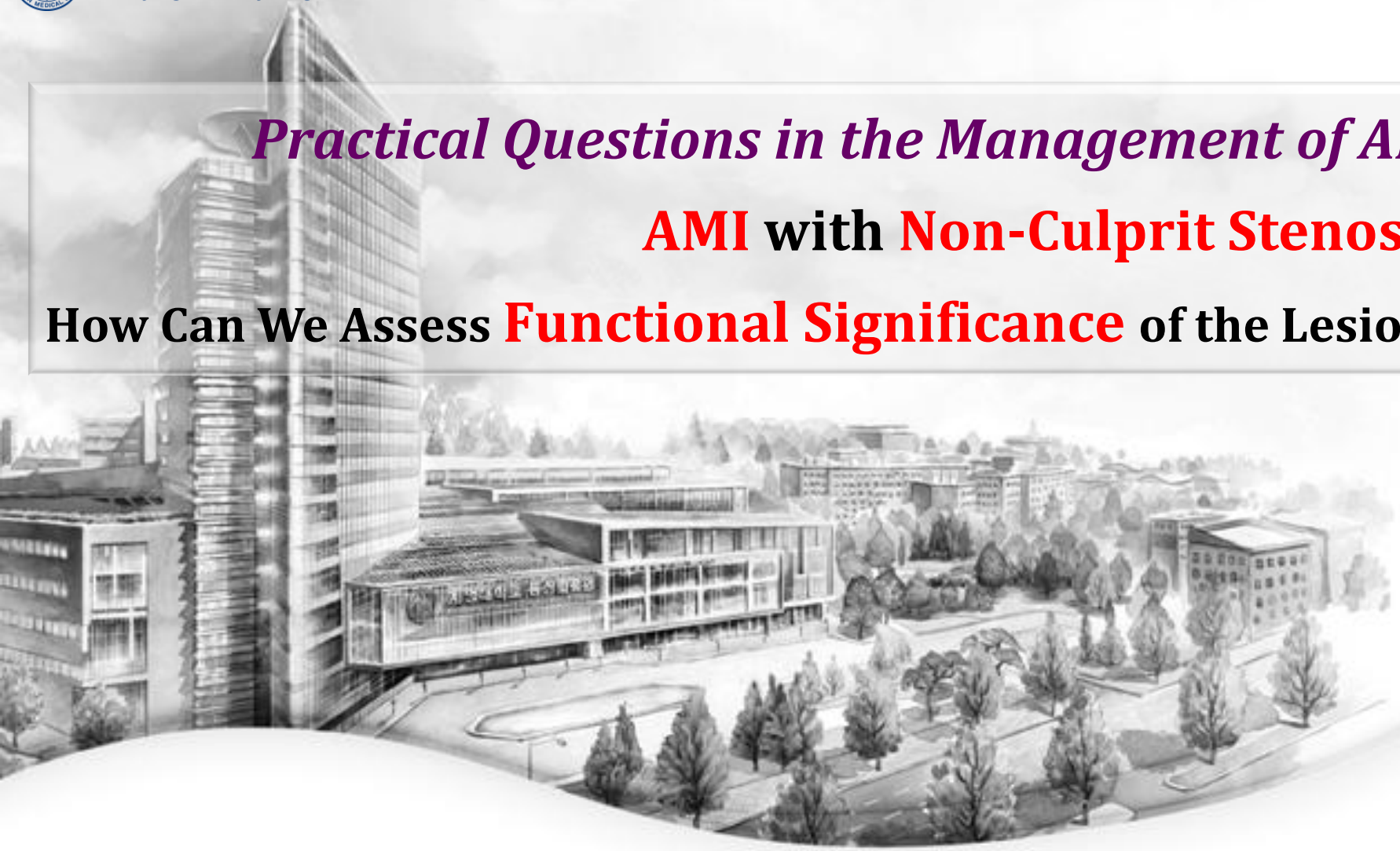
계명대학교 동산의료원
Keimyung University Dongsan Medical Center

Practical Questions in the Management of AMI

AMI with Non-Culprit Stenosis,

How Can We Assess Functional Significance of the Lesions?



Keimyung University Dongsan Medial Center

NAM, Chang-Wook MD, PhD

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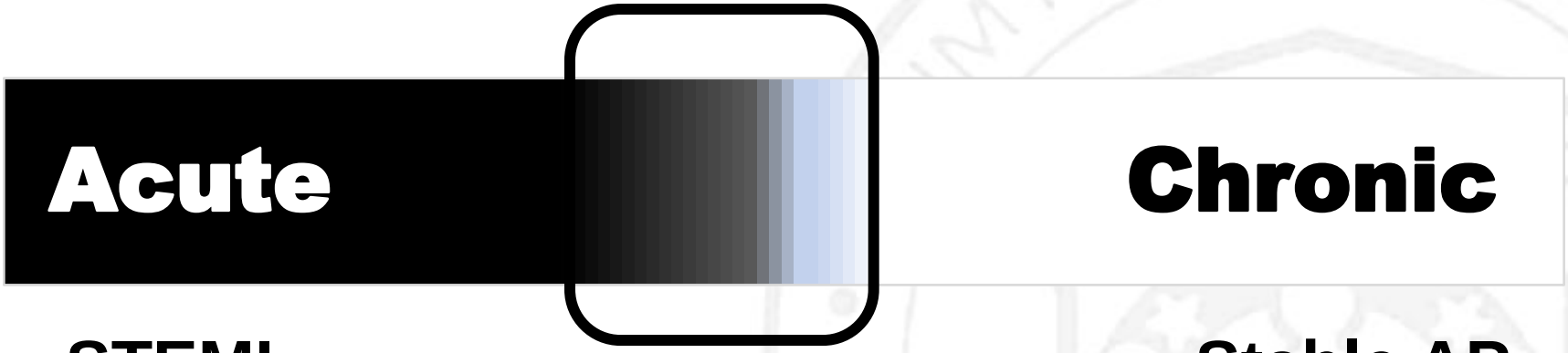
02 **Clinical issues** for the physiologic evaluation of nonculprit lesion in ACS

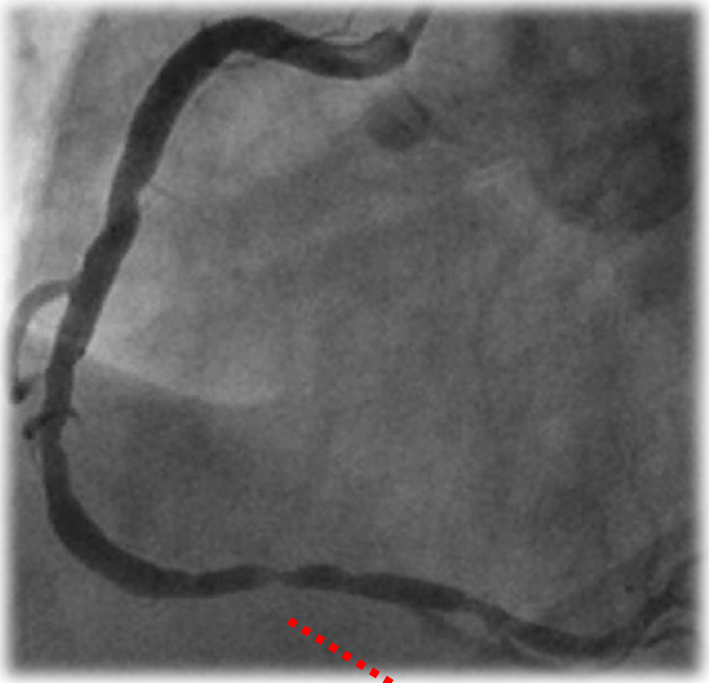
1 Technical issues for the physiologic evaluation of nonculprit lesion in ACS

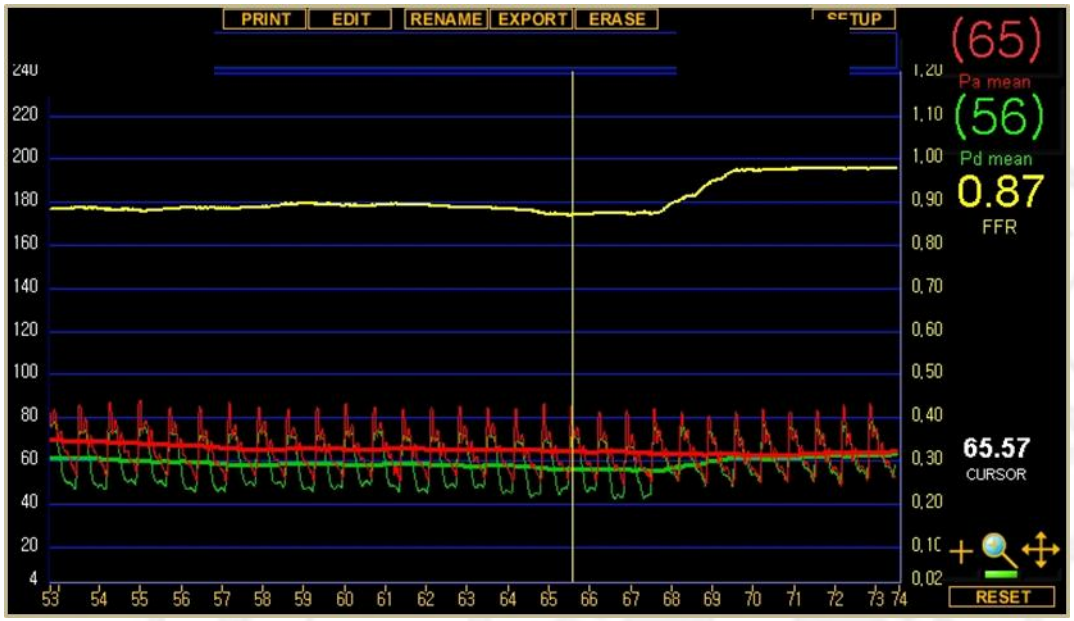
Indication for FFR

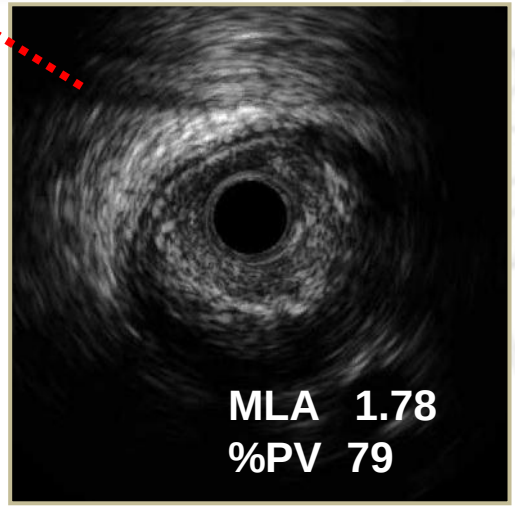
1. Clinically important coronary artery
2. Stable coronary artery disease
3. Inducible maximal hyperemia



