Non Culprit Artery PCI: Indications and Timing

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ACC Middle East Conference 2016

Disclosure

I, Jacqueline Tamis Holland, Have nothing to disclose

Case Example

What is the next most appropriate step for this patient?

- Multi-vessel PCI at the Time of the Index Procedure (MV PCI)
- Staged Multi-vessel PCI (Staged MV PCI)
- Culprit Only PCI and Ischemia Guided Approach to the non-infarct arteries (COR)

ACC/AHA/SCAI Focused Update on Percutaneou Intervention

2013 Recommendat	2015 Focused Update Recommendation	Comment
Class III: Harr	*Class IIb*	
PCI should not performed in a noninfarct arte the time of prir PCI in patients STEMI who are hemodynamica stable.[11–13] (*Le Evidence: B*)	PCI of a noninfarct artery may be considered in selected patients with STEMI and multivessel disease who are hemodynamically stable, either at the time of primary PCI or as a planned staged procedure.[11–24] (*Level of Evidence: B-R*)	lified ımmendation ınged class ı "III: Harm" to ' and expanded : frame in which tivessel PCI could ıerformed).

PCI indicates | myocardial infarc ... EMI, ST-elevation

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Circulation. 2016;133:1135-1147.

Arguments Supporting Multi-vessel PCI at the Time of Index Procedure

- **Multiple rupture plaques seen in setting of acute infarction**
- **Slower than normal flow in non-infarct vessel**
- **Enhancement of regional wall motion of non-infarcted zone Shorter Length of Stay**
- **Convenient "one time only" procedure**
- **Complete revascularization improves outcome**

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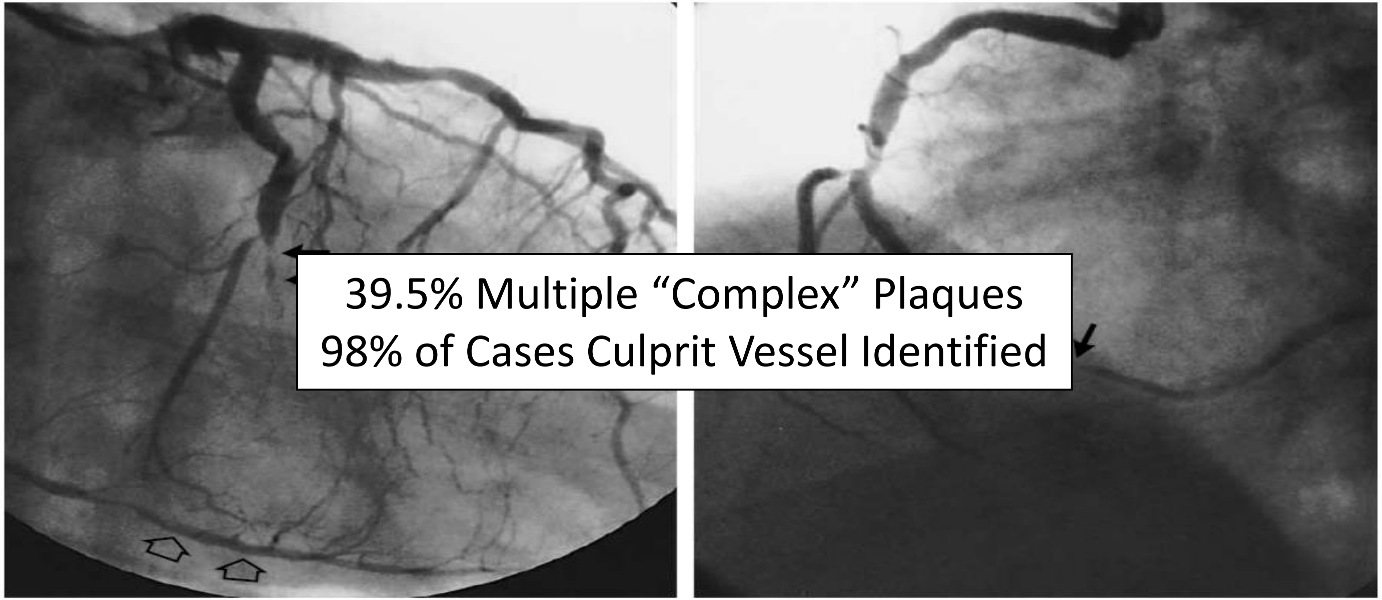
Multiple Complex Plaques are Not Un-Common in STEMI



39.5% Multiple "Complex" Plaques
98% of Cases Culprit Vessel Identified

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N Engl J Med 2000;343:915-22

