

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

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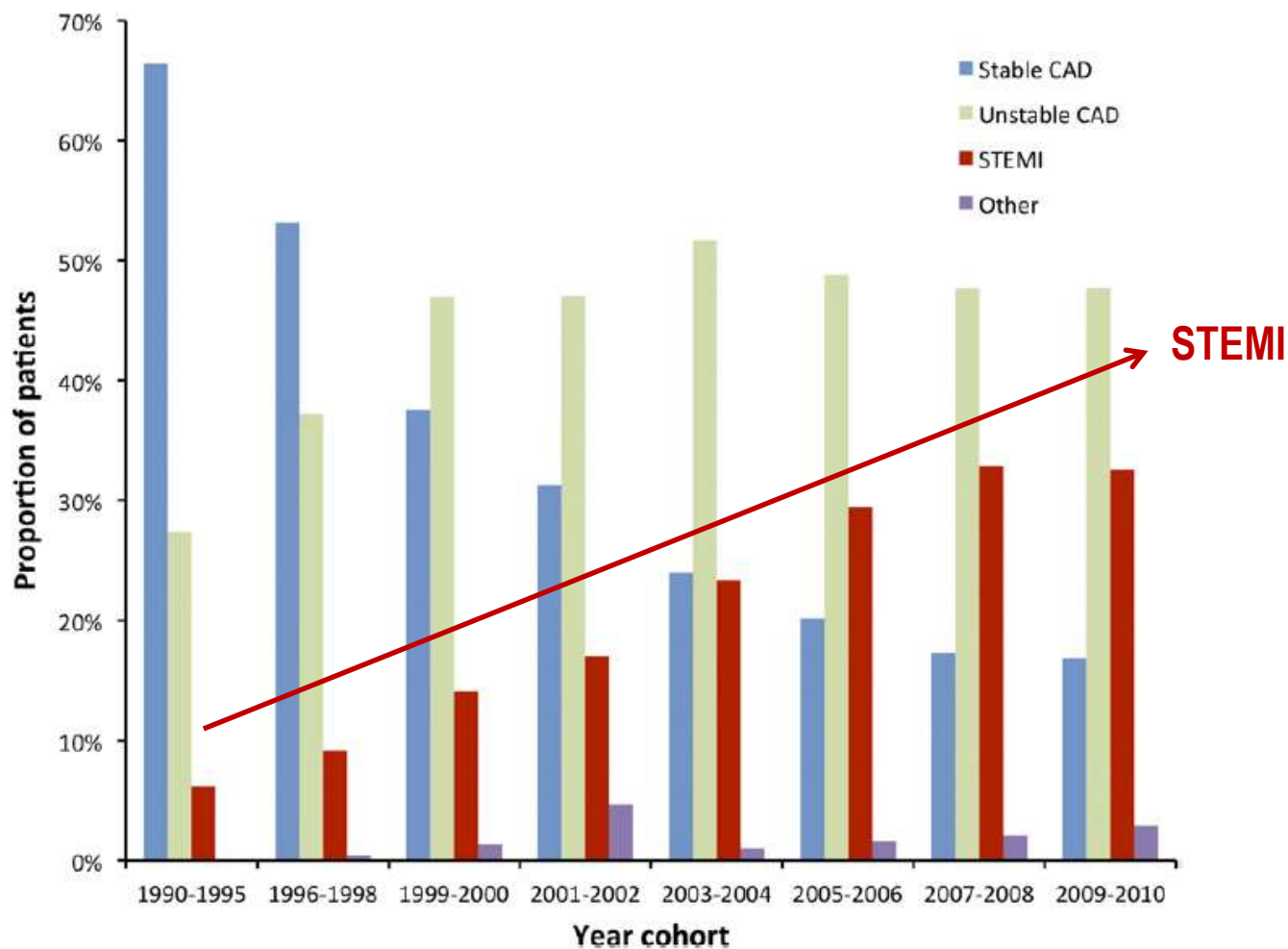
On Behalf of FRAME-AMI Trial Investigators

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Samsung Medical Center, Seoul, Republic of Korea**



