Invasive Assessment of the Microcirculation: *Routine Practice and Future Options*

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest /arrangement or affiliation with the organization(s) listed below

Affiliation/Financial Relationship	Company
Grant/ Research Support:	**St. Jude Medical** **Medtronic** **Acist Medical** **CathWorks**
Consulting Fees/Honoraria:	**HeartFlow**
Major Stock Shareholder/Equity Interest:	
Royalty Income:	
Ownership/Founder:	
Salary:	
Intellectual Property Rights:	
Other Financial Benefit:	

Why is Microvascular Dysfunction Important?

- Up to 30% of patients continue to have angina despite successful coronary revascularization

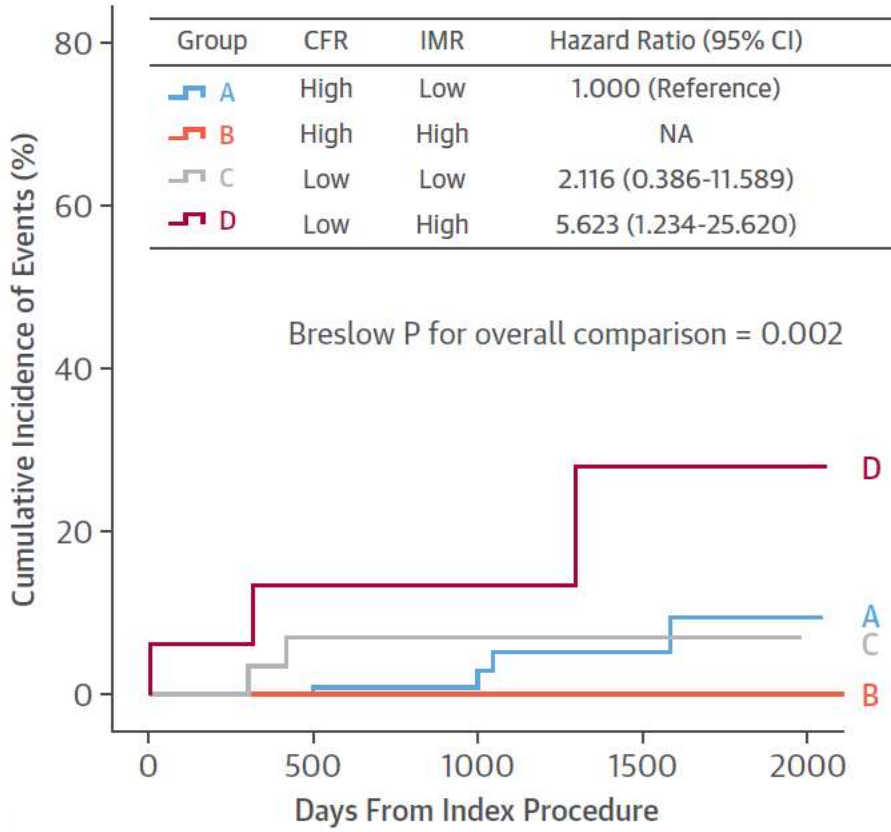
- ~20% of patients with chest pain are found to have no angiographic apparent CAD

- Microvascular dysfunction predicts adverse outcomes in a variety of clinical settings

Importance of the Microcirculation

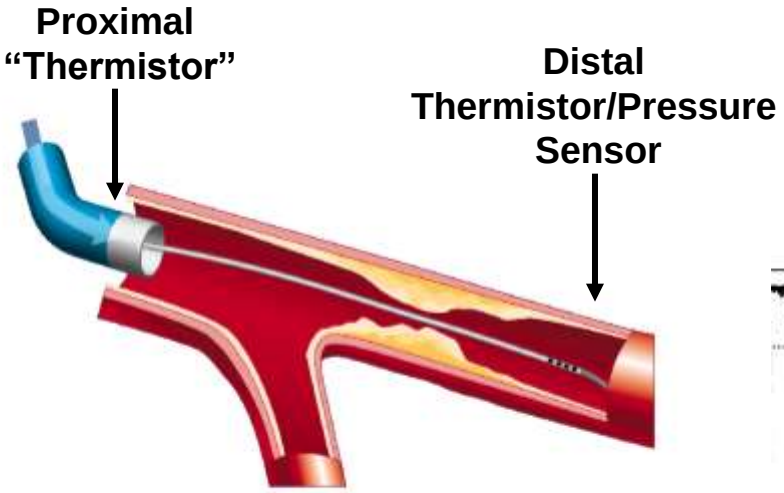
In 313 patients with FFR>0.80, those with low CFR and high IMR (microvascular dysfunction) had significantly higher rate of death, MI, or revascularization.

Group	CFR	IMR	Hazard Ratio (95% CI)	P value
A	High	Low	1.000 (Reference)	NA
B	High	High	NA	NA
C	Low	Low	2.116 (0.386-11.589)	0.388
D	Low	High	5.623 (1.234-25.620)	0.026

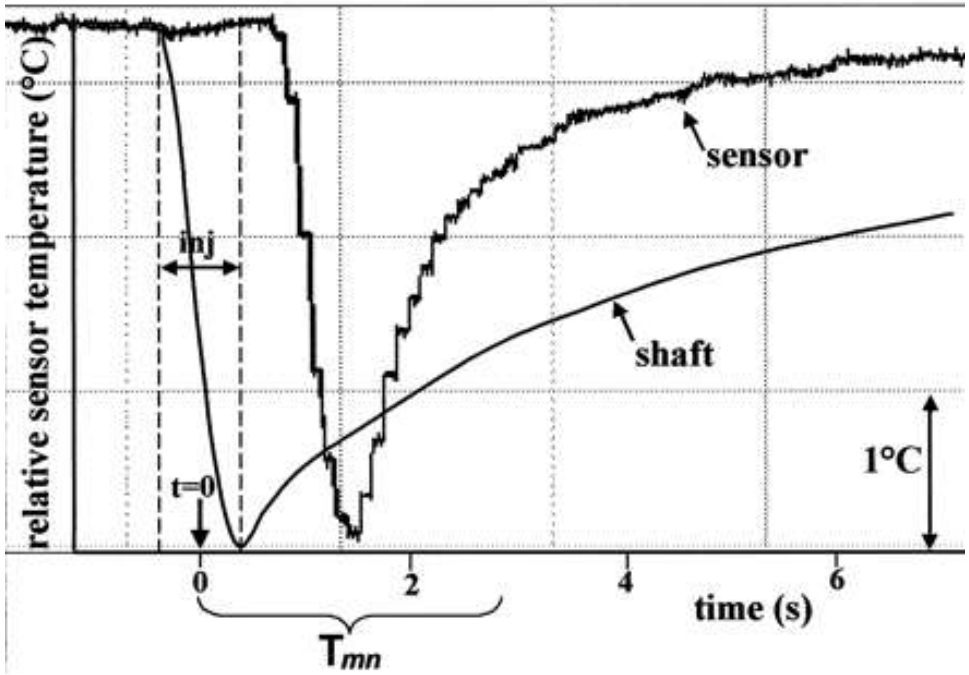


Lee JM, et al. J Am Coll Cardiol 2016;67:1158-69.

