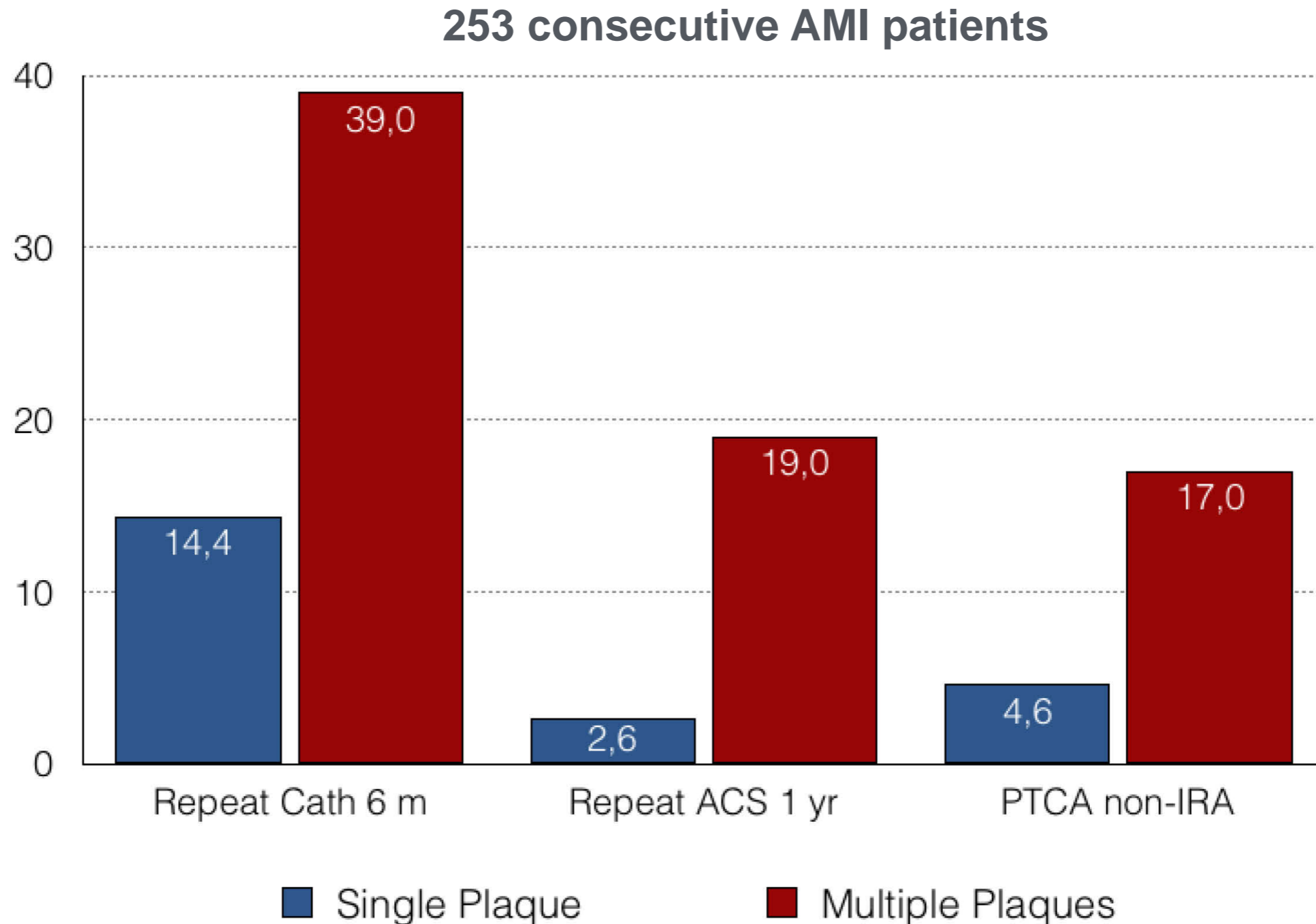
Evolution of STEMI Patient Management

STEMI management has evolved over the past 3 decades based on new clinical data involving technologic and pharmacologic advances



Multiple Coronary Plaques in Patients with STEMI

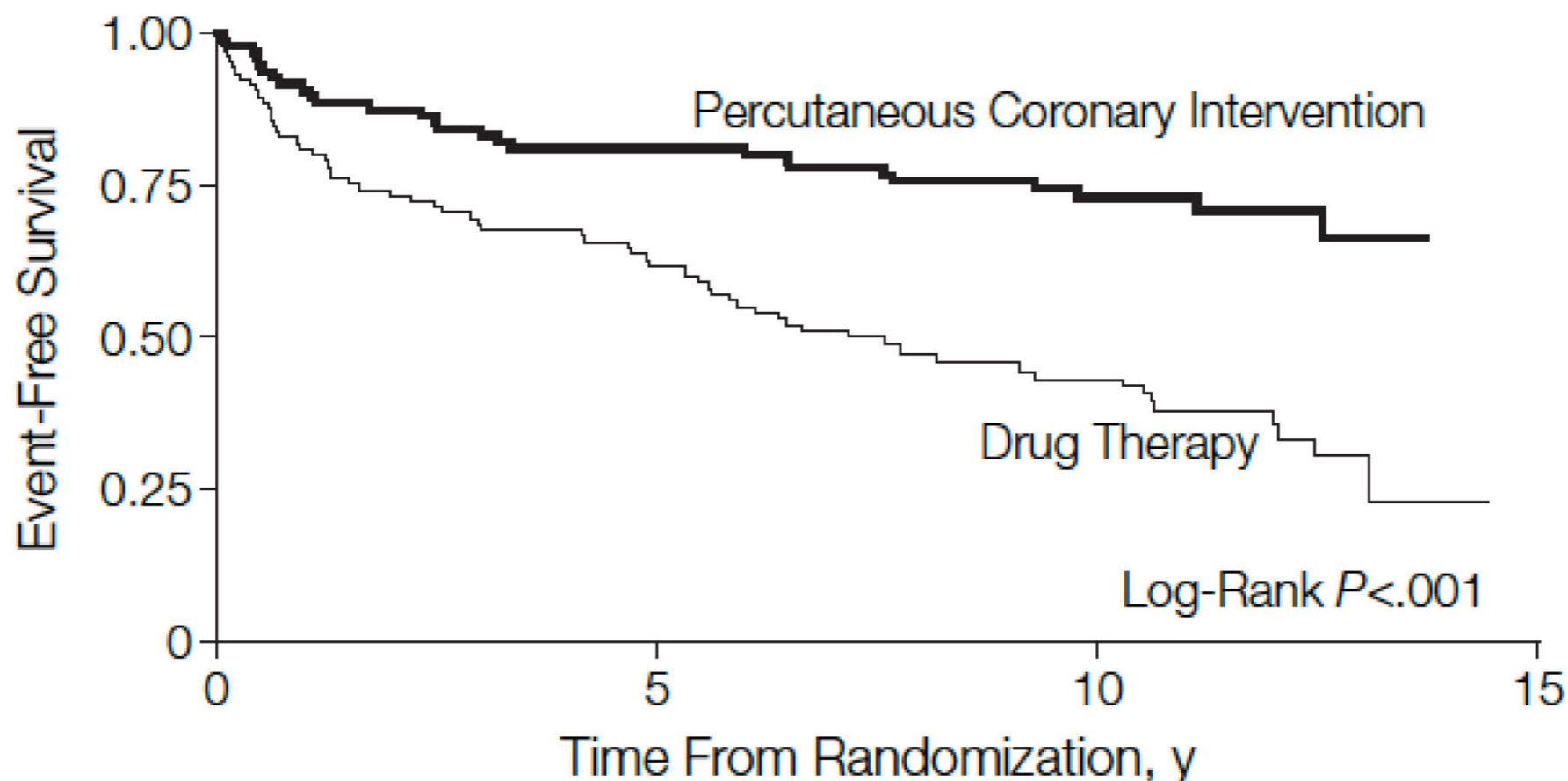
Clinical Outcomes of Patients with Acute Myocardial Infarction and Single or Multiple Complex Coronary Plaques



Complex Coronary Plaques (Thrombus, Ulceration, Plaque Irregularity, Impaired Flow)

Effect of PCI in Silent Ischemia After Myocardial Infarction

Among patients with recent MI and silent myocardial ischemia verified by stress imaging, PCI compared with anti-ischemic drug therapy reduced the long-term risk of MACE



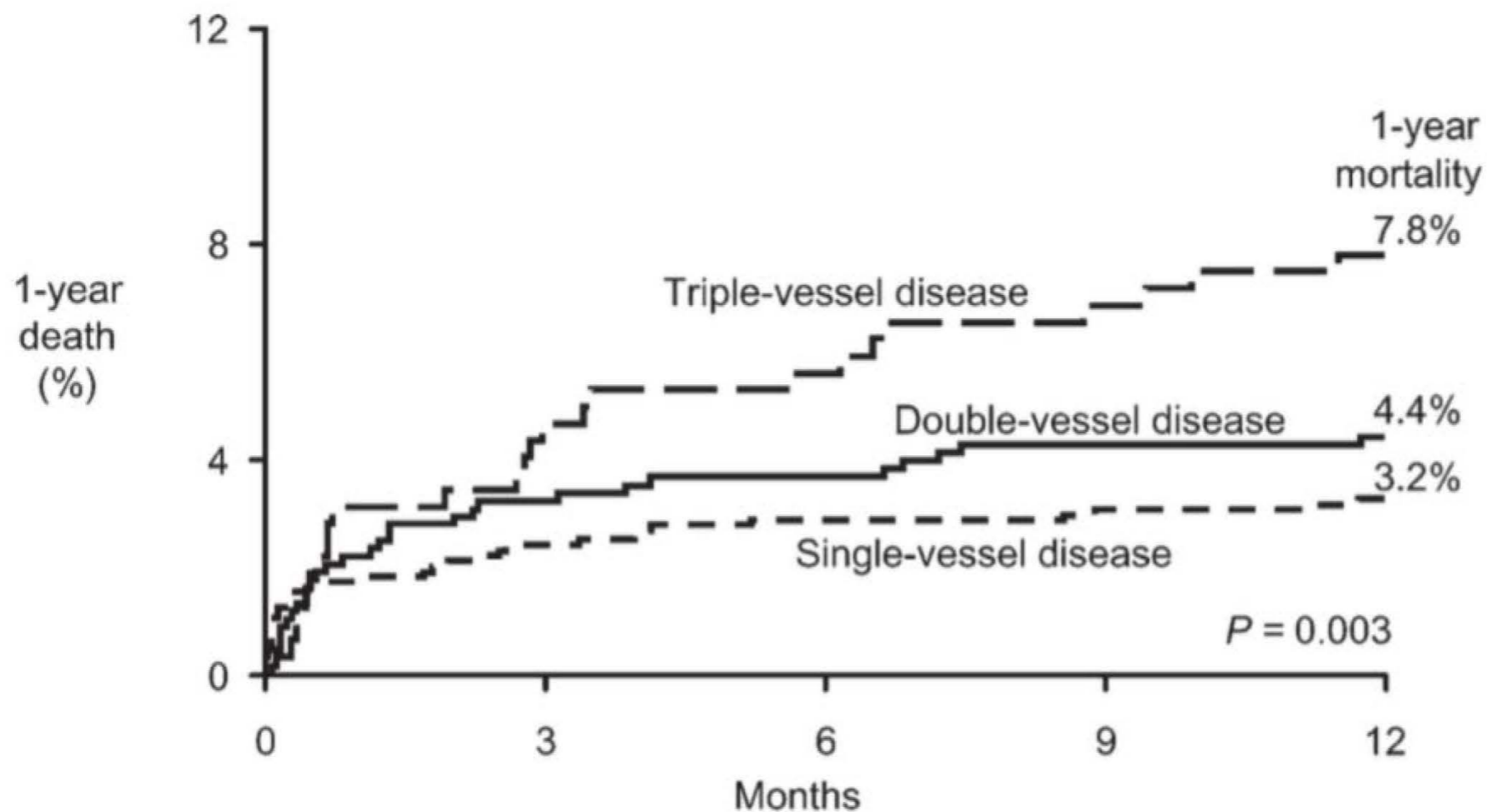
Cardiac death 0,3% vs 2,1% (HR 0,19 [0,05-0,67] p=0,01)
Non-Fatal Recurrent MI 1,2% vs 4,7% (HR 0,31 [0,15-0,65] p=0,002)

Cumulative Incidence of Death According to Number of Vessels

CADILLAC Trial

Cumulative incidence of death according to the presence of single-, double-, or triple-vessel disease

2802 patients enrolled in CADILLAC Trial

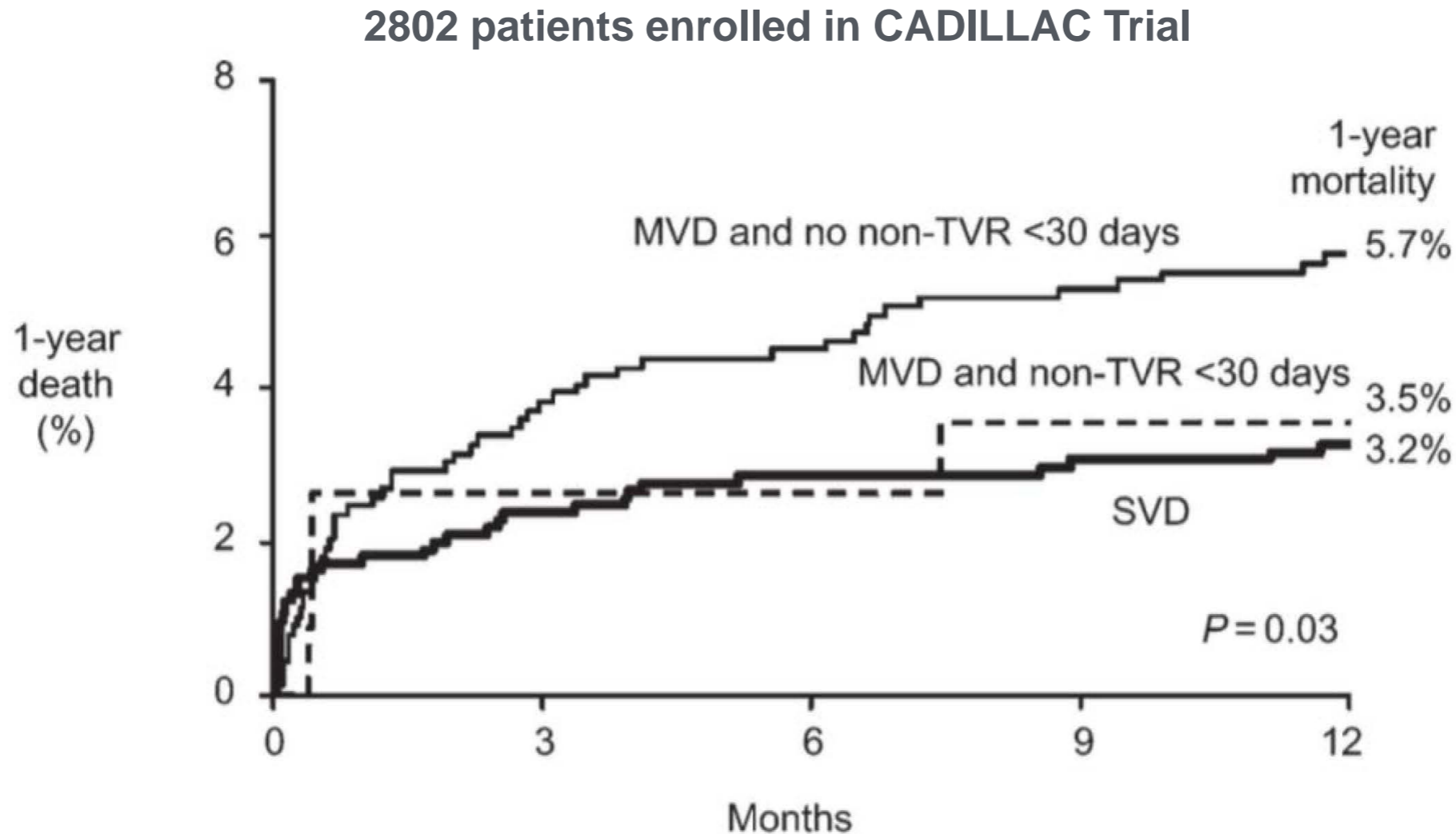


The presence of significant concomitant CAD in vessels remote from the IRA should be recognized as a major adverse prognostic factor in patients with STEMI

Cumulative Incidence of Death According to Number of Vessels

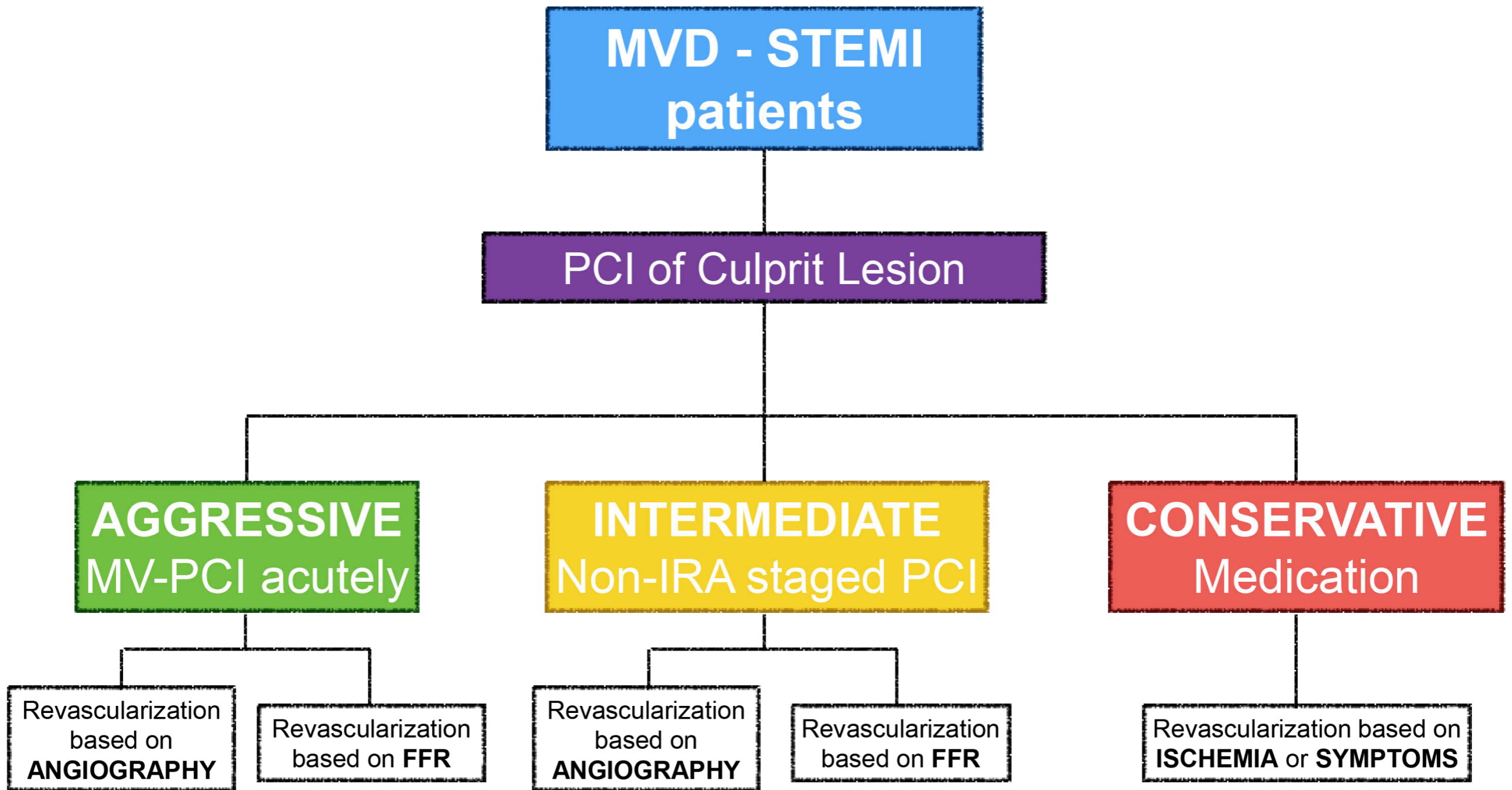
CADILLAC Trial

Cumulative incidence of death in patients with MVD stratified according to whether or not subsequent revascularization was performed within 30 days



Greater survival was evident in patients with multivessel disease in whom revascularization of remote non-infarct-artery-related disease was subsequently performed probably related to deleterious effects of plaque burden and diffuse ischaemia

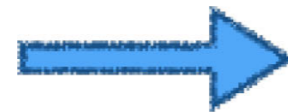
Treatment Strategies in Patients with STEMI and Multivessel Disease



Randomized Trials of Multivessel PCI in STEMI



2013



2017

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Preventive Angioplasty in Myocardial Infarction

David S. Wald, M.D., Joan K. Morris, Ph.D., Nicholas J. Wald, F.R.S., Alexander J. Chase, M.B., B.S., Ph.D., Richard J. Edwards, M.D., Liam O. Hughes, M.D., Colin Berry, M.B., Ch.B., Ph.D., and Keith G. Oldroyd, M.D., for the PRAMI Investigators*

Randomized Trial of Complete Versus Lesion-Only Revascularization in Patients Undergoing Primary Percutaneous Coronary Intervention for STEMI and Multivessel Disease

The CvLPRIT Trial

Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3—PRIMULTI): an open-label, randomised controlled trial

Thomas Engström, Henning Kelbæk, Steffen Helqvist, Dan Eik Højsten, Lene Kløvgaard, Lene Holmvang, Erik Jørgensen, Frants Pedersen, Kari Saunamäki, Peter Clemmensen, Ole De Backer, Jan Ravkilde, Hans-Henrik Tilsted, Anton Boel Villadsen, Jens Aarøe, Svend Eggert Jensen, Bent Raungaard, Lars Køber, for the DANAMI-3—PRIMULTI Investigators*



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Fractional Flow Reserve-Guided Multivessel Angioplasty in Myocardial Infarction

Pieter C. Smits, M.D., Ph.D., Mohamed Abdel-Wahab, M.D., Franz-Josef Neumann, M.D., Bianca M. Boxma-de Klerk, Ph.D., Ketil Lunde, M.D., Carl E. Schotborgh, M.D., Zsolt Piroth, M.D., David Horak, M.D., Adrian Włodarczak, M.D., Paul J. Ong, M.D., Rainer Hambrecht, M.D., Oskar Angerås, M.D., Gert Richardt, M.D., Ph.D., and Elmira Omerovic, M.D., for the Compare-Acute Investigators*



