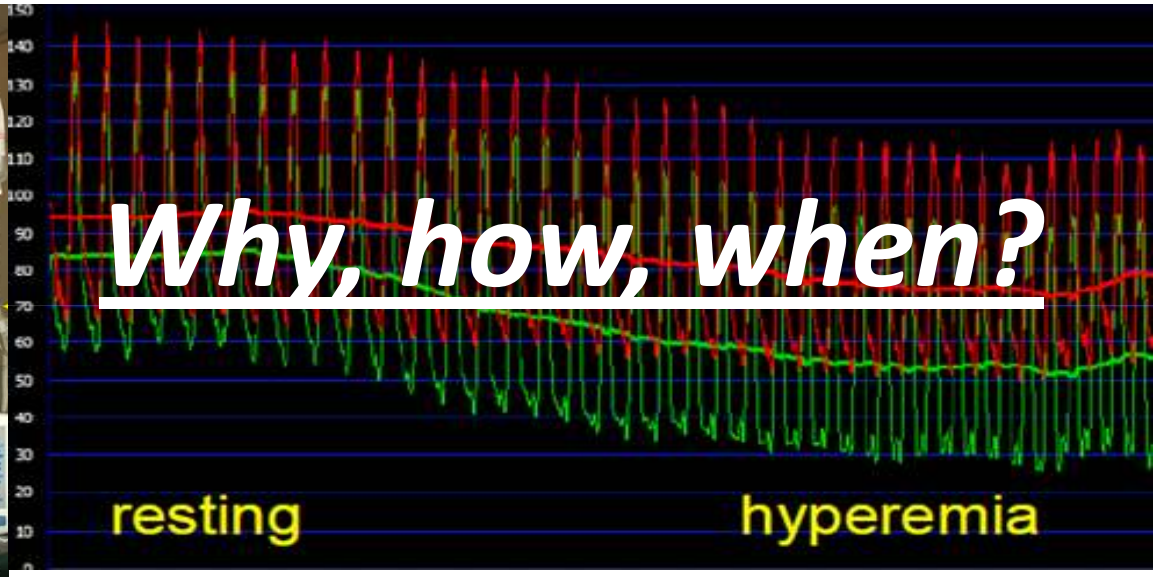
Fractional Flow Reserve (FFR) estimation



GRAIDIS CHRISTOS

EUROMEDICA-KYANOUS STAVROS

Interventional Cardiologist, FSCAI

"Innovations in Interventional Cardiology & Electrophysiology IICE 2013"

14-16 NOVEMBER 2013

ELECTRA PALACE HOTEL, THESSALONIKI

Coronary revascularization should aim at:

1) Relieve symptoms ?

2) Improve outcome ?

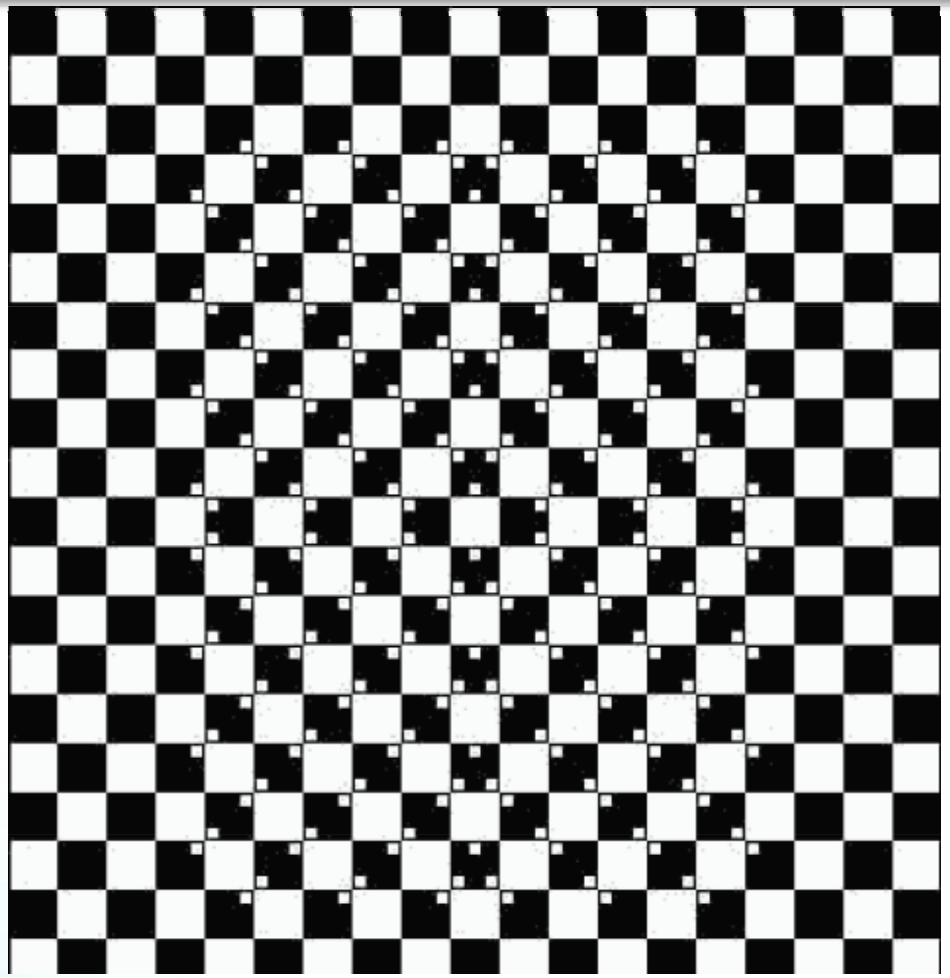
3) Relieve symptoms and improve outcome ?

4) Place a drug eluting stent ?

5) I have no idea

The goal of any treatment is to improve a patient's prognosis and/or symptoms. **Accordingly, any diagnostic tool should help guide decision making in order to achieve optimal treatment for a patient.**

Coronary angiography still plays a pivotal role in invasive imaging of the coronary arteries.

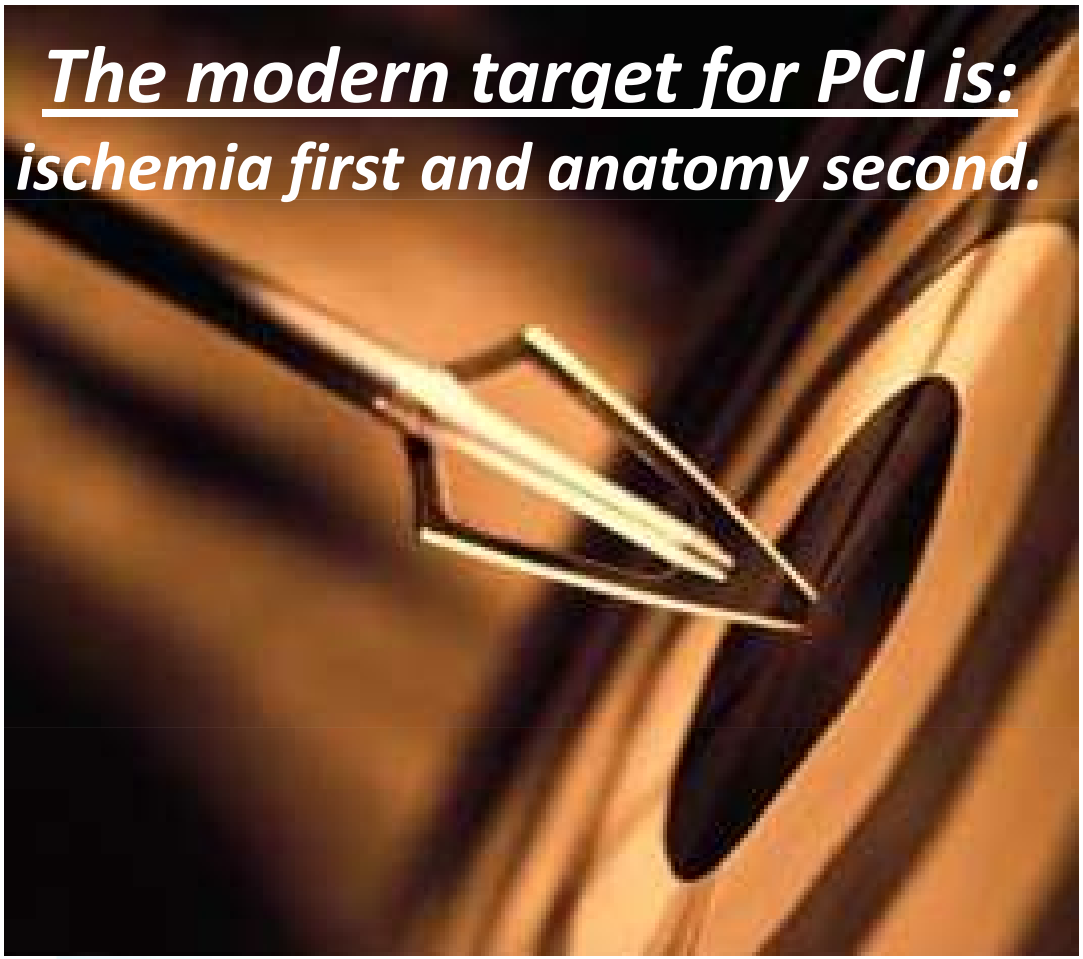


While coronary angiography is widely accepted as the "gold standard" investigation to diagnose coronary artery disease, and has contributed hugely to our understanding of coronary anatomy,

- it is highly subjective and
- does not provide any information about the haemodynamic significance of a stenosis.

ARE THESE HORIZONTAL LINES STRAICHT?

It is important to emphasize that in coronary artery disease, the most important factor related to outcome is the presence and extent of inducible ischemia.

