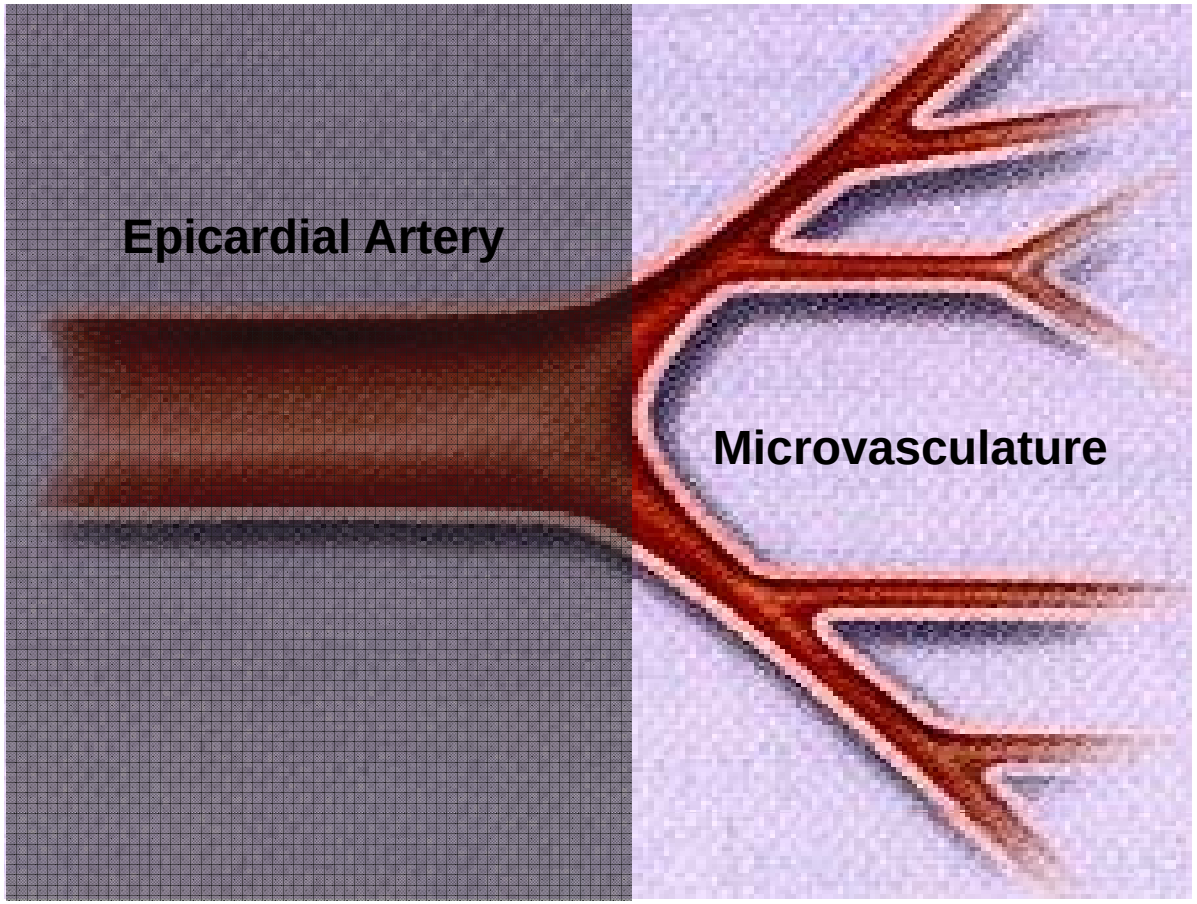
Clinical Application of IMR:
Evidence and Practice

William F. Fearon, MD
Associate Professor
Stanford University Medical Center

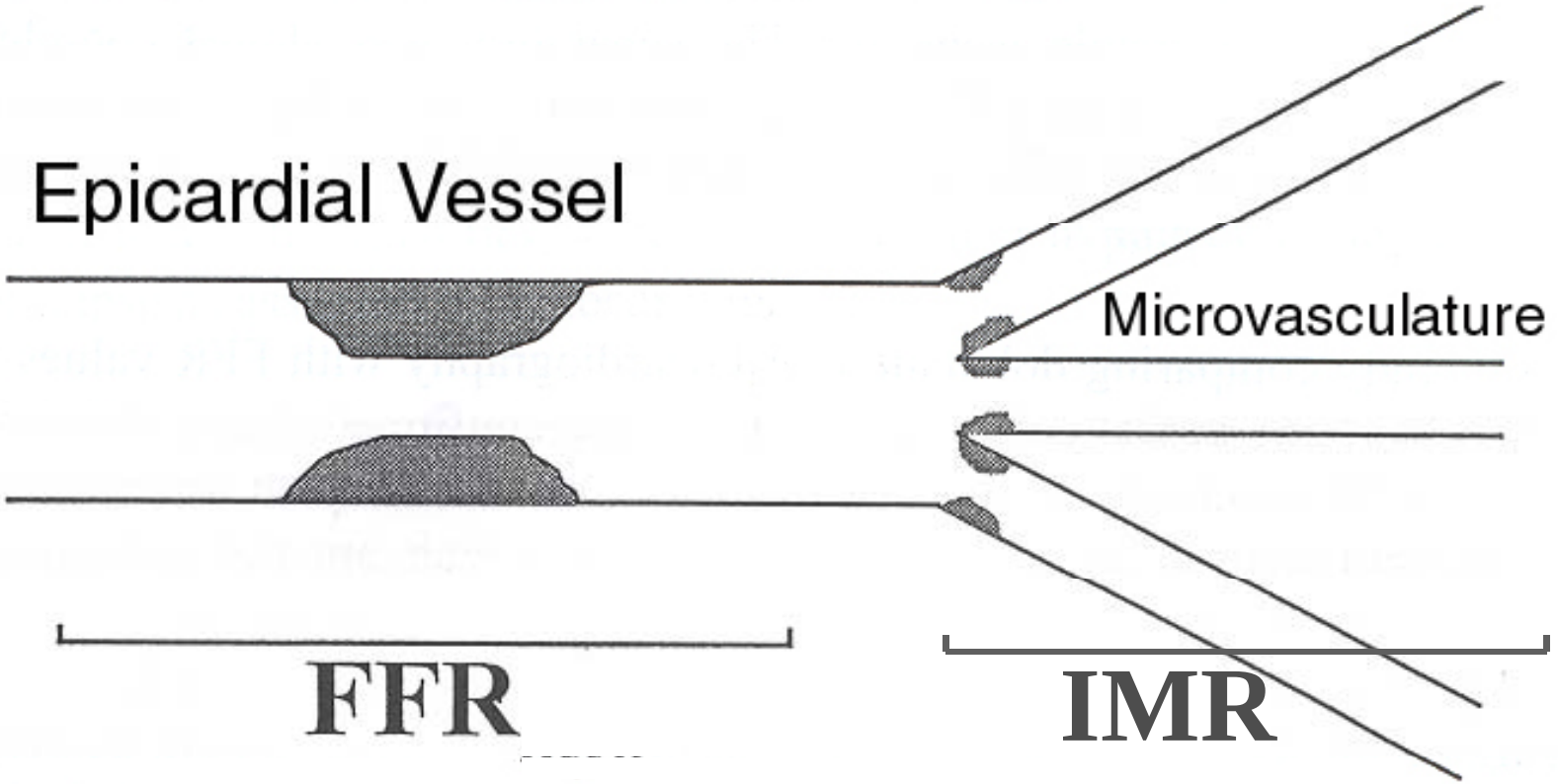


Adapted from Wilson RF. New Engl J Med 1996;334:1735-7

Evaluating the Microvasculature

Techniques	Limitations
Noninvasive: e.g., MRI, PET, Contrast Echo	Not readily available in the cath lab; Require expertise
Angiographic: e.g., Blush score	Qualitative; Useful in large populations
Invasive: e.g., Doppler wire-derived CFR	Interrogates both epicardial vessel and microvasculature; Affected by resting hemodynamics

Index of Microcirculatory Resistance

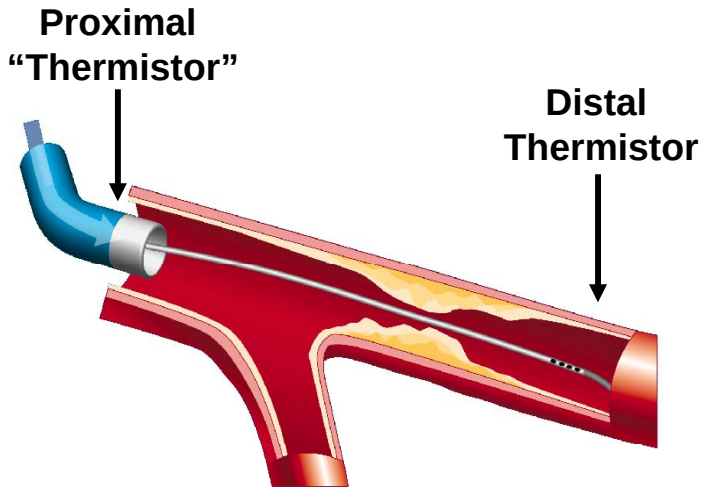


Index of Microcirculatory Resistance

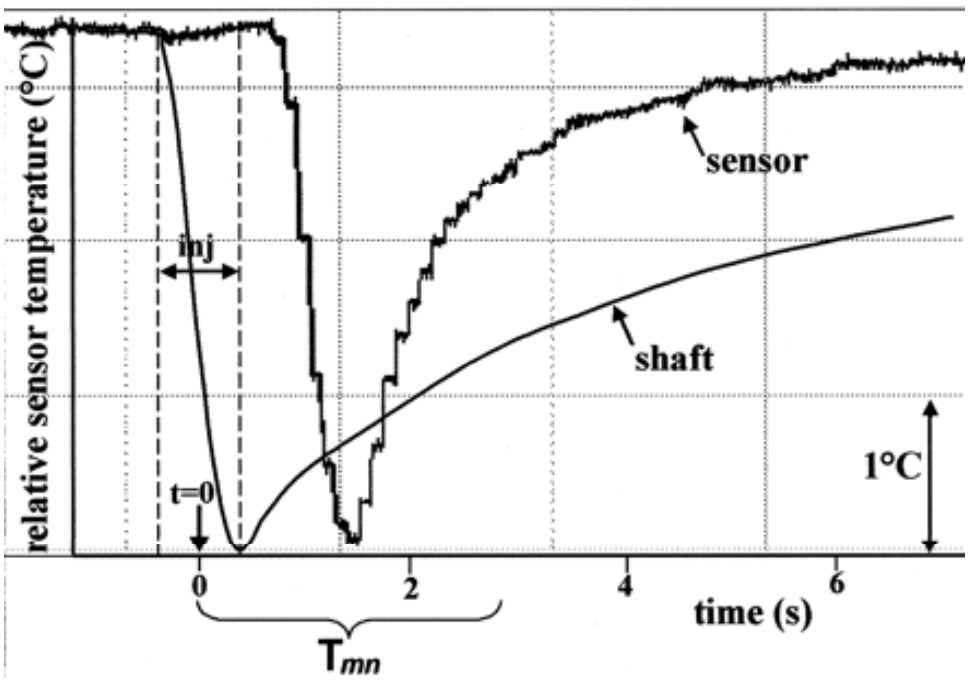
Potential Advantages:

- Readily available in the cath lab
- Specific for the microvasculature
- Quantitative and reproducible
- Predictive of outcomes