FFR in Old MI





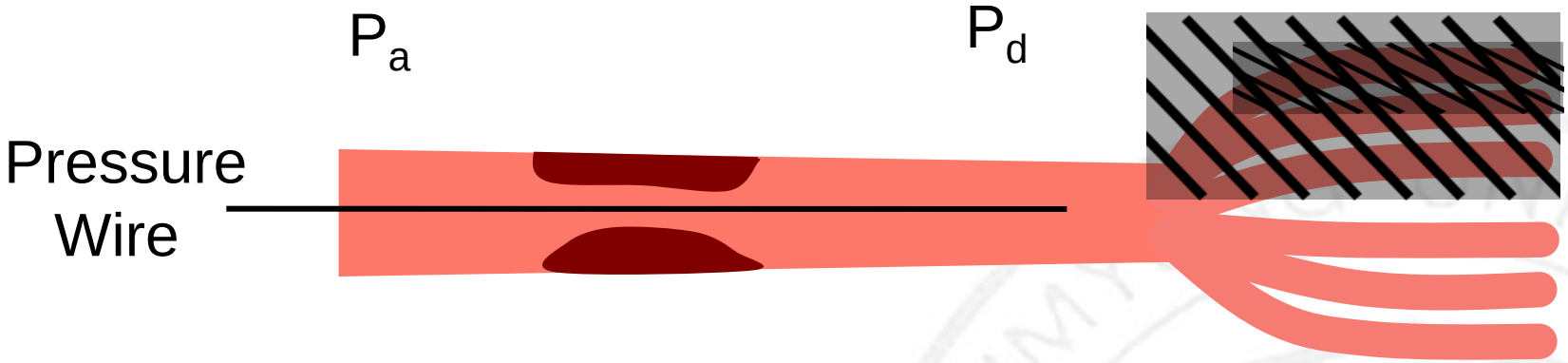


"What You See"

is not always

"What It Is"

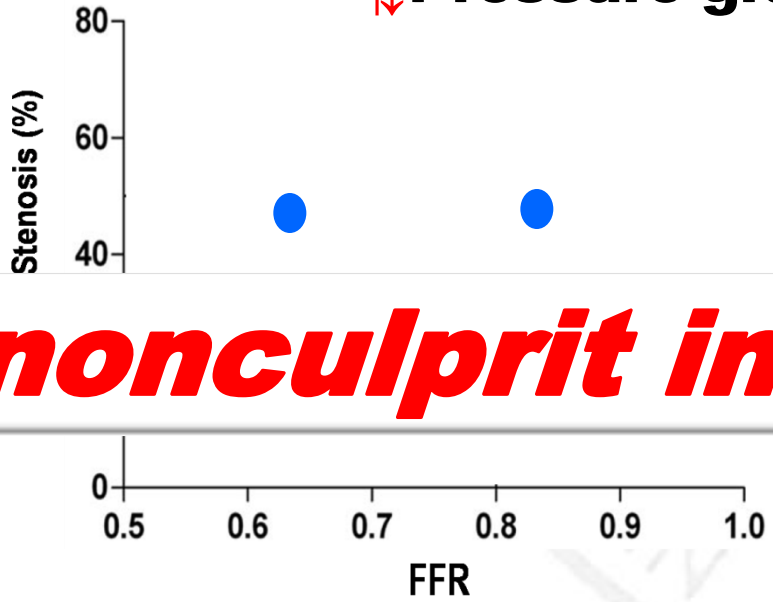
What about FFR in Acute MI?



As time goes on

⇵ **Resistance → ↕Flow↠**

⇅ **Pressure gradient → ↕ FFR**



But, nonculprit in ACS?

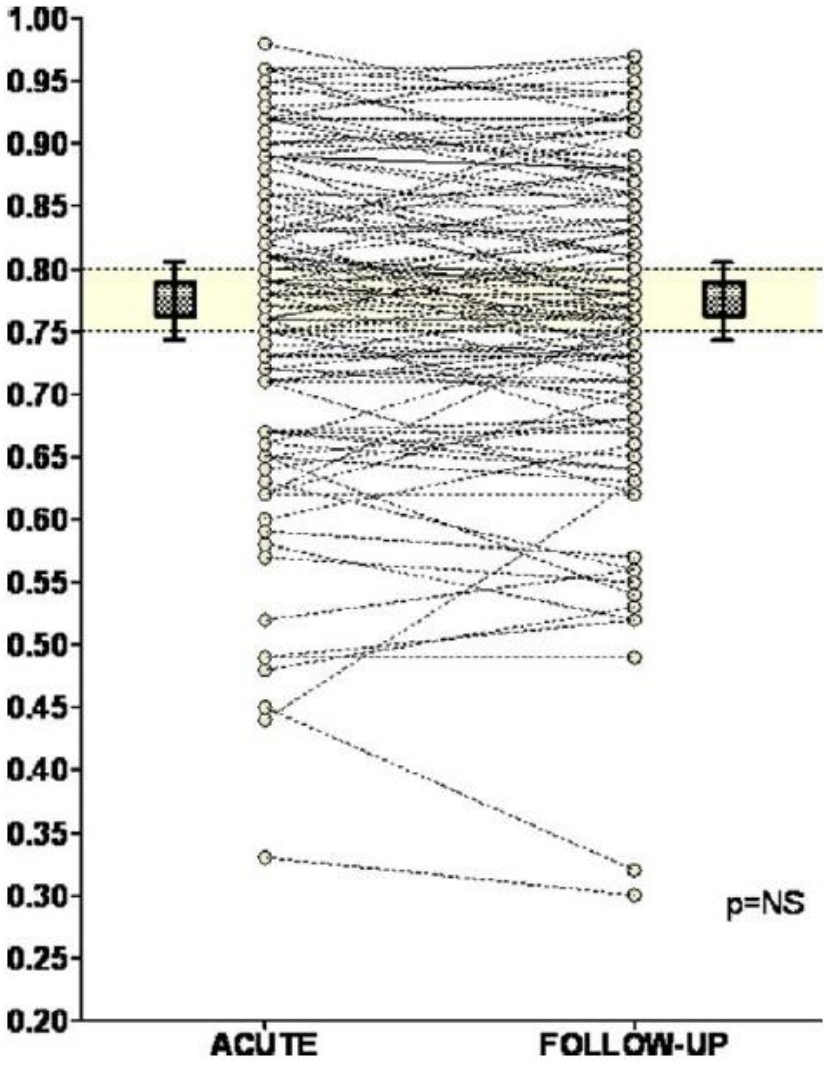
FFR in nonculprit lesion in ACS

- 101 pts(112 nonculprit lesions) undergoing PCI for AMI (75 STEMI, 26 NSTEMI) within 72 h after the onset of chest pain.
- FFR obtained immediately after PCI of the nonculprit stenosis and repeated 35±4 days later.

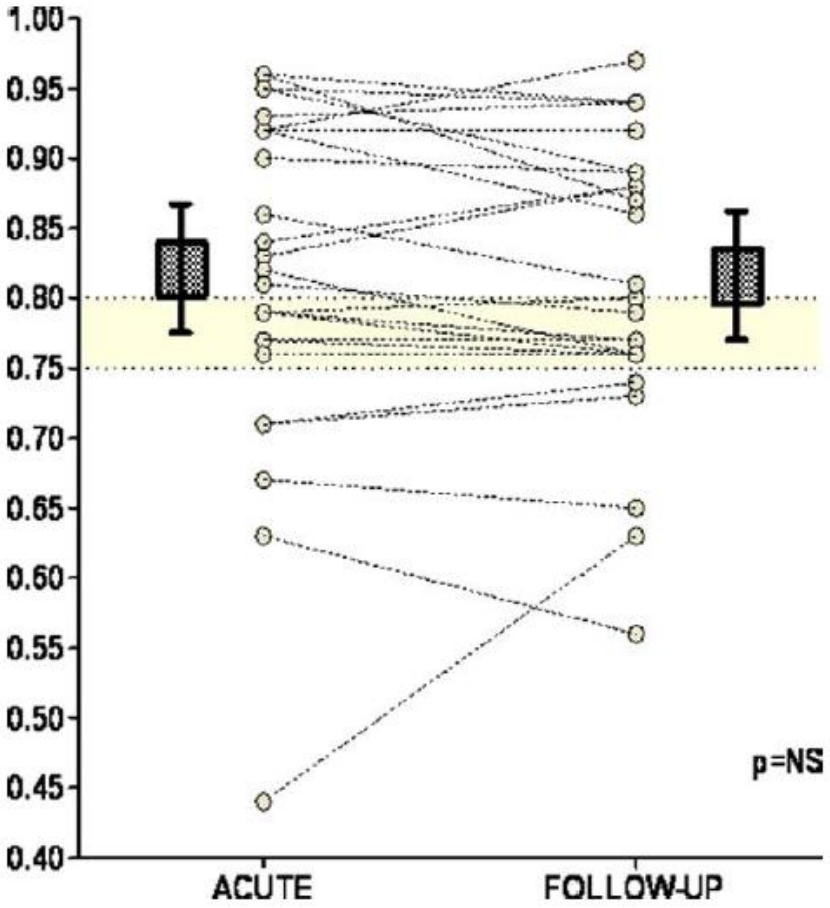
	Acute Phase (n = 101)	Follow-Up (n = 101)	p Value
LVEF (%)	59 ± 15	61 ± 14	NS
LVEDP (mm Hg)	18 ± 7	17 ± 7	NS
FFR nonculprit	0.77 ± 0.13	0.77 ± 0.13	NS
IMR nonculprit (IU)	20 ± 3	24 ± 6	NS
DS nonculprit (%)	56 ± 14	55 ± 14	NS
MLD nonculprit (mm)	1.32 ± 0.46	1.31 ± 0.50	NS
RD nonculprit (mm)	2.9 ± 0.70	2.7 ± 0.70	NS
TIMI flow nonculprit	2.93 ± 0.30	2.97 ± 0.20	NS
cTFC nonculprit	15 ± 6	15 ± 6	NS

