MHIF Research Highlights: May 2020

Thanks to the physicians participating in the five-part, e-series connecting our physicians to the community!

Drs. Steven Bradley, Paul Sorajja, Retu Saxena, Peter Eckman, John Zakaib

mplsheart.org/on-the-pulse

Do you have a perspective about your world during the current pandemic you'd be willing to publish on the MHIF website?

Please let us know by connecting with Jesse Hicks – jhicks@mhif.org

Interested in MHIF Updates During COVID-19?

Visit mplsheart.org/coronavirus/

MHIF FEATURE:

HemoLung Emergency Use of ECCO2R
Dr. Saavedra-Romero

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MHIF Research Tiger Team ready to support HemoLung with 24/7 onsite research coverage!

HOPE DISCOVERED HERE

Minneapolis Heart Institute Foundation

Creating a world without heart and vascular disease

Complete Revascularization in Patients with Multivessel CAD: Is the Story COMPLETE

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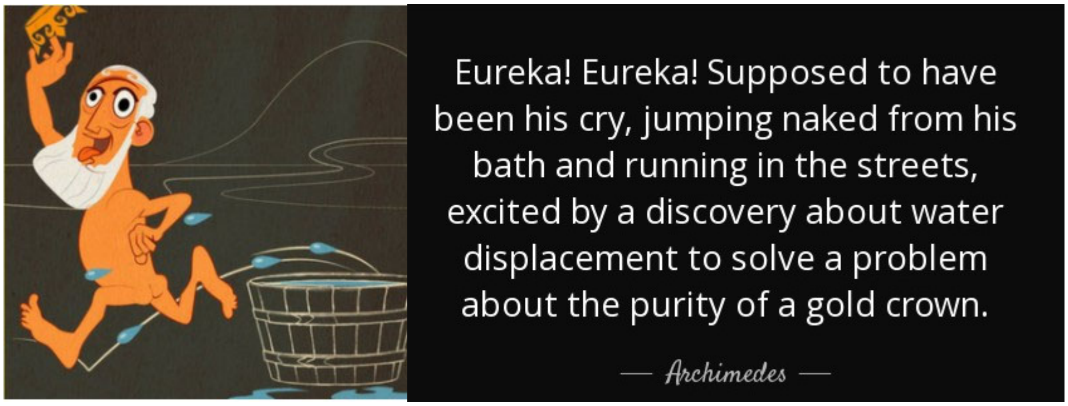
DISCLOSURE

NONE

My mission to IC world started by "Eureka Moment"



Background

1. **Value of complete revascularization in <u>stable CAD</u>.**
2. **Value of complete revascularization in <u>acute MI</u>.**
3. **Value of complete revascularization in <u>cardiogenic shock</u>.**

1- Value of complete revascularization in stable CAD

Background

- Patients undergoing PCI are often found to have multivessel CAD, with 1 or more angiographically significant non-culprit lesions.
- There is uncertainty on how best to manage these non-culprit lesions:
  - Routinely revascularize them with PCI?
  - Manage according to anatomical or functional assessment?
  - Manage them conservatively with guideline-directed medical therapy alone?

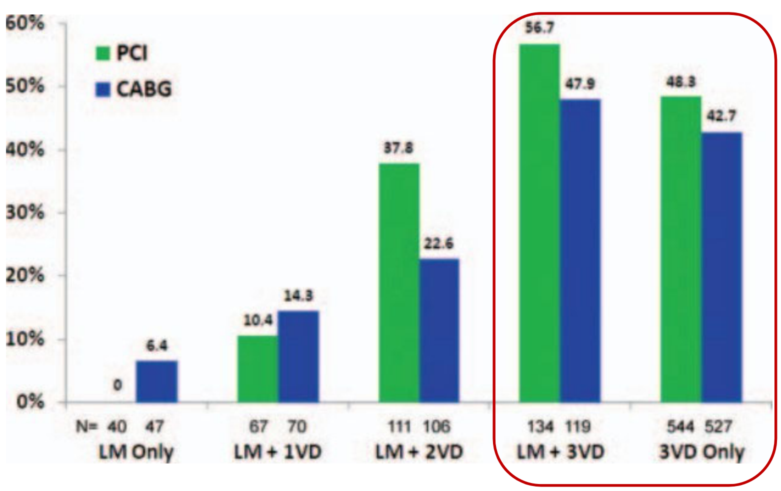
Background

1. Are there standardized definitions for CR/IR available?
2. Is CR a fundamental tenet or is it just a worthwhile objective, for which benefits outweigh the risks? Does it have the same implications for surgeons vs interventional cardiologists
3. Should CR become the standard for comparison of the efficacy of different procedures, eg, should the ability to achieve CR vs IR be used as a criterion to select specific therapeutic options such as PCI vs CABG?
4. Do we perform CR in those patients in whom we can, –and only perform IR when CR is not feasible?
5. Has the FAME[7] study reframed the issues with regard to CR vs IR?
6. Does the effect of CR vs IR depend on the specific arterial segment involved, eg, is CR more important when the LAD is involved?

Gössl et al: Circ Cardiovasc Interv 2012

Prevalence of incomplete revascularization?

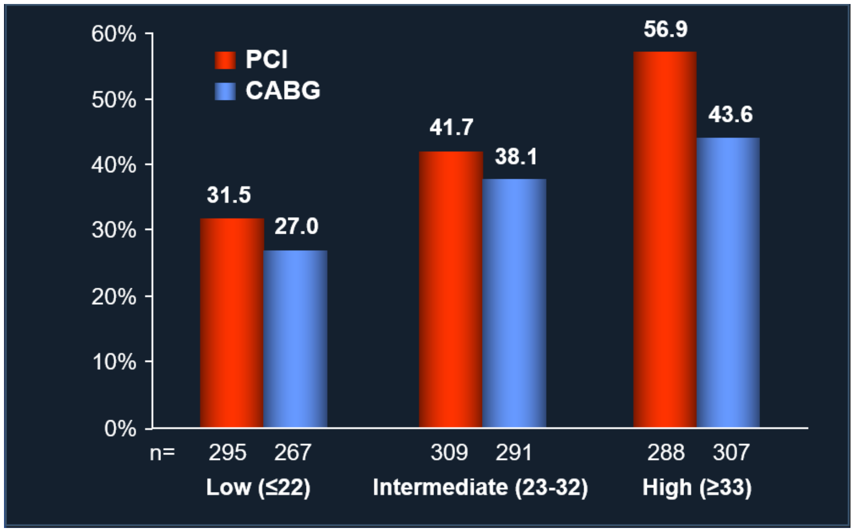
Incomplete revascularization was defined as when a preoperatively identified vessel with a lesion was not revascularized



Almost 50% in patients with 3 VD

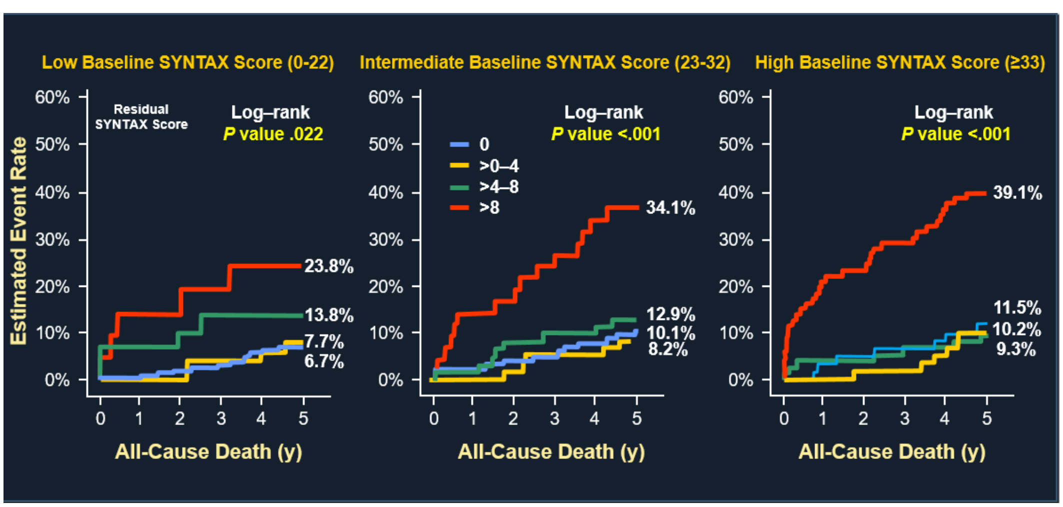
Head et al, Euro J of Cardio-thoracic Surgery 2012;41:535-541

SYNTAX Trial: Incomplete revascularization and SYNTAX SCORE



Head et al, Euro J of Cardio-thoracic Surgery 2012;41:535-541

A residual SYNTAX score >8 after PCI was associated with significant increases in the 5-year risk of death and of the composite of death, MI, and stroke



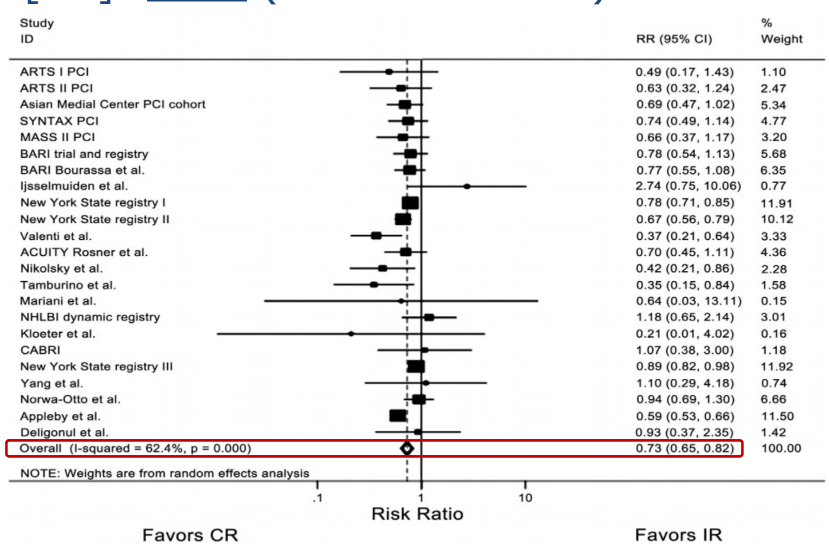
Farooq et al: Circ 2013;128:141

Outcomes After Complete Versus Incomplete Revascularization of Patients with MVD

- Meta-analysis of 35 studies that compared CR vs IR.
- Roughly half of these patients received CR (50.5%).
- IR was more common following PCI vs CABG (56% vs 25%).
- CR was associated with lower long-term mortality as well as reduced MI and repeat coronary revascularization.
- Irrespective of revascularization modality, mortality benefit in regards to CR was consistent across all studies.

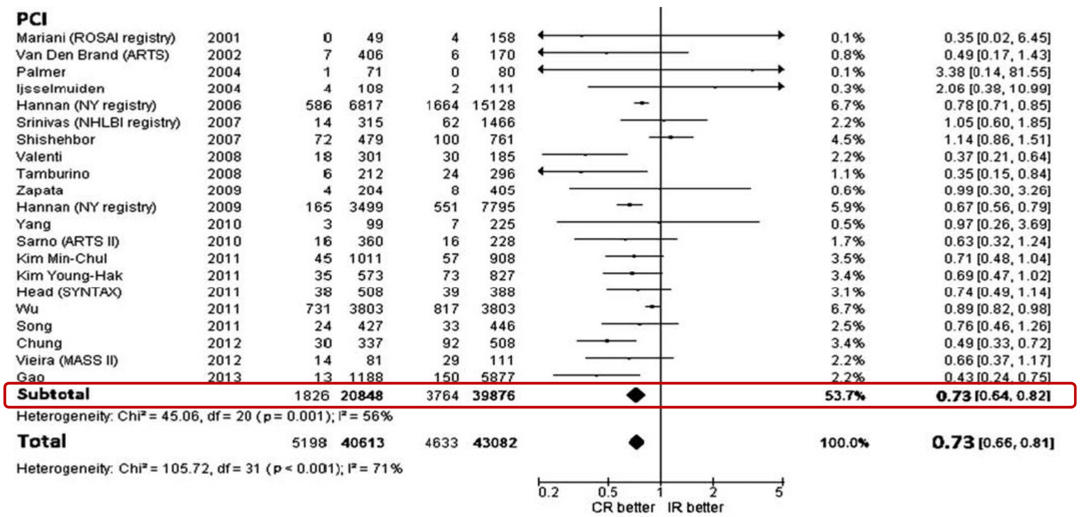
Garcia S et al. *J Am Coll Cardiol*. 2013;62(16):1421-1431.

CR was associated with lower long-term mortality (risk ratio [RR]: **0.73** (CI: 0.65 – 0.82).



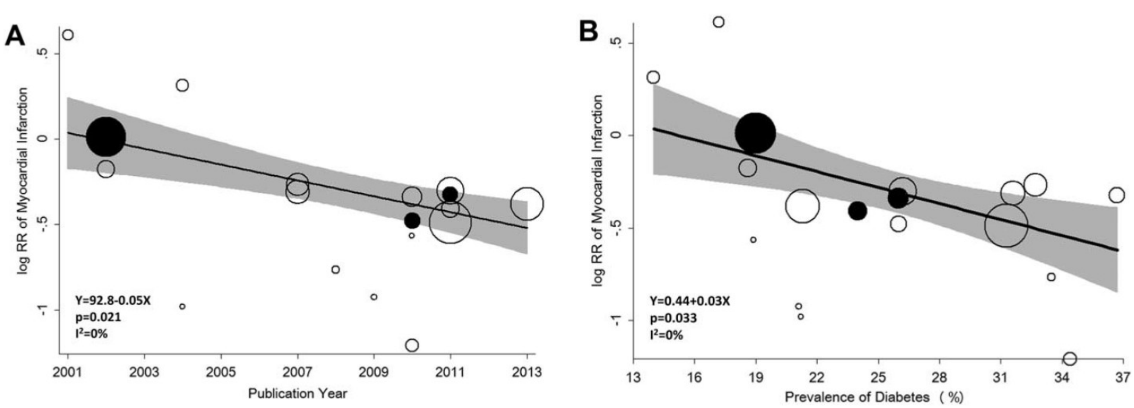
Garcia S et al. *J Am Coll Cardiol*. 2013;62(16):1421-1431.

More recent meta-analysis in 2016: same RR !!



Zimarino et al: CCI 2016, 87:3–12

RR reduction of MI obtained with CR seems stronger in **<u>recent studies</u>** and in populations with a higher prevalence of **<u>diabetes</u>**.



Zimarino et al: CCI 2016, 87:3–12

Everolimus-Eluting Stents or Bypass Surgery for Multivessel Coronary Disease

In this observational study from the New York State registry, the authors compared CABG with PCI using new generation DES

116,915 Patients in New York underwent CABG or PCI for multivessel coronary artery disease for the first time in 2008–2011

↓

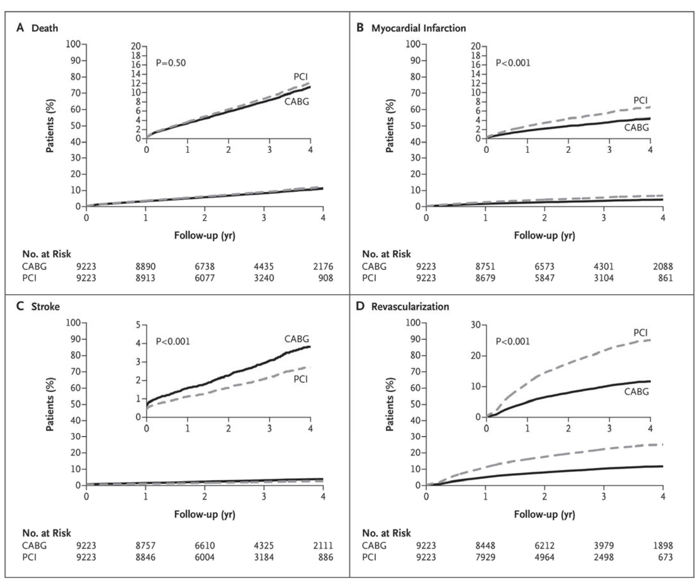
34,819 Were included in study analysis
- 16,876 Underwent isolated CABG
- 17,943 Underwent PCI with everolimus-eluting stent

↓

18,446 Were included in propensity-score–matched analysis
- 9223 Underwent isolated CABG
- 9223 Underwent PCI with everolimus-eluting stent

Bangalore NEJM 2015;372:1213-22

At a mean follow-up of 2.9 years: Compared with CABG, **PCI** was associated with a similar risk of death, **higher risk of MI**, repeat revascularization, but lower risk of stroke.



Bangalore NEJM 2015;372:1213-22

Among the matched pairs, the **higher risk of MI** with PCI vs CABG was significant **only** among those with **incomplete revascularization**.

Table S1. Risk of primary and secondary outcomes in anatomic subgroups

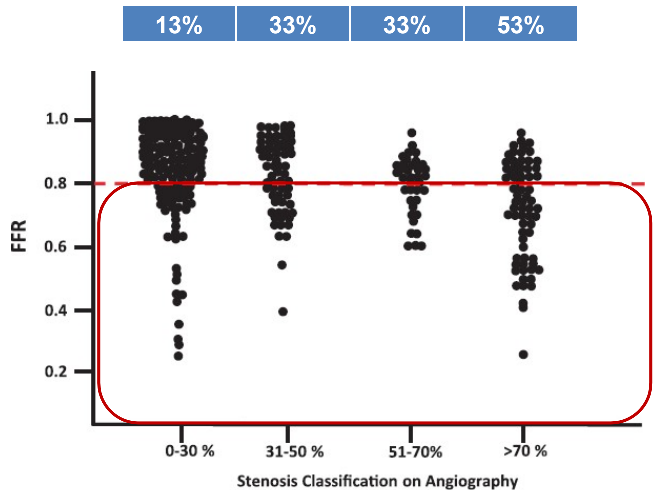
Variables	No. of Patients	No. of Patients with Events	Event Rate (%/Year)	Hazard Ratio (95% CI)	P-value	P-value for interaction
Outcome: Myocardial Infarction						
Complete Revascularization						0.02‡
EES	1911	72	1.43	1.02(0.71,1.47)	0.93	
CABG	1911	80	1.37	Reference		
Incomplete Revascularization†						
EES	7312	390	1.98%	1.66(1.39,1.98)	<0.001	
CABG	7312	242	1.07%	Reference		

Bangalore NEJM 2015;372:1213-22

Does Functional Complete Revascularization Matter?

Angiography alone can be Misleading!!

200 stable patients referred for coronary angiography underwent routine FFR in all patent stentable (≥ 2.25 mm) vessels.



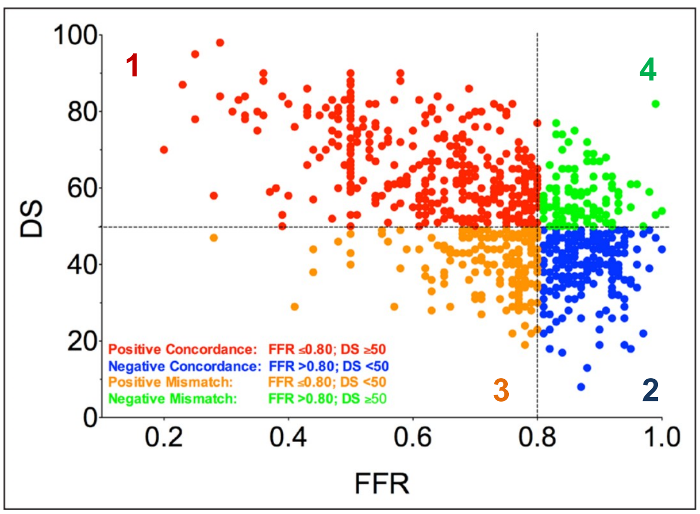
In lesions graded >70% stenosis, the FFR was <0.8 in only 53%.