Increasing Prevalence of ACS

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



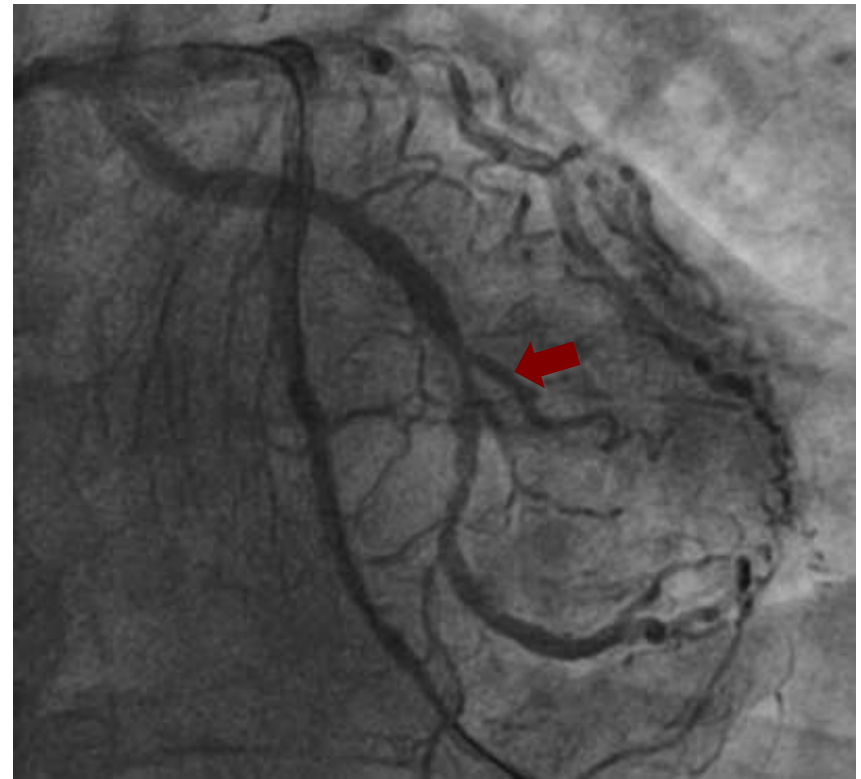
FFR-guided Decision in ACS Setting

- Per-vessel Decision -

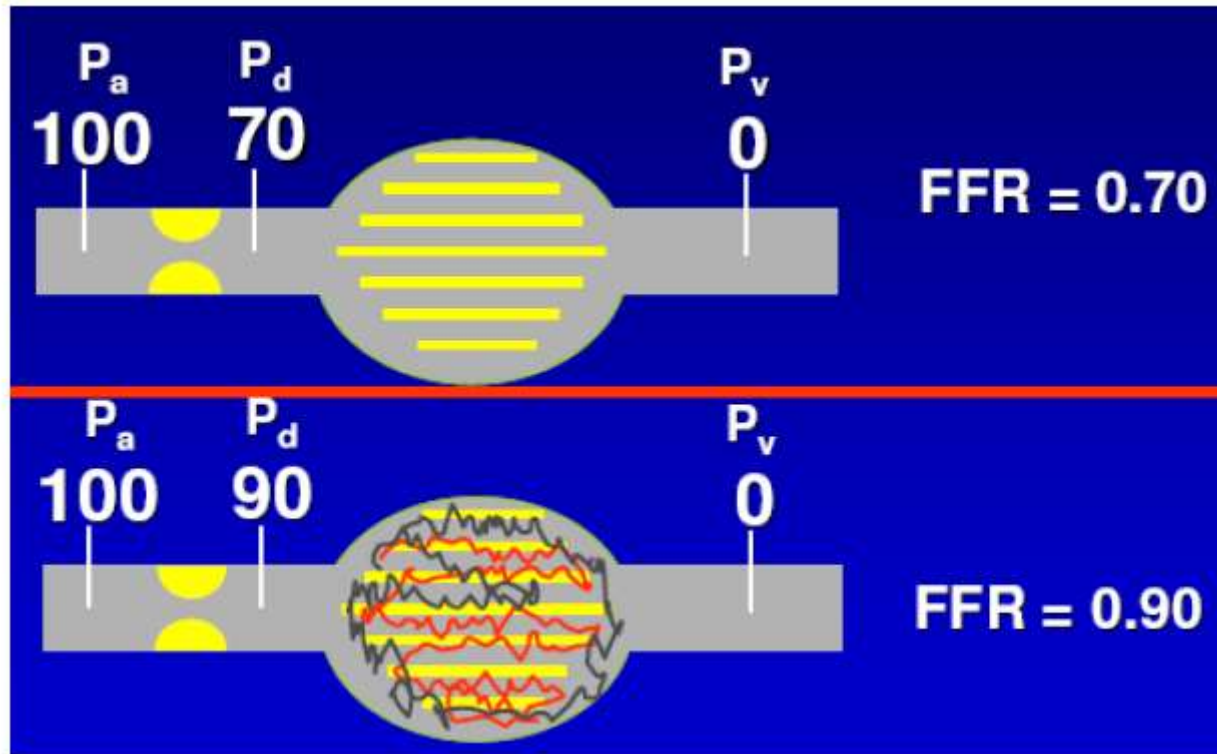
Culprit



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

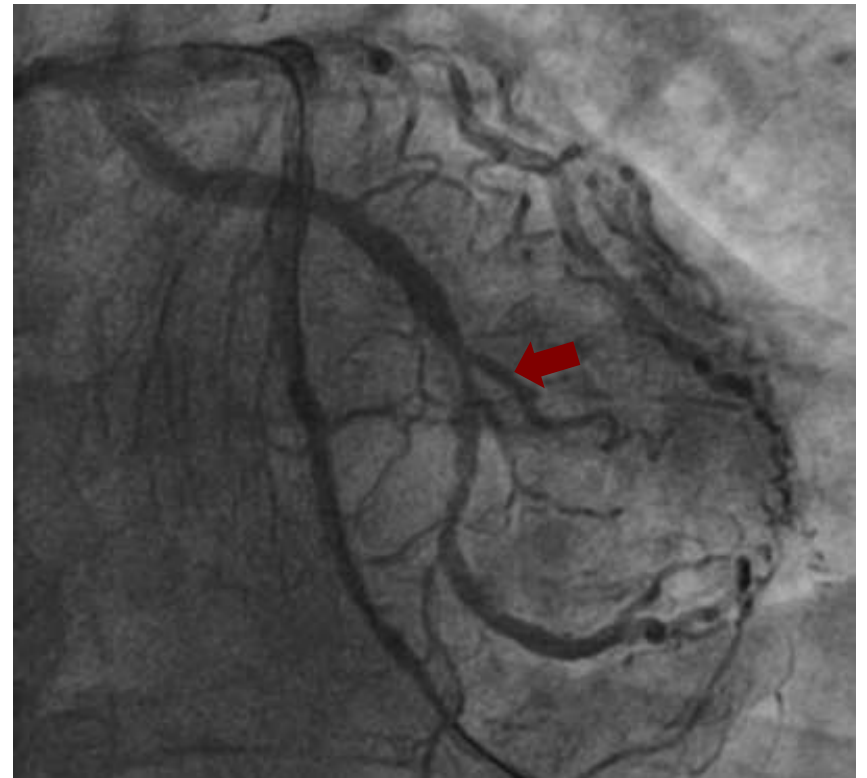
FFR-guided Decision in ACS Setting

- Per-vessel Decision -

Culprit



Non culprit



Multivessel Disease in ACS

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

Muller DW, et al Multivessel coronary artery disease: a key predictor of short-term prognosis after reperfusion therapy for acute myocardial infarction. Thrombolysis and Angioplasty in Myocardial Infarction (TAMI) Study Group. Am Heart J 1991;121:1042-9

Toma M., et al. Non-culprit coronary artery percutaneous coronary intervention during acute ST-segment elevation myocardial infarction: insights from the APEX-AMI trial. European Heart Journal 2010;31:1701-7

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

Effects of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non-Q-wave myocardial infarction. Results of the TIMI IIIB Trial. Thrombolysis in Myocardial Ischemia. Circulation 1994;89:1545–1556.

Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. FRagmin and Fast Revascularisation during InStability in Coronary artery disease Investigators. Lancet 1999;354:708–715.

