Beyond FAME:
The Integration of FFR into Clinical Practice

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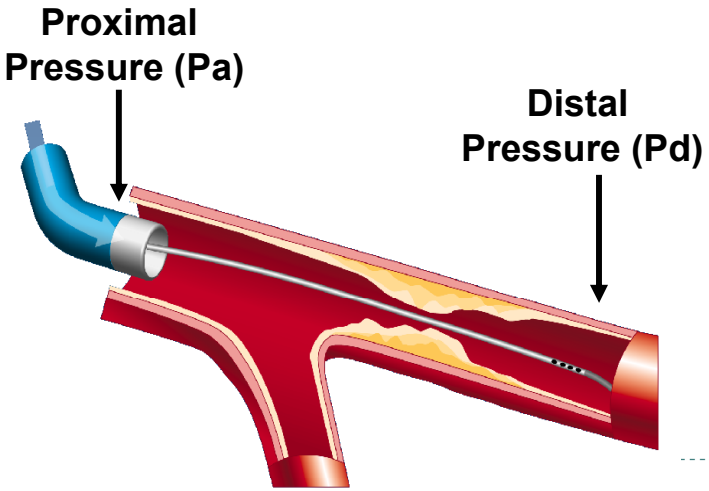
Disclosure Statement of Financial Interest

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

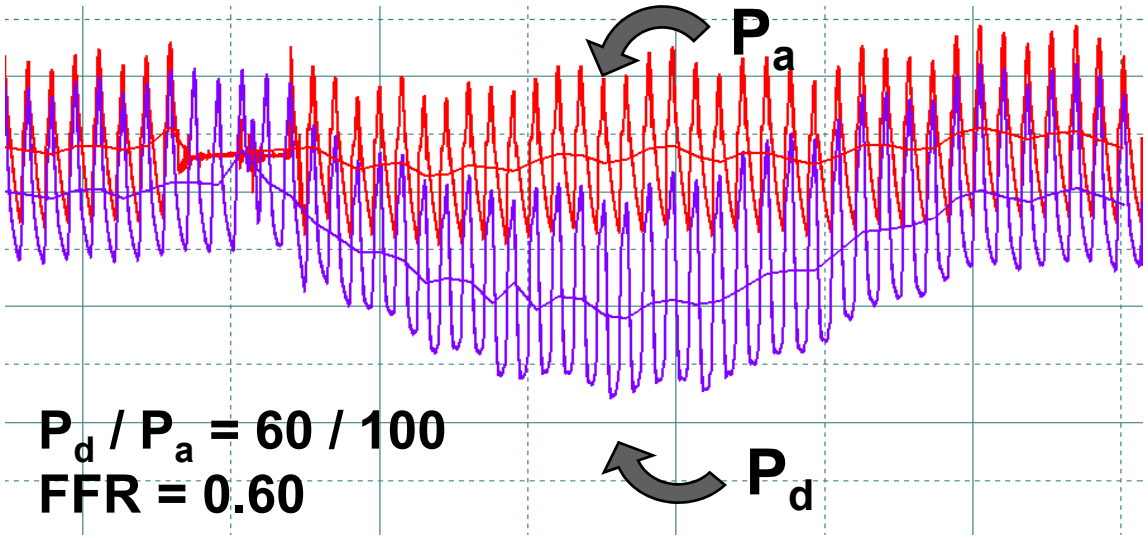
Affiliation/Financial Relationship	Company
Grant/ Research Support:	**St. Jude Medical**
Consulting Fees/Honoraria:	**Tryton Medical**
Major Stock Shareholder/Equity Interest:	
Royalty Income:	
Ownership/Founder:	
Salary:	
Intellectual Property Rights:	
Other Financial Benefit (minor stock options):	**HeartFlow**

