FFR Clinical Trials and Applications: *Changing the Practice of PCI*

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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**
Consulting Fees/Honoraria:	**Tryton Medical**
Major Stock Shareholder/Equity Interest:	
Royalty Income:	
Ownership/Founder:	
Salary:	
Intellectual Property Rights:	
Other Financial Benefit (minor stock options):	**HeartFlow**

Overview:

- Validation and application of FFR in single vessel, intermediate CAD
- FFR in specific subsets:
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  - After myocardial infarction
- FFR in multivessel CAD
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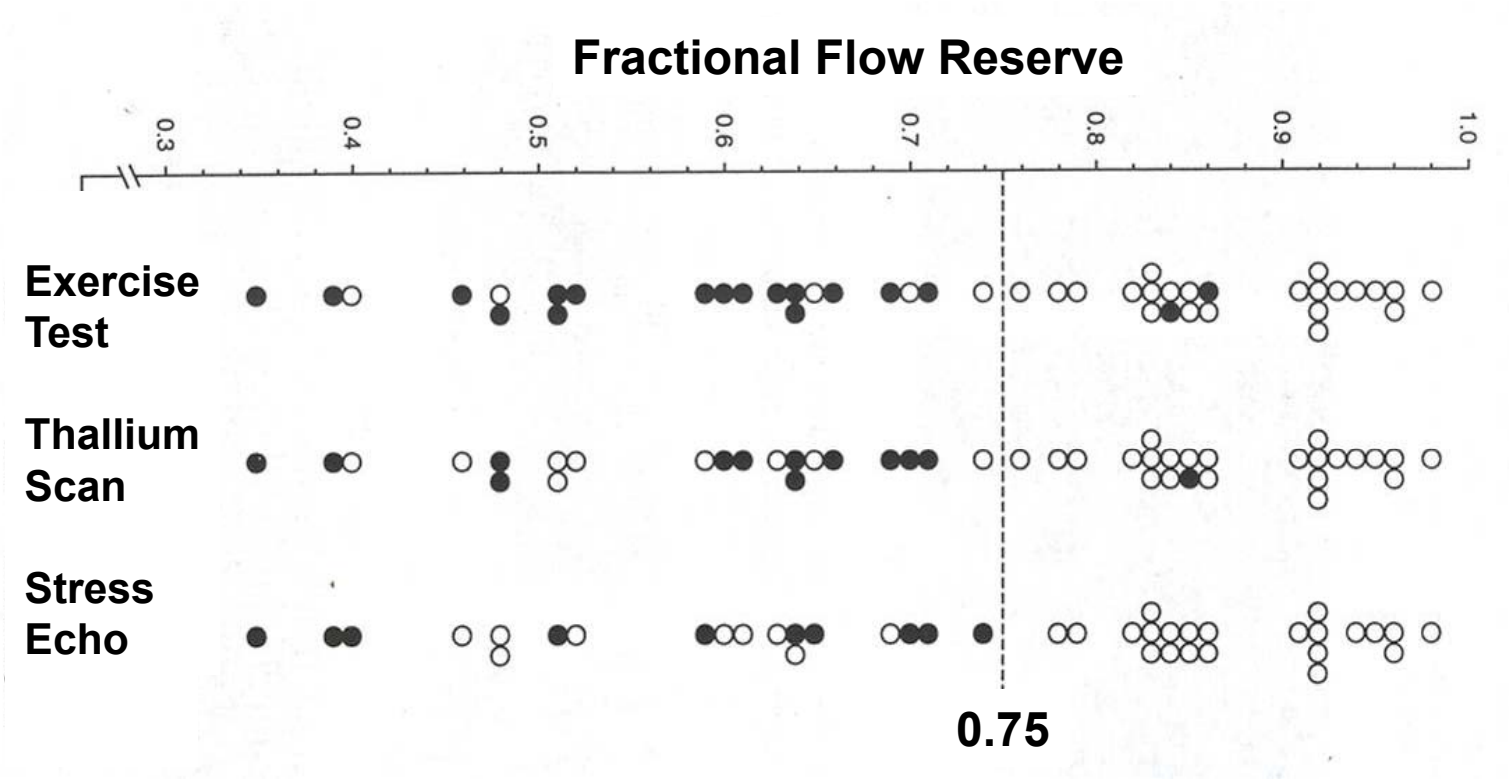
  - FAME 2
  - FAME 3

