Use of FFR for Optimal Management of Multivessel Coronary Artery Disease

Richard G. Bach, MD
Associate Professor of Medicine
Washington University School of Medicine
Director of Cardiac Intensive Care Unit
Barnes-Jewish Hospital
St. Louis, Missouri

Disclosure:

- Research Support/Grants:
  Astra Zeneca, LP, Bristol-Myers Squibb Co, Eli Lilly & Co, and Merck/Schering-Plough Pharmaceuticals
- Consulting (Clinical Event Committees):
  F. Hoffman-La Roche and Wyeth/Pfizer

OUTLINE

- Case presentation
- Clinical trial data: Evidence
- Implications for clinical practice

Case Presentation:

HPI: 69 year-old woman

- 6-8 months vague chest discomfort and shortness of breath with exertion
- Remains active but more fatigued
- Definite decrease in exercise tolerance

Past Medical History

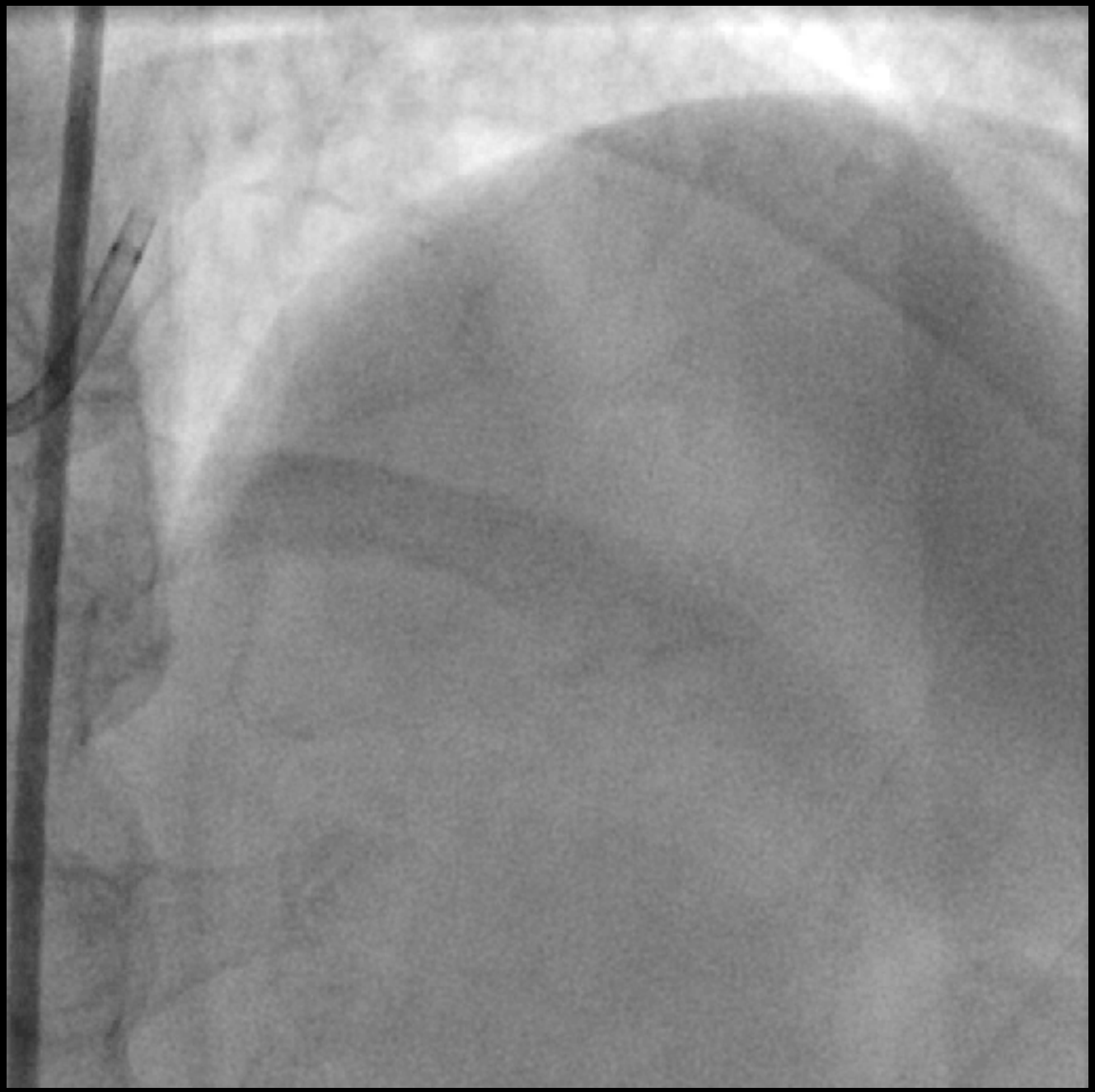
- Hyperlipidemia
- Hypertension
- Obstructive sleep apnea
- Endometrial cancer s/p hysterectomy

Nuclear stress test

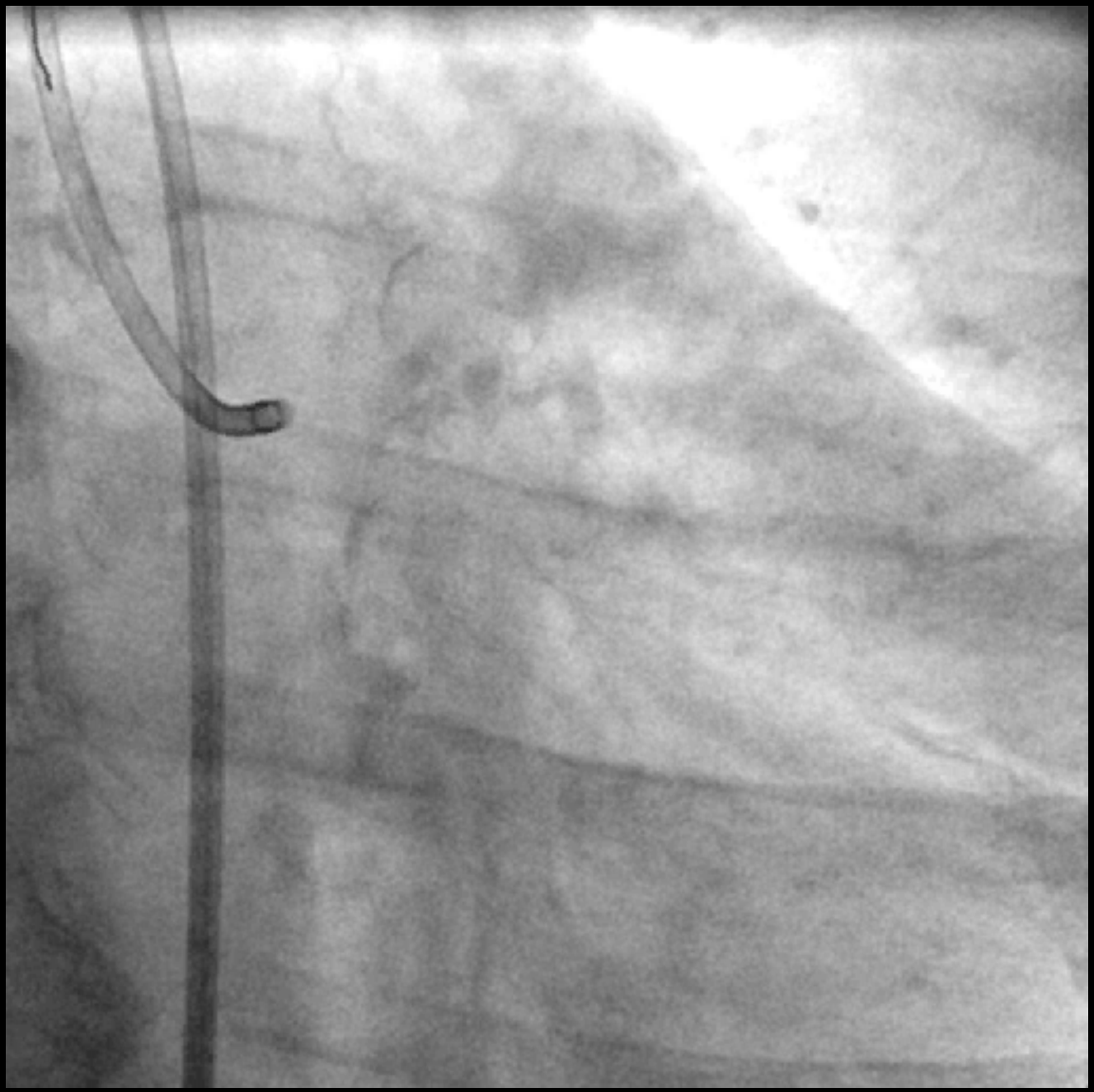
- Completed at an outside facility
- Showed possible apical and inferolateral ischemia;
- Ejection fraction normal
- No discomfort during the test
- No ECG changes reported

Cardiac Catheterization done:

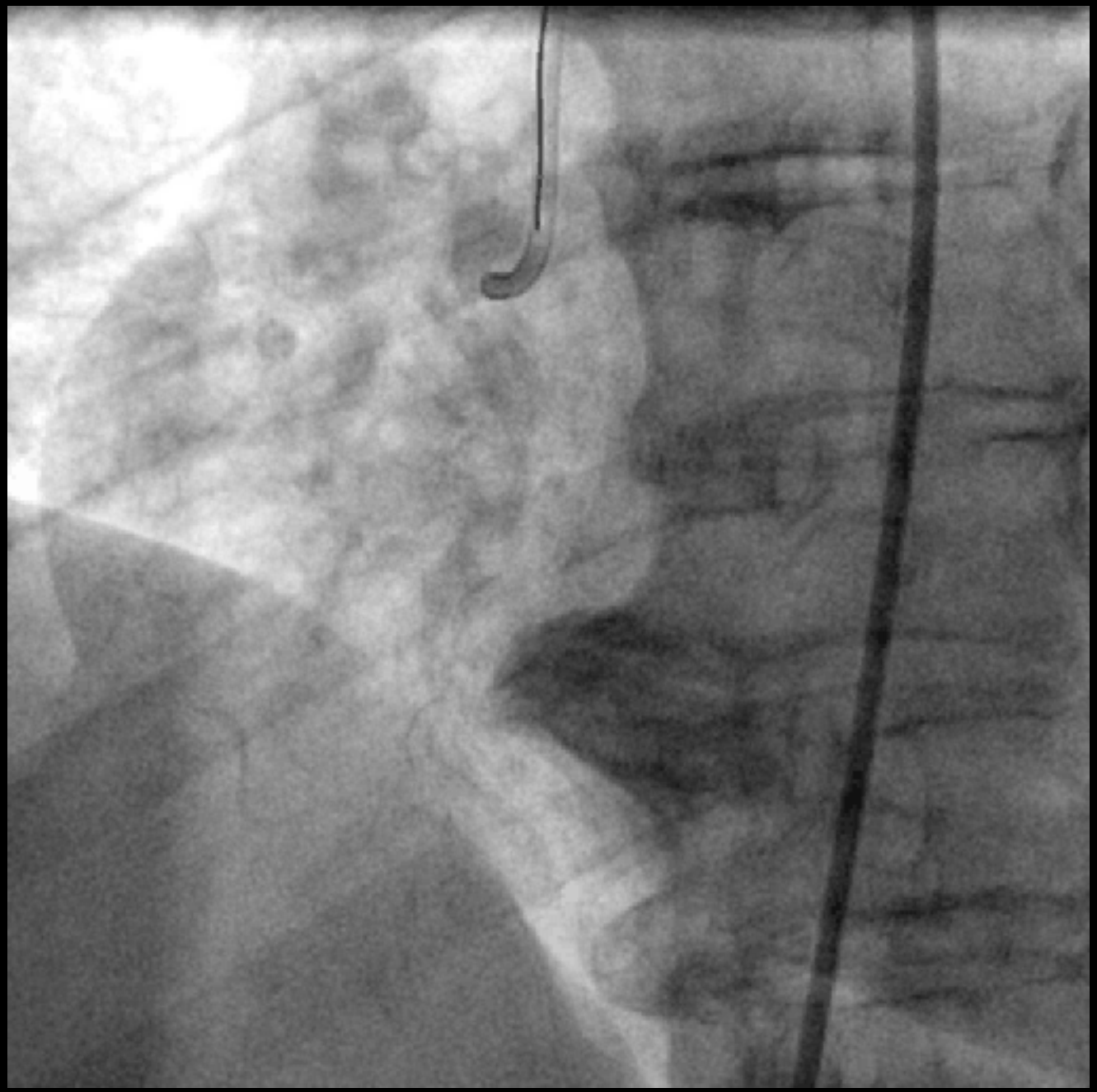
Coronary Angiography



Coronary Angiography



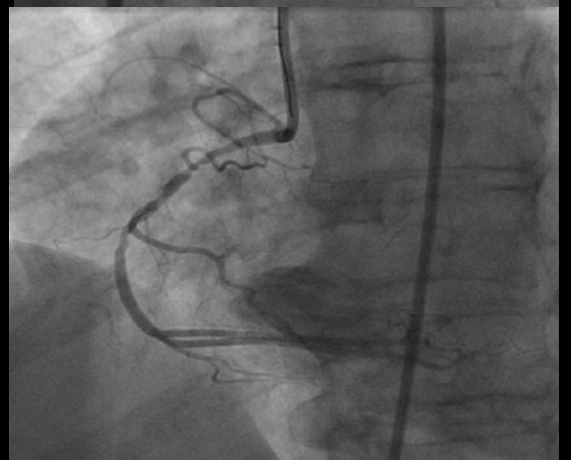
Coronary Angiography



Cardiac catheterization

- “Significant 3-vessel disease”
  - Proximal LAD: 60-70%
  - First OM: 95% at bifurcation
  - Proximal-mid RCA: diffuse 70%

- Referred for CABG
  - Patient hesitant and sought second opinion
  - Referred by new cardiologist for possible PCI



QUESTION:
What is the best option for the management of this patient?

