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

CONTACT:
Kari Williams - kari.williams@allina.com
Carina Benson - carina.benson@allina.com

MHIF Research Tiger Team ready to support HemoLung with 24/7 onsite research coverage!
Complete Revascularization in Patients with Multivessel CAD: Is the Story COMPLETE

Mohamed A. Omer, MD, MSc
Interventional Cardiology Fellow
Abbott Northwestern Hospital

DISCLOSURE

NONE
My mission to IC world started by “Eureka Moment”

Eureka! Eureka! Supposed to have been his cry, jumping naked from his bath and running in the streets, excited by a discovery about water displacement to solve a problem about the purity of a gold crown.

— Archimedes —

Background

1. Value of complete revascularization in stable CAD.
2. Value of complete revascularization in acute MI.
3. Value of complete revascularization in cardiogenic shock.
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 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?


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
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.
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.


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

<table>
<thead>
<tr>
<th>Study ID</th>
<th>RR (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARTS I PCI</td>
<td>0.69 (0.67, 0.71)</td>
<td>1.00</td>
</tr>
<tr>
<td>ARTS II PCI</td>
<td>0.72 (0.68, 0.75)</td>
<td>0.90</td>
</tr>
<tr>
<td>Asian Medical Center PCI cohort</td>
<td>0.75 (0.70, 0.80)</td>
<td>0.60</td>
</tr>
<tr>
<td>SYNTAX PCI</td>
<td>0.74 (0.69, 0.79)</td>
<td>0.70</td>
</tr>
<tr>
<td>MASS II PCI</td>
<td>0.75 (0.70, 0.80)</td>
<td>0.70</td>
</tr>
<tr>
<td>BARI trial registry</td>
<td>0.78 (0.73, 0.83)</td>
<td>0.70</td>
</tr>
<tr>
<td>BARI Trial and registry</td>
<td>0.80 (0.75, 0.85)</td>
<td>0.50</td>
</tr>
<tr>
<td>Greinacher et al.</td>
<td>2.74 (1.90, 3.97)</td>
<td>0.50</td>
</tr>
<tr>
<td>New York State registry I</td>
<td>0.78 (0.71, 0.85)</td>
<td>0.50</td>
</tr>
<tr>
<td>New York State registry II</td>
<td>0.67 (0.60, 0.75)</td>
<td>0.50</td>
</tr>
<tr>
<td>Valenti et al.</td>
<td>0.37 (0.31, 0.44)</td>
<td>0.30</td>
</tr>
<tr>
<td>AGATIC Investigators et al.</td>
<td>0.70 (0.62, 0.78)</td>
<td>0.30</td>
</tr>
<tr>
<td>Nikolsky et al.</td>
<td>0.42 (0.21, 0.86)</td>
<td>0.30</td>
</tr>
<tr>
<td>Tamburino et al.</td>
<td>0.39 (0.15, 0.94)</td>
<td>0.20</td>
</tr>
<tr>
<td>Marince et al.</td>
<td>0.64 (0.52, 0.78)</td>
<td>0.20</td>
</tr>
<tr>
<td>NHIAB dynamic registry</td>
<td>1.18 (0.85, 2.54)</td>
<td>0.10</td>
</tr>
<tr>
<td>Koster et al.</td>
<td>0.21 (0.01, 0.40)</td>
<td>0.10</td>
</tr>
<tr>
<td>CABRIO</td>
<td>1.07 (0.81, 1.43)</td>
<td>0.10</td>
</tr>
<tr>
<td>New York State registry III</td>
<td>0.89 (0.80, 0.99)</td>
<td>0.10</td>
</tr>
<tr>
<td>Yang et al.</td>
<td>1.10 (0.29, 1.45)</td>
<td>0.10</td>
</tr>
<tr>
<td>Nones-Otto et al.</td>
<td>0.94 (0.69, 1.25)</td>
<td>0.10</td>
</tr>
<tr>
<td>Appleby et al.</td>
<td>0.69 (0.53, 0.88)</td>
<td>0.10</td>
</tr>
<tr>
<td>Dejaegere et al.</td>
<td>1.03 (0.37, 3.00)</td>
<td>0.10</td>
</tr>
<tr>
<td>Overall (I² = 53.4%, p = 0.000)</td>
<td>0.73 (0.65, 0.82)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis.

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 **recent studies** and in populations with a higher prevalence of **diabetes**.

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

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.
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

<table>
<thead>
<tr>
<th>Variables</th>
<th>No. of Patients</th>
<th>No. of Patients with Events</th>
<th>Event Rate (%/Year)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P-value</th>
<th>P-value for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome: Myocardial Infarction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete Revascularization</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EES</td>
<td>1911</td>
<td>72</td>
<td>1.43</td>
<td>1.02 (0.71, 1.47)</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>1911</td>
<td>80</td>
<td>1.37</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete Revascularization¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EES</td>
<td>7312</td>
<td>390</td>
<td>1.98%</td>
<td>1.66 (1.39, 1.98)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>7312</td>
<td>242</td>
<td>1.07%</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Stenosis Classification</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-30 %</td>
<td>13%</td>
</tr>
<tr>
<td>31-50 %</td>
<td>33%</td>
</tr>
<tr>
<td>51-70 %</td>
<td>33%</td>
</tr>
<tr>
<td>&gt;70 %</td>
<td>53%</td>
</tr>
</tbody>
</table>

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.

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:
Ischemic vs. Anatomic CAD Burden

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

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.

“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

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

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!


---

**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.

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


**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.

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)

RSS after Angiography - guided PCI

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

Residual SYNTAX Score calculated in FFR-guided patients from FAME

![Graph showing survival free from major adverse cardiac events over time with different residual SYNTAX scores.](image)

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


---

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)

![Graph showing cumulative incidence of events over time with different functional SYNTAX scores.](image)

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.

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

- 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.

