

# Role of FFR in ACS: Still Doubtful?

**Bon-Kwon Koo, MD, PhD**

Seoul National University Hospital, Seoul, Korea



# FFR-guided PCI

Fractional flow reserve (FFR) is the current standard of care for the functional assessment of coronary stenosis.

## 5.4.1. FFR: Recommendation

### CLASS IIa

1. FFR is reasonable to assess angiographic intermediate coronary lesions (50% to 70% diameter stenosis) and can be useful for guiding revascularization decisions in patients with SIHD (12,97, 484–486). (Level of Evidence: A)

### Recommendations for the clinical value of intracoronary diagnostic techniques

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>	Ref. <sup>c</sup>
FFR to identify haemodynamically relevant coronary lesion(s) in stable patients when evidence of ischaemia is not available.	I	A	50,51,713
FFR-guided PCI in patients with multivessel disease.	IIa	B	54

# FFR evidences.....

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Long-Term Clinical  
Outcome After Fractional Flow  
Reserve-Guided Percutaneous  
Intervention in Patients With

Alexandre Berger, MD,\* Kees-Joost Botman, MD,\* Philip A. MacCarthy, MD, PhD, MRCP,\*  
William Wijns, MD, PhD,\* Jozef Bartunek, MD, PhD,\* Guy R. Heyndrickx, MD, PhD,\*  
Nico H. J. Pijls, MD, PhD,† Bernard De Bruyne, MD, PhD\*  
*Aalst, Belgium; and Eindhoven, the Netherlands*



Fractional Flow Reserve versus Angiography  
for Guiding Percutaneous Coronary Intervention



Fractional Flow Reserve-Guided PCI versus Medical Therapy  
in Stable Coronary Disease

## Clinical Investigation and Reports

Coronary Pressure Measurement After Stenting Predicts  
Adverse Events at Follow-Up  
A Multicenter Registry



ers, MD;  
mi, MD;

# FFR in patients with ACS?

Native Coronary Arteries

Stefan Krüger, MD; Karl-Christian Koch, MD; Ira Kaumanns, MD;  
Marc W. Merx, MD; Peter Hawrath, MD; and Rainer Hoffmann, MD

Interventional Cardiology

Clinical outcome in patients with intermediate  
equivocal left main coronary artery disease a  
deferral of surgical revascularization on the basis of  
fractional flow reserve measurements

Michael Lindstaedt, MD,<sup>a</sup> Aydan Yazar, MD,<sup>a</sup> Alfried Germing, MD,<sup>a</sup> Markus K. Fritz, MD,<sup>b</sup>  
Tim Holland-Letz, MSc,<sup>c</sup> Andreas Mügge, MD,<sup>a</sup> and Waldemar Bojara, MD<sup>a</sup> *Bochum, Germany*

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doi:10.1016/j.jacc.2005.04.054

Physiologic Assessment of Jailed Side  
Branch Lesions Using Fractional Flow Reserve

Bon-Kwon Koo, MD, PhD,\* Hyun-Jai Kang, MD, PhD,\* Tae-Jin Youn, MD, PhD,†  
In-Ho Chae, MD, PhD,† Dong-Joo Choi, MD, PhD,† Hyo-Soo Kim, MD, PhD,\*  
Dae-Won Sohn, MD, PhD,\* Byung-Hee Oh, MD, PhD, FACC,\*  
Myoung-Mook Lee, MD, PhD, FACC,\* Young-Bae Park, MD, PhD,<sup>‡</sup>  
Yun-Shik Choi, MD, PhD,\* *Seung-Iae Tack, MD, PhD*

*Seoul, Seongnam, Gyeonggi-*

Physiological evaluation of the provisional  
side-branch intervention strategy for bifurcation  
lesions using fractional flow reserve

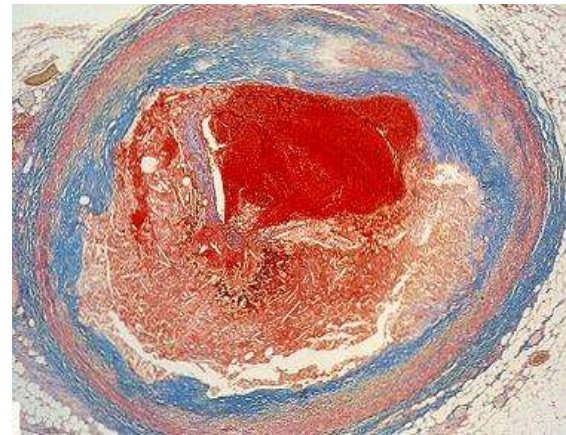
Bon-Kwon Koo<sup>1</sup>, Kyung-Woo Park<sup>1</sup>, Hyun-Jae Kang<sup>1</sup>, Young-Seok Cho<sup>2</sup>,  
Woo-Young Chung<sup>2</sup>, Tae-Jin Youn<sup>2</sup>, In-Ho Chae<sup>2</sup>, Dong-Ju Choi<sup>2</sup>, Seung-Jae Tahk<sup>2</sup>,  
Byung-Hee Oh<sup>1</sup>, Young-Bae Park<sup>1</sup> and Hyo-Soo Kim<sup>1†</sup>

<sup>1</sup>Division of Cardiology, Department of Internal Medicine, Seoul National University College of Medicine, Cardiovascular Center and Cardiovascular Research Institute, Seoul National University Hospital, Yongon-dong 51, Yongsu-gu, Seoul 151-747, Republic of Korea; <sup>2</sup>Heart Center, Samsung Seoul National University Hospital, Gyeonggi-do, Republic of Korea; and <sup>3</sup>Yonsei University School of Medicine, Gyeonggi-do, Republic of Korea

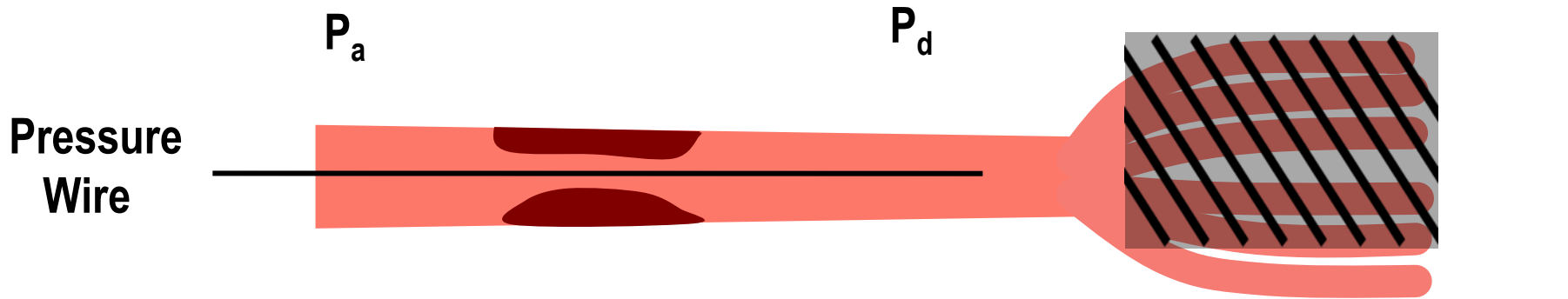
Received 26 March 2005; revised 8 January 2006; accepted 17 January 2006; online publication 28 February 2006