Estimation of Coronary Flow



Calculation of mean transit time



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

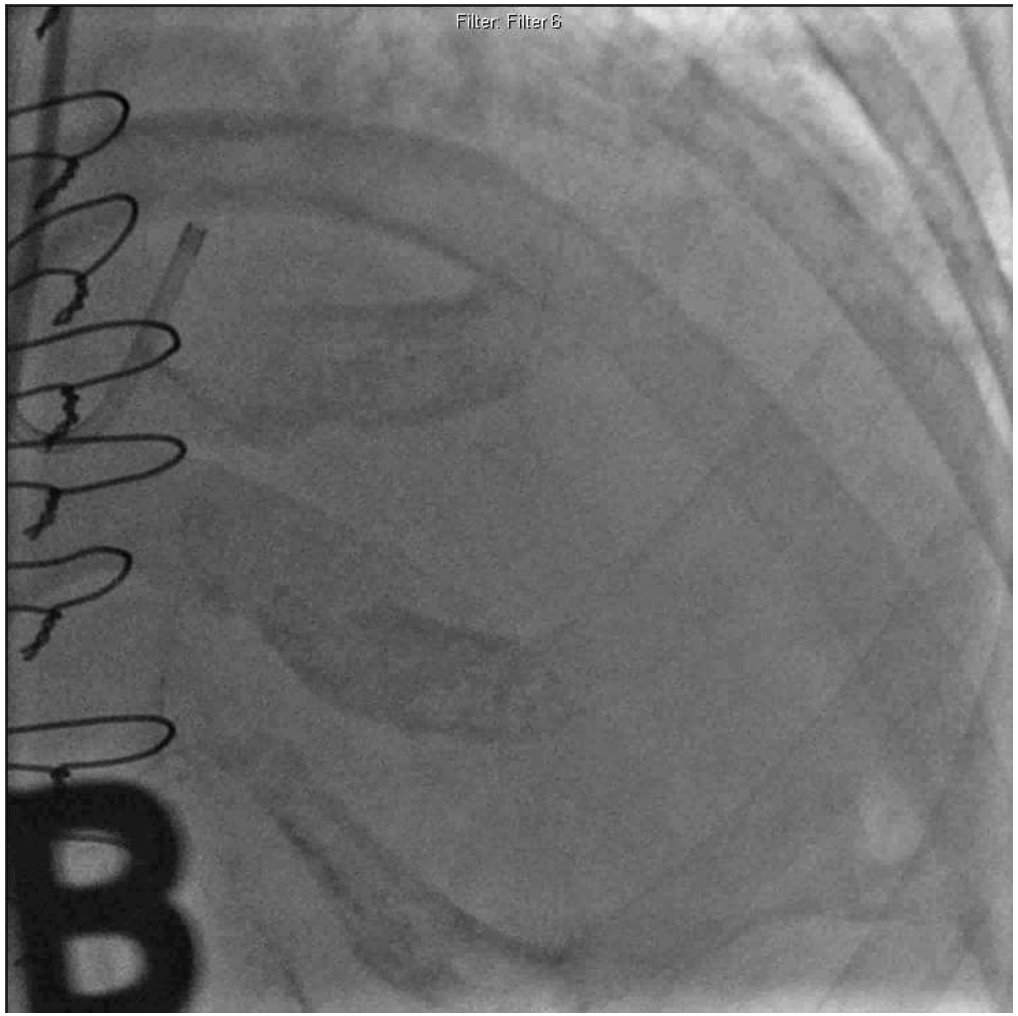
Index of Microcirculatory Resistance:

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

Circulation 2003;107:3129-3132.

IMR Case Example

Cardiac transplant recipient enrolled in study evaluating ACE inhibition



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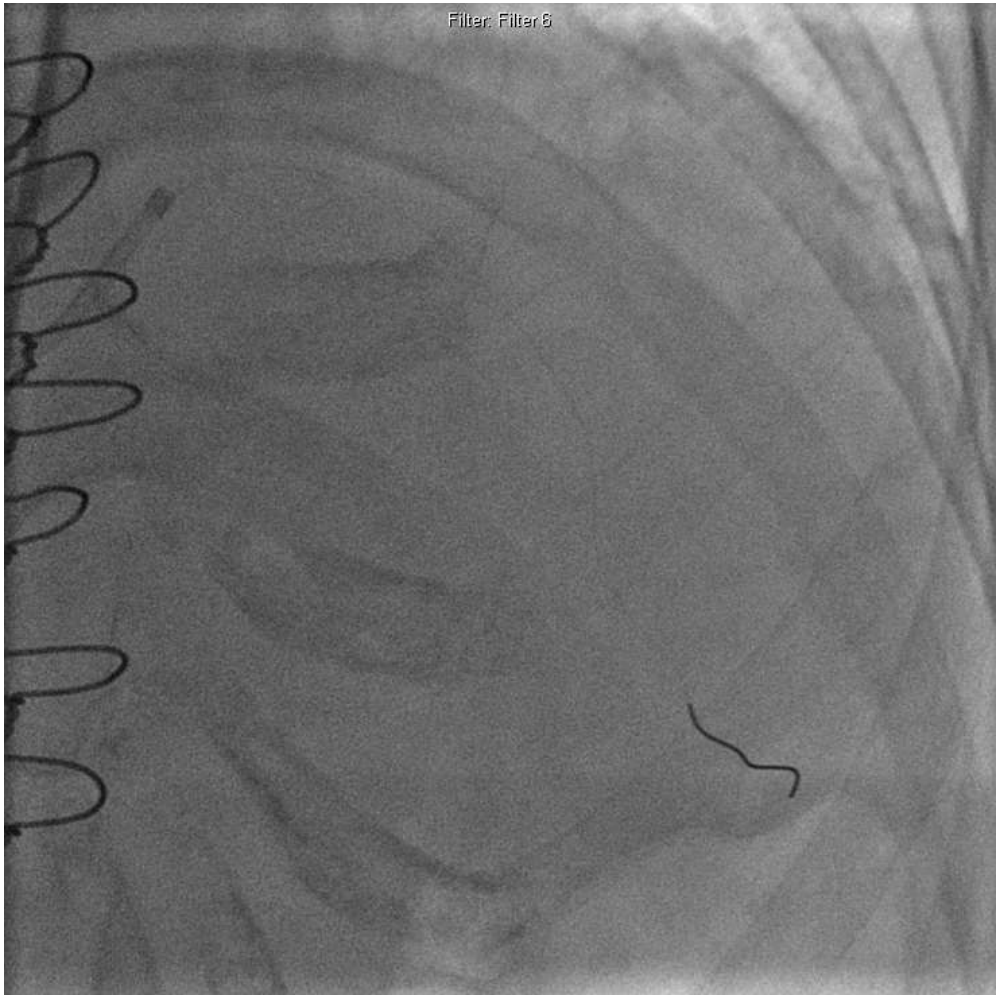


Flushing the System

Hyperemic T_{mn} Measurements

Practical Measurement of IMR

IMR: *Normal Value*

An IMR < 25 is considered normal

- The mean IMR measured in 15 subjects (22 arteries) without any evidence of atherosclerosis and no/minimal risk factors was 19±5.

- The mean IMR measured in 18 subjects with normal stress tests and normal coronary angiography was 18.9±5.6.

