Multivessel Disease in STEMI: FIX THE CULPRIT and GO BACK TO BED!

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Allentown PA

Controversies and Advancements
2016

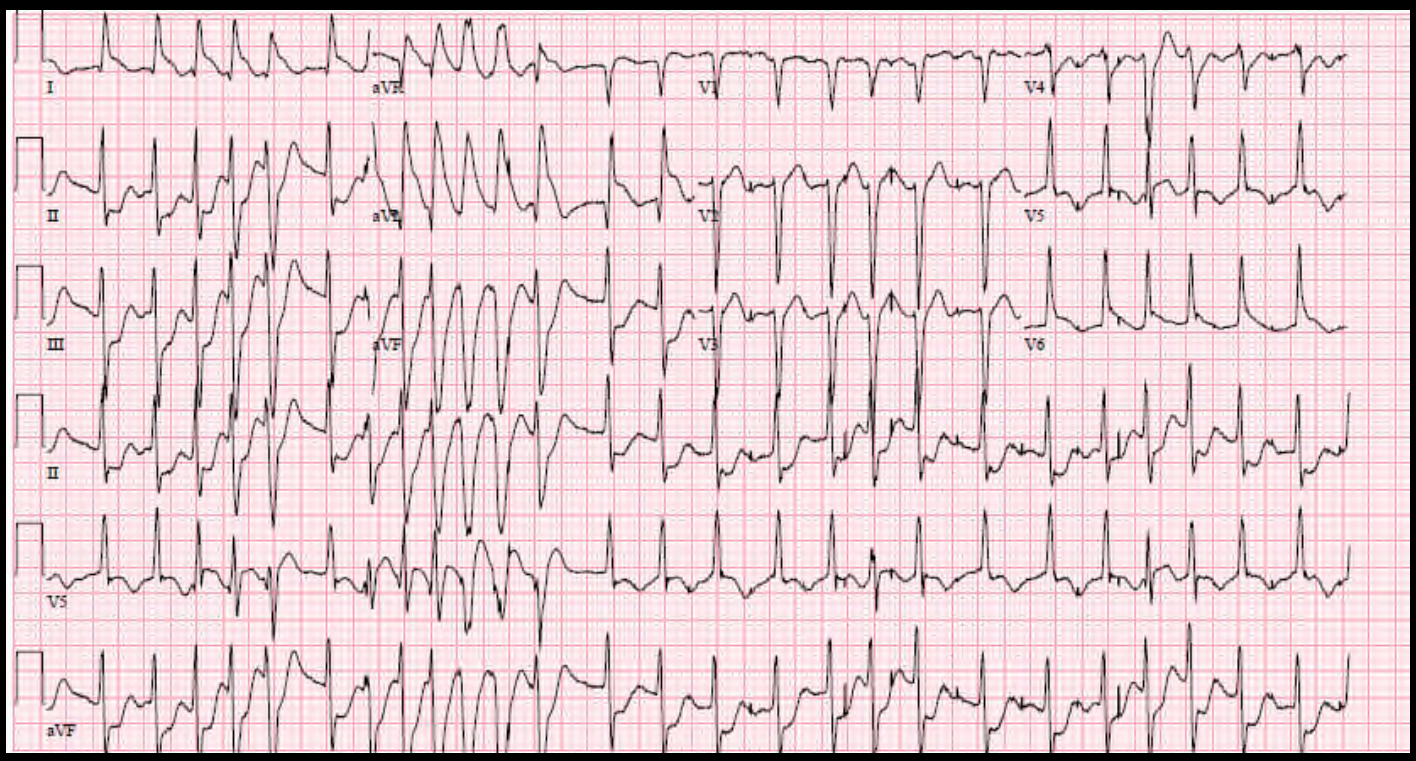
Disclosure

- Medical Advisory Board: Abbott Vascular, Boston Scientific, theMedicinesCompany

Lehigh Valley Hospital

2016 YTD	533 PCI	112 STEMI	21%
FY 2016	1419 PCI	333 STEMI	23%
FY 2015	1293 PCI	259 STEMI	20%

What we aren't talking about



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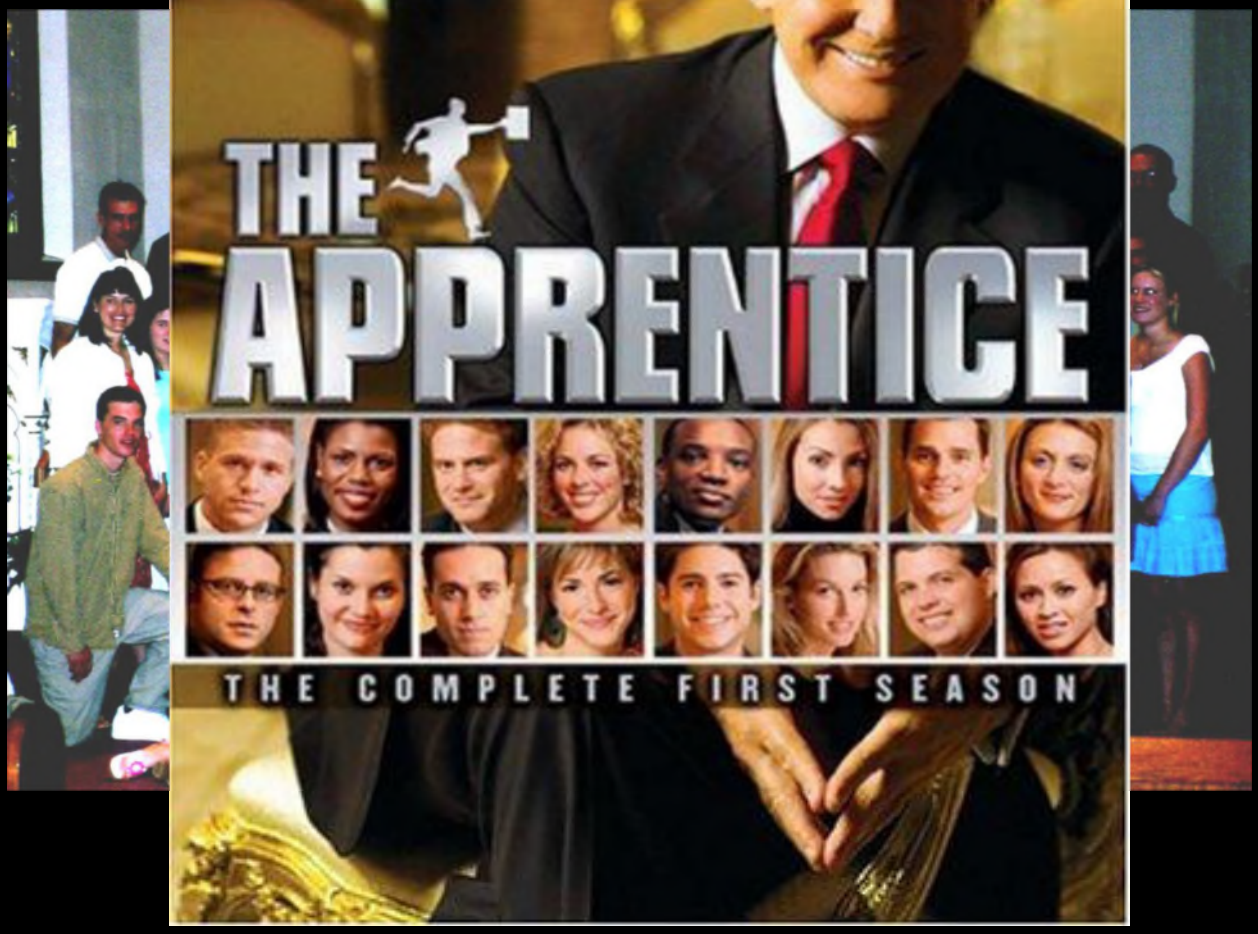
Mr. and Mrs



A sweet story no one should argue with

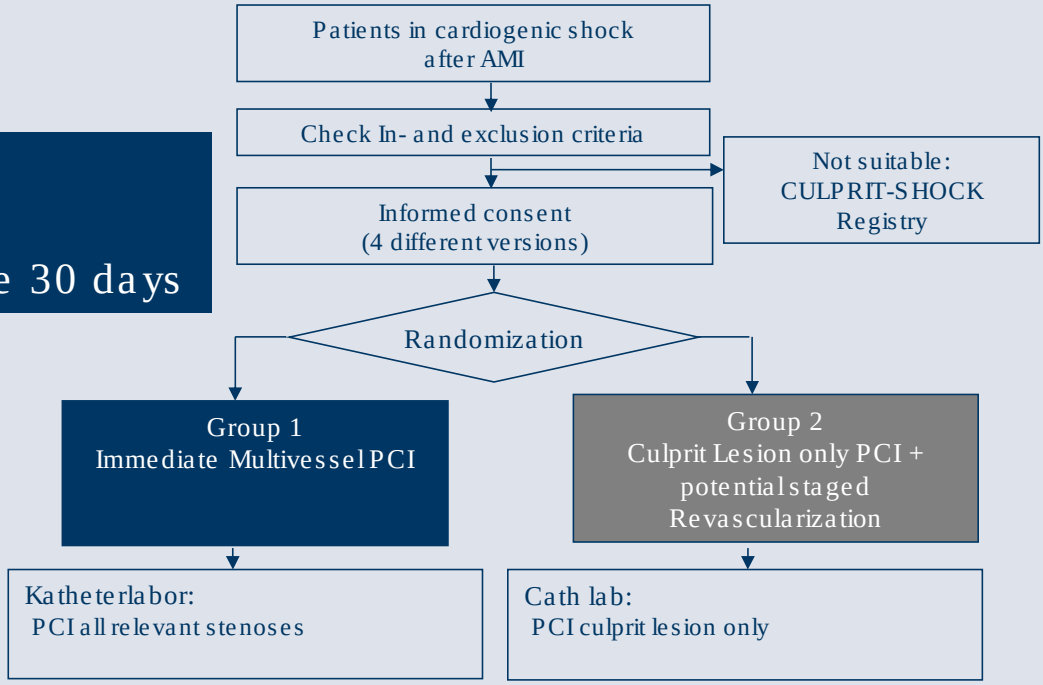
Challenging Dogma

- ¯Everyone in shock should get all their arteries opened: IRA culprit and all the rest_

- Does opening non-culprit artery with TIMI 3 flow and segmental normal wall motion improve shock outcomes?