JACC interv 2010;3:1274

FFR in nonculprit lesion in ACS



The Lowest LVEF Quartile



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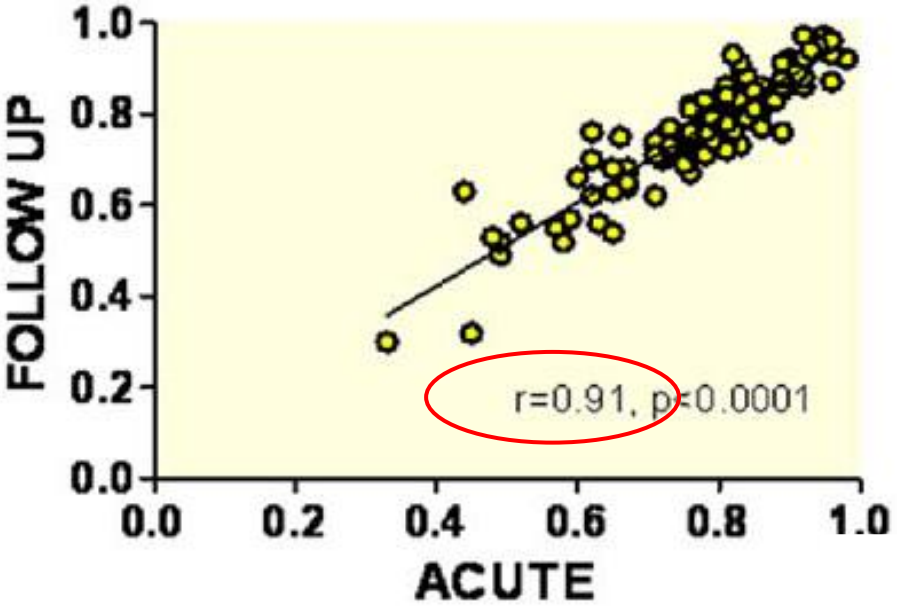
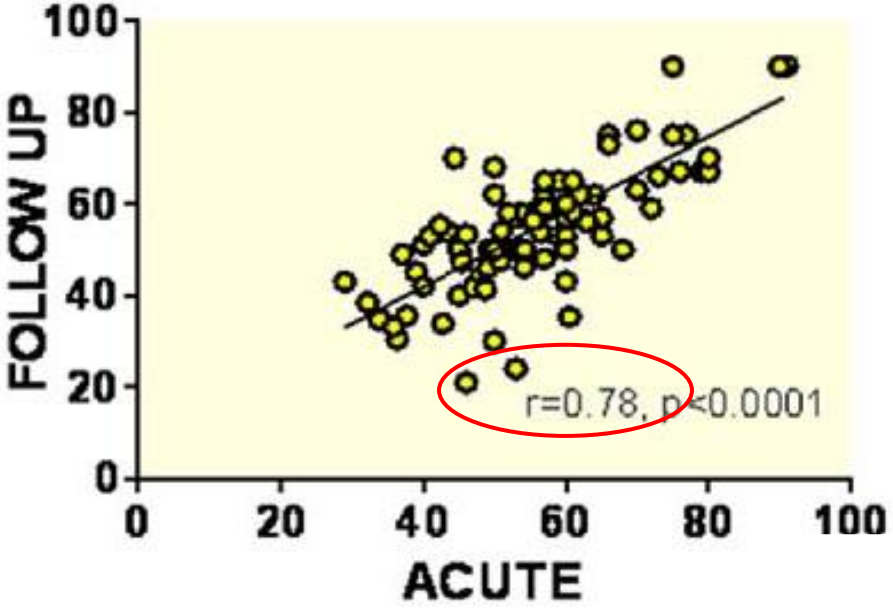
JACC interv 2010;3:1274

FFR in nonculprit lesion in ACS

FFR



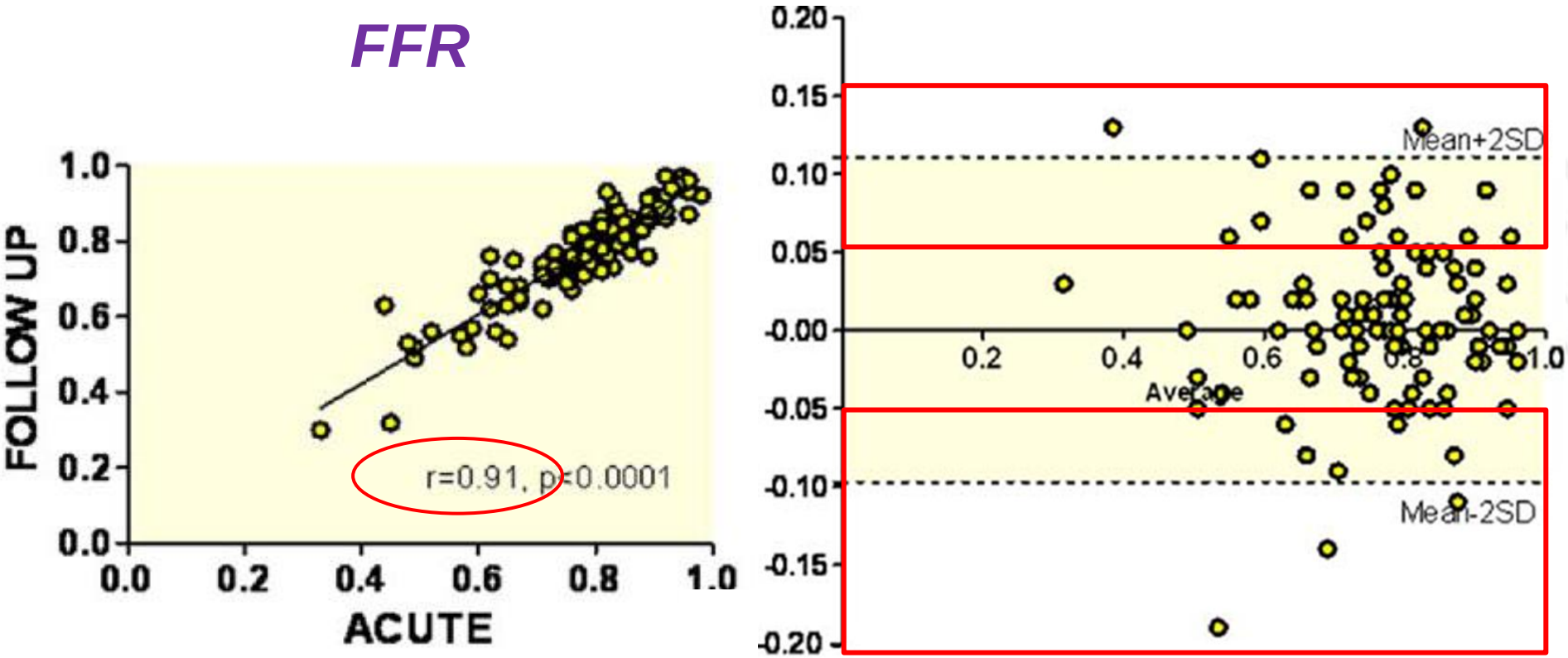
% DS



During the acute phase of ACS, the severity of nonculprit coronary lesions can reliably be assessed by FFR.

JACC interv 2010;3:1274

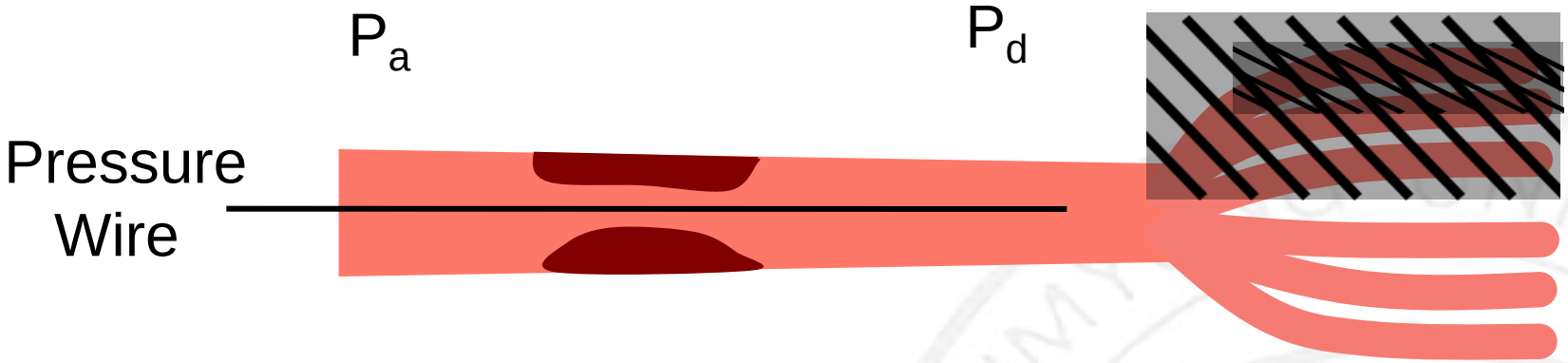
FFR in nonculprit lesion in ACS



There was not a small chance of mismatched FFR over the cut off value for revascularization.

JACC interv 2010;3:1274

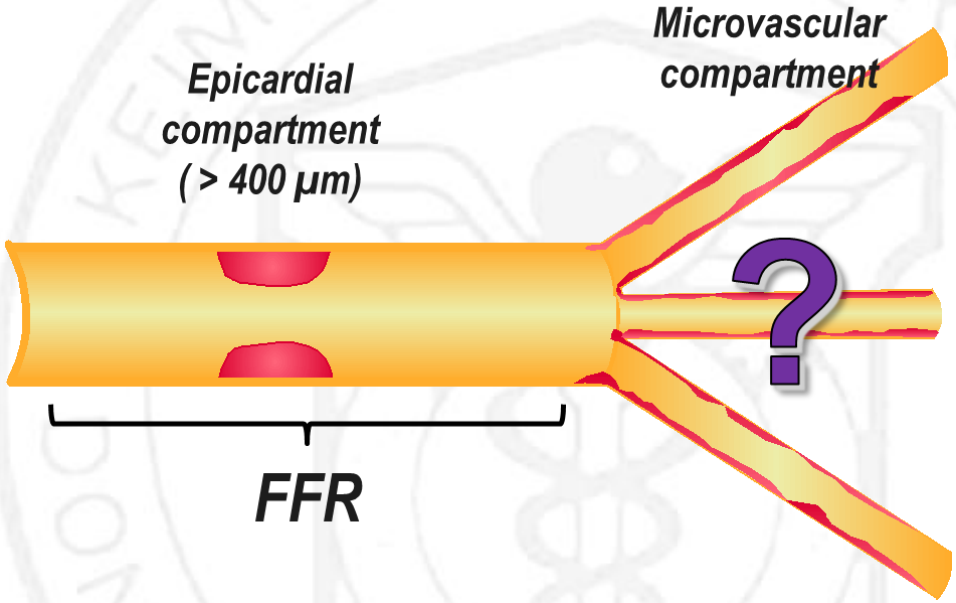
What made the change of FFR?



- Stunning can affect not only infarct related artery but also nonculprit artery.
- Early development of collateral flow

How can we overcome?

But, How can we evaluate invisible "Microvascular system"?



Derivation of IMR

- Pressure = Flow x Resistance
- Resistance = Pressure / Flow
- Flow = $V/T_{mn} \cong 1/T_{mn}$
- IMR = Distal Pressure / $(1 / T_{mn})$

  = Distal Pressure x T_{mn}

at maximal hyperemia…

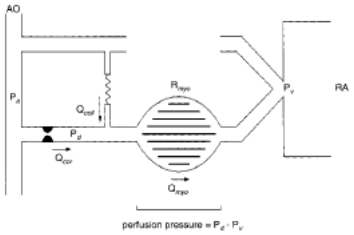


Figure 5. Schematic representing coronary circulation. AO, aorta; RA, right atrium.

myocardial flow, the following algorithm can be applied. In the mathematical derivation of that algorithm, standardized nomenclature will be used as in the initial study introducing the concept of FFR.[9]

Let us use the following terminology: Q_{myo}=myocardial blood flow, Q_{cor}=coronary artery blood flow (equal to F), and Q_c=collateral blood flow, all measured at maximum vasodilation. The "normal" values of these indexes at maximal vasodilation are indicated by the superscript N: Q^N_{myo}, Q^N_{cor}, Q^N_c. Equation 1, in this terminology, states that

(1a) $$Q_{cor} \approx 1/T_{mn}$$

which has also been validated both experimentally and clinically.[11–13]

R_{myo} is myocardial resistance at maximum vasodilation.

