Clinical Value of IMR and CFR for Acute Coronary Syndrome

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Why & How We treat Acute Coronary Syndrome

- We treat ACS to save lives and reduce myocardial damage
- The mainstay of ACS treatment is reperfusion therapy
- Primary & secondary prevention is also important

→ Improve clinical outcomes

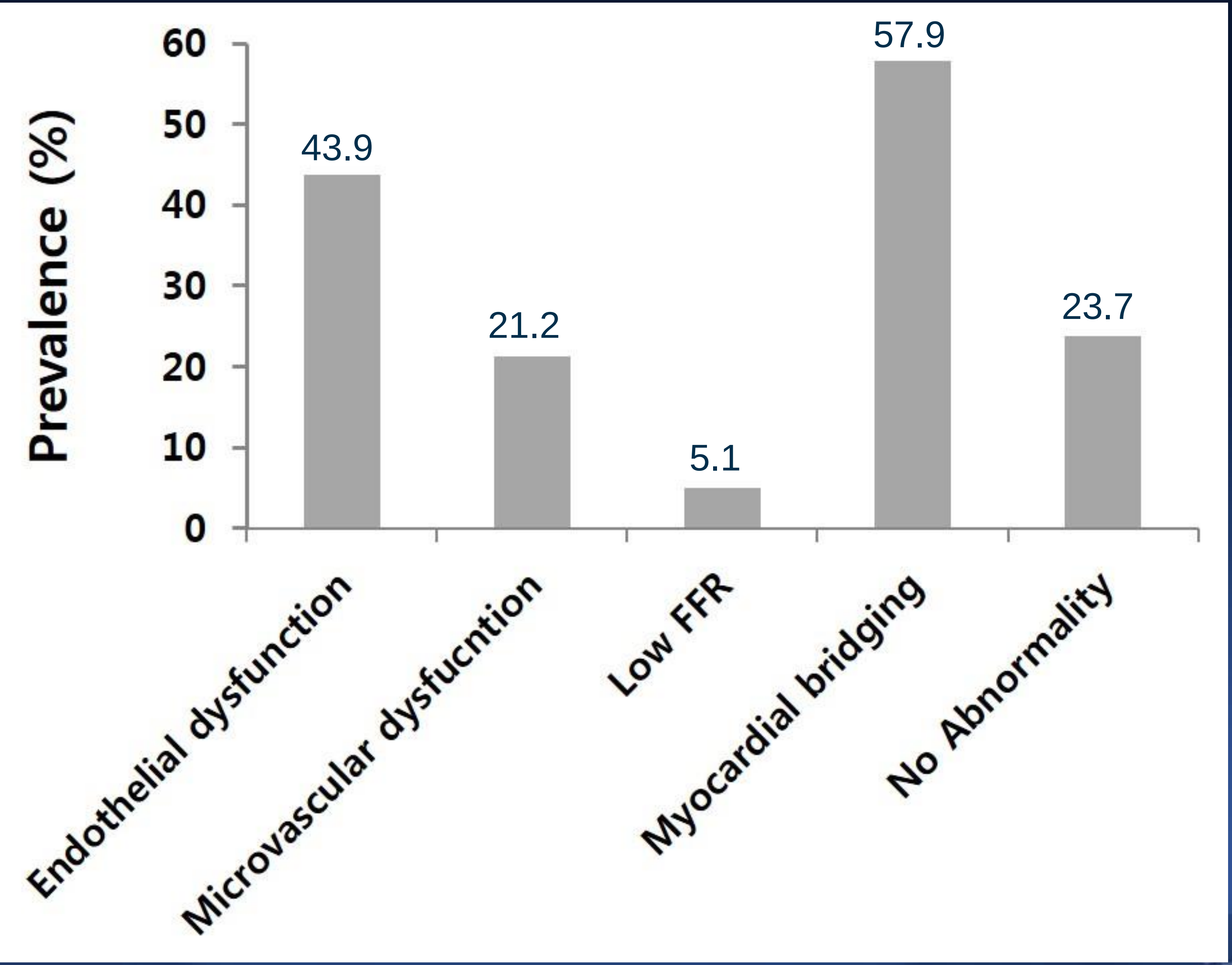
What's the Role of Physiologic Study for ACS Patient

- Provides a natural set of tools to quantify both focal and diffuse disease of a severity that may be associated with improved hard outcomes, independent of symptom relief.
  - FFR → evaluate flow limitation → decision making of revascularization
  - In ACS, multifocal heterogeneous inflammation, endothelial dysfunction, coronary spasm, and downstream smallvessel disease may associate with subsequent nonculprit risk not accounted for by FFR

→ Physiological assessment beyond FFR may uncover a host of abnormalities

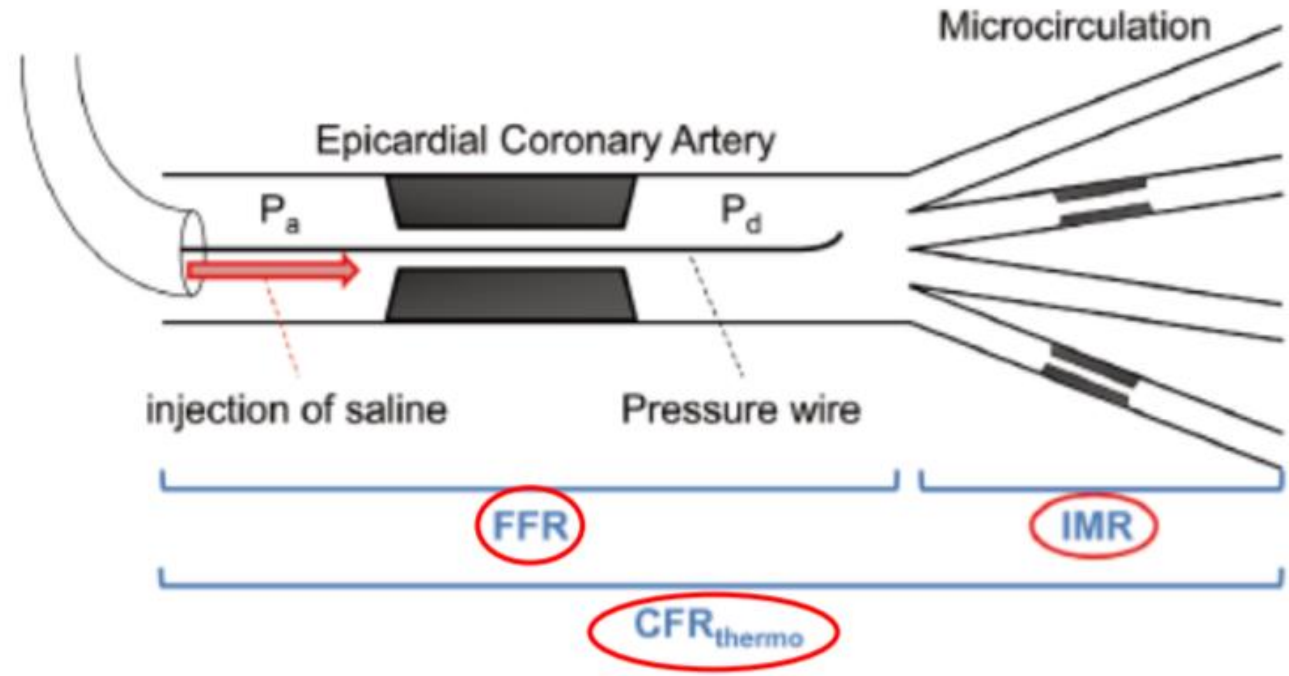
Torino PA et al. NEJM 2009;360:213-24
Lee BK et al. 2015;131:1054-60
Johnson NP et al. JACC 2016;67:2772-88

Prevalence of occult coronary abnormalities on invasive assessment in patients with angina and angiographically normal non-obstructive coronary arteries



Lee BK, Fearon WF et al. *Circulation*. 2015;131:1054–1060

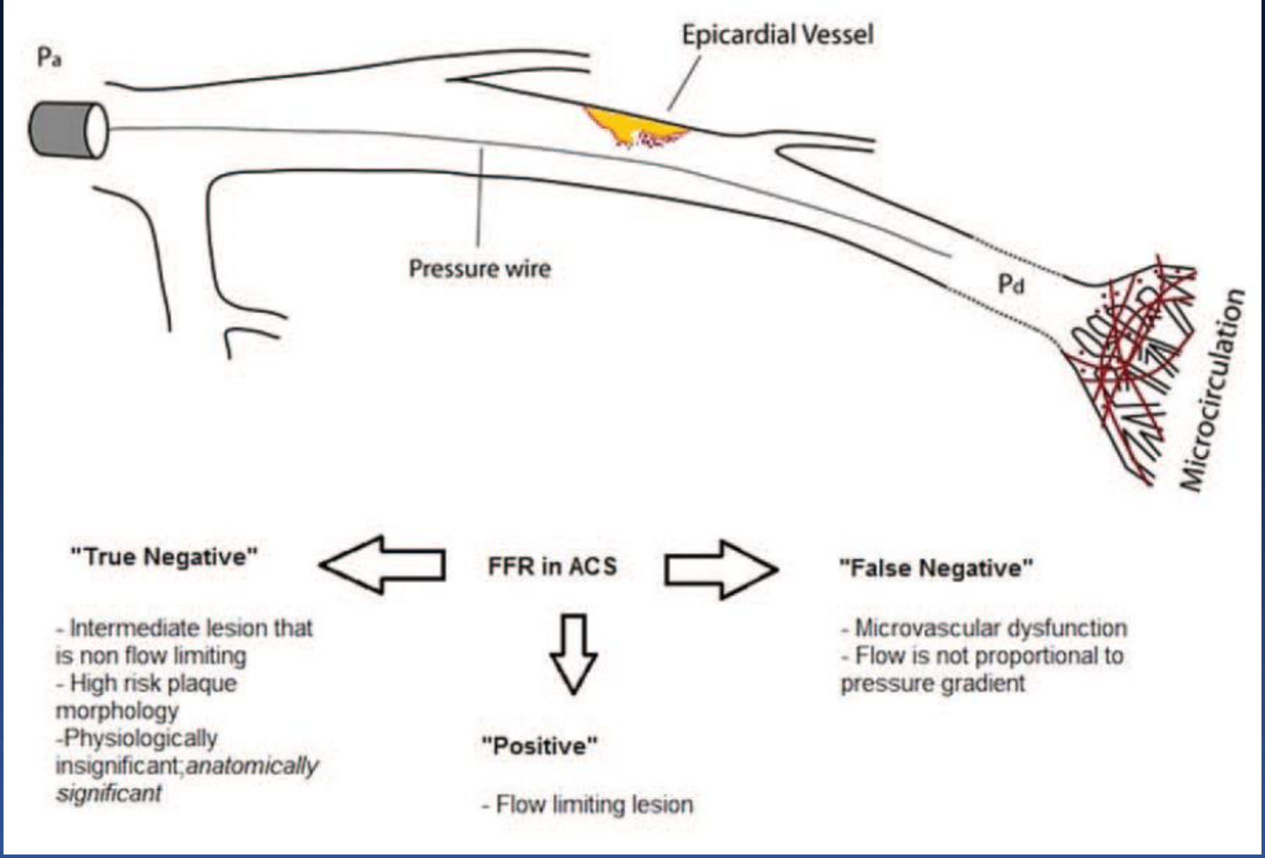
Associated, but Completely Different Physiologic Indexes