ESC Guidelines on Myocardial Revascularization

Recommendations on functional testing and intravascular imaging for lesion assessment

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Classa</th>
<th>Leve lb</th>
</tr>
</thead>
<tbody>
<tr>
<td>When evidence of ischaemia is not available, FFR or IVF FR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>IVUS should be considered to assess the severity of unprotected left main lesions.</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>

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 \(\leq 0.80\) (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

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

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

<table>
<thead>
<tr>
<th>Trial</th>
<th>Same-sitting or Staged</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Di Mario 2004</td>
<td>Index</td>
<td>69</td>
</tr>
<tr>
<td>Politi 2009</td>
<td>Index or staged</td>
<td>149</td>
</tr>
<tr>
<td>Ghanı 2012</td>
<td>Staged (FFR guided)</td>
<td>119</td>
</tr>
<tr>
<td>PRAMI 20131</td>
<td>Index</td>
<td>465</td>
</tr>
<tr>
<td>Culpıt 20142</td>
<td>Index or staged</td>
<td>296</td>
</tr>
<tr>
<td>DANAMI-3 20153</td>
<td>Staged</td>
<td>627</td>
</tr>
<tr>
<td>PRAGUE 13</td>
<td>Staged</td>
<td>214</td>
</tr>
<tr>
<td>Explore</td>
<td>Staged (CTO)</td>
<td>300</td>
</tr>
<tr>
<td>COMPARE-ACUTE4</td>
<td>Mainly index</td>
<td>885</td>
</tr>
</tbody>
</table>


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.
**COMPLETE Trial Design**

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

**EXCLUSION CRITERIA:** Intent to revascularize NCL, planned surgical revascularization, prior CABG

**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

**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

**Global Recruitment**
140 centers, 31 countries

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

---

*Everolimus-eluting stents strongly recommended

**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)

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

**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

**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

---

*Everolimus-eluting stents strongly recommended

**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)

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

**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

**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

---

*Everolimus-eluting stents strongly recommended

**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)

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

**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

**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

---

*Everolimus-eluting stents strongly recommended

**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)

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

**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

**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

---

*Everolimus-eluting stents strongly recommended

**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)

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

**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

**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

---

*Everolimus-eluting stents strongly recommended

**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)

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

**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

**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

---

*Everolimus-eluting stents strongly recommended

**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)

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

**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

**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
**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%

---

**Baseline Characteristics**

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

<table>
<thead>
<tr>
<th></th>
<th>Complete N=2016</th>
<th>Culprit-only N=2025</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sx onset to Culprit PCI (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6 hours</td>
<td>69.4</td>
<td>67.1</td>
</tr>
<tr>
<td>6~12 hours</td>
<td>16.1</td>
<td>17.7</td>
</tr>
<tr>
<td>&gt;12 hours</td>
<td>14.5</td>
<td>15.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Discharge Meds (%)</th>
<th>Complete N=2016</th>
<th>Culprit-only N=2025</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA</td>
<td>99.8</td>
<td>99.5</td>
</tr>
<tr>
<td>P2Y12 Inhibitor</td>
<td>99.4</td>
<td>99.7</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>64.4</td>
<td>63.3</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>9.6</td>
<td>8.3</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>25.6</td>
<td>28.2</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>88.1</td>
<td>89.1</td>
</tr>
<tr>
<td>ACEI/ARB</td>
<td>85.5</td>
<td>84.6</td>
</tr>
<tr>
<td>Statin</td>
<td>98.2</td>
<td>97.2</td>
</tr>
</tbody>
</table>

Procedural Characteristics

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

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

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

Population Health Research Institute

First Co-Primary Outcome: CV Death or New MI

- Hazard Ratio: 0.74
- 95% CI: 0.60-0.91
- P-value: 0.004
- NNT (median 3 years): 37

Second Co-Primary Outcome: CV Death, New MI, or IDR

- Hazard Ratio: 0.51
- 95% CI: 0.43-0.61
- P-value: < 0.001
- NNT (median 3 years): 13

### Efficacy Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Complete Revasc. N=2016</th>
<th>Culprit Lesion Only N=2025</th>
<th>HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Co-Primary Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CV death or MI</td>
<td>158 (7.8)</td>
<td>213 (10.5)</td>
<td>0.74 (0.60-0.91)</td>
<td>0.004</td>
</tr>
<tr>
<td>CV death, MI or IDR</td>
<td>179 (8.9)</td>
<td>339 (16.7)</td>
<td>0.51 (0.43-0.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Key Secondary Outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CV death, MI, IDR, unstable angina or class IV HF</td>
<td>272 (13.5)</td>
<td>426 (21.0)</td>
<td>0.62 (0.53-0.72)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Other Secondary Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>109 (5.4)</td>
<td>160 (7.9)</td>
<td>0.68 (0.53-0.86)</td>
<td>0.002</td>
</tr>
<tr>
<td>IDR</td>
<td>29 (1.4)</td>
<td>160 (7.9)</td>
<td>0.18 (0.12-0.26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unstable Angina</td>
<td>70 (3.5)</td>
<td>130 (6.4)</td>
<td>0.53 (0.40-0.71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CV death</td>
<td>59 (2.9)</td>
<td>64 (3.2)</td>
<td>0.93 (0.65-1.32)</td>
<td>0.68</td>
</tr>
<tr>
<td>All-cause Death</td>
<td>96 (4.8)</td>
<td>106 (5.2)</td>
<td>0.91 (0.69-1.20)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

### Sub-types of MI

<table>
<thead>
<tr>
<th>Subtype of MI</th>
<th>Complete Revasc. N=2016</th>
<th>Culprit Lesion Only N=2025</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSTEMI</td>
<td>66 (3.27)</td>
<td>105 (5.19)</td>
<td>0.63 (0.46-0.85)</td>
</tr>
<tr>
<td>STEMI</td>
<td>43 (2.13)</td>
<td>53 (2.62)</td>
<td>0.81 (0.54-1.22)</td>
</tr>
<tr>
<td><strong>Universal MI Definition</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td>63 (3.13)</td>
<td>128 (6.32)</td>
<td>0.49 (0.36-0.66)</td>
</tr>
<tr>
<td>Type 2</td>
<td>16 (0.79)</td>
<td>13 (0.64)</td>
<td>1.24 (0.60-2.58)</td>
</tr>
<tr>
<td>Type 3</td>
<td>4 (0.20)</td>
<td>1 (0.05)</td>
<td>4.04 (0.45-3.17)</td>
</tr>
<tr>
<td>Type 4a</td>
<td>16 (0.79)</td>
<td>8 (0.40)</td>
<td>2.01 (0.86-4.70)</td>
</tr>
<tr>
<td>Type 4b</td>
<td>8 (0.40)</td>
<td>13 (0.64)</td>
<td>0.62 (0.26-1.49)</td>
</tr>
<tr>
<td>Type 5</td>
<td>1 (0.05)</td>
<td>1 (0.05)</td>
<td>1.00 (0.06-15.92)</td>
</tr>
</tbody>
</table>
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

COMPLETE Trial

STEMI with Multivessel CAD and Successful PCI to the Culprit Lesion

Guideline-Directed Medical Therapy

Co-primary Outcomes:
1. Composite of CV death or new MI
2. Composite of CV death, new MI or IDR
## Baseline Characteristics

