FFR, IMR, CFR Discordance:
Should We Abandon CFR?

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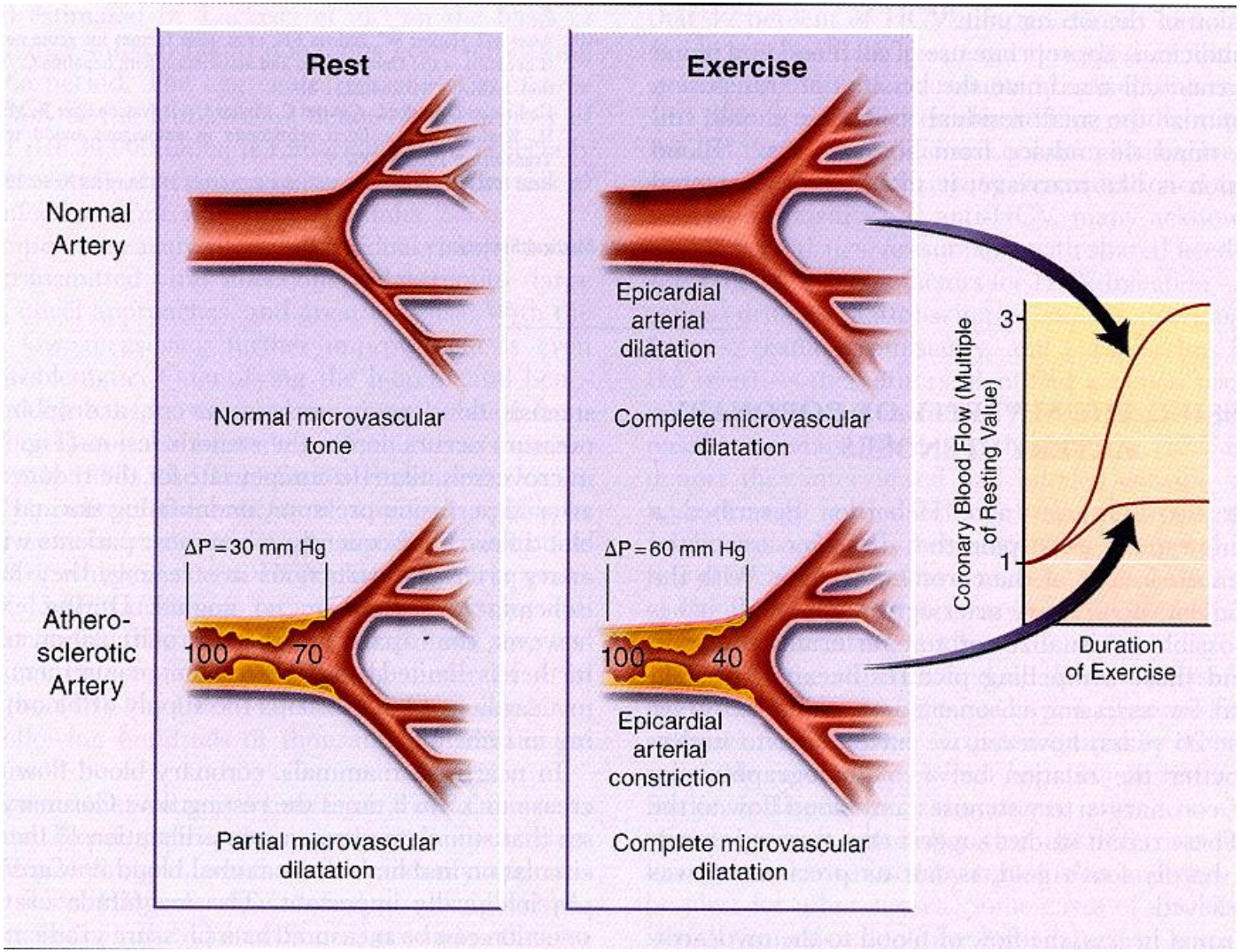
Disclosure Statement of Financial Interest

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, NHLBI
Consulting Fees/Honoraria	Medtronic
Major Stock Shareholder/Equity	
Royalty Income	
Ownership/Founder	
Intellectual Property Rights	
Other Financial Benefit	Minor stock options: HeartFlow

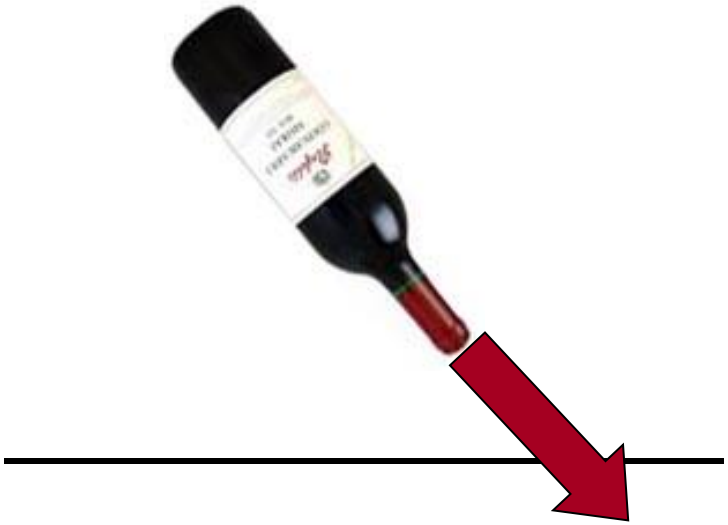
What is Coronary Flow Reserve?



