Guideline Today: Focus on the Culprit

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Presenter Disclosure Information

David R. Holmes, Jr., M.D.

**"Guideline Today:
Focus on the Culprit"**

The following relationships exist related to this presentation:

None

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Why Consider Multivessel PCI in STEMI?
Culprit + Other Significant Lesions

- Multiple IRA
  - Inconclusive ECG
- Improve prognosis
  - Treat shock
  - Reduce ischemic burden
  - Stabilize potentially unstable plaque
- ? Patient preference/convenience
- Cost containment

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dilate

bet'cha can't ~~eat~~ just one!

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Why Avoid Multivessel PCI in STEMI?
Culprit + Staged PCI

- Difficult clinical environment
  - Hemodynamic and electrical instability
- Difficult biochemical environment
  - Prothrombotic and inflammatory
- Increased contrast use
  - Risk of CIN and volume overload
- Overestimation of lesion severity
  - True “oculostenotic reflex”
    - Vasoconstriction, abnormal flow/endothelium
- Risk of hemodynamic spiral and worse prognosis with failed procedure

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ESC 2012

Recommendations	Class	Level
Primary PCI should be limited to the culprit vessel with the exception of cardiogenic shock & persistent ischemia after PCI of the supposed culprit lesion	IIa	B

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ACC/AHA 2013

	COR	LOE
Ischemic symptoms <12 h	I	A
Ischemic symptoms <12 h & 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

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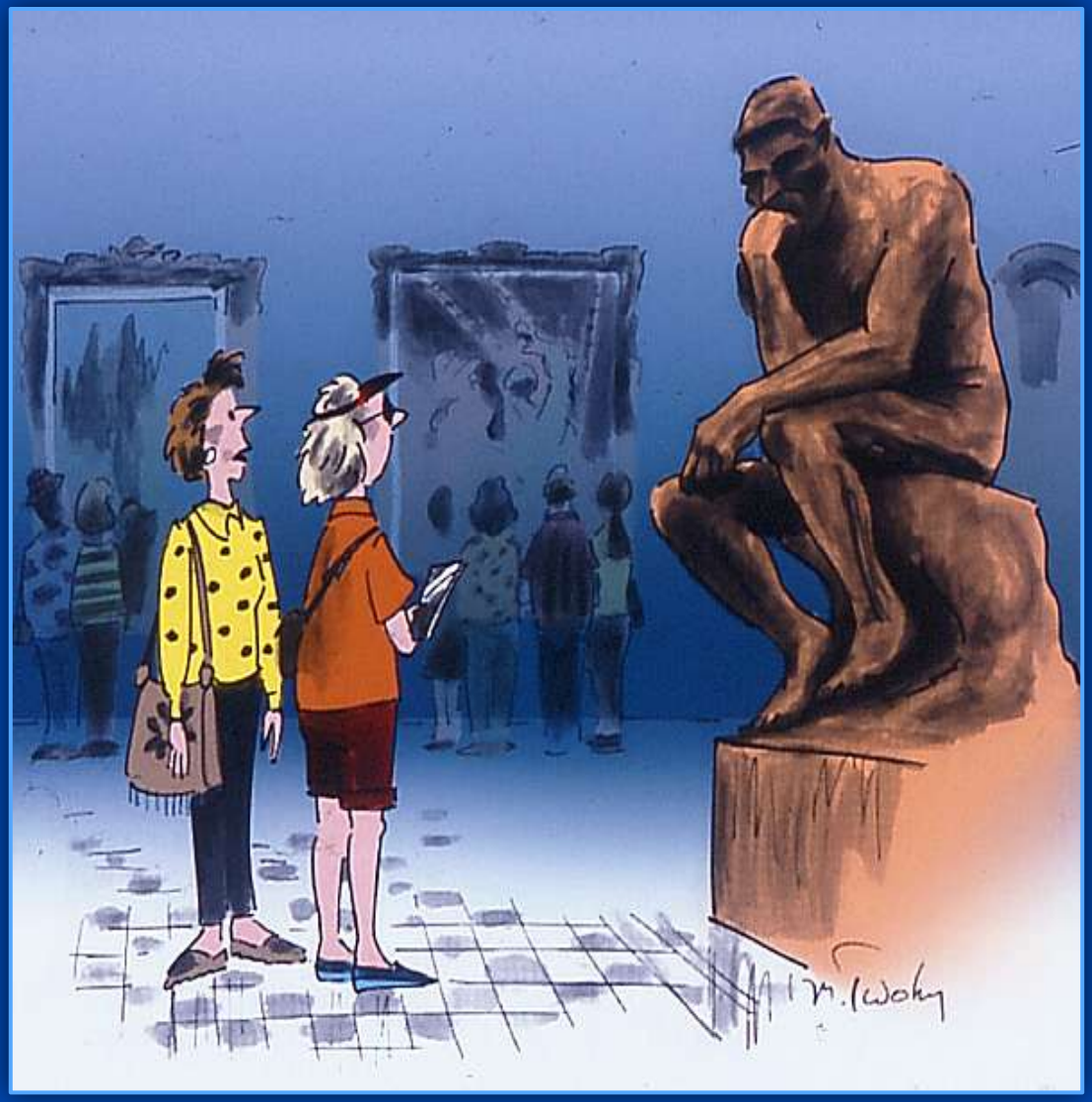

"Personally, I'm a doer."

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Preventive Angioplasty

- Multicenter study
  - 465 patients with STEMI and MVD
- Randomization
  - PCI IRA alone (n=231)
  - Preventive PCI in non-infarct coronary arteries (n=234)
- Primary outcome
  - Composite cardiac death
  - Non fatal MI
  - Refractory angina

Wald et al: NEJM 369:115, 2013

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PRAMI
Clinical Outcomes

Outcome	Preventive PCI (N=234) # of events	No Preventive PCI (N=234) # of events	Hazard Ratio (95% CI)	P
Primary Outcome				
D from cardiac causes, nonfatal MI or refractory angina	21	53	0.35 (0.21-0.58)	<0.001
D from cardiac causes or nonfatal MI	11	27	0.36 (0.18-0.73)	0.004
D from cardiac causes	4	10	0.34 (0.11-1.08)	0.07
Nonfatal MI	7	20	0.32 (0.13-0.75)	0.009
Refractory angina	12	30	0.35 (0.18-0.69)	0.002
Secondary outcomes				
D 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

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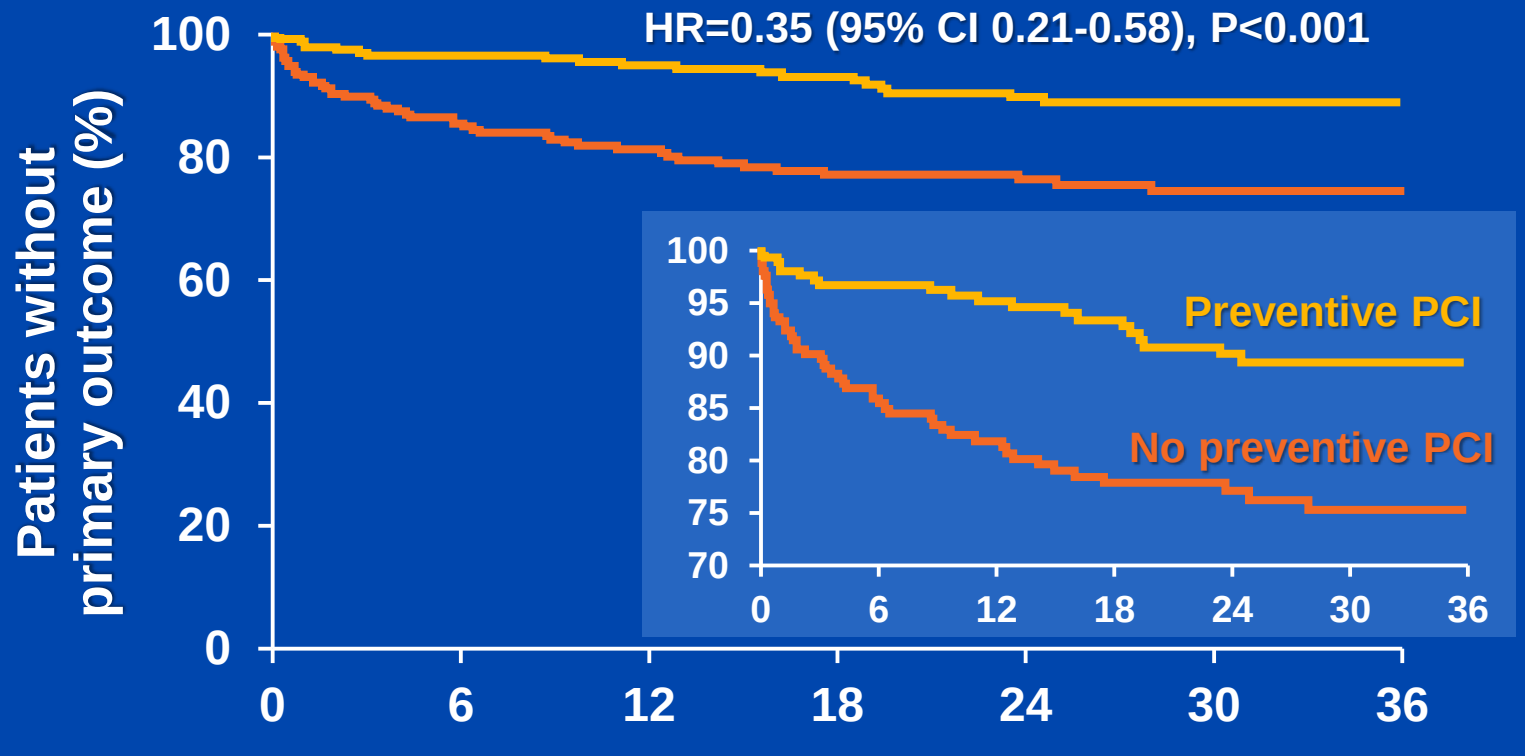
Wald DS et al: N Engl J Med 369:1115-23, 2013

Primary Outcome



At risk (no.)							
Preventive PCI	234	196	166	146	118	89	67
No preventive PCI	231	168	144	122	96	74	50

Wald et al: NEJM 369:115, 2013

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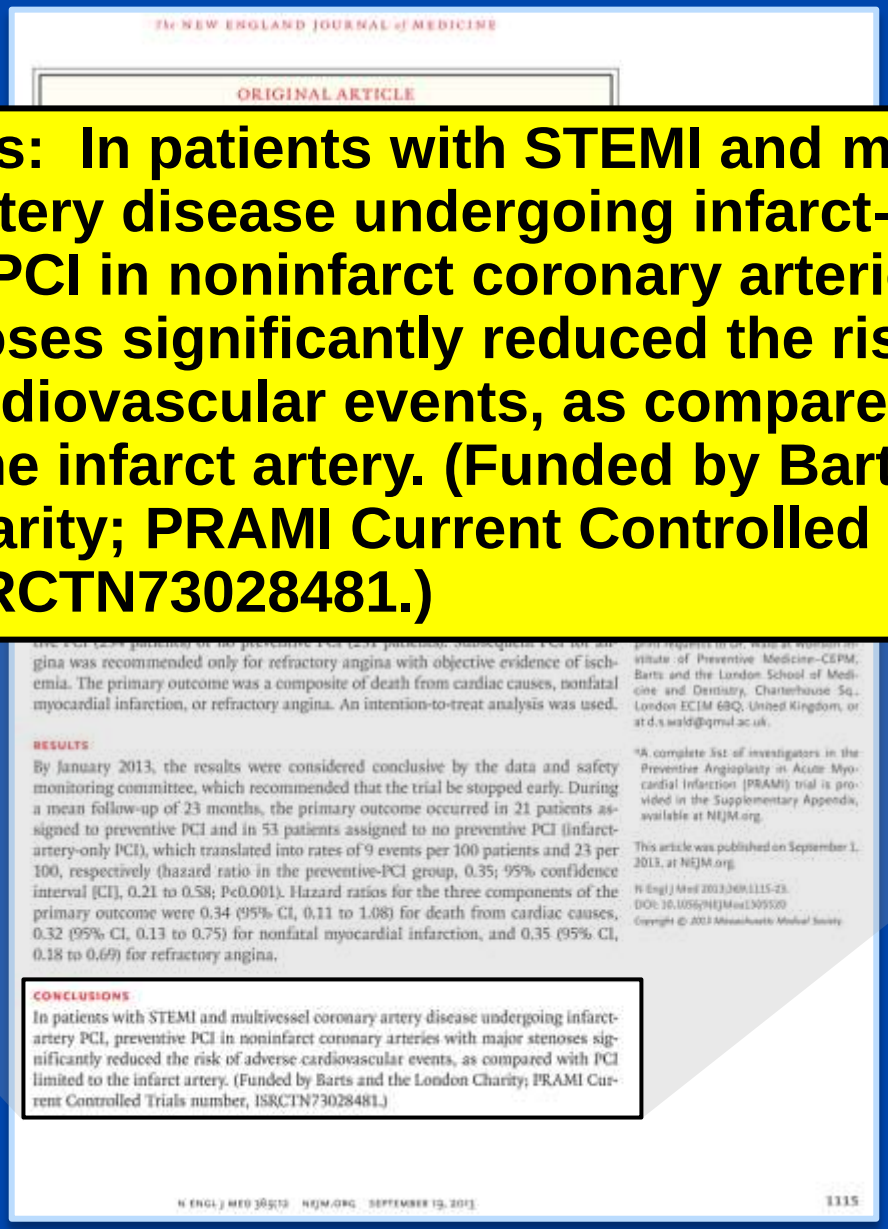
Conclusions: In patients with STEMI and multivessel coronary artery disease undergoing infarct-artery PCI, preventive PCI in noninfarct coronary arteries with major stenoses significantly reduced the risk of adverse cardiovascular events, as compared with PCI limited to the infarct artery. (Funded by Barts and the London Charity; PRAMI Current Controlled Trials number, ISRCTN73028481.)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

gina was recommended only for refractory angina with objective evidence of ischemia. The primary outcome was a composite of death from cardiac causes, nonfatal myocardial infarction, or refractory angina. An intention-to-treat analysis was used.