- **FFR**=P_d/P_a at maximal hyperemia
- **CFR_{thermo}**=$T_{mn}Hyp/T_{mn}Rest$
- **IMR**=$P_d \times T_{mn}Hyp$

Kobayashi et al. Circ J 2014

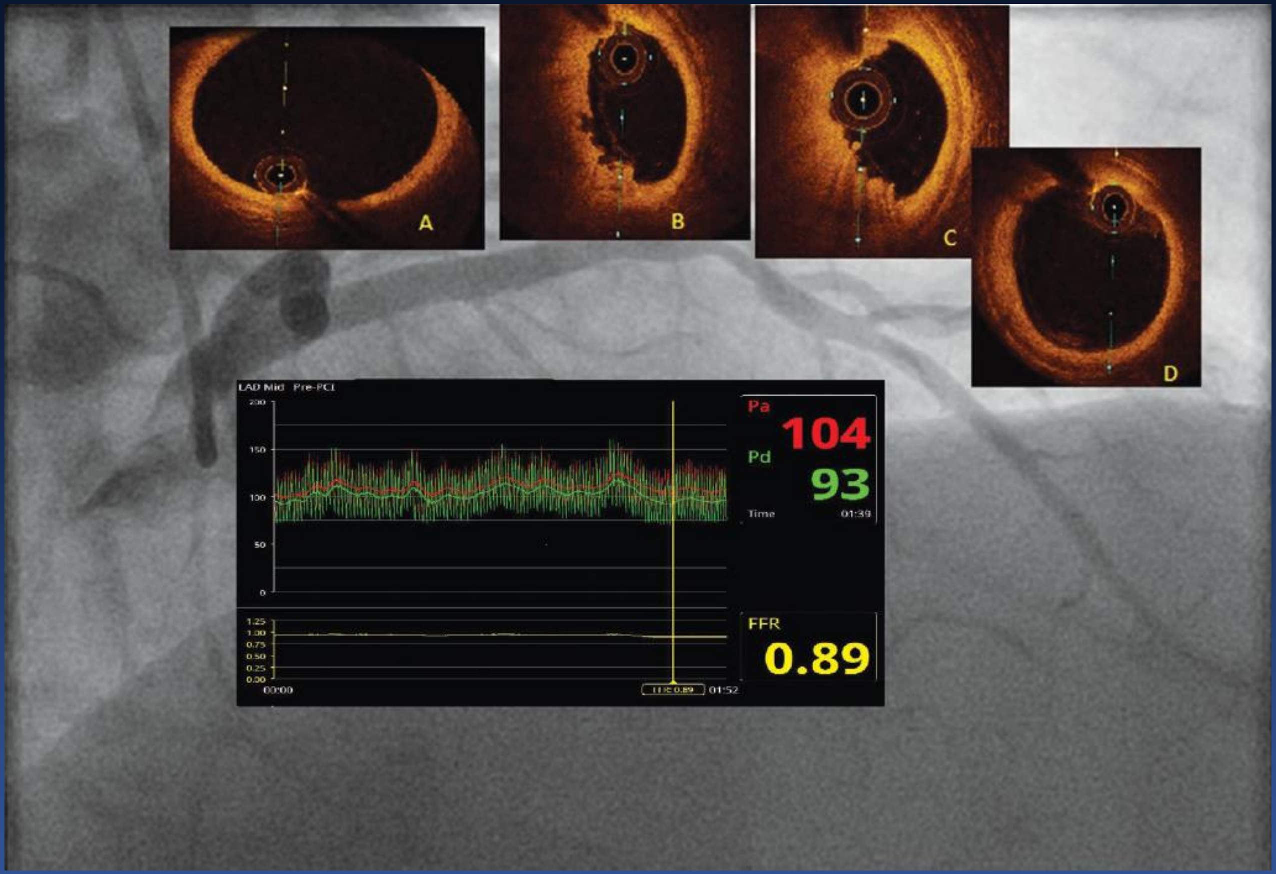
FFR in ACS



- FFR, when used in ACS patients, should be integrated into the entire clinical picture to aid in clinical decision making
- Thresholds for ischemia and long-term outcomes are based on studies on SIHD patients and should not be extrapolated to ACS patients

Hakeem A et al. Curr Opin Cardiol. 2017;32:767-775

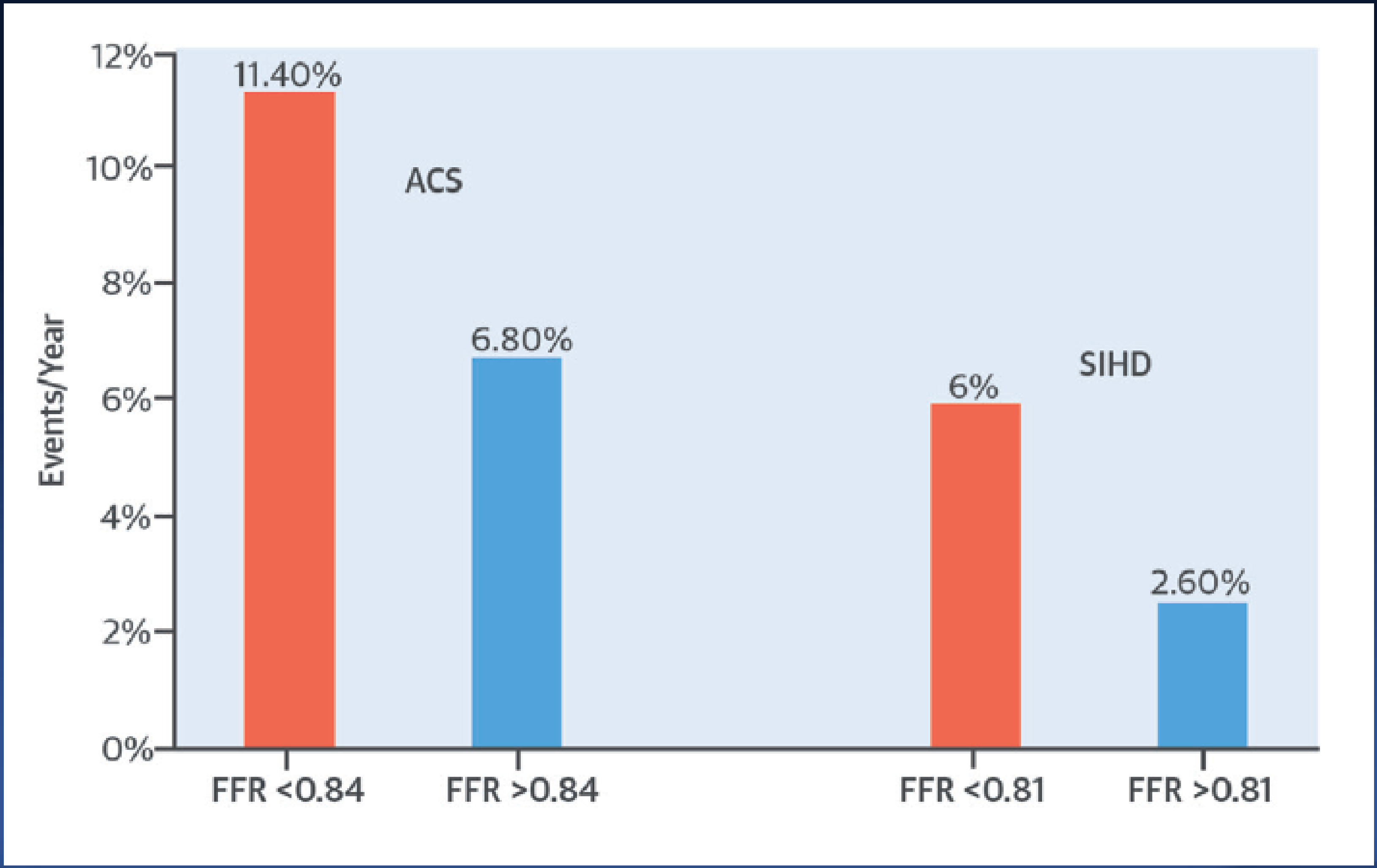
FFR has poor correlation with plaque characteristics



- 70% stenosis in mid LAD on angiography
- FFR=0.89
- Large red thrombus in mid LAD (B &C) with MLA 1.8 mm^2

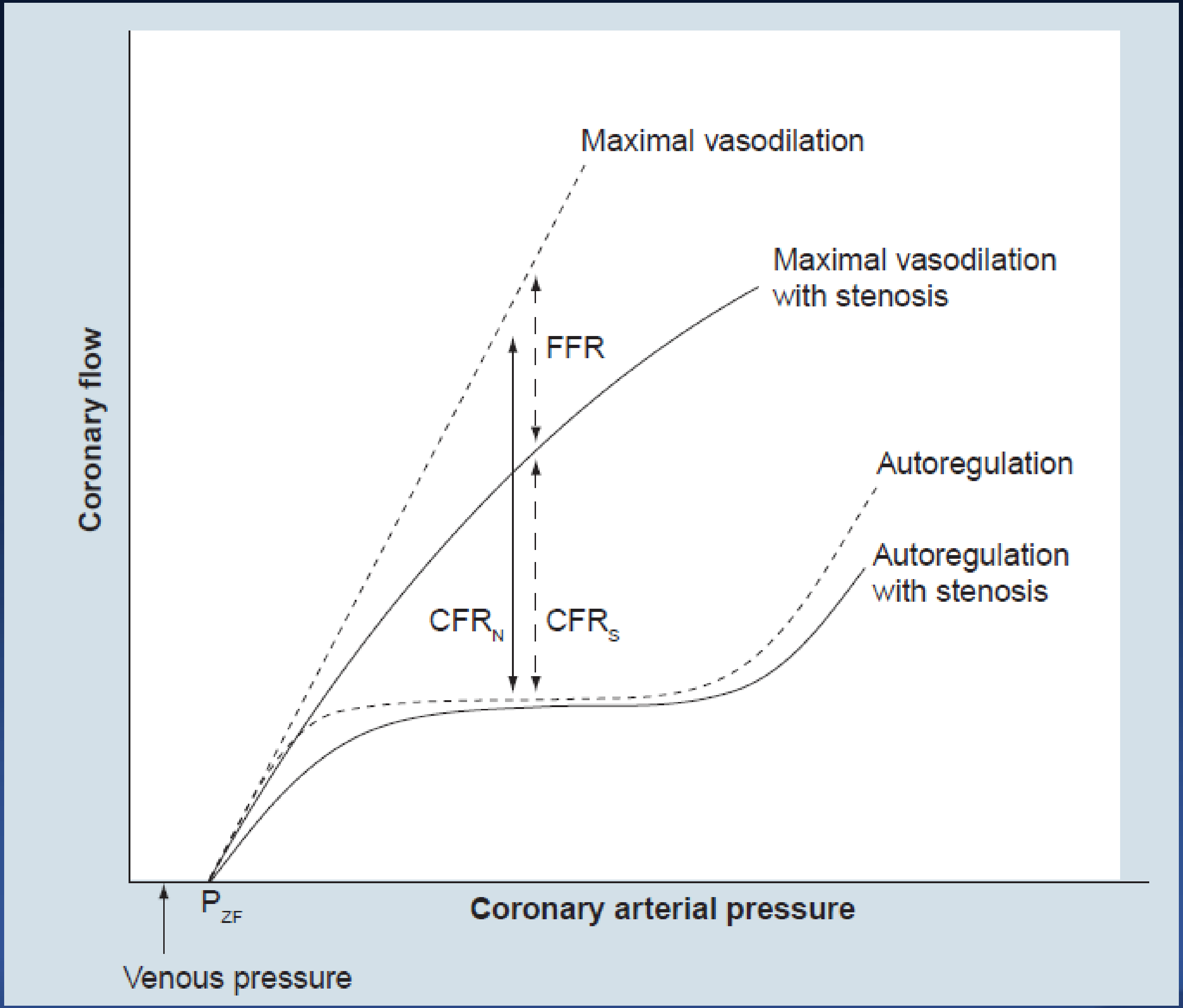
Hakeem A et al. EuroIntervention. 2015;11:e1-2