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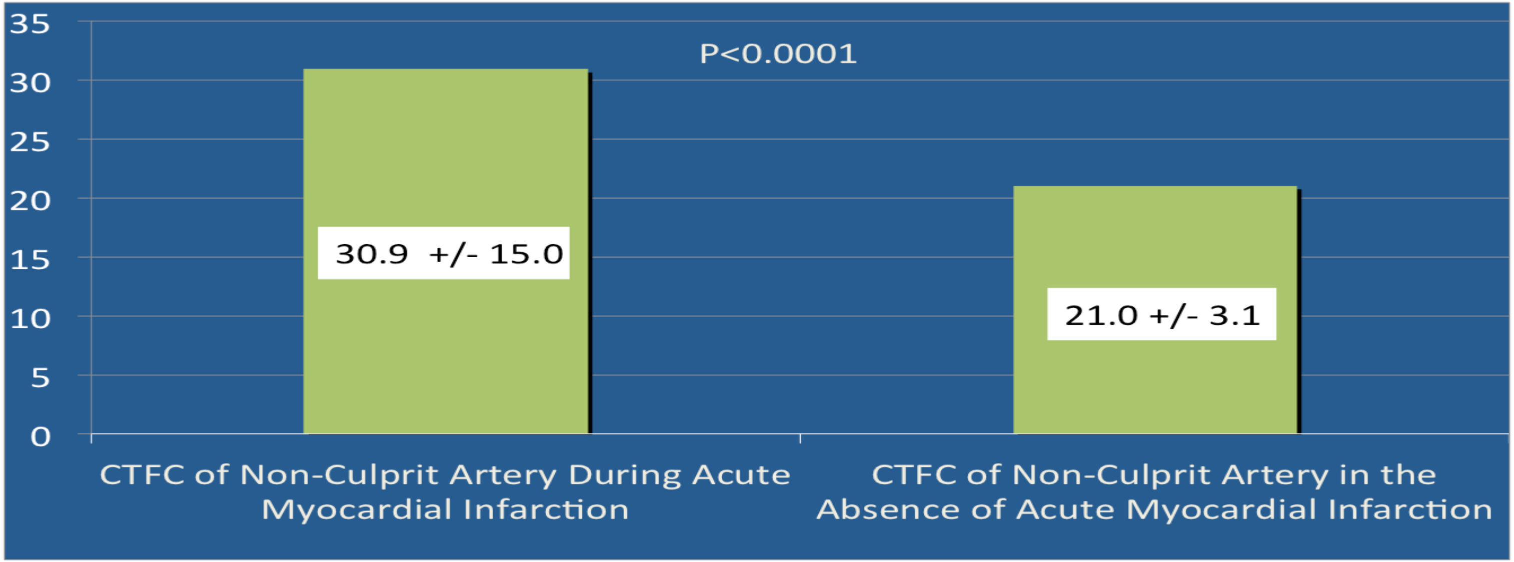
Corrected TIMI Frame Count of Non-Culprit Artery During Acute Infarction



J Am Coll Cardiol 1999;34: 974–82

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Relationship Between Acute Angiographic Variables and In-hospital Mortality

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	Non Survivors (25%, 50%, 75%)	Survivors (25%, 50%, 75%)	X2	P-value
Non-infarct zone (SD/chord)	-2.3, -1.3,+ 0.3	-0.8, +0.4, +1.4	7.6	0.006
Infarct zone (SD/chord)	-3.4, -3.1, -2.1	-3.3, -2.8, -1.9	2.3	0.128
Ejection Fraction (%)	32, 50, 54	45, 53, 61	5.1	0.025

Infarct Zone

Non-infarct Zone

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Circulation 1989;80:245-253

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Arguments Against Multi-vessel PCI in STEMI

- **Exaggerated severity of non culprit stenosis**
- **Potential for severe hemodynamic impairment**
- **Heightened inflammatory and pro-thrombotic state in STEMI**
- **Increased dye load**
- **Increased procedure time/Fluoroscopy**
- **Uncertain Clinical significance of lesion**

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Exaggeration of Non Culprit Artery Stenosis During Acute Infarction

	Infarct Angiogram	Non-Infarct Angiogram	P-value
Minimal Lumen Diameter (mm)	1.53 (.0.51)	1.78 (0.65)	<0.001
Stenosis Non-Culprit (%)	49.3 (14.5)	40.4 (16.6)	<0.0001
Reference Vessel Diameter (mm)	3.1 (0.8)	3.0 (0.8)	0.3

J Am Coll Cardiol 2002;40:911-16

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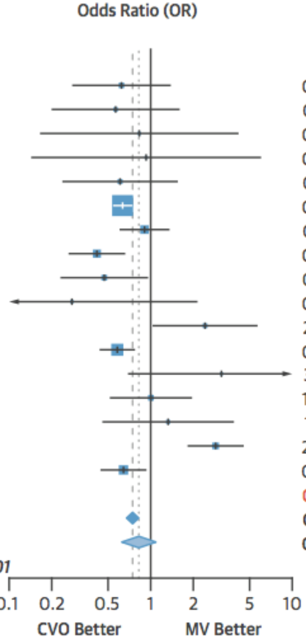
Multi-vessel PCI During Index Procedure
What is the Evidence?