CULPRIT-SHOCK Trial

Primary Endpoint:
Mortality and/or
Severe renal failure 30 days



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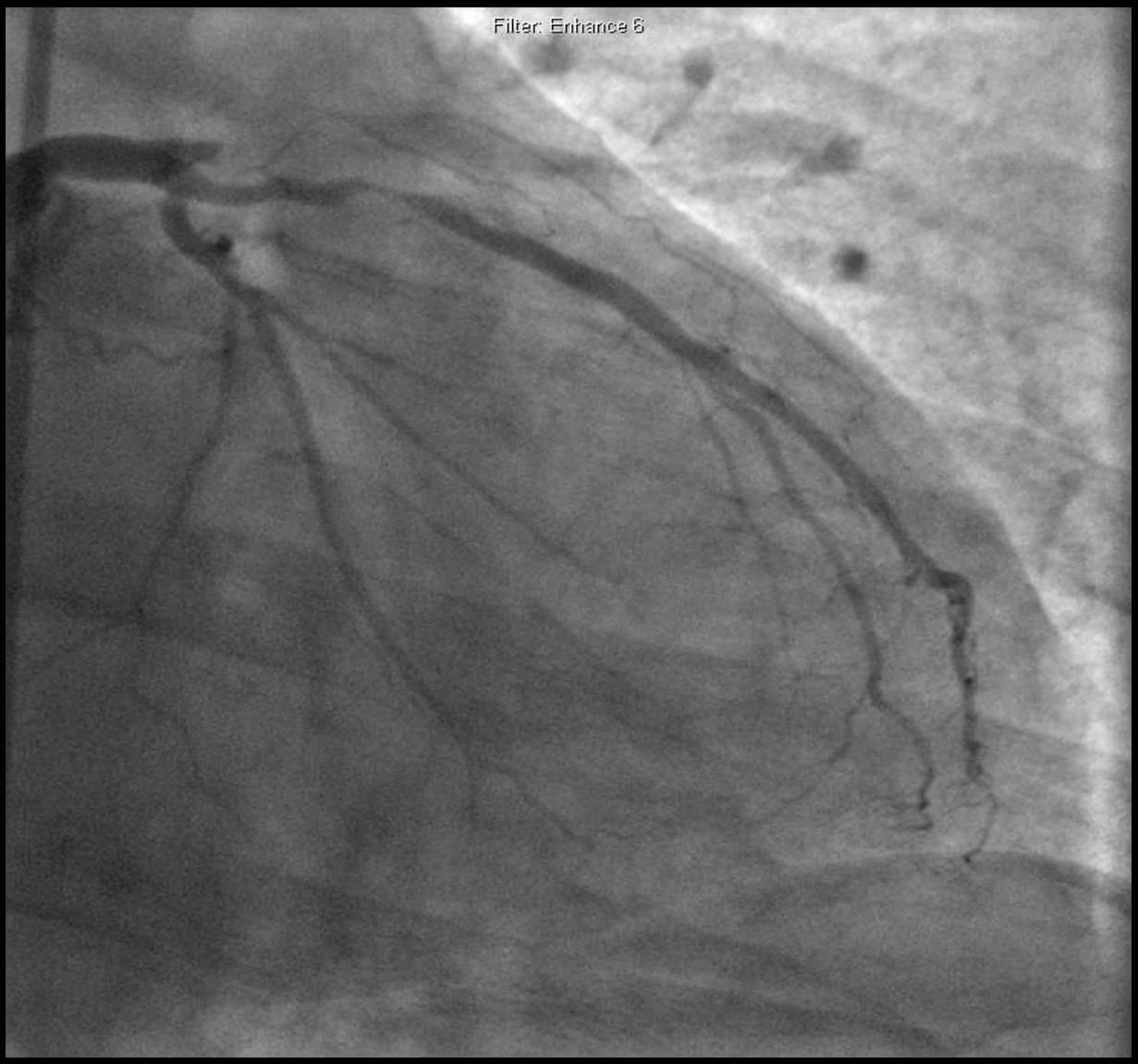
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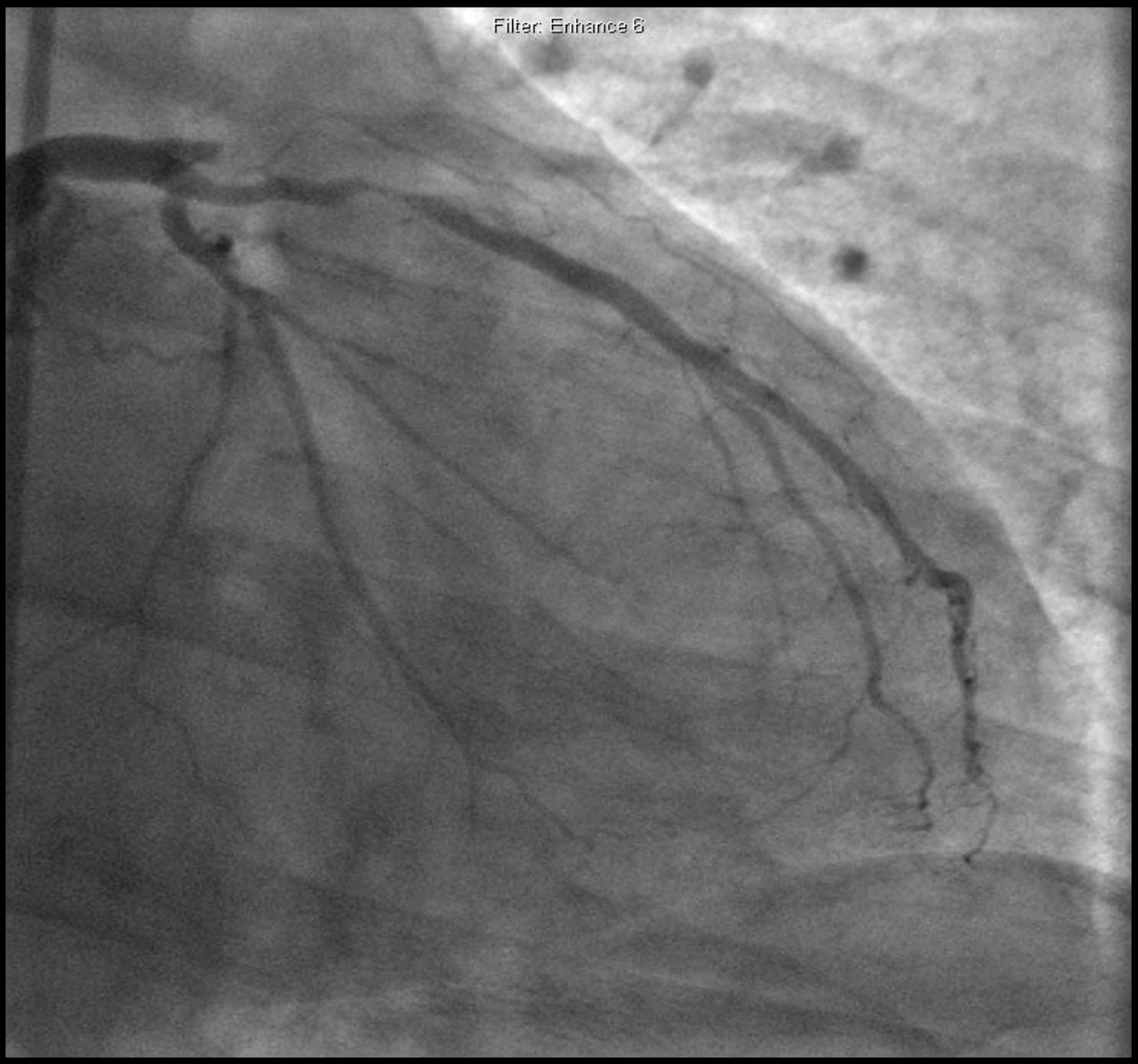
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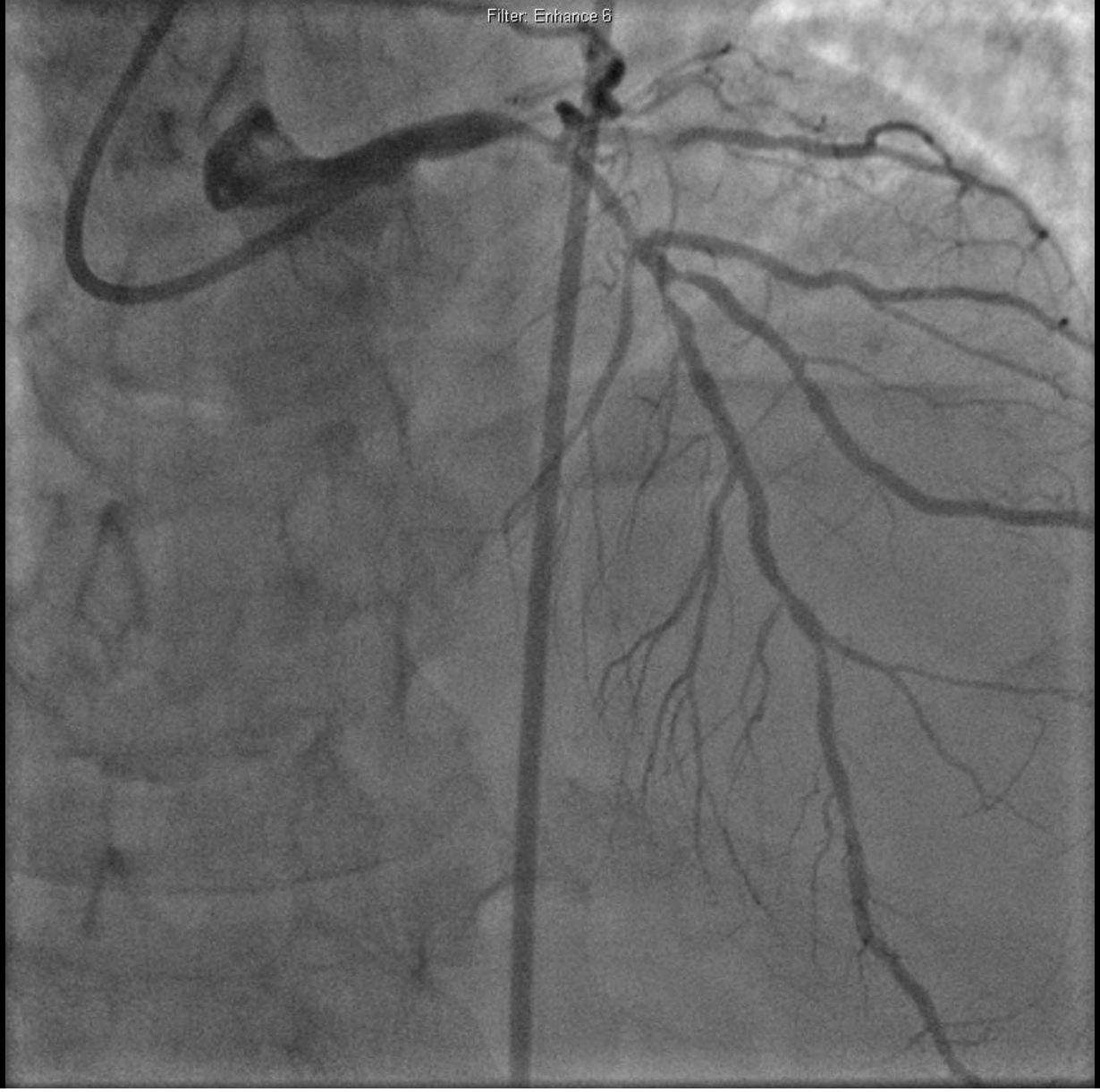
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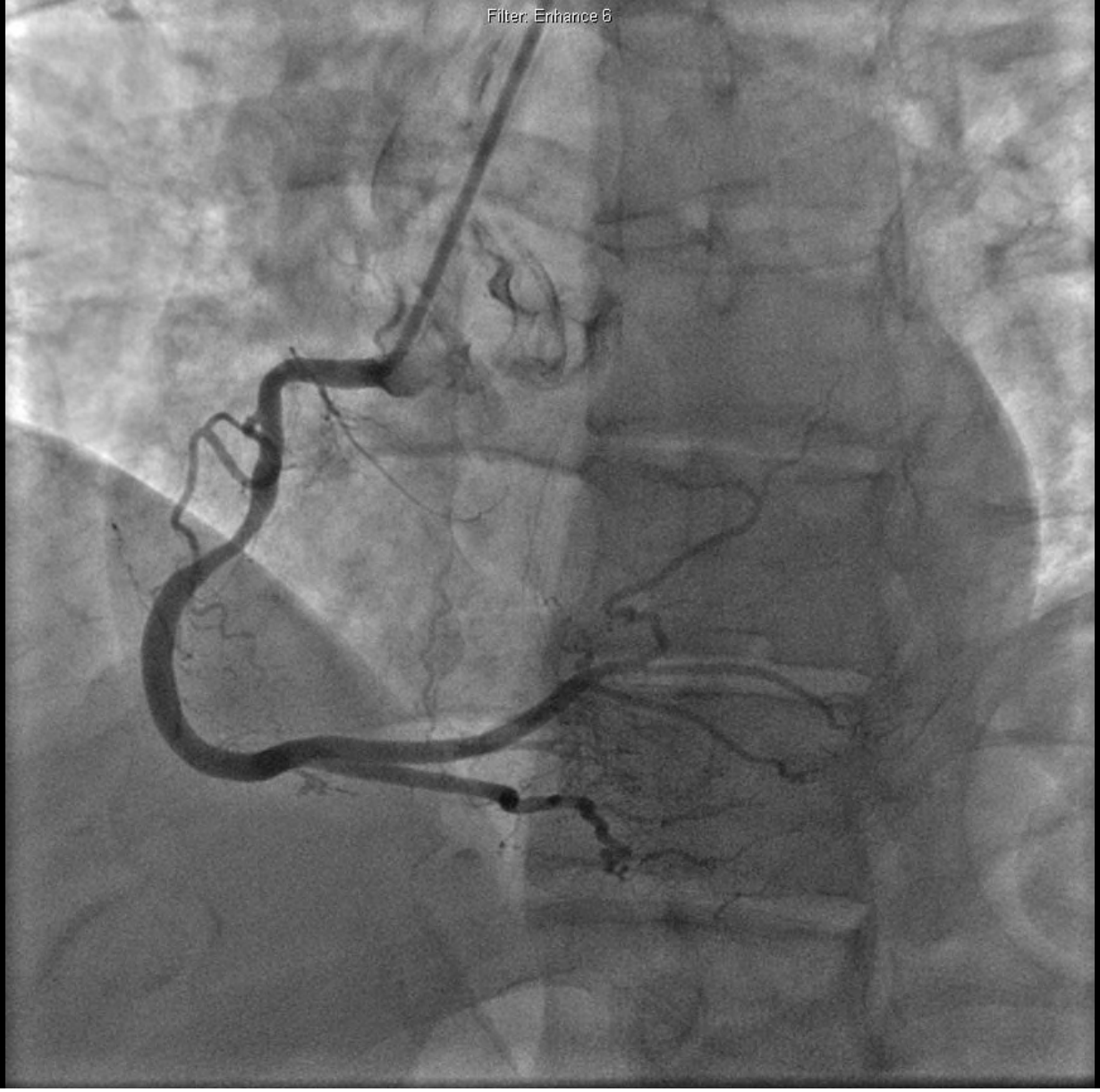
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How to win this debate

