What is the best way to assess coronary perfusion?

Amir Lerman, MD
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Director Cardiovascular Research Center
Mayo Clinic, Rochester, MN

ORIGINAL ARTICLE

Low Diagnostic Yield of Elective Coronary Angiography

Study Population and Rates of Obstructive Coronary Artery Disease

37.6%

62.4 %

C

Multivess

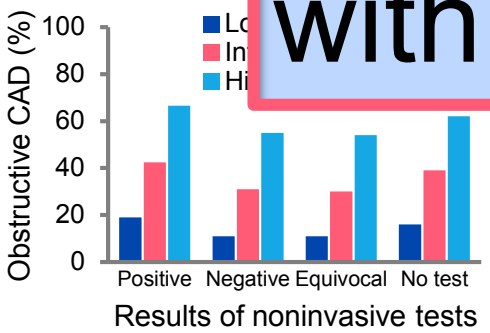
1-vessel

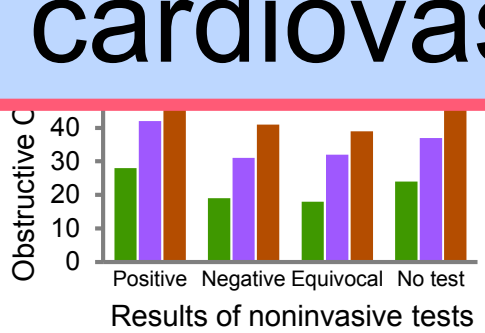
2-vessel

3-vessel

Frami

C





Patel et al: N Engl J Med 362:886, 2010

Research

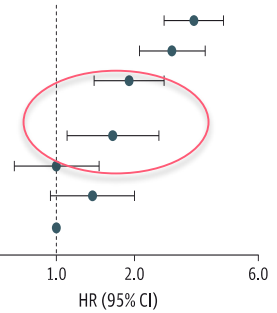
Original Investigation

Nonobstructive Coronary Artery Disease and Risk of Myocardial Infarction

Among 37 674 patients, 8384 patients (22.3%) had non obstructive CAD

Coronary Ischemia and non obstructive coronary artery disease by angiography is common and is associated with cardiovascular events

3-Vessel or left main	239	6036	3.4 (2.6-4.4)
2-Vessel	164	5452	2.8 (2.1-3.7)
1-Vessel	192	9411	1.9 (1.4-2.6)
Nonobstructive CAD			
3-Vessel	27	1133	1.6 (1.1-2.5)
2-Vessel	35	2605	1.0 (0.7-1.5)
1-Vessel	85	4646	1.4 (1.0-2.0)
No apparent CAD	103	8391	1 [Reference]



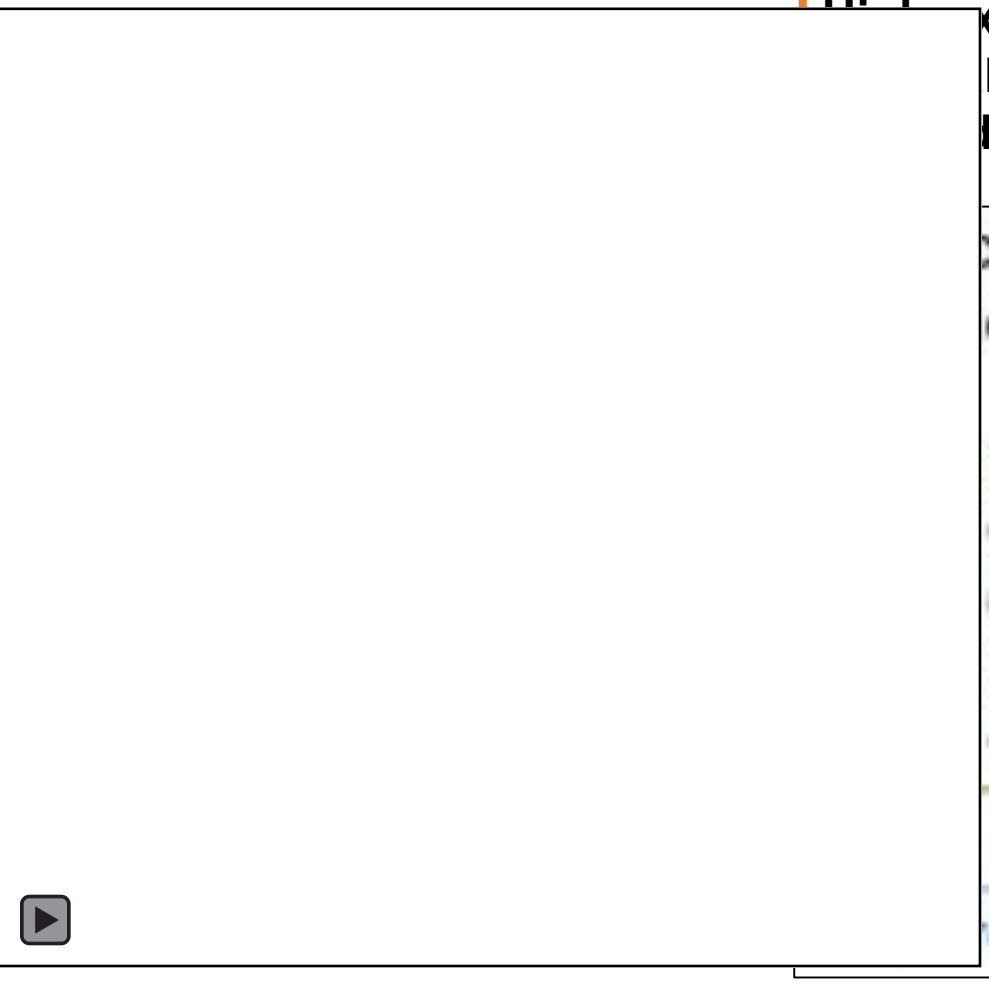
Maddox,JAMA. 2014;312(17):1754-1763..

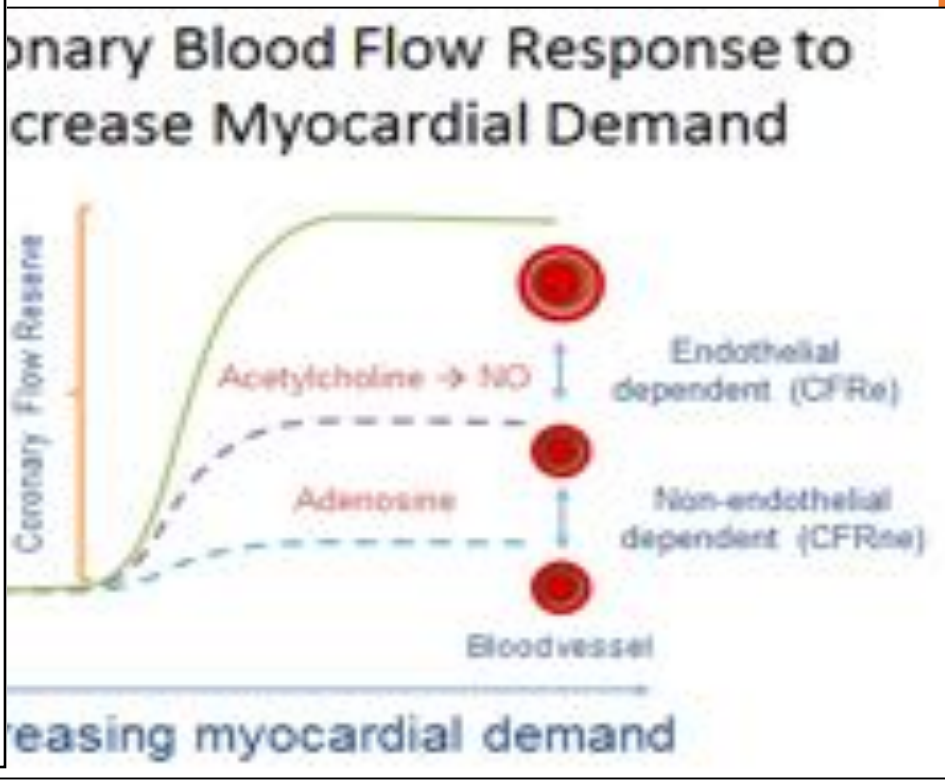
1-Year combined myocardial infarction and mortality

MAYO CLINIC

Coronary Microcirculation

Hi… …xygen extraction 60-80% vs. 20-30% in …l muscle: coronary perfusion is flow …lent

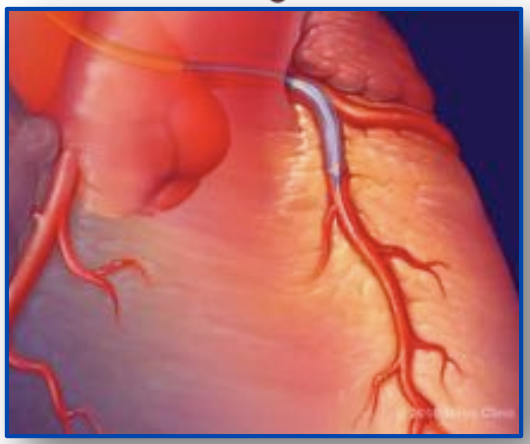


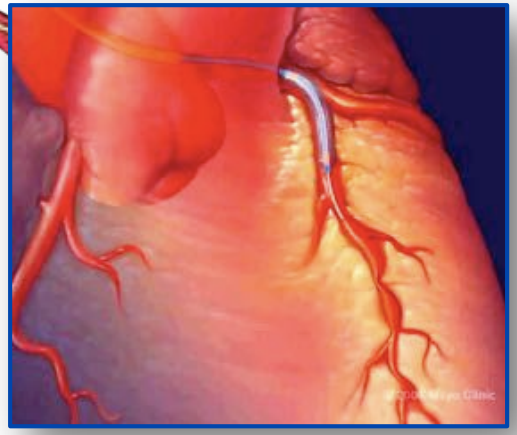


Functional Angiogram Protocol

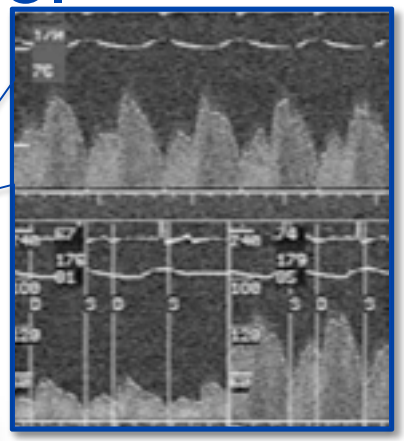
Diagnostic angiography

Adenosine IC 24-72 μg



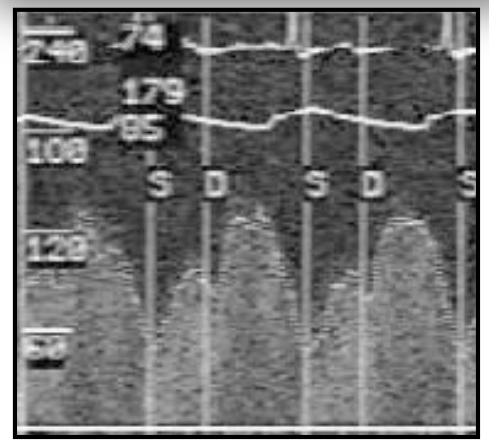


CFR: Non endothelium **microcirculation**

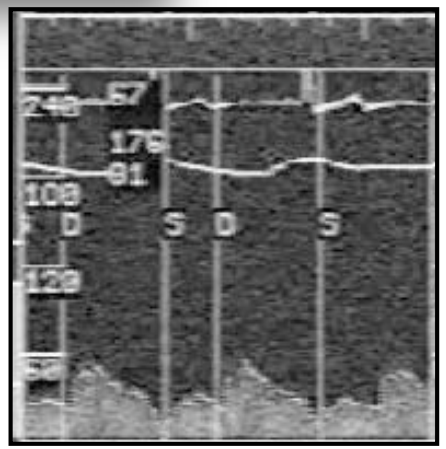


Acetylcholine (endothelium dependent vasodilator)