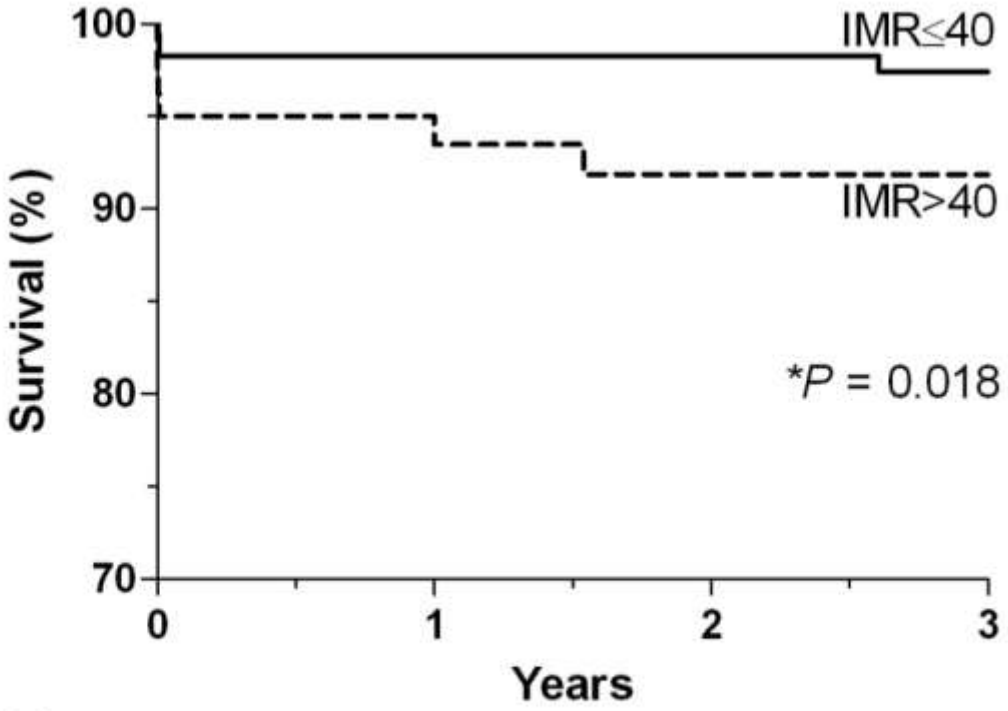
- The mean IMR in 20 subjects with no CAD or risk factors was 14.0 with all values <23.

Melikian, et al. Eurointervention 2010;5:939-945.
Luo, et al. Circ Cardiovasc Interv 2014;7:43-48.
Solberg, et al. Eurointervention 2014;9:1069-75.

When should we be thinking about microvascular dysfunction?

IMR and Outcomes post STEMI

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



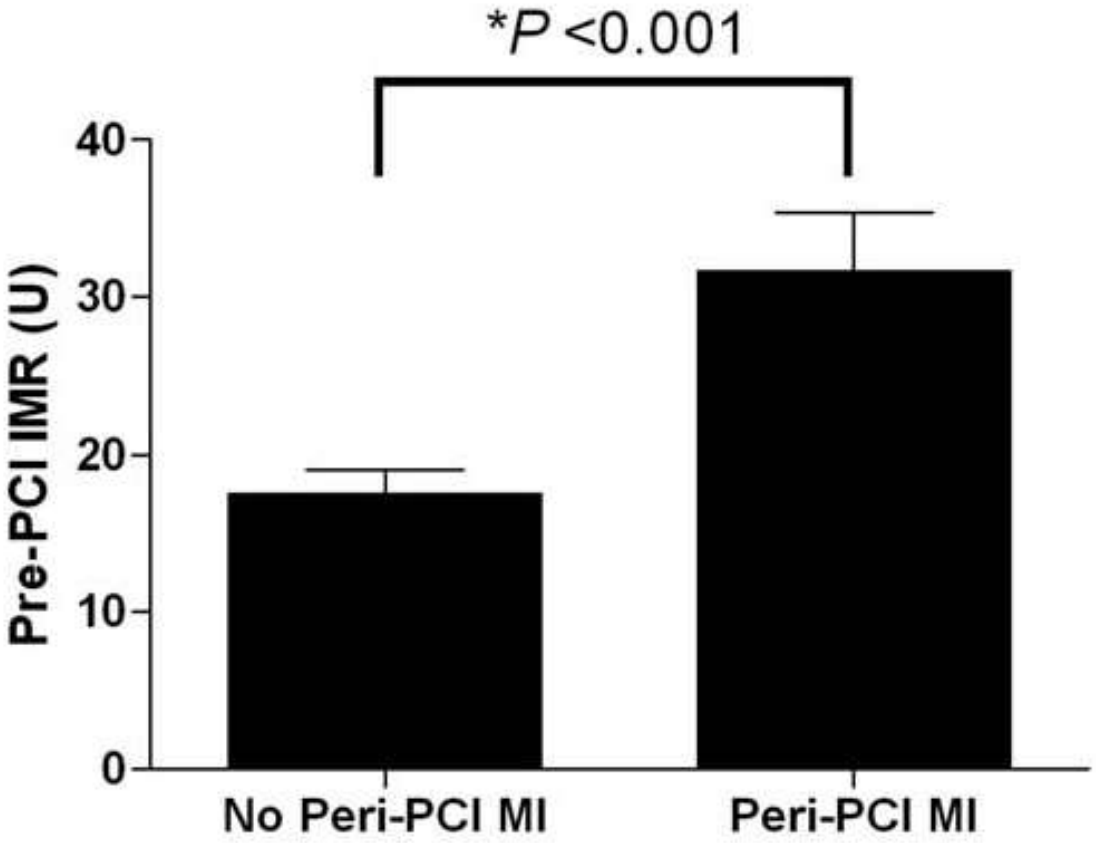
No. at risk:				
IMR ≤40	173	154	149	84
IMR >40	80	69	63	33

IMR was an independent predictor of long-term mortality, while CFR, TMPG, and cTFC were not.

Circulation 2013;127:2436-41.

