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Fractional Flow Reserve: FAME and Practice Guidelines

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Disclosure Statement of Financial Interest

I, William Fearon, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

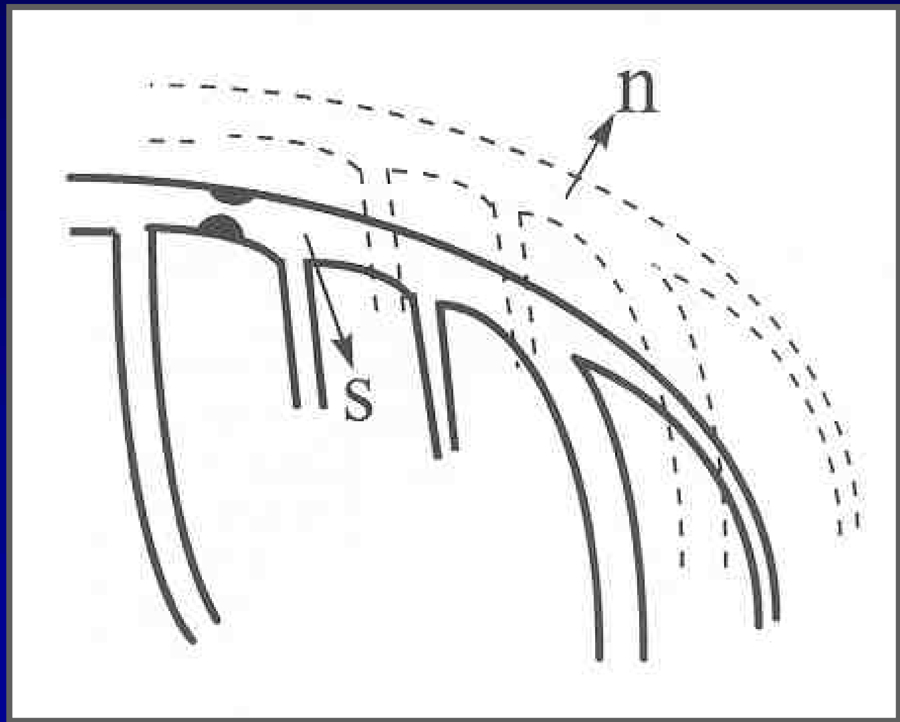
Treatment Options for Multivessel CAD

Medical Treatment		*FFR-Guided PCI*		*CABG*
COURAGE	↔	**FAME**	↔	**SYNTAX**

Fractional Flow Reserve (FFR)

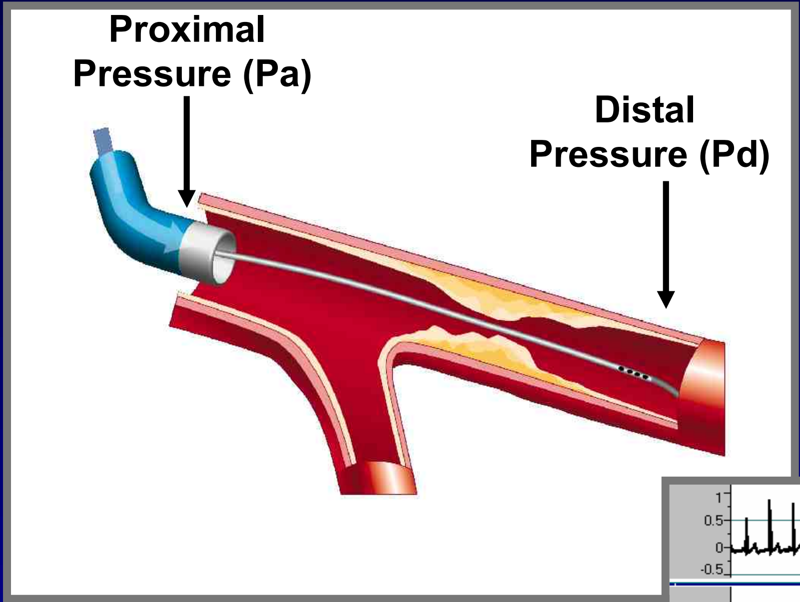
Maximum flow down a vessel in the presence of a stenosis…

…compared to the maximum flow in the hypothetical absence of the stenosis



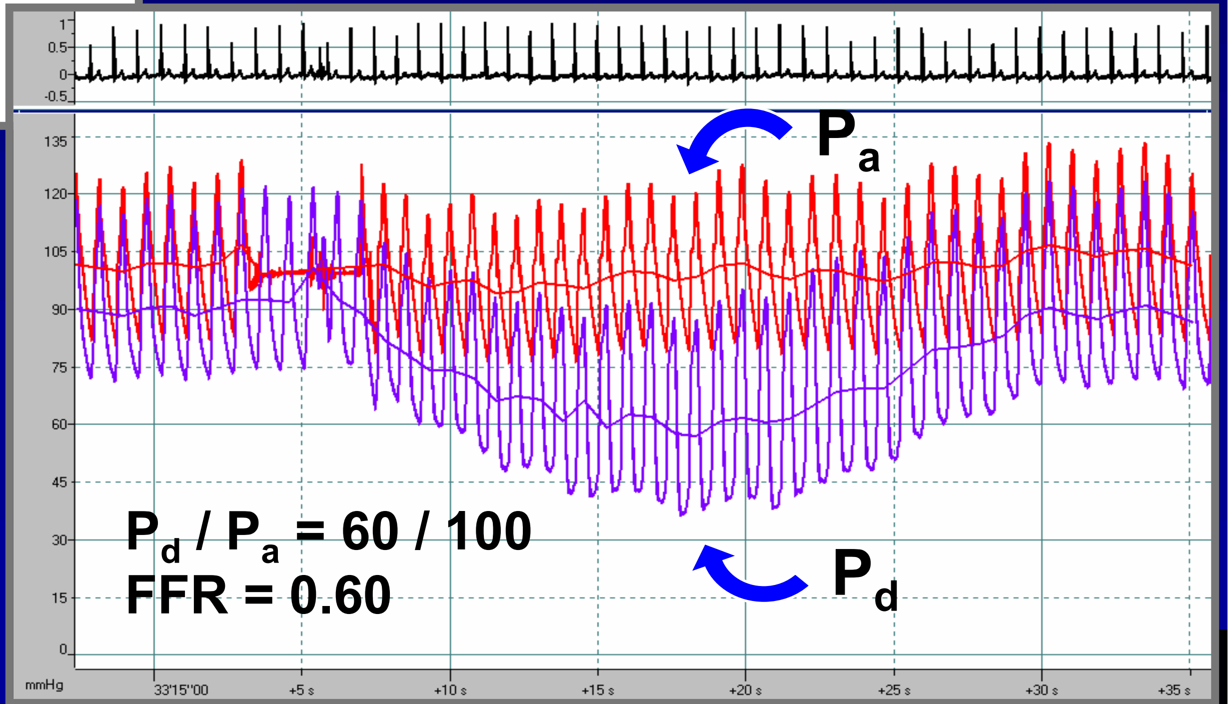
Pijls and De Bruyne, Coronary Pressure
Kluwer Academic Publishers, 2000