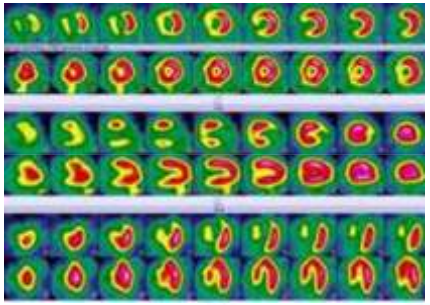


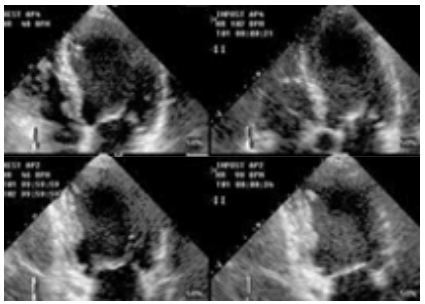
Proof of ischemia, both at a patient level and then at lesion level ,should become a consideration as part of our routine practice.

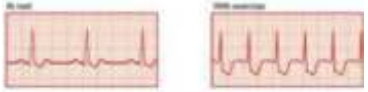
It is of paramount importance to determine whether a stenosis is inducing reversible ischemia—in other words, to assess whether a stenosis is functionally significant

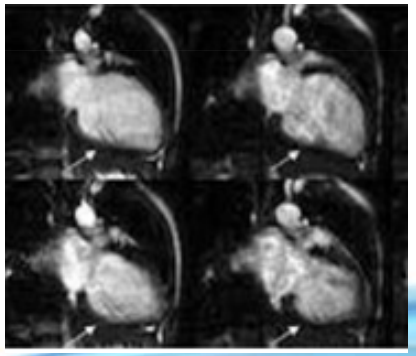
Non invasive functional tests:

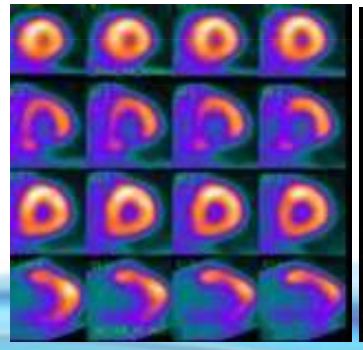
-Exercise elctrocardiogram
-Perfusion scintigraphy
-Stress echocardiography
-Stress MRI
-Positron emission tomography (PET) imaging
-Stress dual-source computed tomography (DSCT)
-Combined/hybrid approaches

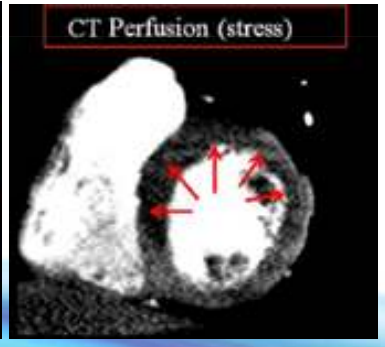




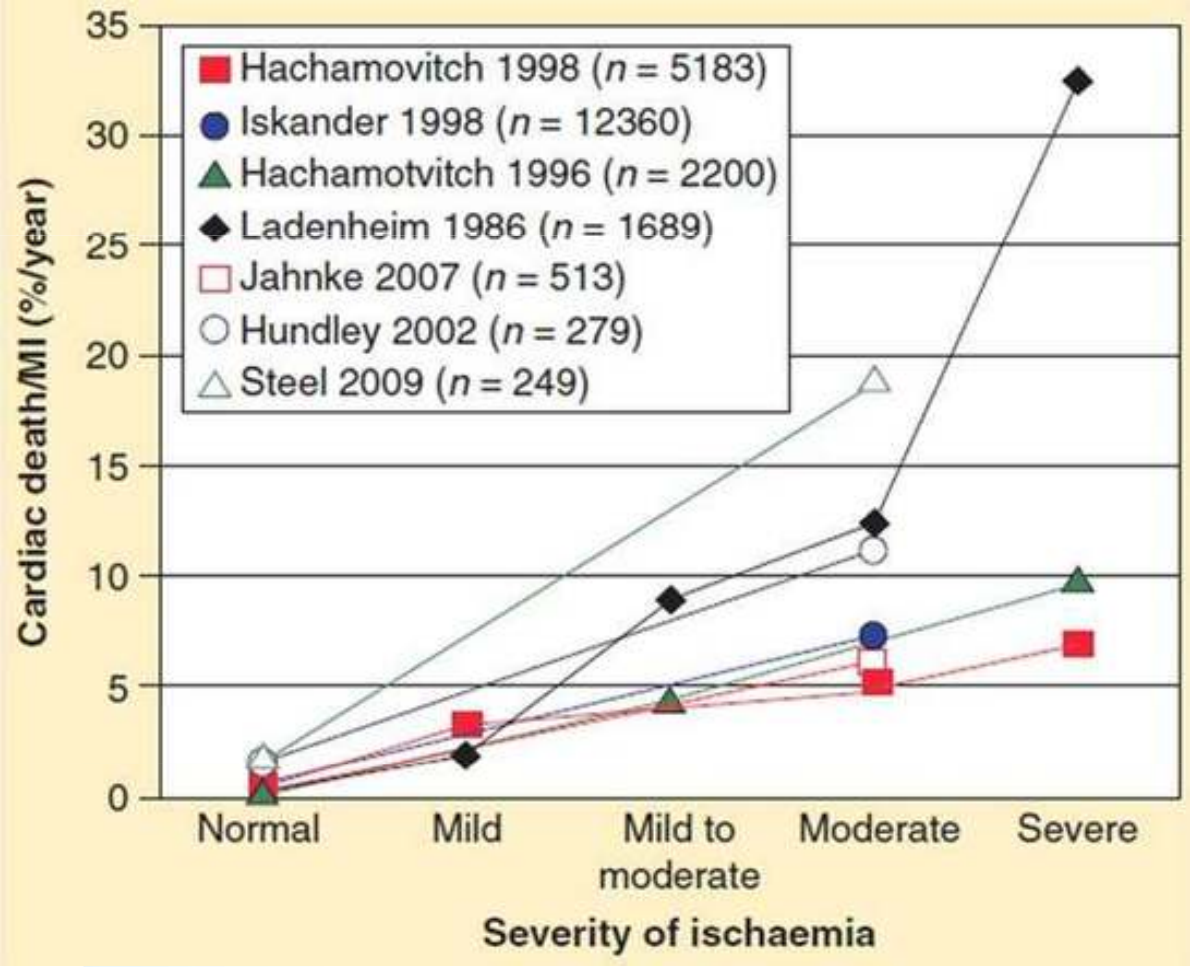








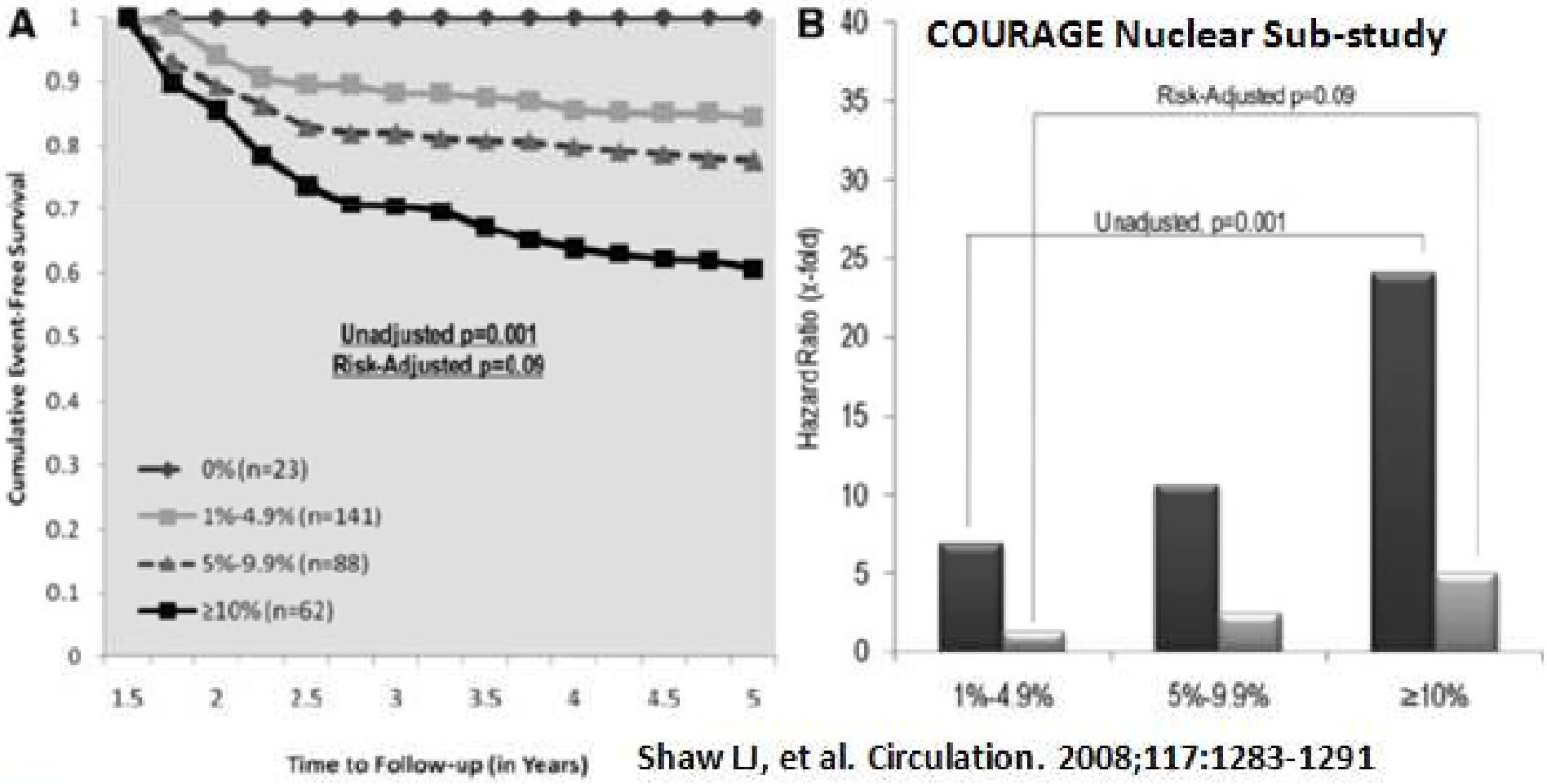
Prediction of cardiac death and nonfatal myocardial infarction (MI) by assessment of ischemia by nuclear imaging/cardiac MRI in seven large studies comprising more than 20,000 patients.