- A COMMON PROBLEM
- 40-50% of patients with STEMI have MV disease
- Nature of non-culprit disease: a mixed bag of challenges!

How to win this debate

- Me: Fix the culprit IRA with a perfect result

  Leave the rest for thoughtful approach—LATER!

- Tim: Just fix them all after you fix the infarct artery….Don't be lazy!

NON-IRA: What we don't know

- Fix it during infarct
- Stent before discharge….?FFR
- Stent in a few weeks….? FFR
- Get a stress test and go from there
- Fix only if symptoms

Why NOT do all the blockages?

Benefits

- Avoid risk of second procedure
- Decrease infarct size by increasing collateral flow?
- Reduce recurrent MI?
- Reduce length of stay?
- Reduce recurrent ischemia?

Why NOT do all the blockages?

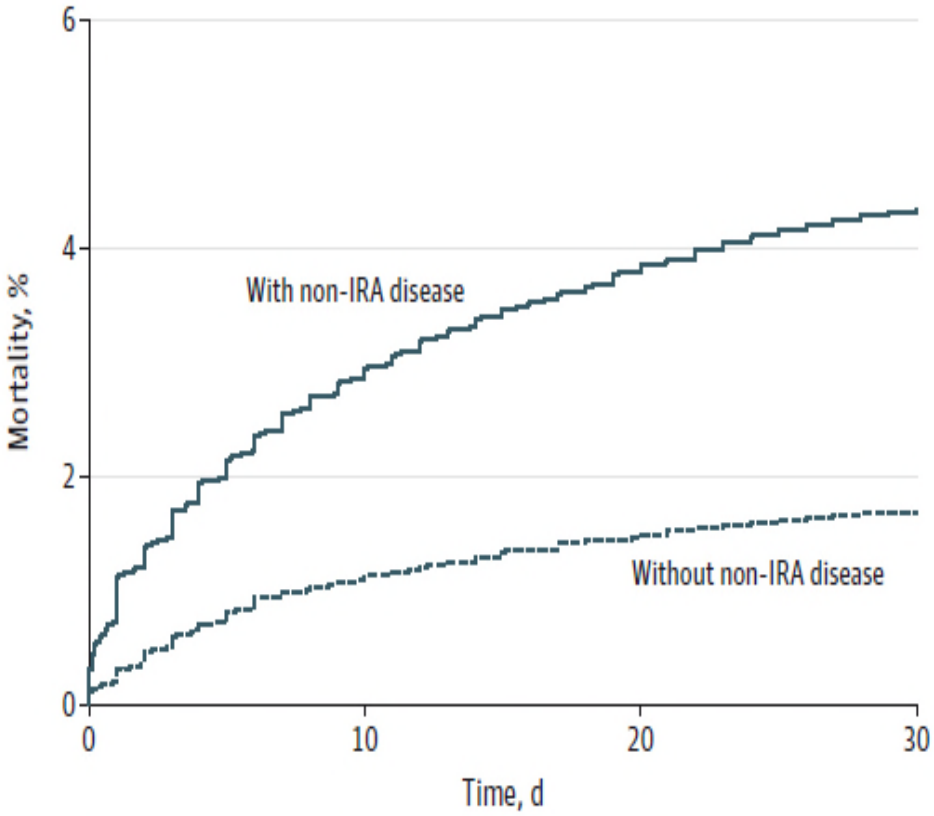
- Risks
  - Increase infarct size
    - Non-IRA PCI related no-reflow, ST
  - Contrast induced nephropathy
  - Increase cost with no clinical benefit
  - Do they all need another PCI?

Tim is tricky: Watch out for him!

- He will quote meta-analyses that are flawed and confounded by including observation registries or RCT's with small trials!

- He will show multiple anecdotal examples to try and prove his point!

Figure 2. Kaplan-Meier Curve for 30-Day Mortality Between Patients With and Without Obstructive Non-Infarct-Related Artery (Non-IRA) Disease



No. at risk				
With non-IRA disease	14916	14479	14335	14115
Without non-IRA disease	13351	13201	13141	13001

2015 ACC/AHA/SCAI Focused Update on PPCI for Patients With STEMI

2013 Recommendation	2015 Focused Update Recommendation	Comment
Class III: Harm	Class IIb	
PCI should not be performed in a noninfarct artery at the time of primary PCI in patients with STEMI who are hemodynamically stable. (LOE: 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 . (LOE: B-R)	Modified recommendation (changed class from ¯III: Harm_ to ¯IIb_ and expanded time frame in which multivessel PCI could be performed).

J Am Coll Cardiol 2016;67:1235-1250

How to win this debate

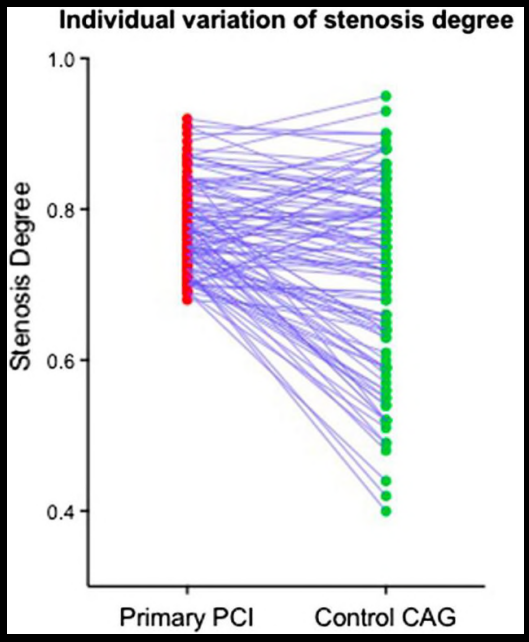
- Why am I right?

- Common sense!