Validation of FFR

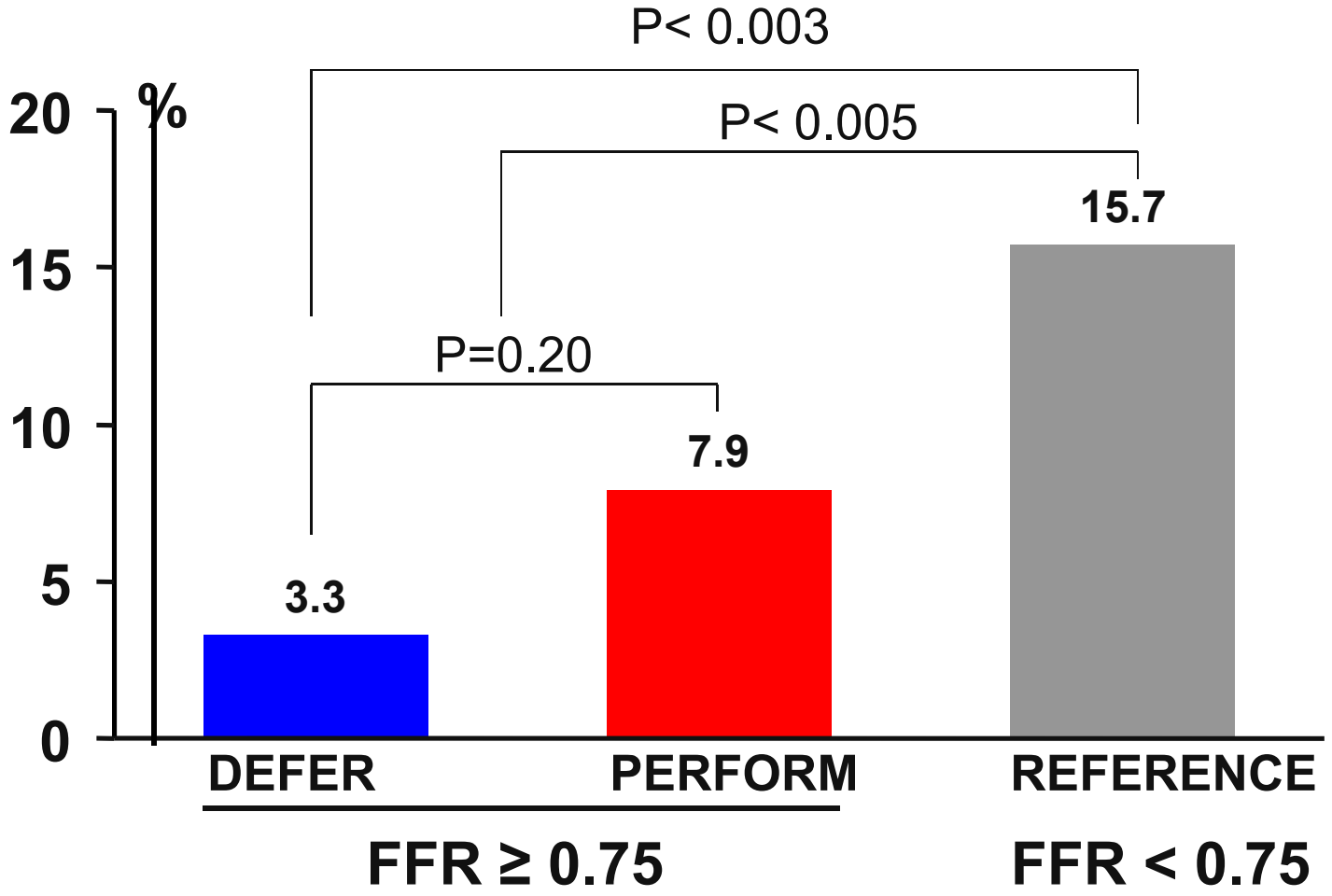


FFR < 0.75 : Sensitivity = 88%
Specificity = 100%

Pijls et al., New Engl J Med 1996;334:1703

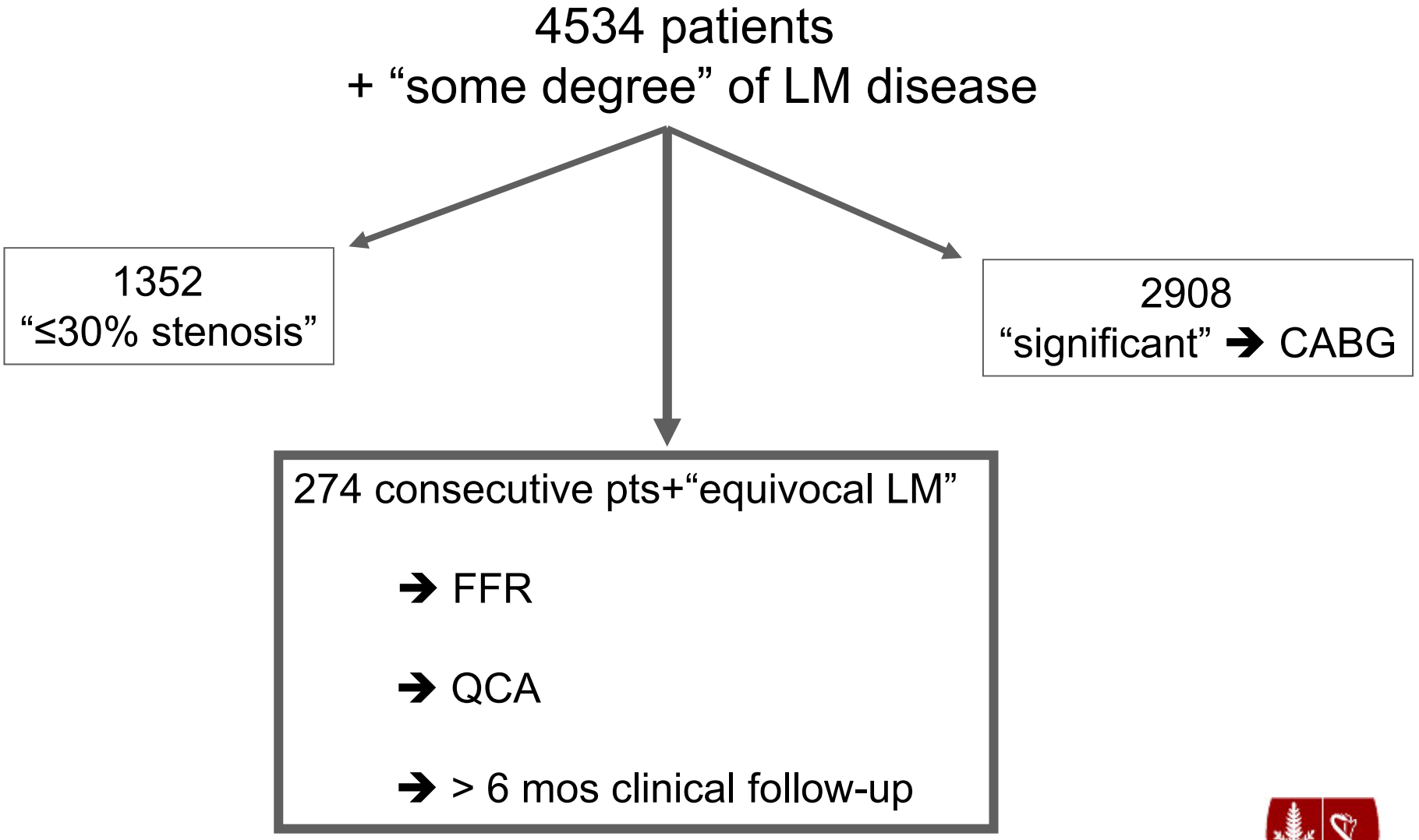
Safety of Deferring PCI Based on FFR

5 Year Cardiac Death and Acute MI rate in DEFER trial



Pijls, et al. J Am Coll Cardiol 2007;49:2105-11

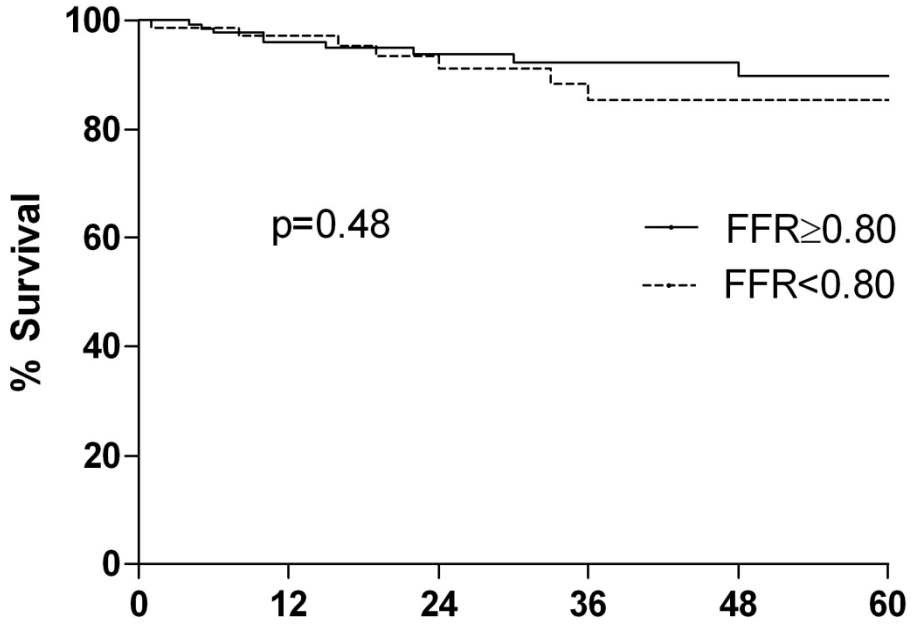
FFR and Intermediate Left Main



Hamilos, et al., Circulation 2009;120:1505

FFR and Intermediate Left Main

Survival Rate

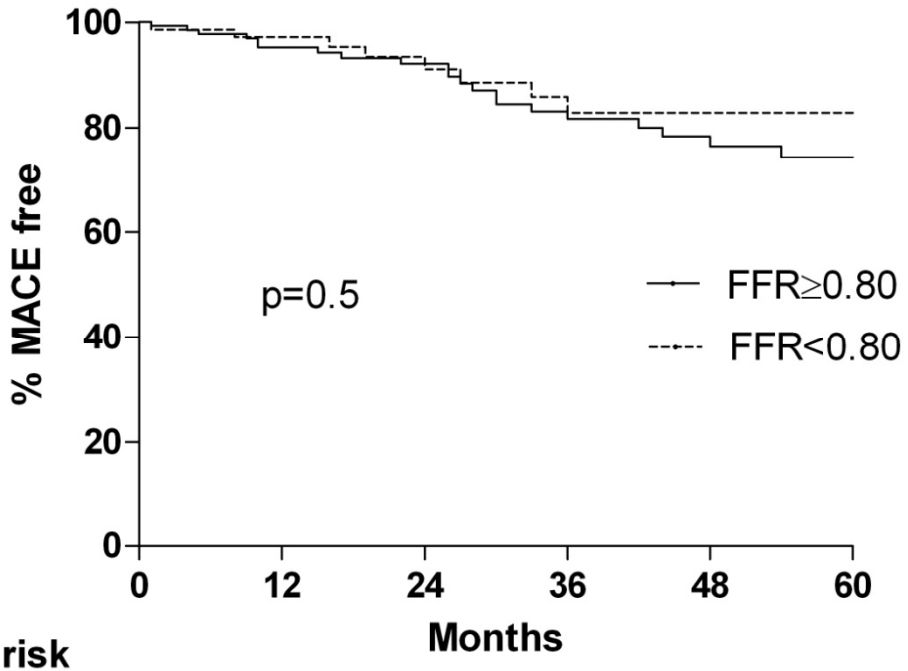


No at risk						
FFR≥0.80	136	103	72	52	38	26
FFR<0.80	73	56	41	30	14	10

Hamilos, et al., Circulation 2009;120:1505

FFR and Intermediate Left Main

MACE Rate



No at risk						
FFR≥0.80	136	106	77	57	42	30
FFR<0.80	73	56	40	29	15	10

Hamilos, et al., Circulation 2009;120:1505

Overview:

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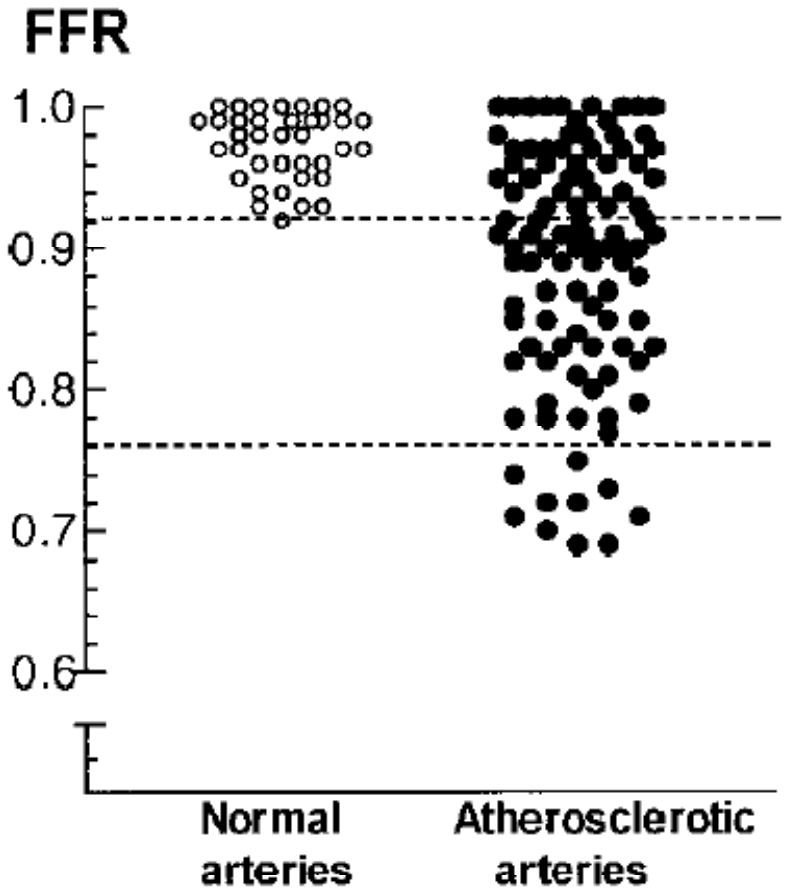
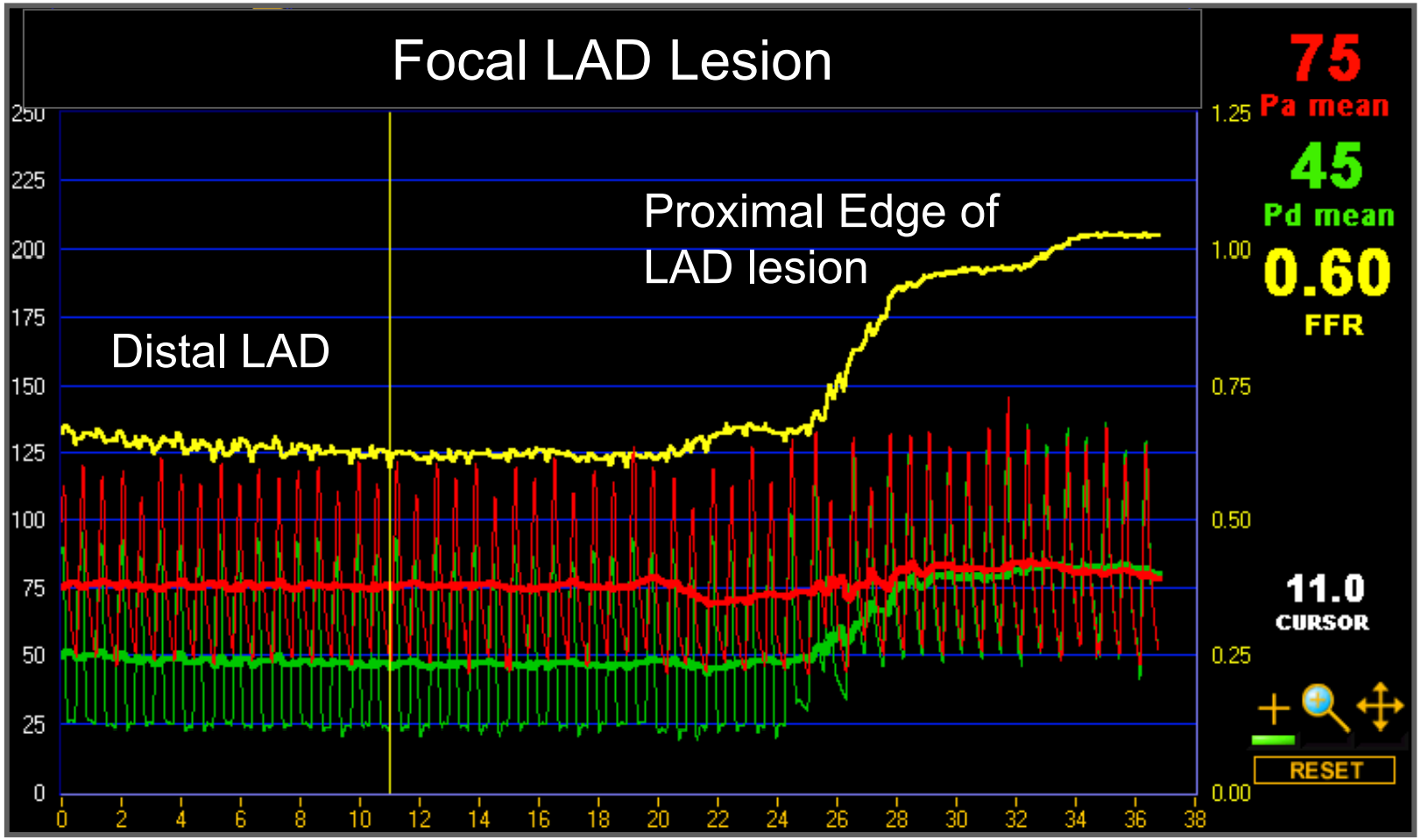
FFR in Diffuse Disease