Estimation of Coronary Flow



Calculation of mean transit time

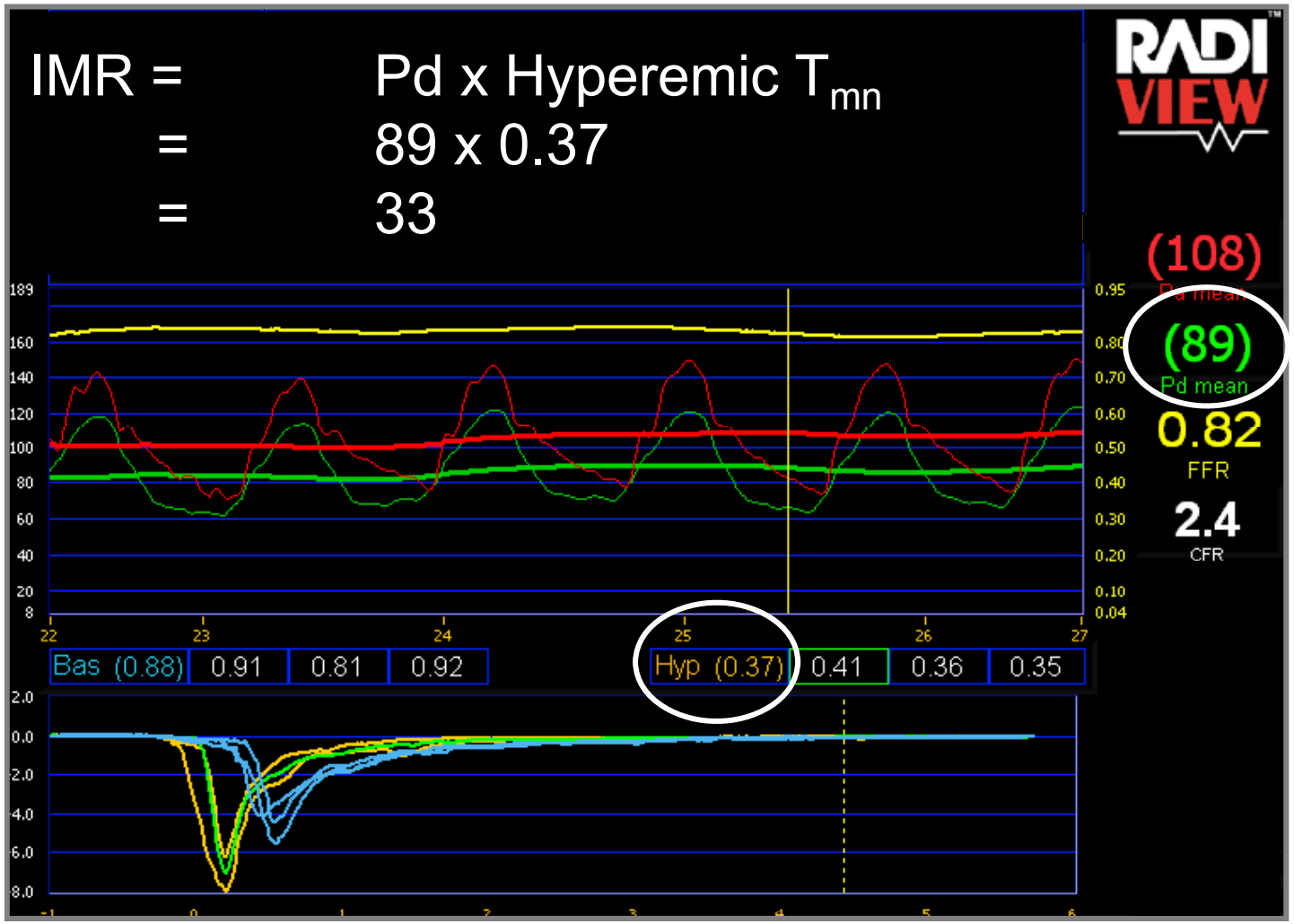


De Bruyne, et al. Circulation 2002;104:2003

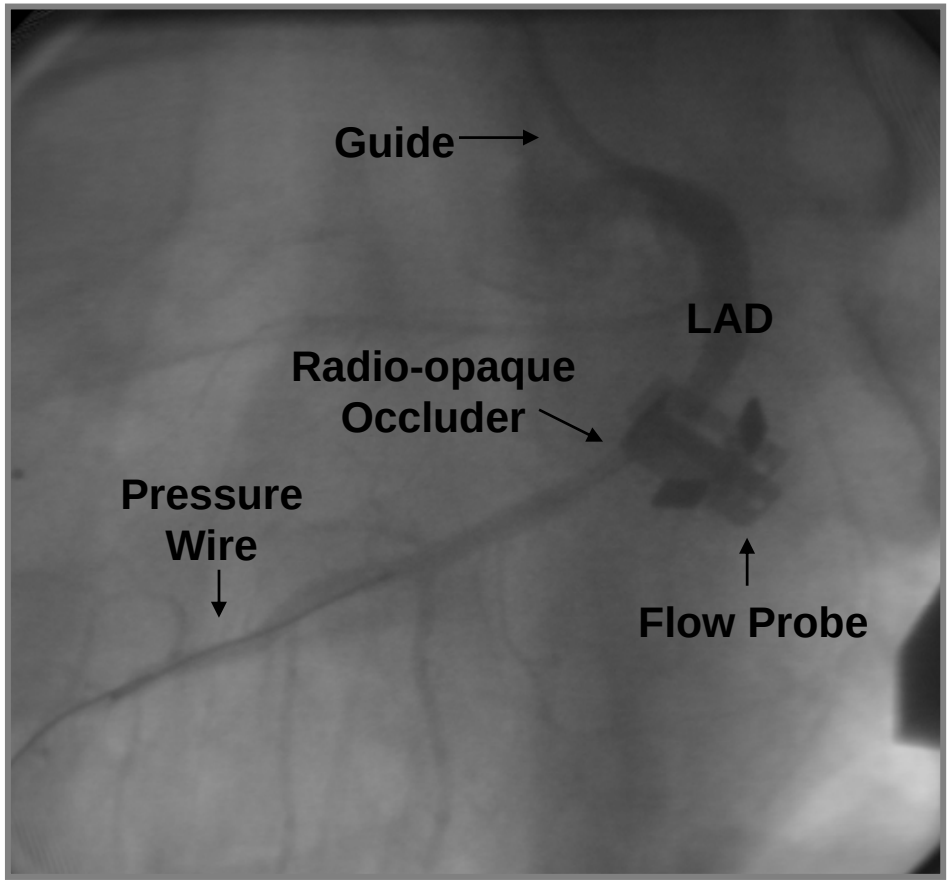
Derivation of IMR:

- Resistance = Δ Pressure / Flow
- Δ Pressure = $P_d - P_v \cong P_d$
- $1 / T_{mn} \cong$ Flow
- IMR = $P_d / (1 / T_{mn})$
- IMR = $P_d \times T_{mn}$ ***at maximal hyperemia…***

Practical Measurement of IMR

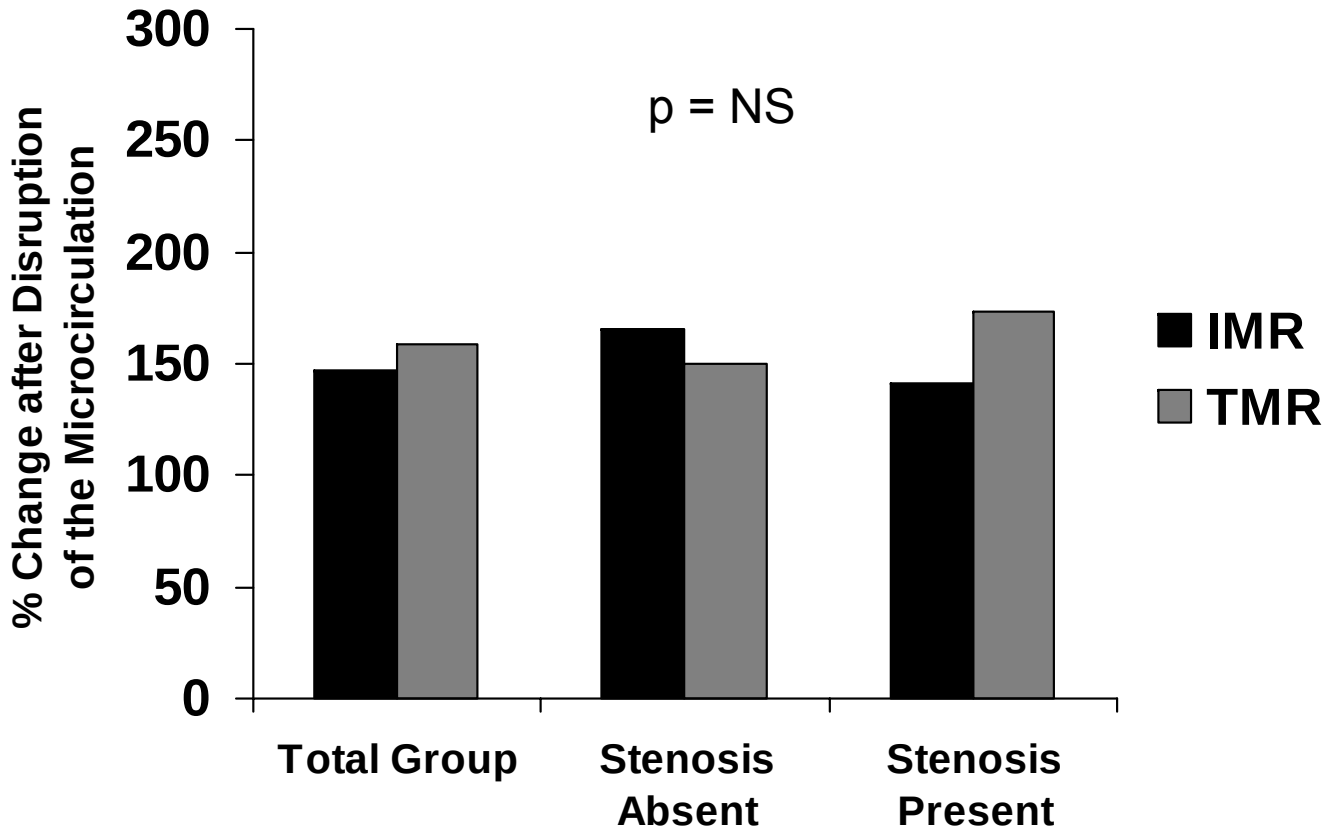


Animal Validation of IMR



Circulation 2003;107:3129-3132.

Animal Validation of IMR



Circulation 2003;107:3129-3132.

Reproducibility of IMR

Effect of Pacing on FFR/CFR/IMR

	Baseline	RV Pacing at 110 bpm
CFR	3.1±1.1	2.3±1.2†
IMR, U	21.8±6.5	22.9±6.9
FFR	0.88±0.07	0.87±0.07

Effect of Blood Pressure on FFR/CFR/IMR

	Baseline	Nitroprusside
CFR	2.9±0.9	2.5±1.2
IMR, U	23.85±6.1	24.00±7.9
FFR	0.88±0.04	0.87±0.05

Change in LV Contractility and FFR/CFR/IMR

	Baseline	Dobutamine
CFR	3.0±1.0	1.7±0.6†
IMR, U	22.2±6.0	23.6±8.2
FFR	0.88±0.06	0.87±0.06

Ng et al. Circulation 2006;113:2054-61.

Why should we assess the coronary microvasculature?

- In stable patients with “normal” coronary arteries, abnormal microvascular function predicts adverse outcome.
- In stable patients undergoing PCI, abnormal microvascular resistance may predict adverse outcome.
- Immediately after STEMI, impaired microvascular function predicts adverse outcome.
- For research purposes.

Why should we assess the coronary microvasculature?

- **In stable patients with “normal” coronary arteries, abnormal microvascular function predicts adverse outcome.**

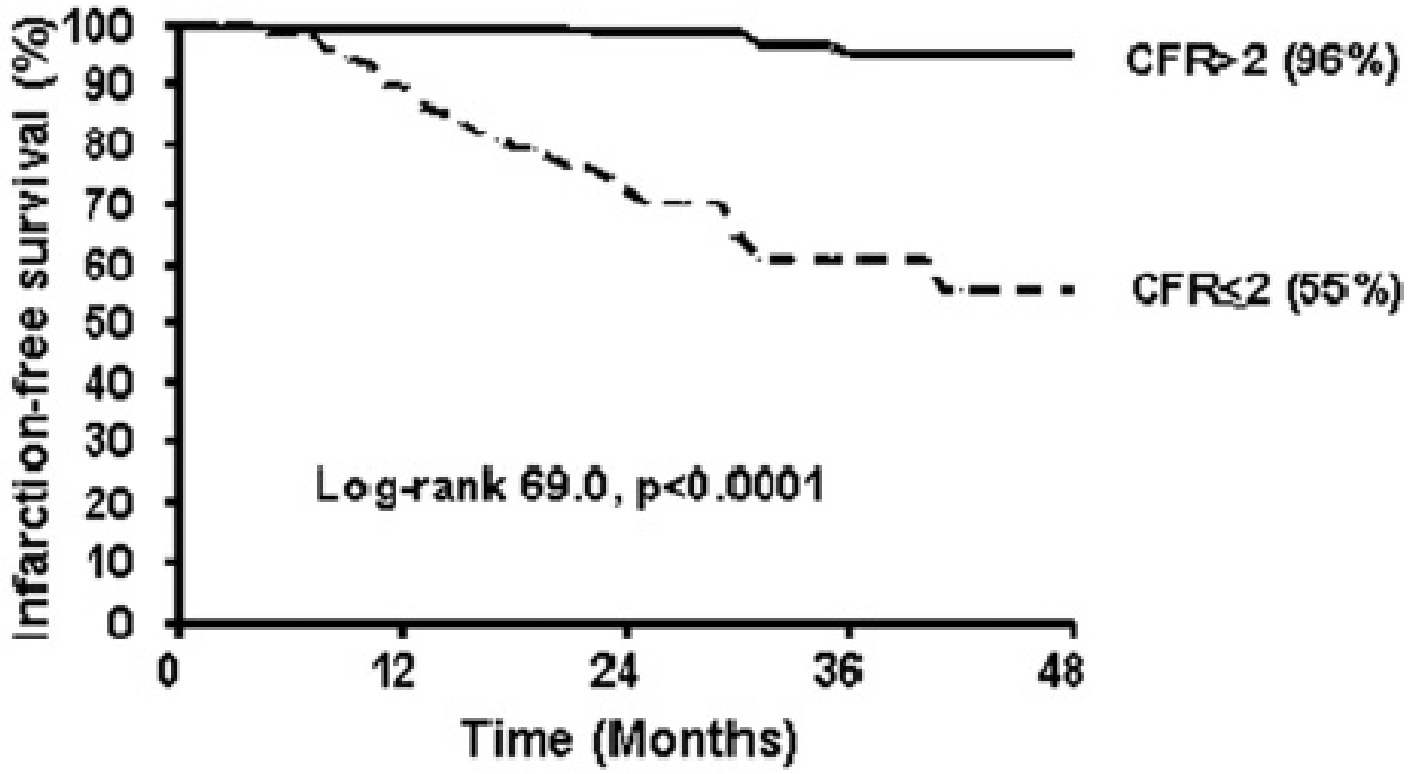
- In stable patients undergoing PCI, abnormal microvascular resistance may predict adverse outcome.

- Immediately after STEMI, impaired microvascular function predicts adverse outcome.

- For research purposes.

Importance of the Microcirculation

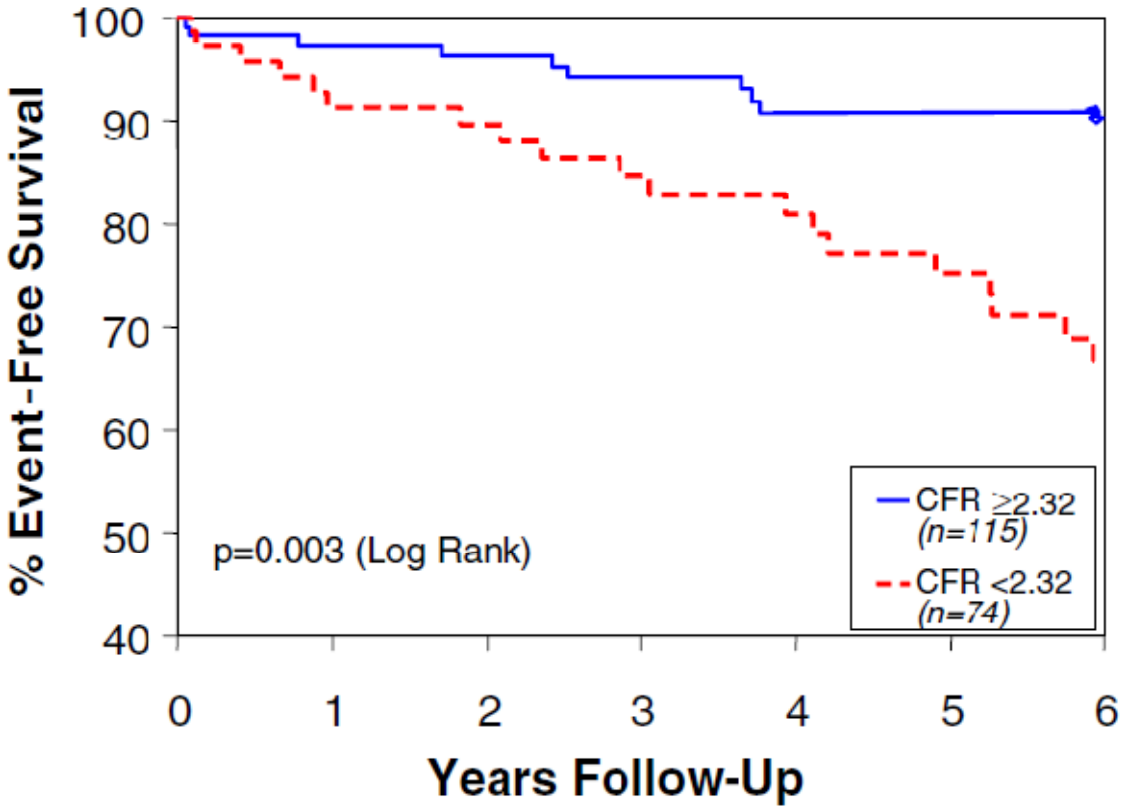
Infarct-Free Survival based on Echo-Derived CFR in 394 Patients with Chest Pain and Normal Coronaries



Sicari, et al. Am J Cardiol 2009;103:626-31.