In patients without ischemia, outcome was excellent.

- The corresponding annual event rates were 0.45% per year for nonischemic MPI patients

In Pts with angiographically documented CAD, the risk of events is proportional to the extent of ischemic burden



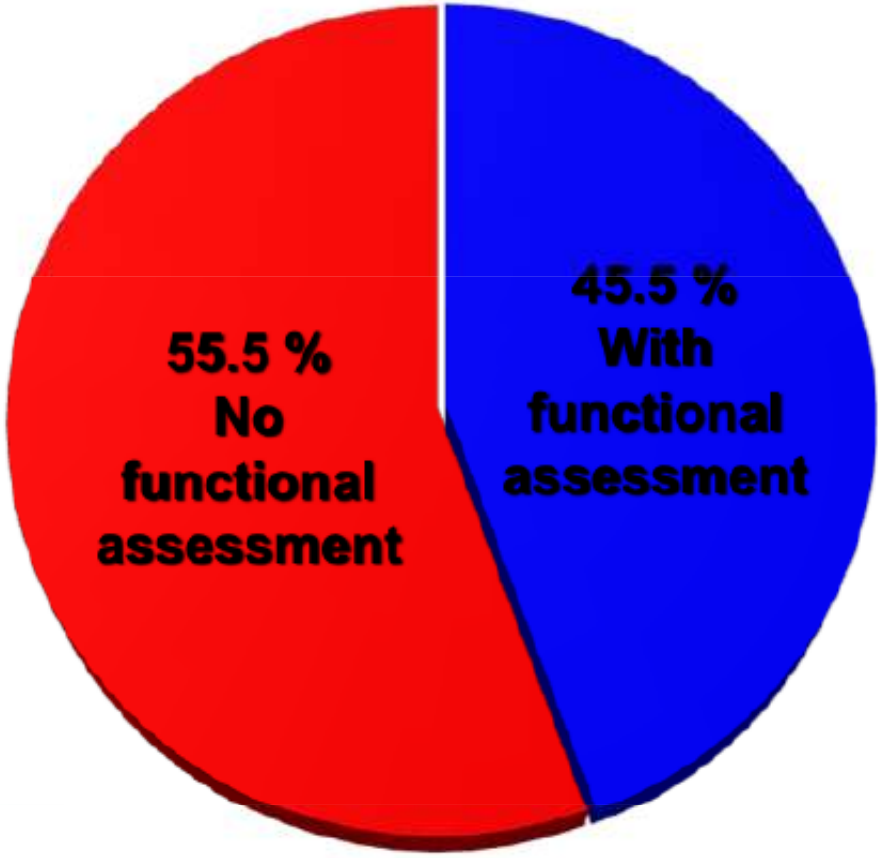
Shaw LJ, et al. Circulation. 2008;117:1283-1291

Concept of fundamental importance

Data suggest that non-ischemic lesions can be managed safely with a non-interventional approach without incurring an increased event rate or mortality, *provided a complete clinical risk assessment has been performed*

Non-Invasive Functional Assessment Before PCI Underutilized

23,887 Medicare Pts Referred for Elective PCI in 2004



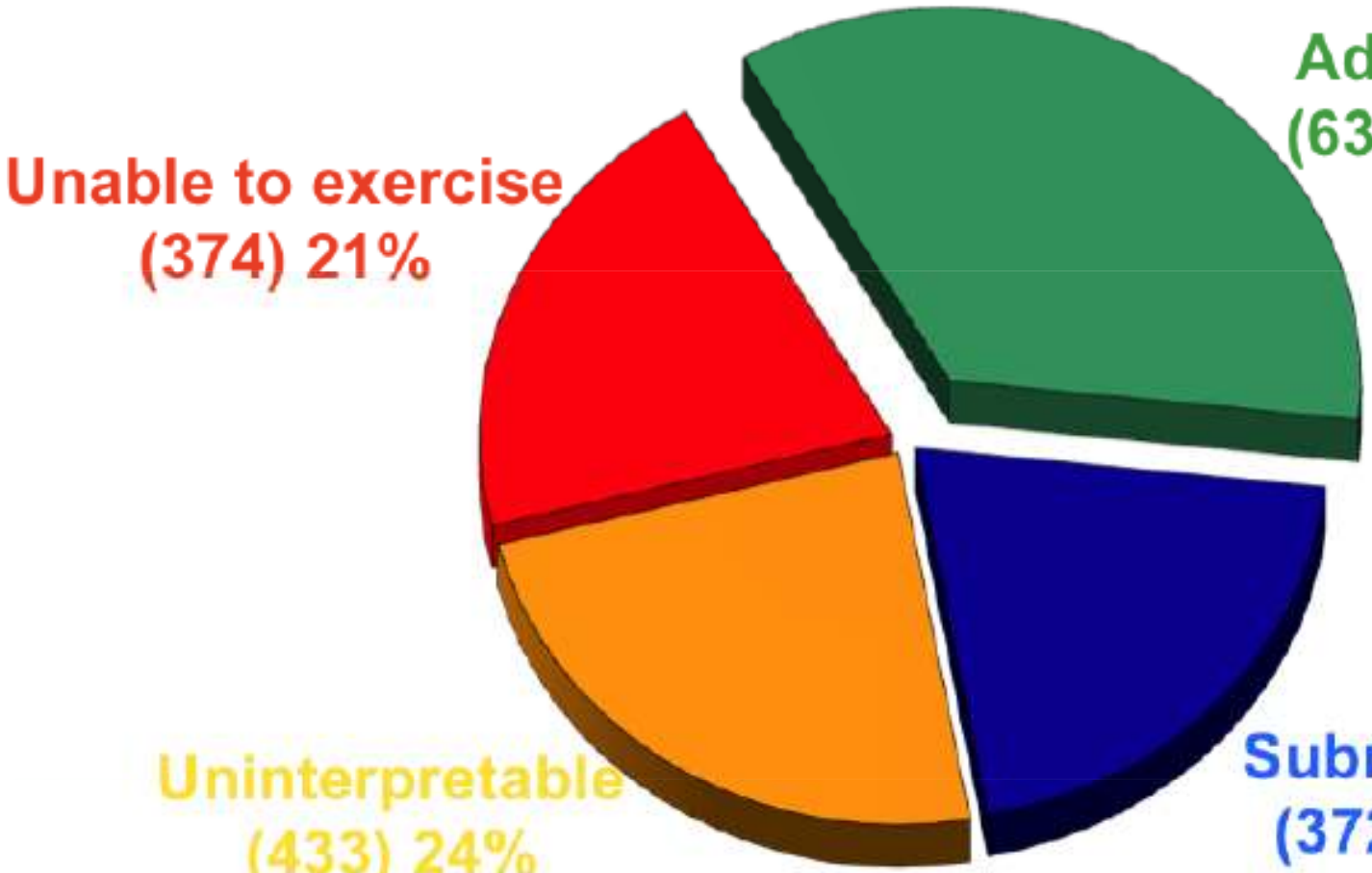
Lower overall rates of prior stress testing in:

- older patients
- patients with angina
- prior CAD,
- prior cardiac catheterization
- COPD (BPCO)
- Congestive heart failure

Lin GA, et al. JAMA 2008;300:1765-1773

The vast majority of patients with suspected coronary artery disease *never undergo any form of non-invasive test* before having a coronary angiogram.

Proportion of Adequate Stress Tests



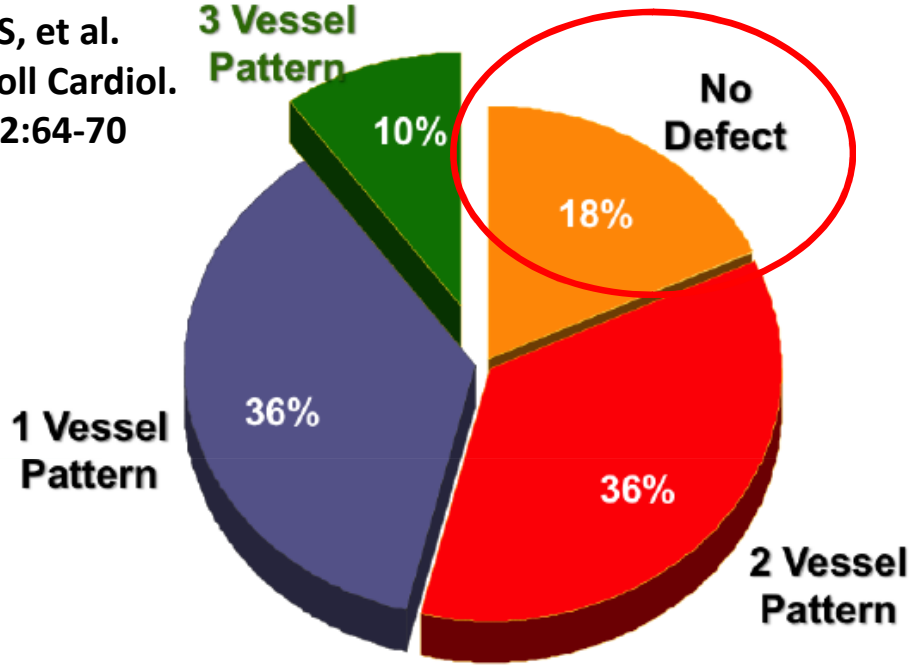
Marwick et al.
Circulation 1994

Inaccuracy of Perfusion SPECT imaging in MVD

Technetium-99m sestamibi singlephoton emission computed tomography, and other classic noninvasive tests often indicate ischemia in patients with multivessel disease ***but fail to distinguish the specific ischemic territories and responsible stenoses.***

143 Severe 3-vessel disease patients and Tc-SPECT

Lima RS, et al.
J Am Coll Cardiol.
2003;42:64-70

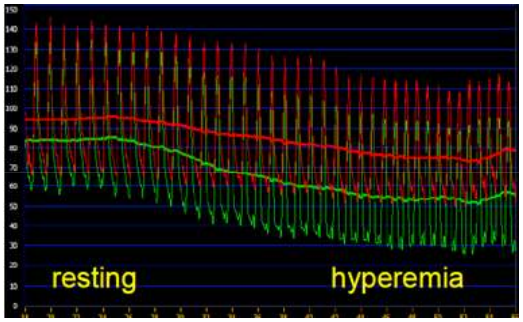


In addition, findings on technetium-99m sestamibi single-photon emission computed tomography **may even be normal in multivessel disease** because of balanced ischemia.