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

## Procedural Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Intended timing of complete revascularization</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Index hospitalization (N=2702)</td>
<td>After discharge (N=1339)</td>
</tr>
<tr>
<td>SYNTAX score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Baseline (including STEMI culprit)</td>
<td>16.1±6.8</td>
<td>16.4±6.6</td>
</tr>
<tr>
<td>• Residual (after index PCI)</td>
<td>7.1±4.8</td>
<td>7.2±4.8</td>
</tr>
<tr>
<td>• Lesion specific (STEMI culprit)</td>
<td>8.6±5.3</td>
<td>8.9±5.3</td>
</tr>
<tr>
<td>• Lesion specific (Non-culprit)</td>
<td>4.5±2.7</td>
<td>4.7±2.7</td>
</tr>
<tr>
<td>• Post NCL lesion PCI=0 (Complete revascularization achieved)</td>
<td>1095/1200 (91.3)</td>
<td>525/598 (87.8)</td>
</tr>
<tr>
<td>Non-culprit lesions location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Left main</td>
<td>7/3543 (0.2)</td>
<td>6/1812 (0.3)</td>
</tr>
<tr>
<td>• Left anterior descending</td>
<td>1379/3543 (38.9)</td>
<td>738/1812 (40.7)</td>
</tr>
<tr>
<td>• Circumflex</td>
<td>1293/3543 (36.5)</td>
<td>633/1812 (34.9)</td>
</tr>
<tr>
<td>• Right coronary artery</td>
<td>864/3543 (24.4)</td>
<td>435/1812 (24.0)</td>
</tr>
<tr>
<td>Non-culprit lesion diameter stenosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 50-69%</td>
<td>28/3468 (0.8)</td>
<td>9/1720 (0.5)</td>
</tr>
<tr>
<td>• 70-79%</td>
<td>1435/3468 (41.4)</td>
<td>805/1720 (46.8)</td>
</tr>
<tr>
<td>• 80-89%</td>
<td>1214/3468 (35.0)</td>
<td>500/1720 (29.1)</td>
</tr>
<tr>
<td>• 90-99%</td>
<td>734/3468 (21.2)</td>
<td>357/1720 (20.8)</td>
</tr>
<tr>
<td>• 100%</td>
<td>57/3468 (1.6)</td>
<td>49/1720 (2.8)</td>
</tr>
<tr>
<td>Index procedure for STEMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Primary PCI</td>
<td>2479 (91.7)</td>
<td>1259 (94.0)</td>
</tr>
<tr>
<td>• Pharmacoinvasive PCI</td>
<td>87 (3.2)</td>
<td>38 (2.8)</td>
</tr>
<tr>
<td>• Rescue PCI</td>
<td>136 (6.0)</td>
<td>42 (3.1)</td>
</tr>
<tr>
<td>Radial access</td>
<td>2143 (79.3)</td>
<td>1120 (83.6)</td>
</tr>
<tr>
<td>Thrombus aspiration</td>
<td>699/2573 (23.7)</td>
<td>323/1166 (27.7)</td>
</tr>
</tbody>
</table>
First Co-Primary Outcome
CV Death or New MI

Index Hospitalization

- Hazard Ratio 0.77
  - 95% CI 0.59-1.00
  - P=0.047

After Discharge

- Hazard Ratio 0.69
  - 95% CI 0.49-0.97
  - P=0.032

Interaction P=0.62

Second Co-Primary Outcome
CV Death, New MI or IDR

Index Hospitalization

- Hazard Ratio 0.47
  - 95% CI 0.38-0.59
  - P<0.001

After Discharge

- Hazard Ratio 0.59
  - 95% CI 0.43-0.79
  - P<0.001

Interaction P=0.27
Landmark Analysis Before and After 45 days
CV Death or New MI

Randomization to 45 Days

>45 days to Study End

Hazard Ratio 0.86
95% CI 0.59-1.24

Hazard Ratio 0.69
95% CI 0.54-0.89

Cumulative Outcome Differences between Complete and Culprit-Lesion-Only PCI over Time

Benefit of complete revascularization over time

No. of events prevented/100 patients treated

Years of Follow-up

Population Health Research Institute

Hamilton Health Sciences

McMaster University

30 of 57
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

3- Value of complete revascularization in AMI with cardiogenic shock
Infarct Artery PCI Only: CULPRIT-SHOCK Provides the Answer!

Holger Thiele, MD
Heart Center Leipzig – University of Leipzig

Anterior STEMI + Cardiogenic Shock
Revascularization Options

Cardiogenic shock

- Culprit Lesion Only
- Culprit lesion only + Staged Revasc.
- 1ry CABG
- Immediate MV-PCI

Randomized Trials Cardiogenic Shock

<table>
<thead>
<tr>
<th>Trial</th>
<th>Follow-up</th>
<th>n/N</th>
<th>n/N</th>
<th>Relative Risk Mortality 95% CI</th>
<th>Relative Risk 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revascularization</td>
<td>1 year</td>
<td>81/152</td>
<td>163/300</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30 days</td>
<td>22/32</td>
<td>46/93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>103/184</td>
<td>209/393</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasopressors</td>
<td>28 days</td>
<td>64/145</td>
<td>99/215</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BOAC-2 (CS subgroup)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inotropes</td>
<td>30 days</td>
<td>5/16</td>
<td>10/16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unverzagt et al.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycoprotein IIb/IIIa inhibitors</td>
<td>30 days</td>
<td>4/19</td>
<td>10/15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRAGUE-18</td>
<td></td>
<td>15/40</td>
<td>26/50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>29/80</td>
<td>46/95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO synthase inhibitors</td>
<td>in hospital</td>
<td>154/370</td>
<td>309/620</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRINITY</td>
<td>30 days</td>
<td>97/201</td>
<td>184/368</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMASH II</td>
<td></td>
<td>30 days</td>
<td>7/16</td>
<td>12/25</td>
<td></td>
</tr>
<tr>
<td>Gutberlet et al.</td>
<td></td>
<td>4/13</td>
<td>9/22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>135/390</td>
<td>205/415</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IABP</td>
<td>30 days</td>
<td>7/19</td>
<td>6/21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IABP-SHOCK I</td>
<td></td>
<td>30 days</td>
<td>119/300</td>
<td>125/319</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>126/319</td>
<td>128/319</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVAD</td>
<td>30 days</td>
<td>9/21</td>
<td>9/20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiele et al.</td>
<td></td>
<td>30 days</td>
<td>9/18</td>
<td>9/18</td>
<td></td>
</tr>
<tr>
<td>Bachofen et al.</td>
<td></td>
<td>30 days</td>
<td>6/13</td>
<td>6/13</td>
<td></td>
</tr>
<tr>
<td>IABP-SHOCK II</td>
<td></td>
<td>30 days</td>
<td>11/24</td>
<td>12/24</td>
<td></td>
</tr>
<tr>
<td>IMPRESS in Severe Shock</td>
<td></td>
<td>30 days</td>
<td>357/77</td>
<td>327/71</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>366/77</td>
<td>339/71</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Early revascularization better
Medical treatment better
Vasopressor better
Norepinephrine better
Levosimendan better
Inotrope better
Control better
Absorb balloon better
Pharmacokinetics better
IABP better
LVAD better
IABP better
Standard treatment better
LVAD better
Placebo better
LVAD better
IABP better
IABP better

Incidence Multivessel CAD – Cardiogenic Shock

<table>
<thead>
<tr>
<th>Study</th>
<th>% Patients with MV-CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>IABP-SHOCK II</td>
<td>79</td>
</tr>
<tr>
<td>SHOCK</td>
<td>87</td>
</tr>
<tr>
<td>TRIUMPH</td>
<td>56</td>
</tr>
<tr>
<td>SHOCK Registry</td>
<td>79</td>
</tr>
</tbody>
</table>

Multivessel PCI in Cardiogenic Shock
European and American Recommendations 2017

Guidelines
- ESC: I, IIa, IIb, III
- ACC/AHA/SCAI: No recommendation

Appropriate Use Criteria
- ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS: A1b

References:
- Ibanez et al. Eur Heart J 2018;39:119-177
- Levine et al. J Am Coll Cardiol2016;67:1235-1250
- Patel et al. J Am Coll Cardiol2017;69:570-591
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)

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).