FFR measured in 37 arteries in 10 patients without CAD and in 107 nonstenotic adjacent arteries in 62 patients with CAD

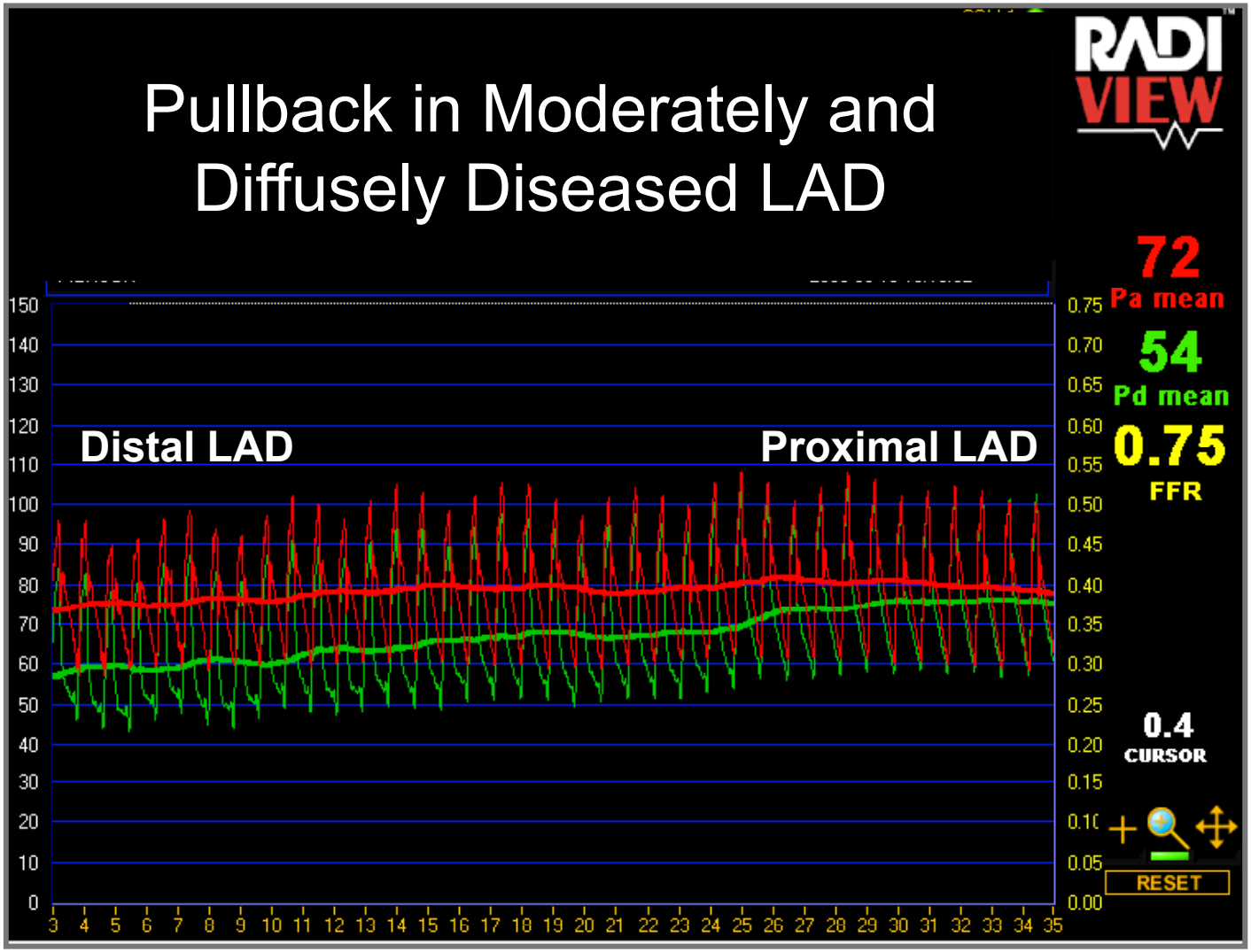


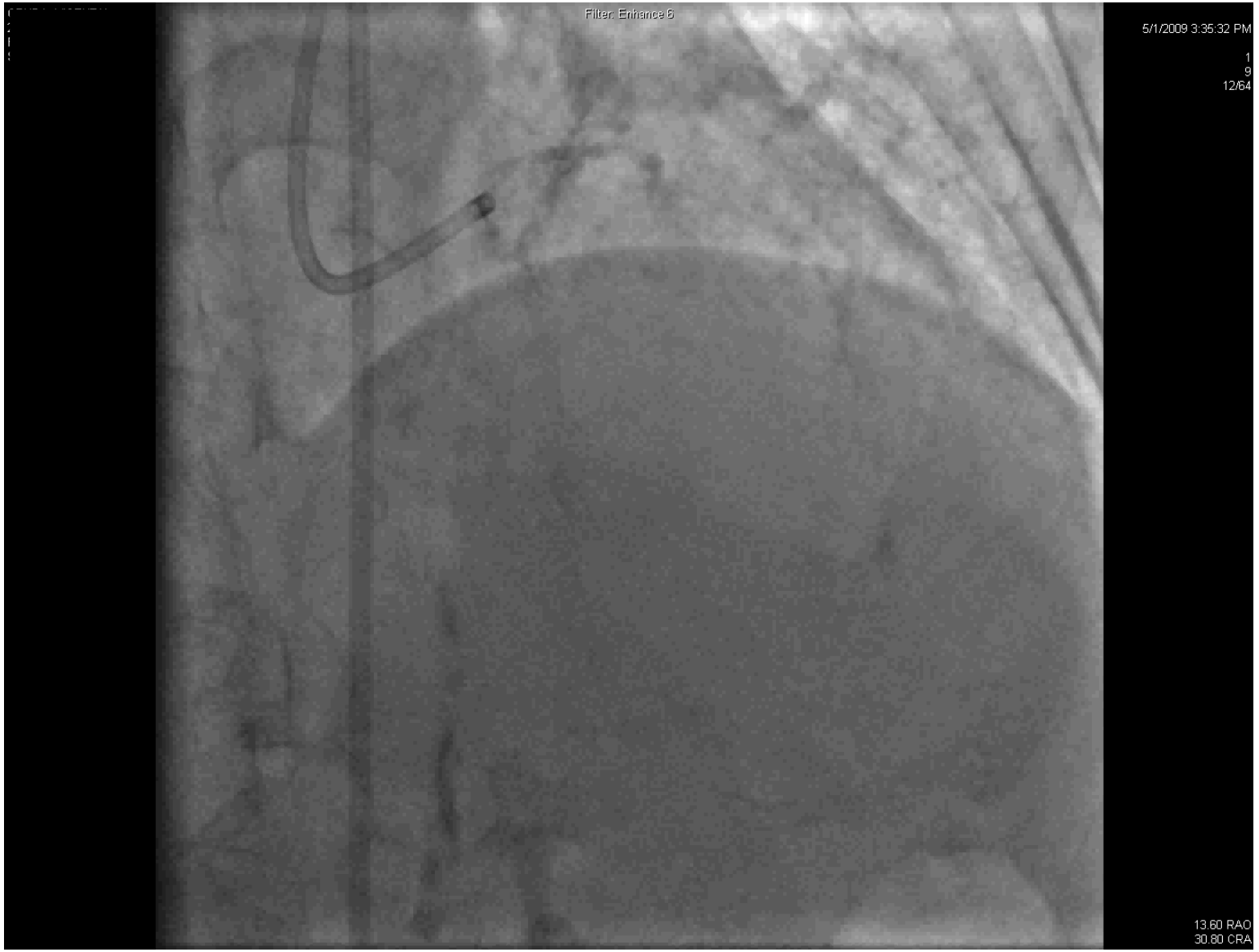
De Bruyne et al. Circulation 2001;104:2401