The time has come to move from coronary angiography to physiological assessment of coronary lesions ?

An ideal parameter should account for the interaction between

- ***epicardial stenosis severity,***
- **extent of the perfusion territory,**
- **myocardial blood flow including collaterals**
- **microvascular function**



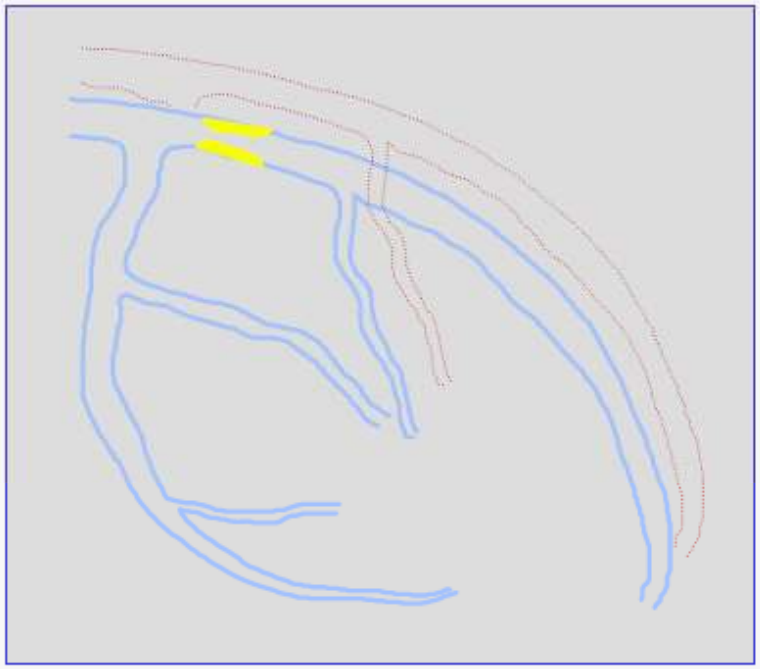
Physiologic evaluation

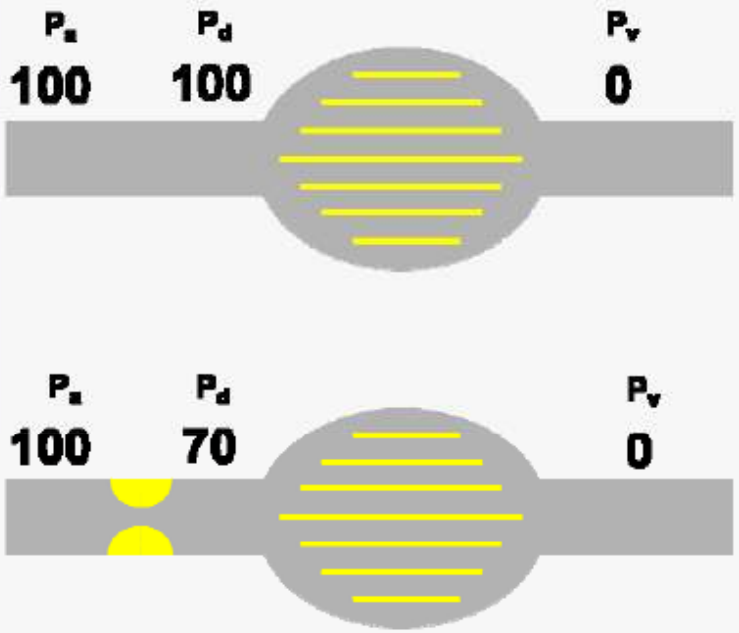
Fractional Flow Reserve- FFR

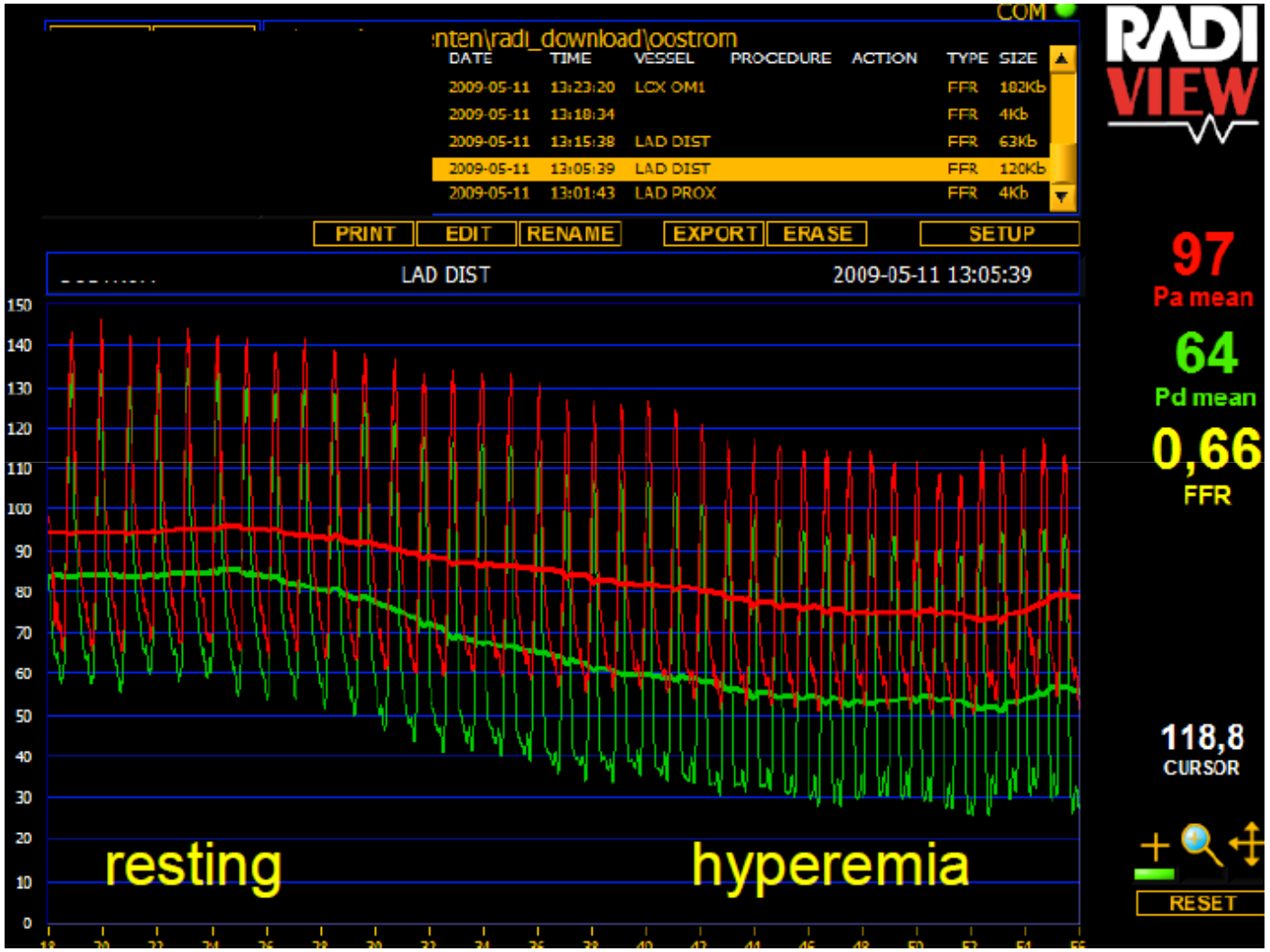
Fractional flow reserve is calculated as the ratio of distal coronary pressure to aortic pressure measured during maximal hyperaemia.

Fractional Flow Reserve (FFR)

$$FFR = \frac{\text{Maximum flow in presence of stenosis}}{\text{Normal maximum flow}} = \frac{Q^{S}_{max}}{Q^{N}_{max}} = \frac{(Pd-Pv)/R}{(Pa-Pv)/R} = \frac{P_d}{P_a}$$



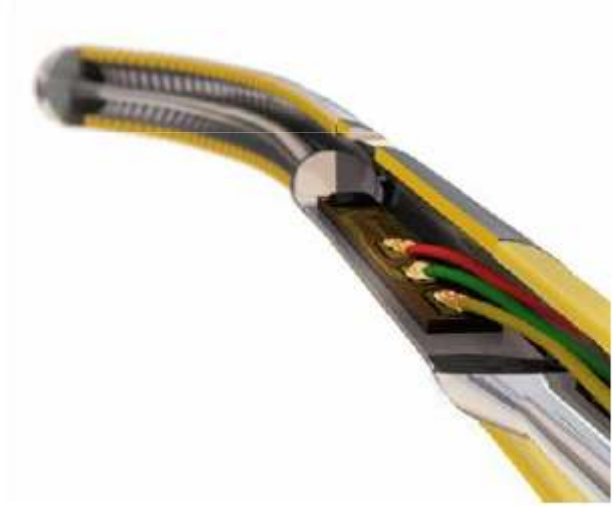




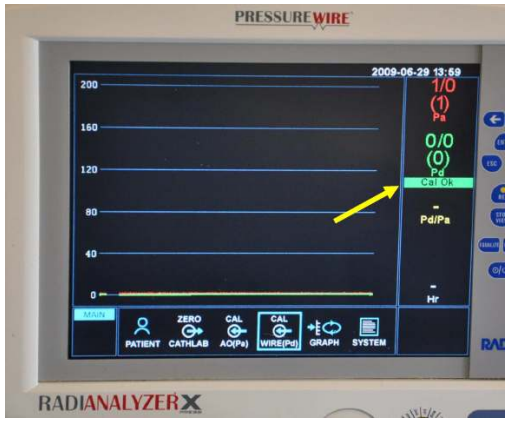
FFR of 0.66 means that the maximum blood flow (and oxygen supply) to the myocardial distribution of the respective artery **only reaches 66% of what it would be if that artery were completely normal.**

- Pressure Wire®

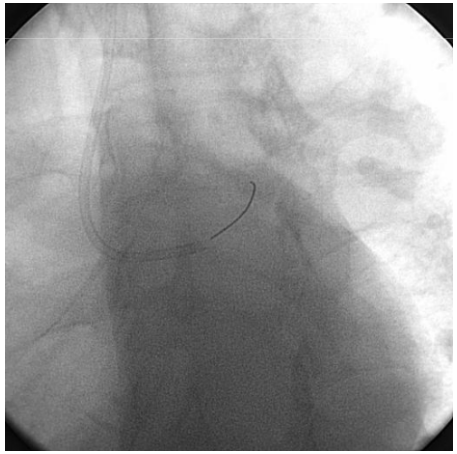
The distal pressure in the coronary artery is measured by a tiny sensor located 3 cm from the tip of an 0.014" guidewire, called PressureWire®.