Thus, in 47% of stenoses graded >70%, the FFR indicated that there was no physiologically significant lesion.

Curzen, et al. Circ Cardiovasc Interv 2014;7:248-55.

Ischemia vs. angiography to predict natural history of CAD

1,029 lesions from 607 medically treated patients in FAME 2

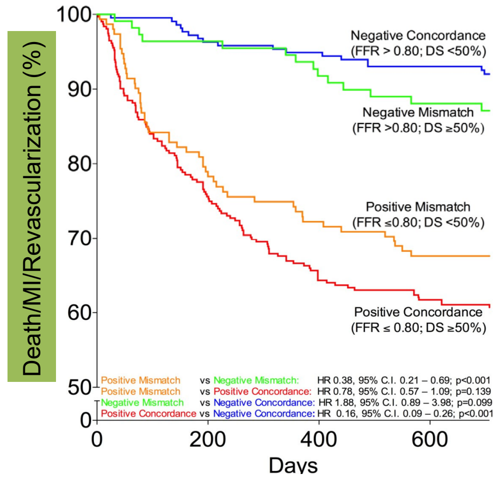


The stenoses were divided into 4 groups according to FFR and %DS values:

Ciccarelli, et al. Circulation 2018;137:1475-85.

Ischemic vs. Anatomic CAD Burden

1,029 lesions from 607 medically treated patients in FAME 2



Negative Concordance : FFR >0.80; DS <50%
Negative Mismatch : FFR >0.80; DS ≥50%
Positive Mismatch : FFR ≤0.80; DS <50%
Positive Concordance : FFR ≤0.80; DS ≥50%

Measurements of FFR should no longer be limited to angiographically intermediate stenosis but should be contemplated in stenoses that are **mild** or **severe** by visual evaluation.

Ciccarelli, et al. Circulation 2018;137:1475-85.

"If all **you** have is a **hammer**, everything looks like a nail"

DEFER Trial 15 Year Follow-Up

181 patients with intermediate lesions and FFR ≥ 0.75 (functionally non-significant stenosis) randomized to: Deferral Vs. performance of PCI

	Defer group (*n* = 91)	**Perform group (*n* = 90)**	***P*-value** Defer vs. Perform
Mortality			
All cause	30 (33.0%)	28 (31.1%)	0.789
Cardiac	5 (5.5%)	4 (4.4%)	1.000
Unknown	13 (14.3%)	11 (12.2%)	0.682
Non-cardiac	12 (13.2%)	13 (14.4%)	0.806
MI			
All	2 (2.2%)	9 (10.0%)	0.033
Target vessel[a]	1 (1.1%)	8 (8.9%)	0.018
Revascularization			
All	39 (42.9%)	31 (34.4%)	0.245
Target vessel	33 (36.3%)	25 (27.8%)	0.221

Rate of MI was significantly lower in the Defer group. 2.2% vs 10.0%, RR 0.22!

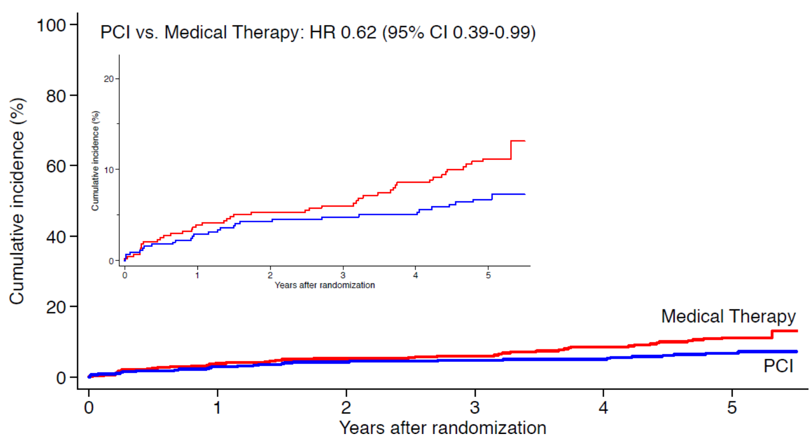
No signs of late 'catch-up' phenomenon!

Zimmermann, et al. Eur Heart J 2015;36:3182-8

FAME 2: Five Year Follow-Up

5 year rate of spontaneous MI in 881 patients with ischemic FFR values randomized to PCI or medical therapy: there is a strong signal towards less MI in the PCI group

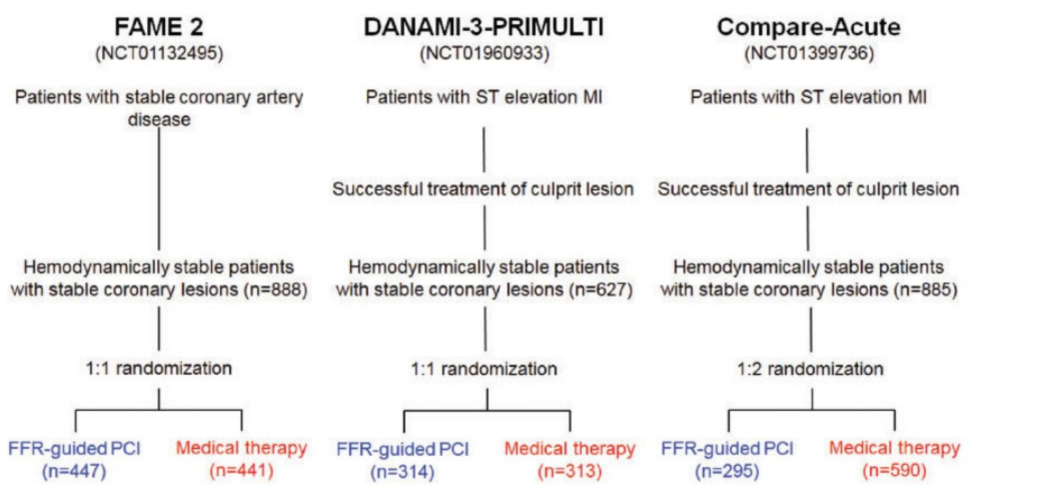
P=0.04



These lesions are NOT safely treated medically.

Xaplanteris, et al. New Engl J Med 2018;379:250-259.

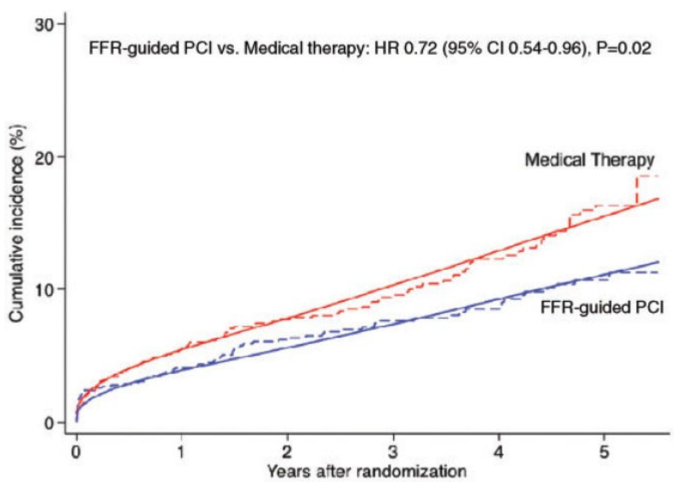
Meta-analysis of FFR-guided PCI vs. medical therapy for patients with stable coronary lesions



Zimmermann, et al. Eur Heart J 2019;40:180-186.

Meta-Analysis of FFR-Guided PCI

2,400 patients with stable (or stabilized) CAD from 3 randomized trials comparing FFR-guided PCI with medical therapy



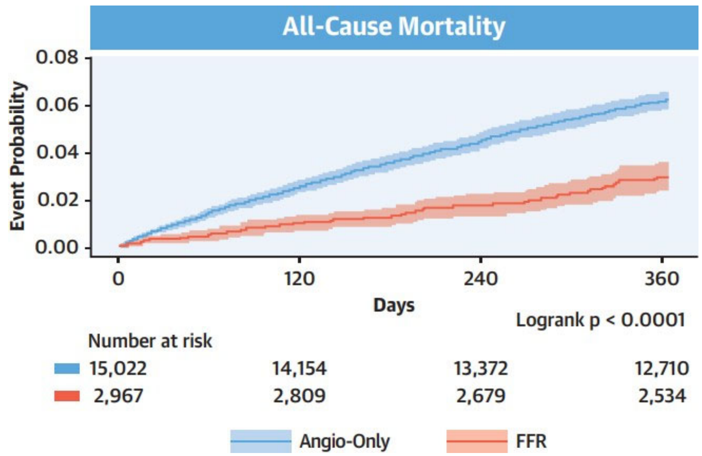
-After a median follow-up of 3 years, a reduction in the composite endpoint of cardiac death or MI was observed with FFR-guided PCI as compared with medical therapy.

-The difference between groups was driven by MI.

Zimmermann, et al. Eur Heart J 2019;40:180-186.

Real World FFR Use

Outcomes of ~18,000 stable patients undergoing PCI at 66 VA hospitals in the US were tracked based on whether or not FFR was used.→ 1-year mortality was 2.8% in the FFR group and 5.9% in the angiography-only group (p < 0.0001)

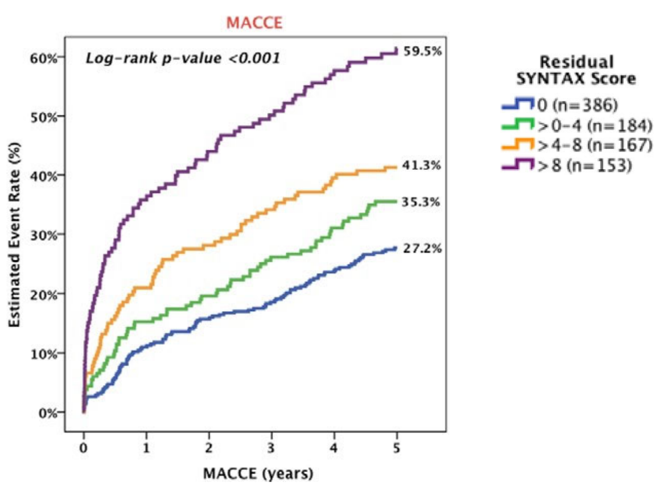


After MV adjustment, FFR-guided revascularization was associated with a 43% lower risk of mortality at 1 year compared with angiography-only revascularization (HR: 0.57; 95% CI: 0.45 to 0.71; p < 0.0001)

Parikh, R.V. et al. J Am Coll Cardiol. 2020;75(4):409-19.

RSS after Angiography - guided PCI

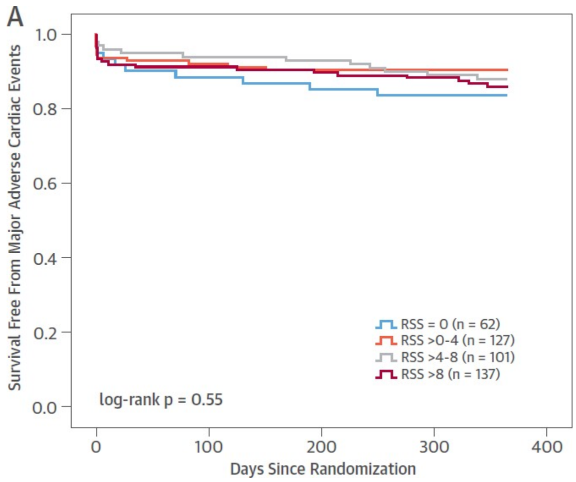
RSS was strongly correlated with outcome in the SYNTAX trial after angiography-guided PCI.



Farooq et al. Circulation 2013;128(2):141-51

Residual SYNTAX Score

Residual SYNTAX Score calculated in FFR-guided patients from FAME

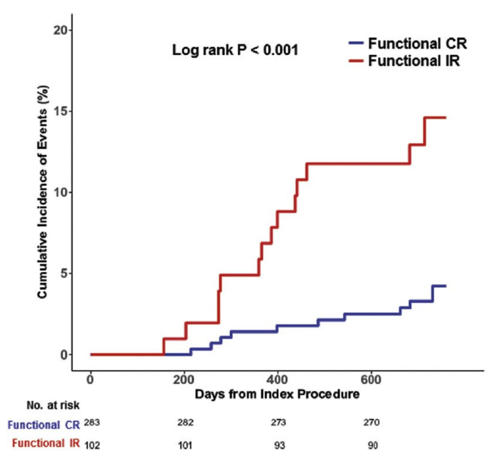


After functionally CR, the residual coronary disease does NOT predict outcomes.

Kobayashi, et al. JACC 2016;67:1701-11.

Residual Functional SYNTAX Score

385 patients underwent 3 vessel FFR and PCI. Functionally CR (residual functional SYNTAX score<1) was compared with functionally IR (rFSS≥1)

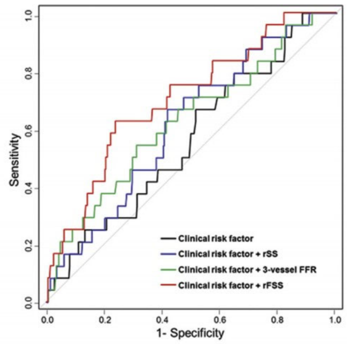


At 2-year follow-up, the functional incomplete revascularization group showed a significantly higher risk for MACEs (14.6% vs. 4.2%; HR: 4.09; 95% CI: 1.82 to 9.21; $p < 0.001$) than the functional CR group.

Choi, et al. J Am Coll Cardiol Intv 2018;11:237-45.

Residual Functional SYNTAX Score

Comparison of Predictive Models for MACEs With 3-Vessel FFR, Residual SYNTAX Score, and Residual Functional SYNTAX Score in Addition to Clinical Risk Factors



Model	Brier Score	C index	95% CI	P value	NRI (Category free)	P value	IDI	P value
Clinical risk factor*	0.0582	0.563	0.447-0.679	0.301	Reference		Reference	
Clinical risk factor + rSS	0.0578	0.618	0.509-0.728	0.053	0.336 (-0.065 - 0.737)	0.101	0.7%	0.122
Clinical risk factor + 3-vessel FFR	0.0575	0.625	0.503-0.747	0.041	0.342 (-0.049 - 0.733)	0.087	1.0%	0.047
Clinical risk factor + rFSS	0.0562	0.701	0.592-0.810	<0.001	0.679 (0.275 - 1.083)	0.001	3.5%	0.002

-The rFSS was defined as residual SYNTAX score measured only in vessels with FFR ≤ 0.8.

-When added to clinical risk factors, rFSS showed the highest integrated discrimination improvement value for MACEs (3.5%; p = 0.002) among 3-vessel FFR, residual SYNTAX score, and rFSS.

Choi, et al. J Am Coll Cardiol Intv 2018;11:237-45.

ESC Guidelines on Myocardial Revascularization

Recommendations on functional testing and intravascular imaging for lesion assessment

Recommendations	Class[a]	Level[b]
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis.[15,17,18,39]	I	A
FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI.[29,31]	IIa	B
IVUS should be considered to assess the severity of unprotected left main lesions.[35–37]	IIa	B

FJ Neumann et al: EHJ- 2019

Is the story complete?

FAME 3 Trial

All Comers with 3 V CAD
(not involving LM)

↓

Heart team identifies lesions for PCI/CABG
and then patient is randomized

FFR-Guided PCI with Resolute DES
Stent all lesions with FFR ≤ 0.80
(n=750)

Perform CABG based on
coronary angiogram
(n=750)

Primary: One Year follow-up for Death, MI, CVA, Revascularization
Key Secondary: Three Year follow-up for Death/MI/CVA
Five year follow-up for Death/MI/CVA

Non-inferior Design

Zimmermann, et al. Am H J 2015;170:619-26.
Zimmermann, et al. Am H J 2019;214:156-157.

Clinical Gold Standard – Patient Outcome Studies in Specific Subgroups

Patient Subgroup	FFR	NHPR	Key Points
Stable IHD, Low Risk	✔	✔	*Defer, Define-Flair, SwedeHeart*
STEMI / NSTEMI	✔	✘	FFR valid in non-culprit ACS vessel if <0.8
SVG Assessment	✔	✘	Physiology accurate, but biology of vein graft deterioration is critical role beyond "ischemia"
Ostial lesion, Left Main	✔	✘	IV hyperemia and caution for left main assessment and proximal LCX or LAD disease
Bypass Graft Failure	✔	✘	Early rate of bypass graft closure in non-physiologically significant vessels
Serial Lesions	?	?	iFR pullback looks promising
Aortic Stenosis & TAVR	?	?	With increasing coronary blood flow after successful AVR, decrease in FFR

Morton Kern: TCT 2019

Conclusion

- Anatomic complete revascularization is associated with improved outcomes after PCI.
- Anatomic complete revascularization with PCI compares favorably with CABG.
- Functionally complete revascularization guided by FFR may result in even better outcomes with PCI.
- We are waiting for the results of the FAME 3 trial next year.

2- Value of complete revascularization in AMI without cardiogenic shock

COMPLETE TRIAL

Background

- Patients undergoing primary PCI to the culprit lesion for STEMI are often found to have multivessel CAD, with 1 or more angiographically significant non-culprit lesions.
- There is uncertainty on how best to manage these non-culprit lesions:
  - *Routinely revascularize them with PCI?*
  - *Manage them conservatively with guideline-directed medical therapy alone?*
- Prior RCT's have shown non-culprit lesion PCI reduces revascularization but none were powered to detect moderate reductions in hard clinical outcomes such as CV death or MI.[1-4]
- Meta-analyses have suggested a possible reduction in CV death or MI, but this result is fragile and no single RCT has been adequately powered to confirm this.[5]

The COMPLETE trial was designed to address this evidence gap.

1. Wald et al. *N Engl J Med* 2013;369:1115-23.
2. Gershlick et al. *J Am Coll Cardiol* 2015;65:963-72.
3. Engstrom et al. *Lancet* 2015;386:665-71.
4. Smits et al. *N Engl J Med* 2017;376:1234-44.
5. Bainey et al. *Can J Cardiol* 2016;32:1542-51.

Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

Hamilton Health Sciences

McMaster University HEALTH SCIENCES

COMPLETE TRIAL

Prior Trials of PCI versus Med Rx in Patients with STEMI and Multivessel Disease

Trial	Same-sitting or Staged	Sample Size
Di Mario 2004	Index	69
Politi 2009	Index or staged	149
Ghani 2012	Staged (FFR guided)	119
PRAMI 2013[1]	Index	465
Cvlprit 2014[2]	Index or staged	296
DANAMI-3 2015[3]	Staged	627
PRAGUE 13	Staged	214
Explore	Staged (CTO)	300
COMPARE-ACUTE[4]	Mainly index	885

1. Wald et al. *N Engl J Med* 2013;369:1115-23.
2. Gershlick et al. *J Am Coll Cardiol* 2015;65:963-72.
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Hamilton Health Sciences McMaster University

COMPLETE TRIAL

Primary Objective

In patients presenting with STEMI and multi-vessel coronary artery disease who have undergone culprit-lesion PCI, the objective is:

To determine whether a strategy of routine, staged non-culprit lesion PCI with the goal of complete revascularization is superior to a strategy of culprit lesion-only PCI in reducing the composite of CV death or new MI.