RESULTS

By January 2013, the results were considered conclusive by the data and safety monitoring committee, which recommended that the trial be stopped early. During a mean follow-up of 23 months, the primary outcome occurred in 21 patients assigned to preventive PCI and in 53 patients assigned to no preventive PCI (infarct-artery-only PCI), which translated into rates of 9 events per 100 patients and 23 per 100, respectively (hazard ratio in the preventive-PCI group, 0.35; 95% confidence interval [CI], 0.21 to 0.58; P<0.001). Hazard ratios for the three components of the primary outcome were 0.34 (95% CI, 0.11 to 1.08) for death from cardiac causes, 0.32 (95% CI, 0.13 to 0.75) for nonfatal myocardial infarction, and 0.35 (95% CI, 0.18 to 0.69) for refractory angina.

CONCLUSIONS

In patients with STEMI and multivessel coronary artery disease undergoing infarct-artery PCI, preventive PCI in noninfarct coronary arteries with major stenoses significantly reduced the risk of adverse cardiovascular events, as compared with PCI limited to the infarct artery. (Funded by Barts and the London Charity; PRAMI Current Controlled Trials number, ISRCTN73028481.)

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*A complete list of investigators in the Preventive Angioplasty in Acute Myocardial Infarction (PRAMI) trial is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on September 1, 2013, at NEJM.org.

N Engl J Med 2013;369:1115-23.
DOI: 10.1056/NEJMoa1305520

Wald et al: NEJM 369:115, 2013

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Systematic Review and Meta-Analysis

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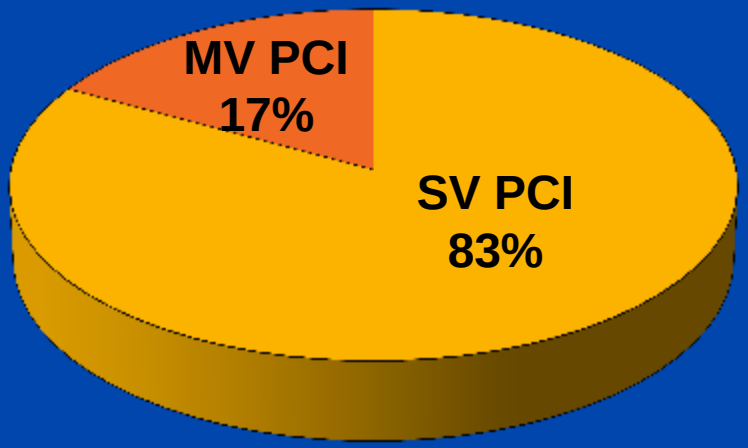
Complete vs Culprit Vessel PCI

- Systematic review and meta-analysis 1996-2011
- Of 507 citations reviewed
  - 26 studies selected
  - 3 randomized
  - 23 non-randomized
  - 46,324 patients



Bainey et al: AHJ 167:1, 2014

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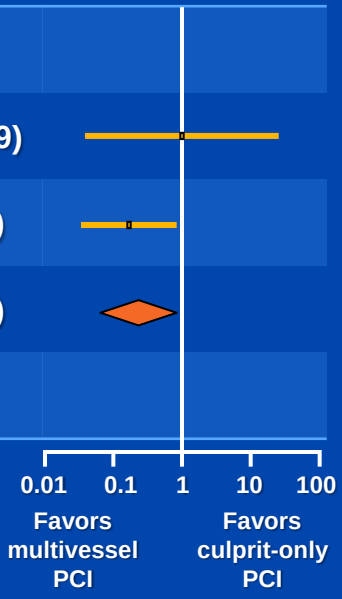
In-Hospital Mortality by Study Approach Randomized Clinical Studies

Study or subgroup	Multivessel PCI Events	Multivessel PCI Total	Culprit-only PCI Events	Culprit-only PCI Total	Weight (%)	Odds ratio M-H, fixed, 95% CI
1.1.1 randomized						
Di Mario 2004	1	52	0	17	0.1	1.02 (0.04, 26.19)
Politi 2009	2	130	7	84	1.7	0.17 (0.03, 0.85)
Subtotal (95% CI)		182		101	1.9	0.24 (0.06, 0.91)
Total events	3		7			

Heterogeneity: Chi^2=0.93, df=1; P=0.33; I^2=0%
Test for overall effect: Z=2.10; P=0.04



Bainey et al: AHJ 167:1, 2014

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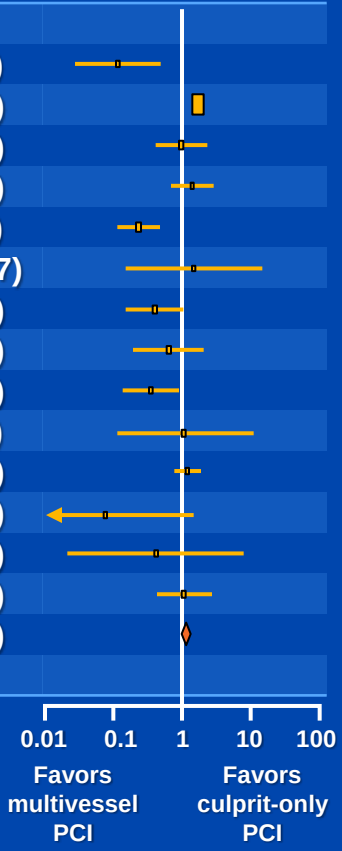
In-Hospital Mortality by Study Approach Observational Studies

Study or subgroup	Multivessel PCI Events	Multivessel PCI Total	Culprit-only PCI Events	Culprit-only PCI Total	Weight (%)	Odds ratio M-H, fixed, 95% CI
1.1.2 randomized						
Barringhaus 2010	2	303	76	1,345	5.7	0.11 (0.03, 0.45)
Cavender 2009	246	3,134	1,321	25,802	54.5	1.58 (1.37, 1.82)
Corpus 2004	8	152	20	354	2.4	0.93 (0.40, 2.16)
Hannan 2010	20	762	15	762	3.0	1.34 (0.68, 2.64)
Hudzik 2009	9	457	136	1,642	12.0	0.22 (0.11, 0.44)
Jin 2007	1	215	3	905	0.2	1.40 (0.15, 13.57)
Kalarus 2007	5	193	40	605	3.9	0.38 (0.15, 0.97)
Katayama 2005	6	20	15	36	1.5	0.60 (0.19, 1.92)
Kong 2006	5	632	31	1,350	4.1	0.34 (0.13, 0.88)
Qarawani 2008	4	95	1	25	0.3	1.05 (0.11, 9.88)
Rahman 2010	29	578	64	1,449	7.2	1.14 (0.73, 1.79)
Rigattieri 2008	0	64	4	46	1.1	0.07 (0.00, 1.40)
Telayna 2002	0	17	6	96	0.4	0.40 (0.02, 7.39)
Varani 2008	13	243	8	156	1.9	1.05 (0.42, 2.58)
Subtotal (95% CI)		6,865		34,573	98.1	1.12 (1.00, 1.27)
Total events	348		1,740			

Heterogeneity: $Chi^2=70.83$, df=13; P<0.00001; $I^2=82\%$
Test for overall effect: Z=1.89; P=0.06



Bainey et al: AHJ 167:1, 2014

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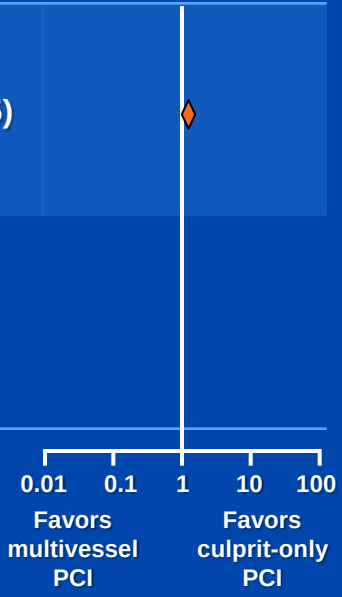
In-Hospital Mortality by Study Approach RCT's and Registries

Study or subgroup	Multivessel PCI Events	Multivessel PCI Total	Culprit-only PCI Events	Culprit-only PCI Total	Weight (%)	Odds ratio M-H, fixed, 95% CI
Total (95% CI)		7,047		34,674	100.0	1.11 (0.98, 1.25)
Total events	351		1,747			

Heterogeneity: Chi^2=77.15, df=15; P<0.00001; I^2=81%
Test for overall effect: Z=1.66; P=0.10
Test for subgroup differences: Chi^2=5.13; df=1; P=0.02; I^2=80.5%



Bainey et al: AHJ 167:1, 2014

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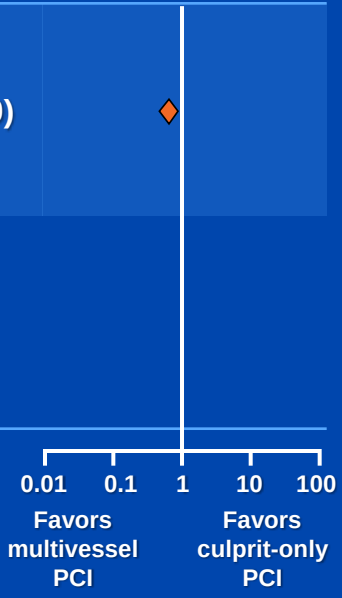
Repeat PCI by Study Method

Study or subgroup	Multivessel PCI Events	Multivessel PCI Total	Culprit-only PCI Events	Culprit-only PCI Total	Weight (%)	Odds ratio M-H, fixed, 95% CI
Total (95% CI)		750		1,738	100.0	0.65 (0.46, 0.90)
Total events	59		144			

Heterogeneity: Chi^2=22.87, df=5; P=0.0004; I^2=78%
Test for overall effect: Z=2.58; P=0.100
Test for subgroup differences: Chi^2=8.10; df=1; P=0.004; I^2=87.7%



Bainey et al: AHJ 167:1, 2014

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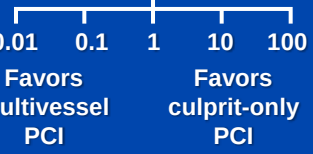
Long-Term Mortality by Timing of Multivessel PCI Staged in Hospital

Study or subgroup	Multivessel PCI Events	Multivessel PCI Total	Culprit-only PCI Events	Culprit-only PCI Total	Weight (%)	Odds ratio M-H, fixed, 95% CI
1.21.2 staged – in-hospital						
Barringhaus 2010	2	252	30	956	9.8	0.25 (0.06, 1.04)
Corpus 2004	12	126	42	354	15.7	0.78 (0.40, 1.54)
Hannan 2010	16	259	116	1,300	28.5	0.67 (0.39, 1.15)
Kalarus 2007	14	193	112	605	39.6	0.34 (0.19, 0.62)
Rigattieri 2008	1	64	7	46	6.3	0.09 (0.01, 0.75)
Subtotal (95% CI)		894		3,261	100.0	0.48 (0.35, 0.67)
Total events	45		307			

Odds ratio M-H, fixed, 95% CI



Heterogeneity: $Chi^2=7.97$, df=4; P=0.09; $I^2=50\%$
Test for overall effect: Z=4.41; P<0.0001

Bainey et al: AHJ 167:1, 2014

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Complete vs culprit-only revascularization for patients with multivessel disease undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: A systematic review and meta-analysis

Kevin R. Bainey, MD, MSC,[a] Shamir R. Mehta, MD, MSC,[b] Tony Lai, MBBS,[b] and Robert C. Welsh, MD[a] *Alberta, and Ontario, Canada*

Background Patients with ST-segment elevation myocardial infarction (STEMI) and multivessel coronary artery disease who undergo primary percutaneous coronary intervention (PCI) are most commonly treated with PCI to the culprit lesion only. Whether a strategy of complete revascularization in these patients is superior is unknown. We performed a meta-analysis comparing the benefits and risks of routine culprit-only PCI vs multivessel PCI in STEMI.

Methods MEDLINE, EMBASE, ISI Web of Science, and The Cochrane Register of Controlled Trials were searched from 1996 to January 2011. Relevant conference abstracts were searched from January 2002 to January 2011. Studies included STEMI with multivessel disease receiving primary PCI. The primary end point was long-term mortality. Data were combined using a fixed-effects model.

Results Of 507 citations, 26 studies (3 randomized, 23 nonrandomized; 46,324 patients, 7886 multivessel PCI and 38,438 culprit-only PCI) were included. There was no significant difference in hospital mortality with multivessel PCI vs culprit-only PCI (odds ratio [OR] 1.11, 95% CI 0.98-1.25, $P = .10$ [randomized OR 0.24, 95% CI 0.06-0.91, $P = .04$; nonrandomized OR 1.12, 95% CI 1.00-1.27, $P = .06$]). However, if multivessel PCI during index catheterization was performed, hospital mortality was increased (OR 1.35, 95% CI 1.19-1.54, $P < .001$). When multivessel PCI was performed as a staged procedure, hospital mortality was lower (OR 0.35, 95% CI 0.21-0.59; $P < .001$; P interaction $< .001$). Reduced long-term mortality (OR 0.74, 95% CI 0.65-0.85, $P < .001$ [randomized OR 0.61, 95% CI 0.28-1.33, $P = .22$; nonrandomized OR 0.75, 95% CI 0.65-0.86, $P < .001$]) and repeat PCI (OR 0.65; 95% 0.46-0.90, $P = .01$ [randomized OR 0.31, 95% CI 0.17-0.57, $P < .001$; nonrandomized OR 0.88, 95% CI 0.59-1.31, $P = .54$]) were observed with multivessel PCI.

Conclusion Overall, staged multivessel PCI improved short- and long-term survival and reduced repeat PCI. Still, large randomized trials are required to confirm the benefits of staged multivessel PCI in STEMI. (Am Heart J 2014;167:1-14.e2.)