IMR *Before* PCI in Stable Patients

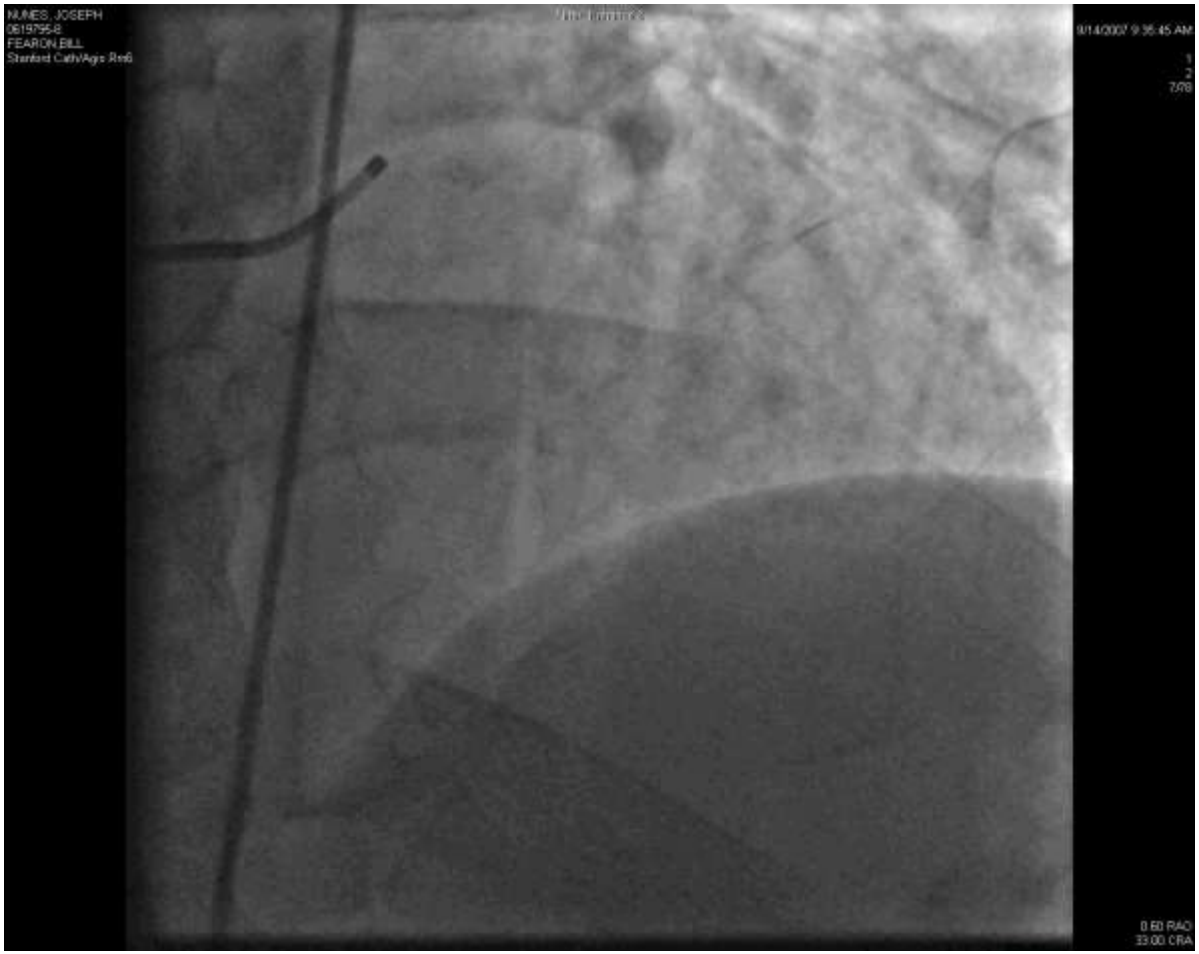
IMR measured before PCI in 50 stable patients undergoing LAD PCI

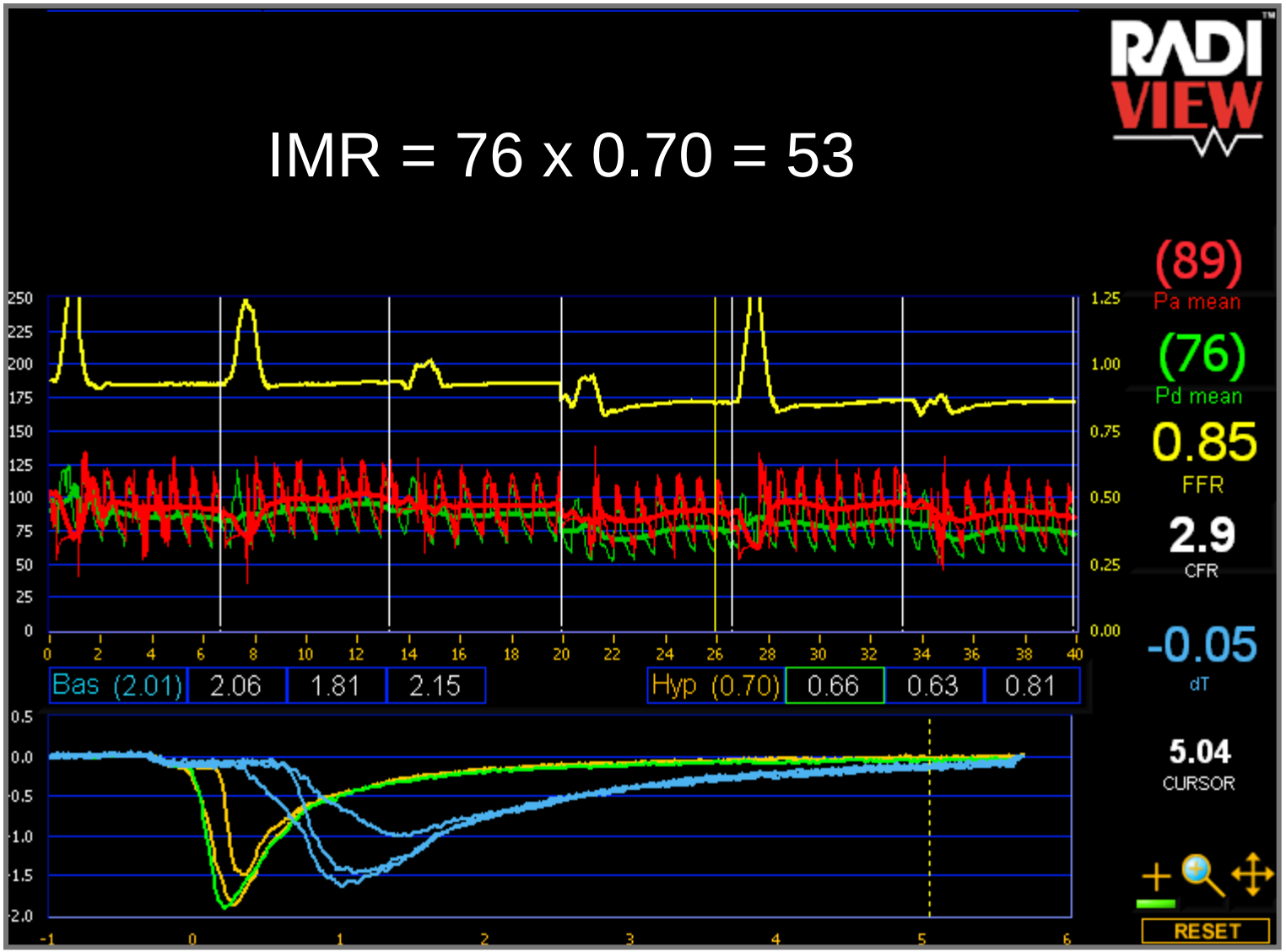


Ng, et al. Circ Cardiovasc Interv 2012;5:515-22.

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
RADI VIEW
(89)
Pa mean
(76)
Pd mean
0.85
FFR
2.9
CFR
-0.05
dT
5.04
CURSOR
RESET
Bas (2.01) 2.06 1.81 2.15
Hyp (0.70) 0.66 0.63 0.81

Chest Pain and “Normal Coronaries”