# Unique features of ACS

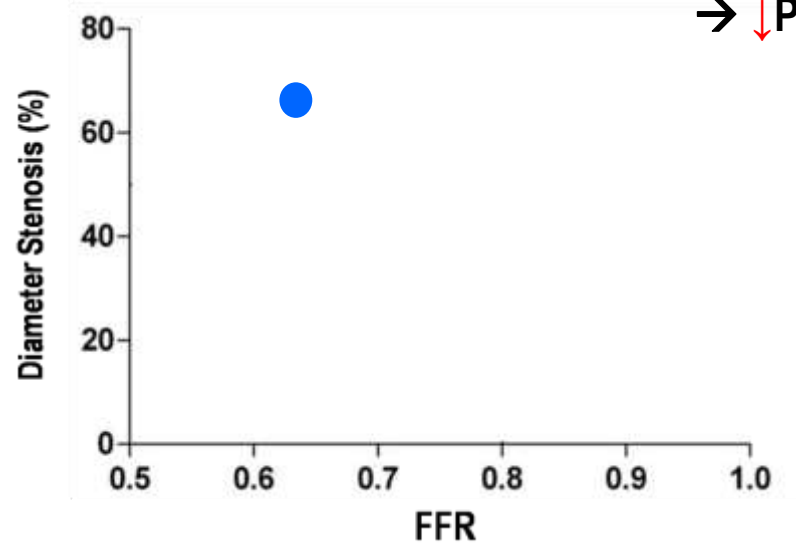
- Unstable clinical condition
- Vulnerable plaque
- Plaque rupture
- Thrombus
- Myocardial damage and microvascular dysfunction



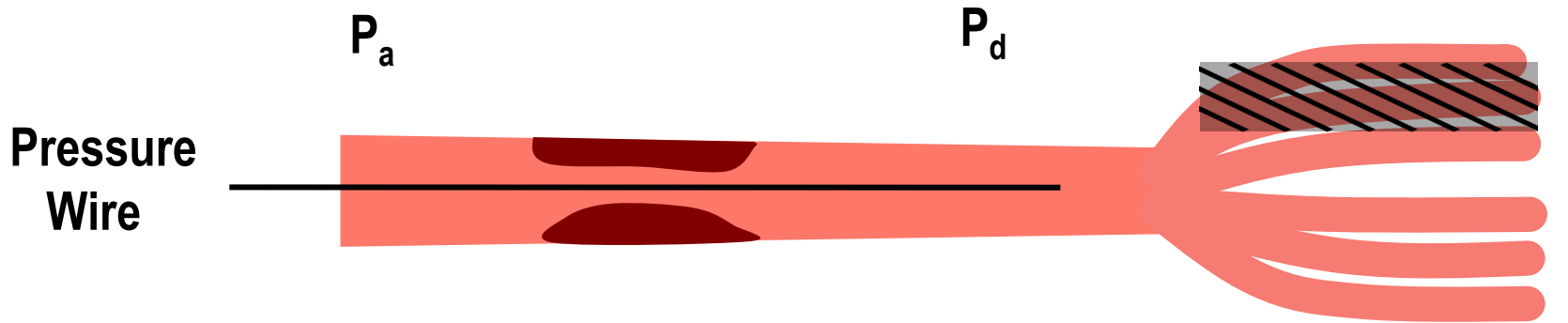
# So, what's wrong with using FFR in ACS, especially in AMI?



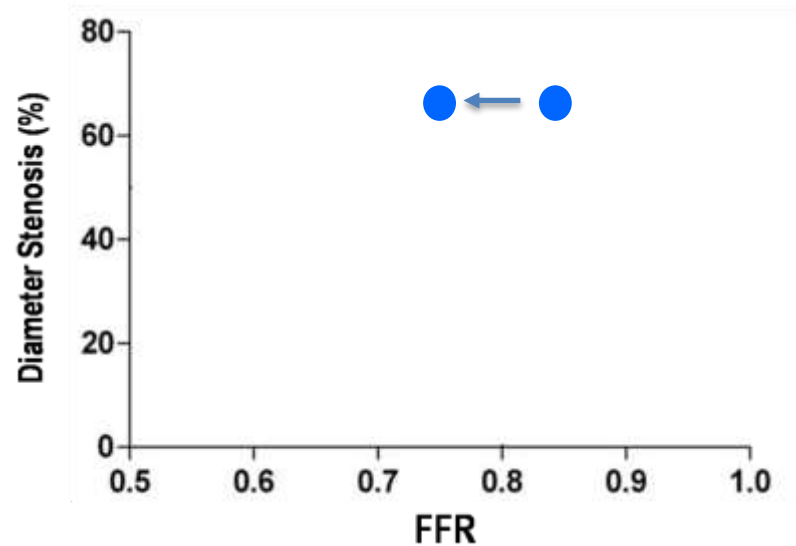
↑ Resistance → ↓ Flow  
→ ↓ Pressure gradient → ↑ FFR