Randomized Trials of Multivessel PCI in STEMI

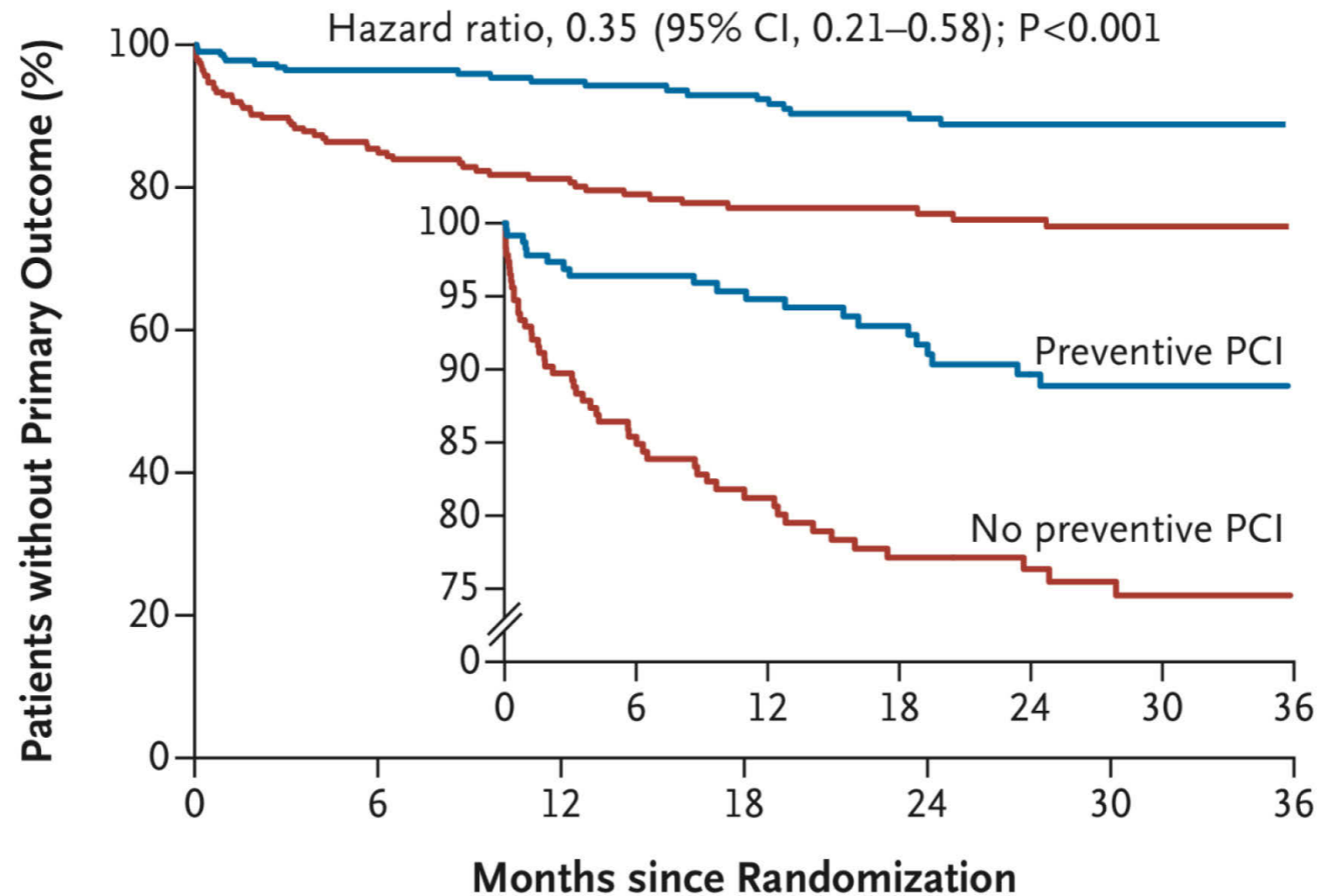
PRAMI Trial

465 patients with STEMI and MVD*, after successful IRA PCI

Preventive Multivessel PCI (n=234)

No preventive PCI (n=231)
(subsequent PCI only recommended for refractory angina with objective evidence of ischemia)

*Angio stenosis >50%



Primary Outcome: death from cardiac causes, non-fatal MI, refractory angina

Randomized Trials of Multivessel PCI in STEMI

PRAMI Trial

The results were considered conclusive by the data and safety monitoring committee, which recommended that the trial be stopped early

Table 3. Prespecified Clinical Outcomes.*

Outcome	Preventive PCI (N = 234) <i>no. of events</i>	No Preventive PCI (N = 231) <i>no. of events</i>	Hazard Ratio (95% CI)	P Value
Primary outcome				
Death from cardiac causes, nonfatal myocardial infarction, or refractory angina†	21	53	0.35 (0.21–0.58)	<0.001
Death from cardiac causes or nonfatal myocardial infarction†	11	27	0.36 (0.18–0.73)	0.004
Death from cardiac causes	4	10	0.34 (0.11–1.08)	0.07
Nonfatal myocardial infarction	7	20	0.32 (0.13–0.75)	0.009
Refractory angina	12	30	0.35 (0.18–0.69)	0.002
Secondary outcomes				
Death from noncardiac causes	8	6	1.10 (0.38–3.18)	0.86
Repeat revascularization	16	46	0.30 (0.17–0.56)	<0.001

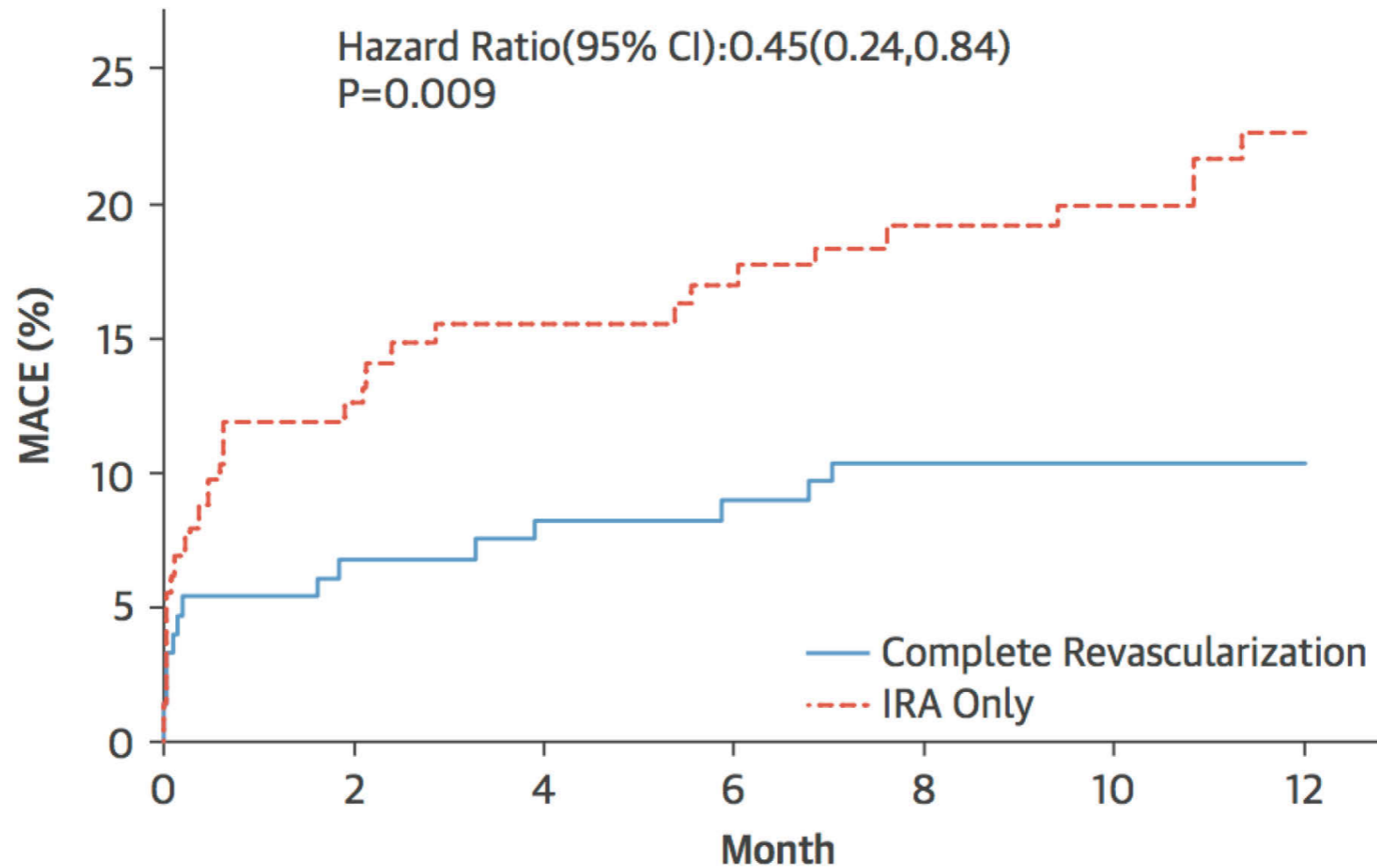
Preventive PCI in noninfarct coronary arteries with major stenoses significantly reduced the risk of adverse CV events, as compared with PCI limited to the infarct artery

Randomized Trials of Multivessel PCI in STEMI

CvLPRIT Trial

296 patients with STEMI and MVD*, after successful IRA PCI	Preventive Multivessel PCI (n=150)
	No preventive PCI (n=146) (subsequent PCI only recommended for refractory angina with objective evidence of ischemia)

*Angio stenosis >70% in 1 view or >50% in 2 views



Primary Outcome: all-cause death, recurrent MI, HF, ischemia-driven revascularization

Randomized Trials of Multivessel PCI in STEMI

CvLPRIT Trial

Clinical Outcomes at 12 months

Event	Preventive PCI N = 150 (%)	NO Preventive PCI N = 146 (%)	HR (95%)	P
Total MACE	15 (10.0)	31 (21.2)	0.45 (0.24, 0.84)	0.009
Mortality	2 (1.3)	6 (4.1)	0.32 (0.06, 1.60)	0.14
Recurrent MI	2 (1.3)	4 (2.7)	0.48 (0.09, 2.62)	0.39
Heart Failure	4 (2.7)	9 (6.2)	0.43 (0.13, 1.39)	0.14
Repeat Revascularization	7 (4.7)	12 (8.2)	0.55 (0.22, 1.39)	0.2

Index admission complete revascularization significantly lowered the rate of the composite primary endpoint at 12 months compared with treating only the IRA

Randomized Trials of Multivessel PCI in STEMI

DANAMI 3 - PRIMULTI

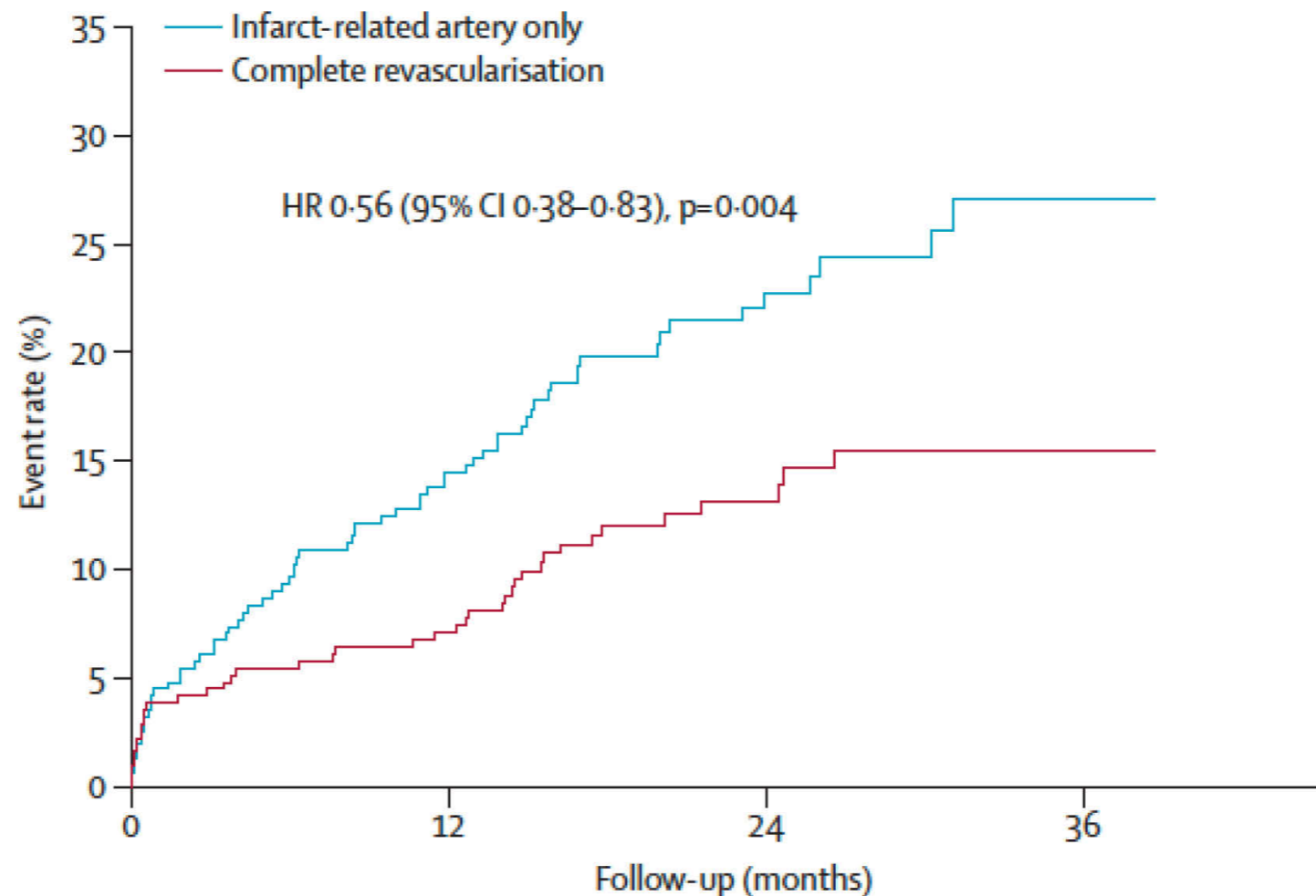
627 patients with STEMI and MVD*, after successful IRA PCI

Staged FFR-guided** Multivessel PCI (n=314)

No further PCI (n=313)
(subsequent PCI only recommended for angina with objective evidence of ischemia)

*Angio stenosis >50%

**FFR>0,80 in 31% of patients



Primary Outcome: all-cause death, ischemia-driven non-target vessel revascularization

Randomized Trials of Multivessel PCI in STEMI

DANAMI 3 - PRIMULTI

Clinical Outcomes at 12 months

	Infarct-related artery only (n=313)	Complete revascularisation (n=314)	Hazard ratio (95% CI)	p	
Primary endpoint*	68 (22%)	40 (13%)	0.56 (0.38-0.83)	0.004	
All-cause mortality	11 (4%)	15 (5%)	1.40 (0.63-3.00)	0.43	
Non-fatal reinfarction	16 (5%)	15 (5%)	0.94 (0.47-1.90)	0.87	
Ischaemia-driven revascularisation	52 (17%)	17 (5%)	0.31 (0.18-0.53)	<0.0001	
Secondary endpoints					
Cardiac death	9 (3%)	5 (2%)	0.56 (0.19-1.70)	0.29	
Cardiac death or non-fatal myocardial infarction	25 (8%)	20 (6%)	0.80 (0.45-1.45)	0.47	
Urgent percutaneous coronary intervention	18 (6%)	7 (2%)†	0.38 (0.16-0.92)	0.03	
Non-urgent percutaneous coronary intervention	27 (9%)	8 (3%)	0.29 (0.13-0.63)	0.002	
Unplanned coronary-artery bypass graft surgery	7 (2%)	3 (1%)	0.43 (0.11-1.70)	0.22	
			Infarct-related artery only (n=313)	Complete revascularisation (n=314)	p
Periprocedural myocardial infarction			0	2 (1%)	0.2
Bleeding requiring transfusion or surgery			4 (1%)	1 (<1%)	0.2
Contrast-induced nephropathy (>50% rise in plasma creatinine)			7 (2%)	6 (2%)	0.8
Stroke			1 (<1%)	4 (1%)	0.2

Complete revascularisation guided by FFR measurements significantly reduces the risk of future events driven by significantly fewer repeat revascularisations, because all-cause mortality and non-fatal reinfarction did not differ between groups

Randomized Trials of Multivessel PCI in STEMI

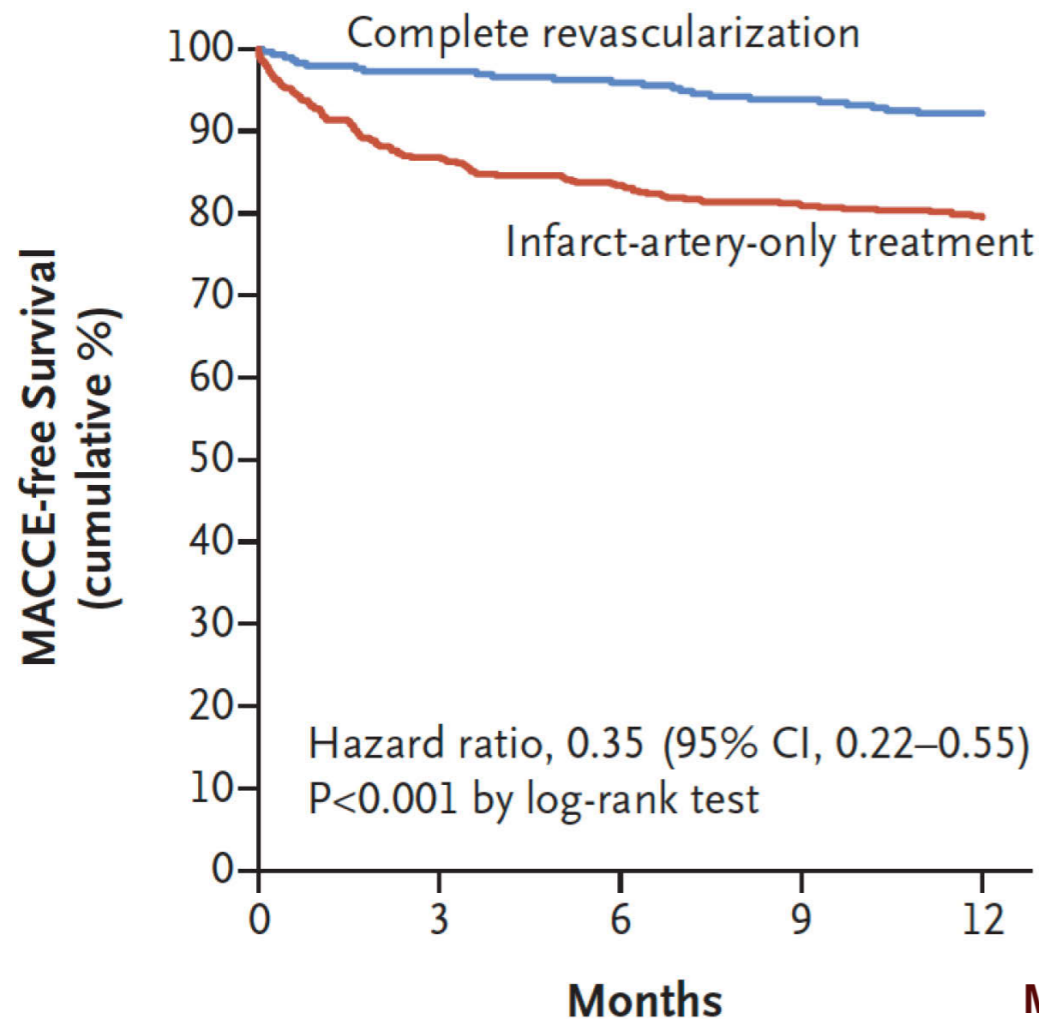
COMPARE ACUTE Trial

885 patients with STEMI and MVD*, after successful IRA PCI

FFR-guided Preventive Multivessel PCI (n=295)

No preventive PCI (n=590)
(subsequent PCI according to ischemia, symptoms or clinical judgement)

*Angio stenosis >50% FFR performed in both groups of treatment



- FFR<0,80 in around 50% of lesions
- In the IRA-PCI, **clinically indicated elective PCI of the N-IRA** (according to ischemia, symptoms or clinical judgement) **within 45 days was not counted as event**
- MV-PCI had N-IRA PCI during index PCI in 83,4%
- DES (EES) in 98,9%

MACCE: all-cause death, recurrent MI, revascularization, cerebrovascular events

59 IRA only PCI patients had N-IRA revascularization within 45 days and were not counted as events

Randomized Trials of Multivessel PCI in STEMI

COMPARE ACUTE Trial

12 months Clinical Outcomes

End Point	Complete Revascularization (N=295)	Infarct-Artery-Only Treatment (N=590)	Hazard Ratio (95% CI)	P Value
	<i>number (percent)</i>			
Primary				
MACCE*	23 (7.8)	121 (20.5)	0.35 (0.22–0.55)	<0.001
Death from any cause	4 (1.4)	10 (1.7)	0.80 (0.25–2.56)	0.70
Cardiac event	3 (1.0)	6 (1.0)	1.00 (0.25–4.01)	1.00
Myocardial infarction	7 (2.4)	28 (4.7)	0.50 (0.22–1.13)	0.10
Spontaneous event	5 (1.7)	17 (2.9)	0.59 (0.22–1.59)	0.29
Periprocedural event	2 (0.7)	11 (1.9)	0.36 (0.08–1.64)	0.19
Revascularization	18 (6.1)	103 (17.5)	0.32 (0.20–0.54)	<0.001
PCI	15 (5.1)	98 (16.6)	0.37 (0.24–0.57)	<0.001
Coronary-artery bypass graft	3 (1.0)	5 (0.8)	1.20 (0.29–5.02)	0.80
Cerebrovascular event	0	4 (0.7)	NA	NA

59 patients in the IRA PCI group had elective non-IRA revascularization within 45 days and did not count as event

MACCE: death from any cause, non-fatal AMI, revascularization, cerebrovascular events at 12 months

Randomized Trials of Multivessel PCI in STEMI

Ongoing Big Randomized Trials



COMPLETE TRIAL

Complete vs culprit-only revascularization to treat multivessel disease after primary PCI for STEMI

STEMI with MVD

Staged non-culprit PCI + OMT vs OMT

3900 patients

Enrollment finished
Results in march 2018

Primary outcome: CV death or new MI 1-4 yr

FULL FULL REVASC TRIAL

FFR-guidance for complete non-culprit revascularization

STEMI or high-risk NSTEMI with MVD

FFR-guided PCI of all non-culprit lesions during index hospitalization vs conservative management

4052 patients

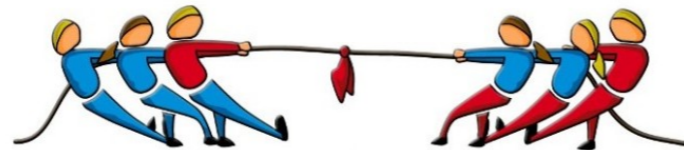
44 patients enrolled on april 28th
Results in october 2019

Primary outcome: all-cause mortality and MI 1 yr

IAM EN MALALTIA MULTIVÀS TRACTAR-HO TOT O NO AGUT O DIFERIT

TRACTAR ALTRES LESIONS QUE LA RESPONSABLE EN LA FASE AGUDA APORTA AVANTATGES

- PART II -



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2014 ESC Myocardial Revascularization Guidelines

Recommendations	Class ^a	Level ^b	Ref ^c
Strategy			
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	234,264–266
Staged revascularization of non-culprit lesions should be considered in STEMI patients with multivessel disease in case of symptoms or ischaemia within days to weeks after primary PCI.	IIa	B	235
Immediate revascularization of significant non-culprit lesions during the same procedure as primary PCI of the culprit vessel may be considered in selected patients.	IIb	B	267
In patients with continuing ischaemia and in whom PCI of the infarct-related artery cannot be performed, CABG should be considered.	IIa	C	

