

Fundamental Fallacies of FFR

**Coronary Vasomotion Disorders International Study Group
(COVADIS): 6th Annual Summit**

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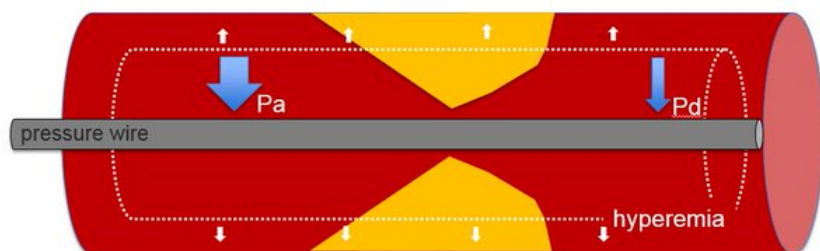
Washington University in St. Louis
SCHOOL OF MEDICINE

Disclosures

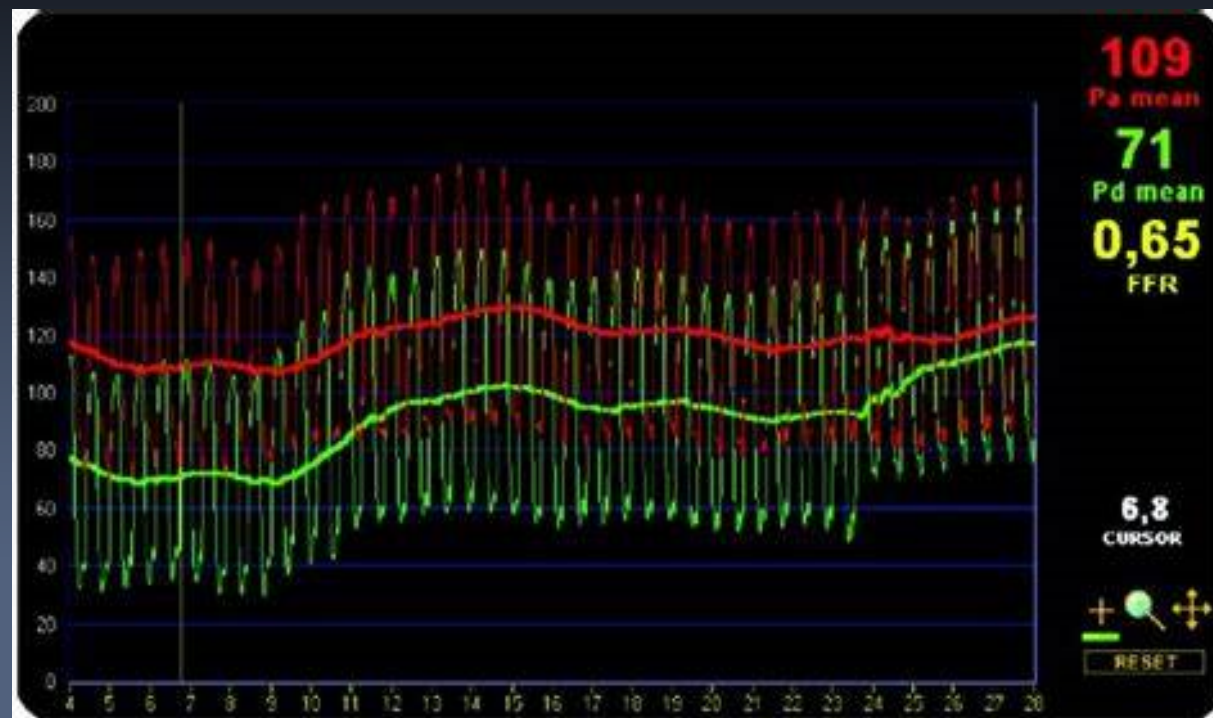
- None
 - I have no financial or intellectual conflicts of interest regarding the topic of today's discussion

Fractional Flow Reserve

FFR, an invasive assessment of coronary physiology

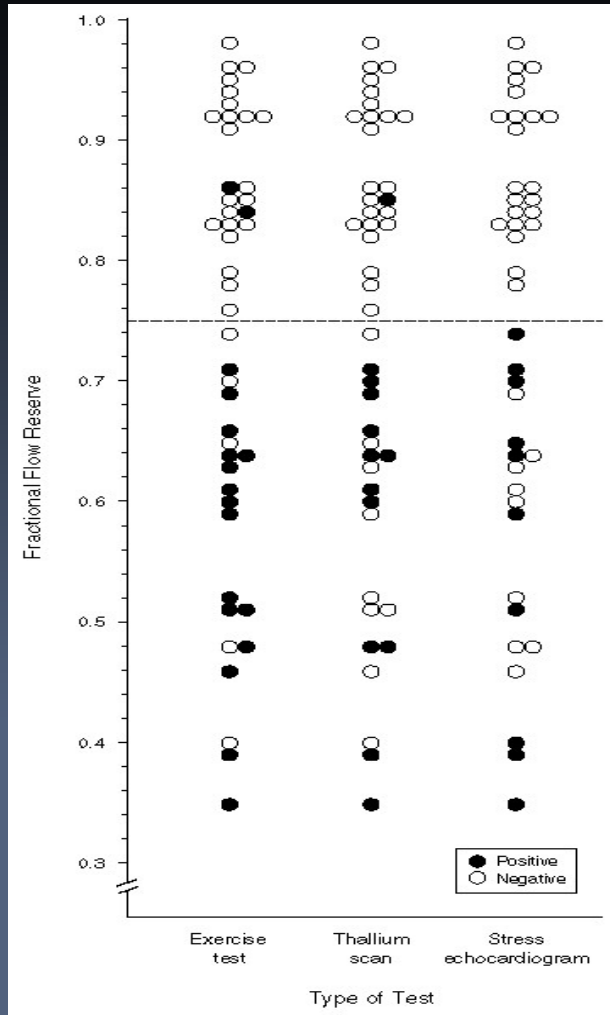


$$\text{Fractional Flow Reserve (FFR)} = \frac{\text{Distal coronary pressure (Pd)}}{\text{Proximal coronary pressure (Pa)}}$$



Derivation of FFR

Angiography Bad--→Calibrate FFR to Stress Tests--→ Stress Tests Calibrated Against Angiography



N=45

ORIGINAL ARTICLE ARCHIVE

Exercise Stress Testing — Correlations among History of Angina, ST-Segment Response and Prevalence of Coronary-Artery Disease in the Coronary Artery Surgery Study (CASS)