A. Medical Therapy (per COURAGE)
B. Calculate the SYNTAX Score to decide on PCI vs. CABG
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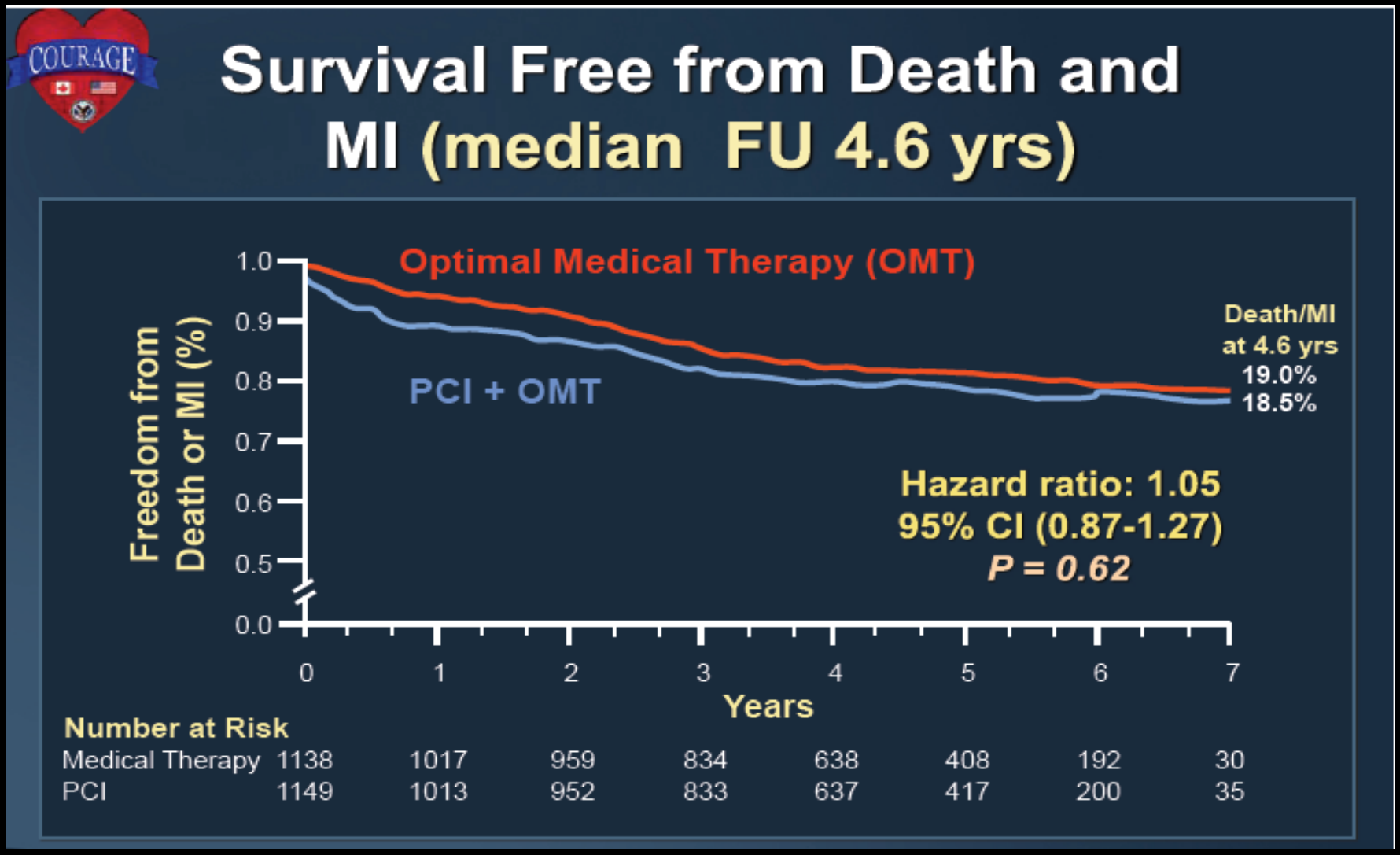
COURAGE: Optimal Medical Therapy



Boden WE et al. *NEJM* 2007;356:1503-16

Issues with ‘COURAGE’

- Randomization
  - *only 6% of total 35,539 pts screened*
- Crossover
  - *33% at median of 4.6 years*
- Increased revascularization rate
  - *6% of PCI used no stents*
  - *97% of stents used were BMS*

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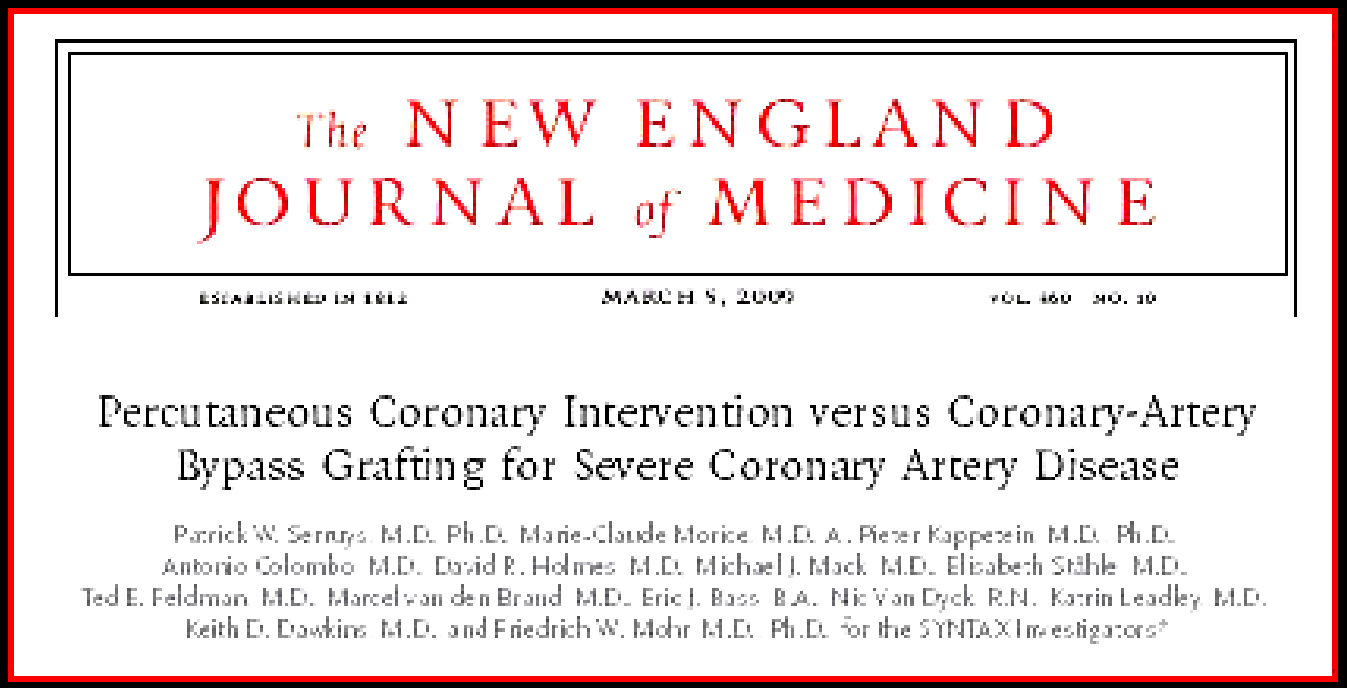
Syntax Trial / Score



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 5, 2009 VOL. 360 NO. 10

Percutaneous Coronary Intervention versus Coronary-Artery Bypass Grafting for Severe Coronary Artery Disease

Patrick W. Serruys M.D. Ph.D. Marie-Claude Morice M.D. A. Pieter Kappetein M.D. Ph.D. Antonio Colombo M.D. David R. Holmes M.D. Michael J. Mack M.D. Elisabeth Ståhle M.D. Ted E. Feldman M.D. Marcel van den Brand M.D. Eric J. Bass B.A. Nic Van Dyck R.N. Katrin Leadley M.D. Keith D. Dawkins M.D. and Friedrich W. Mohr M.D. Ph.D. for the SYNTAX Investigators*

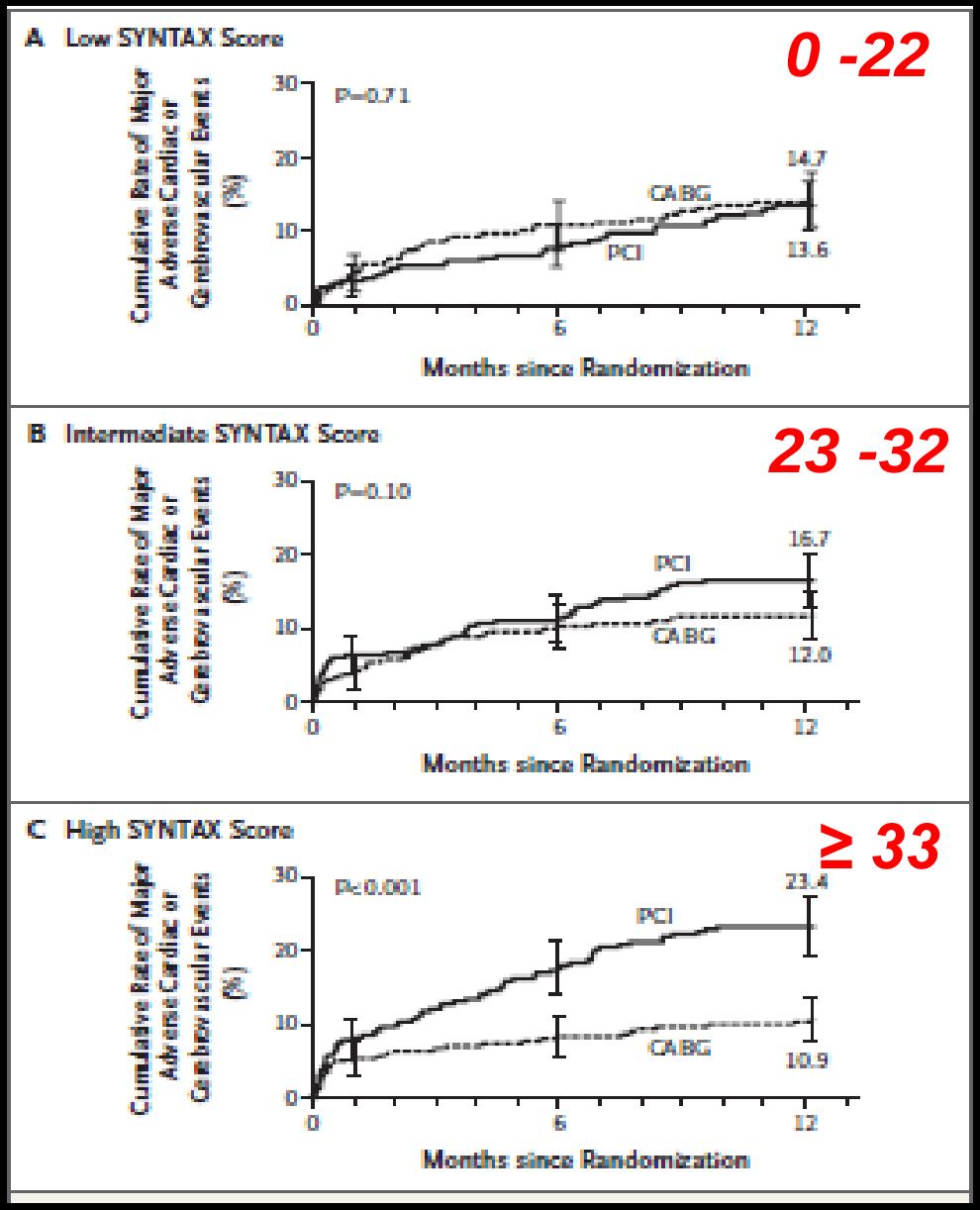
Serruys PW et al. *NEJM* 2009 360:961-72

- 1800 Patients with LM or 3V CAD
- Randomly assigned 1:1 to CABG vs. PCI
- RESULTS:

  1 Yr Mortality: No different

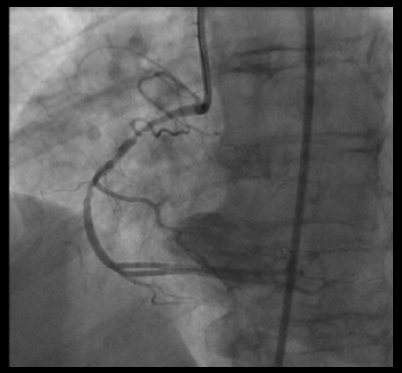
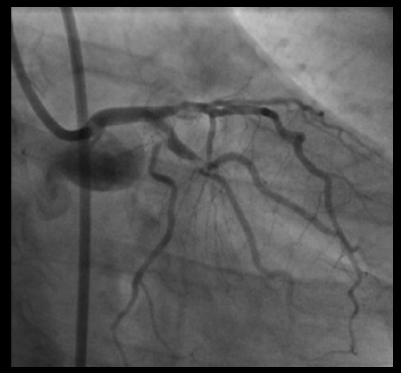
  MACCE @ 1yr favored CABG: 12.4% vs. 17.8%

SYNTAX Results



Serruys PW et al. *NEJM* 2009;360:961-72

Our Patient

Summary

Lesion 1

(segment 1): 1x2=	2
(segment 2): 1x2=	2
Length >20 mm	1
Sub total lesion 1	*5*

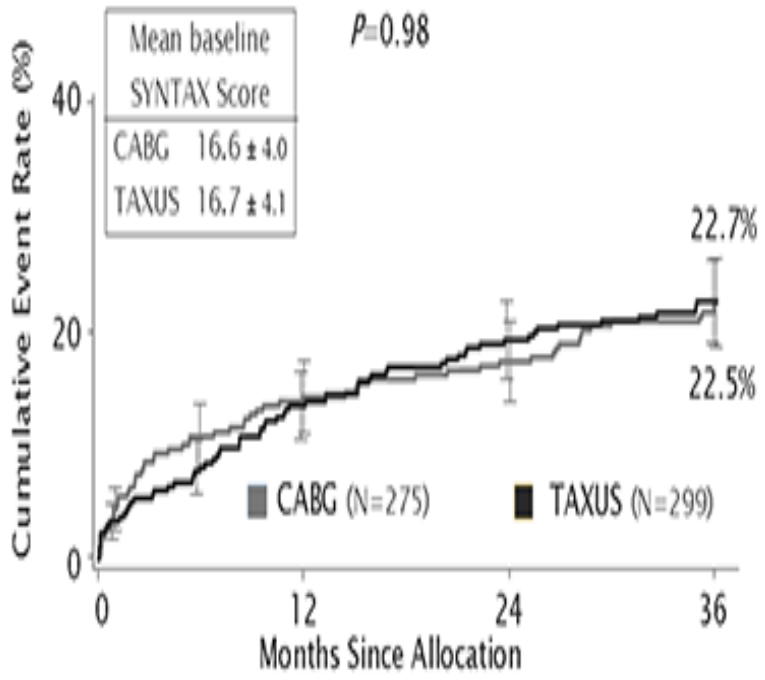
SYNTAX Score = 19

Bifurcation Type: Medina 1,1,1:	2
Sub total lesion 2	*9*

Lesion 3

(segment 12a): 1x2=	2
Bifurcation Type: Medina 1,1,1:	2
Angulation <70º	1
Sub total lesion 3	*5*

TOTAL:	*19*



The cumulative MACCE rate is displayed for the SYNTAX Trial group this score corresponds to.