Fractional Flow Reserve



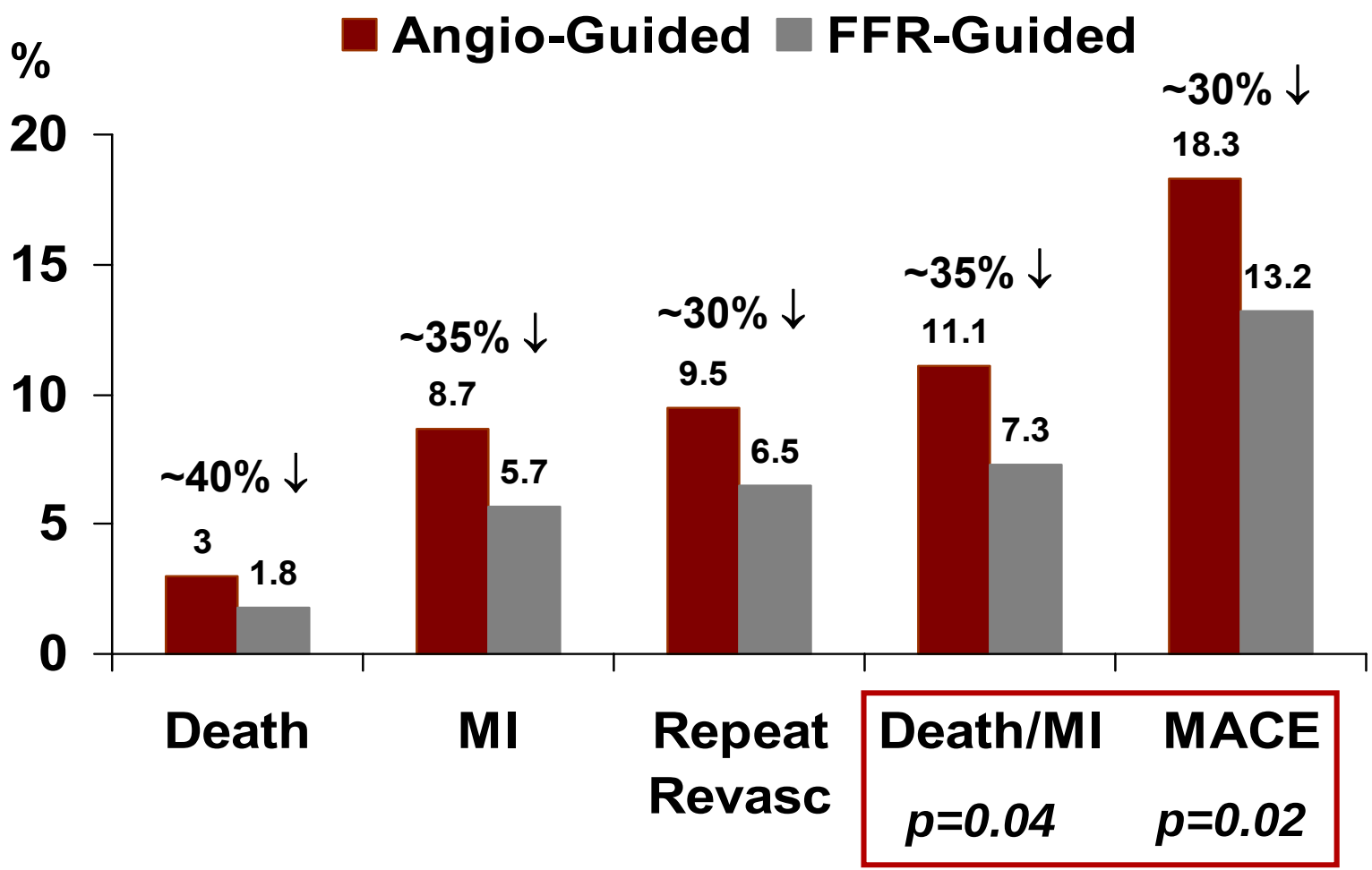
FFR = P_d / P_a

during maximal flow



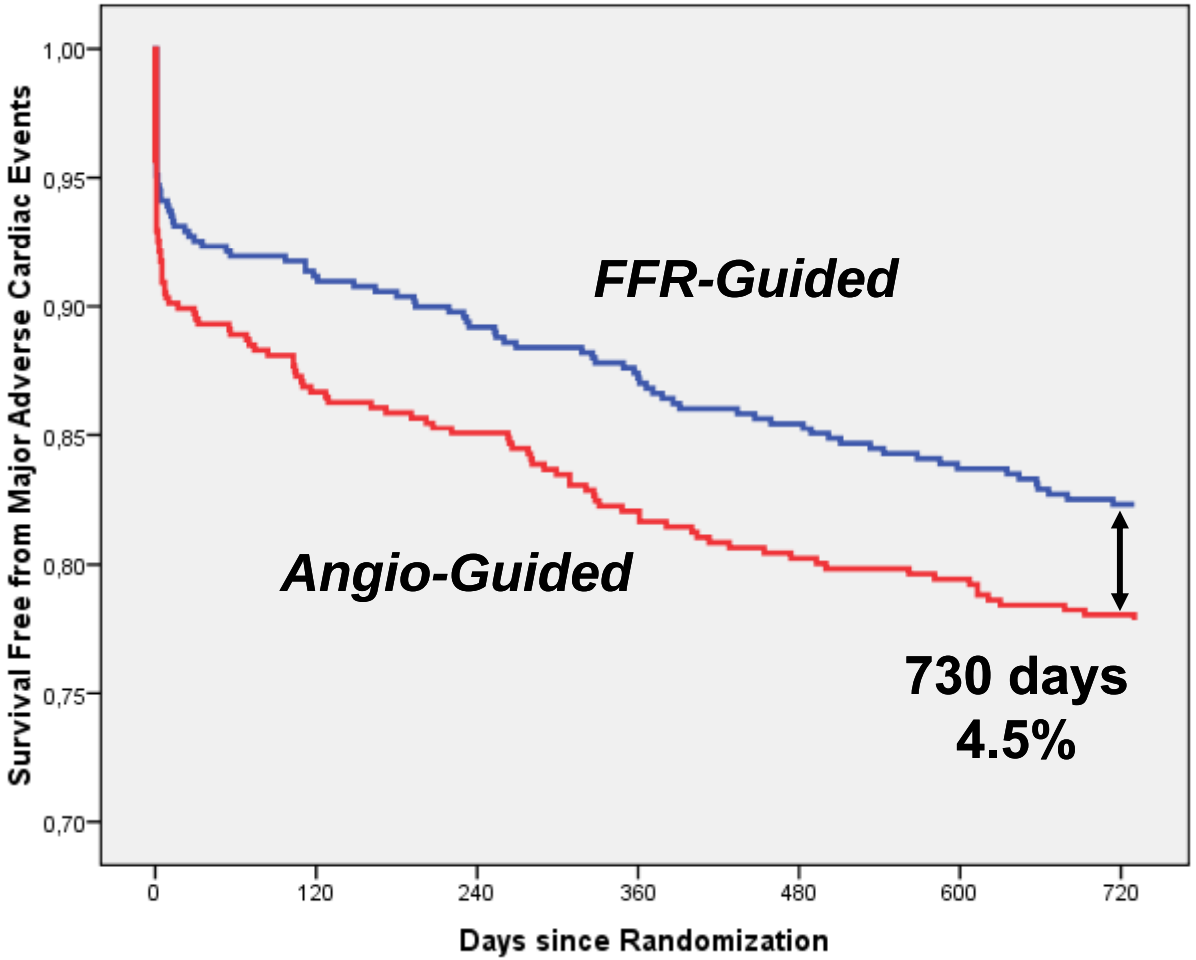
P_d / P_a = 60 / 100
FFR = 0.60

FAME Study: One Year Outcomes



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

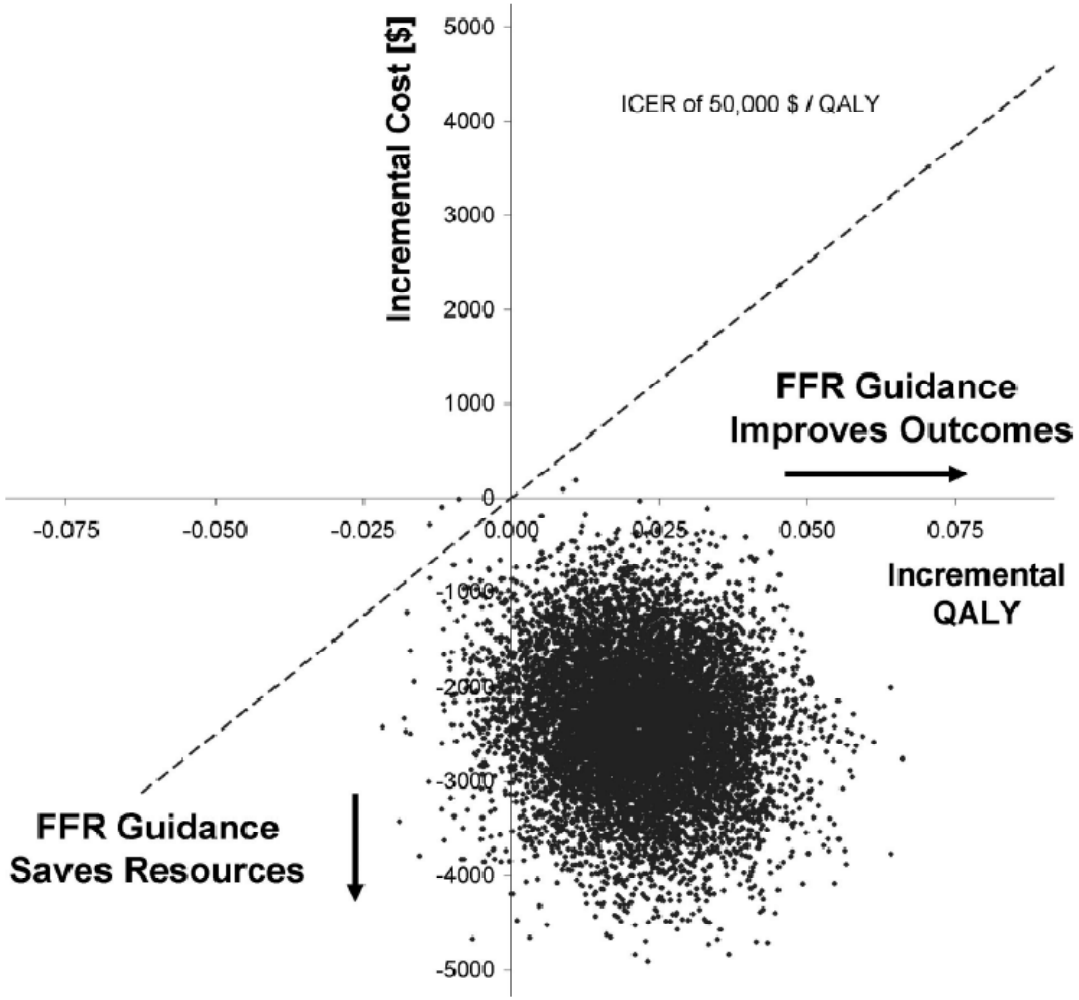
FAME Study: Two Year Outcomes



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.