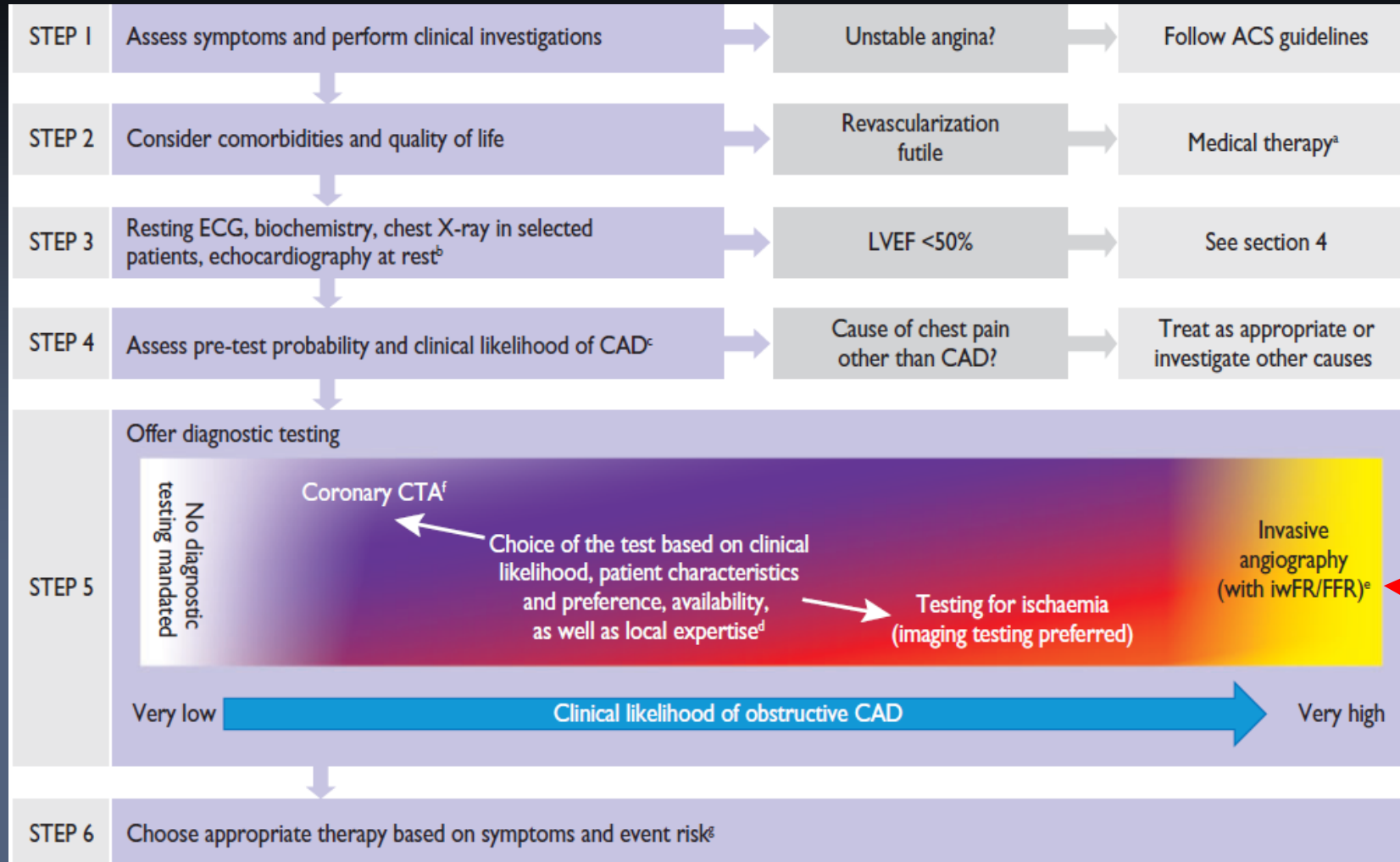
Exercise echocardiography as a screening test for coronary artery disease and correlation with coronary arteriography

**Myocardial Imaging
with Thallium-201 at Rest and during Exercise**

**Comparison with Coronary Arteriography and Resting
and Stress Electrocardiography**

Pijls NH et al. N Engl J Med 1996;334:1703-1708.

2019 ESC Chronic Coronary Syndromes Guidelines



Four Fundamental Fallacies of FFR

1. Ischemia caused by an obstructive epicardial coronary stenosis is on the direct pathway to death/MI and should be a target of revascularization
2. The microvasculature is irrelevant in the assessment of coronary physiology and pathophysiology
3. FFR-guided PCI improves outcomes through targeted lesion selection (FAME)
4. FFR-guided PCI improves outcomes compared to OMT (FAME 2)

Fallacy 1: Ischemia caused by an obstructive epicardial coronary stenosis is on the direct pathway to death/MI and should be a target of revascularization

The Foundational Premise of FFR

MINI-FOCUS ISSUE: OPTICAL COHERENCE TOMOGRAPHY

State-of-the-Art Paper

Functional Measurement of Coronary Stenosis

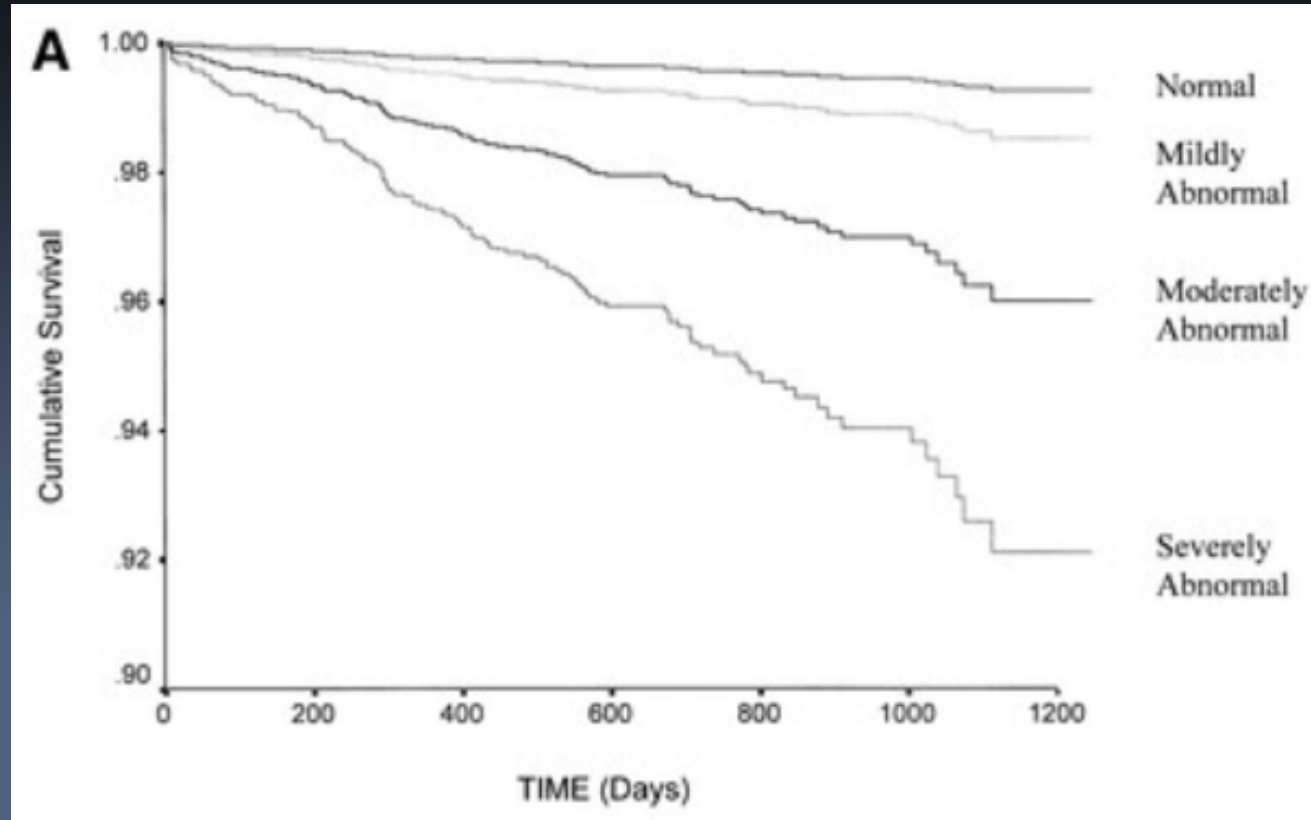
Nico H. J. Pijls, MD, PhD, Jan-Willem E. M. Sels, MD