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

CFR

Hyperemic Flow



Resting Flow

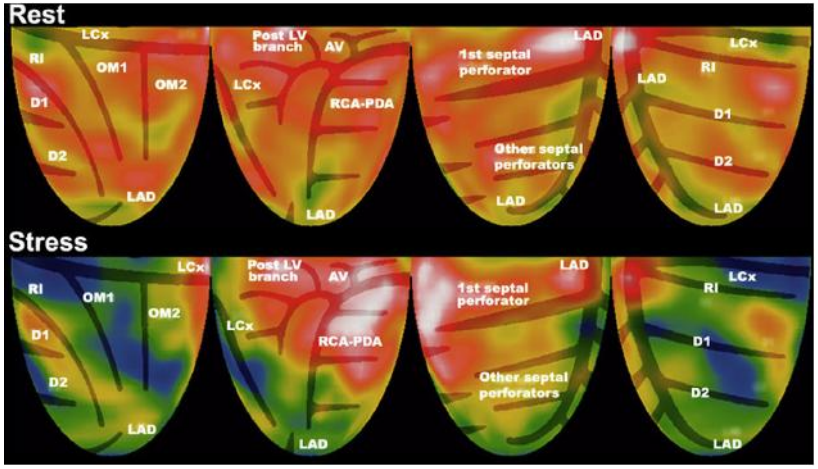
FFR

Hyperemic Flow with Stenosis

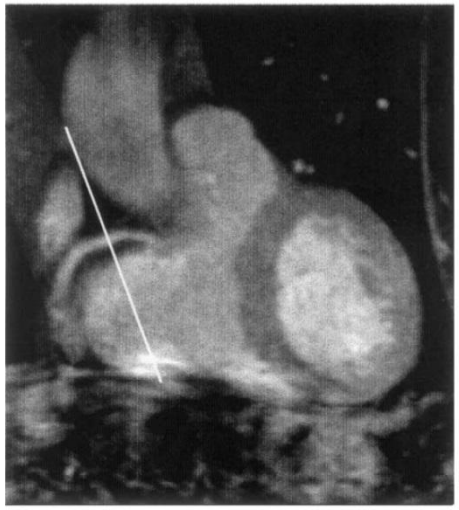
Hyperemic Flow without Stenosis

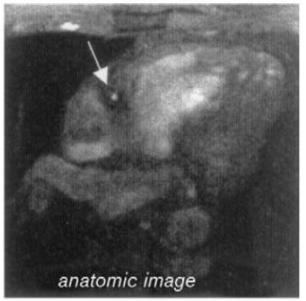
Noninvasive Assessment of CFR

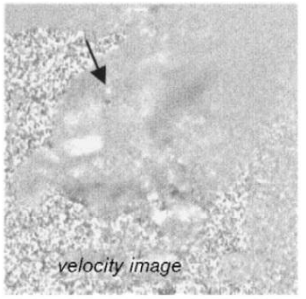
PET



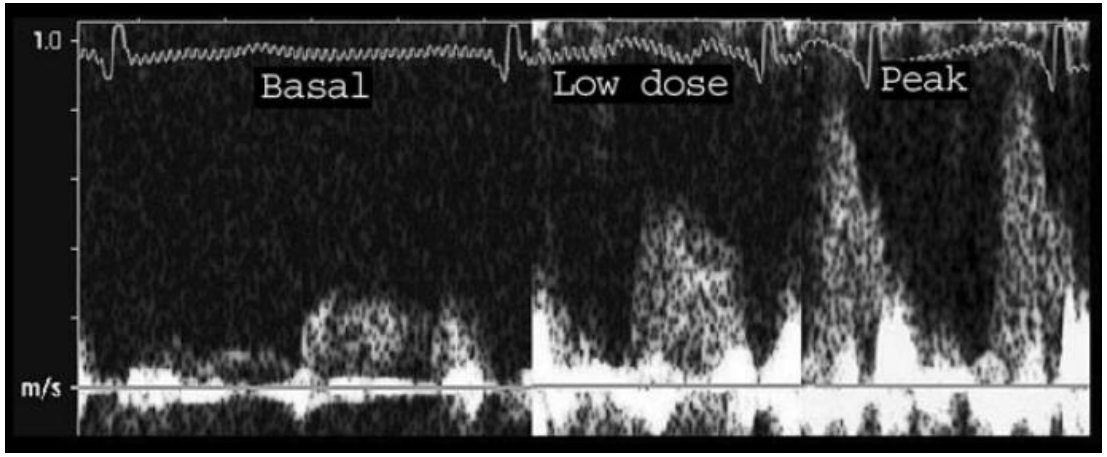
MRI

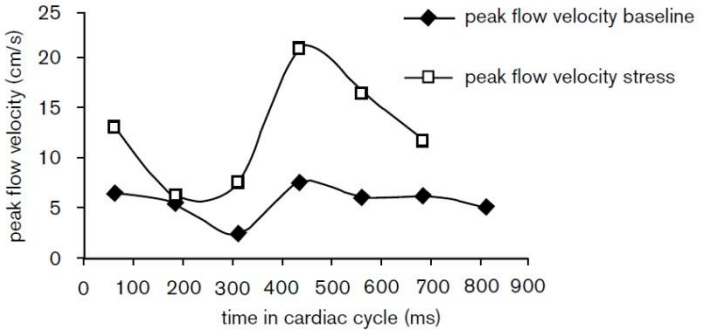






Echo

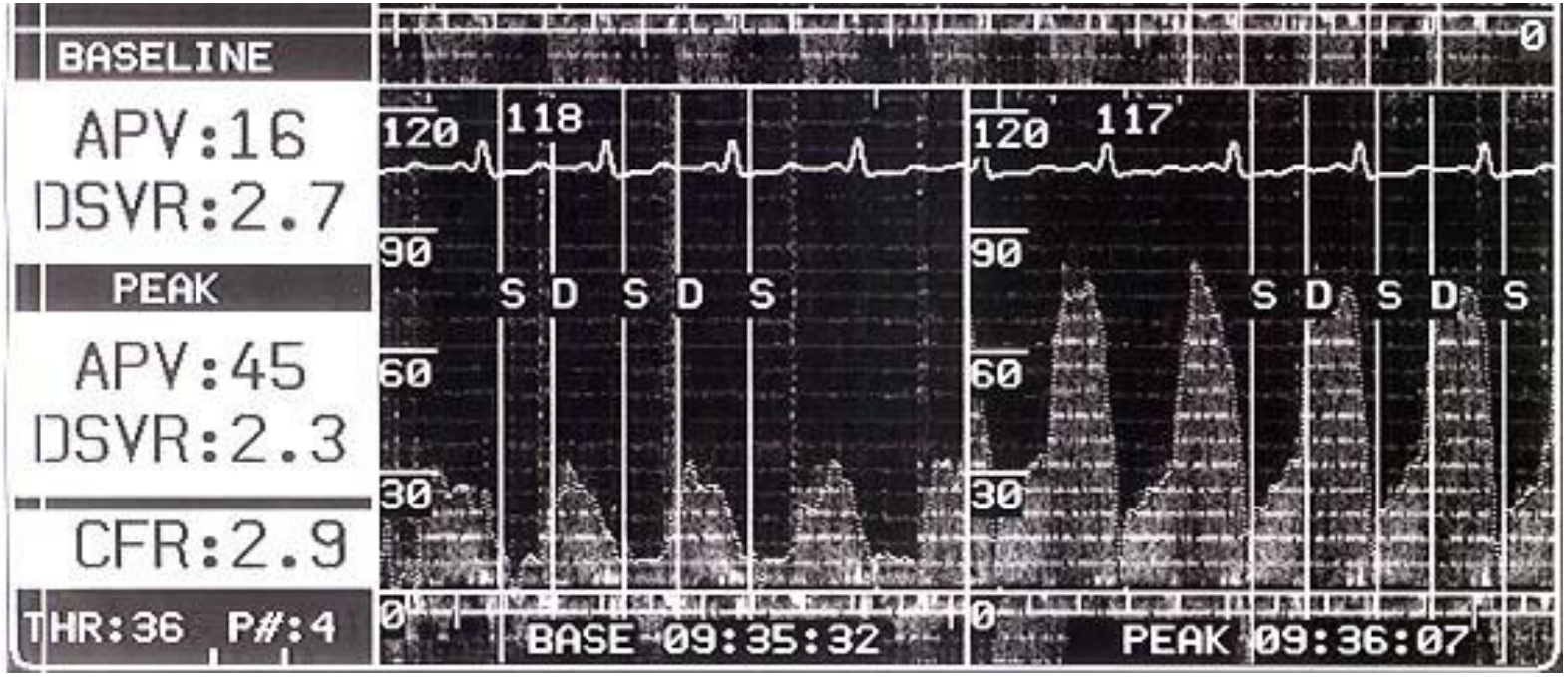




Bedaux, et al. Cor Art Dis 2002;13:365-72.
Meimoun, et al. Eur J Echo 2008;9:449-57.
Gould, et al. J Am Coll Cardiol 2013;62:1639-53.

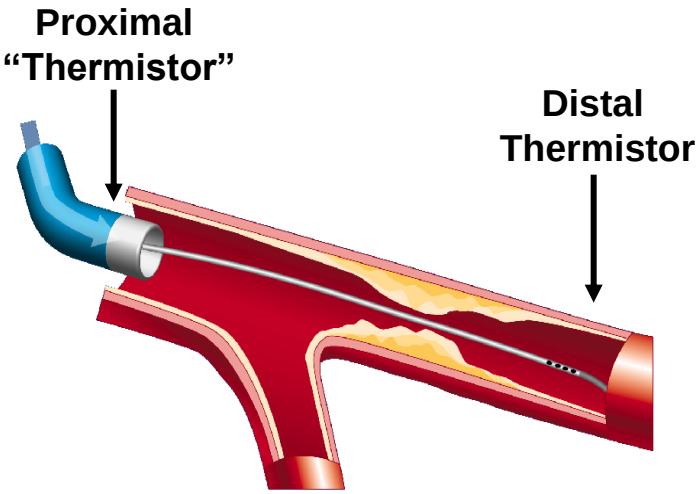
Coronary Flow Reserve

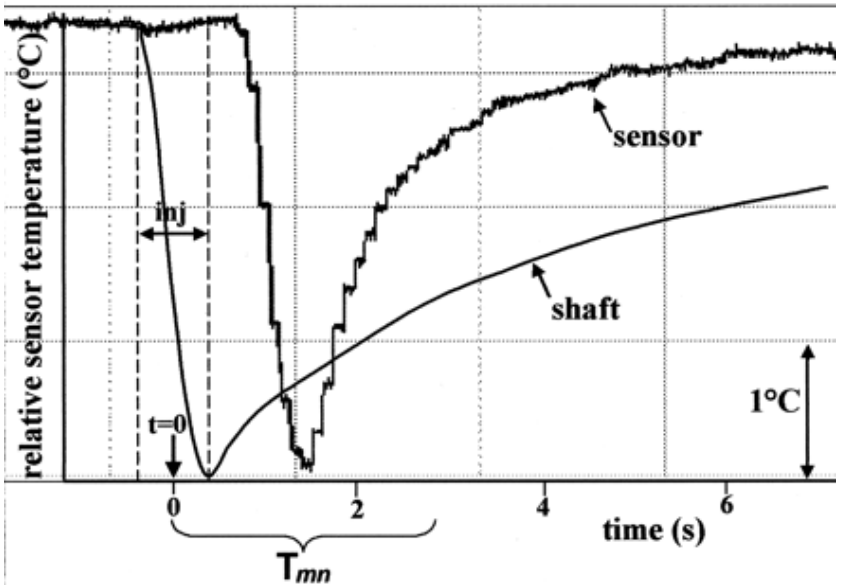
Because flow is proportional to velocity, CFR can be estimated by measuring velocity at rest and at maximal hyperemia

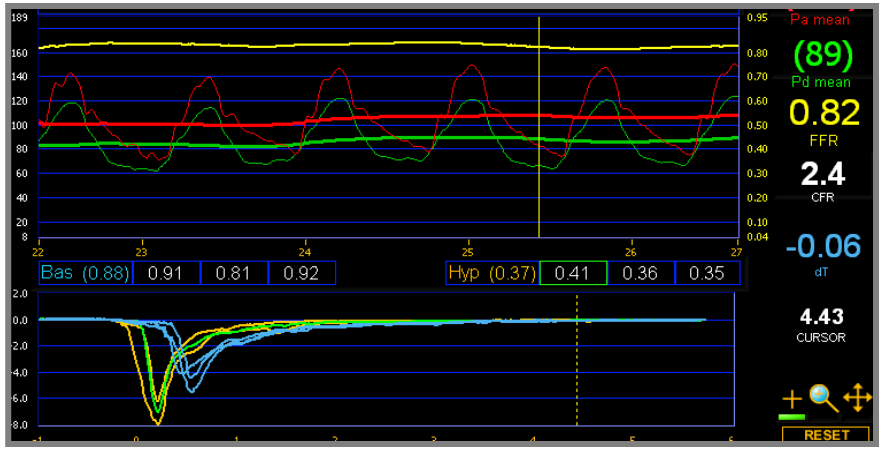


Coronary Flow Reserve

Thermodilution-Derived CFR

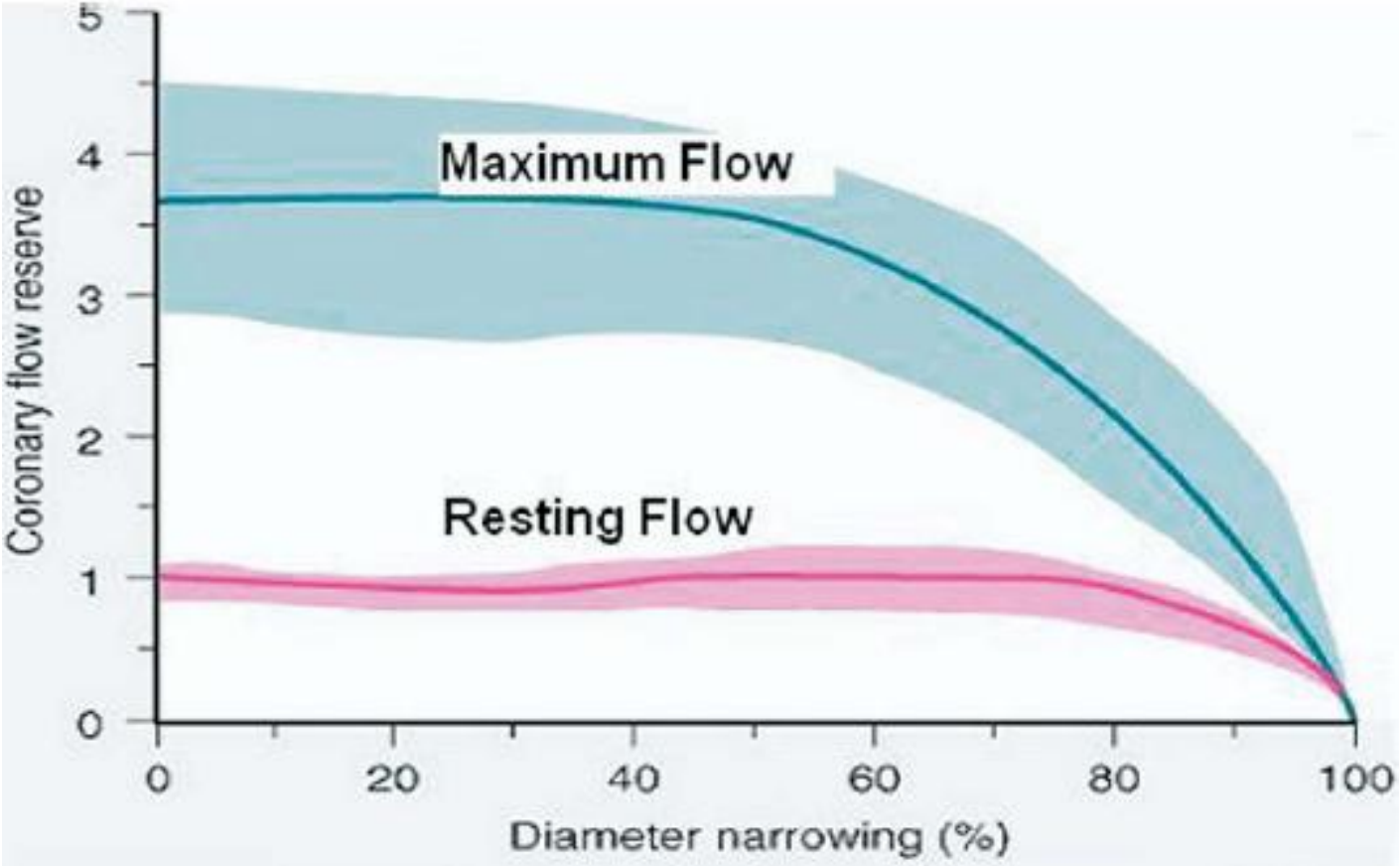






First Description of CFR:

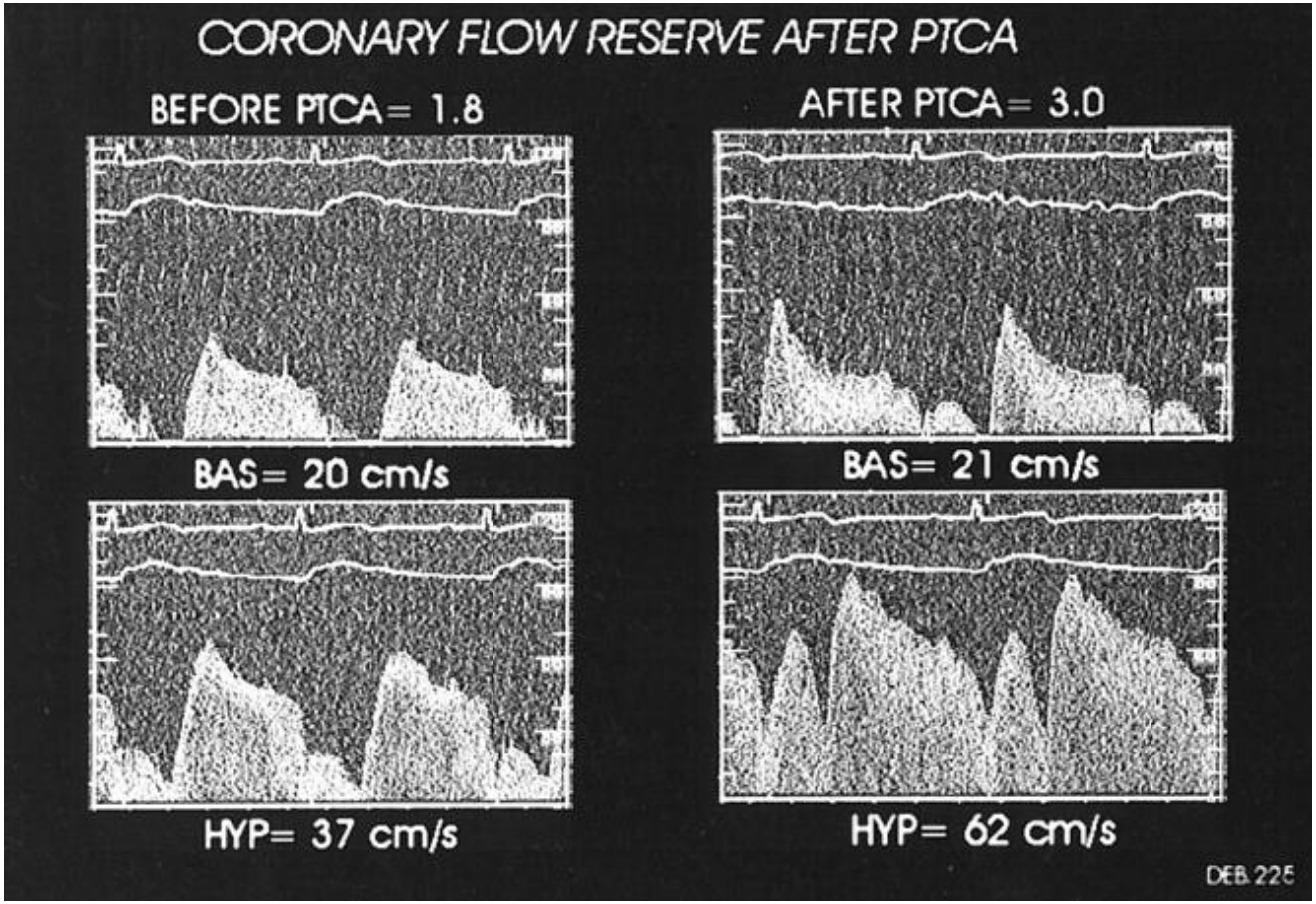
Measurement of myocardial blood flow at rest contains only limited diagnostic information



Gould, et al. Am J Cardiol 1974;33:87-94. (from Braunwald's Heart Disease 2005)

DEBATE Study:

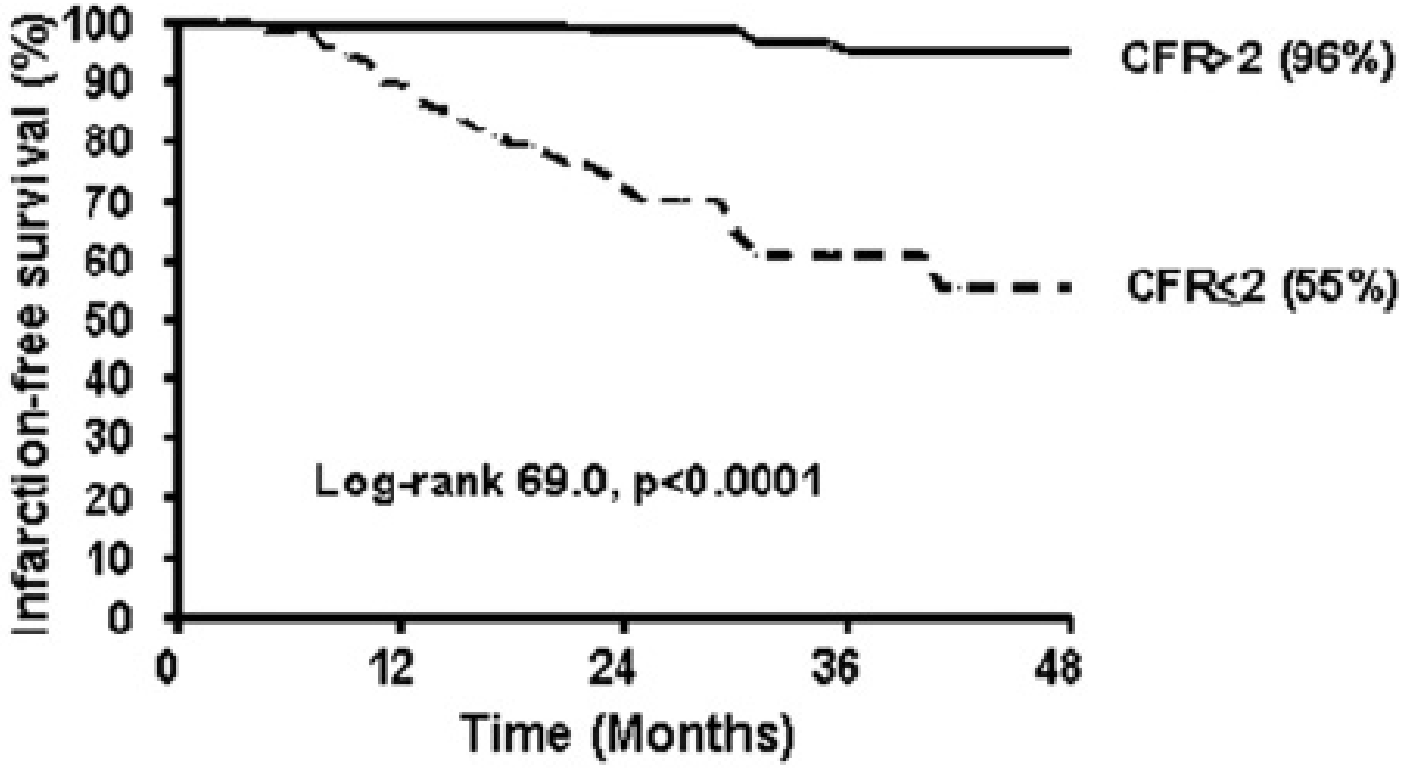
CFR measured in 297 patients after PTCA and found to predict outcomes



Serruys, et al. Circulation 1997;96:3369-77.

Importance of the Microcirculation

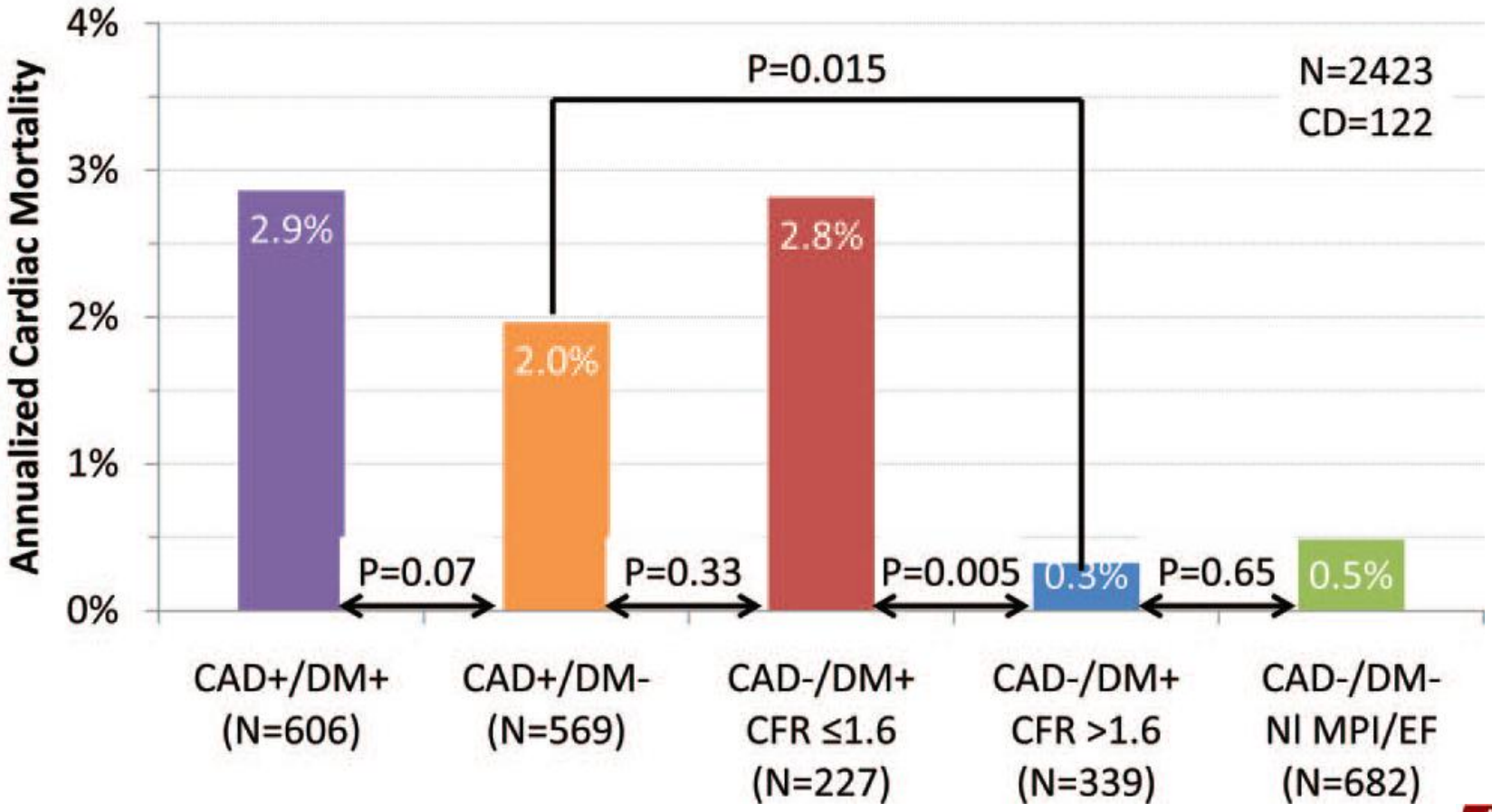
Infarct-Free Survival based on Echo-Derived CFR in 394 Patients with Chest Pain and Normal Coronaries