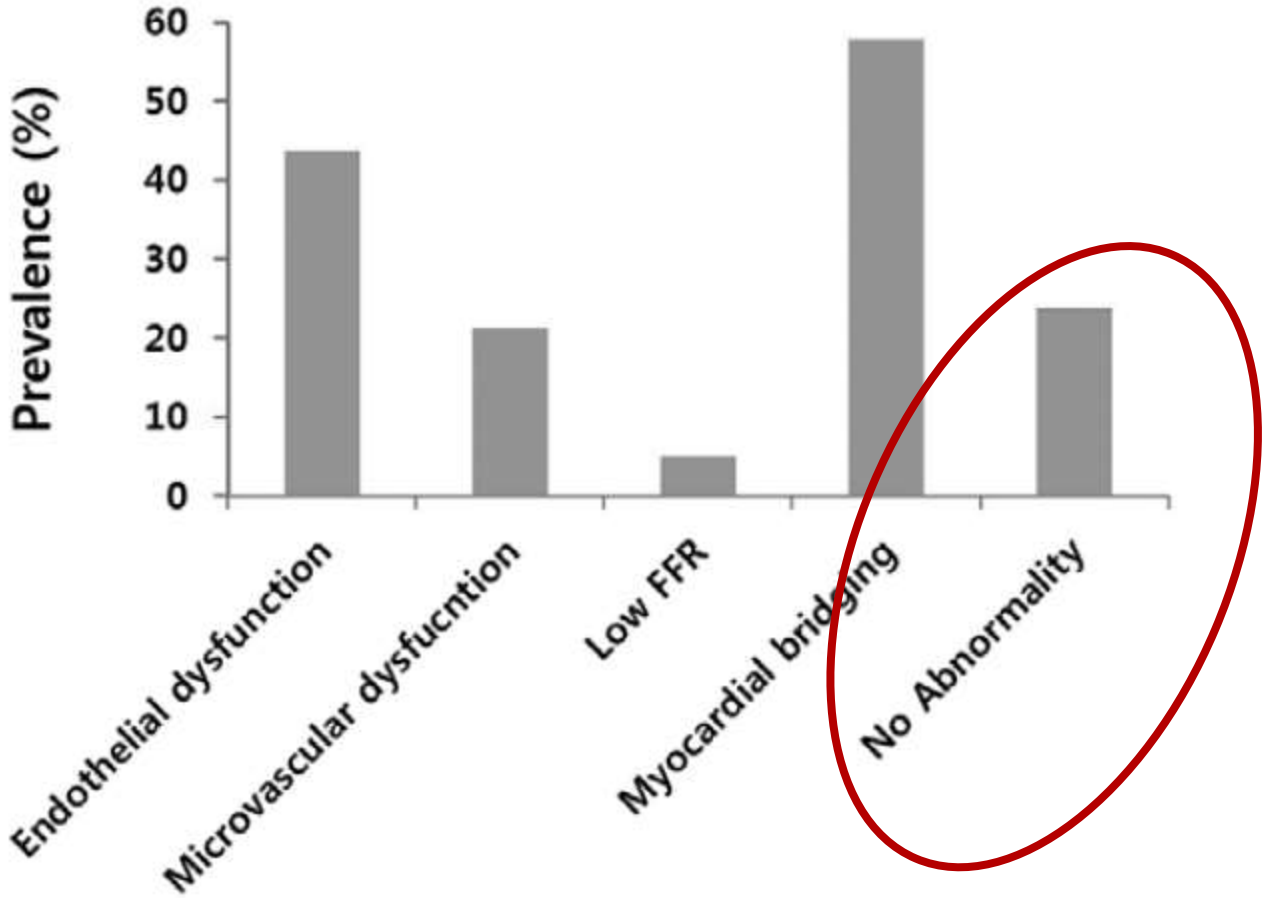
- 139 patients referred for coronary angiography because of symptoms and/or abnormal stress test and found to have “normal” appearing coronaries

- FFR, IMR, CFR, IVUS and acetylcholine challenge were performed down the LAD

Lee BK, et al. Circulation 2015;131:1054-60.

Chest Pain and “Normal Coronaries”

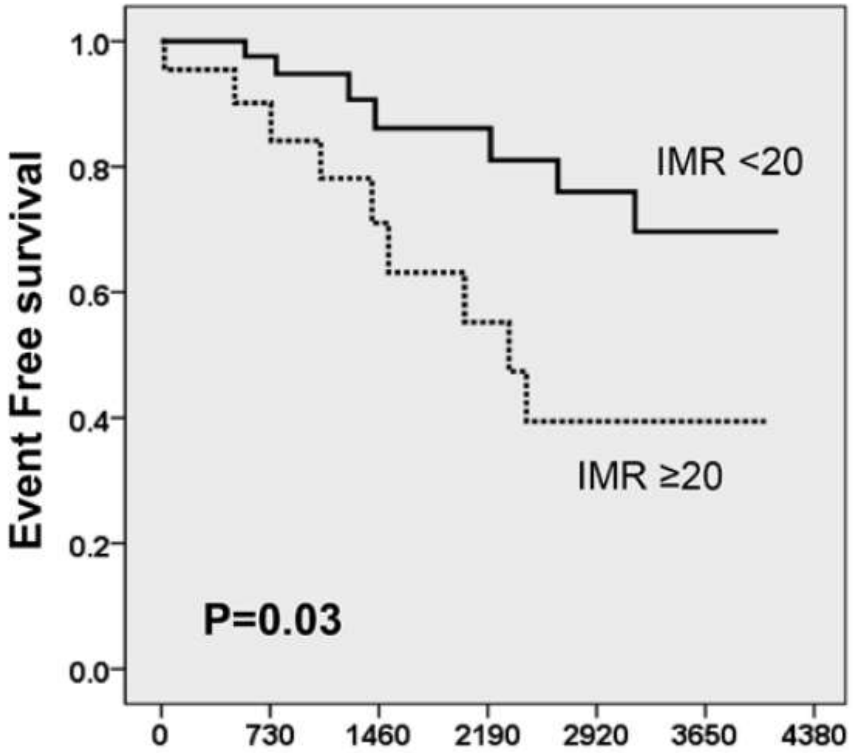
77% of patients had at least one occult coronary circulatory abnormality



Lee BK, et al. Circulation 2015;131:1054-60.

IMR after Heart Transplantation

74 transplant recipients had FFR and IMR measured at baseline and 1 year



Number at risk

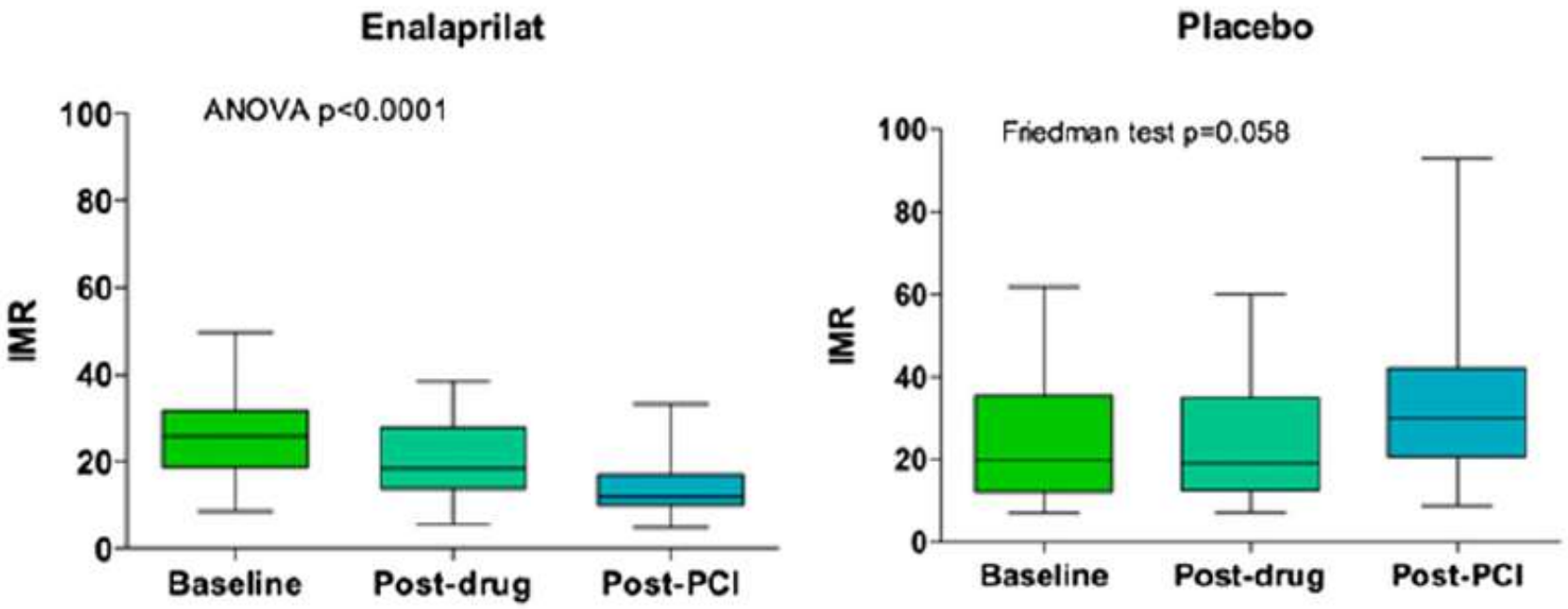
IMR <20	52	36	18	17	15	4
IMR ≥20	22	15	9	7	5	1

IMR ≥ 20 at one year was an independent predictor of long-term death or retransplantation, while IVUS parameters were not.