# So, what's wrong with using FFR in ACS, especially in AMI?



Partial recovery  $\rightarrow$   $\downarrow$  FFR



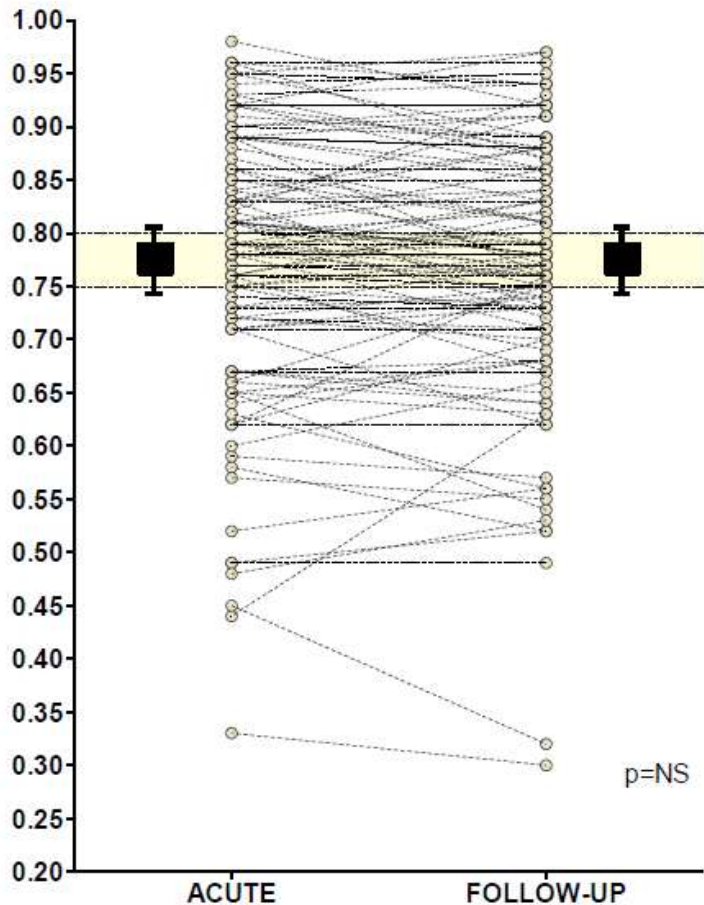
# Influence of MI on FFR

	MI	No MI	<i>P</i>
Target lesion, n	22	21	
Pre-/postintervention, n	7/15	10/11	0.2
Diameter stenosis, %	43 ± 22	44 ± 16	0.9
MLD, mm	1.7 ± 0.8	1.6 ± 0.6	0.6
Length, mm	9.1 ± 4.0	7.3 ± 3	0.1
Reference diameter, mm	2.9 ± 0.5	2.8 ± 0.6	0.6
Flow velocity measurements			
APV (basal), cm/sec	17 ± 7	17 ± 8	0.8
APV (hyperemic), cm/sec	26 ± 13	36 ± 16	0.03
Coronary flow reserve	1.5 ± 0.3	2.1 ± 0.4	< 0.0001
Flow (hyperemic), ml/min	37 ± 26	48 ± 22	0.03
Pressure measurements			
Gradient (hyperemic), mm Hg	13 ± 11	21 ± 13	0.05

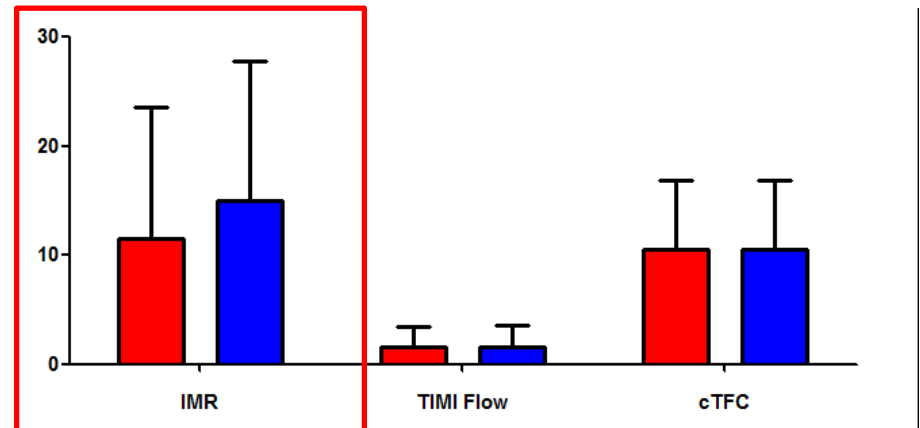
# Then, what about for non-culprit lesions?

101 patients with ACS (75 STEMI, 26 NSTEMI)

112 non-culprit stenoses – FFR at index and F/U ( $35 \pm 24$  days)



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

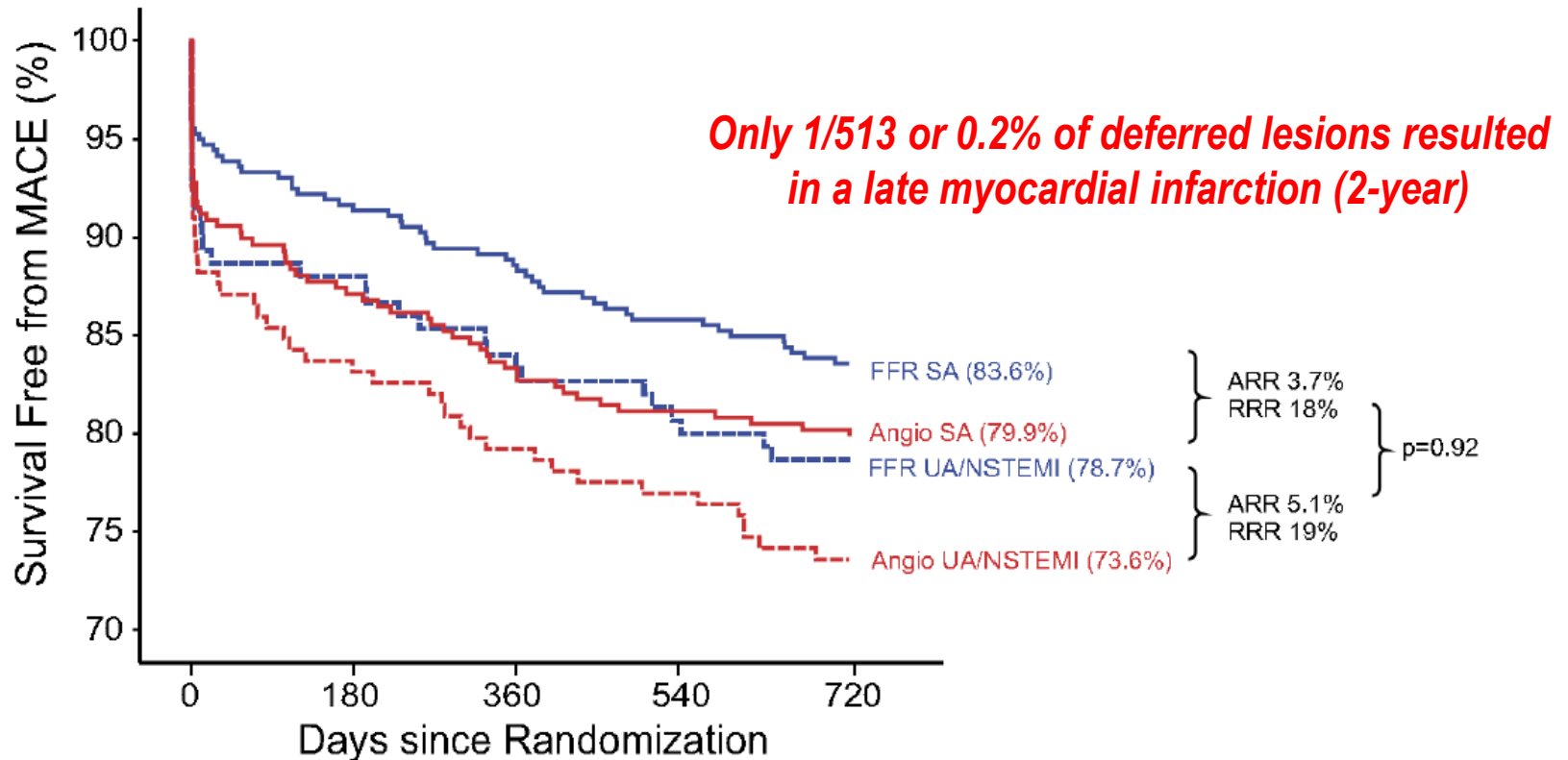


Ntalianis, et al. JACC Intv 2010



# FFR-guided Strategy for NSTEMI/UA (Multivessel)

FAME sub-study (328 patients with NSTEMI/UA)