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

Importance of the Microcirculation

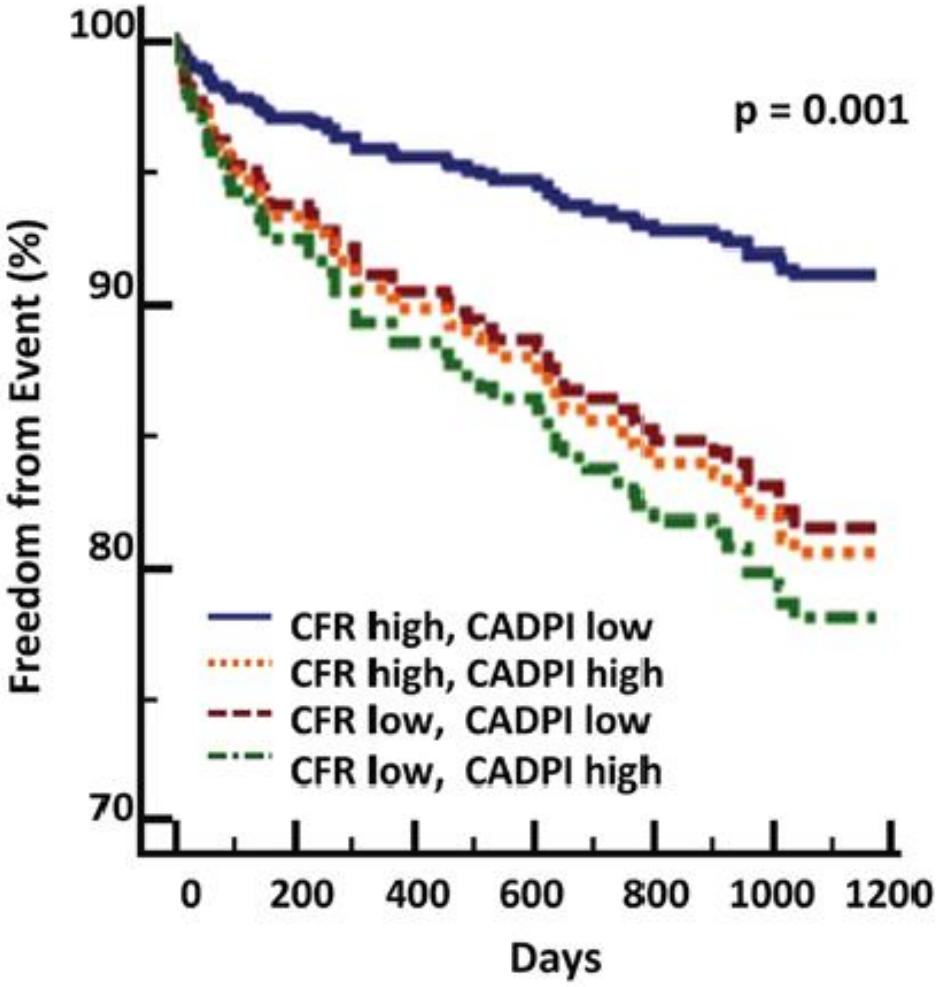
2,423 patients undergoing PET-derived CFR



Murthy, et al. Circulation 2012;126:1858-68.

Importance of the Microcirculation

328 patients undergoing PET-derived CFR and Invasive Angiography



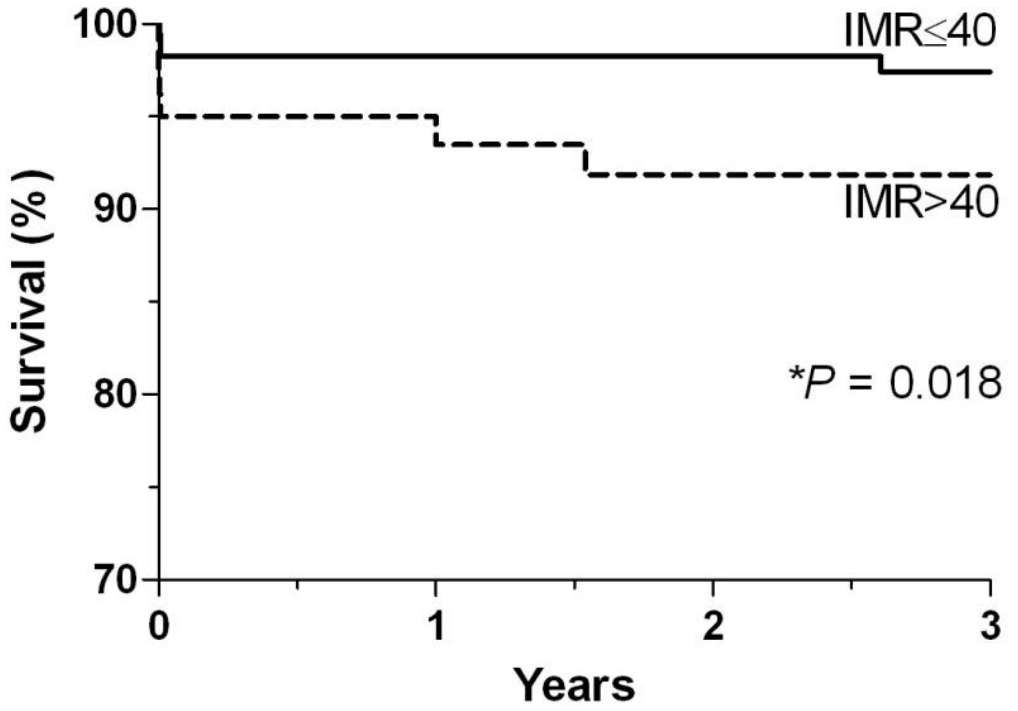
Freedom from cardiac death or CHF admission

CADPI indicates CAD Prognostic Index

Taqueti, et al. Circulation 2015;131:19-27.

Predicting Outcomes: *IMR vs. CFR*

IMR was an independent predictor of survival in 253 STEMI patients while CFR was not.



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

Circulation 2013;127:2436-41.

Predicting Outcomes: *IMR vs. CFR*

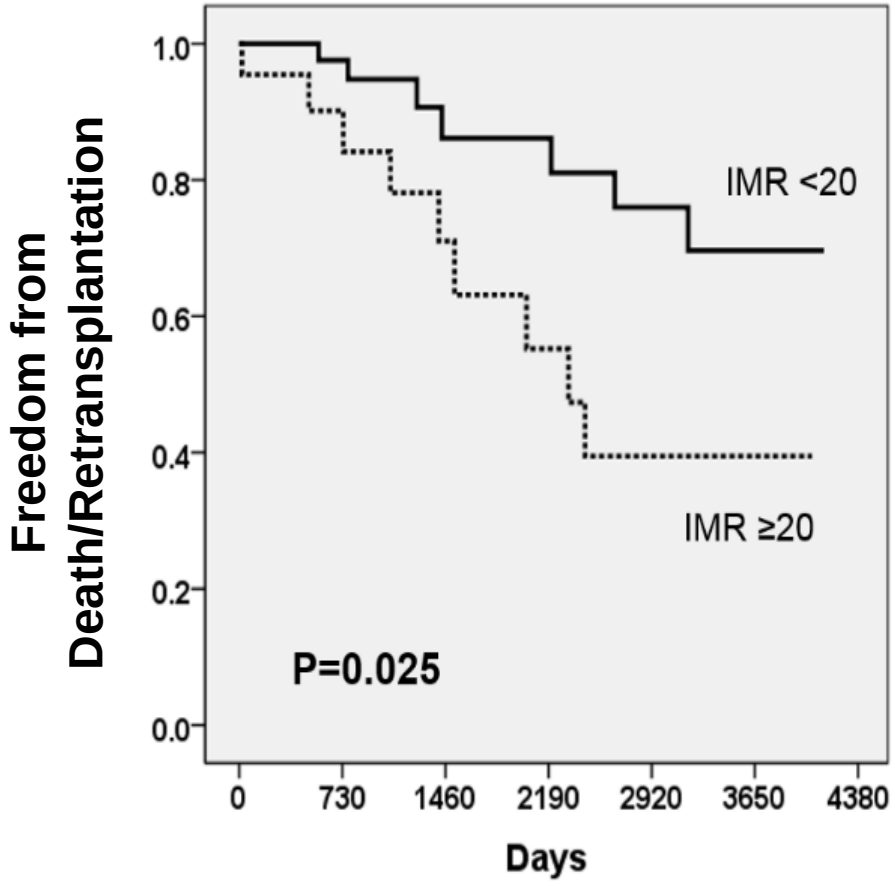
Pre PCI FFR, IMR and CFR measured to predict peri-procedural MI

Variable	Patients With Peripro-cedural Infarction (n=10)	Patients Without Peripro-cedural Infarction (n=40)	*P* Value
Coronary physiology pre-PCI, U			
Coronary wedge pressure	15.7±10.9	16.5±9.2	0.808
Collateral flow index	0.18±0.12	0.20±0.12	0.583
Fractional flow reserve	0.61±0.16	0.58±0.18	0.614
Coronary flow reserve	2.1±1.5	2.1±1.1	0.995
IMR	31.6±11.8	17.6±9.7	<0.001

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

Predicting Outcomes: *IMR vs. CFR*

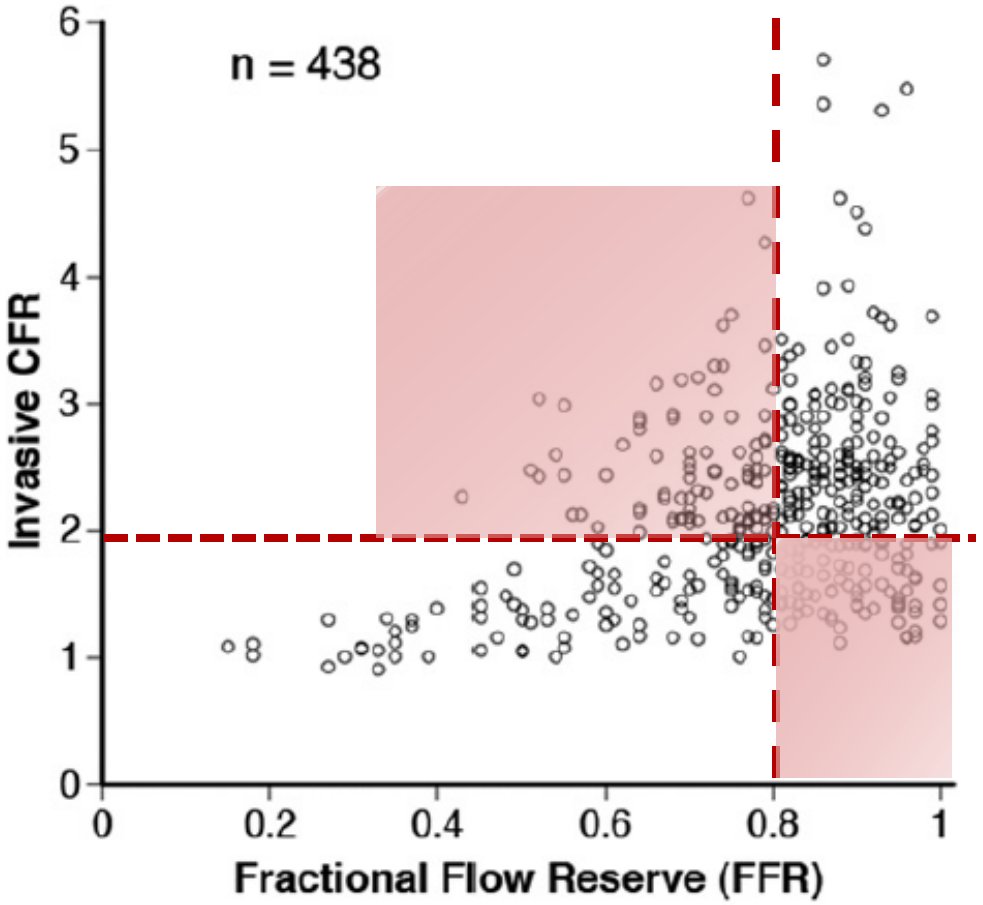
IMR and CFR measured 1 year after heart transplantation in 74 patients with long-term follow-up (mean=4.5 years)



Yang, et al. ACC 2015.