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COMPLETE Trial Design

STEMI WITH MULTIVESSEL CAD AND SUCCESSFUL PCI TO THE CULPRIT LESION
MVD defined as at least one additional non-culprit lesion ≥ 2.5 mm diameter
and ≥70% stenosis or 50-69% with FFR ≤0.80

Exclusion Criteria: Intent to revascularize NCL, planned surgical revascularization, prior CABG

RANDOMIZATION
Stratified for intended timing of NCL PCI:
During initial hospitalization or after discharge (max 45 d)

Actual Time to study NCL PCI in Complete Group (median)
During initial hospitalization: 1 day (IQR 1-3)
After hospital discharge: 23 days (IQR 12.5-33.5)

COMPLETE REVASCULARIZATION
Routine staged PCI* of all suitable non-culprit lesions with the goal of complete revascularization
N=2016

CULPRIT-LESION-ONLY REVASCULARIZATION
No further revascularization of non-culprit lesions, guideline-directed medical therapy alone
N=2025

*Everolimus-eluting stents strongly recommended

Guideline-Directed Medical Therapy
ASA, P2Y12 inhibitor (Ticagrelor strongly recommended), Statin, BB, ACE/ARB + Risk Factor Modification

MEDIAN FOLLOW-UP: 3 YEARS

CO-PRIMARY OUTCOMES:
1. Composite of CV death or new MI
2. Composite of CV death, new MI or IDR

KEY SECONDARY OUTCOME: CV death, new MI, IDR, unstable angina, NYHA class IV heart failure

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Mehta SR et al. *Am Heart J* 2019; 215:157-166.

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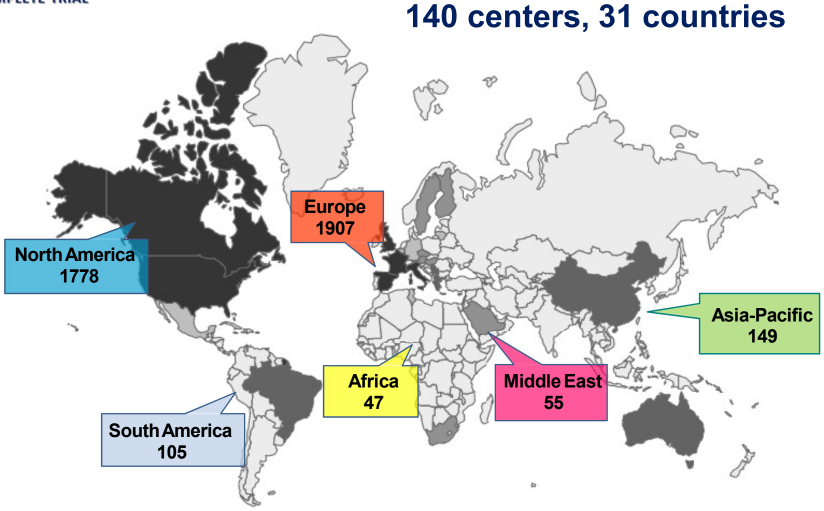
COMPLETE TRIAL

Global Recruitment

140 centers, 31 countries



Australia	Lithuania
Austria	Macedonia
Belgium	Mexico
Brazil	Poland
Canada	Portugal
China	Romania
Colombia	Saudi Arabia
Czech Republic	Serbia
Finland	South Africa
France	Spain
Germany	Sweden
Greece	Switzerland
Hungary	Tunisia
Israel	United Kingdom
Italy	USA
Kuwait	

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COMPLETE TRIAL

Study Power and Follow-up

- **Study Power:** 80% power for CVD/MI and 89% power for CVD/MI/IDR to detect a 22% HRR.

  To preserve the overall type I error rate of 5% for the testing of both co-primary outcomes, the first co-primary outcome was tested at a P value of 0.045 and the second at a P value of 0.0119*
- **Recruitment Period:** February 1, 2013 – March 6, 2017
- **Angiographic Core Lab:** Central review of all coronary angiograms in the trial
- **Analysis:** Intention-to-treat, Cox proportional hazards model, stratified by intended timing of revascularization, stratified log rank test
- **Follow-up (vital status):** 99.1% in *Complete* group and 99.3% *Culprit-Lesion-only* group
- **Crossover in first 45 days:** From *Complete Revasc* to *Culprit-Lesion-only* = 3.9%
  From *Culprit-Lesion-only* to *Complete Revasc* = 4.7%

Population Health Research Institute HEALTH THROUGH KNOWLEDGE

*Mehta SR et al. *Am Heart J* 2019; 215:157-166.

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COMPLETE TRIAL

Baseline Characteristics

	Complete N=2016	Culprit-only N=2025
Age (yrs)	61.6	62.4
Gender (% male)	80.5	79.1
Diabetes (%)	19.1	19.9
Chronic renal insuff. (%)	2.0	2.3
Prior MI (%)	7.3	7.6
Current smoker (%)	40.6	38.9
Hypertension (%)	48.7	50.7
Dyslipidemia (%)	37.9	39.4
Prior PCI (%)	7.0	7.0
Prior stroke (%)	3.2	3.1
Hemoglobin A1C	6.3	6.3
LDL (mmol/L)	3.1	3.1
Creatinine (µmol/L)	84.7	85.2

	Complete N=2016	Culprit-only N=2025
Sx onset to Culprit PCI (%)		
<6 hours	69.4	67.1
6~12 hours	16.1	17.7
>12 hours	14.5	15.3
Discharge Meds (%)		
ASA	99.8	99.5
P2Y12 Inhibitor	99.4	99.7
Ticagrelor	64.4	63.3
Prasugrel	9.6	8.3
Clopidogrel	25.6	28.2
Beta blocker	88.1	89.1
ACEi/ARB	85.5	84.6
Statin	98.2	97.2

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COMPLETE TRIAL

Procedural Characteristics

	Complete N=2016	Culprit-only N=2025
Index PCI for STEMI		
Primary	91.9%	93.1%
Pharmaco-invasive	3.2%	3.0%
Rescue	4.9%	3.9%
Radial access	80.8%	80.7%
Residual diseased vessels		
1	76.1%	77.1%
≥2	23.9%	22.9%
NCL location		
Left main	0.4%	0.1%
LAD	38.0%	41.2%
Proximal LAD	9.8%	10.4%
Mid LAD	21.7%	23.7%
Circumflex	36.4%	35.6%
RCA	25.3%	23.2%

	Complete N=2016	Culprit-only N=2025
NCL diameter	2.8 mm	2.9 mm
Mean NCL stenosis (visual)	79.3%	78.7%
NCL stenosis (visual)		
50-69% and FFR<0.80	0.8%	0.6%
70-79%	41.3%	45.1%
80-89%	33.5%	32.6%
90-99%	22.3%	19.7%
100%	2.1%	2.0%
SYNTAX score (Core Lab)		
Baseline	16.3	16.0
Culprit lesion specific	8.8	8.6
Non-culprit lesion specific	4.5	4.5
Residual (after index PCI)	7.2	7.0

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COMPLETE TRIAL

Procedural Characteristics

	Complete N=2016	Culprit-only N=2025
Index PCI for STEMI		
Primary	91.9%	93.1%
Pharmaco-i		
Rescue		
Radial acces		
Residual diseased vessels		
1	76.1%	77.1%
≥2	23.9%	22.9%
NCL location		
Left main	0.4%	0.1%
LAD	38.0%	41.2%
Proximal LAD	9.8%	10.4%
Mid LAD	21.7%	23.7%
Circumflex	36.4%	35.6%
RCA	25.3%	23.2%

Complete revascularization was achieved in 90.1% after NCL PCI (SYNTAX score = 0)

	Complete N=2016	Culprit-only N=2025
NCL diameter	2.8 mm	2.9 mm
Mean NCL stenosis (visual)	79.3%	78.7%
		0.6%
		45.1%
80-89%	33.5%	32.6%
90-99%	22.3%	19.7%
100%	2.1%	2.0%
SYNTAX score (Core Lab)		
Baseline	16.3	16.0
Culprit lesion specific	8.8	8.6
$\boxed{\text{Non-culprit lesion specific}}$	4.5	4.5
Residual (after index PCI)	7.2	7.0

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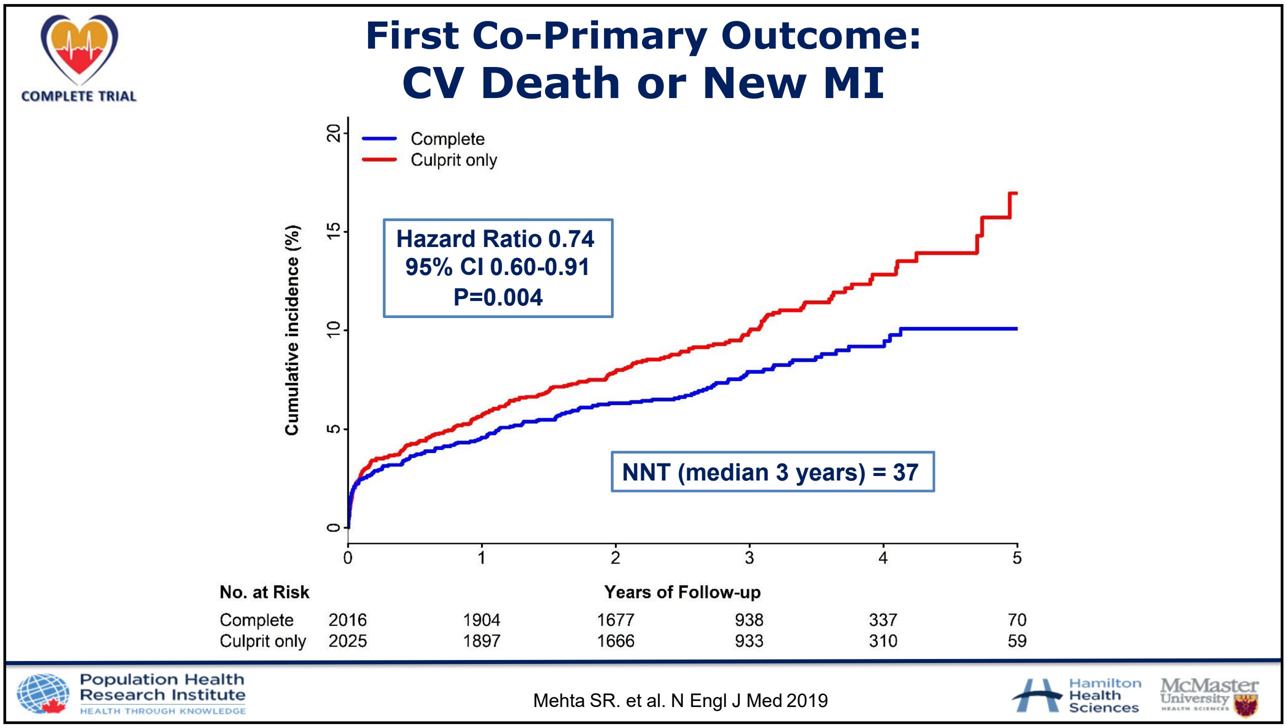
COMPLETE TRIAL
First Co-Primary Outcome:
CV Death or New MI
Complete
Culprit only
Hazard Ratio 0.74
95% CI 0.60-0.91
P=0.004
NNT (median 3 years) = 37
Cumulative incidence (%)
0
5
10
15
20
0 1 2 3 4 5
Years of Follow-up
No. at Risk
Complete 2016 1904 1677 938 337 70
Culprit only 2025 1897 1666 933 310 59
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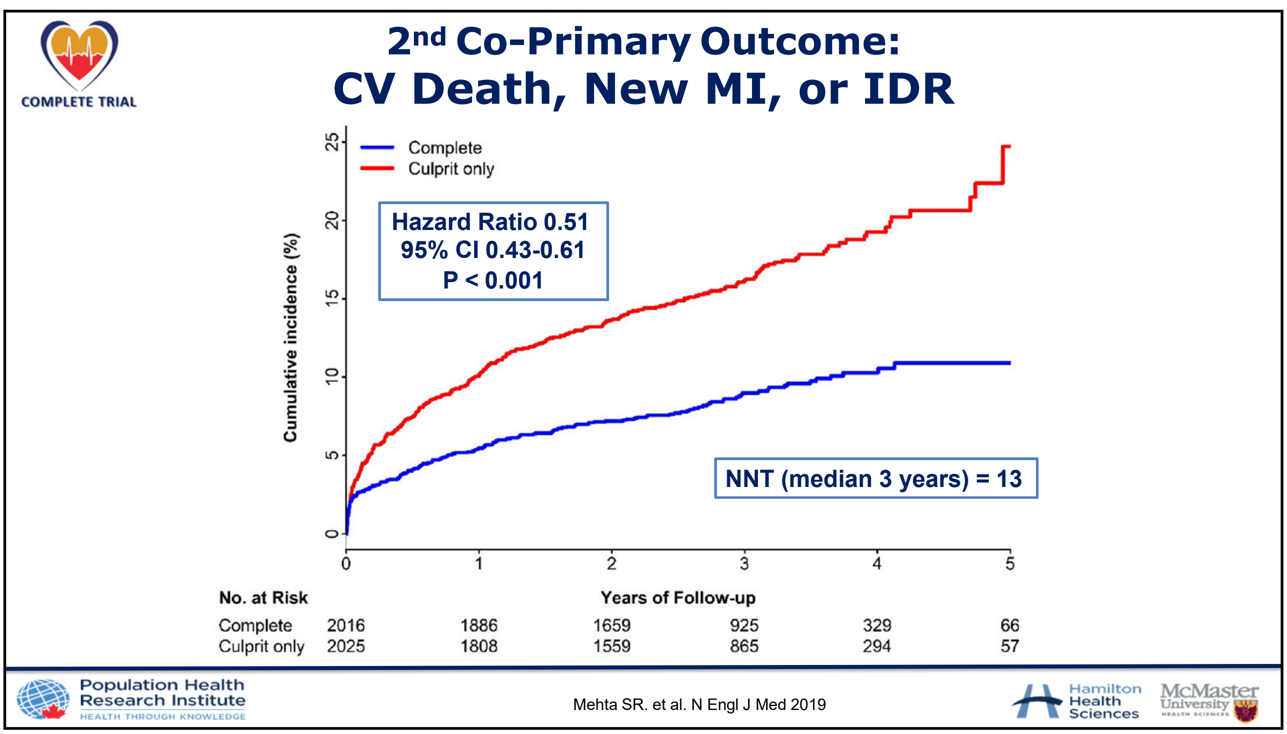
COMPLETE TRIAL
2nd Co-Primary Outcome:
CV Death, New MI, or IDR
Complete
Culprit only
Hazard Ratio 0.51
95% CI 0.43-0.61
P < 0.001
NNT (median 3 years) = 13
Cumulative incidence (%)
0
5
10
15
20
25
0 1 2 3 4 5
Years of Follow-up
No. at Risk
Complete 2016 1886 1659 925 329 66
Culprit only 2025 1808 1559 865 294 57
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COMPLETE TRIAL

Efficacy Outcomes

	Complete Revasc. N=2016		Culprit Lesion Only N=2025		HR (95% CI)	P value
	N (%)	%/year	N (%)	%/year		
Co-Primary Outcomes						
CV death or MI	**158 (7.8)**	**2.7**	**213 (10.5)**	**3.7**	**0.74 (0.60-0.91)**	**0.004**
CV death, MI or IDR	**179 (8.9)**	**3.1**	**339 (16.7)**	**6.2**	**0.51 (0.43-0.61)**	**<0.001**
Key Secondary Outcome						
CV death, MI, IDR, unstable angina or class IV HF	272 (13.5)	4.9	426 (21.0)	8.1	0.62 (0.53-0.72)	<0.001
Other Secondary Outcomes						
MI	109 (5.4)	1.9	160 (7.9)	2.8	0.68 (0.53-0.86)	0.002
IDR	29 (1.4)	0.5	160 (7.9)	2.8	0.18 (0.12-0.26)	<0.001
Unstable Angina	70 (3.5)	1.2	130 (6.4)	2.2	0.53 (0.40-0.71)	<0.001
CV death	59 (2.9)	1.0	64 (3.2)	1.0	0.93 (0.65-1.32)	0.68
All-cause Death	96 (4.8)	1.6	106 (5.2)	1.7	0.91 (0.69-1.20)	0.51

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Sub-types of MI

	Complete Revasc. N=2016		Culprit Lesion Only N=2025		HR (95% CI)
	N (%)	%/year	N (%)	%/year	
Subtype of MI					
NSTEMI	66 (3.27)	1.11	105 (5.19)	1.78	0.63 (0.46-0.85)
STEMI	43 (2.13)	0.72	53 (2.62)	0.88	0.81 (0.54-1.22)
Universal MI Definition					
Type 1	63 (3.13)	1.05	128 (6.32)	2.17	0.49 (0.36-0.66)
Type 2	16 (0.79)	0.26	13 (0.64)	0.21	1.24 (0.60-2.58)
Type 3	4 (0.20)	0.07	1 (0.05)	0.02	4.04 (0.45-36.17)
Type 4a	16 (0.79)	0.27	8 (0.40)	0.13	2.01 (0.86-4.70)
Type 4b	8 (0.40)	0.13	13 (0.64)	0.21	0.62 (0.26-1.49)
Type 5	1 (0.05)	0.02	1 (0.05)	0.02	1.00 (0.06-15.92)

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COMPLETE TRIAL

Timing of Staged Non-Culprit Revascularization

Objectives

1. To determine if there is a difference in the benefit of a strategy of complete revascularization versus culprit-lesion-only PCI according to the intended timing of non-culprit PCI
2. To examine the time course of the benefits of complete vs culprit-lesion-only PCI

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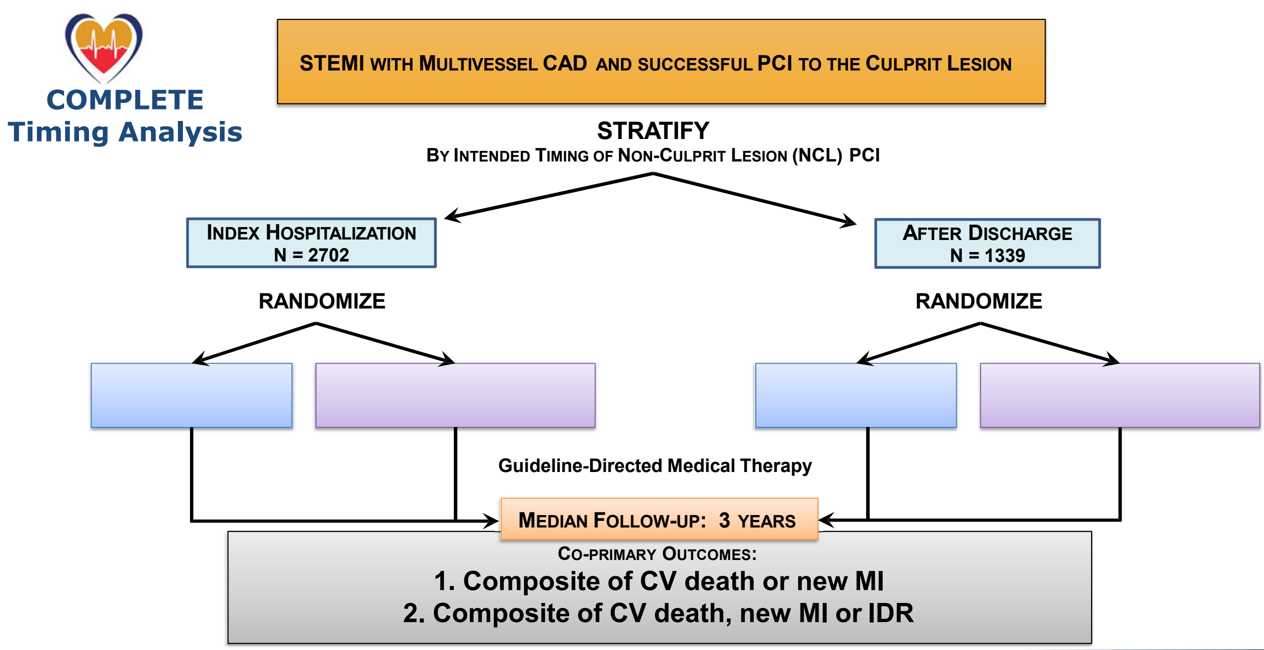