Non-culprit PCI in STEMI multivessel

Previous Guidelines – ESC, ACC/AHA

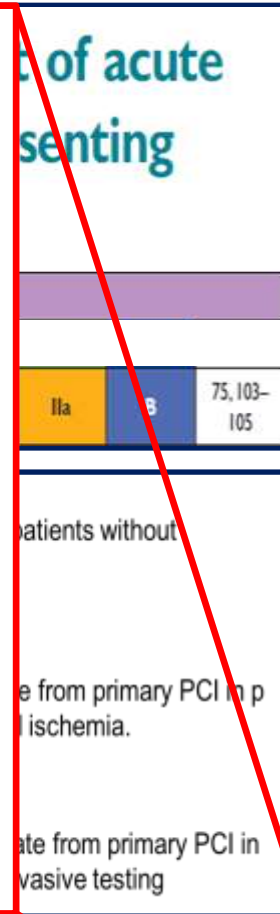
ESC

Based on Very weak evidence

- ① 1 Narrative Review (Holmes DR Jr.)
- ② Retrospective PS matched Study
(Staged non-culprit PCI in same hospitalization N=259 vs. Staged PCI within 60days, N=538)
- ③ Post-hoc analysis of RCT
(Non-culprit PCI 217 patient vs. Culprit only 1984 patient)
- ④ 1 Network meta-analysis
(4 prospective, 14 retrospective analysis -> Only 3 RCTs conducted in 2004, 2004, 2010)

Is This Truly Scientific?

ACC/AHA



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

HR 0.35, $p < 0.001$
(95% CI 0.21-0.58)

65% risk reduction

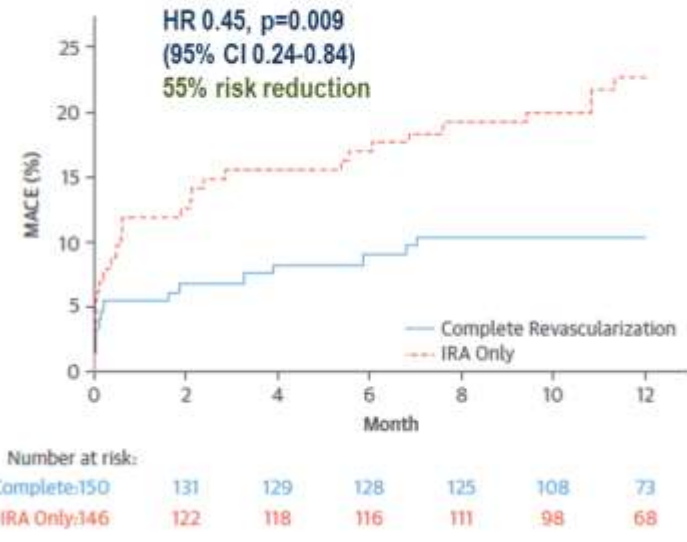
21

Preventive PCI
N=234

53

No preventive PCI
N=231

Preventive PCI for non-culprit lesion >50% DS



**Preventive PCI for non-culprit lesion
> 70% DS or > 50% DS in 2 views**

New Evidences suggests

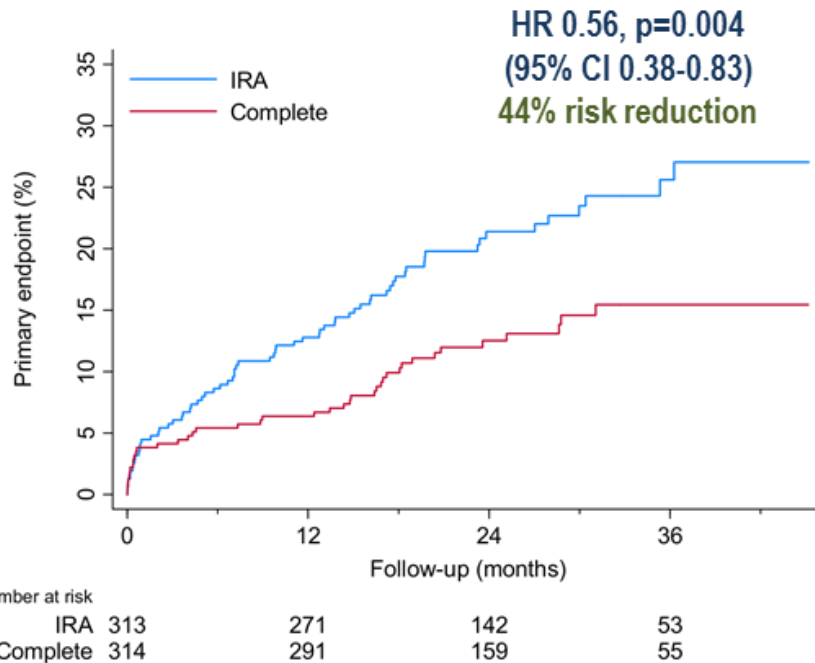
**“Angiography-guided” Complete Revascularization showed
Significant benefit in Patient’s outcome than “Culprit-Only PCI”**

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

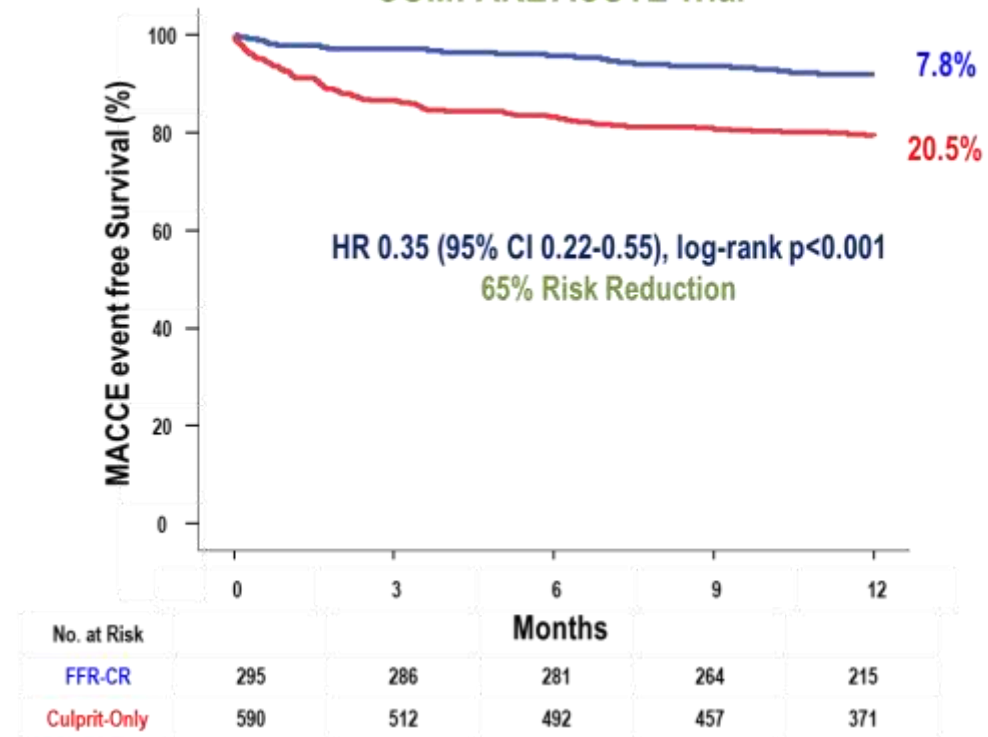
Non-culprit Lesion PCI after Primary PCI in STEMI