FFR Pullback



FFR Pullback

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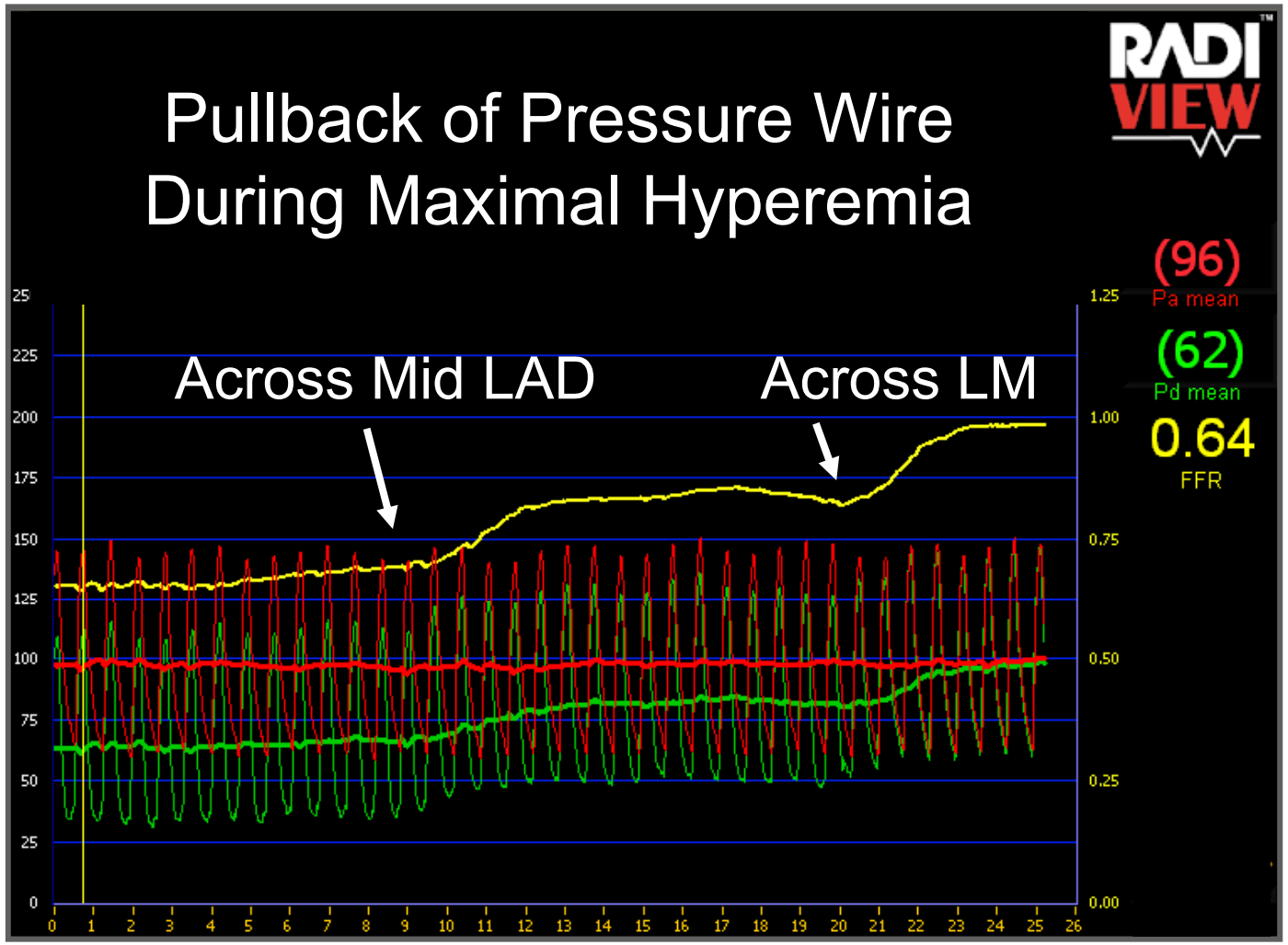
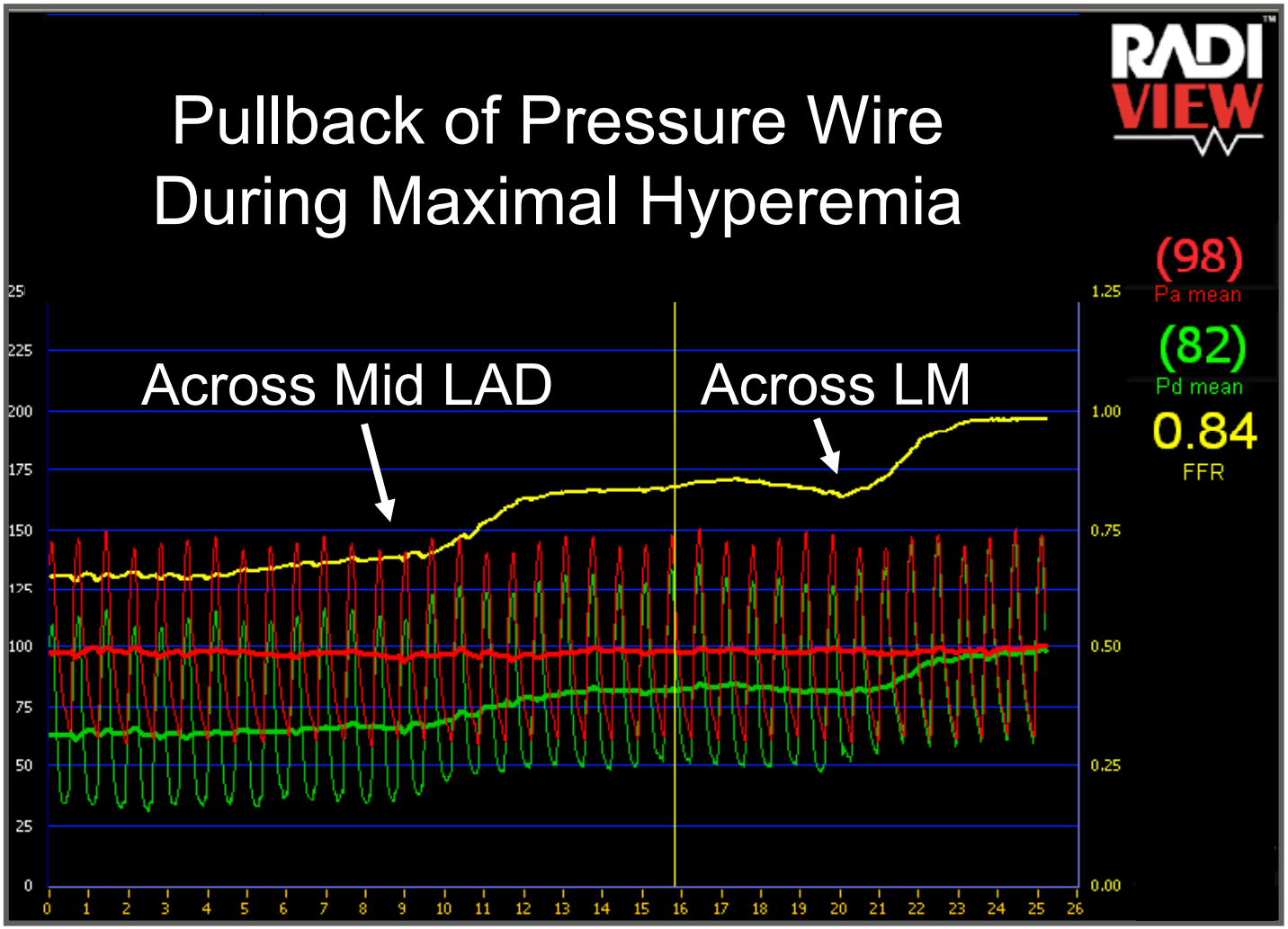
1
9
12/64
13.60 RAO
30.80 CRA