Forest Plots of Observational Studies

Odds Ratio for Long Term Mortality: Culprit Vessel Only vs Multi-vessel PCI at Index PCI

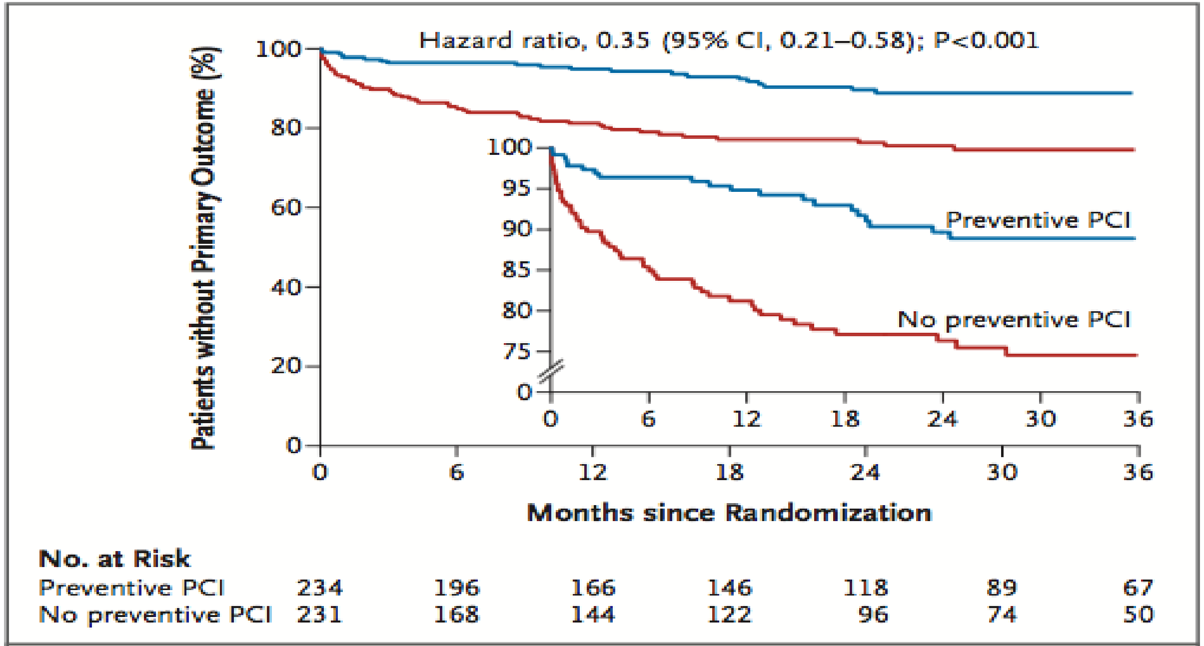
Study	CULPRIT Events	CULPRIT Total	MULTIVESSEL Events	MULTIVESSEL Total	OR	95%-CI
Roe (2001)	13	79	19	79	0.62	[0.28; 1.37]
Corpus (2004)	42	354	5	26	0.57	[0.20; 1.58]
Qarawani (2008)	2	25	9	95	0.83	[0.17; 4.11]
Khattab (2008)	3	45	2	28	0.93	[0.15; 5.93]
Varani (2008)	8	156	12	147	0.61	[0.24; 1.53]
Cavender (2009)	1321	25802	246	3134	0.63	[0.55; 0.73]
Hannan (2010)	54	503	59	503	0.91	[0.61; 1.34]
Toma (2010)	111	1984	27	217	0.42	[0.27; 0.65]
Dziewierz (2010)	57	707	11	70	0.47	[0.23; 0.95]
Mohamad (2011)	3	30	2	7	0.28	[0.04; 2.11]
Bauer (2013)	72	2118	6	419	2.42	[1.05; 5.61]
Jaguszewski (2013)	168	3833	81	1108	0.58	[0.44; 0.76]
Santos (2014)	14	180	2	77	3.16	[0.70; 14.27]
Jeger (2014)	40	1467	12	442	1.00	[0.52; 1.93]
Kim (2014)	15	155	5	67	1.33	[0.46; 3.82]
Manari (2014)	127	706	26	367	2.88	[1.85; 4.48]
Iqbal (2014)	164	2418	41	403	0.64	[0.45; 0.92]
Bayesian hierarchical meta-analysis					0.83	[0.59; 1.15]
Fixed effect model	**2214**	**40562**	**565**	**7189**	**0.75**	**[0.67; 0.82]**
Random effects model					**0.83**	**[0.62; 1.09]**