Annualized MI/TVF Rates on the Basis of Optimal FFR Cutoffs for ACS and SIHD



Hakeem A et al. J Am Coll Cardiol. 2016;68:1181-1191

Coronary Pressure-Flow Relationship & CFR vs FFR



Meuwissen M et al. Interv Cardiol 2009;1:237-55

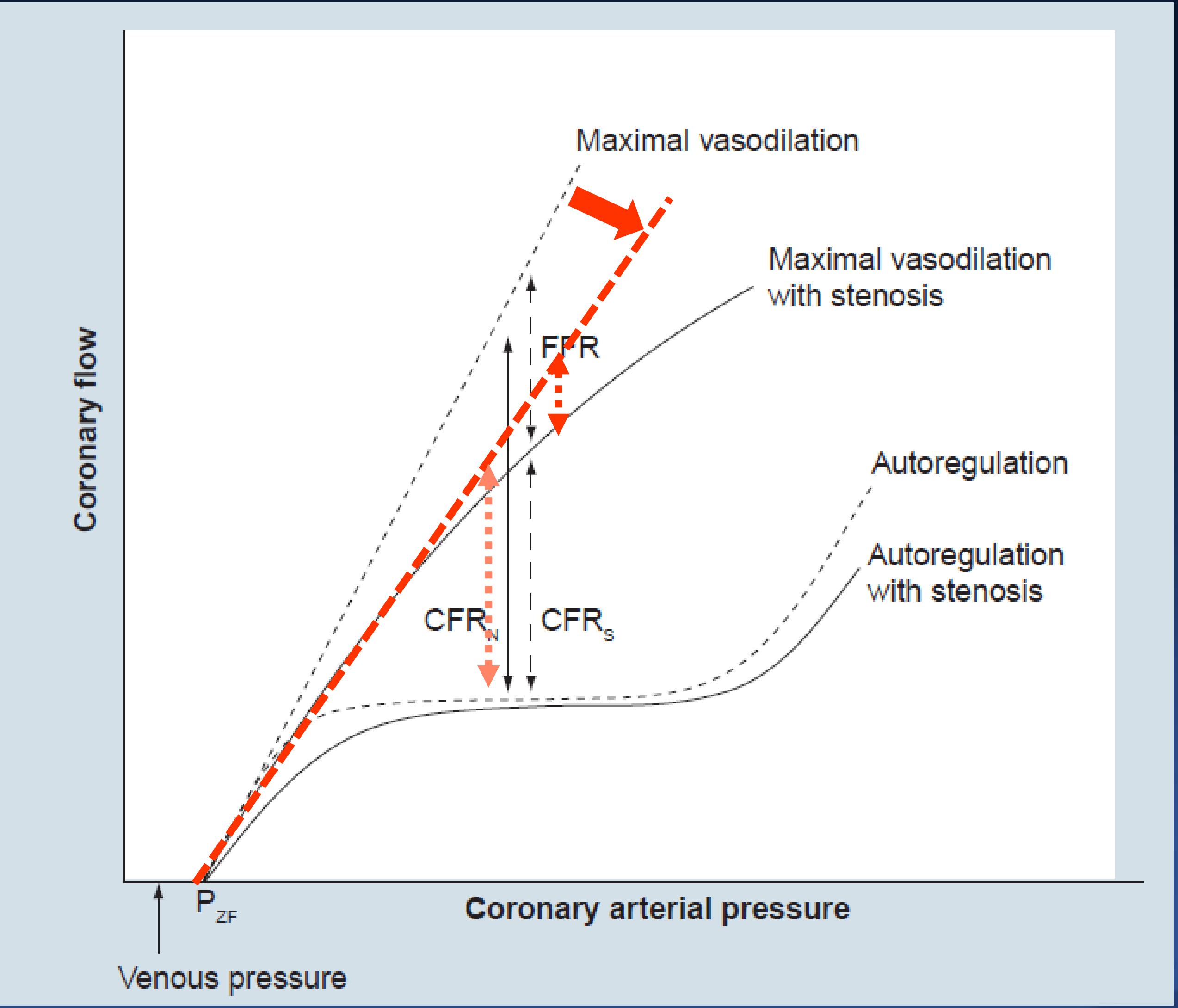
CFR Ischemia Threshold

Coronary flow reserve	n	Ischemic test	BCV	Accuracy (%)	Remarks
Joye *et al.* (1994)	30	MPS	2.0	94	SVD
Miller *et al.* (1994)	33	MPS	2.0	89	SVD
Deychack *et al.* (1995)	17	MPS	1.8	96	SVD
Tron *et al.* (1995)	62	MPS	2.0	84	SVD
Donohue *et al.* (1996)	50	MPS	2.0	88	SVD
Heller *et al.* (1997)	55	MPS	1.7	92	SVD
Schulman *et al.* (1997)	35	X-ECG	2.0	86	SVD
Danzi *et al.* (1998)	30	DSE	2.0	87	SVD
Verberne *et al.* (1999)	37	MPS	1.9	85	SVD
Piek *et al.* (2000)	225	X-ECG	2.1	76	SVD
Abe *et al.* (2000)	46	MPS	2.0	92	SVD
Chamuleau *et al.* (2001)	127	MPS	1.7	76	2- and 3-VD
Duffy *et al.* (2001)	28	DSE	2.0	88	SVD
El-Shafei *et al.* (2001)	48	MPS	1.9	77	SVD
Meuwissen *et al.* (2002)	151	MPS	1.7	75	1- and 2-VD
Voudris *et al.* (2003)	48	MPS	1.7	75	SVD
Salm *et al.* (2005)	20	MPS	1.8	83	SVG
Total	**1042**		**1.9**	**81**	

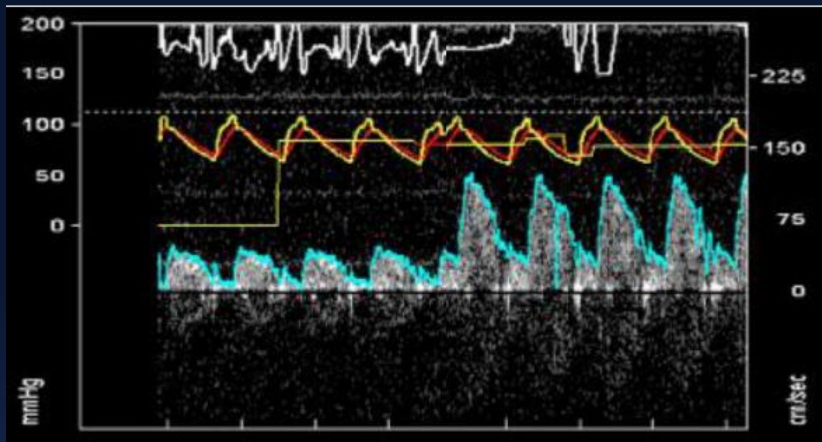
BCV: Best cut-off value (defined as the value with the highest sum of sensitivity and specificity); DSE: Dobutamine stress echocardiography; MPS: Myocardial perfusion scintigraphy; SVD: Single-vessel disease; SVG: Saphenous vein graft; VD: Vessel disease; X-ECG: Exercise electrocardiography.

Meuwissen M et al. Interv Cardiol 2009;1:237-55

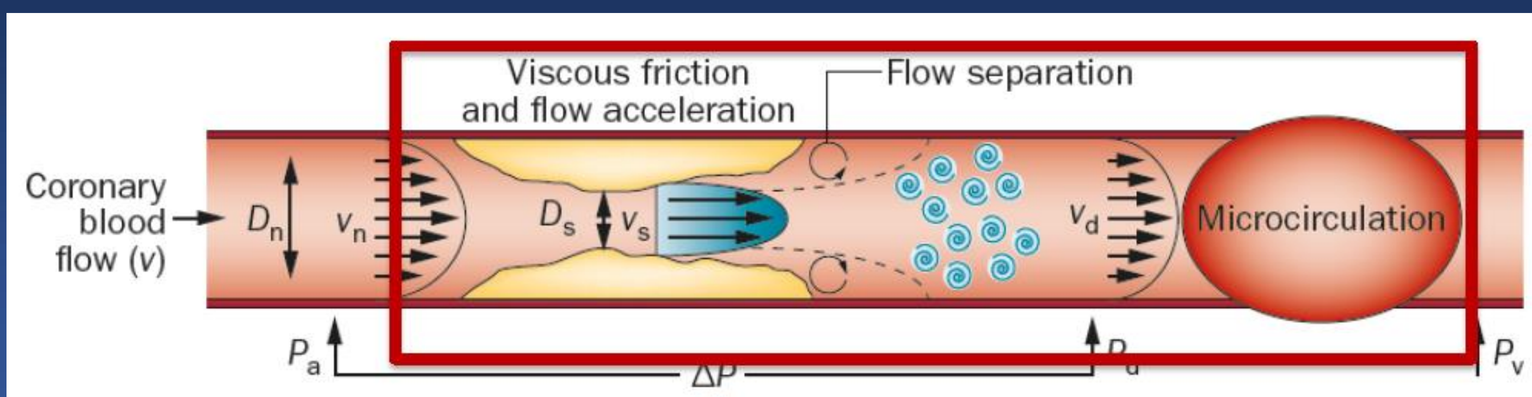
Coronary Pressure-Flow Relationship & CFR vs FFR in ACS