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).

![Image of a table showing the results of the meta-analysis for long-term mortality.](image)

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).

![Image of a table showing the results of the meta-analysis for short-term mortality.](image)

de Waha et al. Eur Heart J Acute Cardiovasc Care. 2018;7:28-37
Meta-analysis long-term Mortality – Registry-Data

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

```
<table>
<thead>
<tr>
<th></th>
<th>MV-PCI</th>
<th>C-PCI</th>
<th>RR</th>
<th>95%CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>IABP-SHOCK II</td>
<td>91/167</td>
<td>149/264</td>
<td>1.04</td>
<td>[0.97-1.24]</td>
<td>19.3%</td>
</tr>
<tr>
<td>KAMIR</td>
<td>16/124</td>
<td>69/366</td>
<td>0.72</td>
<td>[0.43-1.19]</td>
<td>9.0%</td>
</tr>
<tr>
<td>Yang et al.</td>
<td>21/60</td>
<td>85/278</td>
<td>1.14</td>
<td>[0.78-1.69]</td>
<td>12.0%</td>
</tr>
<tr>
<td>Cavender et al.</td>
<td>32/43</td>
<td>101/156</td>
<td>1.15</td>
<td>[0.93-1.42]</td>
<td>18.1%</td>
</tr>
<tr>
<td>Mylotte et al.</td>
<td>37/68</td>
<td>82/163</td>
<td>1.10</td>
<td>[0.56-2.68]</td>
<td>17.2%</td>
</tr>
<tr>
<td>van der Schaaf et al.</td>
<td>22/37</td>
<td>66/124</td>
<td>1.12</td>
<td>[0.95-1.33]</td>
<td>14.3%</td>
</tr>
<tr>
<td>SHOCK</td>
<td>7/9</td>
<td>26/57</td>
<td>1.71</td>
<td>[1.06-2.67]</td>
<td>10.3%</td>
</tr>
<tr>
<td>Overall</td>
<td>226/506</td>
<td>578/1387</td>
<td>1.03</td>
<td>[0.85-1.25]</td>
<td>100%</td>
</tr>
</tbody>
</table>
```

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.
Statistical Methodology

**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

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
Study Flow Chart

1075 patients with acute myocardial infarction (STEMI and NSTEMI) and cardiogenic shock screened

706 randomized

369 excluded

351 randomized to culprit lesion only PCI

344 with full informed consent

301 culprit lesion only PCI

43 immediate multivessel PCI

1 staged CABG

13 urgent PCI

60 staged PCI

310 immediate multivessel PCI

32 culprit lesion only PCI

8 staged PCI

0 staged CABG

5 urgent PCI

344 with 30-day follow-up

341 primary endpoint analysis

344 with 30-day follow-up

1 lost to follow-up

Informed consent

Allocation

Revascularization

Follow-up

Primary endpoint analysis

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

<table>
<thead>
<tr>
<th>Center No.</th>
<th>Case No.</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>4830</td>
<td>10</td>
<td>Initially thrombectomized infarct artery after PCI thrombus in LAD and occlusion of LCx: patient with progression of hemodynamic deterioration</td>
</tr>
<tr>
<td>4113</td>
<td>2 PCIAAD (culprit lesion failed), so PCI RCA instead to improve the condition.</td>
<td></td>
</tr>
<tr>
<td>4830</td>
<td>95</td>
<td>Physician decision based on hemodynamic situation</td>
</tr>
<tr>
<td>9641</td>
<td>9</td>
<td>Pressure gradient detected: significant stenosis in proximal LAD and mid LCX: no benefit of staged revascularization</td>
</tr>
<tr>
<td>7792</td>
<td>7</td>
<td>After stenting of ostial LAD plaque shift to LCx, after that PCI with DES in LCx</td>
</tr>
<tr>
<td>9640</td>
<td>3</td>
<td>Bifurcated lesion</td>
</tr>
<tr>
<td>2311</td>
<td>11</td>
<td>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.</td>
</tr>
<tr>
<td>3920</td>
<td>6</td>
<td>Initially, despite multiple attempts the culprit lesion (RCA) could not be revascularized by multiple guide wires. The acute thrombotic occlusion was located directly proximal to the high-grade calcified stenosis. Therefore, as an ultimate the additional LCX stenosis was intervened because based on ECG this stenosis may also contribute to acute ischemia. In second attempt RCA was left revascularized and stented.</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Culprit only PCI (n=344)</th>
<th>Multivessel PCI (n=342)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years); median (IQR)</strong></td>
<td>70 (60-73)</td>
<td>73 (60-77)</td>
</tr>
<tr>
<td><strong>Male sex; n/total (%)</strong></td>
<td>257/344 (74.9)</td>
<td>267/342 (78.1)</td>
</tr>
<tr>
<td><strong>Prior myocardial infarction; n/total (%)</strong></td>
<td>60/339 (17.7)</td>
<td>53/335 (15.8)</td>
</tr>
<tr>
<td><strong>Prior PCI; n/total (%)</strong></td>
<td>64/339 (18.9)</td>
<td>63/335 (18.8)</td>
</tr>
<tr>
<td><strong>Prior coronary arterial bypass surgery; n/total (%)</strong></td>
<td>20/341 (5.9)</td>
<td>13/337 (3.9)</td>
</tr>
<tr>
<td><strong>Signs of impaired organ perfusion; n/total (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Altered mental status</td>
<td>237/341 (69.5)</td>
<td>224/341 (65.7)</td>
</tr>
<tr>
<td>Cold, clammy skin and extremities</td>
<td>233/338 (68.9)</td>
<td>236/335 (70.4)</td>
</tr>
<tr>
<td>Oliguria</td>
<td>80/334 (24.0)</td>
<td>93/326 (28.5)</td>
</tr>
<tr>
<td>Arterial lactate &gt;2.0 mmol/l</td>
<td>216/334 (64.7)</td>
<td>224/330 (67.9)</td>
</tr>
<tr>
<td>Fibrinolysis &lt;24 h before randomization; n/total (%)</td>
<td>19/341 (5.6)</td>
<td>15/341 (4.4)</td>
</tr>
<tr>
<td><strong>Resuscitation before randomization; n/total (%)</strong></td>
<td>177/341 (51.9)</td>
<td>189/342 (55.3)</td>
</tr>
<tr>
<td><strong>ST-elevation myocardial infarction; n/total (%)</strong></td>
<td>206/335 (61.5)</td>
<td>209/330 (63.3)</td>
</tr>
<tr>
<td><strong>No. of diseased vessels; n/total (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3/343 (0.9)</td>
<td>2/342 (0.6)</td>
</tr>
<tr>
<td>2</td>
<td>122/343 (35.6)</td>
<td>124/342 (36.3)</td>
</tr>
<tr>
<td>3</td>
<td>218/343 (63.6)</td>
<td>216/342 (63.2)</td>
</tr>
<tr>
<td><strong>Patients with at least one CTO; n/total (%)</strong></td>
<td>77/344 (22.4)</td>
<td>82/342 (24.0)</td>
</tr>
<tr>
<td><strong>Left ventricular ejection fraction (%); median (IQR)</strong></td>
<td>33 (25-40)</td>
<td>39 (21-40)</td>
</tr>
</tbody>
</table>