234. Kornowski (HORIZONS AMI)_JACC 2011
 264. Hannan (New York Registry)_JACC Interv 2010
 265. Toma (APEX AMI)_ Eur Heart J 2010
 266. Vlaar (Meta-Analysis)_J Am Coll Cardiol 2011

235. Politi. Heart 2010

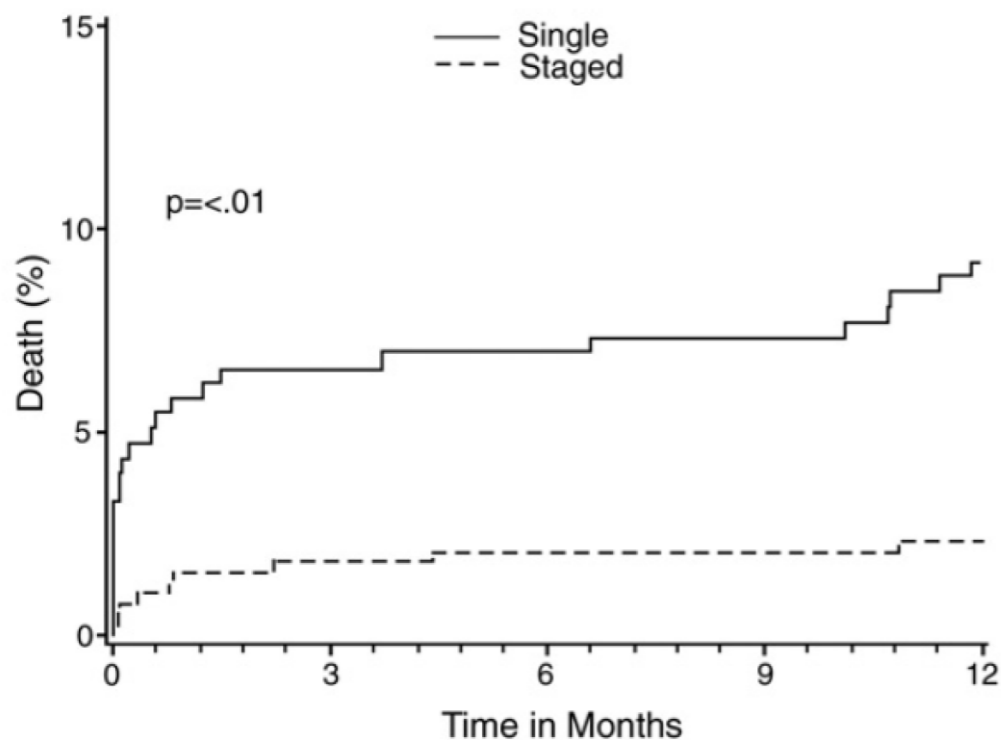
267. Wald. N Engl J Med 2013

HORIZONS AMI Trial

668 of the 3602 STEMI patients enrolled (18.5%) underwent PCI of culprit and nonculprit lesions for multivessel disease

Patients were categorized into a single PCI strategy (n=275) versus staged PCI (n=393)

CONCLUSION: a deferred angioplasty strategy of nonculprit lesions should remain the standard approach in patients with STEMI undergoing primary PCI, as multivessel PCI may be associated with a greater hazard for mortality and stent thrombosis



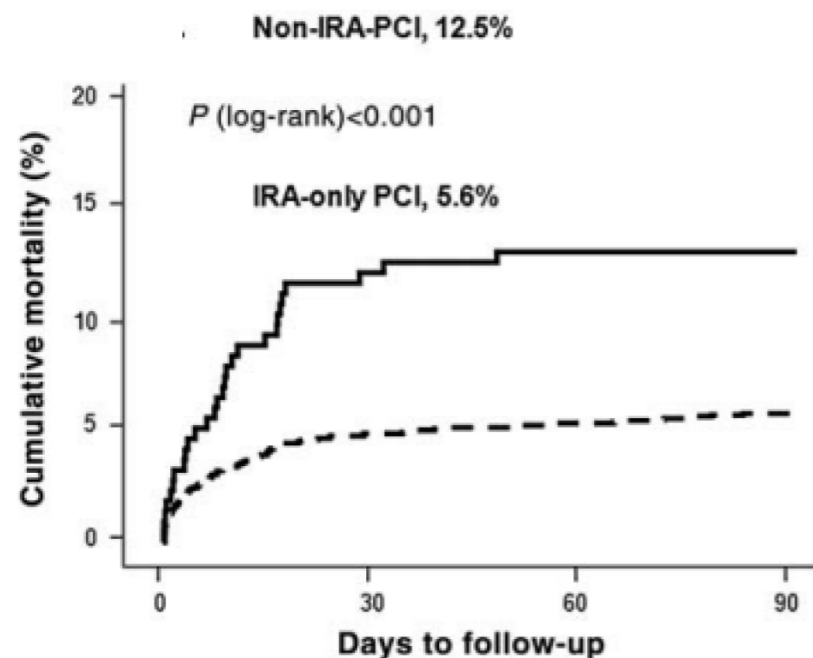
- **Retrospective nonrandomized subanalysis**
- **Specific reason why operator chose a single procedure vs a staged approach was not prospectively collected**
- **Low number of events (31 deaths / 25 cardiac deaths/19 stent thrombosis) -> Multivariate Model Underpowered**
- **BMS vs Taxus Express**

APEX AMI Trial

2201 of the 5373 STEMI patients enrolled (18.5%) underwent PCI of culprit and nonculprit lesions for multivessel disease

Patients were categorized into a single PCI strategy (n =217) versus no PCI (n =1984)

CONCLUSION: Non-culprit coronary interventions were performed at the time of primary PCI in 10% of MVD patients and were significantly associated with increased mortality. Our data support current guideline recommendations discouraging the performance of such procedures in stable primary PCI patients.



- Retrospective nonrandomized subanalysis
- Specific reason why operator chose a single procedure vs a staged approach was not prospectively collected
- Low number of events (135 deaths)-> Multivariate Model Underpowered
- Only 38% DES (1st generation)
- Lack of information on outcomes in patients not treated at the index procedure

2014 EHJ Revascularization Guidelines

Hannan et al, JACC Intv

New York State Registry (3521 patients) 2003-2006

CONCLUSION: Our findings support the ACC/AHA recommendation that culprit vessel PCI be used for STEMI patients with multivessel disease at the time of the index PCI when patients are not hemodynamically compromised. However, staged PCI within 60 days after the index procedure, including during the index admission, is associated with risk-adjusted mortality rates that are comparable with the rate for culprit vessel PCI alone.

Outcome by Subgroup	Culprit Vessel Revascularization at the Time of PPCI	Multivessel Revascularization at the Time of PPCI	Percentage Difference	p Value
All patients	n = 503	n = 503		
Death, %				
In-hospital	2.0	3.4	1.4	0.14
12 months	5.5	7.1	1.6	0.23
24 months	6.6	8.6	2.0	0.17
42 months	10.8	11.8	1.0	0.23
Patients without hemodynamic instability, LVEF <20%, malignant ventricular arrhythmia	n = 458	n = 458		
Death, %				
In-hospital	0.9	2.4	1.5	0.04
12 months	4.2	5.8	1.6	0.13
24 months	4.9	7.2	2.3	0.07
42 months	6.7	10.4	3.7	0.08

Median follow-up – 22.54 months.
LVEF – left ventricular ejection fraction; PPCI – primary percutaneous coronary intervention; STEMI – ST-segment elevation myocardial infarction.

- **Observational study (selection bias)**
- **No information about medical treatment**
- **No information about DES use, but 1st generation**
- **Very low In-hospital mortality in the culprit-only group (0,9%!!)**

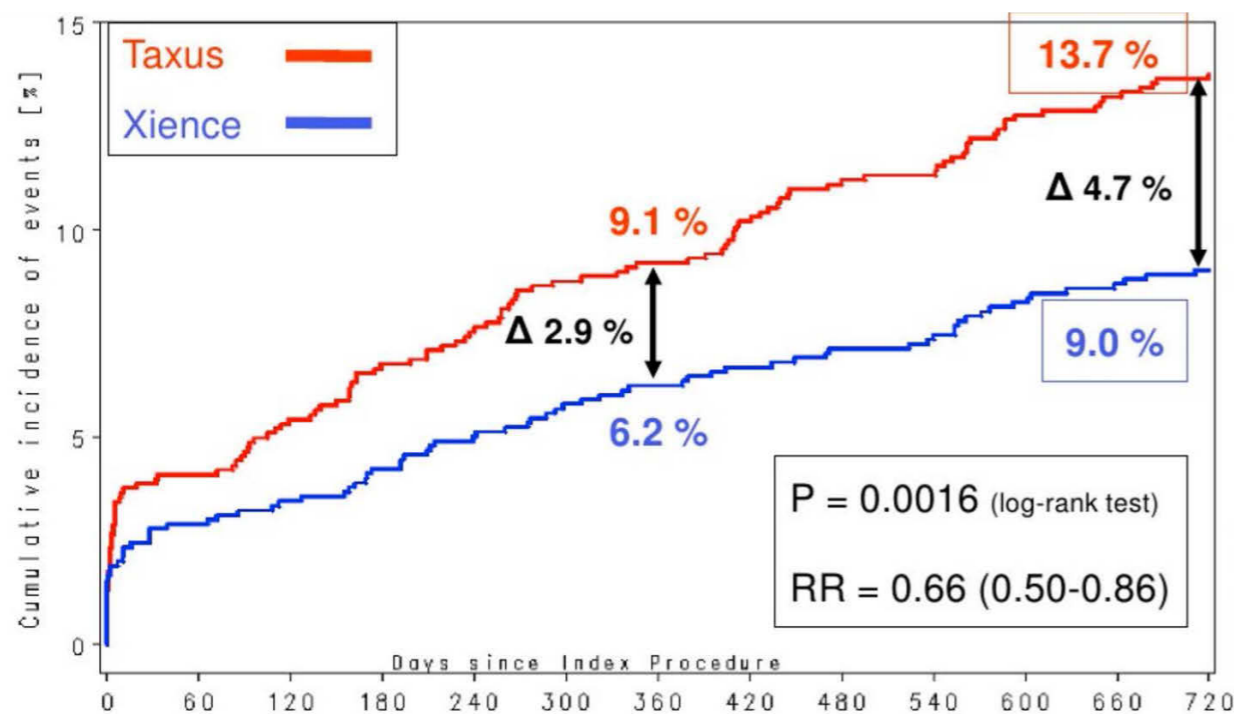
Randomized Trials of Multivessel PCI in STEMI

First Generation vs Contemporary DES

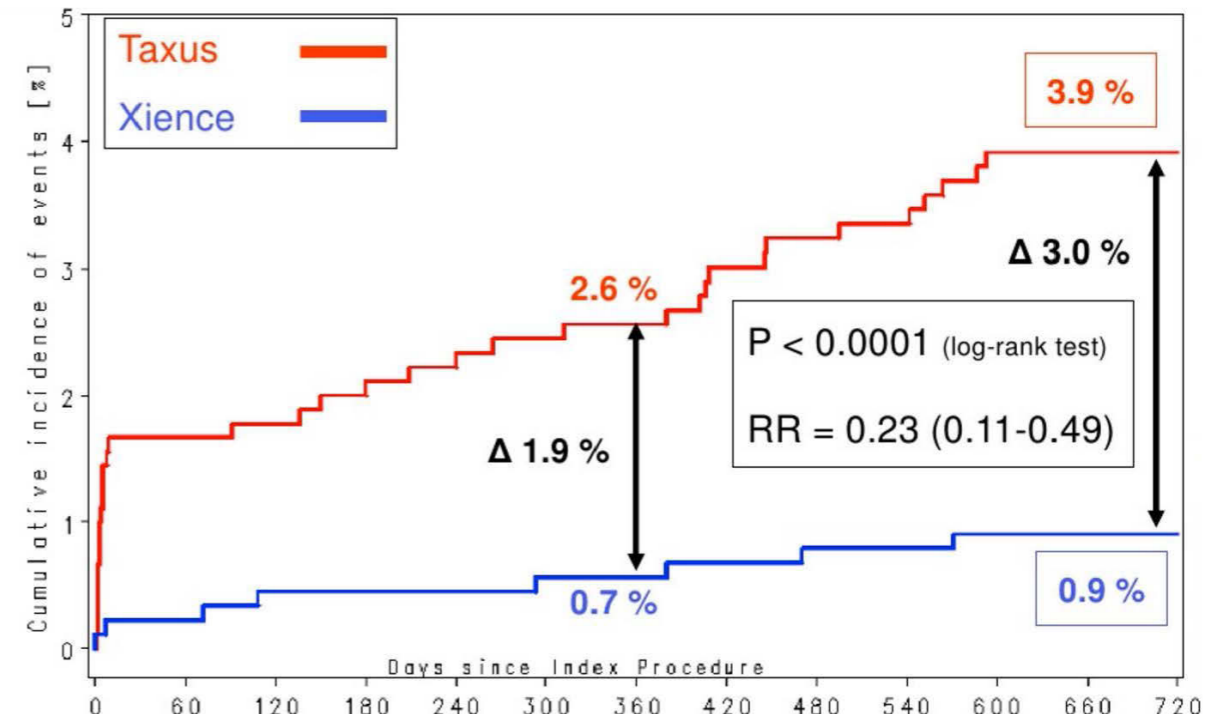
COMPARE Trial

2-Year Follow-Up of a Randomized Controlled Trial of Everolimus- and Paclitaxel-Eluting Stents for Coronary Revascularization in Daily Practice

MACE (all death, non-fatal MI, TVR)

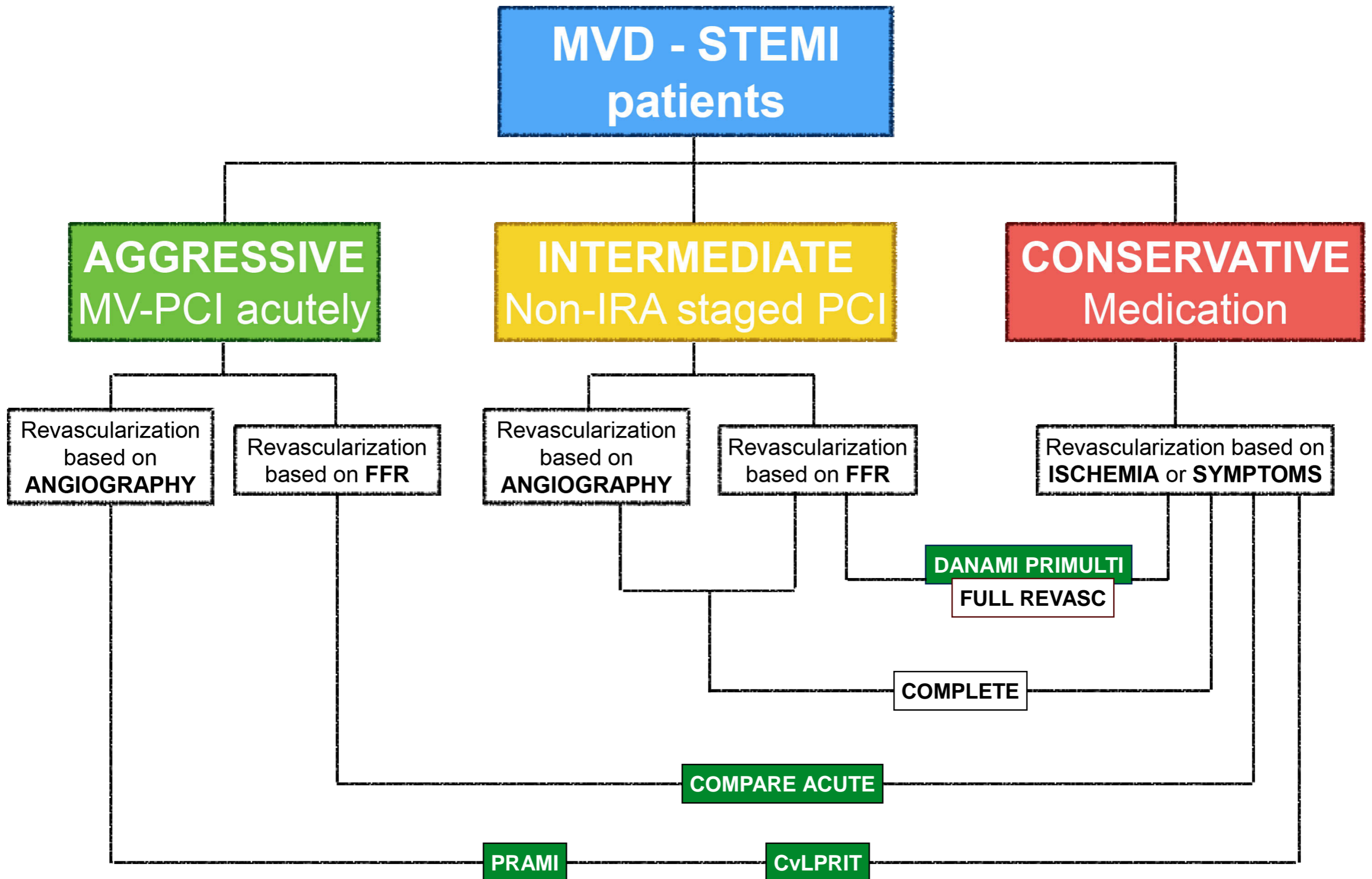


STENT THROMBOSIS



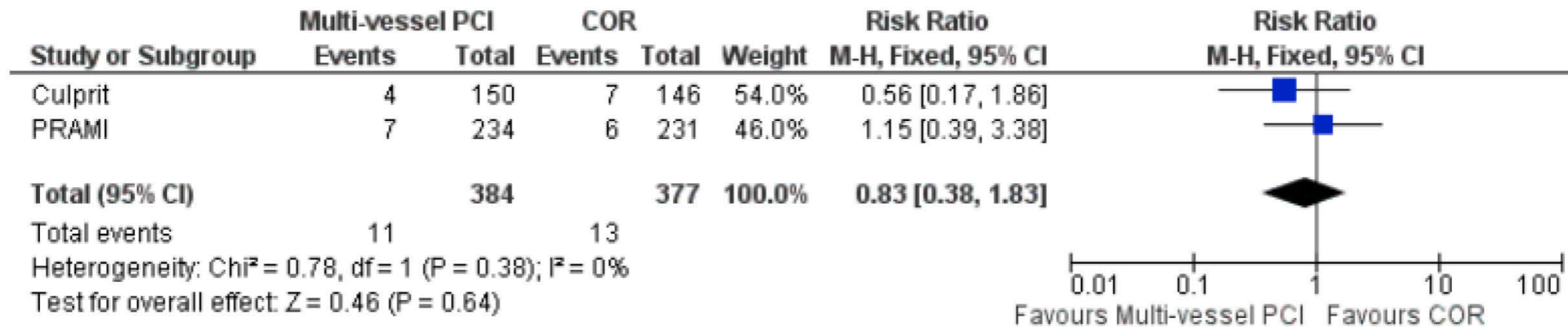
The substantial clinical benefit of the EES over the PES with regard to measures of both safety and efficacy is maintained at 2 years in real-life practice with an increasing benefit in terms of safety and efficacy between 1 year and 2 years

Treatment Strategies in Patients with STEMI and Multivessel Disease

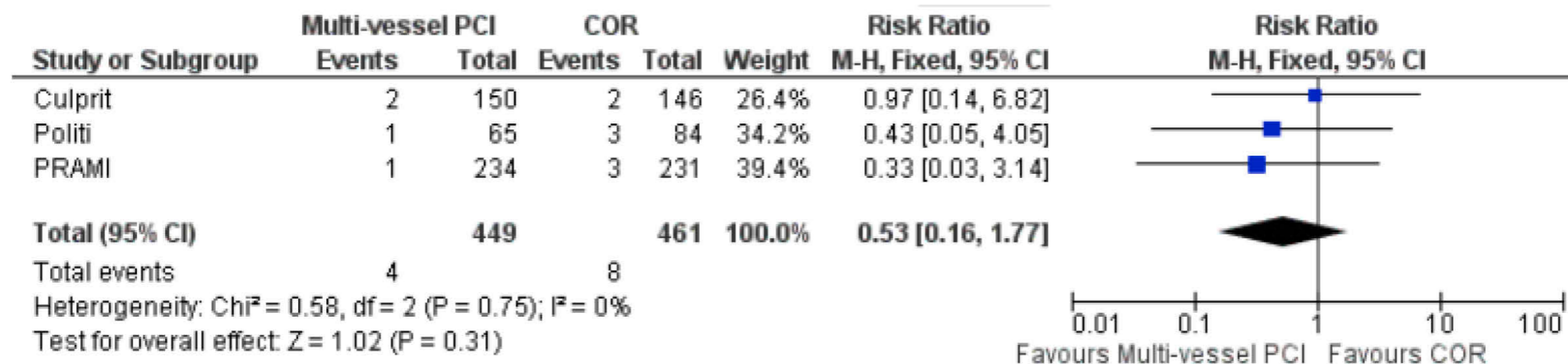


Meta-Analysis of RCT Comparing Multivessel vs Culprit Only PCI

Risk of Major Bleeding in Follow-up

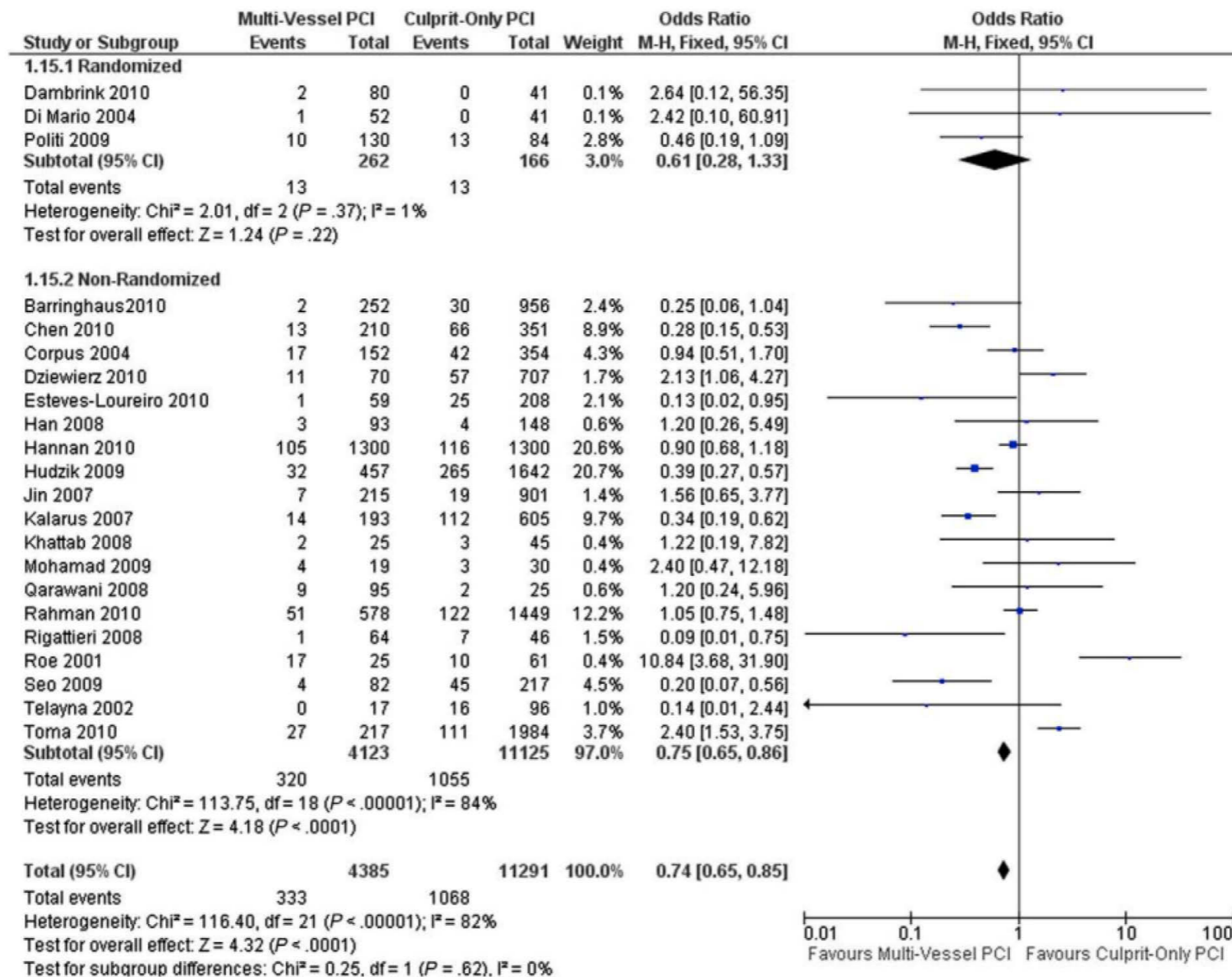


Risk of Contrast-Induced Nephropathy in Follow-up



Meta-Analysis of RCT and nonRCT Comparing Multivessel vs Culprit Only PCI

Long Term Mortality Stratified by Study Method



Multivessel PCI associated with lower long term mortality
OR 0,74 (0,65-0,85) p<0,001