Eindhoven, the Netherlands

- *"In coronary artery disease, the most important factor related to outcome is the presence and extent of inducible ischemia."*
- *"Functionally significant stenoses should be revascularized, if technically possible."*

Association of Ischemia with Cardiac Death

Association $\neq$ Causation

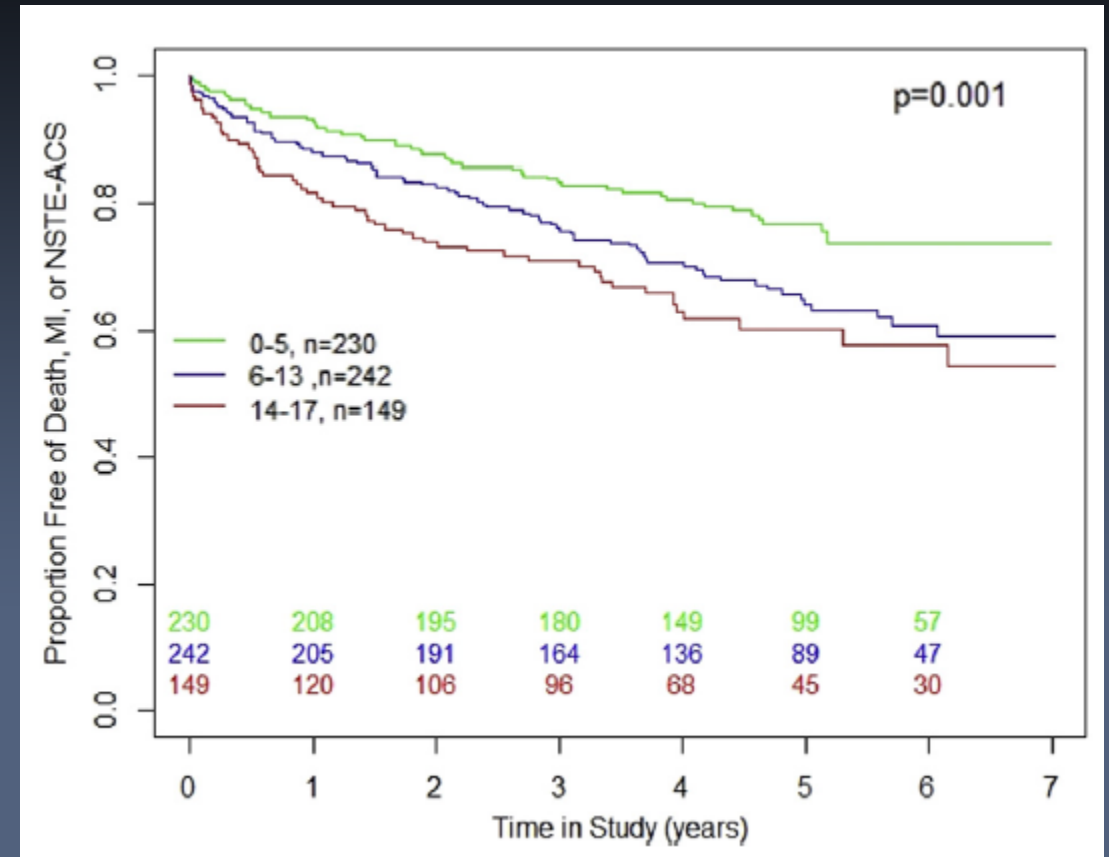
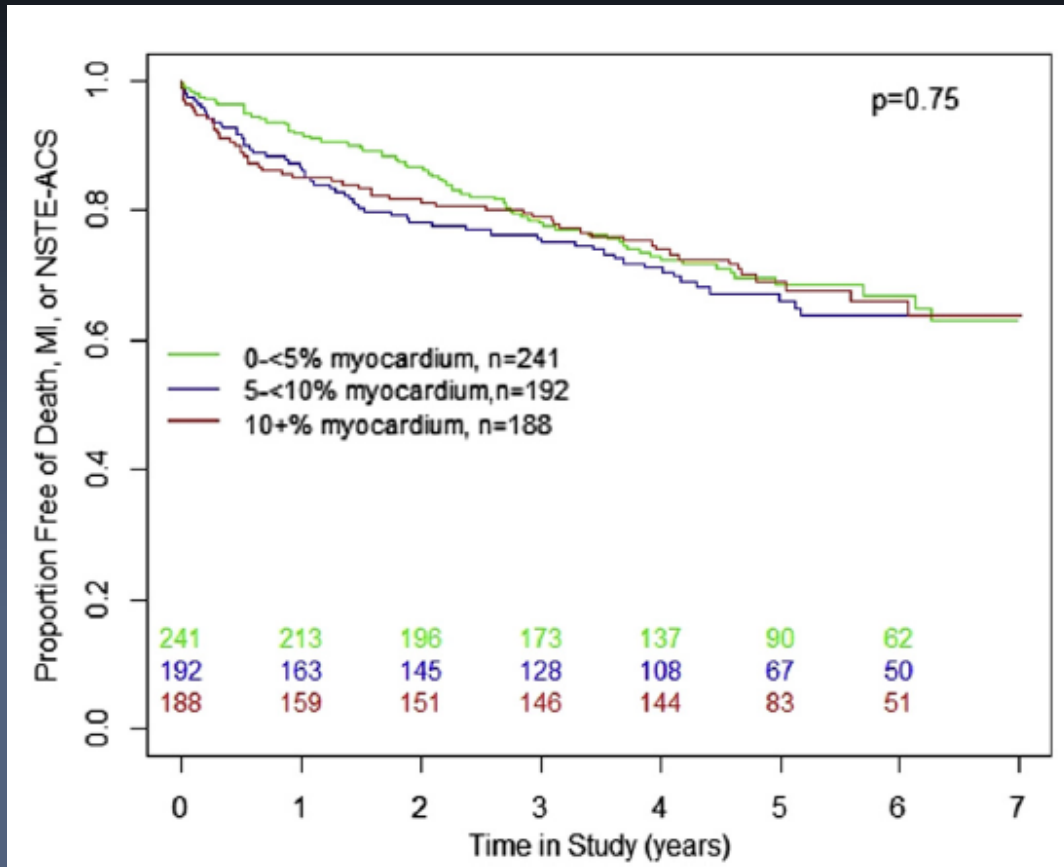