Epicardial



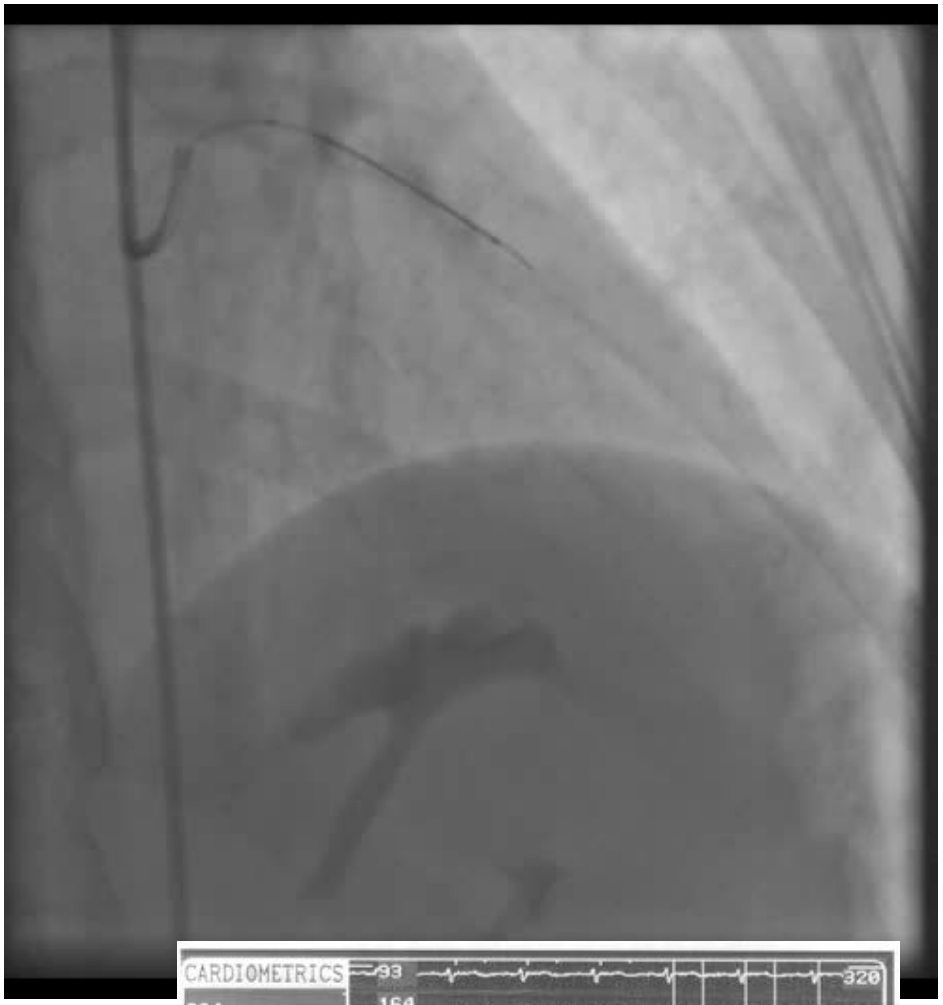
Microcirculation



MAYO CLINIC

50-Year-Old Female With Chest Pain

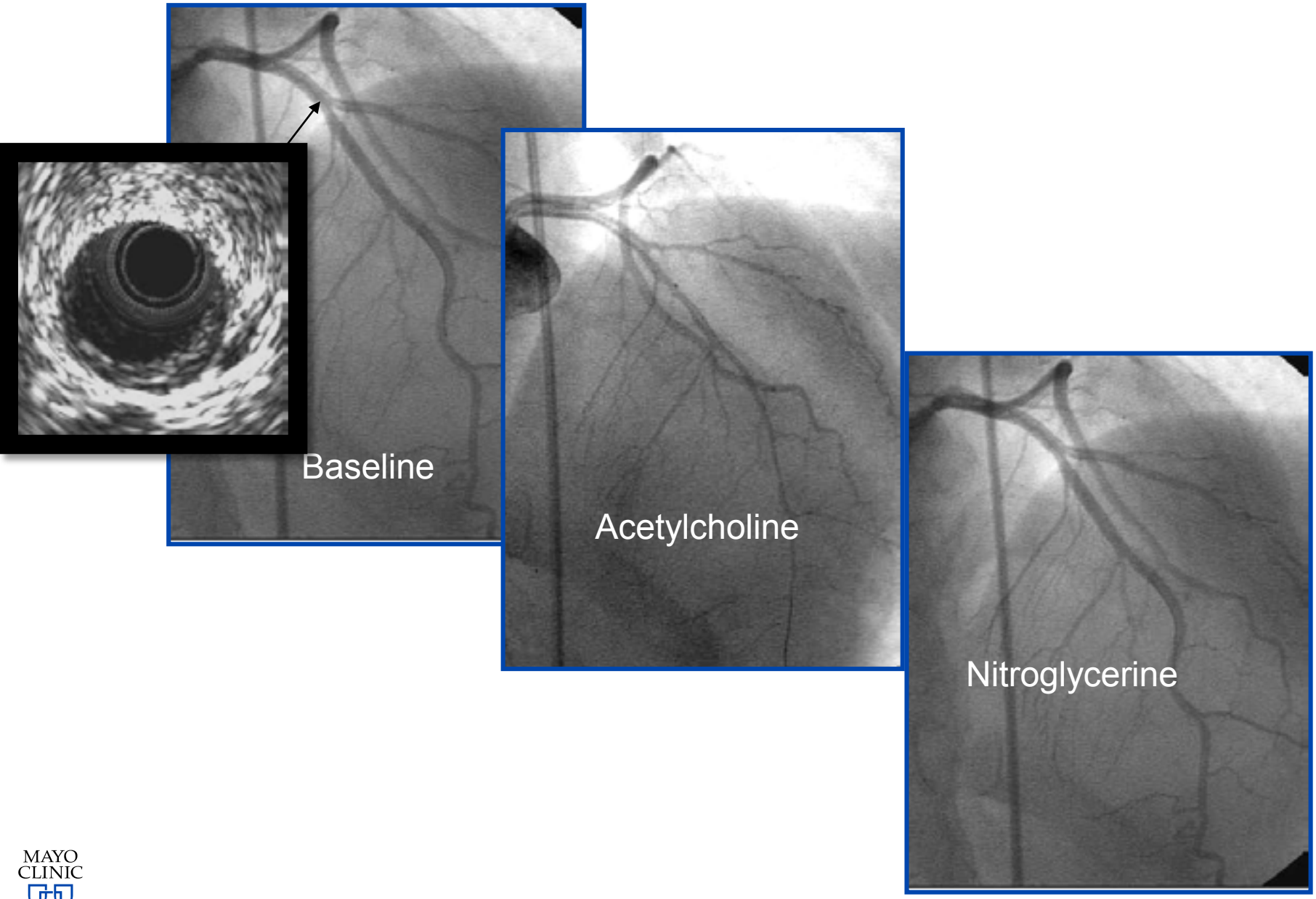
Baseline



Acetylcholine 10-4M

MAYO CLINIC

50-Year-Old Female With Chest Pain

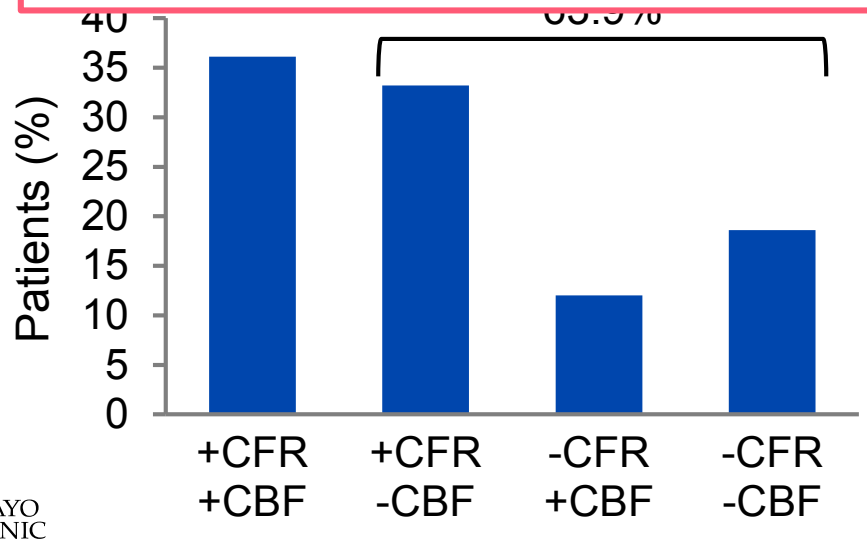


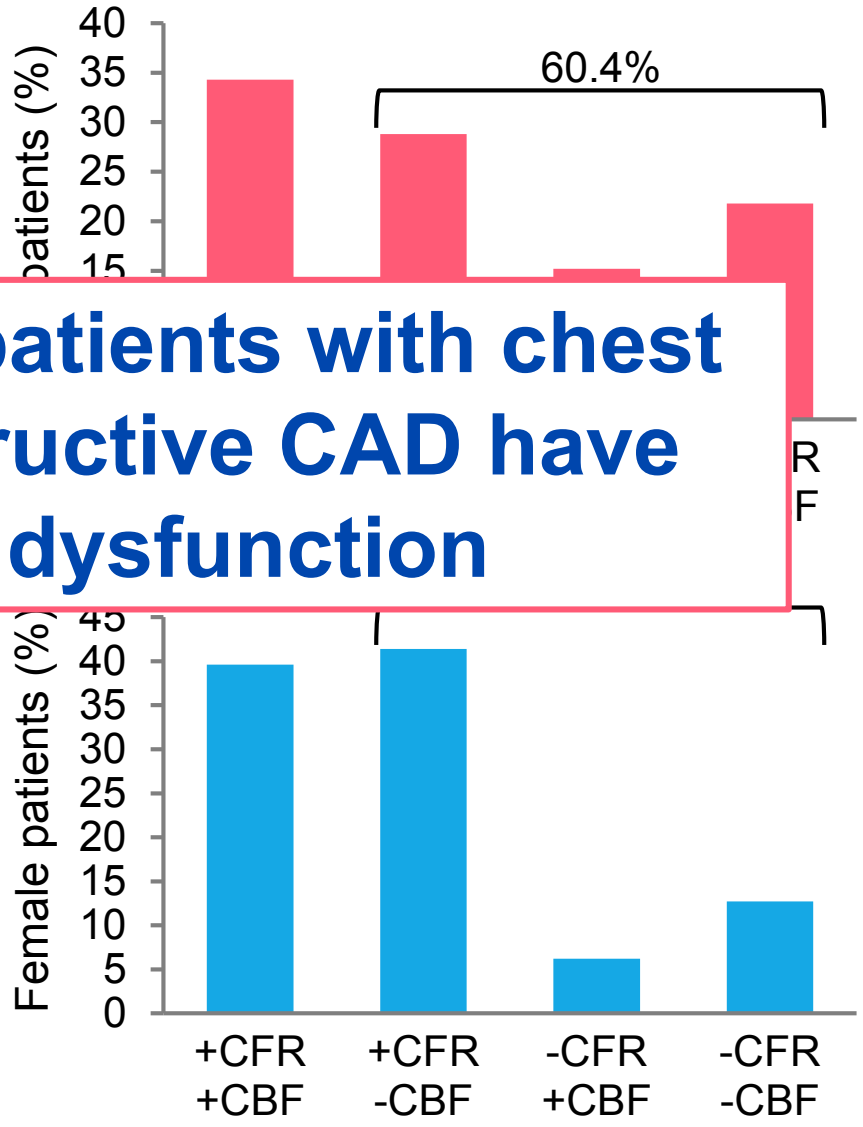
MAYO CLINIC

Prevalence of Microvascular Dysfunction in Patients With Non-Obstructive CAD

1,439 patients with chest pain and non-obstructive CAD at coronary angiography underwent invasive coronary microvessel assessment.

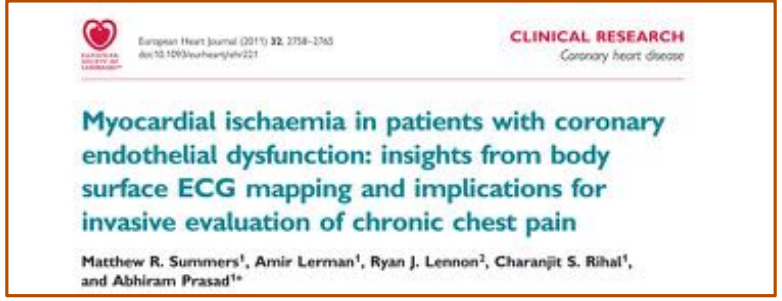
The majority of the patients with chest pain and non-obstructive CAD have microvascular dysfunction





MAYO CLINIC

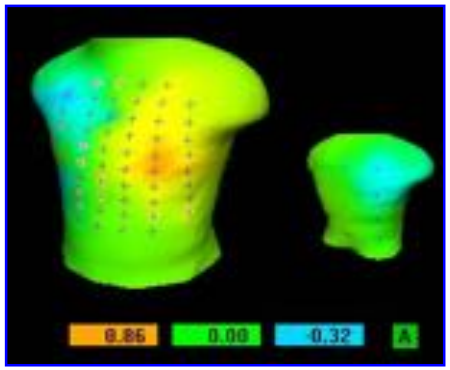
Coronary Endothelial Function: Prime ECG



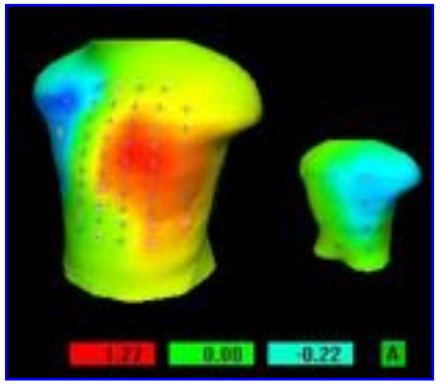
Coronary endothelial function in response to acetylcholine