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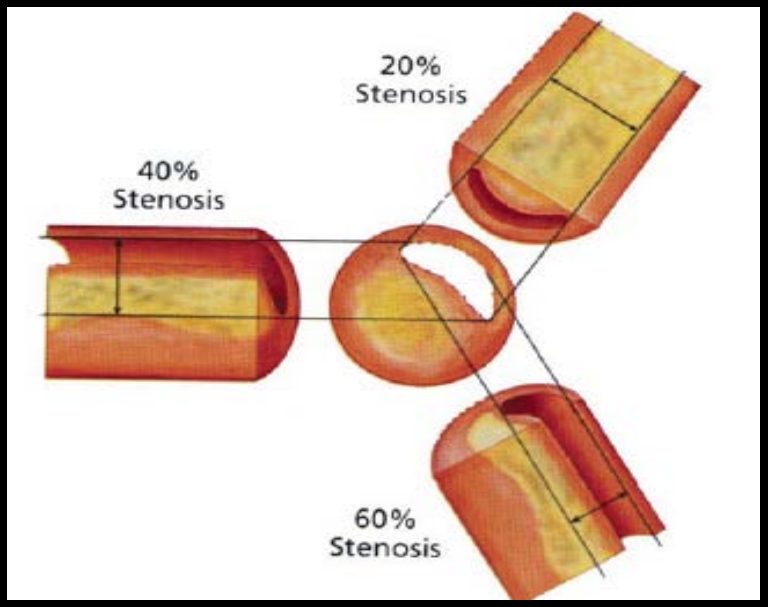
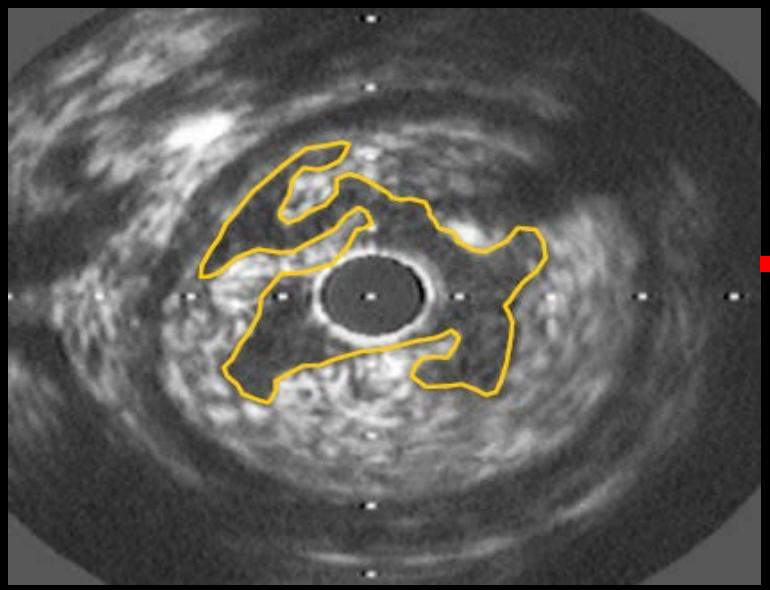
Issues with SYNTAX

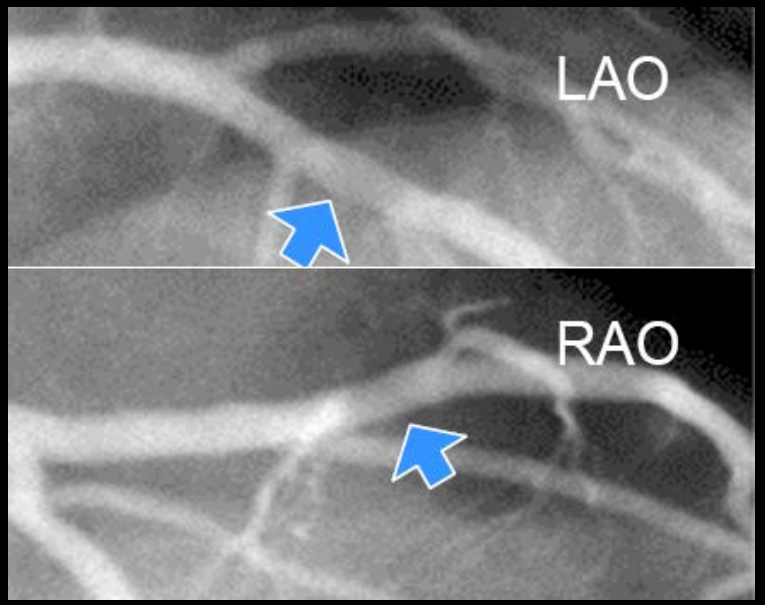
(Including Angiographic Assessment for Revascularization Decisions)

- Large number of stents implanted per patient: 4.6 ± 2.3
- Long length of stented segments: ave 86 ± 48 mm, with stent length >100mm in 33%
- High rate of definite stent thrombosis 3.3 - 4% at 1 year!