### Treatment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Culprit only PCI (n=344)</th>
<th>Multivessel PCI (n=342)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Femoral access; n/total (%)</strong></td>
<td>287/343 (83.7)</td>
<td>277/342 (81.0)</td>
</tr>
<tr>
<td><strong>Radial access; n/total (%)</strong></td>
<td>61/343 (17.8)</td>
<td>66/342 (19.3)</td>
</tr>
<tr>
<td><strong>Stent implanted in culprit lesion; n/total (%)</strong></td>
<td>326/343 (95.0)</td>
<td>324/342 (94.7)</td>
</tr>
<tr>
<td><strong>Drug-eluting stent in culprit lesion; n/total (%)</strong></td>
<td>305/326 (93.6)</td>
<td>308/324 (95.1)</td>
</tr>
<tr>
<td><strong>TIMI-flow III post PCI of culprit lesion; n/total (%)</strong></td>
<td>289/342 (84.5)</td>
<td>293/339 (86.7)</td>
</tr>
<tr>
<td><strong>Immediate PCI of non-culprit lesions; n/total (%)</strong></td>
<td>423/344 (12.7)</td>
<td>372/342 (11.0)</td>
</tr>
<tr>
<td><strong>Immediate complete revascularization; n/total (%)</strong></td>
<td>26/344 (7.6)</td>
<td>277/342 (82.1)</td>
</tr>
<tr>
<td><strong>Total amount of contrast agent (ml); median (IQR)</strong></td>
<td>190 (140-250)</td>
<td>250 (200-350)</td>
</tr>
<tr>
<td><strong>Staged PCI of non-culprit lesions; n/total (%)</strong></td>
<td>60/344 (17.4)</td>
<td>8/341 (2.3)</td>
</tr>
<tr>
<td><strong>Staged coronary artery bypass surgery; n/total (%)</strong></td>
<td>1/344 (0.3)</td>
<td>0/341</td>
</tr>
<tr>
<td><strong>Mechanical circulatory support; n/total (%)</strong></td>
<td>99/344 (28.8)</td>
<td>95/342 (27.8)</td>
</tr>
<tr>
<td><strong>Intraaortic balloon pump; n/total (%)</strong></td>
<td>25/344 (25.3)</td>
<td>26/342 (27.4)</td>
</tr>
<tr>
<td><strong>Impella 2.5; n/total (%)</strong></td>
<td>16/344 (16.2)</td>
<td>18/342 (16.9)</td>
</tr>
<tr>
<td><strong>Impella CP; n/total (%)</strong></td>
<td>30/344 (30.3)</td>
<td>18/342 (16.9)</td>
</tr>
<tr>
<td><strong>TandemHeart; n/total (%)</strong></td>
<td>2/344 (2.0)</td>
<td>0/95</td>
</tr>
<tr>
<td><strong>ECMO; n/total (%)</strong></td>
<td>18/344 (18.2)</td>
<td>27/342 (28.4)</td>
</tr>
<tr>
<td><strong>Mild hypothermia; n/total (%)</strong></td>
<td>111/344 (32.2)</td>
<td>118/340 (34.7)</td>
</tr>
<tr>
<td><strong>Mechanical ventilation; n/total (%)</strong></td>
<td>27/344 (19.4)</td>
<td>282/339 (85.3)</td>
</tr>
<tr>
<td><strong>Duration of mechanical ventilation (days); median (IQR)</strong></td>
<td>2 (1-7)</td>
<td>3 (1-7)</td>
</tr>
<tr>
<td><strong>Duration of intensive care treatment (days); median (IQR)</strong></td>
<td>5 (2-12)</td>
<td>5 (2-11)</td>
</tr>
</tbody>
</table>
CULPRIT-SHOCK Trial – 30-Day Results

Primary study endpoint – 30 days
All-cause mortality or renal replacement therapy