Conclusion: Overall, staged multivessel PCI improved short- and long-term survival and reduced repeat PCI. Still, large randomized trials are required to confirm the benefits of staged multivessel PCI in STEMI

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0002-8703/$ - see front matter

http://dx.doi.org/10.1016/j.ahj.2013.09.018

offer advantages over a strategy of culprit lesion–only PCI because plaque instability may not be limited to the infarct-related artery but may involve other territories in the coronary vasculature.[16] Moreover, complete revascularization has been associated with improved long-term

Bainey et al: AHJ 167:1, 2014

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THINKER

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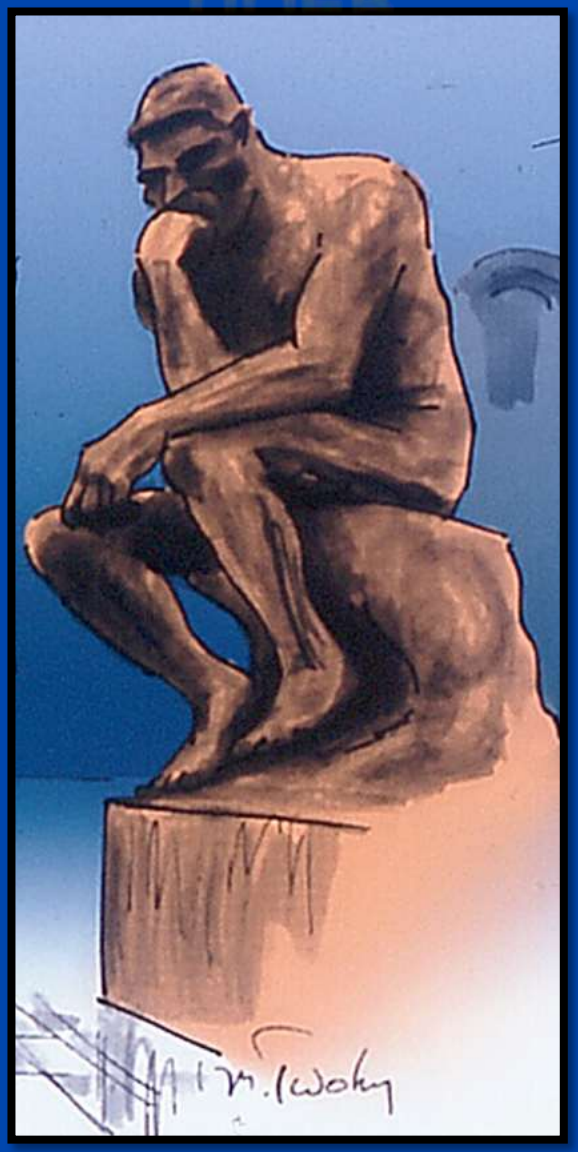

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The feasibility of a procedure is not the best indication for its performance

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OO

- Dec. 31, 2013
  - 58-y.o. male
    - 4 week history of progressive exertional chest pain relieved by rest
    - Day of admission developed persistent pain while driving
  - Arrived in ER with pain
    - ST segment elevation at baseline
    - Treated with Heparin, ASA, clopidogrel
    - Some improvement
    - Transferred by ambulance to St. Mary's

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- Dec. 31, 2013
  - Cardiac Cath
    - Slight lingering pain

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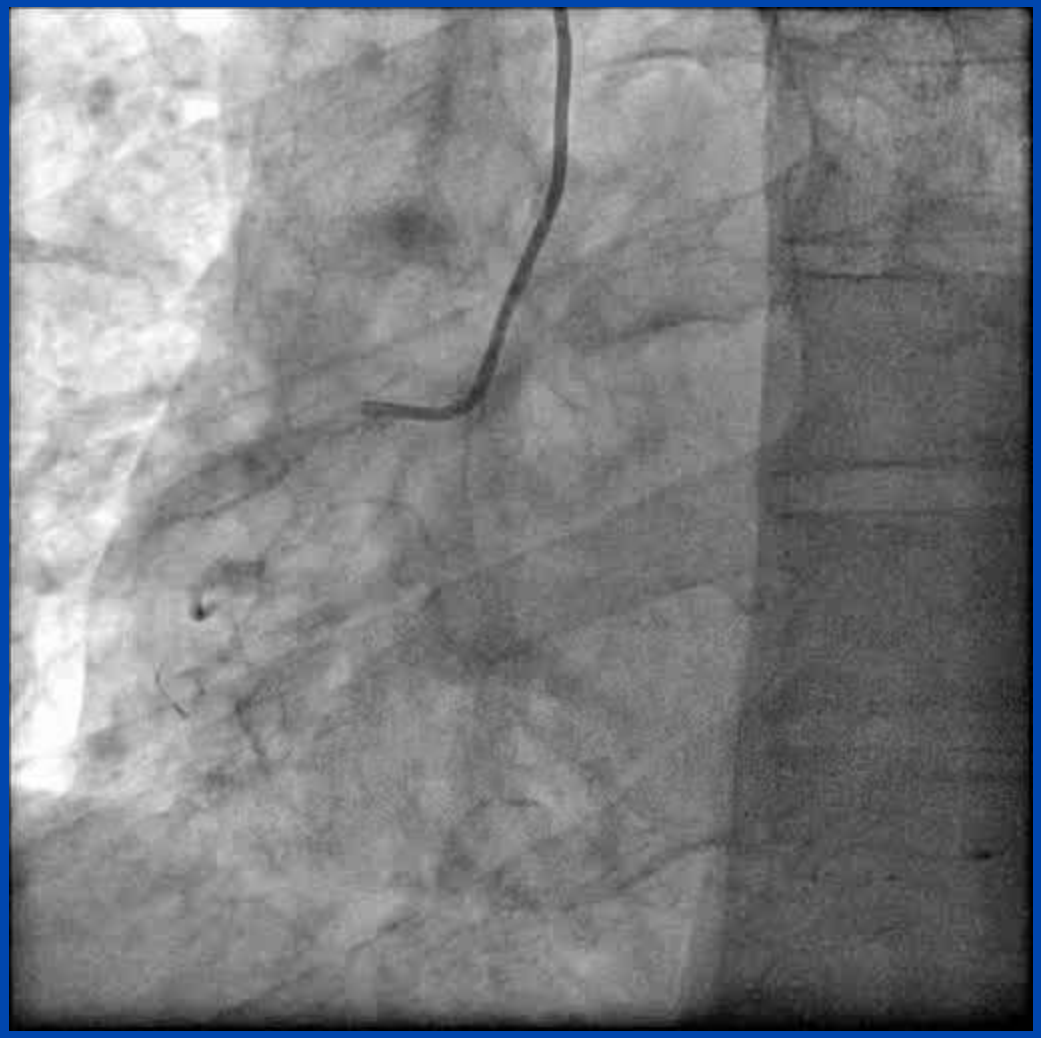

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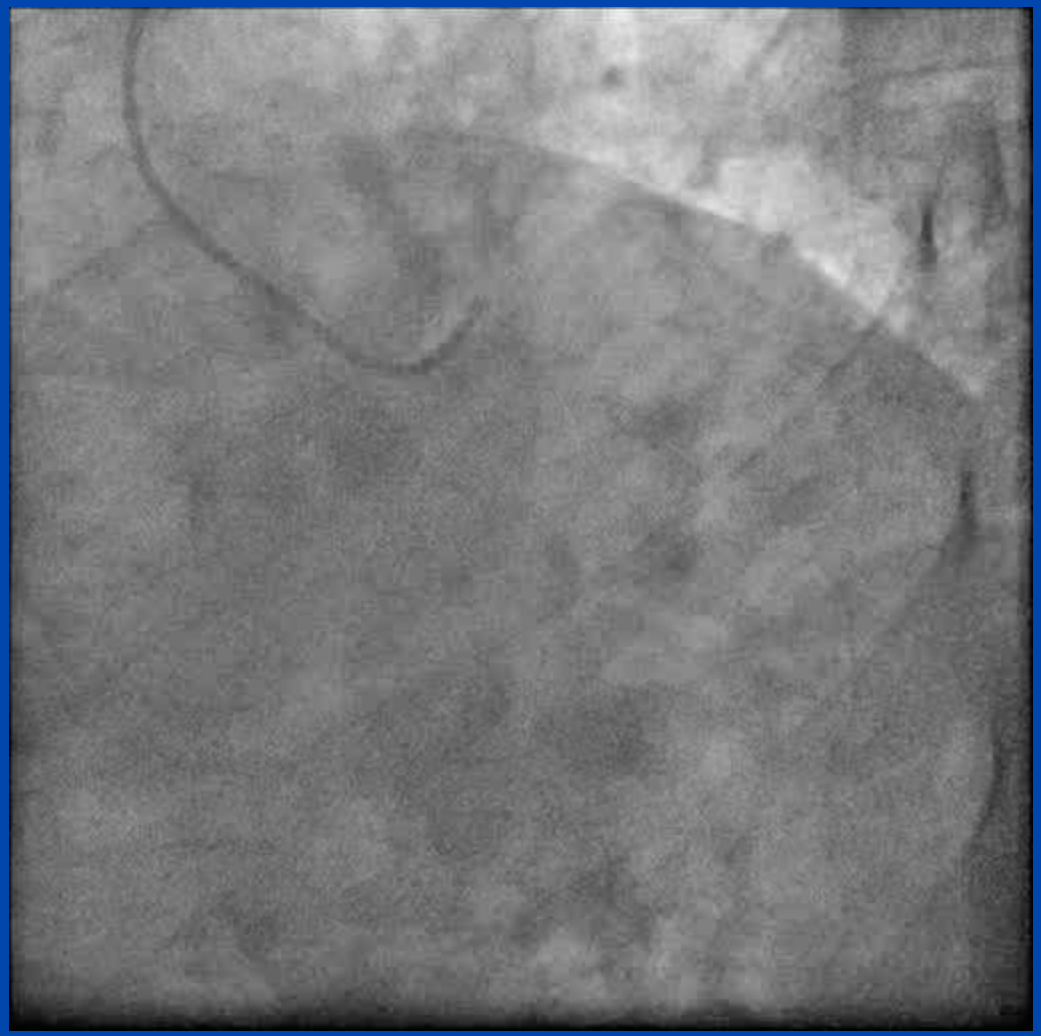

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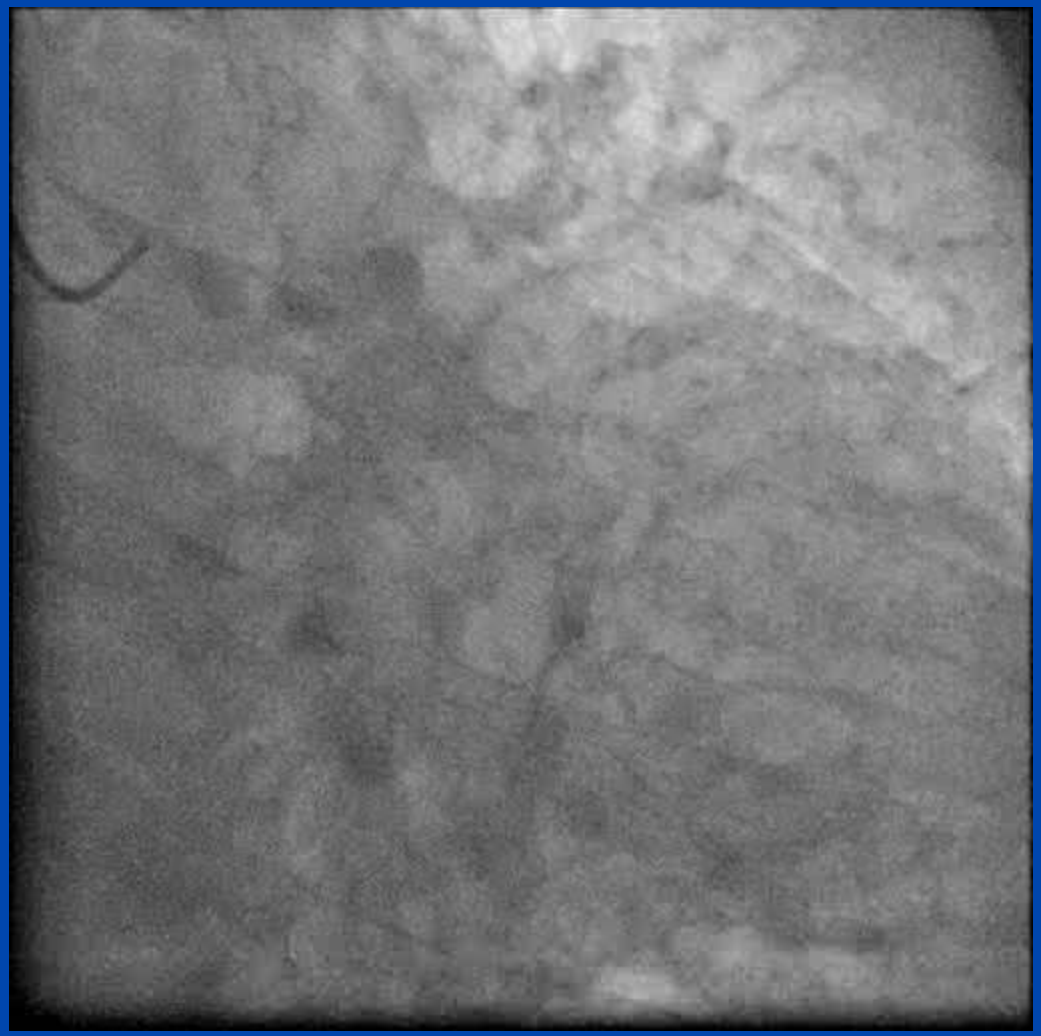