Eighty lead body surface ECG

Baseline

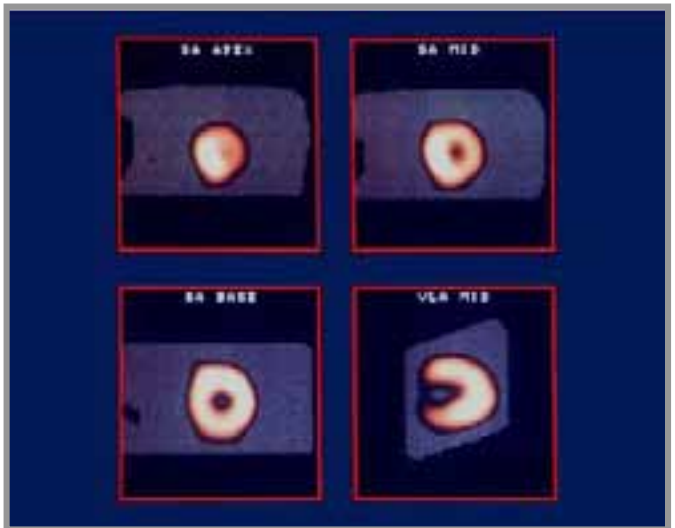


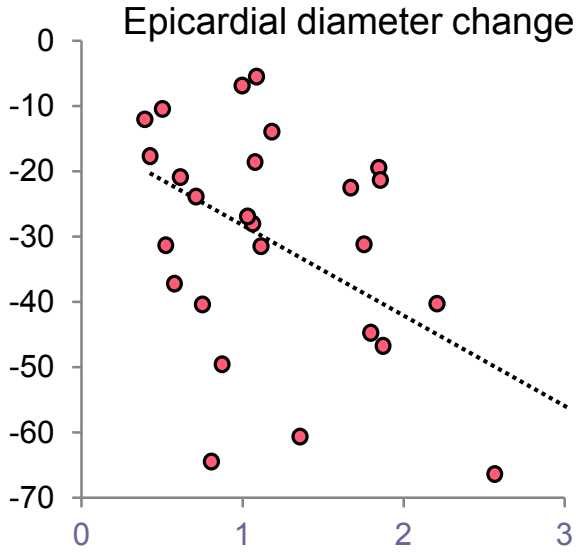
ACH 10^{-4}M



Coronary Endothelial Dysfunction in Humans Is Associated With Myocardial Perfusion Defects

David Hasdai, MD; Raymond J. Gibbons, MD; David R. Holmes, Jr, MD; Stuart T. Higano, MD; Amir Lerman, MD

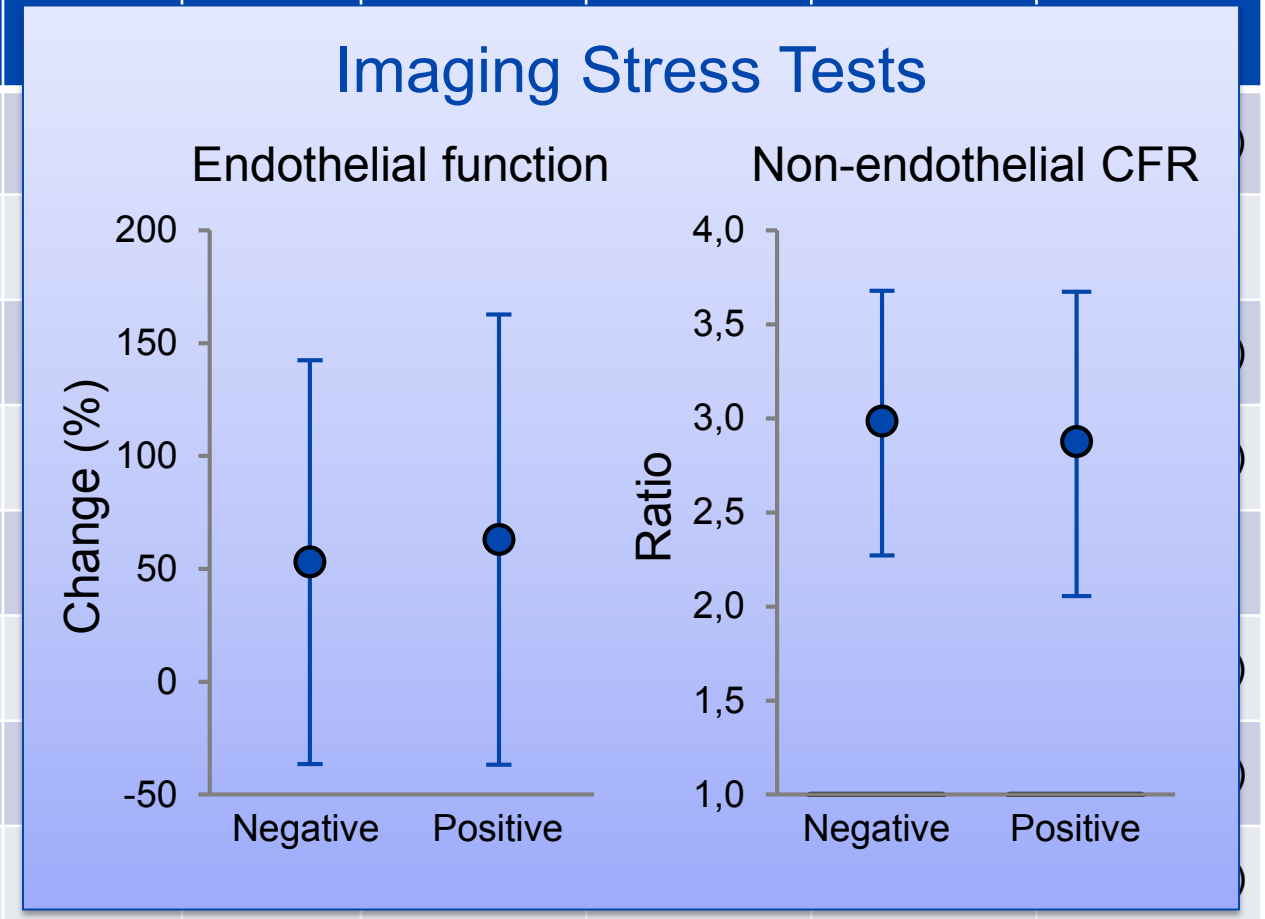




MAYO CLINIC

Association Between Noninvasive Tests and Coronary Microvascular Flow Reserve

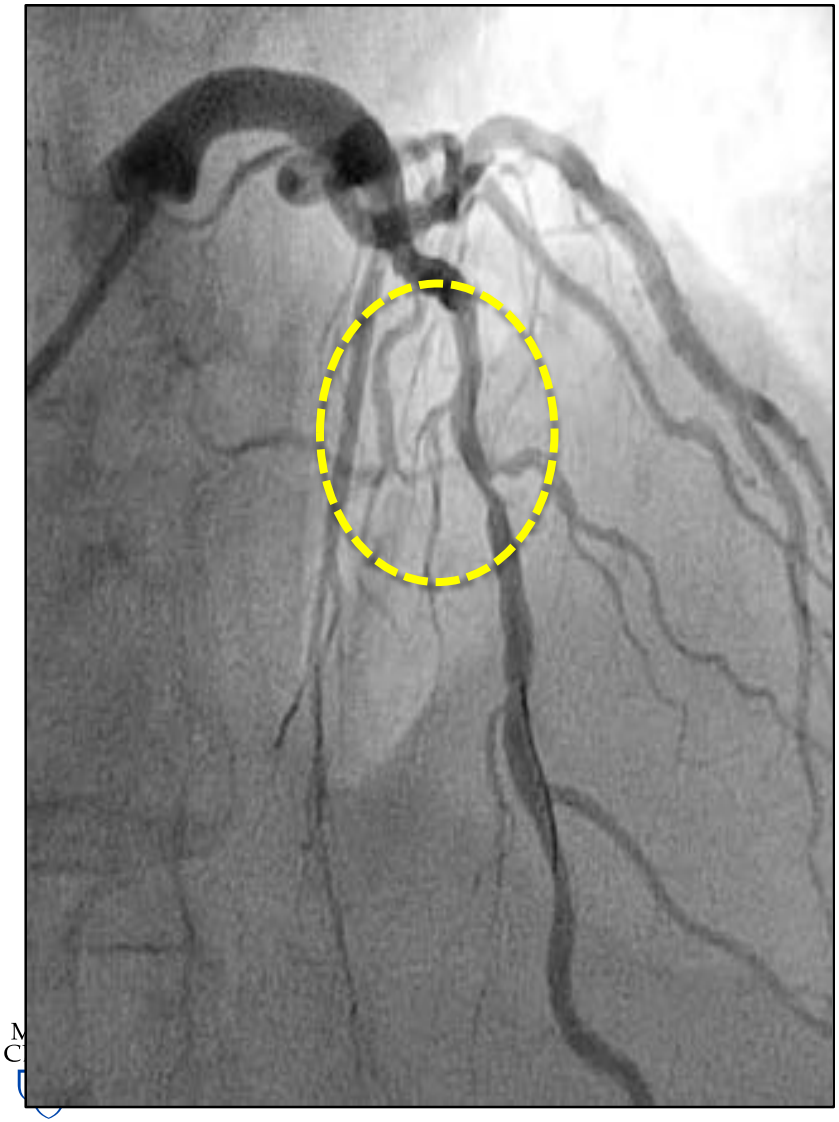
Test
Exercise Echo
Dobutamine Echo
Exercise SPECT
Vasodilator SPECT
Vasodilator PET
All imaging
Exercise ECG
All imaging + ECG



Cassar: Circ, 2009

MAYO CLINIC

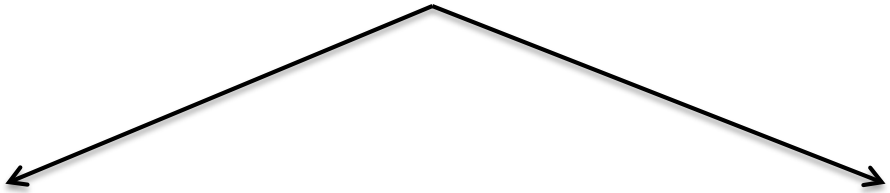
Case: 52 year old accountant with chest pain CFR, epicardial stenoses and microcirculation



CFR provides insight into the overall impairment in flow in the coronary circulation, regardless of its origin in the epicardial vessels (focal or diffuse stenoses), or in the microcirculation.

Many patients with microcirculatory dysfunction present also epicardial stenoses

How do we make resistance stable?