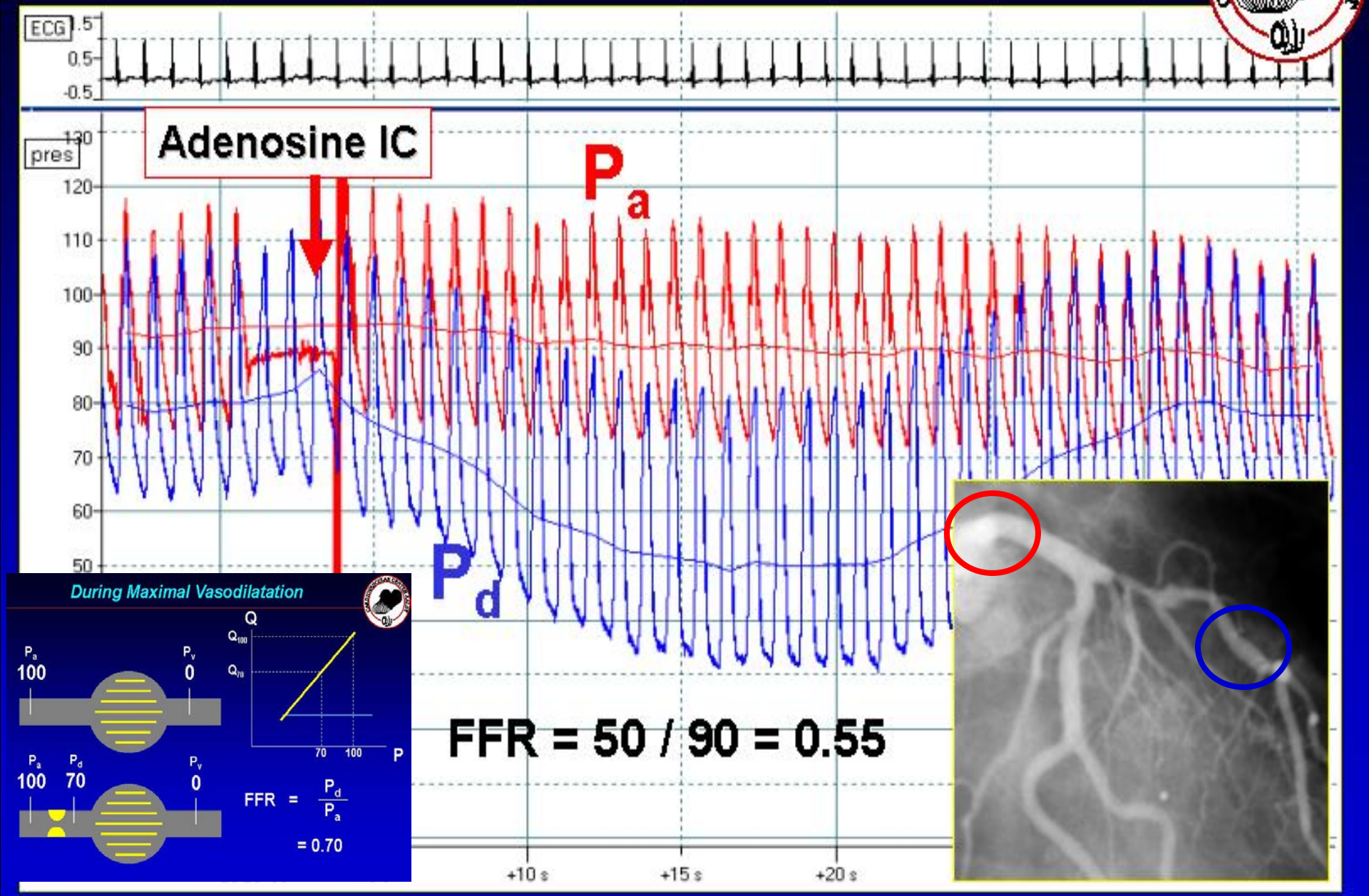
Limitations of Angiography



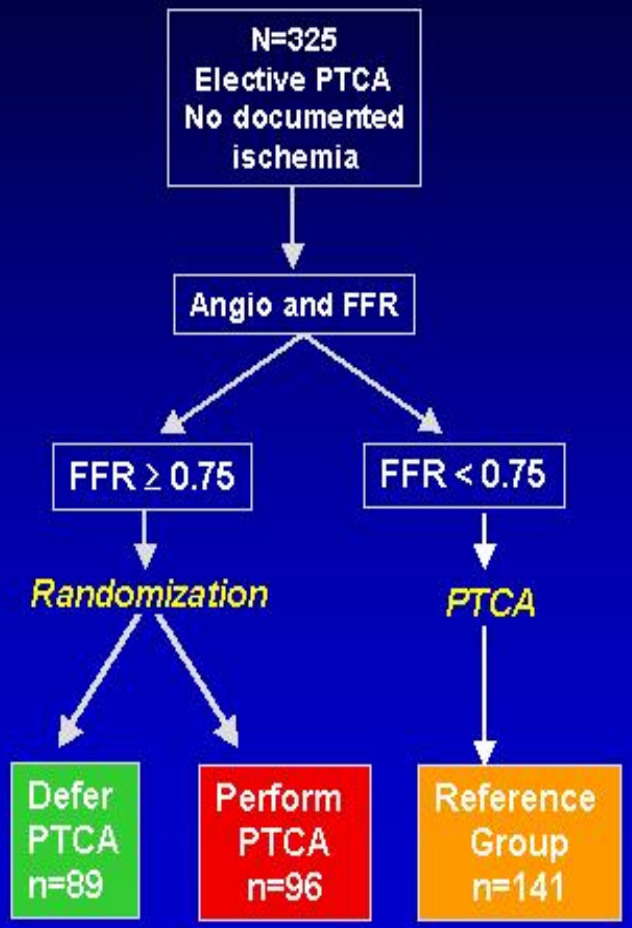


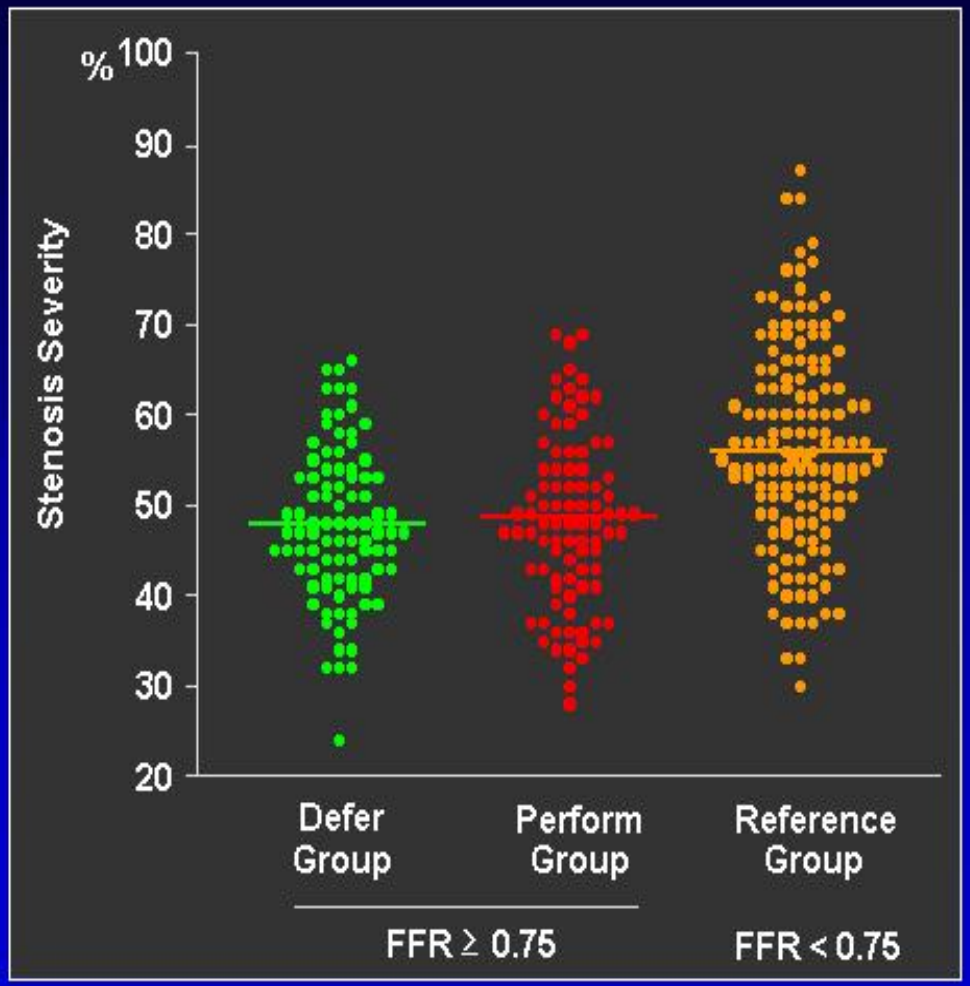


Physiologic Lesion Assessment



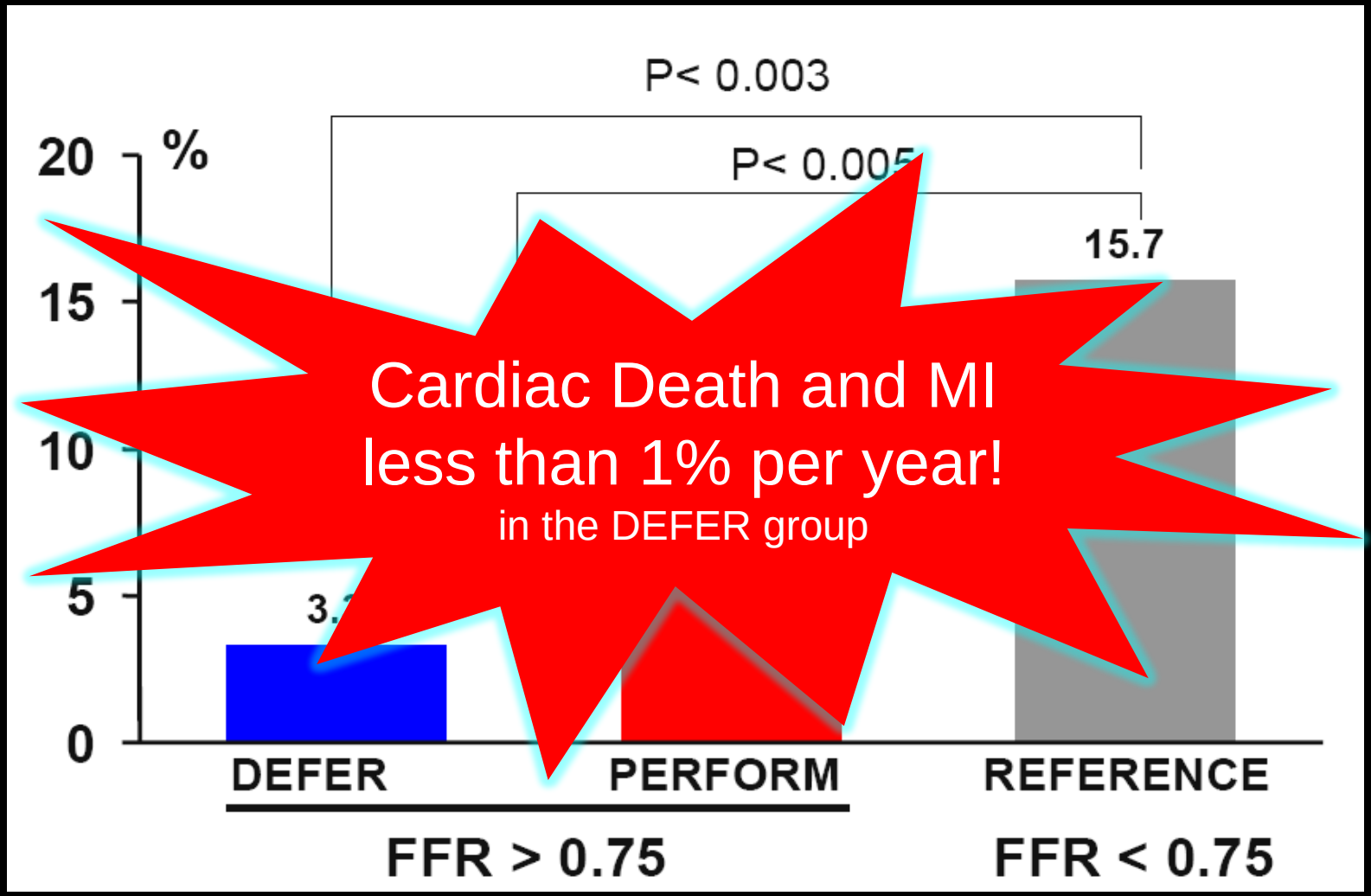
Defer Study: Quantitative Coronary Angiography





Bech GJW et al. *Circulation* 2001;103:2928-2934.

DEFER: 5 Year Cardiac Death and MI



Pijls, et al. JACC 2007

FAME Study

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 15, 2009 VOL. 360 NO. 3

Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention

Pim A.L. Tonino, M.D., Bernard De Bruyne, M.D., Ph.D., Nico H.J. Pijls, M.D., Ph.D., Uwe Siebert, M.D., M.P.H., Sc.D., Fumiaki Ikeno, M.D., Marcel van 't Veer, M.Sc., Volker Klauss, M.D., Ph.D., Ganesh Manoharan, M.D., Thomas Engstrøm, M.D., Ph.D., Keith G. Oldroyd, M.D., Peter N. Ver Lee, M.D., Philip A. MacCarthy, M.D., Ph.D., and William F. Fearon, M.D., for the FAME Study Investigators*

Tonino et al. *NEJM* 2009; 360:213-224

FLOW CHART

Patient with stenoses ≥ 50% in at least 2 of the 3 major epicardial vessels

Indicate all stenoses ≥ 50% considered for stenting

Randomization

Angiography-guided PCI

Stent all indicated stenoses

FFR-guided PCI

Measure FFR in all indicated stenoses

Stent only those stenoses with FFR ≤ 0.80

1-year follow-up

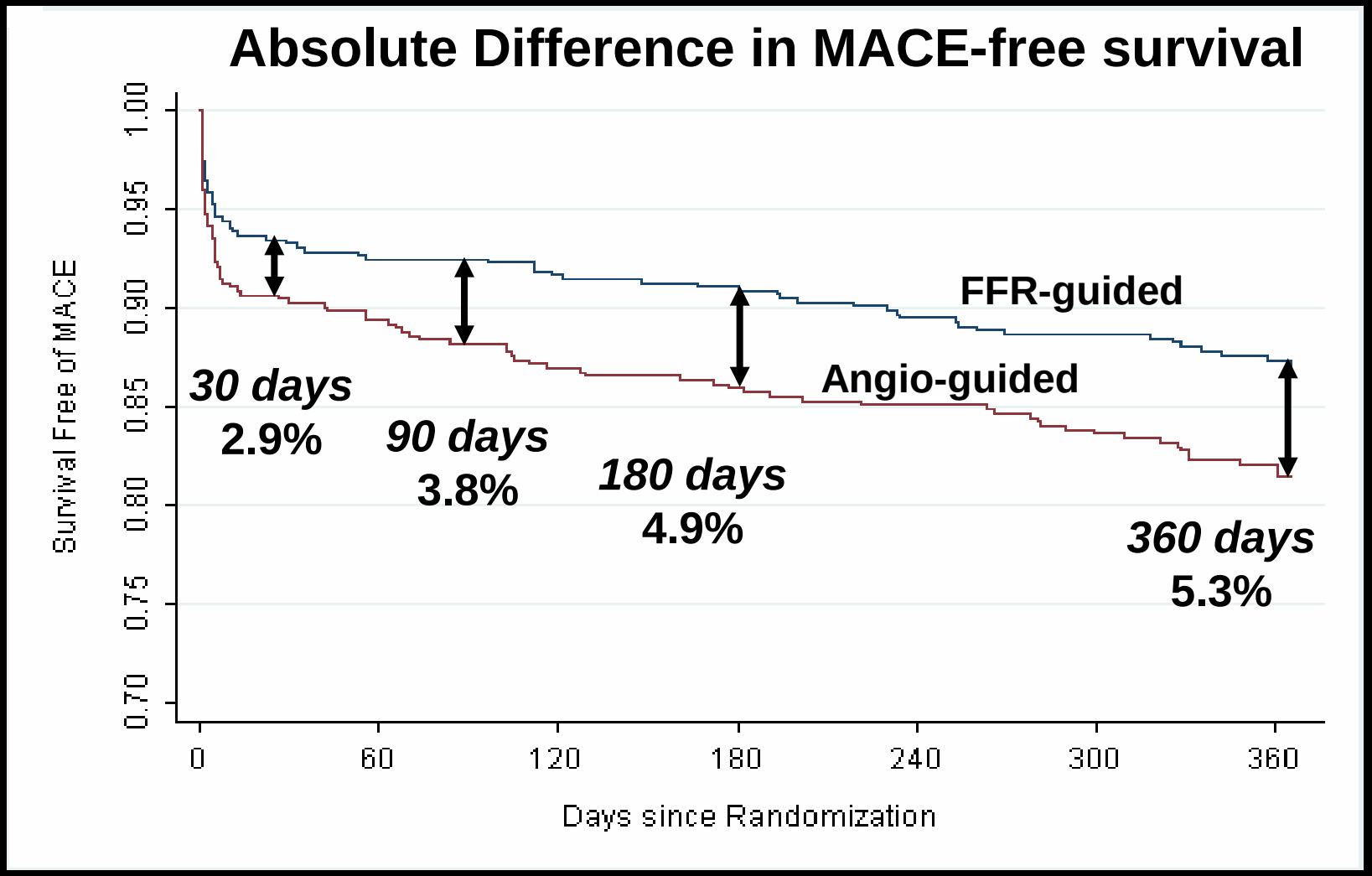
FAME: Procedural Results

	ANGIO-Group n = 496	FFR-Group n = 509	P-value
Mean # of Indicated Lesions per Patient	2.7 ± 0.9	2.8 ± 1.0	0.34
FFR results			
Lesions successfully measured (%)	-	1329 (98%)	-
Lesions with FFR ≤ 0.80 (%)	-	874 (63%)	-
Lesions with FFR > 0.80 (%)	-	513 (37%)	-
Stents per patient	**2.7 ± 1.2**	**1.9 ± 1.3**	**<0.001**
Lesions successfully stented (%)	92%	94%	-
Total DES	1359	980	-

★ FFR-guided group used 0.8 less stents per patient!

Tonino et al. *NEJM* 2009;360:213-224.

FAME study: Event-free Survival



Angiographic Versus Functional Severity of Coronary Artery Stenoses in the FAME Study

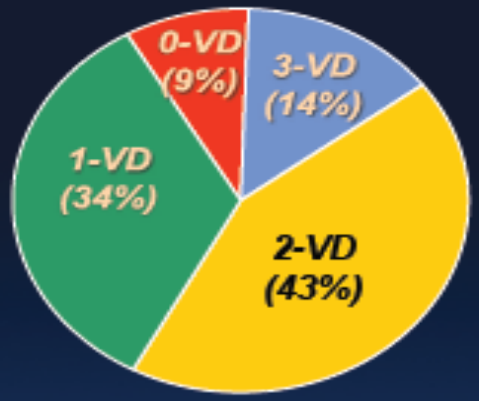
Fractional Flow Reserve Versus Angiography in Multivessel Evaluation

Pim A. L. Tonino, MD,* William F. Fearon, MD,† Bernard De Bruyne, MD, PHD,‡
Keith G. Oldroyd, MD,§ Massoud A. Leesar, MD,‖ Peter N. Ver Lee, MD,¶
Philip A. MacCarthy, MD, PHD,# Marcel van't Veer, MSC, PHD,* Nico H. J. Pijls, MD, PHD*

Eindhoven, the Netherlands; Stanford, California; Aalst, Belgium; Glasgow and London, United Kingdom; Cincinnati, Ohio; and Bangor, Maine