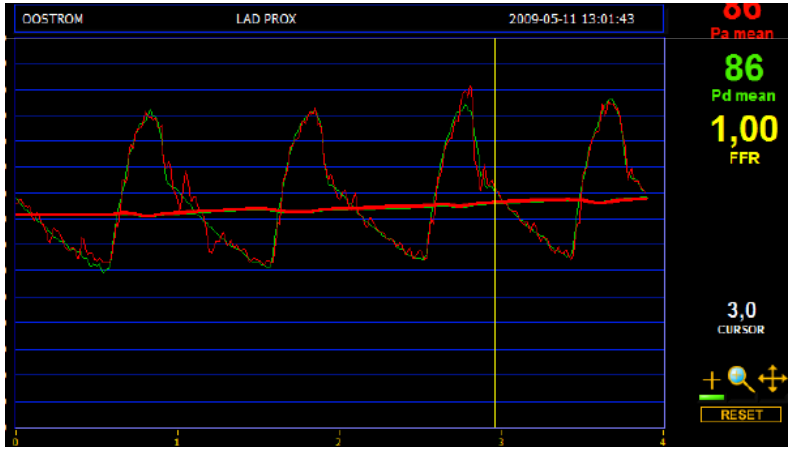


Step 1: Pressure wire and analyzer setting



Step 2: Pa/Pd pressure equalization





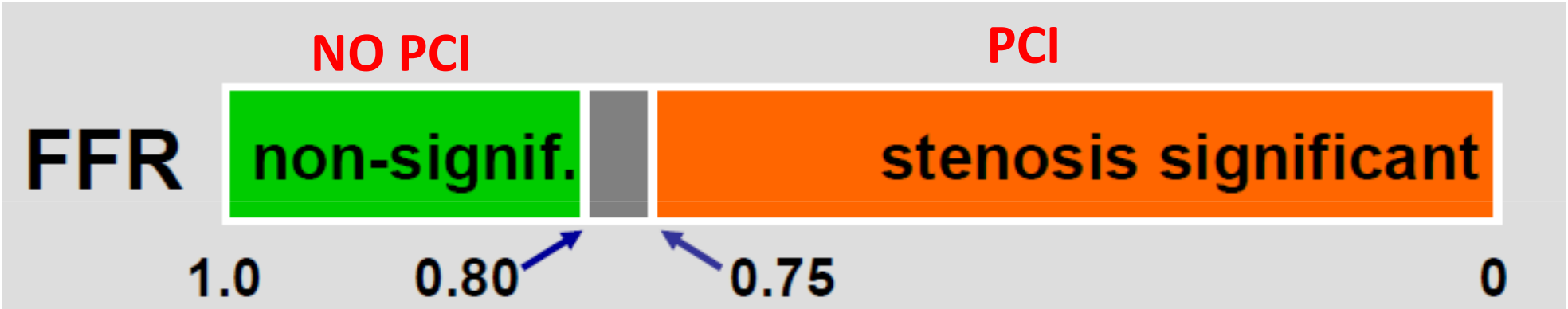
Step3: Wiring, check baseline pressure gradient and induce hyperemia

Features of FFR

- Differently from most physiologic indices, the normal value of the FFR is 1.0 for every patient ,every coronary artery and every segment.
- Not influenced by systemic haemodynamics.(HR, BP, contractility).
- Extremely reproducible, low intra-operator variability, easy to measure (success rate 99 %)
- Independent of gender, and other factors such as hypertension and diabetes.
- *Specifically related to epicardial* lesions, independent of micro-circulation.
- Takes into account the contribution of collaterals.
- High spatial resolution (pull-back).

FFR: ischaemic threshold

A cut-off value reflecting the presence or absence of ischaemiahas been prospectively defined and compared with the "gold standard" non-invasive tests for ischaemia



FFR < 0.75 → always ischaemia (specificity 100 %)

FFR > 0.80 → ischaemia very unlikely (sensitivity 90 %)

De BruyneB et al. *Circulation* ***1995;92:39–46.*** PijlsNH et al. *N EnglJ Med* ***1996;334:1703–08***

• FFR<0.75 excellent diagnostic performance to identify lesions related to reversible myocardial ischemia with an overall predicitive accuracy of 93%

FFR «grey zone»: 0.76-0.79

- In most of cases in which the FFR value falls in the "grey zone", functional non-invasive tests are abnormal, and they become normal after revascularization (*).

- Is recommended to take into account the 0.80 value for the main vessels, whose revascularization has a pronostic value, and to consider the 0.75 value (more restrictive) for the secondary vessels, whose revascularization has a benefit only with respect to symptoms. (**).

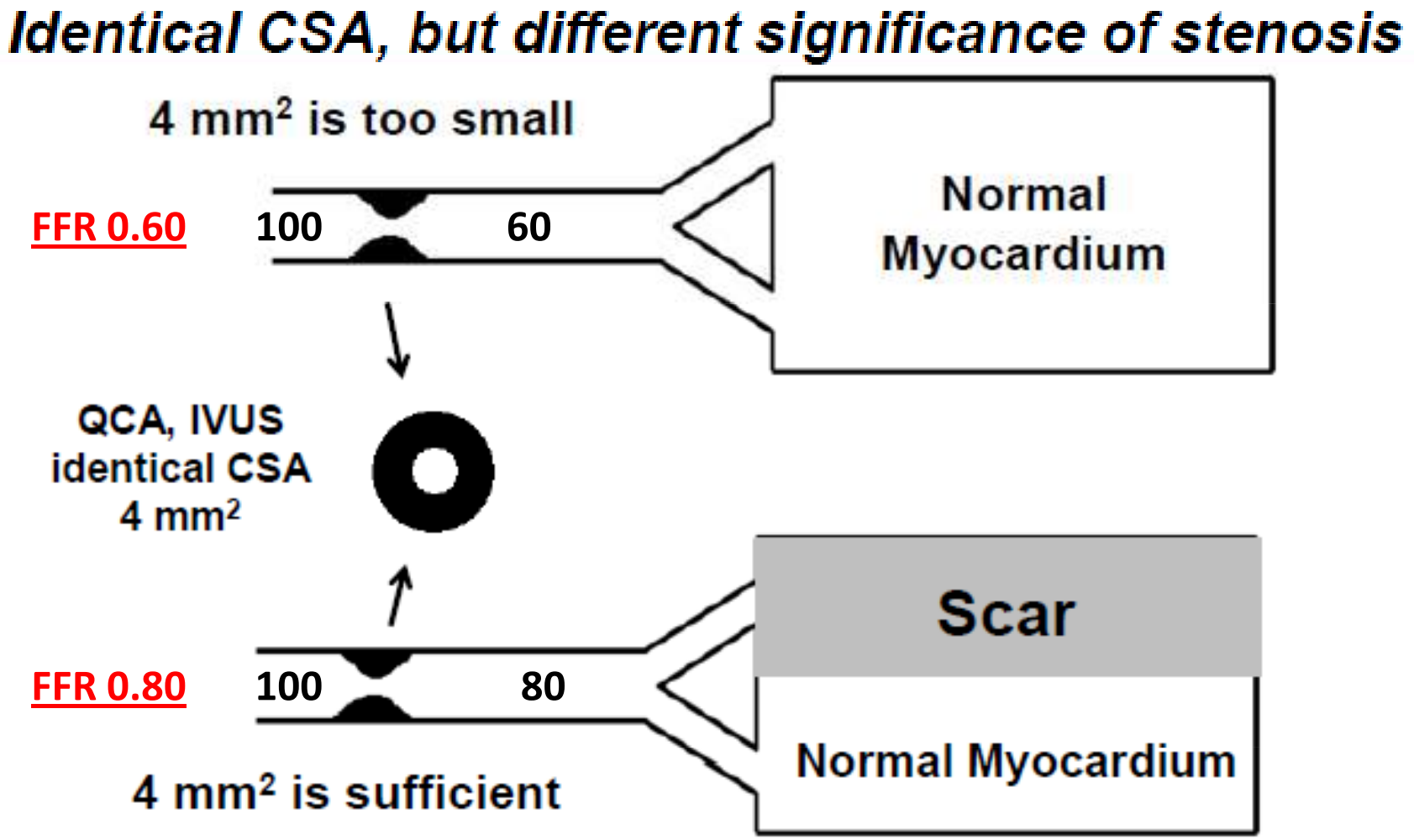
DECISION MAKING MAY BE SUPPORTED BY PATIENT SPECIFIC CLINICAL ASSESMENT

- If single vessel disease, no or atypical complaints, no evidence of ischemia: NO REVASCULARIZATION