Heterogeneity: I−squared=76.6%, tau−squared=0.1929, p<0.0001



J Am Coll Cardiol 2016;68:1066-81

PRAMI Trial



Primary Endpoint:
Composite of Cardiac death, re-MI and refractory angina

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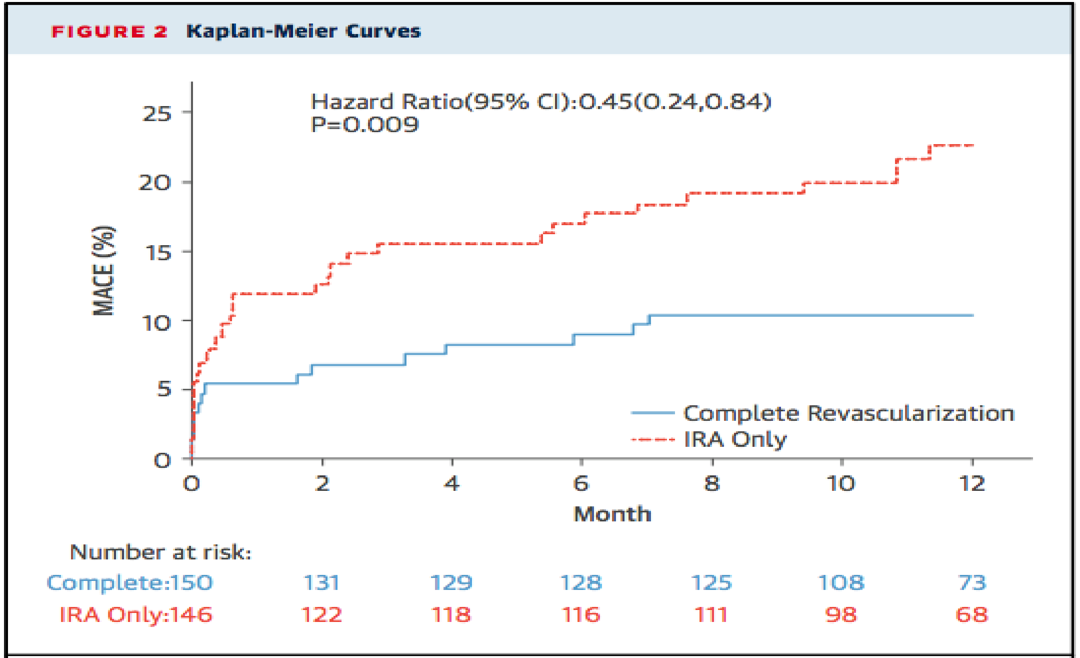
N Engl J Med **2013;369:1115-23**

PRAMI Endpoints

Endpoint	Odds Ratio	P Value
Cardiac Death, Non-Fatal MI or Refractory Angina	0.35, 95% CI (0.21-0.58)	<0.001
Cardiac Death or Non-Fatal MI	0.36, 95% CI (0.18-0.73)	0.004
Cardiac Death	0.34, 95% CI (0.11-1.08)	0.07
Non-Fatal MI	0.32, 95% CI (0.13-0.75)	0.009
Refractory Angina	0.35, 95% CI (0.18-0.69)	0.002

CvlPRIT Trial



Primary Endpoint:
Composite of Death, Re-MI , CHF and Ischemia-driven Revasc

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J Am Coll Cardiol 2015;65:963–72