Religion
Politics

Overestimation of Non-Culprit Stenosis Severity in STEMI (n=81)

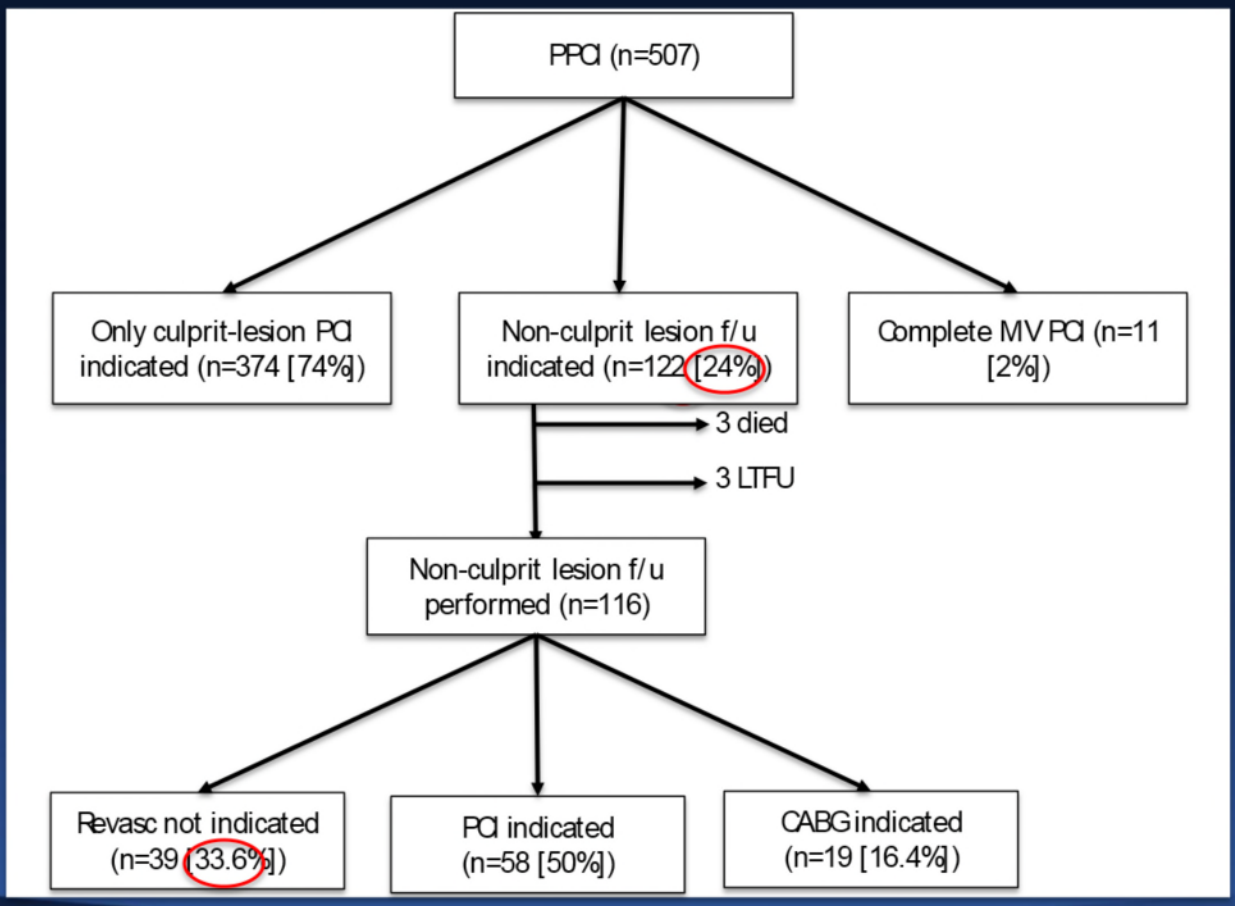
Measurements	Primary PCI	Control CAG	p
Minimum luminal diameter (mm)			
LAD	1.22±0.20	1.30±0.26	<0.001
Cx	1.21±0.31	1.28±0.31	<0.001
RCA	1.28±0.30	1.7±0.28	<0.001



'Critically narrowed' non–culprit arteries at time of PPCI deemed 'non-critical' during control coronary angiography in 13.3%

Donmez E, et al. Int J Cardiovasc Imaging 2016;32:1471-1476

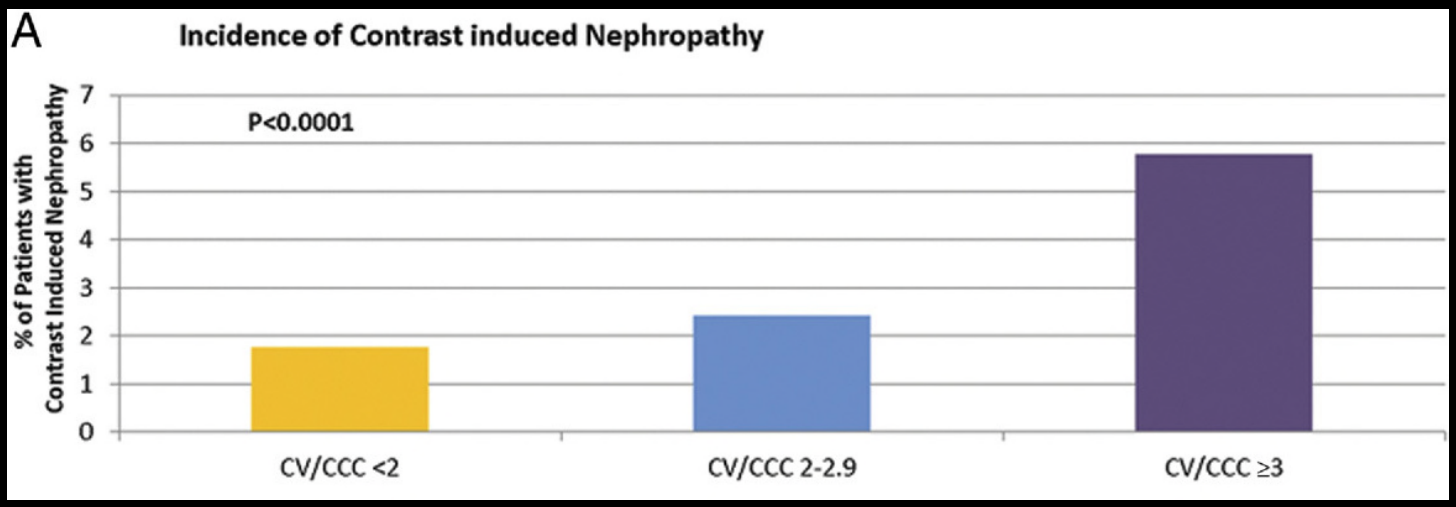
Overestimation of Non-Culprit Stenosis Severity in Setting of STEMI (n=122)



Thim T, et al. Open Heart 2016;3:000427

Contrast dose in CO vs MV PPCI: Increased Risk of CI-AKI

	CO (cc)	MV (cc)	P value
PRAMI	200 (150-260)	300 (210-380)	< 0.001
CVLPRIT	190 (150-250)	250 (190-330)	< 0.0001



Wald DS, et al. N Engl J Med 2013;369:1115-23.
Gershlick AH, et al. J Am Coll Cardiol 2016;65:963-72
Gurm, HS et al. J Am Coll Cardiol 2011;58:907-914

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, Shamir R. Mehta, Tony Lai, Robert C. Welsh

American Heart Journal, Volume 167, Issue 1, 2014, 1–14.e2

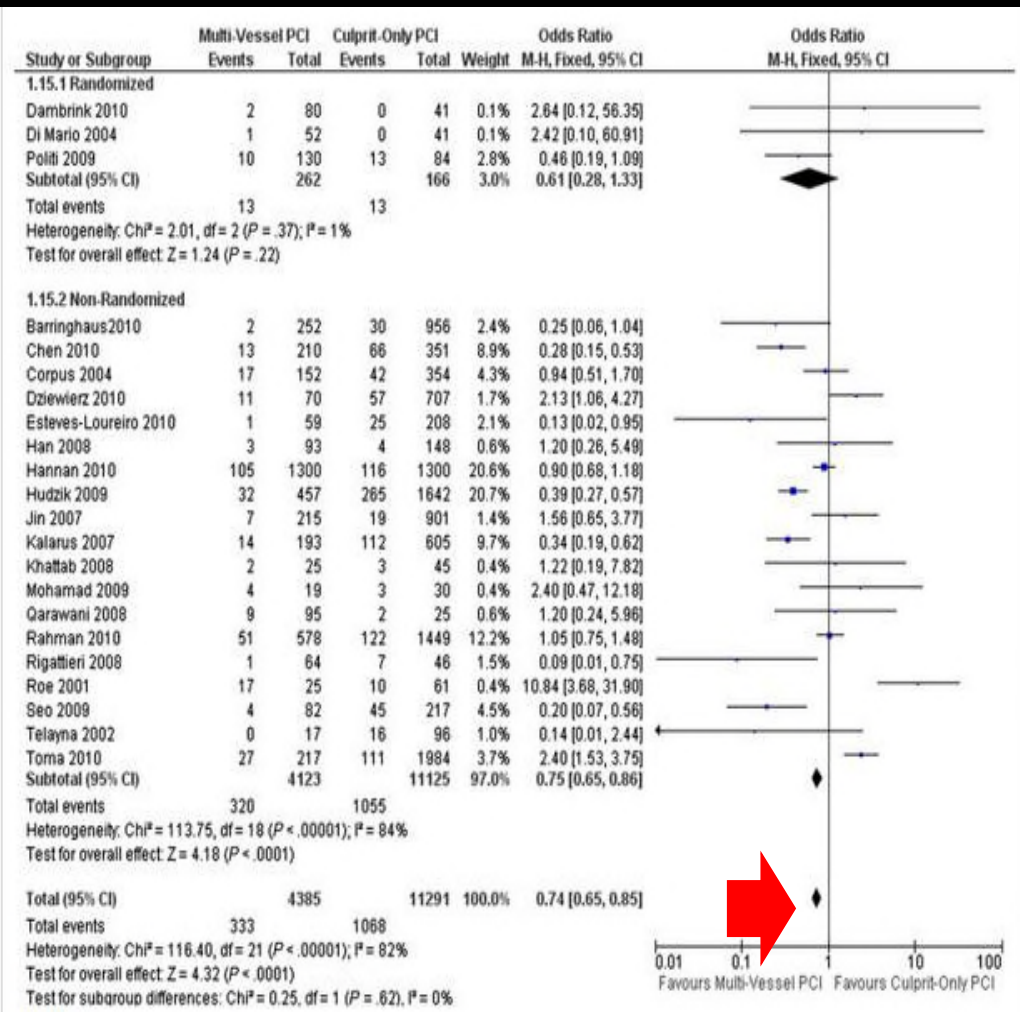
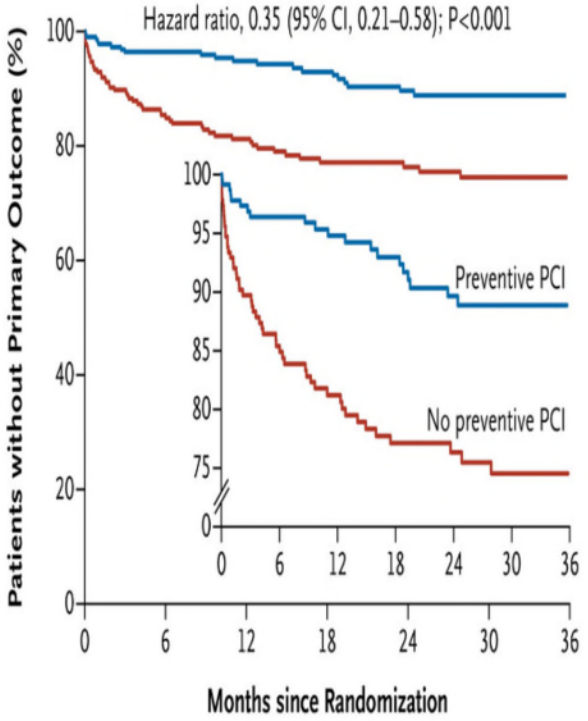


Figure 4.

