
Importance of the Coronary Microvasculature

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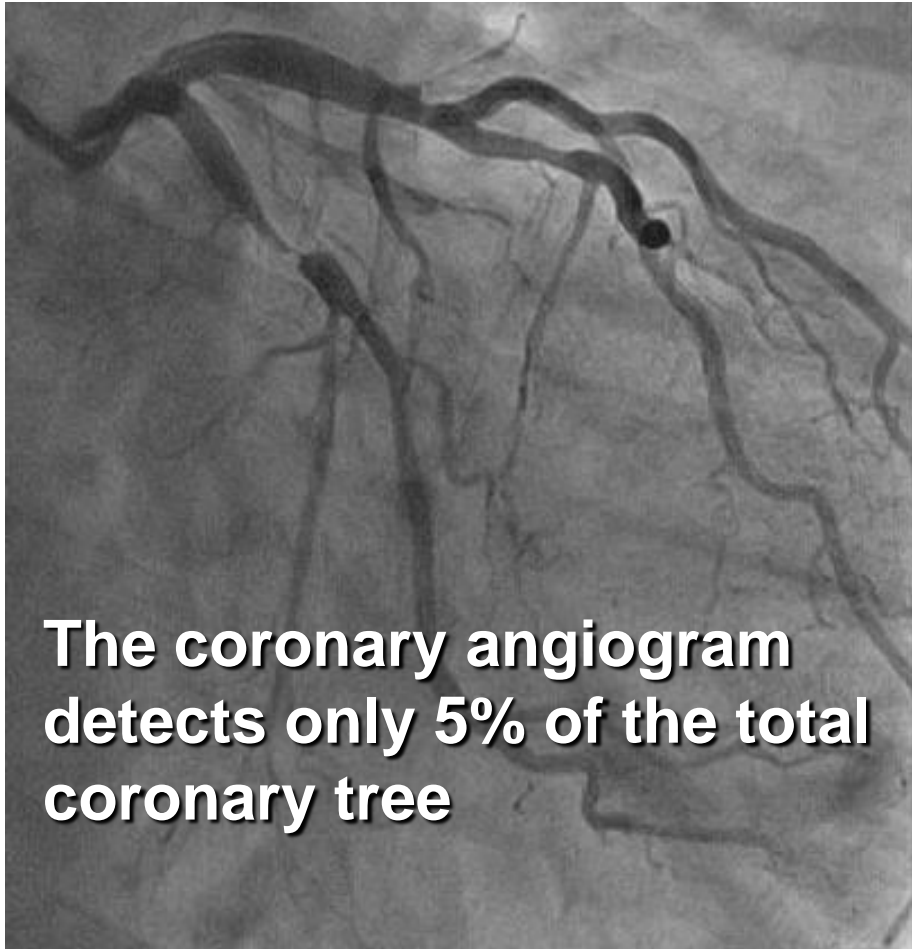
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What is the Microvasculature?

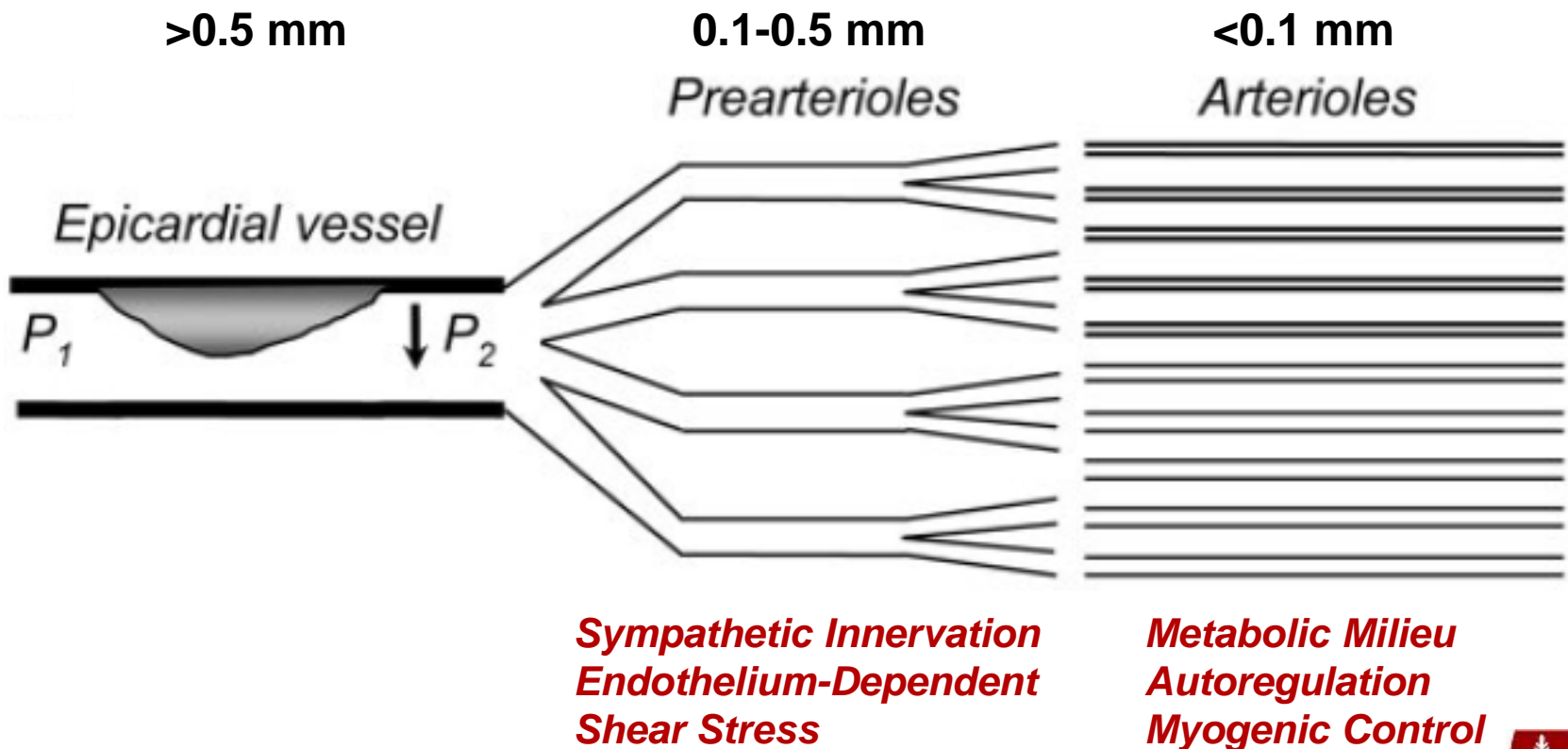


Courtesy of Bernard De Bruyne, MD, PhD



What is the Microvasculature?

Three Compartment Model



Adapted from: Lanza and Crea. Circulation 2010;121:2317-2325.



What is Microvascular Dysfunction?

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What is Microvascular Dysfunction?

- **Coronary microvascular dysfunction (CMD) is defined as abnormal coronary microvascular resistance (either arteriolar or pre-arteriolar) that is clinically evident as an inappropriate coronary blood flow response, impaired myocardial perfusion and/or myocardial ischemia that cannot be accounted for by abnormalities in the epicardial coronary arteries.**



What is Microvascular Dysfunction?

■ Pathophysiology:

□ **Structural**

- Decreased lumen size
- Decreased capillary number

□ **Functional**

- Inappropriate vasoconstrictor response
- Inadequate vasodilator response
- Resulting from an intravascular issue (e.g., endothelial dysfunction) or extravascular issue (e.g., autonomic or humoral dysfunction)