Barriers to Further Integration of FFR into Clinical Practice

- Perceived effect on procedure time
  - FFR and Angio-guided arms had identical procedure times in FAME
- Potential impact on PCI volume ($$)

Anatomic vs. Functional CAD

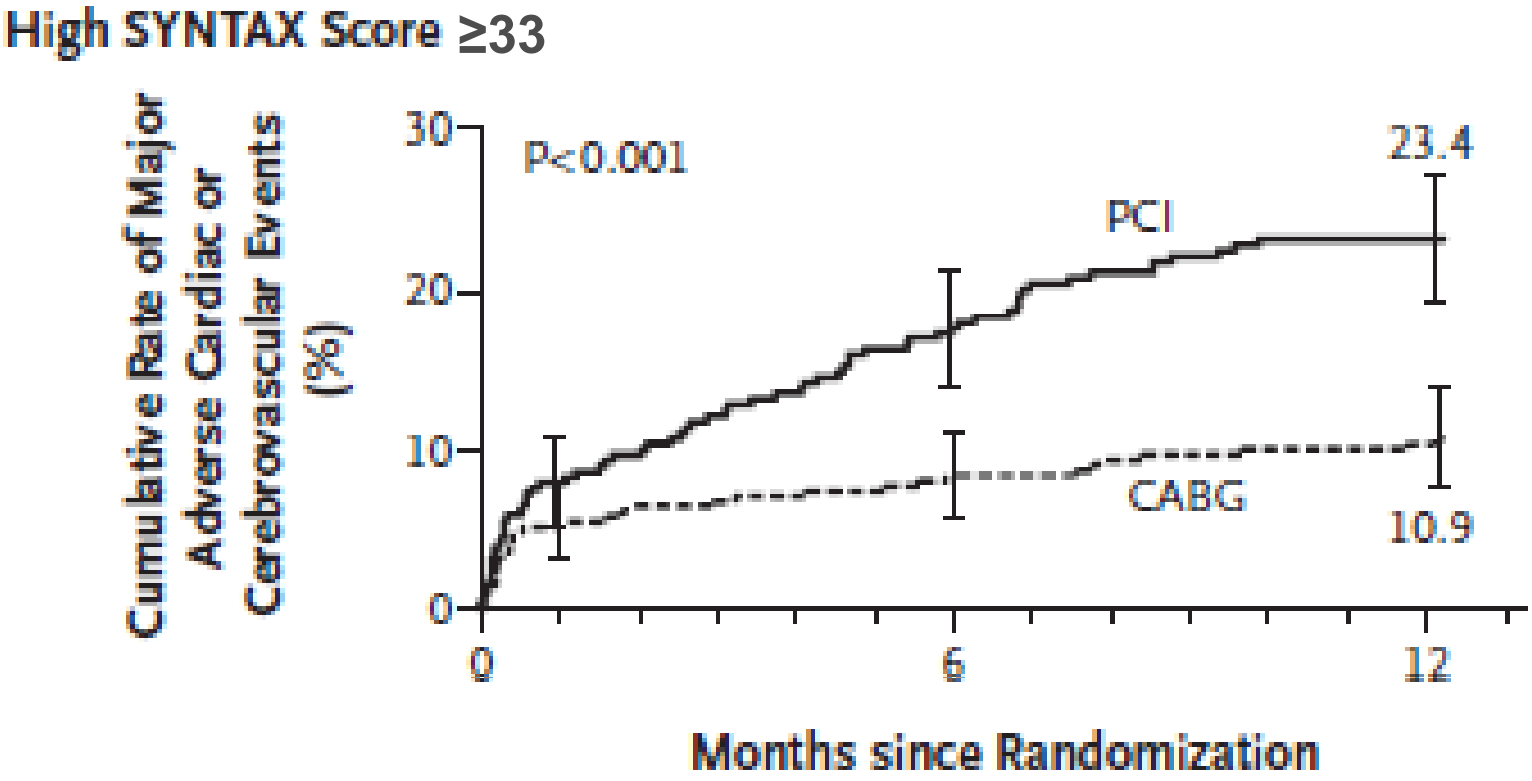
Patients with angiographically 3VD (N=115), proportions per number of diseased vessels after assessment by FFR

Angiographic 3 Vessel Disease

JACC 2010;55:2816-21

Predictive Value of the SYNTAX Score

Improved outcomes in multivessel CAD patients with the highest SYNTAX score treated with CABG



Serruys et al. N Engl J Med 2009;360:961-72

Impact of SYNTAX Score on PCI

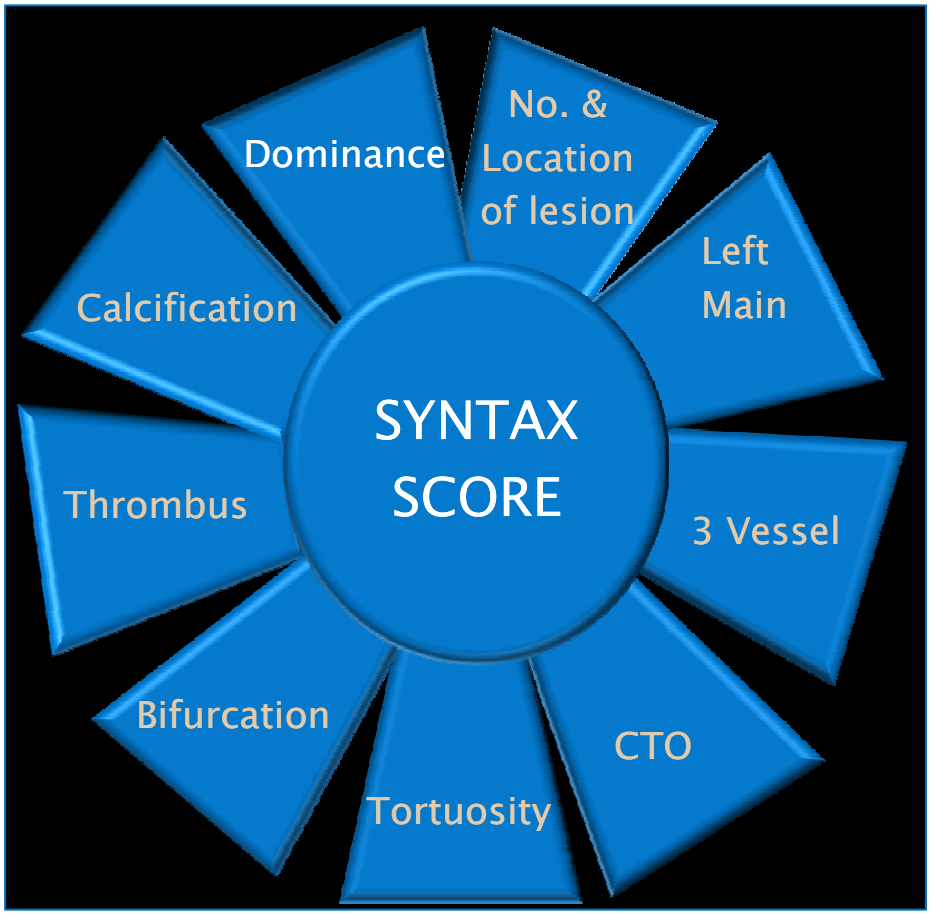
Recently published European guidelines for revascularization