- FFR-guided Complete Revascularization vs. Culprit-Only PCI -

DANAMI-3-PRIMULTI

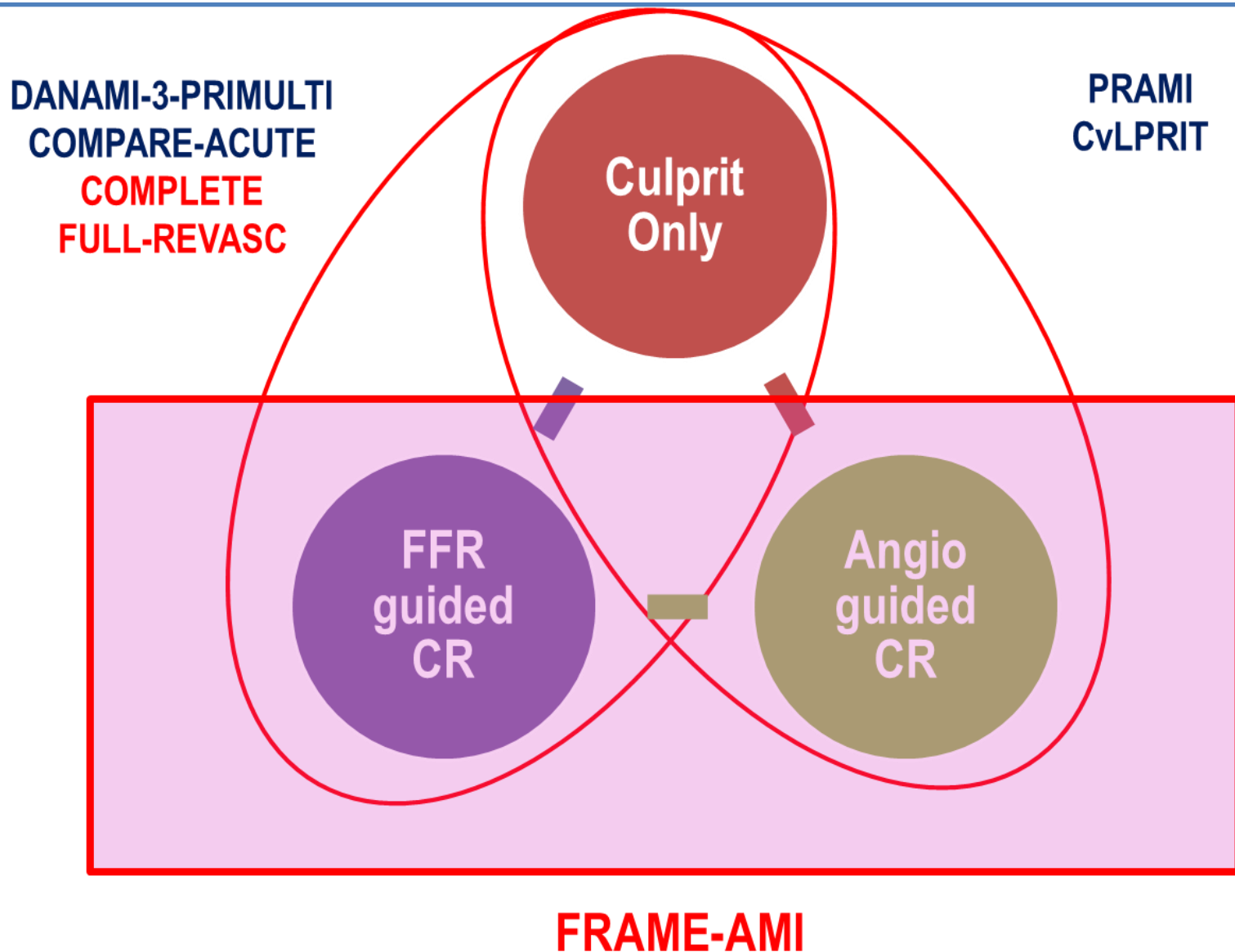


COMPARE ACUTE Trial



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

Non-culprit PCI in STEMI multivessel Updated ESC Guideline



FRAME-AMI Trial (NCT02715518)

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

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

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

FFR-guided Complete Revascularization
(N=646)

FFR \leq 0.80
(IV adenosine or
IC nicorandil)

Perform
Immediate
Revascularization

FFR > 0.80
(IV adenosine or
IC nicorandil)

Defer
Revascularization

*Immediate FFR-guided decision for non-IRA stenosis

Stratified
randomization
Participating Center
STEMI or NSTEMI

Angio-guided Complete Revascularization
(N=646)

>50% stenosis
(Visual or QCA)