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COMPLETE TRIAL

Baseline Characteristics

Characteristic	Intended timing of complete revascularization Index hospitalization (N=2702)	After discharge (N=1339)	P value
Actual complete revascularization	1353 (50.1)	663 (49.5)	
Age – year	62.2±10.7	61.7±10.7	0.18
Gender (male)	2151 (79.6)	1074 (80.2)	0.65
Diabetes	552 (20.4)	235 (17.6)	0.03
Chronic renal insufficiency	61/2586 (2.4)	20/1201 (1.7)	0.17
Prior stroke	88 (3.3)	38 (2.8)	0.47
Body mass index (BMI) – kg/m²	28.3±5.6	28.3±5.0	0.97
Prior myocardial infarction	188 (7.0)	114 (8.5)	0.08
Prior PCI	184 (6.8)	99 (7.4)	0.49
Time from symptom onset to primary PCI			0.34
• **<6 hours**	1821/2678(68.0)	903/1316 (68.6)	
• **6-12 hours**	468/2678(17.5)	208/1316 (15.8)	
• **>12 hours**	389/2678(14.5)	205/1316 (15.6)	
Killip class ≥2	293/2674 (11.0)	137/1317 (10.4)	0.59

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COMPLETE TRIAL

Procedural Characteristics

Characteristic	Intended timing of complete revascularization Index hospitalization (N=2702)	After discharge (N=1339)	P-value
SYNTAX score			
• Baseline (including STEMI culprit)	16.1±6.8	16.4±6.6	0.12
• Residual (after index PCI)	7.1±4.8	7.2±4.8	0.48
• Lesion specific (STEMI culprit)	8.6±5.3	8.9±5.3	0.04
• Lesion specific (Non-culprit)	4.5±2.7	4.7±2.7	0.04
• Post NCL lesion PCI=0 (Complete revascularization achieved)	1095/1200 (91.3)	525/598 (87.8)	0.02
Non-culprit lesions location			
• Left main	7/3543 (0.2)	6/1812 (0.3)	0.77
• Left anterior descending	1379/3543 (38.9)	738/1812 (40.7)	0.20
• Circumflex	1293/3543 (36.5)	633/1812 (34.9)	0.26
• Right coronary artery	864/3543 (24.4)	435/1812 (24.0)	0.83
Non-culprit lesion diameter stenosis			0.12
• 50-69%	28/3468 (0.8)	9/1720 (0.5)	
• 70-79%	1435/3468 (41.4)	805/1720 (46.8)	
• 80-89%	1214/3468 (35.0)	500/1720 (29.1)	
• 90-99%	734/3468 (21.2)	357/1720 (20.8)	
• 100%	57/3468 (1.6)	49/1720 (2.8)	
Index procedure for STEMI			
• Primary PCI	2479 (91.7)	1259 (94.0)	0.01
• Pharmaco-invasive PCI	87 (3.2)	38 (2.8)	0.51
• Rescue PCI	136 (5.0)	42 (3.1)	0.006
Radial access	2143 (79.3)	1120 (83.6)	0.001
Thrombus aspiration	609/2573 (23.7)	323/1166 (27.7)	0.008

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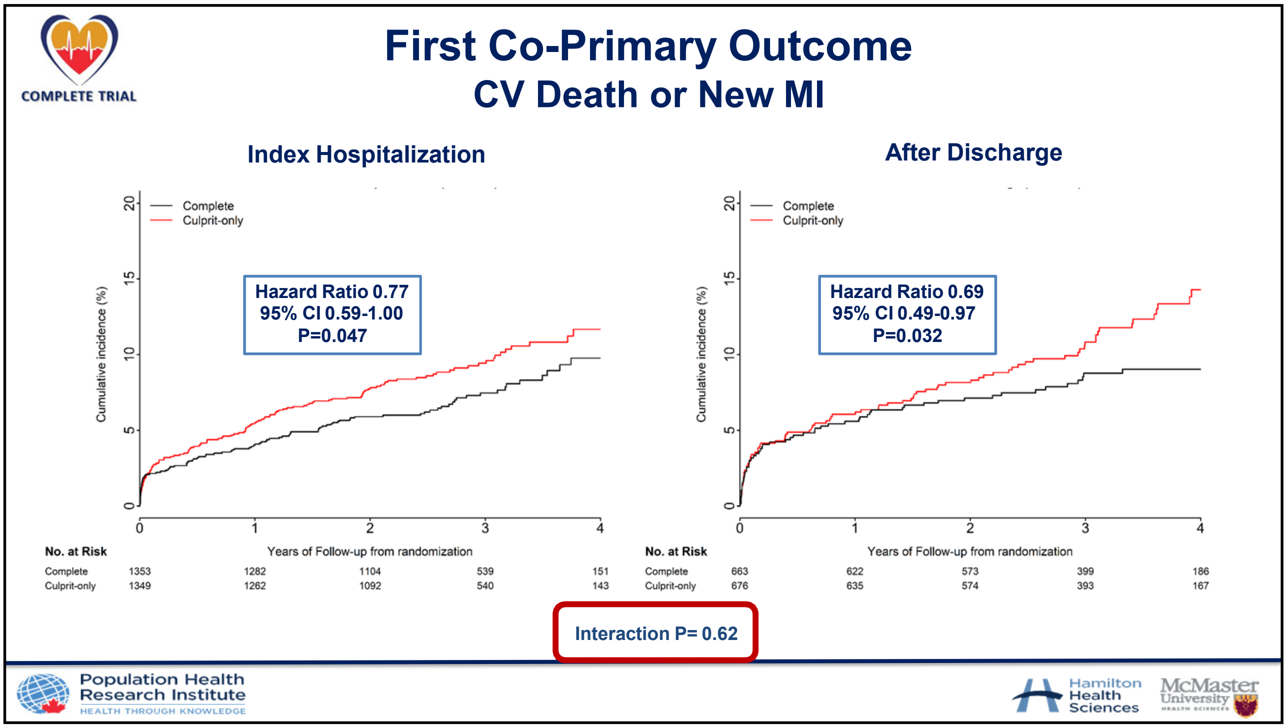
COMPLETE TRIAL
First Co-Primary Outcome
CV Death or New MI
Index Hospitalization
After Discharge
Complete
Culprit-only
Cumulative incidence (%)
Hazard Ratio 0.77
95% CI 0.59-1.00
P=0.047
Hazard Ratio 0.69
95% CI 0.49-0.97
P=0.032
Years of Follow-up from randomization
No. at Risk
Complete 1353 1282 1104 539 151
Culprit-only 1349 1262 1092 540 143
Complete 663 622 573 399 186
Culprit-only 676 635 574 393 167
Interaction P= 0.62
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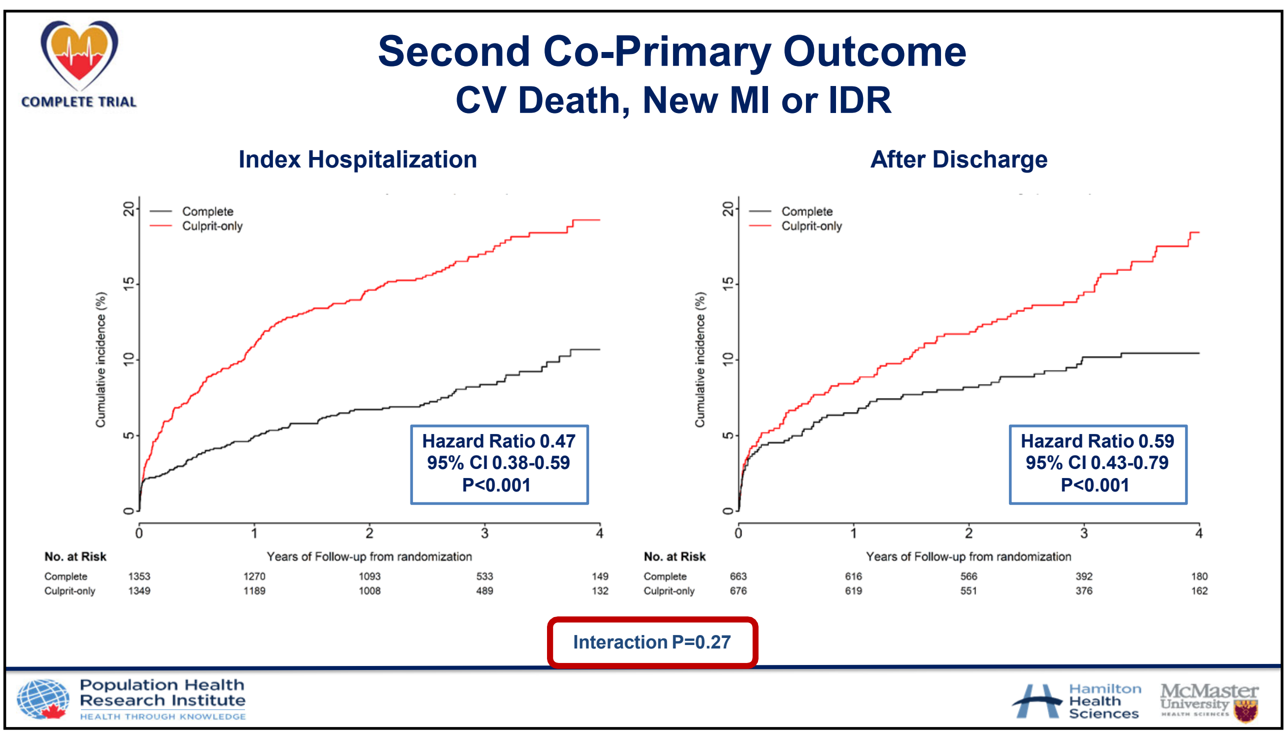
COMPLETE TRIAL
Second Co-Primary Outcome
CV Death, New MI or IDR
Index Hospitalization
After Discharge
Complete
Culprit-only
Cumulative incidence (%)
Hazard Ratio 0.47
95% CI 0.38-0.59
P<0.001
Hazard Ratio 0.59
95% CI 0.43-0.79
P<0.001
Years of Follow-up from randomization
No. at Risk
Complete 1353 1270 1093 533 149
Culprit-only 1349 1189 1008 489 132
Complete 663 616 566 392 180
Culprit-only 676 619 551 376 162
Interaction P=0.27
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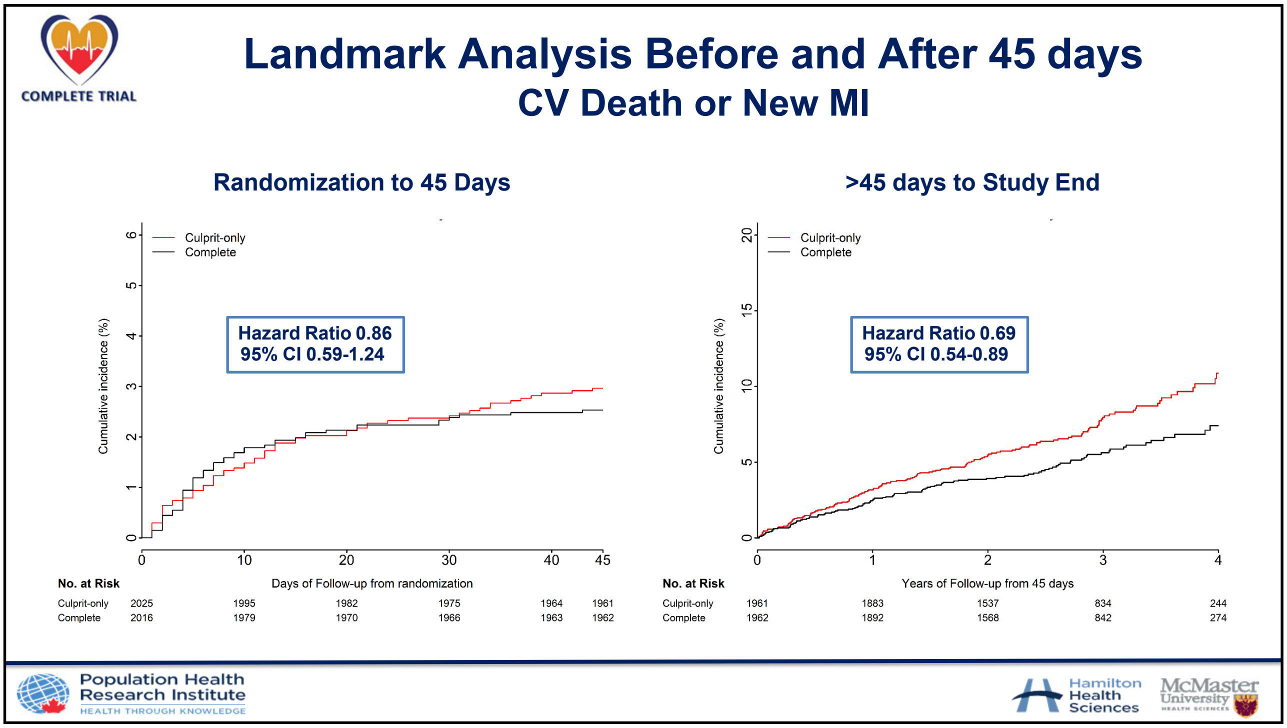
COMPLETE TRIAL
Landmark Analysis Before and After 45 days
CV Death or New MI
Randomization to 45 Days
>45 days to Study End
Culprit-only
Complete
Hazard Ratio 0.86
95% CI 0.59-1.24
Hazard Ratio 0.69
95% CI 0.54-0.89
Cumulative incidence (%)
Days of Follow-up from randomization
Years of Follow-up from 45 days
No. at Risk
Culprit-only 2025 1995 1982 1975 1964 1961
Complete 2016 1979 1970 1966 1963 1962
Culprit-only 1961 1883 1537 834 244
Complete 1962 1892 1568 842 274
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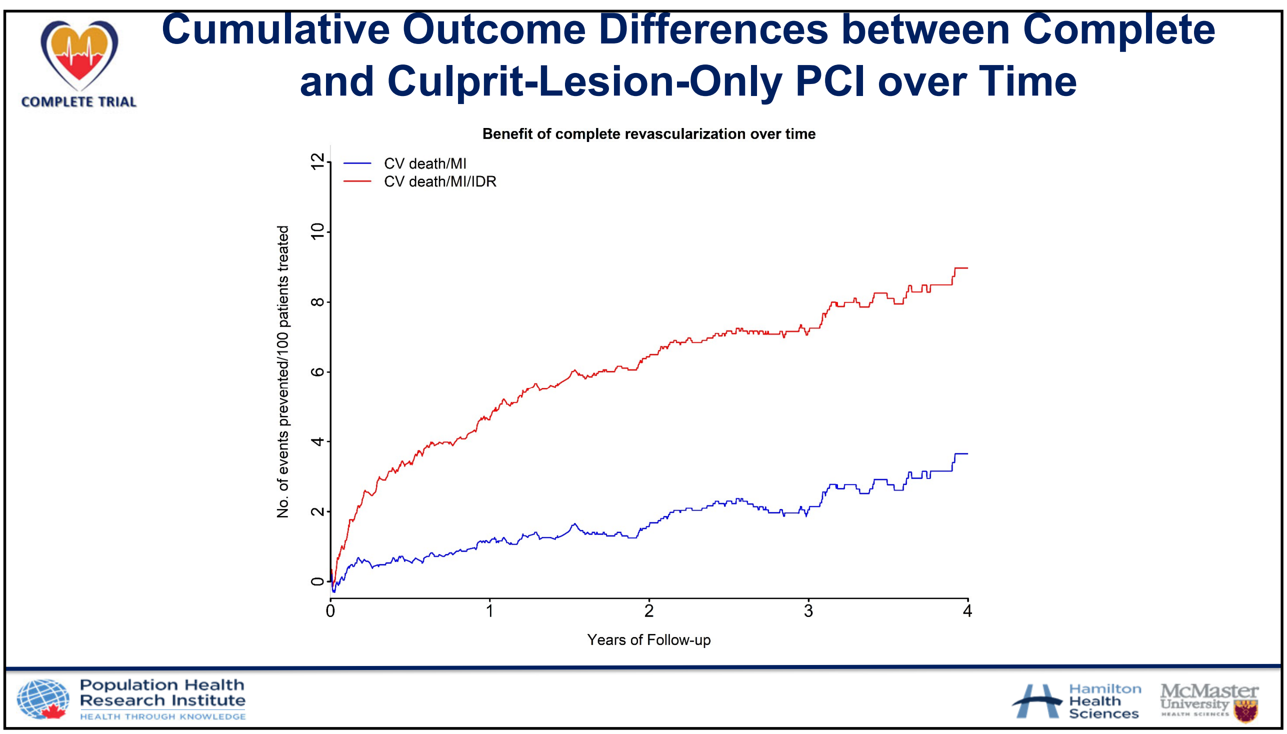
COMPLETE TRIAL
Cumulative Outcome Differences between Complete and Culprit-Lesion-Only PCI over Time
Benefit of complete revascularization over time
CV death/MI
CV death/MI/IDR
No. of events prevented/100 patients treated
Years of Follow-up
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Conclusions

In patients with STEMI and multi-vessel coronary artery disease:

- Compared with culprit-lesion-only PCI, routine non-culprit lesion PCI with the goal of **complete revascularization (residual syntax score =0)**:
  - **Reduced CV death or new MI by 26%** (P=0.004), NNT = 37
  - **Reduced CV death, new MI or IDR by 49%** (P<0.001), NNT = 13
- The benefit of complete revascularization was **similar** in those undergoing non-culprit lesion PCI during the index hospitalization (median 1 day) and several weeks after hospital discharge (median 3 weeks)
- The **benefit** of complete revascularization on hard outcomes (CV death or MI) **emerges** mainly over the **long term** (>45 days).
- There were **NO** significant differences in bleeding, stent thrombosis, AKI or stroke

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3- Value of complete revascularization in AMI with cardiogenic shock

HERZZENTRUM LEIPZIG | UNIVERSITÄT LEIPZIG | Leipzig Heart Institute LHI

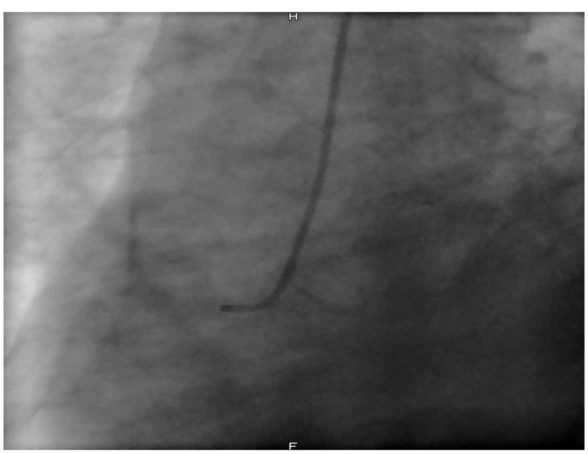
Infarct Artery PCI Only: CULPRIT-SHOCK Provides the Answer!