Forest plot of long-term mortality stratified by study method.

Confounded: Sicker patients with MV dz get fixed …more likely to expire

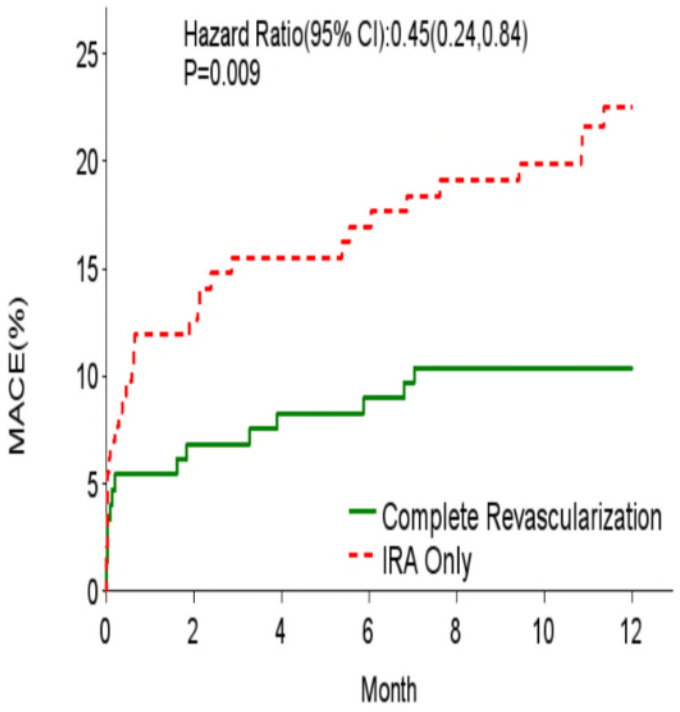
PRAMI



No. at Risk							
Preventive PCI	234	196	166	146	118	89	67
No preventive PCI	231	168	144	122	96	74	50

Wald DSet al. N Engl JMed 2013;369:1115-1123

CvLPRIT



Number at risk:							
Complete:150	131	129	128	125	108	73
IRA Only:146	122	118	116	111	98	68

Gershlick JAm Coll Cardiol. 2015 Mar 17;65(10

PRAMI Trial: 50% or >, Same setting

Variable	Preventive PCI (N=234)	Medical Rx (N=231)	HR (95% CI)	P value
Cardiac Death, MI, RFA	21	53	0.35 (0.21-0.58	<0·001
Cardiac death or MI	11	27	0.36 (0.18-0.73	0.004
All Death	12	16		NS
Cardiac Death	4	11	0.34 (0.11-0.73)	NS
Refract. angina	12	30	0.35 (0.18-0.69)	<0.001

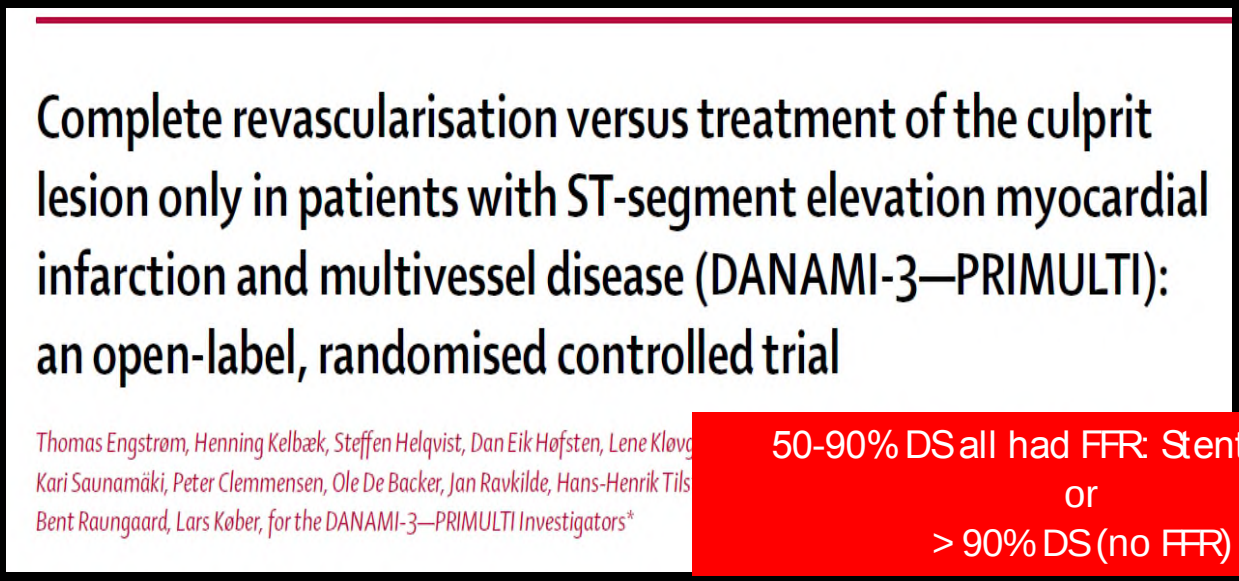
Wald NEJM 2013

Culprit Trial: 70% or >, imd or staged

Variable	Medical Rx (N=146)	PCI (N=150)	HR (95% CI)	P value
MACE N= (%)	31 (21.2)	15 (10.0)	0.45 (0.24, 0.84)	<0·001
All-cause mortality	6 (4.1)	2 (1.3)	0.32 (0.06, 1.60)	0.14
Recurrent MI	4 (2.7)	2 (1.3)	0.48 (0.09, 2.62)	0.39
Heart failure	9 (6.2)	4 (2.7)	0.43 (0.13, 1.39)	0.14
Repeat Revascularisation	12 (8.2)	7 (4.7)	0.55 (0.22, 1.39)	0.2

Gerschlick A. JACC 2014

FFR to guide revascularisation in non-infarct related artery territories



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 Engstrøm, Henning Kelbæk, Steffen Helqvist, Dan Eik Høfsten, Lene Kløv
Kari Saunamäki, Peter Clemmensen, Ole De Backer, Jan Ravkilde, Hans-Henrik Tils
Bent Raungaard, Lars Køber, for the DANAMI-3—PRIMULTI Investigators*

50-90% DS all had FFR: Stent if ↳ 0.80
or
> 90% DS (no FFR)

- Randomised 627 STEMI patients to receive culprit-only or complete revascularisation staged before DC.
- FFR used to guide N-IRA PCI in complete group
- FFR used if lesion diameter stenosis 50-90%.

DANAMI 3 – PRIMULTI Trial: FFR-Guided PCI reduced revasc with no difference in death or MI

A full 31% of lesions 50-90% had FFR >0.80!

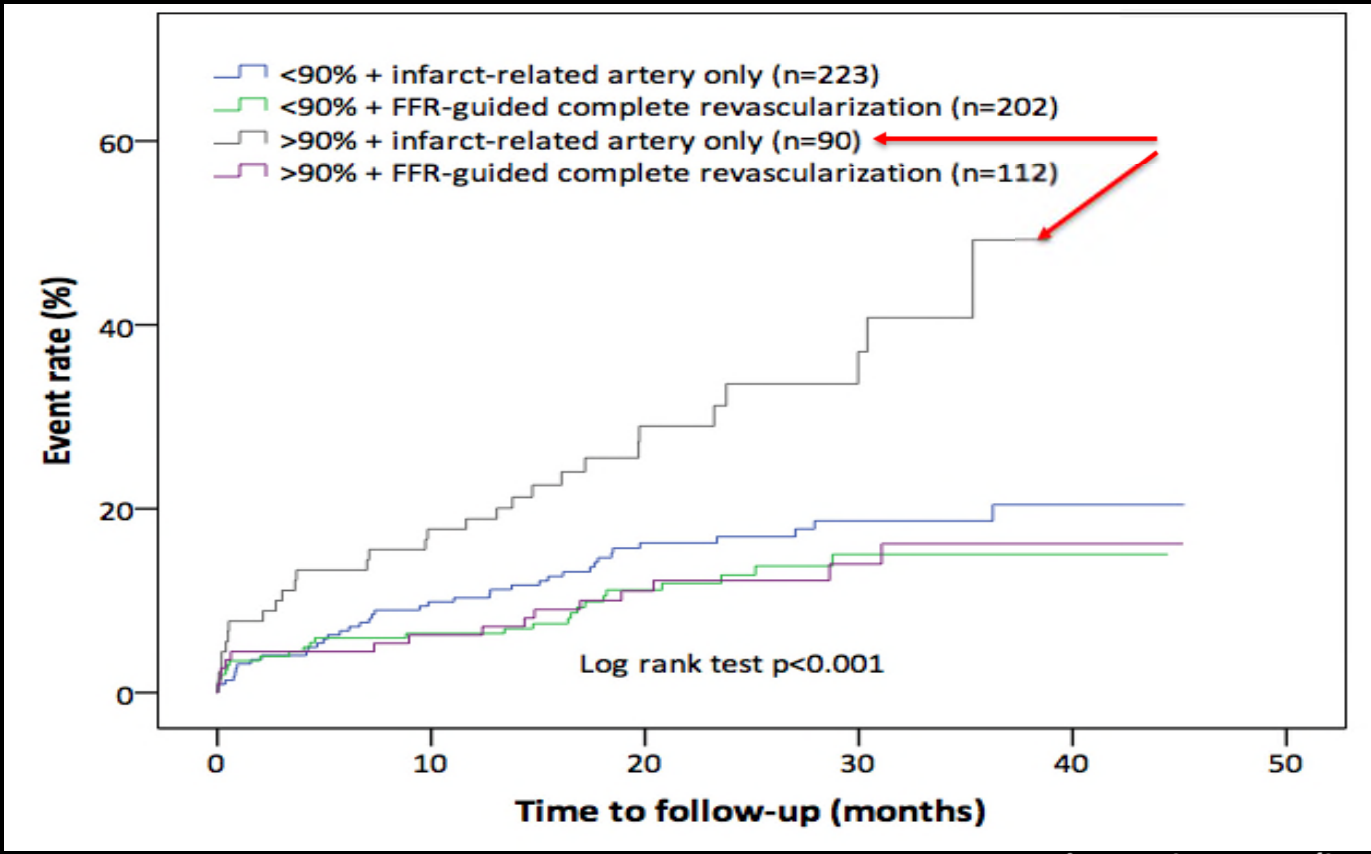
	IRA only	Complete revascularisation		
			0·83]	0·004
	11 (4%)	15 (5%)	1·4 [0·63 – 3·0]	0·43
Nonfatal MI	16 (5%)	15 (5%)	0·94 [0·47 – 1·9]	0·87
Ischemia-driven revascularisation*	52 (17%)	17 (5%)	0·31 [0·18 – 0·53]	<0·001