2014 ESC Myocardial Revascularization Guidelines






Recommendations	Class ^a	Level ^b	Ref ^c
Strategy			
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	234,264–266
Staged revascularization of non-culprit lesions should be considered in STEMI patients with multivessel disease in case of symptoms or ischaemia within days to weeks after primary PCI.	IIa	B	235
Immediate revascularization of significant non-culprit lesions during the same procedure as primary PCI of the culprit vessel may be considered in selected patients.	IIb	B	267
In patients with continuing ischaemia and in whom PCI of the infarct-related artery cannot be performed, CABG should be considered.	IIa	C	

234. Kornowski (HORIZONS AMI)_JACC 2011
 264. Hannan (New York Registry)_JACC Interv 2010
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 266. Vlaar (Meta-Analysis)_J Am Coll Cardiol 2011

235. Politi. Heart 2010

267. Wald. N Engl J Med 2013

2017 SCC Myocardial Revascularization Guidelines?

Recommendations	Class ^a	Level ^b	Ref ^c
Strategy			
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.	 IIb	B	234,264–266
Staged revascularization of non-culprit lesions should be considered in STEMI patients with multivessel disease in case of symptoms or ischaemia within days to weeks after primary PCI.	 I	 A	235
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PRAMI Trial. N Engl J Med 2013
 CvLPRIT Trial. J Am Coll Cardio 2014
 DANAMI PRIMULTI. Lancet 2015
 COMPARE ACUTE. N Engl J Med 2017

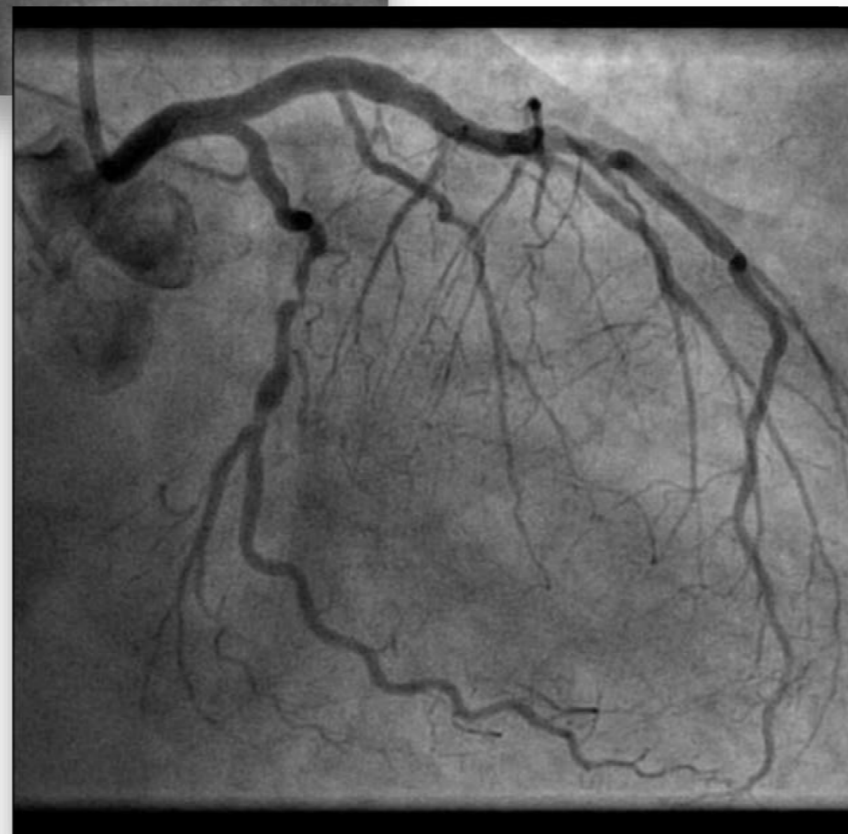
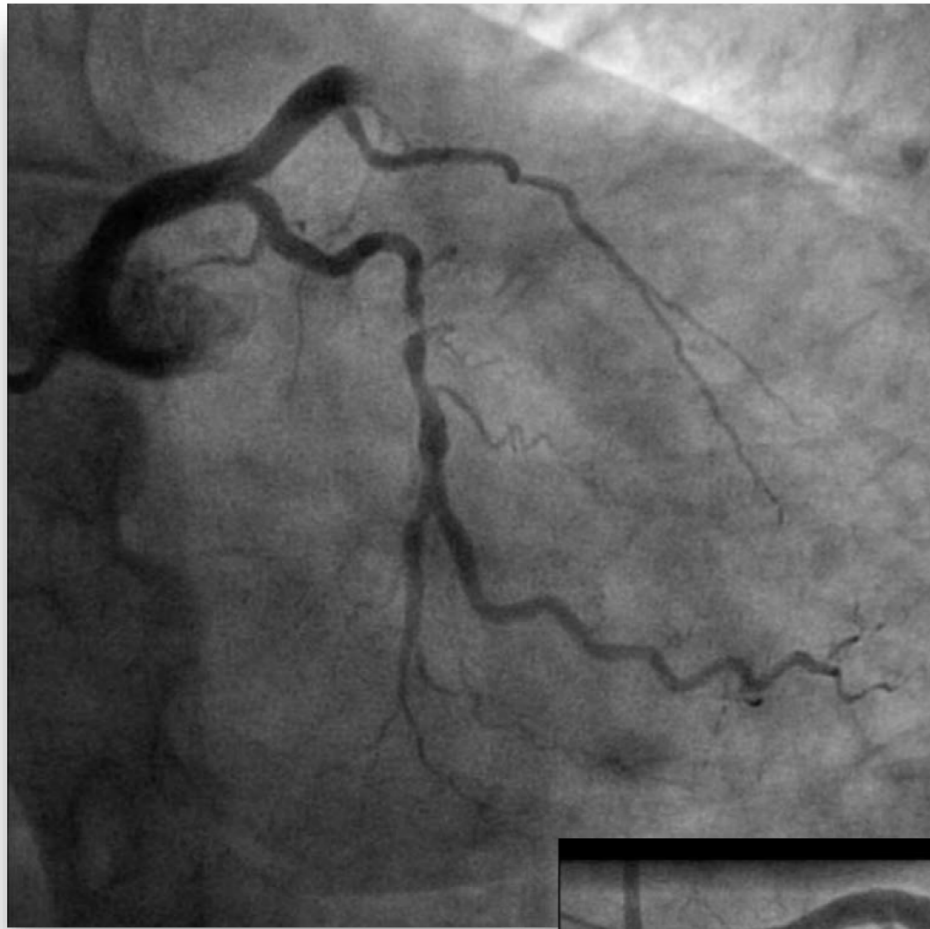


Multivessel revascularization seems the best option in patients with STEMI...



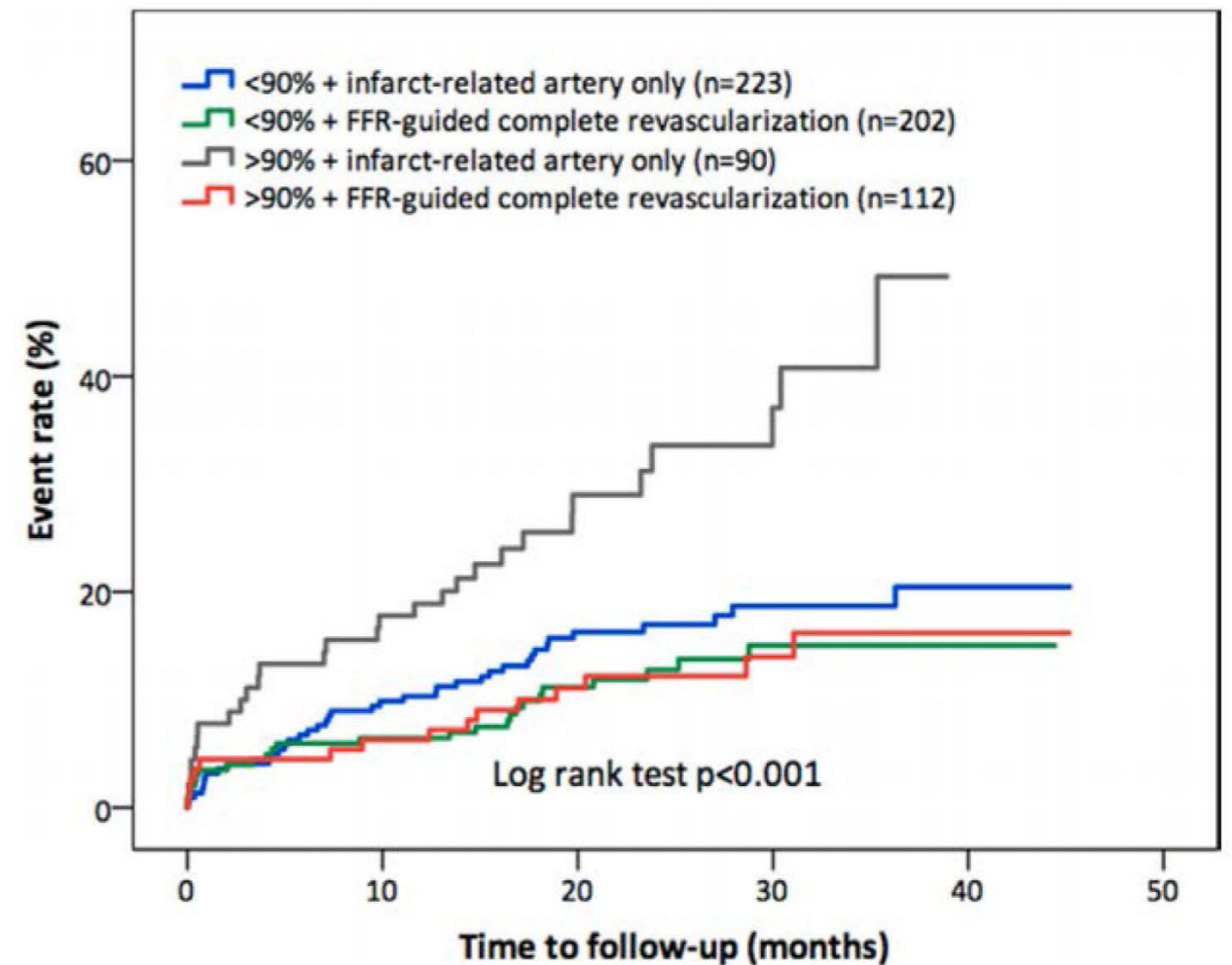
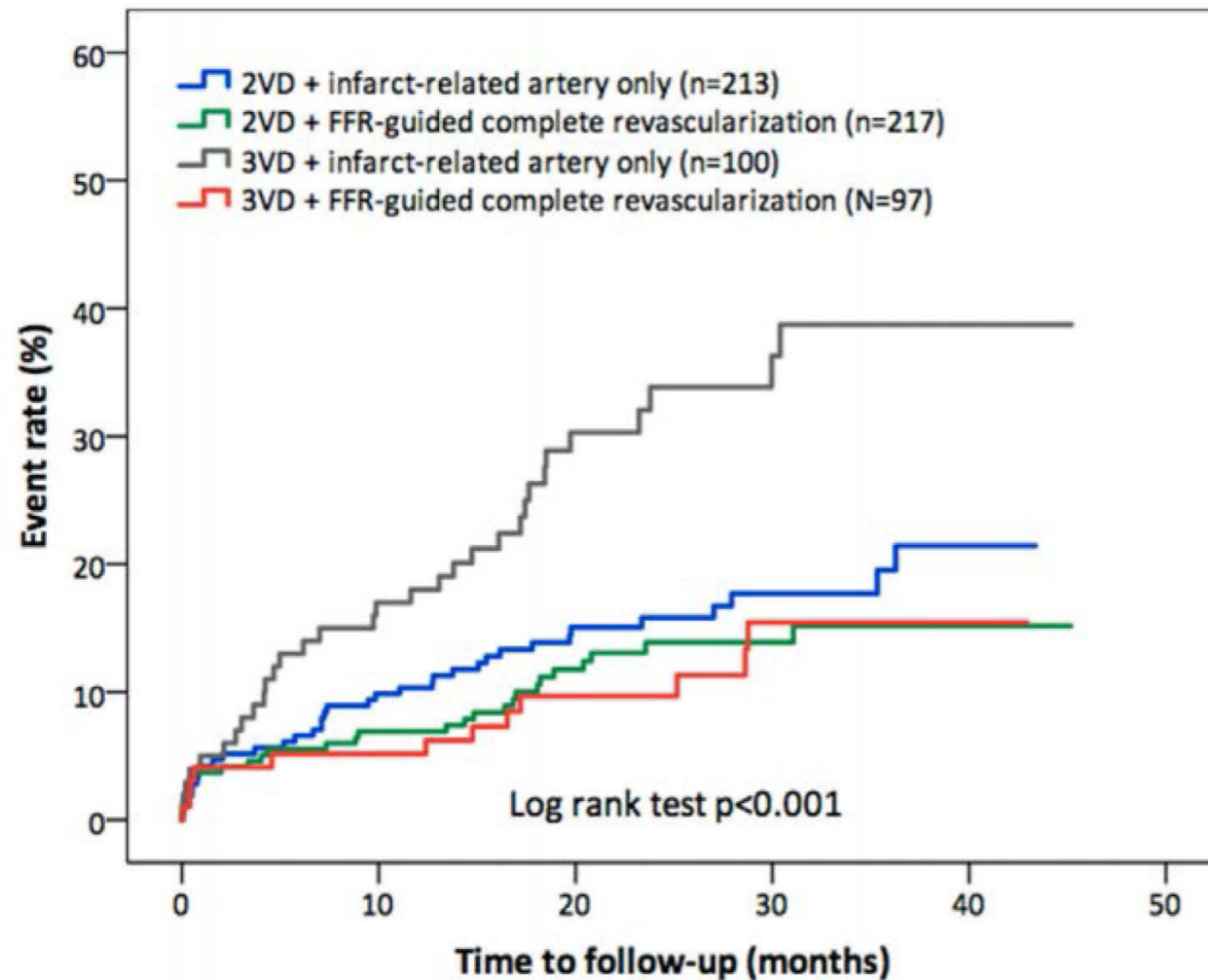
...but should we do it during the index procedure?
(acute multivessel PCI)

Multivessel PCI during the Index Procedure



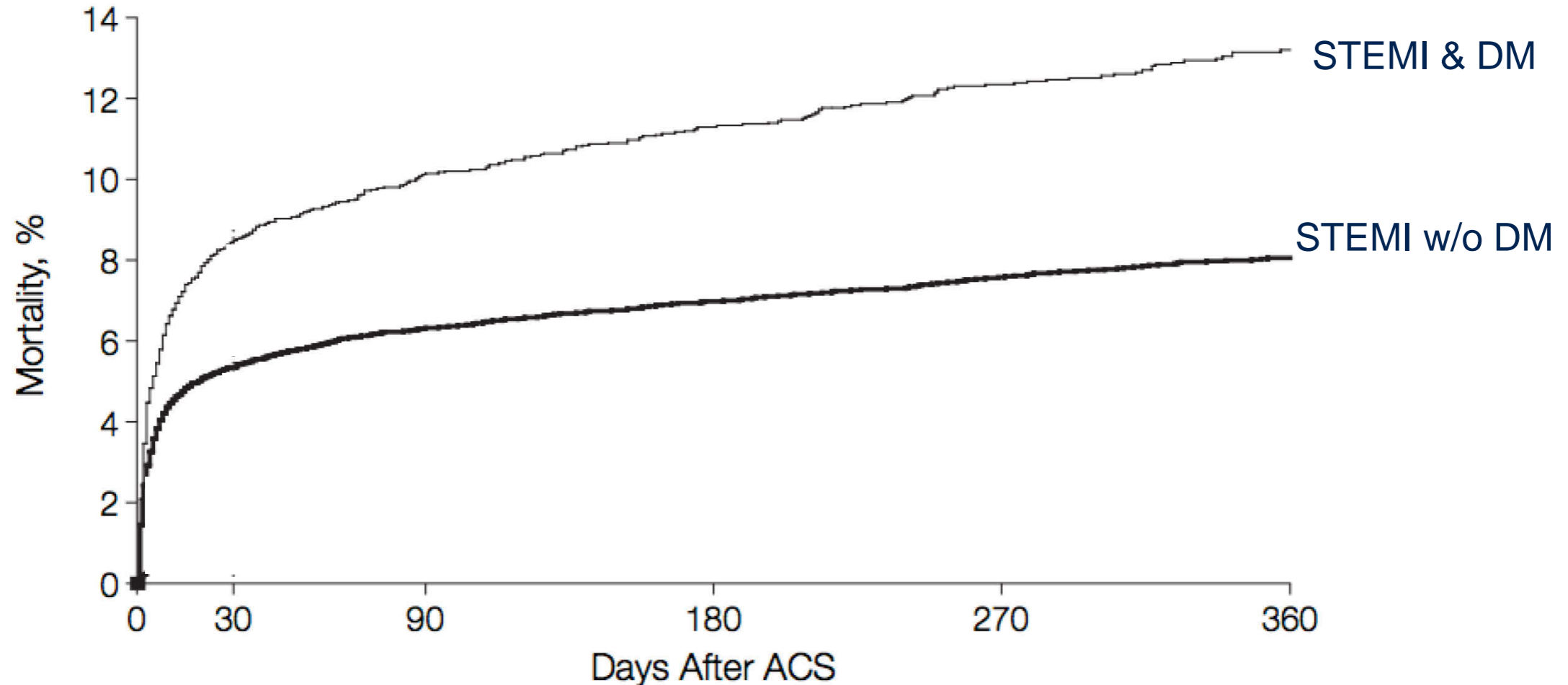
Impact of the Disease Severity on Outcome

The benefit from FFR-guided complete revascularization was dependent in the presence of 3-vessel disease and noninfarct diameter stenosis >90% (particularly pronounced in patients with both these angiographic characteristics)



Impact of the Diabetes on Outcome in STEMI

Diabetes confers a significant adverse prognosis, which highlights the importance of aggressive strategies to manage this high-risk population



Diabetes at presentation was associated with significantly higher mortality 1 year after STEMI (HR, 1.22; 95% CI, 1.08- 1.38)

Current Evidence of Multivessel vs Culprit Lesion PCI in STEMI complicated with Cardiogenic Shock

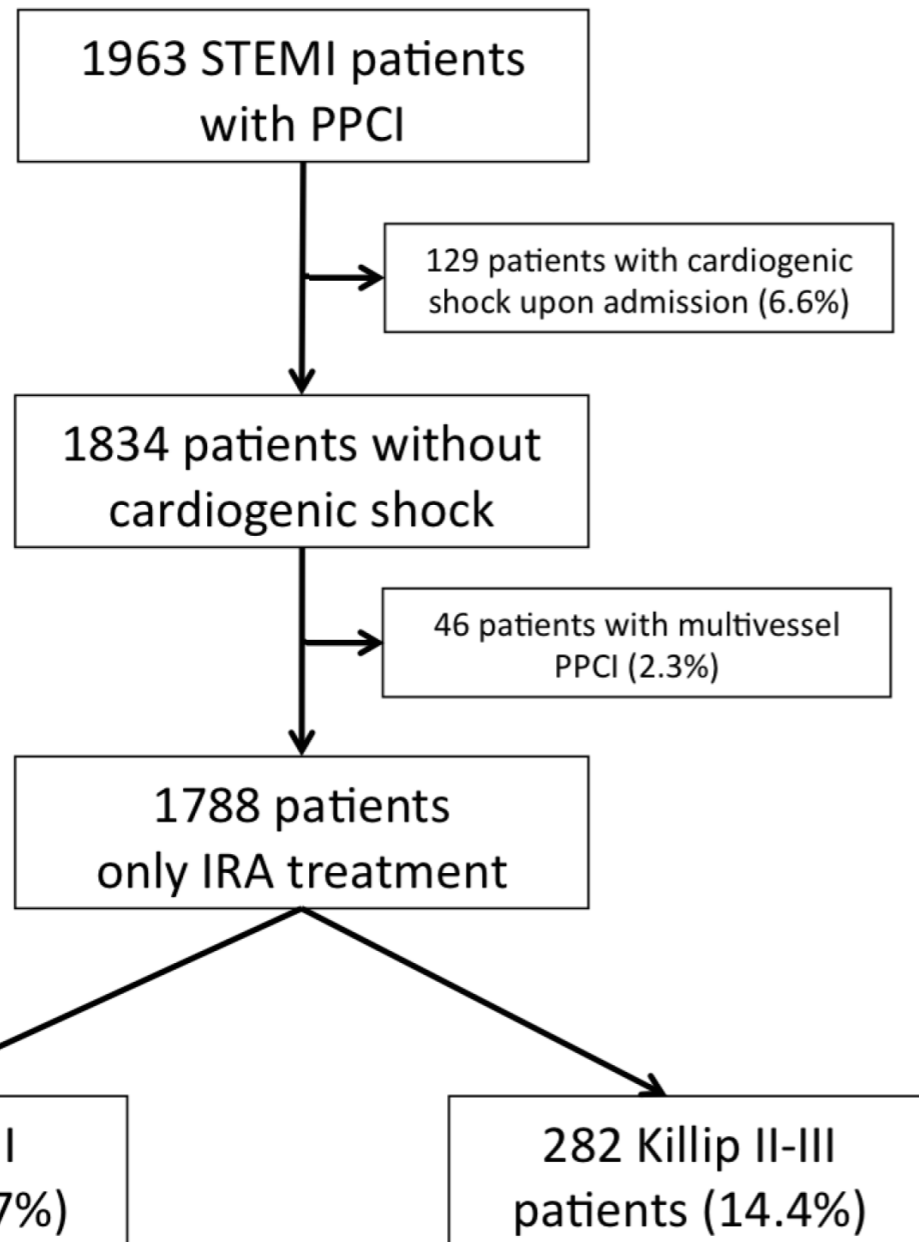
Registry trial	n	Mortality Complete Revascularization	Mortality Incomplete Revascularization	Adjusted OR (95%CI)
Webb ⁸	74	55%*	20%*	2.75 (1.05-7.25)
Van der Schaaf ¹⁹	161	60%*	53%*	Not reported (p=0.05)
Cavender ¹⁸	3087	36.5%	27.8%	1.5 (1.22–1.95)
Bauer ¹⁷	336	48.8%	37.4%	1.28 (0.72–2.28)
Zeymer ²⁰	735	46.8%	35.6%	1.5 (1.1-2.3)
Mylotte ²⁸	169	56.1%†	79.6%†	Not reported (p=0.002)
Cavender ³¹	199	46%	27%	Not reported (p=0.04)
Hussain ²⁷	101	Not reported	Not reported	2.47 (1.14-6.21)
Park ²⁹	510	13.9%	17.9%	Not reported (p=0.18)
Yang ³⁰	338	35.0%	30.6%	1.16 (0.72-1.87)