Is there a discordance?

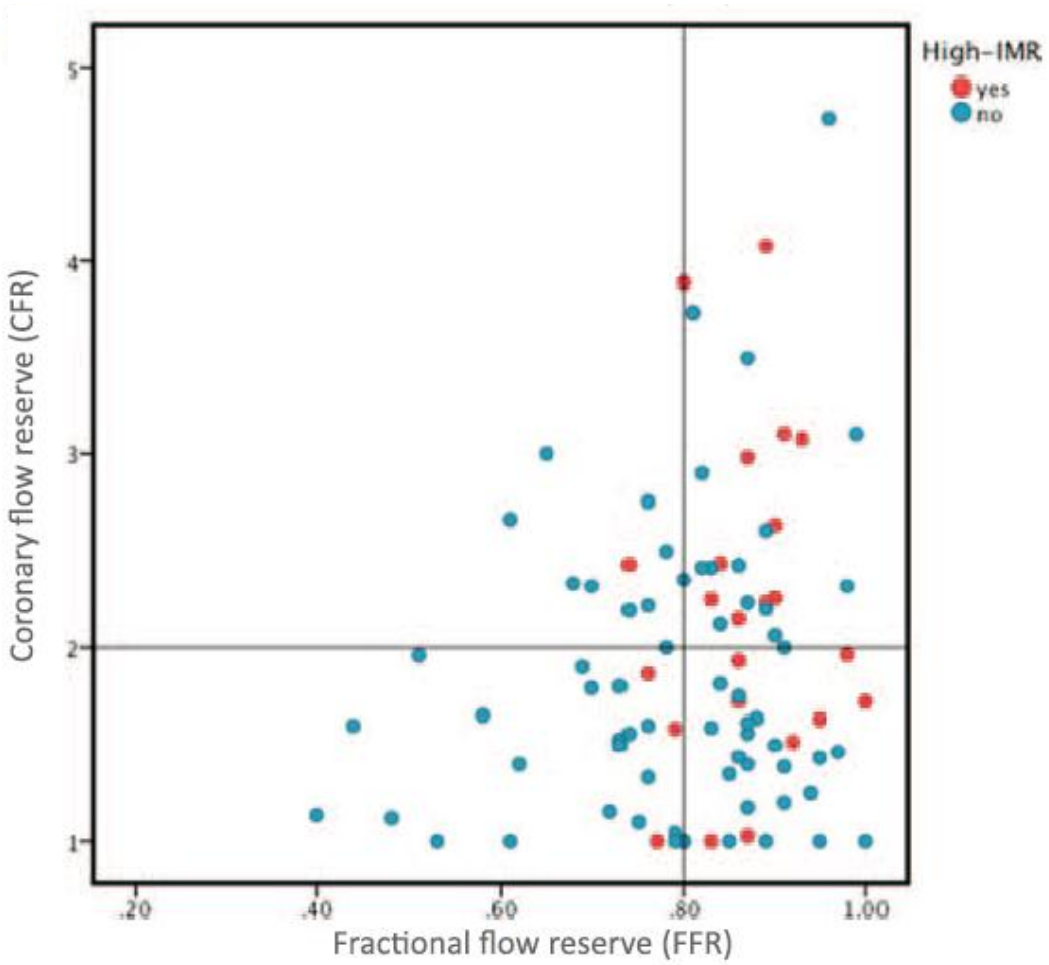
CFR and FFR measured in 438 patients from the literature.



Johnson, et al. J Am Coll Cardiol Img 2012;5:193-202.

Is there a discordance?

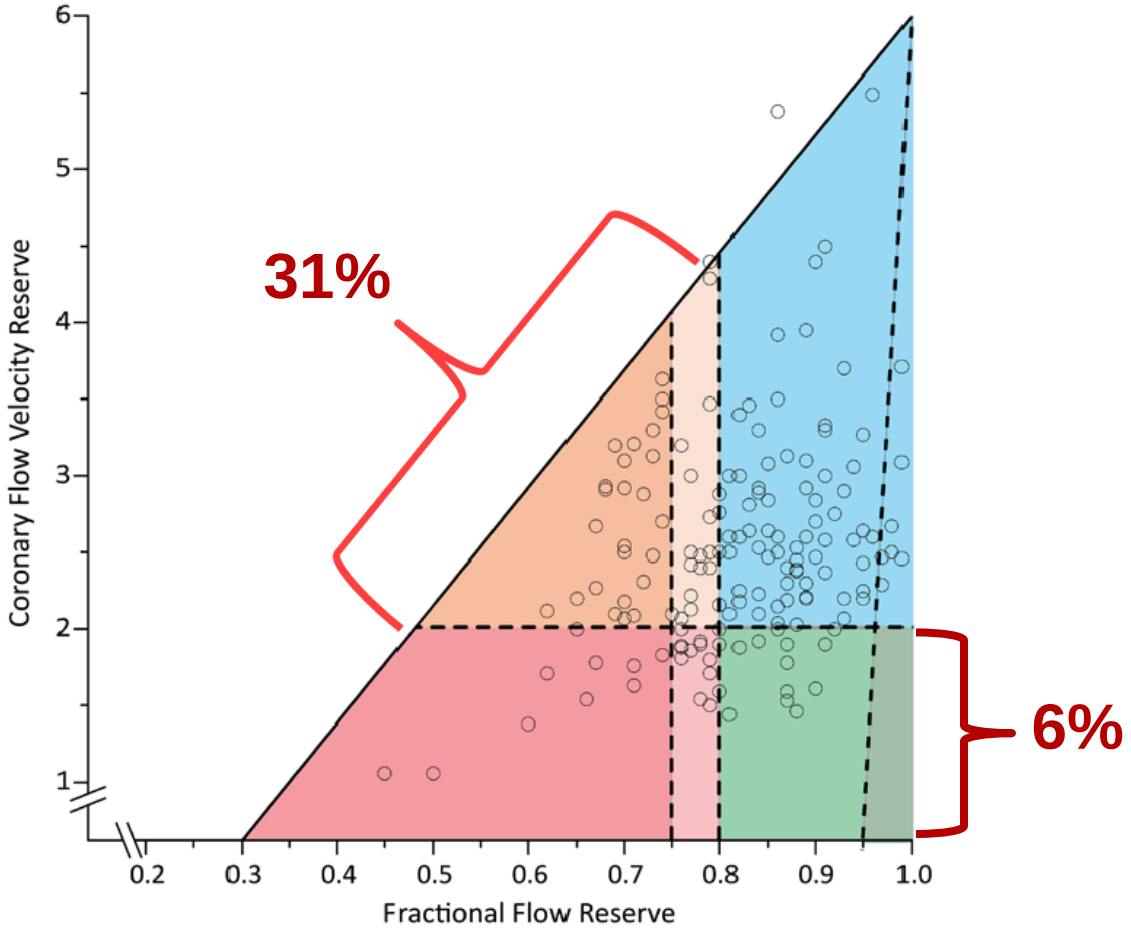
FFR, IMR and CFR measured across 91 lesions in 78 patients.



Echavarria-Pinto, et al. Circulation 2013;128:2557-2566.

Is there a discordance?

CFVR and FFR measured in 157 intermediate stenoses in 157 patients.



van de Hoef, et al. Circ Cardiovasc Interv 2014;7:301-311.

Is the discordance relevant?

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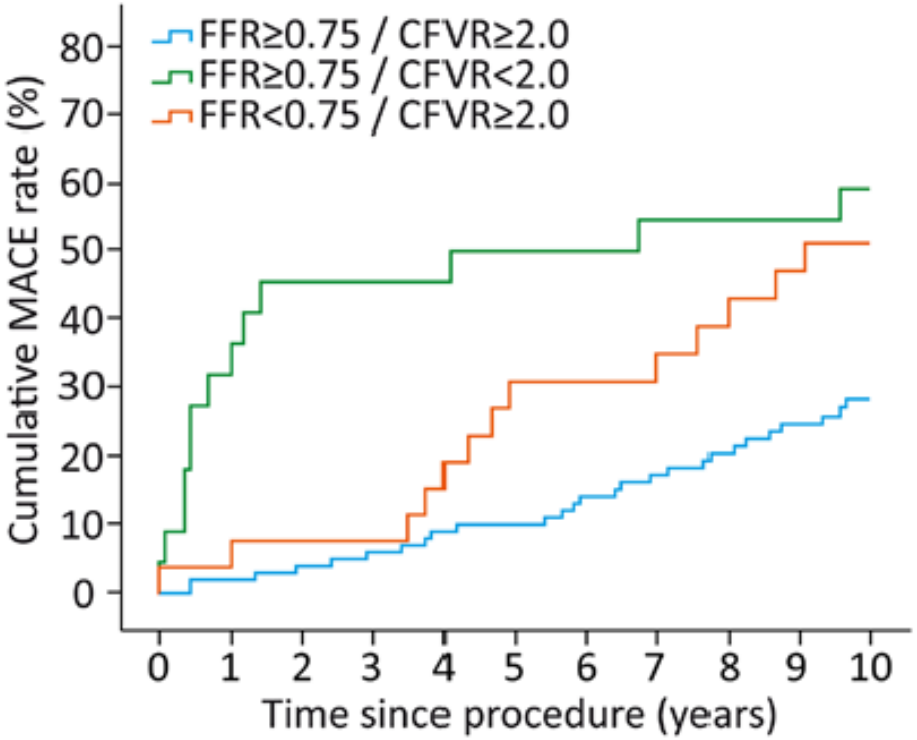

No. at risk:

FFR≥0.75 / CFVR≥2.0	100	95	90	83	74	61
FFR≥0.75 / CFVR<2.0	22	12	12	11	10	8
FFR<0.75 / CFVR≥2.0	26	24	21	18	14	11

MACE is a composite of cardiac death, MI and revascularization.

van de Hoef, et al. Circ Cardiovasc Interv 2014;7:301-311.

