Optimal Treatment Strategy for AMI Patients with Non-culprit Stenosis: Role of Physiology Guidance

Joo Myung Lee, MD, MPH, PhD
On Behalf of FRAME-AMI Trial Investigators

Heart Vascular Stroke Institute,
Samsung Medical Center, Seoul, Republic of Korea
Increasing Prevalence of ACS

144,039 Swedish patients (SCAAR Registry) undergoing PCI (1990-2010)

Fokkema et al. JACC 2013

STEMI
FFR-guided Decision in ACS Setting
- Per-vessel Decision -

Culprit

Non culprit
Impact of Acute MV damage to FFR (Culprit) in ACS

During ACS, Variable degree of MV damage and stunning
Pressure gradient become Smaller, event max hyperemia
Higher FFR and FFR underestimate lesion severity

FFR has limited role in “Clear Culprit Vessel” in ACS patient
FFR-guided Decision in ACS Setting
- Per-vessel Decision -
Multivessel Disease in ACS

- **30-40% in the setting of STEMI**
  


- **44-60% in the setting of NSTEMI**
  

Non-culprit PCI in STEMI multivessel

Previous Guidelines – ESC, ACC/AHA

Based on Very weak evidence

1 Narrative Review (Holmes DR Jr.)
2 Retrospective PS matched Study
   (Staged non-culprit PCI in same hospitalization N=259 vs. Staged PCI within 60 days, N=538)
3 Post-hoc analysis of RCT
   (Non-culprit PCI 217 patient vs. Culprit only 1984 patient)
4 Network meta-analysis

Is This Truly Scientific?

Previous Guidelines basically recommend culprit only PCI in case of STEMI and NSTEMI (except cardiogenic shock)

Based on Very weak evidence
Non-culprit Lesion PCI after Primary PCI - Angio-guided Complete Revascularization vs. Culprit-Only PCI-

PRAMI – cardiac death, non-fatal MI, refractory angina

CvLPRIT – all death, recurrent MI, HF, ischemia-revascularization

New Evidences suggests “Angiography-guided” Complete Revascularization showed Significant benefit in Patient’s outcome than “Culprit-Only PCI”

In terms of hard endpoint (Death, MI \(\rightarrow\) PRAMI) or In terms of soft endpoint (MACE but not death/MI \(\rightarrow\) CvPRIT)

Preventive PCI for non-culprit lesion >50% DS
Preventive PCI for non-culprit lesion > 70% DS or > 50% DS in 2 views
Non-culprit Lesion PCI after Primary PCI in STEMI
- FFR-guided Complete Revascularization vs. Culprit-Only PCI -

**DANAMI-3-PRIMULTI**

HR 0.56, p=0.004
(95% CI 0.38-0.83)
44% risk reduction

- “FFR-guided” Complete Revascularization showed
  Significant benefit in terms of composite endpoints
  (Any Death, MI, I-D revascularization)

**COMPARE ACUTE Trial**

HR 0.35 (95% CI 0.22-0.55), log-rank p<0.001
65% Risk Reduction

Number at risk
IRA 313
Complete 314

0 12 24 36
Follow-up (months)
0 5 10 15 20 25 30 35
Primary endpoint (%)

No. at Risk
<table>
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<tr>
<th>Months</th>
<th>0</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
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<tbody>
<tr>
<td>FFR-CR</td>
<td>295</td>
<td>286</td>
<td>281</td>
<td>264</td>
<td>215</td>
</tr>
<tr>
<td>Culprit-Only</td>
<td>590</td>
<td>512</td>
<td>492</td>
<td>457</td>
<td>371</td>
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COMPARE-ACUTE NEJM 2017 Mar 18; ACC 2017
Non-culprit PCI in STEMI multivessel Updated ESC Guideline

Most recent guideline changed recommendation to Class Iia

However, Unsolved Issues are remained..........

① Best criteria for PCI (FFR, %DS, Vulnerability)

② Timing of Non-IRA PCI (Immediate, Staged, After Discharge)
1292 Patients with Acute Myocardial Infarction with Multivessel Disease (STEMI 646 patients, NSTEMI 646 patients) (>50% by visual estimation in non-IRA)

Primary PCI for IRA

Randomization for Non-IRA stenosis (Stratified by STEMI, NSTEMI)

FFR-guided Complete Revascularization (N=646)

*Immediate FFR-guided decision for non-IRA stenosis

- FFR ≤ 0.80 (IV adenosine or IC nicorandil)
  - Perform Immediate Revascularization
- FFR > 0.80 (IV adenosine or IC nicorandil)
  - Defer Revascularization

Angio-guided Complete Revascularization (N=646)

*Immediate Angio-guided decision for non-IRA stenosis

- >50% stenosis (Visual or QCA)
  - Perform Immediate Revascularization

16 Centers in Korea
Bon-Kwon Koo, Joo-Yong Hahn, Joo Myung Lee, Chang-Wook Nam, Eun-Seok Shin, Joon-Hyung Doh

The non-IRA PCI should be performed during the same intervention, however, exceptions can be made for complex lesions where the operator estimates that the revascularization procedure will require significant contrast overload which may lead to deterioration of cardiac and renal function of the patient.