Fractional Flow Reserve

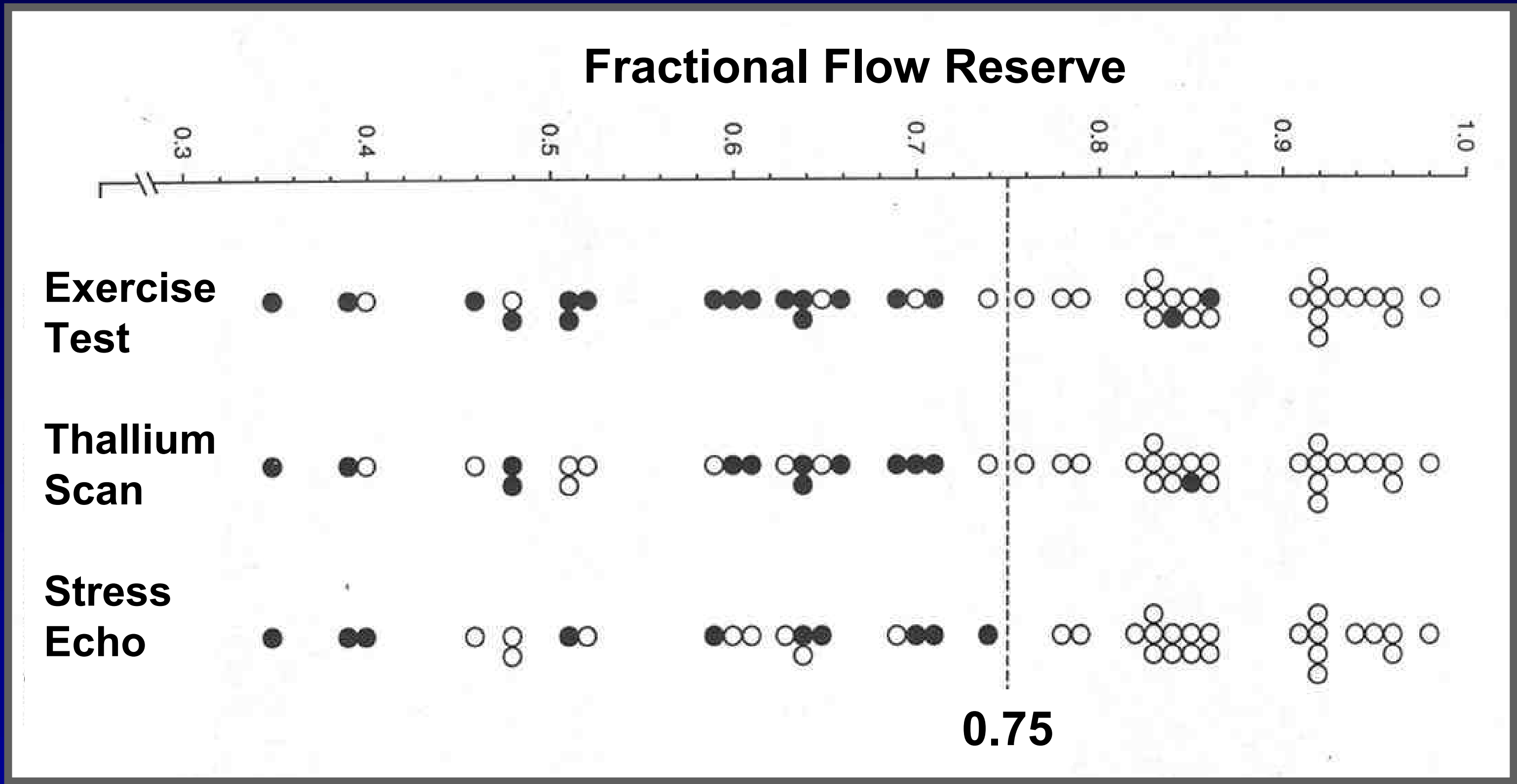


$$FFR = P_d / P_a$$

during maximal flow



FFR in Intermediate Lesions



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

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

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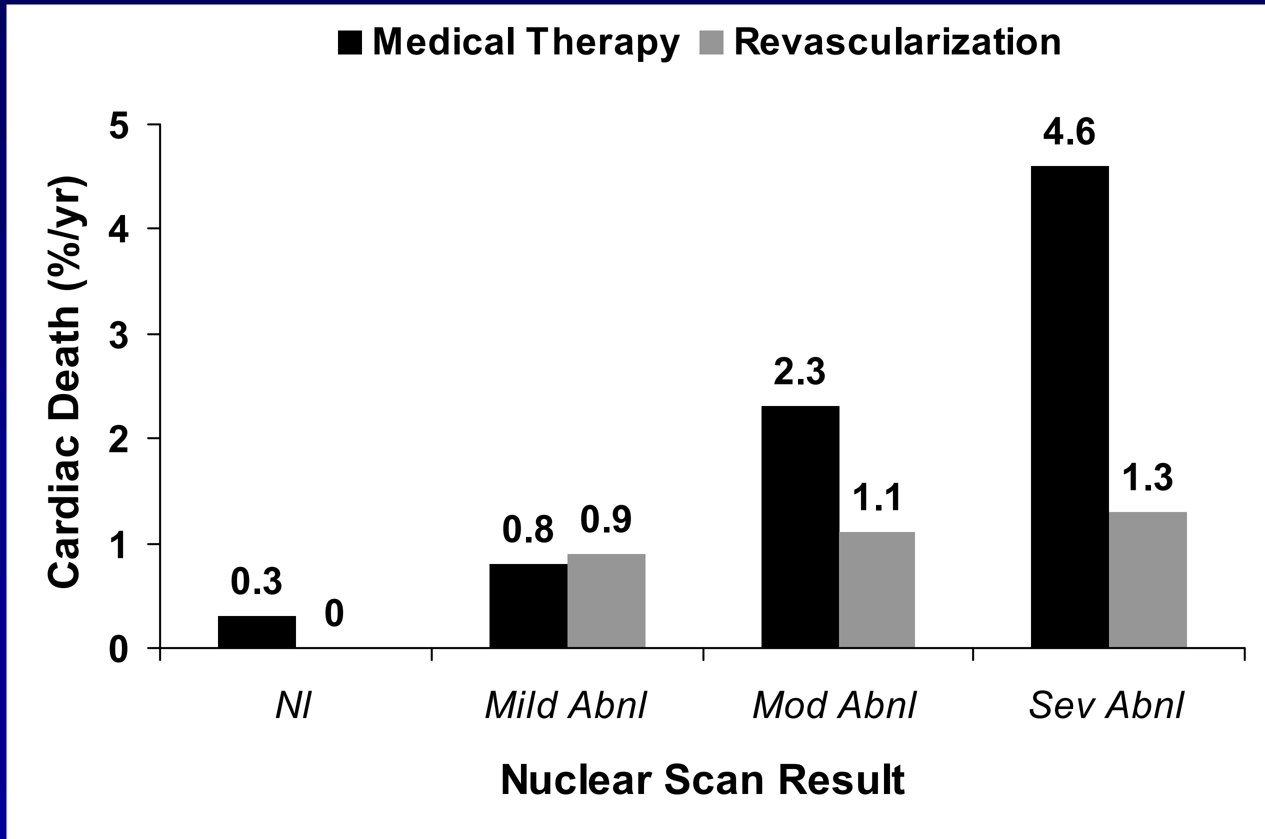
Importance of Revascularization when Ischemia is Present

Nuclear perfusion scans performed in > 5000 patients



Hachamovitch et al. Circulation 1998;97:535-543

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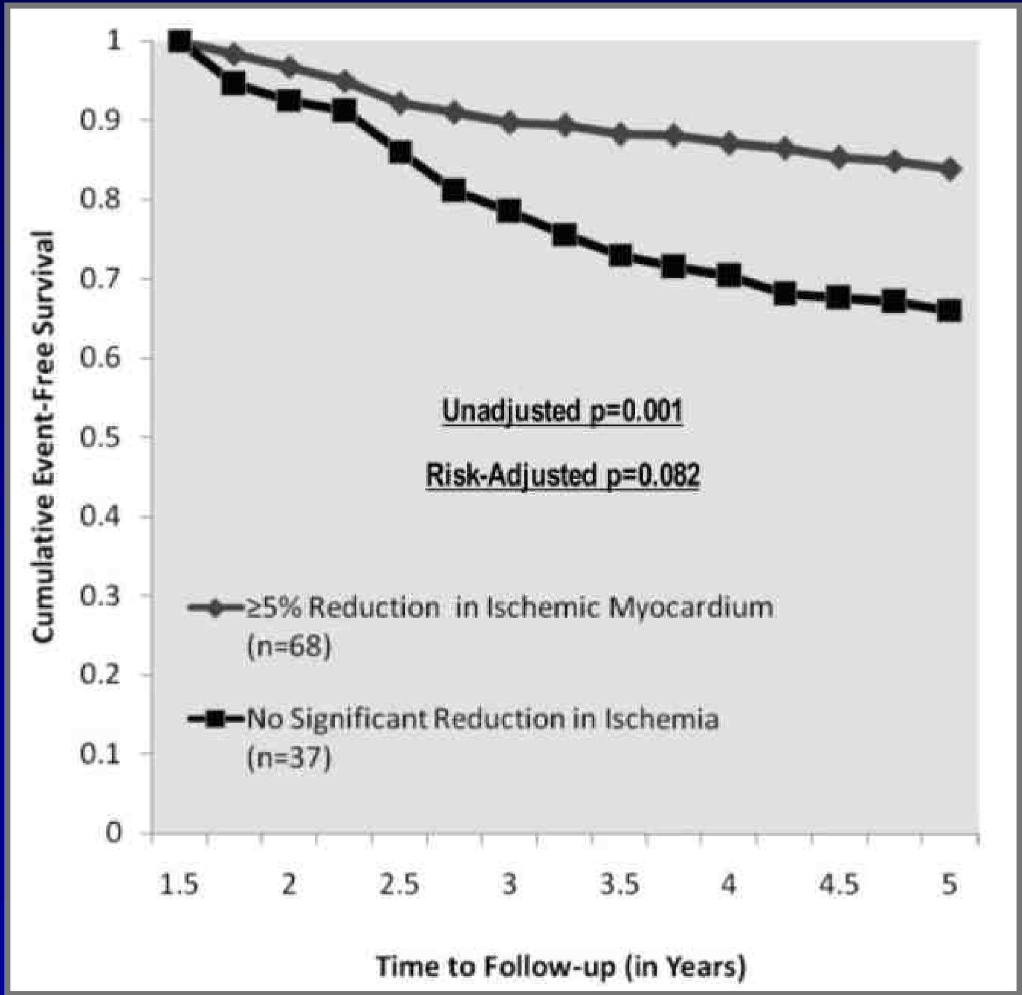
COURAGE Nuclear Substudy

Comparison of death/MI in patients with mod-severe pre-treatment ischemia



Shaw et al. Circulation 2008;117:1283

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Frequency of Stress Testing to Document Ischemia Prior to Elective Percutaneous Coronary Intervention

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Eric Vittinghoff, PhD
Rita F. Redberg, MD, MSc

Context Guidelines call for documenting ischemia in patients with stable coronary artery disease prior to elective percutaneous coronary intervention (PCI).

Objective To determine the frequency and predictors of stress testing prior to elective PCI in a Medicare population.

Design, Setting, and Patients Retrospective, observational cohort study using claims data from a 20% random sample of 2004 Medicare fee-for-service beneficiaries aged 65 years or older who had an elective PCI (N=23 887).

Main Outcome Measures Percentage of patients who underwent stress testing within 90 days prior to elective PCI; variation in stress testing prior to PCI across 306 hospital referral regions; patient, physician, and hospital characteristics that predicted the appropriate use of stress testing prior to elective PCI.

Results In the United States, 44.5% (n=10 629) of patients underwent stress testing within the 90 days prior to elective PCI. There was wide regional variation among the hospital referral regions with stress test rates ranging from 22.1% to 70.6% (national mean, 44.5%; interquartile range, 39.0%-50.9%). Female sex (adjusted odds ratio [AOR], 0.91; 95% confidence interval [CI], 0.86-0.97), age of 85 years or older (AOR, 0.83; 95% CI, 0.72-0.95), a history of congestive heart failure (AOR, 0.85; 95% CI, 0.79-0.92), and prior cardiac catheterization (AOR, 0.45; 95% CI, 0.38-0.54) were associated with a decreased likelihood of prior stress testing. A history of chest pain (AOR, 1.28; 95% CI, 1.09-1.54) and black race (AOR, 1.26; 95% CI, 1.09-1.46) increased the likelihood of stress testing prior to PCI. Patients treated by physicians performing 150 or more PCIs per year were less likely to have stress testing prior to PCI (AOR, 0.84; 95% CI, 0.77-0.93). No hospital characteristics were associated with receipt of stress testing.

Conclusion The majority of Medicare patients with stable coronary artery disease do not have documentation of ischemia by noninvasive testing prior to elective PCI.