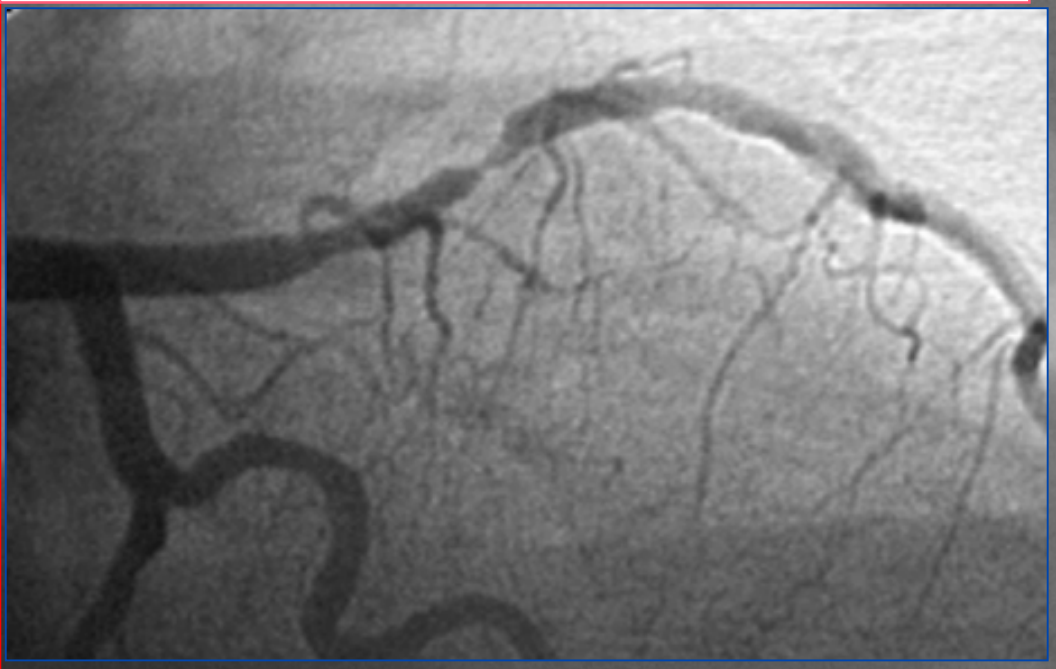


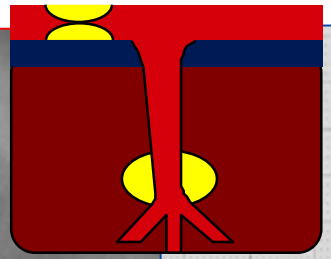
Pharmacological **Physiological**

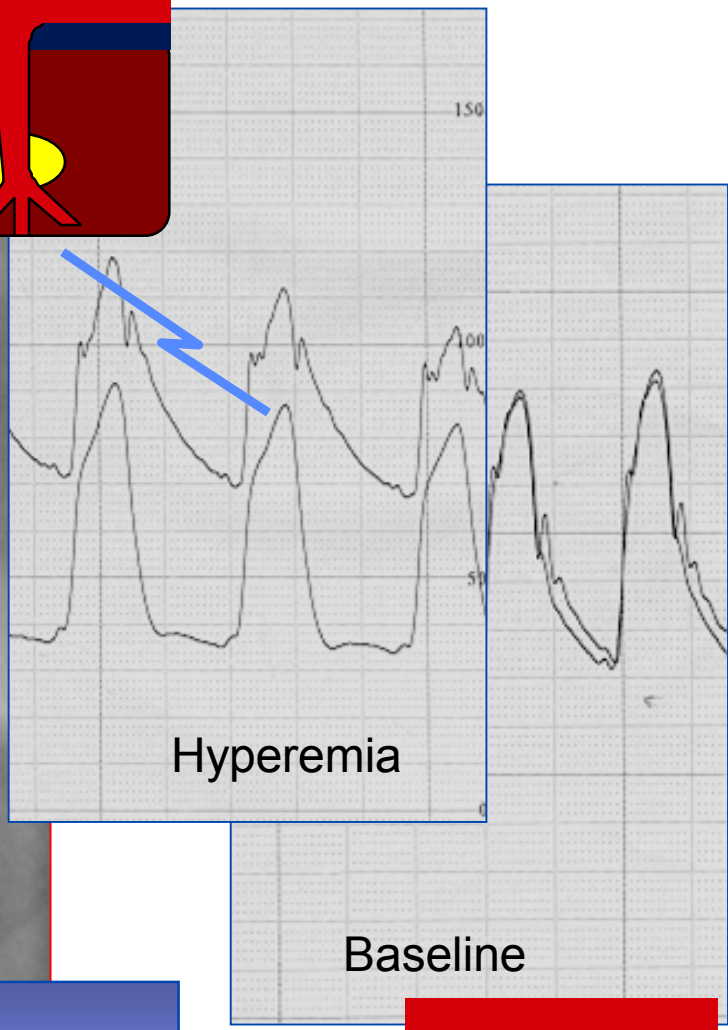
MAYO CLINIC

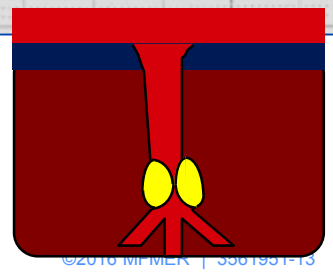
Coronary Stenoses Resting and hyperemic Flow

Hyperemia "uncover" the true gradient across the lesion









- ***Myocardial Fractional Flow Reserve during hyperemia***

$$FFR: = \frac{P_d}{P_A}$$

Fractional Flow Reserve to Determine the Appropriateness of Angioplasty in Moderate Coronary Stenosis

lomized Trial

Bruyne, MD, PhD; Nico H.J. Pijls, MD, PhD;

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Vol. 49, No. 21, 2007
ISSN 0735-1097/07/$32.00
doi:10.1016/j.jacc.2007.01.087

CLINICAL RESEARCH — Interventional Cardiology

Percutaneous Coronary Intervention of Functionally Nonsignificant Stenosis

5-Year Follow-Up of the DEFER Study

Nico H. J. Pijls, MD, PhD,* Pepijn van Schaardenburgh, MD,* Ganesh Man
Eric Boersma, PhD,‡ Jan-Willem Bech, MD, PhD,* Marcel van't Veer, MSc
Jan Hoorntje, MD, PhD,‖ Jacques Koolen, MD, PhD,* William Wijns, MD,
Bernard de Bruyne, MD, PhD†
Eindhoven, Rotterdam, Maastricht, and Zwolle, the Netherlands; and Aalst, Belg

Objectives The purpose of this study was to investigate the appropriateness of stenting stenosis.

Background Percutaneous coronary intervention (PCI) of an intermediate stenosis witho formed, but its benefit is unproven. Coronary pressure-derived fractional flow used to identify a stenosis responsible for reversible ischemia.

Methods In 325 patients scheduled for PCI of an intermediate stenosis, FFR was mea vention. If FFR was ≥0.75, patients were randomly assigned to deferral (Def (Perform group; n = 90) of PCI. If FFR was <0.75, PCI was performed as pl Clinical follow-up was 5 years.

Results There were no differences in baseline clinical characteristics between the 3 tained in 98% of the patients. Event-free survival was not different between and 73%, respectively; p = 0.52), but was significantly worse in the Referra posite rate of cardiac death and acute myocardial infarction in the Defer, Pe 3.3%, 7.9%, and 15.7%, respectively (p = 0.21 for Defer vs. Perform group; both other groups). The percentage of patients free from chest pain at follow Defer and Perform groups.

The NEW ENGLAND JOURNAL of MEDICINE

JANUARY 15, 2009

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.,
Robert M.D.,
Manoharan
Philip A. Mac

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Fractional Flow Reserve–Guided PCI for Stable Coronary Artery Disease

Bernard De Bruyne, M.D., Ph.D., William F. Fearon, M.D., Nico H.J. Pijls, M.D., Ph.D., Emanuele Barbato, M.D., Ph.D., Pim Tonino, M.D., Ph.D., Zsolt Piroth, M.D., Nikola Jagic, M.D., Sven Mobius-Winckler, M.D., Gilles Riouffol, M.D., Ph.D., Nils Witt, M.D., Ph.D., Petr Kala, M.D., Philip MacCarthy, M.D., Thomas Engström, M.D., Keith 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., Andreas Limacher, Ph.D., Eveline Nüesch, Ph.D., and Peter Jüni, M.D., for the FAME 2 Trial Investigators*

ABSTRACT

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 13, 2012 VOL. 367 NO. 11

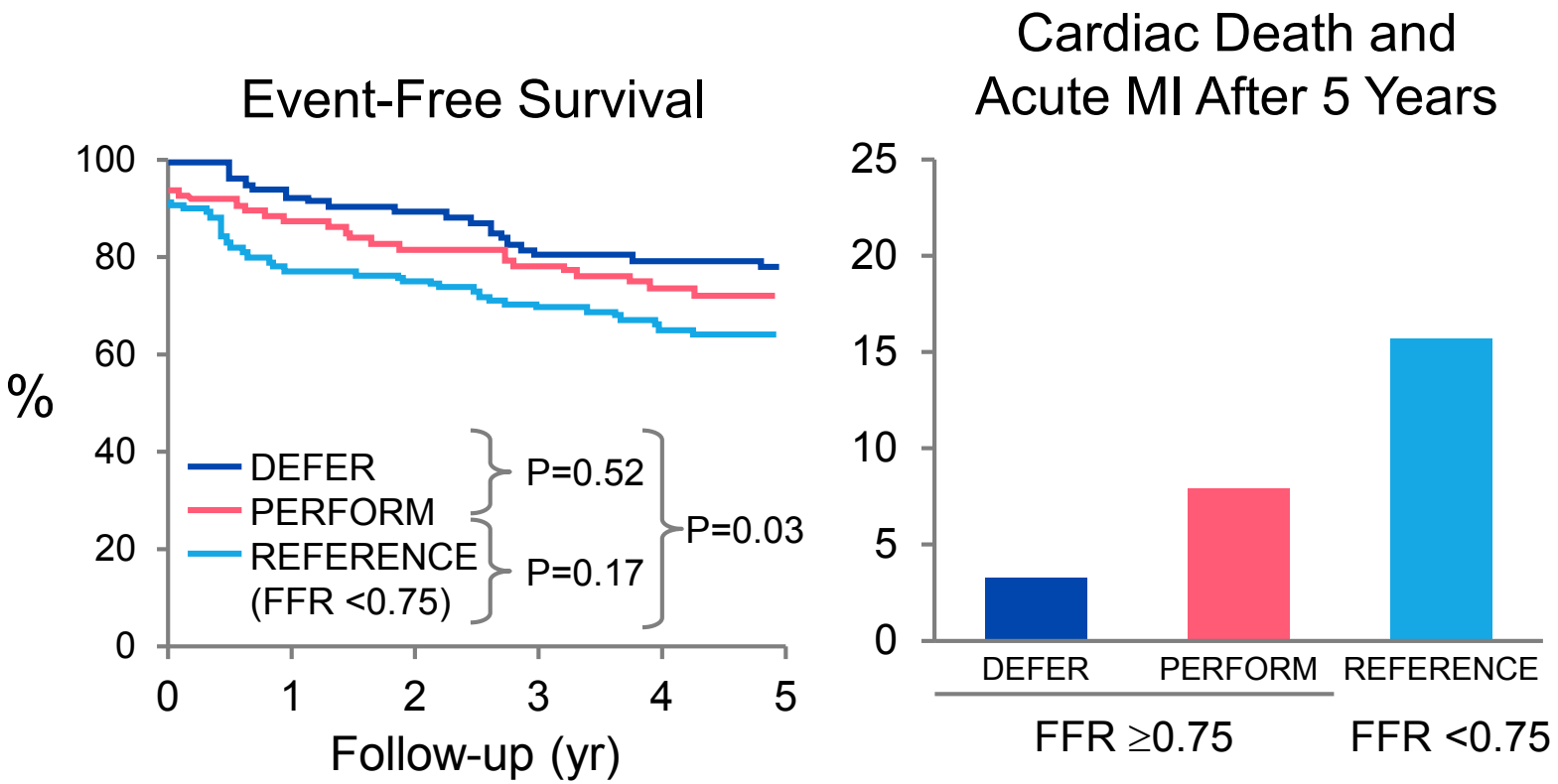
Fractional Flow Reserve–Guided PCI versus Medical Therapy in Stable Coronary Disease

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 Möbius-Winkler, 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*

ABSTRACT

MAY CLIN

5-Year Outcomes – DEFER Trial

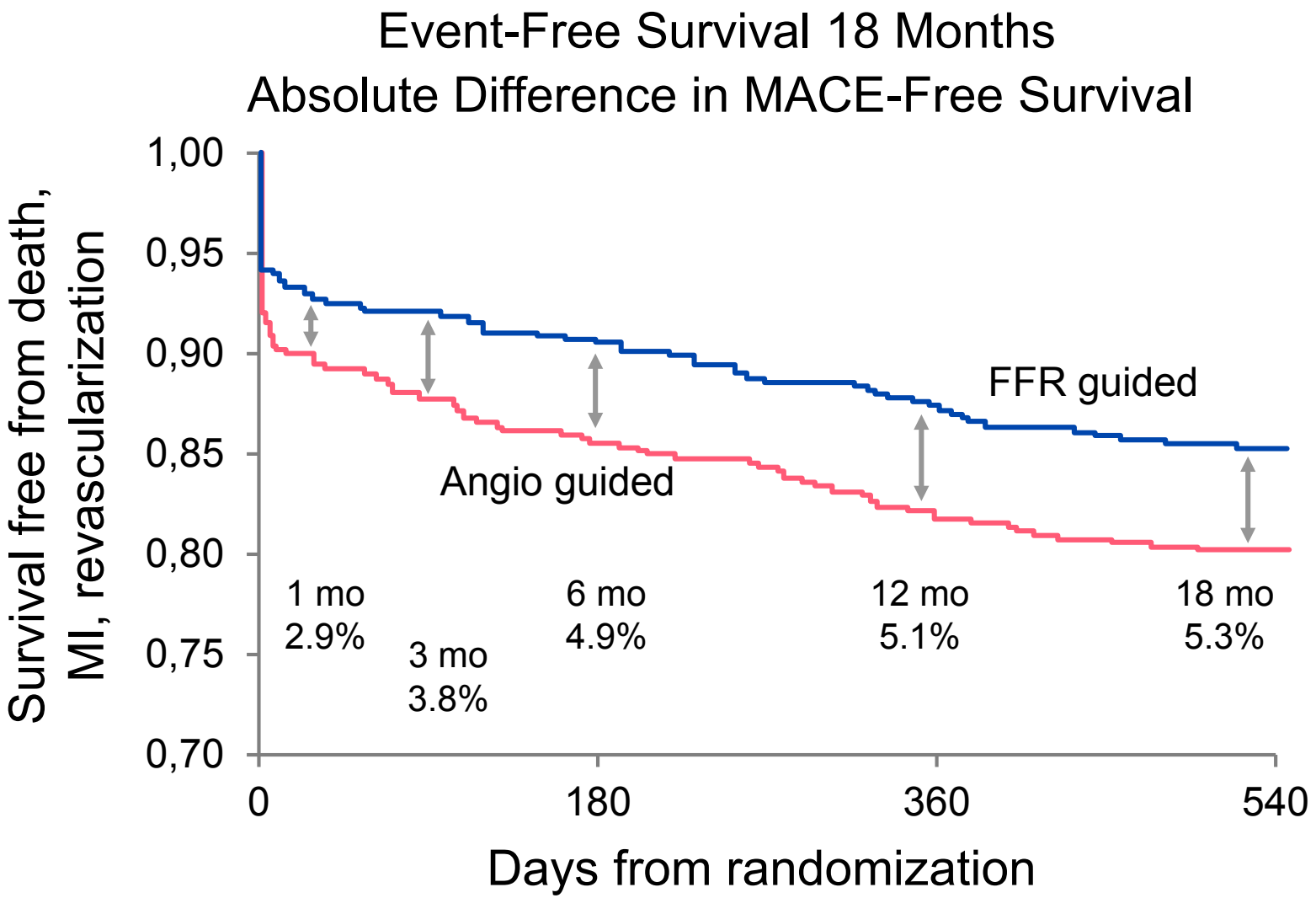


Conclusions: "Five-year outcome after deferral of PCI of an intermediate coronary stenosis based on FFR ≥0.75 is excellent. The risk of cardiac death or myocardial infarction related to this stenosis is <1% per year and not decreased by stenting."