CvlPRIT Endpoints

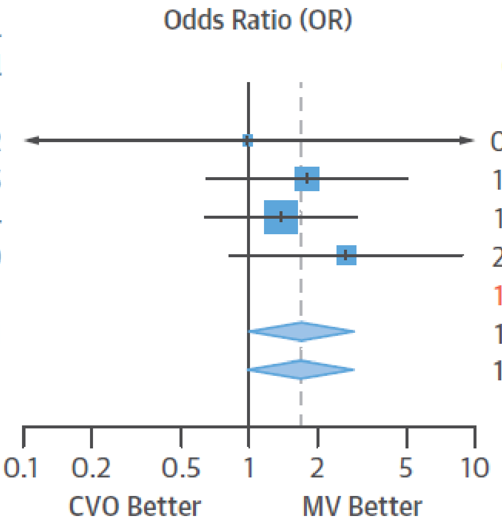
Endpoint	Odds Ratio	P Value
Death, Non-Fatal MI, CHF or Ischemia Driven Revasc	0.45, 95% CI (0.24-0.84)	0.009
Death	0.32, 95% CI (0.06-1.60)	0.14
Non-Fatal MI	0.48, 95% CI (0.09-2.62)	0.39
CHF	0.43, 95% CI (0.13-1.39)	0.14
Repeat Revascularization	0.55, 95% CI (0.22-1.39)	0.2

Forest Plots of Randomized Studies

Odds Ratio for Long Term Mortality: Culprit Vessel Only vs Multi-vessel PCI at Index PCI

	CULPRIT		MULTIVESSEL			
Study	Events	Total	Events	Total	OR	95%-CI
Di Mario (2004)	0	17	1	52	0.98	[0.04; 25.20]
Politi (2010)	13	84	6	65	1.80	[0.64; 5.03]
Wald (2013)	16	231	12	234	1.38	[0.64; 2.98]
Gershlick (2014)	10	146	4	150	2.68	[0.82; 8.76]
Bayesian hierarchical meta-analysis					1.66	[0.84; 3.28]
Fixed effect model	39	478	23	501	1.70	[1.00; 2.91]
Random effects model					1.69	[0.98; 2.89]

Heterogeneity: I−squared=0%, tau−squared=0, p=0.8056



J Am Coll Cardiol 2016;68:1066-81

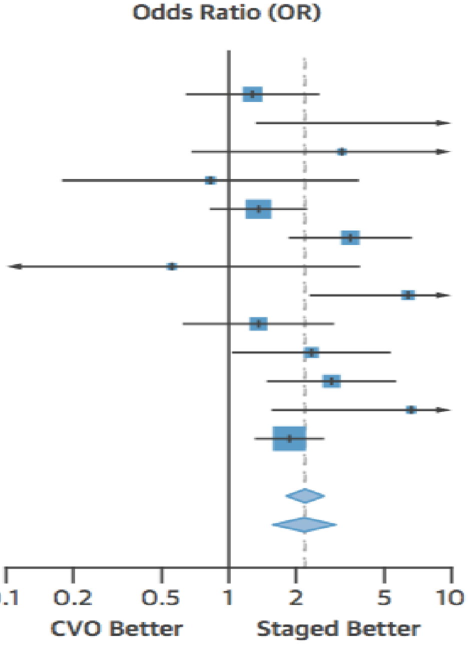
Staged Multi-vessel PCI
What is the Evidence?

Forest Plots of Observational Studies

Odds Ratio for Long Term Mortality: Culprit Vessel Only vs Staged MV PCI

Study	CULPRIT Events	CULPRIT Total	STAGED Events	STAGED Total	OR	95%-CI
Corpus (2004)	42	354	12	126	1.28	[0.65; 2.52]
Rigattieri (2008)	7	46	1	64	11.31	[1.34; 95.44]
Varani (2008)	10	156	2	96	3.22	[0.69; 15.02]
Han (2008)	4	149	3	93	0.83	[0.18; 3.78]
Hannan (2010)	40	538	30	538	1.36	[0.83; 2.22]
Chen (2010)	66	351	13	210	3.51	[1.88; 6.54]
Mohamad (2011)	3	30	2	12	0.56	[0.08; 3.83]
Barringhaus (2011)	106	1345	4	303	6.40	[2.34; 17.49]
Lee (2012)	25	1106	9	538	1.36	[0.63; 2.93]
Kim (2014)	15	155	11	252	2.35	[1.05; 5.25]
Ma (2015)	41	246	13	201	2.89	[1.50; 5.57]
Russo (2015)	38	779	2	259	6.59	[1.58; 27.51]
Toyota (2016)	95	630	59	681	1.87	[1.33; 2.64]
Bayesian hierarchical meta-analysis					2.09	[1.54; 2.88]
Fixed effect model	**492**	**5885**	**161**	**3373**	**2.20**	**[1.82; 2.67]**
Random effects model					**2.18**	**[1.58; 3.01]**