Importance of the Microcirculation

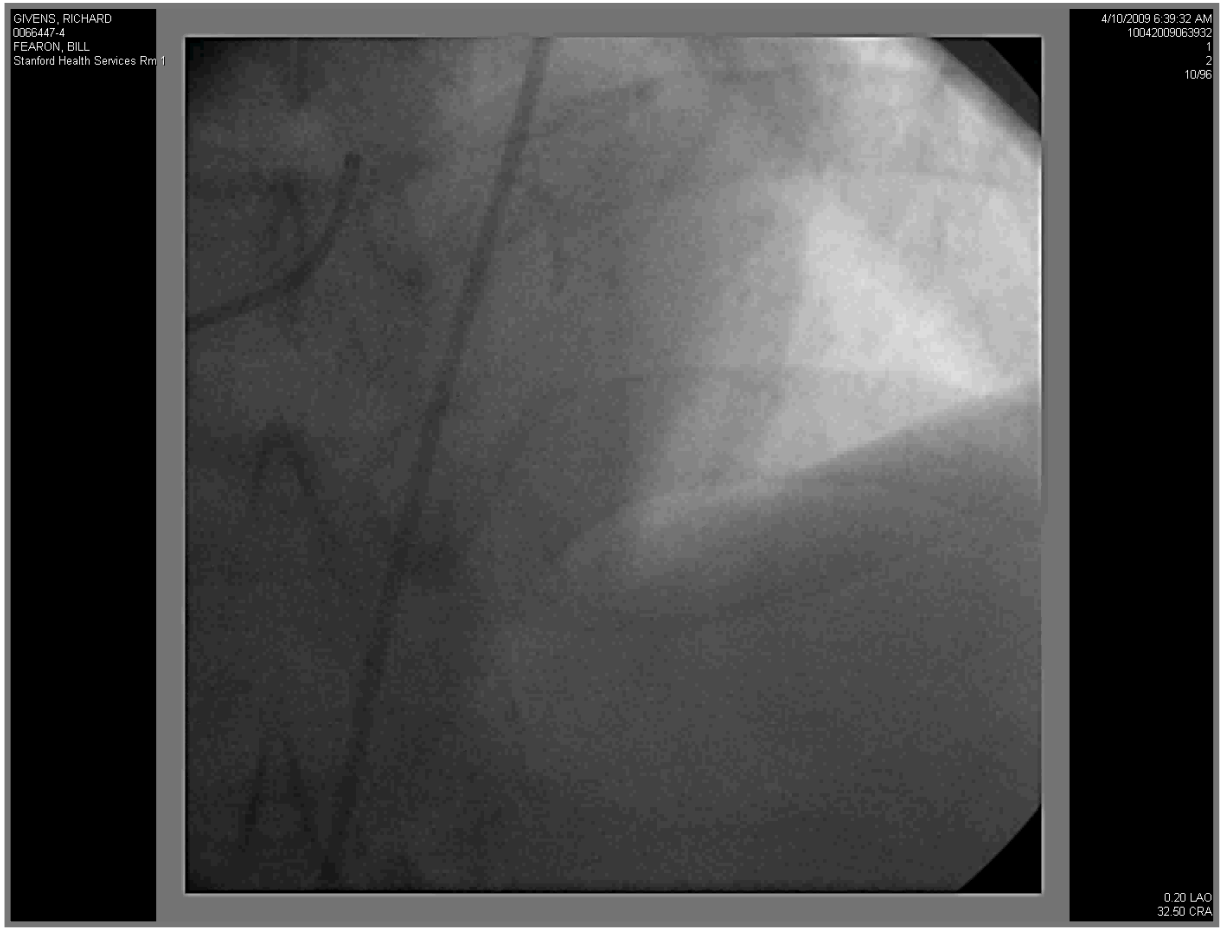
189 women with chest pain and "normal" coronary arteries:
% free of Death, MI, CVA, or CHF



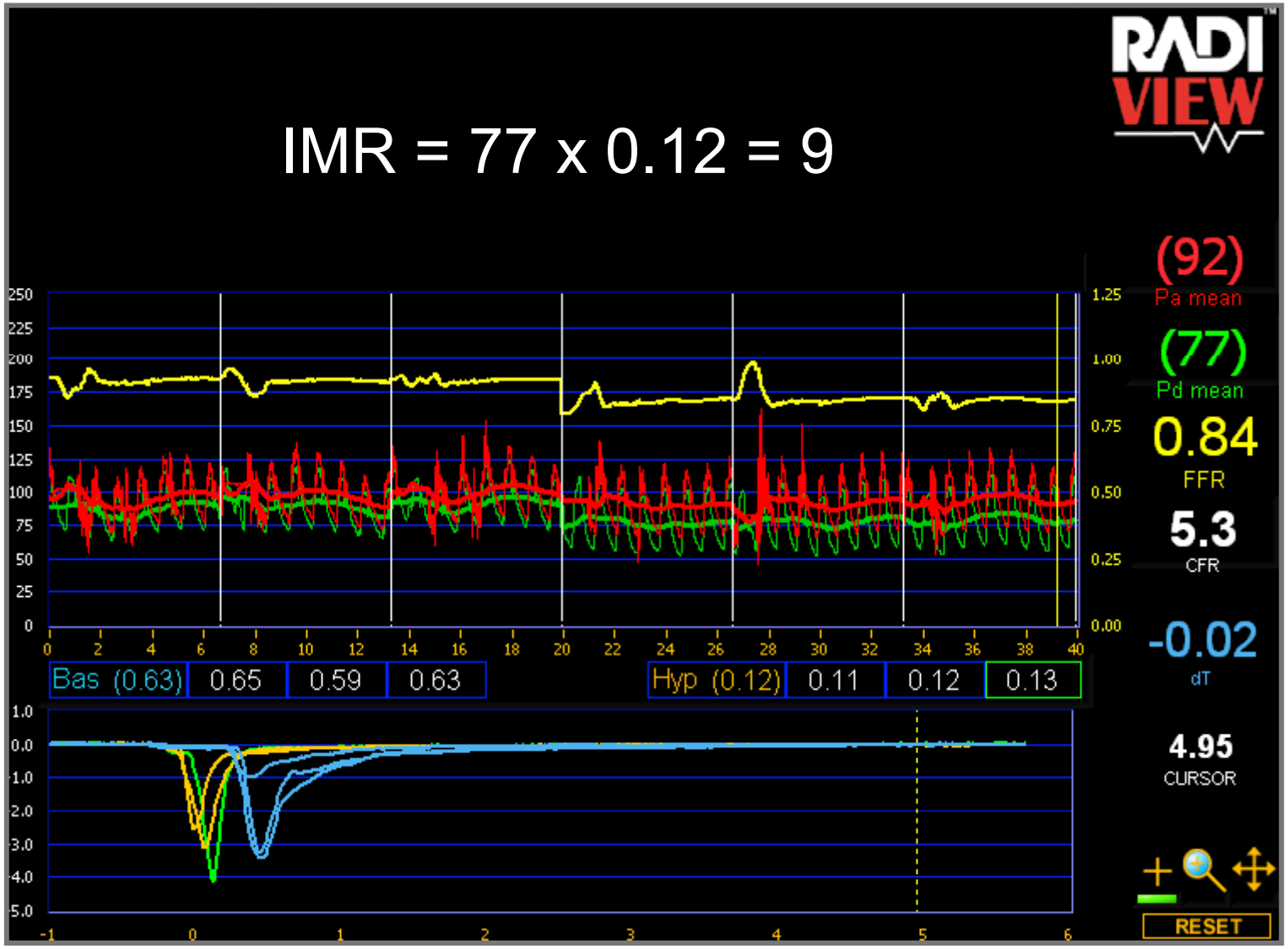
Pepine, et al. J Am Coll Cardiol 2010;55:2825-32.

Clinical Application of IMR

65 year old man with HTN, ↑Chol, and chest pain with anterior ischemia on ETT-Echo

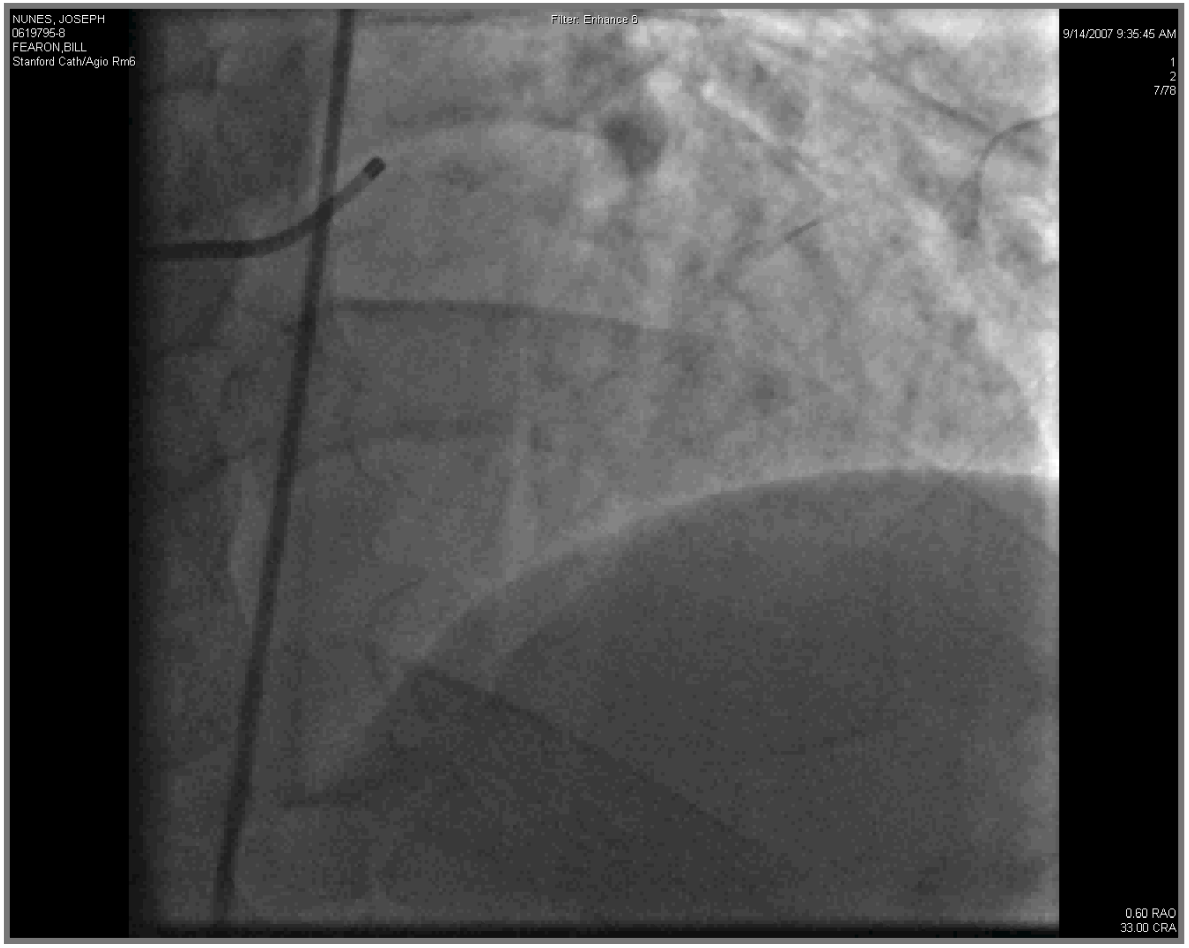


IMR = 77 x 0.12 = 9

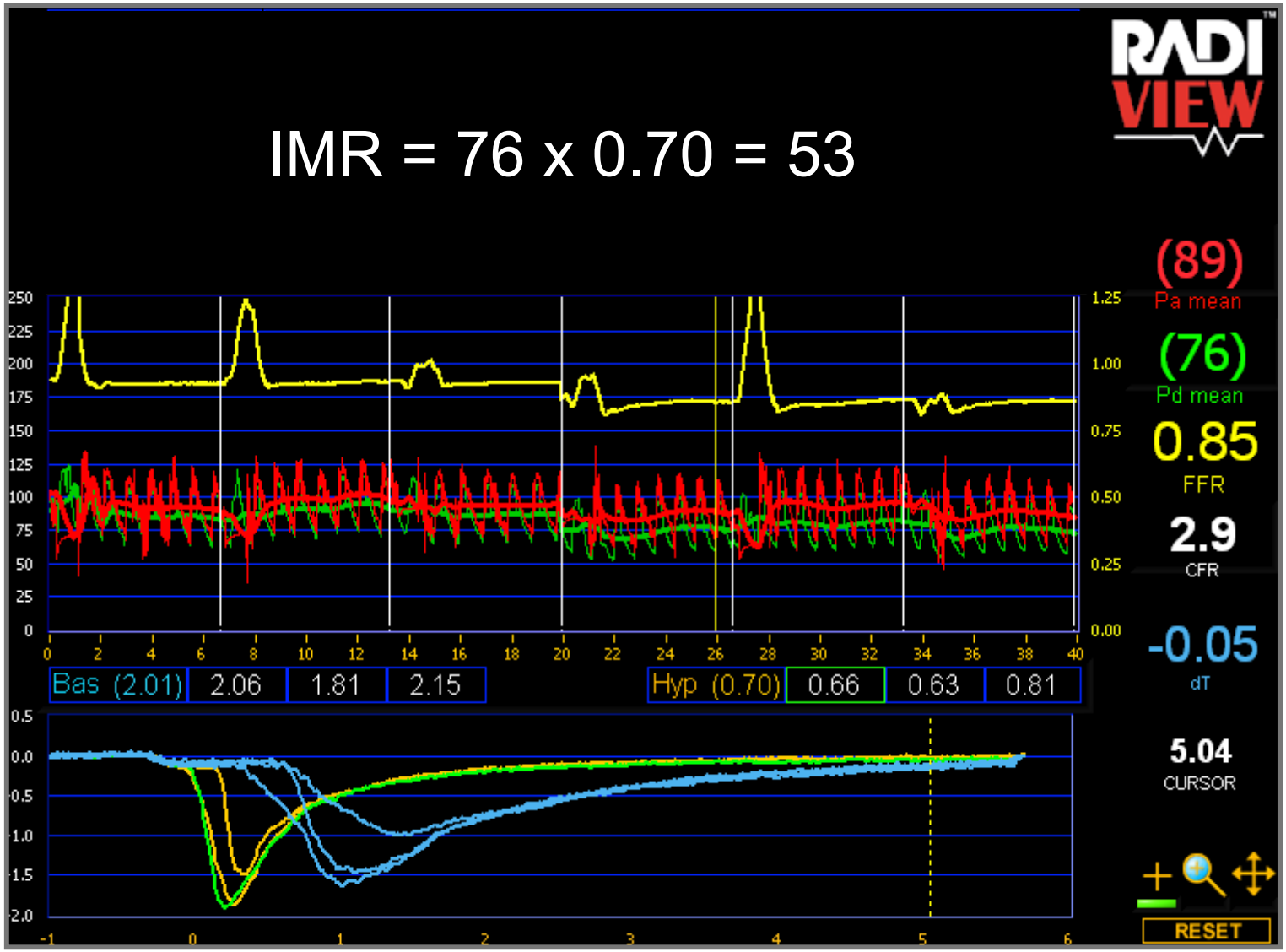

RADI VIEW
(92)
Pa mean
(77)
Pd mean
0.84
FFR
5.3
CFR
-0.02
dT
4.95
CURSOR
RESET
Bas (0.63) 0.65 0.59 0.63
Hyp (0.12) 0.11 0.12 0.13

Clinical Application of IMR

59 year old man with HTN, dyslipidemia and chest pain with emotional stress and septal ischemia on Nuclear Scan