Pijls: JACC, 2007

MAYO CLINIC

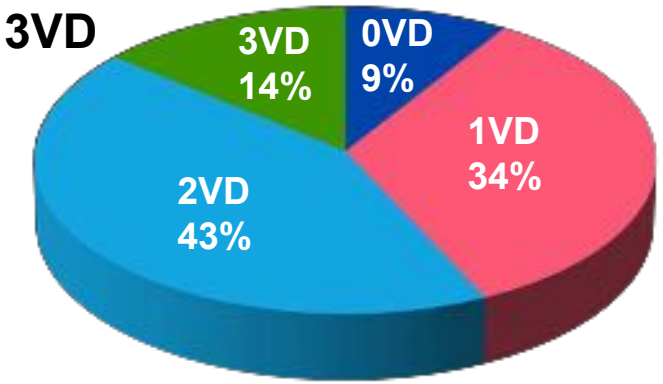
FAME Study



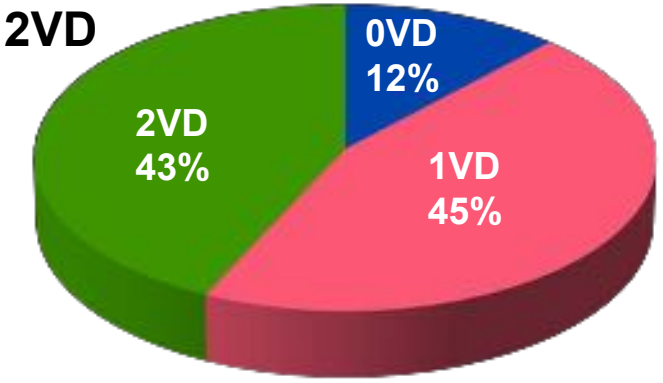
NEJM

MAYO CLINIC

Functional SYNTAX Score Recalculated Counting only Lesions With an FFR <0.8



Only 14% of patients with angiographic 3VD had functional 3VD

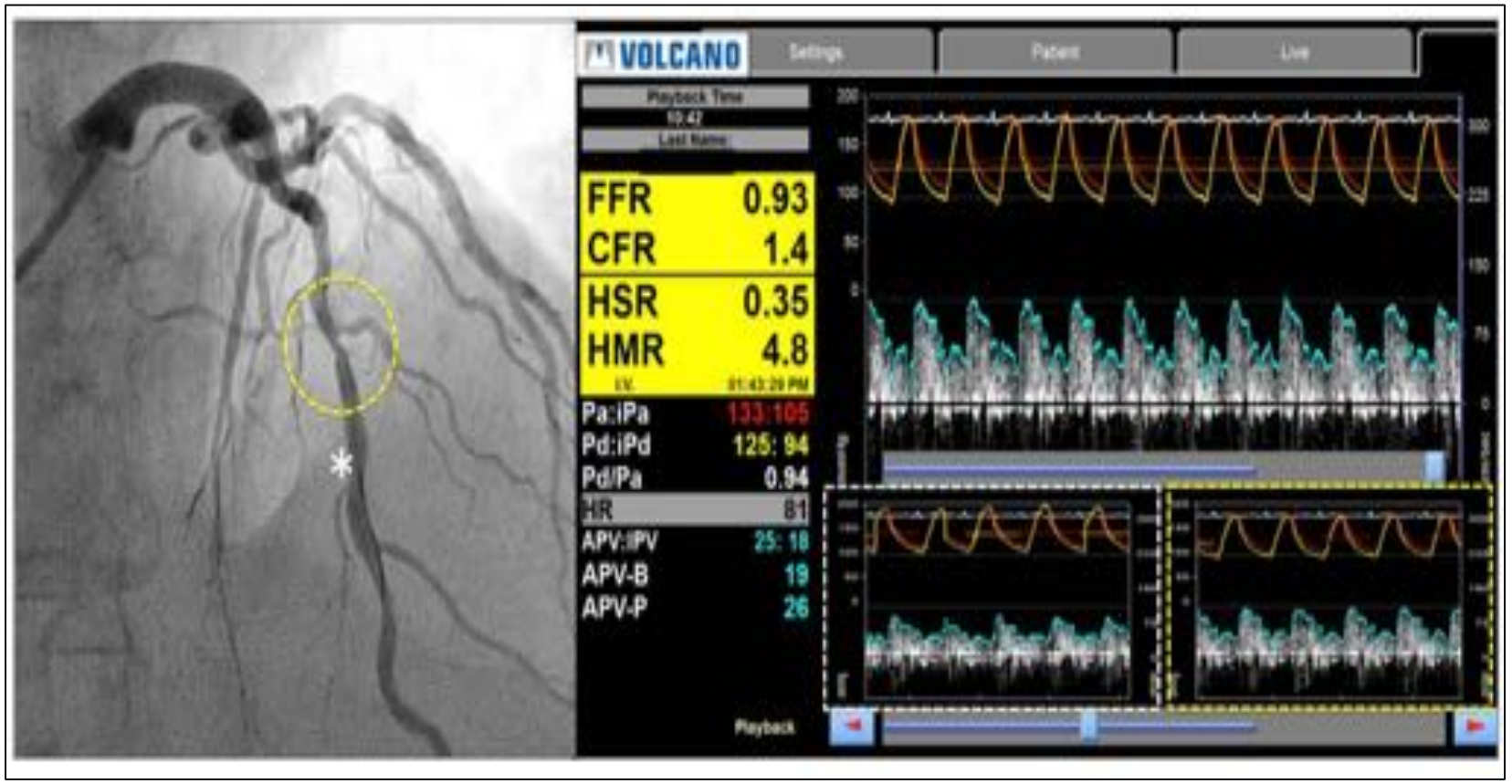


Only 43% of patients with angiographic 2VD had functional 2VD

J Am Coll Cardiol 55(25):2816, 2010

MAYO CLINIC

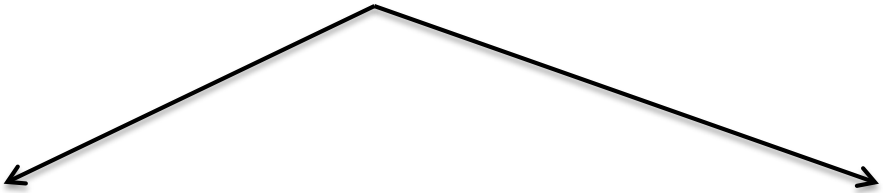
Outlining the involvement of epicardial and microcirculatory domains in ischaemic heart disease



Normal FFR / Decreased CFR / Increased HMR (microcirculatory resistance)

MAYO CLINIC

How do we make resistance stable?



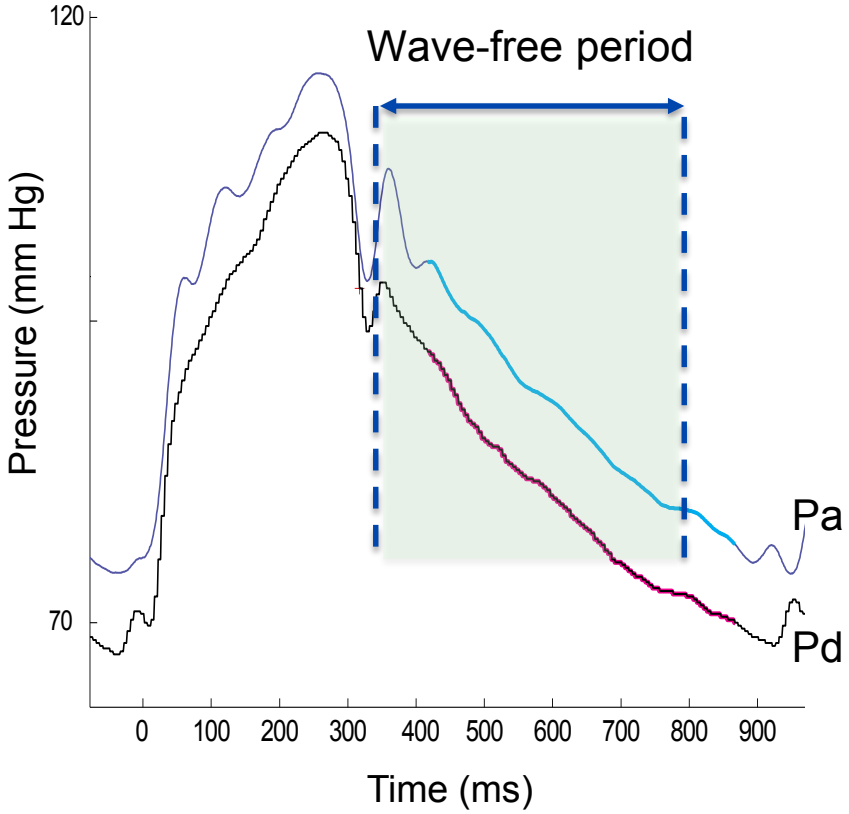
Pharmacological **Physiological**

MAYO CLINIC

Development and Validation of a New Adenosine-Independent Index of Stenosis Severity From Coronary Wave–Intensity Analysis

Results of the ADVISE (ADenosine Vasodilator Independent Stenosis Evaluation) Study

Measure during a wave-free portion of diastole (microvascular resistance constant and minimal)



Contraindications to adenosine

- Bronchospasm
- Heart block
- Dipyramidole can potentiate adenosine effect and cause prolonged heart block
- Patients taking inhibitors of adenosine may require higher doses
  - Theophylline
  - Chocolate
  - Caffeine

MAYO CLINIC

iFR and Clinical Outcome

ORIGINAL ARTICLE

Use of the Instantaneous Wave-free Ratio or Fractional Flow Reserve in PCI

J.E. Davies, S. Sen, H.-M. Dehbi, R. Al-Lamee, R. Petraco, S.S. Nijjer, R. Bhindi, S.J. Lehman, D. Walters, J. Sapontis, L. Janssens, C.J. Vrints, A. Khashaba, M. Laine, E. Van Belle, F. Krackhardt, W. Bojara, O. Going, T. Härle, C. Indolfi, G. Niccoli, F. Ribichini, N. Tanaka, H. Yokoi, H. Takashima, Y. Kikuta, A. Erglis, H. Vinhas, P. Canas Silva, S.B. Baptista, A. Alghamdi, F. Hellig, B.-K. Koo, C.-W. Nam, E.-S. Shin, J.-H. Doh, S. Brugaletta, E. Alegria-Barrero, M. Meuwissen, J.J. Piek, N. van Royen, M. Sezer, C. Di Mario, R.T. Gerber, I.S. Malik, A.S.P. Sharp, S. Talwar, K. Tang, H. Samady, J. Altman, A.H. Seto, J. Singh, A. Jeremias, H. Matsuo, R.K. Kharbanda, M.R. Patel, P. Serruys, and J. Escaned

DEFINE FLAIR

iFR-SWEDEHEART

ORIGINAL ARTICLE

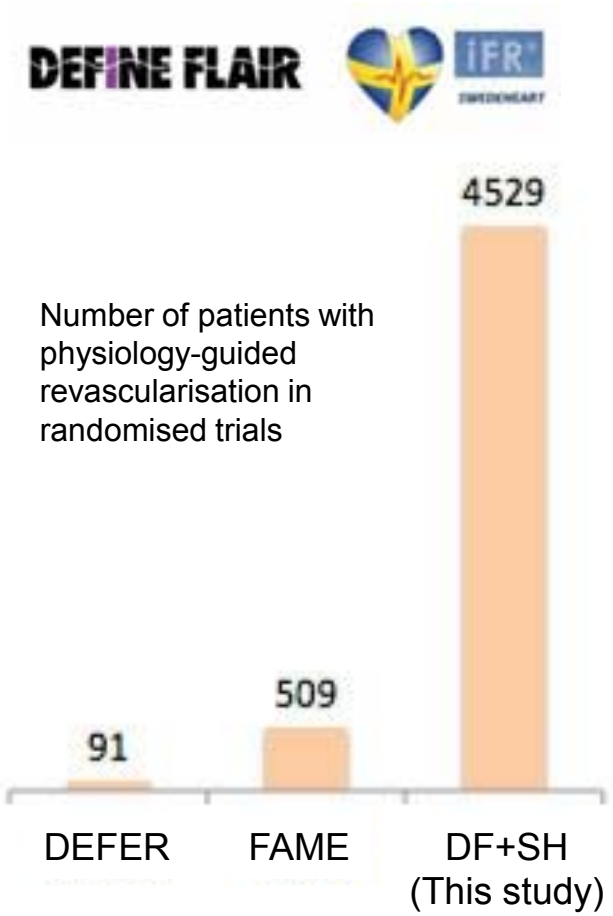
Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI

M. Götberg, E.H. Christiansen, I.J. Gudmundsdottir, L. Sandhall, M. Danielewicz, L. Jakobsen, S.-E. Olsson, P. Öhagen, H. Olsson, E. Omerovic, F. Calais, P. Lindroos, M. Maeng, T. Tödt, D. Venetsanos, S.K. James, A. Kåregren, M. Nilsson, J. Carlsson, D. Hauer, J. Jensen, A.-C. Karlsson, G. Panayi, D. Erlinge, and O. Fröbert, for the iFR-SWEDEHEART Investigators*