Hachamovitch et al. *Circulation*. 1998;97:535–543

Ischemia vs. Atherosclerotic Burden in COURAGE

Ischemic burden:
OR 1.01 (0.98–1.03) P=0.54

Atherosclerotic burden:
OR 1.05 (1.02–1.08) P=0.002

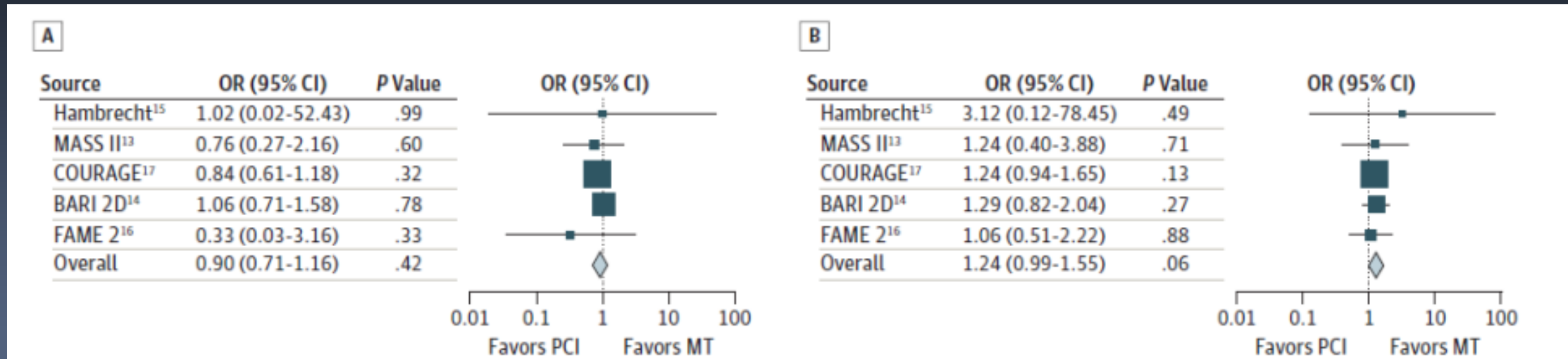


J Am Coll Cardiol Interv 2014;7:195–201

PCI Does Not Reduce Death or MI in Patients with Ischemia

Death

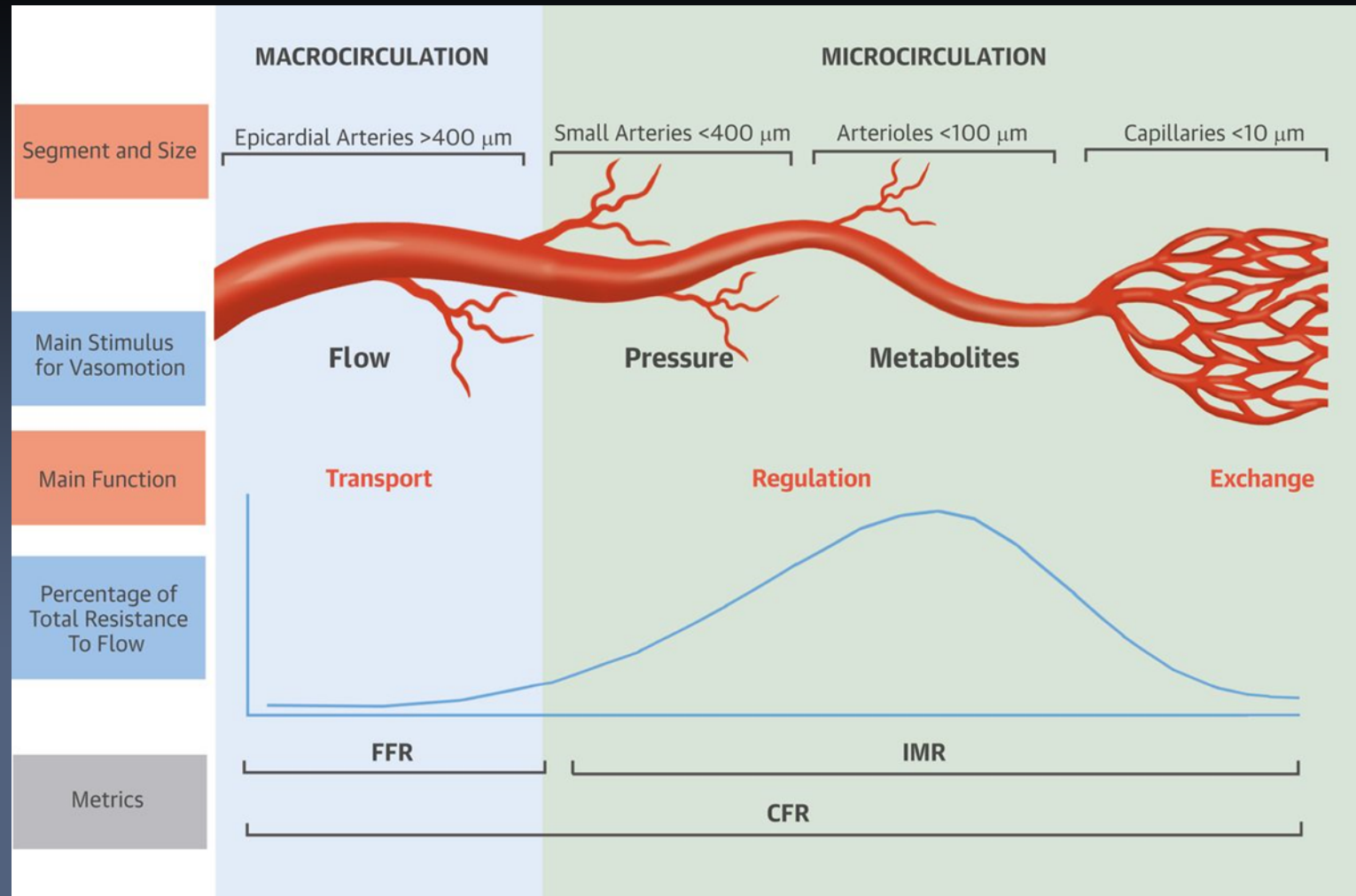
MI



Stergiopoulos et al. JAMA Intern Med. 2014;174(2):232-240

Fallacy 2: The microvasculature is irrelevant in the assessment of coronary physiology and pathophysiology