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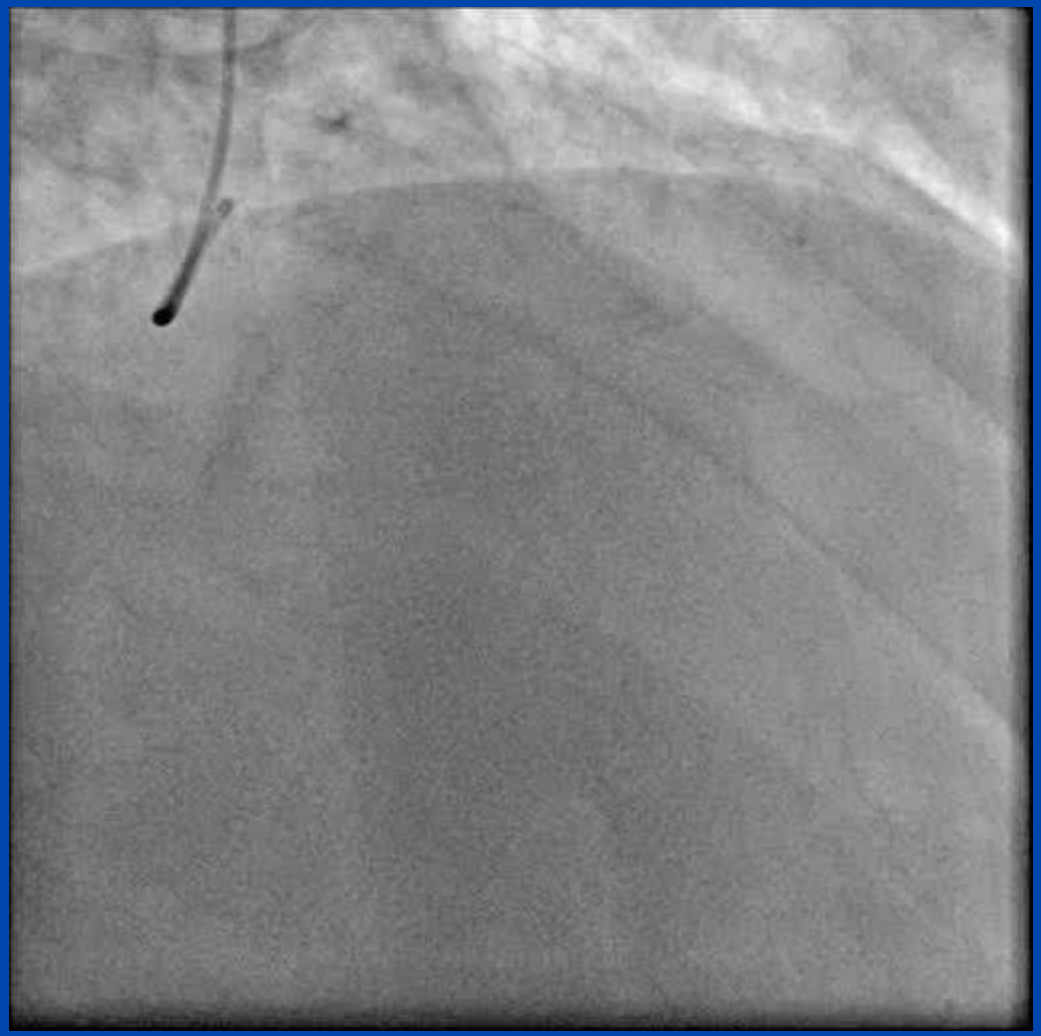

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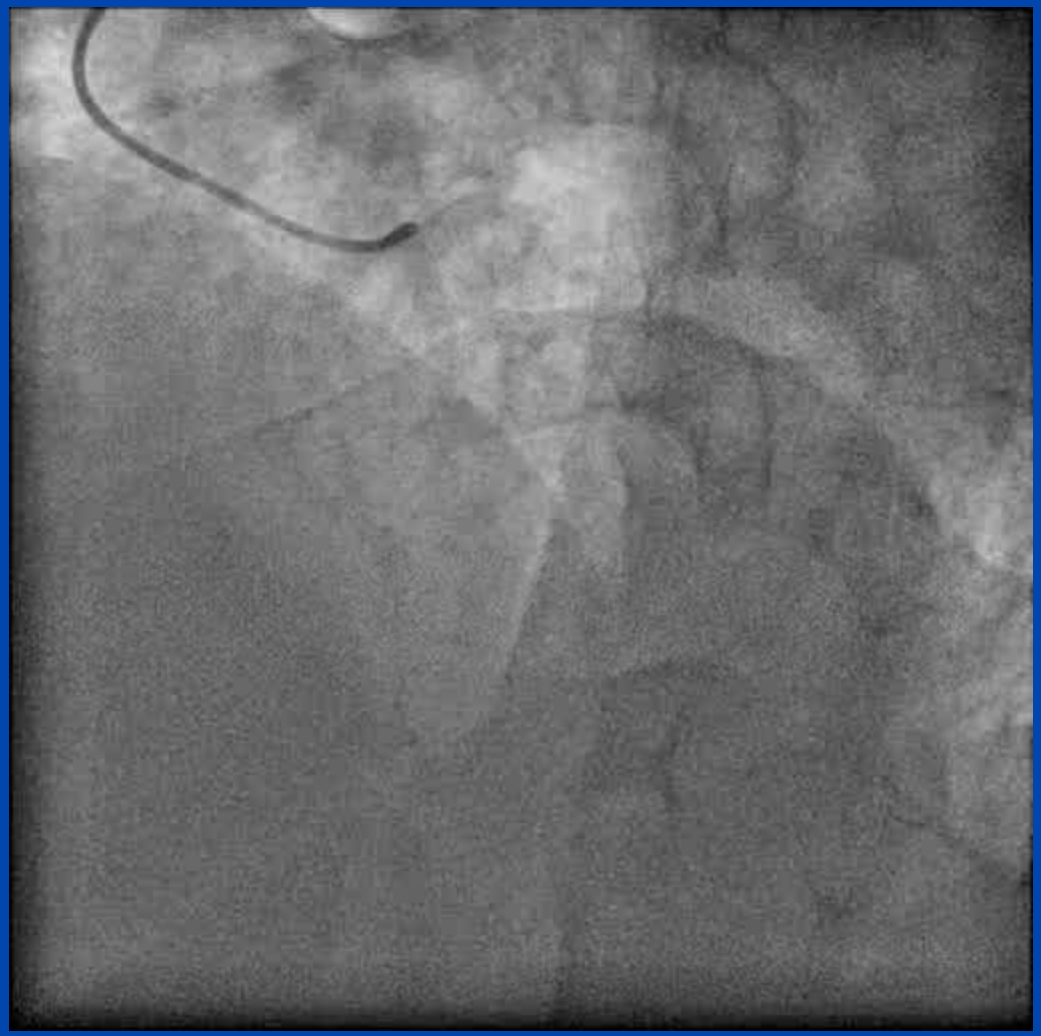

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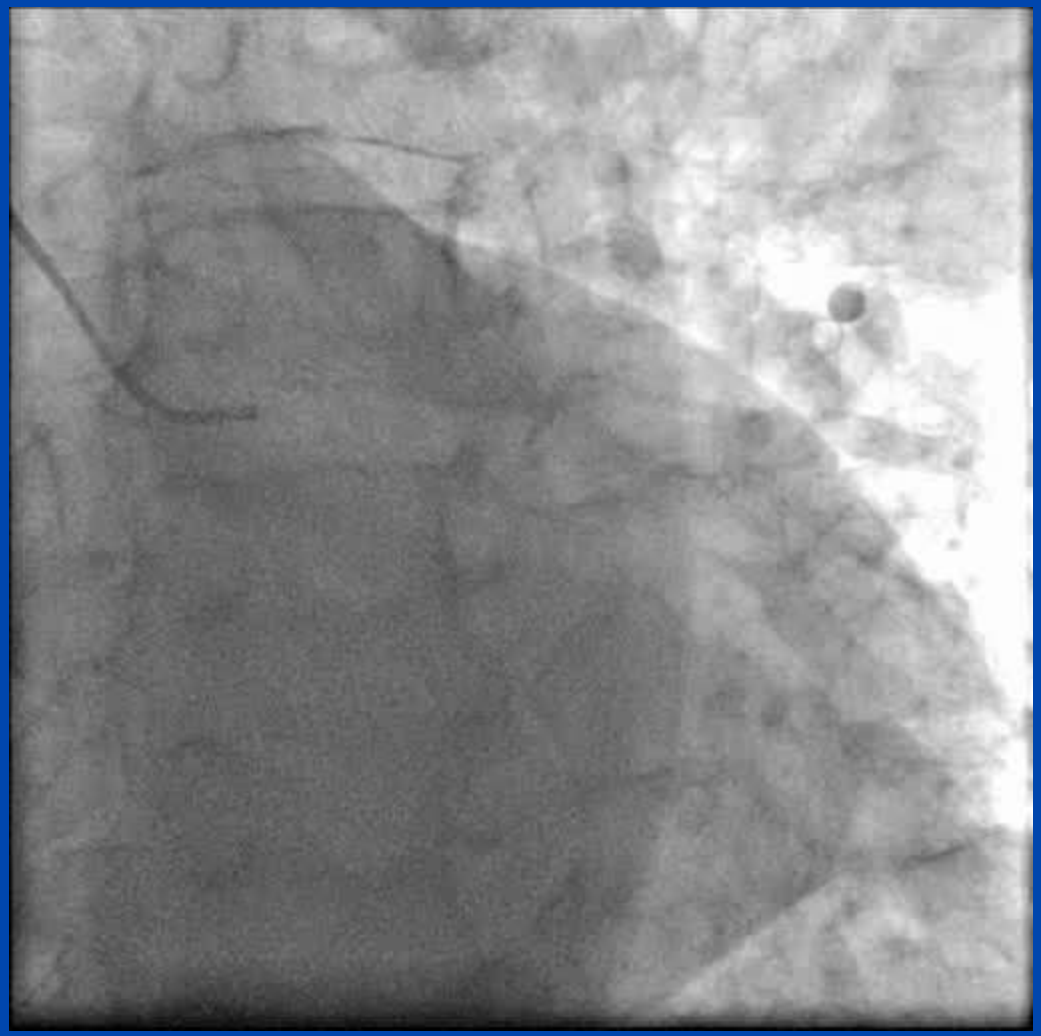

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- Options
  - Dilate and stent LAD
  - Dilate and stent LAD and circumflex

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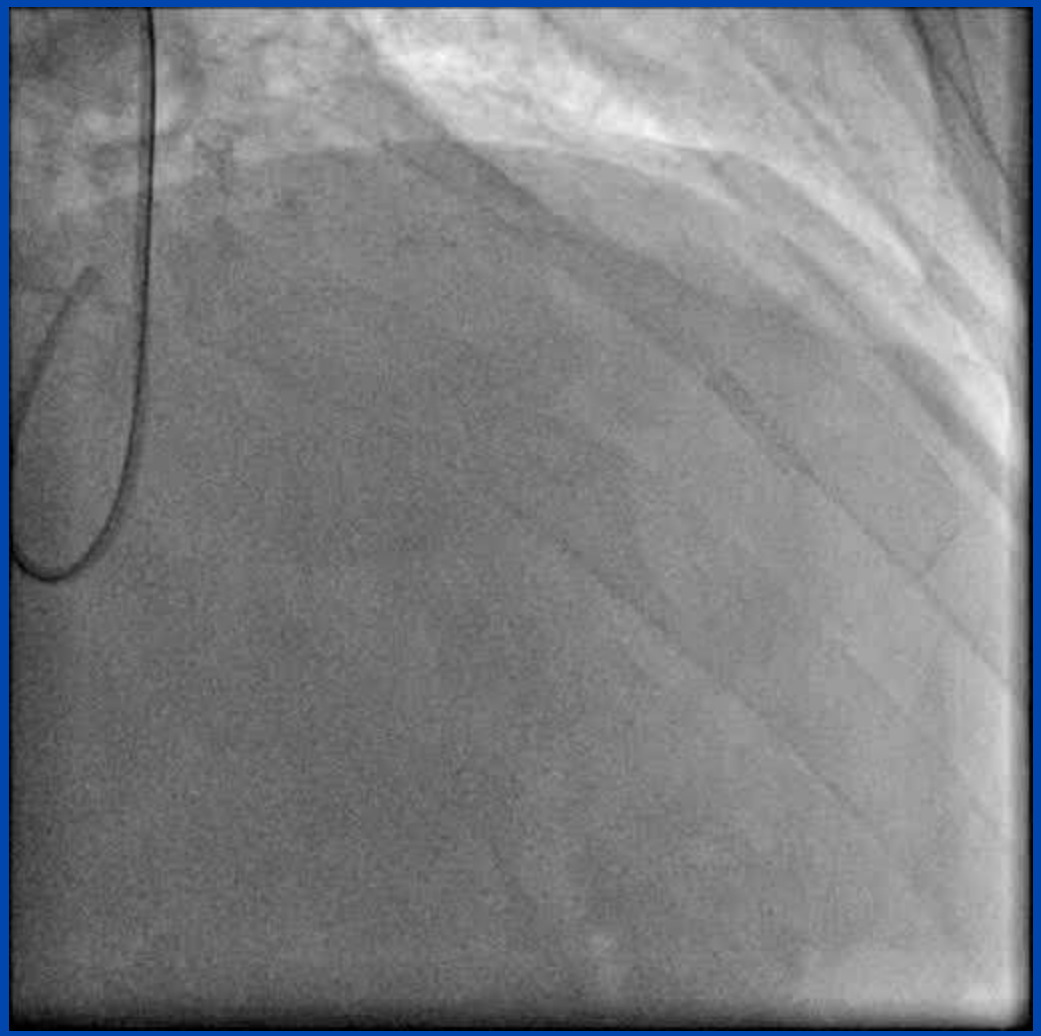

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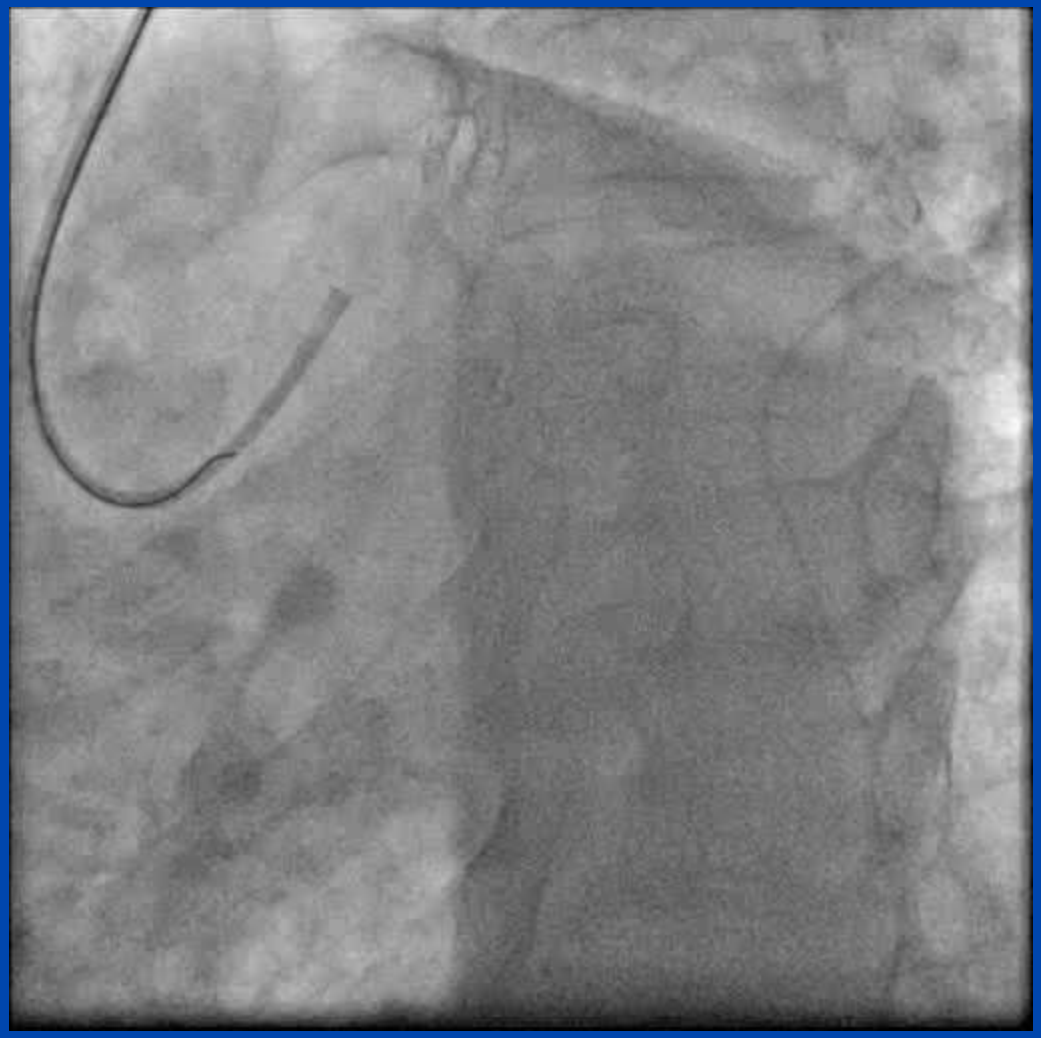