Heterogeneity: I−squared=50.1%, tau−squared=0.1466, p=0.02



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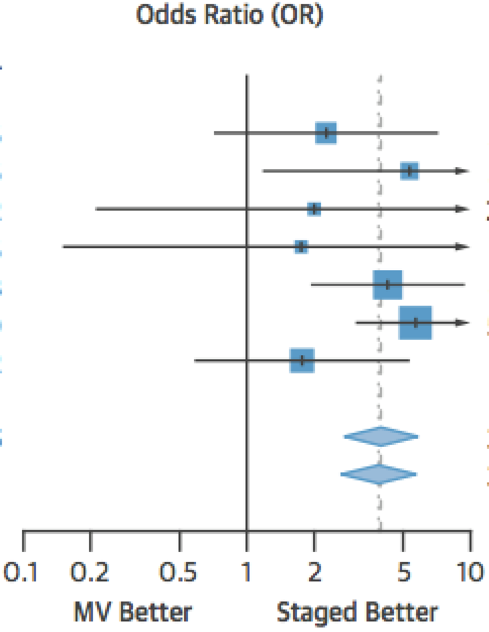
Forest Plots of Observational Studies

Odds Ratio for Long Term Mortality: Staged MV PCI vs MV PCI

Study	MULTIVESSEL Events	MULTIVESSEL Total	STAGED Events	STAGED Total	OR	95%-CI
Corpus (2004)	5	26	12	126	2.26	[0.72; 7.09]
Varani (2008)	15	147	2	96	5.34	[1.19; 23.9]
Mohamad (2011)	2	7	2	12	2.00	[0.21; 18.7]
Maamoun (2011)	2	42	1	36	1.75	[0.15; 20.1]
Kornowski (2011)	25	275	9	393	4.27	[1.96; 9.29]
Jensen (2012)	36	354	16	820	5.69	[3.11; 10.4]
Kim (2014)	5	67	11	252	1.77	[0.59; 5.27]
Bayesian hierarchical meta-analysis					3.59	[2.04; 5.56]
Fixed effect model	90	918	53	1735	3.99	[2.74; 5.80]
Random effects model					3.89	[2.65; 5.70]

Heterogeneity: I−squared=0%, tau−squared=0, p=0.4953



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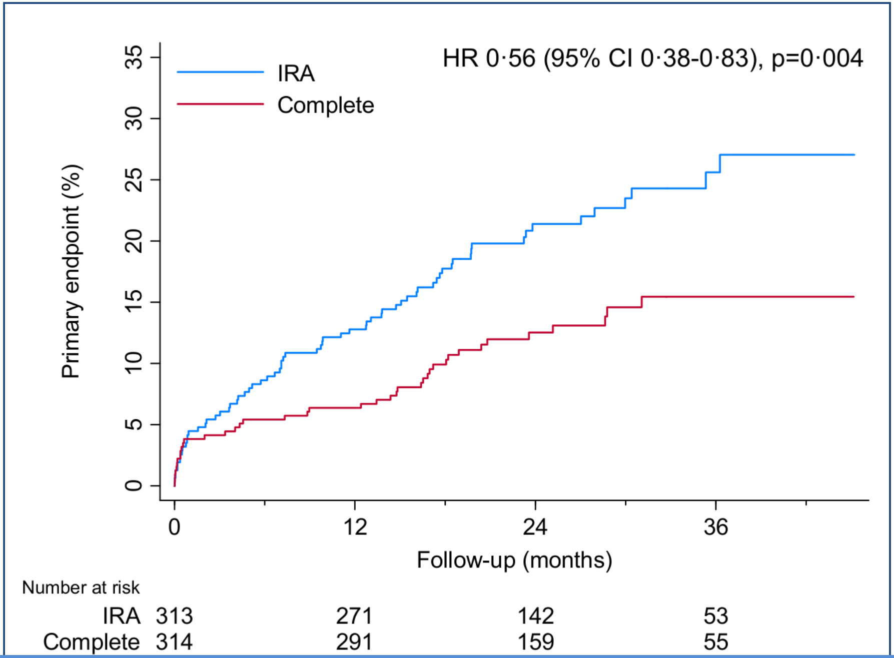
DANAMI-3 PRIMULTI



Primary Endpoint:
Composite of Death, re-MI and Ischemia driven revasc of non-IRA