- If more extensive disease, typical complaints, positive non-invasive test or diabetes: REVASCULARIZATION

*De BruyneB, PijlsNH, et al. *Circulation 2001;104:157–62.* **DeBruyneB,Sarma.J. *Heart2008;94:949 –59.*

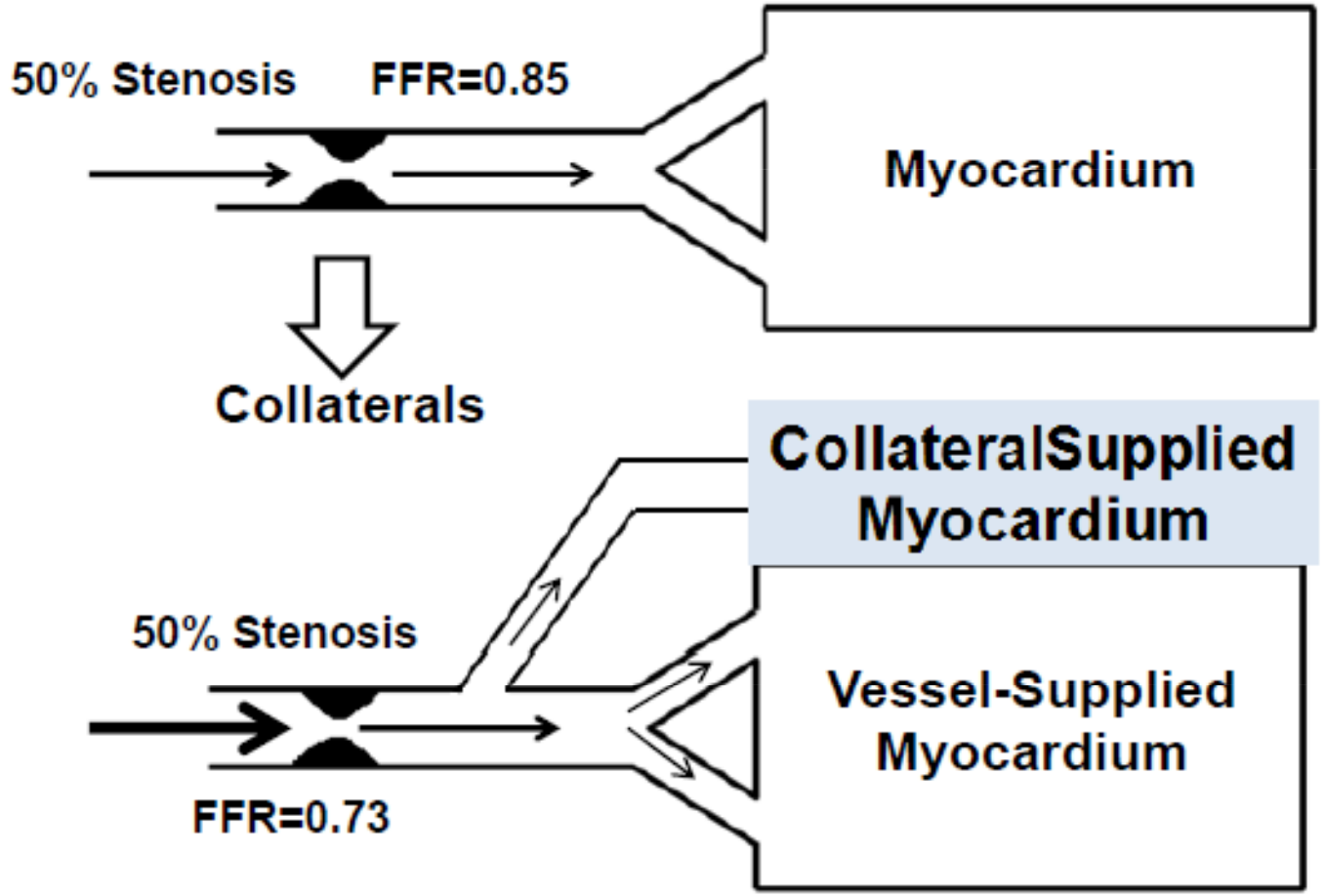
FFR is determined by the size of myocardial mass



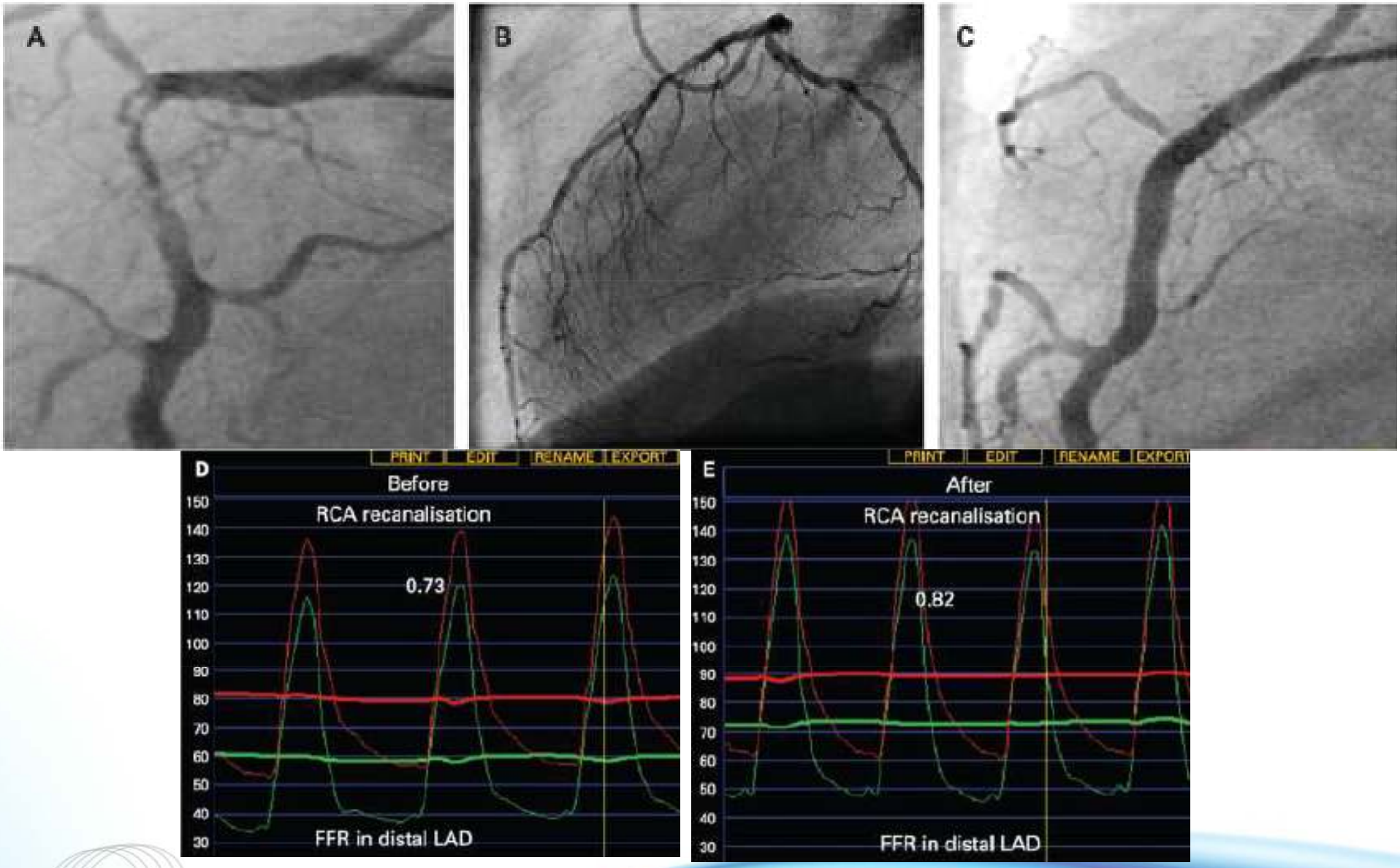
FFR normalizes for the perfusion area: Anatomic severity remains unchanged but physiologic severity has decreased

FFR is determined by the size of myocardial mass

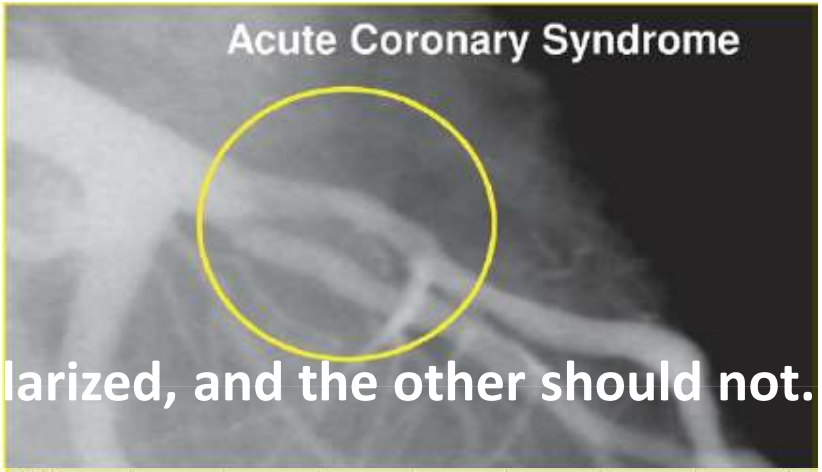
A angiographically not significant stenosis can be significant in FFR measurement because of the total mass of myocardium supplied