MAYO CLINIC

Background: FFR- and iFR-based deferral of coronary revascularisation

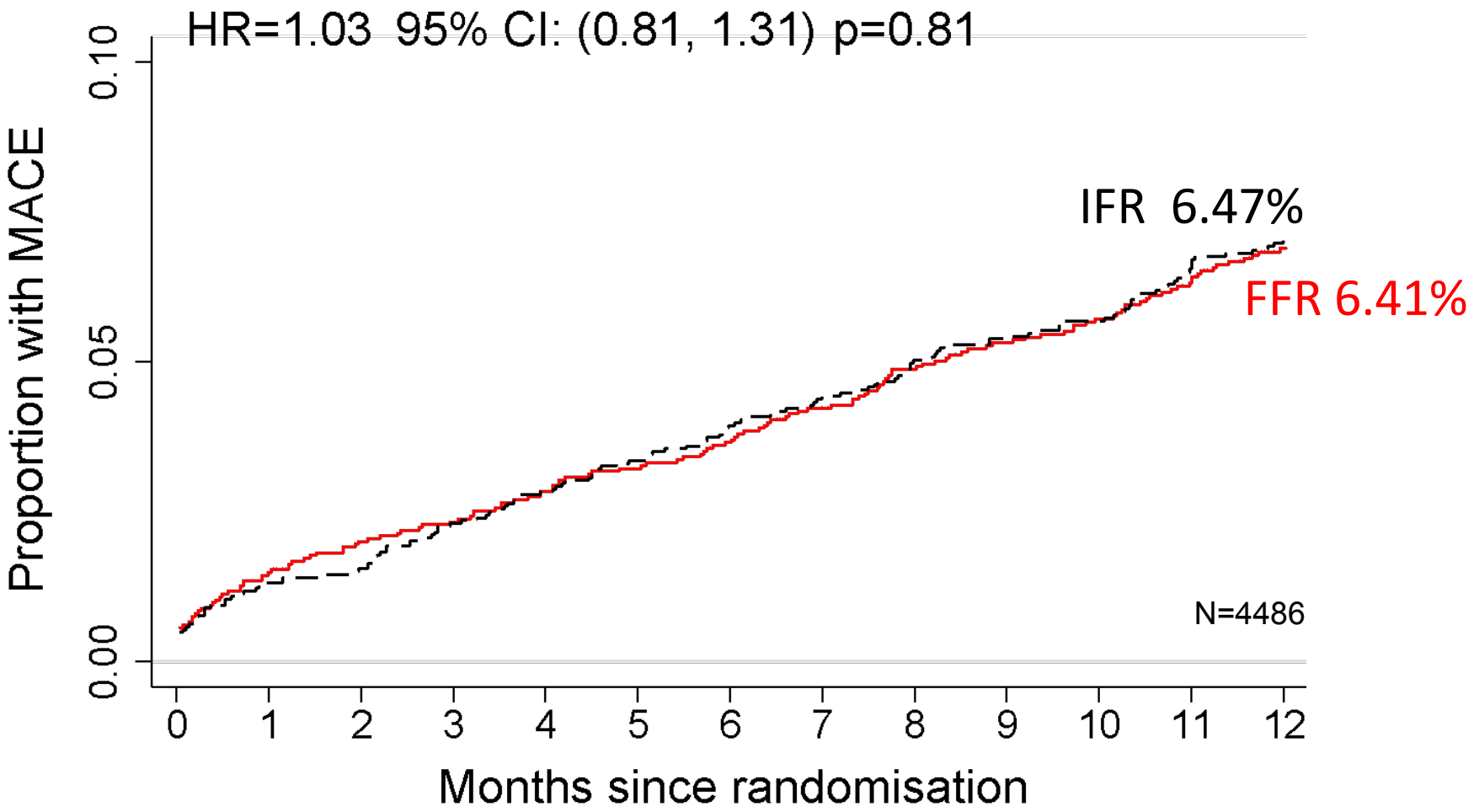
- The DEFINE FLAIR (DF) and iFR SWEDEHEART (SH) trials demonstrated that iFR is as safe as FFR in guiding myocardial revascularisation.
- Yet, it is unknow if this is valid for patients in whom revascularisation is deferred.
- The pooled population of both studies (4529 patients) provides a unique opportunity to investigate the discussed aspects of revascularisation deferral in contemporary clinical practice.



MAYO CLINIC

Davies JE *et al. N Engl J Med* 2017; Götberg M, *et al. N Engl J Med* 2017

MACE in iFR and FFR guided revascularisation (all patients)



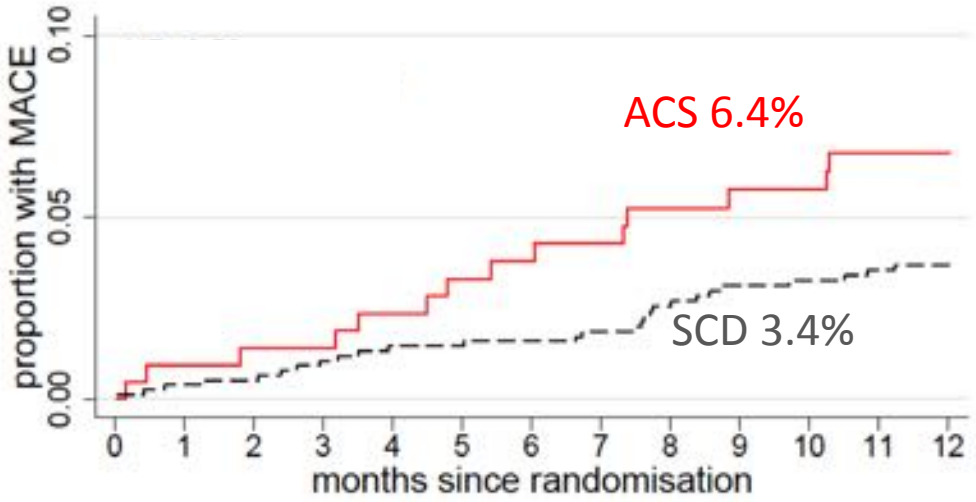
MACE similar and low at 1 year after iFR- and FFR-based revascularisation decision-making

MAYO CLINIC

Unadjusted outcomes after deferral by clinical presentation and iFR or FFR

FFR

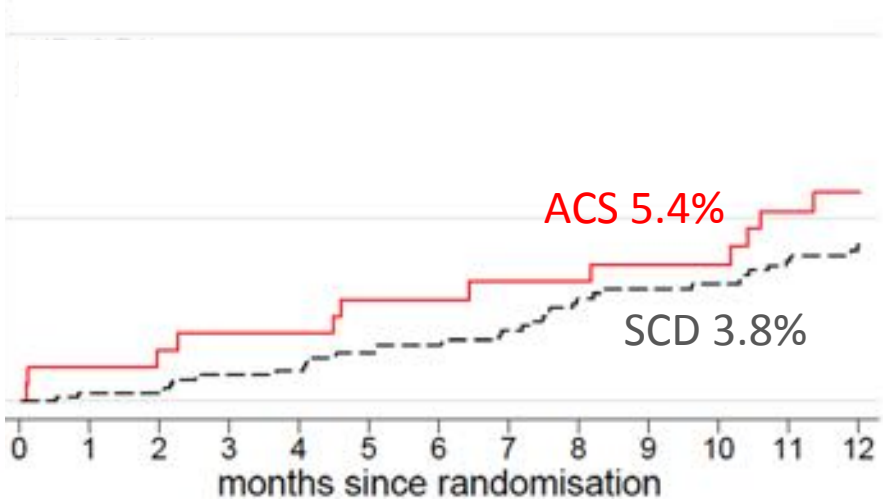
HR 0.52 (0.27-1.00); p<0.05



In FFR-deferred patients, MACE is significantly higher in ACS than SCD

iFR

HR 0.74 (0.38-1.43); p=0.37



In iFR-deferred patients, MACE is similar in ACS and SCD

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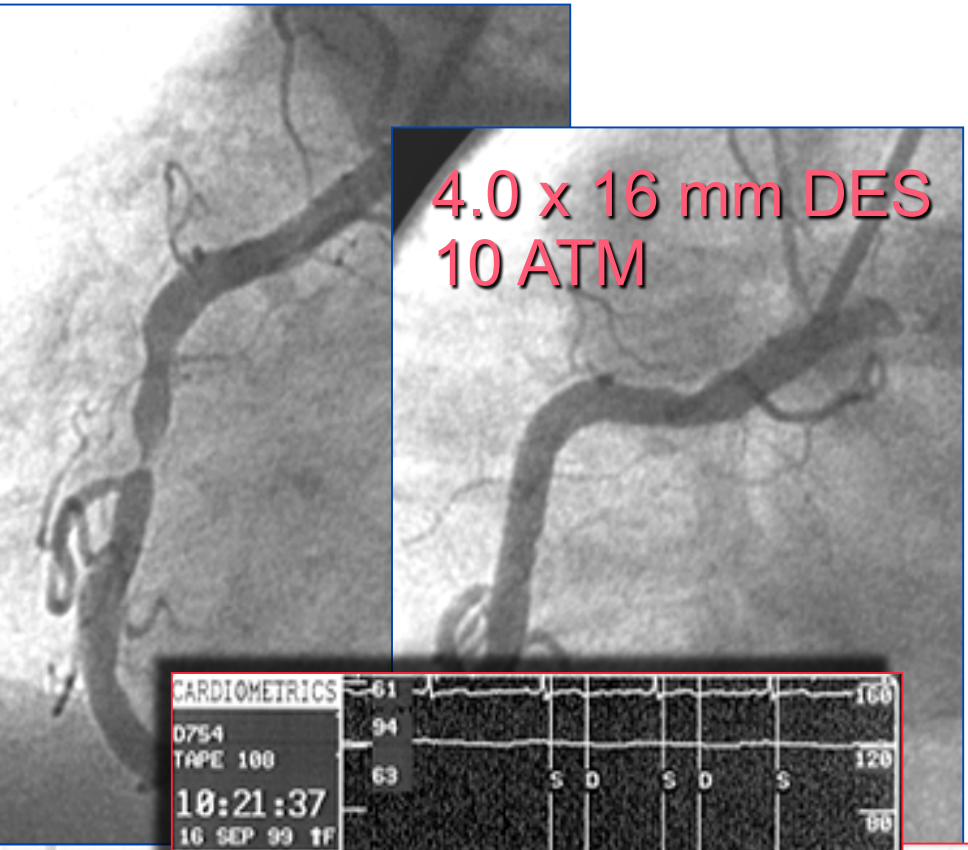
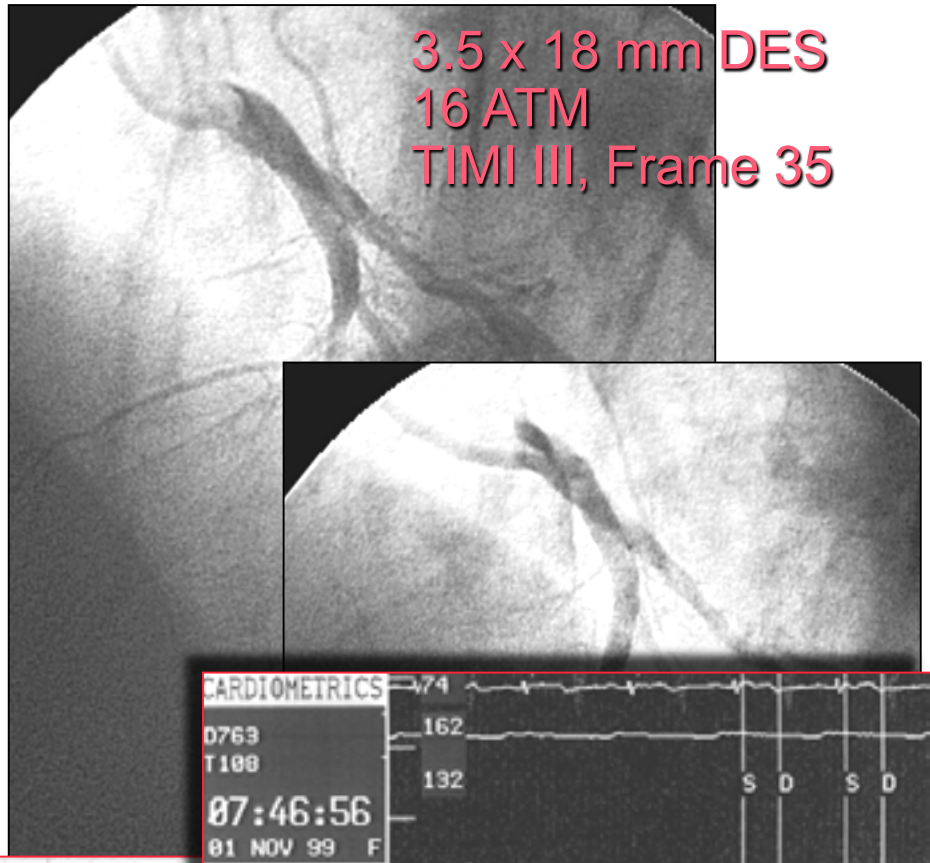
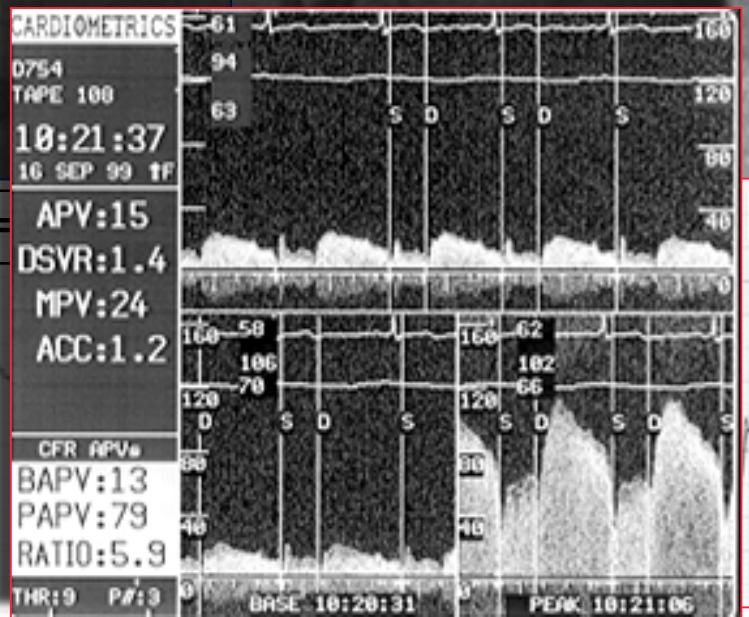
64 year old male, non-smoker, inactive, Admitted with IWMI