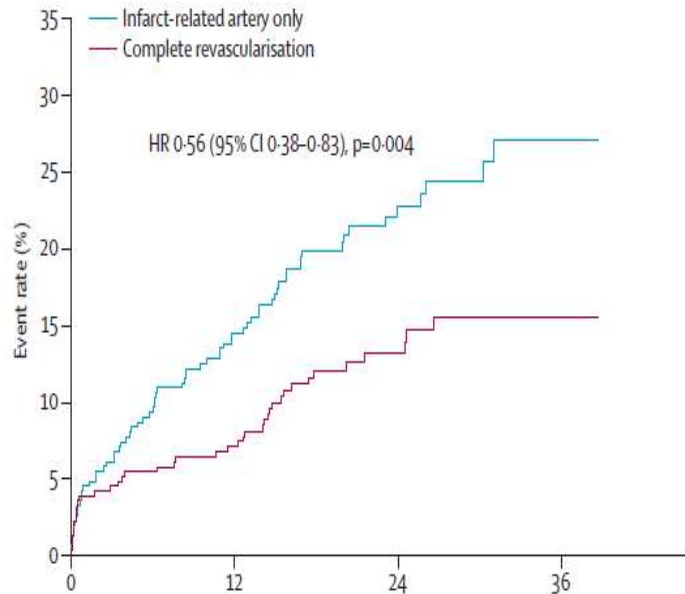


**No difference between SA and UA/NSTEMI**

Sels, et al. JACC Intv 2011

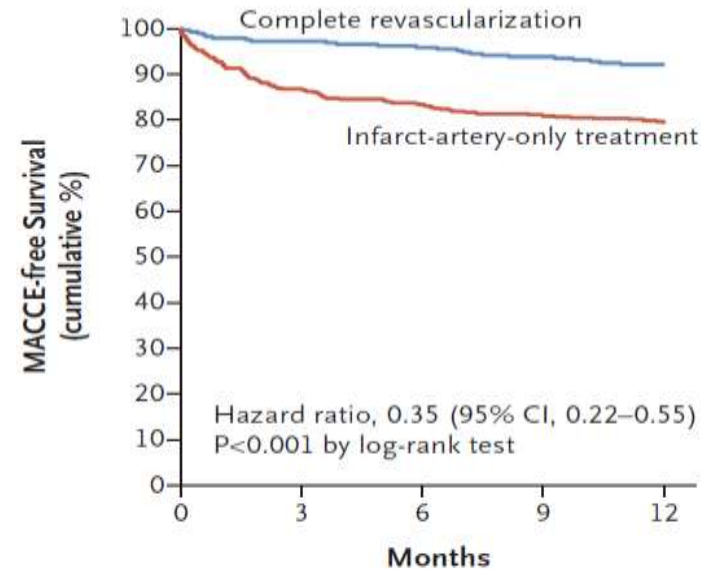
# FFR-Guided CR vs. IRA only in STEMI with MVD

## DANAMI-3-PRIMULTI



Number at risk		Follow-up (months)			
		0	12	24	36
Infarct-related artery only	313	271	142	53	
Complete revascularisation	314	291	159	55	

## COMPARE-ACUTE



No. at Risk		Months				
		0	3	6	9	12
Complete revascularization	295	286	281	264	215	
Infarct artery	590	512	492	457	371	

Engstrom, et al. Lancet 2015;386:665-671  
Smits, et al. N Engl J Med 2017;376:1234-1244

# Why still doubtful?

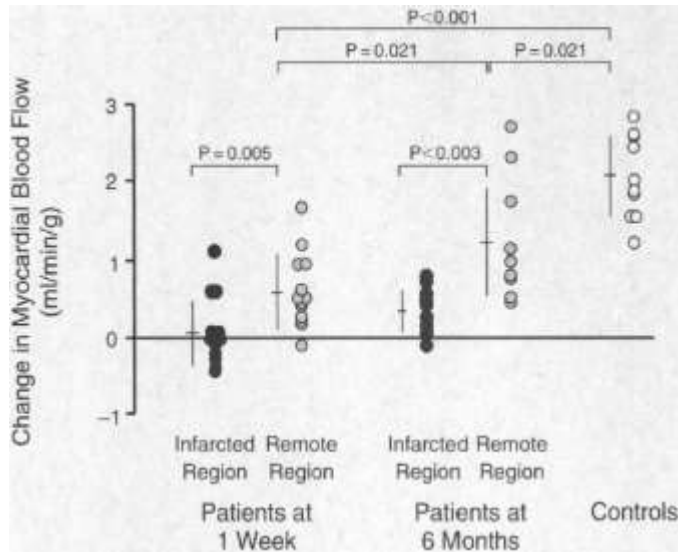
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THE NEW ENGLAND JOURNAL OF MEDICINE

July 28, 1994

## REDUCED CORONARY VASODILATOR FUNCTION IN INFARCTED AND NORMAL MYOCARDIUM AFTER MYOCARDIAL INFARCTION

NEAL G. UREN, M.D., TOM CRAKE, M.D., DAVID C. LEFROY, M.R.C.P., RANIL DE SILVA, PH.D., GRAHAM J. DAVIES, M.D., AND ATTILIO MASERI, M.D.

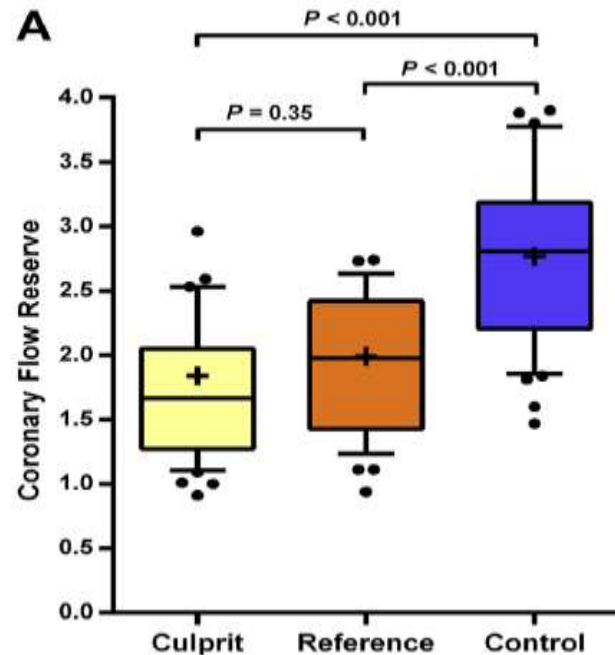


INDEX	MYOCARDIAL BLOOD FLOW (ml/min/g)			CORONARY VASCULAR RESISTANCE (mm Hg · min · g/ml)		
	PET AT 1 WK (N = 13)	PET AT 6 MO (N = 9)	P VALUE	PET AT 1 WK (N = 13)	PET AT 6 MO (N = 9)	P VALUE
<b>Infarcted region</b>						
Basal value	0.81±0.22	0.82±0.21	NS	110.3±48.7	116.9±45.8	NS
Peak after dipyridamole	0.91±0.51	1.20±0.45	0.053	118.0±61.0	107.8±104.4	NS
Coronary vasodilator response	1.12±0.50	1.42±0.37	0.05	—	—	—
<b>Remote region</b>						
Basal value	1.09±0.32†	1.09±0.18‡	NS	76.1±16.7§	83.3±21.0	NS
Peak after dipyridamole	1.70±0.72¶	2.38±0.89	0.006	55.1±18.4¶	43.7±14.8	0.018
Coronary vasodilator response	1.53±0.36**	2.19±0.69¶	0.011	—	—	—