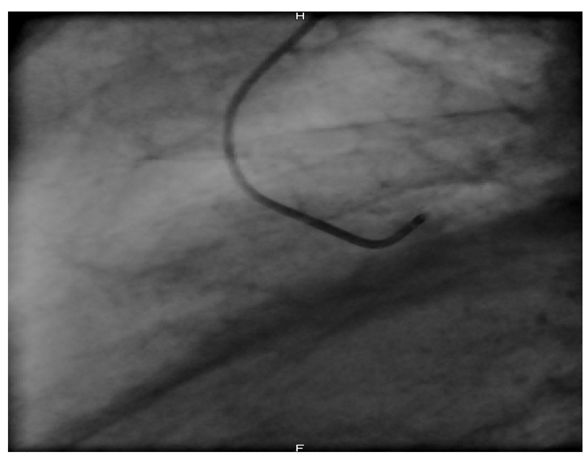
Holger Thiele, MD

Heart Center Leipzig – University of Leipzig

tct2019 | Cardiovascular Research Foundation®

Anterior STEMI + Cardiogenic Shock





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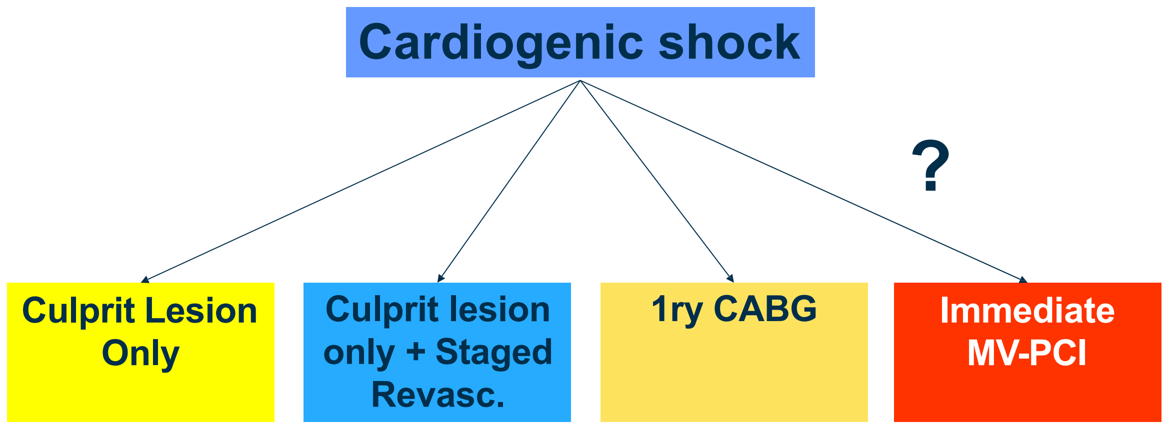
Revascularization Options



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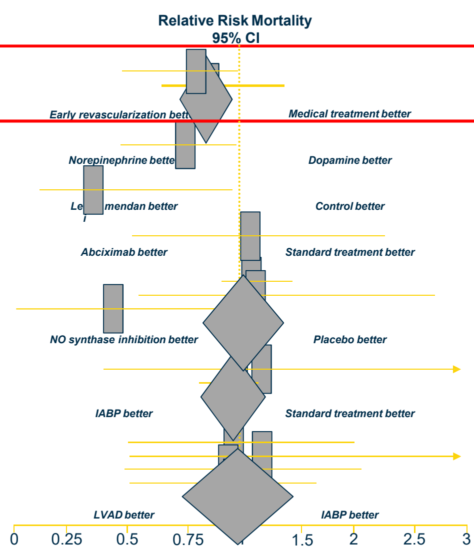
Randomized Trials Cardiogenic Shock

Trial	Follow-up	n/N	n/N	Relative Risk 95% CI
Revascularization				
SHOCK	1 year	81/152	100/150	0.72 (0.54;0.95)
SMASH	30 days	22/32	18/23	0.87 (0.66;1.29)
Total		***103/184***	***118/173***	***0.82 (0.69;0.97)***
Vasopressors				
SOAP-2 (CS subgroup)	28 days	64/145	50/135	0.75 (0.55;0.93)
Inotropes				
Unverzagt et al.	30 days	5/16	10/16	0.33 (0.11;0.97)
Glycoprotein IIb/IIIa inhibitors				
PRAGUE-18	In-hospital	15/40	13/40	1.15 (0.59;2.27)
NO synthase inhibitors				
TRIUMPH	30 days	97/201	76/180	1.14 (0.91;1.45)
SHOCK II	30 days	24/59	7/20	1.16 (0.59;2.69)
Cotter et al.	30 days	4/15	10/15	0.40 (0.13;1.05)
Total		***125/275***	***93/215***	***1.05 (0.85;1.29)***
IABP				
IABP-SHOCK I	30 days	7/19	6/21	1.28 (0.45;3.72)
IABP-SHOCK II	30 days	119/300	123/298	0.96 (0.79;1.17)
Total		***126/319***	***129/319***	***0.98 (0.81;1.18)***
LVAD				
Thiele et al.	30 days	9/21	9/20	0.95 (0.48;1.90)
Burkhoff et al.	30 days	9/19	5/14	1.33 (0.57;3.10)
ISAR-SHOCK	30 days	6/13	6/13	1.00 (0.44;2.29)
IMPRESS in Severe Shock	30 days	11/24	12/24	0.92 (0.51;1.66)
Total		***35/77***	***32/71***	***1.01 (0.70;1.44)***



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Thiele et al. Eur Heart J 2015;36:1223-1230

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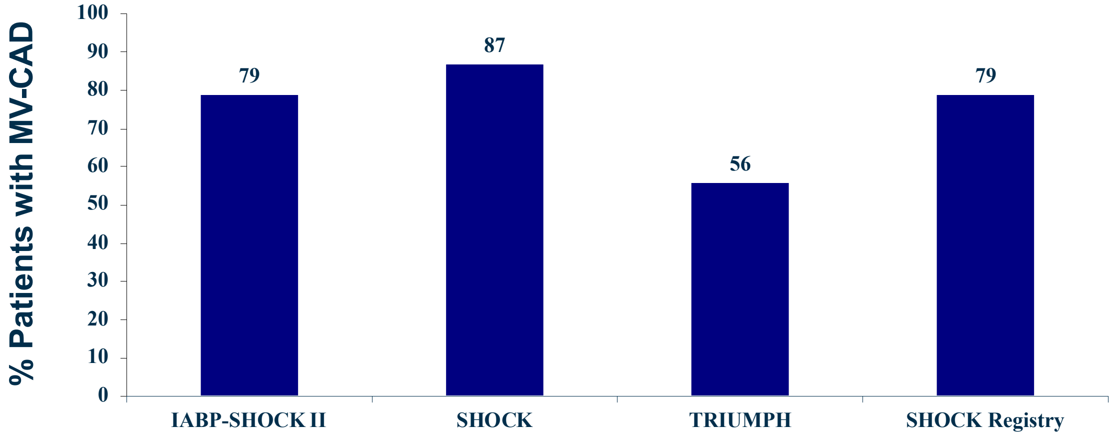
Incidence Multivessel CAD – Cardiogenic Shock



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Multivessel PCI in Cardiogenic Shock European and American Recommendations 2017

Guidelines

ESC

I IIa IIb III

C

ACC/AHA/SCAI

American Heart Association

No recommendation

Appropriate Use Criteria

ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS

American Heart Association

A (9)

Ibanez et al. Eur Heart J 2018;39:119-177
Levine et al. J Am Coll Cardiol 2016;67:1235-1250
Patel et al. J Am Coll Cardiol 2017;69:570-591

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Multivessel PCI in Cardiogenic Shock

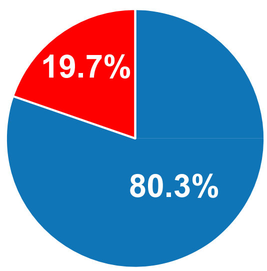
Metaanalysis Mortality – Registry-Data:

10 observational studies published between 2003 and 2016

↓

6,051 patients:

IABP-SHOCK II, ALKK, KAMIR, Yang et al., Cavender et al.; Mylotte et al., van der Schaaf et al., EHS-PCI, NCDR, SHOCK



Culprit only-PCI (n=4,857)

Multivessel-PCI (n=1,194)

tct2019 de Waha et al. Eur Heart J Acute Cardiovasc Care. 2017; epub Cardiovascular® Research Foundation

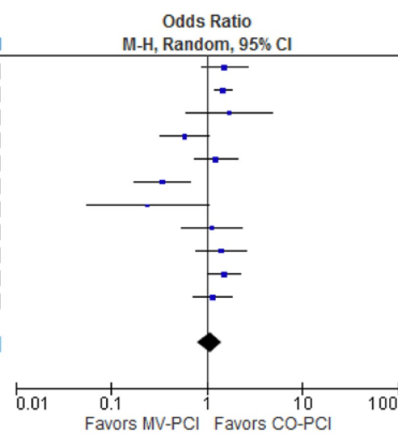
2017 meta-analysis (11 studies): short-term Mortality

NO significant difference in short-term mortality with MV-PCI versus CV-PCI (OR: 1.08; 95% CI, 0.81–1.43; P = 0.61).

Study or Subgroup	MV-PCI Events	MV-PCI Total	CO-PCI Events	CO-PCI Total	Weight	Odds Ratio M-H, Random, 95% CI
Bauer et al. 2012	31	64	81	214	9.7%	1.54 [0.88, 2.71]
Cavender et al. 2009	158	433	737	2654	14.3%	1.49 [1.21, 1.85]
Cavender et al. 2013	14	32	10	32	5.2%	1.71 [0.62, 4.76]
Hambraeus et al. 2016	19	67	106	263	9.4%	0.59 [0.33, 1.05]
Jaguszewski et al. 2013	38	85	62	158	10.1%	1.25 [0.73, 2.13]
Mylotte et al. 2013	36	66	80	103	8.4%	0.34 [0.18, 0.67]
Park et al. 2015	2	83	22	236	3.1%	0.24 [0.06, 1.04]
van der Schaaf et al. 2010	19	37	60	124	7.7%	1.13 [0.54, 2.35]
Yang et al. 2014	19	60	68	278	9.1%	1.43 [0.78, 2.63]
Zeymer et al. 2015	57	121	160	434	11.9%	1.53 [1.02, 2.29]
Zeymer et al. 2016	53	109	89	197	11.0%	1.15 [0.72, 1.84]
Total (95% CI)		**1157**		**4693**	**100.0%**	**1.08 [0.81, 1.43]**
Total events	446		1475			

Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 30.41$, df = 10 (P = 0.0007); $I^2 = 67\%$

Test for overall effect: Z = 0.51 (P = 0.61)

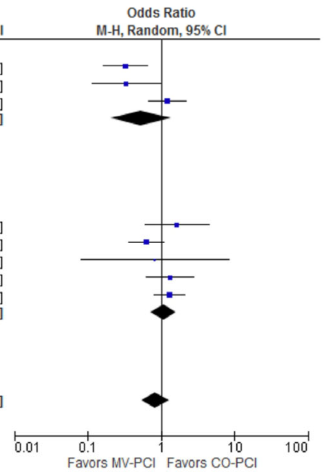


Kolte et al. Circ Cardiovasc Interv. 2017

2017 meta-analysis: long-term Mortality

NO significant difference in long-term mortality with MV-PCI versus CV-PCI (OR: 0.84; 95% CI, 0.54–1.30; P = 0.43).

Study or Subgroup	MV-PCI Events	MV-PCI Total	CO-PCI Events	CO-PCI Total	Weight	Odds Ratio M-H, Random, 95% CI
6-Months Follow-Up						
Mylotte et al. 2013	37	66	82	103	14.3%	0.33 [0.17, 0.65]
Park et al. 2015	4	83	31	236	9.5%	0.33 [0.11, 0.98]
Yang et al. 2014	21	60	85	278	15.7%	1.22 [0.68, 2.20]
Subtotal (95% CI)		**209**		**617**	**39.5%**	**0.54 [0.20, 1.40]**
Total events	62		198			
Heterogeneity: Tau² = 0.57; Chi² = 9.78, df = 2 (P = 0.008); I² = 80%						
Test for overall effect: Z = 1.27 (P = 0.20)						
12-Months Follow-Up						
Cavender et al. 2013	19	32	15	32	10.4%	1.66 [0.62, 4.46]
Hambraeus et al. 2016	24	67	124	263	16.2%	0.63 [0.36, 1.09]
Jeger et al. 2014	1	20	3	50	3.1%	0.82 [0.08, 8.43]
van der Schaaf et al. 2010	22	37	65	124	13.4%	1.33 [0.63, 2.80]
Zeymer et al. 2016	63	108	102	197	17.4%	1.30 [0.81, 2.09]
Subtotal (95% CI)		**264**		**666**	**60.5%**	**1.07 [0.73, 1.57]**
Total events	129		309			
Heterogeneity: Tau² = 0.05; Chi² = 5.39, df = 4 (P = 0.25); I² = 26%						
Test for overall effect: Z = 0.36 (P = 0.72)						
Total (95% CI)		**473**		**1283**	**100.0%**	**0.84 [0.54, 1.30]**
Total events	191		507			
Heterogeneity: Tau² = 0.23; Chi² = 19.29, df = 7 (P = 0.007); I² = 64%						
Test for overall effect: Z = 0.79 (P = 0.43)						
Test for subgroup differences: Chi² = 1.73, df = 1 (P = 0.19), I² = 42.2%						



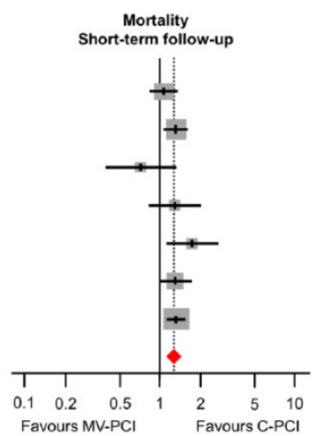
Kolte et al. Circ Cardiovasc Interv. 2017

Meta-analysis short-term Mortality – Registry-Data

Short-term mortality was **37.5%** in patients undergoing MV-PCI compared with **28.8%** in CV-PCI patients (risk ratio 1.26, 95% confidence interval 1.12–1.41, *p*=0.001).

	MV-PCI Events	MV-PCI Total	C-PCI Events	C-PCI Total	RR	95%CI	Weight
IABP-SHOCK II	75	167	119	284	1.07	[0.86-1.33]	18.5%
ALKK	81	173	201	562	1.31	[1.08-1.33]	21.1%
KAMIR	13	124	56	386	0.72	[0.41-1.28]	3.9%
Yang et al.	19	60	68	278	1.29	[0.85-1.98]	6.6%
Cavender et al.	20	43	42	156	1.73	[1.14-2.61]	7.0%
EHS-PCI	40	82	95	254	1.30	[0.99-1.71]	13.5%
NCDR	158	433	737	2654	1.31	[1.14-1.51]	29.3%
Overall	**406**	**1082**	**1318**	**4574**	**1.26**	**[1.12-1.41]**	**100%**

Heterogeneity: τ²=0.007, I²=31.0%, p=0.19
Test for overall effect: p=0.001



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de Waha et al. Eur Heart J Acute Cardiovasc Care. 2018;7:28-37

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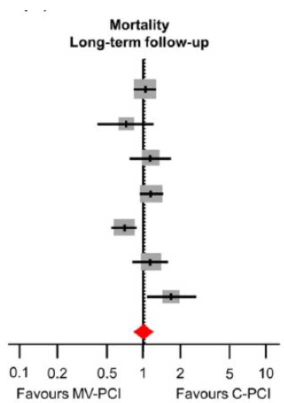
Meta-analysis long-term Mortality – Registry-Data

Long-term mortality did NOT differ significantly between the two revascularization groups.

	MV-PCI		C-PCI		RR	95%CI	Weight
	Events	Total	Events	Total			
IABP-SHOCK II	91	167	149	284	1.04	[0.87-1.24]	19.3%
KAMIR	16	124	69	386	0.72	[0.43-1.19]	9.0%
Yang et al.	21	60	85	278	1.14	[0.78-1.69]	12.0%
Cavender et al.	32	43	101	156	1.15	[0.93-1.42]	18.1%
Mylotte et al.	37	66	82	103	0.70	[0.56-0.89]	17.2%
van der Schaaf et al.	22	37	66	124	1.12	[0.82-1.53]	14.3%
SHOCK	7	9	26	57	1.71	[1.09-2.67]	10.3%
Overall	**226**	**506**	**578**	**1387**	**1.03**	**[0.85-1.25]**	**100%**

Heterogeneity: $\tau^2=0.043$, $I^2=67.8\%$, $p=0.005$
Test for overall effect: $p=0.77$



tct2019 de Waha et al. Eur Heart J Acute Cardiovasc Care. 2018;7:28-37 Cardiovascular® Research Foundation

Hypothesis

Culprit lesion only PCI (with possible staged revascularization)

is superior to immediate multivessel PCI in multivessel coronary artery disease patients with cardiogenic shock complicating acute myocardial infarction.

tct2019 Thiele et al. Am Heart J. 2016;172:160-169 Cardiovascular® Research Foundation

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HERZZENTRUM

Statistical Methodology

CULPRIT-SHOCK

Primary Study Endpoint:
- 30-day all-cause mortality or renal replacement therapy

Secondary Study Endpoints:
- 30-day all-cause mortality
- Renal failure with requirement of renal replacement therapy
- Time to hemodynamic stabilization
- Duration of catecholamine therapy
- Serial creatinine-clearance
- Length of ICU-stay
- SAPS-II score
- Requirement and length of mechanical ventilation
- All-cause death within 6 and 12 months follow-up
- Recurrent infarction within 30-days, 6 and 12 months follow-up
- Death or recurrent infarction at 6 and 12 months follow-up
- Rehospitalization for congestive heart failure within 30 days, 6-, and 12-months follow-up
- Death/recurrent infarction/rehospitalization for congestive heart failure within 30 days, 6-, and 12-months follow-up
- Need for repeat revascularization (PCI and/or CABG) within 30 days, 6-, and 12-months follow-up
- Peak creatine kinase, creatine kinase-MB and troponin level during hospital stay

Sample Size:
- Estimated 50% event rate in multivessel PCI versus 38% in culprit lesion only group for primary endpoint
- 1 interim analysis (50% of patients)
- 2-sided test Chi²-test; power: 80%, alpha=0.048 for final analysis → 684 patients
- To compensate losses in follow-up → 706 patients

tct2017 Thiele et al. Am Heart J. 2016;172:160-169 Cardiovascular Research Foundation

CULPRIT-SHOCK Trial

Investigator-initiated European multicenter trial; 1:1 randomization

PI + Coordination:
Holger Thiele
Co-PI:
Uwe Zeymer
Steffen Desch

National Coordinators (83 centers):
- Kurt Huber
- Gilles Montalescot
- Jan Piek
- Holger Thiele
- Pranas Serpytis
- Janina Stepinska
- Christiaan Vrints
- Marko Noc
- Keith Oldroyd
- Stefan Windecker
- Stefano Savonitto

tct2019 Thiele et al. Am Heart J. 2016;172:160-169 Cardiovascular® Research Foundation