All-cause mortality – 30 days

CULPRIT-SHOCK Trial – Subgroups

<table>
<thead>
<tr>
<th>Baseline Variable</th>
<th>Multivessel PCI</th>
<th>Culprit lesion only PCI</th>
<th>Relative Risk (95% CI)</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>148/256 (55.6)</td>
<td>166/307 (54.3)</td>
<td>0.76 (0.64-0.91)</td>
<td>0.11</td>
</tr>
<tr>
<td>Female</td>
<td>417/736 (56.7)</td>
<td>466/862 (55.8)</td>
<td>1.02 (0.77-1.35)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50 years</td>
<td>31/56 (16.8)</td>
<td>67/127 (52.8)</td>
<td>0.50 (0.31-0.82)</td>
<td>0.04</td>
</tr>
<tr>
<td>50-75 years</td>
<td>11/26 (42.3)</td>
<td>62/121 (51.6)</td>
<td>1.05 (0.69-1.58)</td>
<td>0.85</td>
</tr>
<tr>
<td>&gt;75 years</td>
<td>7/22 (31.8)</td>
<td>70/115 (60.5)</td>
<td>1.03 (0.65-1.64)</td>
<td>0.90</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>196/345 (57.4)</td>
<td>209/372 (55.3)</td>
<td>0.86 (0.62-1.19)</td>
<td>0.47</td>
</tr>
<tr>
<td>Yes</td>
<td>66/116 (56.6)</td>
<td>58/103 (56.6)</td>
<td>0.79 (0.58-1.07)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>114/205 (56.6)</td>
<td>86/180 (47.1)</td>
<td>0.82 (0.62-1.09)</td>
<td>0.96</td>
</tr>
<tr>
<td>Yes</td>
<td>68/129 (52.7)</td>
<td>102/225 (45.6)</td>
<td>0.79 (0.58-1.07)</td>
<td></td>
</tr>
<tr>
<td>Type of infarction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSTEMI</td>
<td>54/97 (55.7)</td>
<td>45/84 (49.0)</td>
<td>0.82 (0.62-1.09)</td>
<td>0.96</td>
</tr>
<tr>
<td>STEMI</td>
<td>128/223 (54.9)</td>
<td>106/191 (55.6)</td>
<td>0.82 (0.62-1.09)</td>
<td></td>
</tr>
<tr>
<td>STEMI type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior infarction</td>
<td>38/68 (55.9)</td>
<td>57/105 (54.2)</td>
<td>0.80 (0.59-1.09)</td>
<td>0.37</td>
</tr>
<tr>
<td>Non-anterior infarction</td>
<td>50/72 (69.4)</td>
<td>47/107 (43.9)</td>
<td>0.43 (0.32-0.56)</td>
<td>0.003</td>
</tr>
<tr>
<td>Previous infarction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>154/251 (61.6)</td>
<td>128/270 (46.9)</td>
<td>0.80 (0.62-1.06)</td>
<td>0.43</td>
</tr>
<tr>
<td>Yes</td>
<td>26/53 (49.1)</td>
<td>25/50 (50.0)</td>
<td>0.78 (0.53-1.17)</td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-vessel disease</td>
<td>54/124 (43.5)</td>
<td>48/122 (39.3)</td>
<td>0.78 (0.58-1.01)</td>
<td>0.96</td>
</tr>
<tr>
<td>3-vessel disease</td>
<td>124/215 (57.7)</td>
<td>106/186 (56.0)</td>
<td>0.87 (0.73-1.03)</td>
<td></td>
</tr>
<tr>
<td>Chronic total occlusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>146/230 (64.4)</td>
<td>121/207 (49.1)</td>
<td>0.81 (0.54-1.20)</td>
<td>0.36</td>
</tr>
<tr>
<td>Yes</td>
<td>42/66 (63.6)</td>
<td>27/77 (35.1)</td>
<td>0.67 (0.40-1.08)</td>
<td></td>
</tr>
</tbody>
</table>
### Multivessel PCI in Shock - Guideline Evolution

**ESC STEMI Guidelines 2017 → Revascularization Guidelines 2018**

#### 2017

- I
- Ila
- IIb
- III

#### 2018

- I
- IIa
- IIb
- III

---

### Metaanalysis Mortality – Registry-Data

#### Short-term follow-up

<table>
<thead>
<tr>
<th>Study</th>
<th>MV-PCI Events</th>
<th>MV-PCI Total</th>
<th>C-PCI Events</th>
<th>C-PCI Total</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>IABP-SHOCK II</td>
<td>75</td>
<td>167</td>
<td>119</td>
<td>266</td>
<td>1.97</td>
<td>[0.60-1.33]</td>
</tr>
<tr>
<td>AMIR</td>
<td>31</td>
<td>173</td>
<td>293</td>
<td>562</td>
<td>1.31</td>
<td>[0.81-1.36]</td>
</tr>
<tr>
<td>KAMIR</td>
<td>11</td>
<td>128</td>
<td>96</td>
<td>256</td>
<td>0.72</td>
<td>[0.41-1.26]</td>
</tr>
<tr>
<td>Yang et al.</td>
<td>19</td>
<td>80</td>
<td>88</td>
<td>278</td>
<td>1.29</td>
<td>[0.80-1.28]</td>
</tr>
<tr>
<td>Cavender et al.</td>
<td>28</td>
<td>63</td>
<td>42</td>
<td>136</td>
<td>1.73</td>
<td>[1.16-2.81]</td>
</tr>
<tr>
<td>EHS-PCI</td>
<td>49</td>
<td>82</td>
<td>86</td>
<td>236</td>
<td>1.26</td>
<td>[0.81-1.71]</td>
</tr>
<tr>
<td>MEHS</td>
<td>108</td>
<td>433</td>
<td>737</td>
<td>2583</td>
<td>1.21</td>
<td>[1.04-1.41]</td>
</tr>
<tr>
<td>Overall</td>
<td>406</td>
<td>1082</td>
<td>1318</td>
<td>4574</td>
<td>1.26</td>
<td>[1.12-1.41]</td>
</tr>
</tbody>
</table>

**Heterogeneity:** I²=58.6%, τ²=0.19  
**Test for overall effect:** p=0.001

#### Long-term follow-up

<table>
<thead>
<tr>
<th>Study</th>
<th>MV-PCI Events</th>
<th>MV-PCI Total</th>
<th>C-PCI Events</th>
<th>C-PCI Total</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>IABP-SHOCK II</td>
<td>75</td>
<td>167</td>
<td>119</td>
<td>266</td>
<td>1.94</td>
<td>[0.67-1.24]</td>
</tr>
<tr>
<td>AMIR</td>
<td>31</td>
<td>173</td>
<td>293</td>
<td>562</td>
<td>0.72</td>
<td>[0.43-1.19]</td>
</tr>
<tr>
<td>Yang et al.</td>
<td>19</td>
<td>80</td>
<td>88</td>
<td>278</td>
<td>1.16</td>
<td>[0.74-1.58]</td>
</tr>
<tr>
<td>Cavender et al.</td>
<td>28</td>
<td>63</td>
<td>42</td>
<td>136</td>
<td>1.10</td>
<td>[0.83-1.42]</td>
</tr>
<tr>
<td>Mylotte et al.</td>
<td>22</td>
<td>43</td>
<td>751</td>
<td>159</td>
<td>0.70</td>
<td>[0.44-1.09]</td>
</tr>
<tr>
<td>van der Schuer et al.</td>
<td>20</td>
<td>37</td>
<td>86</td>
<td>172</td>
<td>1.12</td>
<td>[0.86-1.49]</td>
</tr>
<tr>
<td>SHOCK</td>
<td>7</td>
<td>8</td>
<td>86</td>
<td>207</td>
<td>1.11</td>
<td>[0.84-1.48]</td>
</tr>
<tr>
<td>Overall</td>
<td>226</td>
<td>506</td>
<td>578</td>
<td>1387</td>
<td>1.03</td>
<td>[0.85-1.25]</td>
</tr>
</tbody>
</table>

**Heterogeneity:** I²=54.6%, τ²=0.68  
**Test for overall effect:** p=0.77

---

MHIF Cardiovascular Grand Rounds – May 11, 2020
1-Year All-Cause Mortality or Renal Replacement Therapy

Number at risk:
- Culprit-lesion-only PCI: 344, 179, 174, 171, 167, 165, 142
- Immediate multivessel PCI: 341, 149, 149, 145, 142, 139, 122

Patients Who Died or Underwent Renal Replacement Therapy (%)
Relative Risk (95% CI) 0.87 (0.76-0.99); P=0.048

1-Year All-Cause Mortality – Landmark Analysis

Number at risk:
- Multivessel PCI: 165, 161, 160, 156, 152, 149, 131
- Culprit-lesion-only PCI: 195, 186, 181, 178, 174, 172, 147

Patients Who Died from Any Cause (%)
Relative Risk (95% CI) 1.08 (0.60-1.93); P=0.86

Relative Risk (95% CI) 0.84 (0.72-0.98); P=0.03
Shock vs no Shock – Different Animals?