FAME:
Angiographic vs. Functional NDV

Pts with angiographic 3VD
(%DS >50%)
N=115



Tonino PAL et al. *JACC* 2010;55:2816

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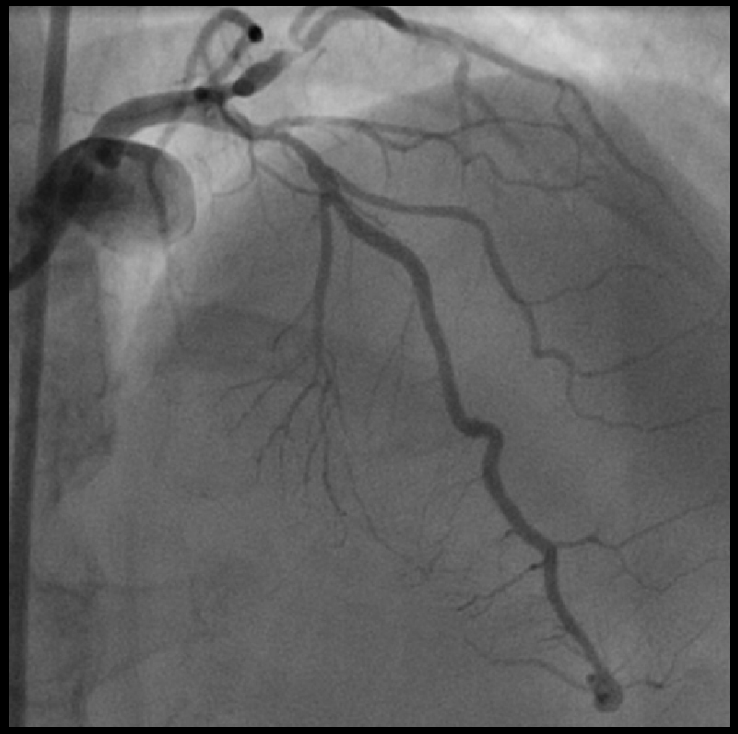
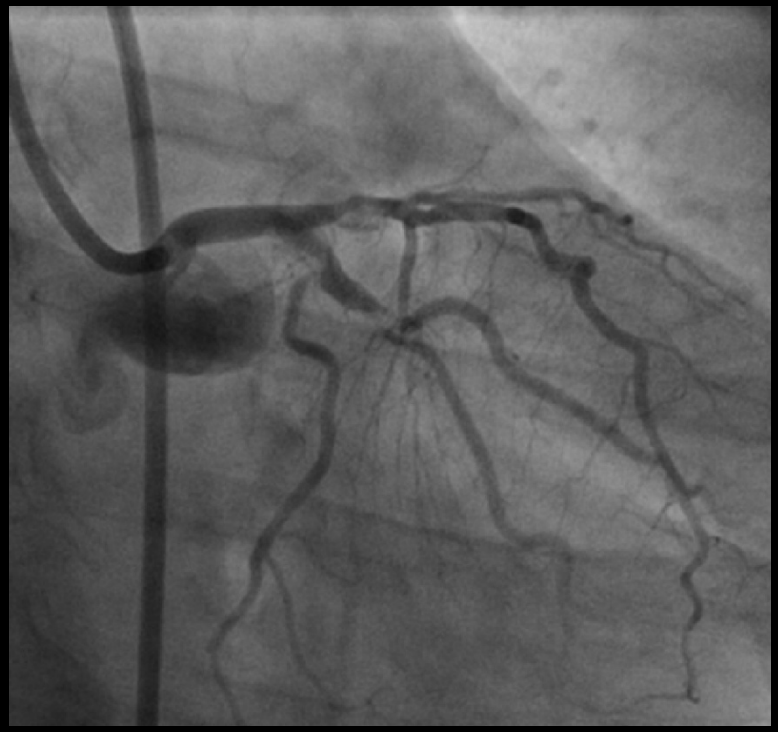
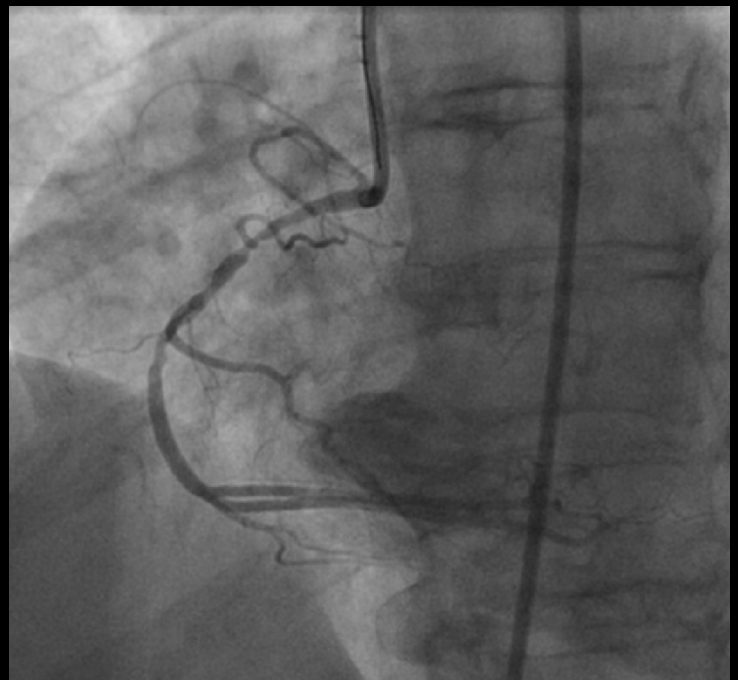
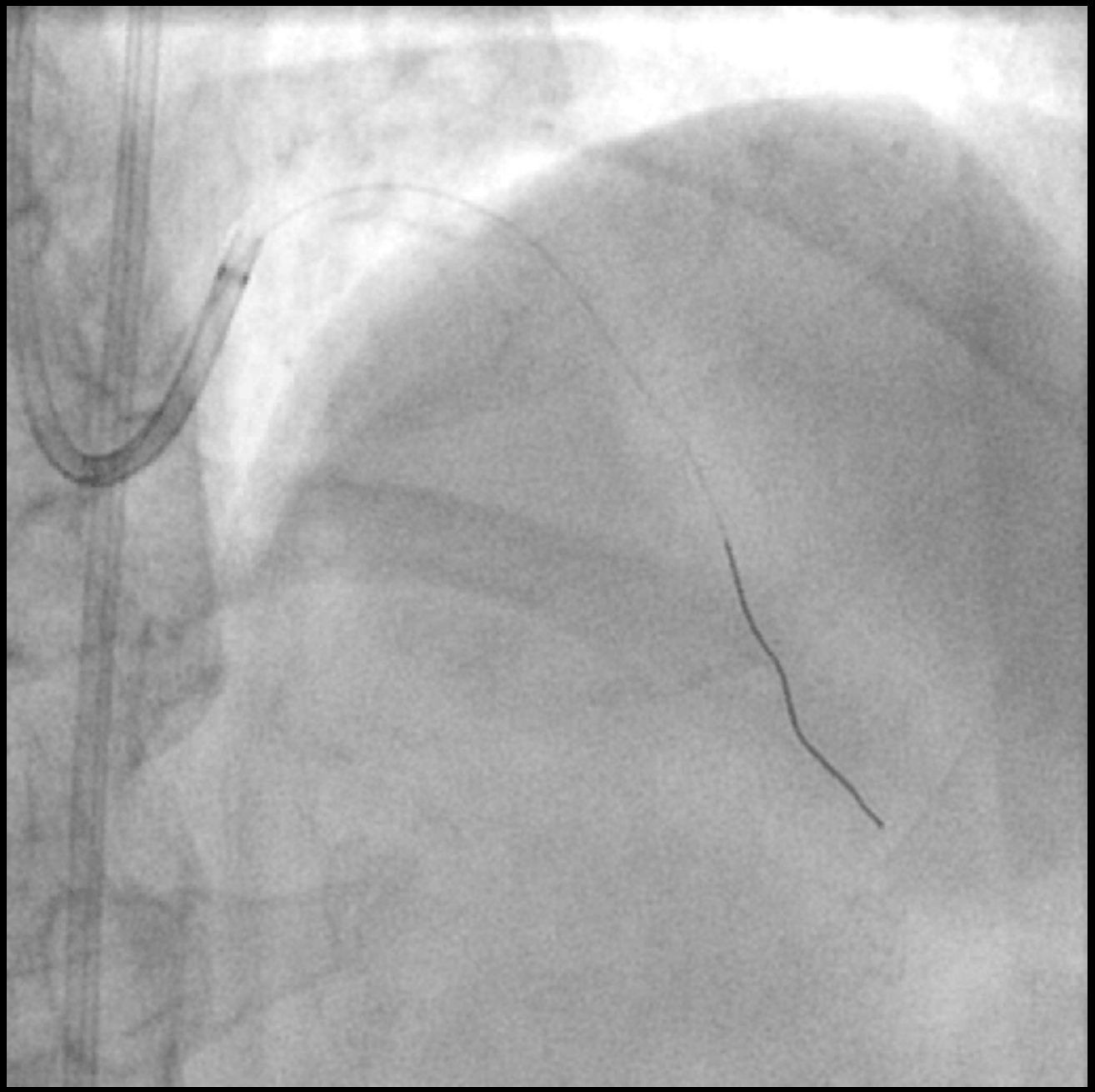
Our Patient







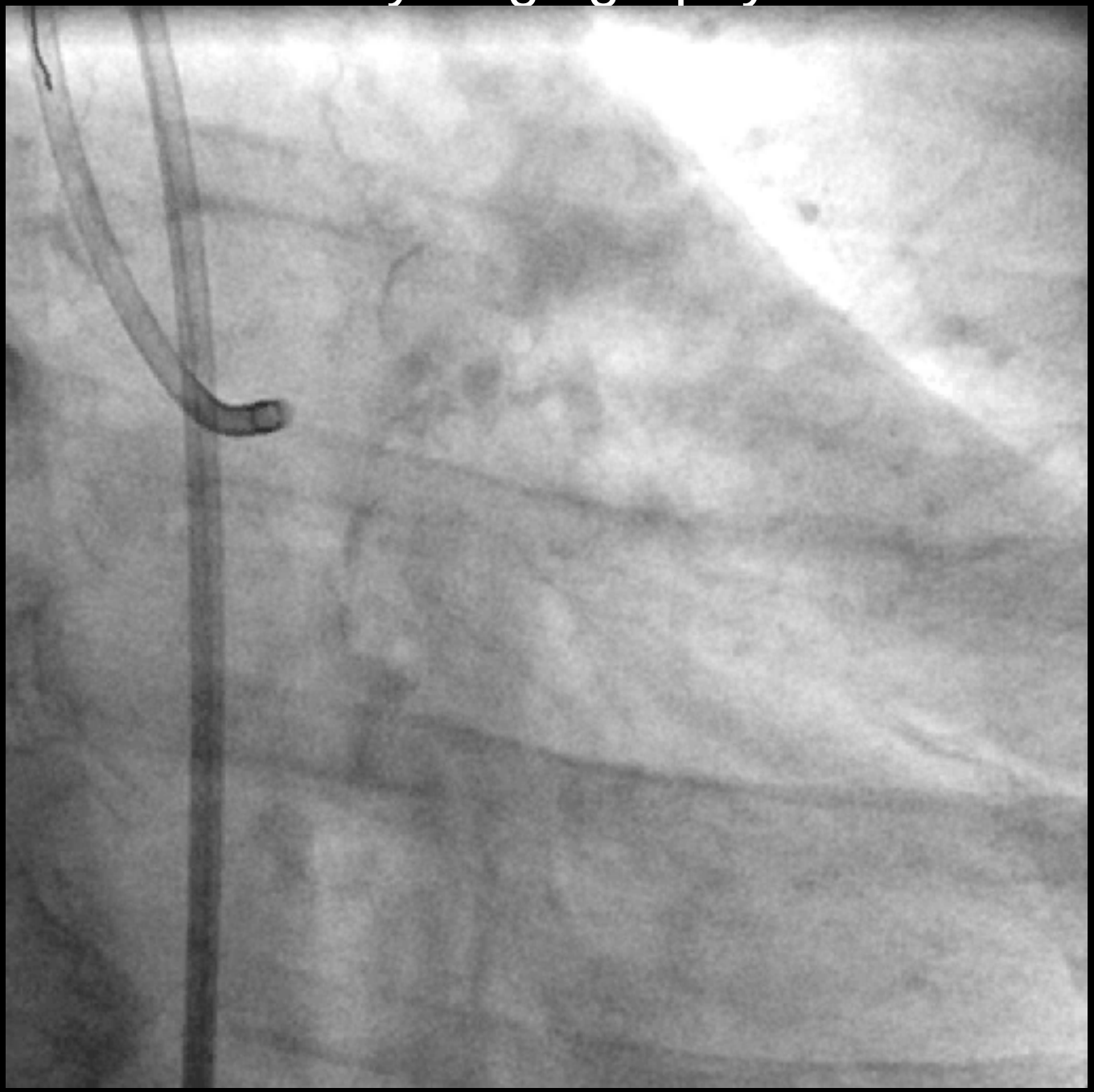
Coronary Angiography: LAD FFR



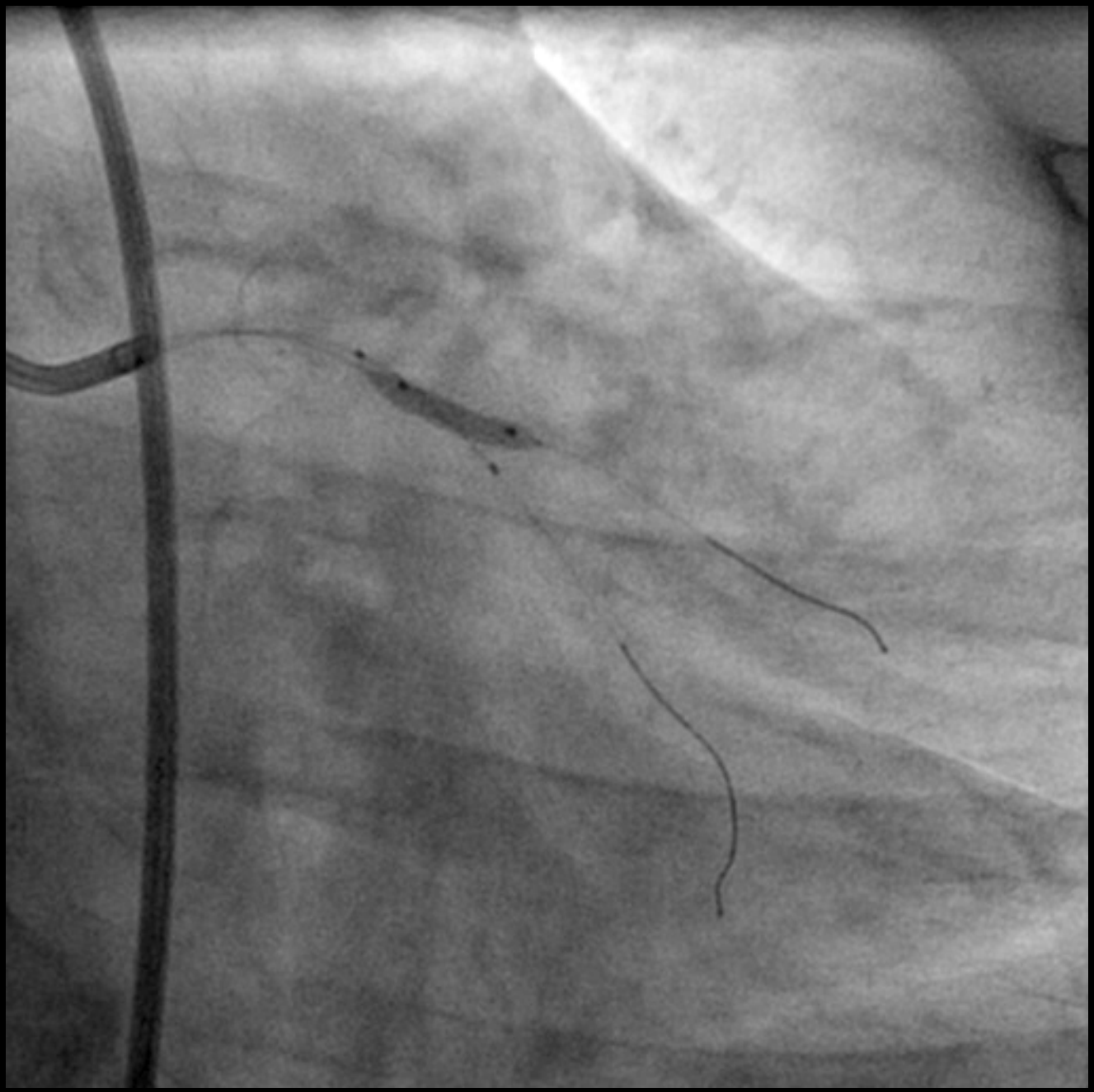
FFR Assessment: LAD

- Eccentric, calcified, hazy 70% lesion
  - Pressure wire (Volcano Prestige) equalized in the left main and passed into the mid LAD
  - Resting FFR decreased to 0.95
- Adenosine 60mcg and 120mcg
  - FFR 0.89, 0.91
- *Final result*
  - *Lesion physiologically not significant…*
  - *PCI Deferred*