## Changes in Coronary Blood Flow After Acute Myocardial Infarction

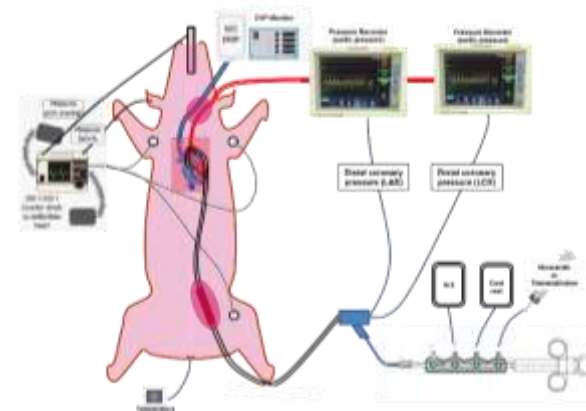
Insights From a Patient Study and an Experimental Porcine Model

Gaas A. de Waard, MD,<sup>1</sup> Maurits R. Hollander, MD,<sup>2</sup> Paul F.A. Teunissen, MD,<sup>3</sup> Matthijs F. Jansen, MD,<sup>4</sup> Elise S. Eerenberg, MD,<sup>5</sup> Aernout M. Beek, MD, PhD,<sup>6</sup> Koen M. Marques, MD, PhD,<sup>7</sup> Peter M. van de Ven, PhD,<sup>8</sup> Ingrid M. Garrelts, MSc,<sup>9</sup> A.H. Jan Danser, PhD,<sup>10</sup> Dick J. Duncker, MD, PhD,<sup>11</sup> Niels van Royen, MD, PhD<sup>12</sup>



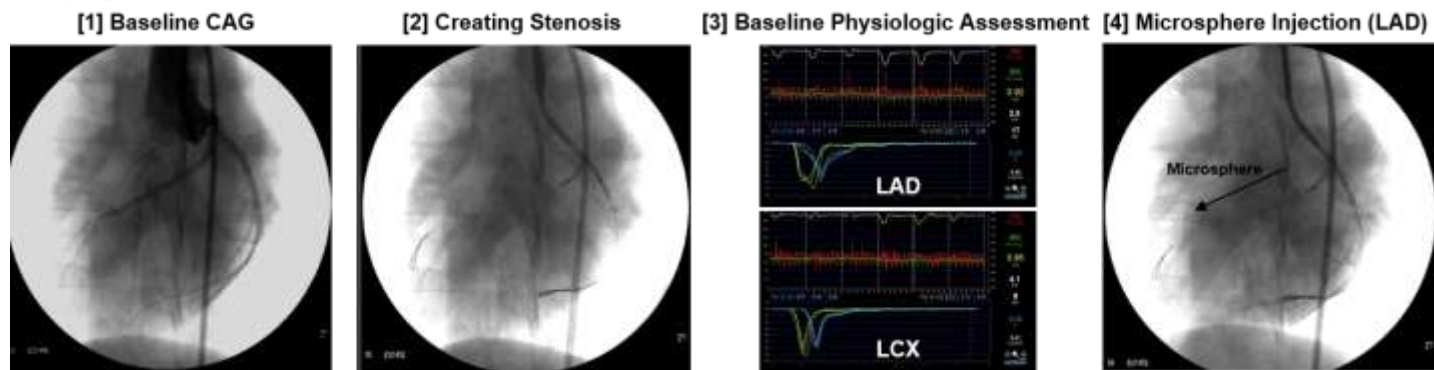
de Waard, et al. JACC Intv 2016





# Influence of Local Myocardial Damage on Index of Microcirculatory Resistance and Fractional Flow Reserve in Target and Nontarget Vascular Territories in a Porcine Microvascular Injury Model

Joo Myung Lee, MD, MPH, PhD,<sup>a</sup> Hyun Kuk Kim, MD, PhD,<sup>b</sup> Kyung Seob Lim, DVM, PhD,<sup>c</sup> Jun-Kyu Park, PhD,<sup>d</sup> Ki Hong Choi, MD,<sup>e</sup> Jonghanne Park, MD,<sup>e</sup> Doyeon Hwang, MD,<sup>e</sup> Tae-Min Rhee, MD,<sup>f</sup> Jeong Hoon Yang, MD,<sup>g,h</sup> Eun-Seok Shin, MD, PhD,<sup>b</sup> Chang-Wook Nam, MD, PhD,<sup>i</sup> Joon-Hyung Doh, MD, PhD,<sup>j</sup> Joo-Yong Hahn, MD, PhD,<sup>g</sup> Bon-Kwon Koo, MD, PhD,<sup>k,l</sup> Myung Ho Jeong, MD, PhD<sup>g</sup>



LAD (Microsphere injection)

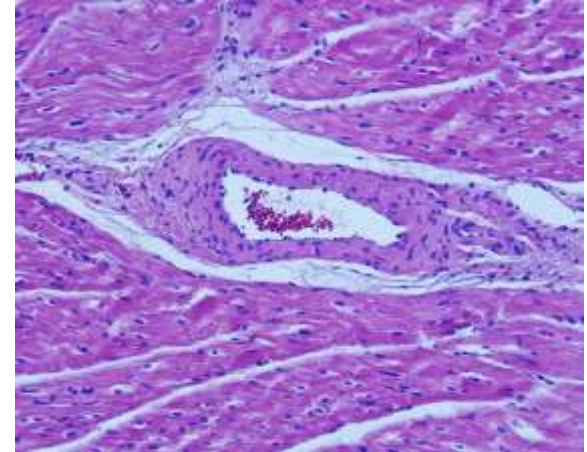
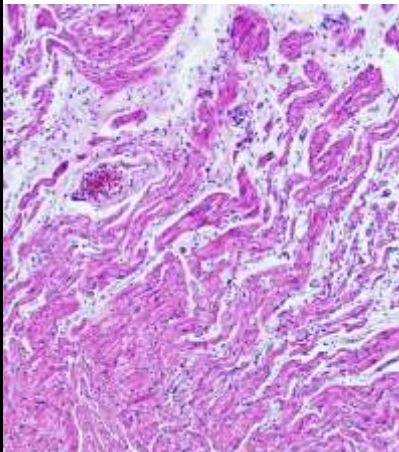
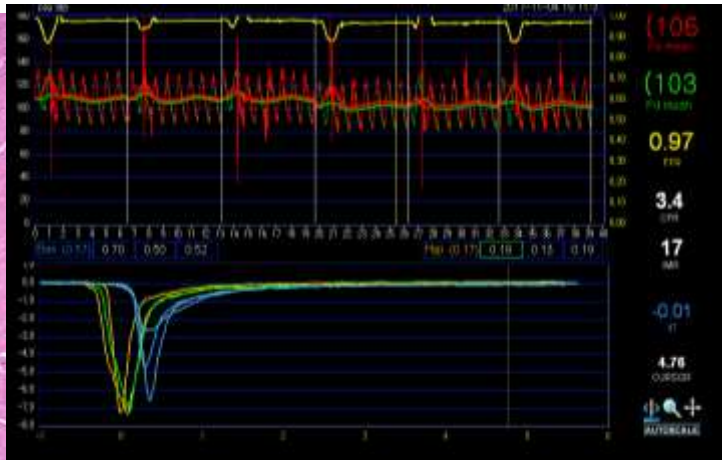