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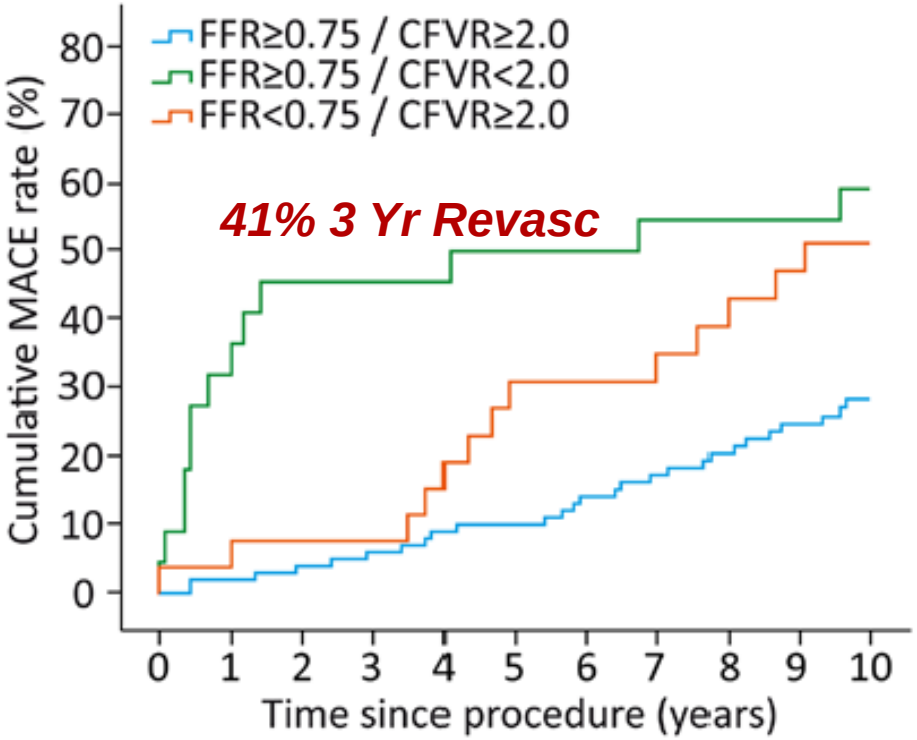

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FFR<0.75 / CFVR≥2.0	26	24	21	18	14	11

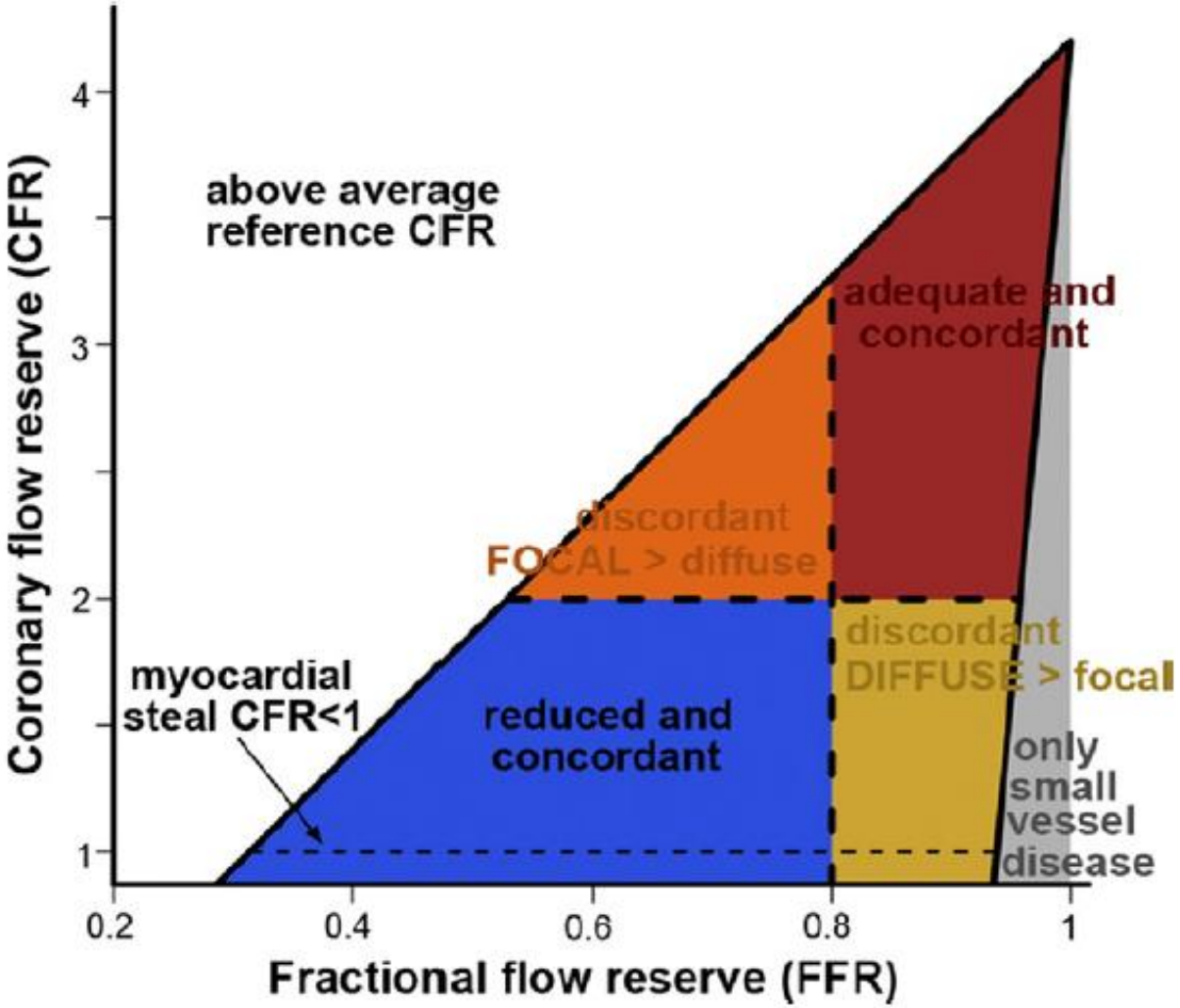
5 Year Death/MI Rate

14% (3/22)
20% (5/26)

6% (6/100)

van de Hoef, et al. Circ Cardiovasc Interv 2014;7:301-311.

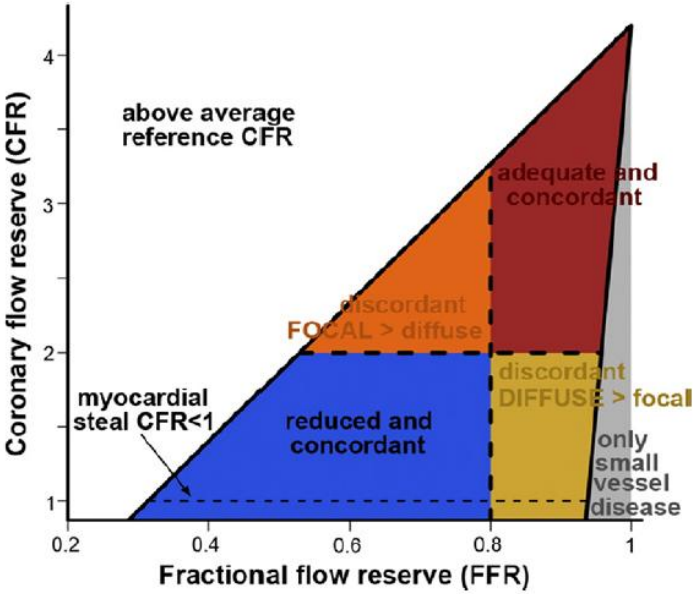
Why is there a discordance?



Johnson, et al. J Am Coll Cardiol Img 2012;5:193-202.

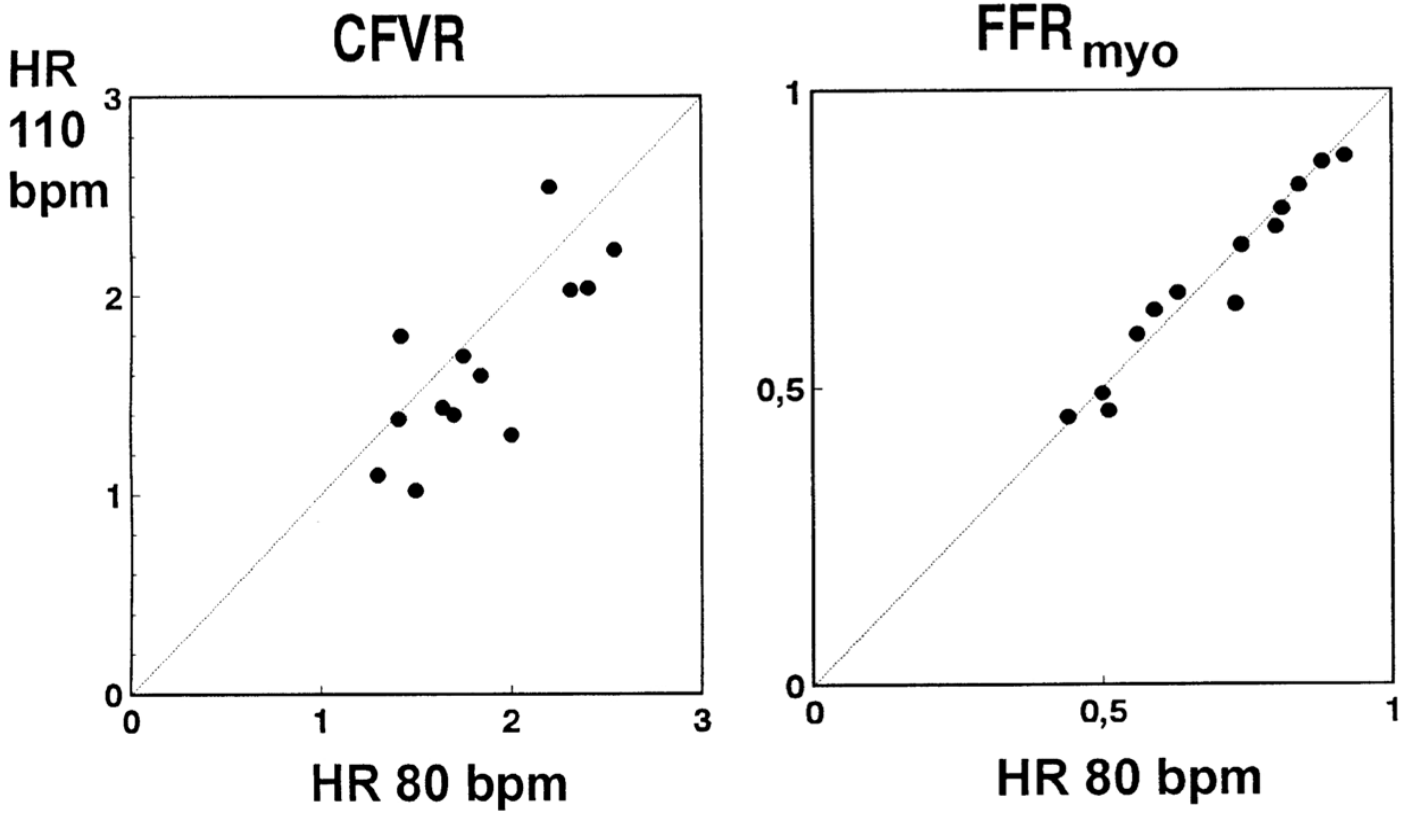
Limitations of CFR

- No clearly defined normal value
- Does not distinguish epicardial from microvascular disease
- Affected by resting hemodynamics