Subset of CAD by anatomy	Favours CABG	Favours PCI	Ref.
1VD or 2VD - non-proximal LAD	IIb C	I C	—
1VD or 2VD - proximal LAD	I A	IIa B	30, 31, 50, 51
3VD simple lesions, full functional revascularization achievable with PCI, SYNTAX score ≤22	I A	IIa B	4, 30–37, 53
3VD complex lesions, incomplete revascularization achievable with PCI, SYNTAX score >22	I A	III A	4, 30–37, 53
Left main (isolated or 1VD, ostium/shaft)	I A	IIa B	4, 54
Left main (isolated or 1VD, distal bifurcation)	I A	IIb B	4, 54
Left main + 2VD or 3VD, SYNTAX score ≤32	I A	IIb B	4, 54
Left main + 2VD or 3VD, SYNTAX score ≥33	I A	III B	4, 54

Wijns W, Kolh P, et al. Eur Heart J 2010

SYNTAX Score

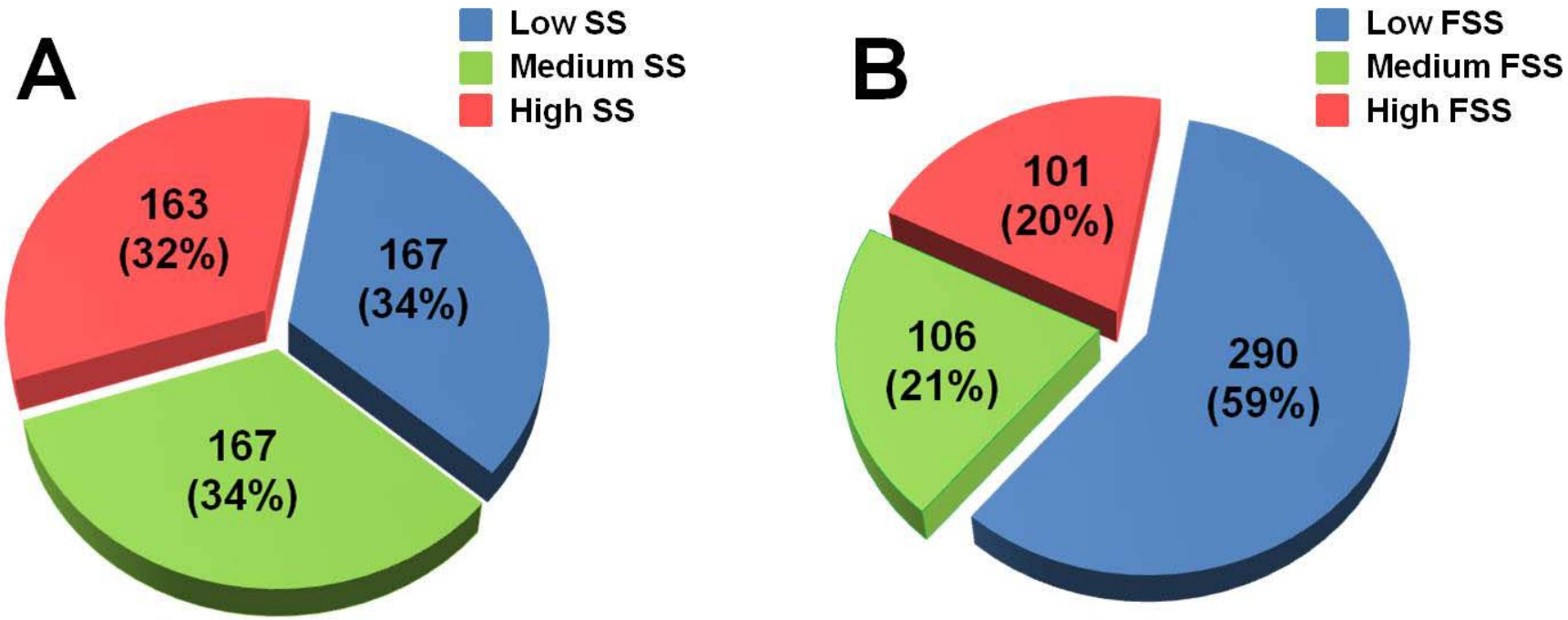
- Angiography-based scoring system aimed at determining coronary lesion complexity
- Because it is angiography-based, it is inherently limited by the accuracy of the coronary angiogram



Can we enhance the SYNTAX Score?

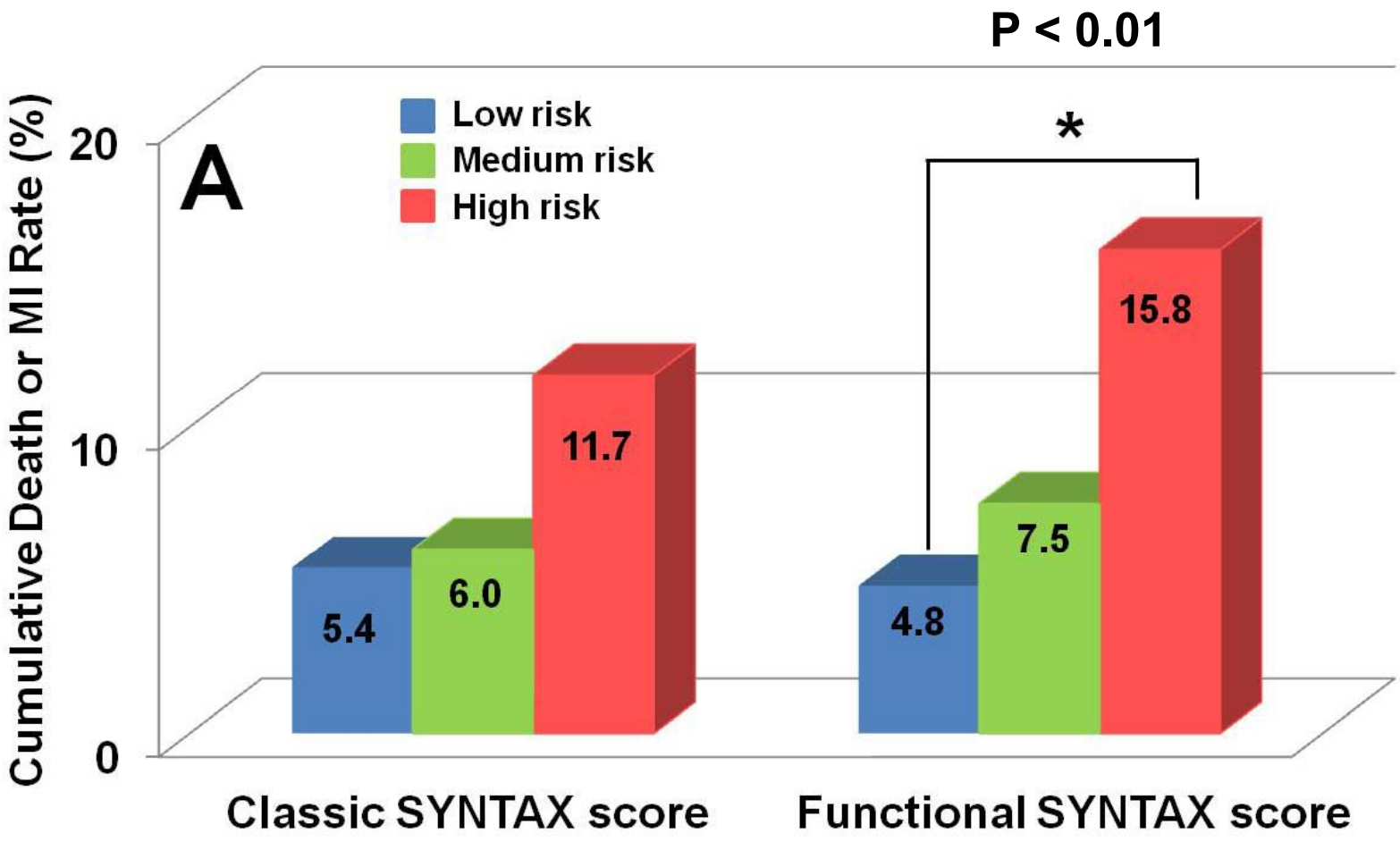
- By incorporating FFR into the SYNTAX score, termed “Functional SYNTAX Score” (FSS), can we:
  - Convert high/medium risk SYNTAX score patients to a lower risk group?
  - Improve our risk stratification of patients with multivessel CAD undergoing PCI?