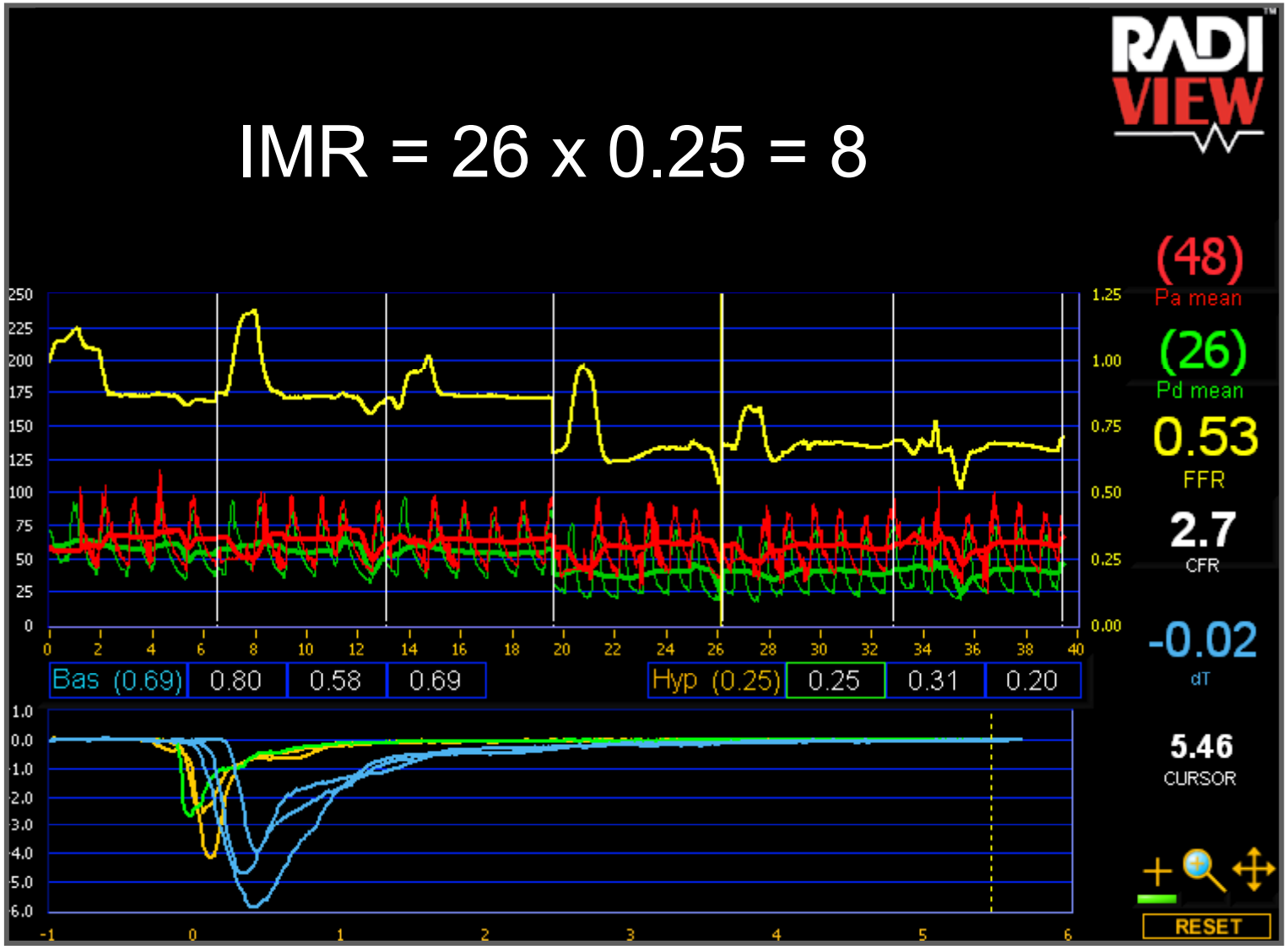
IMR = 76 x 0.70 = 53



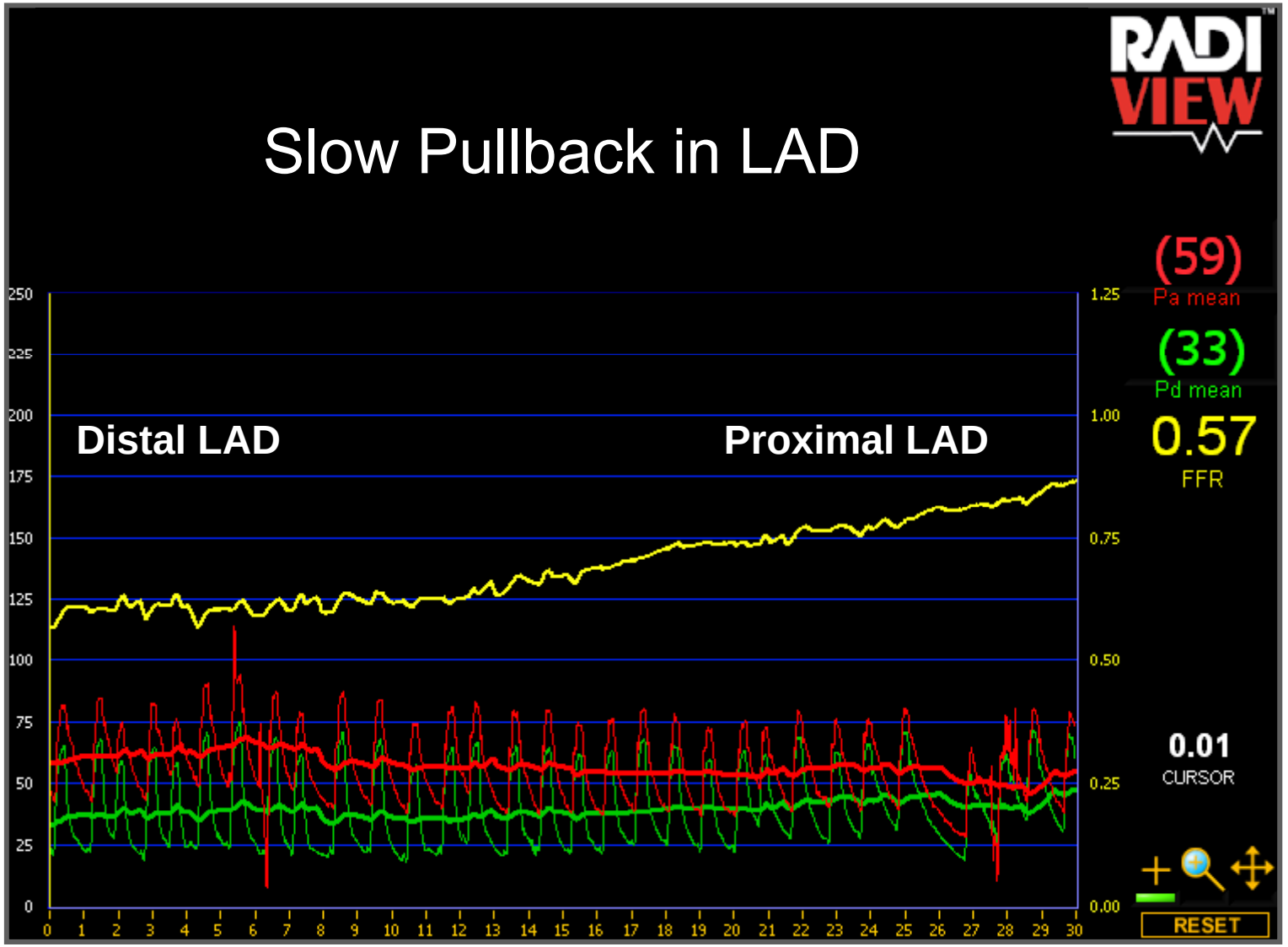
Clinical Application of IMR

68 year old man HTN and tobacco use with negative stress echo 4 months ago, but increasingly severe classic exertional angina

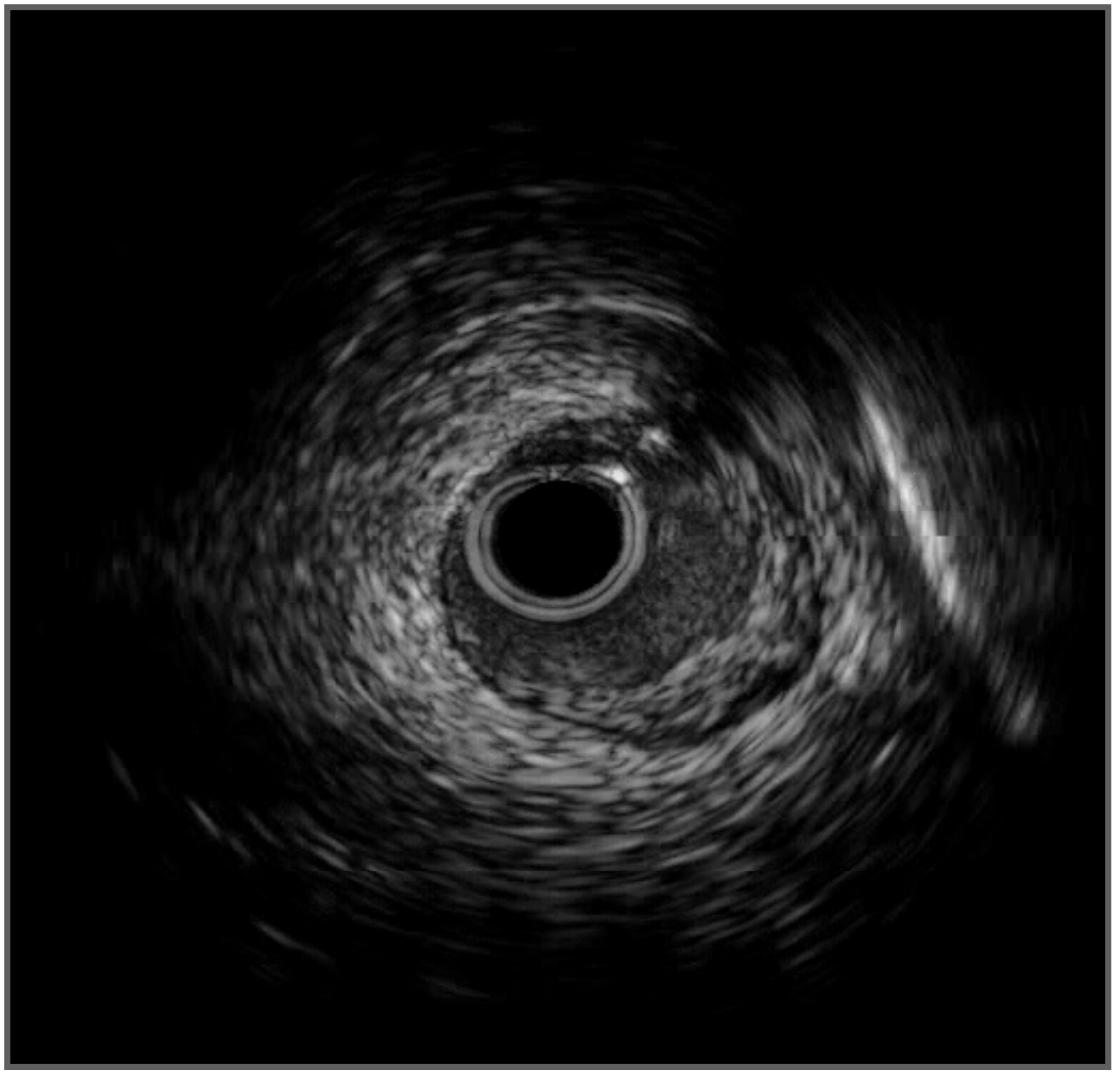
IMR = 26 x 0.25 = 8


RADI VIEW
(48)
Pa mean
(26)
Pd mean
0.53
FFR
2.7
CFR
-0.02
dT
5.46
CURSOR
RESET
Bas (0.69) 0.80 0.58 0.69
Hyp (0.25) 0.25 0.31 0.20

Slow Pullback in LAD



IVUS of LAD

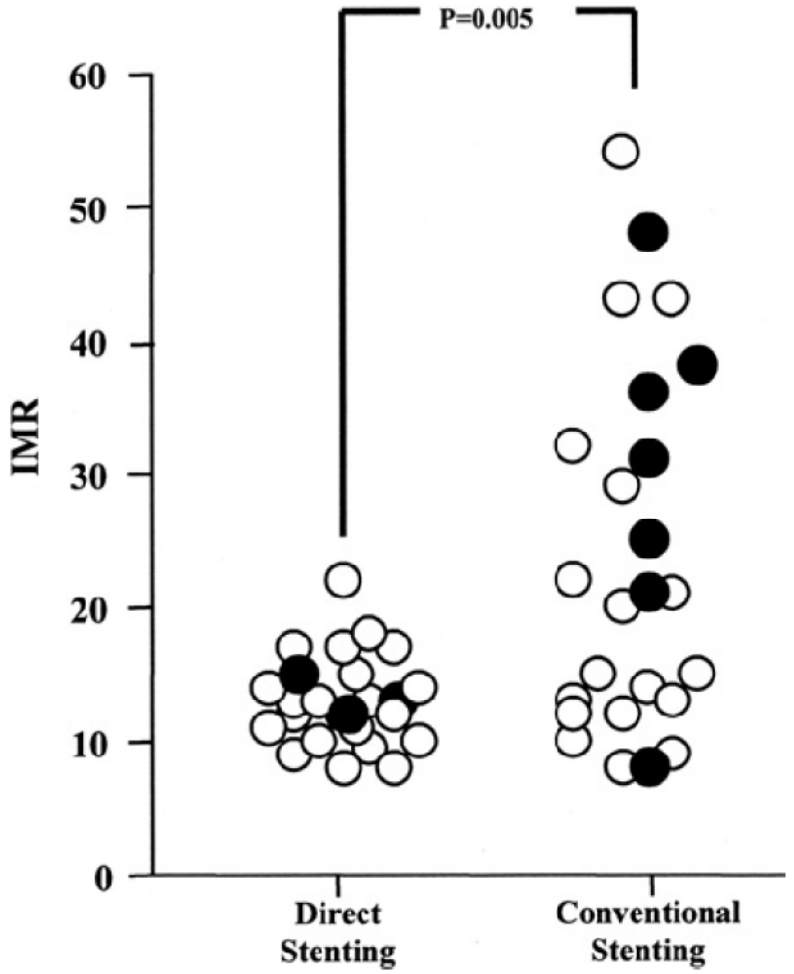


Why should we assess the coronary microvasculature?

- In stable patients with “normal” coronary arteries, abnormal microvascular function predicts adverse outcome.
- In stable patients undergoing PCI, abnormal microvascular resistance may predict adverse outcome.
- Immediately after STEMI, impaired microvascular function predicts adverse outcome.
- For research purposes.