The CULPRIT-SHOCK trial will address the question of optimal revascularization strategy in patients with multivessel disease and acute myocardial infarction complicated by cardiogenic shock

Impact of Heart Failure on Outcome in STEMI

HUGTP Experience (2007-2013)

Patients with STEMI treated with Primary PCI and Multivessel Disease



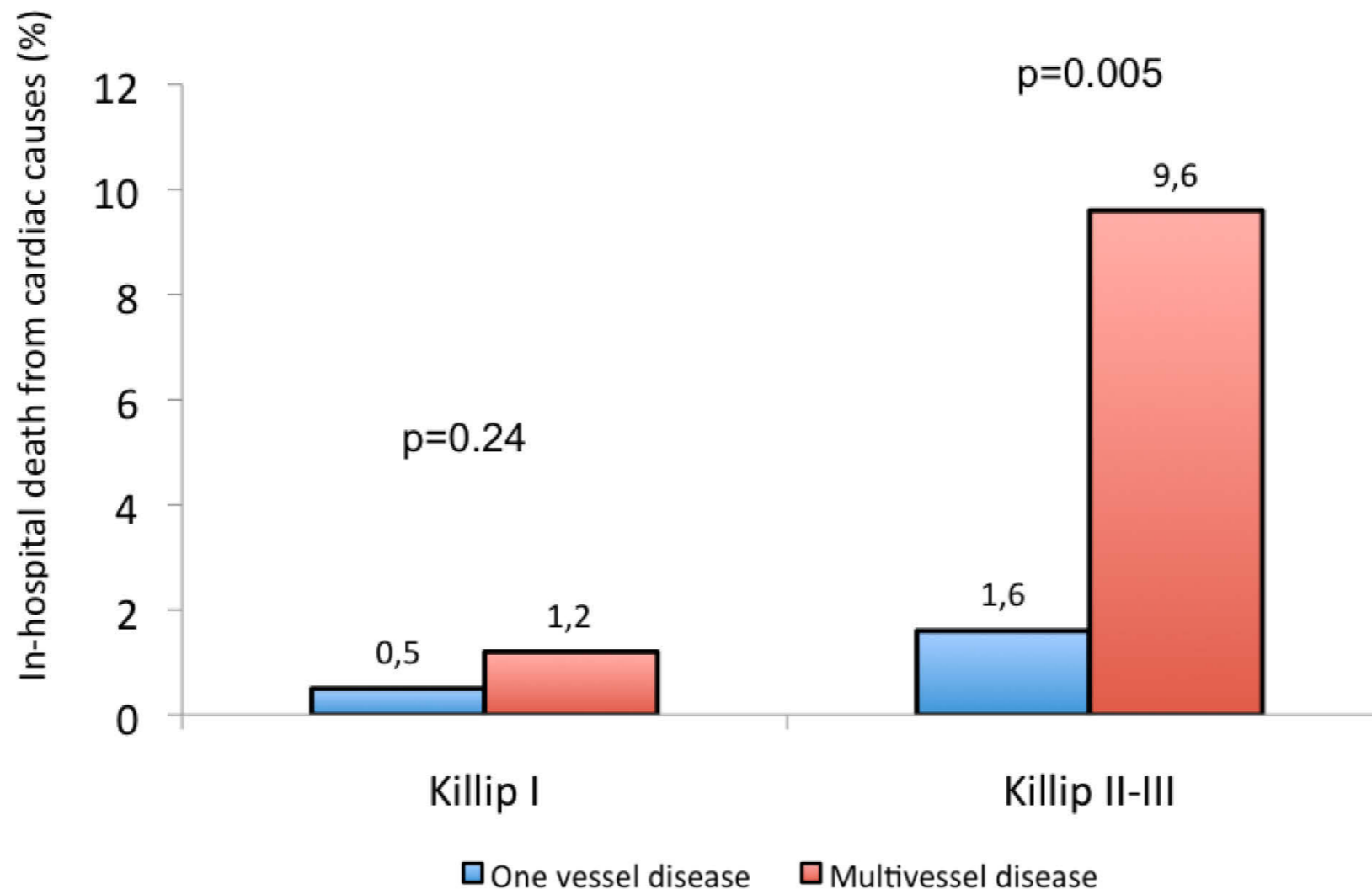
	Killip 1 N=1 506	Killip 2-3 N=282	P
Age, years	63±13	66±14	<0,0001
Females, n(%)	299(19.9)	78(27.7)	0,003
Hypertension, n(%)	751(49.9)	169(59.9)	0,001
Dyslipidemia, n(%)	771(51.2)	134(47.5)	0,14
Diabetes, n(%)	332(22.0)	92(32.6)	<0,0001
Smoking, n(%)	676(44.9)	112(39.7)	0,06
Kidney failure, n(%)	124(8.2)	61(21.6)	<0,0001
Peripheral vascular disease, n(%)	127(8.4)	49(17.4)	<0,0001
Previous infarction, n(%)	122(8.1)	43(15.2)	<0,0001
Previous PCI, n(%)	115(7.6)	36(12.8)	0,005
Multivessel disease, n(%)	694(46.1)	156(55.3)	0,003
Radial access, n(%)	1442(95.8)	269(95.4)	0,44
Thrombectomy, n(%)	1170(77.7)	213(75.5)	0,23
Anti IIb/IIIa, n(%)	1122(74.5)	193(68.4)	0,02
DTDT<120 min, n(%)	1010(67.1)	177(62.8)	0,17
Symptoms to reperfusion <120 min, n(%)	979(65.0)	171(60.6)	0,17

Impact of Heart Failure on Outcome in STEMI

HUGTP Experience (2007-2013)

Patients with STEMI treated with Primary PCI and Multivessel Disease

In-Hospital Cardiac Death



Multivessel disease was associated with a 6-fold higher in-hospital cardiac mortality (1.6% vs. 9.6%; p=0.005)

Impact of Heart Failure on Outcome in STEMI

HUGTP Experience (2007-2013)

Patients with STEMI treated with Primary PCI and Multivessel Disease

Multivariate Analysis of Cardiac Death During Admission in Patients with Multivessel Disease

	RR	P
Age	1.11 (1.05-1.17)	<0.0001
Renal failure	2.04 (0.88-4.70)	0.09
Use of anti-glycoprotein IIb/IIIa agents	0.32 (0.12-0.86)	0.024
Heart failure at admission (killip>1)	5.19 (2.35-11.41)	<0.0001

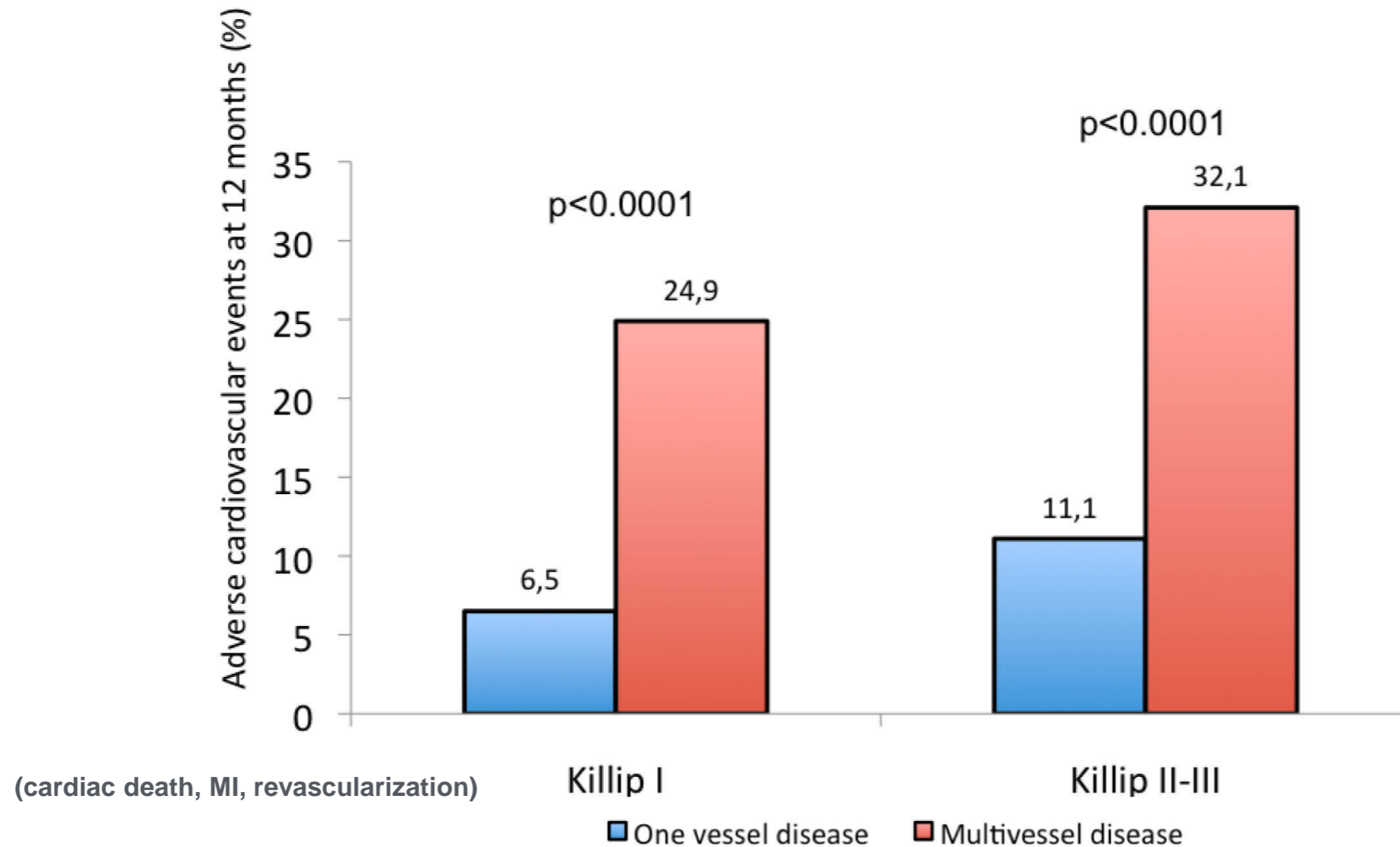
In patients with multivessel disease, Killip II-III at admission was the strongest predictor of in-hospital cardiac mortality

Impact of Heart Failure on Outcome in STEMI

HUGTP Experience (2007-2013)

Patients with STEMI treated with Primary PCI and Multivessel Disease

Adverse Cardiovascular Events at 12 months



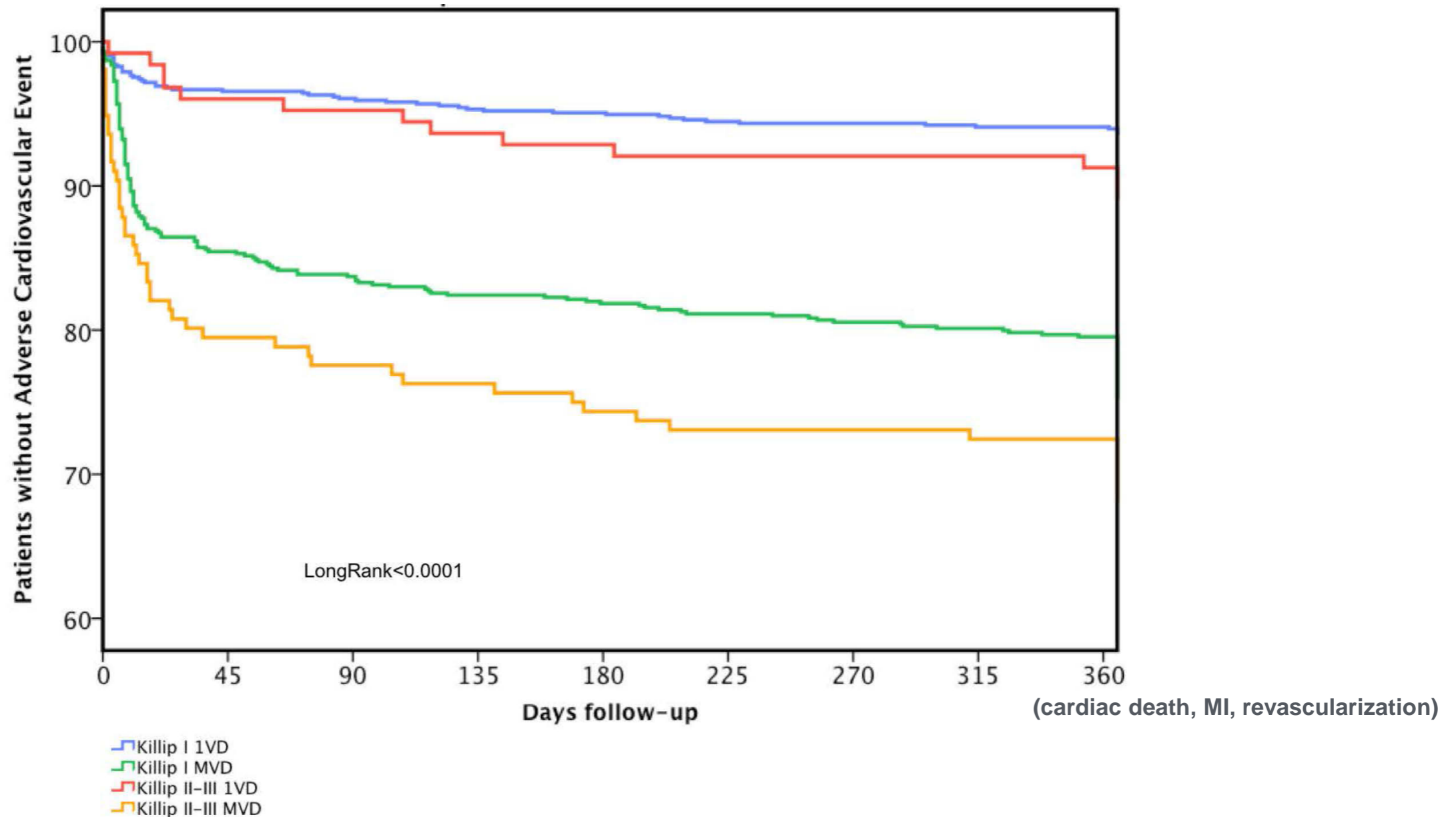
Multivessel disease was associated with a higher incidence of ACE in both groups

Impact of Heart Failure on Outcome in STEMI

HUGTP Experience (2007-2013)

Patients with STEMI treated with Primary PCI and Multivessel Disease

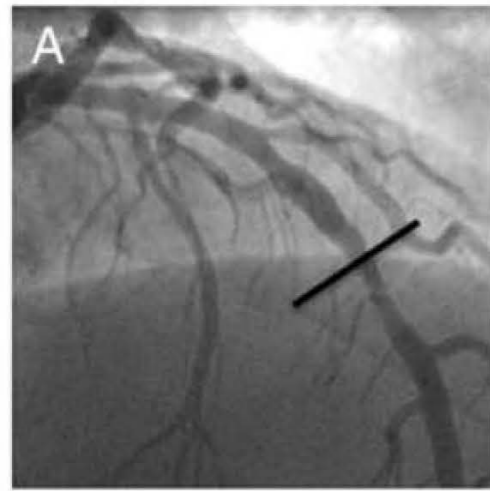
Kaplan-Meier Curves for Adverse Cardiovascular Events



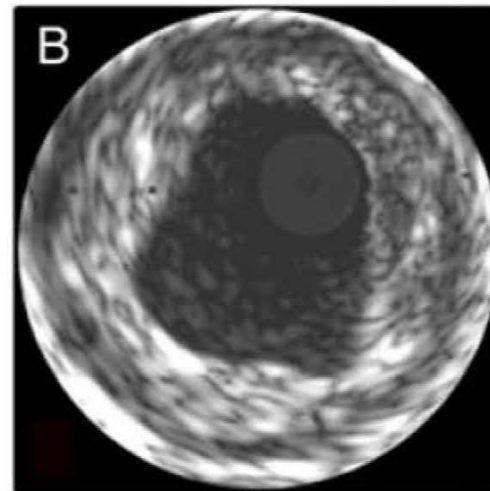
Remarkably, single-vessel disease curves were associated with favorable outcomes and could be superimposed for Killip I and Killip II-III patients

Meta-Analysis of RCT Comparing Multivessel vs Culprit Only PCI

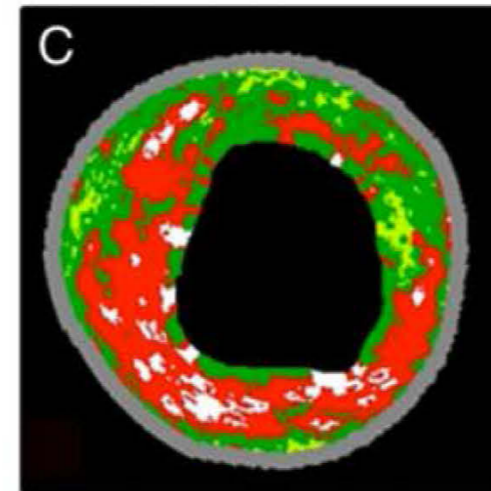
Multimodality imaging of a distal left anterior descending artery lesion by angiography



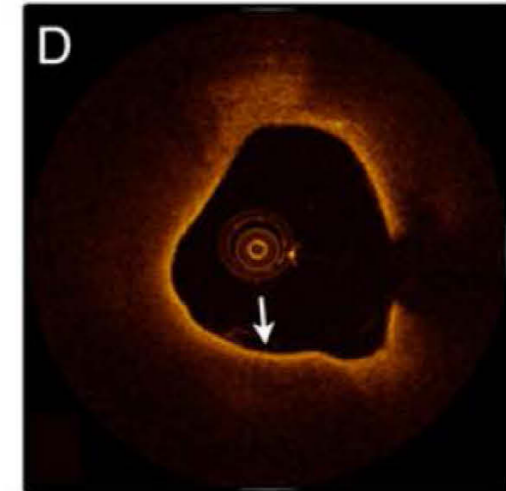
Lumen stenosis
Angiography



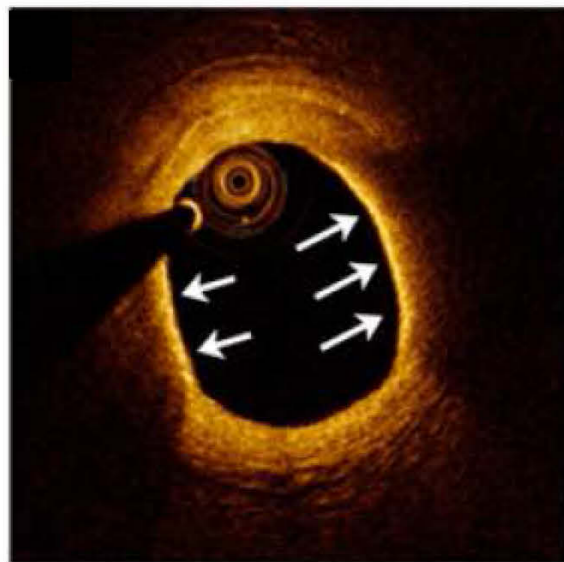
Atheroma / Vessel wall
IVUS



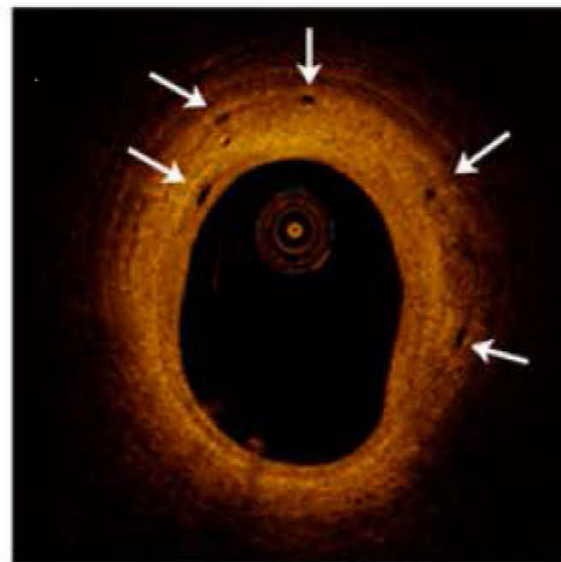
Plaque composition
IVUS-VH



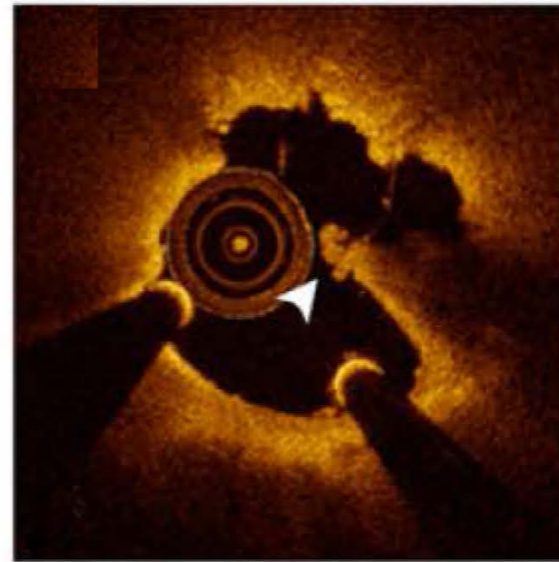
Thin fibrous cap
OCT



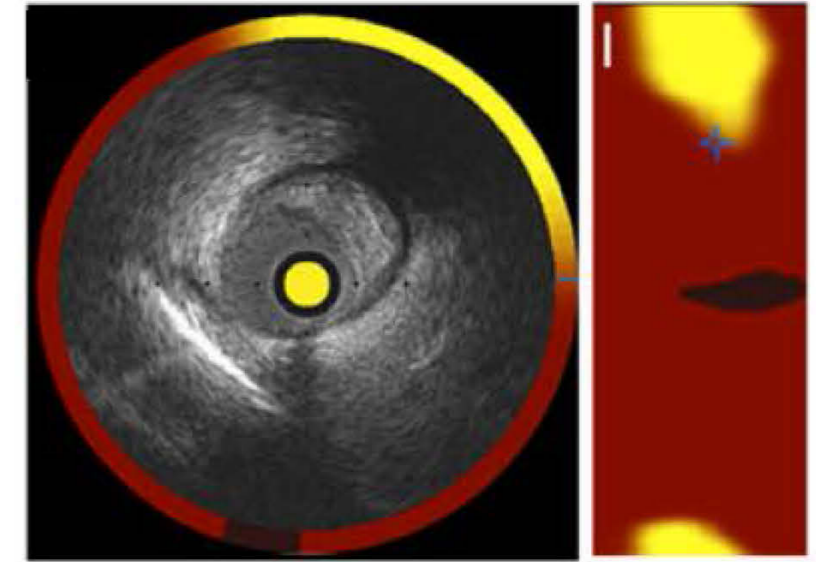
Macrophages



Microvessels



Plaque rupture



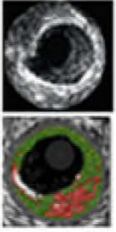
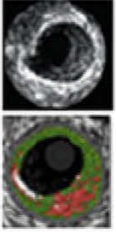
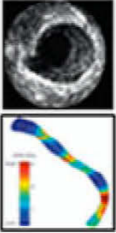
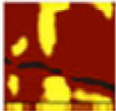
Lipid-rich plaque