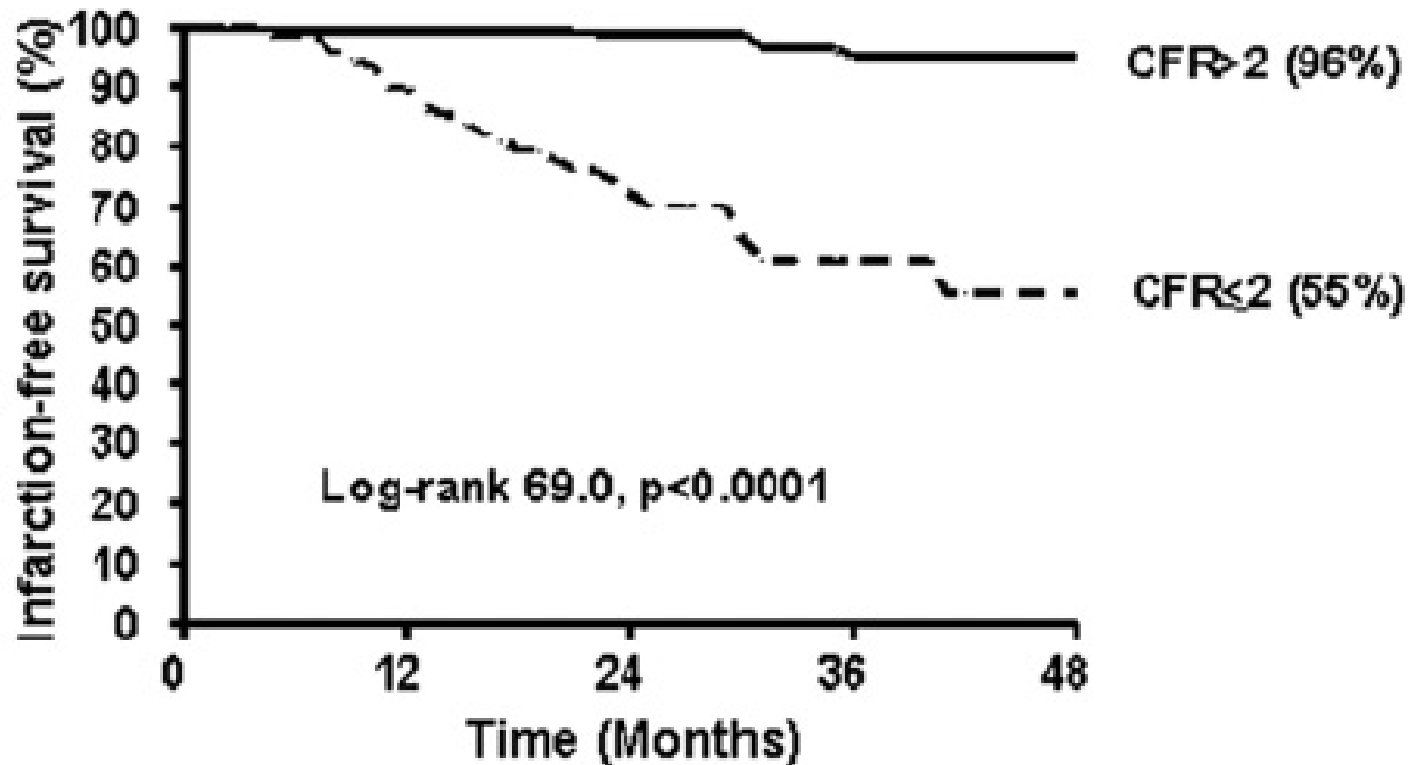
Why is Microvascular Dysfunction Important?

- Up to 30% of patients continue to have angina despite successful coronary revascularization
- ~20% of patients with chest pain are found to have no angiographic apparent CAD
- Microvascular dysfunction predicts adverse outcomes in a variety of clinical settings