IMR after PCI in Stable Patients

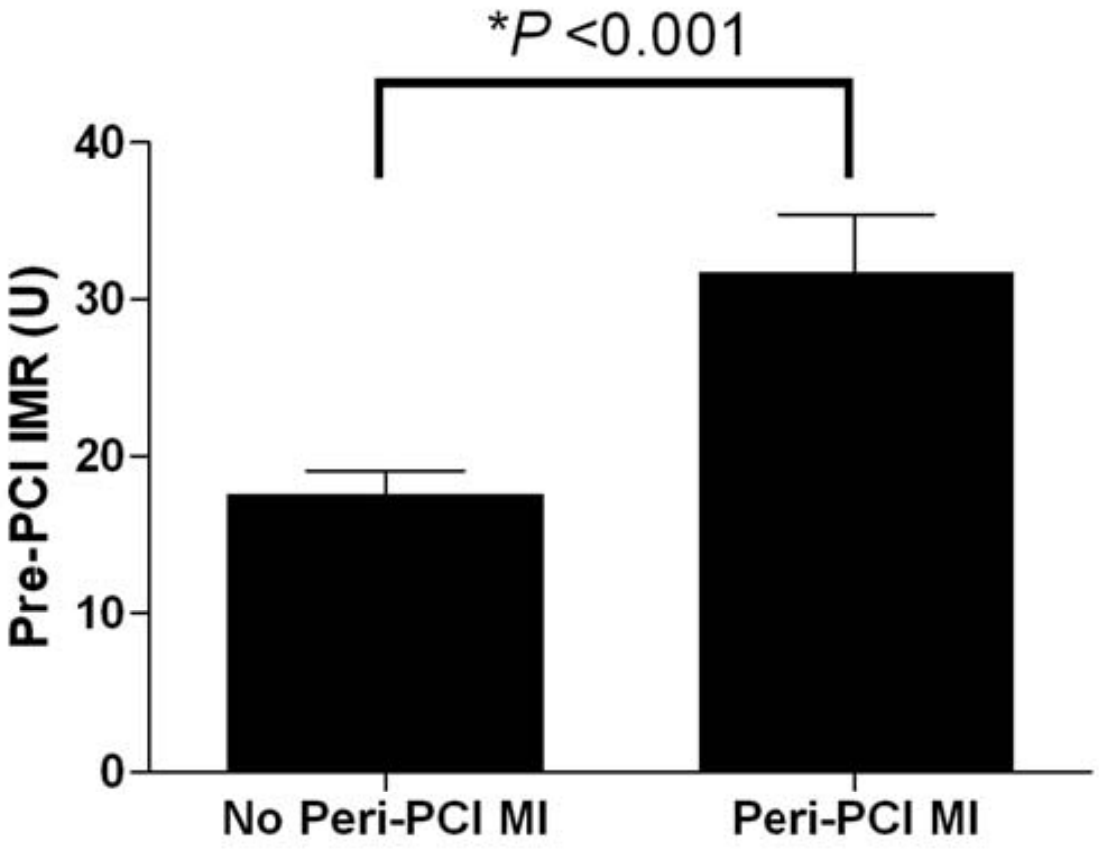
- **50 patients randomized to conventional stenting with predilatation versus direct stenting**
- **IMR measured after PCI and correlated with troponin release**
- **In the 10 patients with elevated Tn post PCI, IMR was 24.7 ±13.3 vs. 16.9 ±10.2, p=0.04.**



Cuisset, et al. J Am Coll Cardiol;2008:51:1060

IMR *Before* PCI in Stable Patients

IMR measured before PCI in 50 stable patients undergoing LAD PCI



Yong, et al. AHA 2010.

IMR *Before* PCI in Stable Patients

IMR measured before PCI in 50 stable patients undergoing LAD PCI

Multivariable Regression Analysis

Variable	*P*	Odds ratio	95% Confidence interval
IMR	0.002	1.25	1.08 – 1.43
Beta-blocker	0.064	13.97	0.97 – 200.56
Post-dilation	0.072	0.09	0.01 – 1.24
Total inflation time	0.115	1.01	0.99 – 1.03
Stent length	0.35	1.08	0.92 – 1.27

Yong, et al. AHA 2010.

Why should we assess the coronary microvasculature?

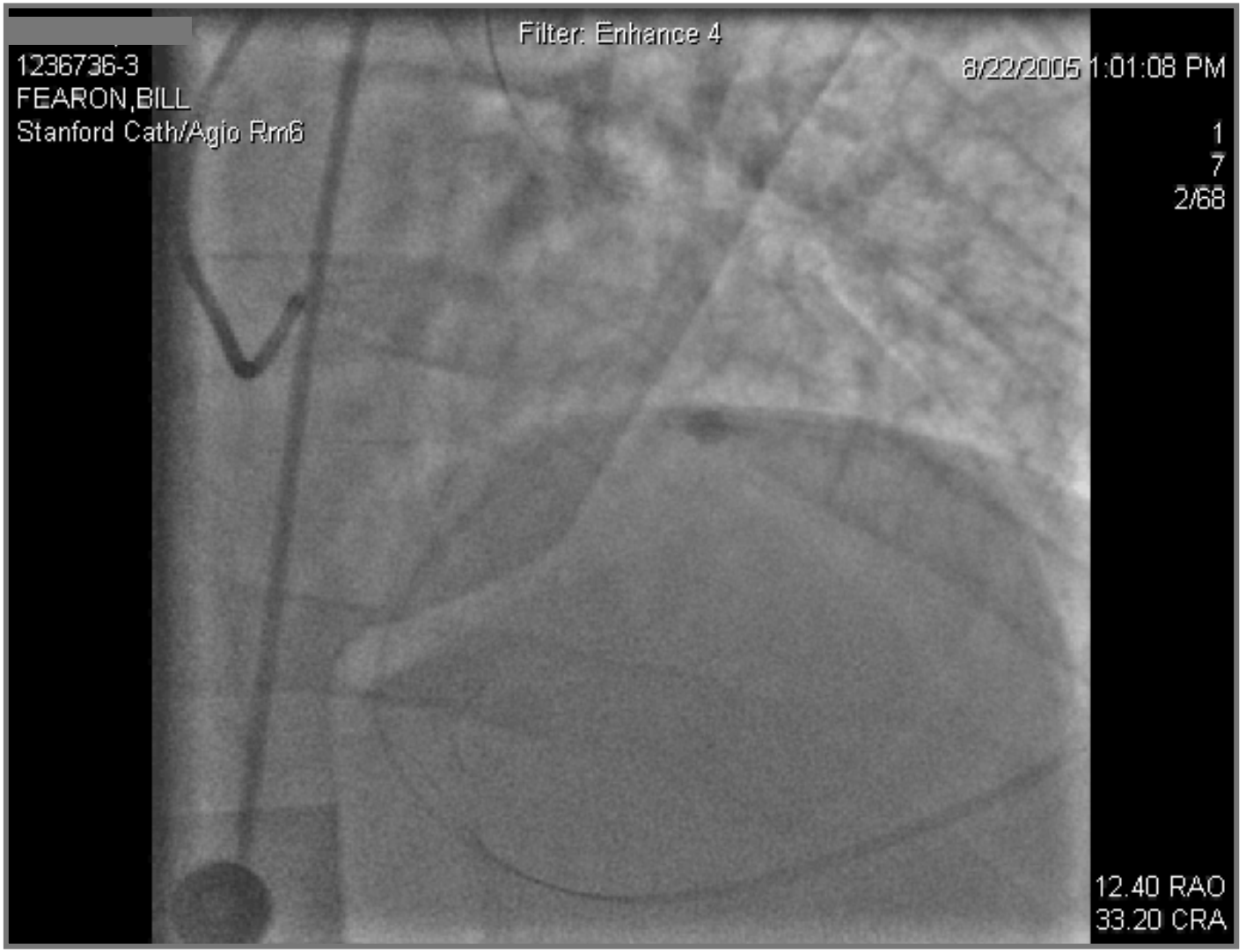
- In stable patients with “normal” coronary arteries, abnormal microvascular function predicts adverse outcome.
- In stable patients undergoing PCI, abnormal microvascular resistance may predict adverse outcome.
- Immediately after STEMI, impaired microvascular function predicts adverse outcome.
- For research purposes.

A Tale of Two MI's

STEMI Case 1

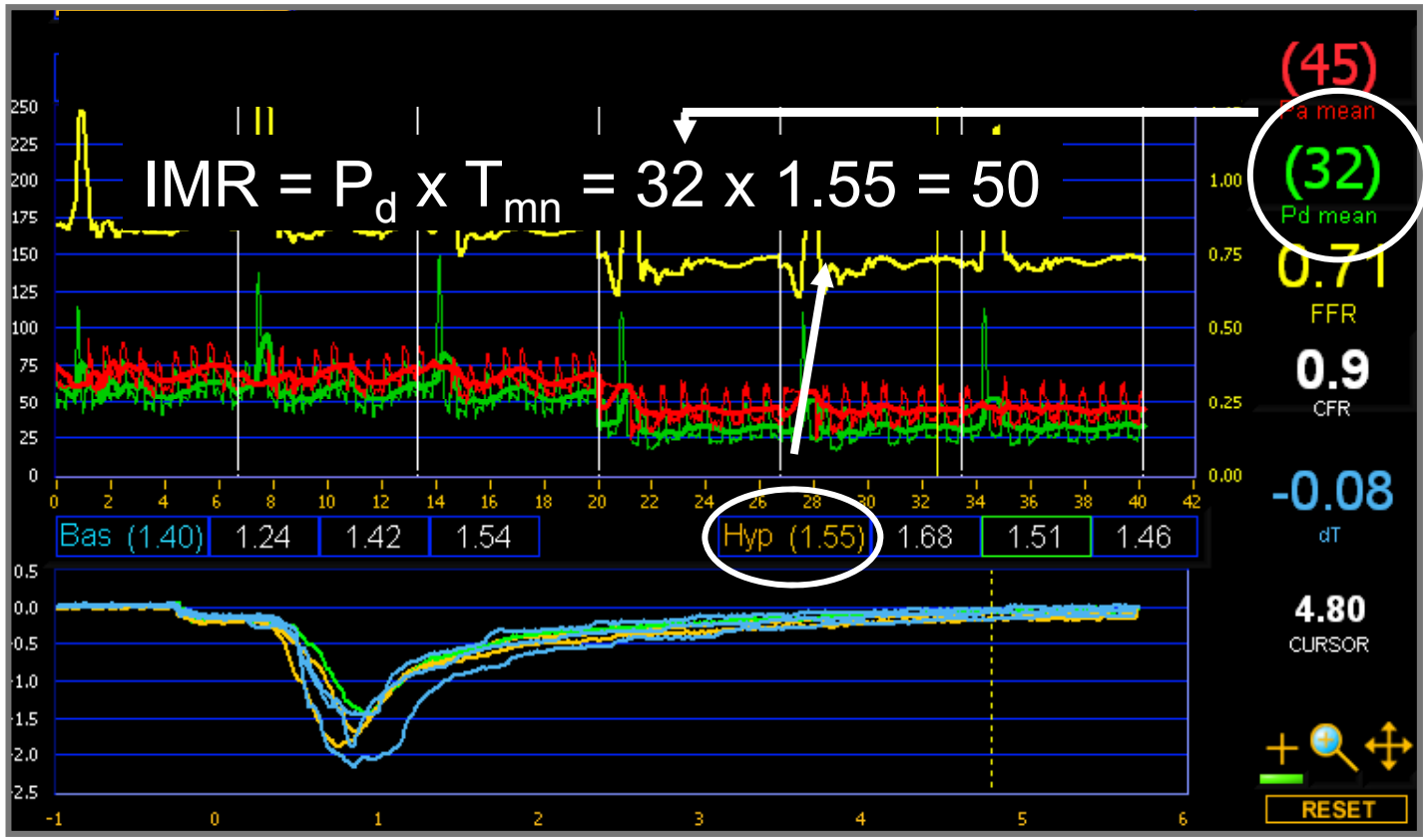
- 65 year old man with HTN presents with recurrent chest pain and ST segment elevation in leads V_1 to V_3 after failed lytics

- He was taken emergently to the cath lab roughly 5½ hours after symptom onset


Filter: Enhance 4
1236736-3
FEARON,BILL
Stanford Cath/Agio Rm6
8/22/2005 1:01:08 PM
1
7
2/68
12.40 RAO
33.20 CRA


Filter: Enhance 4
1236736-3
FEARON,BILL
Stanford Cath/Agio Rm6
8/22/2005 1:01:08 PM
1
20
2/104
14.40 RAO
33.40 CRA