Engstrøm, Lancet 2

So far, RCT not definitive

- PRAMI: 5 years to recruit, excluded many, stopped early by DSMB
- Culprit: small, MACE positive, not individual components
- Danami-3: FFR driven if 50-90%. 1/3 50-90% FFR not ischemic
- None address issue of safety re: go home and come back

Primary endpoint according to severity of non-infarct related stenosis – DANAMI-3-PRIMULTI

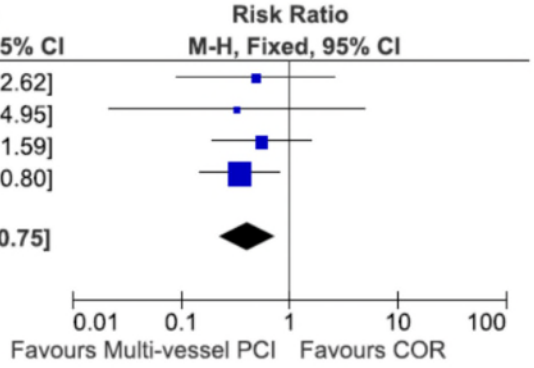


Lønborg Circ Interv (in press)

Re AMI

Study or Subgroup	Multi-vessel PCI Events	Total	COR Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Culprit	2	150	4	146	11.9%	0.49 [0.09, 2.62]
HELP AMI	1	52	1	17	4.4%	0.33 [0.02, 4.95]
Politi	6	130	7	84	24.9%	0.55 [0.19, 1.59]
PRAMI	7	234	20	231	58.9%	0.35 [0.15, 0.80]
Total (95% CI)		**566**		**478**	**100.0%**	**0.41 [0.23, 0.75]**
Total events	16		32			

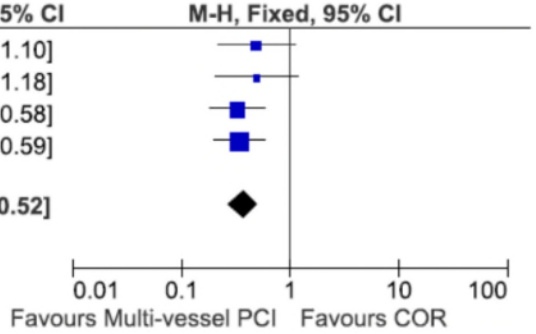
Heterogeneity: Chi² = 0.53, df = 3 (P = 0.91); I² = 0%
Test for overall effect: Z = 2.90 (P = 0.004)



Re-vascularization

Study or Subgroup	Multi-vessel PCI Events	Total	COR Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Culprit	8	150	16	146	15.4%	0.49 [0.21, 1.10]
HELP AMI	9	52	6	17	8.6%	0.49 [0.20, 1.18]
Politi	14	130	28	84	32.2%	0.32 [0.18, 0.58]
PRAMI	16	234	46	231	43.9%	0.34 [0.20, 0.59]
Total (95% CI)		**566**		**478**	**100.0%**	**0.37 [0.27, 0.52]**
Total events	47		96			

Heterogeneity: Chi² = 1.11, df = 3 (P = 0.77); I² = 0%
Test for overall effect: Z = 5.85 (P < 0.00001)



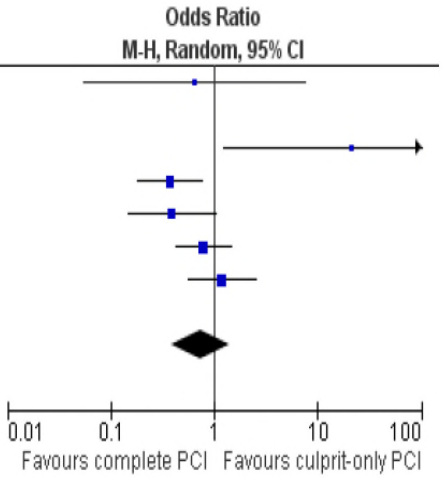
Add DANAMI -3 and PRAGUE

Meta analyses less convincing

Study or Subgroup	Multi-Vessel PCI Events	Total	Culprit-Only PCI Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Di Mario 2004	2	52	1	17	5.6%	0.64 [0.05, 7.53]	2004
Politi 2009	0	0	0	0		Not estimable	2009
Ghani Dambrink 2012	16	79	0	40	4.4%	21.05 [1.23, 360.59]	2012
Wald 2013	11	234	27	231	23.2%	0.37 [0.18, 0.77]	2013
Gershlick 2014	6	150	14	146	18.6%	0.39 [0.15, 1.05]	2014
Engstrom 2015	20	314	25	313	25.4%	0.78 [0.43, 1.44]	2015
Hlinomaz 2015	17	106	15	108	22.7%	1.18 [0.56, 2.51]	2015
Total (95% CI)		**935**		**855**	**100.0%**	**0.73 [0.38, 1.39]**	
Total events	72		82				

Heterogeneity: Tau² = 0.33; Chi² = 12.18, df = 5 (P = 0.03); I² = 59%

Test for overall effect: Z = 0.96 (P = 0.34)



combined endpoint of death / recurrent myocardial infarction.

Meta-Analysis of 7 RCTs
MV vs. CO-PCI Strategy for STEMI (n=1,939)

Outcome	Incidence (Complete %/Culprit %)	RR	95% CI	P-value	I^2%
Mortality or MI	7.8/10.4	0.69	0.42–1.12	0.14	51
MACE	14.7/24.4	0.61	0.45–0.81	<0.001	54
All-cause mortality	4.6/5.6	0.85	0.57–1.26	0.41	0
MI	5.2/6.0	0.74	0.38–1.44	0.38	49
Urgent revascularization	9.2/19.0	0.46	0.29–0.70	<0.001	61
Major bleeding	2.2/2.5	0.83	0.41–1.71	0.62	1
Contrast-induced nephropathy	1.6/1.7	0.94	0.42–2.12	0.89	0

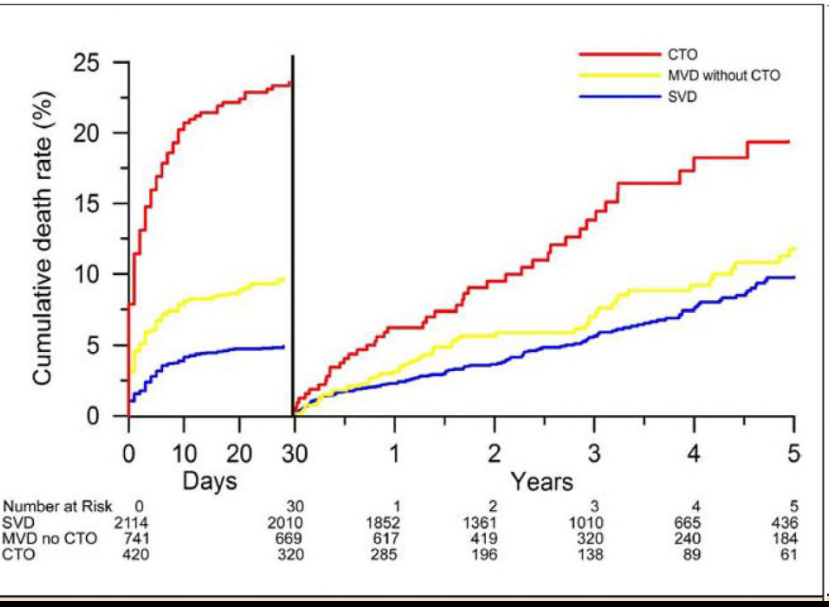
Elgendy IY, et al. Catheter Cardiovsac Interv 2016;88:501-505

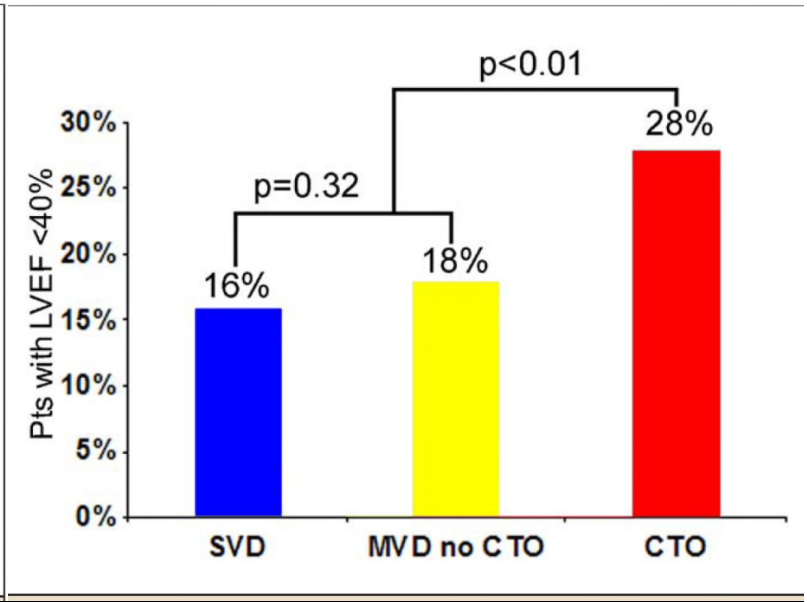
Call Mom

IS Tim really going to argue we should fix all non-culprit blockages at the same time ….based on these small RCT's and mx meta's I can't understand?