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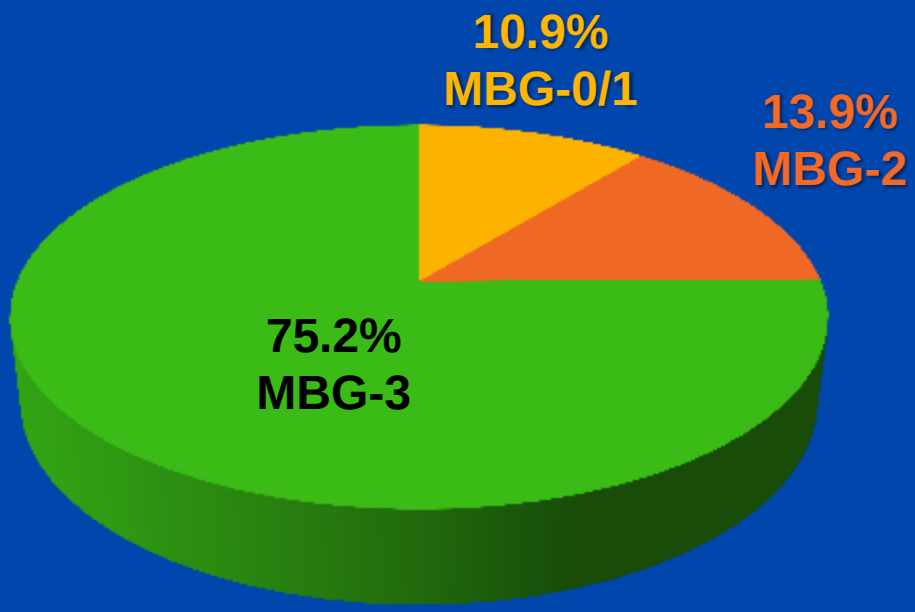
Nonculprit Vessel MBG Affect in ACS

- Angiographic ACUITY substudy
- 3,826 NSTE-ACS patients treated with PCI
- Objective: Assess impact of myocardial hypoperfusion in areas remote from IRA vessel on outcome
- Worst culprit lesion determined in 3,426



Lansky, et al: J Am Coll Cardiol Intv 7:266-75, 2014

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Impact of Nonculprit Vessel Myocardial Perfusion on Outcomes of Patients Undergoing Percutaneous Coronary Intervention for Acute Coronary Syndromes

Analysis From the ACUITY Trial (Acute Catheterization and Urgent Intervention Triage Strategy)

Conclusions: Reduced myocardial perfusion in an area supplied by a nonculprit vessel is associated with increased short- and long-term mortality rates in NSTE-ACS patients undergoing PCI. Furthermore, worst nonculprit MBG is able to risk-stratify patients with normal baseline flow of the culprit vessel.

Methods The angiographic substudy of the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial included 6,921 NSTE-ACS patients. Complete 3-vessel assessments of baseline coronary TIMI (Thrombolysis In Myocardial Infarction) flow grade and myocardial blush grade (MBG) were performed. We examined the outcomes of PCI-treated patients according to the worst nonculprit vessel MBG identified per patient.

Results Among the 3,826 patients treated with PCI, the worst nonculprit MBG was determined in 3,426 (89.5%) patients, including 375 (10.9%) MBG 0/1 patients, 475 (13.9%) MBG 2 patients, and 2,576 (75.2%) MBG 3 patients. Nonculprit MBG 0/1 was associated with worse baseline clinical characteristics. Patients with nonculprit MBG 0/1 versus MBG 3 had increased rates of 30-day (3.0% vs. 0.7%, $p < 0.0001$) and 1-year (4.4% vs. 1.0%, $p < 0.0001$) death. Similar results were found among patients with pre-procedural TIMI flow grade 3 in the culprit vessel, where nonculprit vessel MBG 0/1 (hazard ratio: 2.81 [95% confidence interval: 1.63 to 4.84], $p = 0.0002$) was the strongest predictor of 1-year mortality.

Conclusions Reduced myocardial perfusion in an area supplied by a nonculprit vessel is associated with increased short- and long-term mortality rates in NSTE-ACS patients undergoing PCI. Furthermore, worst nonculprit MBG is able to risk-stratify patients with normal baseline flow of the culprit vessel. (J Am Coll Cardiol Intv 2014;7:266–75) © 2014 by the American College of Cardiology Foundation

Lansky et al: JACC Intv 7:266, 2014

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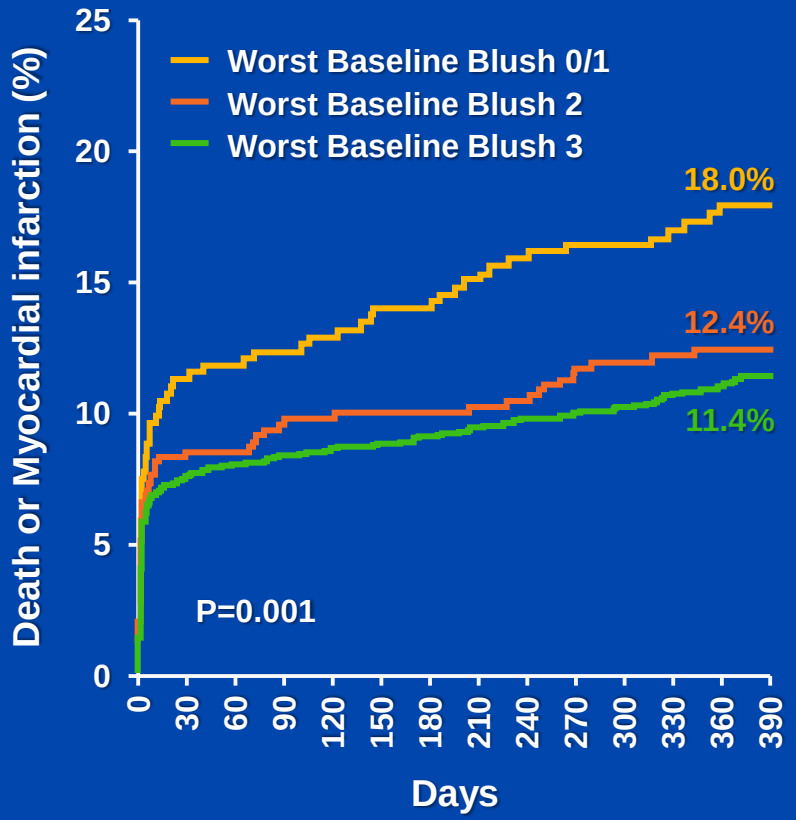
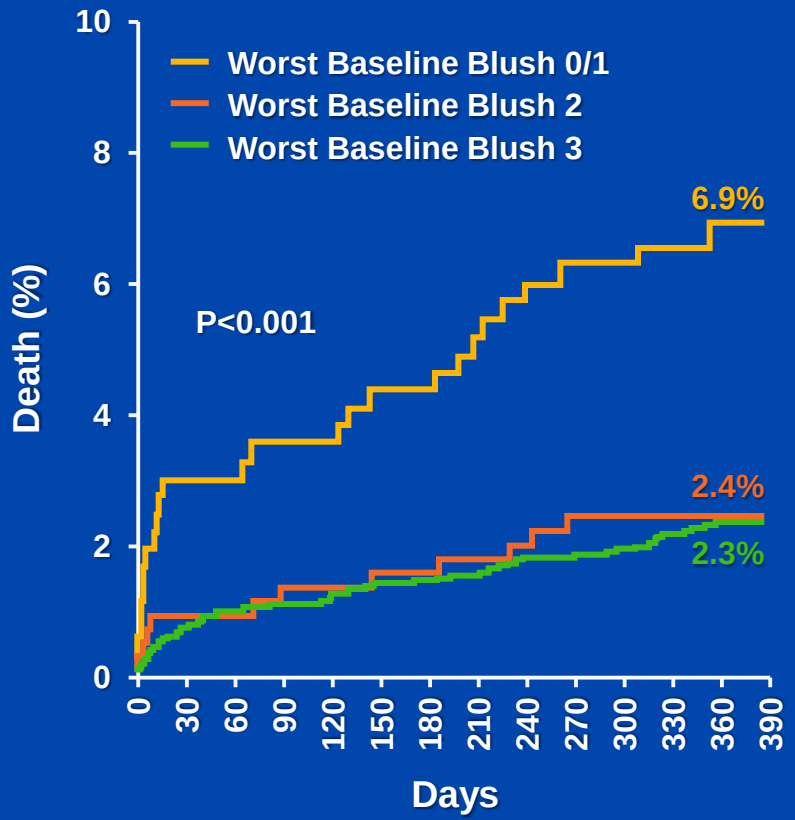
Time-to-Event Curves in Overall PCI Population



No. at risk

Worst Baseline Blush 0/1	375	317	311	301	215
Worst Baseline Blush 2	475	413	410	401	301
Worst Baseline Blush 3	2,576	2,284	2,262	2,231	1,584



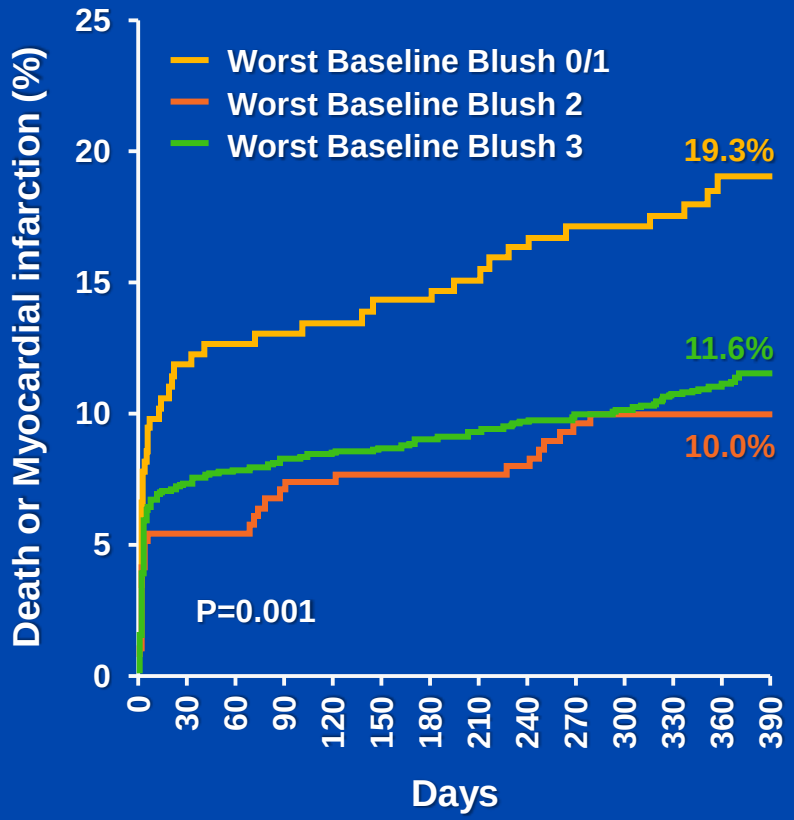
No. at risk

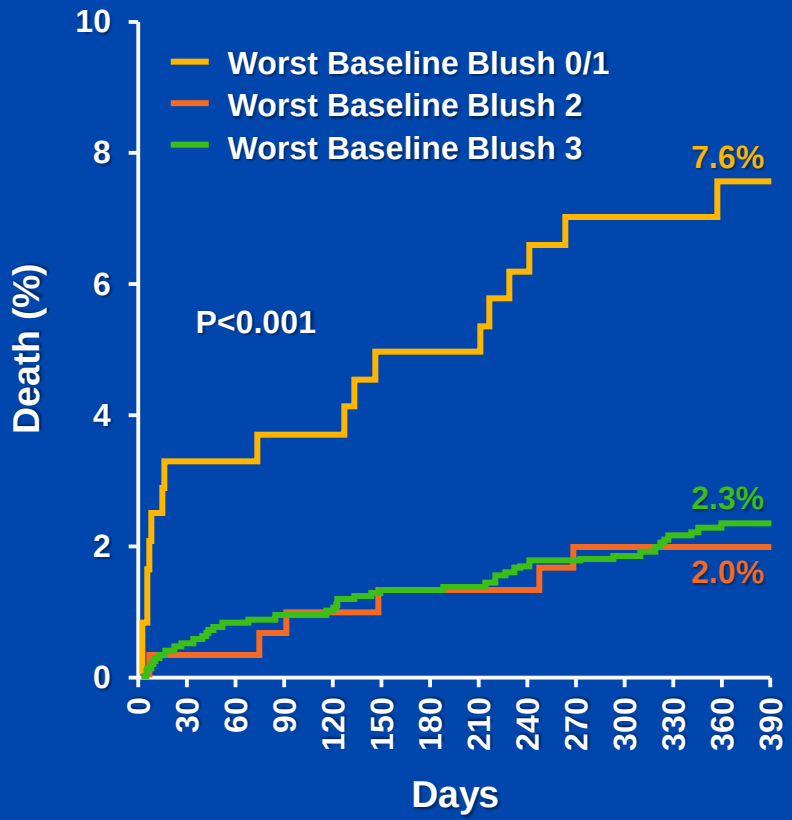
Worst Baseline Blush 0/1	375	350	347	339	247
Worst Baseline Blush 2	475	453	449	444	338
Worst Baseline Blush 3	2,576	2,465	2,453	2,436	1,730