“Resting” Hemodynamics and CFR

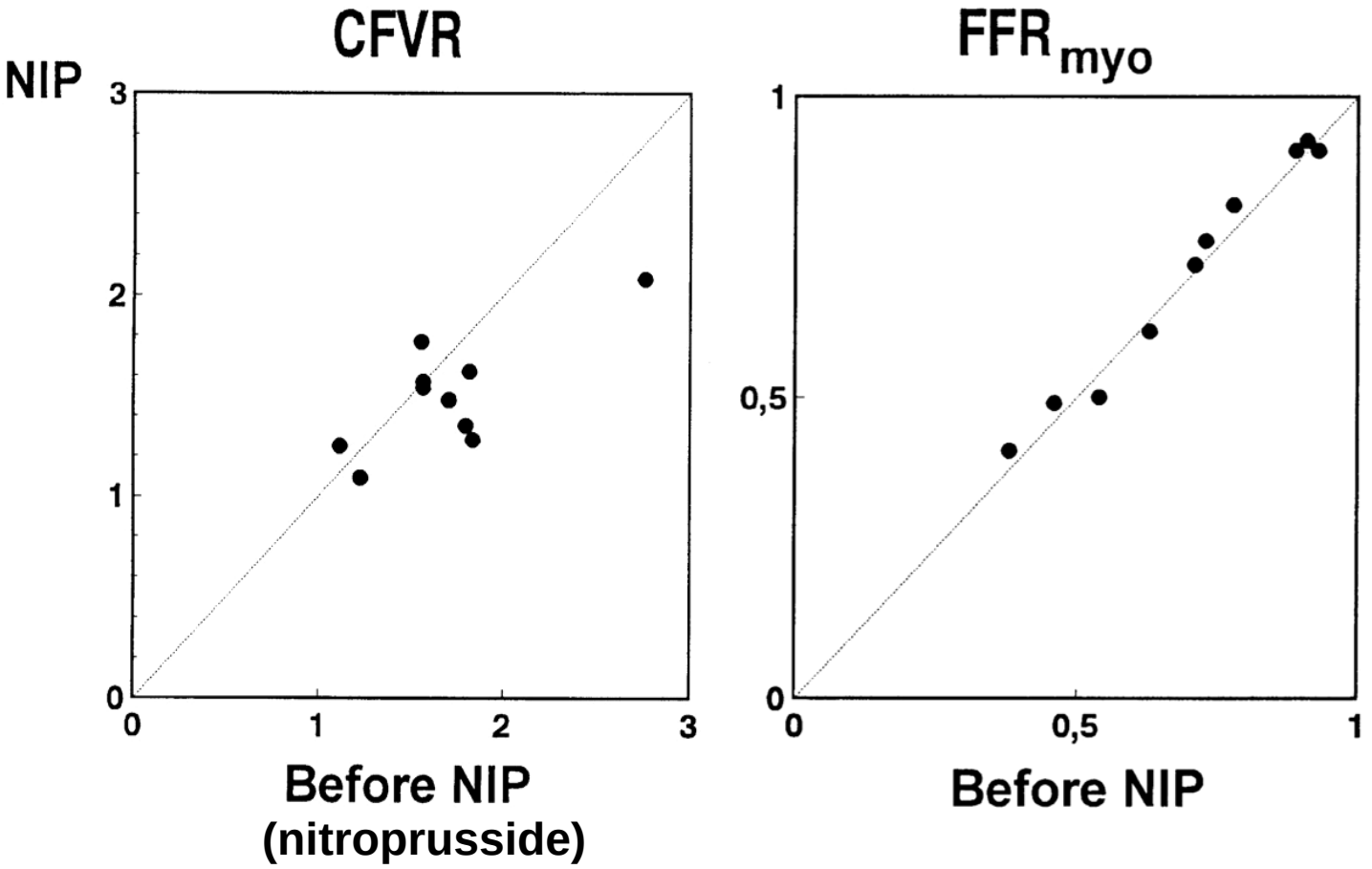
Effect of changing heart rate on CFVR and FFR



De Bruyne, et al. Circulation 1996;94:1842-1849.

“Resting” Hemodynamics and CFR

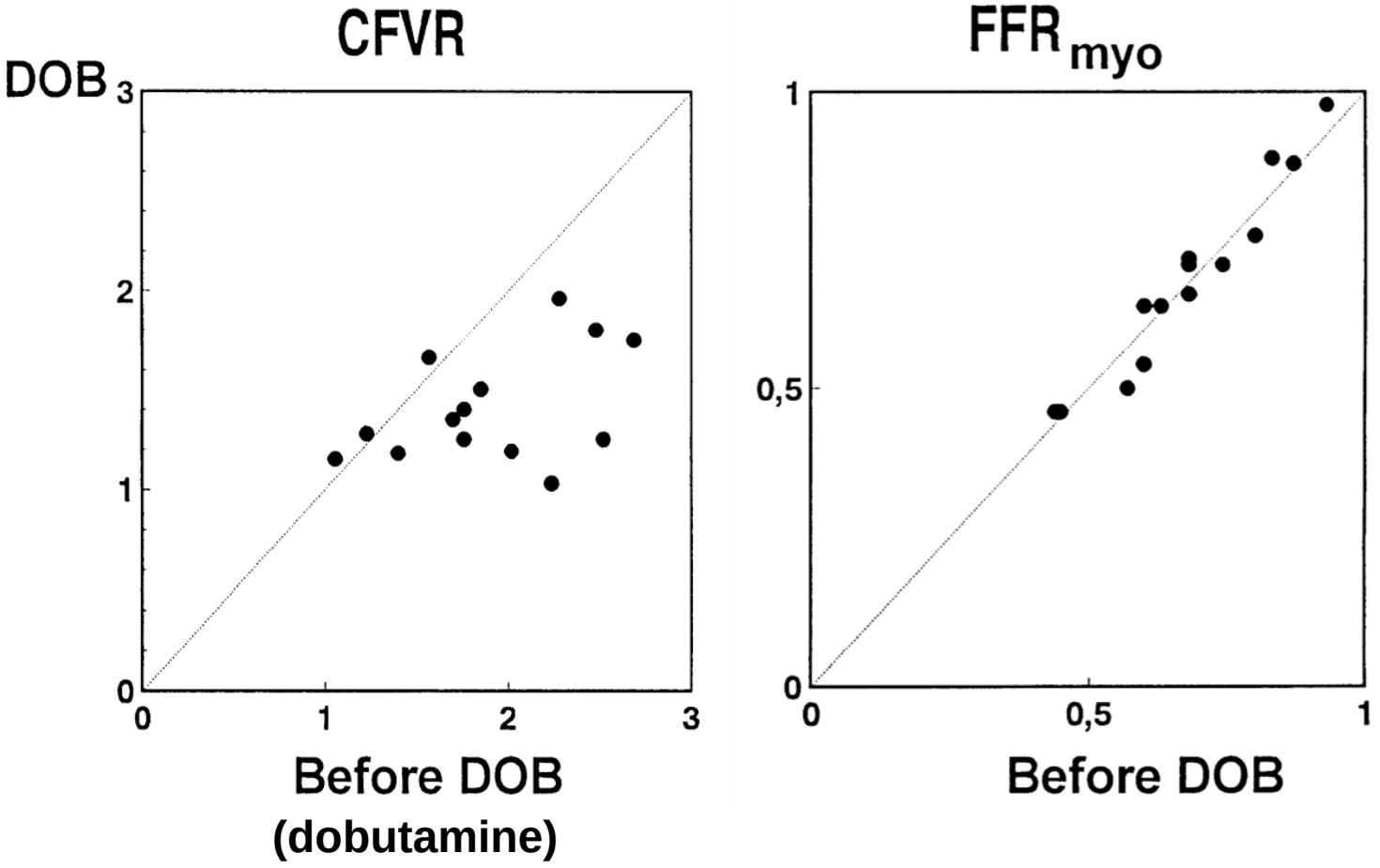
Effect of changing blood pressure on CFVR and FFR



De Bruyne, et al. Circulation 1996;94:1842-1849.

“Resting” Hemodynamics and CFR

Effect of changing contractility on CFVR and FFR



De Bruyne, et al. Circulation 1996;94:1842-1849.

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.

† $p<0.05$

Sex Differences and CFR

FFR, 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).
- This was primarily due to a shorter resting T_{mn} in women (p=0.005), suggesting increased resting coronary flow.
- Hyperemic T_{mn} was identical (p=0.79).
- On multivariate analysis, female sex was an independent predictor of lower CFR and shorter resting T_{mn}, but not a predictor of IMR or hyperemic T_{mn}.

Kobayashi, et al. J Am Coll Cardiol Interv 2015;in press.

Sex Differences and CFR

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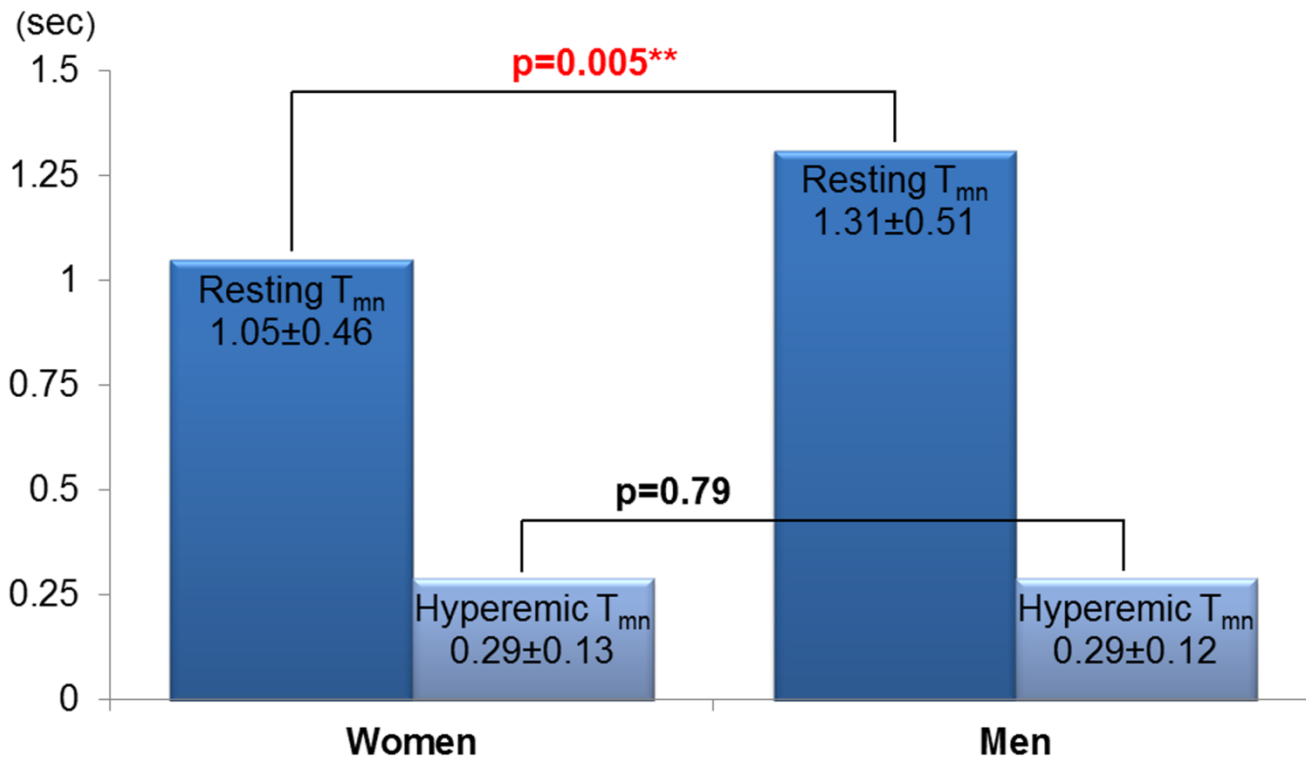

T_{mn}: an inverse correlate to absolute coronary flow

Kobayashi, et al. J Am Coll Cardiol Interv 2015;in press.