IMR during STEMI



*IMR = **50***

*Peak CK=**3754***

*Initial EF=**37%***

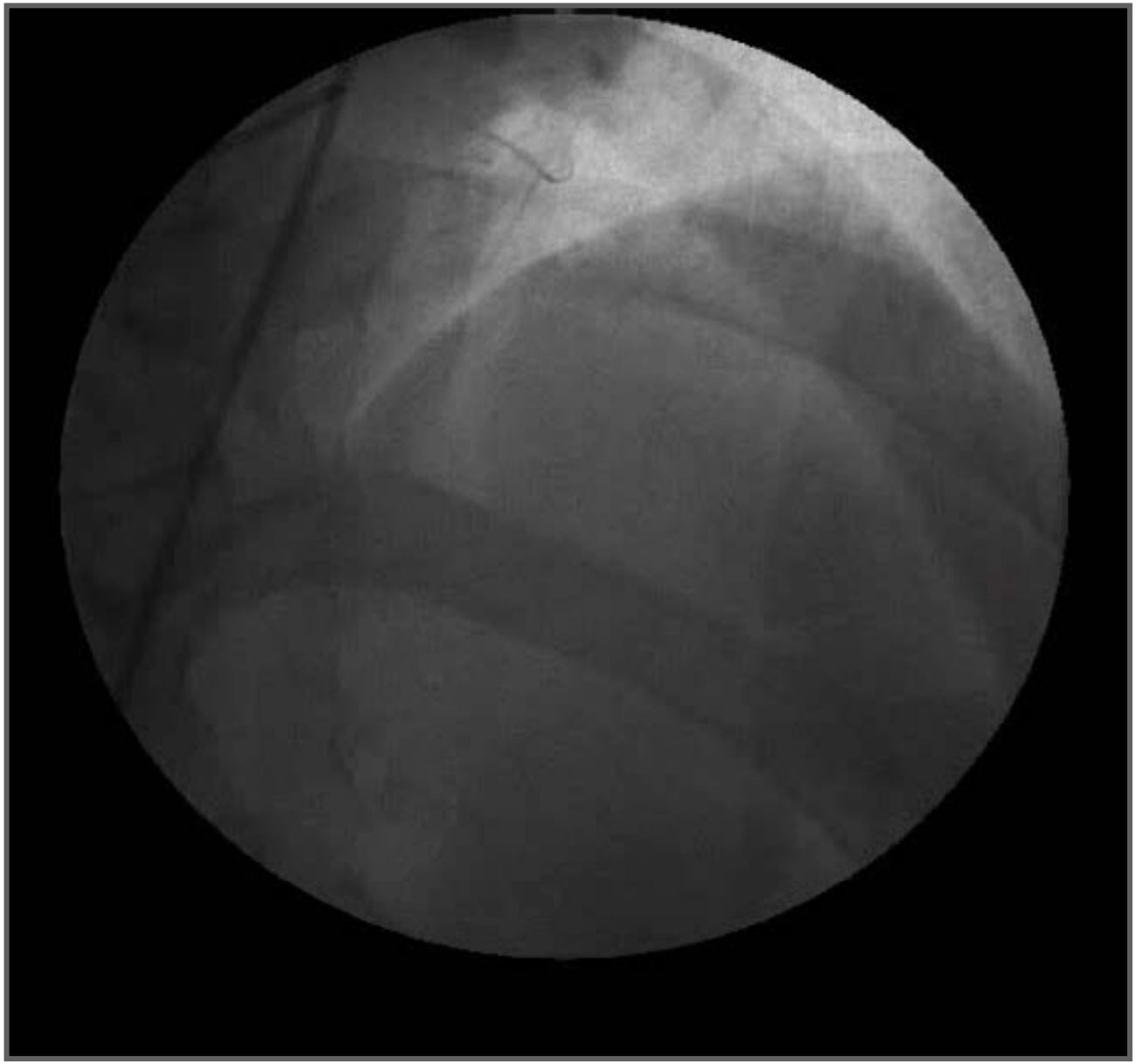
*F/U EF=**37%***

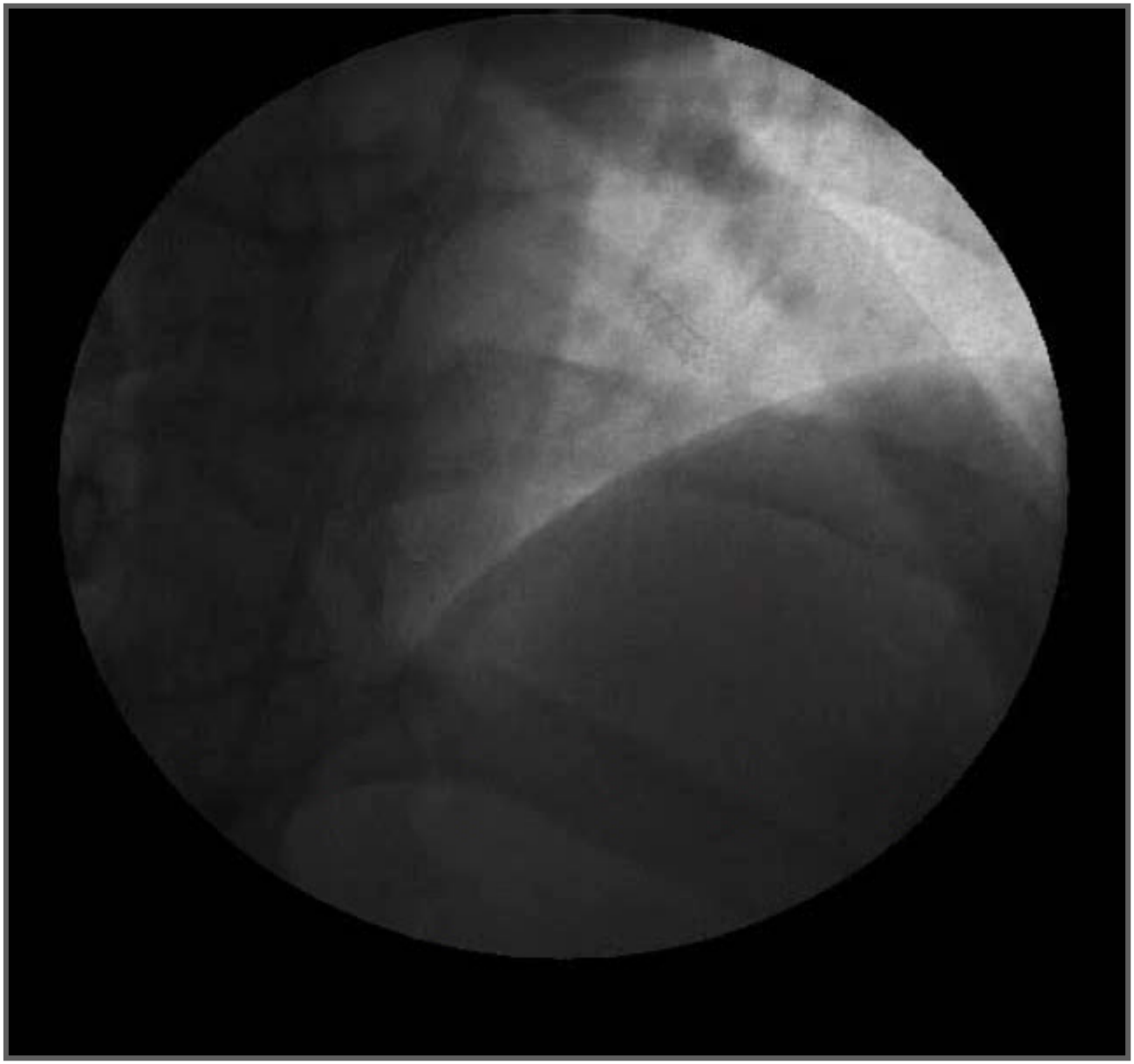
A Tale of Two MI's

STEMI Case 2

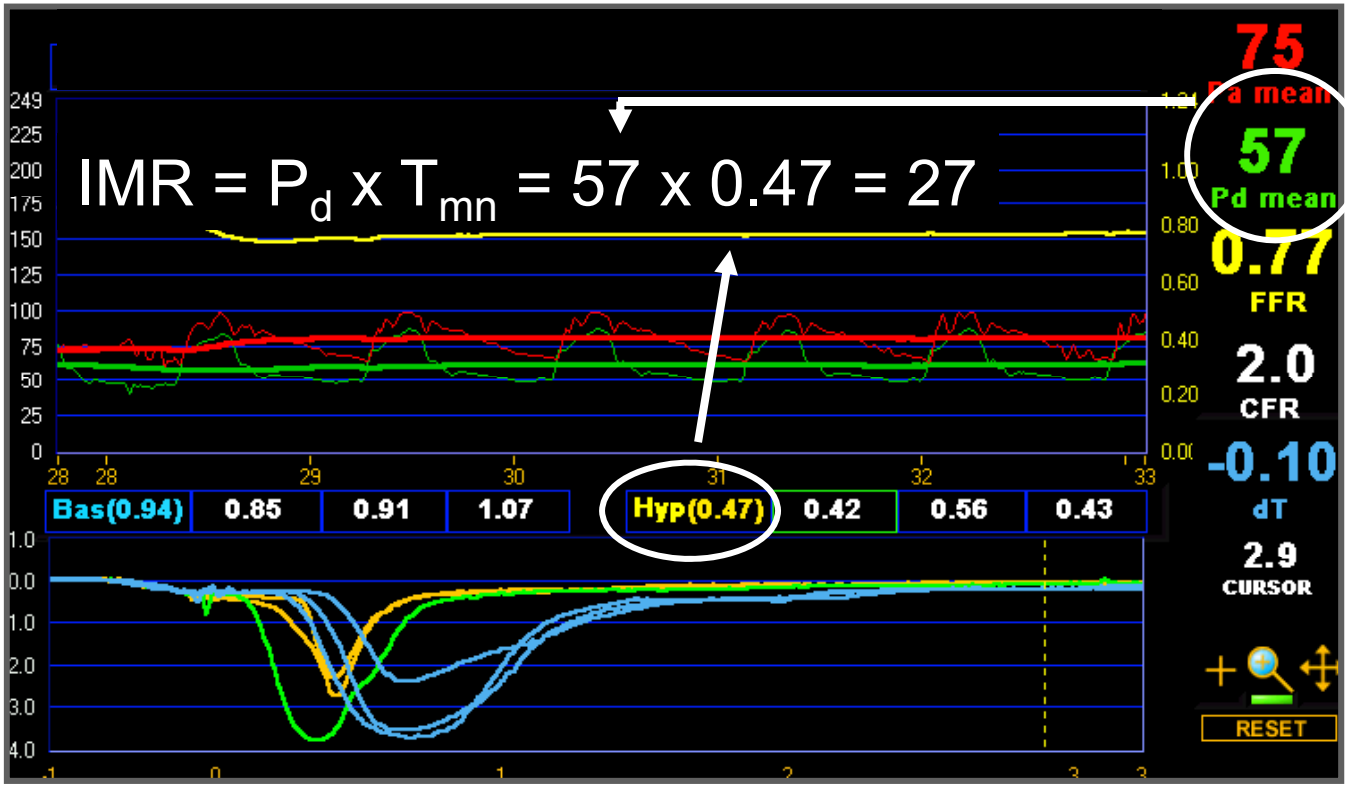
- 52 year old man with HTN and dyslipidemia presents with recurrent chest pain and ST segment elevation in leads V_2-V_4 after failed lytics

- He was taken emergently to the cath lab roughly 8 hours after symptom onset





IMR during STEMI



*IMR = **27***

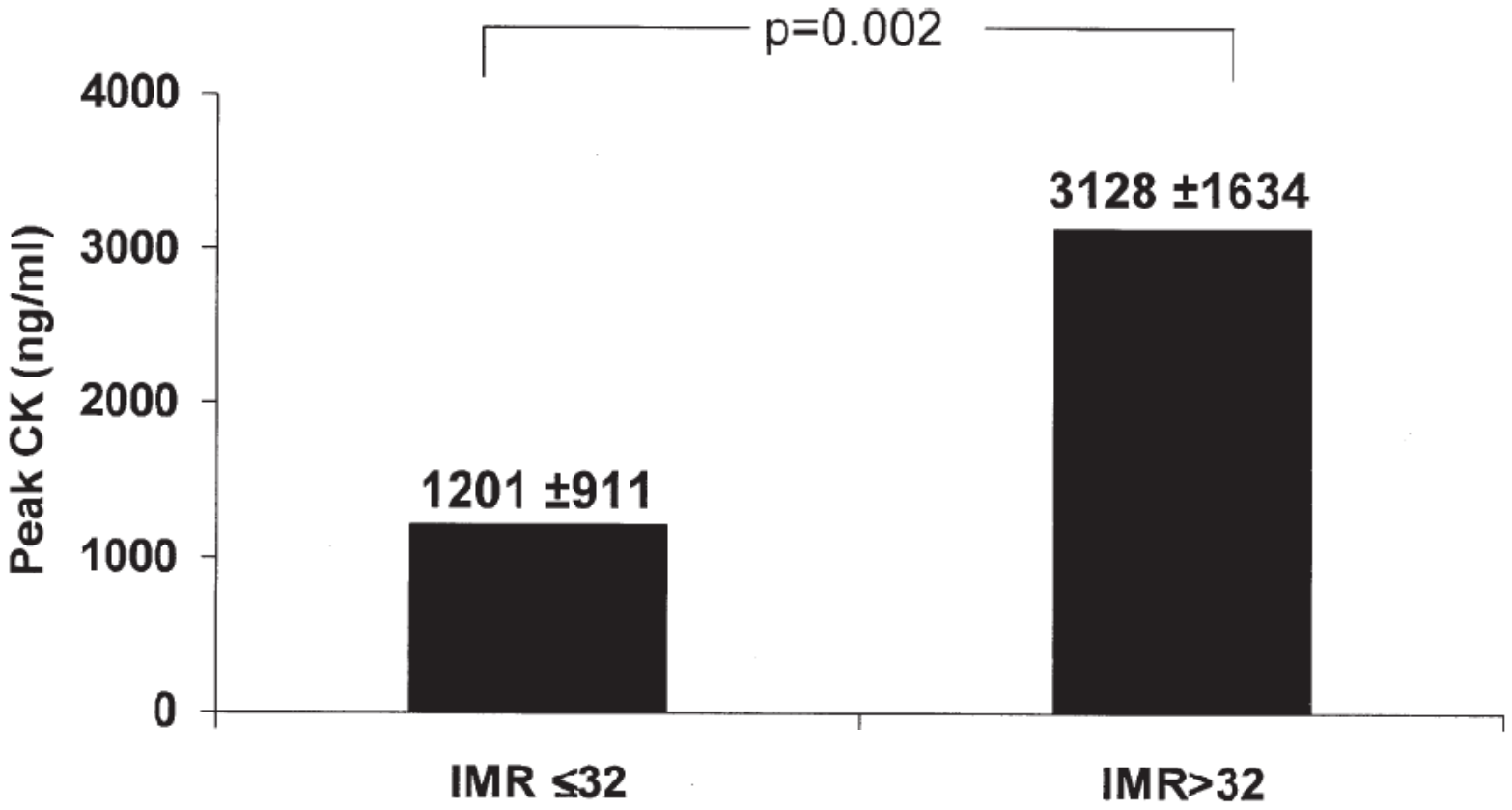
*Peak CK=**1008***

*Initial EF=**42%***

*F/U EF=**62%***

Predictive Value of IMR after PCI for STEMI

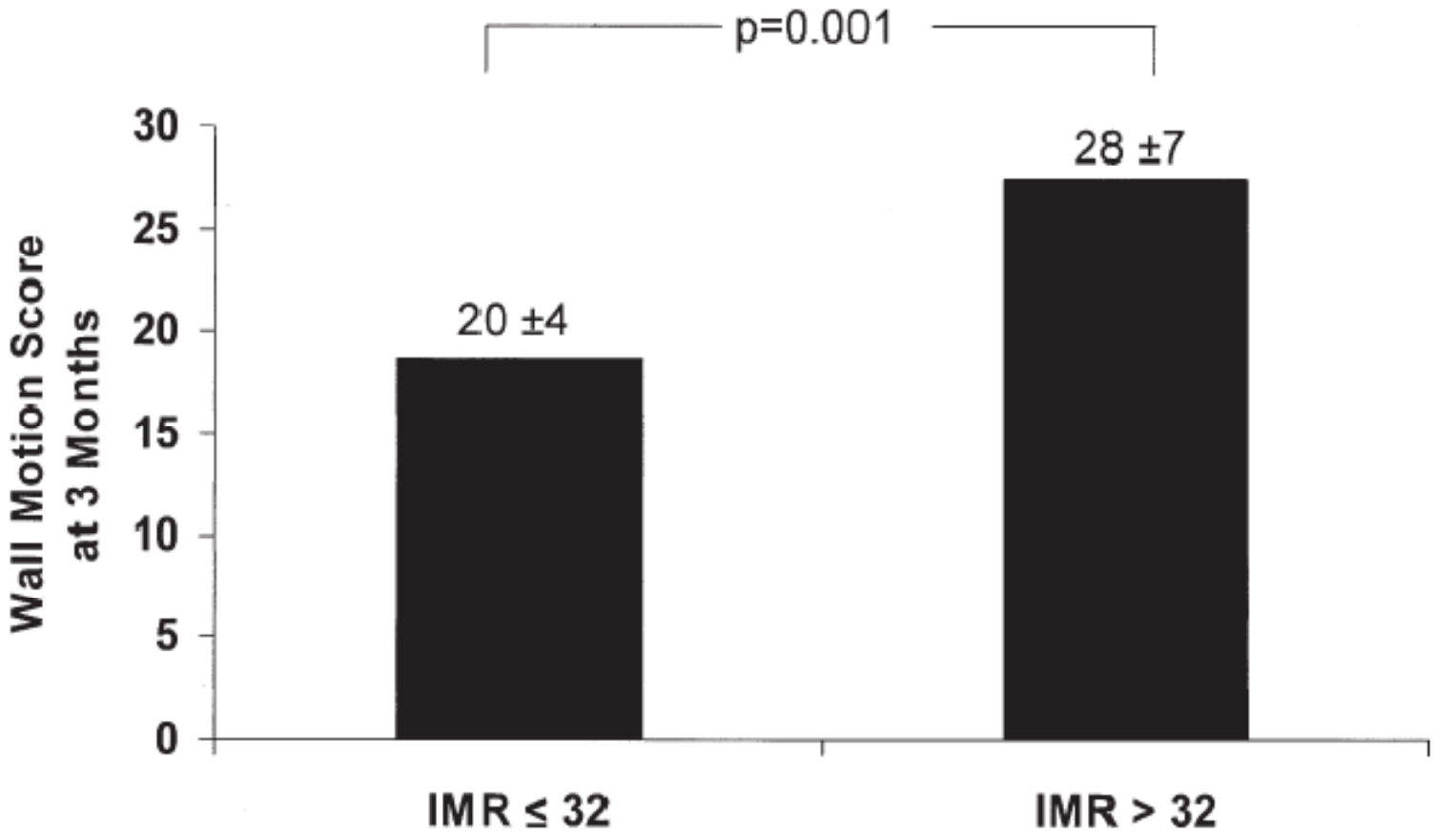
IMR predicts peak CK in patients with STEMI