First co-primary outcome
CV death, or new MI

- Complete
- Culprit only

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>Years of follow-up</th>
<th>Cumulative incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete 2016</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Complete 2025</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Culprit only 2025</td>
<td>1666</td>
<td>0</td>
</tr>
<tr>
<td>Culprit only 2025</td>
<td>310</td>
<td>0</td>
</tr>
</tbody>
</table>

- Complete
- Culprit only

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>Years of follow-up</th>
<th>Cumulative incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete 2016</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Complete 2025</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Culprit only 2025</td>
<td>1666</td>
<td>0</td>
</tr>
<tr>
<td>Culprit only 2025</td>
<td>310</td>
<td>0</td>
</tr>
</tbody>
</table>

NNT (median 3 years) = 37
Hazard Ratio 0.74
95% CI 0.60; 0.91
P=0.004

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

- Complete
- Culprit only

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>Years of follow-up</th>
<th>Cumulative incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete 2016</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Complete 2025</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Culprit only 2025</td>
<td>1666</td>
<td>0</td>
</tr>
<tr>
<td>Culprit only 2025</td>
<td>310</td>
<td>0</td>
</tr>
</tbody>
</table>

NNT (median 3 years) = 13
Hazard Ratio 0.51
95% CI 0.43; 0.61
P<0.001

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

Revascularization Options

Cardiogenic shock

- Culprit Lesion Only
- Culprit lesion only + Staged Revasc.
- CABG
- Immediate MV-PCI
1-Year Repeat Revascularization

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

- Patients Who Underwent Repeat Revascularization (%)
  - Immediate multivessel PCI: 32.3%
  - Culprit-lesion-only PCI: 9.4%

Revascularization Options

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

- Culprit Lesion Only
- Culprit lesion only + Staged Revasc.
- CABG
- Immediate MV-PCI

Thiele et al. NEJM 2018;379:1699-1710
CV-PCI vs MV-PCI in patients with NSTEMI
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

![Flowchart showing study population](Image)
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
Table 1: Baseline characteristics

<table>
<thead>
<tr>
<th>Variable (%)</th>
<th>Before matching</th>
<th>After matching</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Multivessel PCI</td>
<td>Culprit Vessel PCI</td>
</tr>
<tr>
<td></td>
<td>n = 9,791</td>
<td>n = 15,533</td>
</tr>
<tr>
<td>Patient demographics:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean years</td>
<td>69.2 ± 11.9</td>
<td>69.2 ± 11.7</td>
</tr>
<tr>
<td>Female</td>
<td>3384 (34.6%)</td>
<td>4974 (32.0%)</td>
</tr>
<tr>
<td>Race - White</td>
<td>81 (83.1%)</td>
<td>1390 (84.7%)</td>
</tr>
<tr>
<td>BMI</td>
<td>29.2 ± 6.9</td>
<td>29.2 ± 8.7</td>
</tr>
<tr>
<td>Primary expected payer:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>6452 (65.9%)</td>
<td>10217 (65.8%)</td>
</tr>
<tr>
<td>Medicaid</td>
<td>1319 (13.5%)</td>
<td>2035 (13.1%)</td>
</tr>
<tr>
<td>Private insurance</td>
<td>5462 (55.8%)</td>
<td>8658 (55.7%)</td>
</tr>
<tr>
<td>No-insurance</td>
<td>590 (6.0%)</td>
<td>957 (6.2%)</td>
</tr>
<tr>
<td>Medical history:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current/Recent Smoker</td>
<td>2353 (24.1%)</td>
<td>4015 (25.9%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>8176 (83.6%)</td>
<td>13105 (84.4%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>7204 (73.7%)</td>
<td>11609 (74.9%)</td>
</tr>
<tr>
<td>EF of Premature CAD</td>
<td>1354 (13.8%)</td>
<td>2485 (15.8%)</td>
</tr>
<tr>
<td>Prior MI</td>
<td>3454 (35.3%)</td>
<td>6146 (39.5%)</td>
</tr>
<tr>
<td>Prior Heart Failure</td>
<td>3290 (33.6%)</td>
<td>5083 (32.7%)</td>
</tr>
<tr>
<td>Prior Valve Surgery</td>
<td>232 (2.6%)</td>
<td>487 (3.1%)</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>3080 (31.4%)</td>
<td>5582 (34.7%)</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>1666 (16.4%)</td>
<td>4726 (30.4%)</td>
</tr>
<tr>
<td>Currently on Dialysis</td>
<td>117 (11.4%)</td>
<td>1490 (33.5%)</td>
</tr>
<tr>
<td>Cerebrovascular Disease</td>
<td>1997 (20.4%)</td>
<td>3211 (20.7%)</td>
</tr>
<tr>
<td>Peripheral Arterial Disease</td>
<td>2210 (22.6%)</td>
<td>3577 (22.9%)</td>
</tr>
<tr>
<td>Chronic Lung Disease</td>
<td>2149 (22.0%)</td>
<td>3655 (23.4%)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>5206 (53.1%)</td>
<td>7999 (51.3%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable (%)</th>
<th>Standardized Difference (10%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Culprit Vessel PCI</td>
</tr>
<tr>
<td></td>
<td>n = 7,864</td>
</tr>
<tr>
<td></td>
<td>52 of 57</td>
</tr>
</tbody>
</table>