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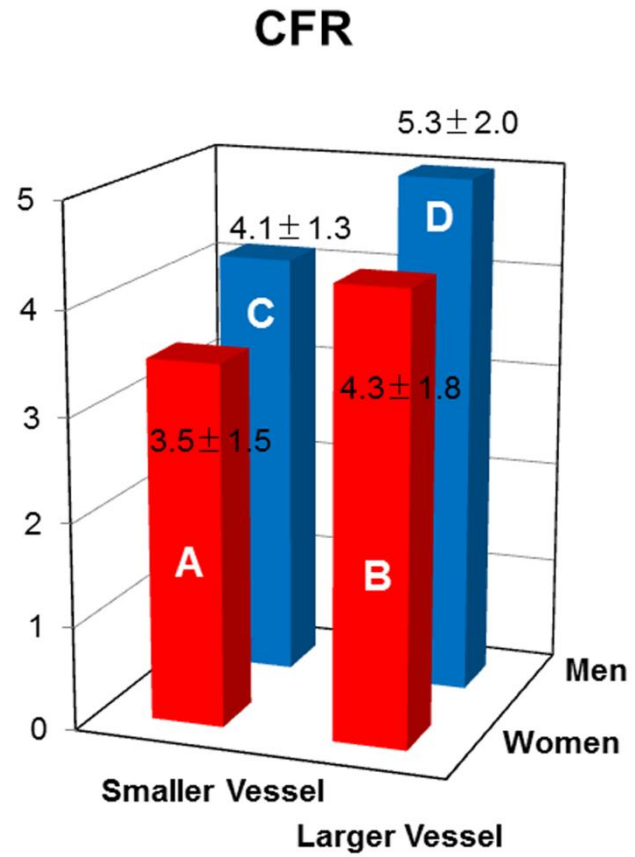
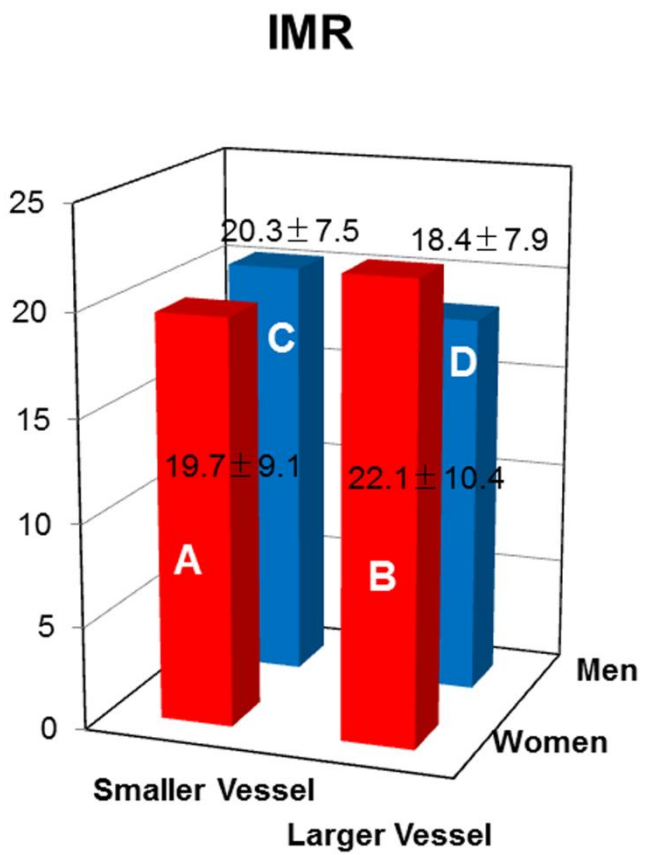


ANOVA p=0.002 (A vs. D, p=0.002)

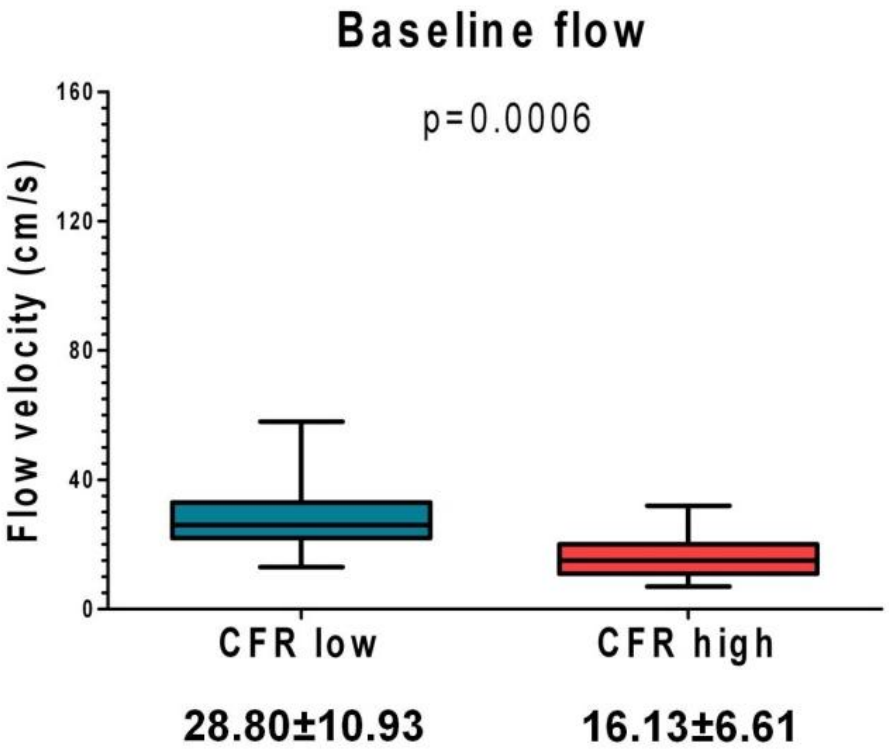


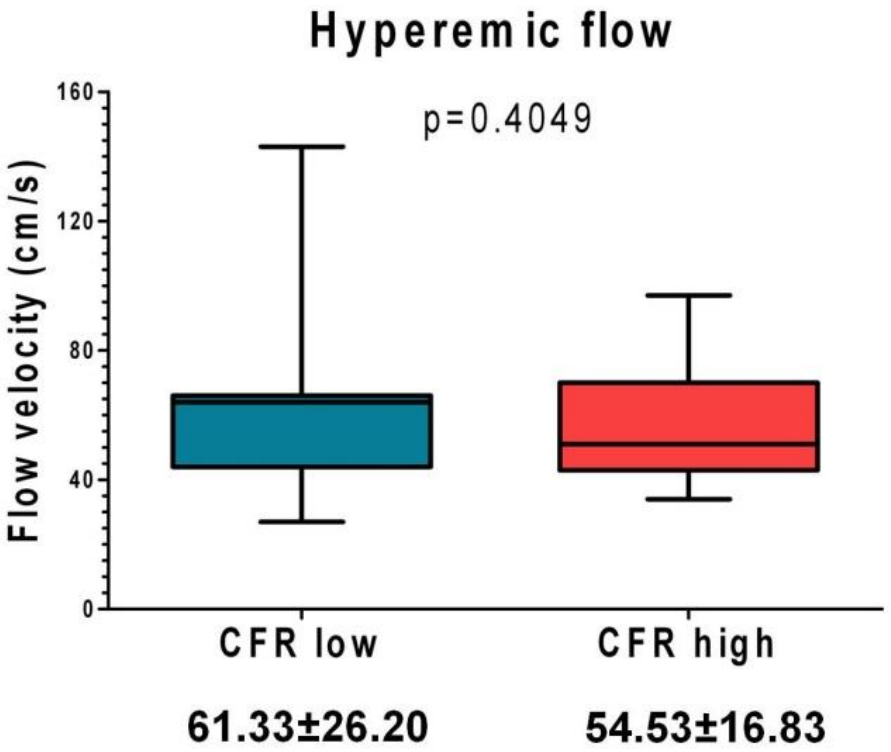
ANOVA p=0.41

Kobayashi, et al. J Am Coll Cardiol Interv 2015;in press.

“Resting Flow” and CFR

Doppler wire-derived CFR measured in 30 patients

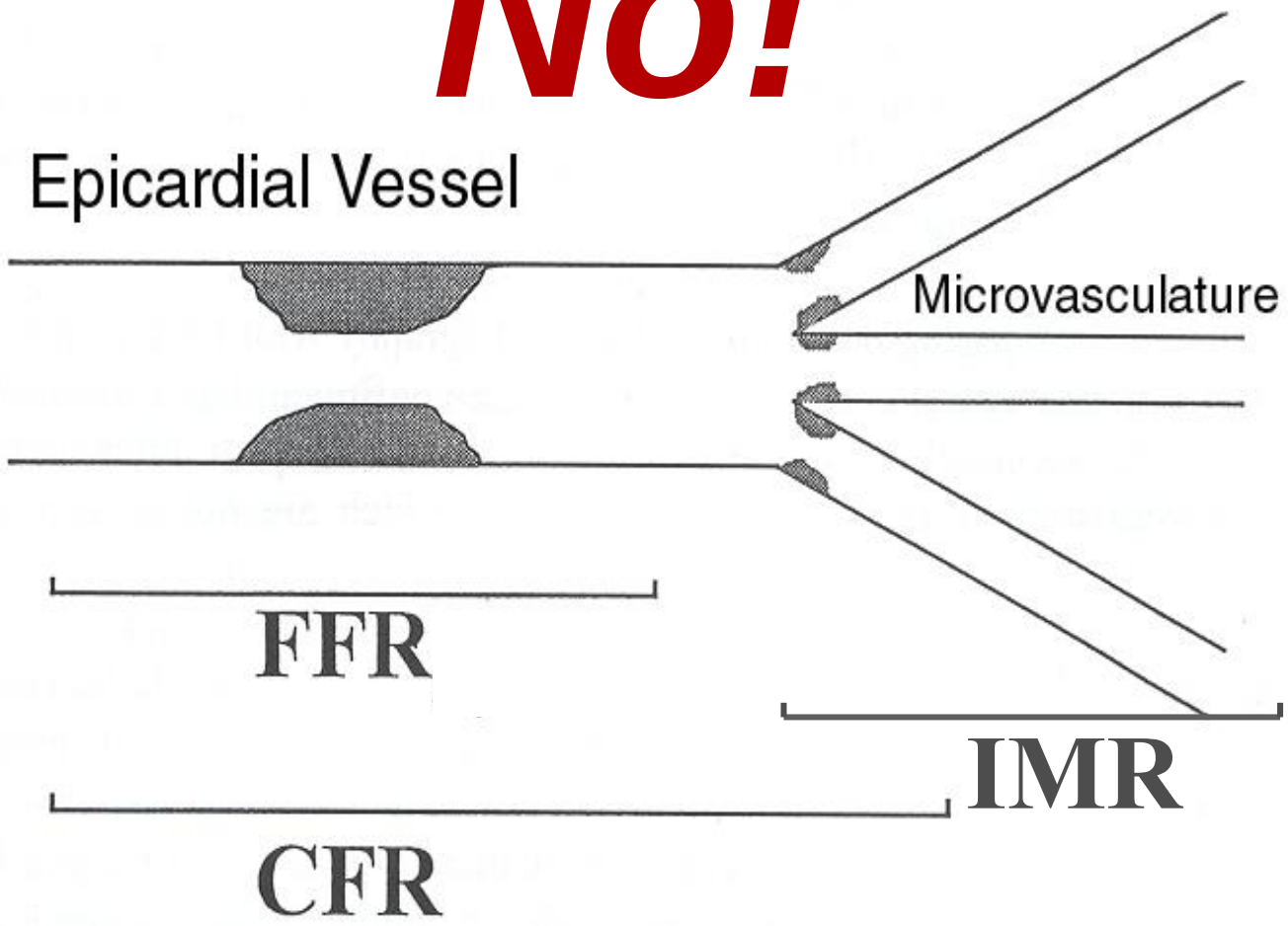




Adjedj, et al. J Am Coll Cardiol Interv 2015;in press.

Is there a discordance?

No!



Should we abandon CFR?

- Despite the aforementioned limitations, noninvasively derived CFR is clearly prognostic and therefore useful.
- In the cath lab, when dealing with an individual patient, FFR remains the gold standard for identifying epicardial disease capable of inducing ischemia and for guiding PCI.
- In the cath lab, IMR is more reproducible and specific for assessing the microvasculature and may be more predictive of outcomes.