Yang HM, et al. Circulation 2016;133:1945-50.

Effects of ACE I on the Microvasculature

Randomized comparison of IC enalaprilat vs. placebo in 40 patients peri-PCI



Mangiacapra F, et al. J Am Coll Cardiol 2013;61:615-21.

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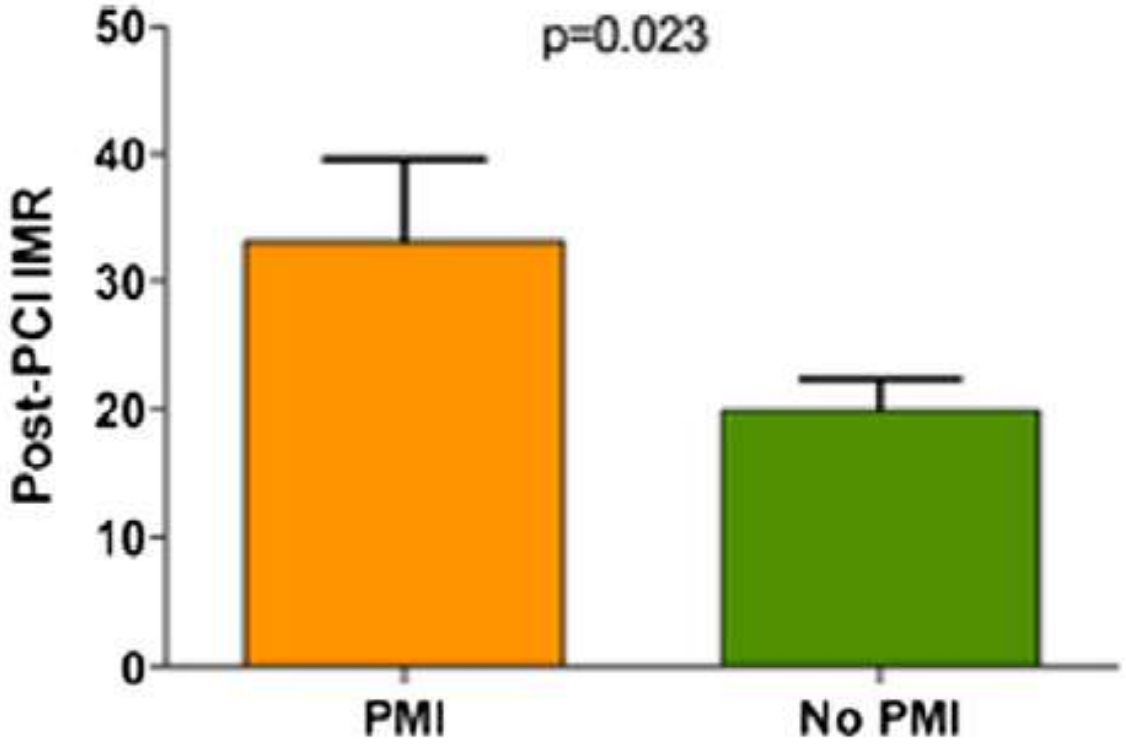


Post-PCI IMR predicts myocardial infarction

Mangiacapra F, et al. J Am Coll Cardiol 2013;61:615-21.

Ramipril after Heart Transplant

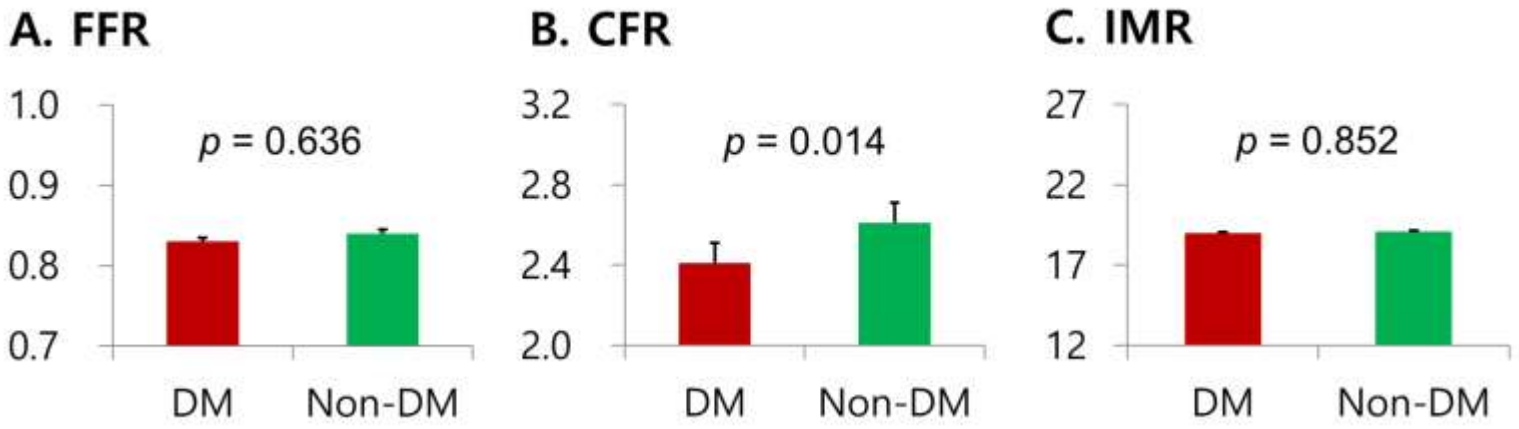
Randomized comparison of ramipril vs. placebo early after cardiac transplantation

Variable	Baseline	One year	p value
Placebo, n = 23			
FFR	0.89 ± 0.04	0.90 ± 0.04	0.39
CFR	4.1 ± 1.8	4.1 ± 2.2	0.60
IMR*	17.4 ± 8.4	21.5 ± 20.0	0.72

J Am Coll Cardiol 2017;in press.