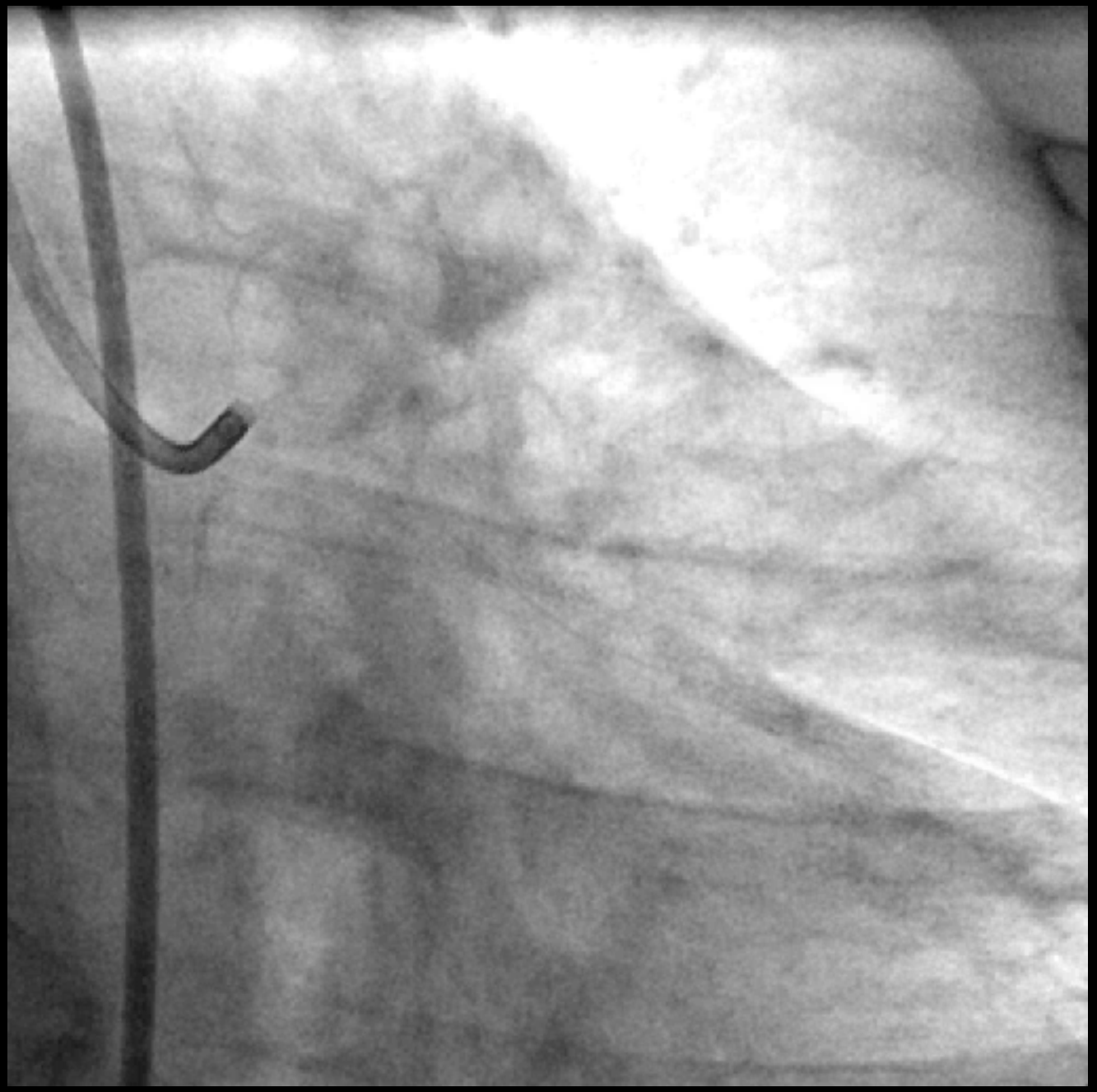
Coronary Angiography: LCA



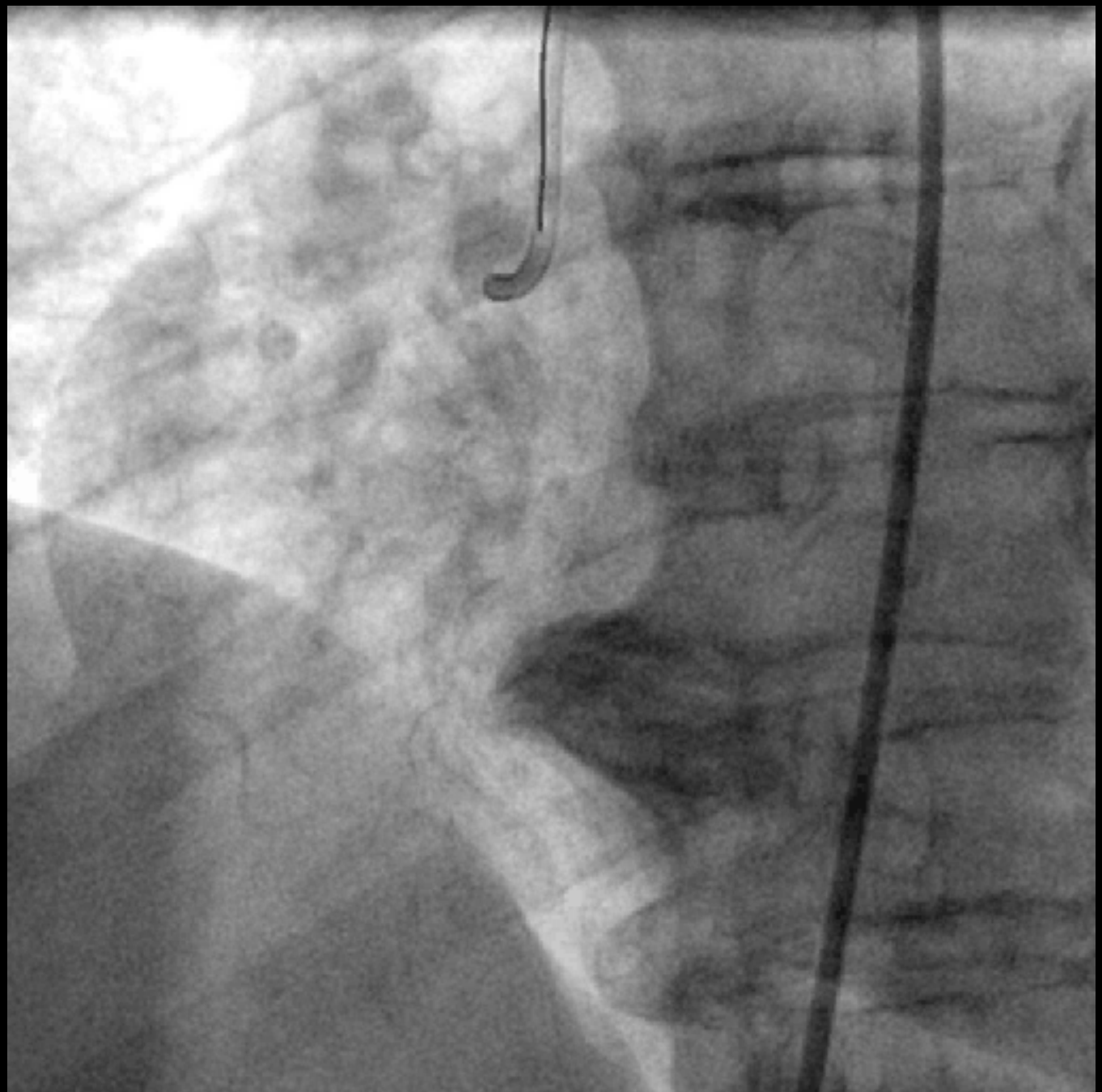
PCI of Bifurcating OM with JBT



Post-PCI of OM

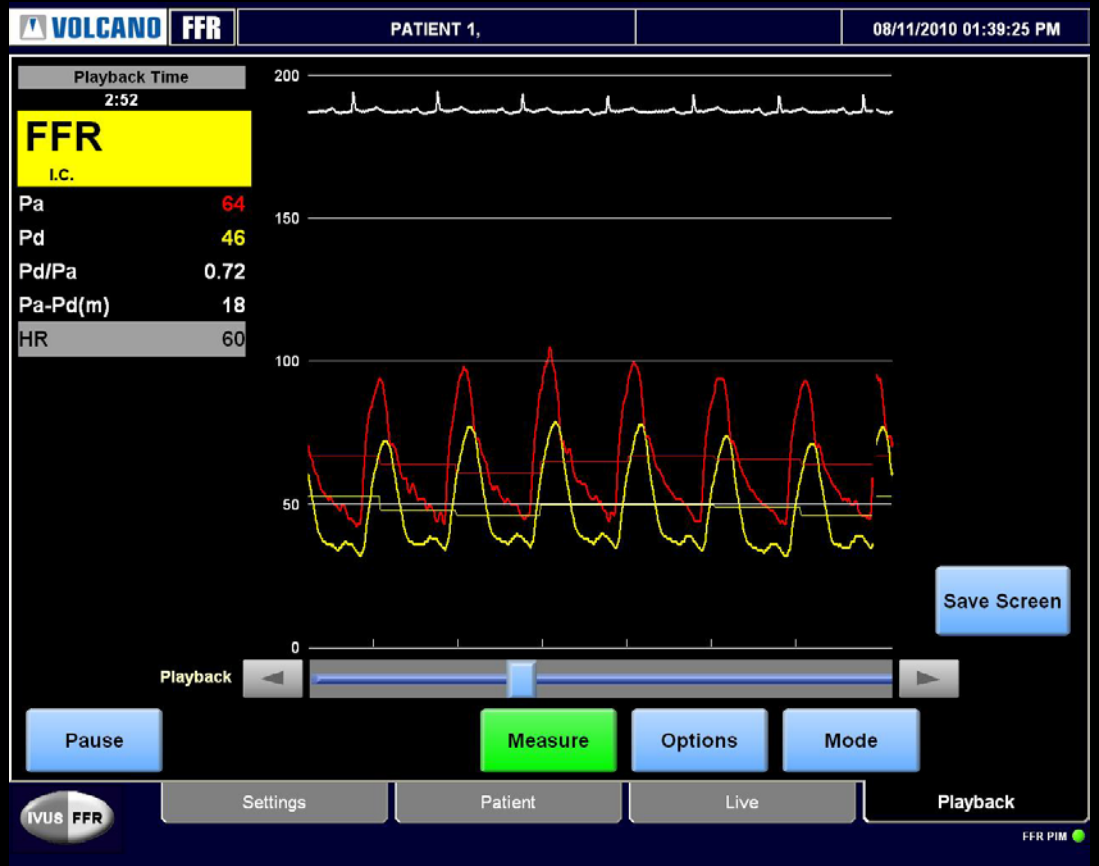


Coronary Angiography: RCA

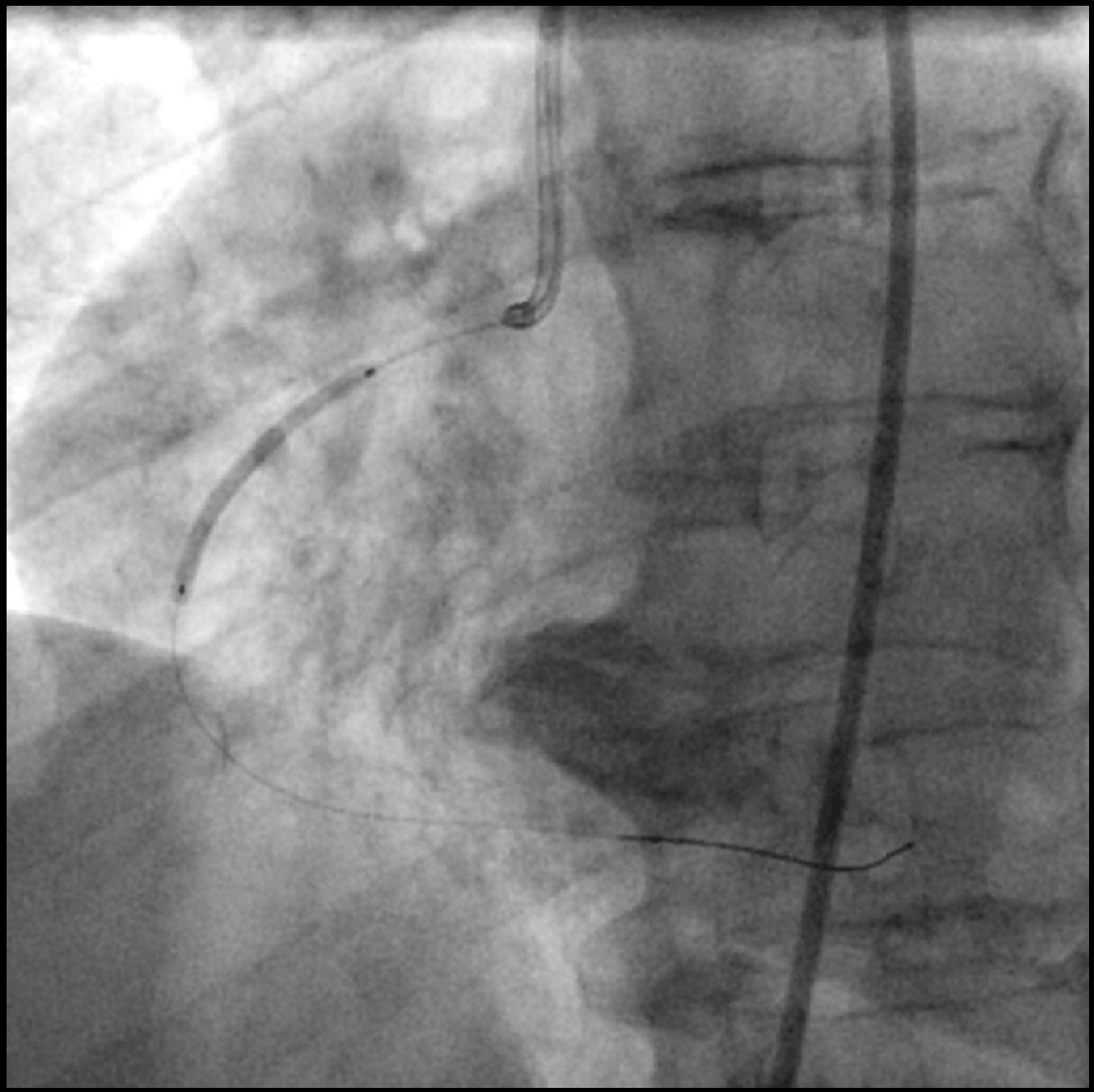


FFR Assessment: RCA

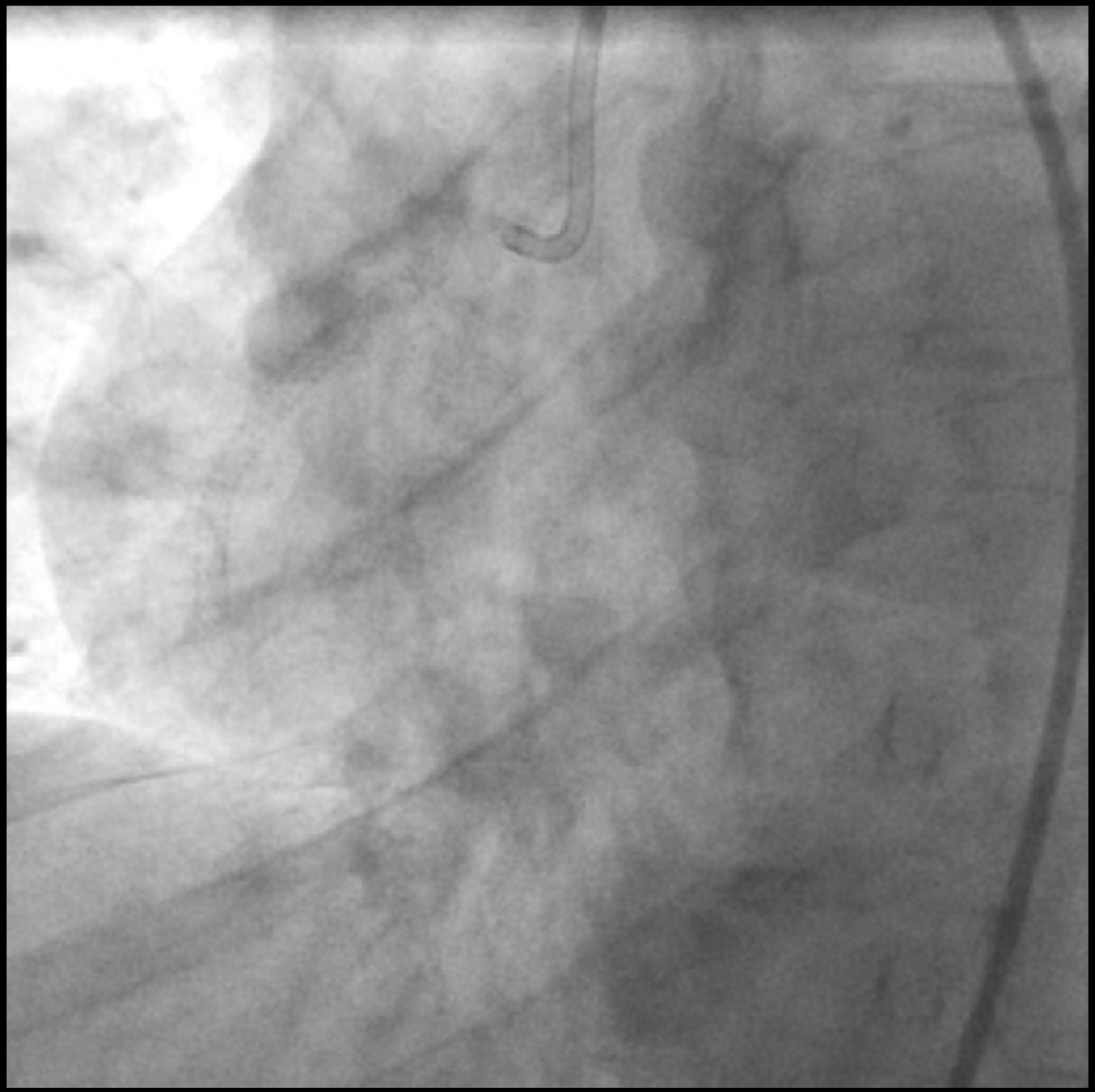
- Eccentric, hazy, long 70% lesion
  - Volcano Prestige wire equalized in the proximal RCA and passed distally into the PDA
- Adenosine 30 mcg
  - FFR 0.72
- *Final result*
  - *Physiologically significant*



PCI of RCA



Post-PCI of RCA



Follow-up…

- Patient with uncomplicated recovery…discharged in good condition
- ASA indefinitely
- Clopidogrel minimum one year
- Clinically improved…
  - No further chest tightness reported
  - Improved exercise tolerance

Conclusions