Lansky et al: JACC Intv 7:266, 2014

MAYO CLINIC

Time-to-Event Curves in Patients With Culprit TIMI Flow Grade 3





No. at risk					
Worst Baseline Blush 0/1	244	208	205	198	139
Worst Baseline Blush 2	316	282	279	272	197
Worst Baseline Blush 3	1,876	1,666	1,649	1,628	1,146

No. at risk					
Worst Baseline Blush 0/1	244	231	228	223	162
Worst Baseline Blush 2	316	302	298	295	214
Worst Baseline Blush 3	1,876	1,799	1,790	1,777	1,249

Lansky et al: JACC Intv 7:266, 2014

MAYO CLINIC

Multivariate Analysis of Death/MI & Death in Patients With TIMI Flow Grade 3 in Culprit Vessel

	HR (95% CI)	P
Death/MI		
Nonculprit MBG 0/1 vs 2/3	1.58 (1.12-2.21)	0.009
Prior MI	1.41 (1.09-1.65)	0.01
Renal insufficiency	2.44 (1.88-3.18)	<0.0001
Baseline cardiac biomarker elevation or ST-segment deviation	1.57 (1.20-2.07)	0.001
3-vessel disease	1.45 (1.12-1.88)	0.006
Death		
Nonculprit MBG 0/1 vs 2/3	2.41 (1.37-4.22)	0.002
Age, 10-year increments	2.05 (1.62-2.59)	<0.0001
Diabetes	2.22 (1.37-3.62)	0.001

Lansky et al: JACC Intv 7:266, 2014

MAYO CLINIC

Why

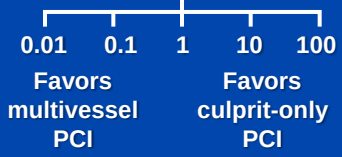
- Single trials never really provide the correct answer unless they agree with what we believe
- Single trials are anecdotes
- Trials are underpowered
- Heterogeneity versus homogeneity
- Our bibliographies need bulking up

MAYO CLINIC

In-Hospital Mortality by Timing of Multivessel Disease At Index Catheterization

	Multivessel PCI		Culprit-only PCI				
Study or subgroup	Events	Total	Events	Total	Weight (%)	Odds ratio M-H, fixed, 95% CI	Odds ratio M-H, fixed, 95% CI
1.20.1 immediately – index catheterization							
Cavender 2009	246	3,134	1,321	25,802	74.7	1.58 (1.37, 1.82)	
Corpus 2004	5	26	20	354	0.6	3.98 (1.36, 11.65)	
Hannan 2010	17	503	15	762	3.3	1.74 (0.86, 3.52)	
Hudzik 2009	9	457	136	1,642	16.5	0.22 (0.11, 0.44)	
Jin 2007	1	215	3	905	0.3	1.40 (0.15, 13.57)	
Katayama 2005	6	20	15	36	2.1	0.60 (0.19, 1.92)	
Qarawani 2008	4	95	1	25	0.4	1.05 (0.11, 9.88)	
Varani 2008	12	147	8	156	2.0	1.64 (0.65, 4.15)	
Subtotal (95% CI)		4,597		29,682	100.0	1.35 (1.19, 1.54)	
Total events	300		1,519				

Heterogeneity: $Chi^2=37.86$, df=7; $P<0.00001$; $I^2=82\%$
Test for overall effect: $Z=4.53$; $P<0.00001$

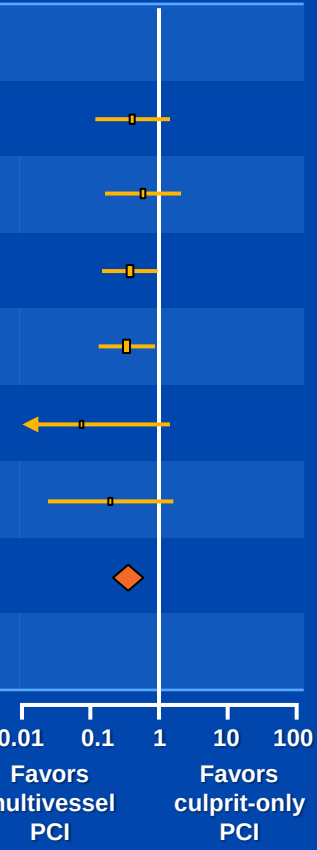


Bainey et al: AHJ 167:1, 2014

MAYO CLINIC

In-Hospital Mortality by Timing of Multivessel Disease During Index Hospitalization

Study or subgroup	Multivessel PCI Events	Multivessel PCI Total	Culprit-only PCI Events	Culprit-only PCI Total	Weight (%)	Odds ratio M-H, fixed, 95% CI
1.20.2 staged – index hospitalization						
Corpus 2004	3	126	20	354	15.2	0.41 (0.12, 1.39)
Hannan 2010	3	259	15	762	11.2	0.58 (0.17, 2.03)
Kalarus 2007	5	193	40	605	27.9	0.38 (0.15, 0.97)
Kong 2006	5	632	31	1,350	29.1	0.34 (0.13, 0.88)
Rigattieri 2008	0	64	4	46	7.7	0.07 (0.00, 1.40)
Varani 2008	1	96	8	156	8.9	0.19 (0.02, 1.58)
Subtotal (95% CI)		4,597		29,682	100.0	1.35 (1.19, 1.54)
Total events	300		1,519			



Heterogeneity: $Chi^2=2.10$, df=5; P=0.83; $I^2=0\%$
Test for overall effect: Z=4.03; P<0.0001
Test for subgroup differences: $Chi^2=25.42$; df=1; P=96.1%

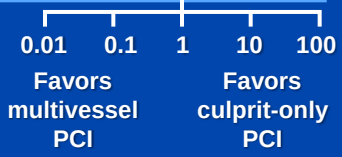
Bainey et al: AHJ 167:1, 2014

MAYO CLINIC

Long-Term Mortality by Timing of Multivessel PCI At time of index Catherization

	Multivessel PCI		Culprit-only PCI				
Study or subgroup	Events	Total	Events	Total	Weight (%)	Odds ratio M-H, fixed, 95% CI	Odds ratio M-H, fixed, 95% CI
1.21.1 index catheterization							
Corpus 2004	5	26	42	354	2.0	1.77 (0.63, 4.94)	
Dziewierz 2010	11	70	57	707	3.8	2.13 (1.06, 4.27)	
Esteves-Loureiro 2010	1	59	25	208	4.8	0.13 (0.02, 0.95)	
Hannan 2010	59	503	116	1,300	25.2	1.36 (0.97, 1.89)	
Hudzik 2009	32	457	265	1,642	47.3	0.39 (0.27, 0.57)	
Jin 2007	7	215	19	901	3.1	1.56 (0.65, 3.77)	
Khattab 2008	2	25	3	45	0.9	1.22 (0.19, 7.82)	
Mohamad 2009	2	7	3	30	0.4	3.60 (0.47, 27.35)	
Qarawani 2008	9	95	2	25	1.3	1.20 (0.24, 5.96)	
Roe 2001	17	25	10	61	0.8	10.84 (3.68, 31.90)	
Seo 2009	4	82	45	217	10.4	0.20 (0.07, 0.56)	
Subtotal (95% CI)		1,564		5,490	100.0	0.85 (0.70, 1.03)	
Total events	149		587				

Heterogeneity: $Chi^2=68.36$, df=10; $P<0.00001$; $I^2=85\%$
Test for overall effect: Z=1.66; P=0.10

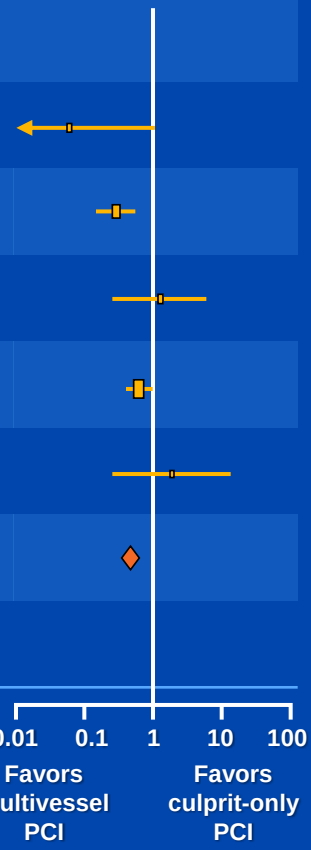


Bainey et al: AHJ 167:1, 2014

MAYO CLINIC

Long-Term Mortality by Timing of Multivessel PCI Elective Outpatient

Study or subgroup	Multivessel PCI Events	Multivessel PCI Total	Culprit-only PCI Events	Culprit-only PCI Total	Weight (%)	Odds ratio M-H, fixed, 95% CI
1.21.3 staged – elective outpatient						
Barringhaus 2010	0	252	30	956	10.0	0.05 (0.00, 0.99)
Chen 2010	13	210	66	351	36.3	0.28 (0.15, 0.53)
Han 2008	3	93	4	148	2.3	1.20 (0.26, 5.49)
Hannan 2010	30	538	116	1,300	50.2	0.60 (0.40, 0.91)
Mohamad 2009	2	12	3	30	1.1	1.80 (0.26, 12.41)
Subtotal (95% CI)		1,105		2,785	100.0	0.46 (0.33, 0.64)
Total events	48		219			



Heterogeneity: $Chi^2=9.38$, df=4; P=0.05; $I^2=57\%$
Test for overall effect: Z=4.70; P<0.0001
Test for subgroup difference: $Chi^2=14.69$; df=2; P=0.0006; $I^2=86.4\%$

Bainey et al: AHJ 167:1, 2014

MAYO CLINIC

Culprit vs Staged Procedure

- New York State Registry
- 4,024 patients with MVD undergoing primary PCI 2003-2006
- Objective:
  - Assess in-hospital and long-term mortality as a function of PCI strategy
- 3 analyses
  - Culprit vessel PCI vs MV PCI during index procedure
  - Culprit vessel PCI vs staged MV PCI during index hospitalization
  - Culprit vessel PCI vs staged MV PCI within 60 days

Hannan et al: J AM Coll Cardiol Intv 3:22, 2010

MAYO CLINIC

Mortality Rates for MV Disease STEMI Patients by Revascularization

Outcome by subgroup	Culprit vessel revasc at time of PPCI	MV revasc at time of PPCI	P
All patients	n=503	n=503	
Death, %			
In-hospital	2.0	3.4	0.14
12 months	5.5	7.1	0.23
24 months	6.6	8.6	0.17
42 months	10.8	11.8	0.23

Hannan et al: J AM Coll Cardiol Intv 3:22, 2010

MAYO CLINIC

Mortality Rates for MV Disease STEMI Patients With Culprit Vessel PCI

Outcome by subgroup	Culprit vessel revasc	Staged MV revasc during index hosp. stay	P
All patients	n=259	n=259	
Death, %			
In-hospital	1.9	1.2	0.48
12 months	5.5	3.9	0.53
24 months	7.4	6.3	0.71
42 months	8.4	6.3	0.72

Hannan et al: J AM Coll Cardiol Intv 3:22, 2010

MAYO CLINIC

Mortality Rates for MV Disease STEMI Patients With Culprit Vessel PCI

Outcome by subgroup	Culprit vessel revasc patients alive at 60 days	MV revasc within 60 days	P
All patients	n=538	n=538	
Death, %			
12 months	3.3	1.3	0.04
24 months	4.3	3.7	0.21
42 months	7.4	5.6	0.17

Hannan et al: J AM Coll Cardiol Intv 3:22, 2010

MAYO CLINIC

Culprit Vessel Percutaneous Coronary Intervention Versus Multivessel and Staged Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction Patients With Multivessel Disease

Conclusions: Our findings support the American College of Cardiology/American Heart Association (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.

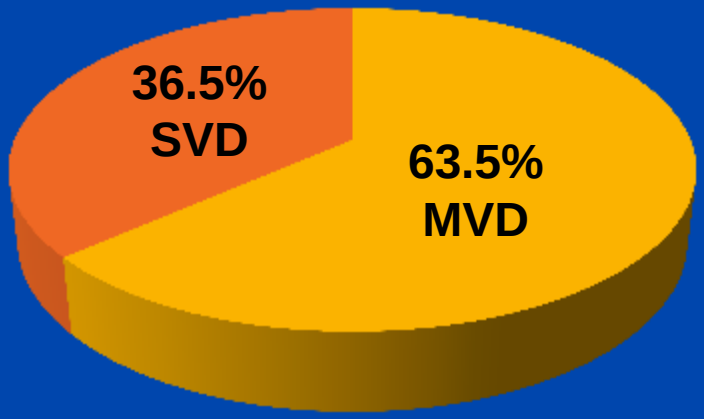
Results A total of 3,521 patients (87.5%) underwent culprit vessel PCI during the index procedure. A total of 259 of them underwent staged PCI during the index admission and 538 patients underwent staged PCI within 60 days of the index procedure. For patients without hemodynamic compromise, culprit vessel PCI during the index procedure was associated with lower in-hospital mortality than multivessel PCI during the index procedure (0.9% vs. 2.4%, $p = 0.04$). Patients undergoing staged multivessel PCI within 60 days after the index procedure had a significantly lower 12-month mortality rate than patients undergoing culprit vessel PCI only (1.3% vs. 3.3%, $p = 0.04$).