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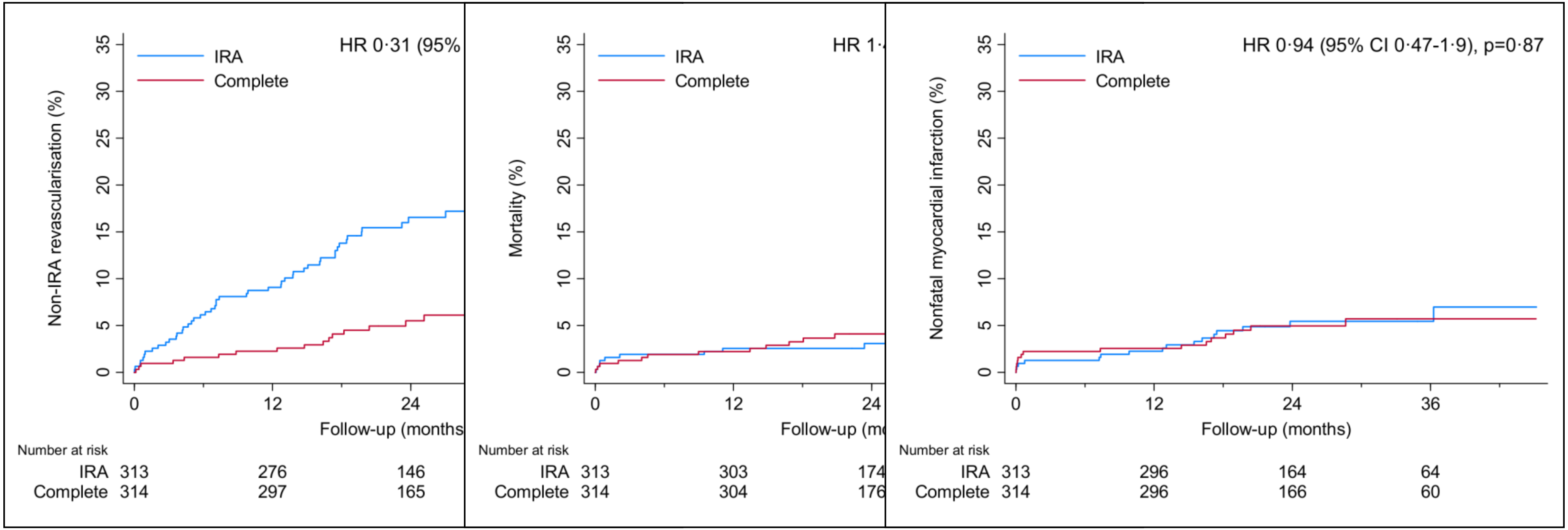
The Lancet 2015;386:665-71

DANAMI-3 PRIMULTI



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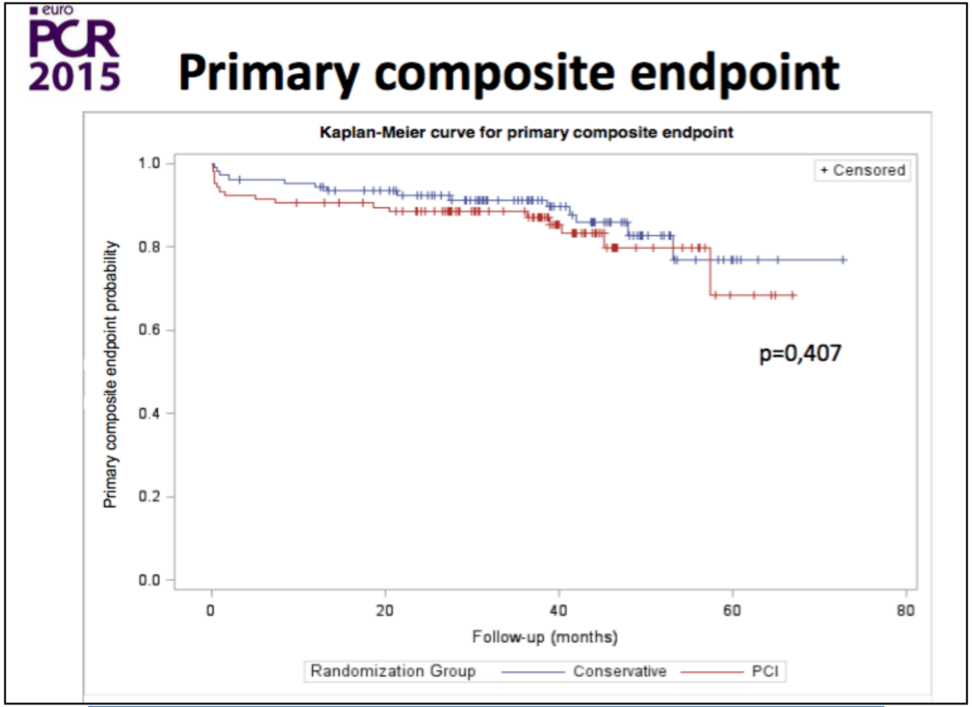
PRAGUE-13