Myocardial flow equals the sum of coronary artery flow and collateral flow, so:

$$Q_{myo} = Q_{cor} + Q_c$$

Furthermore, it is assumed that $Q^N_c = 0$ and that $Q^N_{myo} = Q^N_{cor}$.

FFR_{myo} and FFR_{cor} are defined as follows[6]: $FFR_{myo} = Q_{myo}/Q^N_{myo}$ and $FFR_{cor} = Q_{cor}/Q^N_{cor}$.

The different pressures are defined as follows: P_a=aortic pressure, P_d=distal coronary pressure at maximum vasodilation, P_w=coronary wedge pressure, and P_v=central venous pressure, all at maximum dilation.

It has been demonstrated that FFR_{cor} and FFR_{myo} can be expressed in terms of pressures as follows[6]:

(4) $$FFR_{cor} = \frac{P_d - P_w}{P_a - P_w}$$

and

(5) $$FFR_{myo} = \frac{P_d - P_v}{P_a - P_v}$$

TMR equals:

$$R_{myo} = \frac{P_d - P_v}{Q_{myo}}$$

By multiplying the numerator and denominator by Q_{cor}, this can be rewritten as:

$$R_{myo} = \frac{P_d - P_v}{Q_{myo}} = \frac{P_d - P_v}{Q_{cor}} \cdot \frac{Q_{cor}}{Q_{myo}}$$

$$R_{myo} = (P_d - P_v) \cdot T_{mn} \cdot \left(\frac{Q_{cor}}{Q_{myo}}\right)$$

$$= (P_d - P_v) \cdot T_{mn} \cdot \frac{Q_{cor}}{Q^N_{cor}} \cdot \frac{Q^N_{cor}}{Q_{myo}}$$

Because $Q^N_{cor} = Q^N_{myo}$, we obtain

$$R_{myo} = (P_d - P_v) \cdot T_{mn} \cdot \frac{Q_{cor}}{Q^N_{cor}} \cdot \frac{Q^N_{cor}}{Q_{myo}}$$

$$= (P_d - P_v) \cdot T_{mn} \cdot \frac{FFR_{cor}}{FFR_{myo}}$$

Therefore,

(6a) $$IMR = (P_d - P_v) \cdot T_{mn} \cdot \frac{FFR_{cor}}{FFR_{myo}}$$

or in case P_v is close to zero,

(6b) $$IMR = P_d \cdot T_{mn} \cdot \frac{FFR_{cor}}{FFR_{myo}}$$

Note that if there are no collaterals, as in the case of a normal artery, $FFR_{cor} = FFR_{myo}$ and Equation 6b equals Equation 3, as should be the case.

Equation 6a can be rewritten in terms of measured pressures by substitution of Equations 4 and 5 as follows:

$$IMR \approx (P_d - P_v) \cdot T_{mn} \cdot \left(\frac{P_d - P_w}{P_a - P_w}\right) \div \left(\frac{P_d - P_v}{P_a - P_v}\right)$$

$$- (P_d - P_v) \cdot T_{mn} \cdot \left(\frac{P_d - P_w}{P_a - P_w}\right) \cdot \left(\frac{P_a - P_v}{P_d - P_v}\right)$$

$$- (P_d - P_v) \cdot T_{mn} \cdot \left(\frac{P_d - P_w}{P_a - P_w}\right)$$

And by neglecting P_v, we obtain

(7a) $$IMR \approx P_a \cdot T_{mn} \cdot \left(\frac{P_d - P_w}{P_a - P_w}\right)$$

or expressed in a different way,

(7b) $$IMR \approx P_a \cdot T_{mn} \cdot FFR_{cor}$$

In summary, Equation 7a constitutes the general form of IMR, universally applicable in both the presence and absence of a significant stenosis. If studies are performed in patients without significant epicardial disease, the simpler Equation 3 can be used for IMR. In addition, when Doppler-derived indexes of microvascular resistance are used,[4–7] they should be corrected in a similar way as in Equation 6b by multiplying them by (FFR_{cor}/FFR_{myo}).

Finally, it is clear that overestimation of microvascular resistance when collateral flow is neglected increases with increasing stenosis severity and with increasing recruitable collateral flow. This percentage overestimation can be defined as

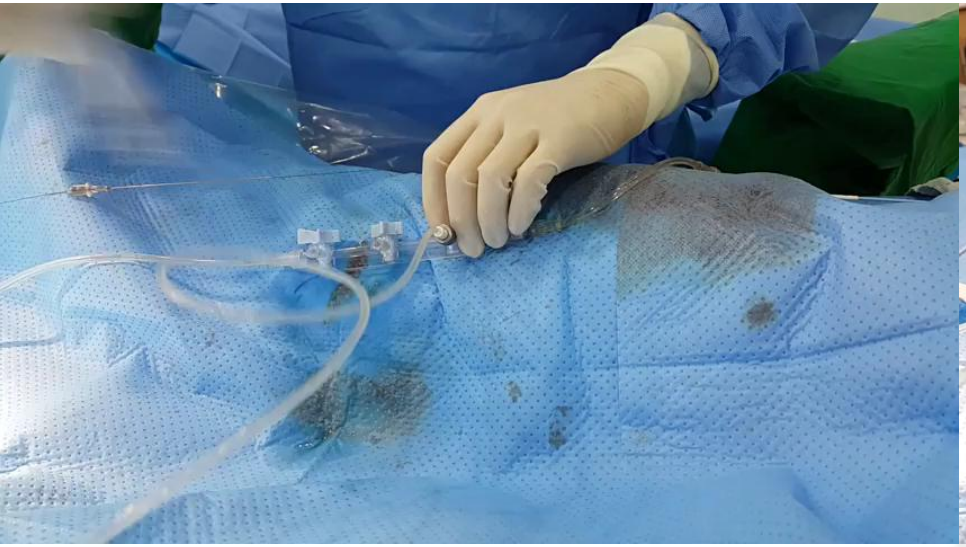
$$\left(\frac{IMR_{uncorr}}{IMR}\right) - 1 \cdot 100\%$$

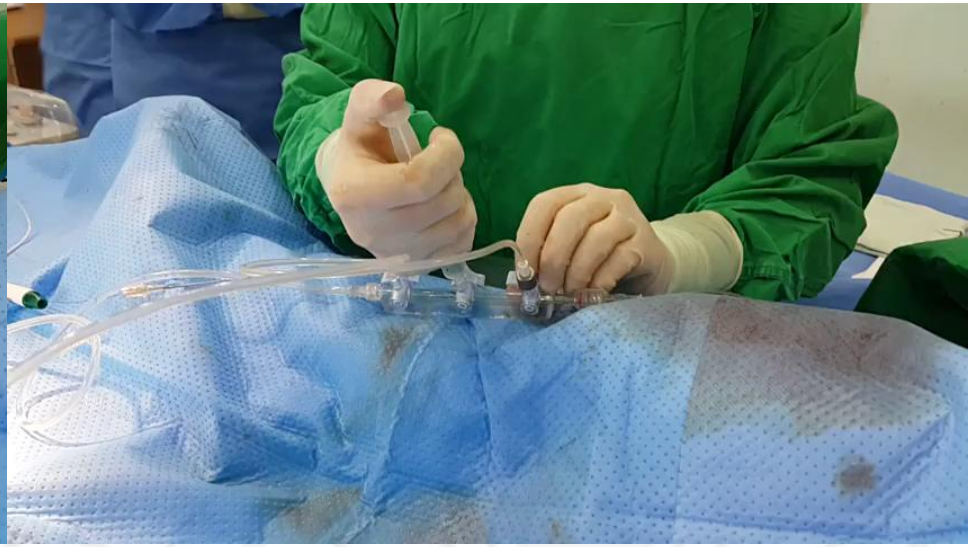
(8) $$- \left(\frac{P_d \cdot T_{mn}}{P_a \cdot T_{mn}[(P_d - P_w)/(P_a - P_w)]}\right) - 1 \cdot 100\%$$

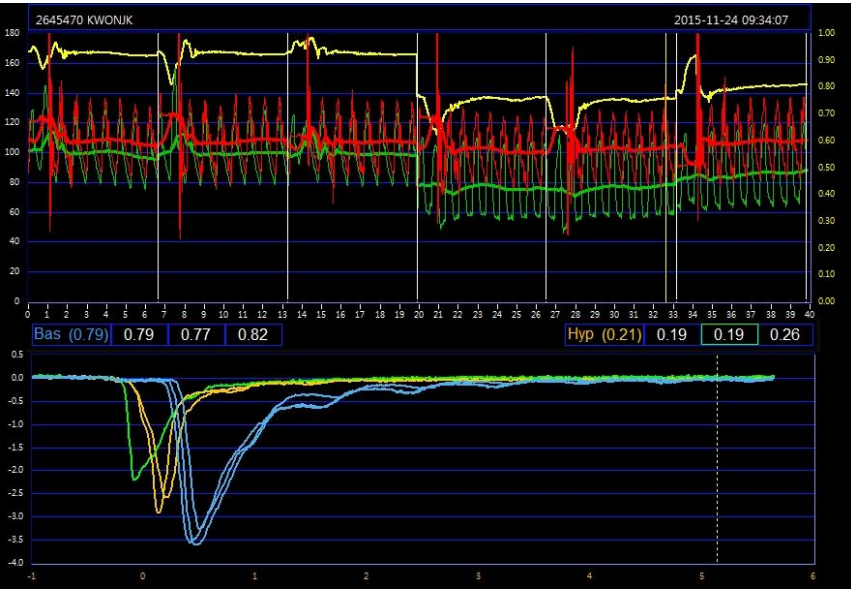
$$- \left(\frac{P_d}{P_a} \cdot \left(\frac{P_a - P_w}{P_d - P_w}\right) - 1\right) \cdot 100\%$$

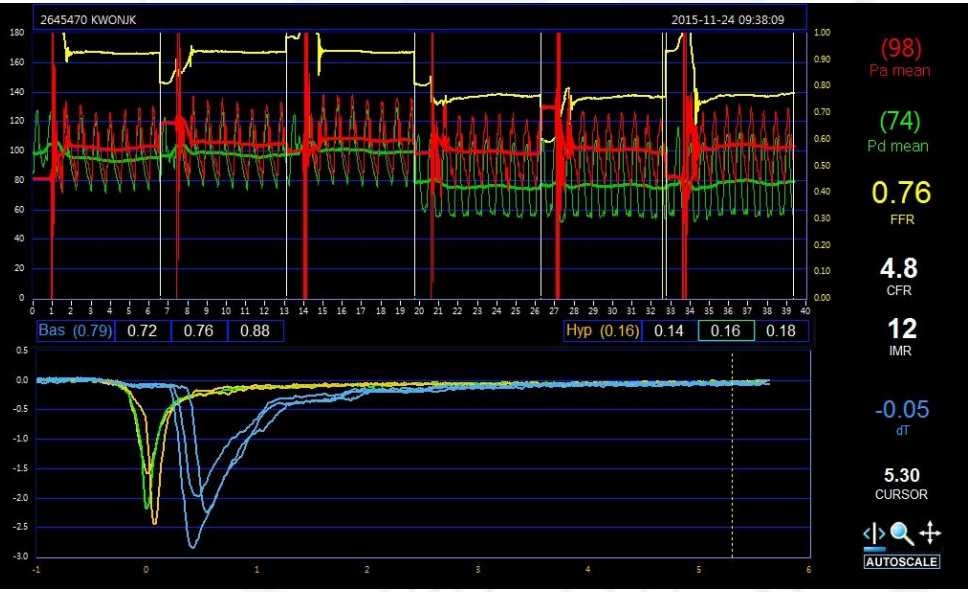
Fearon, et al. Circulation 2003;107:3129