Conclusions Our findings support the American College of Cardiology/American Heart Association (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. (J Am Coll Cardiol Intv 2010;3:22–31)

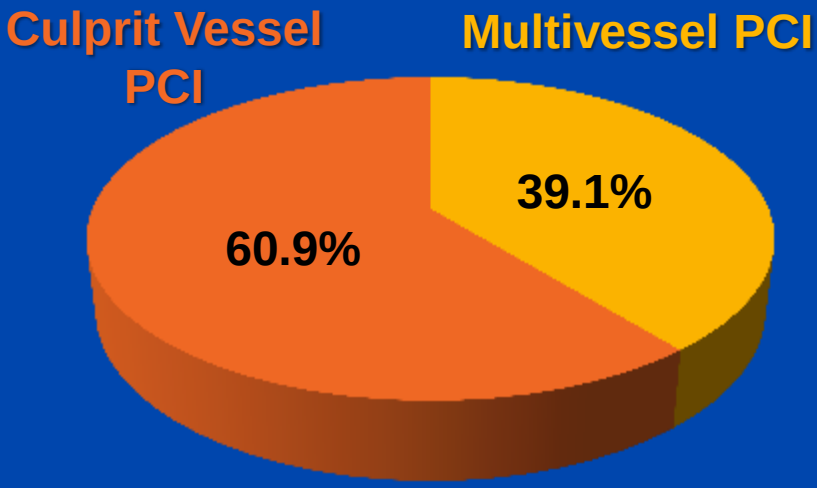
MAYO CLINIC

Primary PCI, Resuscitated Arrest
Cardiogenic Shock

- Multicenter prospective observational study consecutive STEMI patients
- 11,530 patients



266 resuscitated cardiac arrest and shock



MVD

Mylotte et al: J Am Coll Cardiol Intv 6:115, 2013

MAYO CLINIC

Clinical Outcomes

	All Pts (n=266)	SVD (n=97)	MVD (n=169)	P
Death in Cath Lab	21 (7.9)	8 (7.2)	13 (7.7)	0.999
Death within 24 h	78 (29.3)	28 (28.9)	50 (29.6)	0.999
Reinfarction	5 (1.9)	2 (2.1)	3 (1.8)	0.999
Repeat emerg PCI	10 (3.8)	1 (1.0)	9 (5.3)	0.999
Recurrent cardiac arrest	87 (32.7)	33 (34.0)	54 (32.0)	0.786
6-mo mortality	174 (65.4)	55 (56.7)	119 (70.4)	0.032
Shock death	102 (59.6)	26 (47.3)	76 (65.5)	0.03
Arryhthmic death	21 (12.3)	7 (12.7)	14 (12.1)	0.999
Anoxic death	45 (26.3)	21 (38.2)	24 (20.7)	0.017
Sepsis death	3 (1.8)	1 (1.8)	2 (1.7)	0.999
Composite of recurrent cardiac arrest & shock death	149 (56.0)	46 (47.4)	103 (60.9)	0.04

MAYO CLINIC

Mylotte et al: J Am Coll Cardiol Intv 6:115, 2013

Clinical Outcomes

	Culprit-only Primary PCI (n=103)	MV Primary PCI (n=66)	P
Death in Cath Lab	8 (7.8)	5 (7.6)	0.999
Death within 24 h	35 (34.0)	15 (22.7)	0.125
Reinfarction	1 (1.0)	2 (3.0)	0.561
Repeat emerg PCI	5 (4.9)	4 (6.1)	0.738
Recurrent cardiac arrest	36 (35.0)	18 (27.3)	0.316
6-mo mortality	82 (79.6)	37 (56.1)	0.0017
Shock death	54 (67.5)	22 (61.1)	0.532
Arryhthmic death	9 (11.3)	5 (13.9)	0.76
Anoxic death	16 (20.0)	8 (22.2)	0.807
Sepsis death	1 (1.3)	1 (2.8)	0.999
Composite of recurrent cardiac arrest & shock death	70 (68.0)	33 (50.0)	0.024

MAYO CLINIC

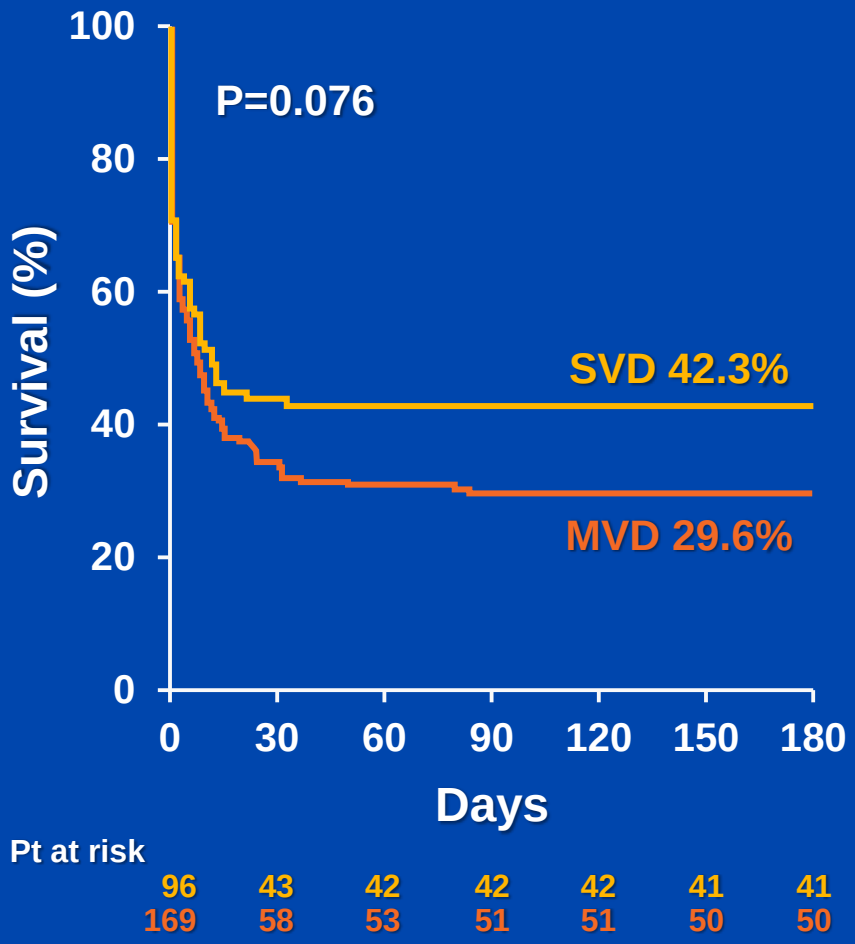
Mylotte et al: J Am Coll Cardiol Intv 6:115, 2013

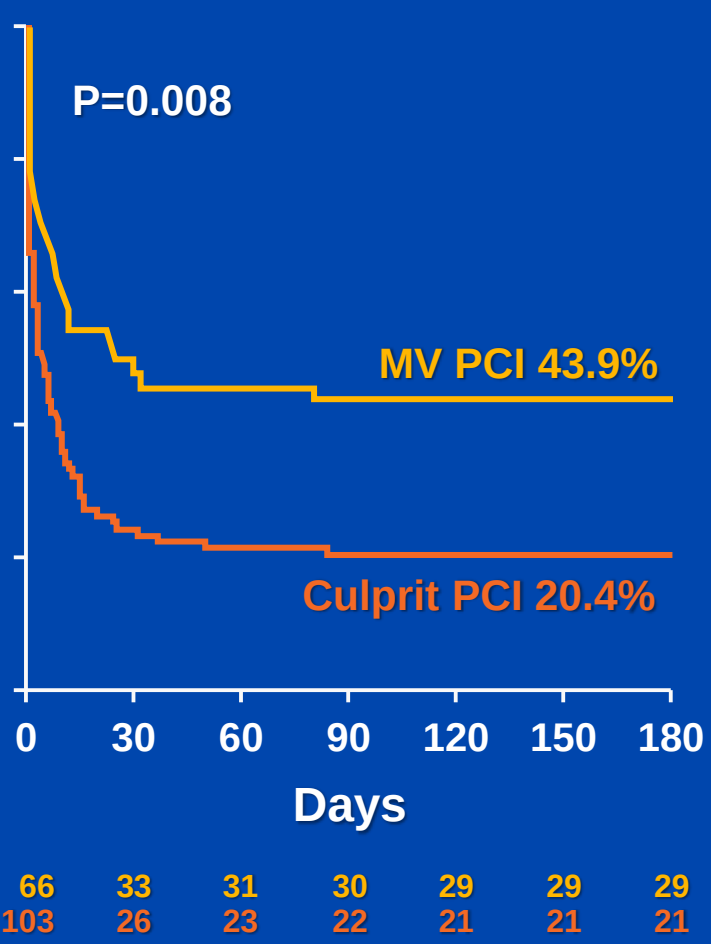
	Simple Cox Regression			Multiple Cox Regression		
	HR	95% CI	P	HR	95% CI	P
RCA IRA	0.68	0.43-1.05	0.083	0.54	0.34-0.85	0.009
LM IRA	0.59	0.33-1.08	0.085	0.55	0.30-1.01	0.054
Non-target CTO	1.29	0.95-1.91	1.23			
MVD	1.26	0.92-1.73	0.156			
Pre-PCI TIMI flow grade 0	1.19	0.80-1.77	0.396			
Thrombus aspiration	0.99	0.65-1.50	0.945			
MV PCI	0.55	0.37-0.81	0.003	0.53	0.36-0.80	0.002
PCI success	0.59	0.39-0.90	0.014	0.65	0.43-1.00	0.047
Hypothermia	0.79	0.47-1.35	0.391			

MAYO CLINIC

Mylotte et al: J Am Coll Cardiol Intv 6:115, 2013

Primary Endpoint at 6 Months





Mylotte et al: J Am Coll Cardiol Intv 6:115, 2013

MAYO CLINIC

Primary Percutaneous Coronary Intervention in Patients With Acute Myocardial Infarction, Resuscitated Cardiac Arrest, and Cardiogenic Shock

The Role of Primary Multivessel Revascularization

Objectives This study sought to assess the impact of multivessel (MV) primary percutaneous coronary intervention (PCI) on clinical outcomes in patients with ST-segment elevation myocardial infarction (STEMI) presenting with cardiogenic shock (CS) and resuscitated cardiac arrest (CA).

characteristics were similar in those with MVD undergoing culprit-only (60.9%) or MV (39.1%) primary PCI. However, 6-month survival was significantly greater in patients who underwent MV PCI (43.9% vs. 20.4%, p = 0.0017). This survival advantage was mediated by a reduction in the composite of recurrent CA and death due to shock (p = 0.024) in MV PCI patients. In those with MVD, culprit artery PCI success (hazard ratio [HR]: 0.63; 95% confidence interval [CI]: 0.41 to 0.96, p = 0.030) and MV primary PCI (HR: 0.57; 95% CI: 0.38 to 0.84, p = 0.005) were associated with increased 6-month survival.

Conclusions The results of this study suggest that in STEMI patients with MVD presenting with CS and CA, MV primary PCI may improve clinical outcome. Randomized trials are required to verify these results. (J Am Coll Cardiol Intv 2013;6:115–25) © 2013 by the American College of Cardiology Foundation

Conclusions: The results of this study suggest that in STEMI patients with MVD presenting with CS and CA, MV primary PCI may improve clinical outcome. Randomized trials are required to verify these results. (J Am Coll Cardiol Intv 2013;6:115-25)
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Mylotte et al: J Am Coll Cardiol Intv 6:115, 2013

MAYO CLINIC

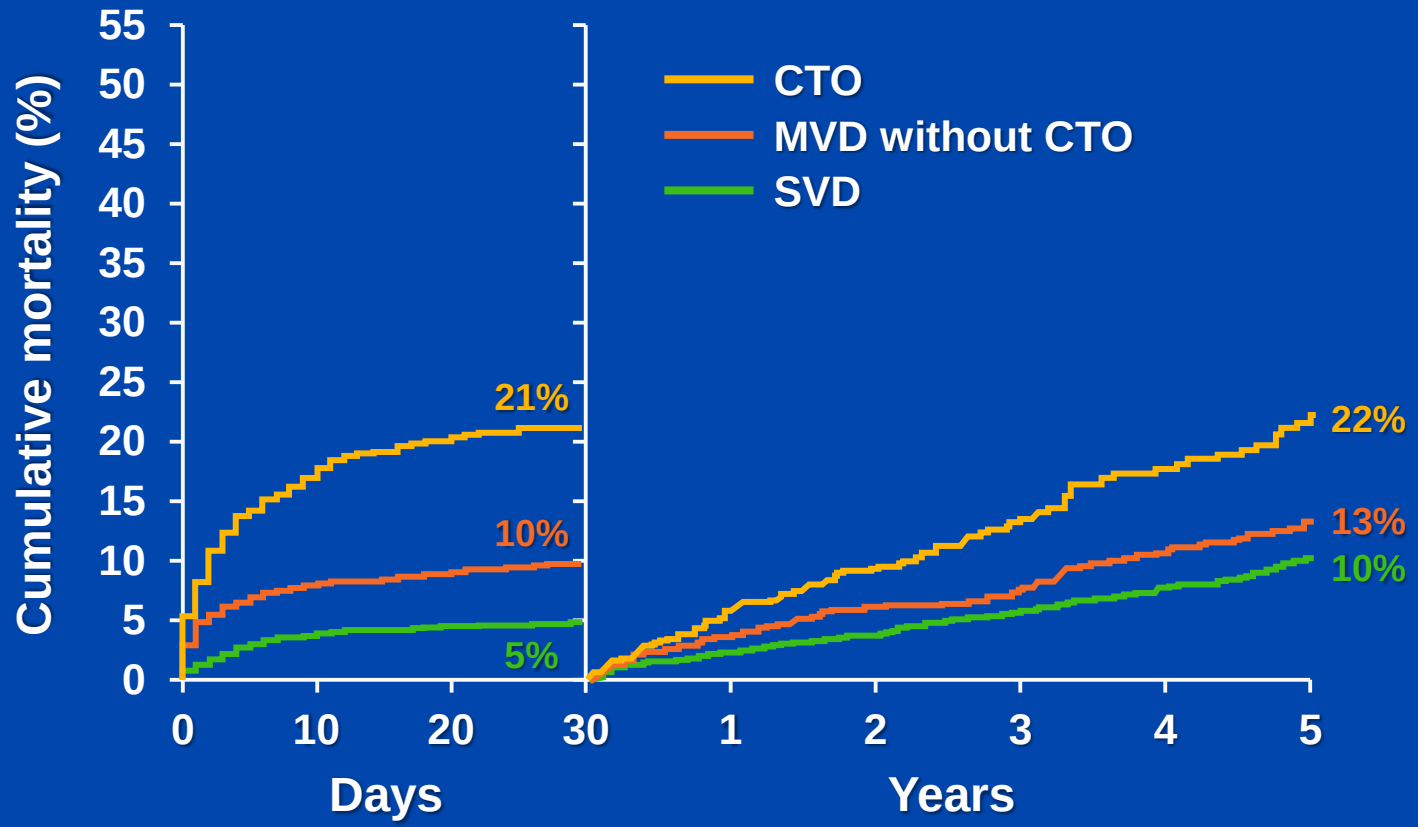
MVD, STEMI, CTO, Shock

- Evaluate prognostic importance of MVD +/- CTO in STEMI patients +/- shock
- Cohort 5,018 consecutive unselected STEMI patients
  - STEMI without shock 88%
  - STEMI with shock 12%
  - SVD 64%
  - MVD with CTO 23%
  - MVD without CTO 13%