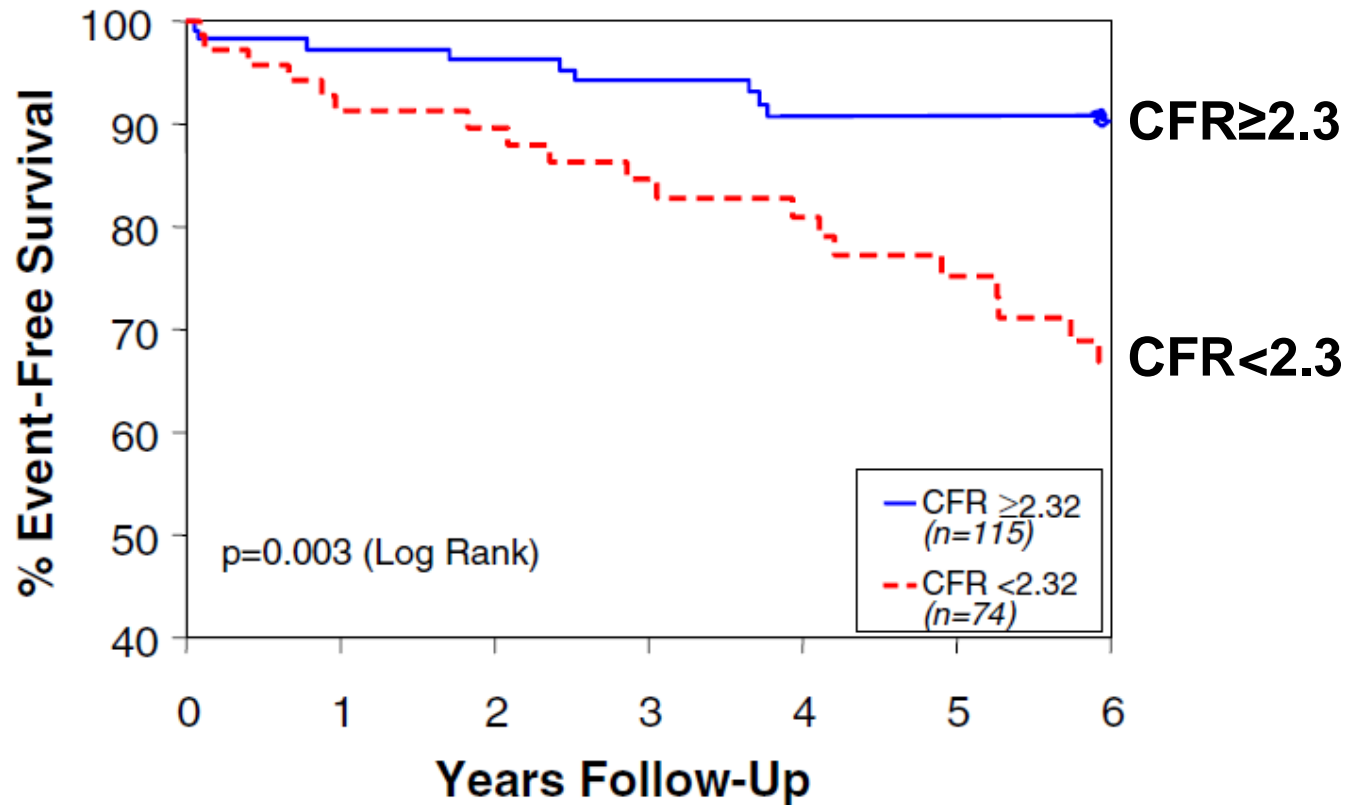
Importance of Microvascular Dysfunction

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



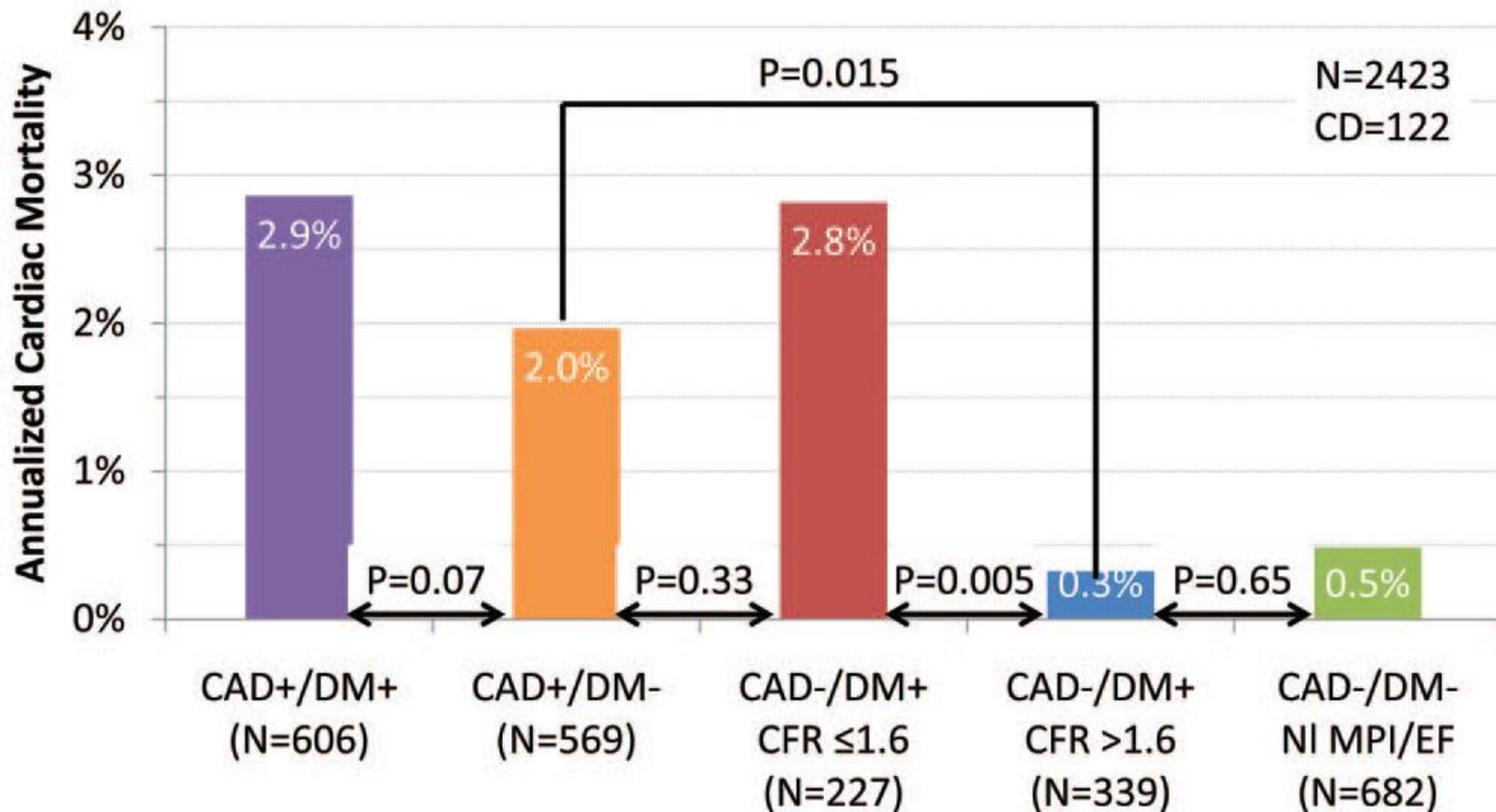
Importance of the Microcirculation

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



Importance of the Microcirculation

2,423 patients undergoing PET-derived CFR



Assessment of the Microvasculature

- Can be a challenging diagnosis
 - Heterogeneous patient population
 - Variety of pathogenetic mechanisms
 - Poor anatomic resolution
 - Potentially patchy nature of the disease
- Therefore, assessment of the microvasculature is primarily *functional* and not *anatomic*



Evaluating the Microcirculation...

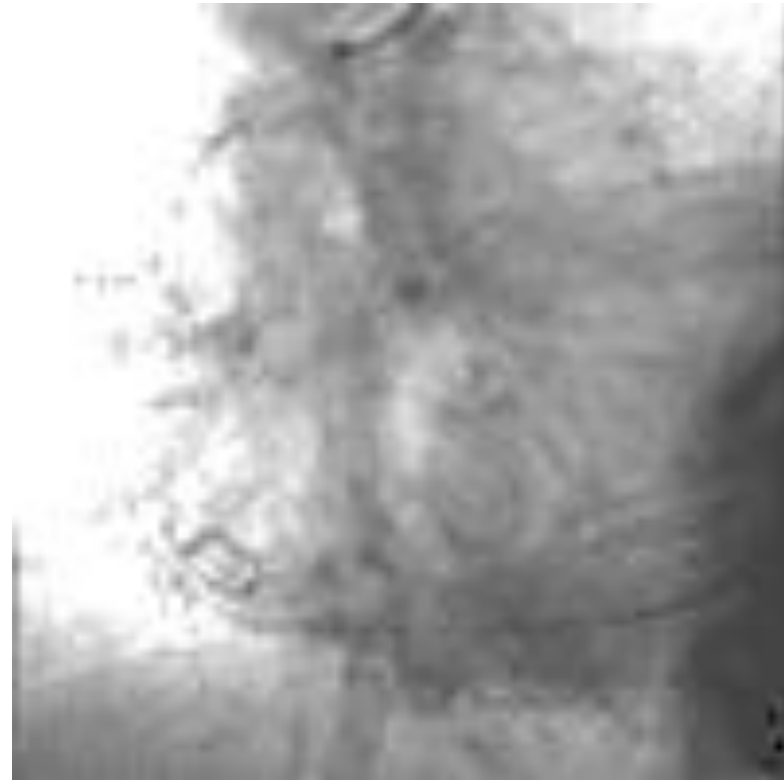
...in the Cath Lab

TIMI Myocardial Perfusion Grade:

- Easy to obtain
- Specific for microvasculature
- Predictive of outcomes in large studies

Drawbacks:

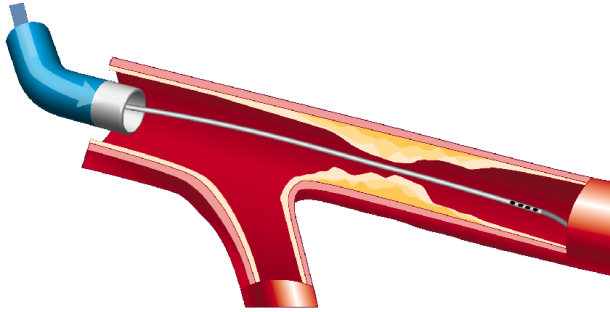
- Qualitative
- Interobserver variability
- Not as useful in smaller studies