- In appropriately selected patients with multivessel CAD, a strategy of FFR-guided PCI can provide symptomatic benefit with strong evidence of superior outcomes, even at reduced cost.

Heart & Vascular Center

BARNES-JEWISH Hospital
BJC HealthCare

Washington University in St. Louis
Physicians

NATIONAL LEADERS IN MEDICINE

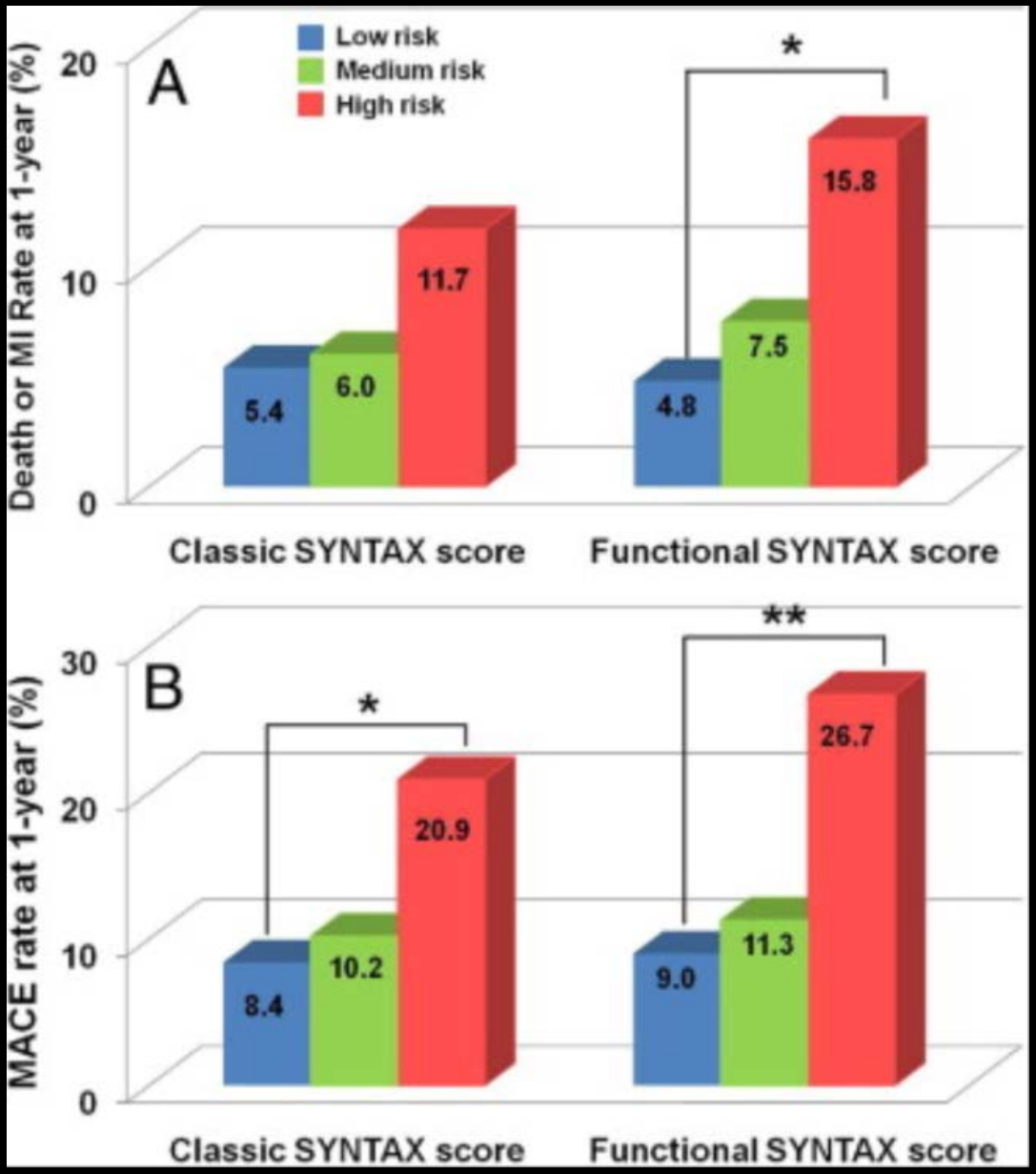
FAME: Patient Outcomes

	ANGIO-Group n = 496	FFR-Group n = 509	P-value
Events at 1 year, # (%)			
Death, MI, CABG, or repeat-PCI	91 (18.4)	67 (13.2)	0.02
Death	15 (3.0)	9 (1.8)	0.19
Death or MI	55 (11.1)	37 (7.3)	0.04
CABG or repeat PCI	47 (9.5)	33 (6.5)	0.08
Total # of MACE	113	76	0.02

- ★ MACE rates in the FFR-guided group are 28% lower than the Angio-guided group!
- ★ Death or MI in the FFR-guided group is 34% lower than in the Angio-guided group!

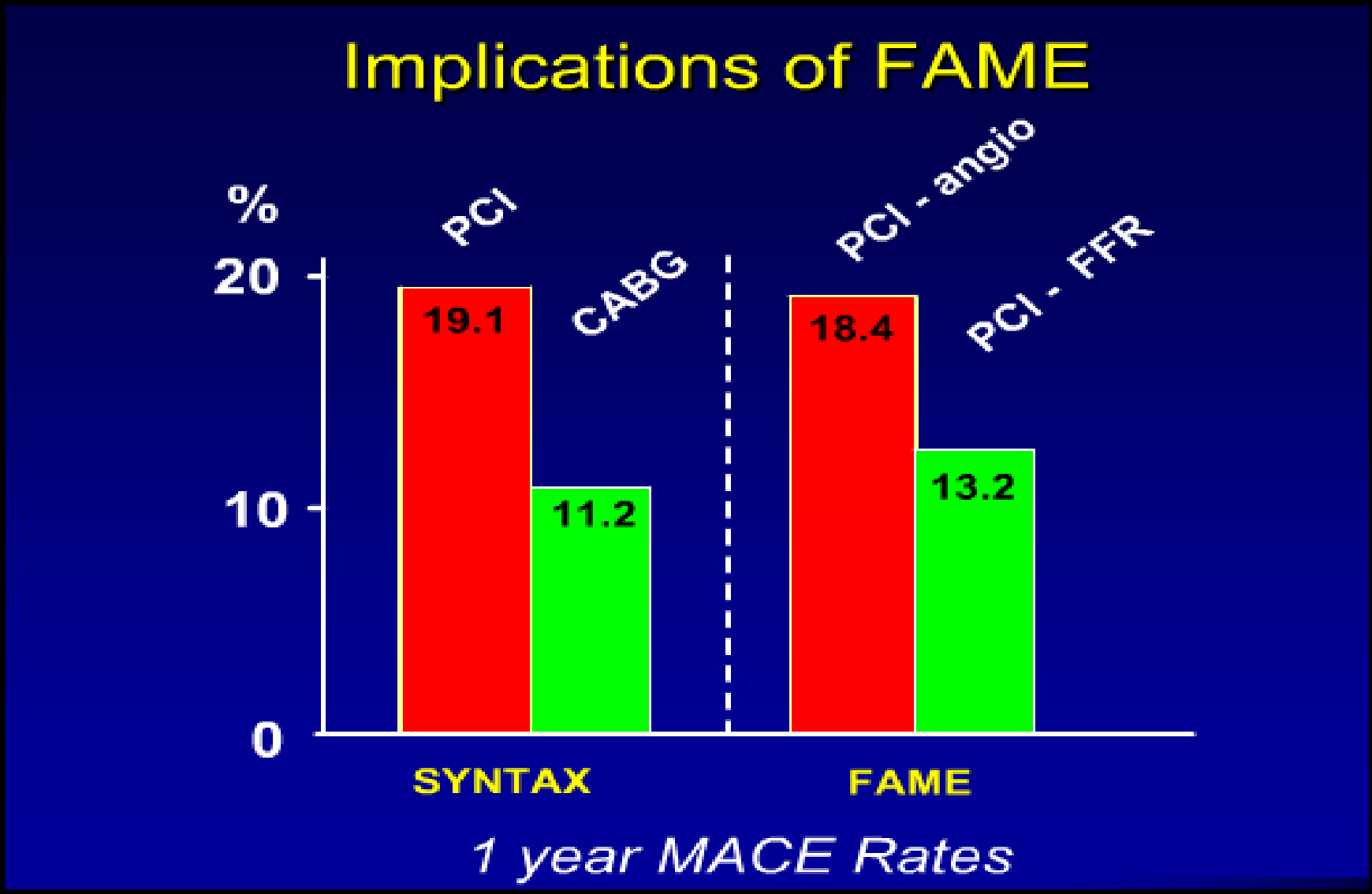
Tonino et al. *NEJM* 2009;360:213-224.