J Am Coll Cardiol 2008;51:560-5

Predictive Value of IMR after PCI for STEMI

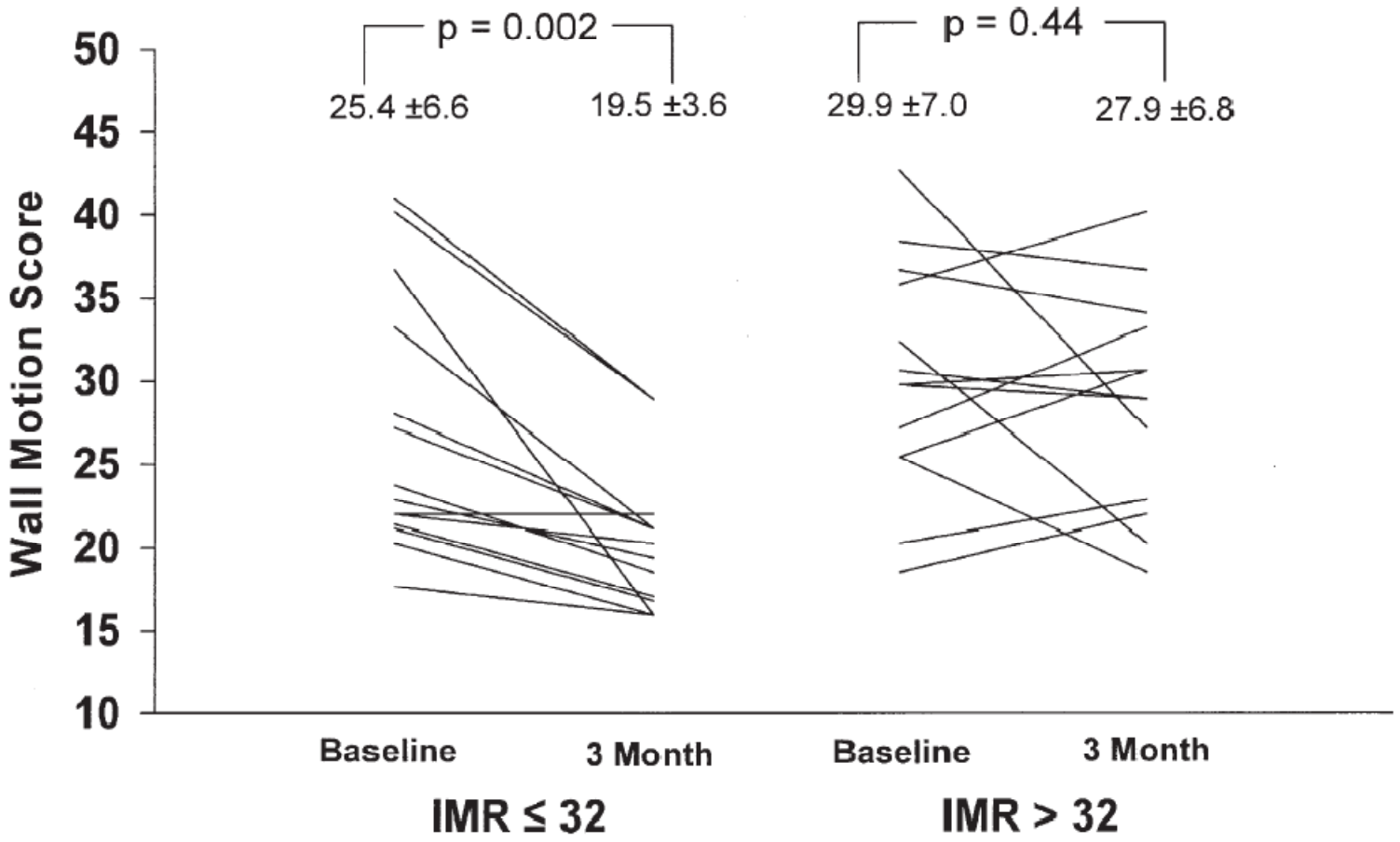
IMR predicts LV function 3 months after STEMI



J Am Coll Cardiol 2008;51:560-5.

Predictive Value of IMR after PCI for STEMI

IMR predicts which patients will have improved LV function after STEMI



J Am Coll Cardiol 2008;51:560-5.

Predictive Value of IMR after PCI for STEMI

Correlation between measures of microvascular function and peak CK and 3-month wall motion score

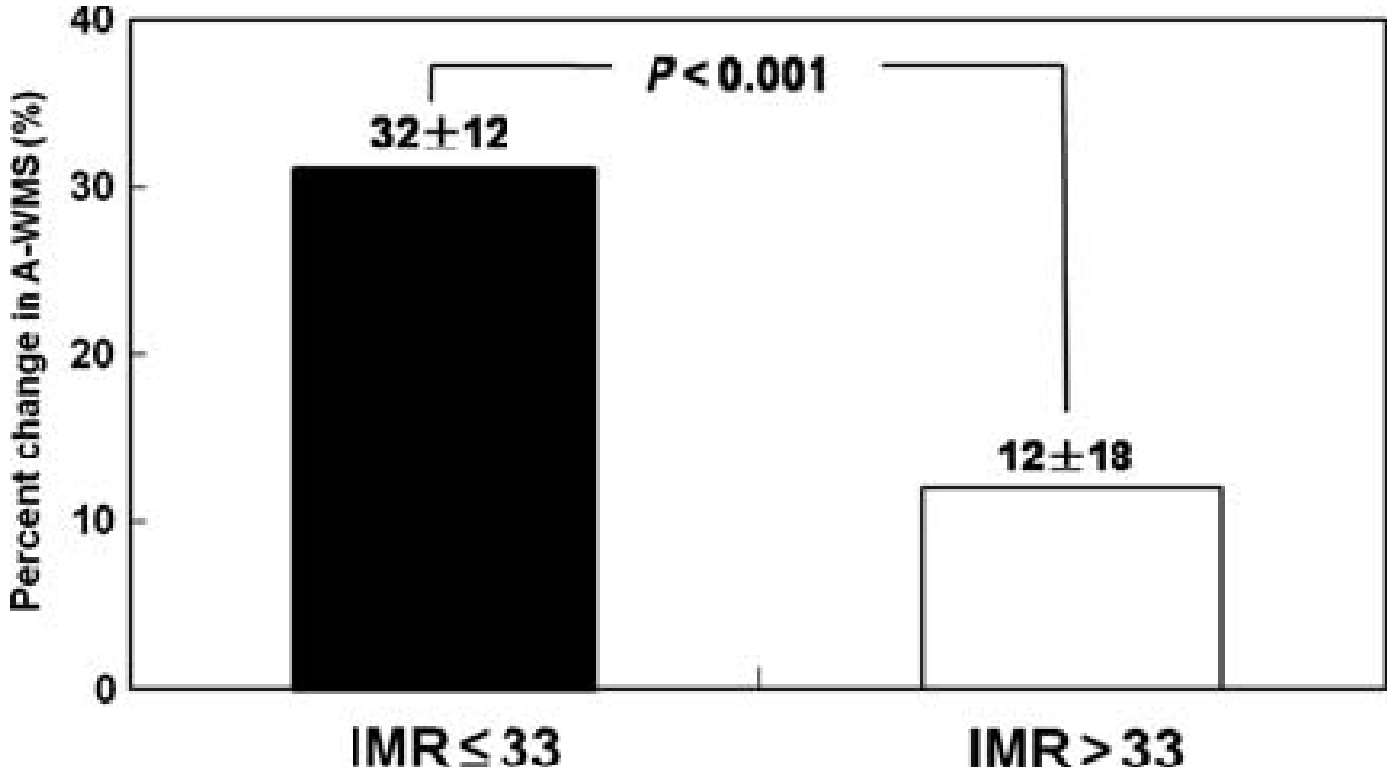
Variable	Peak CK	3-Month WMS
IMR	0.61*	0.59†
TMPG	0.05	0.12
CFR	−0.32	−0.35
ST-segment resolution	−0.35	−0.34
cTFC	−0.02	0.06

*p = 0.0005, †p = 0.002, p = NS for all others.

J Am Coll Cardiol 2008;51:560-5.

Predictive Value of IMR after PCI for STEMI

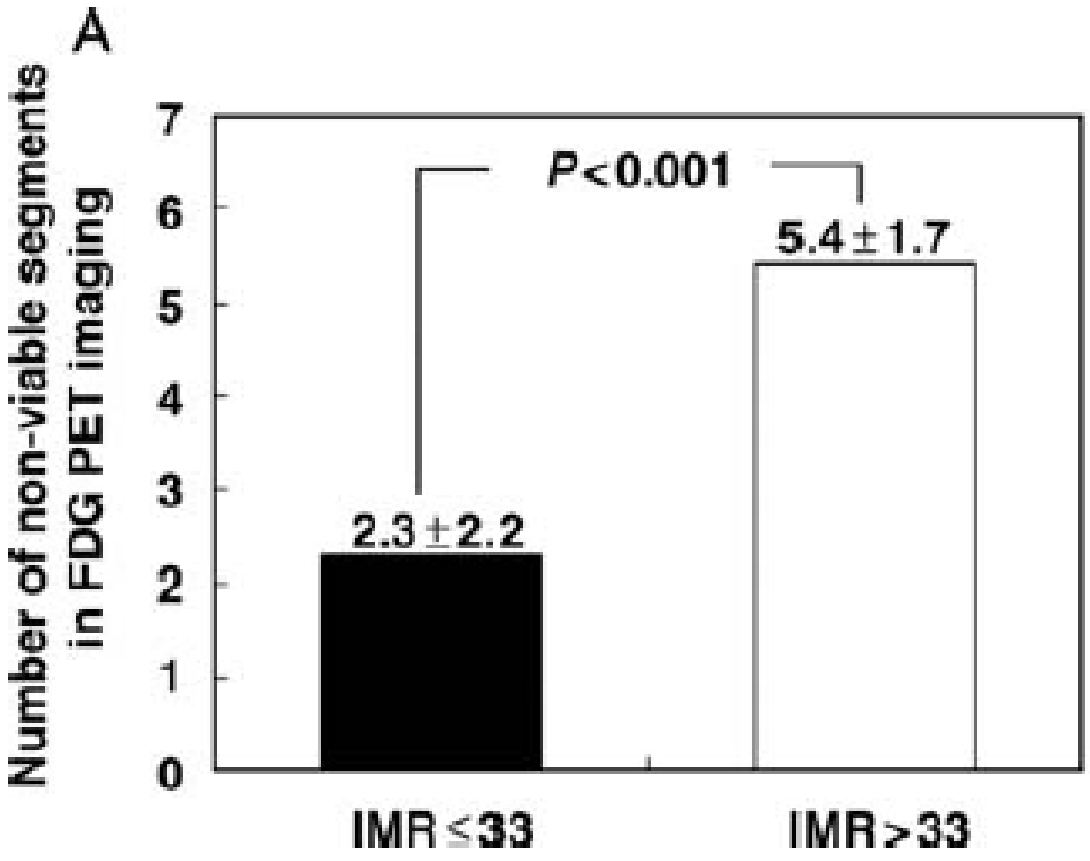
Relation between IMR and recovery of LV function in 40 STEMI patients



Lim HS, et al Eur Heart J 2009;30:2854-60.

Predictive Value of IMR after PCI for STEMI

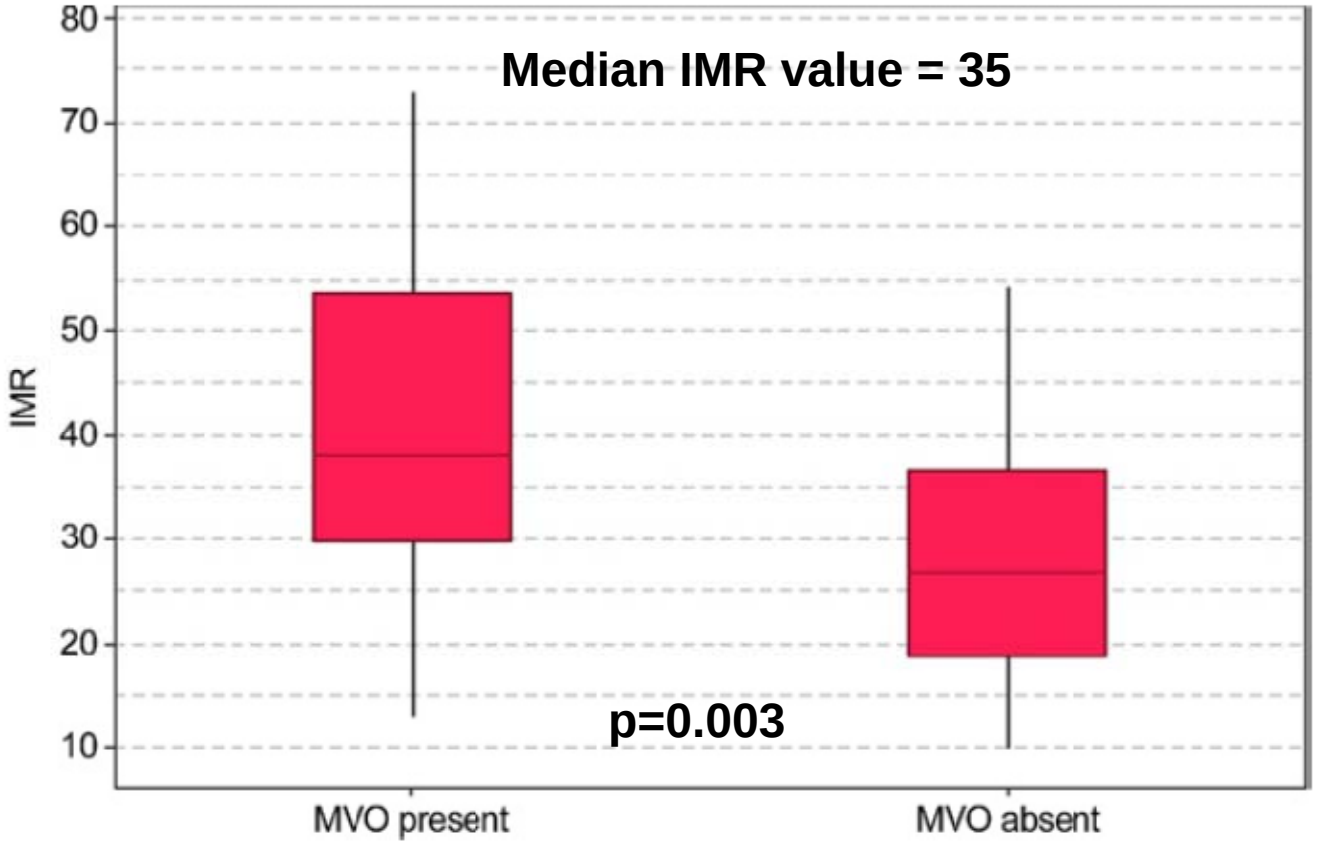
Relation between IMR and PET viability in 40 STEMI patients



Lim HS, et al Eur Heart J 2009;30:2854-60.