LCX (No microsphere injection)

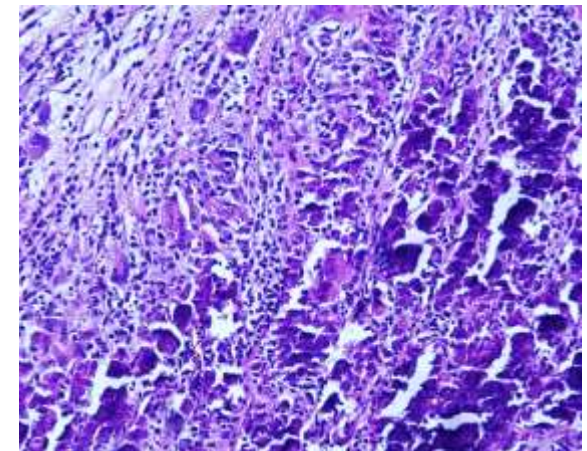
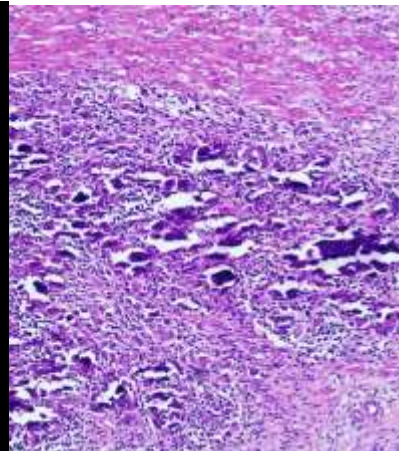
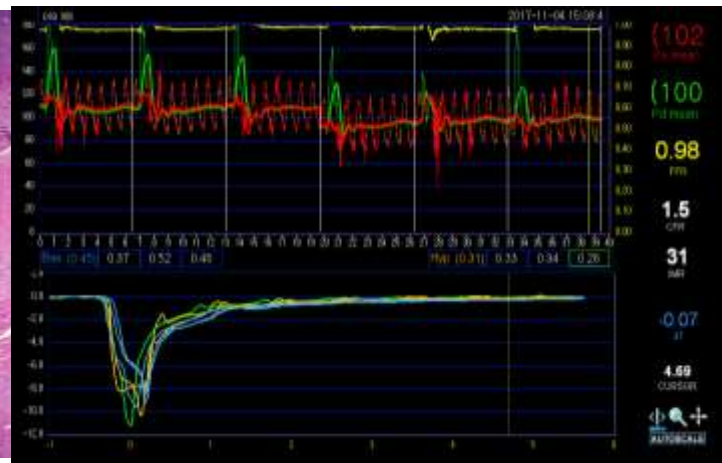


# Pathologic change vs. IMR

## No microvascular injury



## Microsphere injection



Courtesy of HK Kim, MD, PhD

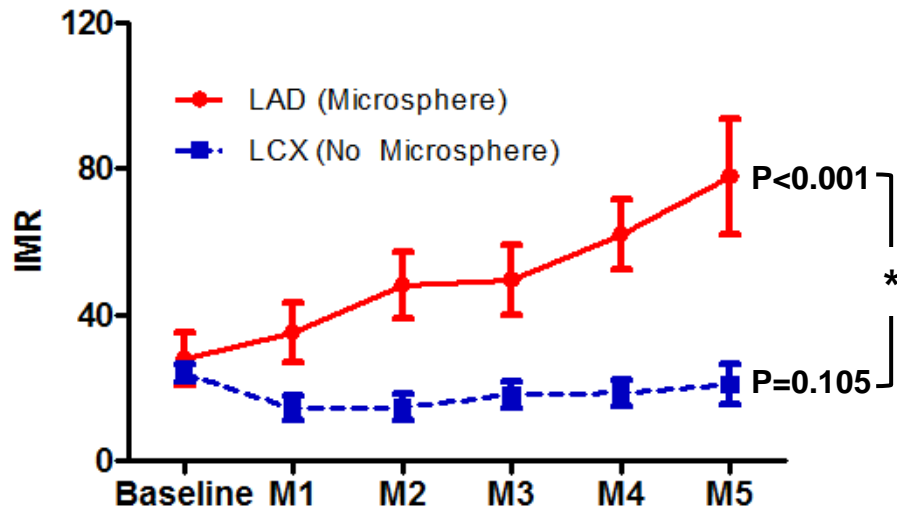
# Baseline characteristics

Animals (N=12)	
Body weight, kg	25.0 (24.0-27.0)
Interrogated Vessels (N=24)	
Reference vessel diameter, mm	
LAD	2.90 (2.83-3.09)
LCX	2.88 (2.51-3.61)
Area stenosis, %	
LAD	48.1 (40.8-50.4)
LCX	47.9 (31.1-62.9)
Fractional flow reserve	
LAD	0.92 (0.81-0.95)
LCX	0.95 (0.93-0.97)
Index of microcirculatory resistance	
LAD	16.2 (9.2-24.5)
LCX	17.3 (9.9-23.9)