Such procedures can be performed in a staged procedure during the same hospitalization.

Analysis at 24 months after Index Procedure

<table>
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<tr>
<th>Primary Endpoint</th>
<th>A composite of All death, Any Myocardial Infarction, Any Revascularization</th>
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<tbody>
<tr>
<td>Secondary Endpoints</td>
<td>All-cause mortality, any myocardial infarction with or without periprocedural MI, any revascularization, cerebrovascular accident, angina symptom score (Seattle Angina Questionnaire), ARC-defined stent thrombosis, incidence of contrast induced nephropathy</td>
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</table>
FFR use in Non-culprit lesions in STEMI

40 STEMI patients, PS matched with 40 Stable Angina without obstructive lesion

A. CFR (Doppler)  B. Resting APV  C. Hyperemic APV

Blunted hyperemic response in STEMI setting
Possibility of underestimation of non-culprit lesion severity by using FFR

Is This True ???
FFR use in Non-culprit lesions in STEMI/NSTEMI

101 patients with ACS (75 STEMI, 26 NSTEMI)
112 non-culprit stenoses – FFR at index and F/U (35 ± 24 days)

- In only 2/112 non-culprit stenoses was the FFR > 0.80 during ACS and < 0.75 at follow-up
FFR use in Non-culprit lesions in STEMI/NSTEMI

101 patients with ACS (75 STEMI, 26 NSTEMI)
112 non-culprit stenoses – FFR at index and F/U (35±24 days)

- Microvascular resistance in non-culprit was not changed from baseline to follow-up

Ntalianis et al. JACC Intv 2010;3:1274
Secondary MV damage
- Regional Problem, Preclinical Validation -

Inducing Overt MV damage in LAD with Repeated IC injection of Microsphere 50um \((1.8 \times 10^4\text{ microspheres/ml})\)
Artificial Stenosis was created in both LAD and LCX (mean %AS 48.1%)

→ Comprehensive assessment in LAD (culprit) and LCX (non-culprit)
Microvascular damage can be considered as “Regional Problem” in culprit vessel territory only.
MV damage in AMI setting
- Results: Resting Index -

Additional Experiments with more severe baseline stenosis
(Subject N=3, total 135 repeated measurements)

LAD (Microsphere)

LCX (No Microsphere)

Significant Increase of Resting Pd/Pa and iFR in LAD
No Changes of Resting Pd/Pa and iFR in LCX

* Please note, the baseline Pd/Pa 0.78±0.03, baseline iFR 0.70±0.03 in LAD
FFR for Non-Culprit Stenosis Evaluation
- Real World Patient Data (Samsung Medical Center) -

100 AMI with Multivessel Disease (FFR/CFR/IMR at Acute stage) vs. 203 Stable IHD Patients (Part of IMR registry, NCT02186093)
iFR / FFR for Non-Culprit Stenosis Evaluation - Real World Patient Data (Samsung Medical Center) -

100 AMI with Multivessel Disease (FFR/CFR/IMR at Acute stage) vs. 203 Stable IHD Patients (Part of IMR registry, NCT02186093)

Fractional Flow Reserve

Interaction P (SIHD vs. AMI) = 0.371
iFR / FFR for Non-Culprit Stenosis Evaluation
- Real World Patient Data (Samsung Medical Center) -

100 AMI with Multivessel Disease (FFR/CFR/IMR at Acute stage)
vs. 203 Stable IHD Patients (Part of IMR registry, NCT02186093)

Instantaneous Wave Free Ratio

Interaction P (SIHD vs. AMI) = 0.335
Per-vessel level decision in ACS patients

- For the “Clear Culprit Lesion” of Acute STEMI and NSTEMI, FFR may be unreliable due to microvascular damage and stunning.

- For the “Non-Culprit Lesion” of STEMI and NSTEMI (multivessel), FFR-guided decision making is reasonable and reliable.

- Although use of iFR needs more clinical data, our results support clinical relevance of iFR for non-culprit stenosis, even in the acute setting.

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<tr>
<th></th>
<th>SIHD</th>
<th>NSTE-ACS</th>
<th>STEMI (acute)</th>
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<tbody>
<tr>
<td>Clear Culprit</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Non-culprit</td>
<td>+</td>
<td>+</td>
<td>+</td>
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Per-patient level decision in ACS with multivessel disease

- In STEMI with multivessel disease, FFR-guided complete revascularization for non-culprit lesion improves clinical outcome than culprit-only PCI (DANAMI-3-PRIMULTI, COMPARE-ACUTE).

- In STEMI/NSTEMI with multivessel disease, More evidence is needed to compare FFR-guided CR vs. Angio-guided CR. FRAME-AMI Trial will clarify this issue.