Focus on FFR Obscures the Critical Role of the Microvasculature

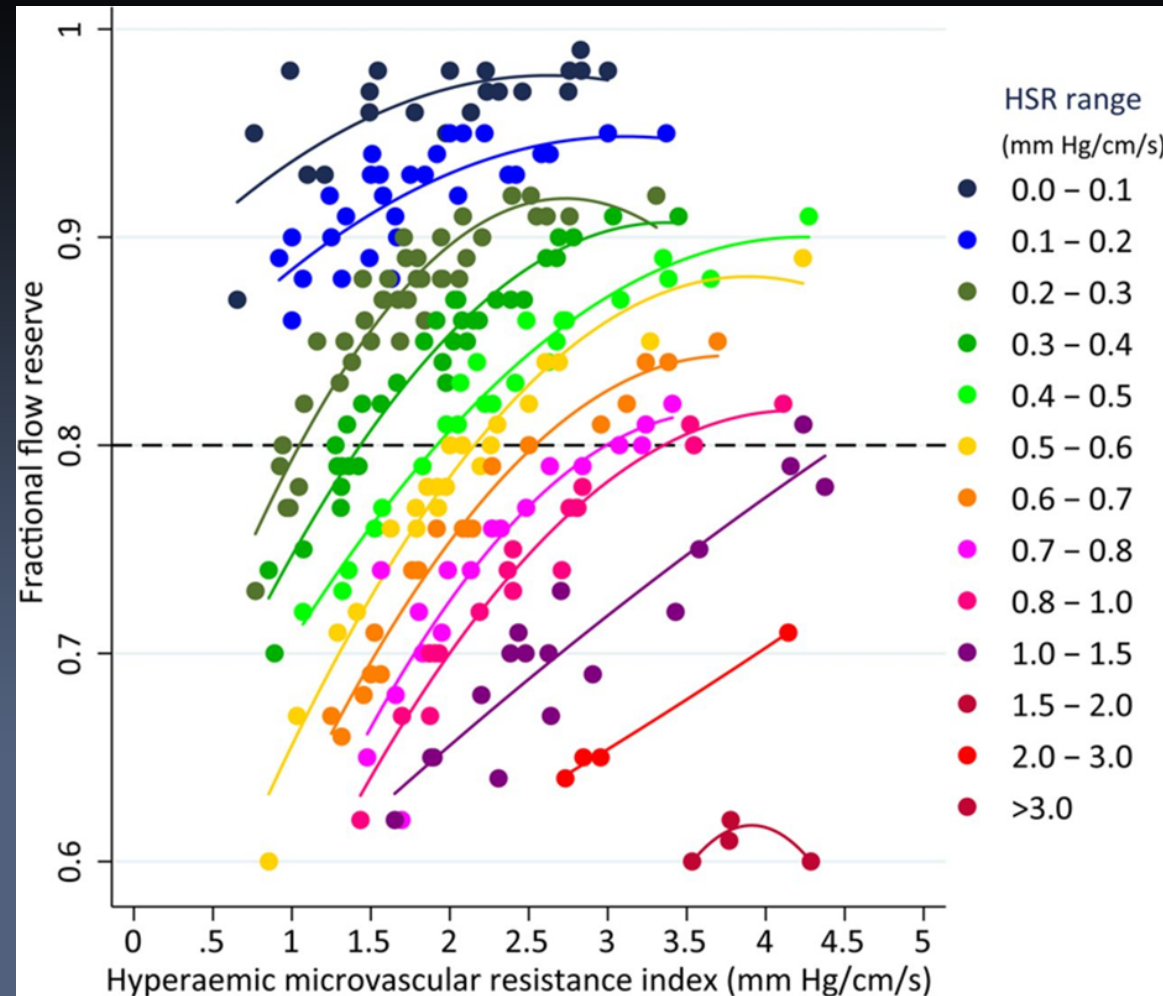


CFR=Coronary flow reserve

IMR=index of microcirculatory resistance= $P_d \times T_{mn}$

Impact of Coronary Microvascular Dysfunction on FFR- Worst Case Scenario

HMR =
mean distal coronary
pressure/
mean distal flow velocity at
maximum hyperemia



For a given epicardial
disease severity, FFR
increases with
increasing HMR (MVD)

Tim P van de Hoef et al. Heart 2014;100:951-959

FFR May Miss Diffuse Atherosclerosis

RESEARCH CORRESPONDENCE

Coronary Microvascular Dysfunction Is Associated With Significant Plaque Burden and Diffuse Epicardial Atherosclerotic Disease