Perform
Immediate
Revascularization

*Immediate Angio-guided decision for non-IRA stenosis

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

Primary Endpoint

A composite of All death, Any Myocardial Infarction, Any Revascularization

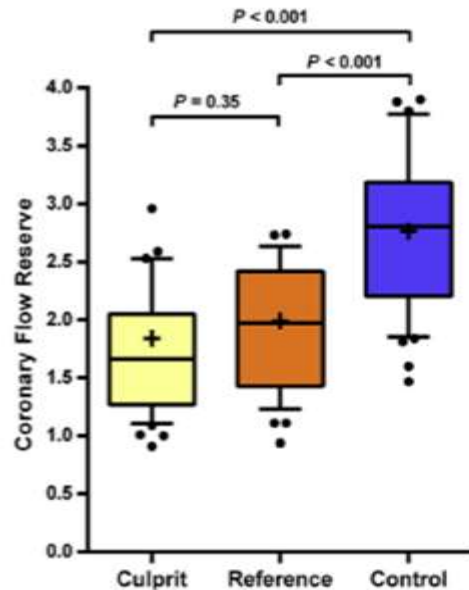
Secondary Endpoints

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

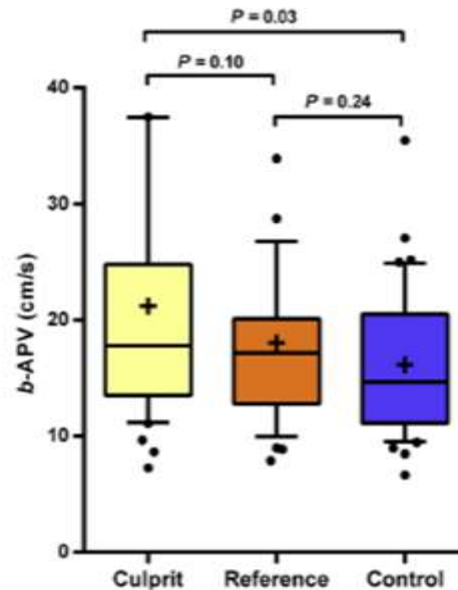
FFR use in Non-culprit lesions in STEMI

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

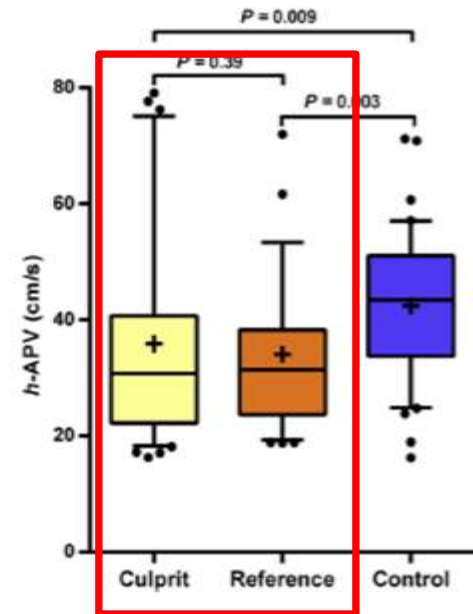
A. CFR (Doppler)



B. Resting APV



C. Hyperemic APV



Blunted hyperemic response in STEMI setting

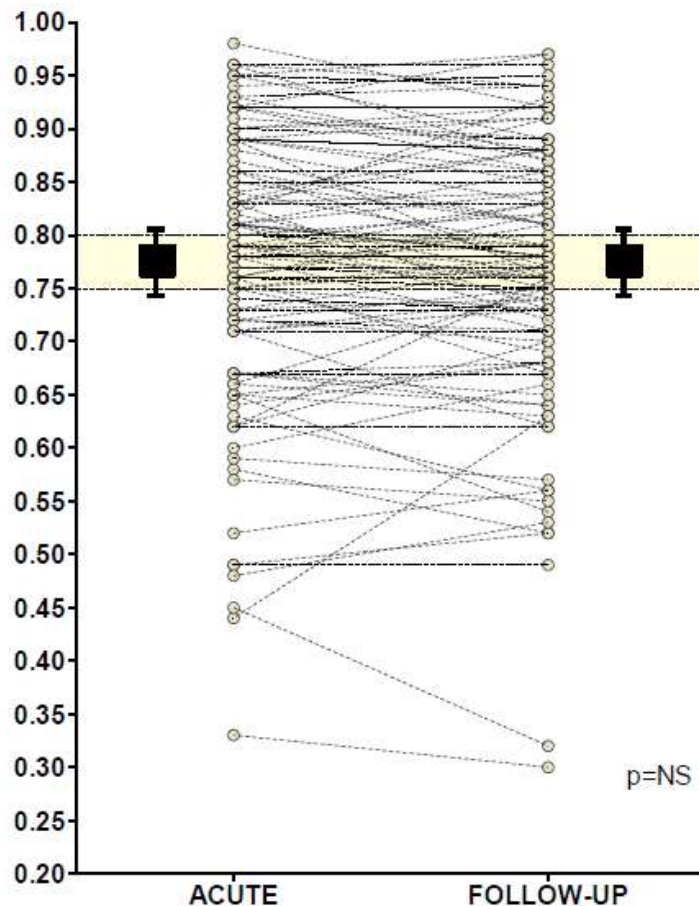
Possibility of underestimation of non-culprit lesion severity by using FFR