OCT

NIRS

Meta-Analysis of RCT Comparing Multivessel vs Culprit Only PCI

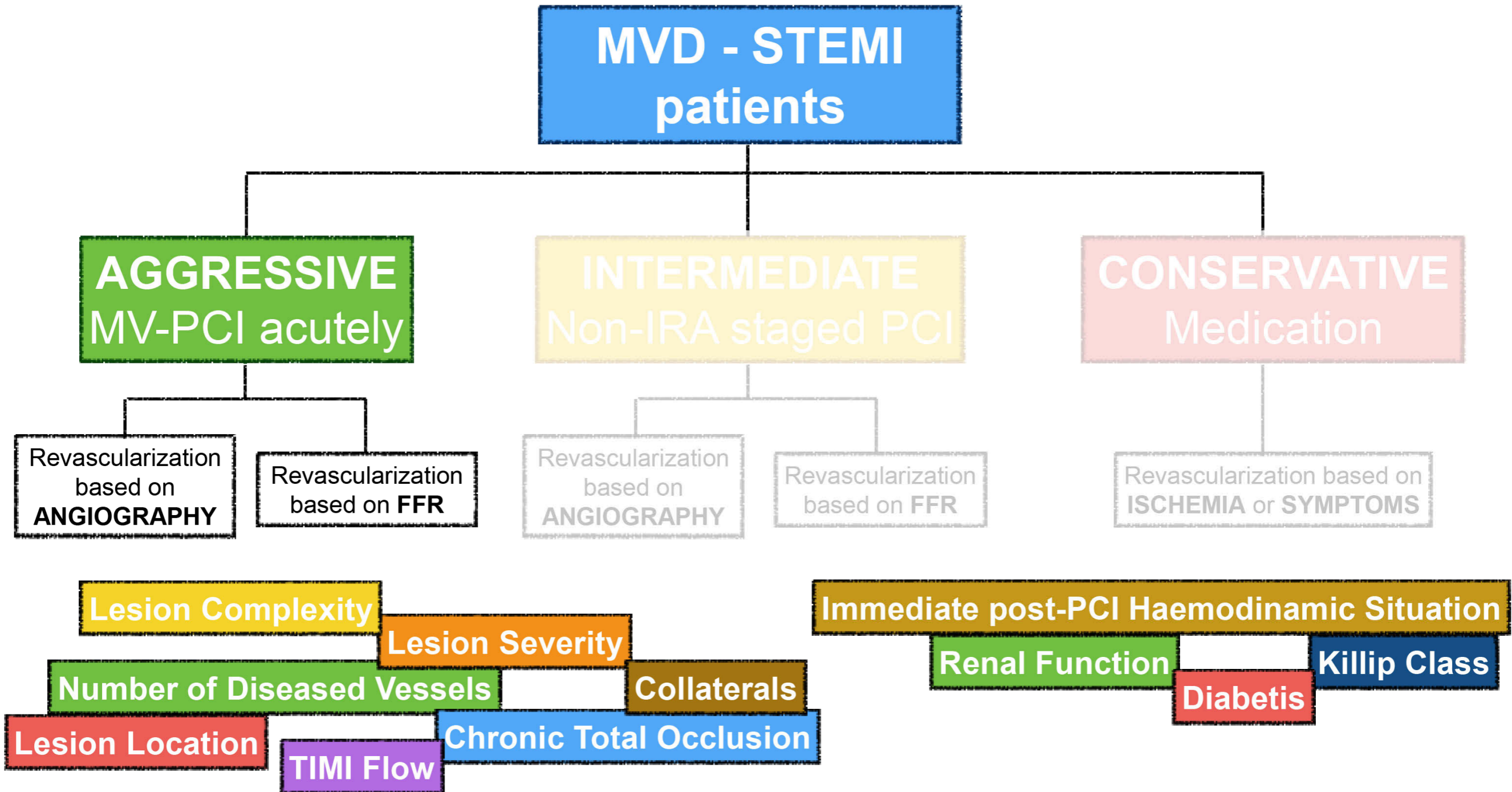
Summary of the positive and negative predictive values of intracoronary imaging–derived variables for prediction of clinical outcomes

Study	Modality	Lesion characteristic(s)	Clinical endpoint	Positive predictive value	Negative predictive value
PROSPECT <i>n</i> =697	 IVUS & IVUS-VH	PB \geq 70% & MLA $<$ 4mm ² & IVUS-VH TCHA	MACE	18%	98%
ATHEROREMO IVUS <i>n</i> =581	 IVUS & IVUS-VH	PB \geq 70% & MLA $<$ 4mm ² & IVUS-VH TCHA	MACE	23%	93%
PREDICTION <i>n</i> =506	 IVUS & ESS	PB \geq 58% & Low ESS $<$ 1.0 Pa	PCI	41%	92%
ATHEROREMO NIRS <i>n</i> =203	 NIRS	LCBI _{4mm} $>$ 43	MACE	12%	99%

These methodologies have established a **link between in vivo plaque characteristics and subsequent coronary events**, thereby improving **individual risk stratification**, paving the way for risk-tailored systemic therapies and **raising the option for pre-emptive interventions**

Treatment Strategies in Patients with STEMI and Multivessel Disease

There are about 60 possible scenarios based on combinations of angiographic and clinical findings in individual patients



Conclusions

Multivessel disease should be recognized as a major adverse prognostic factor in patients with STEMI

Multivessel disease in STEMI is not a single entity and thus the treatment approach should be individualized

Randomized controlled trials (PRAMI, CvLPRIT, DANAMI-3 PRIMULTI, COMPARE ACUTE) showed that preventive PCI is safe and improves outcomes mainly driven by the need of repeat revascularization

Patients who are asymptomatic and have negative functional tests and no evidence for silent ischaemia after their first STEMI should currently be treated conservatively

Future studies should clarify whether complete revascularization should be done acutely during the index procedure or at later time and whether it has an effect on hard endpoints

The every day real-life clinical practice brings much more different clinical scenarios. It is unlikely that any randomized clinical trial in the future can be able to fully address this complexity and thus, **experienced, wise clinical judgement will probably remain the most important factor in this difficult situation**

IAM EN MALALTIA MULTIVÀS TRACTAR-HO TOT O NO AGUT O DIFERIT

TRACTAR ALTRES LESIONS QUE LA RESPONSABLE EN LA FASE AGUDA APORTA AVANTATGES

- PART II -



Oriol Rodríguez Leor
Institut del Cor Germans Trias i Pujol
Badalona



germanstriashospital



2014 ESC Myocardial Revascularization Guidelines

Recommendations	Class ^a	Level ^b	Ref ^c
Strategy			
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	234,264–266
Staged revascularization of non-culprit lesions should be considered in STEMI patients with multivessel disease in case of symptoms or ischaemia within days to weeks after primary PCI.	IIa	B	235
Immediate revascularization of significant non-culprit lesions during the same procedure as primary PCI of the culprit vessel may be considered in selected patients.	IIb	B	267
In patients with continuing ischaemia and in whom PCI of the infarct-related artery cannot be performed, CABG should be considered.	IIa	C	

234. Kornowski (HORIZONS AMI)_JACC 2011
 264. Hannan (New York Registry)_JACC Interv 2010
 265. Toma (APEX AMI)_ Eur Heart J 2010
 266. Vlaar (Meta-Analysis)_J Am Coll Cardiol 2011

235. Politi. Heart 2010

267. Wald. N Engl J Med 2013

Windecker S et al. 2014 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2014;35:2541-2619

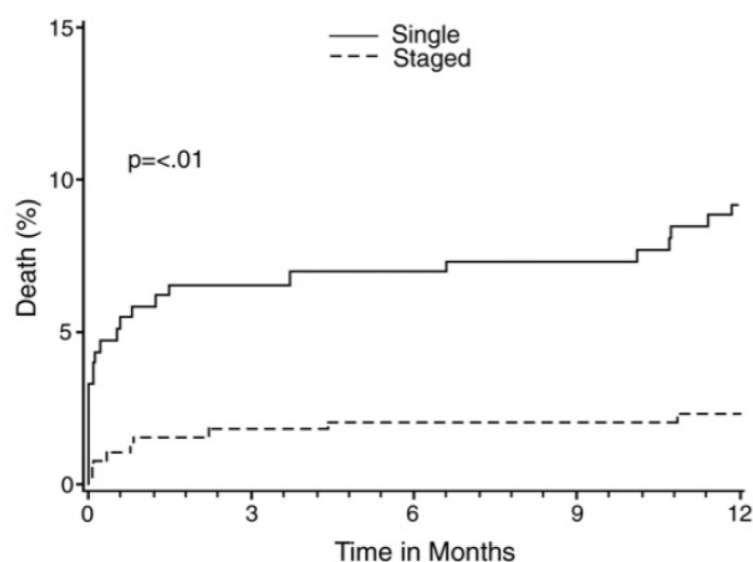
2014 EHJ Revascularization Guidelines

HORIZONS AMI Trial

668 of the 3602 STEMI patients enrolled (18.5%) underwent PCI of culprit and nonculprit lesions for multivessel disease

Patients were categorized into a single PCI strategy (n=275) versus staged PCI (n=393)

CONCLUSION: a deferred angioplasty strategy of nonculprit lesions should remain the standard approach in patients with STEMI undergoing primary PCI, as multivessel PCI may be associated with a greater hazard for mortality and stent thrombosis



- Retrospective nonrandomized subanalysis
- Specific reason why operator chose a single procedure vs a staged approach was not prospectively collected
- Low number of events (31 deaths / 25 cardiac deaths/19 stent thrombosis) -> Multivariate Model Underpowered
- BMS vs Taxus Express

Kornowski R et al. Prognostic impact of staged vs "ontime" multivessel PCI in acute myocardial infarction. Analysis from the HORIZONS-AMI Trial. J Am Coll Cardiol 2011; 58:704-711

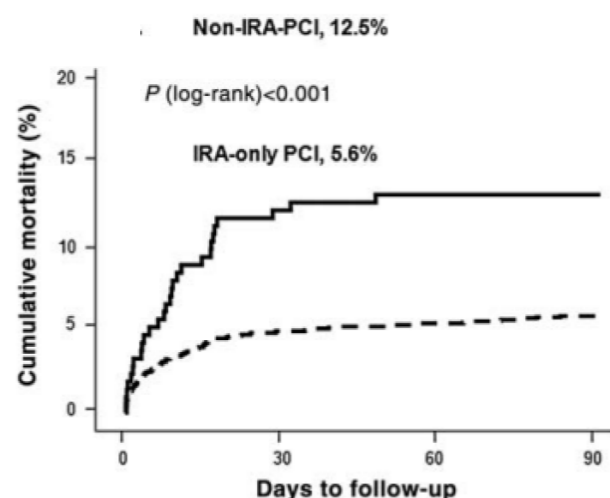
2014 EHJ Revascularization Guidelines

APEX AMI Trial

2201 of the 5373 STEMI patients enrolled (18.5%) underwent PCI of culprit and nonculprit lesions for multivessel disease

Patients were categorized into a single PCI strategy (n =217) versus no PCI (n =1984)

CONCLUSION: Non-culprit coronary interventions were performed at the time of primary PCI in 10% of MVD patients and were significantly associated with increased mortality. Our data support current guideline recommendations discouraging the performance of such procedures in stable primary PCI patients.



- Retrospective nonrandomized subanalysis
- Specific reason why operator chose a single procedure vs a staged approach was not prospectively collected
- Low number of events (135 deaths)-> Multivariate Model Underpowered
- Only 38% DES (1st generation)
- Lack of information on outcomes in patients not treated at the index procedure

Toma M et al. Non-culprit coronary artery percutaneous coronary intervention during acute ST-segment elevation myocardial infarction: insights from the APEX-AMI trial. Eur Heart J. 2010;31:1701-7

2014 EHJ Revascularization Guidelines

Hannan et al, JACC Intv

New York State Registry (3521 patients) 2003-2006

CONCLUSION: Our findings support the ACC/AHA recommendation that culprit vessel PCI be used for STEMI patients with multivessel disease at the time of the index PCI when patients are not hemodynamically compromised. However, staged PCI within 60 days after the index procedure, including during the index admission, is associated with risk-adjusted mortality rates that are comparable with the rate for culprit vessel PCI alone.

Outcome by Subgroup	Culprit Vessel Revascularization at the Time of PPCI	Multivessel Revascularization at the Time of PPCI	Percentage Difference	p Value
All patients	n = 503	n = 503		
Death, %				
In-hospital	2.0	3.4	1.4	0.14
12 months	5.5	7.1	1.6	0.23
24 months	6.6	8.6	2.0	0.17
42 months	10.8	11.8	1.0	0.23
Patients without hemodynamic instability, LVEF <20%, malignant ventricular arrhythmia	n = 458	n = 458		
Death, %				
In-hospital	0.9	2.4	1.5	0.04
12 months	4.2	5.8	1.6	0.13
24 months	4.9	7.2	2.3	0.07
42 months	6.7	10.4	3.7	0.08

Median follow-up – 22.54 months.
LVEF – left ventricular ejection fraction; PPCI – primary percutaneous coronary intervention; STEMI – ST-segment elevation myocardial infarction.

- **Observational study (selection bias)**
- **No information about medical treatment**
- **No information about DES use, but 1st generation**
- **Very low In-hospital mortality in the culprit-only group (0,9%!!)**

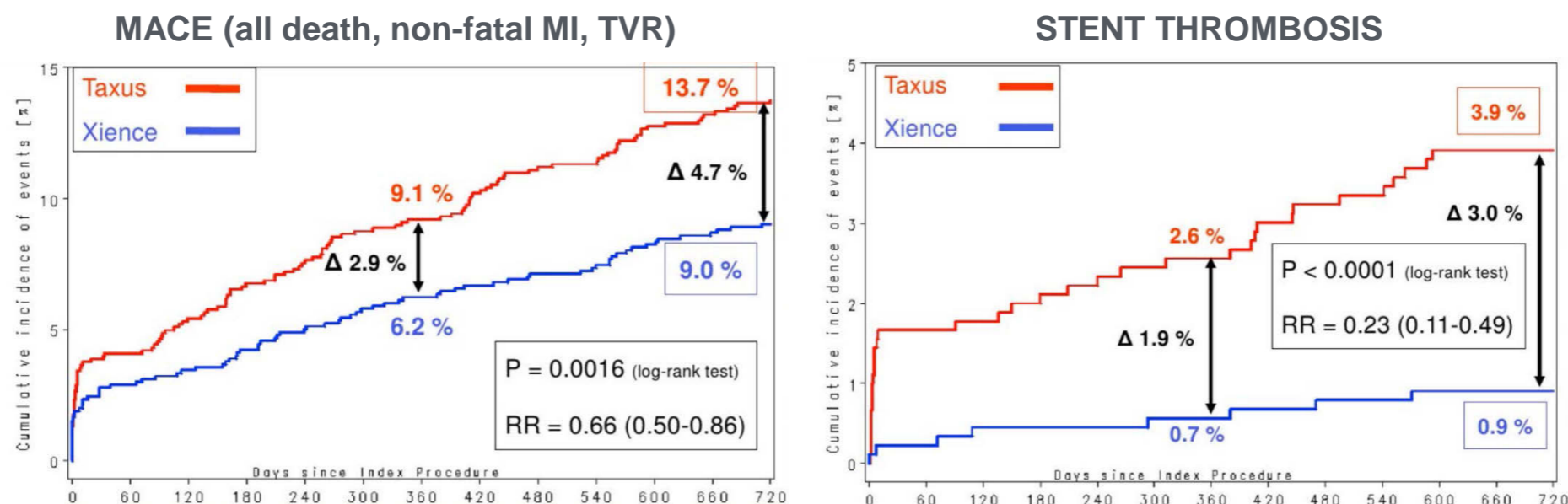
Hannan EL et al. Culprit vessel PCI vs multivessel and staged PCI for STEMI in patients with multivessel disease. J Am Coll Cardiol Intv 2010;3:22-31

Randomized Trials of Multivessel PCI in STEMI

First Generation vs Contemporary DES

COMPARE Trial

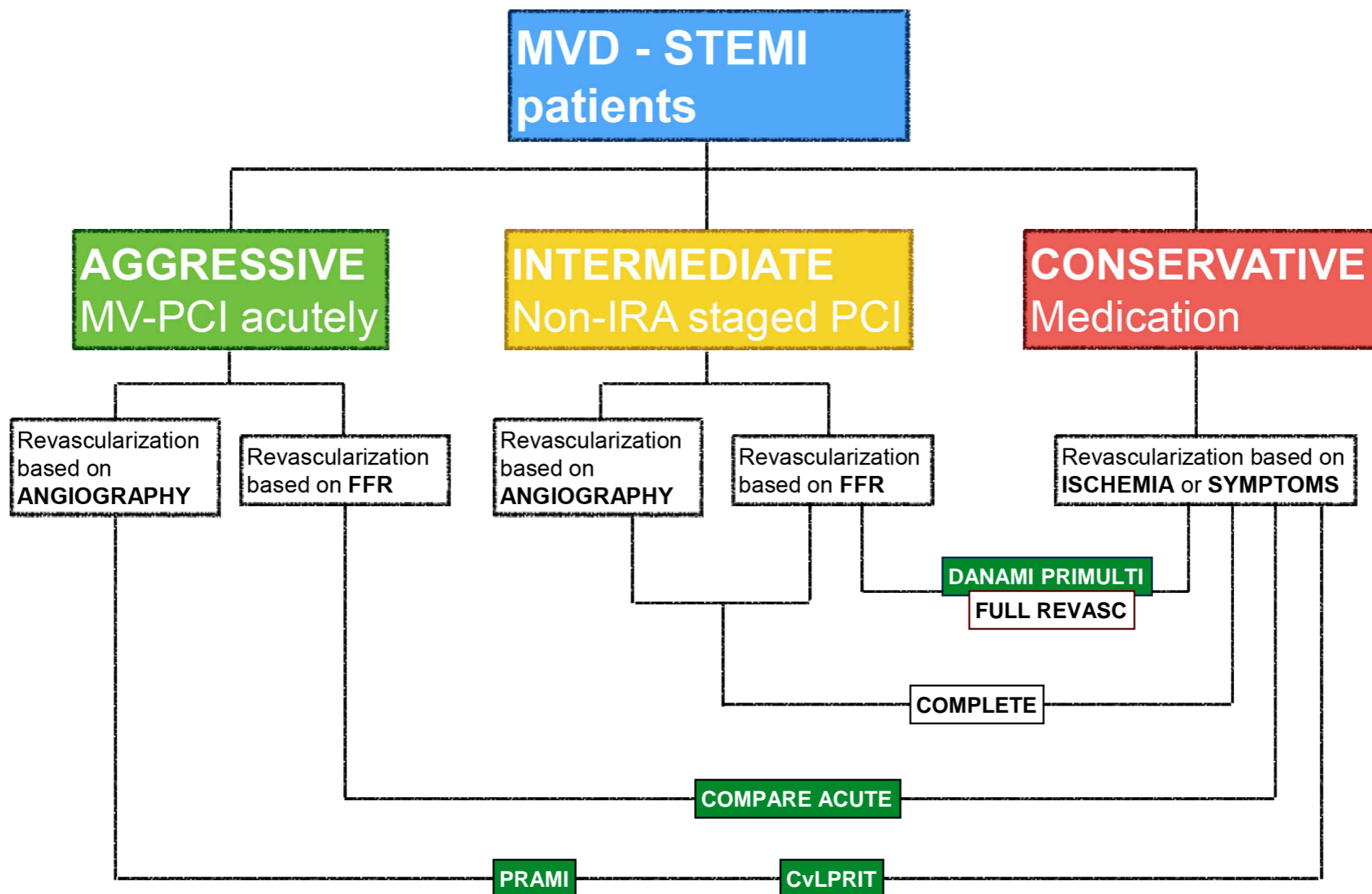
2-Year Follow-Up of a Randomized Controlled Trial of Everolimus- and Paclitaxel-Eluting Stents for Coronary Revascularization in Daily Practice



The substantial clinical benefit of the EES over the PES with regard to measures of both safety and efficacy is maintained at 2 years in real-life practice with an increasing benefit in terms of safety and efficacy between 1 year and 2 years

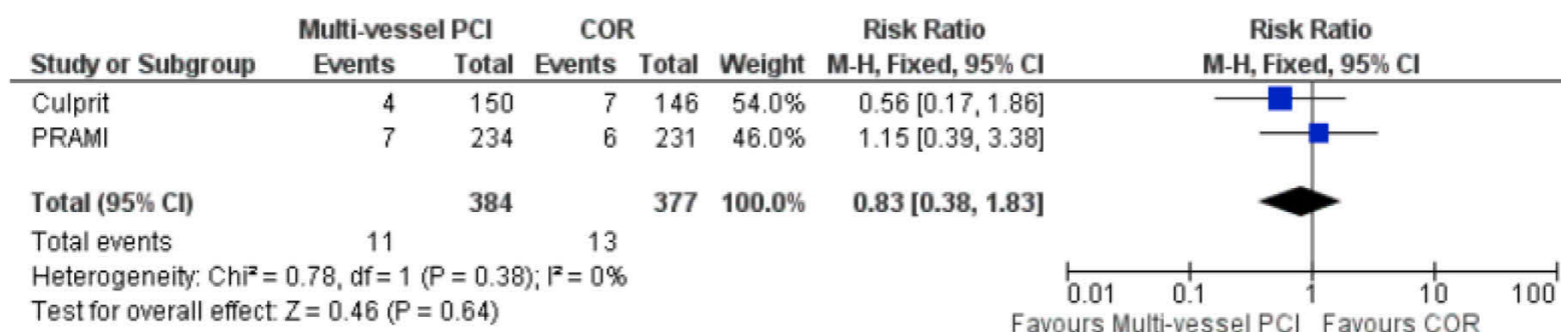
Smits PC et al. 2-Year Follow-Up of a Randomized Controlled Trial of Everolimus- and Paclitaxel-Eluting Stents for Coronary Revascularization in Daily Practice. J Am Coll Cardiol 2011; 58:11-8