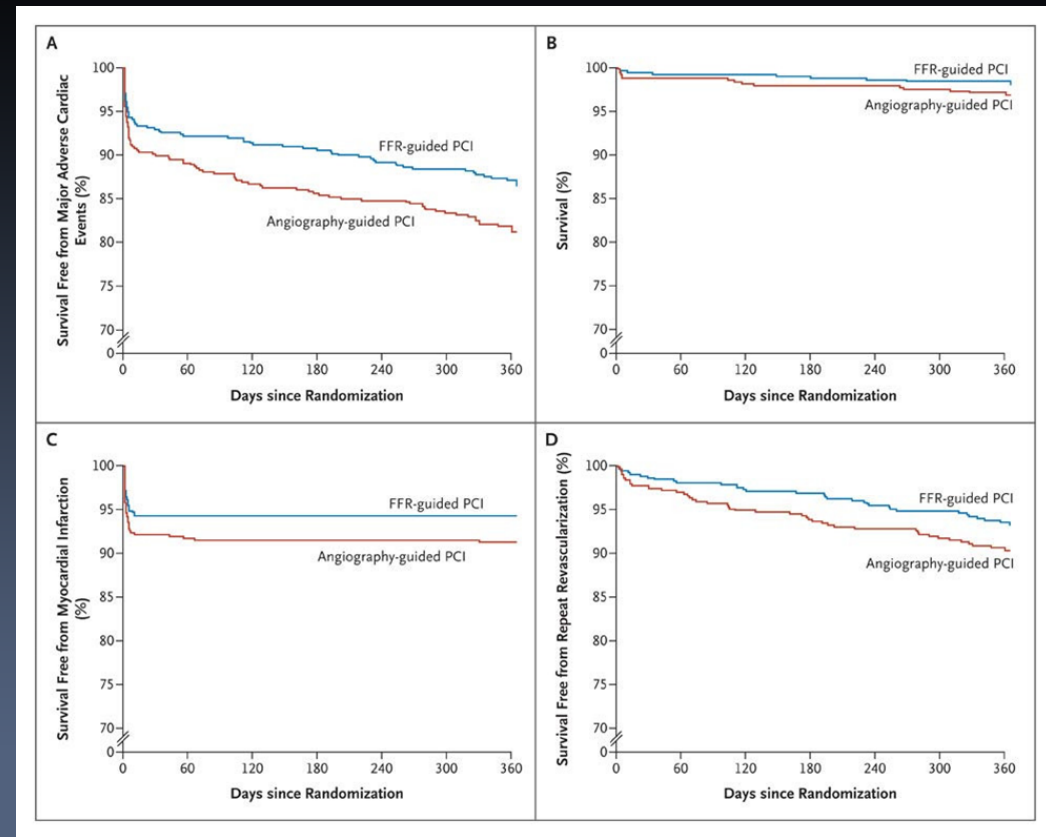
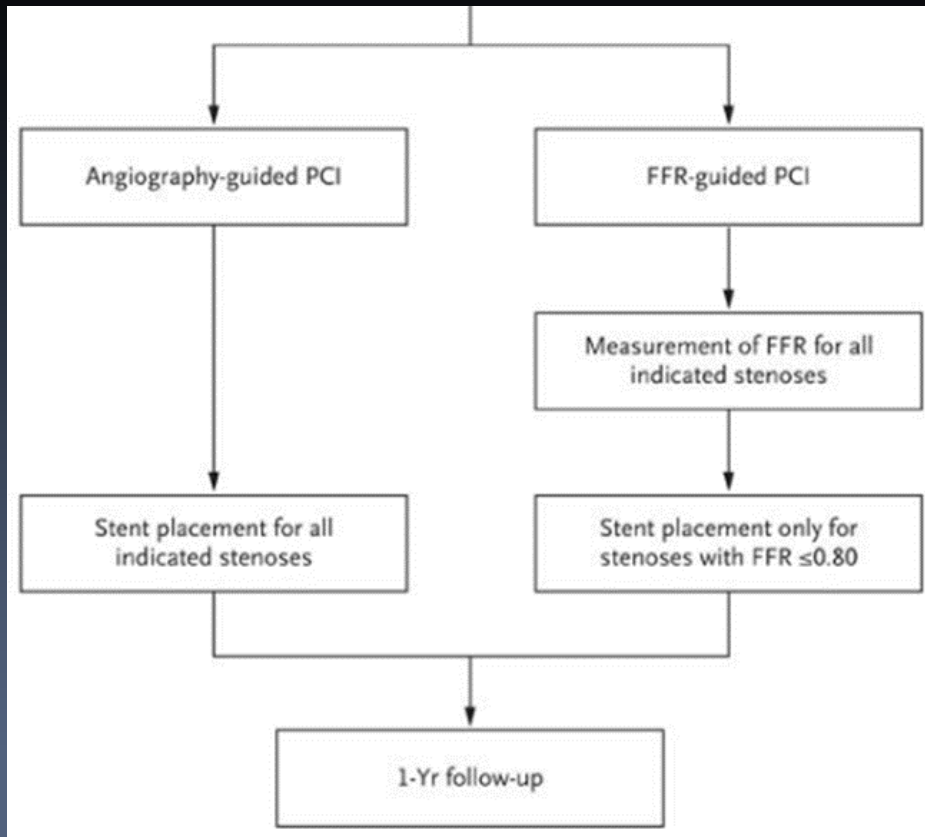
TABLE 1 Patients and Vessels Characteristics

	All Patients (N = 77)	CMD (Abnormal HMR) (n = 30)	No CMD (Normal HMR) (n = 47)	p Value*
Age, yrs	56 ± 10	60 ± 9	53 ± 10	0.003
Male	39 (51)	15 (50)	24 (51)	0.99
Hypertension	55 (71)	23 (77)	32 (68)	0.45
Diabetes mellitus	18 (23)	12 (40)	6 (13)	0.012
Dyslipidemia	59 (77)	22 (73)	37 (79)	0.59
Total cholesterol	163 ± 36	161 ± 33	164 ± 37	0.85
HDL cholesterol	44 ± 12	44 ± 11	44 ± 13	0.96
LDL cholesterol	95 ± 32	92 ± 35	98 ± 30	0.42
HMR	1.9 ± 0.7	2.62 ± 0.49	1.47 ± 0.32	<0.001
FFR	0.93 ± 0.06	0.94 ± 0.05	0.92 ± 0.07	0.13
EEM area, mm ²	15.7 ± 4.3	16.2 ± 4.4	15.4 ± 4.3	0.55
Lumen area, mm ²	9.7 ± 3.2	9.5 ± 3.2	9.8 ± 3.1	0.75
MLA, mm ²	5.1 ± 2.4	4.7 ± 1.8	5.3 ± 2.8	0.76
Plaque area, mm ²	6.9 ± 7.5	8.3 ± 10.7	6.0 ± 4.3	0.14
Minimum PB%	18.8 ± 9.8	21.9 ± 9.8	16.8 ± 9.4	0.02
Median PB%	37 ± 15.3	41.3 ± 13.0	34.3 ± 16.1	0.04
Maximum PB%	61.3 ± 18.1	67.4 ± 15.3	57.5 ± 18.9	0.037
Percentage of IVUS frames with PB ≥40%	41 ± 35	50.1 ± 34.3	34.2 ± 33.5	0.039

JACC: Cardiovascular Interventions 2019; 12: 1516–20

Fallacy 3: FFR-guided PCI improves outcomes through targeted lesion selection

FAME Trial



In **37%** of lesions, the FFR was greater than 0.80 and PCI was not performed.