JAMA. 2008;300(15):1765-1773 www.jama.com

In the United States, percutaneous coronary intervention (PCI) has become a common treatment strategy for patients with stable coronary artery disease (CAD) and such patients now account for the majority of PCIs performed.[1,2] However, multiple studies have established that some important outcomes for patients with stable CAD (death and risk of future myocardial infarction) do not differ between patients treated with PCI plus optimal medical therapy and patients treated with optimal medical therapy alone.[3-10] The addition of PCI does offer quicker relief of angina than medical therapy alone but also carries an increased risk of repeat revascularization, late-stent thrombosis, and a decreased

JAMA 2008;300:1765

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FFR vs. Nuclear Perfusion Scan in MVD

67 patients with angiographic 2 or 3 vessel CAD

B

		MPI	
		positive	negative
FFR	< 0.80	38	42
	> 0.80	24	97

Melikian et al. J Am Coll Cardiol Int 2010;3:307-14

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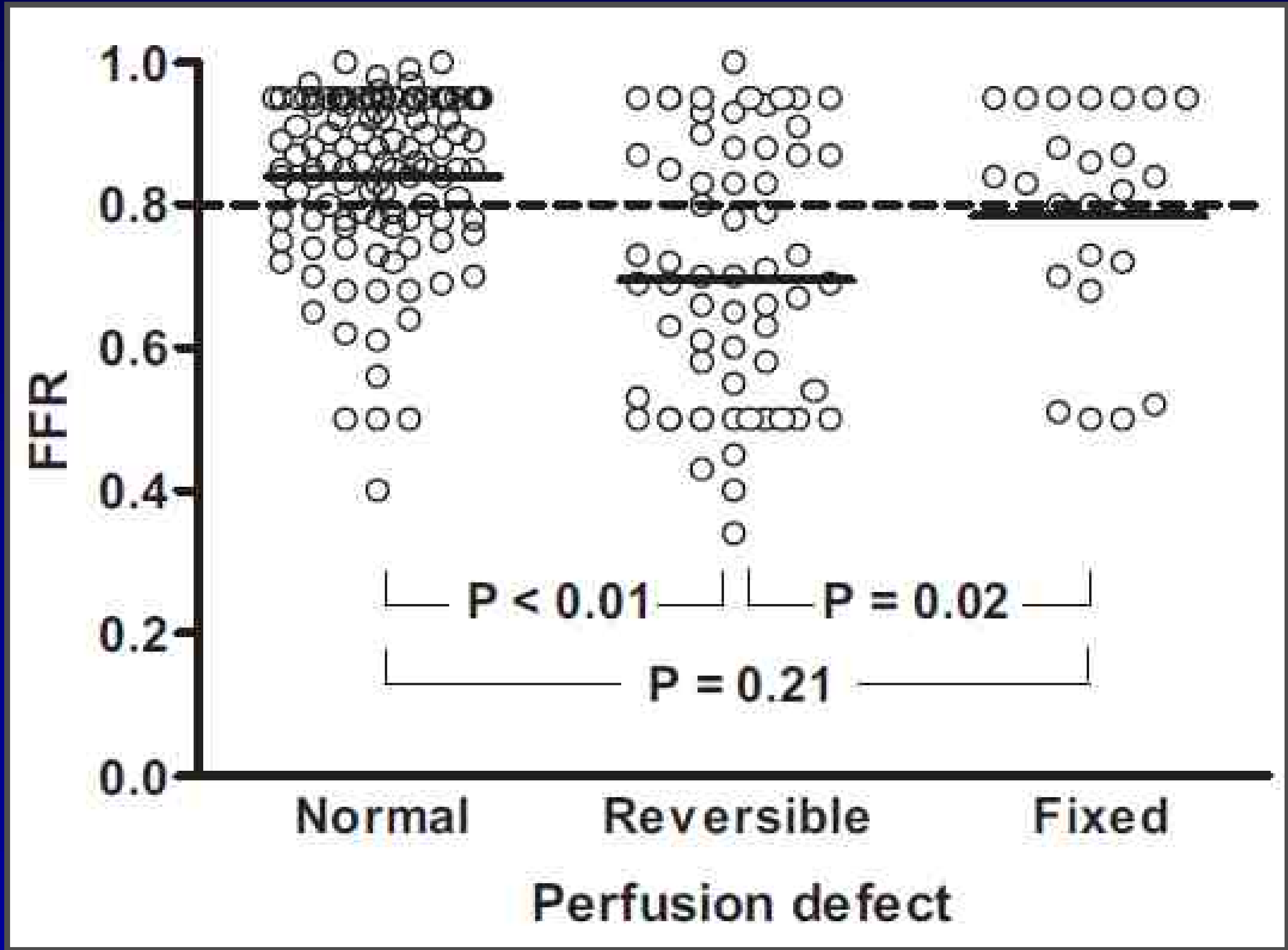
FFR vs. Nuclear Perfusion Scan in MVD

67 patients with angiographic 2 or 3 vessel CAD



Melikian et al. J Am Coll Cardiol Int 2010;3:307-14

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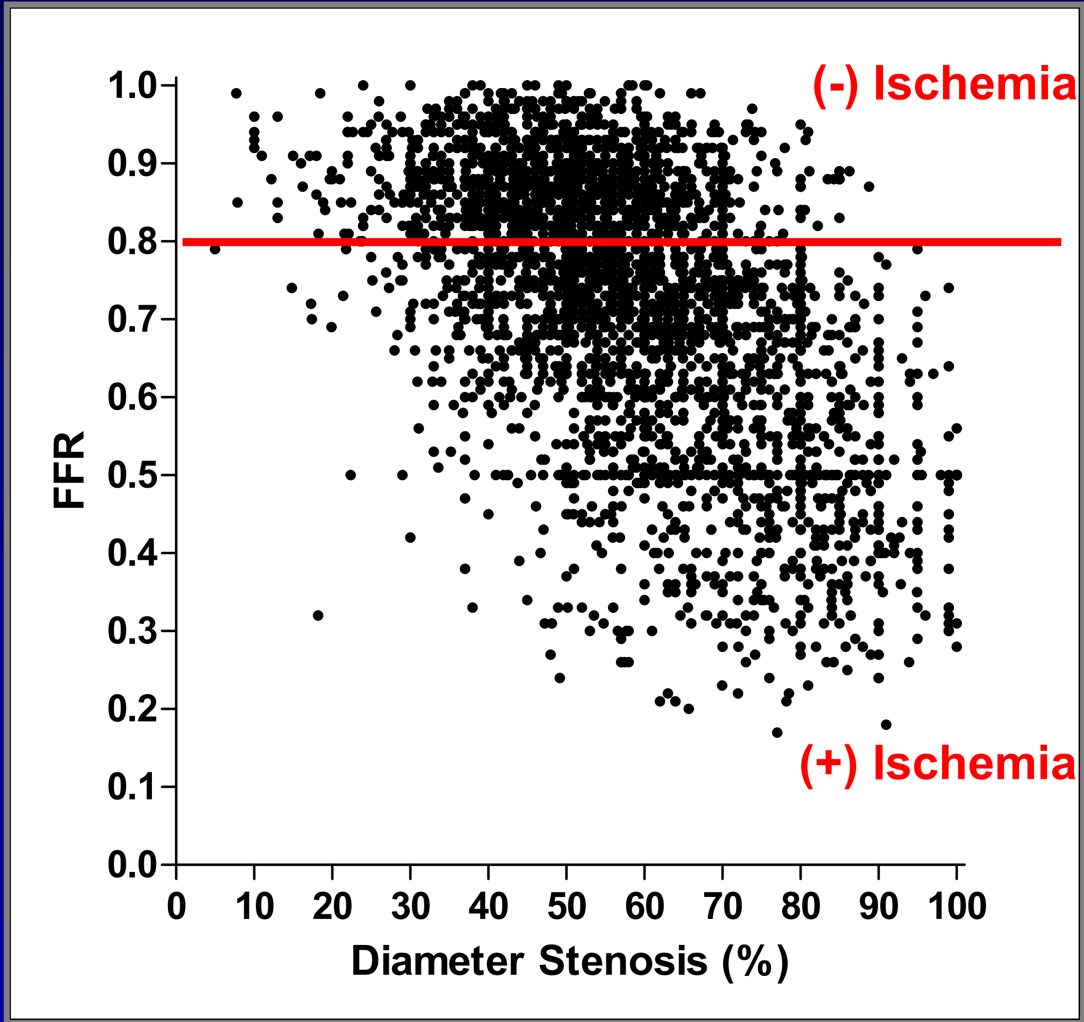
Limitation of Angiography