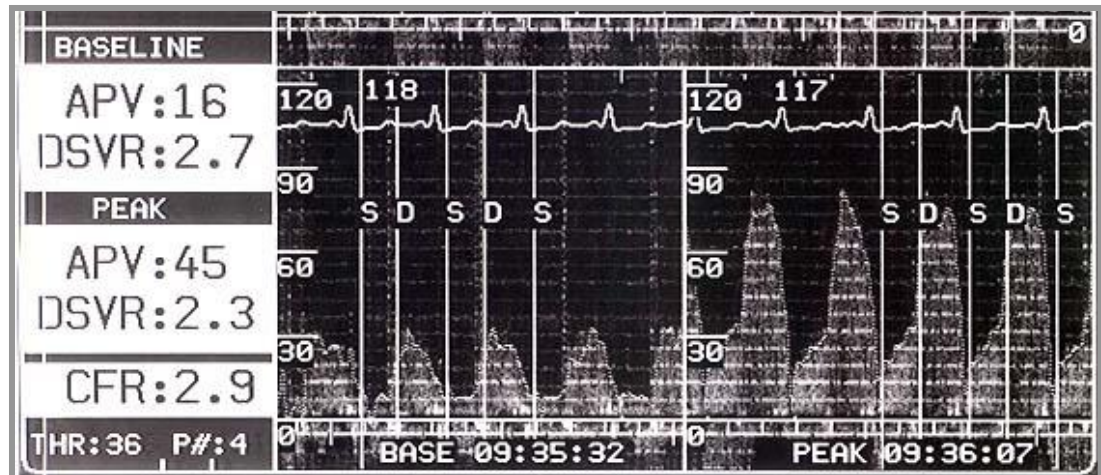
www.perfuse.org



Doppler Wire Coronary Flow Reserve

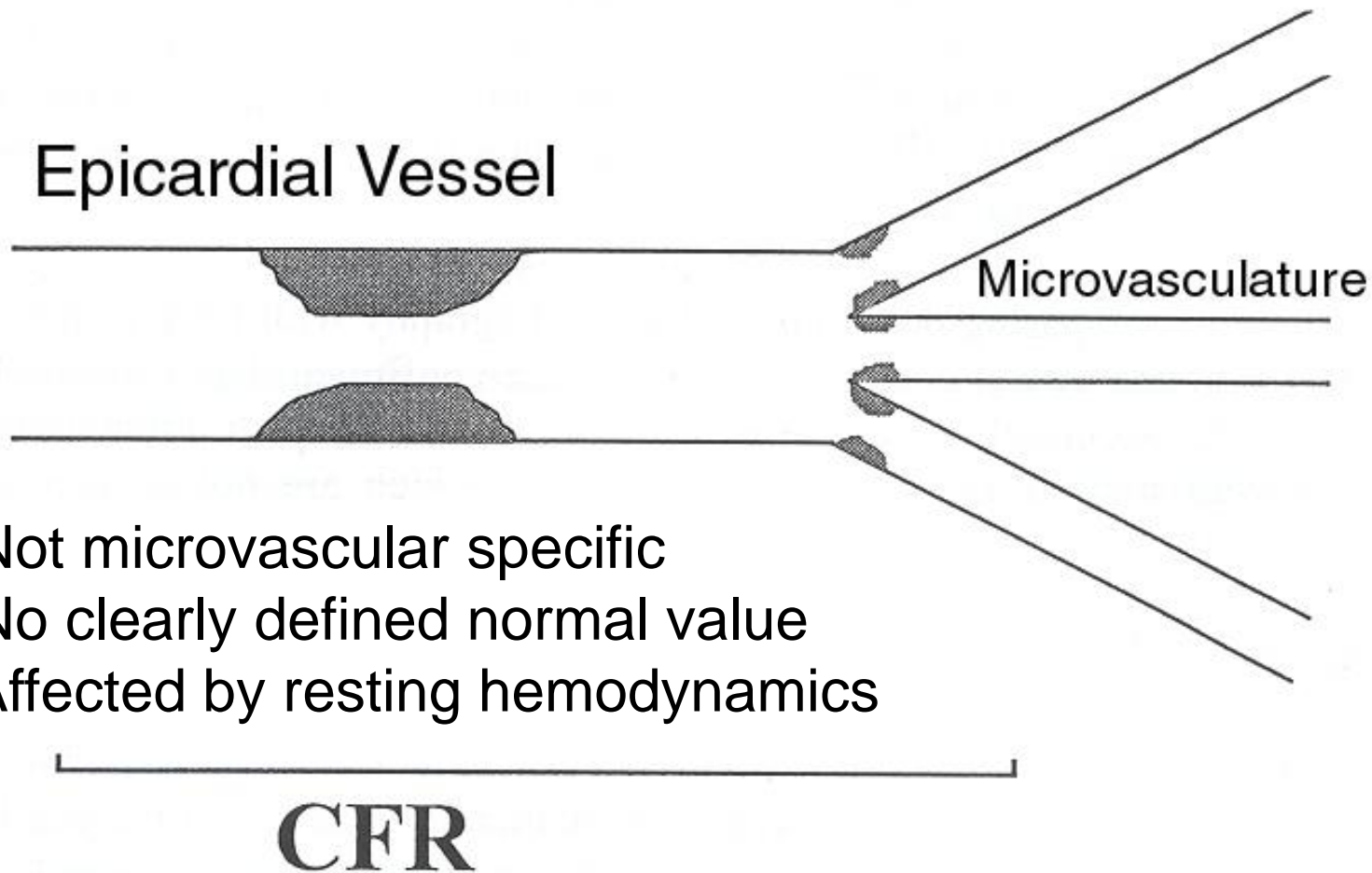


$$CFR = \frac{\text{Hyperemic Flow}}{\text{Resting Flow}}$$



Coronary Wire-Based Assessment

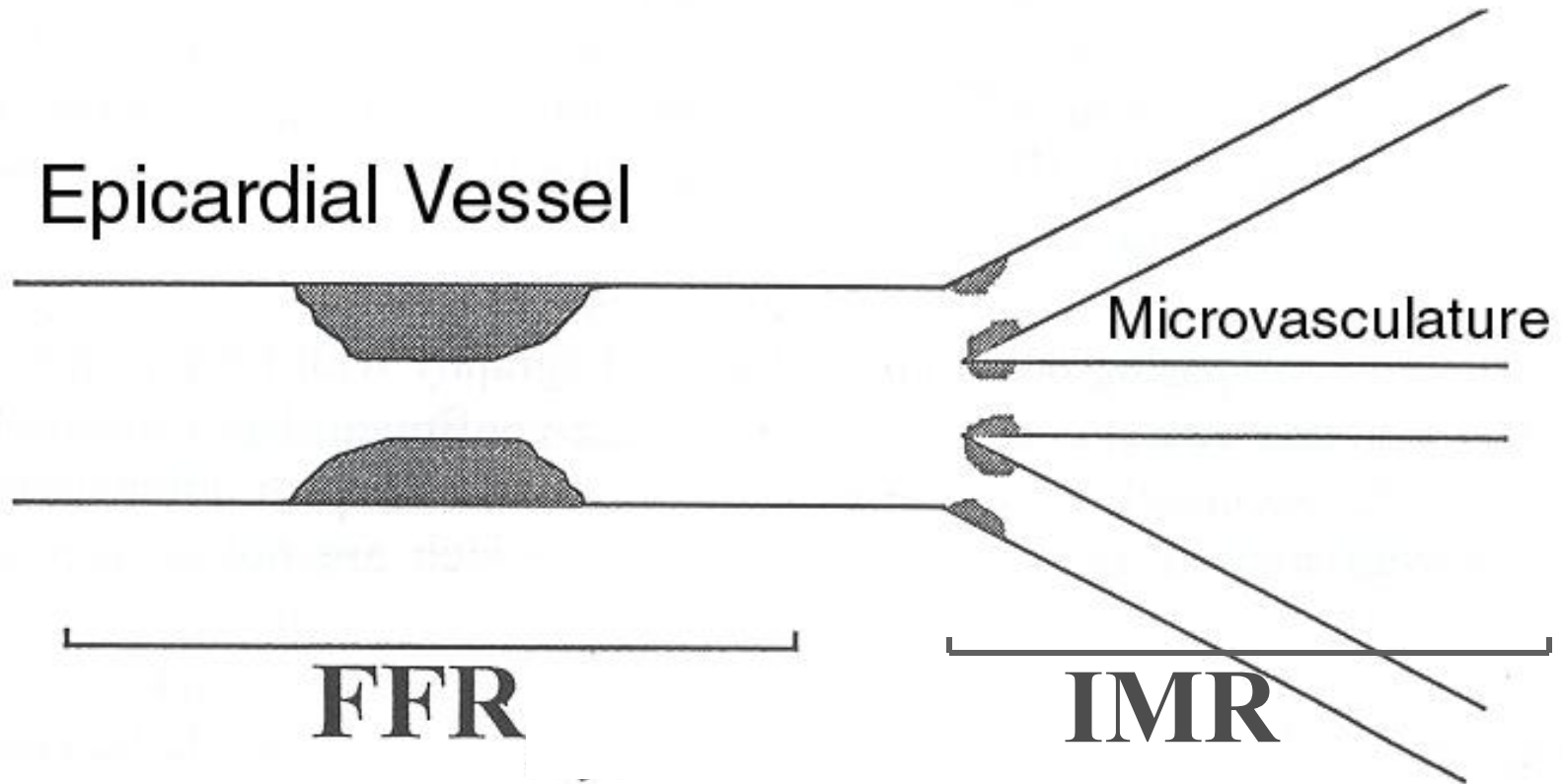
Coronary Flow Reserve



- Not microvascular specific
- No clearly defined normal value
- Affected by resting hemodynamics



Index of Microcirculatory Resistance



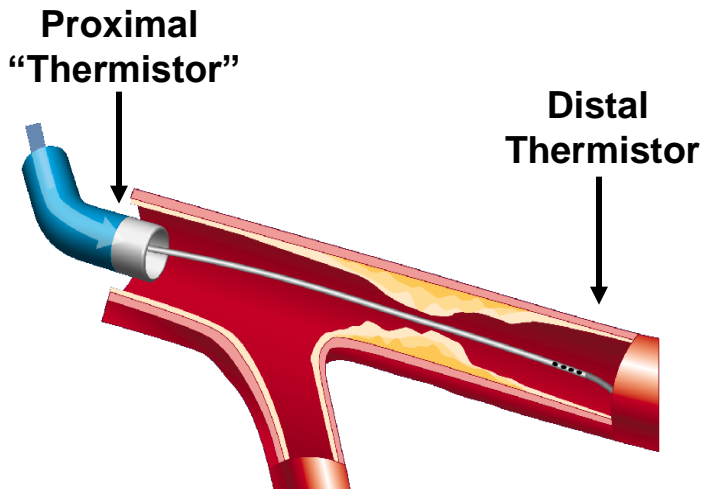
Index of Microcirculatory Resistance

Potential Advantages:

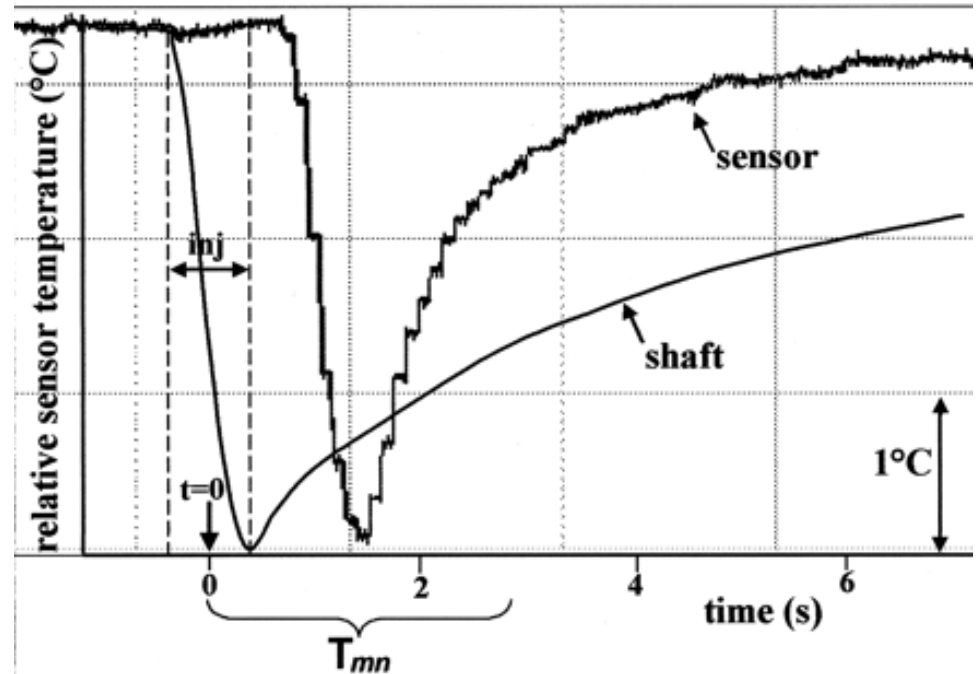
- ❑ Readily available in the cath lab
- ❑ Specific for the microvasculature
- ❑ Quantitative and reproducible
- ❑ Predictive of outcomes