Measurement of IMR









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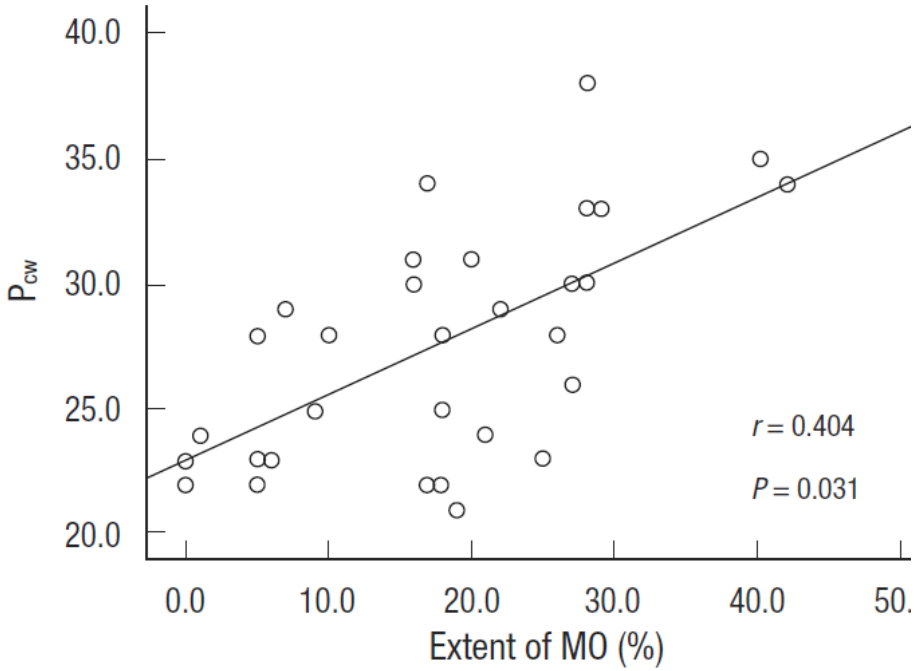
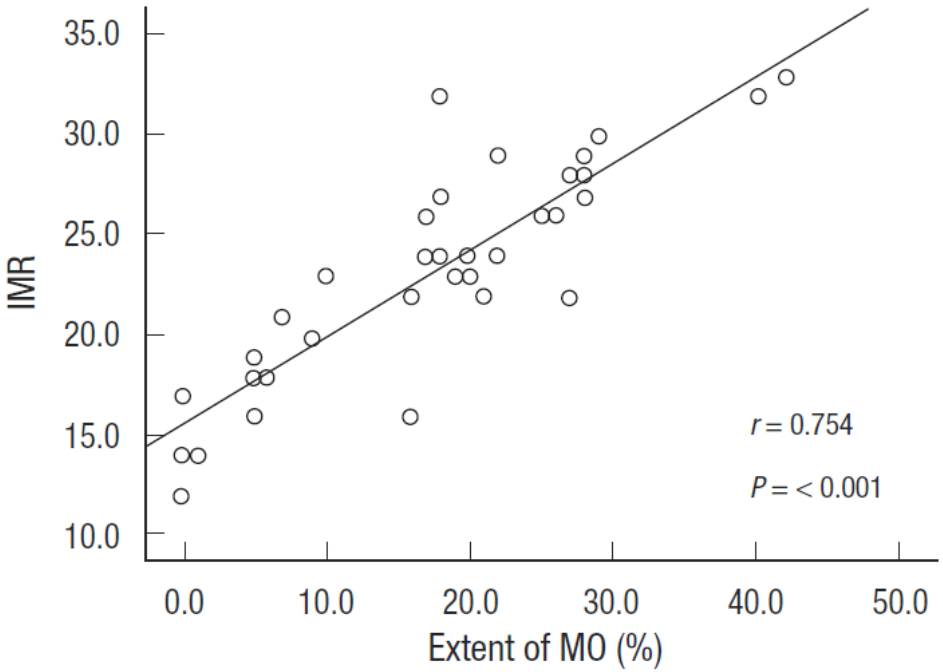
IMR in AMI

- **34 patients with first anterior AMI**
- **Extent of microvascular obstruction (MO) in MRI**





J Korean Med Sci 2012; 27: 1044-1050

Physiologic assessment of Nonculprit lesions in ACS

1. Measure FFR of nonculprit lesion in ACS after PCI of culprit lesion.
2. When FFR is significant, treat it.
3. When it is nonsignificant,

→ Perform IMR measurement of nonculprit lesion.

→ Check the residual lesion in culprit artery.

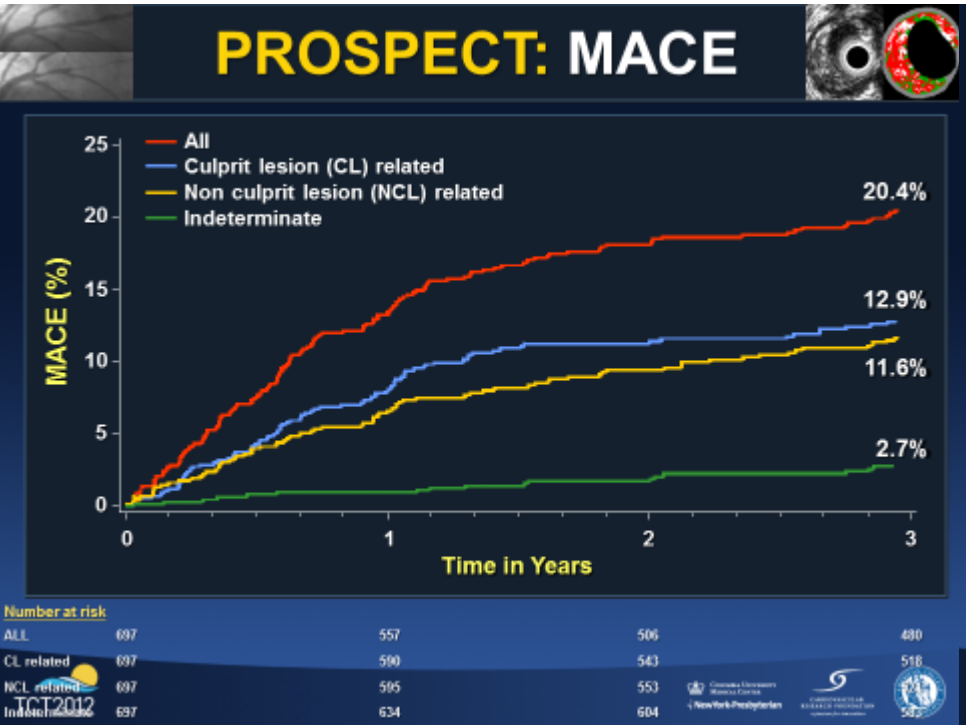
2 Clinical issues for the physiologic evaluation of nonculprit lesion in ACS