CTO drives excess mortality in MVD

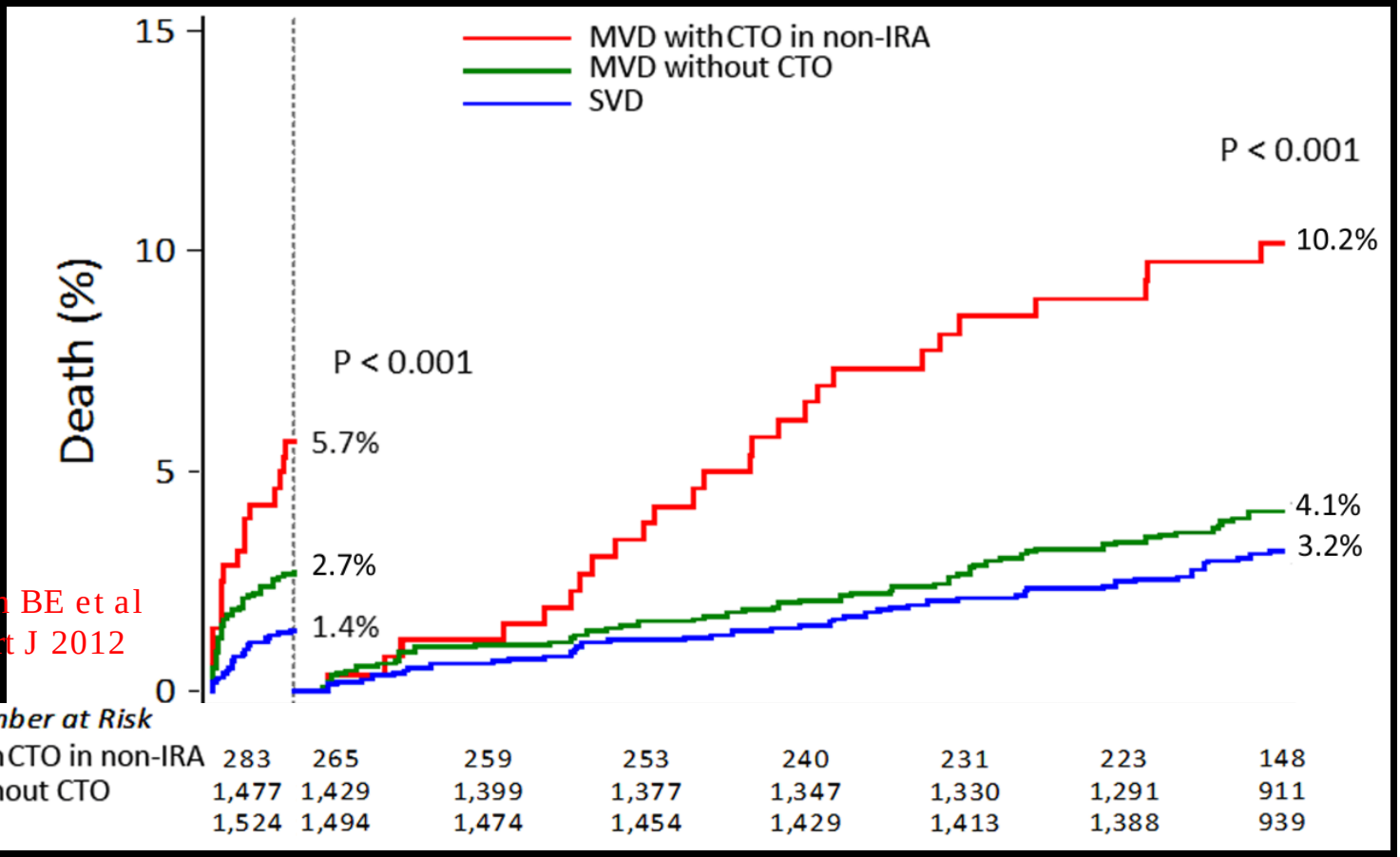
- CTO in non-IRA in 10% of STEMI patients
- Reduced LV function in MVD patients mainly driven by presence of CTO





Van der Schaaf et al, Heart, 2006
Claessen et al. JACC: Cardiovascular Interventions, 2009

substudy from the HORIZONS-AMI trial



Claessen BE et al
Eur Heart J 2012

Explore Trial Design

XPLORE

- Patients

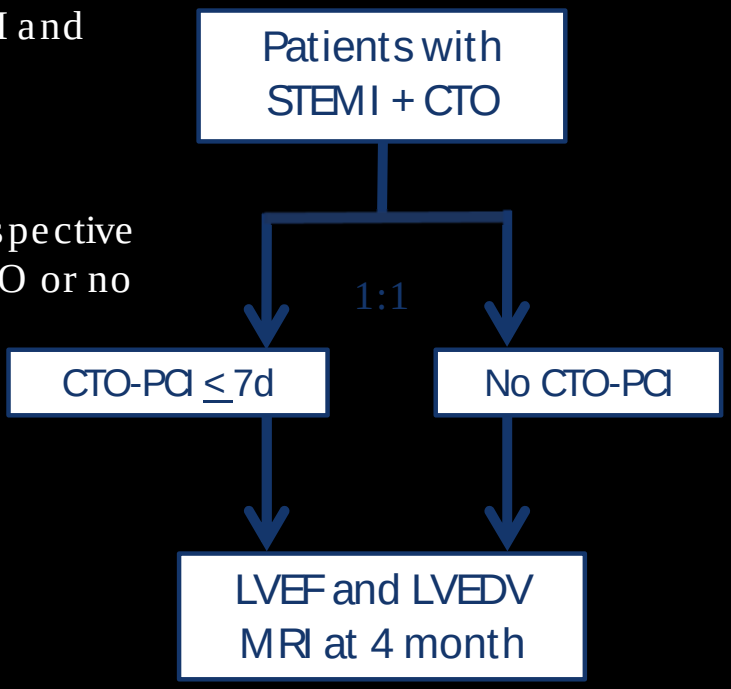
  Patients with STEMI treated with pPCI and with a non-infarct related CTO.

- Design

  Global, multi-center, randomized, prospective two-arm trial with either PCI of the CTO or no CTO intervention after STEMI.
  Blinded evaluation of endpoints.

- Objective

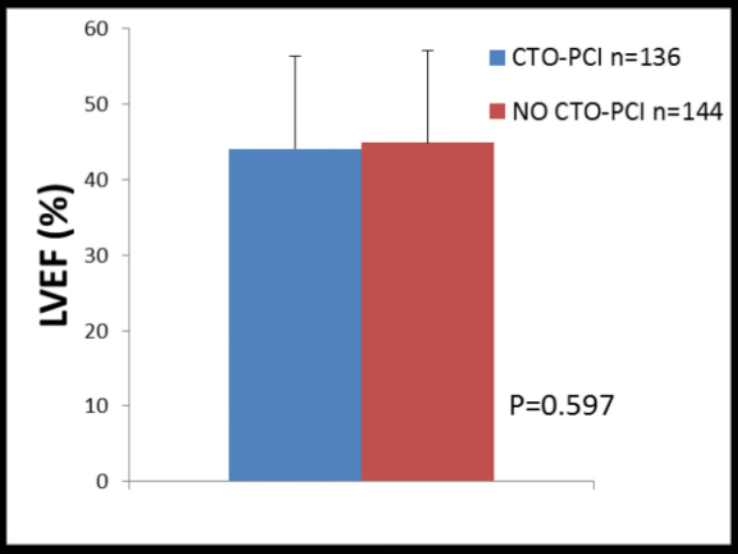
  To determine whether PCI of the CTO within 7 days after STEMI results in a higher LVEF and a lower LVEDV assessed by MRI at 4 months

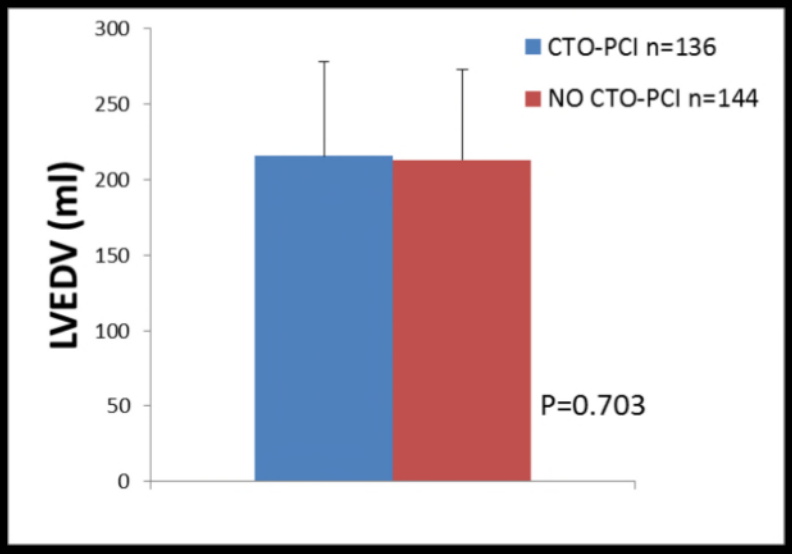


Henriques JP et al, JACC, 2016

EXPLORE Trial Outcome

- Early CTO-PCI :
  - not associated with higher LVEF and lower LVEDV @ 4 months





Henriques JP et al, JACC, 2016

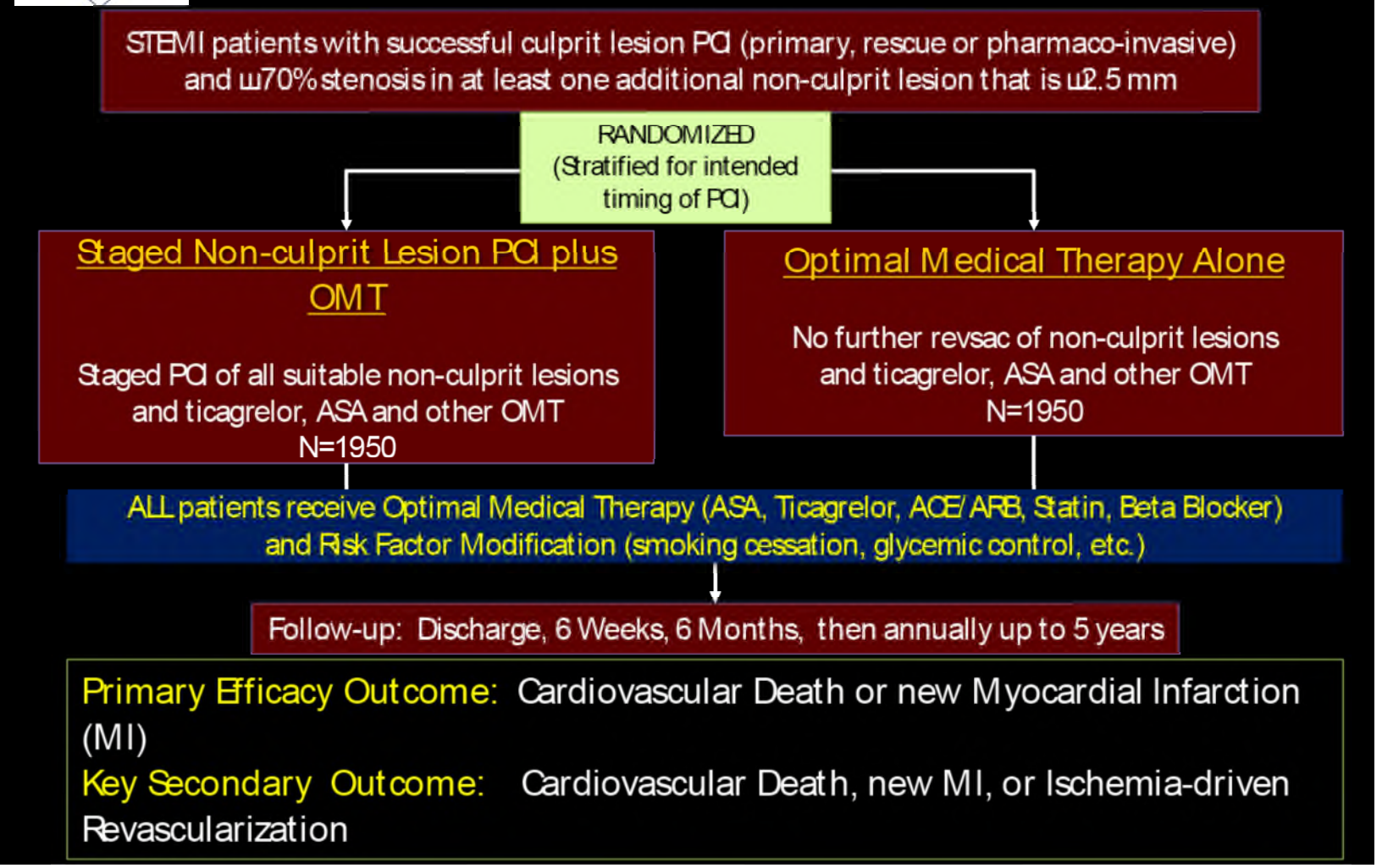
TABLE 4 Adjudicated Clinical Outcomes From Randomization to 4-Month Follow-Up