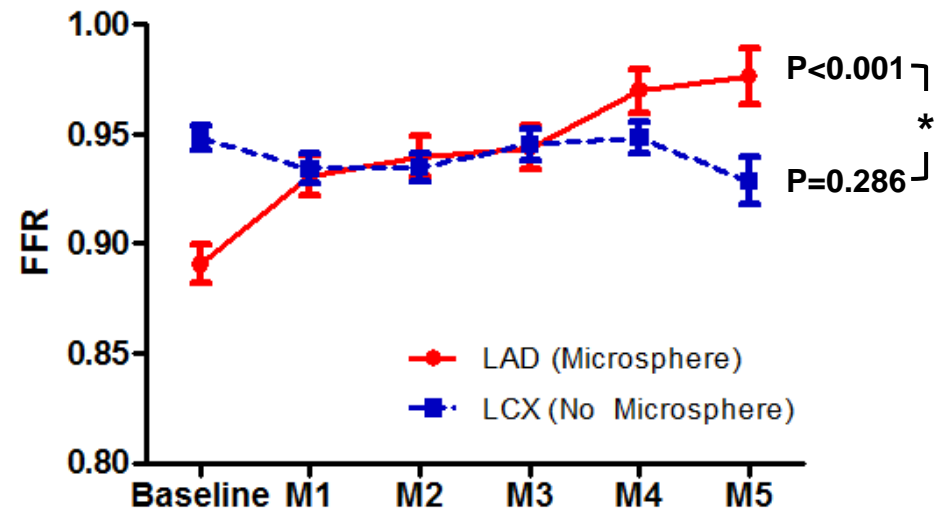
Lee JM & Kim HK, ....., Koo BK, Jeong MH, JACC Intv, 2018

# Changes in Culprit/Non-culprit vessels

## IMR



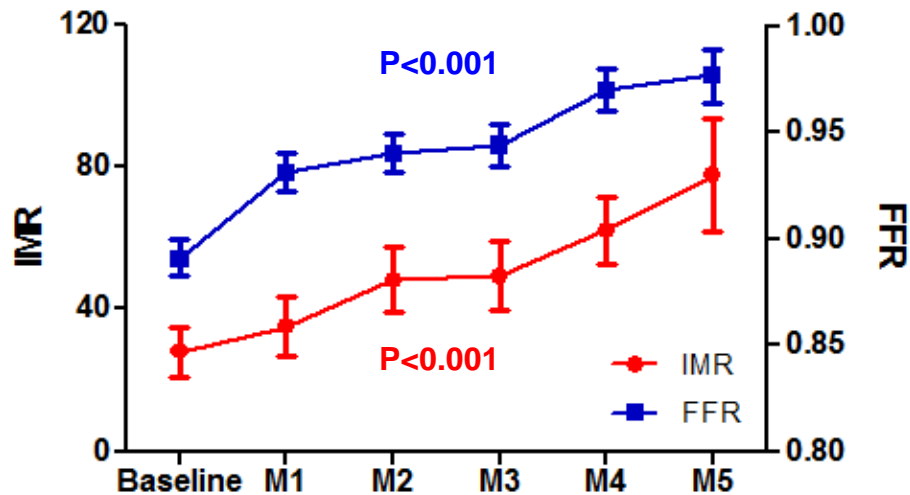
## FFR



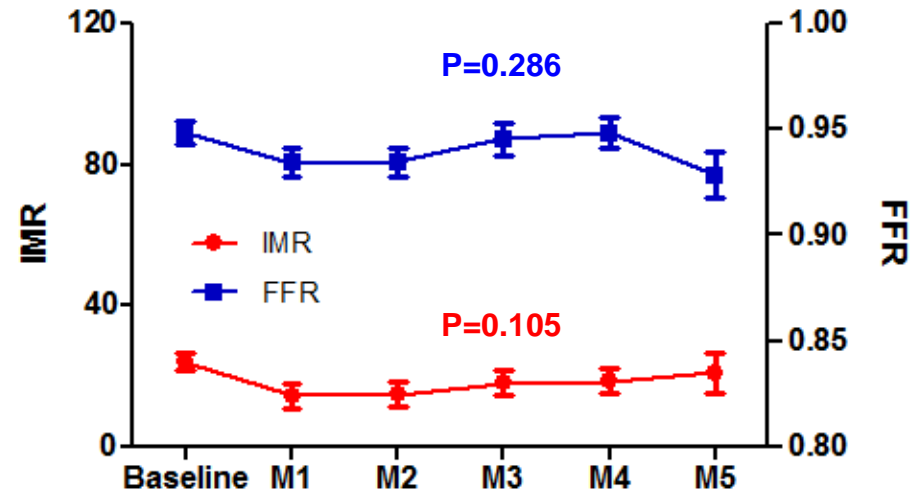
Lee JM & Kim HK, ....., Koo BK, Jeong MH, JACC Intv, 2018

# Changes in Culprit/Non-culprit vessels

## LAD (Culprit)



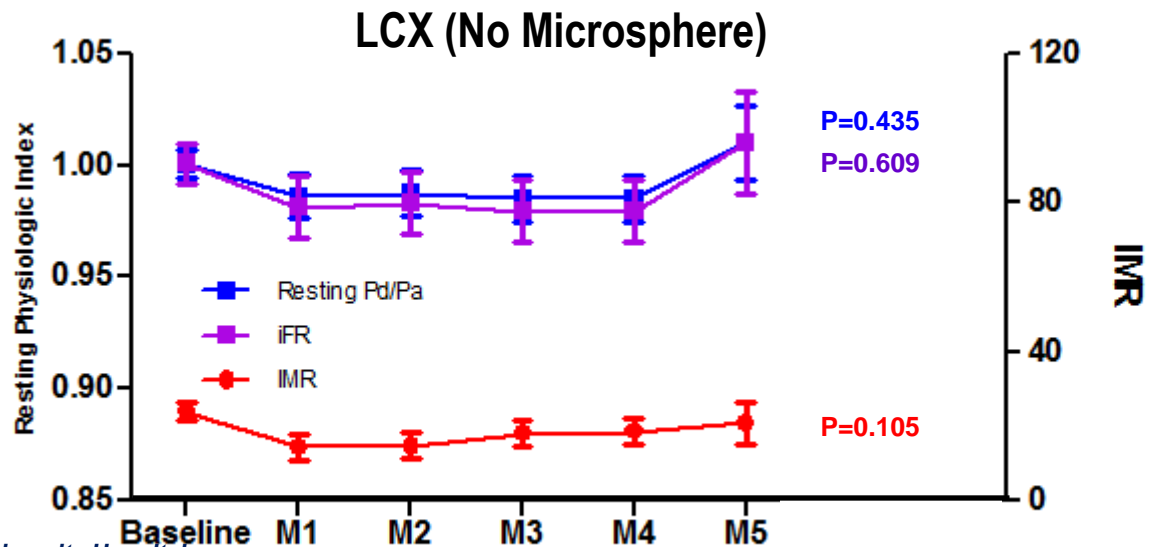
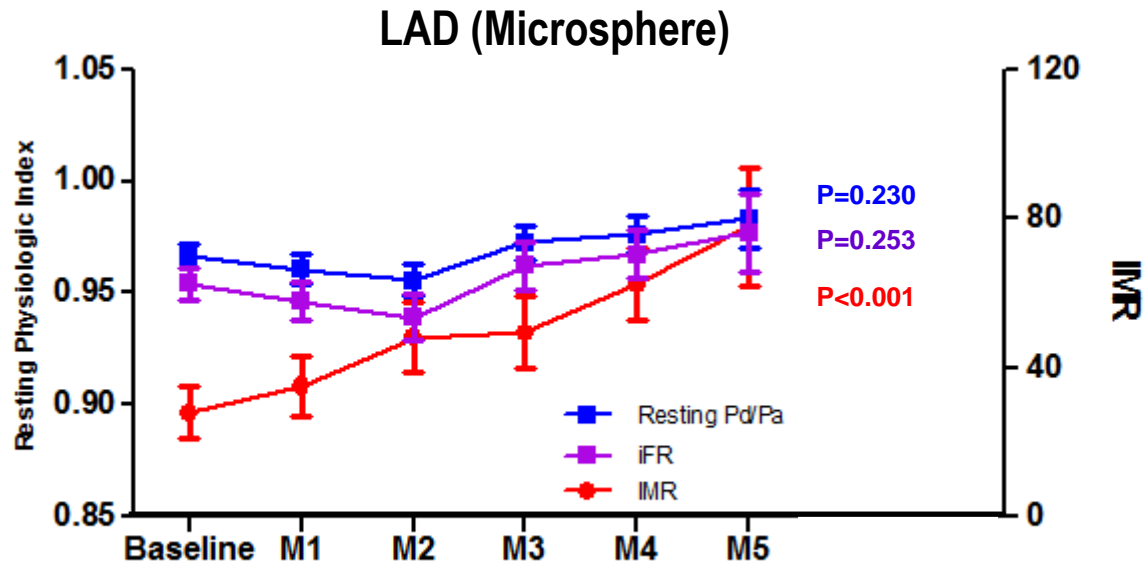
## LCX (Non-culprit)