Comparison of QCA to FFR in over 3,000 lesions



Courtesy of Bernard De Bruyne, MD, PhD

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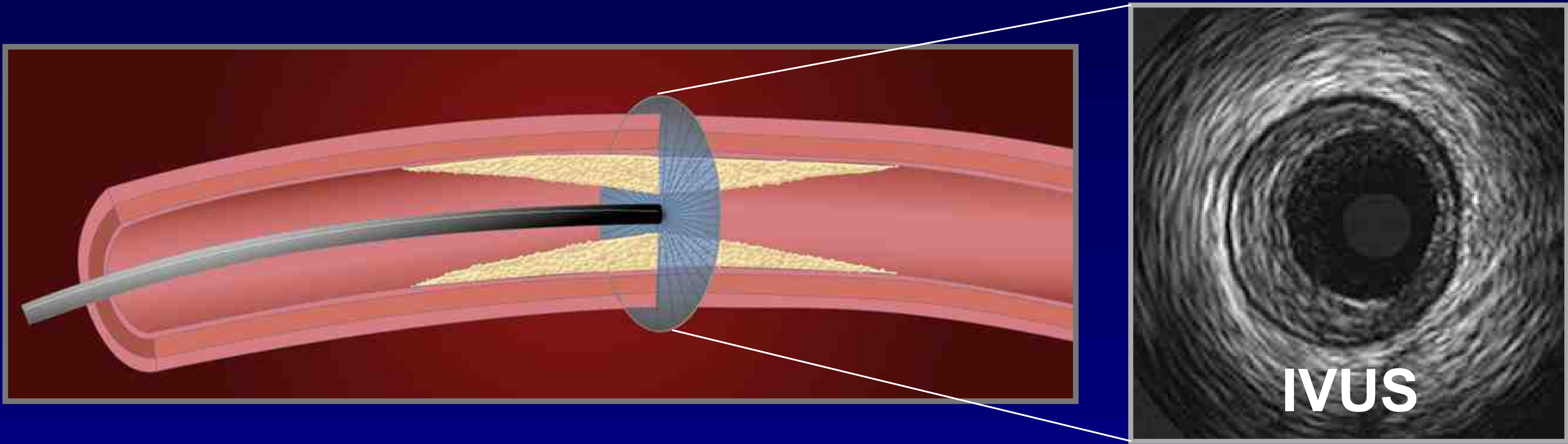
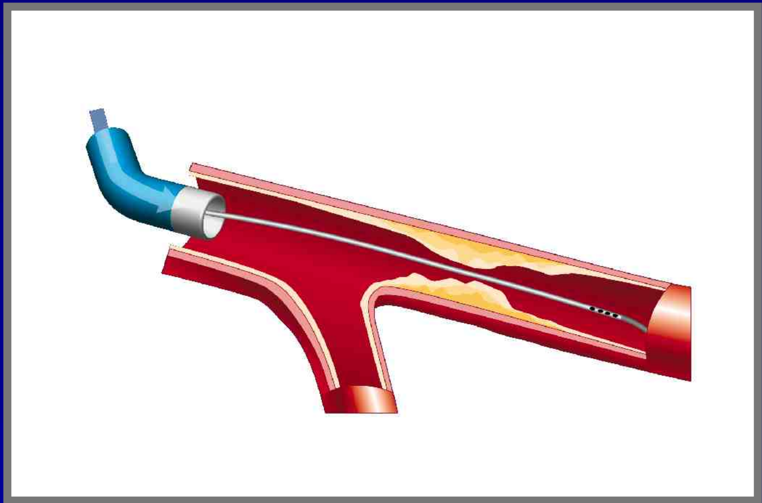
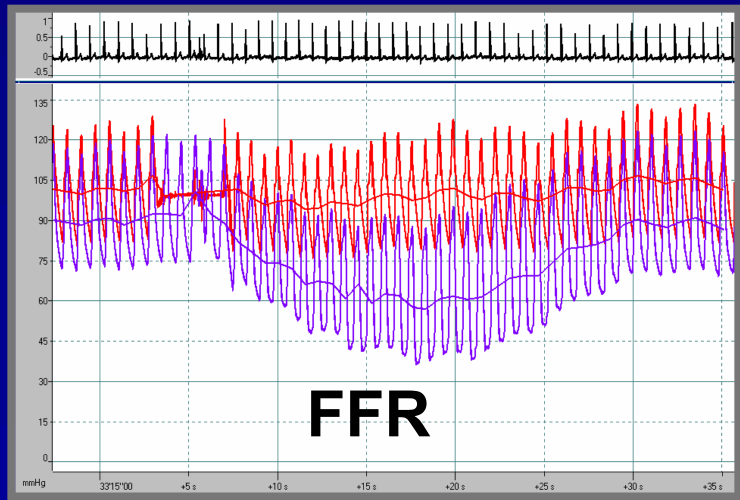
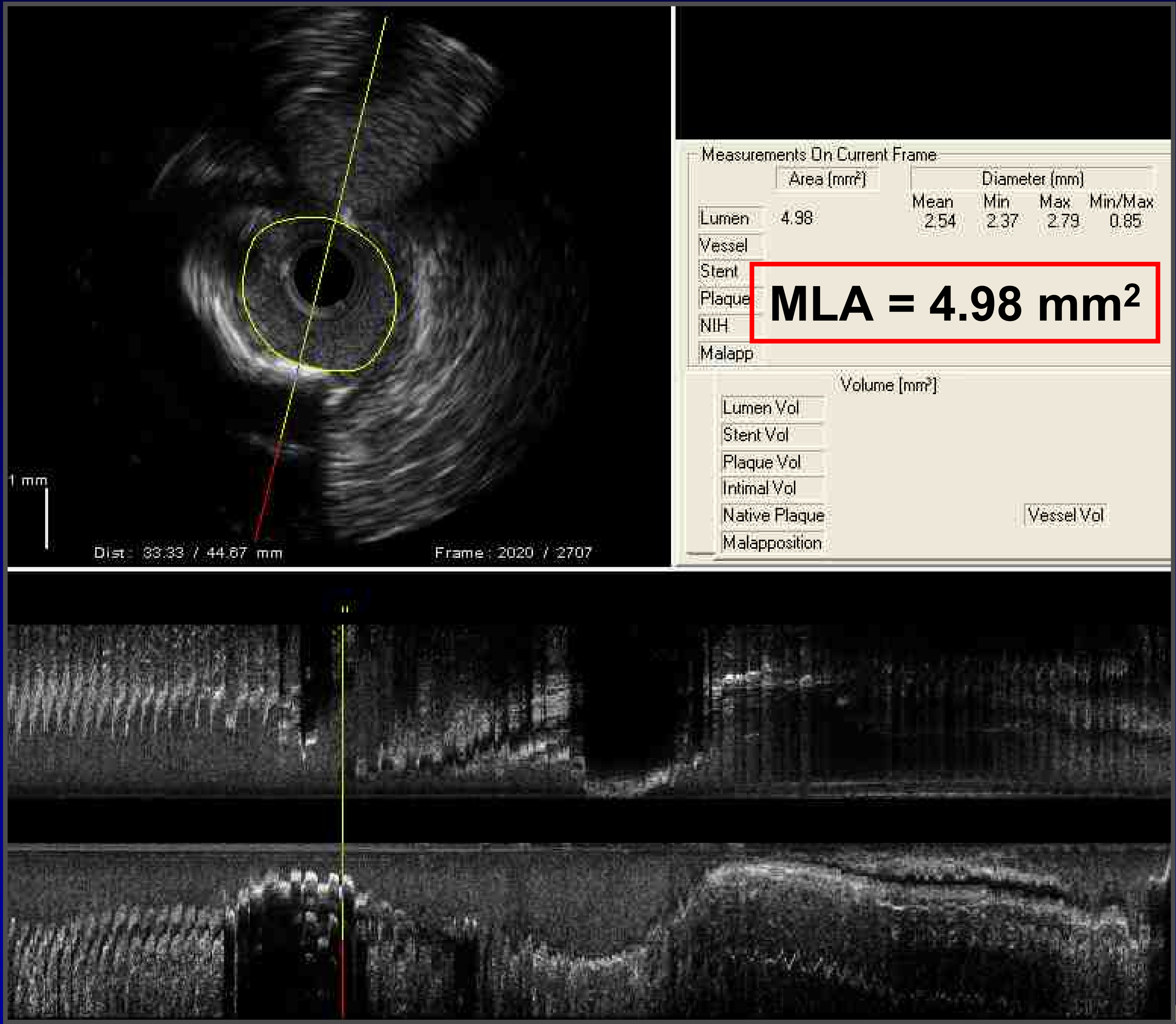
Why FFR instead of IVUS?









1 mm
Dist : 33.33 / 44.67 mm
Frame : 2020 / 2707
Measurements On Current Frame
Area (mm²)
Diameter (mm)
Mean
Min
Max
Min/Max
Lumen
4.98
2.54
2.37
2.79
0.85
Vessel
Stent
Plaque
NIH
Malapp
MLA = 4.98 mm²
Volume (mm³)
Lumen Vol
Stent Vol
Plaque Vol
Intimal Vol
Native Plaque
Malapposition
Vessel Vol

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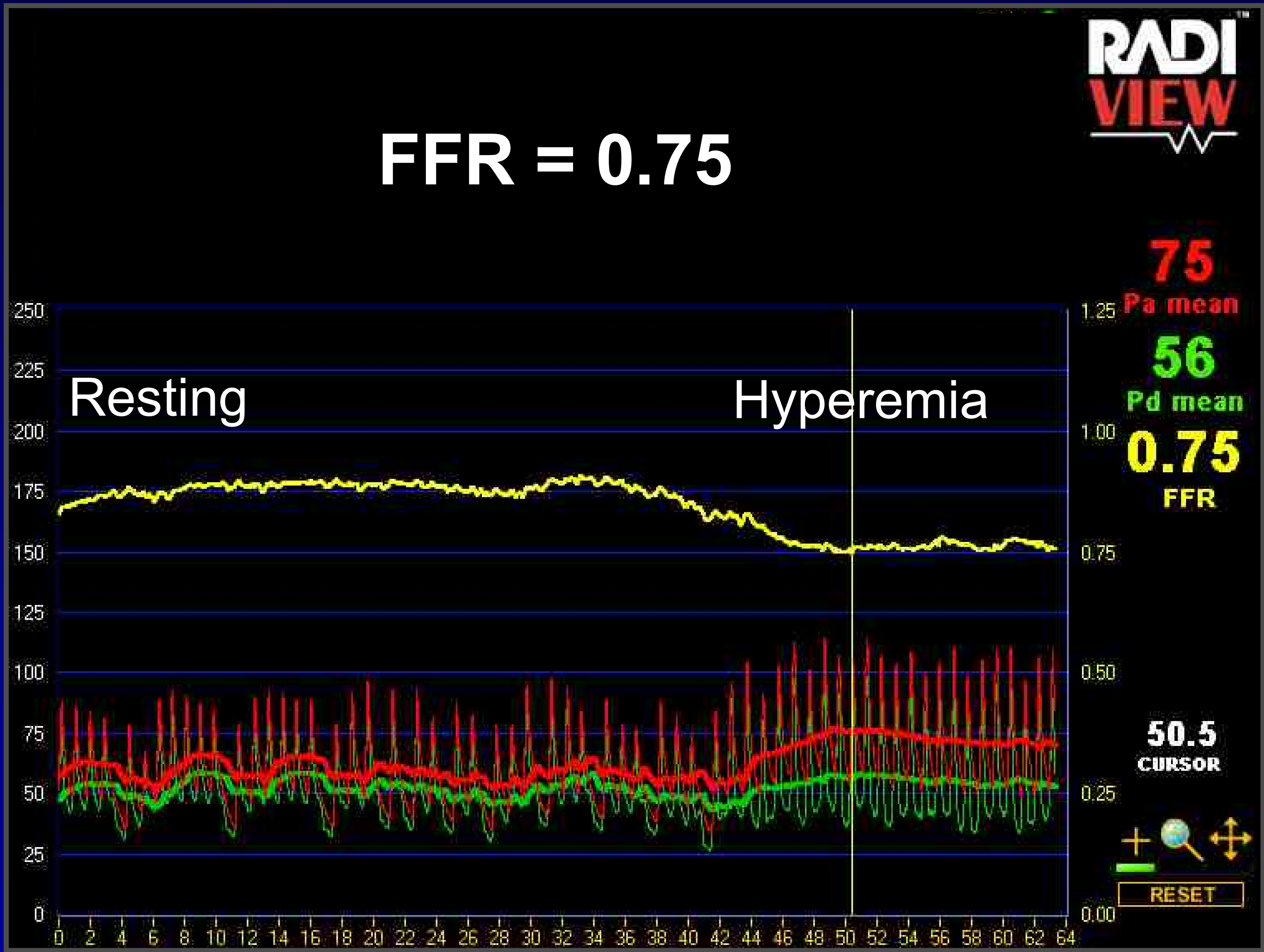
FFR = 0.75
RADI VIEW
Resting
Hyperemia
75
Pa mean
56
Pd mean
0.75
FFR
50.5
CURSOR
RESET
250
225
200
175
150
125
100
75
50
25
0
1.25
1.00
0.75
0.50
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0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42 44 46 48 50 52 54 56 58 60 62 64