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)**

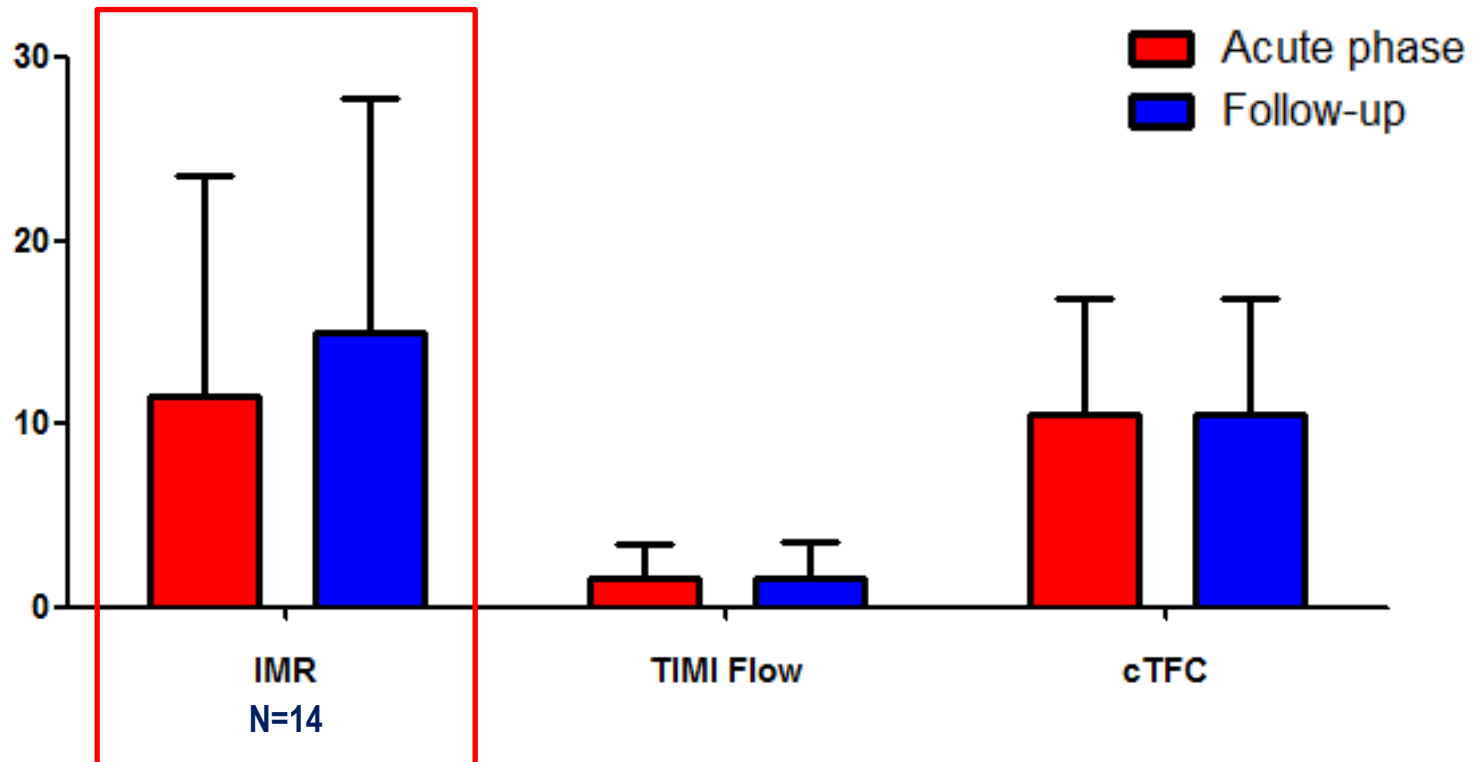


- In only 2/112 non-culprit stenoses was the FFR > 0.80 during ACS and < 0.75 at follow-up

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

Secondary MV damage

- Regional Problem, Preclinical Validation -

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

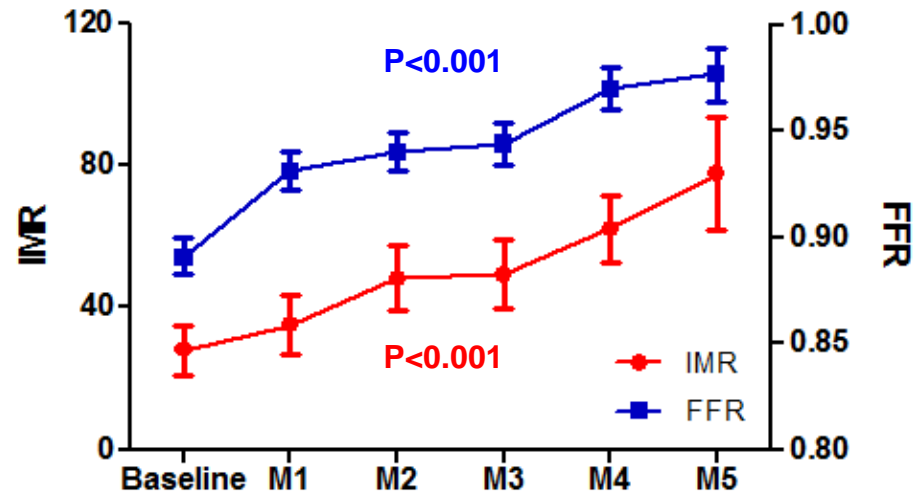
➔ Comprehensive assessment in LAD (culprit) and LCX (non-culprit)



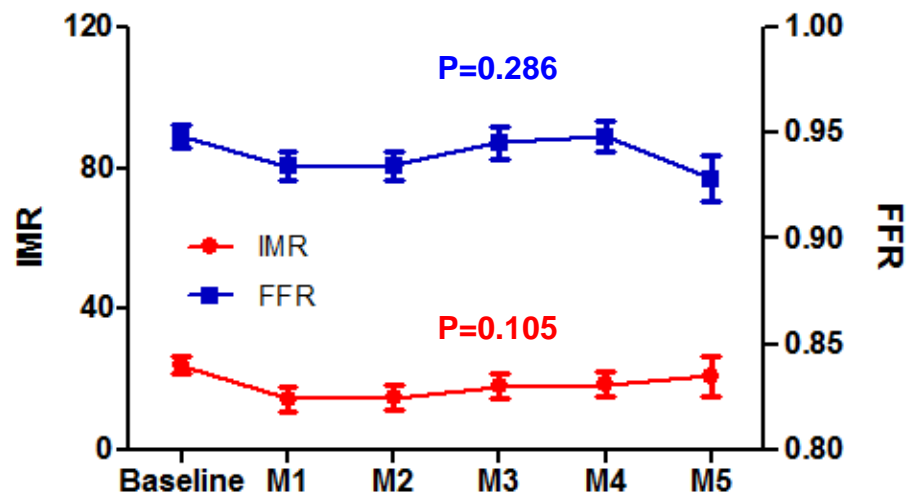
MV damage in AMI setting

- Results : According to Vessels -

LAD (Microsphere)



LCX (No Microsphere)



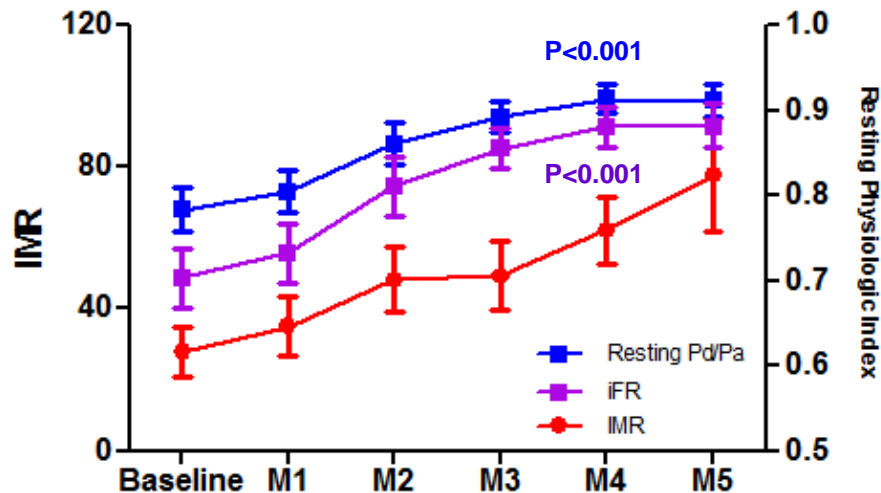
Microvascular damage can be considered as
“Regional Problem” in culprit vessel territory only