Coronary Flow Reserve (CFR)



Coronary flow reserve = $\frac{\text{Hyperemic}}{\text{baseline}}$ flow



CFR domain

van de Hoef, et al. Nat Rev Cardiol 2013

Non-invasive CFR Measurment also Available

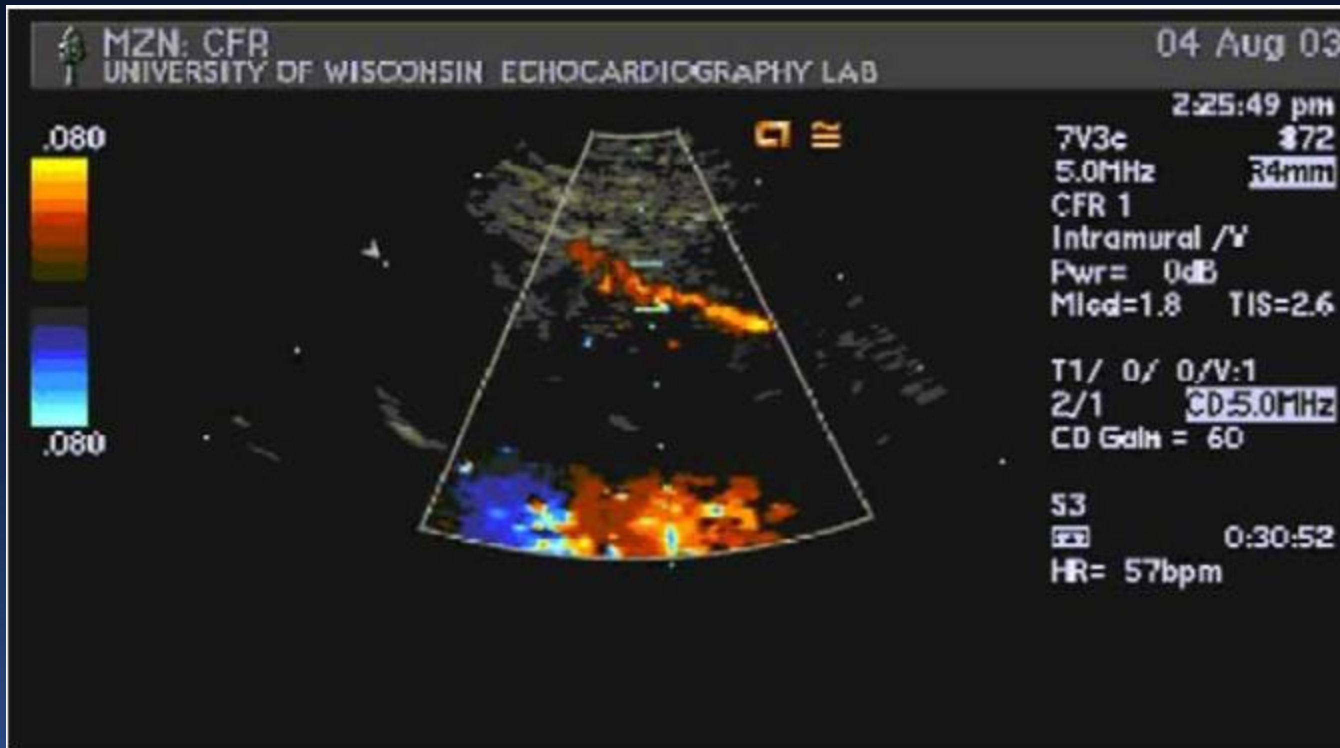


Figure 1 Blood flow in the left anterior descending coronary artery obtained using a modified, low parasternal long axis view.

Korcarz CE et al. J Am Soc Echocardiogr 2004;17:704-7

Non-invasive CFR Measurment also Available

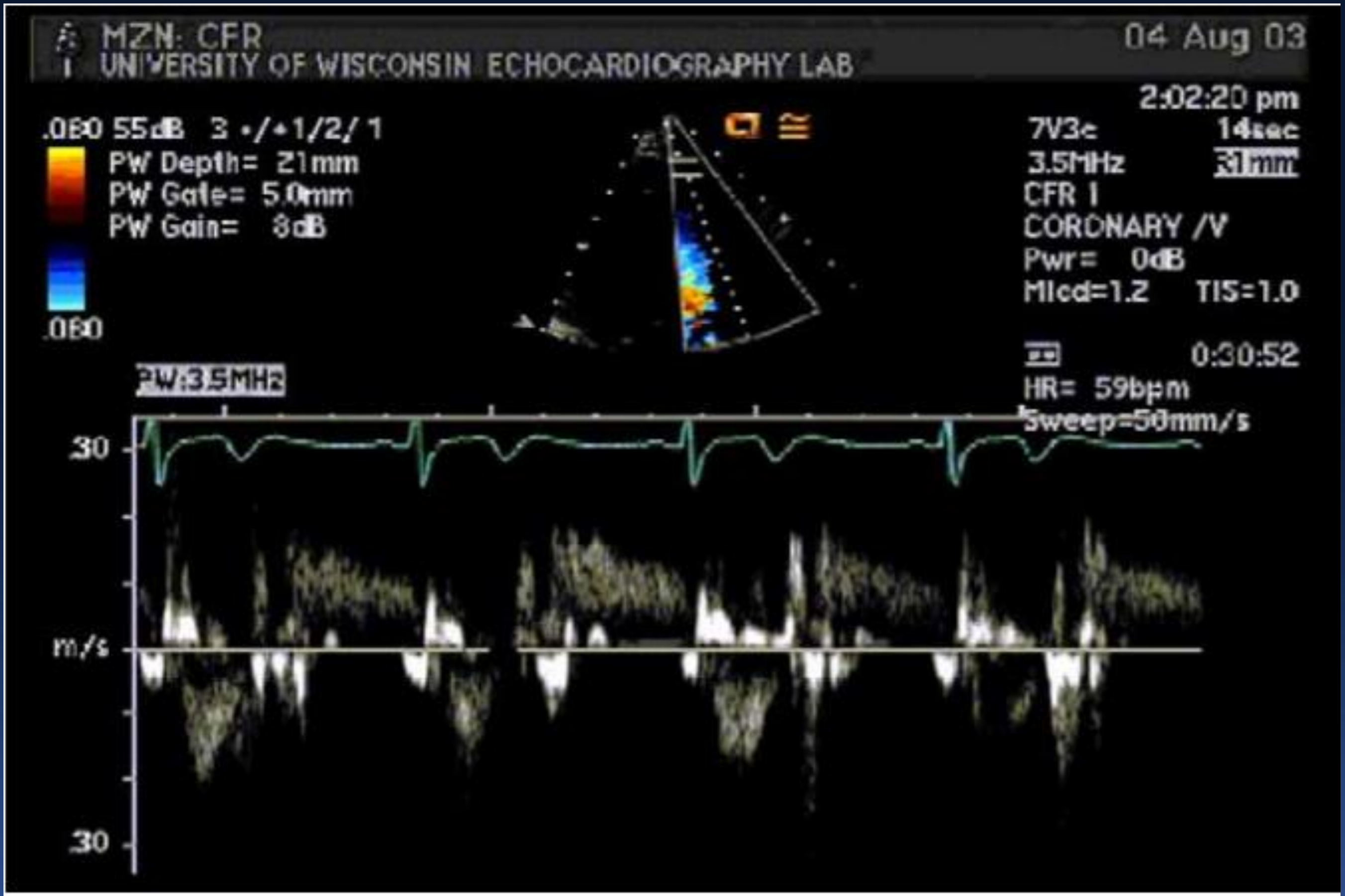
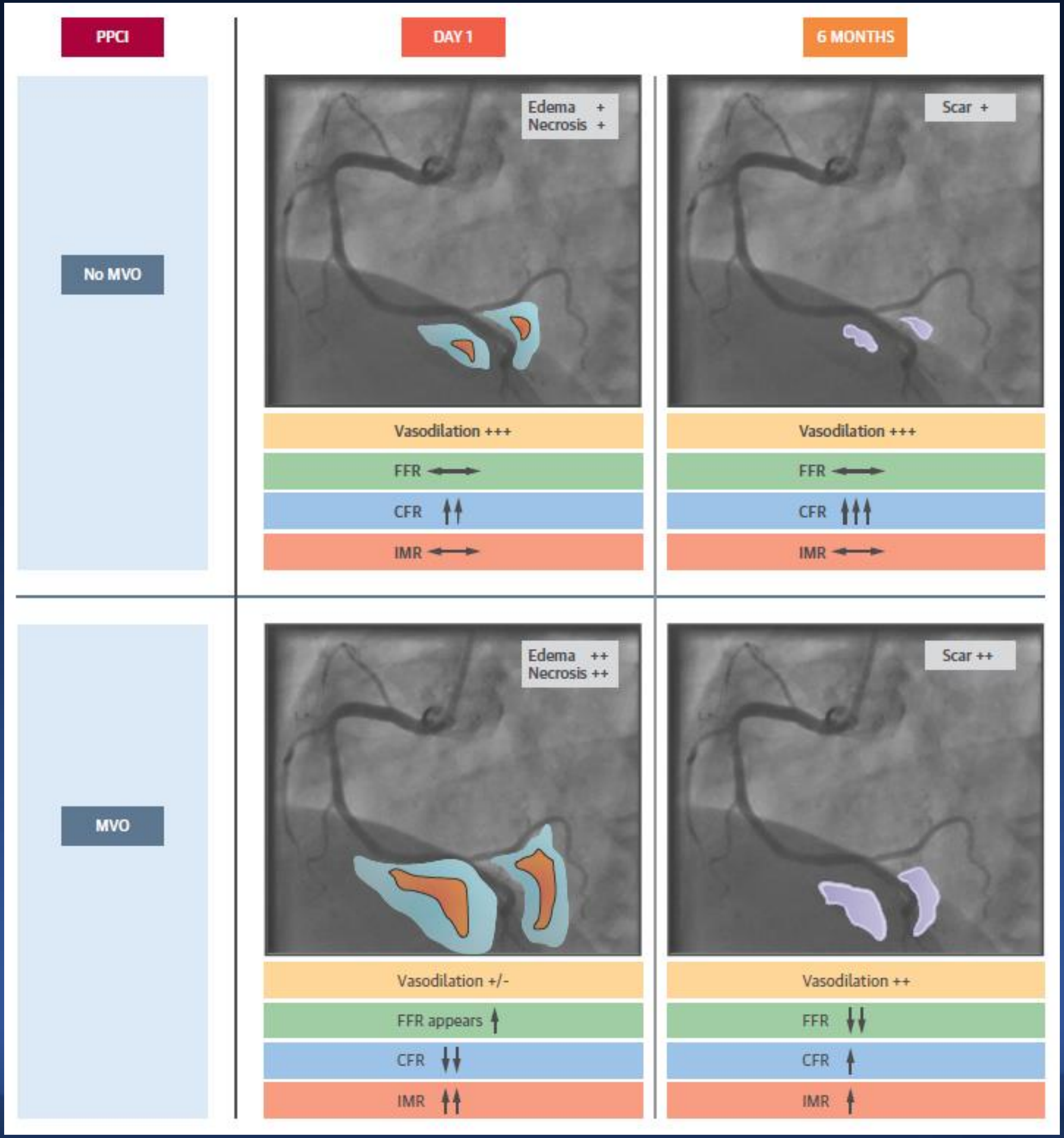


Figure 2 Typical spectral Doppler flow in the left anterior descending coronary artery.