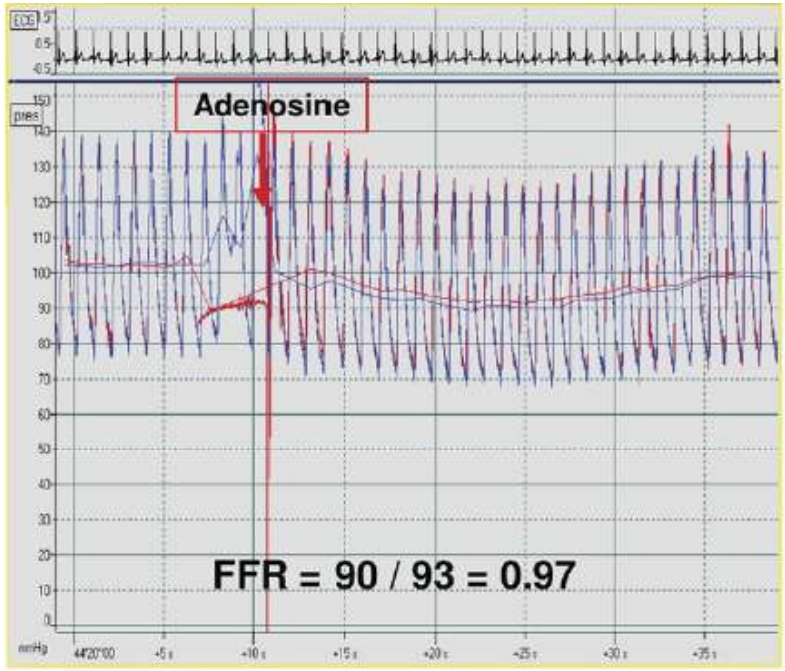
FFR with collateral contribution

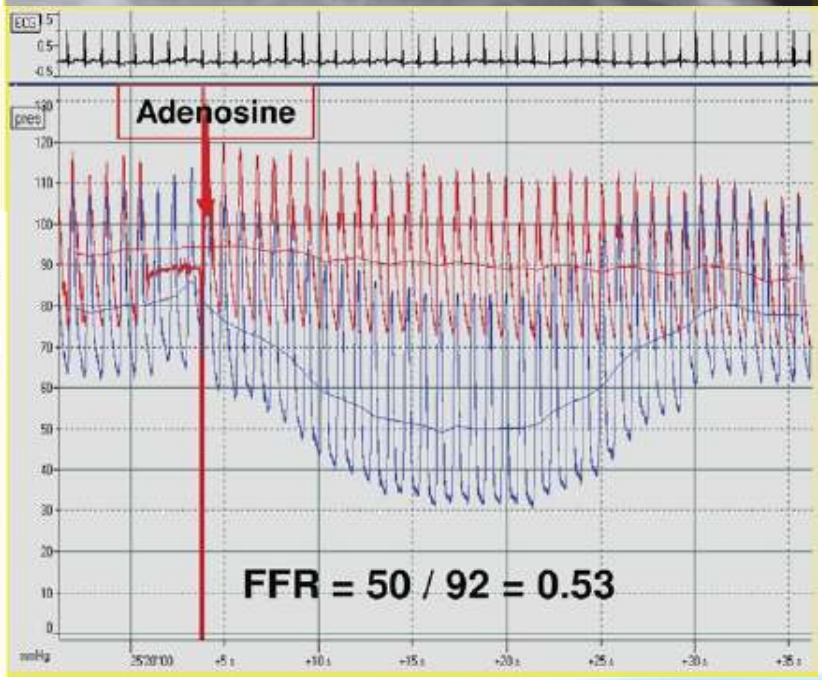


VISUAL-FUNCTIONAL MISMATCH



One of them should be revascularized, and the other should not.





2 angiographically similar stenoses may have a completely different hemodynamic severity.

FFR is determined by many lesion specific local factors at maximal hyperemia

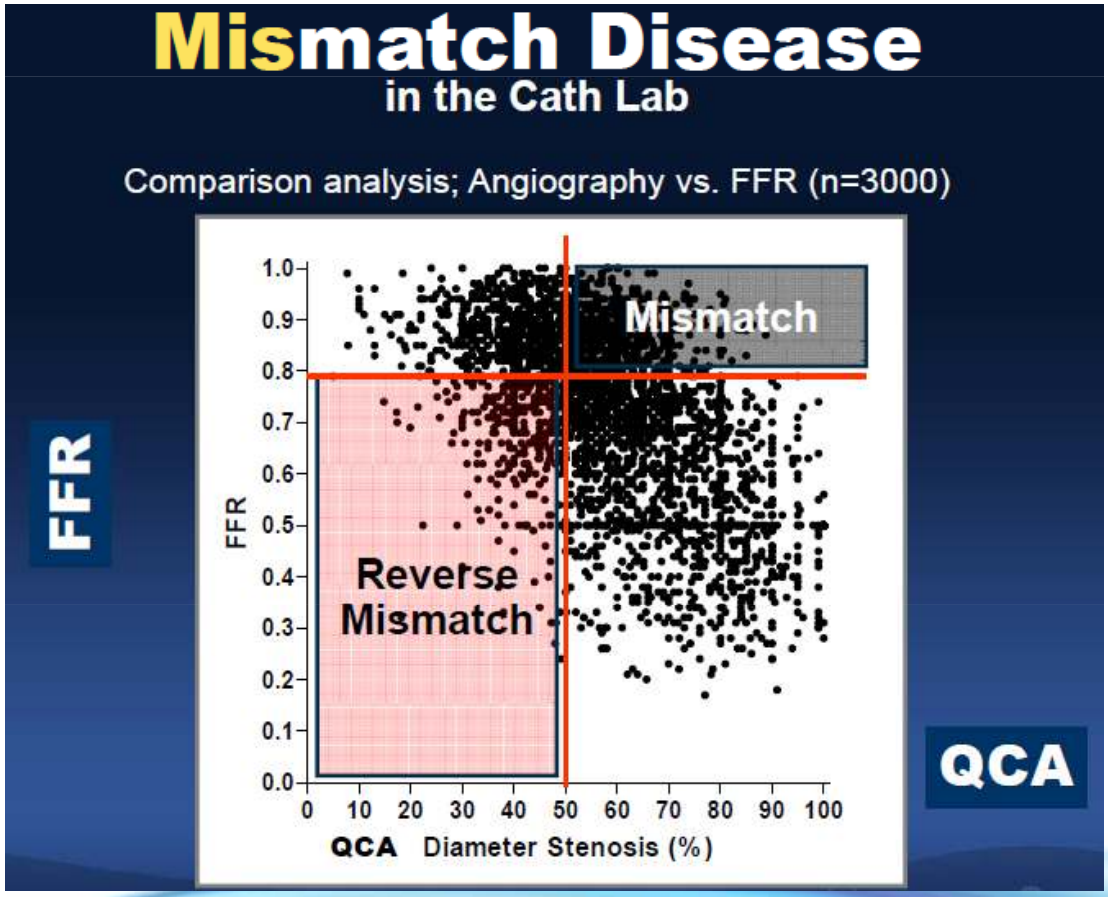
Lesion severity determined by coronary angiography has not been well-correlated with the physiologic significance of the stenosis. However, the reasons why mismatches between the two, are still poorly understood.

Mismatch

Significant Stenosis (>50%) with Negative FFR

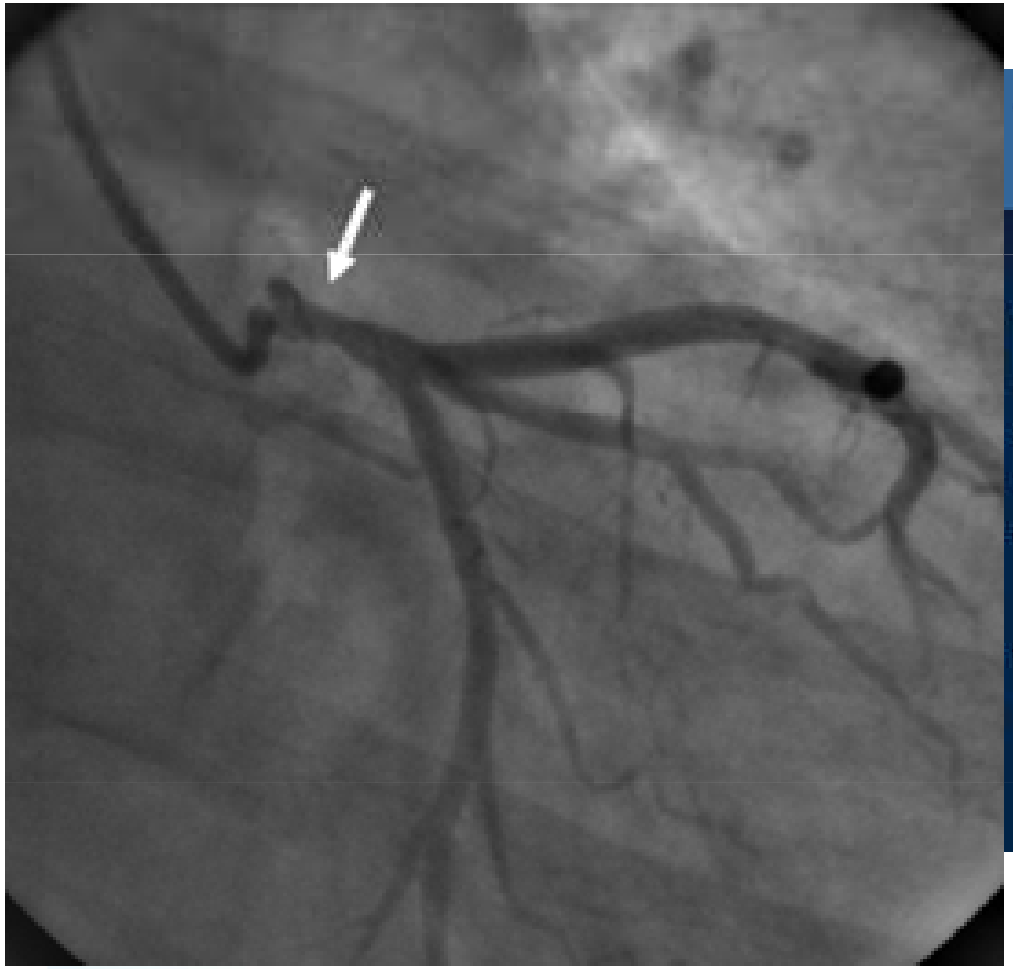
Reverse Mismatch

Insignificant Stenosis (<50%) with Positive FFR



Visual - Functional Mismatch

Reverse Mismatch



Visual Estimation : 30%

FFR : 0.70

IVUS MLA: 4.5 mm2

Treadmill test: + stage 2

Thallium spect : + large LAD

FFR is influenced by Many Lesion Specific Factors

The same degree of stenosis can make a different FFR value according to the different lesion morphologic factors.