FSS Reclassifies > 30% of Cases



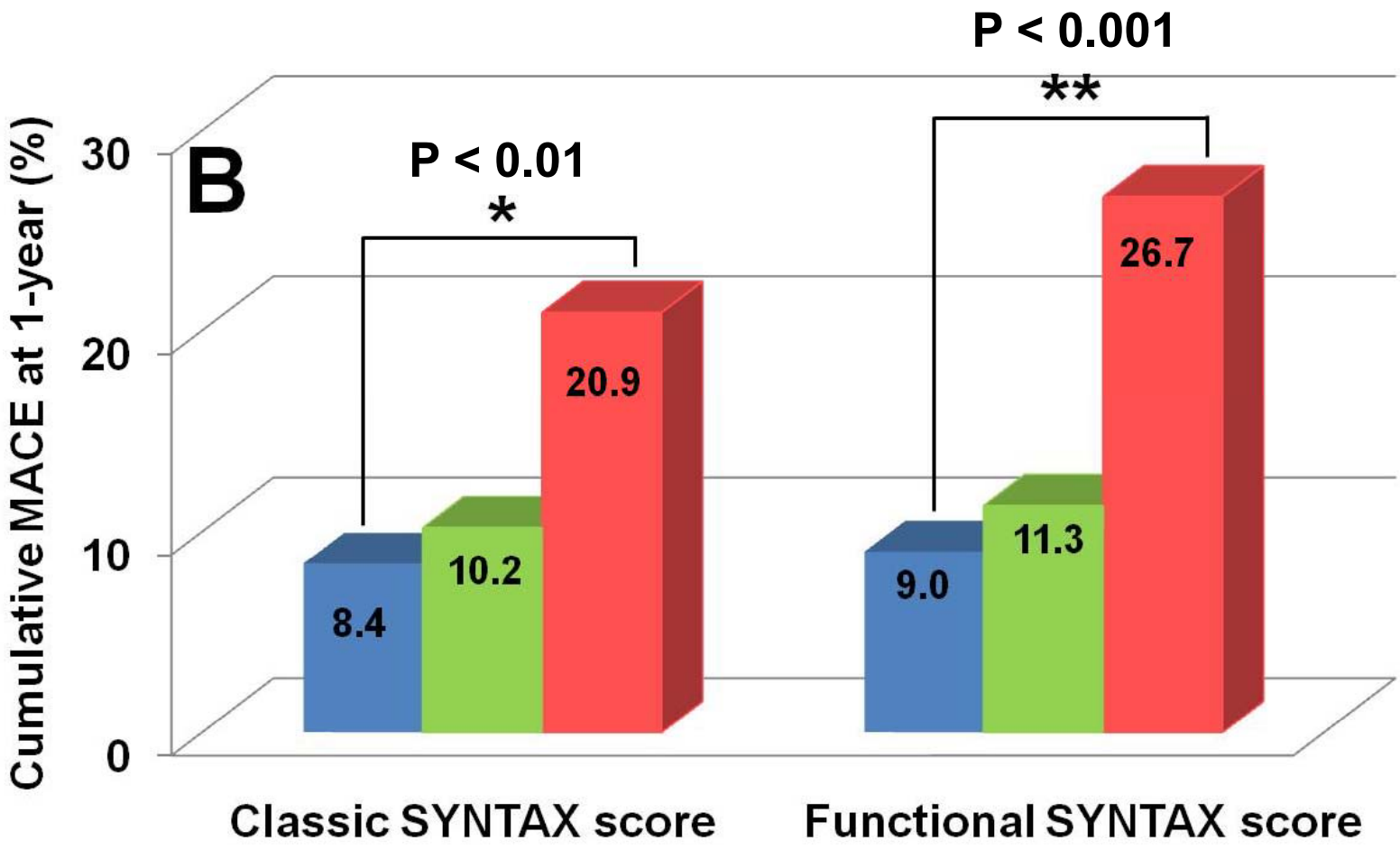
Nam CW, et al. J Am Coll Cardiol 2011 (Submitted)

FSS Discriminates Risk for Death/MI



Nam CW, et al. J Am Coll Cardiol 2011 (Submitted)

FSS Discriminates Risk for MACE



Nam CW, et al. J Am Coll Cardiol 2011 (Submitted)

Can FFR Increase PCI Volume?

- The mean FSS decreased by ~25% compared to the mean SS
- 43% of patients with a SS > 22 moved to an FSS < 22

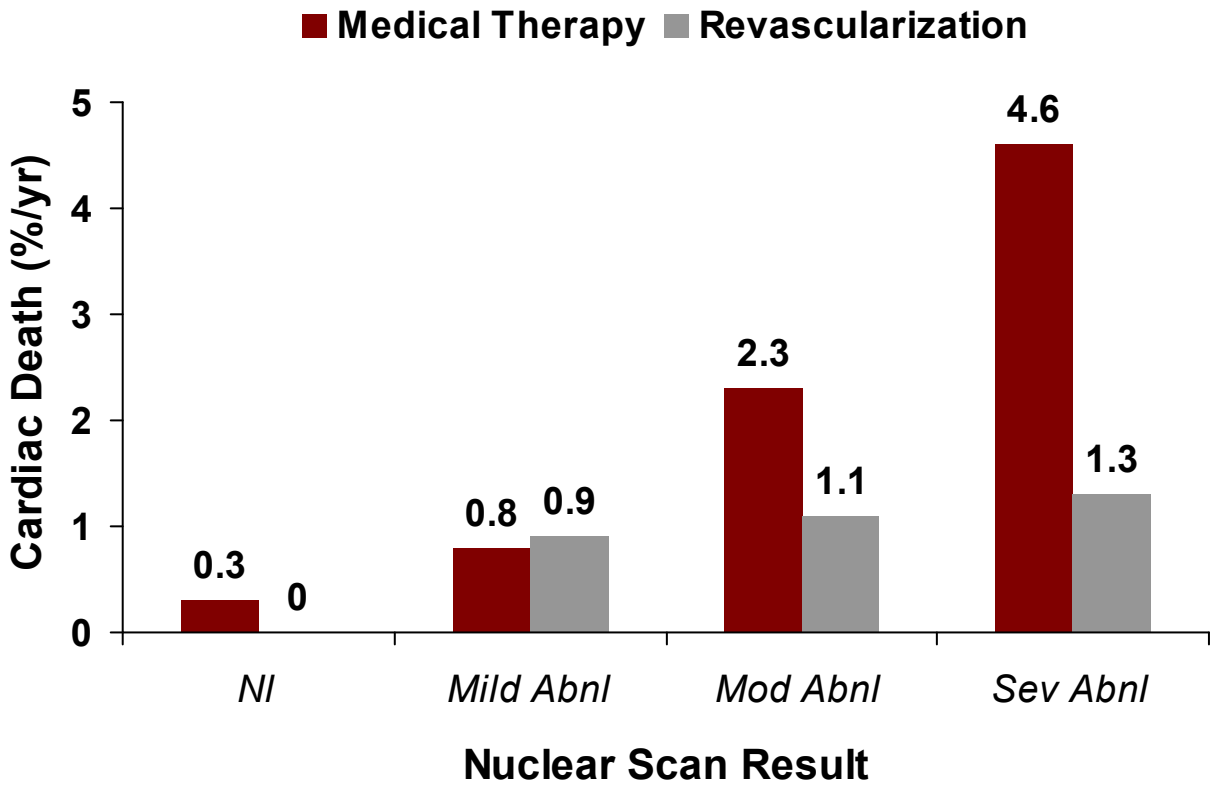
Nam CW, et al. J Am Coll Cardiol 2011 (Submitted)