54 year old male, smoker, Admitted with AWMI

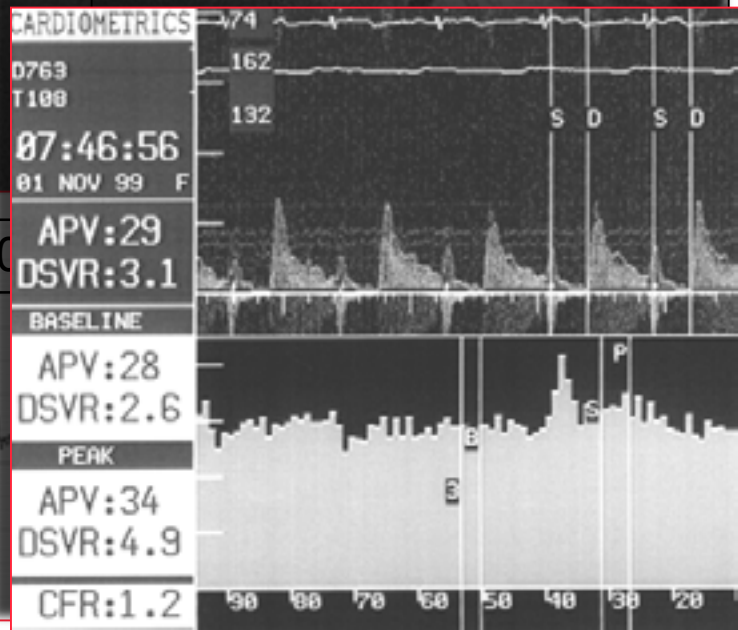




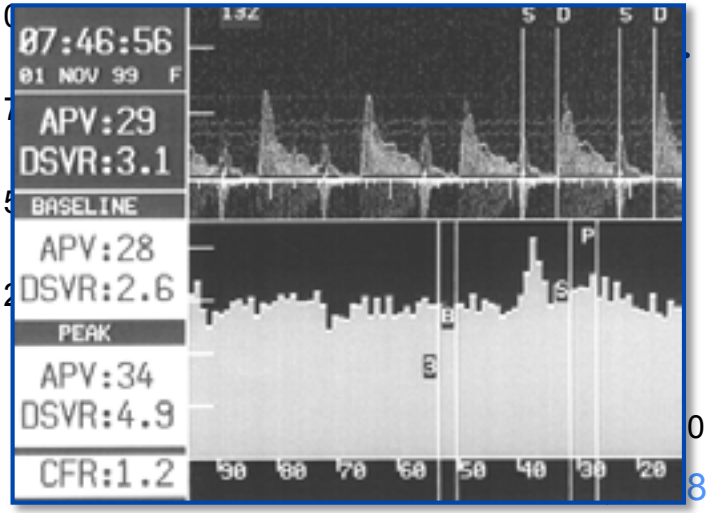
FFR =



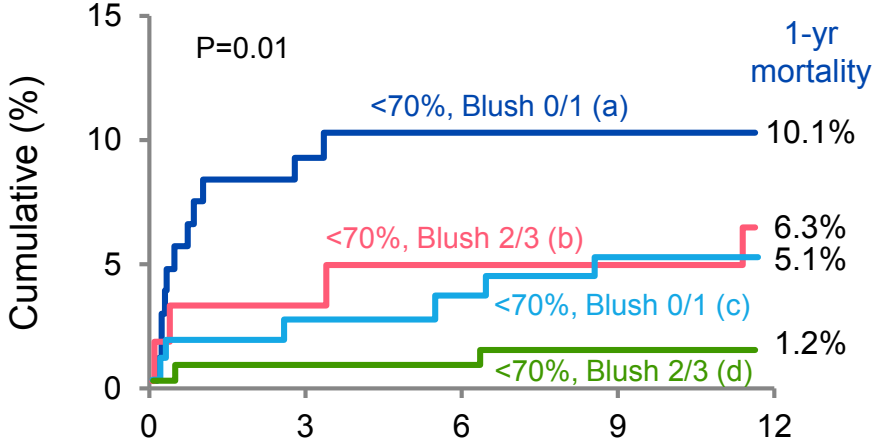
FFR = 1.00



Angiographic TIMI Flow and CFR

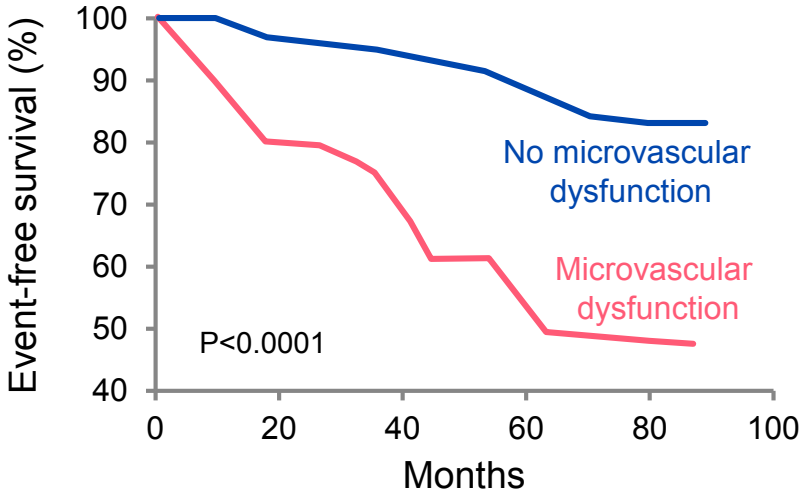


ST-Segment Recovery and Myocardial Blush Grade



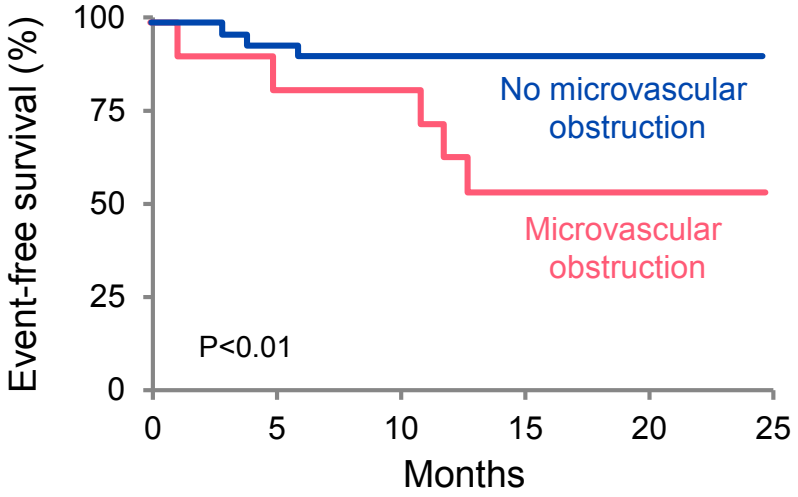
Sorajja et al: Eur Heart J, 2005

Myocardial Contrast Echo



Bologneseet al: Circulation, 2004

Magnetic Resonance Imaging



Wu et al: Circulation, 1998

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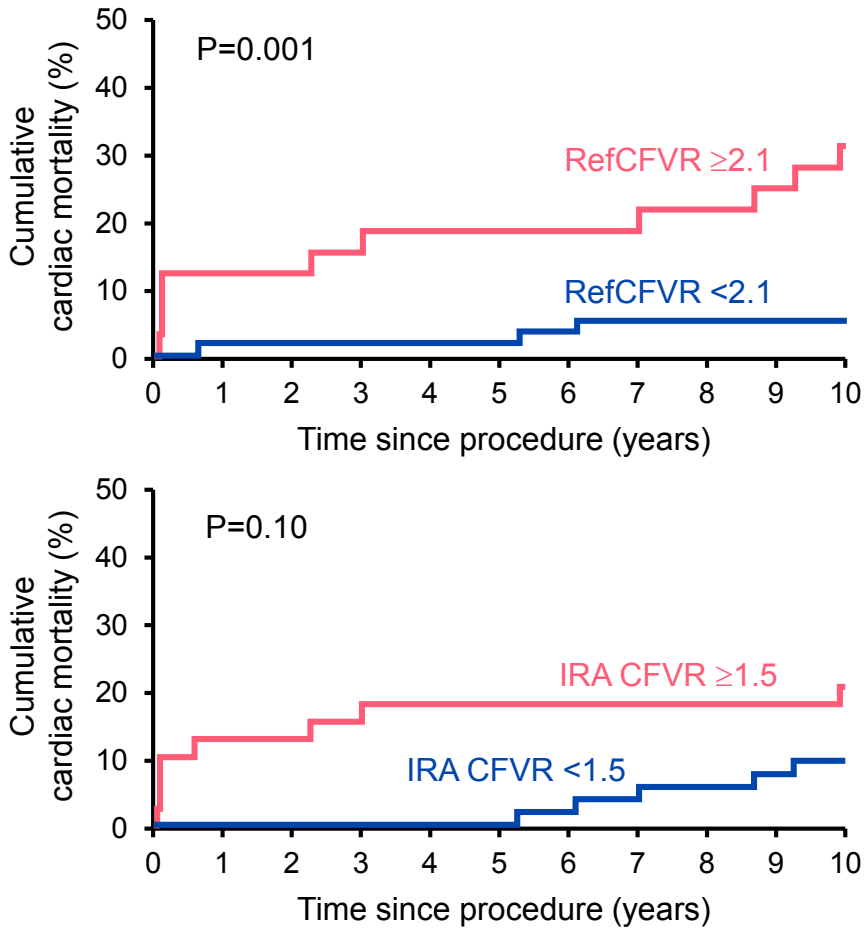
Impact of Coronary Microvascular Function on Long-term Cardiac Mortality in Patients With Acute ST-Segment–Elevation Myocardial Infarction

- intracoronary Doppler flow velocity was measured in the infarct-related artery,, as well as in a reference vessel to determine reference vessel CFVR

Conclusions

- Microvascular dysfunction, determined after primary percutaneous coronary intervention for acute anterior wall ST-segment–elevation myocardial infarction *both at the IRA and the remote* area are associated with a significantly increased long-term cardiac mortality