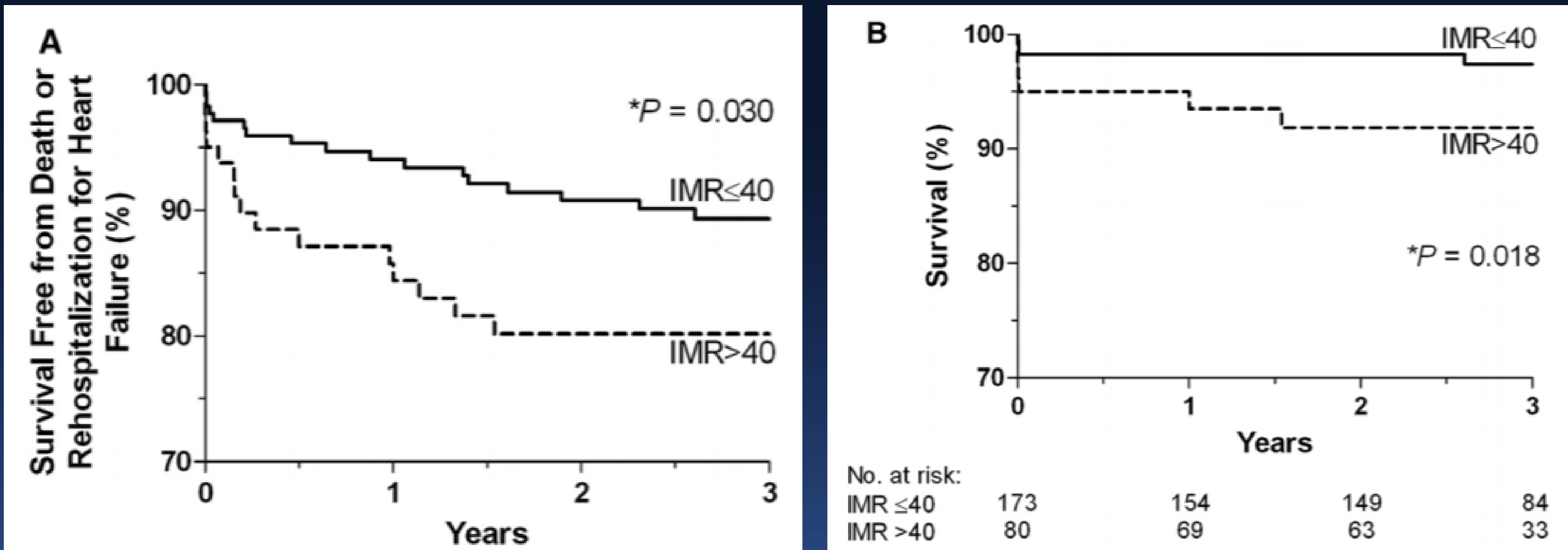
Korcarz CE et al. J Am Soc Echocardiogr 2004;17:704-7

Impact of MVO on the Microcirculation and FFR After ST-Segment Elevation Myocardial Infarction



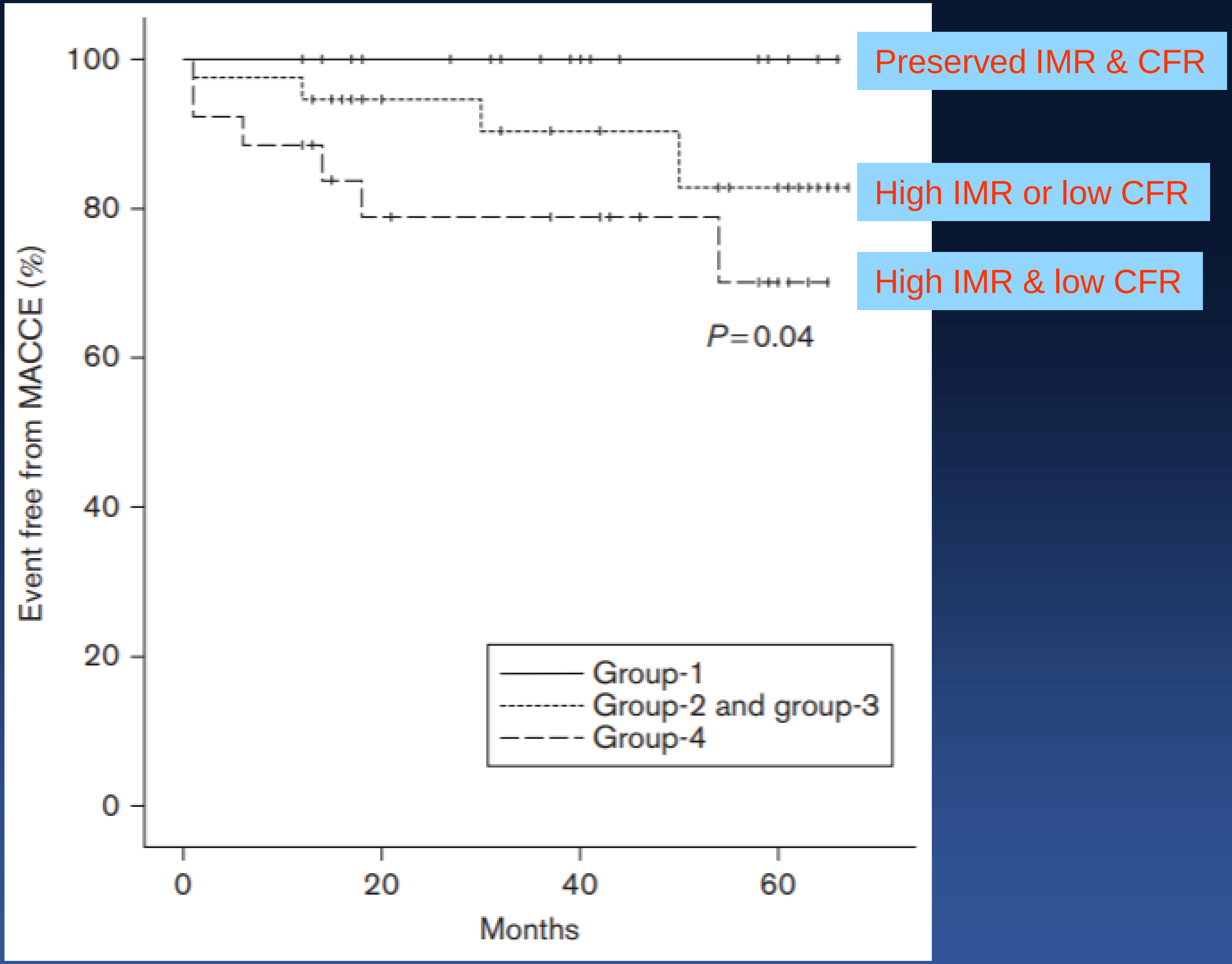
Cuculi F et al. JACC 2014;64:1894-904

Prognostic Value of the IMR after Primary PCI for STEMI



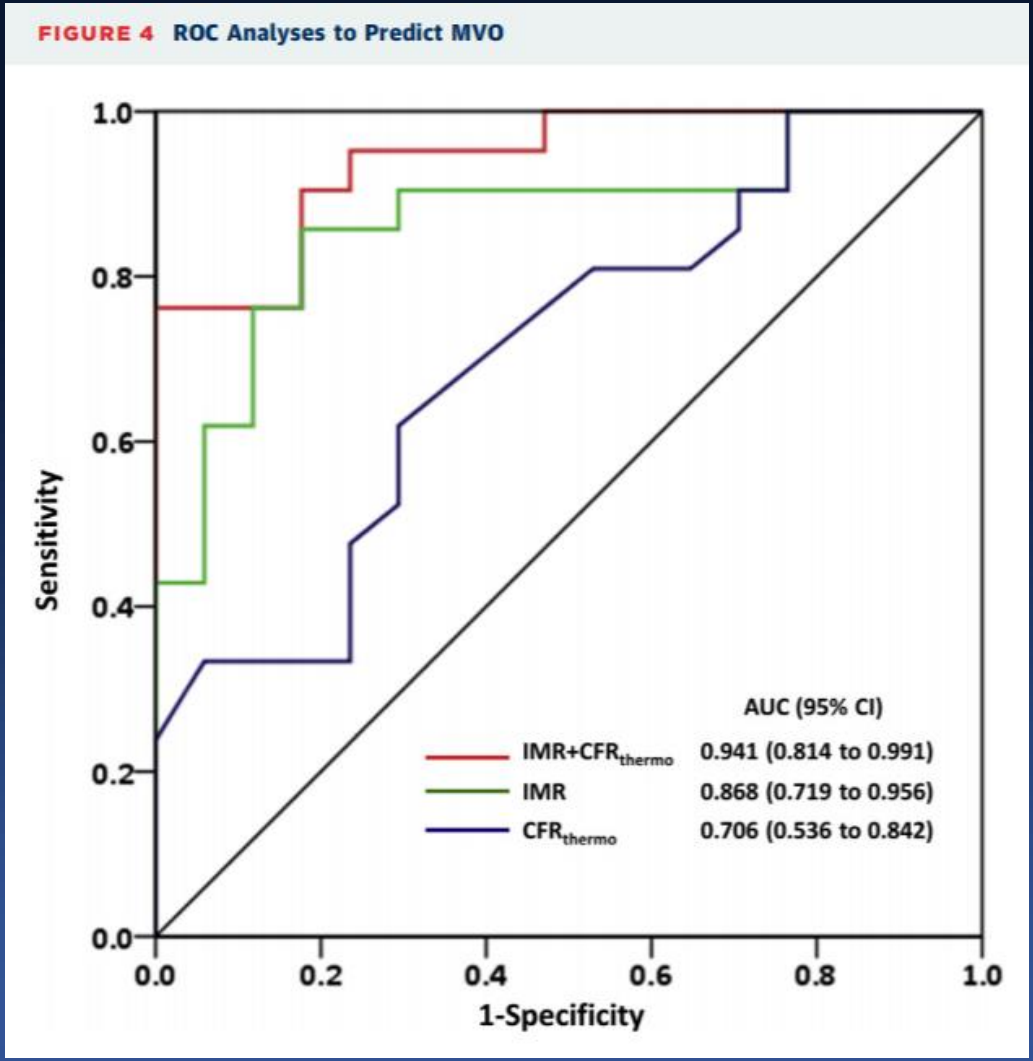
Fearon WF et al. Circulation 2013;127:2436-441