Results

<table>
<thead>
<tr>
<th>Variable (%)</th>
<th>Before matching</th>
<th>After matching</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Multivessel PCI</td>
<td>Culprit Vessel PCI</td>
</tr>
<tr>
<td></td>
<td>n = 8,791</td>
<td>n = 15,533</td>
</tr>
<tr>
<td>Cath Lab Visit:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI Status</td>
<td>10.8</td>
<td></td>
</tr>
<tr>
<td>Urgent</td>
<td>4871 (49.2%)</td>
<td>7268 (46.9%)</td>
</tr>
<tr>
<td>Emergent</td>
<td>5728 (58.1%)</td>
<td>6539 (42.1%)</td>
</tr>
<tr>
<td>Salvage</td>
<td>962 (9.8%)</td>
<td>1190 (7.7%)</td>
</tr>
<tr>
<td>Cardiac Arrest Within 24 Hours</td>
<td>3272 (12.4%)</td>
<td>4024 (24.4%)</td>
</tr>
<tr>
<td></td>
<td>1872 (23.6%)</td>
<td>1804 (23.7%)</td>
</tr>
<tr>
<td>Pro-PCL LV EF</td>
<td>5.9 ± 21.9</td>
<td>56.5 ± 21.7</td>
</tr>
<tr>
<td></td>
<td>33.1 ± 14.9</td>
<td>35.2 ± 15.2</td>
</tr>
<tr>
<td>GFR</td>
<td>5.9 ± 21.9</td>
<td>56.5 ± 21.7</td>
</tr>
<tr>
<td>LVEF</td>
<td>4338.5 (55.1%)</td>
<td>436 (52.5%)</td>
</tr>
<tr>
<td>Other MCA</td>
<td>2523 (21.7%)</td>
<td>1506 (19.7%)</td>
</tr>
<tr>
<td>Arterial access</td>
<td>2 (2.2)</td>
<td>2 (2.2)</td>
</tr>
<tr>
<td>Femoral access</td>
<td>8648 (88.8%)</td>
<td>13755 (86.8%)</td>
</tr>
<tr>
<td>Radial access</td>
<td>1072 (11.0%)</td>
<td>1644 (10.6%)</td>
</tr>
<tr>
<td>Other</td>
<td>68 (0.7%)</td>
<td>131 (0.8%)</td>
</tr>
<tr>
<td>Contrast volume:</td>
<td>230.4 ± 109.1</td>
<td>183.4 ± 89.9</td>
</tr>
<tr>
<td>Fluoroscopy Time</td>
<td>26.3 ± 17.3</td>
<td>18.5 ± 13.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable (%)</th>
<th>Standardized Difference (10%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Culprit Vessel PCI</td>
</tr>
<tr>
<td></td>
<td>n = 7,864</td>
</tr>
<tr>
<td></td>
<td>52 of 57</td>
</tr>
</tbody>
</table>

52 of 57
Results

<table>
<thead>
<tr>
<th>Variable (%)</th>
<th>Before matching</th>
<th>Culprit Vessel PCI</th>
<th>Standardized Difference (10%)</th>
<th>After matching</th>
<th>Culprit Vessel PCI</th>
<th>Standardized Difference (10%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Multivessel PCI</td>
<td>multivessel PCI</td>
<td></td>
<td></td>
<td>multivessel PCI</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n= 5,791</td>
<td>n= 15,533</td>
<td></td>
<td>n= 7,864</td>
<td>n= 7,864</td>
<td></td>
</tr>
<tr>
<td>Disease and intervened vessels</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left main disease</td>
<td>3584 (36.6%)</td>
<td>3243 (20.9%)</td>
<td>35.3</td>
<td>2109 (26.8%)</td>
<td>2181 (27.7%)</td>
<td>2.1</td>
</tr>
<tr>
<td>LAD disease</td>
<td>8746 (89.3%)</td>
<td>12958 (83.4%)</td>
<td>17.3</td>
<td>6904 (87.8%)</td>
<td>6852 (87.1%)</td>
<td>2.0</td>
</tr>
<tr>
<td>RCA disease</td>
<td>7187 (73.4%)</td>
<td>12768 (82.3%)</td>
<td>21.3</td>
<td>5990 (76.0%)</td>
<td>6029 (76.7%)</td>
<td>1.5</td>
</tr>
<tr>
<td>LCx disease</td>
<td>8069 (82.4%)</td>
<td>11625 (74.9%)</td>
<td>18.5</td>
<td>6346 (80.7%)</td>
<td>6307 (80.2%)</td>
<td>1.3</td>
</tr>
<tr>
<td>Prior LAD disease</td>
<td>6000 (61.5%)</td>
<td>7784 (50.1%)</td>
<td>27.6</td>
<td>4437 (56.4%)</td>
<td>4424 (56.3%)</td>
<td>0.1</td>
</tr>
<tr>
<td>Left main intervened</td>
<td>3243 (33.1%)</td>
<td>873 (5.6%)</td>
<td>24.1</td>
<td>1919 (24.9%)</td>
<td>609 (7.7%)</td>
<td>46.6</td>
</tr>
<tr>
<td>LAD intervened</td>
<td>7112 (73.8%)</td>
<td>5564 (35.8%)</td>
<td>46.4</td>
<td>6025 (76.6%)</td>
<td>3144 (60.0%)</td>
<td>80.0</td>
</tr>
<tr>
<td>RCA intervened</td>
<td>4046 (41.3%)</td>
<td>4397 (28.3%)</td>
<td>27.6</td>
<td>3553 (45.2%)</td>
<td>1938 (24.6%)</td>
<td>44.1</td>
</tr>
<tr>
<td>LCx intervened</td>
<td>7023 (71.7%)</td>
<td>4697 (30.2%)</td>
<td>91.3</td>
<td>5631 (71.6%)</td>
<td>2173 (27.6%)</td>
<td>97.9</td>
</tr>
<tr>
<td>LAD culprit</td>
<td>4705 (48.0%)</td>
<td>5564 (35.8%)</td>
<td>24.9</td>
<td>3575 (45.5%)</td>
<td>3144 (60.0%)</td>
<td>11.1</td>
</tr>
<tr>
<td>RCA culprit</td>
<td>1970 (20.1%)</td>
<td>4397 (28.3%)</td>
<td>19.2</td>
<td>1731 (22.3%)</td>
<td>1938 (24.6%)</td>
<td>3.6</td>
</tr>
<tr>
<td>LCx culprit</td>
<td>3831 (39.1%)</td>
<td>4697 (30.2%)</td>
<td>18.8</td>
<td>3016 (38.4%)</td>
<td>2173 (27.6%)</td>
<td>22.9</td>
</tr>
<tr>
<td>Left main culprit</td>
<td>2133 (22.6%)</td>
<td>875 (5.6%)</td>
<td>52.6</td>
<td>1352 (17.2%)</td>
<td>609 (7.7%)</td>
<td>28.9</td>
</tr>
<tr>
<td>Chronic total occlusion PCI</td>
<td>877 (9.0%)</td>
<td>807 (5.2%)</td>
<td>14.7</td>
<td>745 (9.5%)</td>
<td>430 (5.5%)</td>
<td>15.3</td>
</tr>
<tr>
<td>Pre-PCI TIMI0</td>
<td>3038 (31.0%)</td>
<td>5112 (32.9%)</td>
<td>4.0</td>
<td>2592 (33.0%)</td>
<td>2638 (33.5%)</td>
<td>1.2</td>
</tr>
<tr>
<td>Class C lesion</td>
<td>8146 (83.2%)</td>
<td>10744 (69.2%)</td>
<td>33.4</td>
<td>6516 (80.3%)</td>
<td>6309 (80.2%)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Clinical Outcomes

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

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

## 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.


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 term 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 inhospital mortality but similar long-term survival compared with culprit vessel PCI.

3- Further well-designed RCTs are still needed!