Microvascular Dysfunction and DM

IMR, CFR and FFR measured in 681 propensity matched patients (227 with DM)

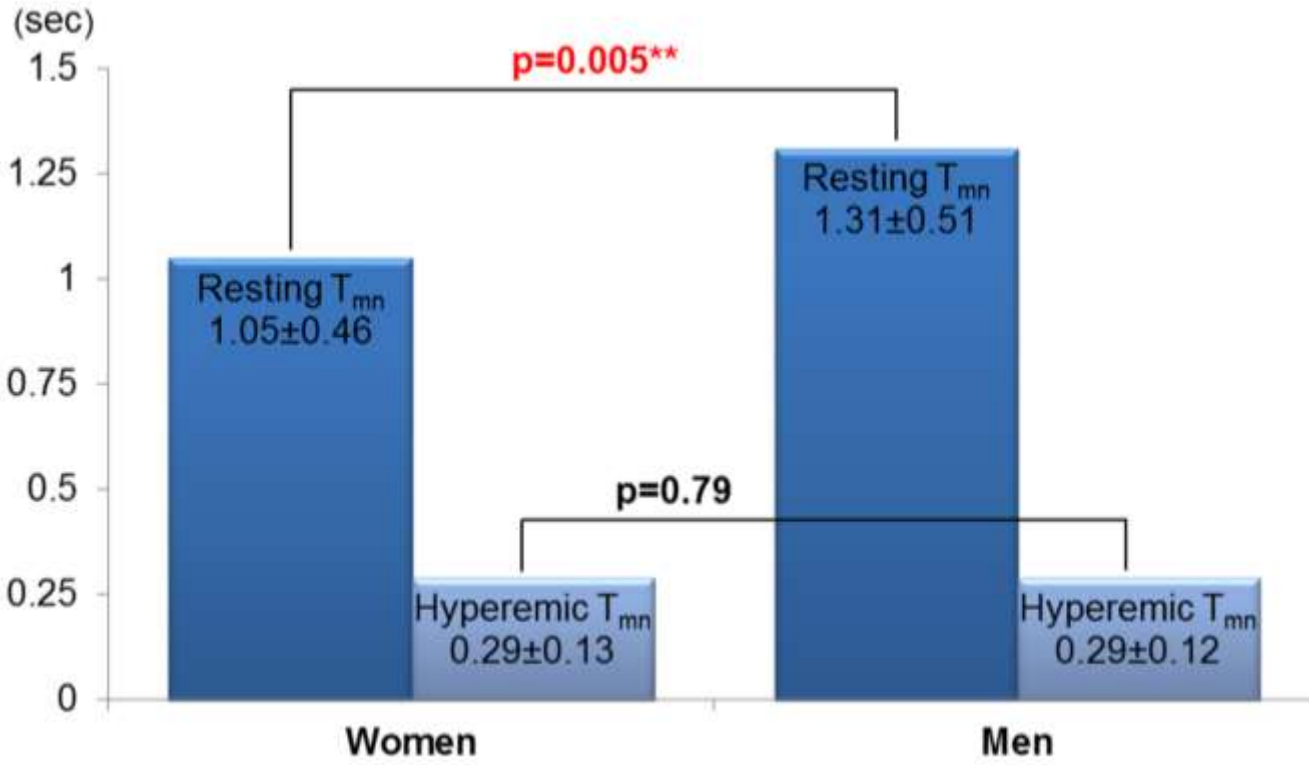


Lee JH, et al. Submitted

Microvascular Dysfunction and DM

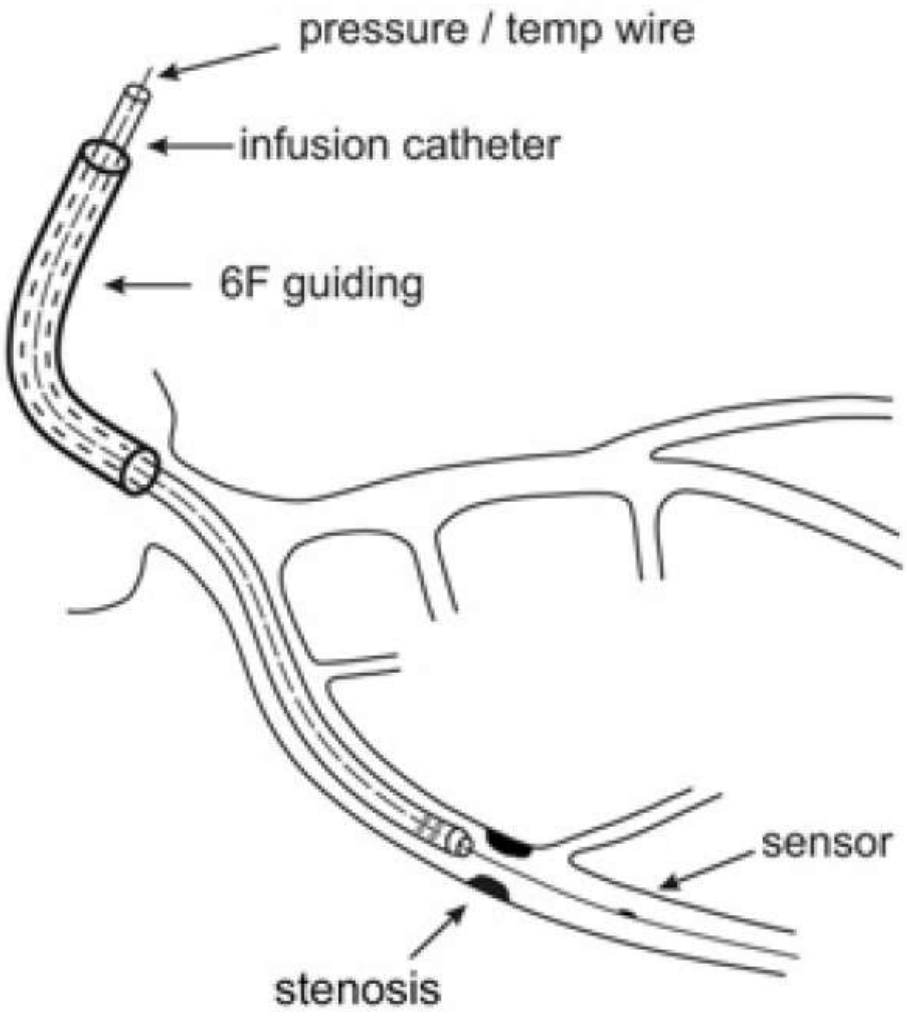
IMR and CFR measured in 157 patients (40 men) with "normal" coronaries

- IMR was similar between the sexes (20.7±9.8 vs. 19.1±8.0, p=0.45), but CFR was lower in women (3.8±1.6 vs. 4.8±1.9, p=0.004).



Kobayashi, et al. J Am Coll Cardiol Interv 2015;8:1433-41.