Prognostic Value of the IMR+CFR after Primary PCI for STEMI



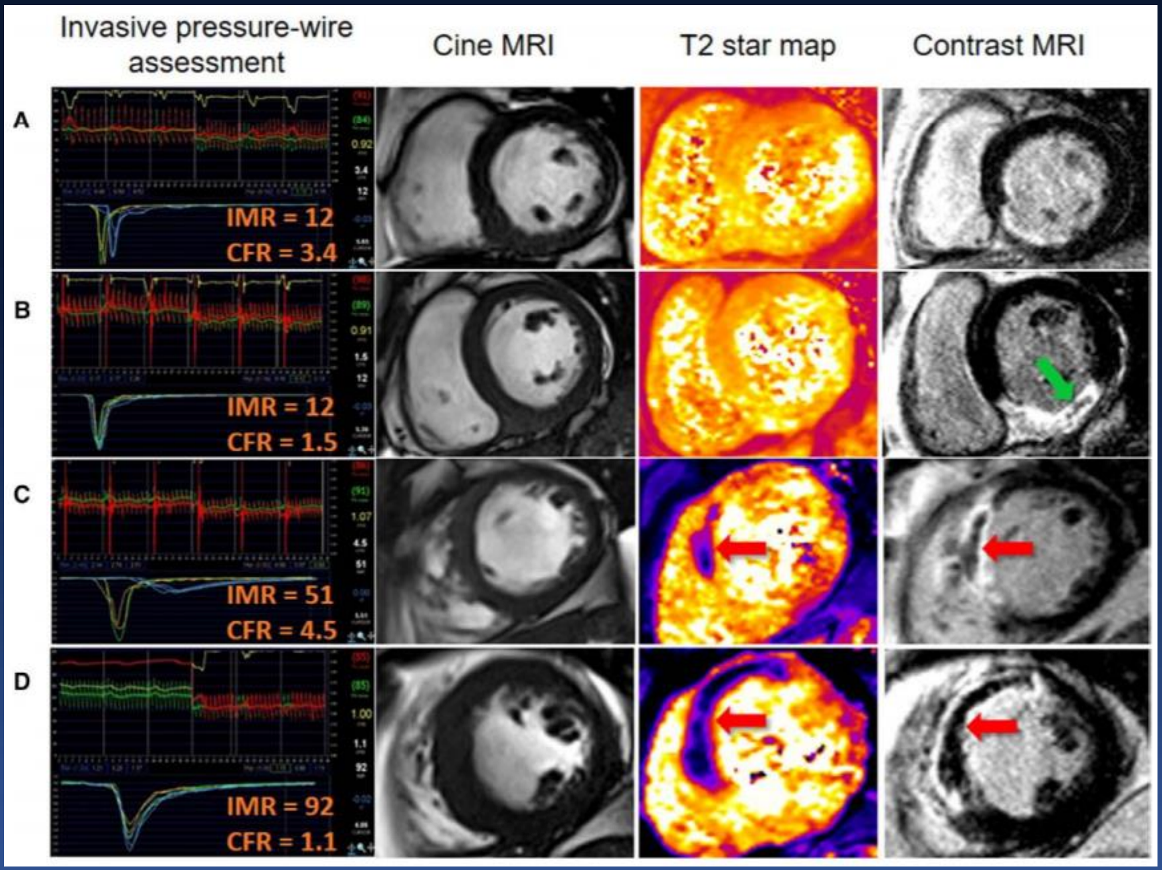
Park SD et al. Coronary Artery Disease 2016;27:34-39

Prognostic Value of the IMR+CFR after Primary PCI for STEMI



Ahn SG et al. JACC Cardiovasc Interv 2016;9:793-801

IMR Alone is Sufficient for Prognostication after STEMI

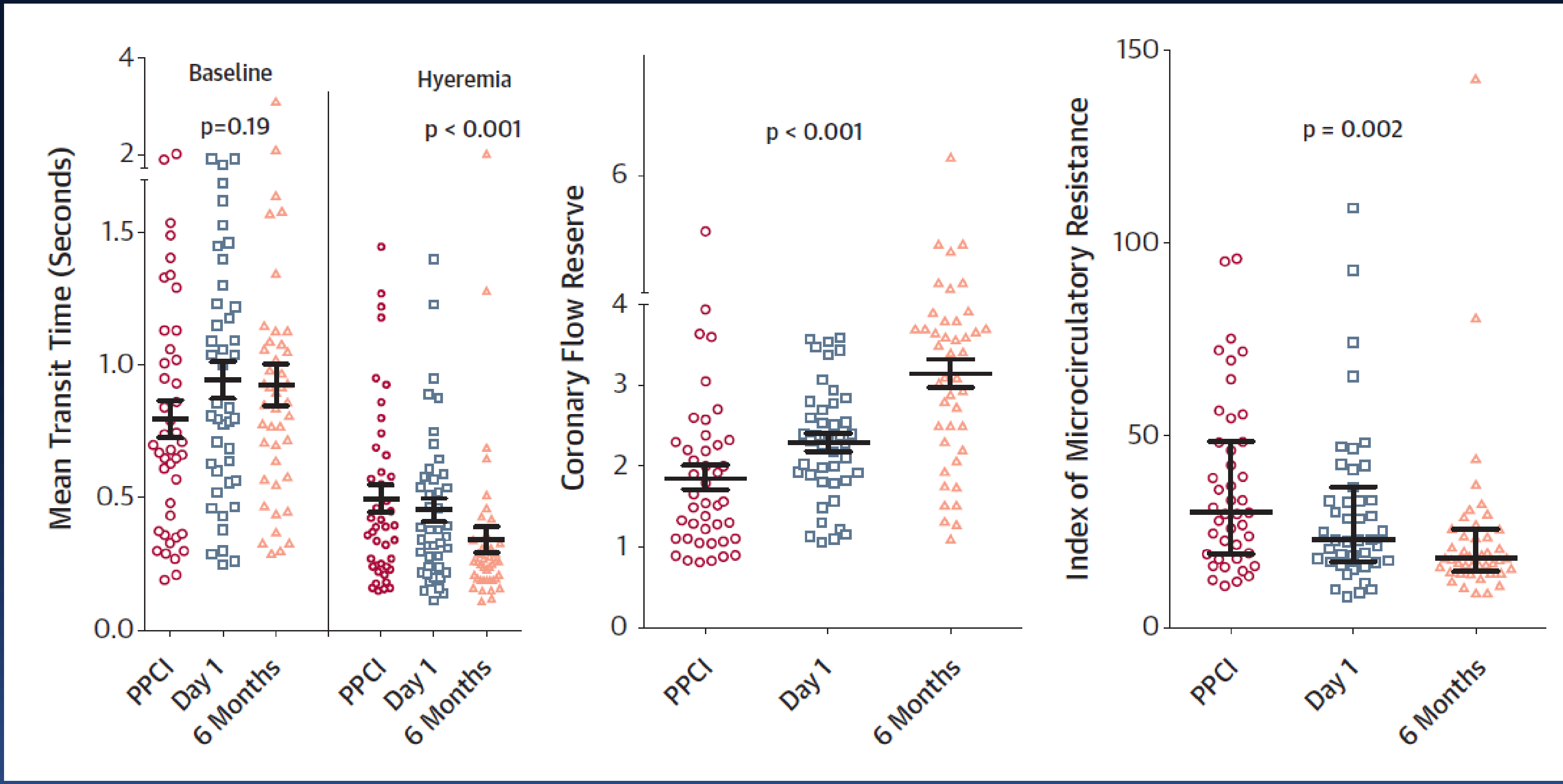


Associations	OR (95% CI)	*P* Value
Univariable associations		
IMR>40	4.36 (2.10–9.06)	<0.001
IMR (for a 5-unit change)	1.08 (1.05–1.12)	<0.001
IMR>median	2.16 (1.01–4.61)	0.047
CFR≤2.0, IMR>40	4.37 (2.13–8.97)	<0.001
CFR≤median, IMR>median	2.96 (1.24–7.08)	0.015
CFR (for a 0.2-unit change)	0.92 (0.82–1.02)	0.124
CFR≤median	1.74 (0.81–3.72)	0.153
CFR≤2.0	1.17 (0.50–2.72)	0.721
Multivariable associations		
Model A (n=283)		
IMR>40	4.70 (2.10–10.53)	<0.001
Cigarette smoker	2.49 (1.01–6.14)	0.048
Hypertension	2.84 (1.26–6.42)	0.012
IMR>40, CFR ≤2.0	5.01 (2.22–11.33)	<0.001
Cigarette smoker	2.69 (1.08–6.69)	0.033
Hypertension	2.84 (1.26–6.42)	0.12
Model B (n=282)		
IMR >40	4.42 (1.93–10.10)	<0.001
No ST-segment resolution	2.49 (1.01–6.15)	0.049
TIMI frame count after PCI	1.00 (0.97–1.03)	0.823
IMR>40, CFR≤2.0	4.46 (1.96–10.15)	<0.001
No ST-segment resolution	2.58 (1.04–6.38)	0.041
TIMI frame count after PCI	1.00 (0.97–1.03)	0.866