	CTO PCI (n = 148)	No CTO PCI (n = 154)	p Value
Major adverse cardiac events			
Cardiac death	4 (2.7)	0 (0.0)	0.056
Myocardial infarction	5 (3.4)	3 (1.9)	0.49
Periprocedural*	4 (2.7)	1 (0.6)	–
Spontaneous or recurrent	2 (1.4)	2 (1.3)	–
CABG operation	–	1 (0.6)	–
MACE	8 (5.4)	4 (2.6)	0.25

Henriques JP et al, JACC, 2016

A randomize ffectiveness study of α ulprit-only revascularization strategies to treat multi-vessel disease after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction

COMPLETE Study Design



Primary Efficacy Outcome: Cardiovascular Death or new Myocardial Infarction (MI)

Key Secondary Outcome: Cardiovascular Death, new MI, or Ischemia-driven Revascularization

Ongoing Trials

	n	Immediate Strategy	Subsequent Strategy for Untreated Non-Culprit Lesions	FFR Strategy
COMPARE-ACUTE	800	Culprit Only vs FFR Guided Complete	"Guideline Based" PCI in Culprit Only Group	DS > 50% - FFR (blinded in culprit only group)
COMPLETE	3900	Culprit Only In Both Groups	Staged Complete Revasc (PCI) Within 6 weeks	DS 50-70% - FFR DS > 70% - Stent
FULL REVASC	4052	Culprit Only vs FFR Guided Complete During Index Admission (Immediate or Staged)	"PRAMI" CONTROL Symptom or ischaemia driven revasc only. No mandatory ischaemia testing	DS 50-90% - FFR DS > 90% - Stent

MVD in the setting of STEMI- not a simple question

STEMI

↓

Significant N-IRA lesion

↓

Will the patient be better off/worse off if it is treated with PCI?

Final thoughts

What I have to concede to Tim:

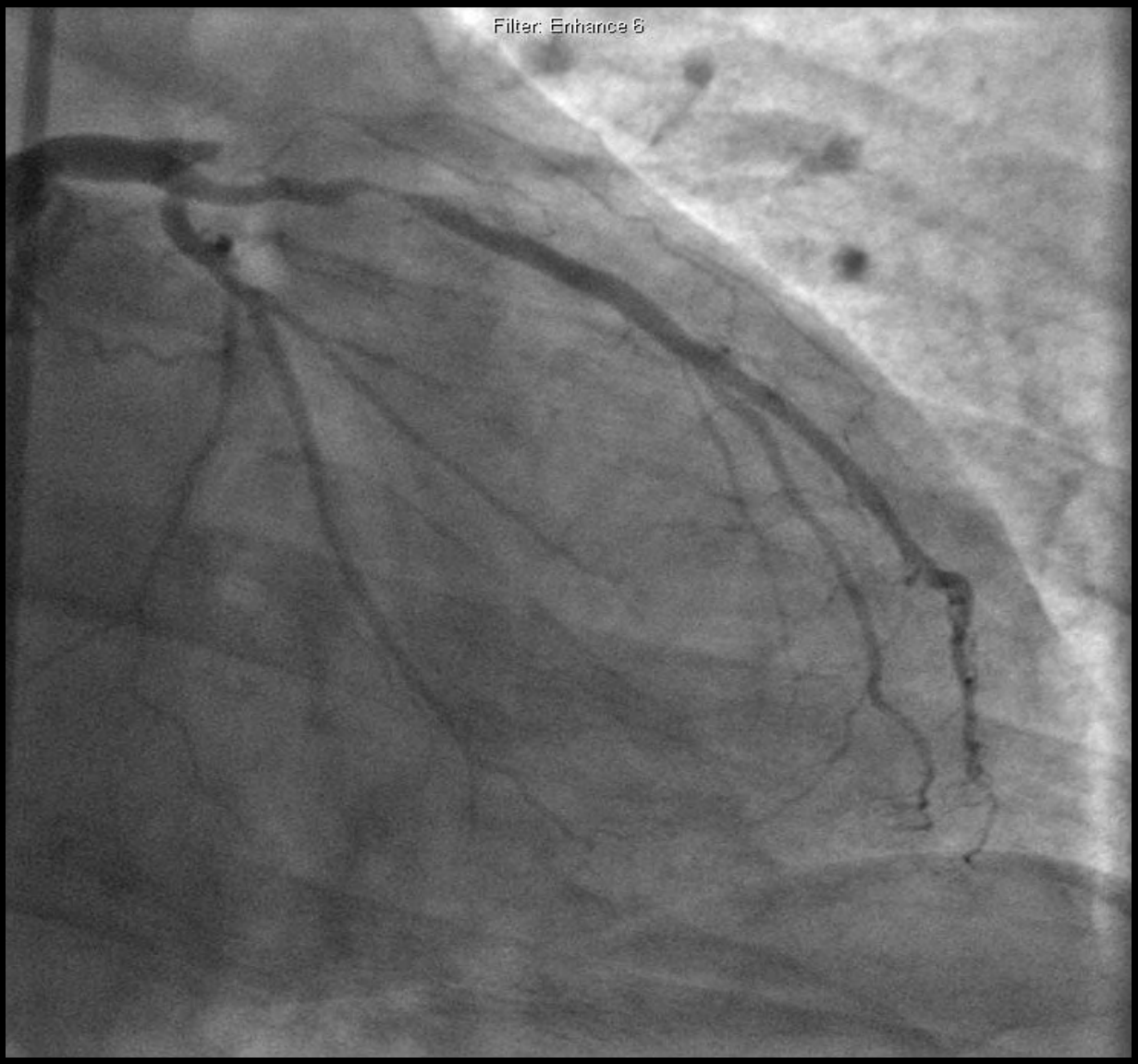
meta of 7 RCT's shows no increase in CIN with MV PCI same setting or before DC

What Tim has to concede to me:

If Danami 3 is right and 31% of 50-90% lesions are FFR negative….we will be doing a lot of unnecessary stenting!

Final thoughts

- No one trial will likely settle this debate
- BE A DOCTOR..No-Reflow in IRA, don't' play with fire in non-IRA!
- At least we have some data to make choices and not end up in Guideline-Jail
- More powerful studies on the way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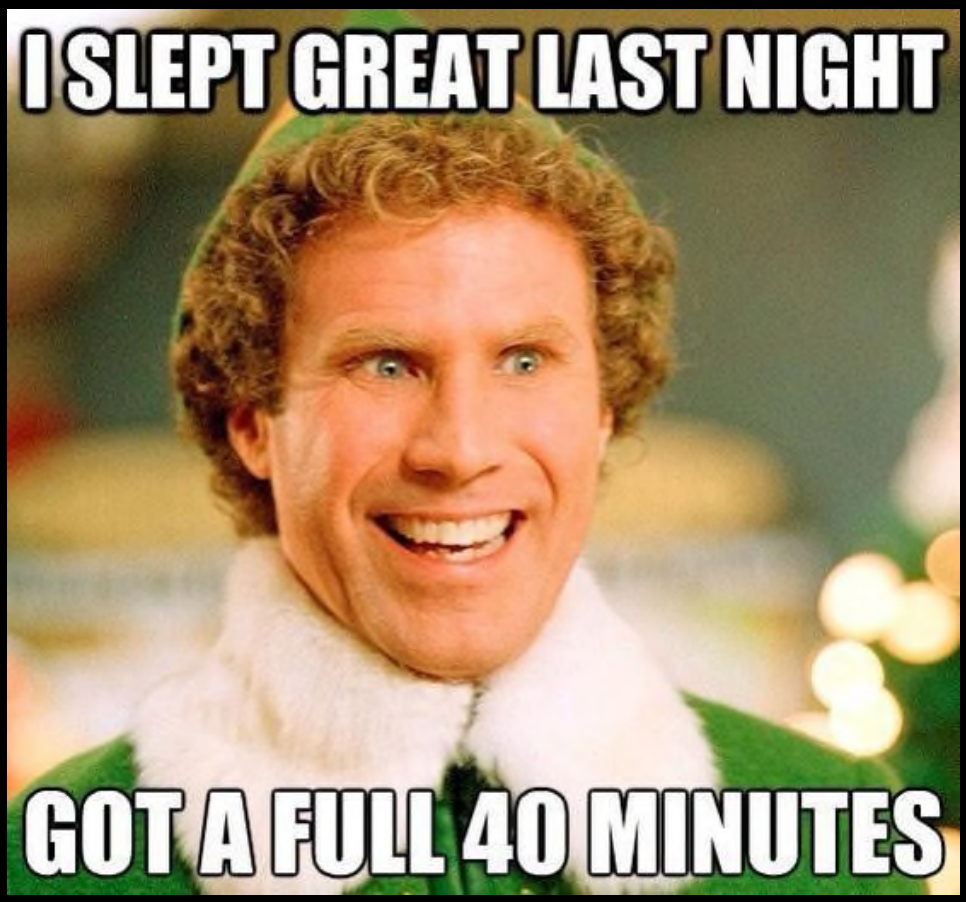
Most of my call nights...



See what Tim comes up with
But I think…I won!