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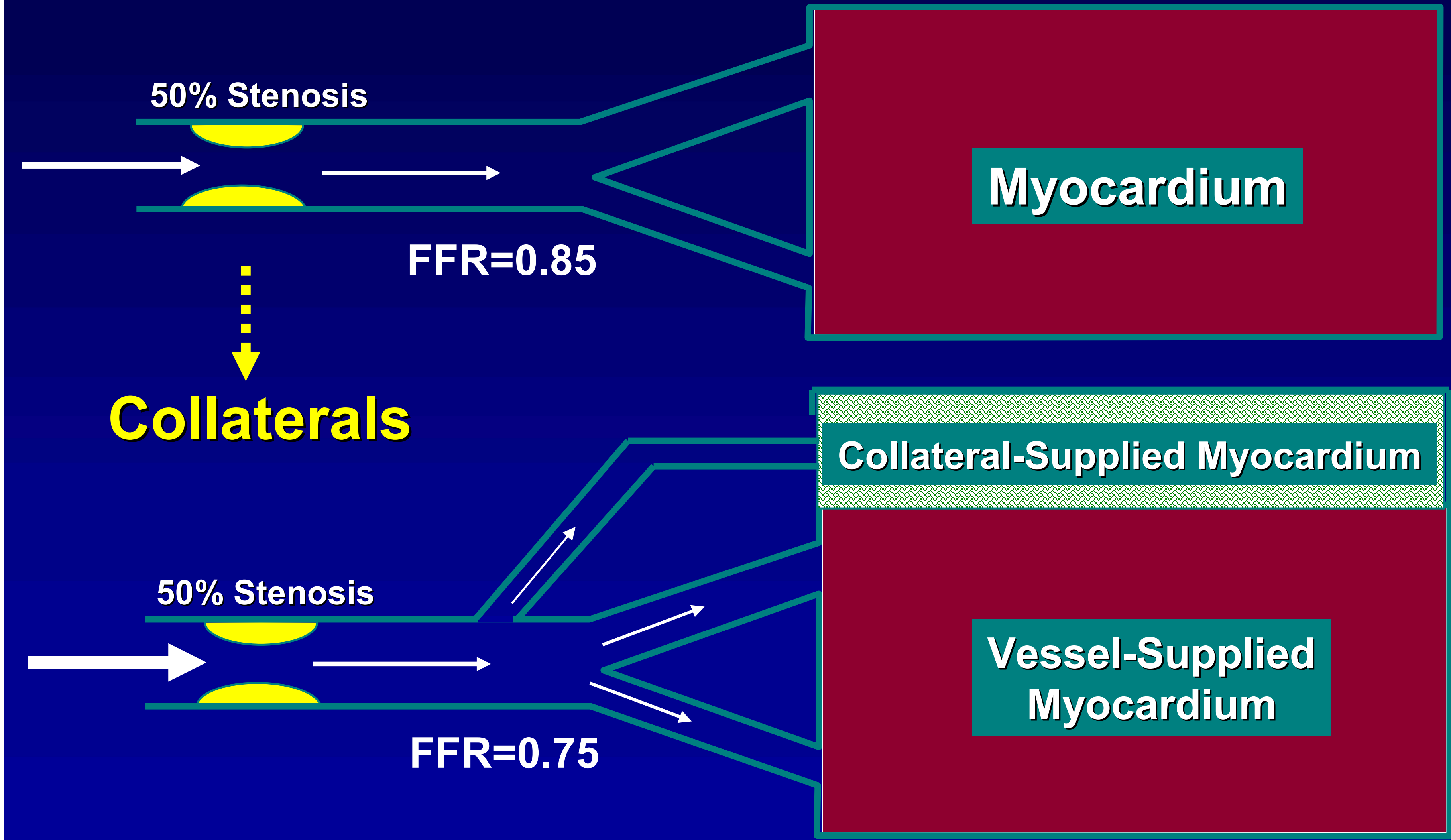
Disconnect between Anatomy and Physiology



…During Maximal Hyperemia

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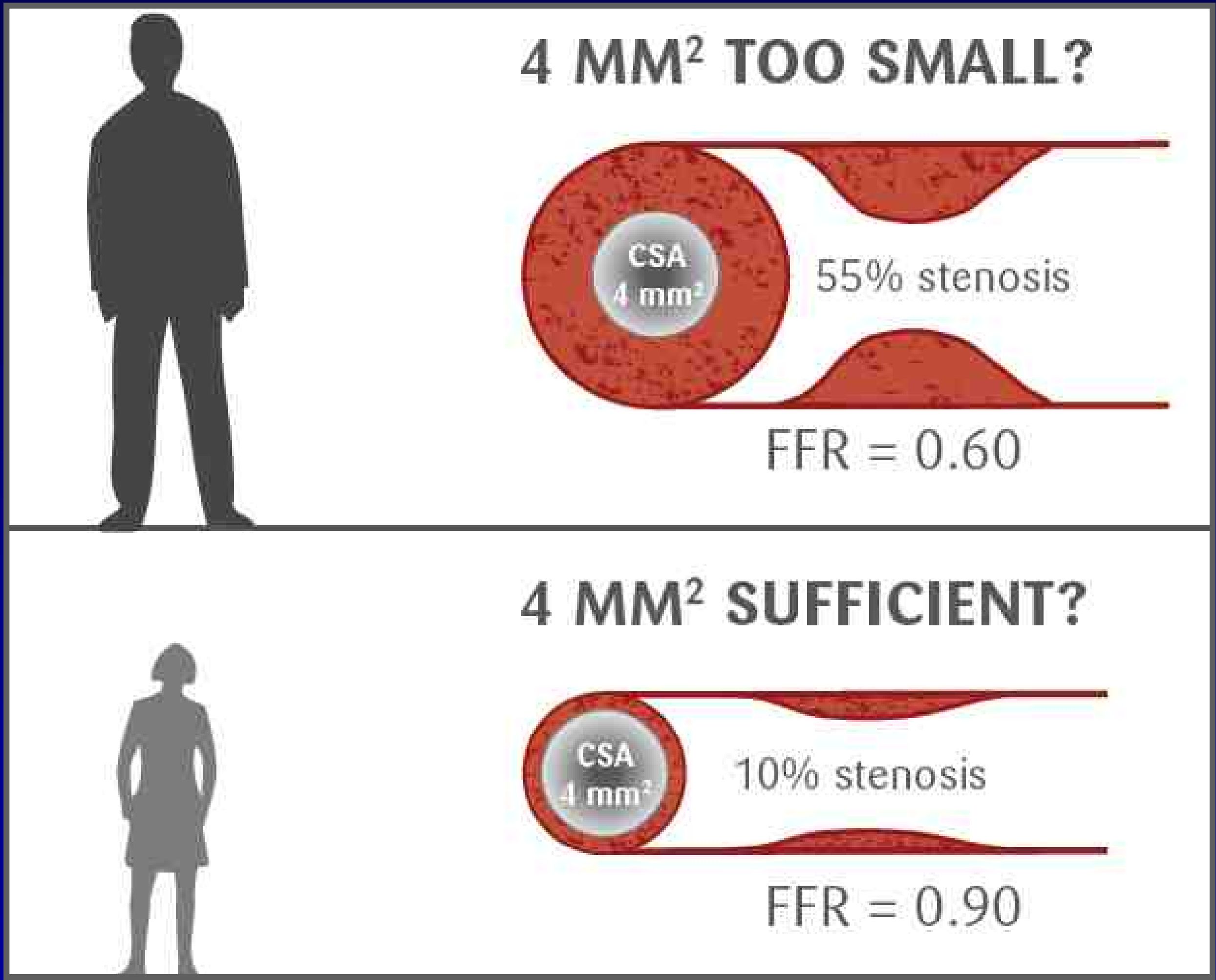
IVUS cutoff is affected by size of vessel



STATE-OF-THE-ART PAPER

Assessment of Intermediate Severity Coronary Lesions in the Catheterization Laboratory

Jonathan Tobis, MD, Babak Azarbal, MD, Leo Slavin, MD

Los Angeles, California

demonstrated benefit in guiding therapy in small trials in patients with ACS.

The no-reflow phenomenon, defined by the acute reduction in coronary flow in the setting of a patent epicardial coronary artery is an uncommon complication of PCI (0.6% to 2.0%) (103). More frequently, it occurs during rotational atherectomy, interventions involving SVGs, and AMI (103). Up to 30% of PCIs performed in the setting of AMI are complicated by the "no-reflow" phenomenon where no blood flow proceeds distally despite a successful balloon dilatation or stent insertion (104,105). Although, the precise pathophysiology of no-reflow is still uncertain, various mechanisms, including microvascular spasms, distal embolization of thrombus or atherosclerotic debris, oxygen-free radical-mediated endothelial injury, or capillary inflammatory injury have been proposed (103). Intravascular ultrasound can predict lesions at higher risk for "no-reflow" after PCI, owing to the plaque mass and loose tissue components of the plaque (105). In addition, IVUS can rule out other causes of poor flow after PCI such as coronary dissection or residual stenosis (106).

Ostial lesions. Analogous to assessment of lesion severity in bifurcation stenoses, assessment of ostial lesion severity is confounded by vessel overlap with the aorta, angulation, and deep seating of the catheter beyond the ostial lesion (107). In a study of 46 patients where 55 ostial lesions were evaluated, 20 of 25 patients (80%) determined to have stenosis severity of 70% or greater had an FFR ≥0.75 (86). Although sensitivity of angiography in this study was 100%, the specificity was only 55%; there was an excellent correlation between presence of ischemia by noninvasive stress imaging studies and FFR.