Estimation of Coronary Flow



Calculation of mean transit time



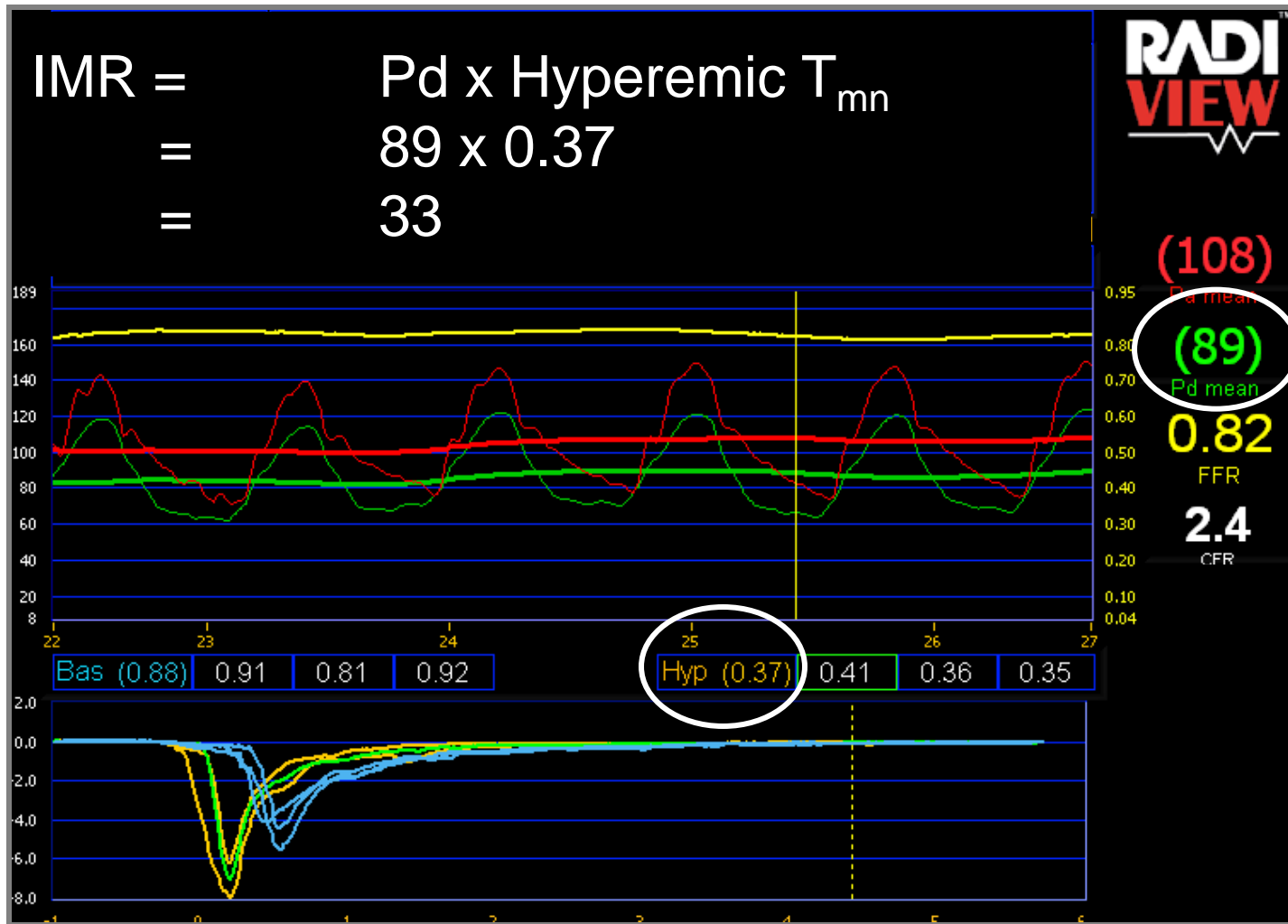
Derivation of IMR:

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

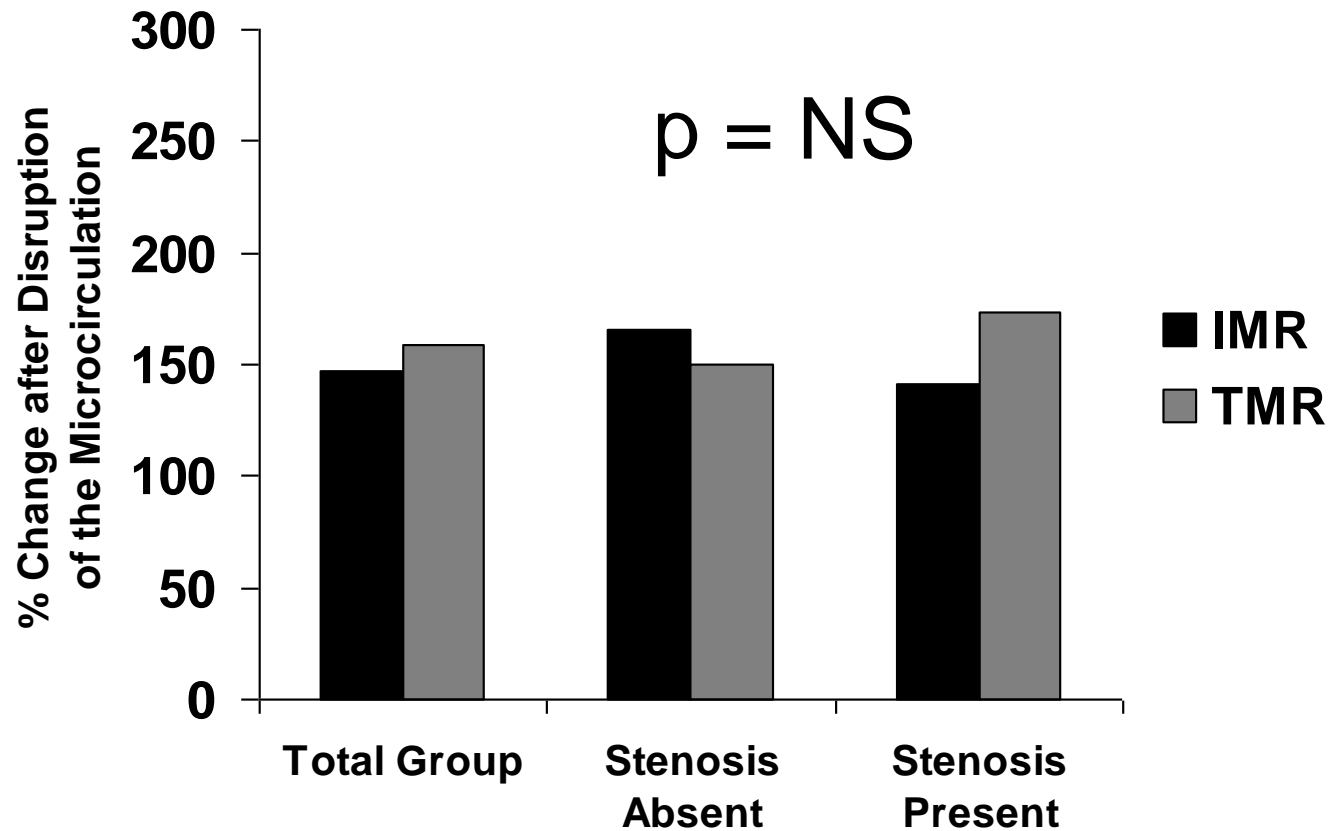
*at maximal
hyperemia...*



Practical Measurement of IMR



Animal Validation of IMR



Reproducibility of IMR

Effect of Pacing on FFR/CFR/IMR

	Baseline	RV Pacing at 110 bpm
CFR	3.1 ± 1.1	$2.3 \pm 1.2^\dagger$
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	$1.7 \pm 0.6^\dagger$
IMR, U	22.2 ± 6.0	23.6 ± 8.2
FFR	0.88 ± 0.06	0.87 ± 0.06



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 primary PCI for STEMI, impaired microvascular function predicts adverse outcome.