FFR in Tandem Lesions



FFR in Tandem Lesions



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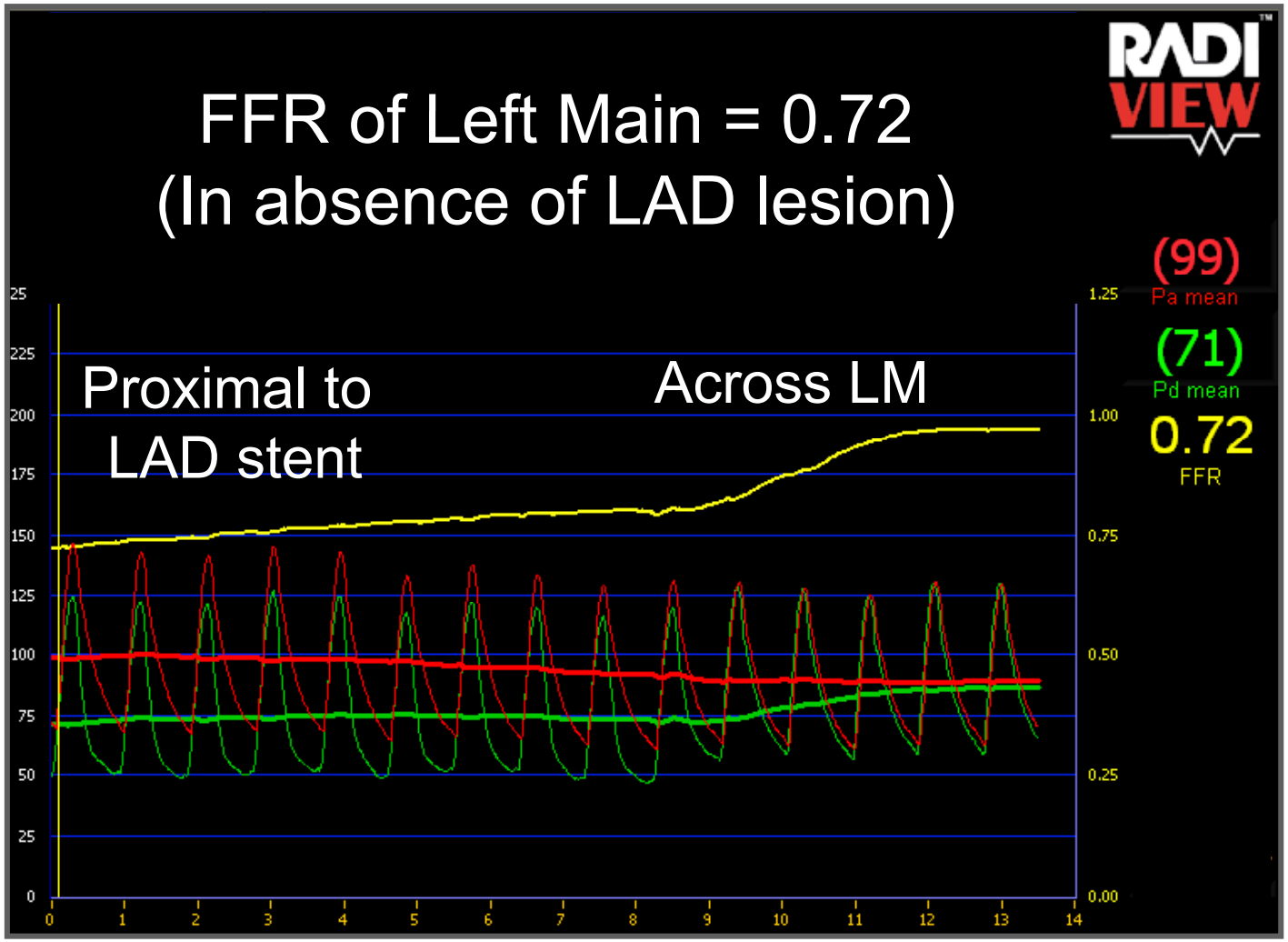
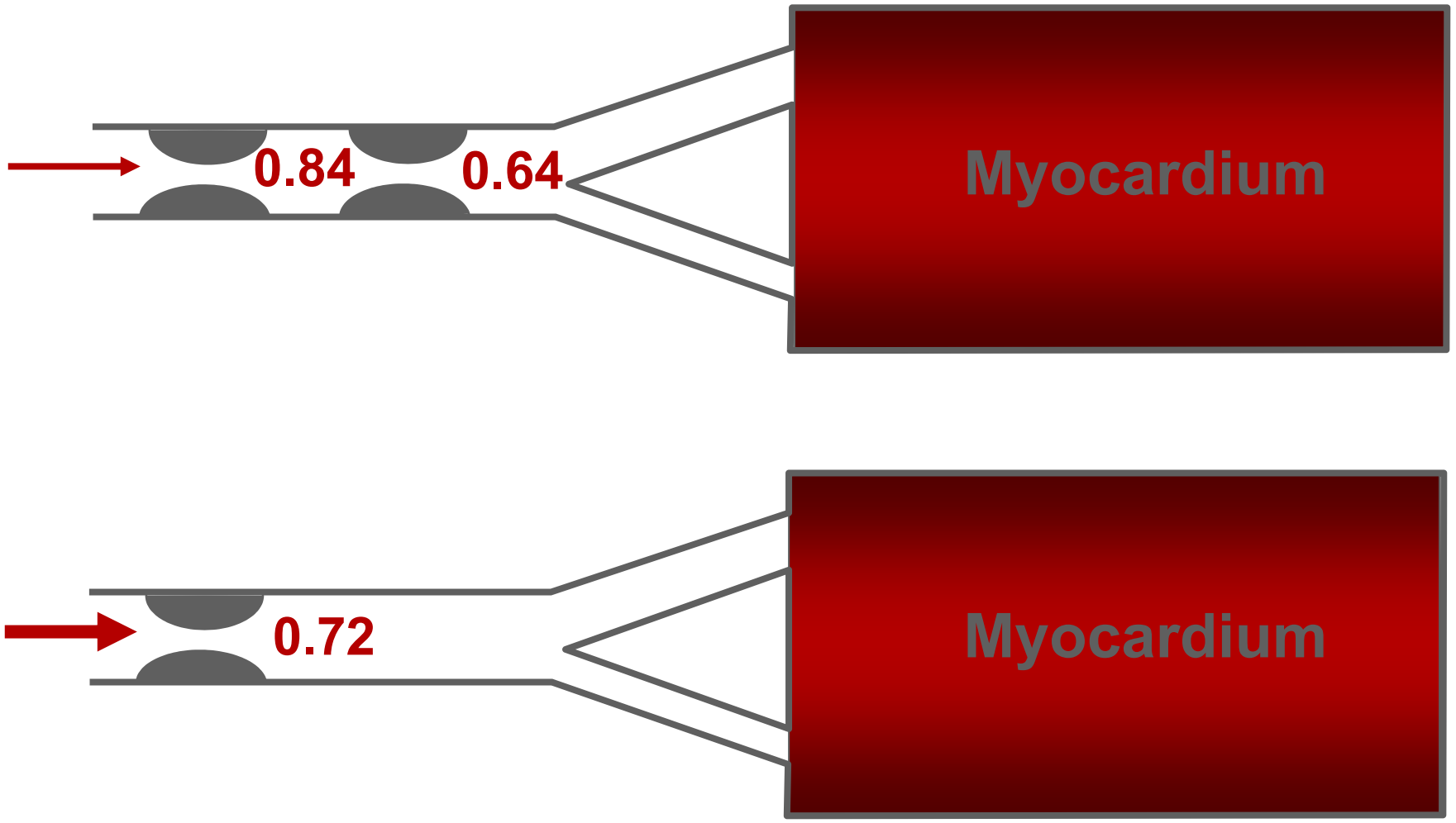
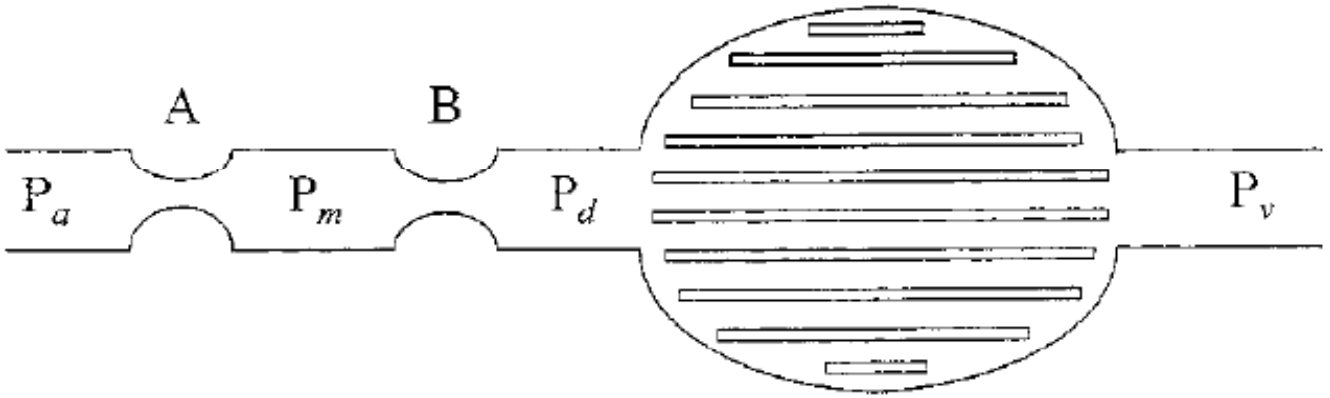


Effect of Tandem Lesions



Tandem Lesions

Scientific Aspects



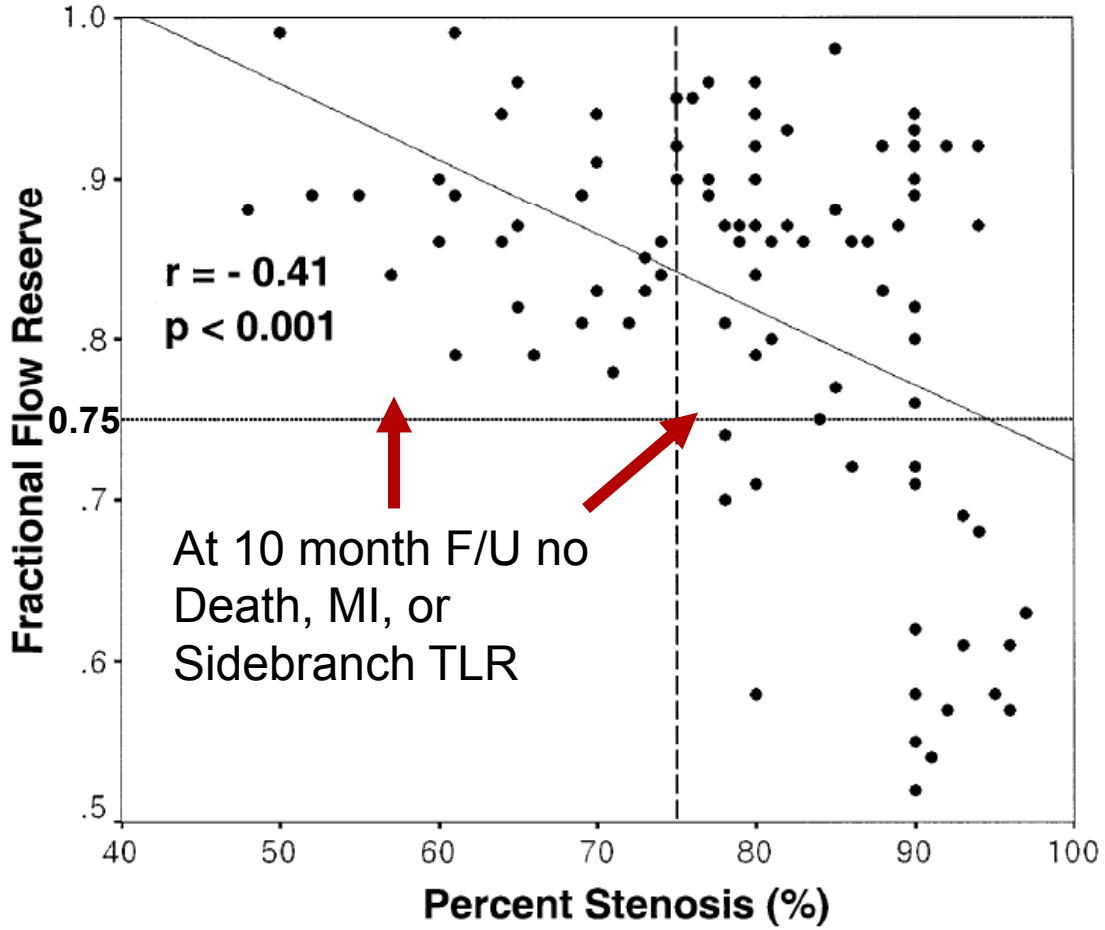
$$FFR(A)_{pred} = \frac{P_d - (P_m/P_a)\,P_w}{P_a - P_m + P_d - P_w}$$

$$FFR(B)_{pred} = 1 - \frac{(P_a - P_w)(P_m - P_d)}{P_a(P_m - P_w)}\,.$$

De Bruyne, et al. Circulation 2000;101:1840-7.
Pijls, et al. Circulation 2000;102:2371-7.