Barriers to Further Integration of FFR into Clinical Practice

- Perceived effect on procedure time
  - FFR and Angio-guided arms had identical procedure times in FAME
- Potential impact on PCI volume ($$)
- Preoccupation with anatomic complete revascularization, instead of focusing on *functionally complete revascularization*

Ischemia and Outcomes

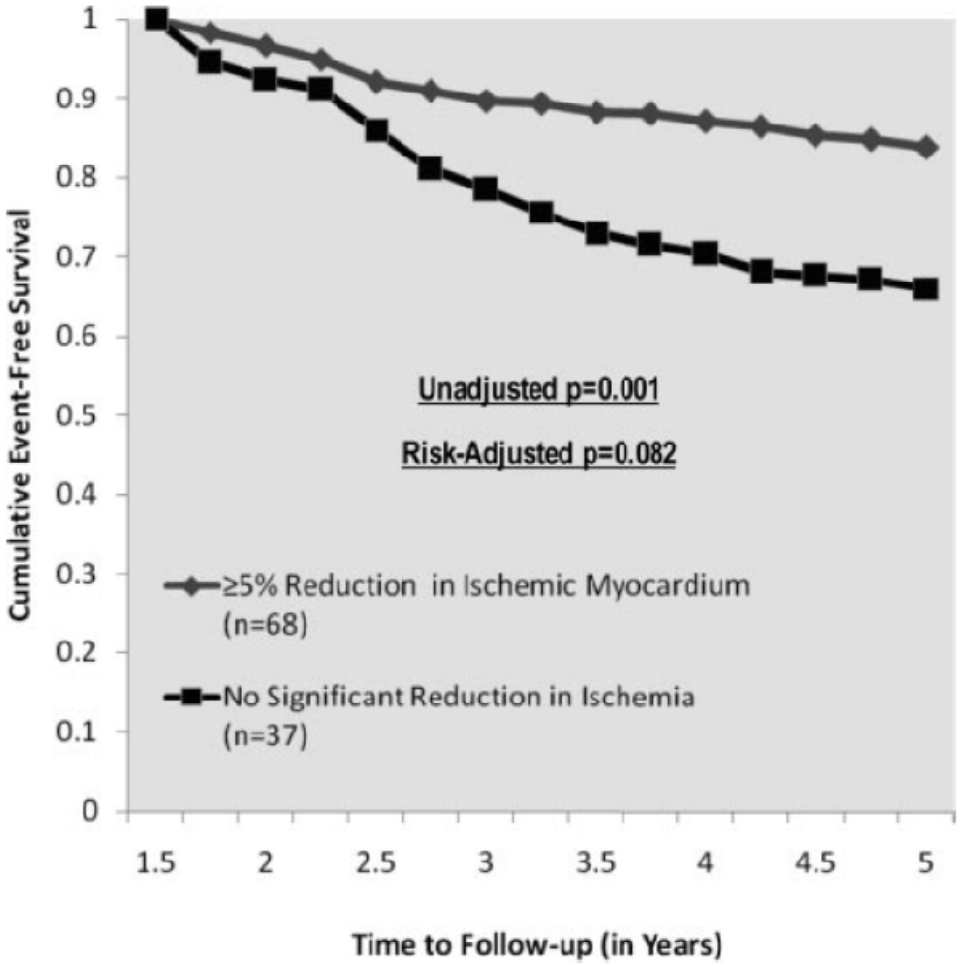
Nuclear perfusion scans performed in > 5000 patients



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

Relief of Ischemia Improves Outcomes

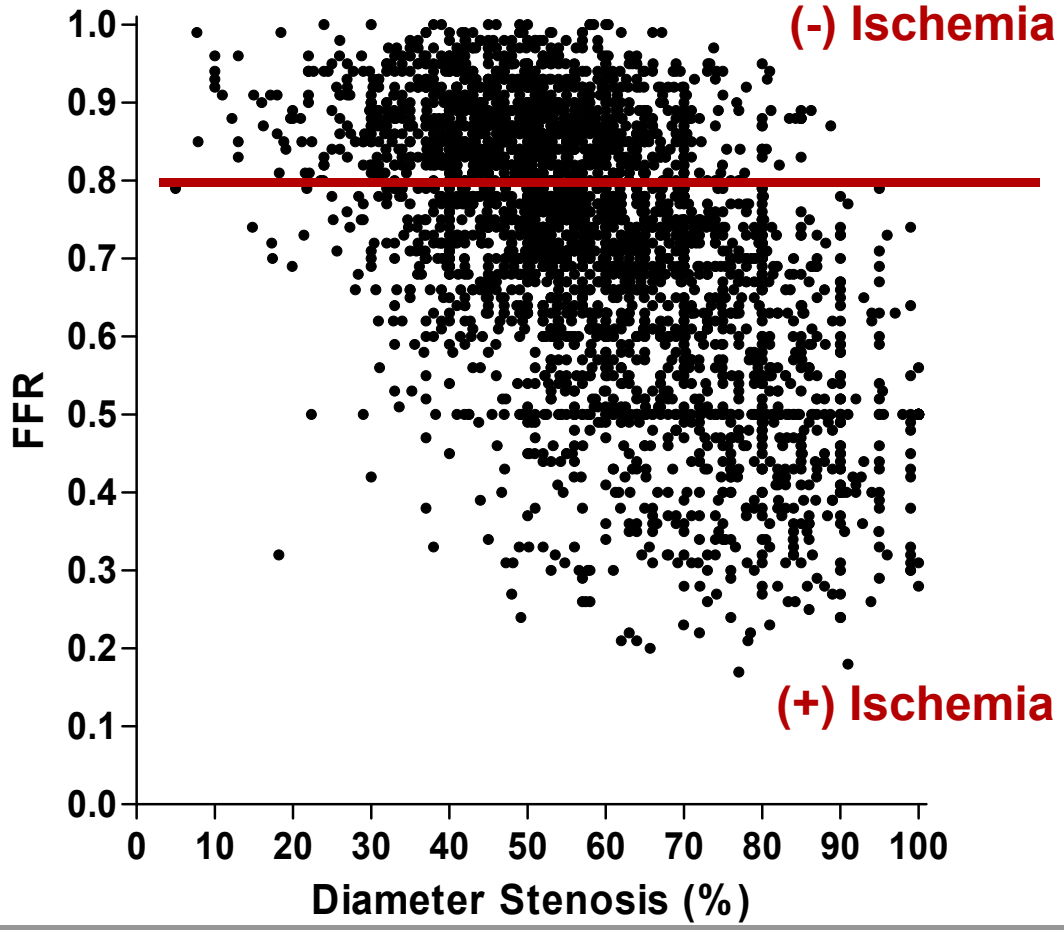
Death/MI in patients with mod-severe pre-treatment ischemia