No additive role of CFR to predict all-cause death or re-hospitalization

Carrick D et al. Circulation 2016;134:1833-847

Evolution of Mean Transit Times, CFR, and IMR After STEMI

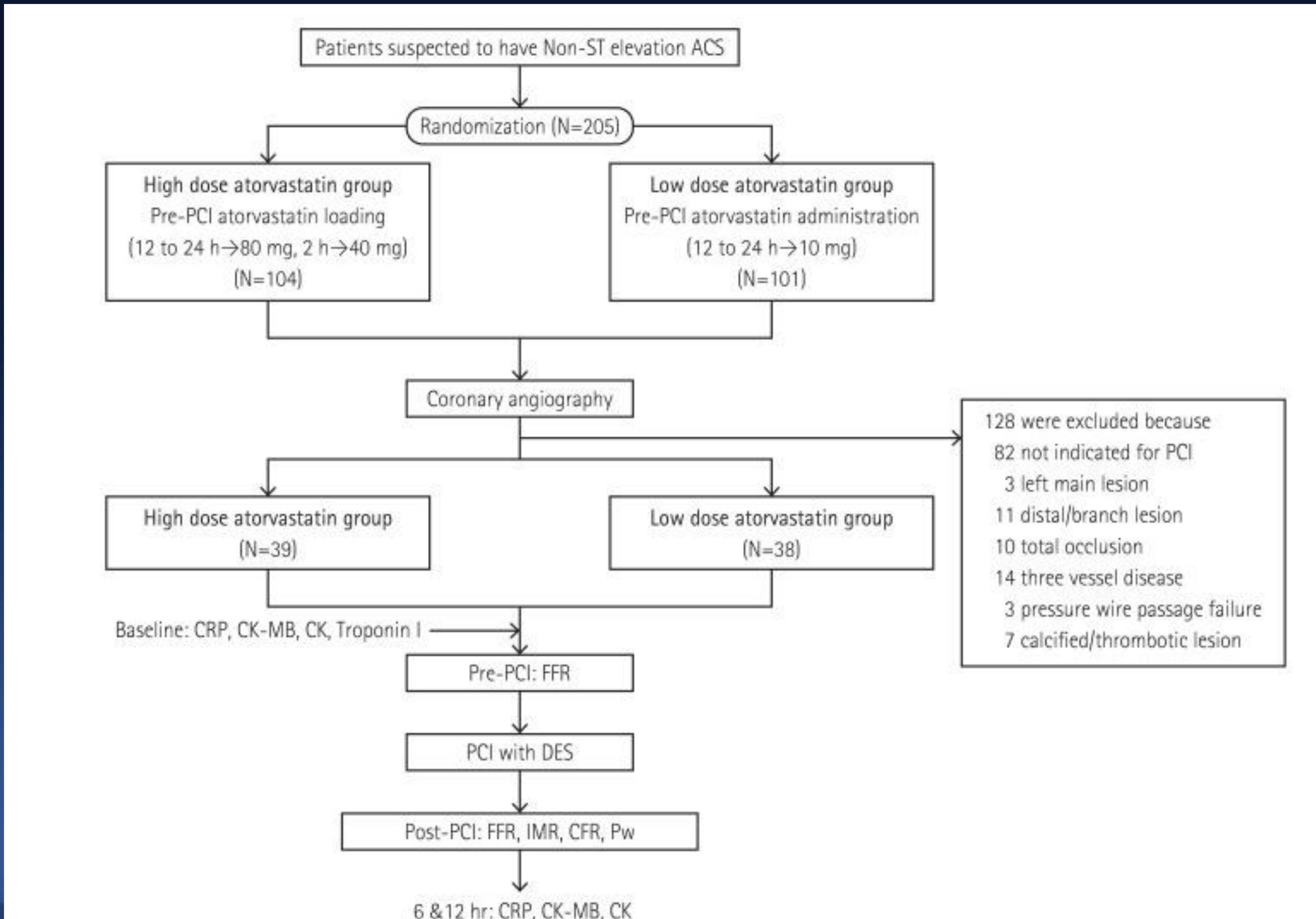


- After STEMI, serial invasive measurements in the culprit artery showed decreasing microvascular resistance and increasing CFR over the subsequent 6 months, reflecting some myocardial recovery after an acute event.

→ Measurement of CFR & IMR may provide insights beyond FFR

Cuculi F et al. JACC 2014;64:1894-904

Study Design of the RESIST-ACS Trial



Lee BK, Koo BK et al. *Korean Circ J* 2016;46:472-80

CK-MB Levels Before and After Stenting

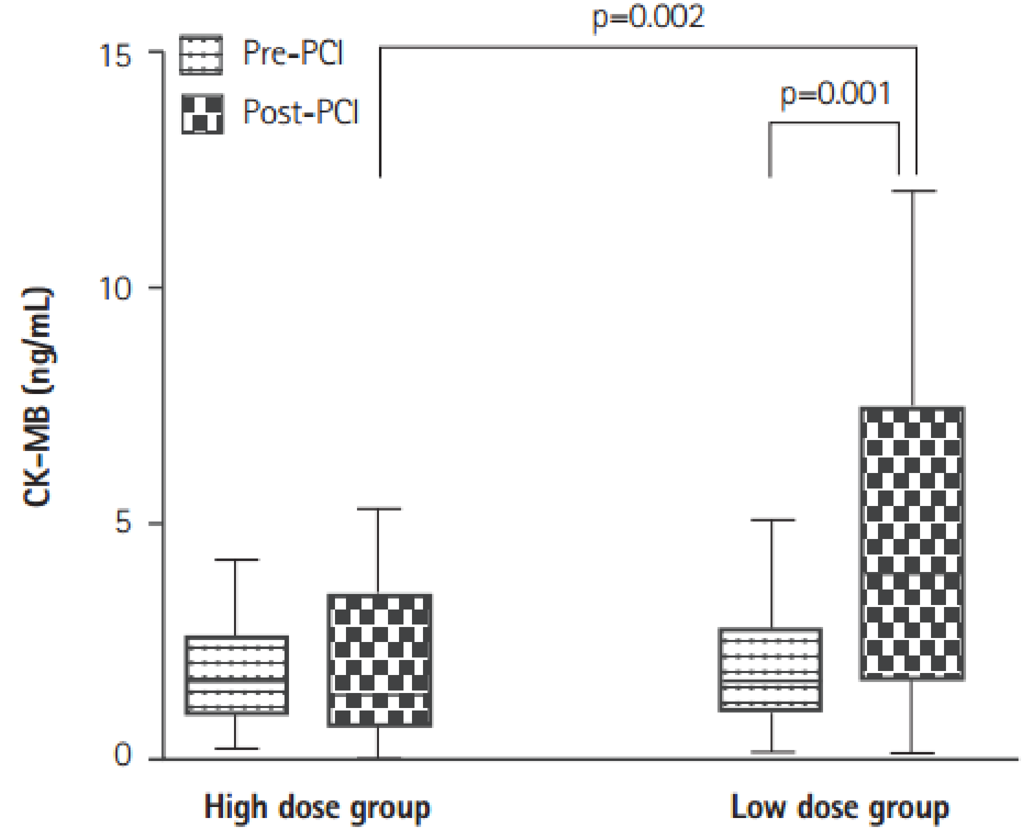
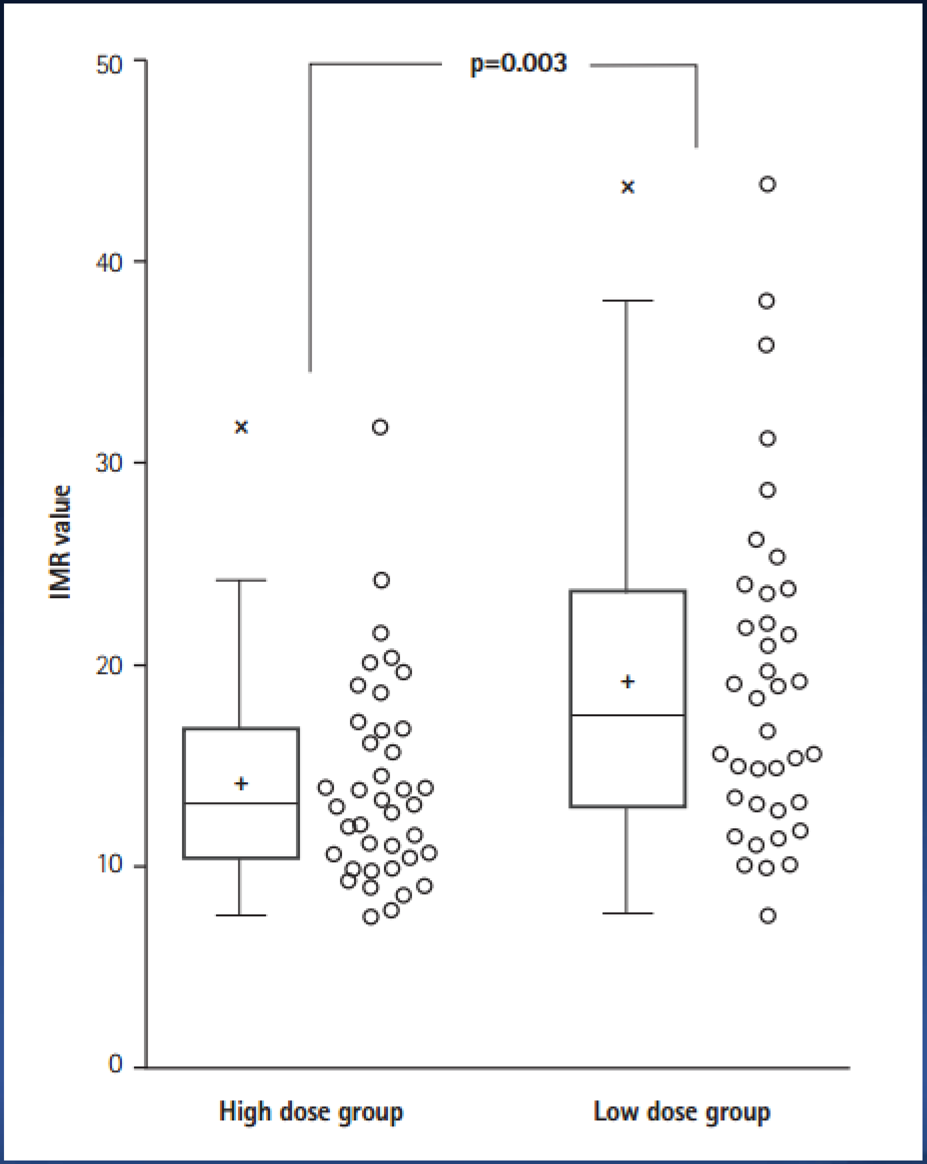


Fig. 3. Box plots comparing CK-MB levels before and after stenting in the two groups. The median, interquartile range (IQR) and 1.5 IQR for each group are shown. Comparison was performed by Man-Whitney and Wilcoxon tests. CK-MB: creatine kinase-myocardial isoenzyme, PCI: percutaneous coronary intervention.