Bifurcation Lesions

FFR in 97 "Jailed" Side Branches



Koo, et al. J Am Coll Cardiol 2005;46:633-7.

Acute Microvascular Damage and FFR

STEMI

Variable Degree of Reversible Microvascular Stunning

Maximum Achievable Flow is Less

Smaller Gradient and Higher FFR across Any Given Stenosis

With time, the microvasculature may recover, maximum achievable flow may increase, and a larger gradient with a lower FFR may be measured across a given stenosis

Chronic Microvascular Damage and FFR

Old Myocardial Infarction

→ *Irreversible Microvascular Damage*

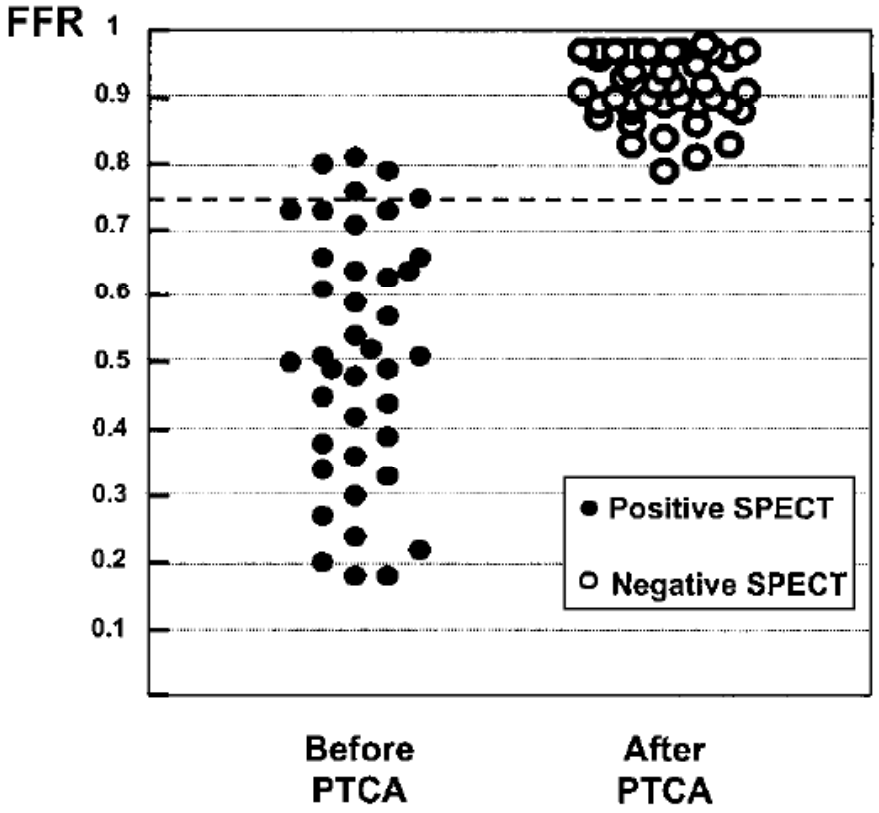
→ *Maximum Achievable Flow is Less*

→ *Smaller Gradient and Higher FFR across Any Given Stenosis*

In the setting of chronic microvascular dysfunction, the higher FFR is not falsely elevated, but reflects the smaller amount of viable myocardium supplied by the vessel and still provides information about the expected gain in flow after PCI

FFR in Chronic MI (Culprit Vessel)

Comparison of FFR in 57 patients with an MI ≥ 6 days old to SPECT imaging before and after PCI



	MIBI + n = 40	MIBI - n = 40
FFR≥0.75 n = 45	5	40
FFR<0.75 n = 35	35	0

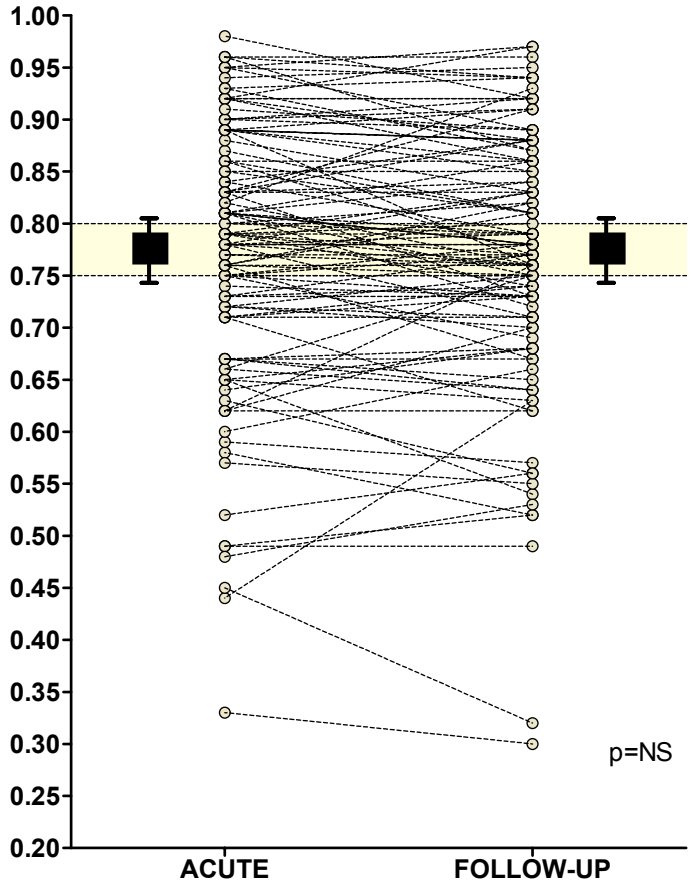
Concordance = 94%

κ = 0.87; P<0.0001

De Bruyne, et al. Circulation 2001;104:157-162

FFR STEMI (Non-Culprit Vessels)

- ***101 patients with an acute coronary syndrome***
- ***112 non culprit stenoses measured acutely and 35±24 days later***



In only 2/112 stenoses was the FFR >0.80 during the ACS and <0.75 at follow-up.