Lee JM & Kim HK, ....., Koo BK, Jeong MH, JACC Intv, 2018



# Changes in Culprit/Non-culprit vessels: Resting Indexes



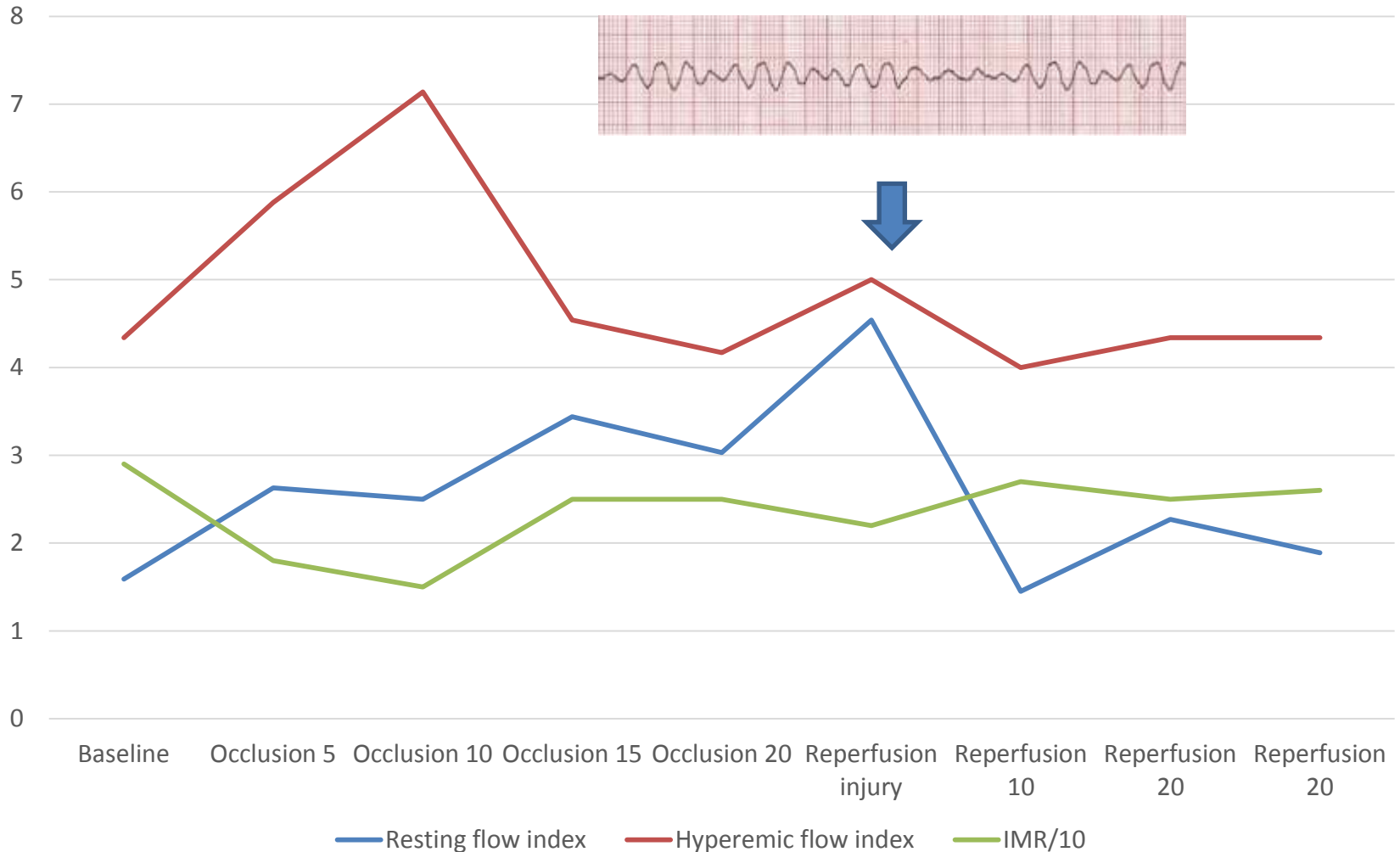
## Fractional Flow Reserve in Nonculprit Vessel During STEMI Reliable or Prone to Error?\*

Marc D. Feldman, MD, Amit K. Gupta, MD

Why is there a discrepancy with the older published reports? There were weaknesses in prior studies.

The study by Uren et al. (10) was conducted in the fibrinolysis era in subjects more than a week after infarct and is not reflective of current practice. de Waard et al (11) used an intracoronary Doppler wire for their study, which introduces variability in measurements due to the unpredictable location of the Doppler crystal in the coronary lumen, resulting in inconsistent signal acquisition. As a result, only two-thirds of measurements could be used in their final analysis. This may have led to underestimation of

# Stable IMR in a non-culprit vessel in a balloon occlusion model



Courtesy of HK Kim, MD, PhD

# Role of FFR in ACS: ~~Still Doubtful?~~



**TABLE 1** Indications for FFR-Based Decision Making

Vessel	SIHD	NSTE-ACS	STEMI
Clear culprit	Yes	No	No
Nonculprit	Yes	Yes	Yes

FFR = fractional flow reserve; NSTE-ACS = non-ST-segment elevation acute coronary syndrome; SIHD = stable ischemic heart disease; STEMI = ST-segment elevation myocardial infarction.

**JUST DO IT!**