Lee BK, Koo BK et al. *Korean Circ J* 2016;46:472-80

Distribution of Post-PCI IMR Values



Lee BK, Koo BK et al. *Korean Circ J* 2016;46:472-80

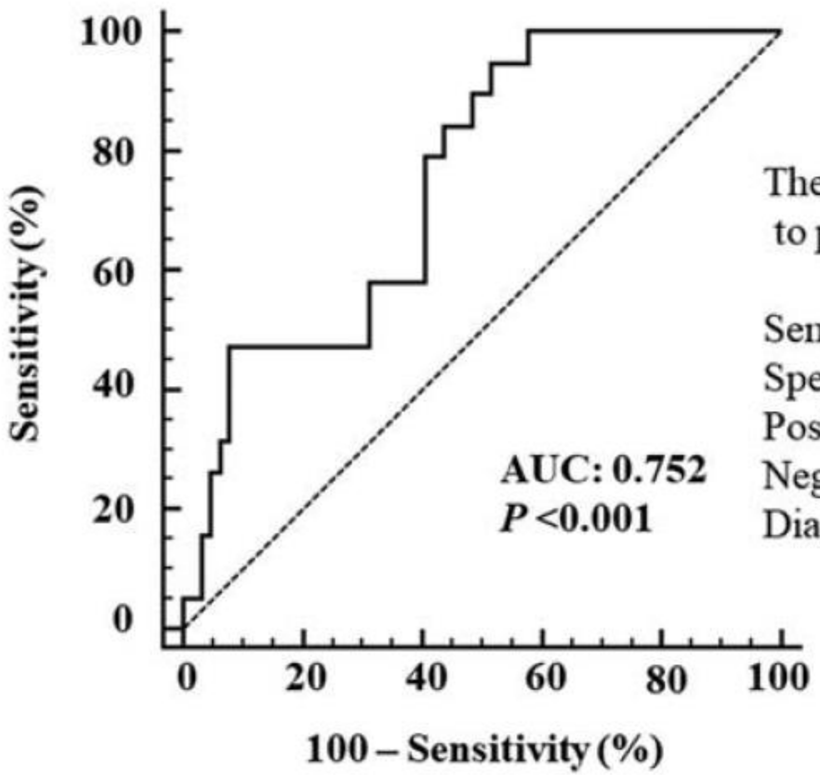
The Comparison Between Patients with and without Long-term Clinical Adverse Event

	Event (+) group; *N* = 19	Event (−) group; *N* = 64	*P* value
Age, y	67.9 ± 9.7	62.4 ± 9.3	0.027
Physiologic parameters after PCI			
Pa, mmHg	86 ± 15	87 ± 12	0.92
Pd, mmHg	78 ± 14	78 ± 13	1.00
Tmn at rest, sec	0.87 (0.56–1.46)	0.65 (0.49–1.10)	0.15
Tmn at hyperemia, sec	0.40 (0.31–0.58)	0.23 (0.13–0.37)	0.001
FFR	0.92 (0.84–0.98)	0.89 (0.86–0.95)	0.72
CFR	1.82 (1.36–3.81)	2.55 (1.90–4.21)	0.041
IMR	27.2 (22.9–46.5)	16.3 (10.7–29.2)	0.001

- Post-PCI IMR value showed a significant relationship with long-term prognosis in patients with NSTE-ACS who were treated with an early invasive strategy, while post-PCI FFR did not.

Murai T et al. Catheter Cardiovasc Interv. 2018;1-12

Can IMR Predict MACE after PCI?

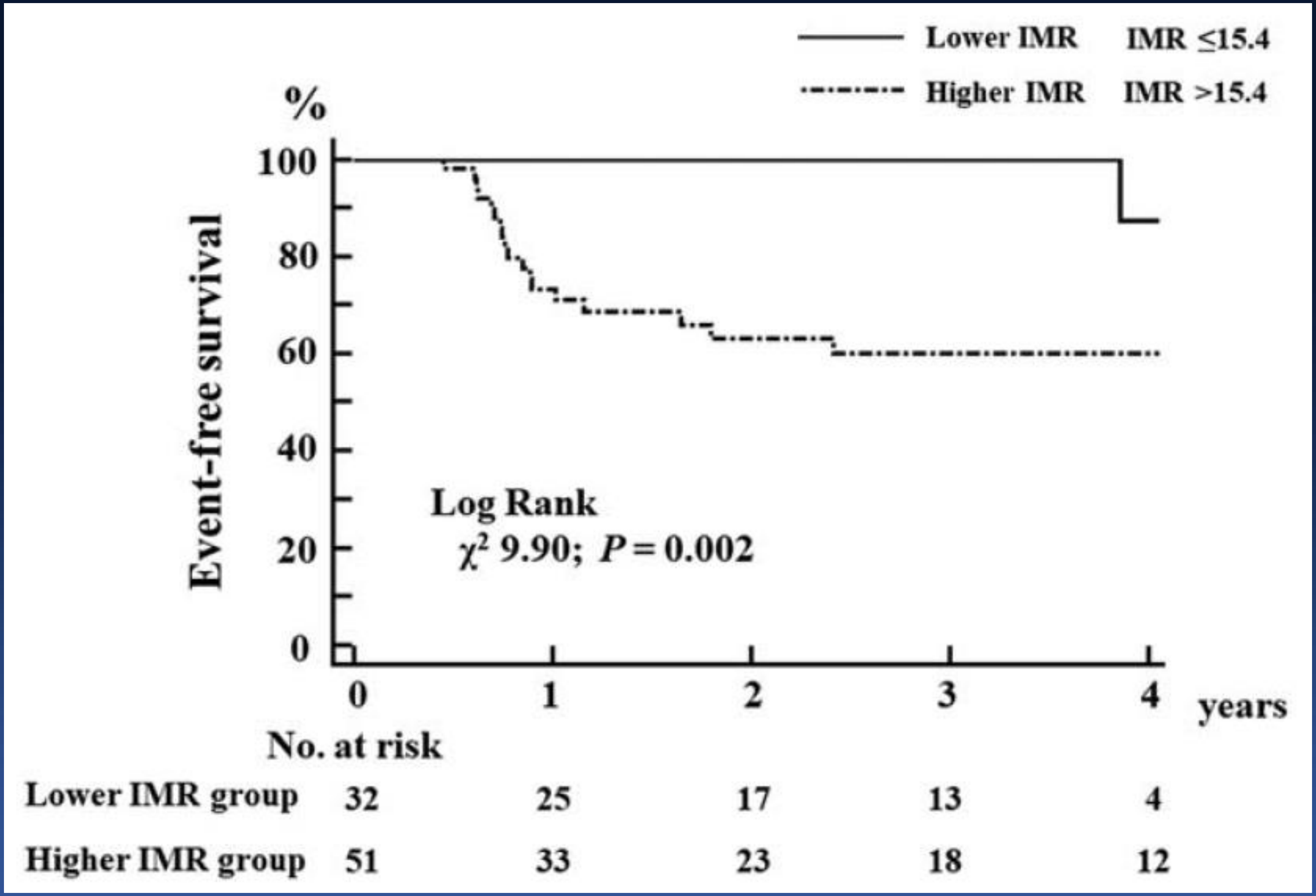


The best post-PCI IMR cutoff value to predict MACE: >15.4

Sensitivity	: 94.7%
Specificity	: 48.4%
Positive predict value	: 35.3%
Negative predict value	: 96.9%
Diagnostic accuracy	: 59.0%

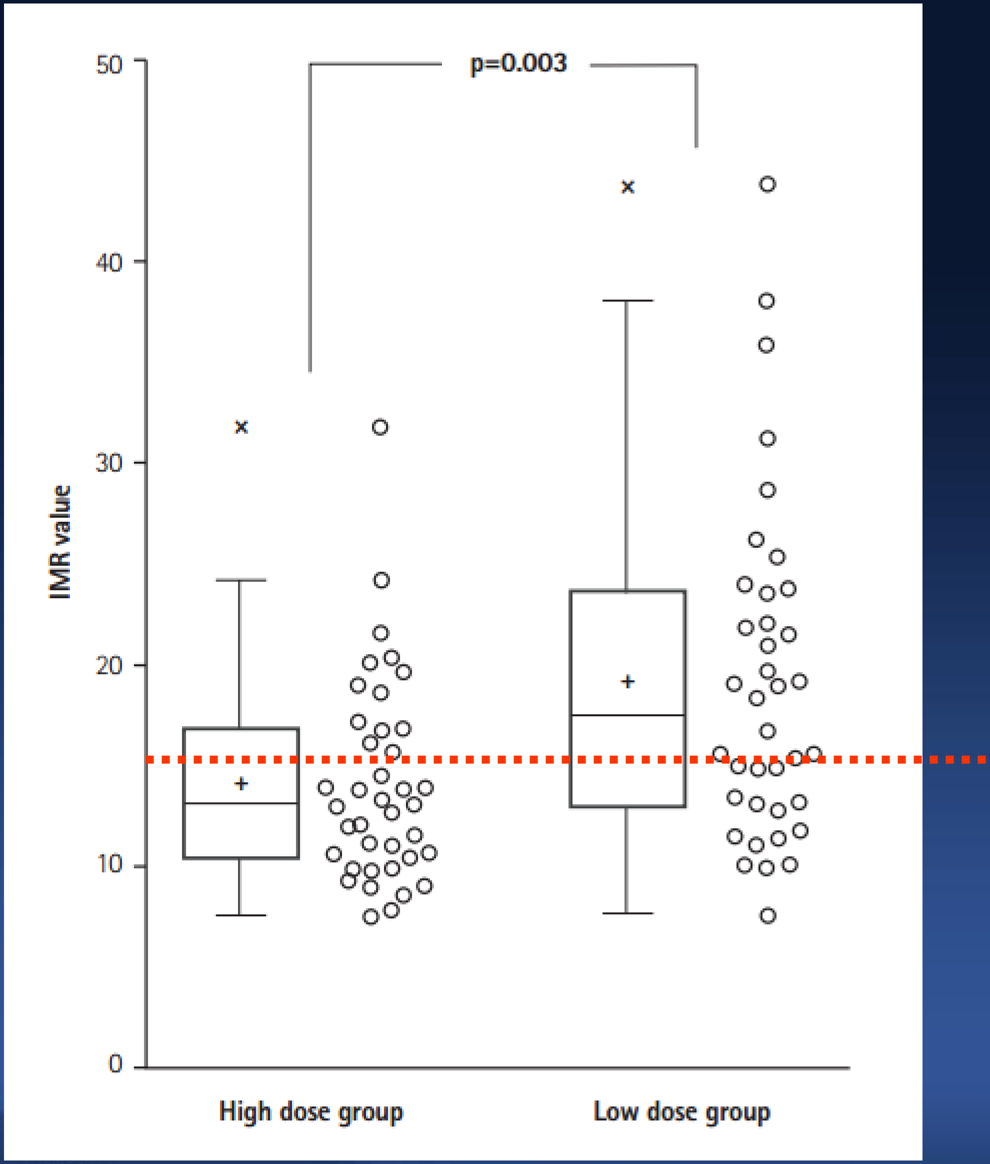
Murai T et al. Catheter Cardiovasc Interv. 2018;1-12

Can IMR Predict MACE after PCI?



Murai T et al. Catheter Cardiovasc Interv. 2018;1-12

I'm Happy to See This!



15.4

Murai T et al.
Catheter Cardiovasc Interv. 2018;1-12

Lee BK, Koo BK et al. *Korean Circ J* 2016;46:472-80

Take Home Message

- For patients with acute coronary disease, coronary physiology may potentially refine treatment of the culprit lesion
- Simultaneous measurement of high-fidelity pressure and velocity also opens up new avenues to gain physiological information from the entire coronary circulation
- Measuring IMR and CFR helps to predict clinical outcome after acute coronary syndrome
- Novel systemic therapies for cardiovascular disease, such as methotrexate and PCSK9 inhibitors, are currently being tested in general populations, and coronary physiology may provide a risk stratification tool to refine their cost-effective use