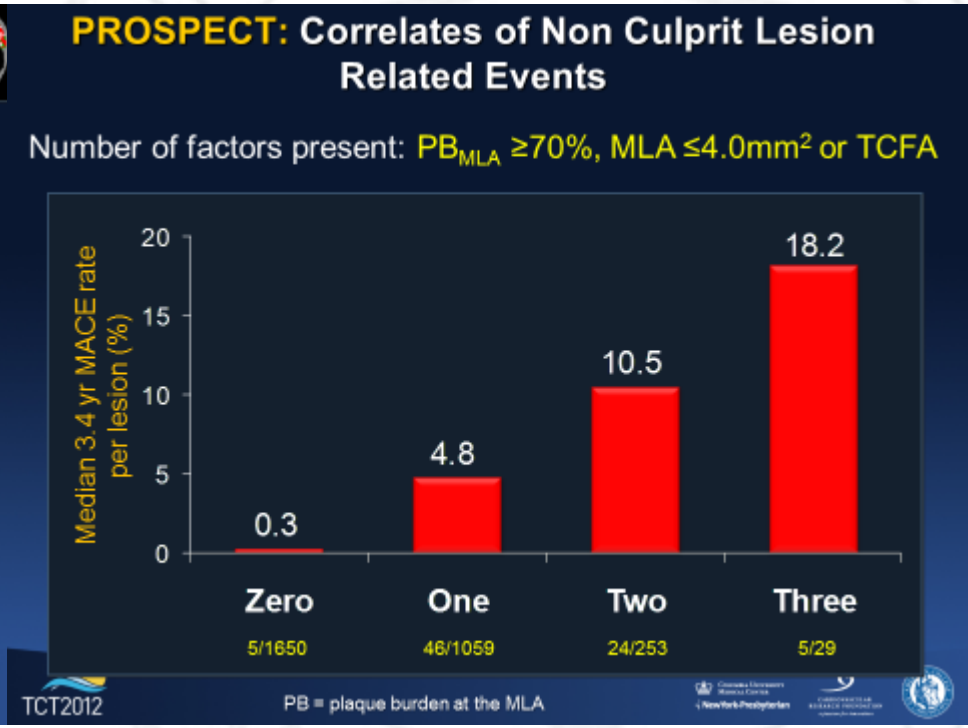
The PROSPECT Trial

700 pts with ACS

undergoing PCI of 1 or 2 major coronary arteries

at up to 40 sites in the U.S. and Europe

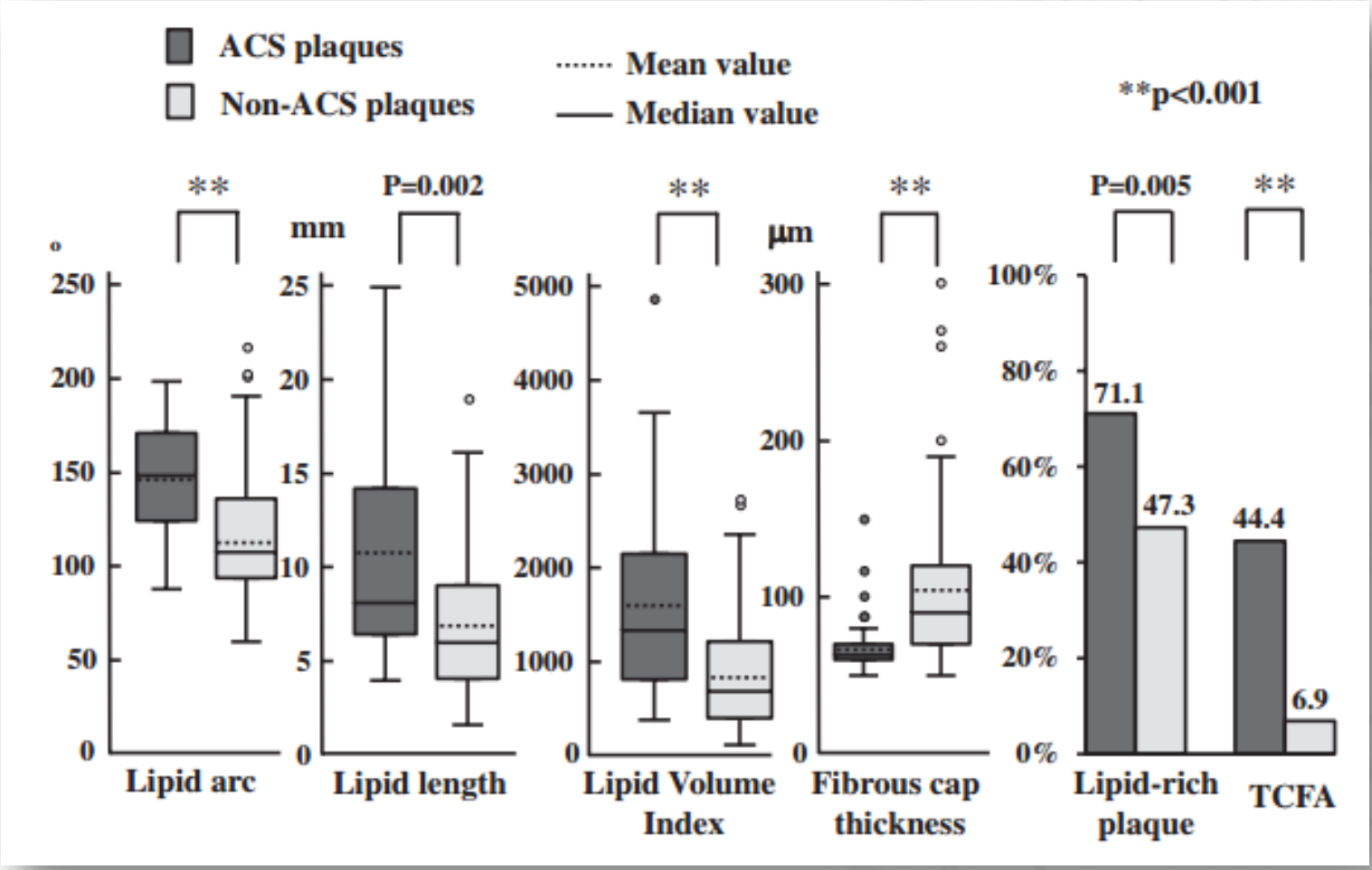




Adapted slide from Dr Gregg W. Stone

Pancoronary Plaque Vulnerability in ACS

3-vessel OCT imaging were selected from the MGH OCT Registry. **248 nonculprit plaques** were found in 104 patients: 45 plaques in 17 ACS patients and 203 plaques in 87 non-ACS patients.



Circ Cardiovasc Imaging. 2012;5:433-440

3-year Outcomes after FFR-guided Defer

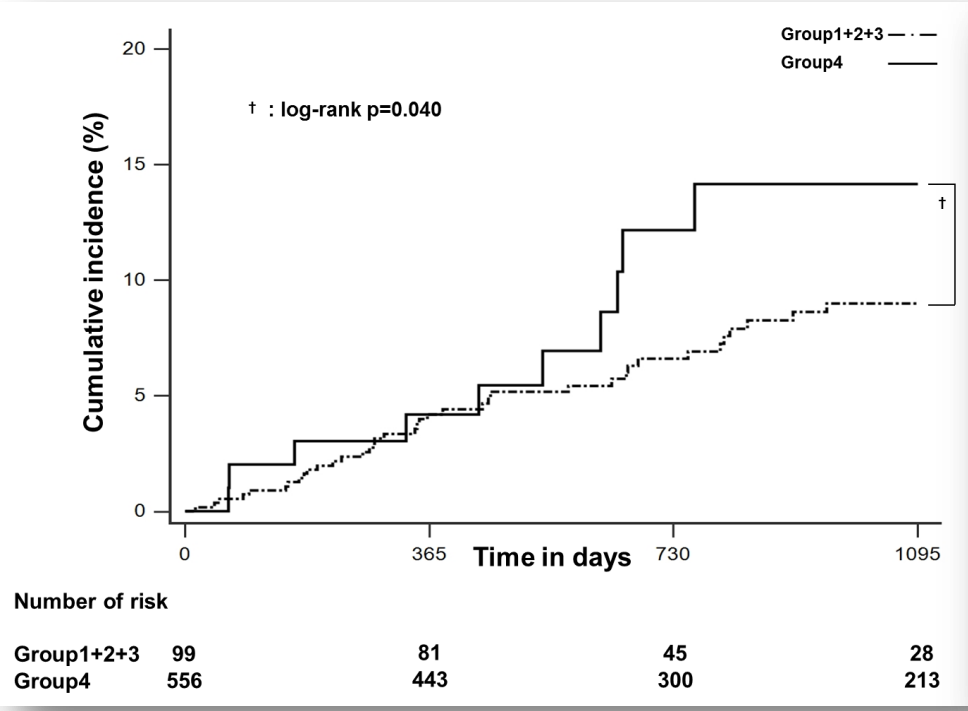
Among 1294 patients and 1628 lesions in Korean FFR registry, 665 patients with 781 deferred coronary lesions, categorized 4 groups according to FFR; group 1: >0.95, group 2: 0.86–0.95, group 3: 0.81–0.85, and group 4: <0.80, MACE defined as the composites of all death, MI, and TVR

Characteristic	Group 1 (n=89)	Group 2 (n=398)	Group 3 (n=189)	Group 4 (n=105)	P
Target vessel					**<0.001**
LAD	**17 (19.1)**	**200 (50.3)**	**130 (68.8)**	**82 (78.1)**	
Non-LAD	**72 (80.9)**	**198 (49.7)**	**59 (31.2)**	**23 (21.9)**	
QCA					
Reference diameter, mm	**3.18 ± 0.68**	**3.02 ± 0.55**	**2.86 ± 0.43**	**2.75 ± 0.52**	**<0.001**
MLD, mm	**1.77 ± 0.60**	**1.58 ± 0.46**	**1.36 ± 0.43**	**1.27 ± 0.36**	**<0.001**
% DS	**44.62 ± 12.61**	**47.5 ± 12.83**	**52.41 ± 14.22**	**53.60 ± 12.52**	**<0.001**
Lesion length, mm	**14.94 ± 8.80**	**17.09 ± 8.51**	**21.63 ± 11.67**	**25.61 ± 15.01**	**<0.001**
FFR	**0.98 ± 0.01**	**0.90 ± 0.03**	**0.83 ± 0.01**	**0.75 ± 0.06**	**<0.001**

Submitted data from Korean FFR registry

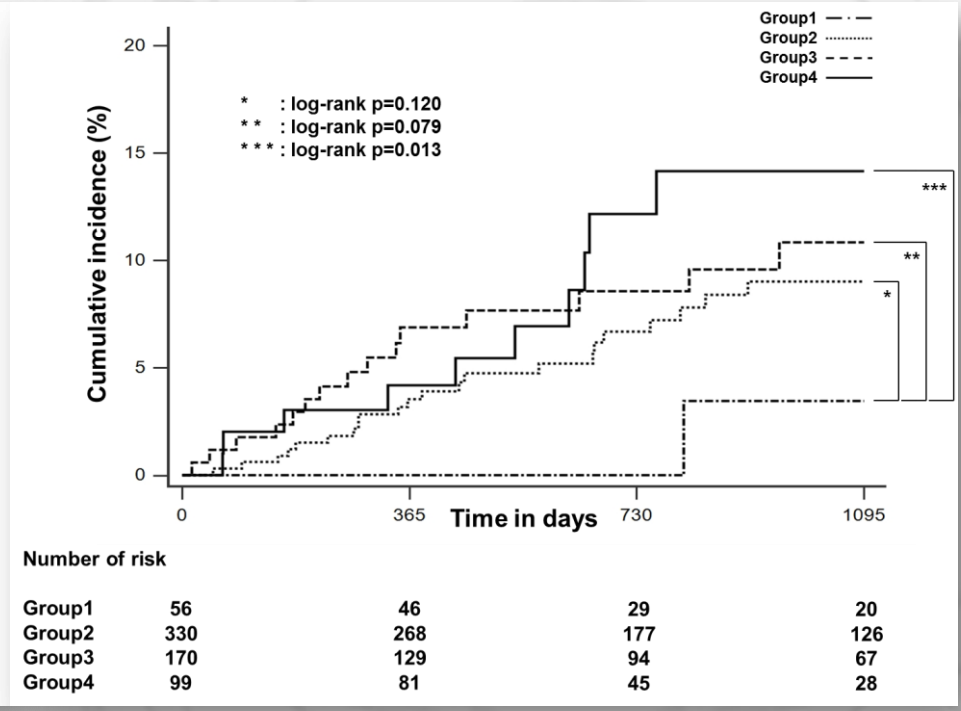
3-year Outcomes after FFR-guided Defer

Among 1294 patients and 1628 lesions in Korean FFR registry, 665 patients with 781 deferred coronary lesions, categorized 4 groups according to FFR; group 1: >0.95, group 2: 0.86–0.95, group 3: 0.81–0.85, and group 4: <0.80, MACE defined as the composites of all death, MI, and TVR