Intravascular ultrasound is also helpful for diagnosing and treating ostial lesions. Intravascular ultrasound can delineate the extent of stenosis as well as the plaque burden at the ostial location, although heavy calcification limits the penetration of the ultrasound images. Precise placement of the stent at the aorta-ostial juncture is often challenging when using fluoroscopic guidance. The corresponding position of the IVUS catheter on the fluoroscopic image at the cross section where the ostium is observed on the ultrasound image can be very useful in ensuring correct stent placement. Without moving the image intensifier, the stent is placed in the same position as the IVUS catheter was when the aorta-ostial juncture was seen by ultrasound. After PCI, IVUS is helpful to confirm that the entire ostium has been covered by the stent, which will decrease the chance of restenosis.

Comparison of IVUS and FFR

Although IVUS does not provide direct estimation of the hemodynamic severity of a coronary lesion, several studies have demonstrated a strong correlation between anatomic data obtained from IVUS and ischemia by myocardial perfusion SPECT imaging (108), CFR (109), and FFR (110,111). Briguori et al. (111) evaluated 53 lesions in 43 patients with both IVUS and FFR. Receiver operating characteristic curve analysis demonstrated that the following IVUS parameters correlated with an abnormal FFR value (≤0.75) (in order of decreasing sensitivity and specificity): >70% area stenosis, minimal lumen diameter ≤1.8 mm, minimal lumen cross-sectional area ≤4.0 mm², and lesion length >10 mm. Another study by Takagi et al. (110) evaluated 51 lesions in 42 patients with both FFR and IVUS. Intravascular ultrasound parameters that best correlated with an FFR value ≤0.75 were >60% area stenosis and a minimal lumen cross-sectional area <3.0 mm². By providing precise information on vessel size, extent of the atherosclerosis, and plaque characteristics, IVUS images help guide PCI strategy, equipment selection, and assessment of the adequacy of the results.

Fractional flow reserve provides important physiologic information on the hemodynamic severity of a coronary lesion and is helpful in the cardiac catheterization laboratory to determine whether PCI should be performed without stopping the procedure and sending the patient for a noninvasive stress test. Fractional flow reserve is easy to perform and provides an accurate and lesion-specific index of functional severity of coronary stenosis that correlates with noninvasive tests of myocardial ischemia in patients with intermediate lesions (112). Fractional flow reserve has been compared with IVUS as a measurement for optimal stent deployment. One retrospective analysis showed that FFR ≥0.94 after stent deployment had a concordance rate of 91% with IVUS and displayed accuracy in guiding stent deployment (55). However, another study revealed that FFR ≥0.96 did not reliably predict an optimum stent result (113). The correlation between adverse outcomes after angioplasty and stenting and the FFR index has been evaluated. Bech et al. (114), in 60 patients, showed excellent clinical outcomes at 2 years in patients with diameter stenosis ≤35%, and FFR ≥0.90. Pijls et al. (56) showed that a post-stent FFR ≥0.90 was associated with low incidence of the composite end point of death, MI, or total vessel revascularization at 6 months.

The heterogeneity of the patients studied in the multiple registries and differences in methodology between studies create difficulty in evaluating the efficacy of IVUS and FFR in specific clinical settings. There are no randomized,

tion laboratory to provide critical anatomic and functional data that permit more accurate decisions in the management of the patient. In our laboratory, both methods are used: FFR is preferred to identify whether an intermediate lesion is functionally significant, and IVUS is preferred when assessing the anatomy of a lesion for sizing, position of plaque, and adequacy of stent deployment.

FFR is preferred to identify whether an intermediate lesion is functionally significant, and IVUS is preferred when assessing the anatomy of a lesion for sizing, position of plaque and adequacy of stent deployment.

J Am Coll Cardiol 2007;49:839-48.

Fractional Flow Reserve

versus

Angiography for

Multivessel

Evaluation

New Engl J Med 2009;360:213-24

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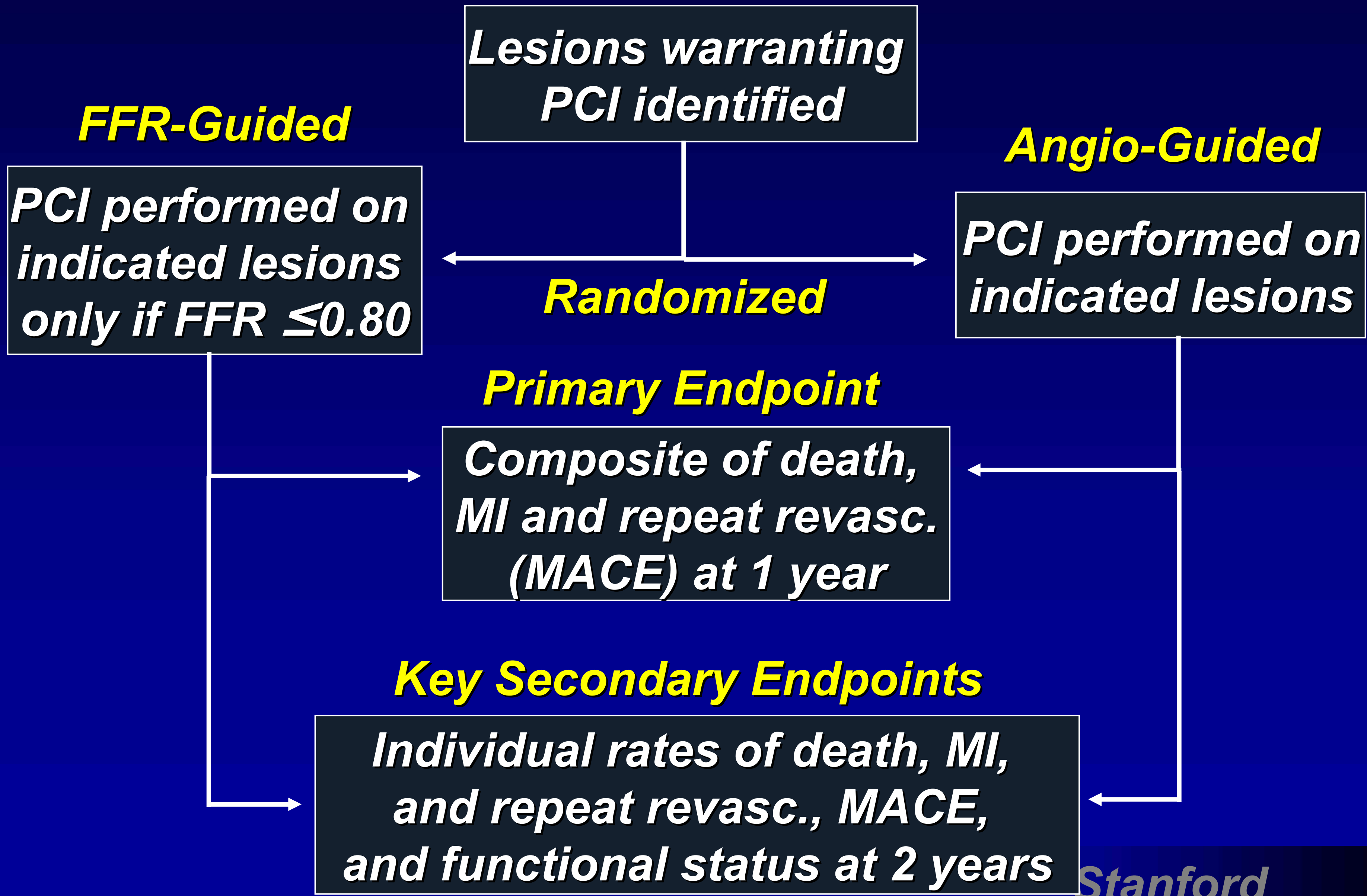
Flow Chart



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Baseline Characteristics

	Angio-Guided n = 496	FFR-Guided n = 509	P Value
Age, mean ±SD	64±10	65±10	0.47
Male, %	73	75	0.30
Diabetes, %	25	24	0.65
Hypertension, %	66	61	0.10
Current smoker, %	32	27	0.12
Hyperlipidemia, %	73	72	0.62
Previous MI, %	36	37	0.84
NSTE ACS, %	36	29	0.11
Previous PCI , %	26	29	0.34
LVEF, mean ±SD	57±12	57±11	0.92
LVEF < 50% , %	27	29	0.47

Procedural Characteristics

	Angio-Guided n = 496	FFR-Guided n = 509	P Value
Indicated lesions / patient	2.7±0.9	2.8±1.0	0.34
Stents / patient	2.7 ± 1.2	1.9 ± 1.3	<0.001

Procedural Characteristics

	Angio-Guided n = 496	FFR-Guided n = 509	P Value
Indicated lesions / patient	2.7±0.9	2.8±1.0	0.34
Stents / patient	2.7 ± 1.2	1.9 ± 1.3	<0.001
Procedure time (min)	70 ± 44	71 ± 43	0.51
Contrast agent used (ml)	302 ± 127	272 ± 133	<0.001
Equipment cost (US $)	6007	5332	<0.001
Length of hospital stay (days)	3.7 ± 3.5	3.4 ± 3.3	0.05