Functional SYNTAX Score



Nam CW et al.
JACC 2011;
58(12):1211-1218

FAME vs. SYNTAX



The NEW ENGLAND JOURNAL of MEDICINE

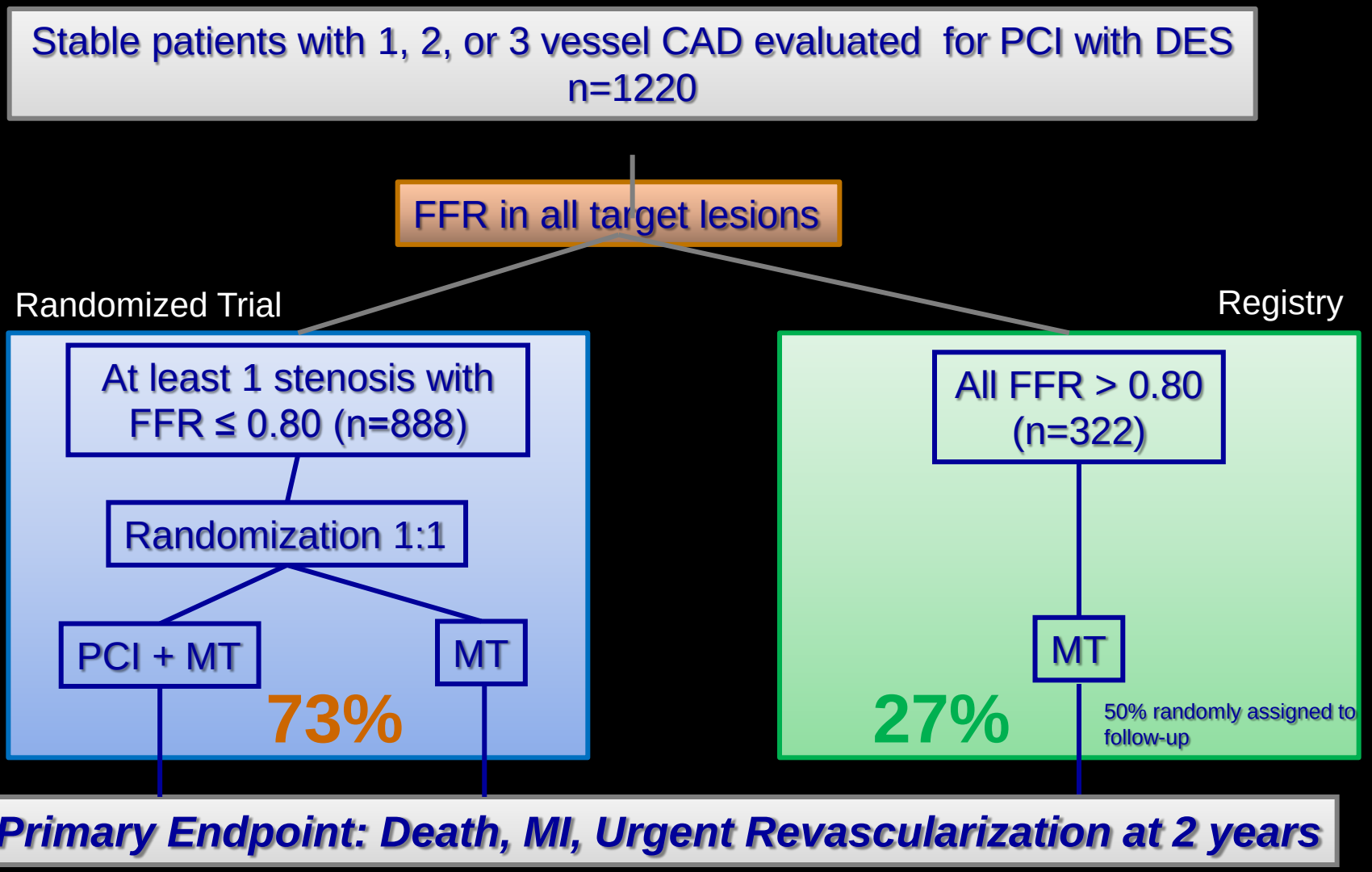
ORIGINAL ARTICLE

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

Bernard De Bruyne, M.D., Ph.D., Nico H.J. Pijls, M.D., Ph.D.,
Bindu Kalesan, M.P.H., Emanuele Barbato, M.D., Ph.D.,
Pim A.L. Tonino, M.D., Ph.D., Zsolt Piroth, M.D., Nikola Jagic, M.D.,
Sven Mobius-Winckler, M.D., Gilles Rioufol, M.D., Ph.D., Nils Witt, M.D., Ph.D.,
Petr Kala, M.D., Philip MacCarthy, M.D., Thomas Engström, M.D.,
Keith G. Oldroyd, M.D., Kreton Mavromatis, M.D., Ganesh Manoharan, M.D.,
Peter Verlee, M.D., Ole Frobert, M.D., Nick Curzen, B.M., Ph.D.,
Jane B. Johnson, R.N., B.S.N., Peter Jüni, M.D., and William F. Fearon, M.D.,
for the FAME 2 Trial Investigators*

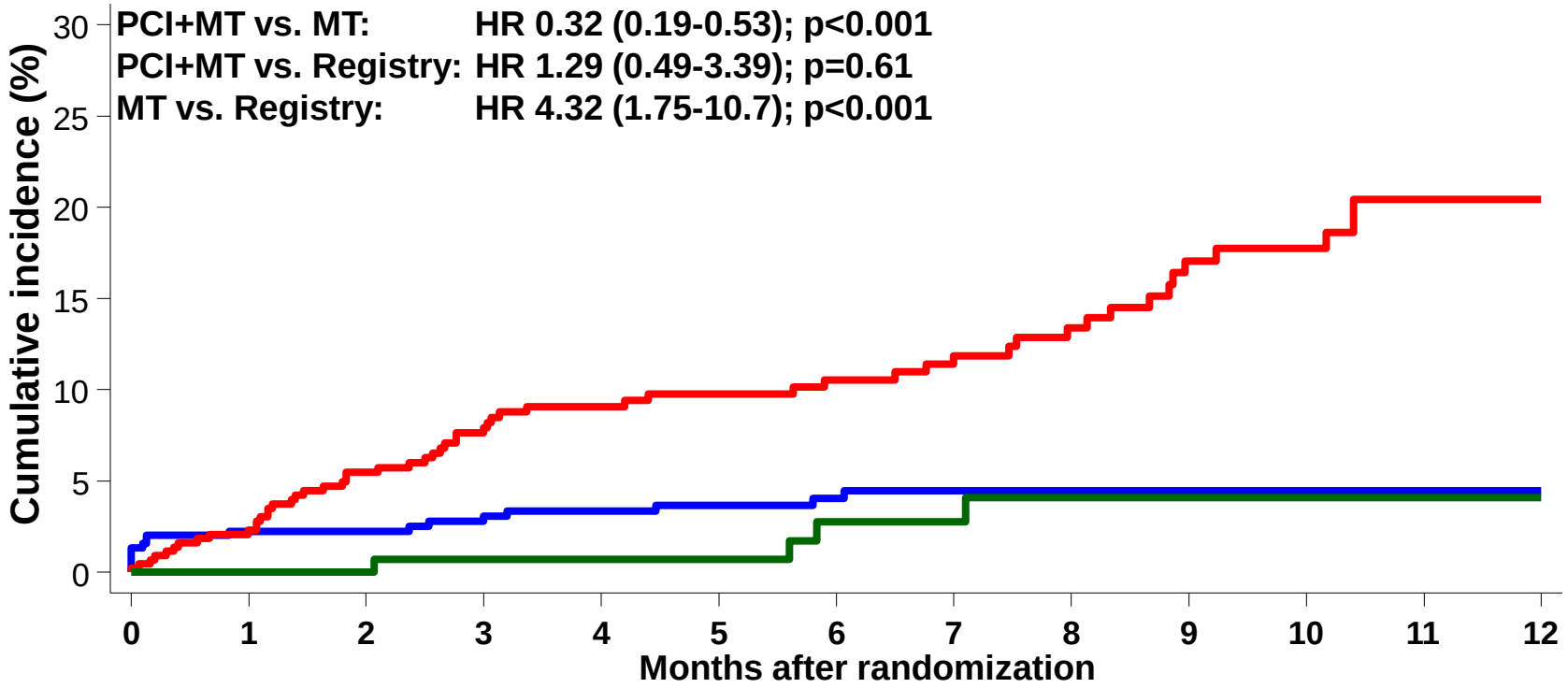
De Bruyne B et al. *NEJM* 2012;367:991-1001

FAME 2: Trial Design



De Bruyne B et al. *NEJM* 2012;367:991-1001

FAME 2: Primary Outcome: Death, MI, Unplanned Hospitalization with Urgent Revascularization



No. at risk

MT	441	414	370	322	283	253	220	192	162	127	100	70	37
PCI+MT	447	414	388	351	308	277	243	212	175	155	117	92	53
Registry	166	156	145	133	117	106	93	74	64	52	41	25	13

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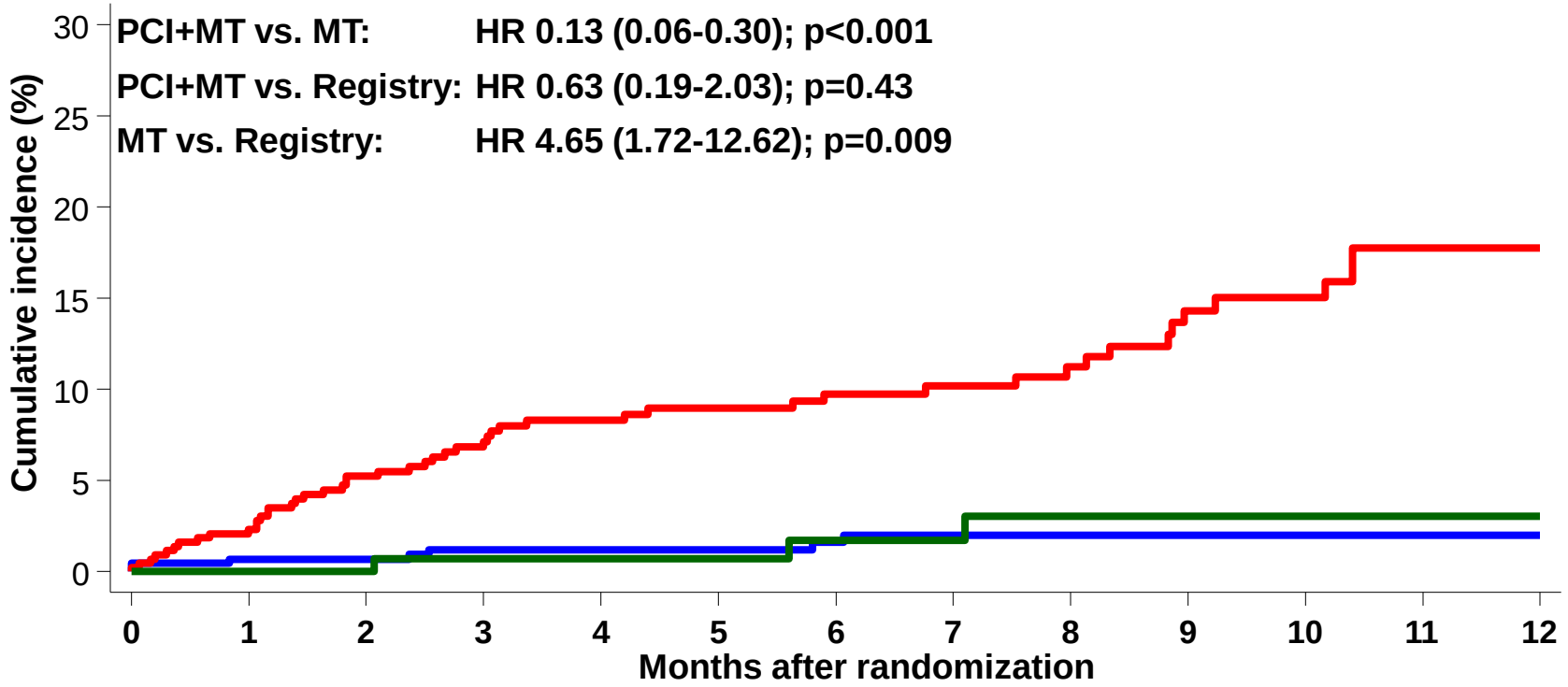
FAME 2: Urgent Revascularization



No. at risk

MT	441	414	371	325	286	256	223	195	164	129	101	71	38
PCI+MT	447	421	395	356	315	285	248	217	180	160	119	93	53
Registry	166	156	145	133	117	106	94	75	65	53	42	26	13

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FAME 2: Conclusions

- In patients with stable coronary artery disease, FFR-guided PCI, improves patient outcome as compared with medical therapy alone
- This improvement is driven by a dramatic decrease in the need for urgent revascularization for ACS
- In patients with functionally non-significant stenoses medical therapy alone resulted in an excellent outcome, regardless of the angiographic appearance of the stenoses

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