Absolute Coronary Flow

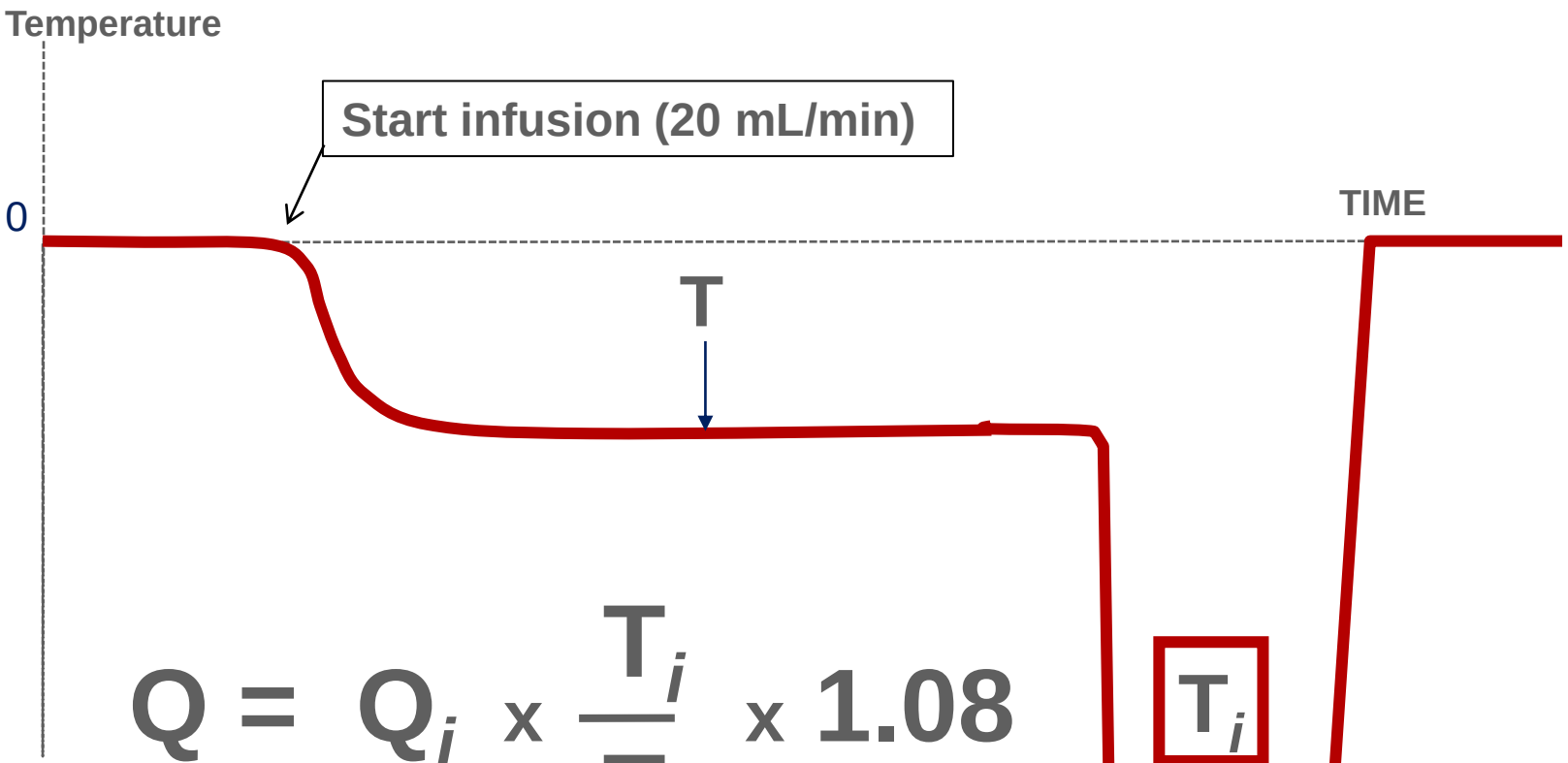


Nico Pijls, MD, PhD

Aarnoudse W, et al. J Am Coll Cardiol 2007;50:2294

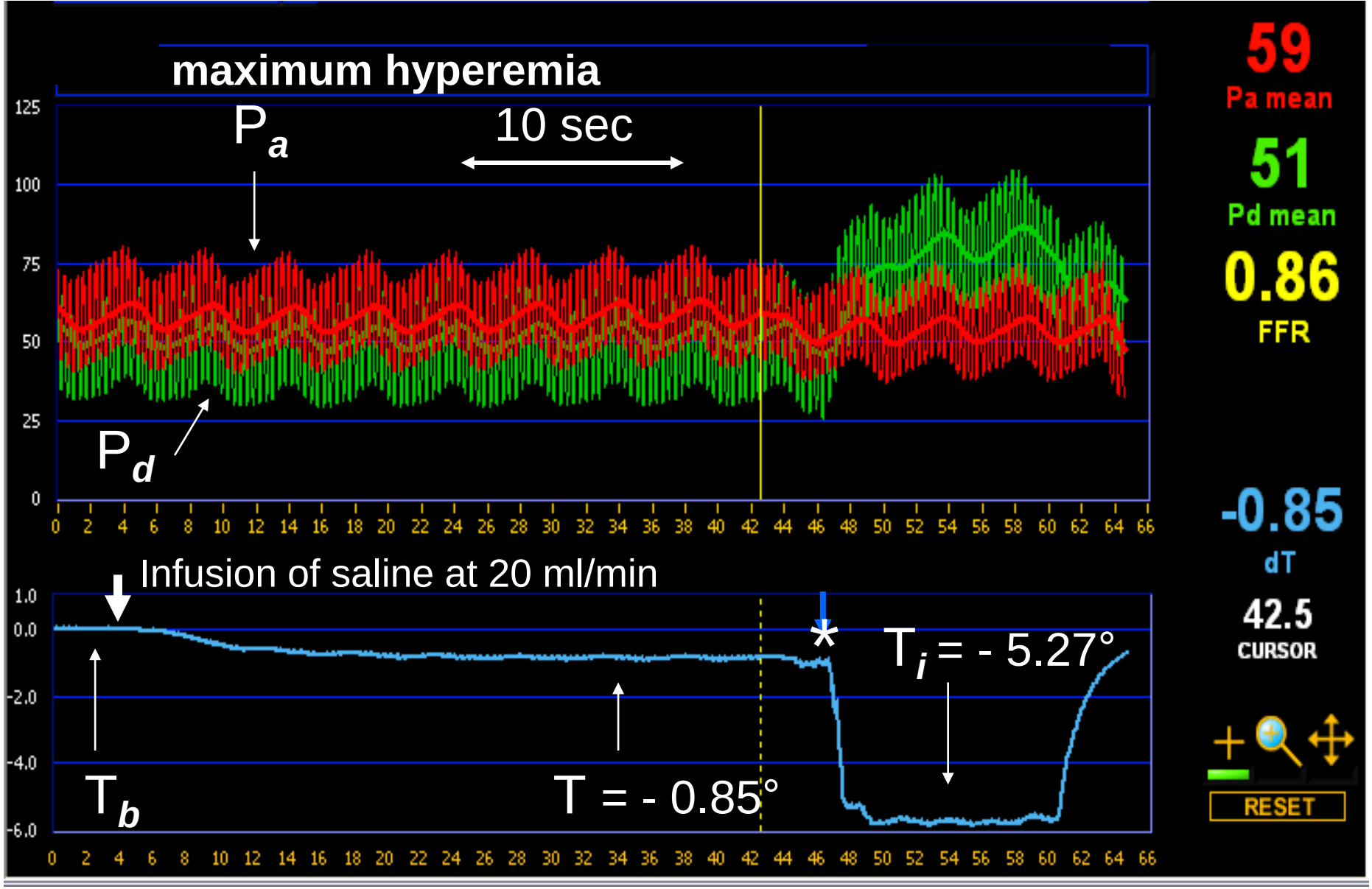
Absolute Coronary Flow

Indicator Dilution Theory: Continuous Infusion



Bernard De Bruyne, MD, PhD

Aarnoudse W, et al. J Am Coll Cardiol 2007;50:2294



Q*b* = 20 x (-5.27 / -0.85) x 1.08 = 134 ml/min

Nico Pijls, MD, PhD

Conclusion

- Microvascular dysfunction is an important contributor to adverse outcome
- We now can rapidly and easily assess microvascular function by measuring IMR
- IMR is predictive of adverse outcomes in a number of settings
- Measuring absolute coronary flow may further refine our ability to assess the microvasculature