MV damage in AMI setting

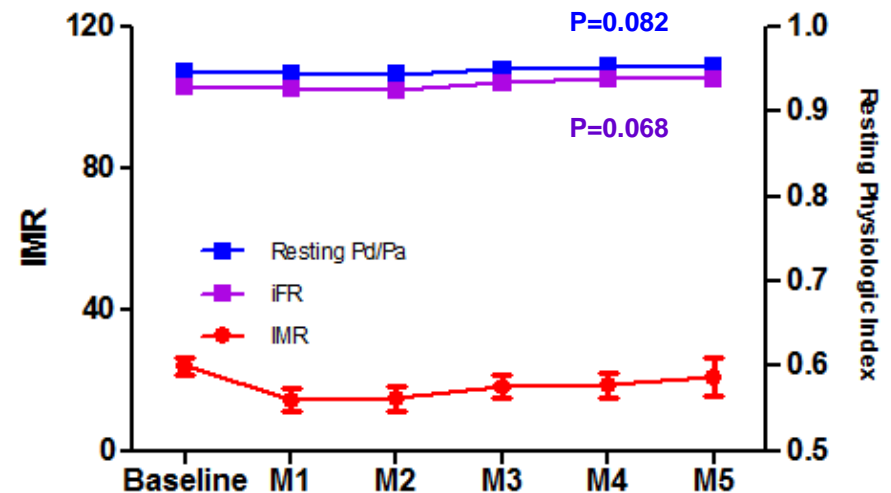
- Results : Resting Index? -

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

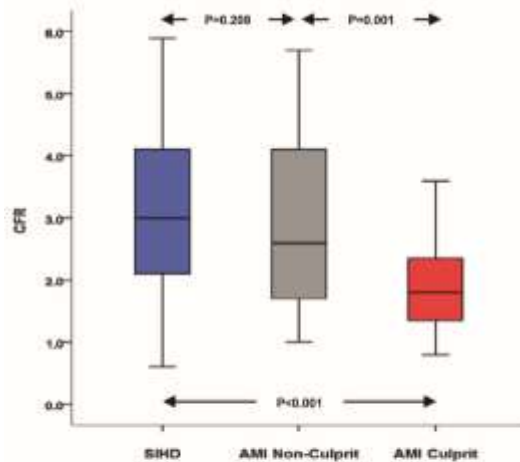
* Please note, the baseline Pd/Pa 0.78 ± 0.03 , baseline iFR 0.70 ± 0.03 in LAD

FFR for Non-Culprit Stenosis Evaluation

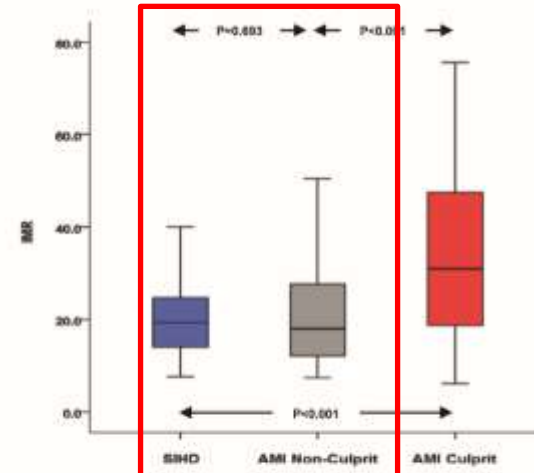
- Real World Patient Data (Samsung Medical Center) -