Ntalianis, et al. JACC: Cardiovasc Interv 2010;3:1274

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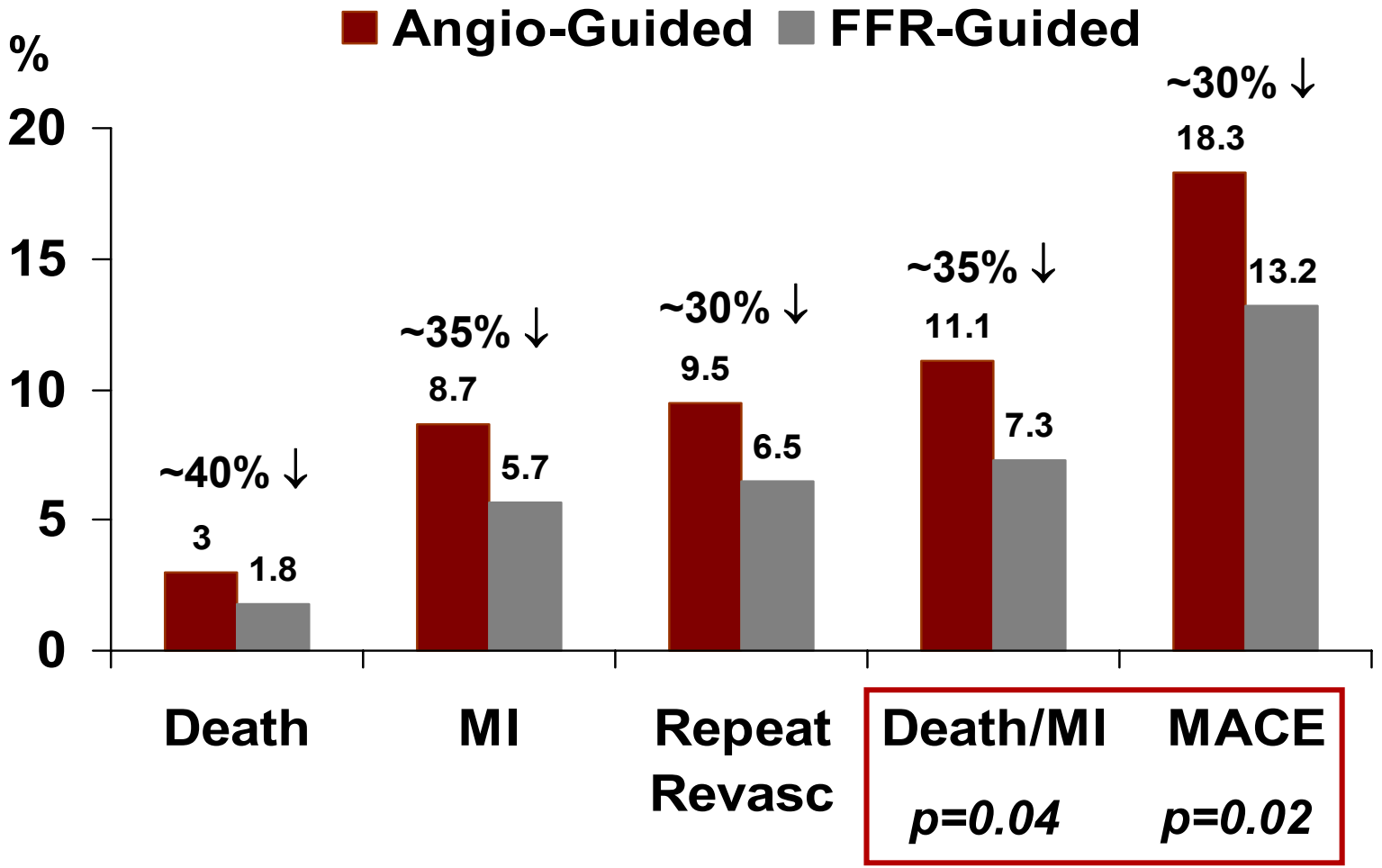
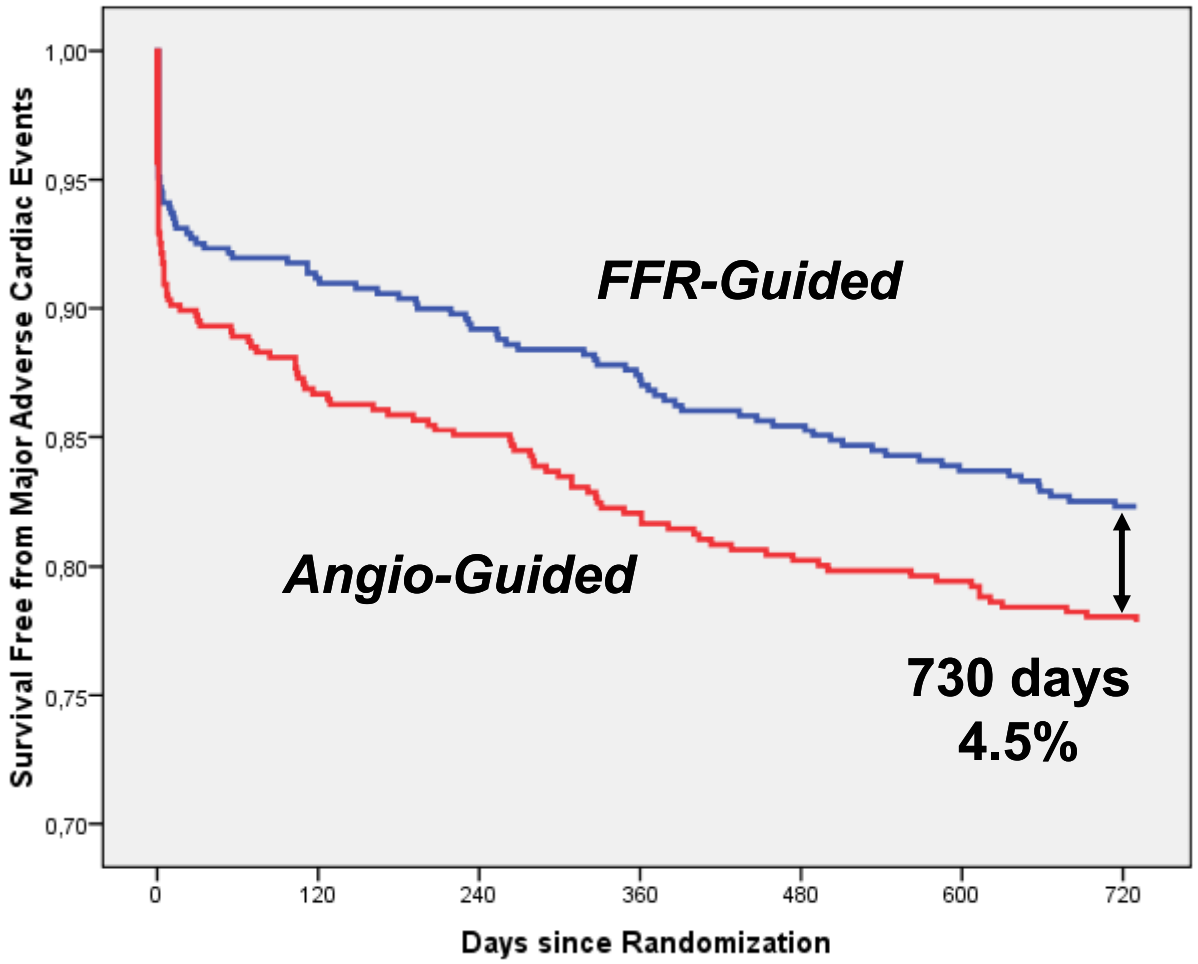
FAME Study: One Year Outcomes



New Engl J Med 2009;360:213-24.

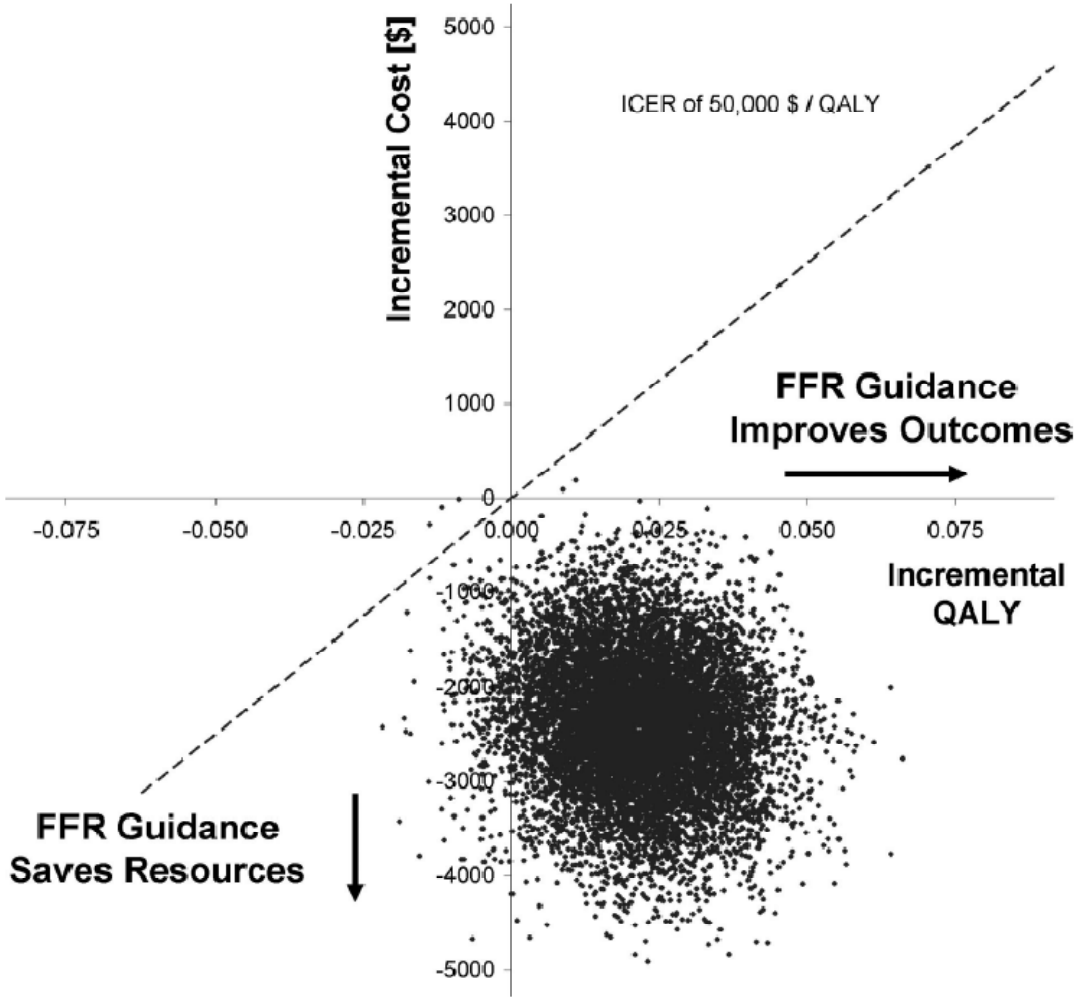
FAME Study: Two Year Outcomes



J Am Coll Cardiol 2010;56:177-184

FAME: Economic Evaluation

Bootstrap Analysis



FFR-guided PCI saved >$2,000 per patient at one year compared to Angio-guided PCI

Circulation 2010;122:2545-50.

Anatomic vs. Functional CAD

Patients with angiographically 3VD (N=115), proportions per number of diseased vessels after assessment by FFR