Shaw, et al. Circulation 2008;117:1283

Limitation of Angiography

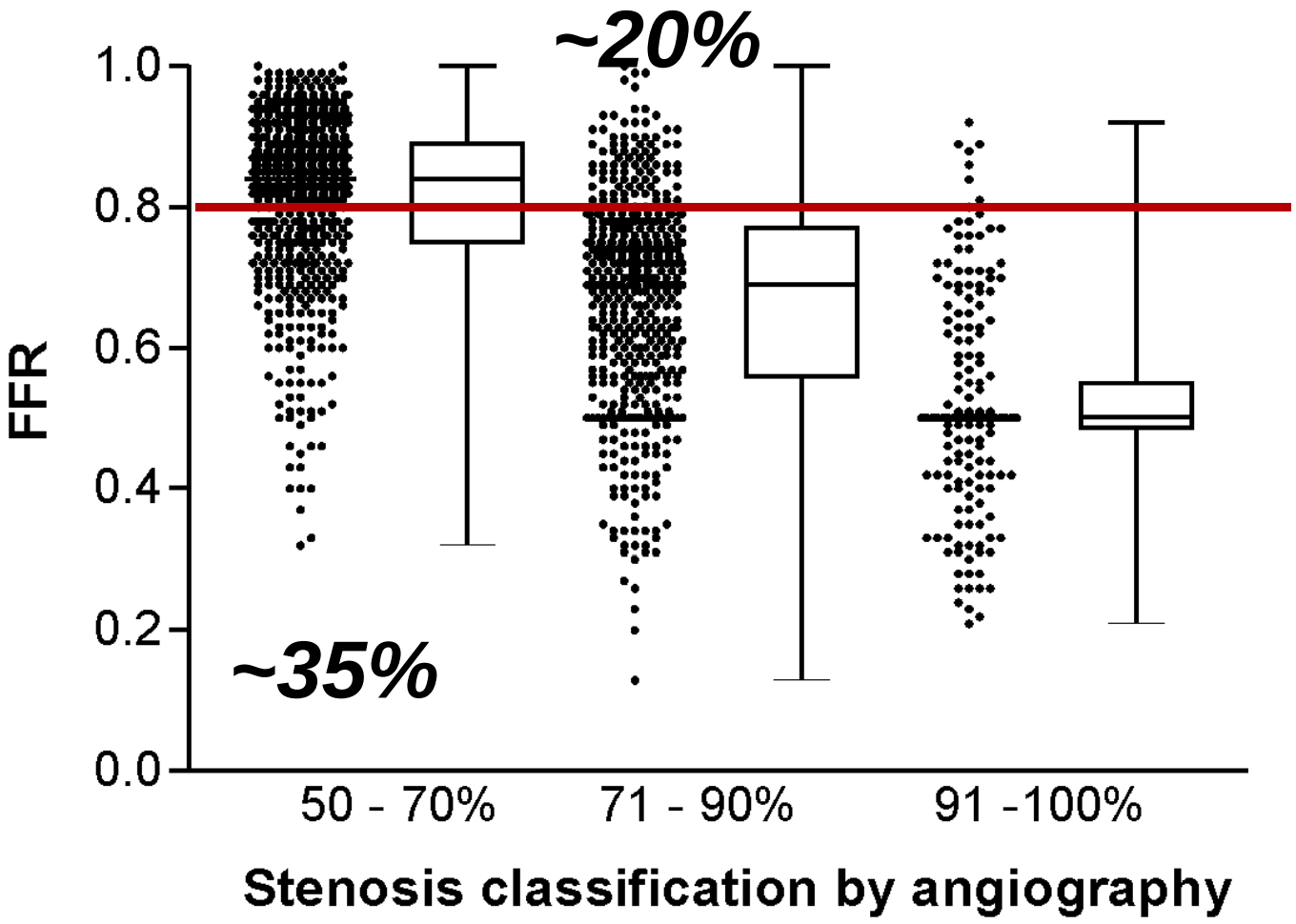
Comparison of QCA to FFR in over 3,000 lesions



Courtesy of Bernard De Bruyne, MD, PhD

Limitation of Angiography

1329 lesions in the FFR-guided arm of the FAME Study



J Am Coll Cardiol 2010;55:2816-21.

What happens to deferred lesions?

Two Year Follow-up of Lesions Deferred in FAME

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**

↓

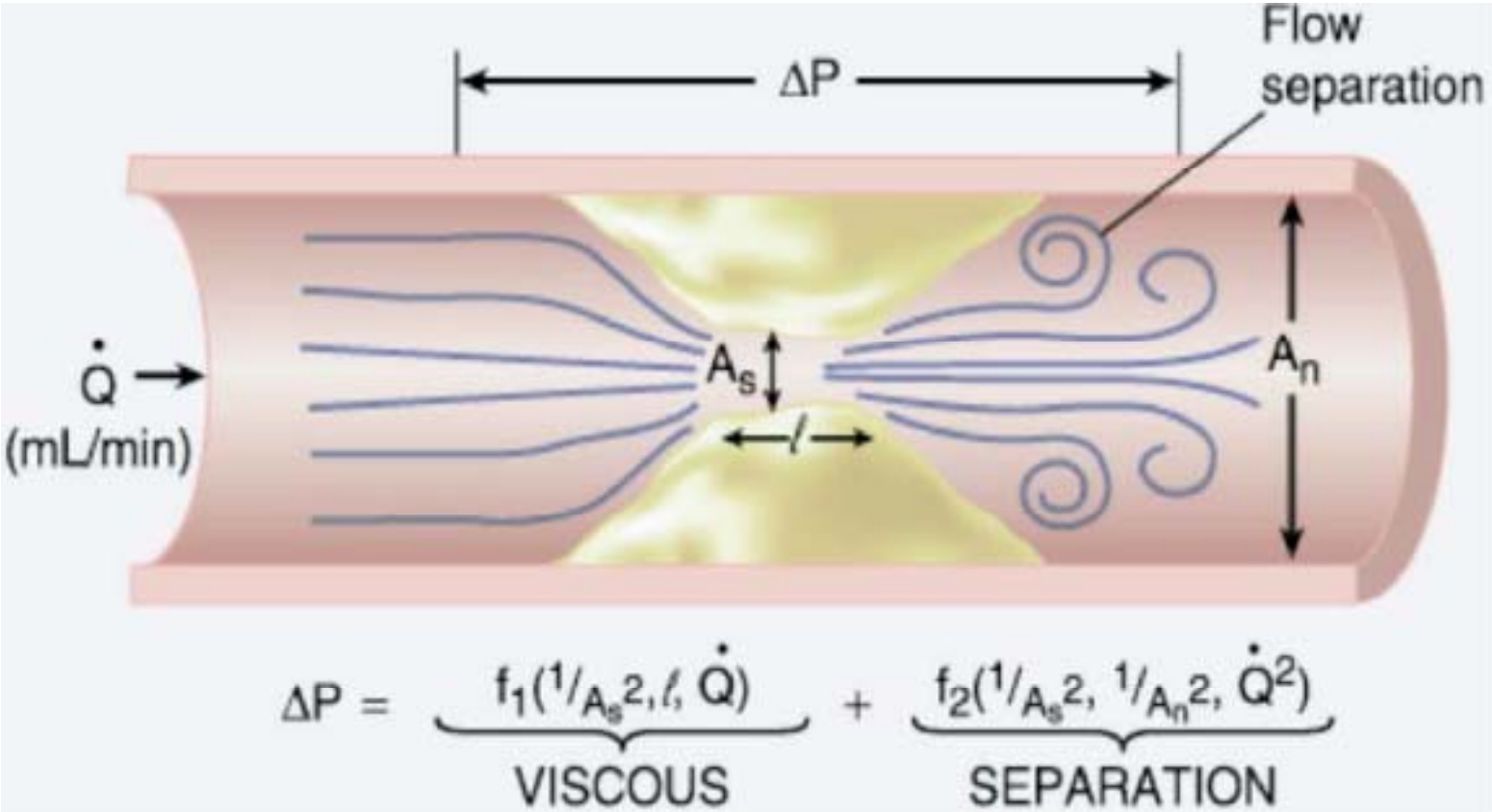
1 Myocardial Infarction due to an Originally Deferred Lesion

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

J Am Coll Cardiol 2010;56:177-84

Why is Myocardial Ischemia Bad?