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

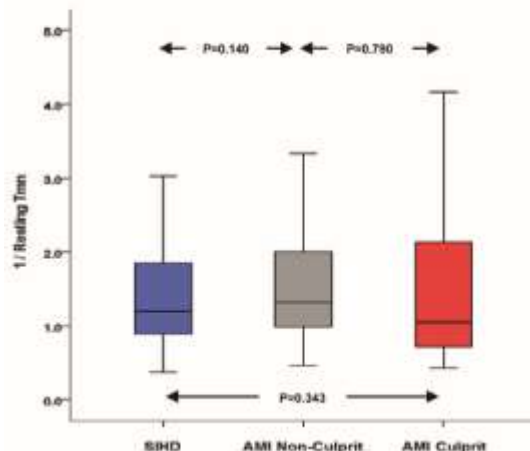
A. Coronary Flow Reserve



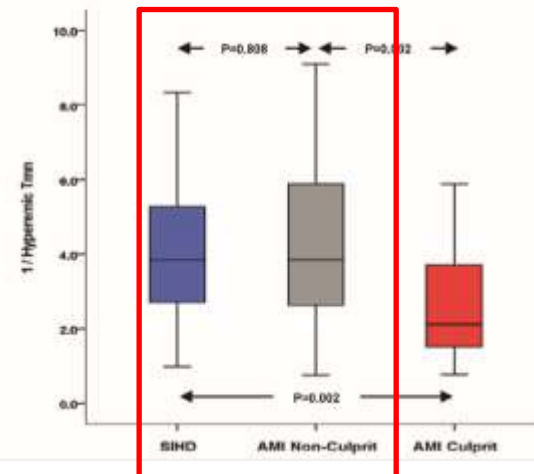
B. Index of Microcirculatory Resistance



C. Resting Coronary Flow Velocity Index



D. Hyperemic Coronary Flow Velocity Index

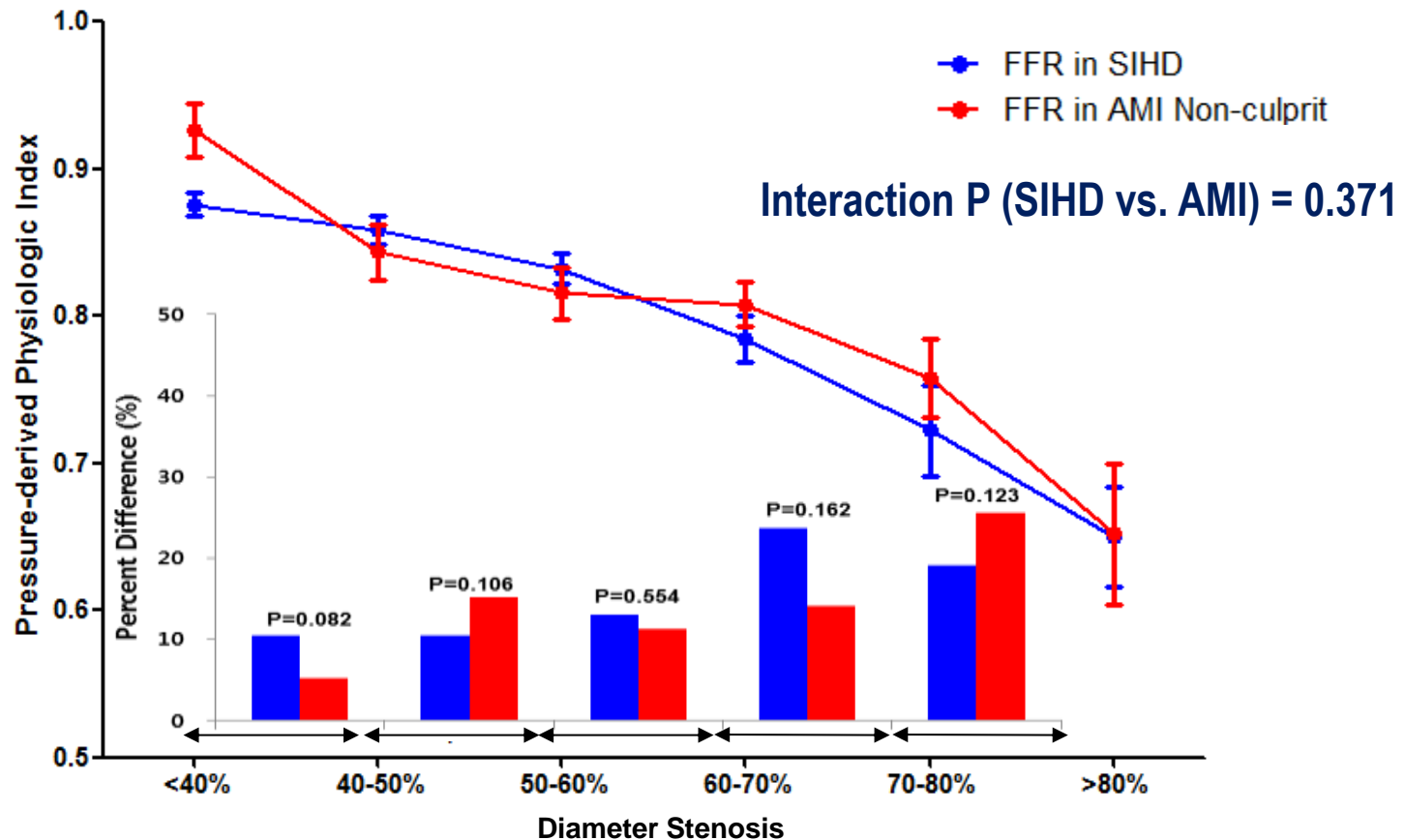


iFR / FFR for Non-Culprit Stenosis Evaluation

- 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

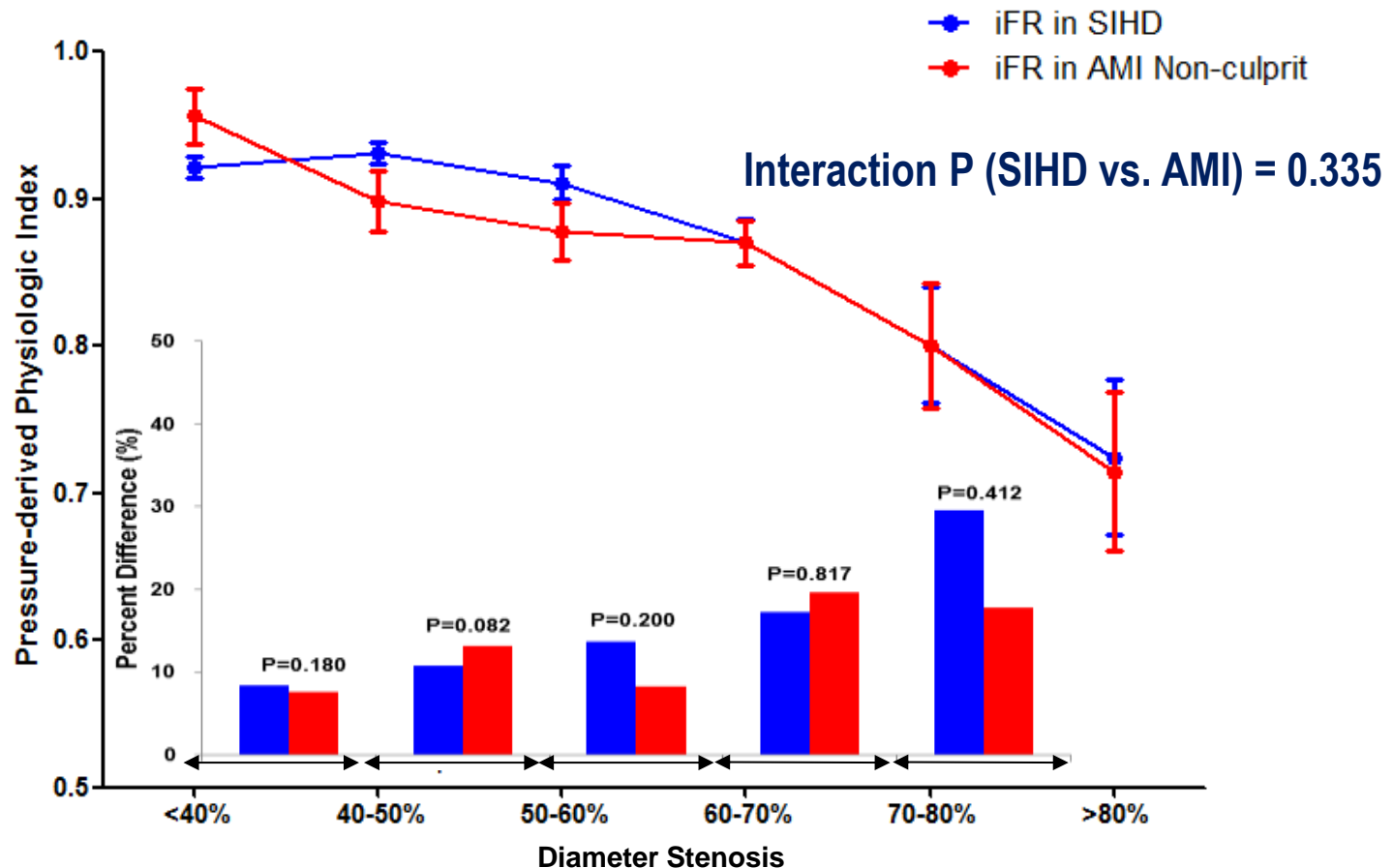


iFR / FFR for Non-Culprit Stenosis Evaluation

- 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



Summary

➤ 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.

	SIHD	NSTE-ACS	STEMI (acute)
Clear Culprit	+	-	-
Non-culprit	+	+	+

Summary

➤ 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.