MAYO CLINIC

Hoebers et al: Eur J Heart Fail 15:425, 2013

MVD, STEMI, CTO and Shock
Total Cohort



No. at risk

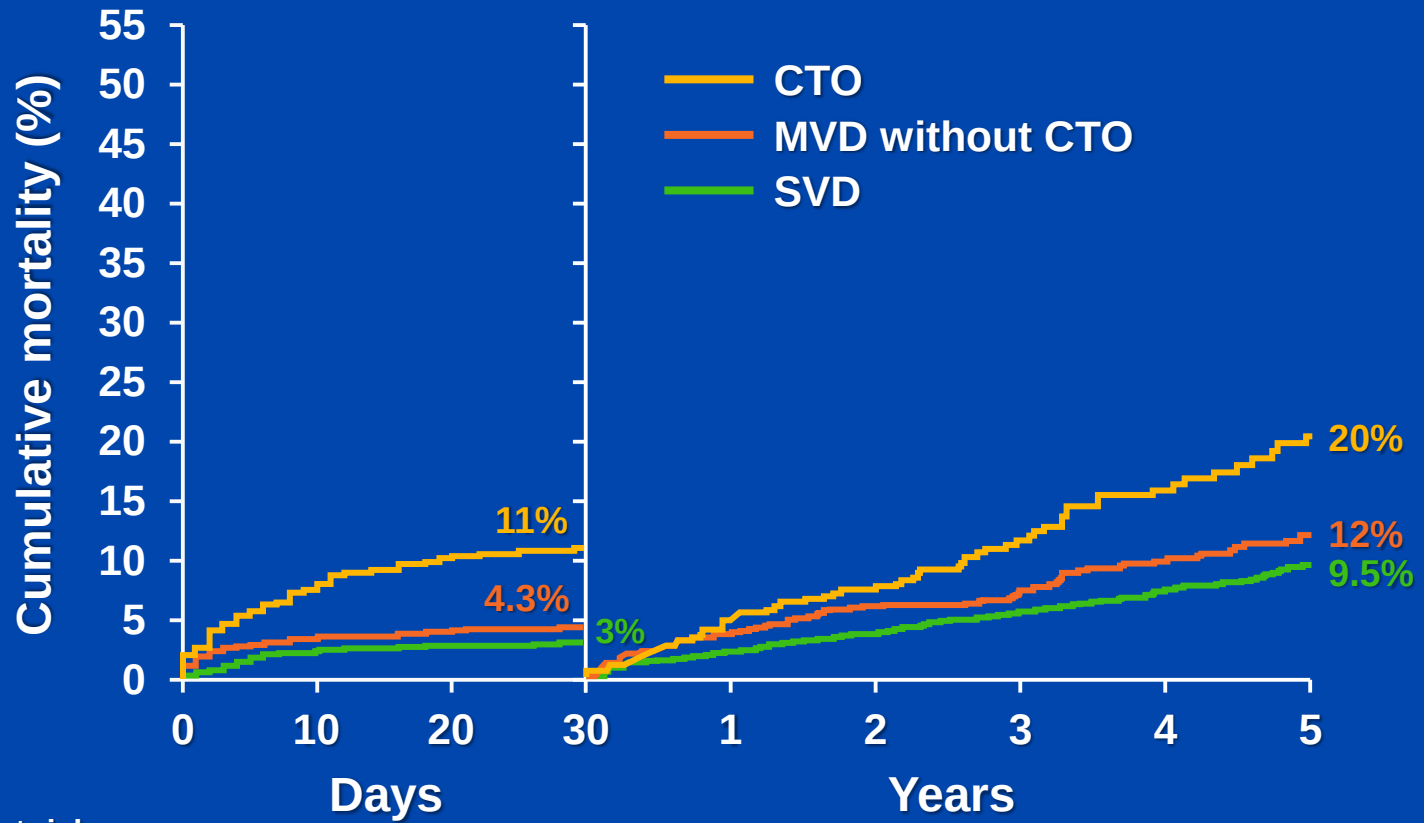
CTO	666	524	496	413	299	225	162
MVD without CTO	1,153	1,036	997	844	636	459	337
SVD	3,199	3,040	2,964	2,505	1,905	1,439	1,045

Hoebers et al: Eur J Heart Fail 15:425, 2013

MAYO CLINIC

MVD, STEMI, CTO and Shock

Patients Without Shock



No. at risk

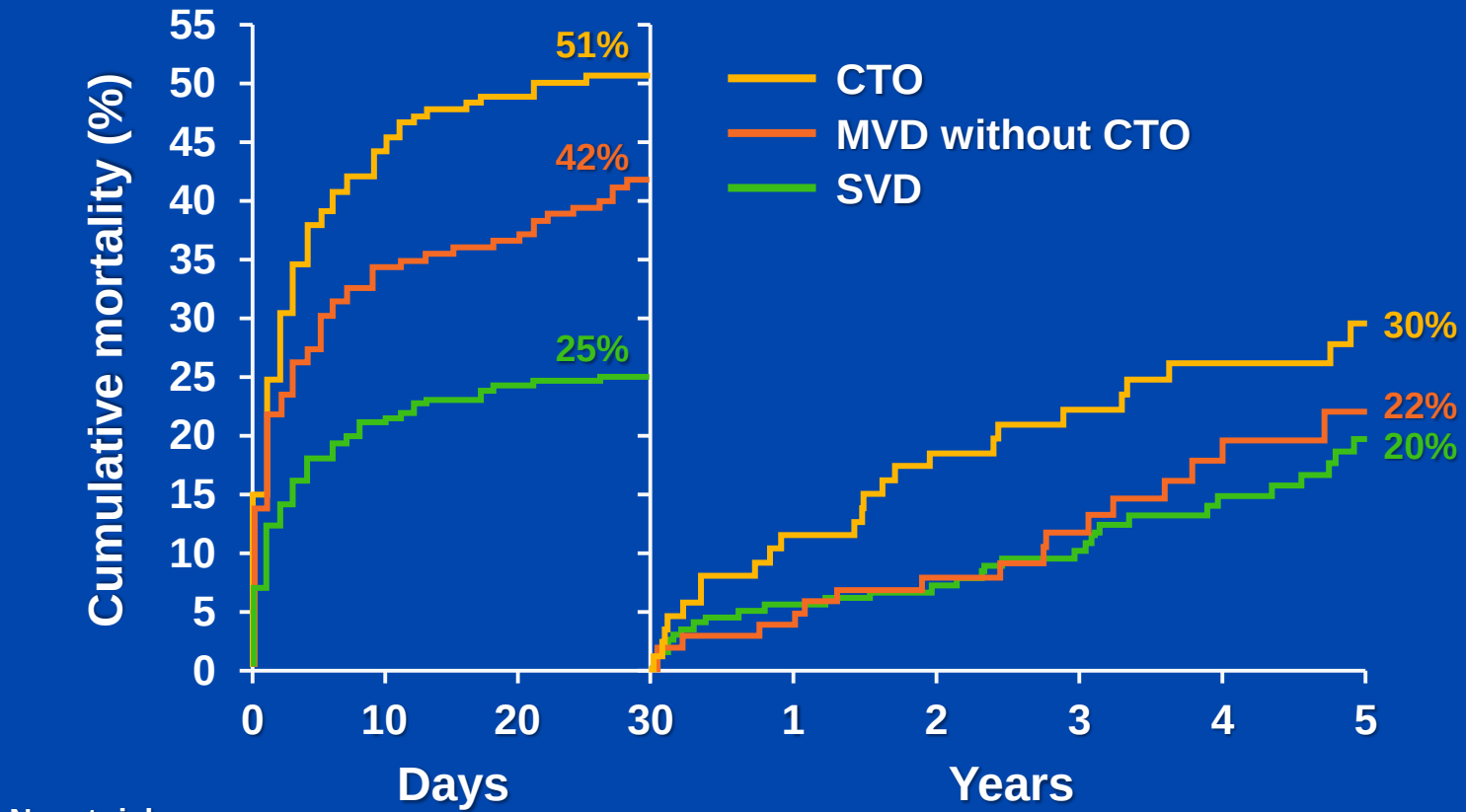
CTO	492	438	420	343	238	172	123
MVD without CTO	978	935	900	758	573	414	308
SVD	2,939	2,846	2,781	2,338	1,776	1,336	975

Hoebers et al: Eur J Heart Fail 15:425, 2013

MAYO CLINIC

MVD, STEMI, CTO and Shock

Patients With Shock



No. at risk

CTO	174	86	76	70	61	53	39
MVD without CTO	175	101	97	86	63	45	29
SVD	260	230	183	167	129	101	70

Hoebers et al: Eur J Heart Fail 15:425, 2013

MAYO CLINIC

MVD, STEMI, CTO, Shock
Conclusions

- In STEMI without shock, MVD is only associated with short and long-term mortality when a co-existing CTO is present
- In STEMI with shock, MVD is associated with increased 30 day mortality with or without a CTO

MAYO CLINIC

Hoebers et al: Eur J Heart Fail 15:425, 2013

HORIZONS AMI
Chronic Total Occlusion

- Background
  - STEMI Patients
    - 40-60% have MVD
    - 10% have a CTO of non IRA
- What is the importance of the CTO

Claessen et al: EHJ 33:768, 2012

MAYO CLINIC

HORIZONS AMI

- Of 3,283 patients with STEMI
  - 1,524 SVD (46.4%)
  - 1,477 MVD without CTO (45.0%)
  - 283 MVD with CTO (8.6%)

Claessen et al: EHJ 33:768, 2012

MAYO CLINIC

HORIZONS AMI

- MVD with CTO
  - Older
  - More often female
  - More HBP
  - Diabetes
  - Prior MI
  - History CHF
  - Prior CABG

Claessen et al: EHJ 33:768, 2012

MAYO CLINIC

Predictors of Early (0-30 days) Mortality

Variable	HR (95% CI)	P
MVD with CTO vs SVD	2.88 (1.41-5.88)	0.004
Killip class 2-4 (vs.0/1)	2.40 (1.39-4.14)	0.002
Age (per 10-yr increase)	2.11 (1.69-2.64)	<0.0001
MVD without CTO vs SVD	1.75 (1.00-3.06)	0.0495
WBC (per 1000 U increase)	1.14 (1.09-1.20)	<0.0001
Final TIMI flow grade 3	0.48 (0.27-0.83)	0.009
1 or more stents implanted	0.26 (0.15-0.47)	<0.0001

MAYO CLINIC

Claessen et al: EHJ 33:768, 2012

Predictors of Overall 3-Year Mortality

Variable	HR (95% CI)	P
Hx CHF	2.77 (1.67-4.60)	<0.0001
MVD with CTO vs SVD	2.27 (1.47-3.52)	0.0002
Killip class 2-4 (vs.0/1)	1.99 (1.39-2.86)	0.0002
Age (per 10-yr increase)	1.88 (1.58-2.24)	<0.0001
Hx prior MI	1.56 (1.07-2.28)	0.02
Cr clearance <60mL/min	1.54 (1.05-2.22)	0.03
WBC (per 1000 U increase)	1.10 (1.06-1.14)	<0.0001
Final TIMI flow grade 3	0.57 (0.40-0.83)	0.003
1 or more stents implanted	0.53 (0.33-0.85)	0.008
MVD without CTO vs SVD	1.33 (0.95-1.86)	0.10

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Conclusions: In patients with STEMI undergoing primary PCI in the HORIZONS-AMI trial, MVD with or without a CTO in a non-IRA was an independent predictor of early mortality. The presence of a CTO in a non-IRA was also an independent predictor of increased late mortality to 3 years.

Aims We sought to investigate the impact of multivessel disease (MVD) with and without a chronic total occlusion (CTO) in a non-infarct-related artery (IRA) on mortality in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI).

Methods and results In the HORIZONS-AMI trial, of 3283 patients undergoing primary PCI, 1524 patients (46.4%) had single-vessel disease (SVD), 1477 (45.0%) had MVD without a CTO, and 283 (8.6%) had MVD with a CTO in a non-IRA. Compared with SVD patients and MVD patients without a CTO, patients with a non-IRA CTO were significantly less likely to achieve post-procedural TIMI 3 flow ($P = 0.0003$), more often had absent myocardial blush ($P = 0.0002$), and less frequently achieved complete ST-segment resolution ($P = 0.0001$). By multivariable analysis, MVD with CTO in a non-IRA was an independent predictor of both 0- to 30-day mortality [hazard ratio (HR) 2.88, 95% confidence interval (CI) 1.41–5.88, $P = 0.004$] and 30-day to 3-year mortality (HR 1.98, 95% CI 1.19–3.29, $P = 0.009$), while MVD without a CTO was a significant predictor for 0- to 30-day mortality (HR 2.20, 95% CI 1.00–3.06, $P = 0.049$) but not late mortality.

Conclusion In patients with STEMI undergoing primary PCI in the HORIZONS-AMI trial, MVD with or without a CTO in a non-IRA was an independent predictor of early mortality. The presence of a CTO in a non-IRA was also an independent predictor of increased late mortality to 3 years.

Keywords ST-segment elevation myocardial infarction • Chronic total occlusion • Multivessel disease

Introduction

Acute ST-segment elevation myocardial infarction (STEMI) typically arises from sudden thrombotic occlusion of a coronary artery.[1] Prompt restoration of epicardial blood flow reduces infarct size and mortality.[2] Mechanical reperfusion by primary percutaneous coronary intervention (PCI) with stent implantation is currently the preferred treatment for STEMI patients.[3] Approximately 40–60% of the STEMI patients have multivessel disease (MVD) and ~10% of the patients have a chronic total occlusion (CTO) in a non-infarct-related artery (IRA).[3,4] Multivessel disease is regarded as a risk factor associated with worse outcome after STEMI.[5] However, some studies have suggested that MVD may only be of prognostic importance if a CTO in a non-IRA is present.[4,6,7]

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