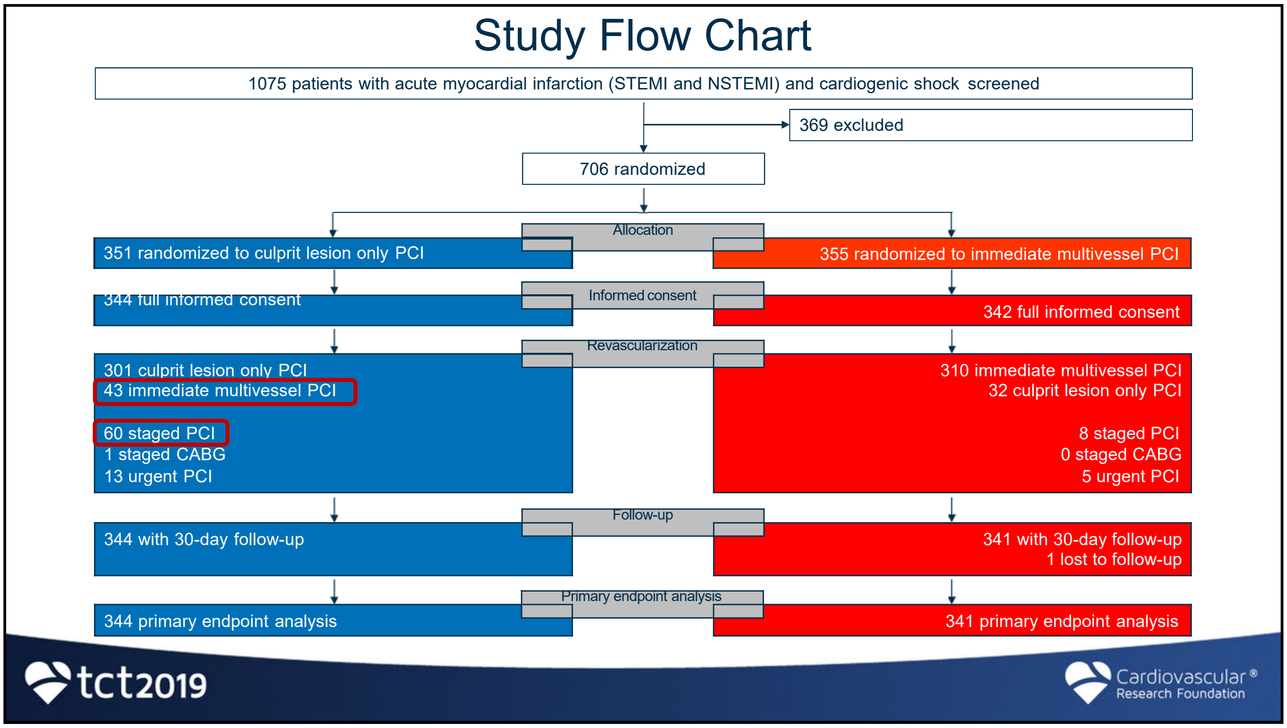

Table S1 – Individual Case Reports of Cross-overs from Culprit-Only PCI to Immediate Multivessel PCI

Center No.	Case No.	Value
4830	10	initially thrombotic occlusion ostial LAD, after PCI thrombus in LCX and occlusion of LCX, patient with progression of hemodynamic deterioration
4113	2	PCI LAD (culprit lesion) failed, so PCI RCA instead to improve the condition.
4830	95	Physician decision, not based on hemodynamic situation
9843	1	massive cardiogenic shock significant stenosis also in proximal LAD and mid LCX => possibly no benefit of staged revascularization
7792	7	After stenting of ostial LAD plaque shift to LCX, after that PCI with DEB in LCX
9640	3	bifurcation lesion
2311	11	Initially operator believed the segment 12 belongs to the LAD and performed additional stenting. Finally the segment 12 should be classified as a part of LCX. The stenosis of the main branch of LCX and the RCA were not treated.
3920	6	Initially, despite multiple attempts the culprit lesion (RCA) could not be recanalized by multiple guide wires. The acute thrombotic occlusion was located directly proximal to a high-grade calcified stenosis. Therefore, as ultima ratio the additional LCX stenosis was intervened because based on ECG this stenosis may also have contributed to acute ischemia. In second attempt RCA was successfully recanalized and stented.
3920	8	After PCI of culprit lesion in LCX there is a new significant lesion in left main which requires PCI to LAD. After left main PCI no-reflow in LAD with subsequent PCI of LAD. Additional stenoses remain in RCA, distal LAD und obtuse marginal.
6912	5	Otherwise stent-placement (culprit lesion) in non-diseased vessel would not have been feasible
5603	2	There was a stenosis extending from left main to LCX after PCI, that's why both stenoses were stented.
3873	8	A second presumably also acute occlusion was noticed after PCI of culprit lesion: RDP. This lesion was therefore threated in the same PCI setting. Other lesions were left untreated.
7553	2	By implantation stent in LAD there was a plaque shift in LCX -> Culotte stenting in main stem and LCX was absolute necessary
7553	5	Persistent hemodynamic instability despite high catecholamine doses with indication for Impella implantation
4145	13	diffuse coronary atherosclerosis, the proximal culprit lesion continues to segment 2
7553	17	severe left main stem stenosis
6912	7	Progressive stenosis of ostial LCX after PCI of culprit lesion
5603	7	The PCI was done on the extension of culprit lesion.
2311	15	Live saving step to achieve better perfusion under ECLS therapy
7553	23	hemodynamically relevant main stem stenosis
5233	6	Bifurcation of the circumflex artery and the left descending artery
6767	10	operator preference

43 patients crossed over from culprit-lesion only PCI to MV PCI (for reasons including lack of hemodynamic improvement, discovery of new lesions after initial PCI, and plaque shifts), potentially leading to bias toward including more complex and comorbid patients in the MV PCI group. This may lead to overestimation of the benefit of culprit-lesion only PCI.

Baseline Characteristics

Characteristic	Culprit only PCI (n=344)	Multivessel PCI (n=342)
Age (years); median (IQR)	70 (60-78)	70 (60-77)
Male sex; n/total (%)	257/343 (74.9)	267/342 (78.1)
Prior myocardial infarction; n/total (%)	60/339 (17.7)	53/335 (15.8)
Prior PCI; n/total (%)	64/339 (18.9)	63/335 (18.8)
Prior coronary arterial bypass surgery; n/total (%)	20/341 (5.9)	13/337 (3.9)
Signs of impaired organ perfusion; n/total (%)		
Altered mental status	237/341 (69.5)	224/341 (65.7)
Cold, clammy skin and extremities	233/338 (68.9)	236/335 (70.4)
Oliguria	80/334 (24.0)	93/326 (28.5)
Arterial lactate >2.0 mmol/l	216/334 (64.7)	224/330 (67.9)
Fibrinolysis <24 h before randomization; n/total (%)	19/341 (5.6)	15/341 (4.4)
Resuscitation before randomization; n/total (%)	177/341 (51.9)	189/342 (55.3)
ST-elevation myocardial infarction; n/total (%)	206/335 (61.5)	209/330 (63.3)
No. of diseased vessels; n/total (%)		
1	3/343 (0.9)	2/342 (0.6)
2	122/343 (35.6)	124/342 (36.3)
3	218/343 (63.6)	216/342 (63.2)
Patients with at least one CTO; n/total (%)	77/344 (22.4)	82/342 (24.0)
Left ventricular ejection fraction (%); median (IQR)	33 (25-40)	30 (21-40)

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Treatment

Characteristic	Culprit only PCI (n=344)	Multivessel PCI (n=342)	
Femoral access; n/total (%)	287/343 (83.7)	277/342 (81.0)	0.36
Radial access; n/total (%)	61/343 (17.8)	66/342 (19.3)	0.61
Stent implanted in culprit lesion; n/total (%)	326/343 (95.0)	324/342 (94.7)	0.86
Drug-eluting stent in culprit lesion; n/total (%)	305/326 (93.6)	308/324 (95.1)	0.41
TIMI-flow III post PCI of culprit lesion; n/total (%)	289/342 (84.5)	293/338 (86.7)	0.46
Immediate PCI of non-culprit lesions; n/total (%)	43/344 (12.5)	310/342 (90.6)	<0.001
Immediate complete revascularization; n/total (%)	26/344 (7.6)	277/342 (81.2)	<0.001
Total amount of contrast agent (ml); median (IQR)	190 (140-250)	250 (200-350)	<0.001
Staged PCI of non-culprit lesions; n/total (%)	60/344 (17.4)	8/341 (2.3)	<0.001
Staged coronary artery bypass surgery; n/total (%)	1/344 (0.3)	0/341	>0.99
Mechanical circulatory support; n/total (%)	99/344 (28.8)	95/342 (27.8)	0.77
Intraaortic balloon pump; n/total (%)	25/99 (25.3)	26/95 (27.4)	0.74
Impella 2.5; n/total (%)	16/99 (16.2)	18/95 (18.9)	0.61
Impella CP; n/total (%)	30/99 (30.3)	18/95 (18.9)	0.07
TandemHeart; n/total (%)	2/99 (2.0)	0/95	0.50
ECMO; n/total (%)	18/99 (18.2)	27/95 (28.4)	0.09
Mild hypothermia; n/total (%)	111/344 (32.3)	118/340 (34.7)	0.50
Mechanical ventilation; n/total (%)	273/344 (79.4)	282/339 (83.2)	0.20
Duration of mechanical ventilation (days); median (IQR)	3 (1-7)	3 (1-7)	0.97
Duration of intensive care treatment (days); median (IQR)	5 (2-12)	5 (2-11)	0.61

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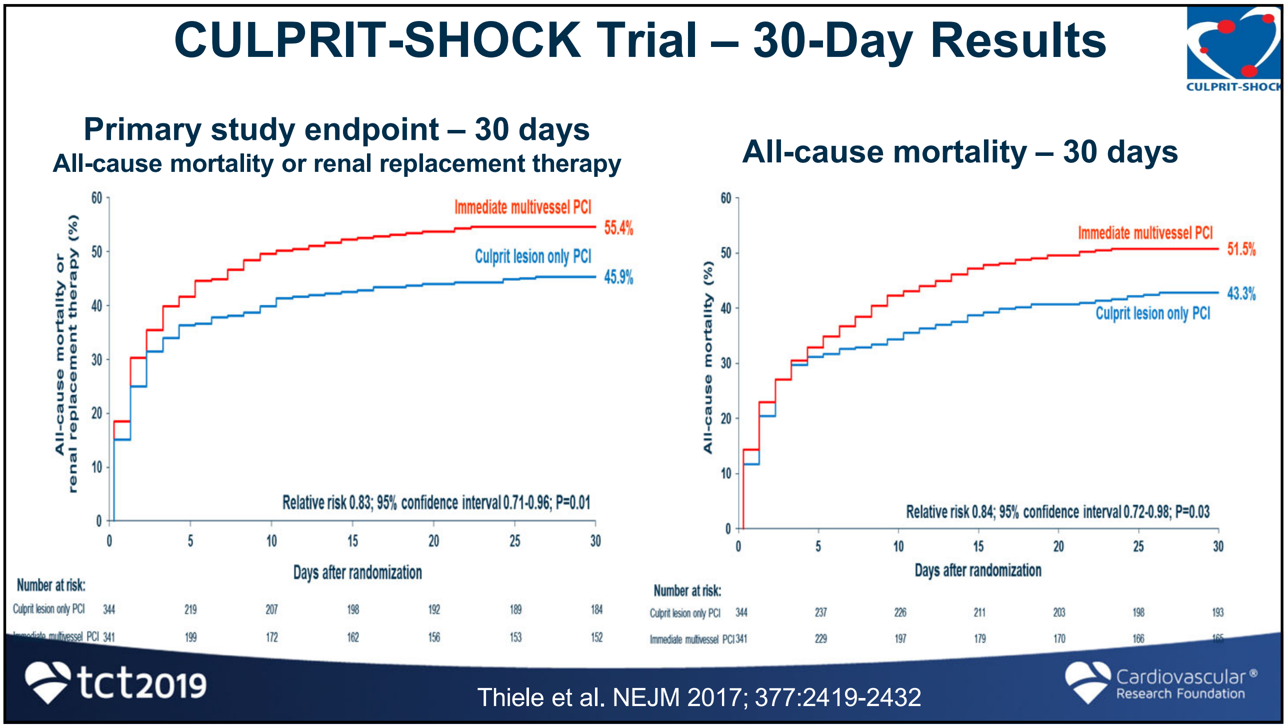
CULPRIT-SHOCK Trial – 30-Day Results
CULPRIT-SHOCK
Primary study endpoint – 30 days
All-cause mortality or renal replacement therapy
All-cause mortality or renal replacement therapy (%)
Immediate multivessel PCI
55.4%
Culprit lesion only PCI
45.9%
Relative risk 0.83; 95% confidence interval 0.71-0.96; P=0.01
Days after randomization
Number at risk:
Culprit lesion only PCI 344 219 207 198 192 189 184
Immediate multivessel PCI 341 199 172 162 156 153 152
All-cause mortality – 30 days
All-cause mortality (%)
Immediate multivessel PCI
51.5%
43.3%
Culprit lesion only PCI
Relative risk 0.84; 95% confidence interval 0.72-0.98; P=0.03
Days after randomization
Number at risk:
Culprit lesion only PCI 344 237 226 211 203 198 193
Immediate multivessel PCI 341 229 197 179 170 166 165
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Thiele et al. NEJM 2017; 377:2419-2432
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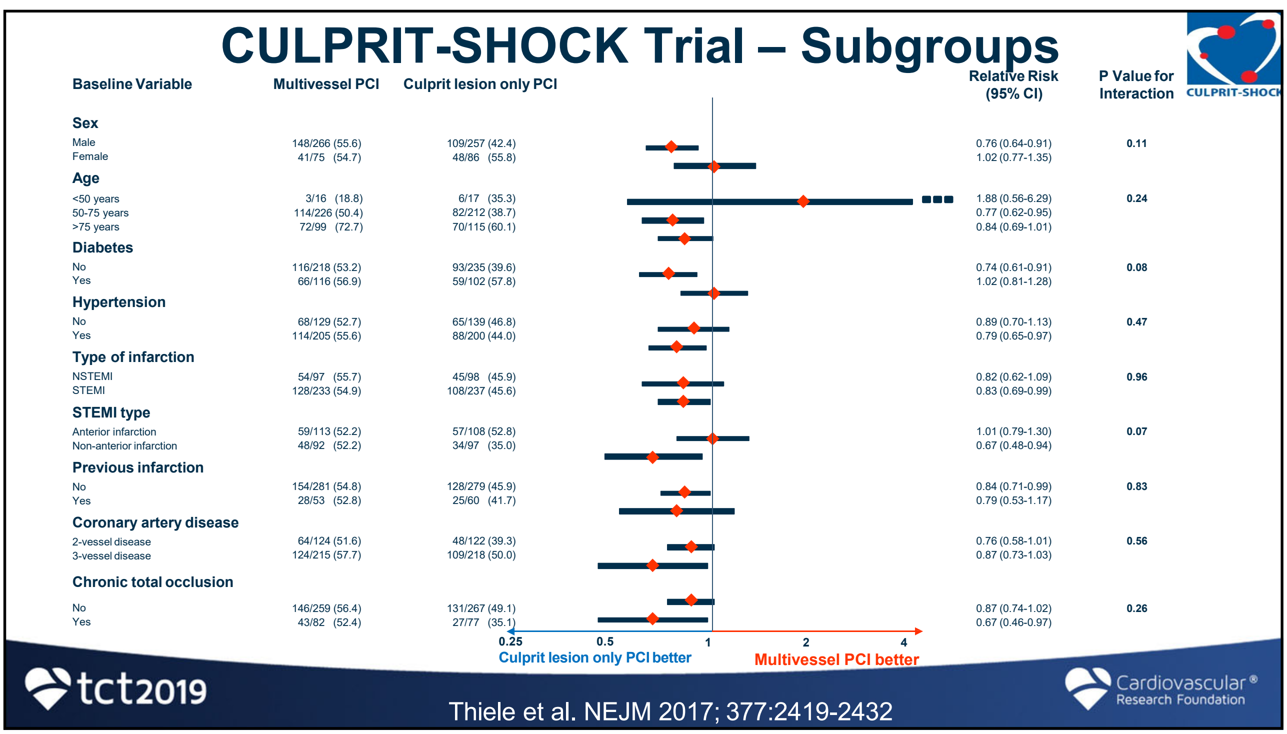
CULPRIT-SHOCK Trial – Subgroups
CULPRIT-SHOCK
Baseline Variable | Multivessel PCI | Culprit lesion only PCI | Relative Risk (95% CI) | P Value for Interaction
Sex
Male 148/266 (55.6) 109/257 (42.4) 0.76 (0.64-0.91) 0.11
Female 41/75 (54.7) 48/86 (55.8) 1.02 (0.77-1.35)
Age
<50 years 3/16 (18.8) 6/17 (35.3) 1.88 (0.56-6.29) 0.24
50-75 years 114/226 (50.4) 82/212 (38.7) 0.77 (0.62-0.95)
>75 years 72/99 (72.7) 70/115 (60.1) 0.84 (0.69-1.01)
Diabetes
No 116/218 (53.2) 93/235 (39.6) 0.74 (0.61-0.91) 0.08
Yes 66/116 (56.9) 59/102 (57.8) 1.02 (0.81-1.28)
Hypertension
No 68/129 (52.7) 65/139 (46.8) 0.89 (0.70-1.13) 0.47
Yes 114/205 (55.6) 88/200 (44.0) 0.79 (0.65-0.97)
Type of infarction
NSTEMI 54/97 (55.7) 45/98 (45.9) 0.82 (0.62-1.09) 0.96
STEMI 128/233 (54.9) 108/237 (45.6) 0.83 (0.69-0.99)
STEMI type
Anterior infarction 59/113 (52.2) 57/108 (52.8) 1.01 (0.79-1.30) 0.07
Non-anterior infarction 48/92 (52.2) 34/97 (35.0) 0.67 (0.48-0.94)
Previous infarction
No 154/281 (54.8) 128/279 (45.9) 0.84 (0.71-0.99) 0.83
Yes 28/53 (52.8) 25/60 (41.7) 0.79 (0.53-1.17)
Coronary artery disease
2-vessel disease 64/124 (51.6) 48/122 (39.3) 0.76 (0.58-1.01) 0.56
3-vessel disease 124/215 (57.7) 109/218 (50.0) 0.87 (0.73-1.03)
Chronic total occlusion
No 146/259 (56.4) 131/267 (49.1) 0.87 (0.74-1.02) 0.26
Yes 43/82 (52.4) 27/77 (35.1) 0.67 (0.46-0.97)
0.25 0.5 1 2 4
Culprit lesion only PCI better
Multivessel PCI better
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Thiele et al. NEJM 2017; 377:2419-2432
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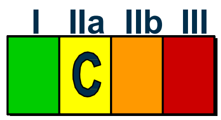
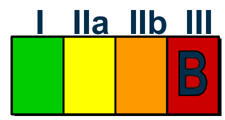
Multivessel PCI in Shock - Guideline Evolution

ESC STEMI Guidelines 2017 → Revascularization Guidelines 2018

2017



2018



tct2019

Ibanez et al. Eur Heart J 2018;39:119-177
Neumann et al. Eur Heart J 2019;40:87-165

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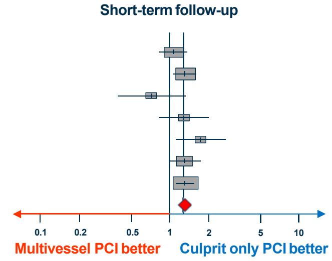
Metaanalysis Mortality – Registry-Data