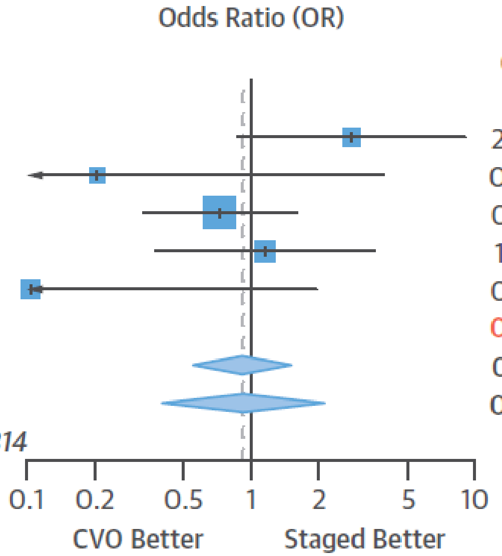
Primary Endpoint:
Composite of Death, Re-MI and Stroke

Forest Plots of Randomized Studies

Odds Ratio for Long Term Mortality: Culprit Vessel Only vs Staged MV PCI

Study	CULPRIT Events	CULPRIT Total	STAGED Events	STAGED Total	OR	95%-CI
Politi (2010)	13	84	4	65	2.79	[0.87; 9.01]
Ghani (2012)	0	41	4	80	0.20	[0.01; 3.90]
Engstrom (2015)	11	313	15	314	0.73	[0.33; 1.61]
Hinomaz (2015)	7	108	6	106	1.16	[0.38; 3.56]
Henriques (2015)	0	154	4	148	0.10	[0.01; 1.95]
Bayesian hierarchical meta-analysis					0.94	[0.31; 2.09]
Fixed effect model	31	700	33	713	0.91	[0.55; 1.51]
Random effects model					0.92	[0.40; 2.12]

Heterogeneity: I–squared=43.6%, tau–squared=0.3606, p=0.1314



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Summary of Evidence of Pooled Results

Type of Study	
Observational Studies of MV PCI vs COR	MV PCI worse
Observational Studies of Staged PCI vs COR	Staged PCI better
Observational Studies of MV PCI vs Staged PCI	Staged PCI better
Randomized Studies of MV PCI vs COR	MV PCI better
Randomized Studies of Staged PCI vs COR	Staged PCI with similar outcomes to COR

Things to Consider

Observational Studies

- Not randomized/subject to bias
- Unknown Circumstances leading to PCI
- Multi-vessel PCI at index procedure marker for higher risk (or lower risk) patient?
- Staged multi-vessel PCI a marker for lower risk?

Randomized Studies

- PRAMI stopped prematurely
- Trials underpowered to detect difference in individual outcomes
- Open label design might bias softer endpoints
- Varying study results
- Limited information on clinical or lesion selection criteria.

On Going Randomized Trials

Randomized Controlled Trial	Design	Size (n)	Composite Primary Endpoint
COCUA NCT01180218	Culprit-only primary PCI vs MV primary PCI	646	1-year cardiac death, STEMI, ischemia-driven TVR
ASSIST-MI NCT01818960	Culprit-only primary PCI vs MV primary PCI	250	90-day infarct size by CMR
CULPRIT SHOCK NCT01927549	Culprit-only primary PCI vs MV primary PCI in cardiogenic shock	706	30-day death or acute kidney injury requiring renal replacement therapy
FIT NCT01160900	Culprit-only primary PCI vs staged PCI	180	30-day death, MI 1-year stent thrombosis, TVR
COMPLETE NCT01740479	Culprit-only primary PCI vs staged PCI (<72 hr) with FFR for lesions 50%-70% DS	3900	4-year death, MI
ZES for STEMI NCT01781715	MV primary PCI vs staged (3-15 days) PCI	120	1-year death, MI, revascularization
CompareAcute NCT01399736	MV primary PCI with FFR vs ischemia-guided PCI	885	1-year death, MI, cerebrovascular events, revascularization
CROSS-AMI NCT01179126	Staged PCI (index hospitalization) vs ischemia-guided PCI	400	1-year cardiovascular death, MI, revascularization, HF hospitalization

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Factors Favoring MV PCI During the Index PCI	Factors Favoring Staged MV PCI
Ongoing chest pain	Stable symptoms
Shock	Prolonged procedure to open the infarct artery
Arrhythmias	Complex lesion in non-infarct artery
Very large, potentially unstable non-culprit lesion with large area of myocardium at risk	Chronic kidney disease
Infarct Artery required little time/dye	Un-cooperative patient
Anticipated simple PCI of non-infarct artery	Patient Preference
Obstacles to returning to lab	Cath Lab team preference

In other words…..

DO WHAT IS CLINICALLY APPROPRIATE!