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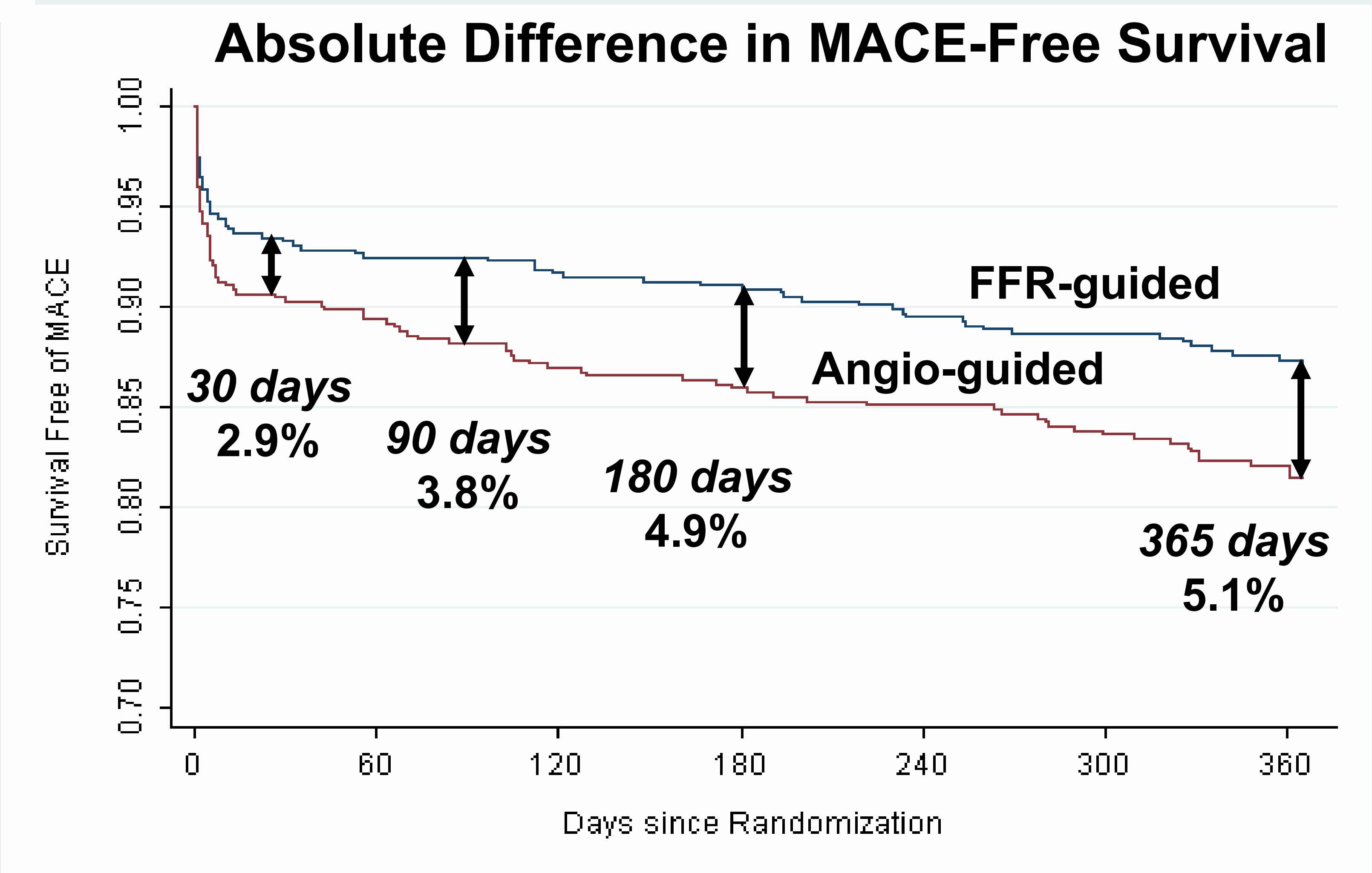
Adverse Events at 1 Year

	Angio-Guided n = 496	FFR-Guided n = 509	P Value
Total no. of MACE	113	76	
Death	15 (3.0)	9 (1.8)	0.19
Myocardial Infarction	43 (8.7)	29 (5.7)	0.07
Small / peri-PCI (CK-MB 3-5xNl)	16	12	
Other infarctions ("late or large")	27	17	
CABG or repeat PCI	47 (9.5)	33 (6.5)	0.08
Death or Myocardial Infarction	55 (11.1)	37 (7.3)	0.04
Death, MI, CABG, or re-PCI	91 (18.3)	67 (13.2)	0.02

Event-free Survival



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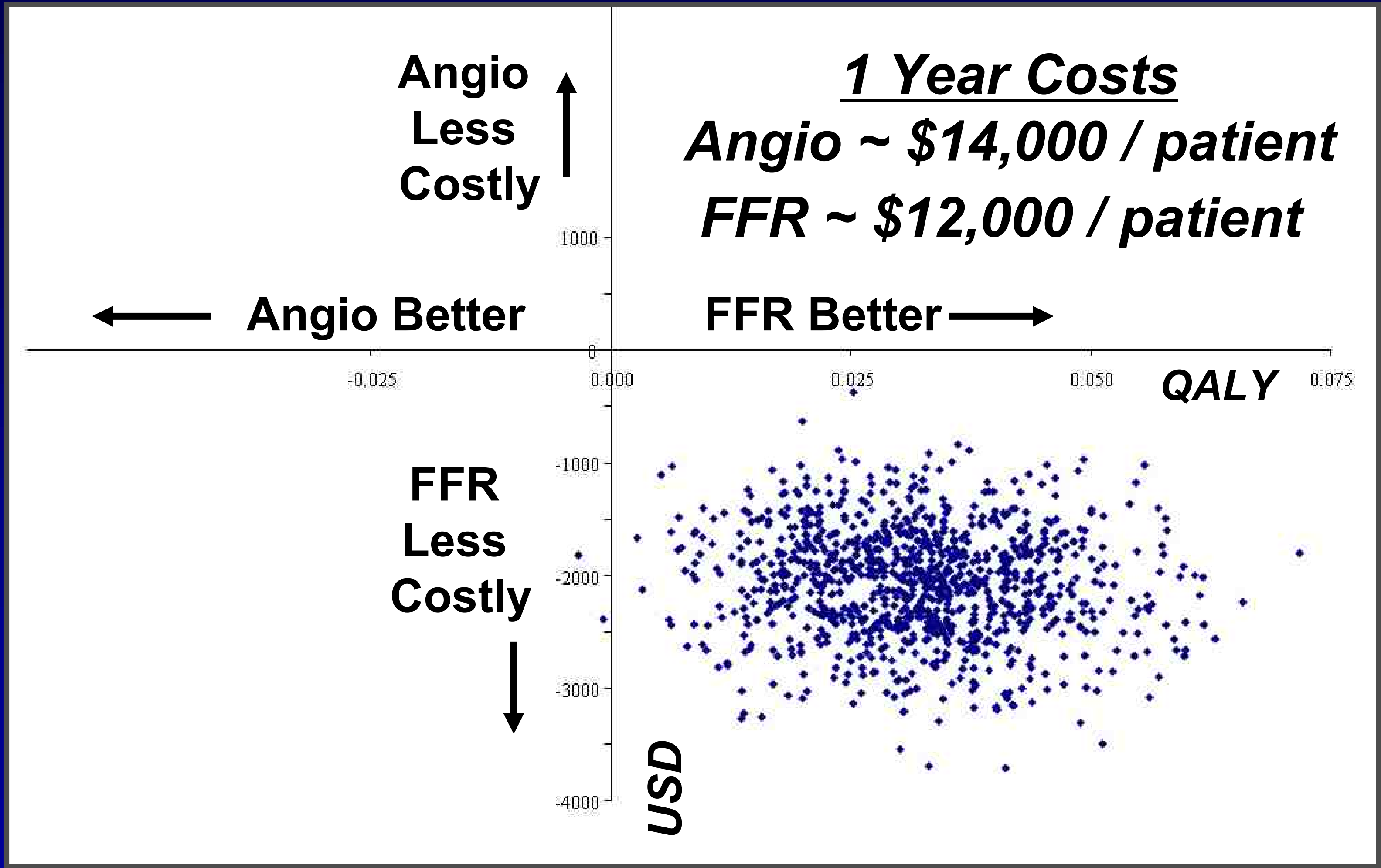
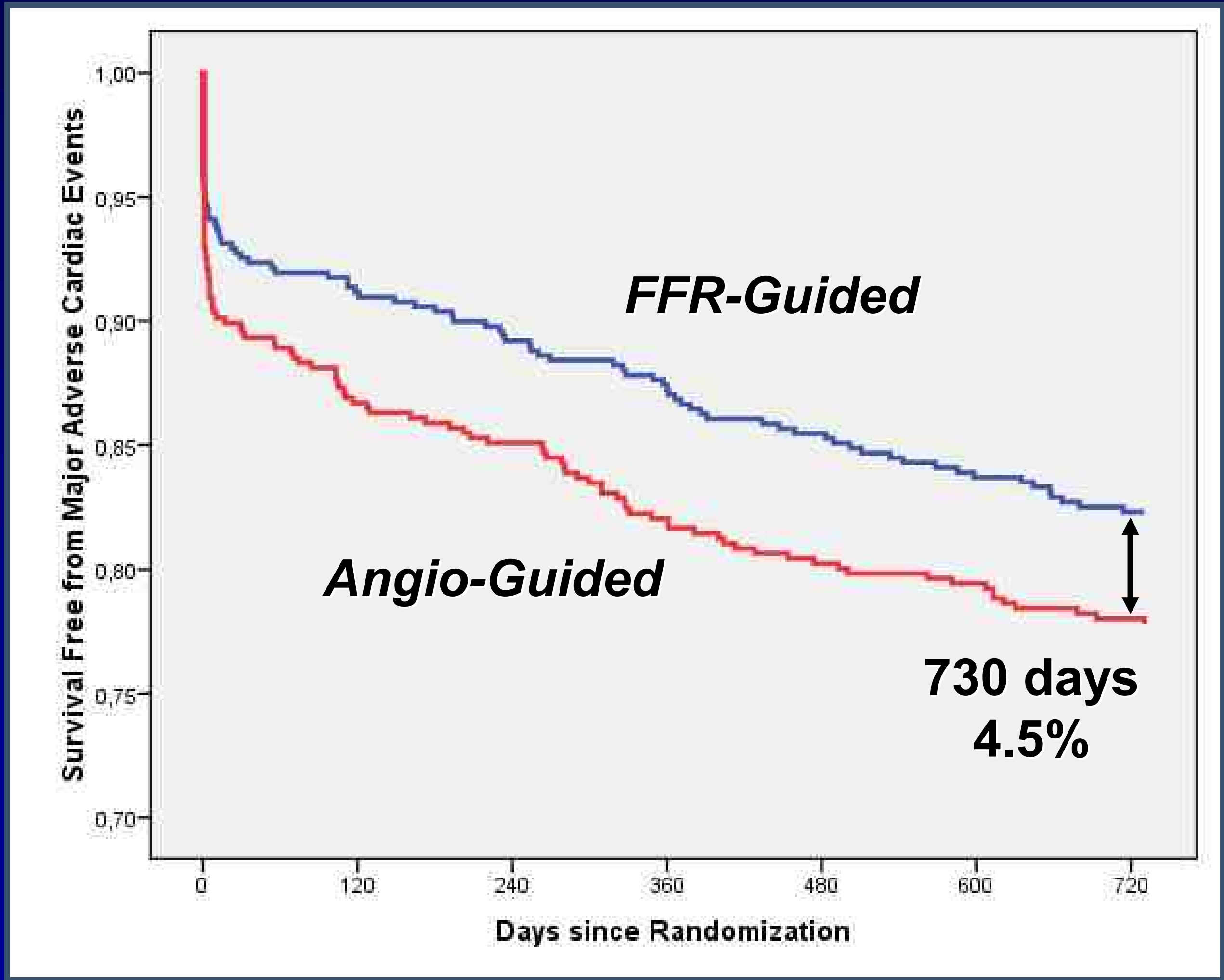
1 Year Economic Evaluation