Kaplan-Meier estimates and log-rank comparison of cumulative cardiac mortality. A) Reference vessel coronary flow velocity reserve (refCFVR) and B) Infarct-related artery (IRA) CFVR



van de Hoef et al: Circ Cardiovasc Interv. 6:207, 2013

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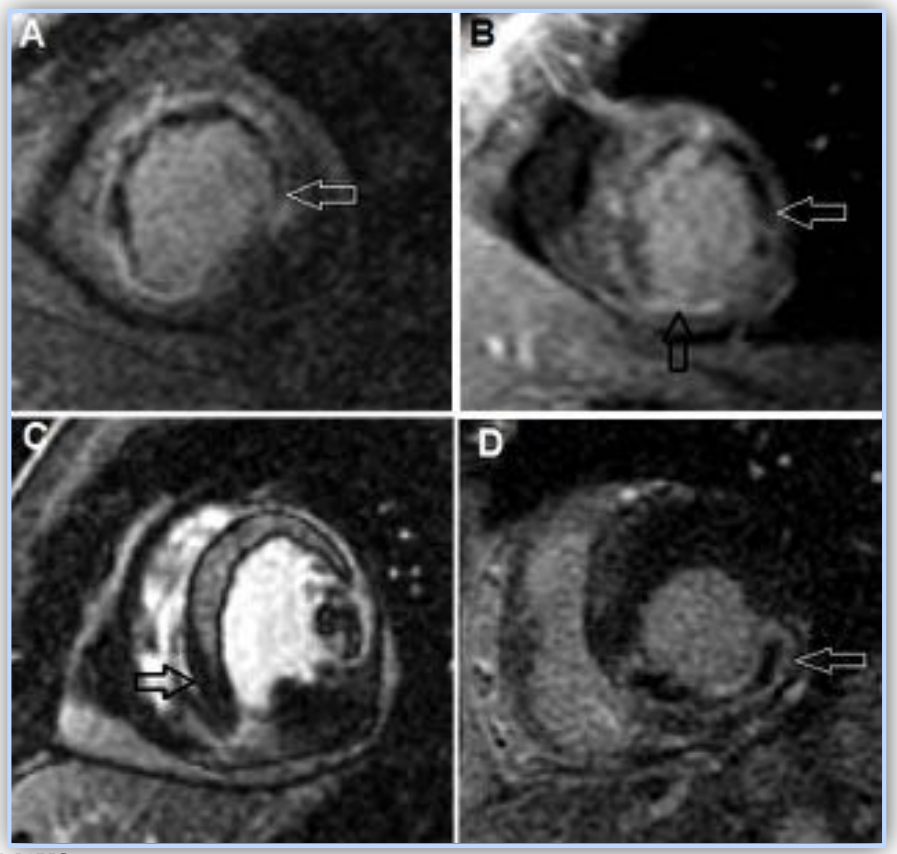
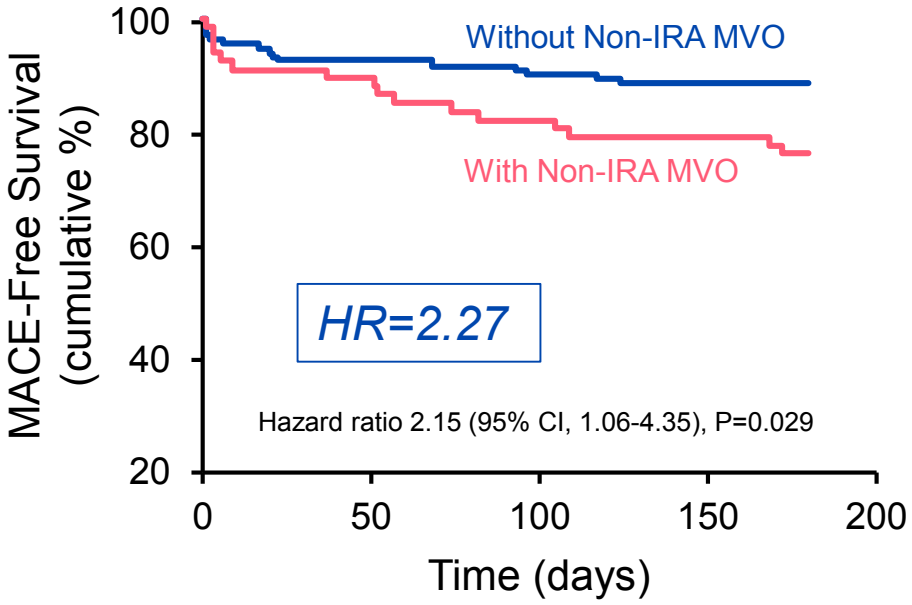
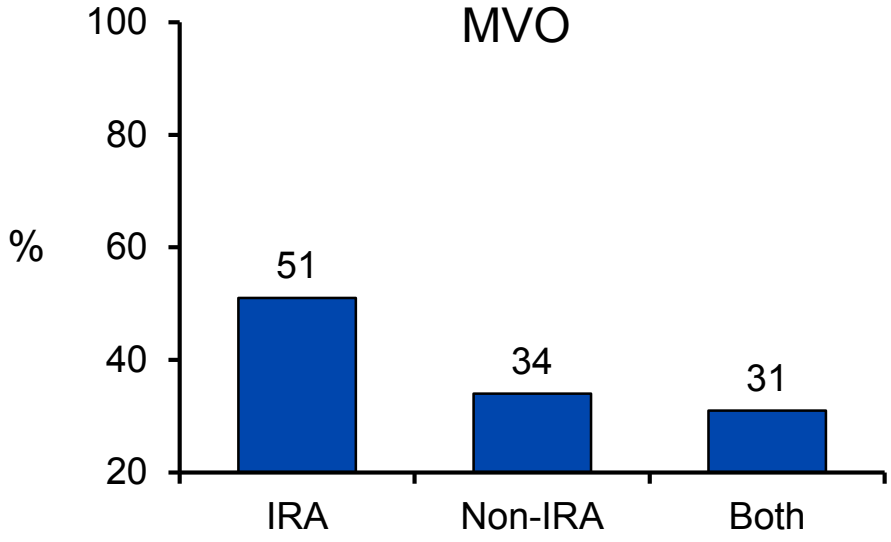
Microvascular Obstruction in Non-Infarct Related Coronary Arteries

- 199 patients followed PCI for STEMI
- Cardiac MRI within one week
- IRA and non-IRA segments (AHA)







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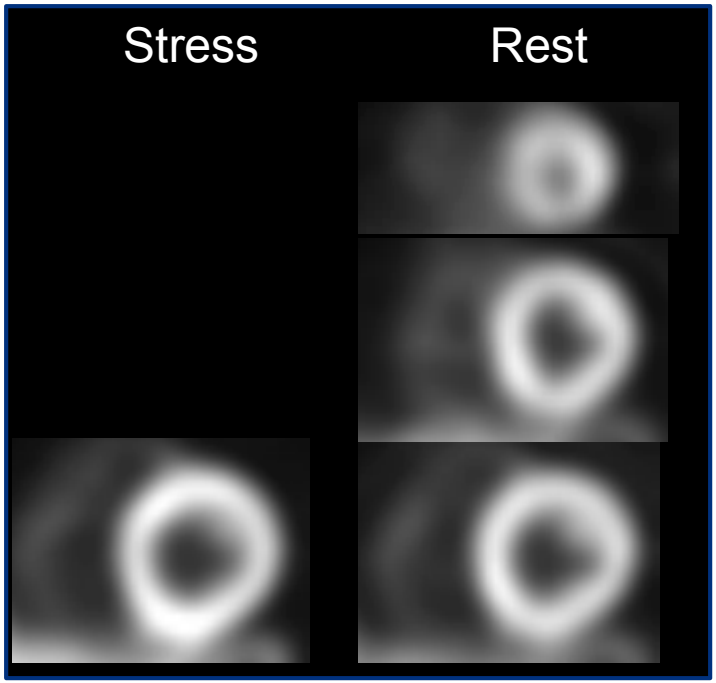
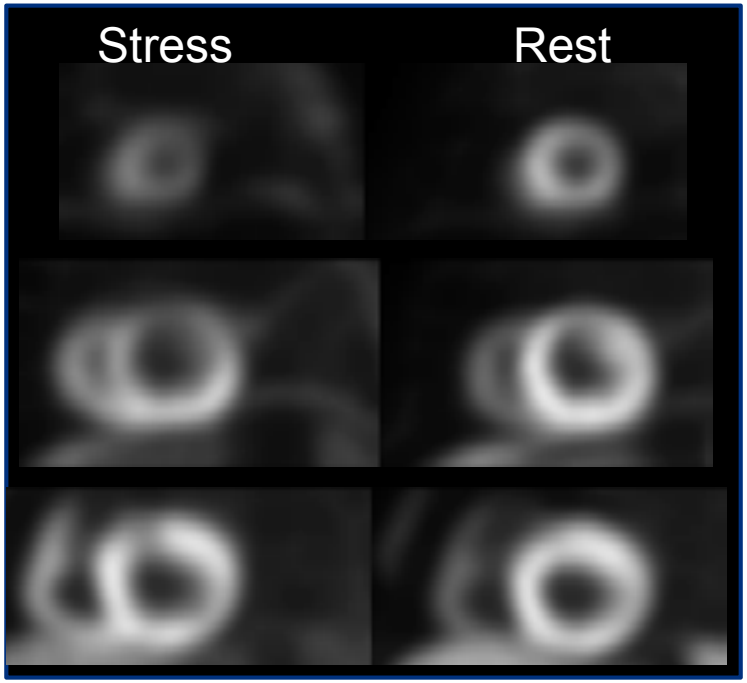
PET MPI with N-13 ammonia and MBF





	Stress	Rest	MFR
LAD	2.11	0.95	2.22
LCx	1.92	0.93	2.06
RCA	1.68	0.88	1.91

	Stress	Rest	MFR
LAD	1.58	0.85	1.86
LCx	1.98	0.95	2.08
RCA	1.73	0.85	2.03

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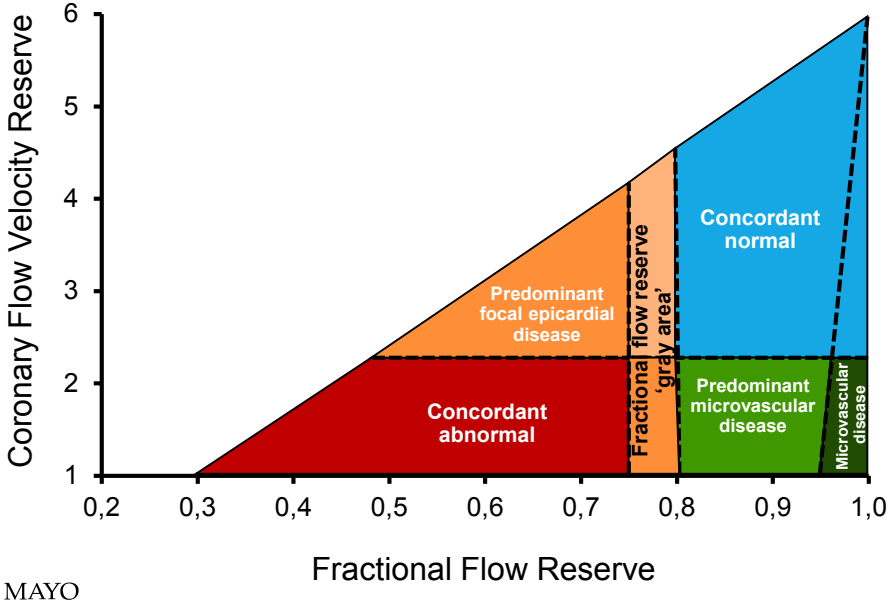
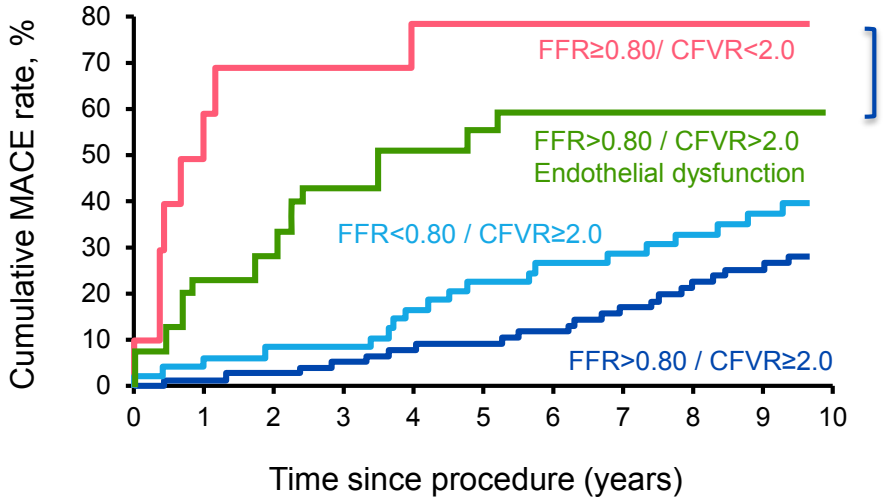
Coronary Hemodynamics

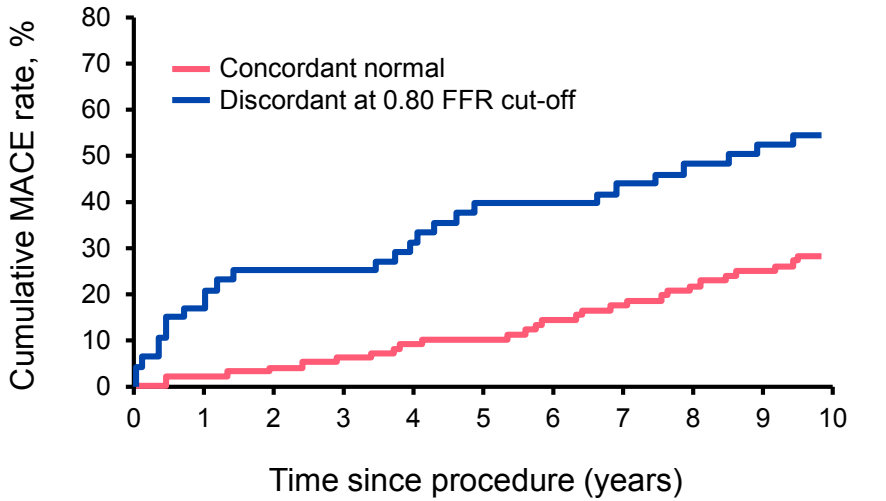
Physiological Basis and Long-Term Clinical Outcome of Discordance Between Fractional Flow Reserve and Coronary Flow Velocity Reserve in Coronary Stenoses of Intermediate Severity

- 157 patients, evaluated by FFR and CFVR
- Long-term follow-up was performed to document the occurrence of major adverse cardiac events: cardiac death, myocardial infarction, or target vessel revascularization. Discordance between FFR and CFVR occurred in 31% and 37% of stenoses at the 0.75, and 0.80 FFR cut-off value
- Discordance of CFVR with FFR originates from the involvement of the coronary microvasculature



MACE Indicates Major Adverse Cardiac Event





van de Hoef et al: Circ Cardiovasc Interv 7:301, 2014

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