Short-term follow-up

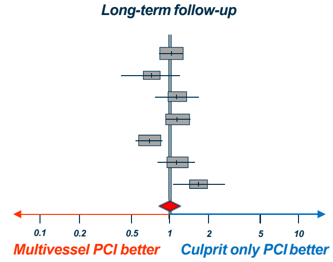
	MV-PCI		C-PCI		RR	95%CI
	Events	Total	Events	Total		
IABP-SHOCK II	75	167	119	284	1.07	[0.86-1.33]
ALKK	81	173	201	562	1.31	[1.08-1.33]
KAMIR	13	124	56	386	0.72	[0.41-1.28]
Yang et al.	19	60	68	278	1.29	[0.85-1.98]
Cavender et al.	20	43	42	156	1.73	[1.14-2.61]
EHS-PCI	40	82	95	254	1.30	[0.99-1.71]
NCDR	158	433	737	2654	1.31	[1.14-1.51]
Overall	**406**	**1082**	**1318**	**4574**	**1.26**	**[1.12-1.41]**



Heterogeneity: τ^2=0.007, I^2=31.0%, p=0.19
Test for overall effect: p=0.001

Long-term follow-up

	MV-PCI		*C-PCI*		*RR*	*95%CI*
	Events	*Total*	*Events*	*Total*		
IABP-SHOCK II	*91*	*167*	*149*	*284*	*1.04*	*[0.87-1.24]*
KAMIR	*16*	*124*	*69*	*386*	*0.72*	*[0.43-1.19]*
Yang et al.	*21*	*60*	*85*	*278*	*1.14*	*[0.78-1.69]*
Cavender et al.	*32*	*43*	*101*	*156*	*1.15*	*[0.93-1.42]*
Mylotte et al.	*37*	*66*	*82*	*103*	*0.70*	*[0.56-0.89]*
van der Schaaf et al.	*22*	*37*	*66*	*124*	*1.12*	*[0.82-1.53]*
SHOCK	*7*	*9*	*26*	*57*	*1.71*	*[1.09-2.67]*
Overall	***226***	***506***	***578***	***1387***	***1.03***	***[0.85-1.25]***



Heterogeneity: τ^2=0.043, I^2=67.8%, p=0.005
Test for overall effect: p=0.77

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de Waha et al. Eur Heart J Acute Cardiovasc Care. 2018;7:28-37

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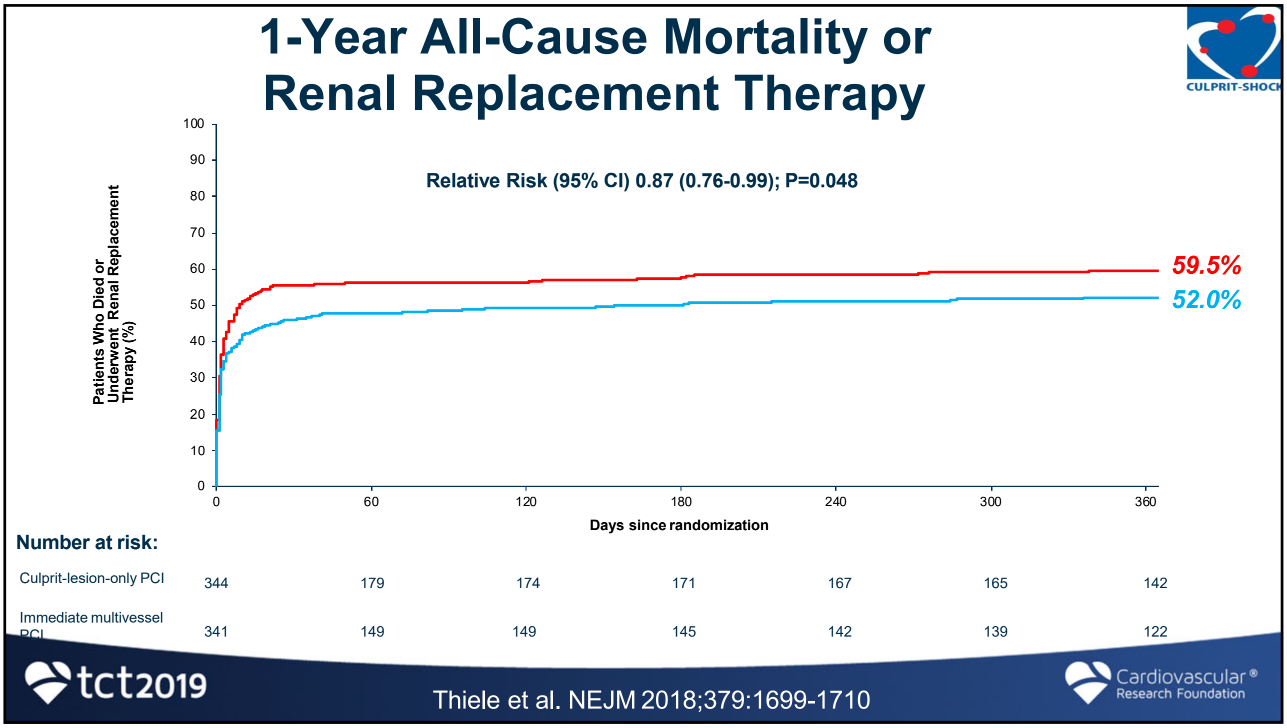
1-Year All-Cause Mortality or
Renal Replacement Therapy
CULPRIT-SHOCK
Relative Risk (95% CI) 0.87 (0.76-0.99); P=0.048
Patients Who Died or Underwent Renal Replacement Therapy (%)
100
90
80
70
60
50
40
30
20
10
0
59.5%
52.0%
0
60
120
180
240
300
360
Days since randomization
Number at risk:
Culprit-lesion-only PCI 344 179 174 171 167 165 142
Immediate multivessel PCI 341 149 149 145 142 139 122
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Thiele et al. NEJM 2018;379:1699-1710
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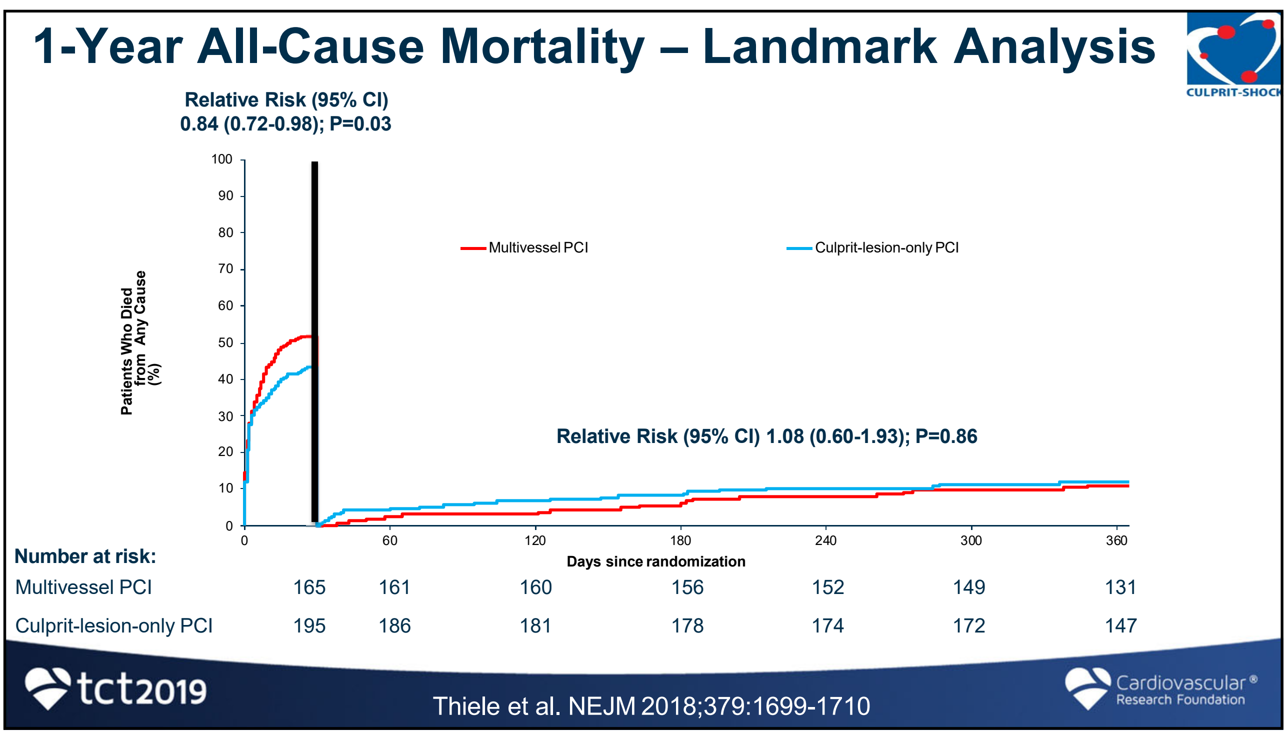
1-Year All-Cause Mortality – Landmark Analysis
CULPRIT-SHOCK
Relative Risk (95% CI)
0.84 (0.72-0.98); P=0.03
Patients Who Died from Any Cause (%)
100
90
80
70
60
50
40
30
20
10
0
Multivessel PCI
Culprit-lesion-only PCI
Relative Risk (95% CI) 1.08 (0.60-1.93); P=0.86
0
60
120
180
240
300
360
Days since randomization
Number at risk:
Multivessel PCI 165 161 160 156 152 149 131
Culprit-lesion-only PCI 195 186 181 178 174 172 147
tct2019
Thiele et al. NEJM 2018;379:1699-1710
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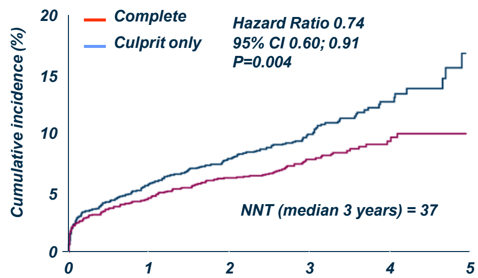
Shock vs no Shock – Different Animals?

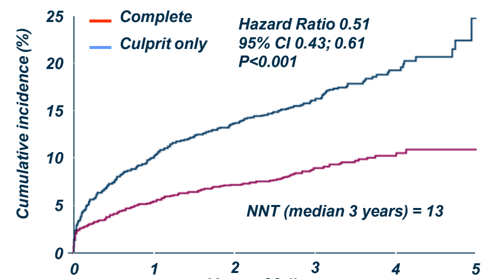
First co-primary outcome
CV death, or new MI



Number at risk						
Complete	2016	1904	1677	938	337	70
Culprit only	2025	1897	1666	933	310	59

Driven by:
MI HR 0.68 (0.53; 0.86)
Type 1 MI (STEMI & NSTEMI) HR 0.49 (0.36; 0.66)

2nd co-primary outcome
CV death, MI, or IDR



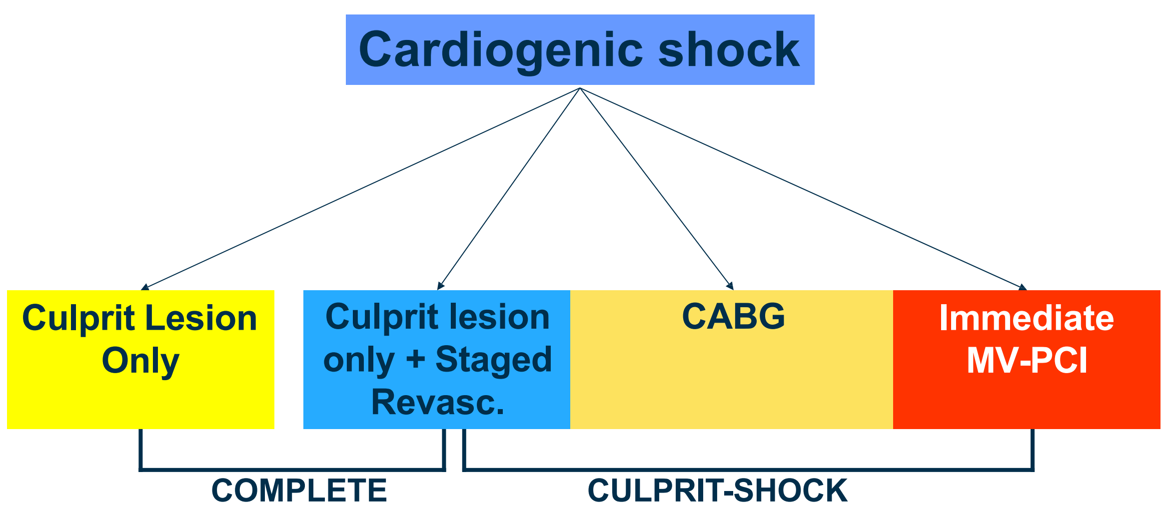
Number at risk						
Complete	2016	1886	1659	925	329	66
Culprit only	2025	1808	1559	865	294	57

Driven by:
Revasc (ischaemia) HR 0.18 (0.12; 0.26)
Unstable angina HR 0.53 (0.40; 0.71)

Complete revascularization achieved in 90.1% after NCL PCI (SYNTAX score = 0)

tct2019 Metha et al. NEJM 2019 Cardiovascular Research Foundation

Revascularization Options



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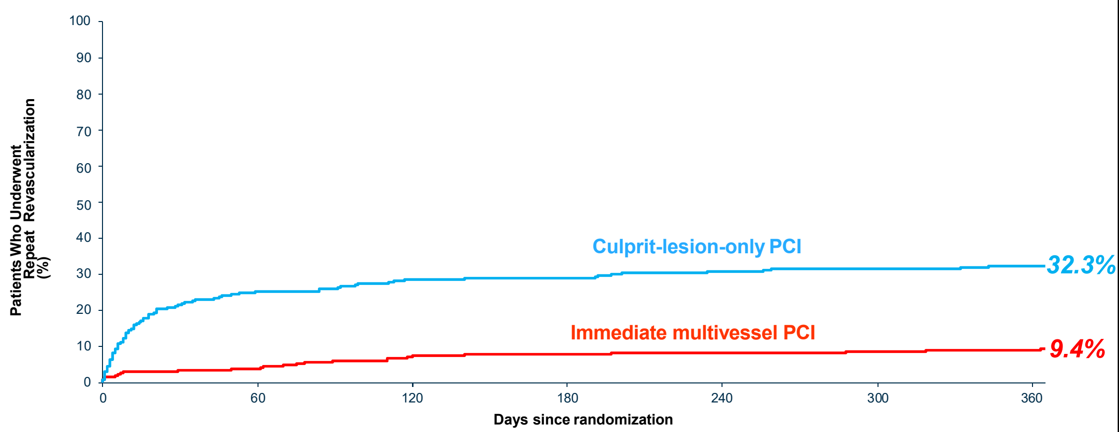
1-Year Repeat Revascularization

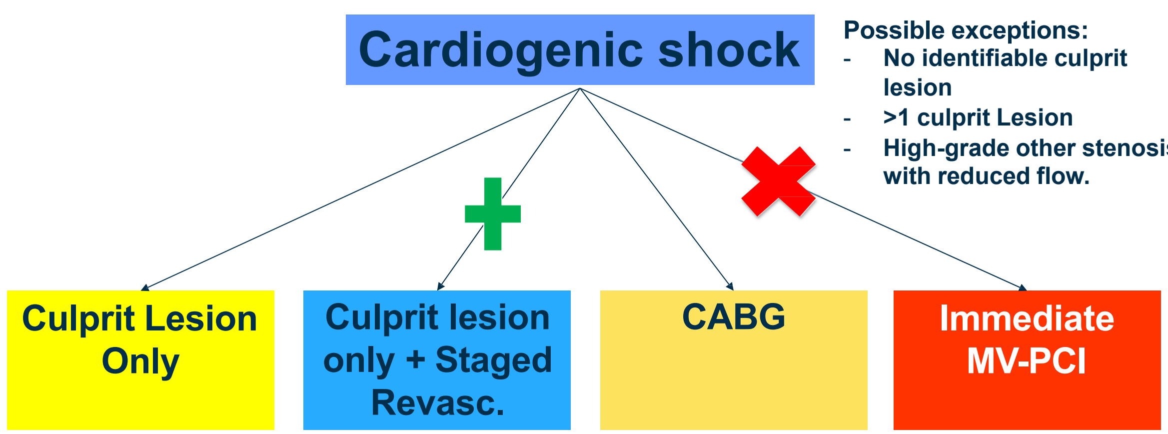
CULPRIT-SHOCK



Number at risk:							
Culprit-lesion only PCI	344	256	245	244	237	234	223
Multivessel PCI	341	327	316	313	312	311	293

tct2019 Thiele et al. NEJM 2018;379:1699-1710 Cardiovascular® Research Foundation

Revascularization Options



Possible exceptions:
- No identifiable culprit lesion
- >1 culprit Lesion
- High-grade other stenosis with reduced flow.

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CV-PCI vs MV-PCI in patients with NSTEMI

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Journal of the American College of Cardiology
Volume 74, Issue 13 Supplement, October 2019
DOI: 10.1016/j.jacc.2019.08.969

PDF Article

VENTRICULAR ASSIST AND MANAGEMENT OF CARDIOGENIC SHOCK - 3

TCT-822 Culprit Vessel Only Versus Multivessel Percutaneous Coronary Intervention in Patients With NSTEMI and Cardiogenic Shock: Insights From the NCDR CathPCI Registry

Mohamed Omer, Emmanouil Brilakis, Kevin Kennedy, Islam Elgendy, Philip Jones, Jonathan Enriquez, Suzanne Arnold, Paul Chan and John Spertus

Background

- In the case of cardiogenic shock, possible advantages of multivessel PCI include an enhanced perfusion of the peri-infarct area, which may improve LV function and potentially reduce infarct size.
- Additionally, multivessel PCI could prevent recurrent ischemia in non-infarct related lesions.
- However, this PCI strategy may also lead to harm due to increased procedural time, more contrast use and increased thrombogenicity.

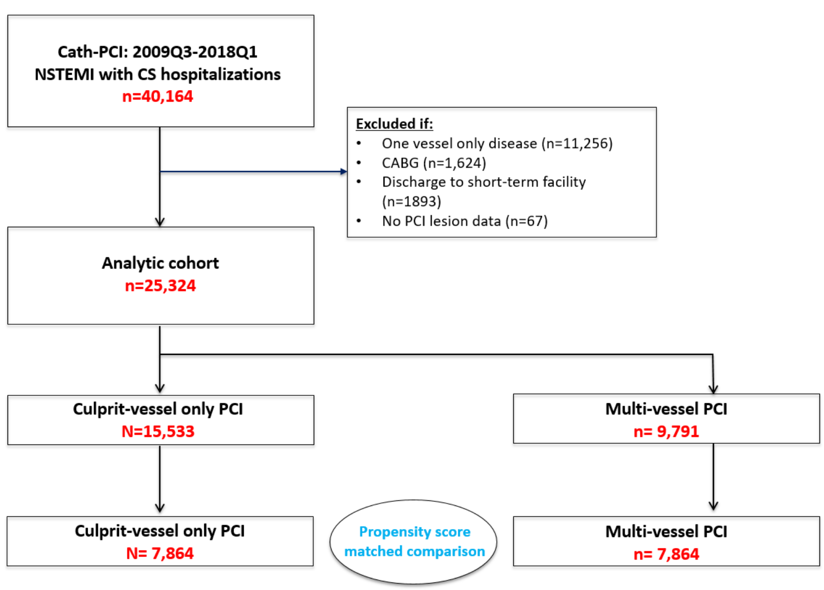
Objectives

- To describe the frequency of multi-vessel PCI in patients with NSTEMI presenting with cardiogenic shock.
- To compare the association of these strategies with short- and long-term outcomes in the National Cardiovascular Data CathPCI Registry.