J Am Coll Cardiol 2010;55:2816-21

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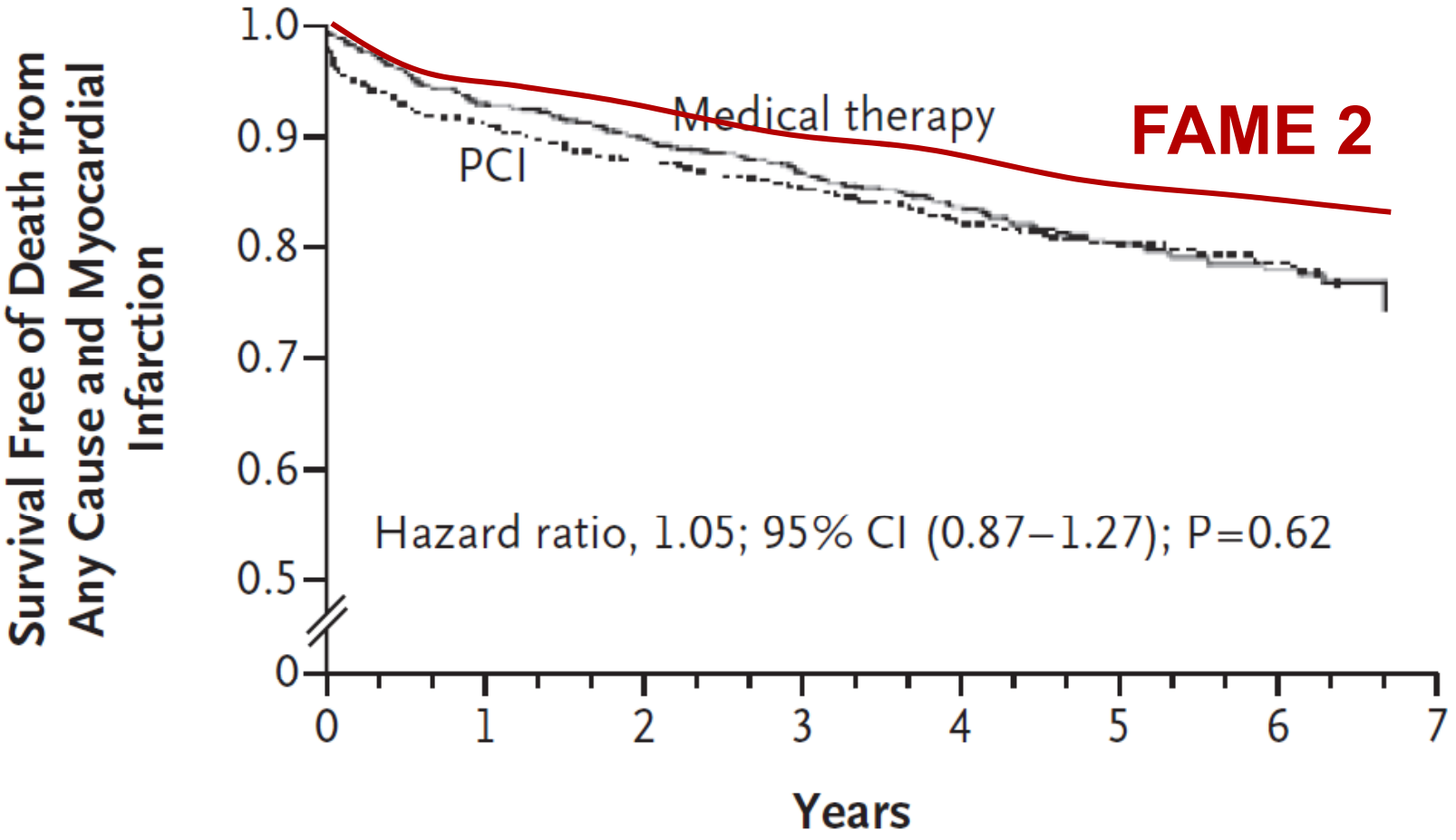
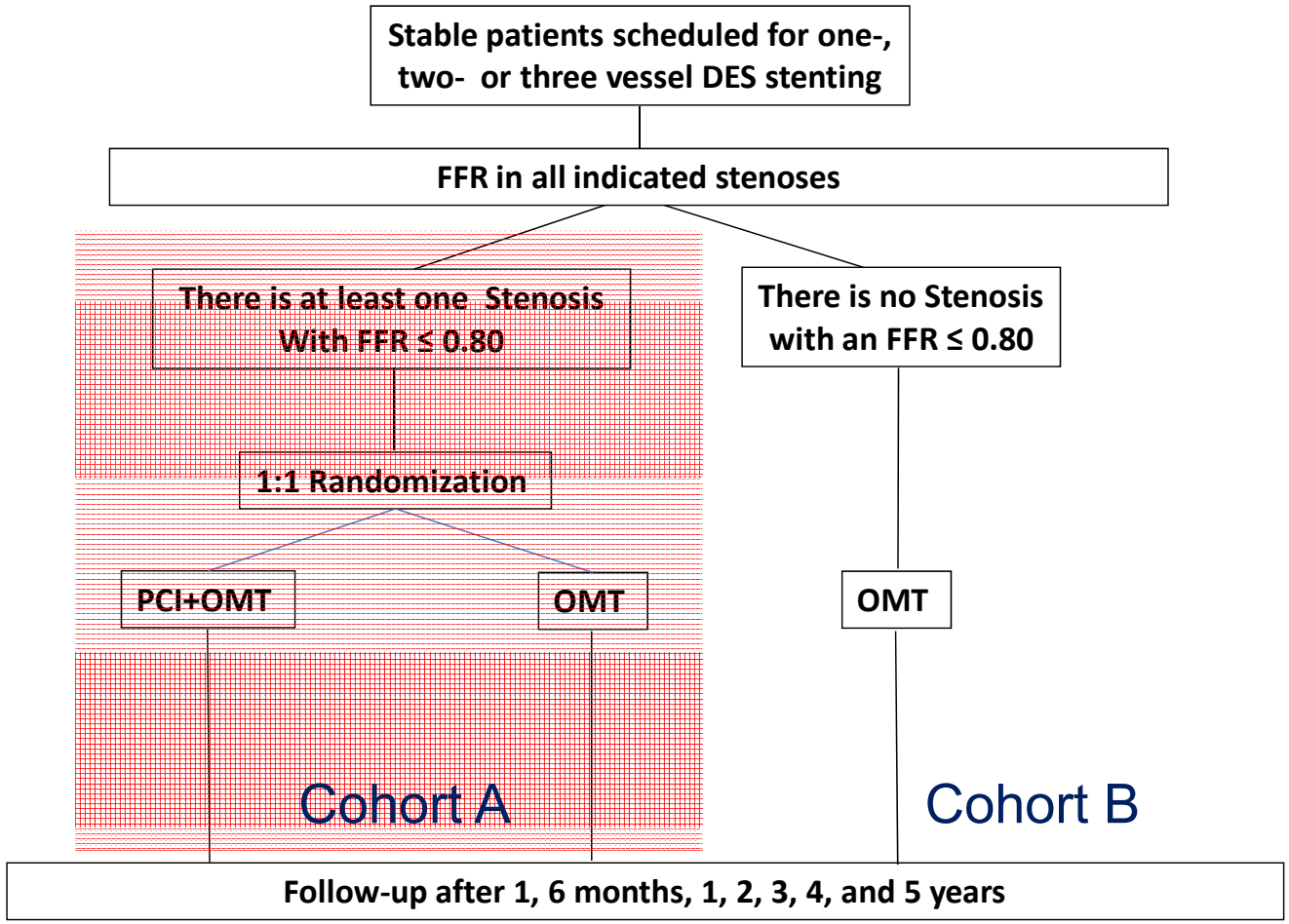
FAME 2

Death and MI in the COURAGE study



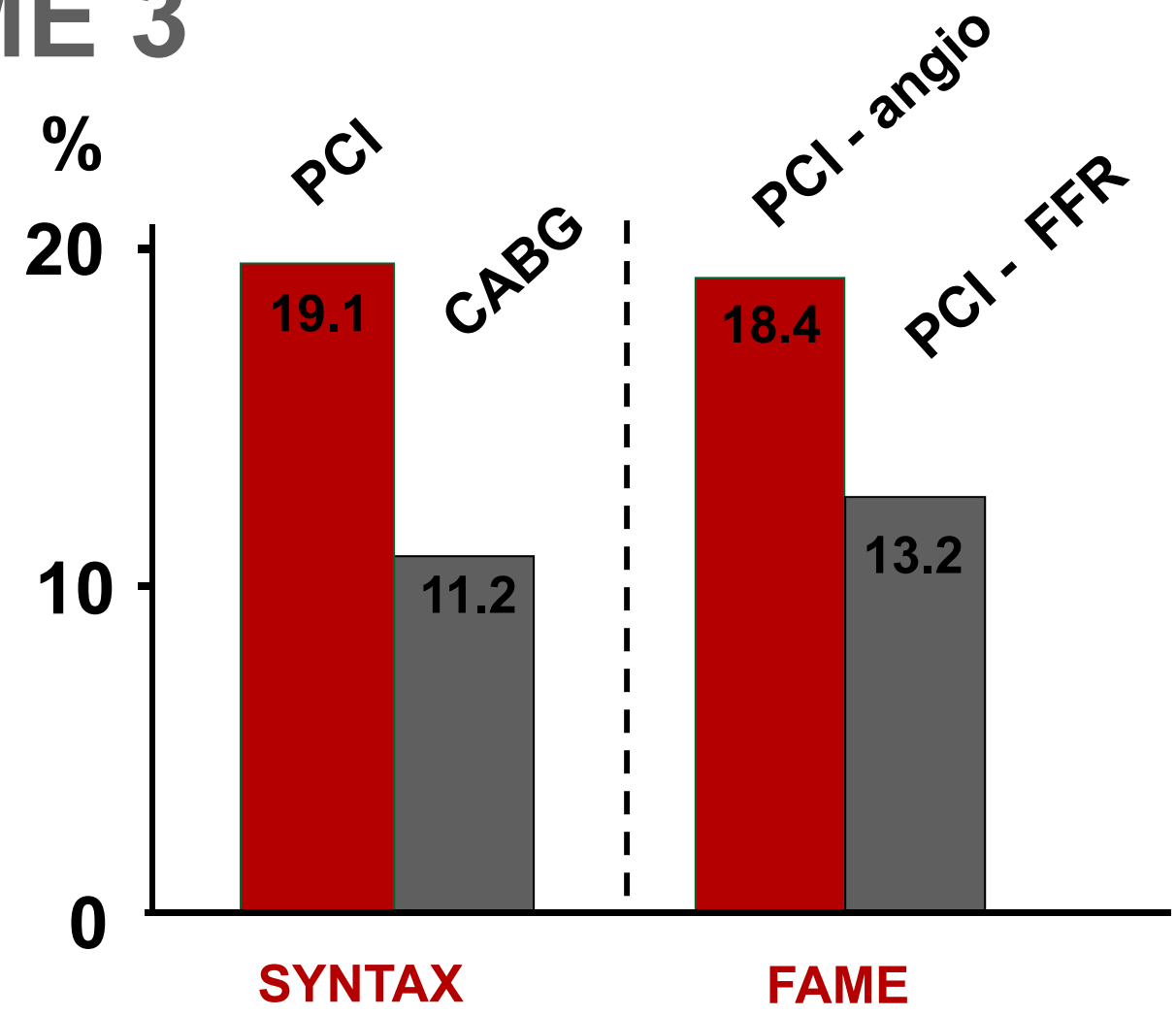
Boden et al., New Engl J Med 2007;356:1503-16.

FAME 2



Primary Endpoint: Death, MI, Urgent TVR at 2 years

FAME 3



1 year MACE Rates

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Summary:

The numerous FFR clinical trials and applications have refocused PCI from "Anatomic Revascularization" to "Functional Revascularization" (i.e. stenting ischemic lesions and medically treating nonischemic ones)