Bootstrap Simulation



2 Year Survival Free of MACE



Late Breaking Trial, TCT 2009

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Adverse Events at 2 Years

	Angio-Guided n = 496	FFR-Guided n = 509	P Value
Total no. of MACE	**139**	**105**	
Individual Endpoints			
Death	19 (3.8)	13 (2.6)	0.25
Myocardial Infarction	48 (9.7)	31 (6.1)	0.03
CABG or repeat PCI	61 (12.3)	53 (10.4)	0.35
Composite Endpoints			
Death or Myocardial Infarction	63 (12.7)	43 (8.4)	0.03
Death, MI, CABG, or re-PCI	110 (22.2)	90 (17.7)	0.07

2 Year Outcome of Deferred Lesions

513 Deferred Lesions in 509 FFR-Guided Patients

↓ ***2 Years***

31 Myocardial Infarctions → **22 Peri-procedural**

↓

9 Late Myocardial Infarctions → **8 Due to a New Lesion or Stent-Related**

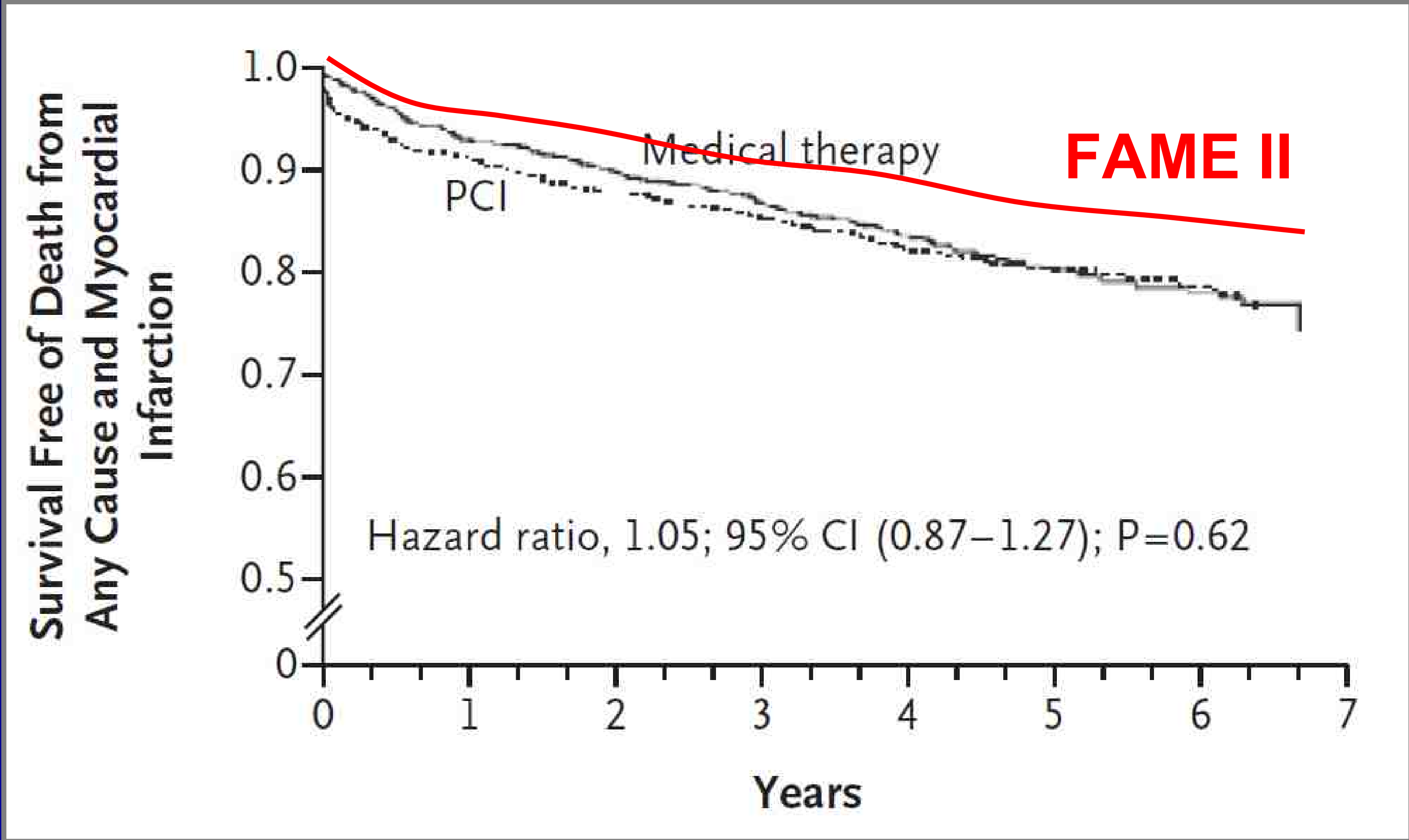
↓

1 Myocardial Infarction due to an Originally Deferred Lesion

Only 1/513 or 0.2% of deferred lesions resulted in a late myocardial infarction

Implications of FAME

Death and MI in the COURAGE study



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

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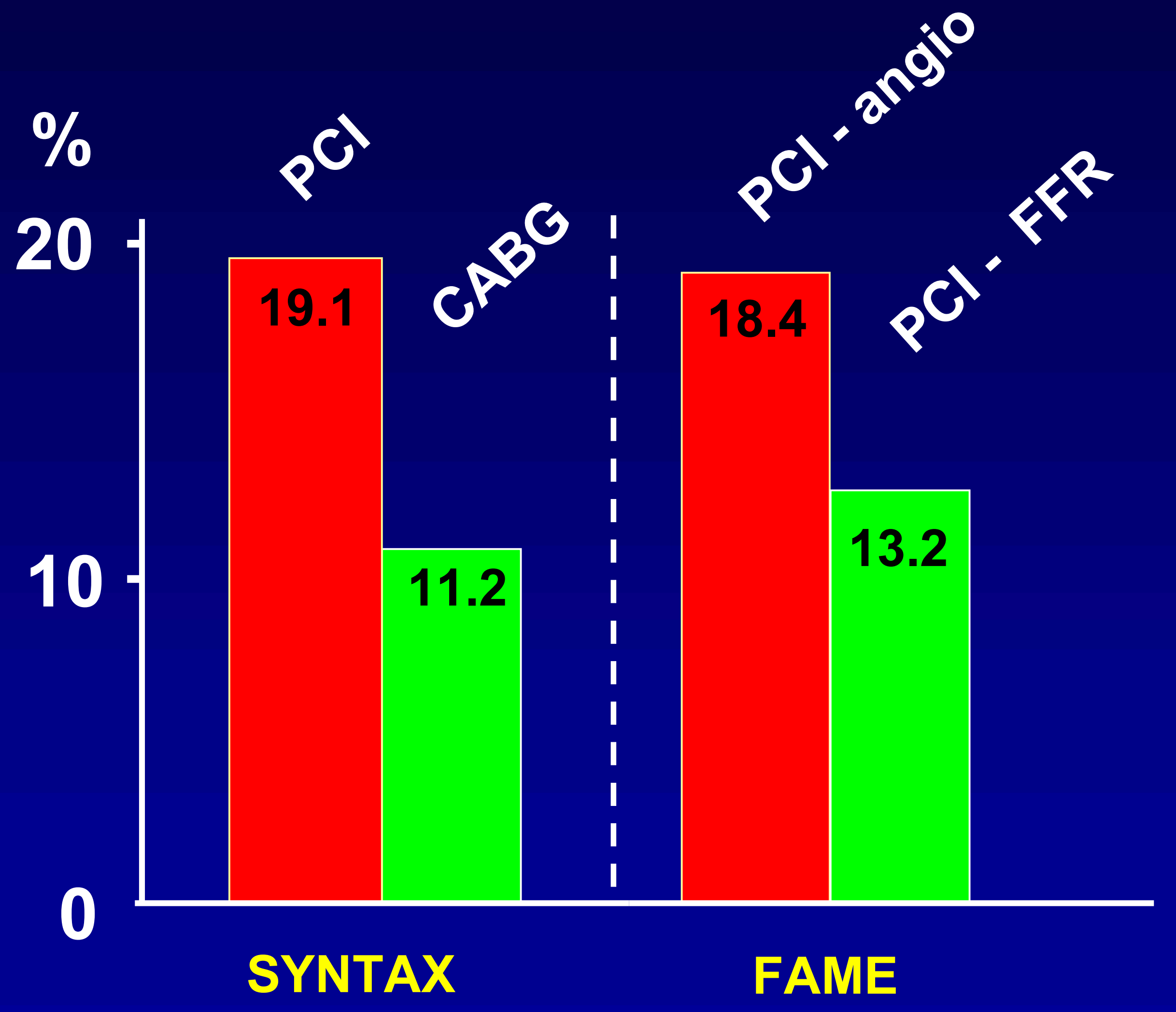
Implications of FAME



1 year MACE Rates

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2009 PCI Guidelines Update

1. **FFR can be useful to determine if PCI is warranted, particularly if the noninvasive test is absent or equivocal. It is reasonable to use FFR for assessing the need for PCI of intermediate lesions (IIa)**

2. **FFR is not warranted to assess an angiographically significant stenosis if there is angina present and an unequivocally positive stress test in a concordant vascular distribution (III)**

Circulation 2009;120:2271-2306

Final Thoughts:

- FFR-guided PCI improves outcomes and saves money compared to angio-guided
- FFR-guided PCI may help identify stable CAD which would benefit from PCI as compared to medical therapy alone
- FFR-guided PCI may result in equivalent outcomes compared to CABG