Data Source

- The **NCDR CathPCI** registry prospectively collects data on patient characteristics, procedural details, and in-hospital outcomes of patients receiving diagnostic angiography or PCI from >1,000 sites across the US to support quality improvement.
- Patients > 65 years who underwent PCI between 2009 and 2013 at hospitals participating in the NCDR CathPCI Registry were linked to **Medicare** fee-for-service claims to obtain long-term survival data for this analysis.
- Based on the revascularization strategy, patients were classified into CV-PCI only intervention or multivessel PCI groups (culprit vessel in addition to immediate additional vessel PCI).

Study Population



Study Outcomes

The primary outcome:

- The occurrence of procedural complications, including in-hospital mortality, bleeding events within 72 hours, requirement of RBC transfusion, stroke, new requirement for dialysis and pericardial tamponade.

The secondary outcome:

- 7-year all-cause mortality.

Statistical analysis

- Baseline characteristics, PCI procedural findings, and in hospital outcomes were compared between patients with CV-PCI versus multivessel PCI.

- To better balance the groups for comparison, we conducted a pre-specified **propensity score analysis**. The propensity score for an individual was defined as the conditional probability of receiving a particular treatment (in this case multivessel revascularization) given the individual's covariates.

Statistical analysis

To estimate these scores, we created a logistic regression model to predict the use of multivessel PCI conditioned on the following covariates:

- Demographic variables (age, sex, race, insurance)
- Clinical risk factors: (BMI, GFR, DLD, HTN, DM, family history of premature CAD, smoking, history of MI, history of heart failure, prior valve surgery, prior PCI, prior CABG, current haemodialysis treatment, cerebrovascular disease, PAD, chronic lung disease)
- Year of PCI
- Disease severity (CCS class I- IV angina within 2 weeks, heart failure within 2 weeks, NYHA class IV heart failure, cardiomyopathy, cardiac arrest within 24 hours)
- Pre-PCI procedure information (MCS device use and arterial access site)
- Pre-procedural medications: glycoprotein IIb/IIIa inhibitors
- Lesion characteristics: left main disease, lesion complexity class C.

Statistical analysis

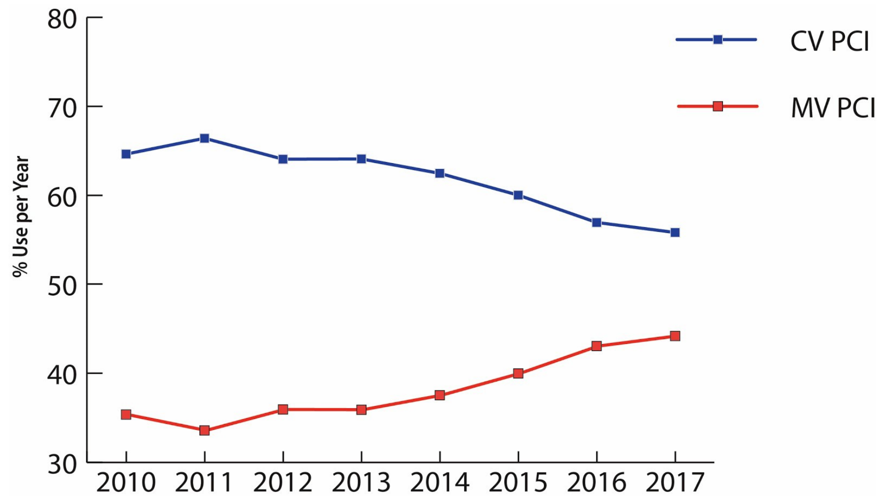
-We then performed a **1:1** nearest neighbor match on the logit of the propensity score within a caliper width of 0.2 times the standard deviation of the logit of the propensity score.

-The success of matching was examined by comparing standardized differences in the distribution of the covariates between the 2 treatment strategies; a difference of <10% was considered acceptable.

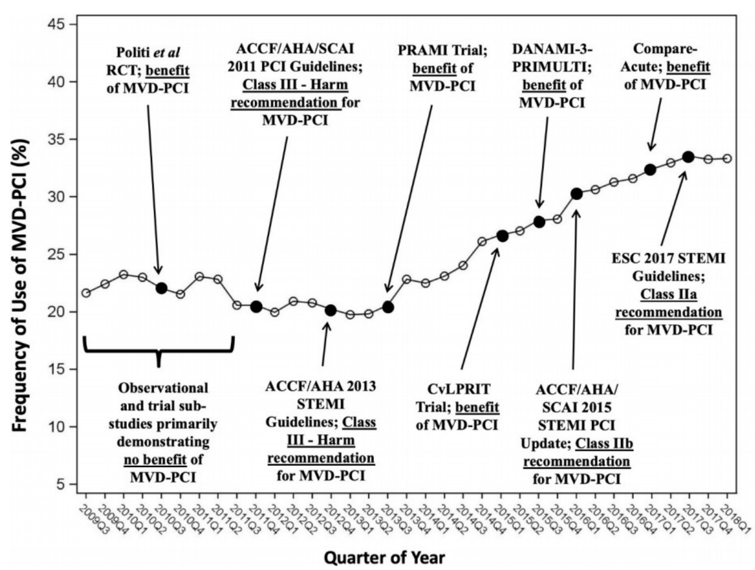
- **Conditional logistic regression** was used to produce odds ratios and 95% confidence intervals.

-Finally, **Cox proportional hazard analysis** were used to show event rates over time using survivors at discharge from the matched groups.

Trends of MV-PCI over the study period



Trends of MV-PCI in STEMI population



Secemsky et al ACC 2020

Table 1: Baseline characteristics

Variable (%)	Before matching: Multivessel PCI n= 9,791	Before matching: Culprit Vessel PCI n= 15,533	Standardized Difference (10%)	After matching: Multivessel Vessel PCI n= 7,864	After matching: Culprit Vessel PCI n= 7,864	Standardized Difference (10%)
Patient demographics:						
Age, mean years	69.2 ± 11.9	69.2 ± 11.7	0.3	69.0 ± 11.9	69.0 ± 11.8	0.1
Female	3384 (34.6%)	4974 (32.0%)	5.4	2671 (34.0%)	2646 (33.6%)	0.7
Race - White	8136 (83.1%)	13160 (84.7%)	4.4	6563 (83.5%)	6587 (83.8%)	1.0
BMI	29.2 ± 6.9	29.2 ± 8.7	0.1	29.1 ± 6.9	29.2 ± 8.1	0.8
Primary expected payer						
Medicare	6452 (65.9%)	10217 (65.8%)	0.3	5126 (65.2%)	5103 (64.9%)	0.6
Medicaid	1319 (13.5%)	2035 (13.1%)	1.1	1064 (13.5%)	1066 (13.6%)	0.1
Private insurance	5462 (55.8%)	8658 (55.7%)	0.1	4344 (55.2%)	4391 (55.8%)	1.2
No-insurance	590 (6.0%)	957 (6.2%)	0.6	503 (6.4%)	505 (6.4%)	0.1
Medical history						
Current/Recent Smoker	2353 (24.1%)	4015 (25.9%)	4.1	1968 (25.0%)	1963 (25.0%)	0.1
Hypertension	8176 (83.6%)	13105 (84.4%)	2.2	6567 (83.5%)	6588 (83.8%)	0.7
Dyslipidemia	7204 (73.7%)	11609 (74.9%)	2.6	5785 (73.6%)	5769 (73.4%)	0.5
FH of Premature CAD	1354 (13.8%)	2453 (15.8%)	5.5	1147 (14.6%)	1155 (14.7%)	0.3
Prior MI	3454 (35.3%)	6146 (39.6%)	8.9	2823 (35.9%)	2844 (36.2%)	0.6
Prior Heart Failure	3290 (33.6%)	5083 (32.7%)	1.9	2586 (32.9%)	2589 (32.9%)	0.1
Prior Valve Surgery	252 (2.6%)	487 (3.1%)	3.4	219 (2.8%)	212 (2.7%)	0.5
Prior PCI	3040 (31.1%)	5542 (35.7%)	9.8	2524 (32.1%)	2526 (32.1%)	0.1
Prior CABG	1606 (16.4%)	4726 (30.4%)	33.6	1545 (19.6%)	1561 (19.8%)	0.5
Currently on Dialysis	1119 (11.4%)	1440 (9.3%)	7.1	809 (10.3%)	811 (10.3%)	0.1
Cerebrovascular Disease	1997 (20.4%)	3211 (20.7%)	0.7	1564 (19.9%)	1595 (20.3%)	1.0
Peripheral Arterial Disease	2210 (22.6%)	3557 (22.9%)	0.8	1701 (21.6%)	1686 (21.4%)	0.5
Chronic Lung Disease	2149 (22.0%)	3635 (23.4%)	3.5	1768 (22.5%)	1792 (22.8%)	0.7
Diabetes Mellitus	5296 (54.1%)	7959 (51.3%)	5.7	4158 (52.9%)	4151 (52.8%)	0.2

Results

Variable (%)	Before matching: Multivessel PCI n= 9,791	Before matching: Culprit Vessel PCI n= 15,533	Standardized Difference (10%)	After matching: Multivessel Vessel PCI n= 7,864	After matching: Culprit Vessel PCI n= 7,864	Standardized Difference (10%)
Cath Lab Visit						
PCI Status			10.8			0.5
Urgent	4817 (49.2%)	7268 (46.8%)		3807 (48.4%)	3812 (48.5%)	
Emergent	3728 (38.1%)	6539 (42.1%)		3135 (39.9%)	3133 (39.8%)	
Salvage	962 (9.8%)	1190 (7.7%)		683 (8.7%)	686 (8.7%)	
Cardiac Arrest w/in 24 Hours	2215 (22.6%)	4024 (25.9%)	7.7	1871 (23.8%)	1864 (23.7%)	0.2
Heart failure within 2 weeks	5769 (58.9%)	7635 (49.2%)	19.7	4333 (55.1%)	4341 (55.2%)	0.2
Pre-PCI LV EF	33.1 ± 14.9	35.2 ± 15.2	14.0	34.0 ± 15.0	33.8 ± 14.9	1.5
GFR	55.9 ± 21.9	56.5 ± 21.7	2.6	56.4 ± 21.8	56.5 ± 22.0	0.7
IABP	4397 (44.9%)	5648 (36.4%)	17.5	3372 (42.9%)	3413 (43.4%)	1.1
Other MCS	2123 (21.7%)	1506 (9.7%)	33.4	1169 (14.9%)	1139 (14.5%)	1.1
Arterial access			2.2			1.4
Femoral access	8648 (88.4%)	13755 (88.6%)		6945 (88.3%)	5538 (88.7%)	
Radial access	1072 (11.0%)	1644 (10.6%)		863 (11.0%)	856 (10.9%)	
Other	68 (0.7)	131 (0.8%)		56 (0.7%)	48 (0.6%)	
GPIIbIIIa use	2853 (29.2%)	4707 (30.3%)	2.6	2381 (30.3%)	2375 (30.2%)	0.2
Contrast volume	230.4 ± 109.1	183.4 ± 89.9	47.0	228.7 ± 106.3	183.1 ± 91.4	46.0
Fluoroscopy Time	26.3 ± 17.3	18.5 ± 13.5	50.7	25.1 ± 16.3	19.1 ± 14.0	39.1

Results

Variable (%)	Before matching			After matching		
	Multivessel PCI n= 9,791	Culprit Vessel PCI n= 15,533	Standardized Difference (10%)	Multivessel Vessel PCI n= 7,864	Culprit Vessel PCI n= 7,864	Standardized Difference (10%)
Diseased and intervened vessels						
Left main disease	3584 (36.6%)	3243 (20.9%)	35.3	2109 (26.8%)	2181 (27.7%)	2.1
LAD disease	8746 (89.3%)	12958 (83.4%)	17.3	6904 (87.8%)	6852 (87.1%)	2.0
RCA disease	7187 (73.4%)	12768 (82.2%)	21.3	5980 (76.0%)	6029 (76.7%)	1.5
LCx disease	8069 (82.4%)	11625 (74.8%)	18.5	6346 (80.7%)	6307 (80.2%)	1.3
Prox LAD disease	6000 (61.3%)	7784 (50.1%)	22.6	4437 (56.4%)	4424 (56.3%)	0.3
Left main intervened	3241 (33.1%)	875 (5.6%)	74.1	1919 (24.4%)	609 (7.7%)	46.6
lAD intervened	7712 (78.8%)	5564 (35.8%)	96.4	6025 (76.6%)	3144 (40.0%)	80.0
RCA intervened	4046 (41.3%)	4397 (28.3%)	27.6	3553 (45.2%)	1938 (24.6%)	44.1
LCx intervened	7025 (71.7%)	4697 (30.2%)	91.3	5631 (71.6%)	2173 (27.6%)	97.9
LAD culprit	4700 (48.0%)	5564 (35.8%)	24.9	3575 (45.5%)	3144 (40.0%)	11.1
RCA culprit	1970 (20.1%)	4397 (28.3%)	19.2	1751 (22.3%)	1938 (24.6%)	5.6
LCx culprit	3831 (39.1%)	4697 (30.2%)	18.8	3016 (38.4%)	2173 (27.6%)	22.9
Left main culprit	2313 (23.6%)	875 (5.6%)	52.6	1352 (17.2%)	609 (7.7%)	28.9
Chronic total occlusion PCI	877 (9.0%)	807 (5.2%)	14.7	745 (9.5%)	430 (5.5%)	15.3
Pre-PCI TIMI0	3038 (31.0%)	5112 (32.9%)	4.0	2592 (33.0%)	2638 (33.5%)	1.2
Class C lesion	8146 (83.2%)	10744 (69.2%)	33.4	6316 (80.3%)	6309 (80.2%)	0.2

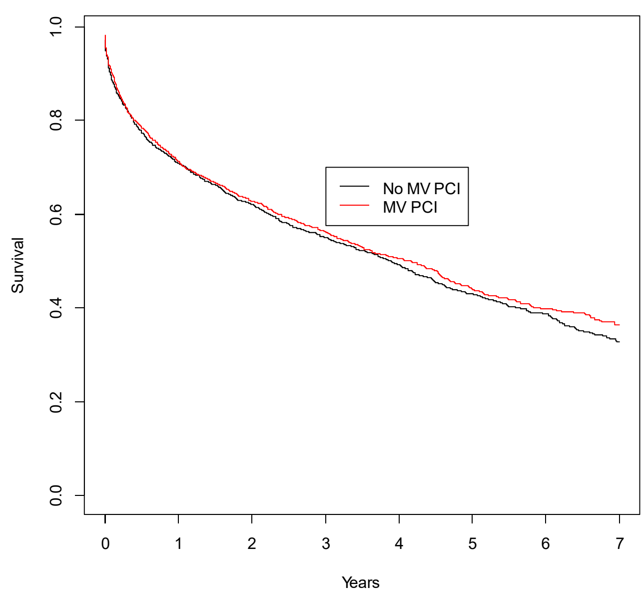
Clinical Outcomes

	Before matching			After matching		
	Multivessel PCI n= 9,791	Culprit Vessel PCI n= 15,533	P-Value	Multivessel Vessel PCI n= 7,864	Culprit Vessel PCI n= 7,864	P-Value
In-hospital mortality	3204 (32.7%)	4942 (31.8%)	0.13	2432 (30.9%)	2706 (34.4%)	**<0.001**
Bleeding Event within 72 Hours	1431 (14.6%)	1487 (9.6%)	<0.001	1039 (13.2%)	845 (10.8%)	**<0.001**
Blood Transfusion	2504 (25.6%)	2759 (17.8%)	<0.001	1815 (23.1%)	1530 (19.5%)	**<0.001**
New Requirement for Dialysis	613 (6.3%)	689 (4.4%)	<0.001	447 (5.7%)	358 (4.5%)	**0.001**
Tamponade	39 (0.4%)	34 (0.2%)	0.009	29 (0.4%)	22 (0.3%)	0.32
Stroke	209 (2.1%)	249 (1.6%)	0.001	152 (1.9 %)	146 (1.9%)	0.73

3- Subgroup analysis

Cohort	MVPCI vs Not Odds ratio for Mortality, 95% CI	p-value	Interaction P-value
Full	0.85 (.79, .91)	<.001	NA
Age>65	.81 (.74, .90)	<.001	0.34
Age<=65	.90 (.78, 1.04)	.035	
Male	.87 (.80, .96)	.005	0.51
Female	.82 (.71, .95)	.007	
DM	.91 (.82, 1.02)	.109	0.14
No DM	.79 (.70, .89)	<.001	
Mech Support	.65 (.52, .80)	<.001	0.006
No Mech Support	.90 (.83, .97)	<.001	

4- Cox Proportional Hazard Regression Model for Long-term Survival



Hazard ratio, MV vs CV 0.96 (0.88, 1.04), p=.279

Discussion

- Nearly 2 in 5 patients underwent multivessel PCI over time, with an increasing prevalence for multivessel PCI over time.

- Compared with CV-PCI, patients undergoing multivessel PCI had lower adjusted in-hospital mortality, but similar long-term mortality at 7 year follow-up.

- These results have important clinical implications because they are applicable to the general US population requiring acute interventional care.

Discussion

The discrepancy of the in-hospital mortality results of our study compared to CULPRIT-SHOCK is likely related to several differences in the design of the two studies.

1- CUPRIT-SHOCK compared **MV-PCI** to **culprit-only PCI with staged revascularization** if necessary. As a result, in the culprit-lesion only PCI group, 12.5% underwent immediate multivessel revascularization and 17.7% underwent staged multivessel revascularization. Overall, 30.2% of the culprit-lesion-only PCI group was actually treated by multivessel PCI.

In contrast, our study compared patients who underwent **culprit vessel PCI** with those that underwent **immediate multivessel PCI**. The percentage of staged PCI was < 5% in both groups. Therefore, multivessel PCI is defined very differently in both studies and cannot be considered equivalent.

Discussion

2- There may be difference in the patient population included in the analysis. In the CULPRIT-SHOCK trial, ~ **40%** of the cohort were **NSTEMI**, **50%** of the patients had **resuscitation** before randomization and the rate of **MCS** use was relatively low (**28%**).

However, our study **exclusively** included **NSTEMI** patients, **25%** of whom had **cardiac arrest** and the rate of **MCS use was 55**%.

Furthermore, Anderson et al. showed that NSTEMI patients with shock carried a greater burden of comorbidities compared to patients with STEMI. The incidence of diabetes, PAD, prior MI and prior CABG were more common in our study compared with CULPRIT-SHOCK study.

Anderson et al: Circ Cardiovasc Qual Outcomes 2013;6:708-15

Discussion

3- In the CULPRIT-SHOCK trial, **23%** of patients had one or more CTO and **all CTOs were attempted** in the multivessel PCI group according to the predetermined trial protocol.

In contrast, in our study, CTO PCI were performed in **~ 9.5 %** of the MV-PCI patients.

This may have contributed to less contrast load and less requirement for dialysis observed in our study compared to the CULPRIT-SHOCK (5.7% vs 16.4%).

Conclusion

1-In patients with multivessel coronary artery disease and cardiogenic shock complicating AMI (**STEMI and NSTEMI**), **culprit lesion only PCI** with possible staged revascularization **reduced short tem mortality at 30 days**. However, the 1-year mortality data was similar between the two groups.

2- US registry real-world data showed that ~ 40% of **NSTEMI** patients with MVD and cardiogenic shock are managed with a strategy of **multivessel PCI**. This strategy was associated with **lower adjusted in-hospital mortality** but similar long-term survival compared with culprit vessel PCI.

3- Further well-designed RCTs are still needed!