Treatment Strategies in Patients with STEMI and Multivessel Disease

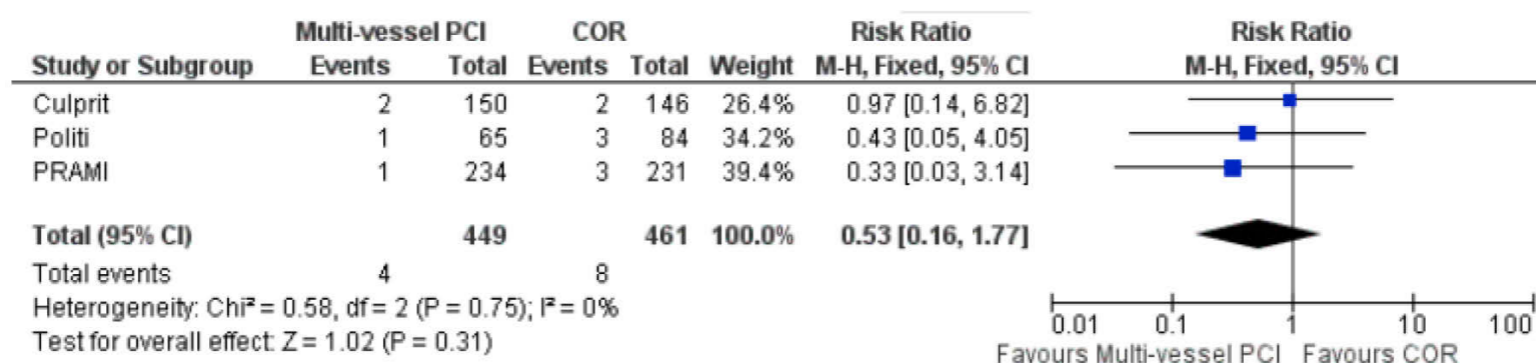


Meta-Analysis of RCT Comparing Multivessel vs Culprit Only PCI

Risk of Major Bleeding in Follow-up



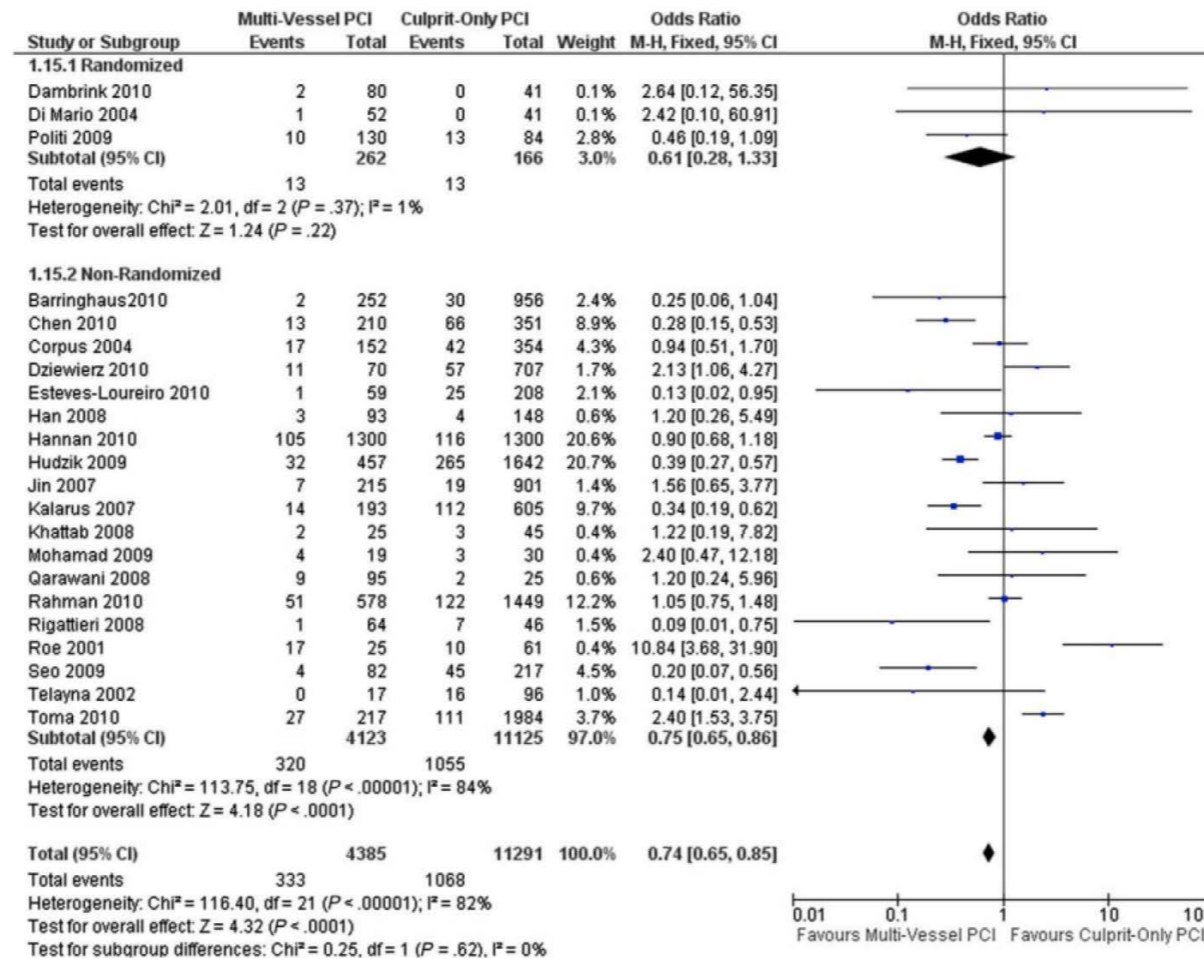
Risk of Contrast-Induced Nephropaty in Follow-up



EI-Hayek GE et al. Meta-analysis of randomized controlled trials comparing multi-vessel vs culprit only revascularization for patients with STEMI and multivessel disease. Am J Cardiol;2015;115:1481

Meta-Analysis of RCT and nonRCT Comparing Multivessel vs Culprit Only PCI

Long Term Mortality Stratified by Study Method



Multivessel PCI associated with lower long term mortality
OR 0,74 (0,65-0,85) $p < 0,001$

Bainey KR et al. Complete vs culprit-only revascularization for patients with MVD undergoing primary PCI for STEMI: a systematic review and meta-analysis. Am Heart J;2014;167:1-14

2014 ESC Myocardial Revascularization Guidelines

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2017 SCC Myocardial Revascularization Guidelines?

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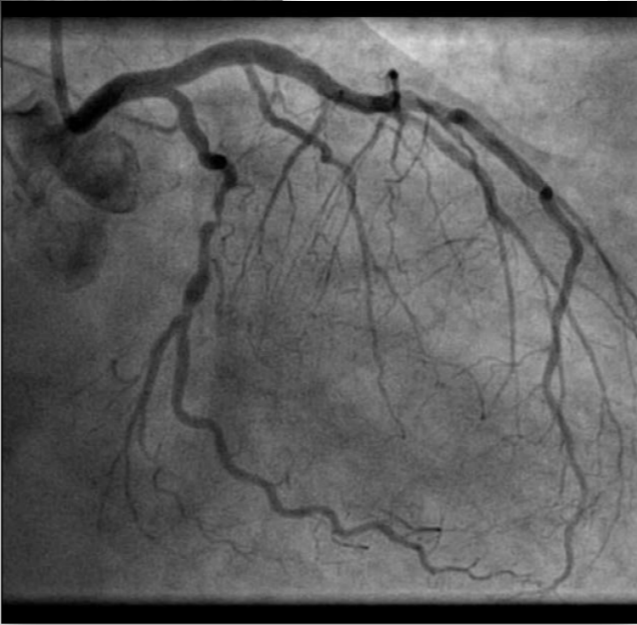
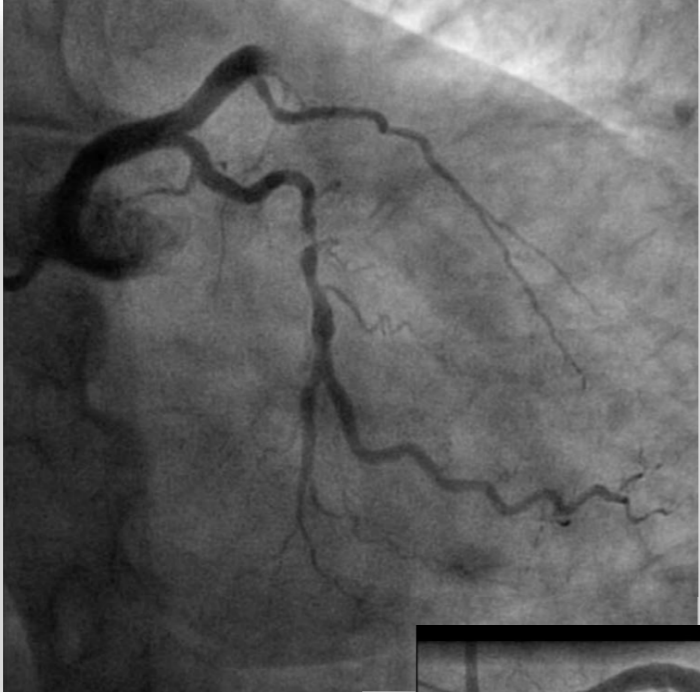
PRAMI Trial. N Engl J Med 2013
 CvLPRIT Trial. J Am Coll Cardio 2014
 DANAMI PRIMULTI. Lancet 2015
 COMPARE ACUTE. N Engl J Med 2017

Multivessel revascularization seems the best option in patients with STEMI...



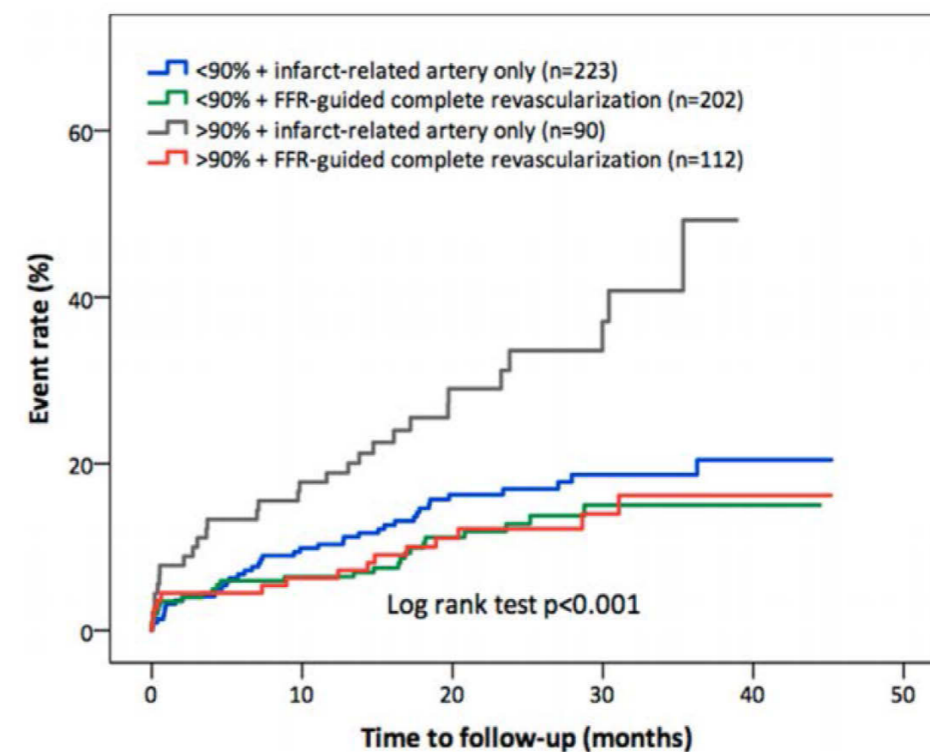
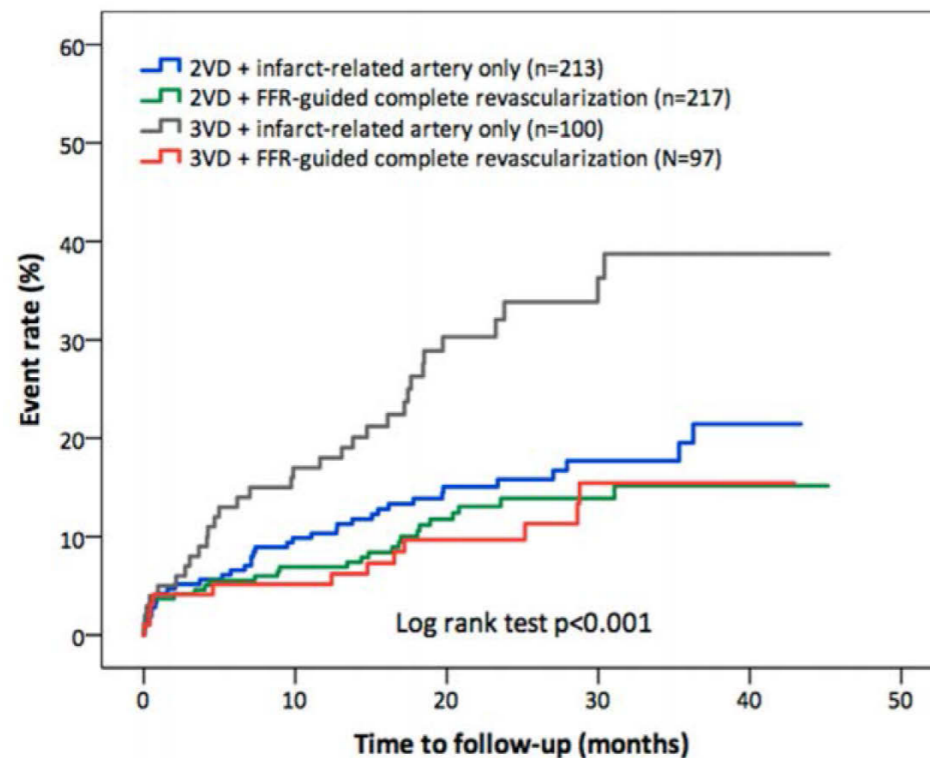
...but should we do it during the index procedure?
(acute multivessel PCI)

Multivessel PCI during the Index Procedure



Impact of the Disease Severity on Outcome

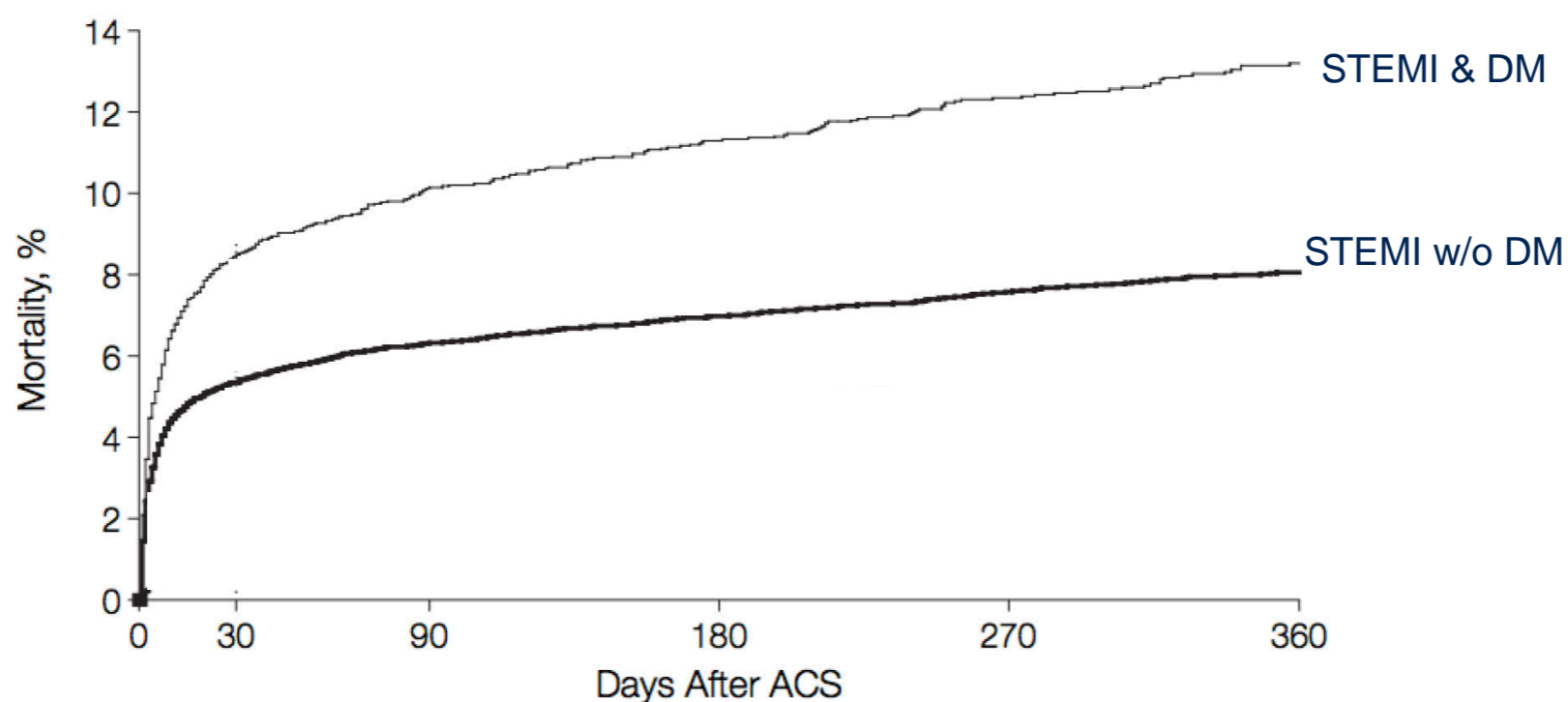
The benefit from FFR-guided complete revascularization was dependent in the presence of 3-vessel disease and noninfarct diameter stenosis >90% (particularly pronounced in patients with both these angiographic characteristics)



Lønborg J et al. FFR-guided complete revascularization improves the prognosis of patients with STEMI and severe nonculprit disease. A DANAMI 3 PRIMULTI substudy. *Circ Cardiovasc Interv* 2017;10:e004460

Impact of the Diabetes on Outcome in STEMI

Diabetes confers a significant adverse prognosis, which highlights the importance of aggressive strategies to manage this high-risk population



Diabetes at presentation was associated with significantly higher mortality 1 year after STEMI (HR, 1.22; 95% CI, 1.08- 1.38)

Donahoe SM et al. **Diabetes and Mortality Following Acute Coronary Syndromes.** JAMA 2007;298:765-775

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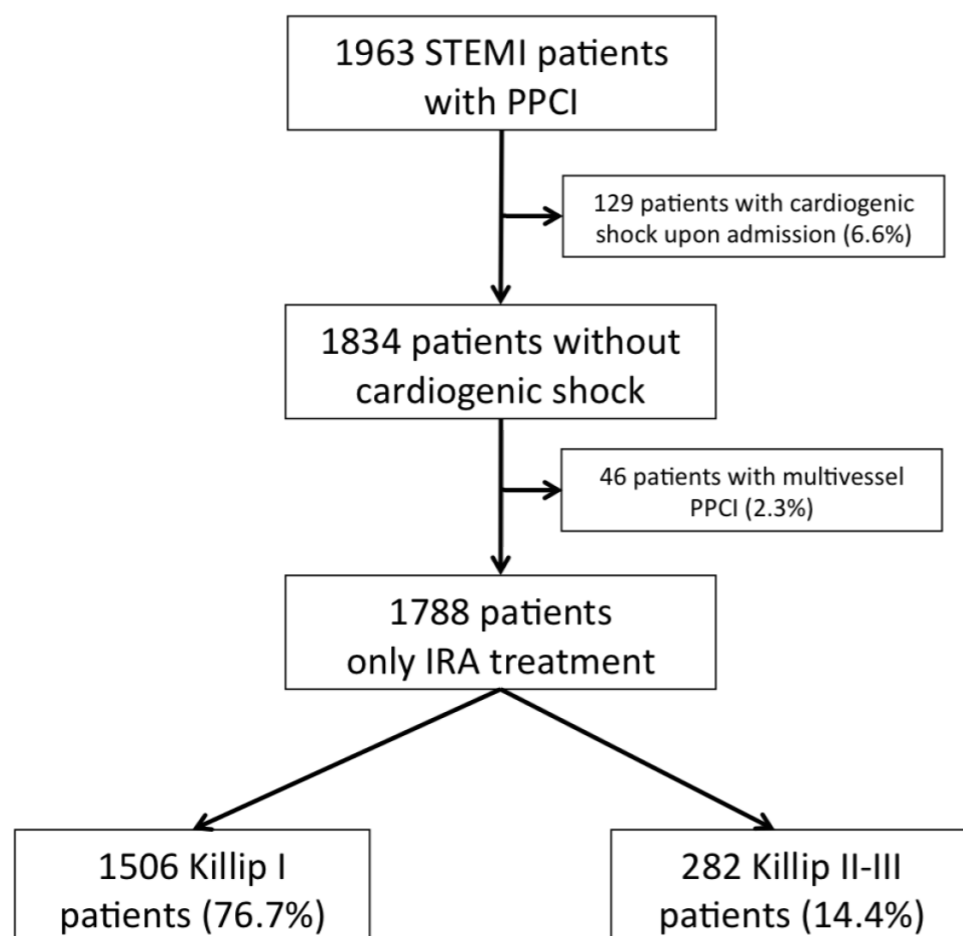
The CULPRIT-SHOCK trial will address the question of optimal revascularization strategy in patients with multivessel disease and acute myocardial infarction complicated by cardiogenic shock

Thiele H et al. Multivessel versus culprit lesion only PCI plus potential staged revascularization in patients with STEMI complicated by cardiogenic shock: Design and rationale of CULPRIT-SHOCK trial. Am Heart J;2016;172:160-169

Impact of Heart Failure on Outcome in STEMI

HUGTP Experience (2007-2013)