Predictive Value of IMR after PCI for STEMI

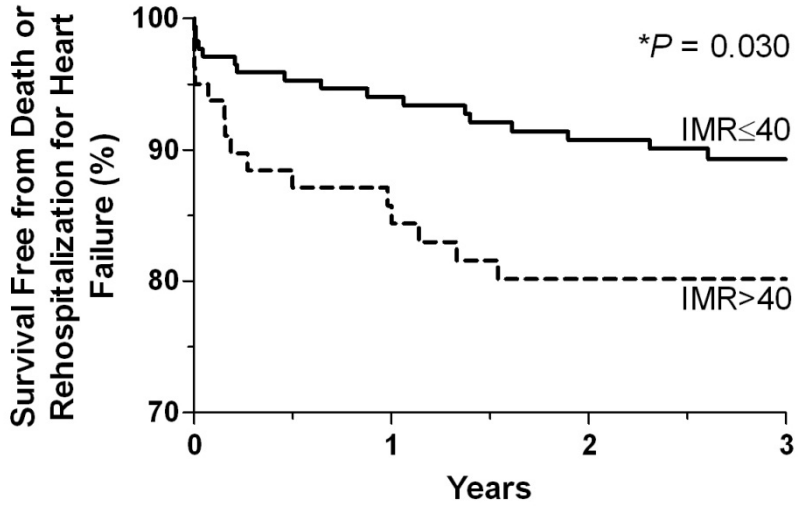
Correlation between IMR and cardiac MR assessment of microvascular obstruction in 57 patients after STEMI

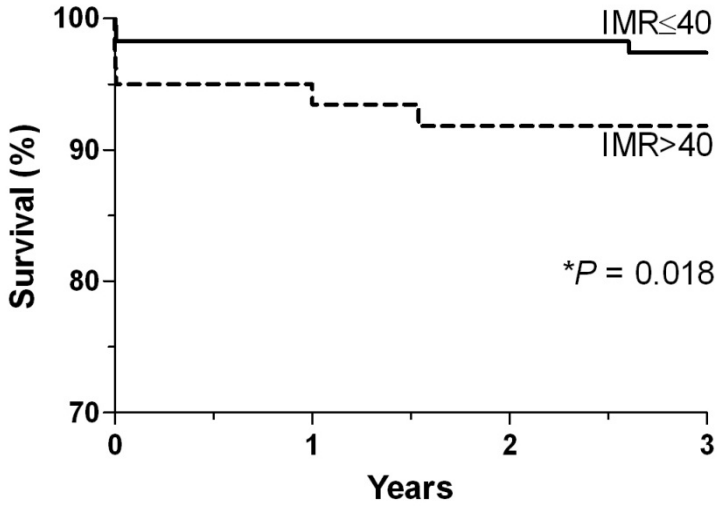


McGeoch et al. J Am Coll Cardiol Intv 2010;3:715-22.

Prospective, Longitudinal IMR post STEMI study

IMR measured at the time of STEMI in 253 patients





No. at risk:								
IMR ≤40	173	148	138	76	173	154	149	84
IMR >40	80	63	55	28	80	69	63	33

Yong, et al. ACC 2012

Prospective, Longitudinal IMR post STEMI study

Predictors of Death

A. Univariable Predictors with P <0.1	***P*-value**	**Odds ratio**	**95% Confidence interval**
IMR >40	0.028	3.95	1.16 – 13.50
FFR ≤0.8	0.09	3.16	0.84 – 11.94
TMPG	0.038	0.34	0.14 – 0.89

B. Independent Predictors in Multivariate Analysis	***P*-value**	**Odds ratio**	**95% Confidence interval**
FFR ≤0.8	0.033	4.47	1.13 – 17.65
IMR >40	0.046	3.68	1.03 – 13.22

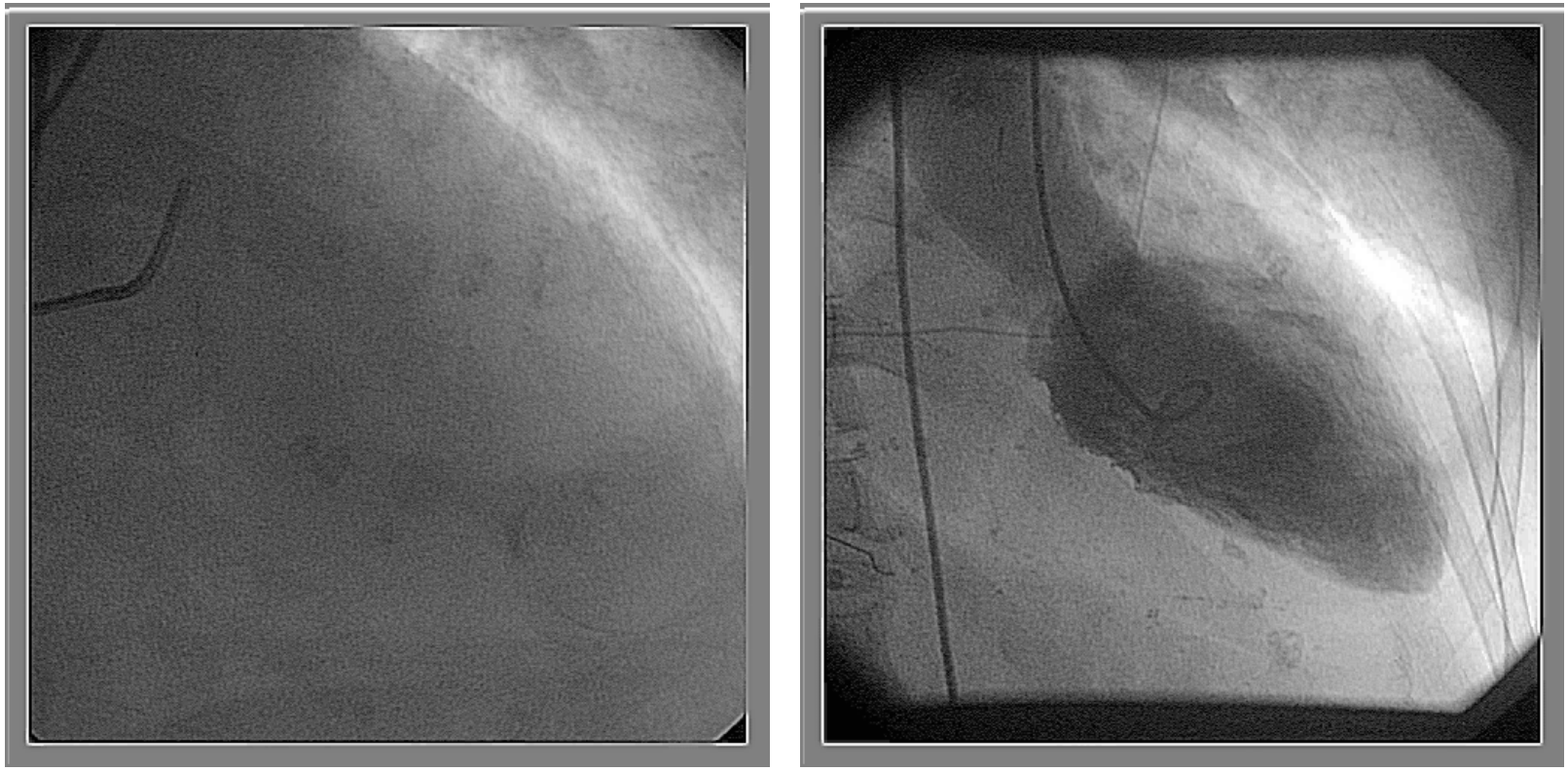
Yong, et al. ACC 2012

Why should we assess the coronary microvasculature?

- In stable patients with “normal” coronary arteries, abnormal microvascular function predicts adverse outcome.
- In stable patients undergoing PCI, abnormal microvascular resistance may predict adverse outcome.
- Immediately after STEMI, impaired microvascular function predicts adverse outcome.
- For research purposes.

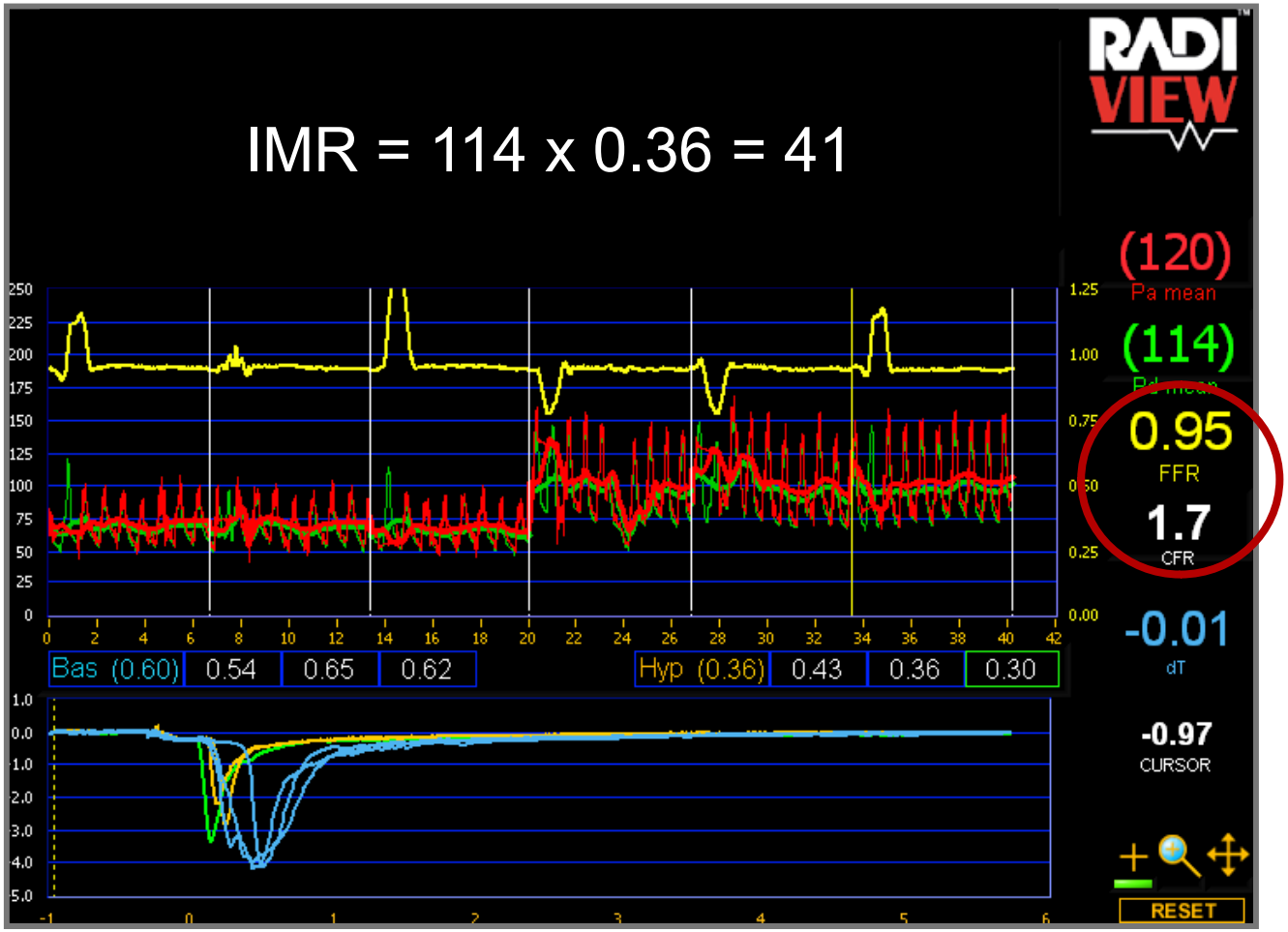
Research Applications of IMR:

Tako-Tsubo (Stress Cardiomyopathy)



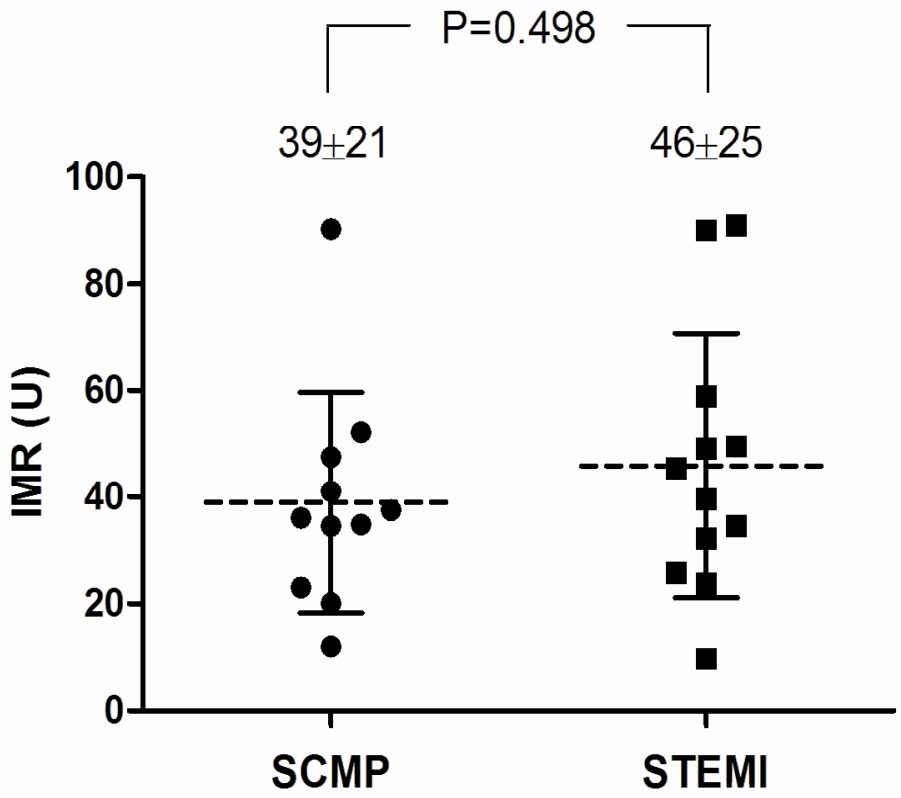
Research Applications of IMR:

Tako-Tsubo (Stress Cardiomyopathy)



Research Applications of IMR:

Tako-Tsubo (Stress Cardiomyopathy)



Kim HS, et al. J Am Coll Cardiol 2011;58:2430-1.

Limitations of IMR

- Invasive
- Interpatient and intervessel variability?
  - Sensor distance
- Independent of epicardial stenosis
  - Coronary wedge pressure

Clinical Applications of IMR

Take Home Messages:

- The microvasculature can be assessed easily and reliably by measuring IMR.
- In stable patients with “normal” coronary arteries, simultaneous assessment of FFR and IMR can guide therapy.
- IMR predicts outcomes in acute MI; emerging data suggest its utility in stable PCI patients, as well.