Number of risk

Group1+2+3	99	81	45	28
Group4	556	443	300	213



Number of risk

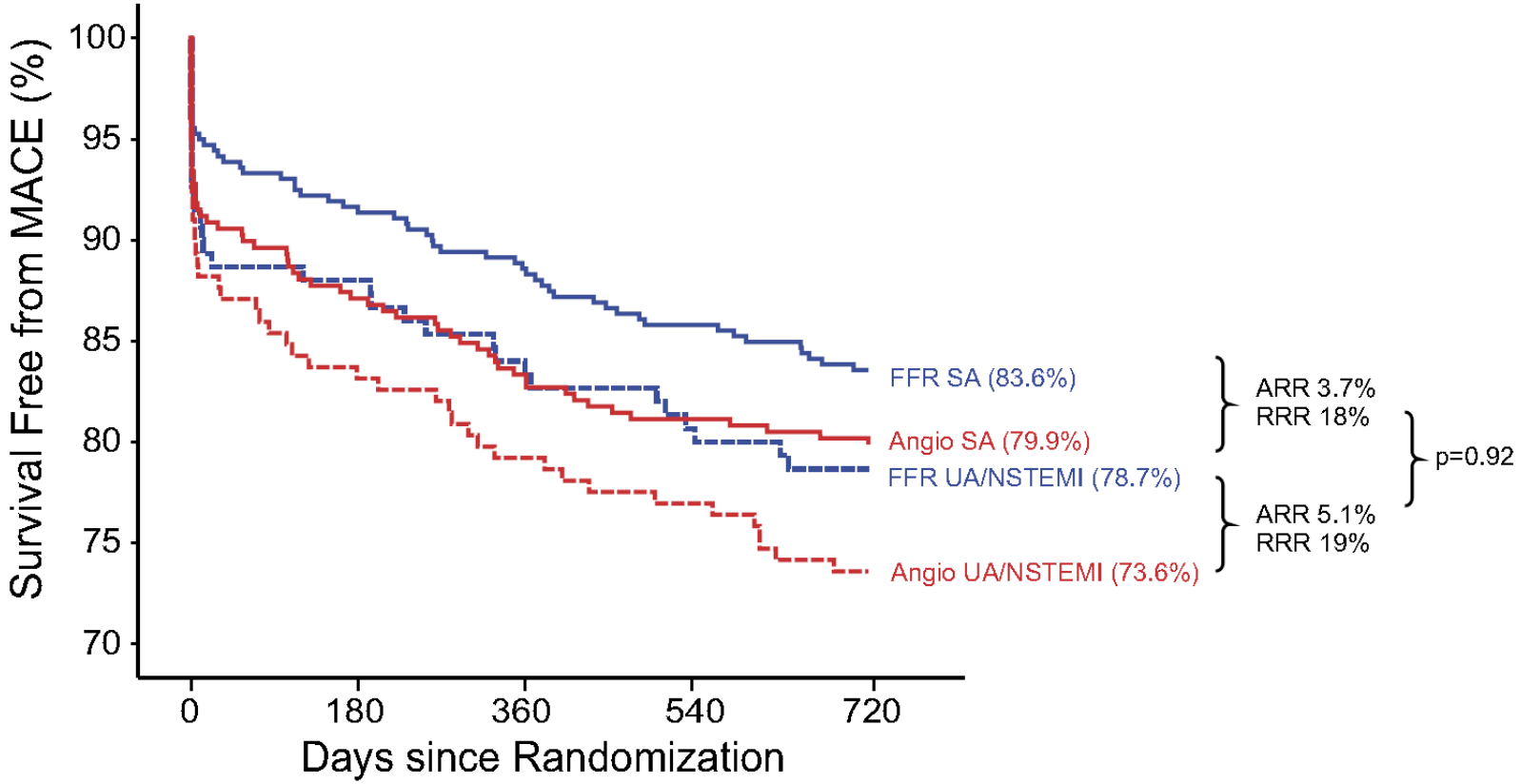
Group1	56	46	29	20
Group2	330	268	177	126
Group3	170	129	94	67
Group4	99	81	45	28

3-year Outcomes after FFR-guided Defer

	Subjects with FFR >0.8					
	Univariate analysis			Multivariate analysis		
	HR	95% CI	P	HR	95% CI	P
Age	1.02	0.99–1.06	0.133			
Male	1.05	0.55–1.98	0.890			
Diabetes mellitus	1.75	0.93–3.27	0.082			
Dyslipidemia	1.17	0.63–2.18	0.612			
Smoking	1.61	0.83–3.11	0.156			
Previous MI	2.56	1.08–6.08	0.034	1.20	0.44–3.30	0.725
Previous PCI or CABG	2.64	1.41–4.94	0.002	**2.37**	**1.13–5.01**	**0.023**
ACS	2.46	1.31–4.61	0.005	**2.35**	**1.18–4.65**	**0.015**
LVEF	0.96	0.93–0.99	0.006	0.98	0.95–1.01	0.232
Multi-VD	2.25	1.16–4.34	0.016	1.45	0.72–2.92	0.298
LAD	0.45	0.24–0.84	0.012	0.57	0.30–1.10	0.095
Reference diameter	1.26	0.72–2.20	0.424			
% DS	1.02	1.00–1.05	0.081			
Lesion length>20 mm	1.33	0.69–2.57	0.392			
Previous PCI-MLD	0.71	0.36–1.38	0.308			
FFR	0.96	0.90–1.02	0.188			

Submitted data from Korean FFR registry

FFR in UA or NSTEMI: FAME



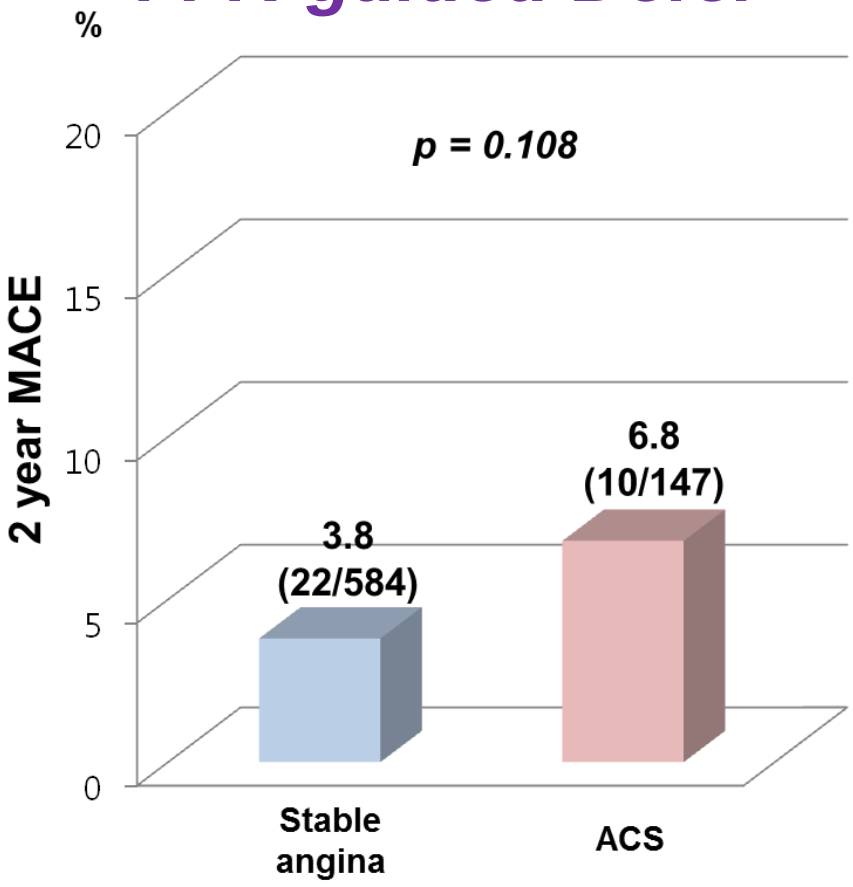
The benefit of using FFR to guide PCI in MVD does not differ between ACS, compared with SA

Sels JW et al. JACC interv 2011;4:1183

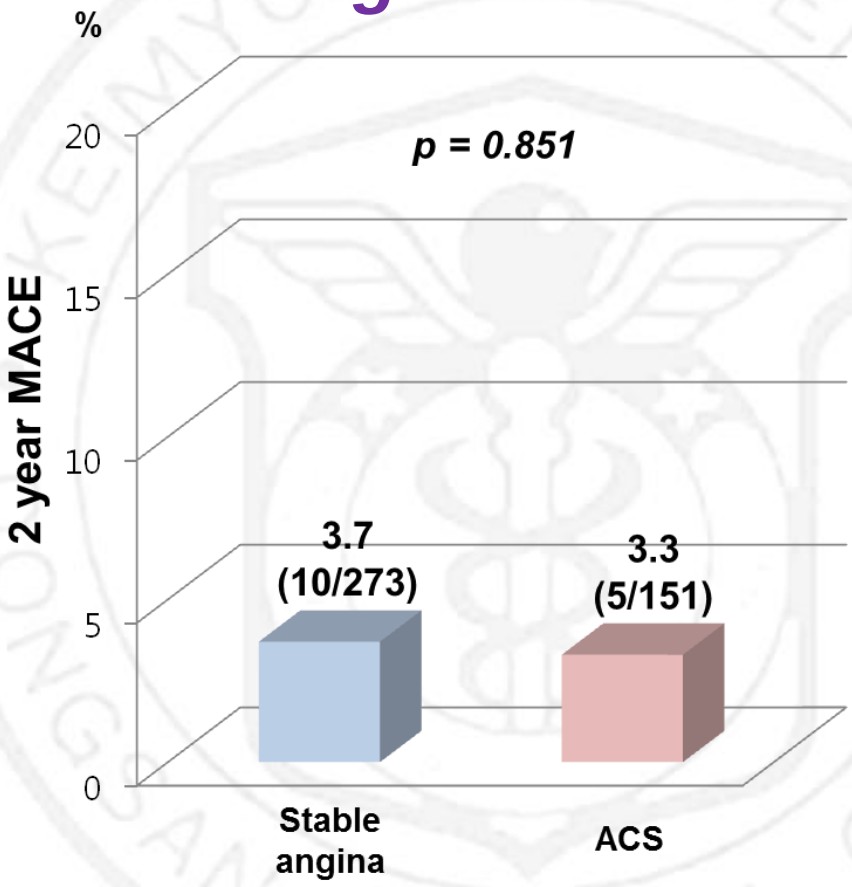
Korean FFR registry

Only FFR-guided decision made 1155 patients

FFR-guided Defer



FFR-guided PCI



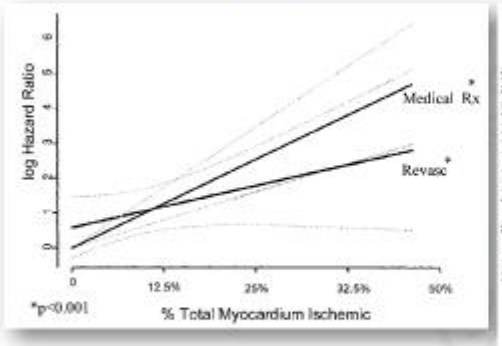
Keimyung University, Korea

Presented at 2013 KSC

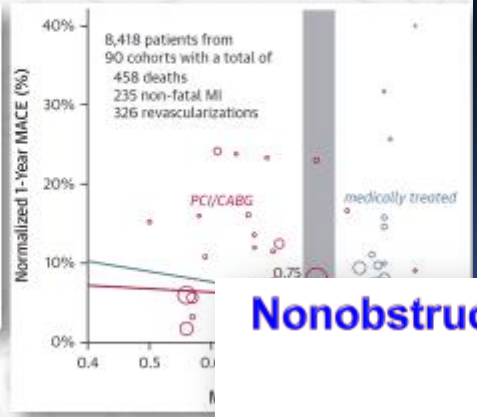
What we can to do for nonculprit lesion of ACS

FFR & Burden of ischemia

Burden of Ischemia



FFR



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The ***PREVENT***ive Implantation of Bioresorbable Vascular Scaffold on Stenosis With Functionally Insignificant Vulnerable Plaque

PREVENT Trial

Any Epicardial Coronary Stenosis (DS>50% by visual estimation)
with *FFR >0.80* and with *Two* of the following

1. MLA ≤4.0mm^2
2. Plaque Burden$_{MLA}$ >70%
3. Lipid-Rich Plaque on NIRS ($_{max}$LCBI$_{4mm}$>315)
4. TCFA defined by OCT or VH-IVUS