Determinants of an abnormal FFR

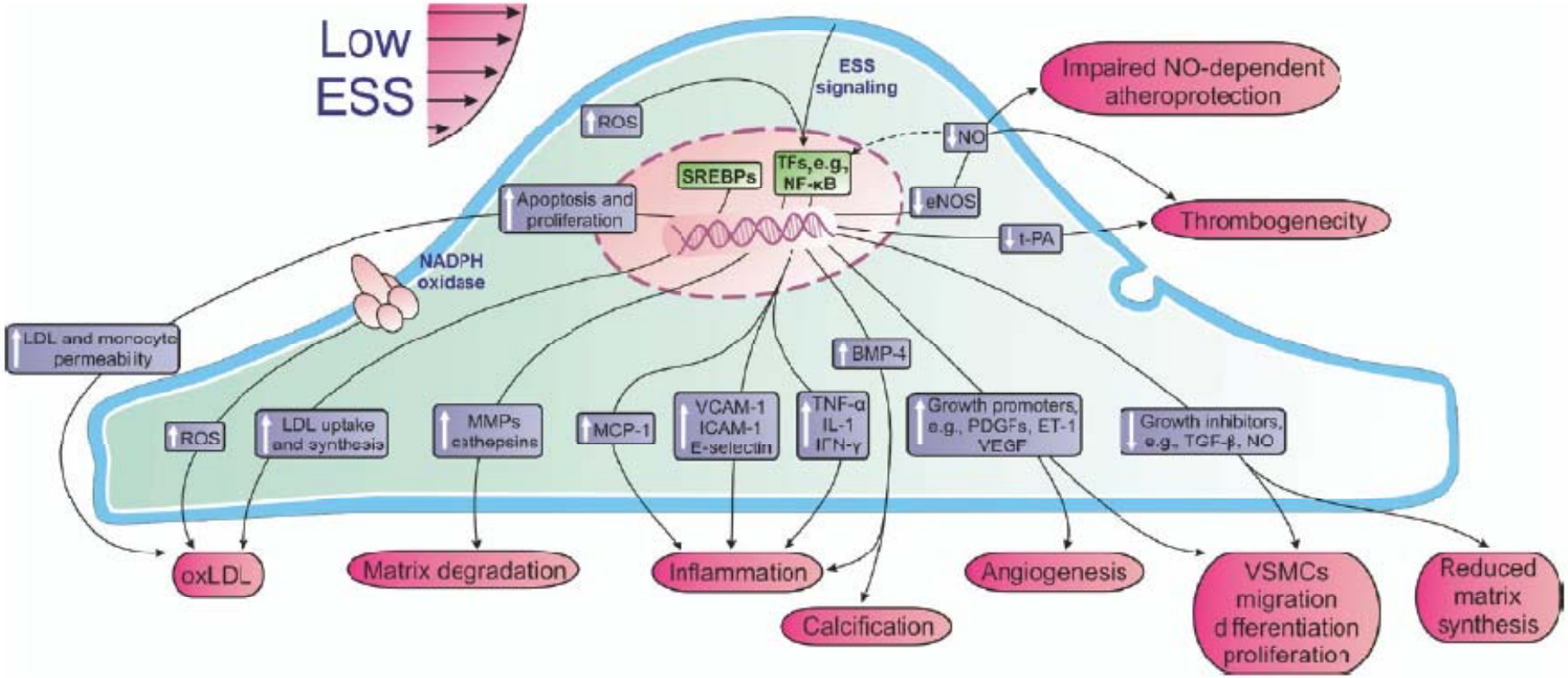


Braunwald's Heart Disease 2005, 7th edition, vol.2, p.1112.

Why is Myocardial Ischemia Bad?

Does Ischemia Lead to Plaque Vulnerability?

Low shear stress down-regulates vasoprotective factors and up-regulates inflammatory, oxidative stress, and thrombogenic factors

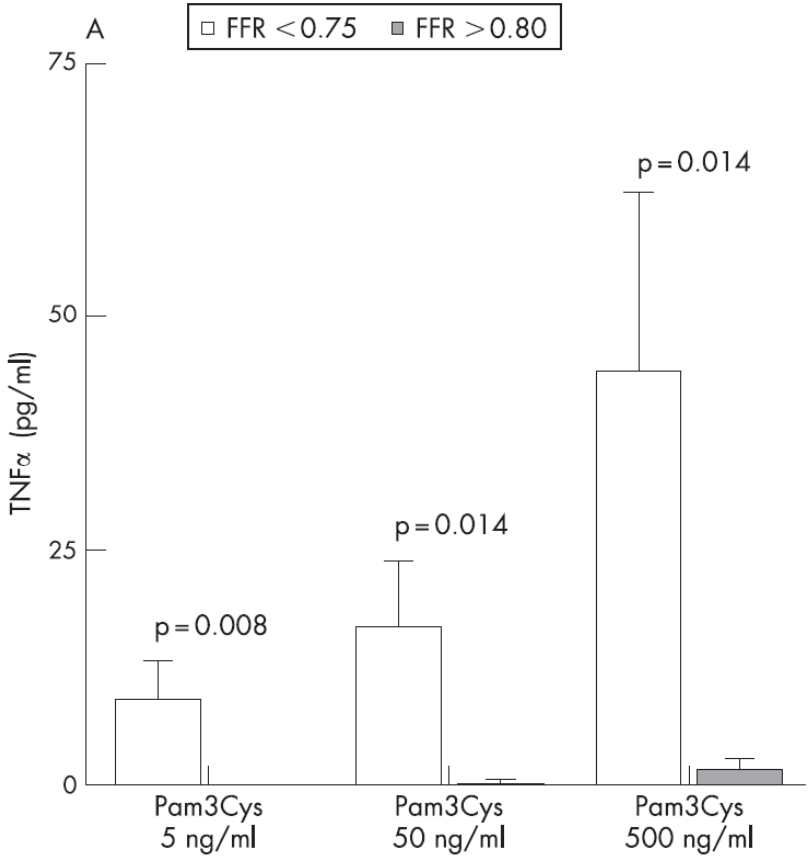


Chatzizisis et al. J Am Coll Cardiol 2007;49:2379

Why is Myocardial Ischemia Bad?

Does Ischemia Lead to Plaque Vulnerability?

Increased production of TNF-α correlates with fractional flow reserve measured in 70 patients referred for PCI



Versteeg, et al. Heart 2008;94:770

Integration of FFR into Practice

- FFR-Guided PCI
  - Improves patient outcomes
  - Saves Money
  - Does not prolong procedure times
  - Identifies lesions (and patients) which (who) will benefit most from PCI

We need to shift our focus from anatomic complete revascularization to "Functionally Complete Revascularization" (i.e. stenting ischemic lesions and medically treating nonischemic ones)