Chest Pain and “Normal Coronaries”

- 139 patients referred for coronary angiography because of symptoms and/or abnormal stress test and found to have “normal” appearing coronaries
- FFR, IMR, CFR, IVUS and acetylcholine challenge were performed down the LAD



Chest Pain and “Normal Coronaries”

Patient Characteristic	n=139
Age (years)	54 ± 11
Female	77%
Hypertension	53%
Diabetes	23%
Dyslipidemia	63%
Tobacco Use	8%
Typical Angina	32%
Positive Stress Test	42%



Chest Pain and “Normal Coronaries”

- 21% had an IMR ≥ 25
 - 5% had an FFR ≤ 0.80
 - 44% had epicardial endothelial dysfunction
 - 43% had a myocardial bridge
-
- **42% had nonischemic FFR, normal IMR, no significant endothelial dysfunction**



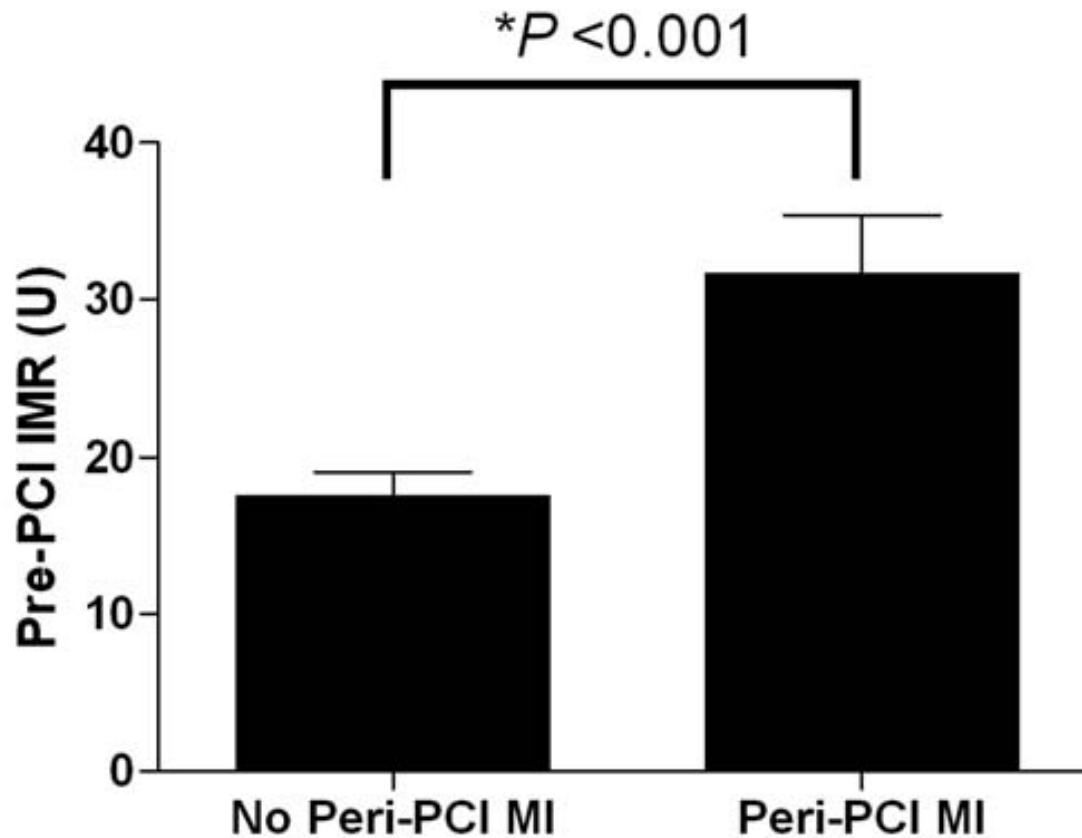
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IMR Before PCI in Stable Patients

IMR measured before LAD PCI in 50 stable patients



IMR *Before* PCI in Stable Patients

IMR measured before LAD PCI in 50 stable patients

Multivariable Regression Analysis

Variable	<i>P</i>	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



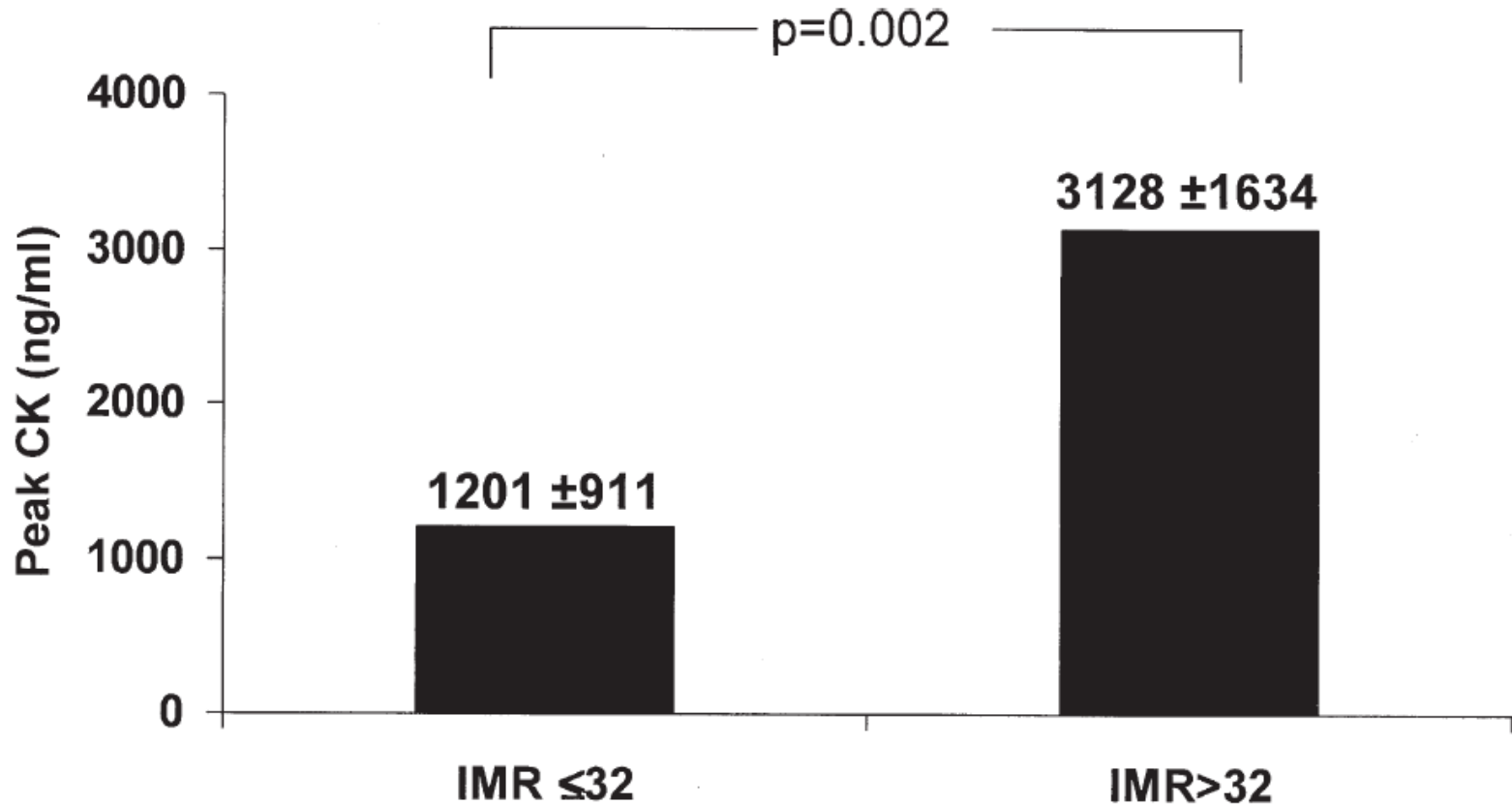
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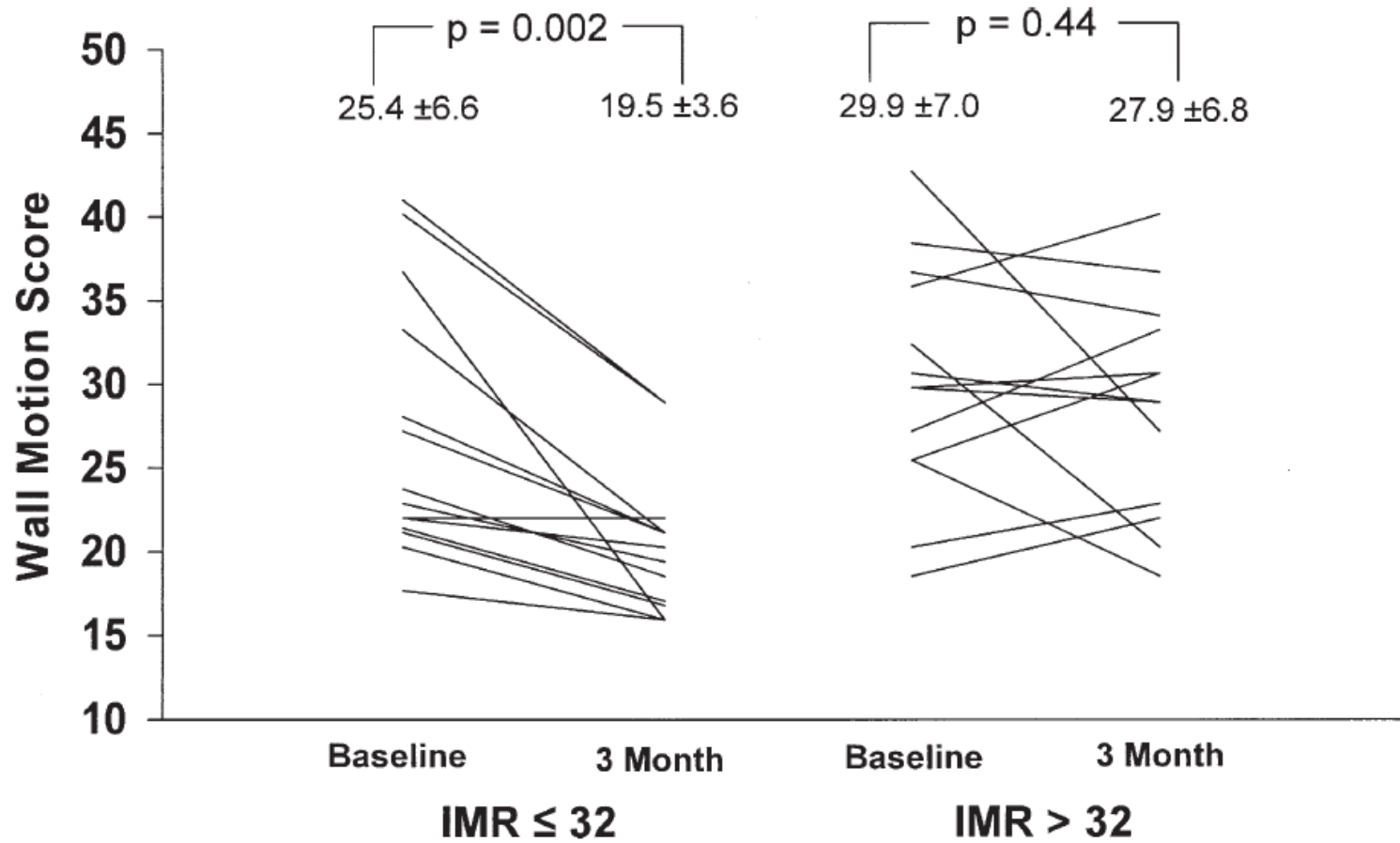
Predictive Value of IMR after PCI for STEMI