Patients with STEMI treated with Primary PCI and Multivessel Disease

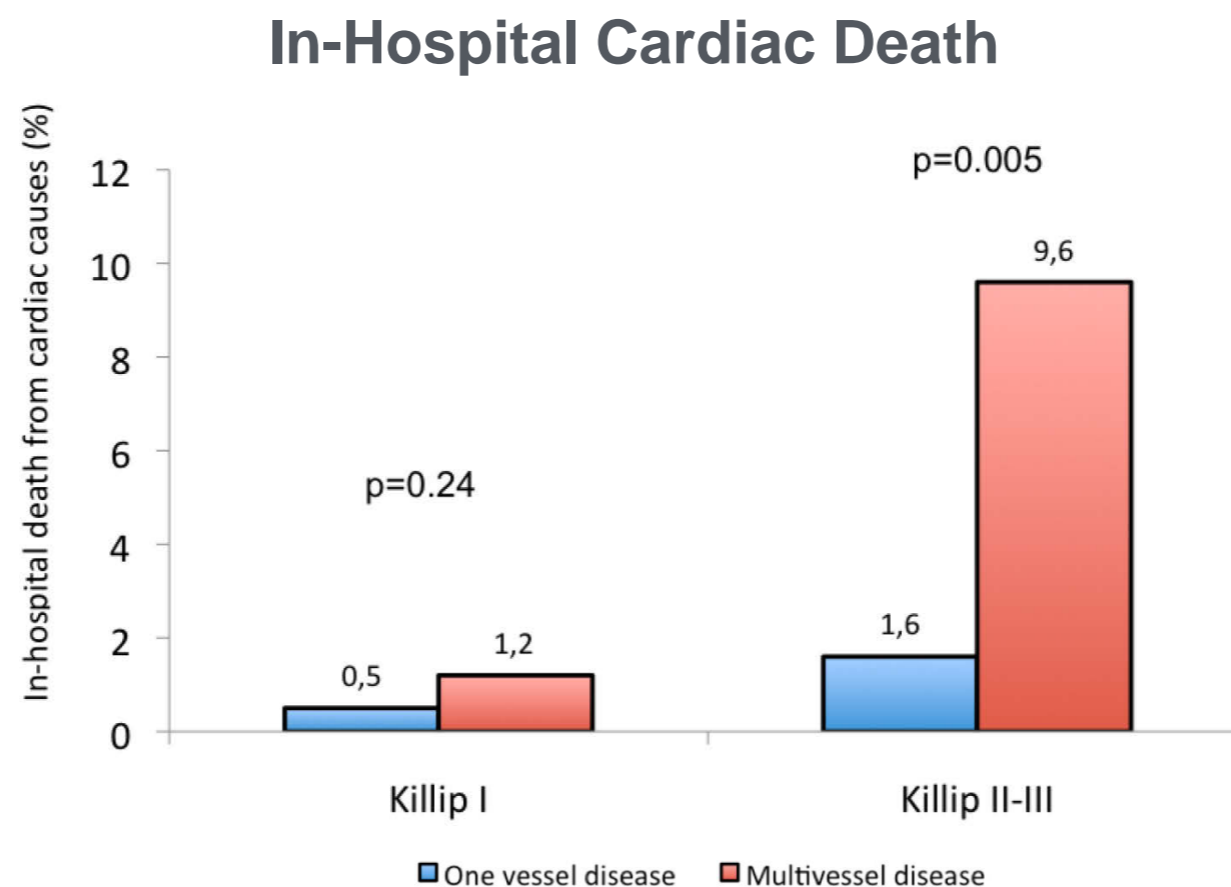


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Previous PCI, n(%)	115(7.6)	36(12.8)	0,005
Multivessel disease, n(%)	694(46.1)	156(55.3)	0,003
Radial access, n(%)	1442(95.8)	269(95.4)	0,44
Thrombectomy, n(%)	1170(77.7)	213(75.5)	0,23
Anti IIb/IIIa, n(%)	1122(74.5)	193(68.4)	0,02
DTDT<120 min, n(%)	1010(67.1)	177(62.8)	0,17
Symptoms to reperfusion <120 min, n(%)	979(65.0)	171(60.6)	0,17

Impact of Heart Failure on Outcome in STEMI

HUGTP Experience (2007-2013)

Patients with STEMI treated with Primary PCI and Multivessel Disease



Multivessel disease was associated with a 6-fold higher in-hospital cardiac mortality (1.6% vs. 9.6%; p=0.005)

Impact of Heart Failure on Outcome in STEMI

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Multivariate Analysis of Cardiac Death During Admission in Patients with Multivessel Disease

	RR	P
Age	1.11 (1.05-1.17)	<0.0001
Renal failure	2.04 (0.88-4.70)	0.09
Use of anti-glycoprotein IIb/IIIa agents	0.32 (0.12-0.86)	0.024
Heart failure at admission (killip>1)	5.19 (2.35-11.41)	<0.0001

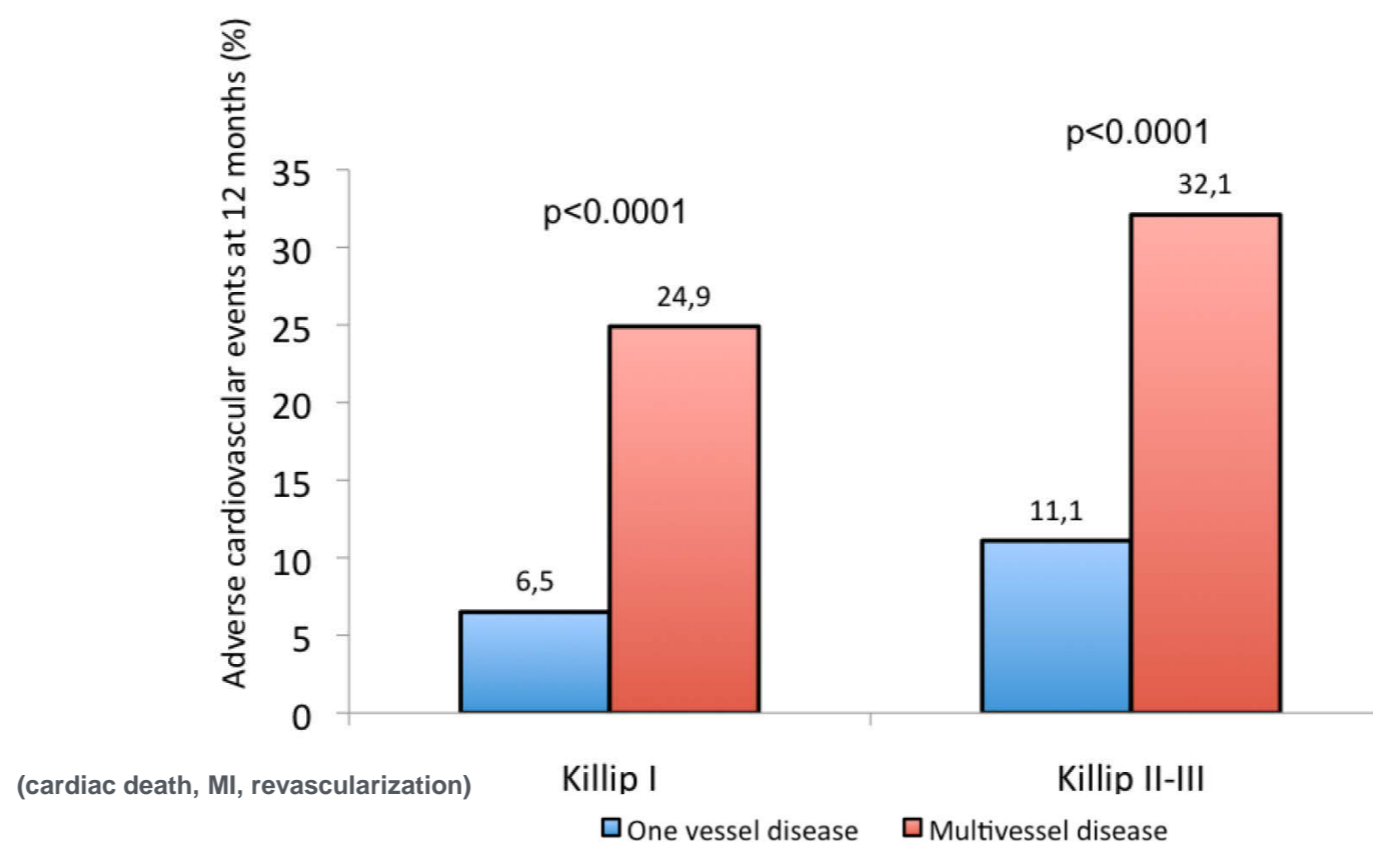
In patients with multivessel disease, Killip II-III at admission was the strongest predictor of in-hospital cardiac mortality

Impact of Heart Failure on Outcome in STEMI

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Adverse Cardiovascular Events at 12 months



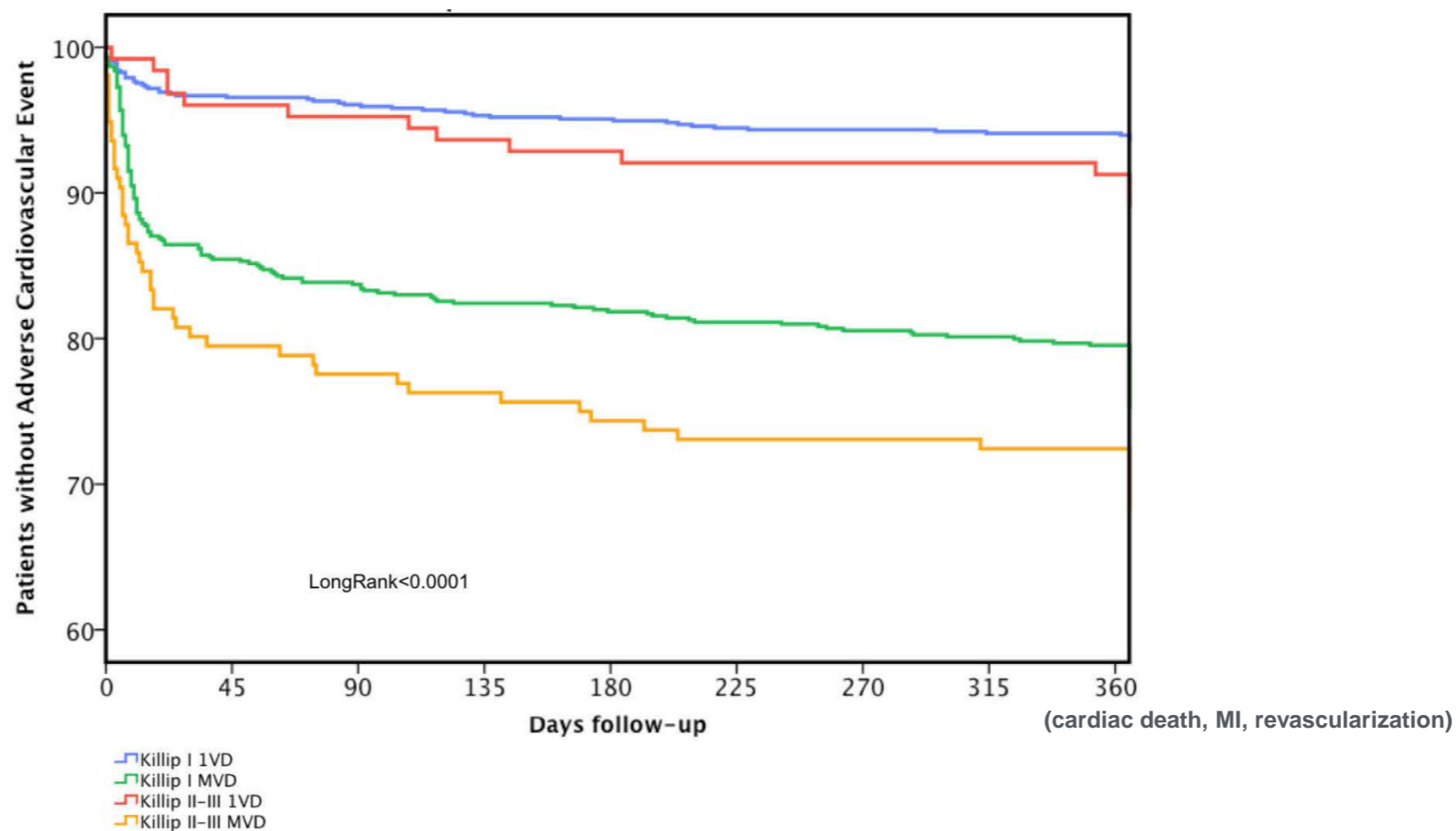
Multivessel disease was associated with a higher incidence of ACE in both groups

Impact of Heart Failure on Outcome in STEMI

HUGTP Experience (2007-2013)

Patients with STEMI treated with Primary PCI and Multivessel Disease

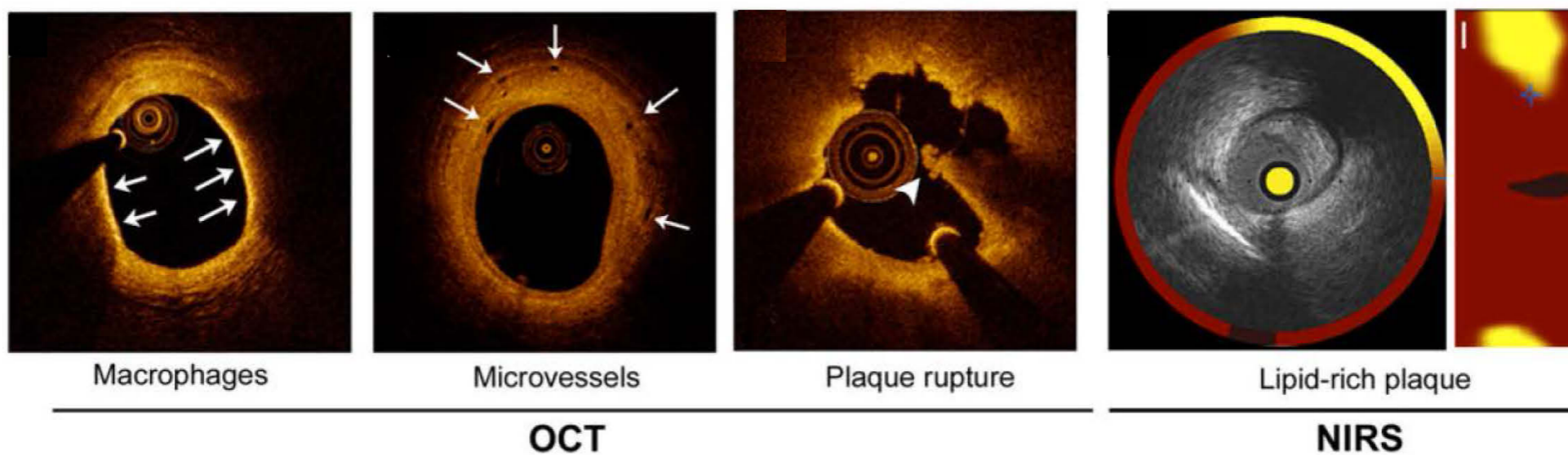
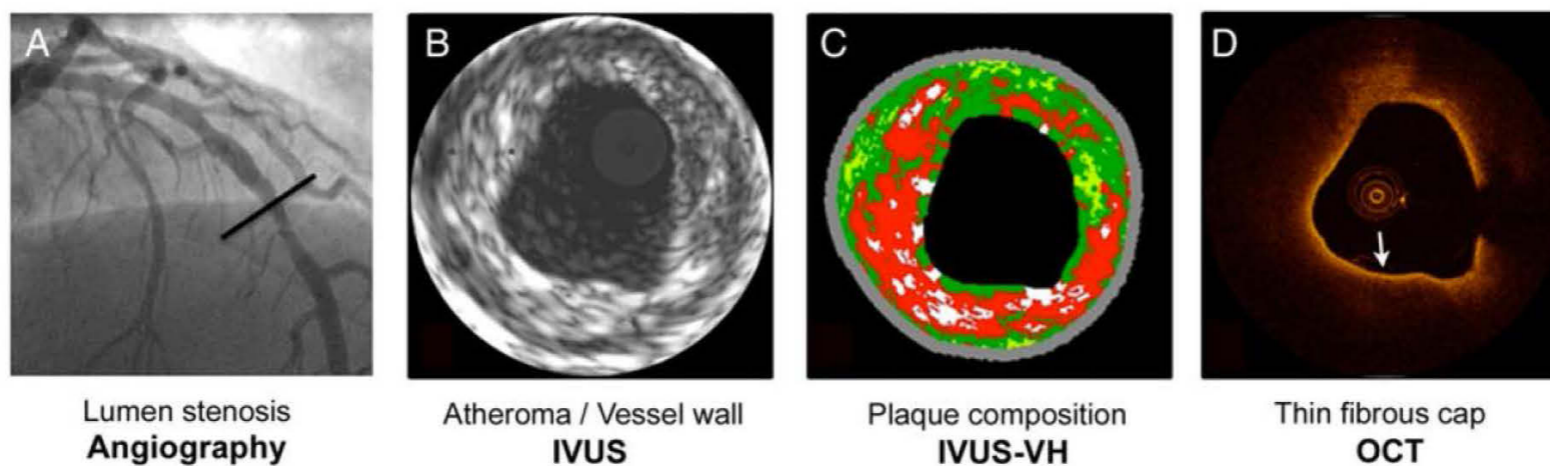
Kaplan-Meier Curves for Adverse Cardiovascular Events



Remarkably, single-vessel disease curves were associated with favorable outcomes and could be superimposed for Killip I and Killip II-III patients

Meta-Analysis of RCT Comparing Multivessel vs Culprit Only PCI

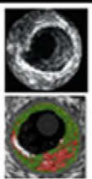
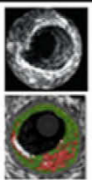
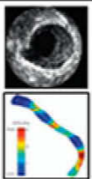

Multimodality imaging of a distal left anterior descending artery lesion by angiography



Koskinas KC et al. Intracoronary imaging of coronary atherosclerosis: validation for diagnosis, prognosis and treatment. Eur Heart J;2016;37:524-535

Meta-Analysis of RCT Comparing Multivessel vs Culprit Only PCI

Summary of the positive and negative predictive values of intracoronary imaging–derived variables for prediction of clinical outcomes

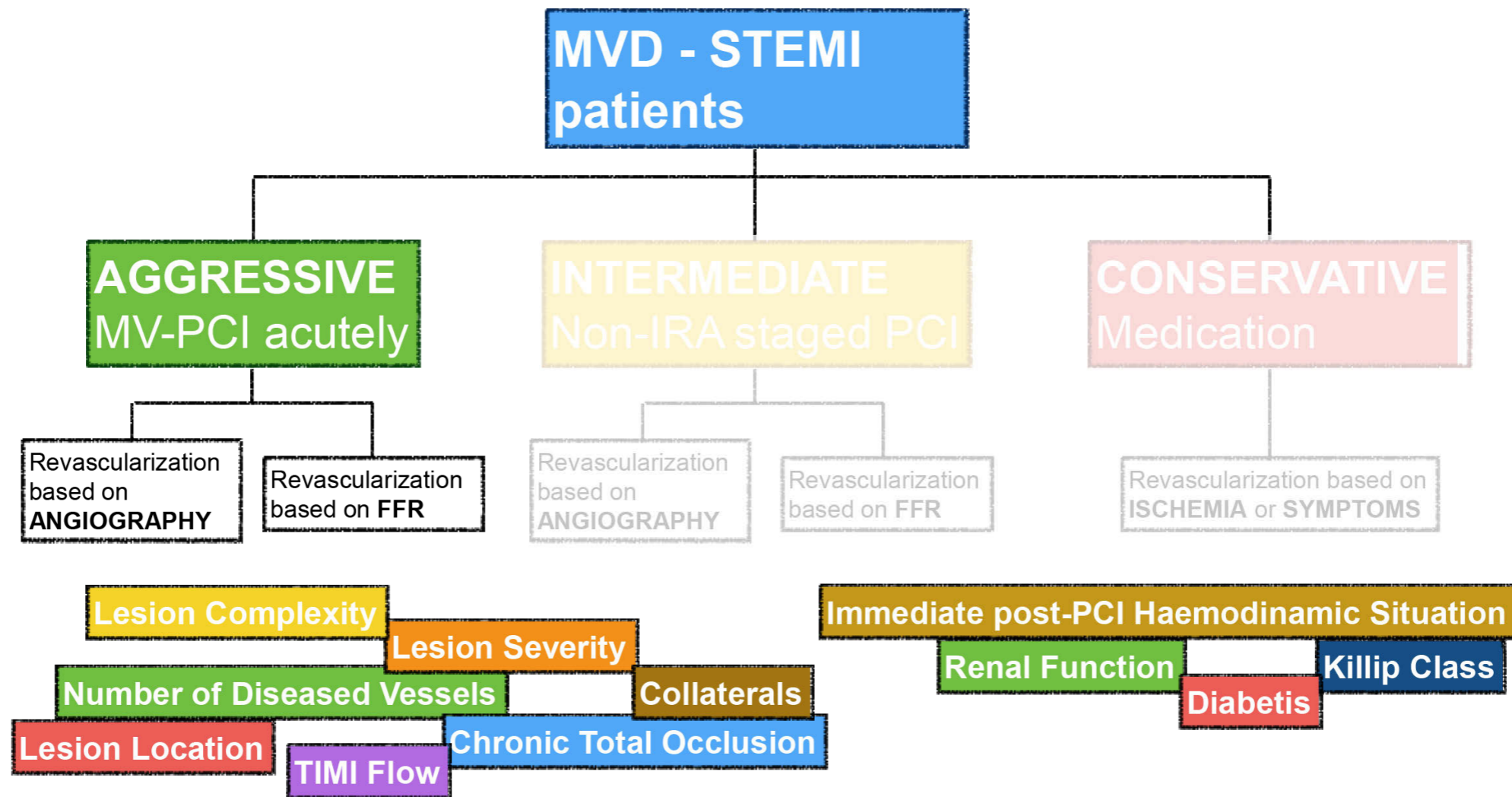
Study	Modality	Lesion characteristic(s)	Clinical endpoint	Positive predictive value	Negative predictive value
PROSPECT <i>n</i> =697	 IVUS & IVUS-VH	PB \geq 70% & MLA $<$ 4mm ² & IVUS-VH TCHA	MACE	18%	98%
ATHEROREMO IVUS <i>n</i> =581	 IVUS & IVUS-VH	PB \geq 70% & MLA $<$ 4mm ² & IVUS-VH TCHA	MACE	23%	93%
PREDICTION <i>n</i> =506	 IVUS & ESS	PB \geq 58% & Low ESS $<$ 1.0 Pa	PCI	41%	92%
ATHEROREMO NIRS <i>n</i> =203	 NIRS	LCBI _{4mm} $>$ 43	MACE	12%	99%

These methodologies have established a **link between in vivo plaque characteristics and subsequent coronary events**, thereby **improving individual risk stratification**, paving the way for risk-tailored systemic therapies and **raising the option for pre-emptive interventions**

Koskinas KC et al. Intracoronary imaging of coronary atherosclerosis: validation for diagnosis, prognosis and treatment. Eur Heart J;2016;37:524-535

Treatment Strategies in Patients with STEMI and Multivessel Disease

There are about 60 possible scenarios based on combinations of angiographic and clinical findings in individual patients



Conclusions

Multivessel disease should be recognized as a major adverse prognostic factor in patients with STEMI

Multivessel disease in STEMI is not a single entity and thus the treatment approach should be individualized

Randomized controlled trials (PRAMI, CvLPRIT, DANAMI-3 PRIMULTI, COMPARE ACUTE) showed that preventive PCI is safe and improves outcomes mainly driven by the need of repeat revascularization

Patients who are asymptomatic and have negative functional tests and no evidence for silent ischaemia after their first STEMI should currently be treated conservatively

Future studies should clarify whether complete revascularization should be done acutely during the index procedure or at later time and whether it has an effect on hard endpoints

The every day real-life clinical practice brings much more different clinical scenarios. It is unlikely that any randomized clinical trial in the future can be able to fully address this complexity and thus, **experienced, wise clinical judgement will probably remain the most important factor in this difficult situation**



thank you!