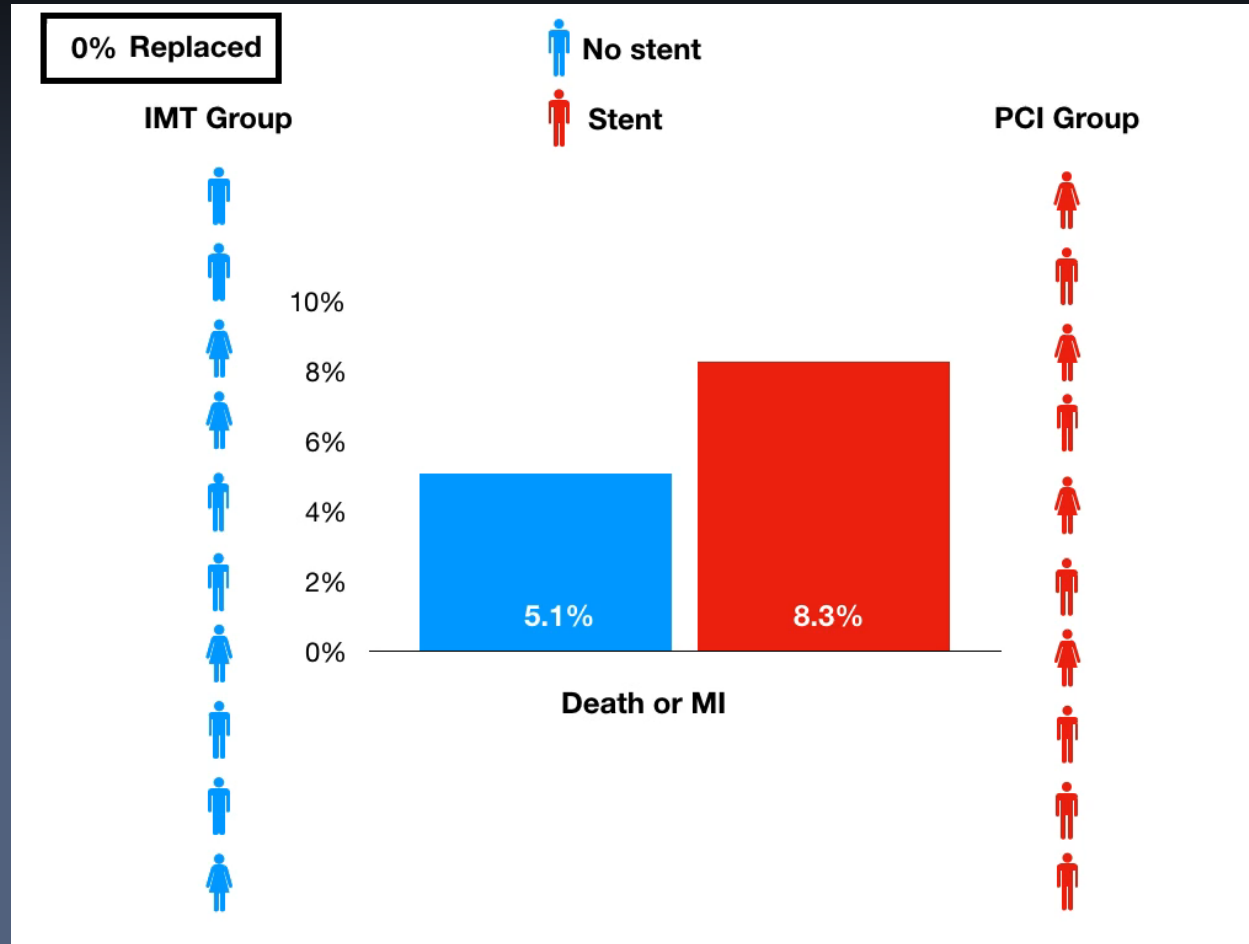
	Angio	FFR	Relative Risk
Death or MI-no (%)	55(11.1)	37(7.3)	0.66 (0.44-0.98)

N Engl J Med 2009; 360:213-224

Critical Unanswered Question

Was the reduction in death/MI seen with FFR-guided PCI the result of avoidance of hemodynamically insignificant lesions or simply the result of putting in 37% fewer stents?

A BARI 2D Simulation: Random(as opposed to FFR-guided) Selection of Patients for Deferral of PCI



Fallacy 4: FFR-guided PCI improves outcomes compared to OMT

FAME 2

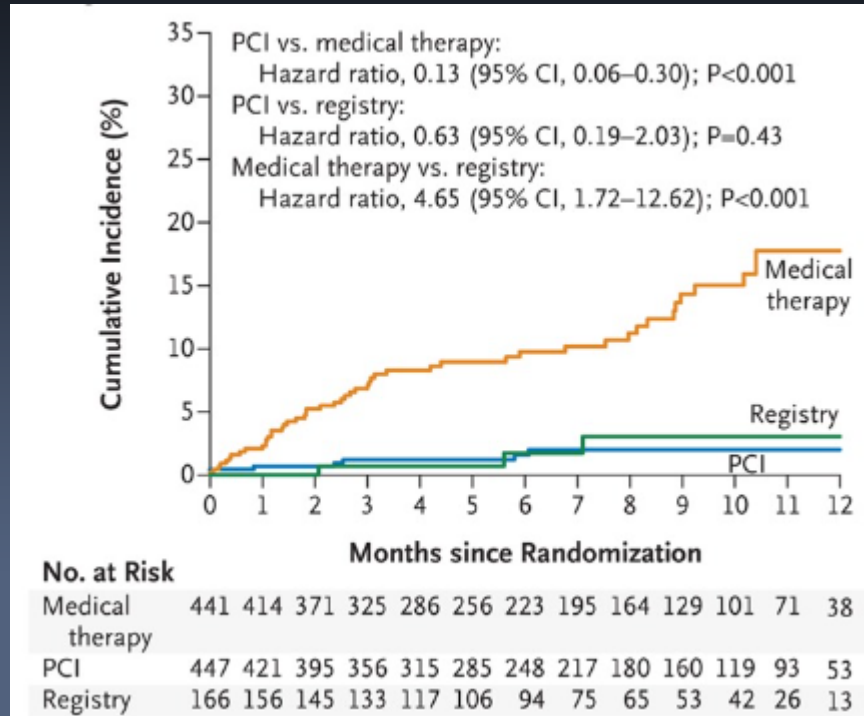
ORIGINAL ARTICLE

Fractional Flow Reserve–Guided PCI versus Medical Therapy in Stable Coronary Disease