R

OMT
N=800

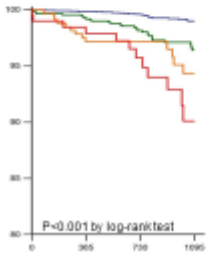
ngina

arm at 2 years)

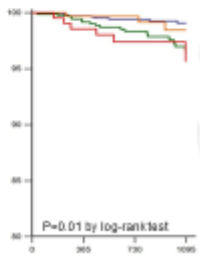
Nonobstructive CAD

SIS Quartiles

Even-free survival without statin

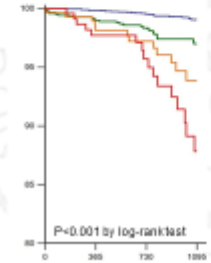


Even-free survival with statin

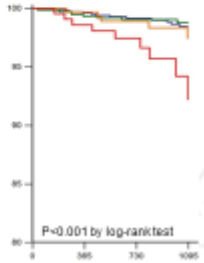


Calcium score Quartiles

Even-free survival without statin



Even-free survival with statin



Keimyung University, Korea

Cho YK, Nam CW et al. 2014 AHA, KSC

Keimyung University, Korea

Late Benefit, but not only from Lipid: Plaque Stabilization…

EASY-FIT

70 Patients with U
Naïve to statin

int: Fibrous Cap
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months

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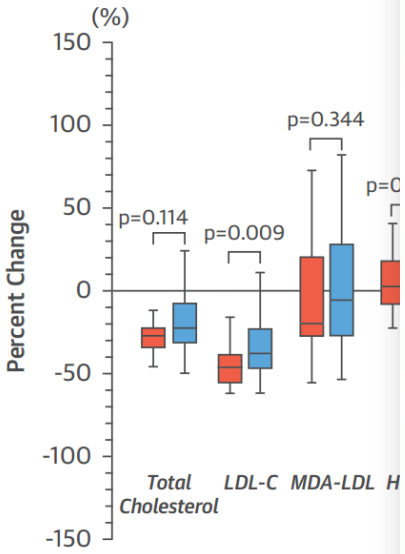

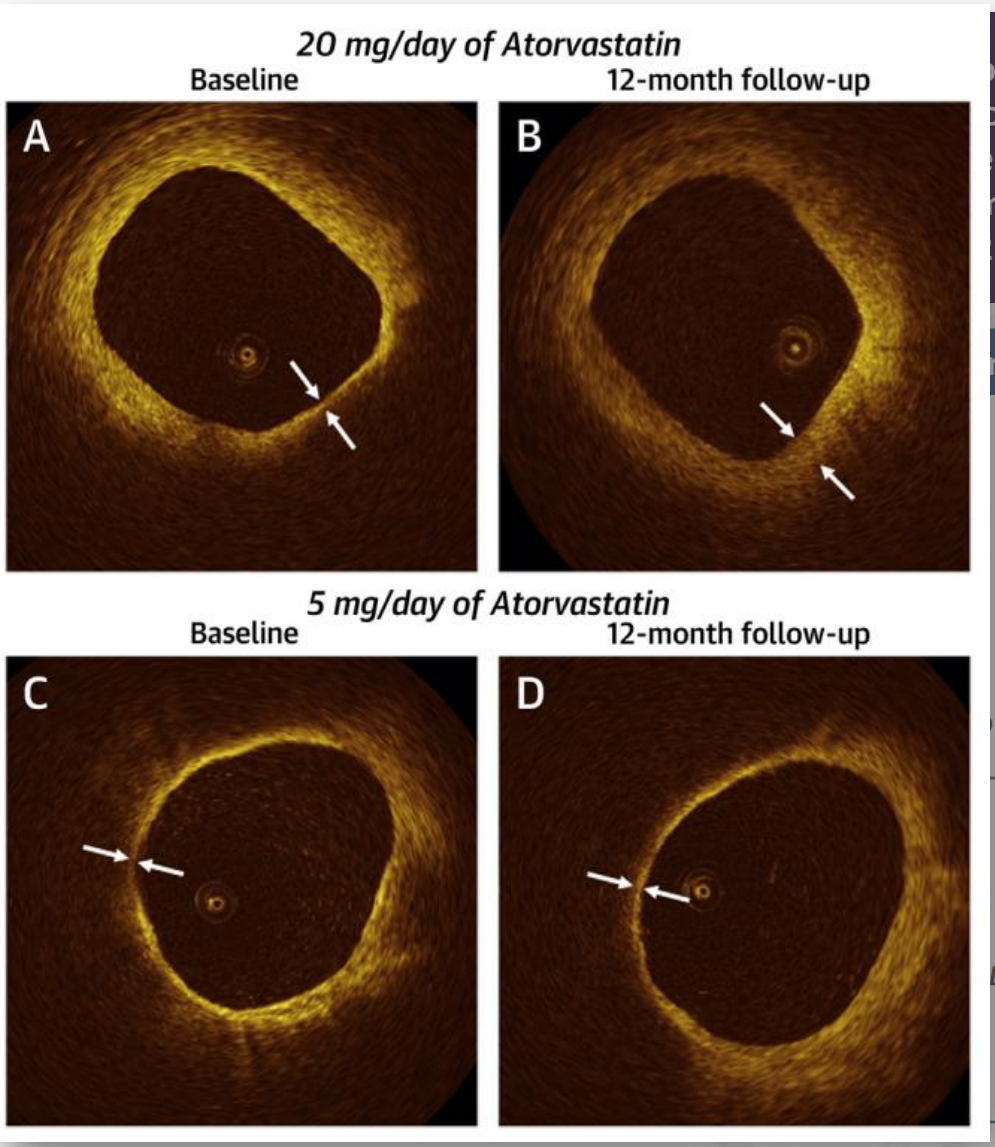

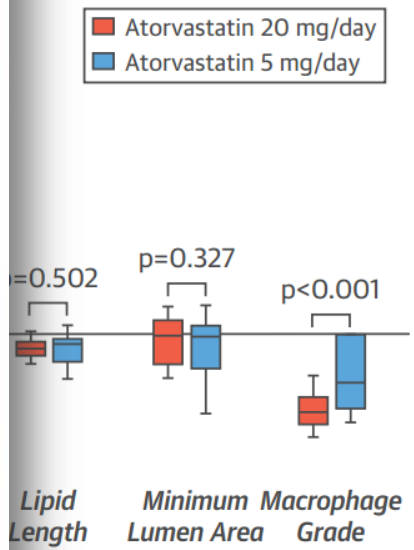

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J Am Coll Cardiol 2014;64:2207

Take Home Message

01 **Technical issues for the physiologic evaluation of nonculprit lesion in ACS**

02 **Clinical issues for the physiologic evaluation of nonculprit lesion in ACS**

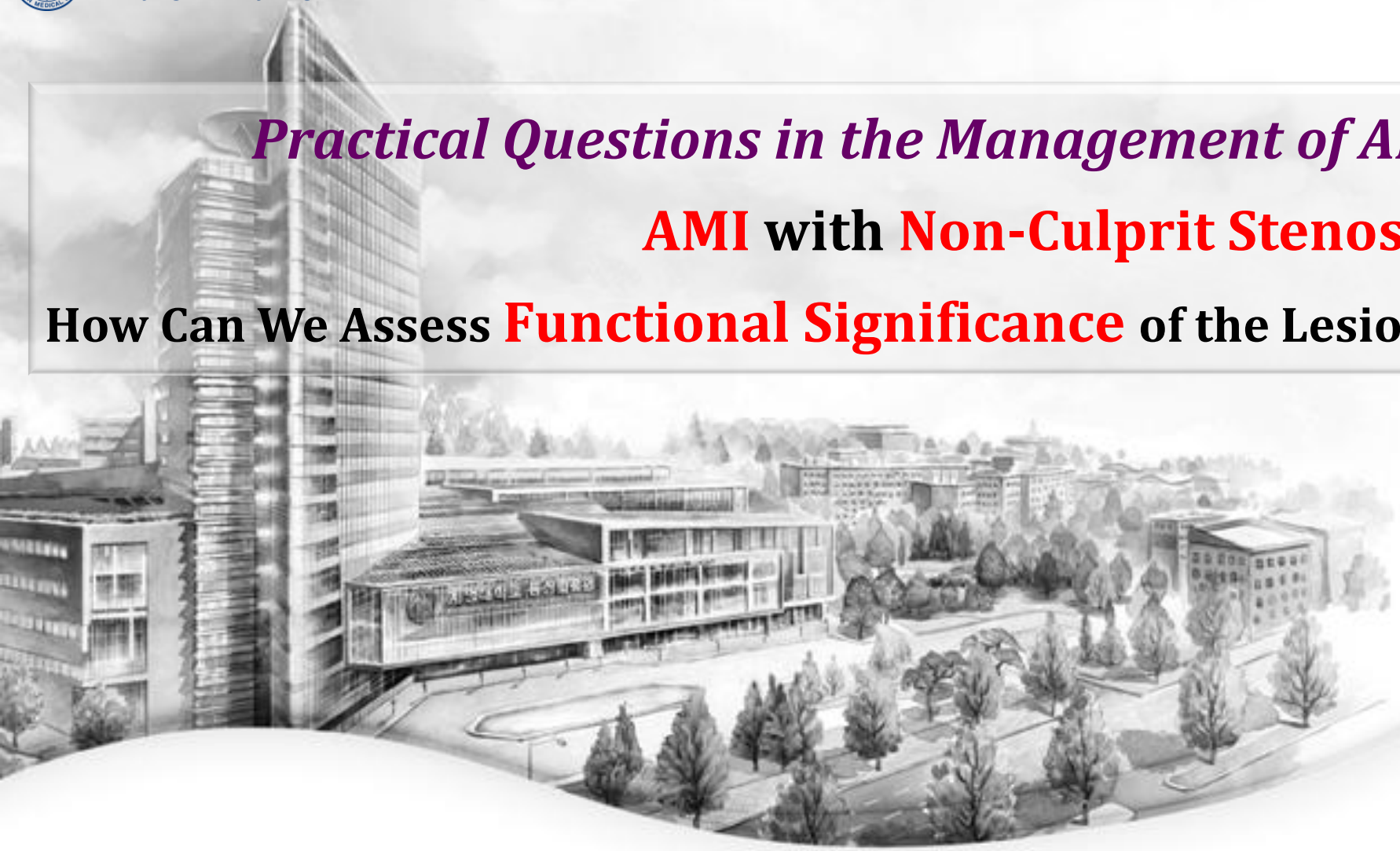
- The severity of nonculprit lesion in ACS can reliably be assessed by FFR. However, several technical issues are still exist as barriers of this application.
- Clinical outcome of FFR guided treatment in nonculprit lesion of ACS was acceptable. However, large trial to confirm this strategy should be warranted.

계명대학교 동산의료원
Keimyung University Dongsan Medical Center

Practical Questions in the Management of AMI

AMI with Non-Culprit Stenosis,

How Can We Assess Functional Significance of the Lesions?



Keimyung University Dongsan Medial Center

NAM, Chang-Wook MD, PhD

Thank You