IMR predicts peak CK in patients with STEMI



Predictive Value of IMR after PCI for STEMI

IMR predicts which patients will have improved LV function after STEMI



Predictive Value of IMR after PCI for STEMI

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

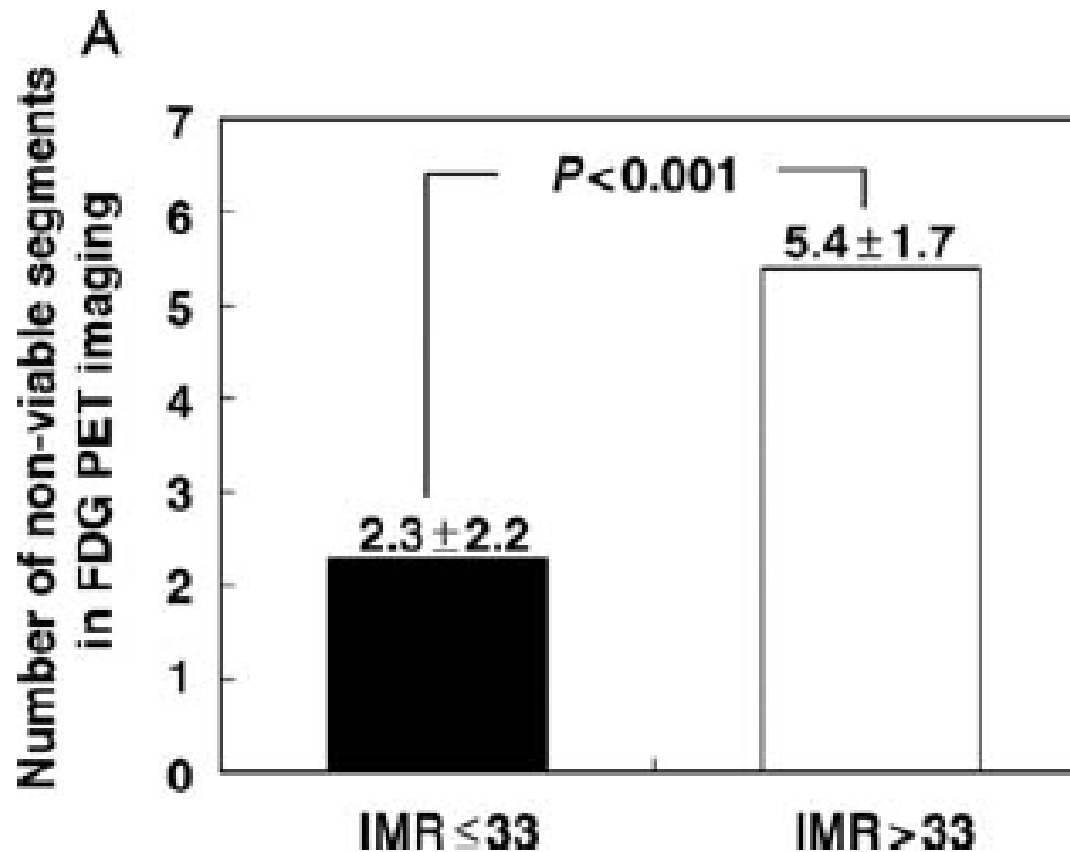
Variable	Peak CK	3-Month WMS
IMR	0.61*	0.59†
TMPG	0.05	0.12
CFR	−0.32	−0.35
ST-segment resolution	−0.35	−0.34
cTFC	−0.02	0.06

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



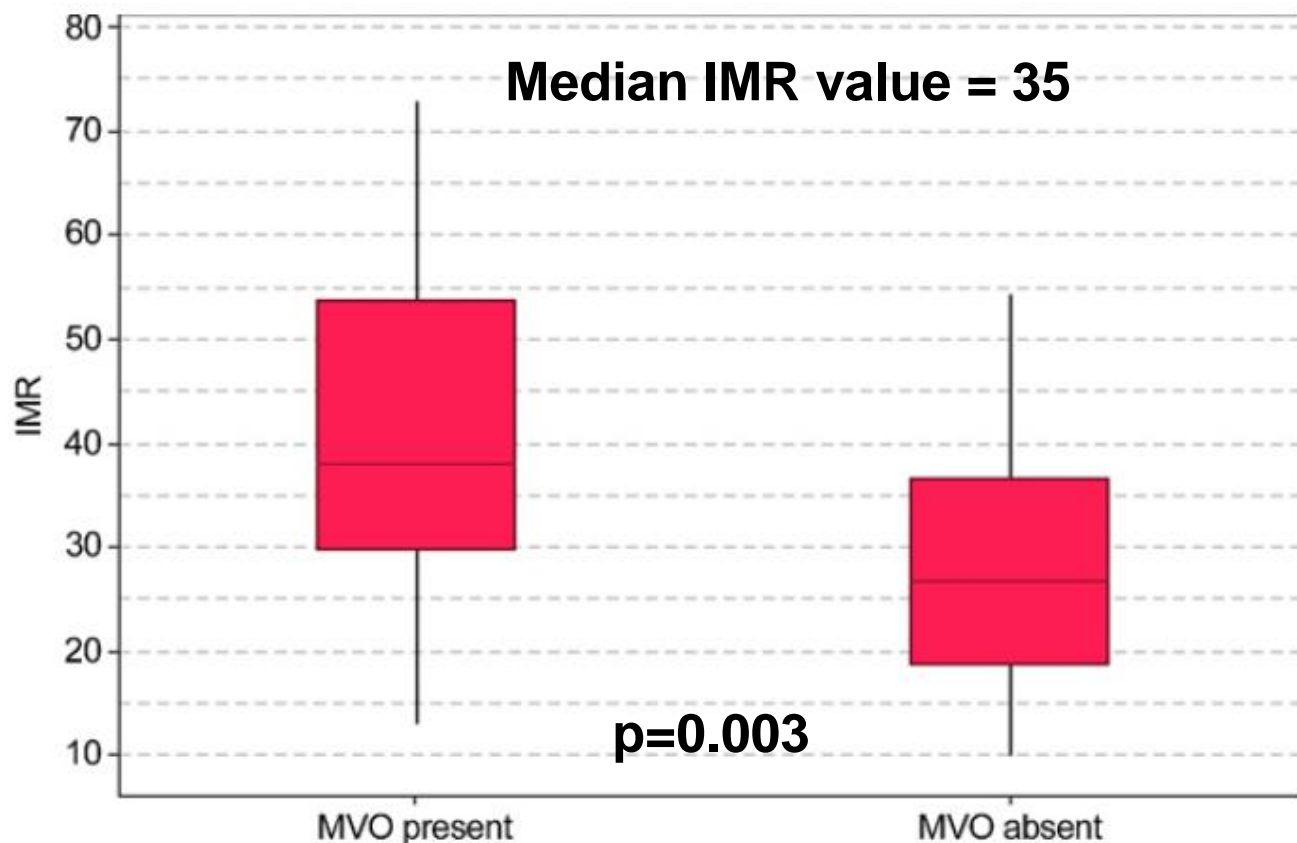
Predictive Value of IMR after PCI for STEMI