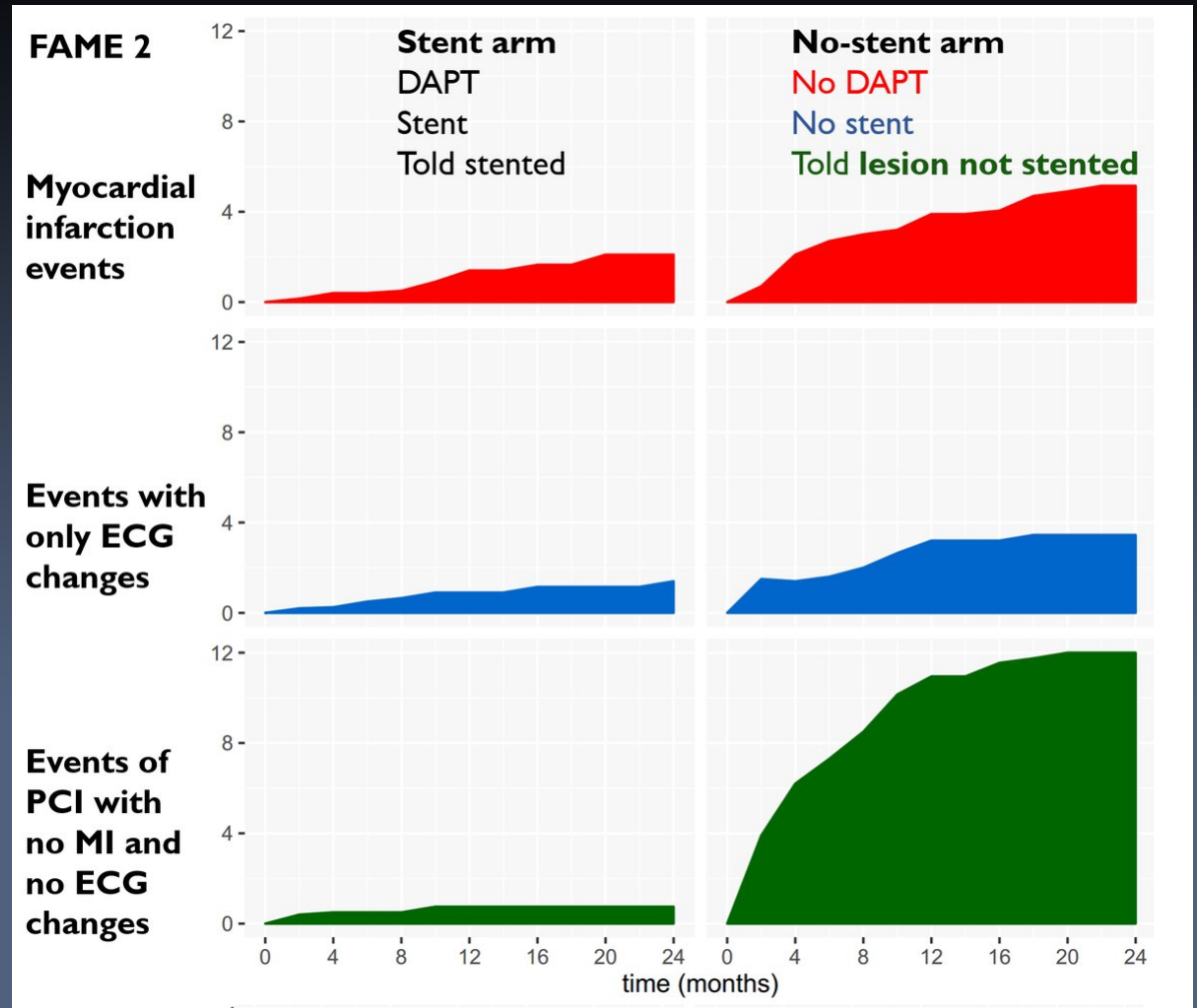
F/U		N	Death (%)			MI (%)		
			PCI	MT	P	PCI	MT	P
213 days	NEJM	888	0.2	0.7	0.31	3.4	3.2	0.89
3 years	Circ	888	2.7	3.6	0.43	6.3	7.7	0.41
5 years	NEJM	784	5.1	5.2	0.98 (0.55-1.75)	8.1	12	0.66(0.43-1.00)

N Engl J Med 2012; 367:991-1001

What About the Urgent Revascularizations? 'Faith Healing' and 'Subtraction Anxiety' in FAME 2

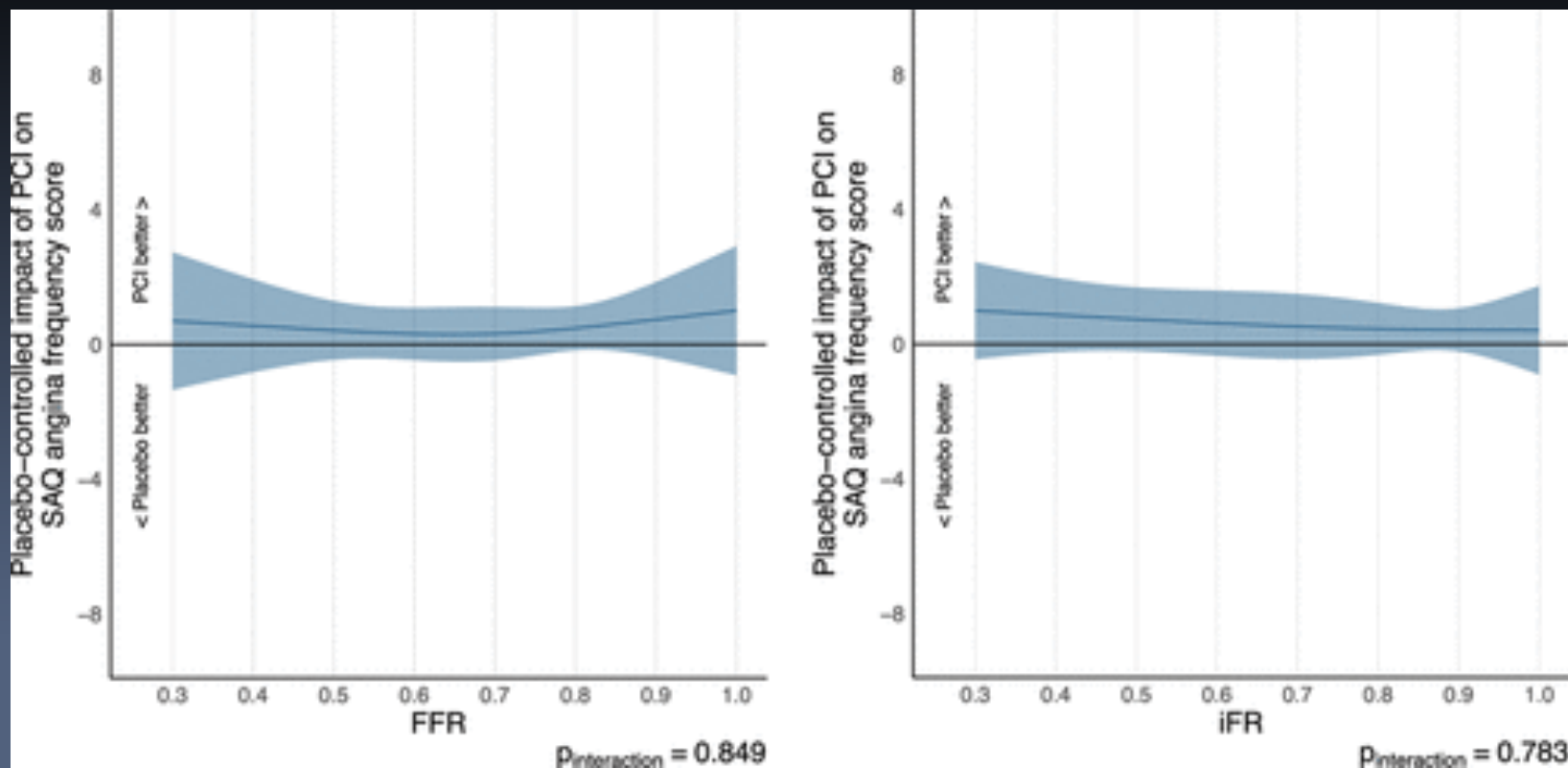


N Engl J Med 2012; 367:991-1001



Circulation: Cardiovascular Quality and Outcomes. 2018;11:e004665

Impact of Baseline FFR on Angina Relief in ORBITA



Circulation. 2018;138:1780–1792

Conclusions

- FFR, in isolation, is of no value in the evaluation of patients with suspected ischemia
- The ESC guidelines continue to promote an outdated paradigm for evaluation of suspected ischemia
- Ideally, the entire coronary vasculature should be assessed for a comprehensive understanding of the pathophysiology and preferred treatment of individual patients

Thank You!