Relation between IMR and PET viability in 40 STEMI patients



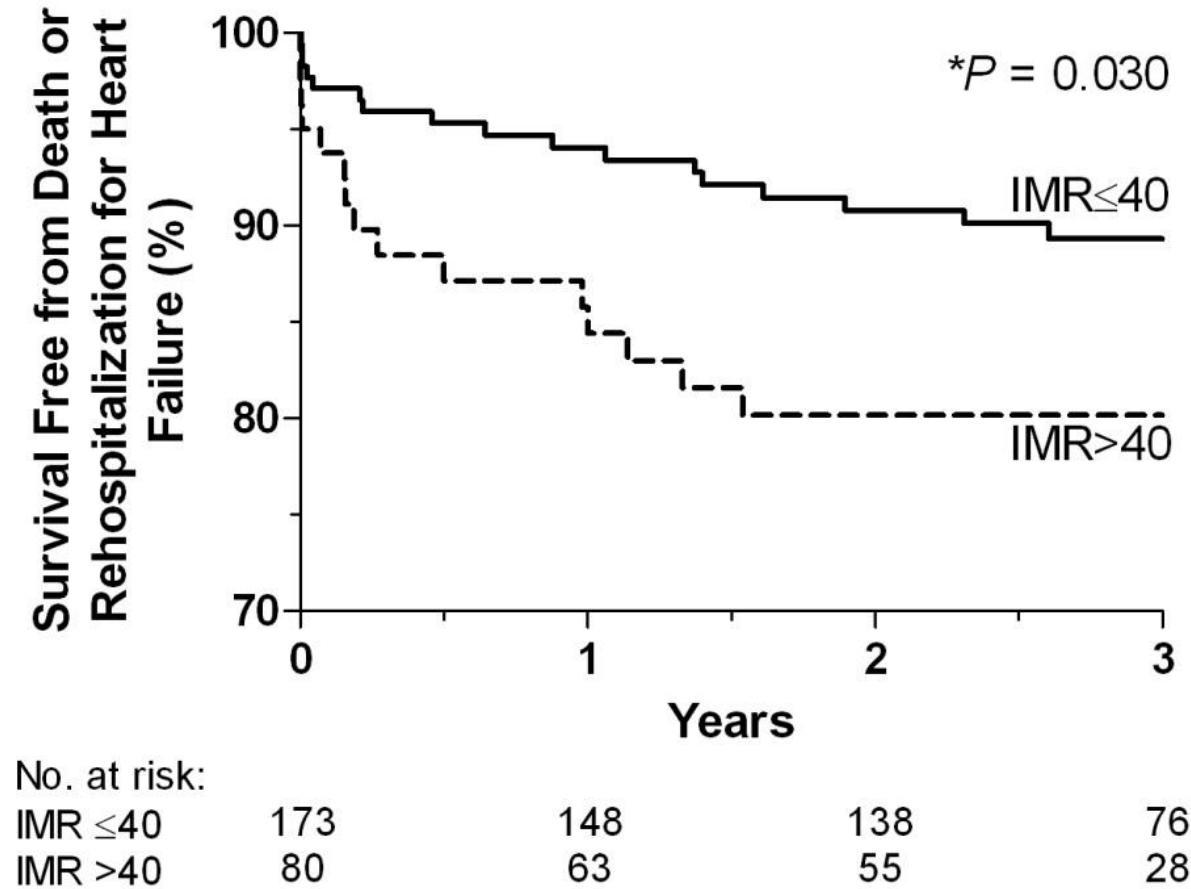
Predictive Value of IMR after PCI for STEMI

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



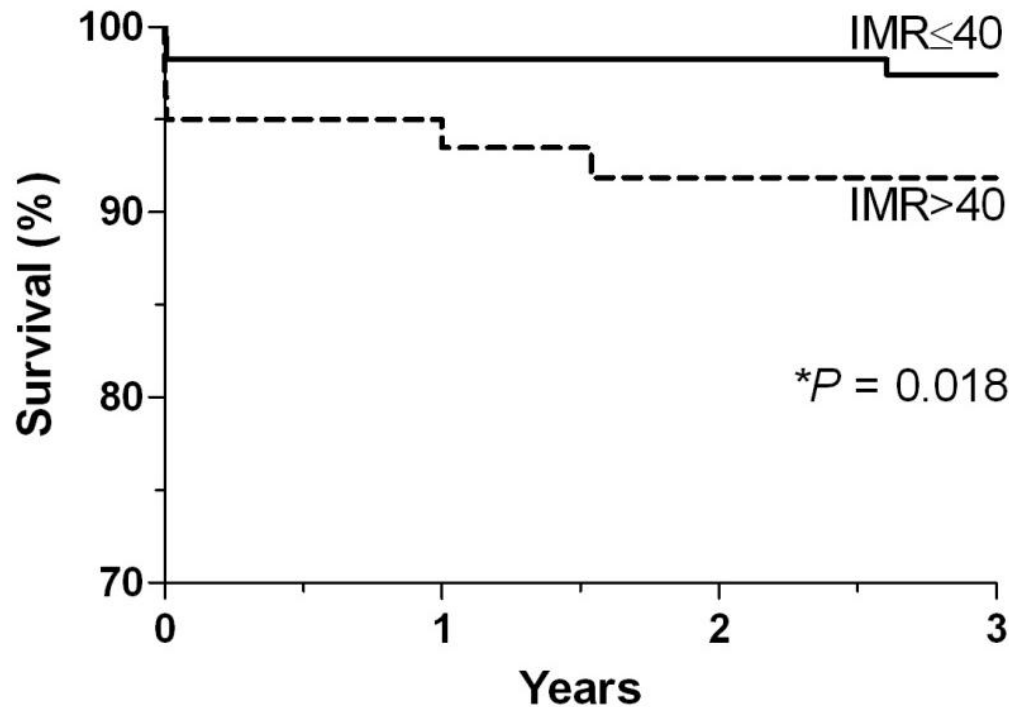
IMR and Outcomes post STEMI

Multicenter study evaluating relationship between IMR and longer-term outcomes in 253 STEMI patients



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Multicenter study evaluating relationship between IMR and longer-term outcomes in 253 STEMI patients



No. at risk:

IMR ≤ 40	173	154	149	84
IMR > 40	80	69	63	33



IMR and Outcomes post STEMI

Multicenter study evaluating relationship between IMR and longer-term outcomes in 253 STEMI patients

Physiologic and clinical predictors of death

	<i>P</i> Value	Hazard Ratio	95% CI
Univariable predictors			
IMR >40	0.028	3.95	1.16–13.50
FFR ≤ .8	0.09	3.16	0.84–11.94
TIMI myocardial perfusion grade <3	0.084	2.96	0.87–10.14
Multivariable predictors			
IMR >40	0.020	4.34	1.26–15.00



Conclusions:

- The coronary microvasculature is an oft-ignored entity.
- The etiology of coronary microvascular dysfunction is complex and multifactorial.
- Microvascular dysfunction is associated with worse outcomes.
- The invasive assessment of microvascular function will likely play an increasingly important role in patient evaluation.