- Degree of diameter stenosis
- Reference vessel diameter (myocardium)
- Lesion morphology
- Eccentricity
- Lesion length
- Plaque burden, Plaque rupture
- Surface roughness (thrombus)
- Viscous friction, flow separation, turbulence, and eddies

FFR, a very sensitive index integrating various local factors, is more reliable than angiographically determined stenosis severity.

FFR : Applications

- ✓Intermediate Stenoses
- ✓Multivessel disease
- ✓Left main
- ✓Ostial lesions
- ✓Bifurcations (before and after PCI of the «mother» vessel)
- ✓Multiple stenoses, diffuse disease
- ✓PCI results
- ✓ACS

FFR IN INTERMEDIATE LESIONS

One of the standard indications for FFR is the precise assessment of the functional consequences of a given coronary stenosis with unclear hemodynamic significance

ACCF/AHA/SCAI Guidelines for PCI (2011)

5.4.1. FFR: Recommendation

Class IIa

1. FFR is reasonable to assess angiographic intermediate coronary lesions (50% to 70% diameter stenosis) and can be useful for guiding revascularization decisions in patients with SIHD.[12,97,484–486] *(Level of Evidence: A)*

CLASS IIa
Benefit >> Risk
Additional studies with focused objectives needed
IT IS REASONABLE to perform procedure/administer treatment

LEVEL A
Multiple populations evaluated*
Data derived from multiple randomized clinical trials or meta-analyses

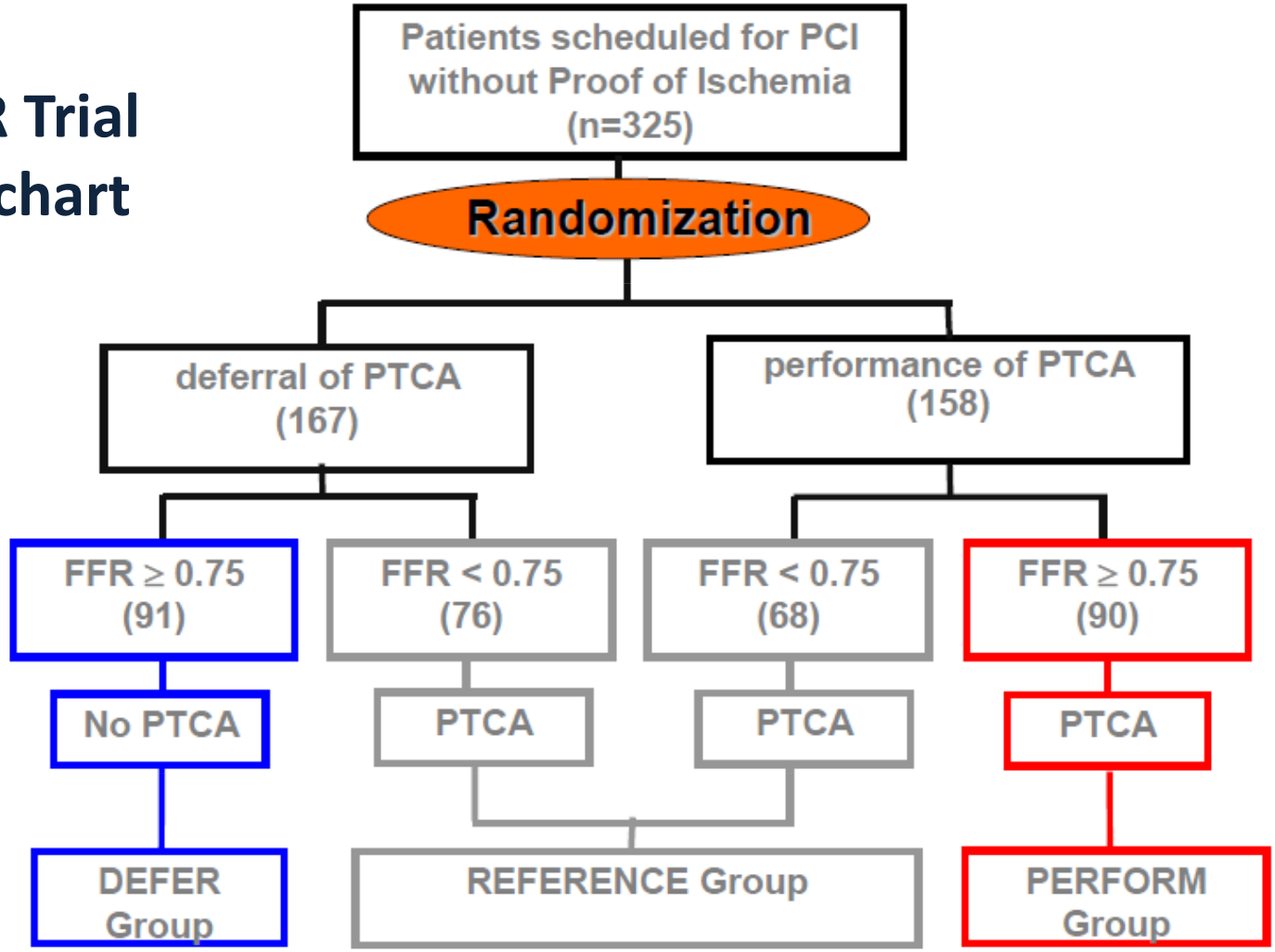
Circulation. ***2011***;*124:e574-e651*

✓**Intermediate lesions (40-70%) are the most common in patients with CAD (47% in FAME) and with great variability in interpretation**

✓Furthermore, results of different noninvasive tests are often contradictory, which renders appropriate clinical decision making difficult.

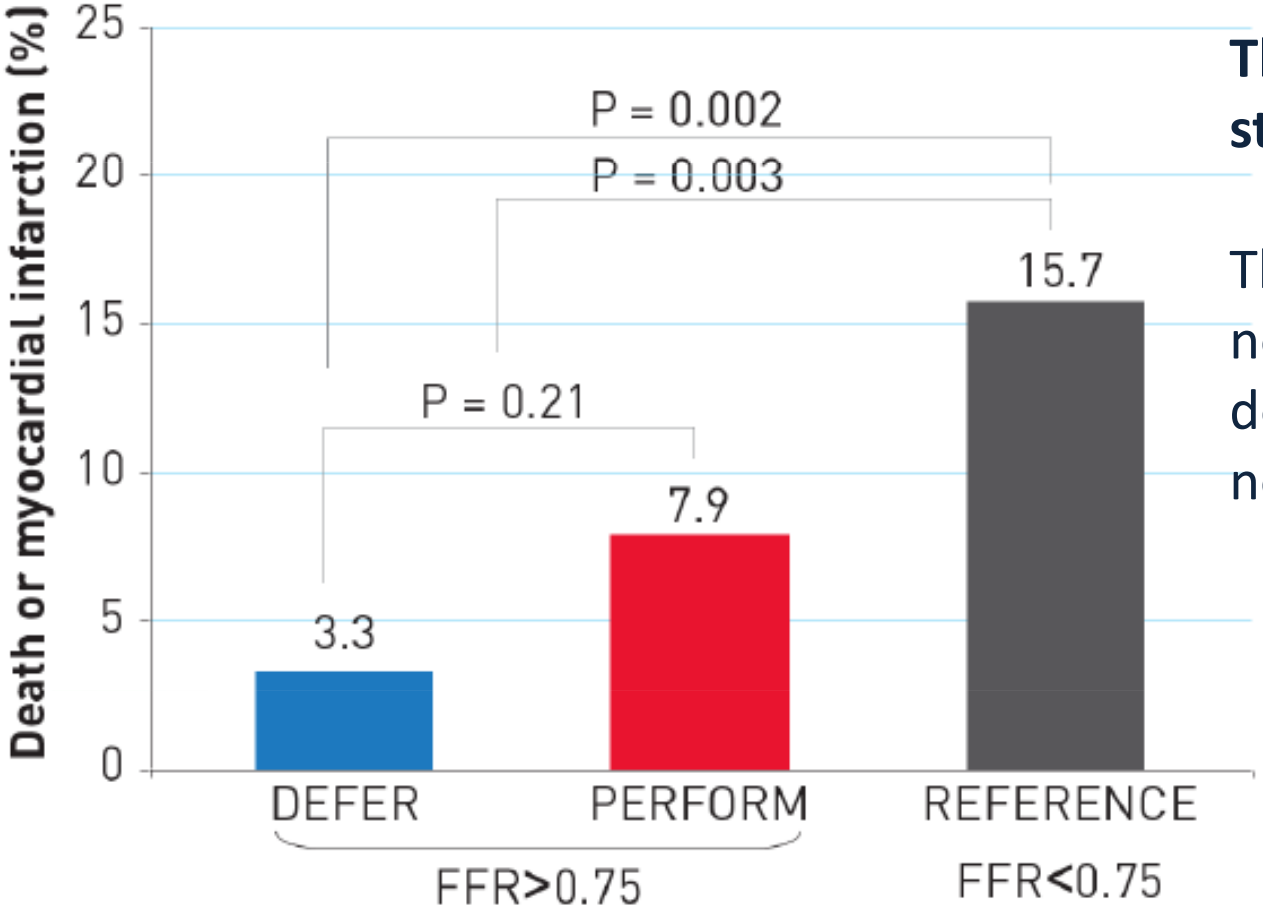
Safety of Deferring PCI Based on FFR

DEFER Trial
Flow chart



Safety of Deferring PCI Based on FFR

DEFER Trial: 5-Year Follow-up



The prognosis of "non-ischaemic" stenosis (FFR > 0.75) is excellent

The risk that a hemodynamically nonsignificant stenosis will cause death or AMI is<1% per year and is not decreased by stenting.

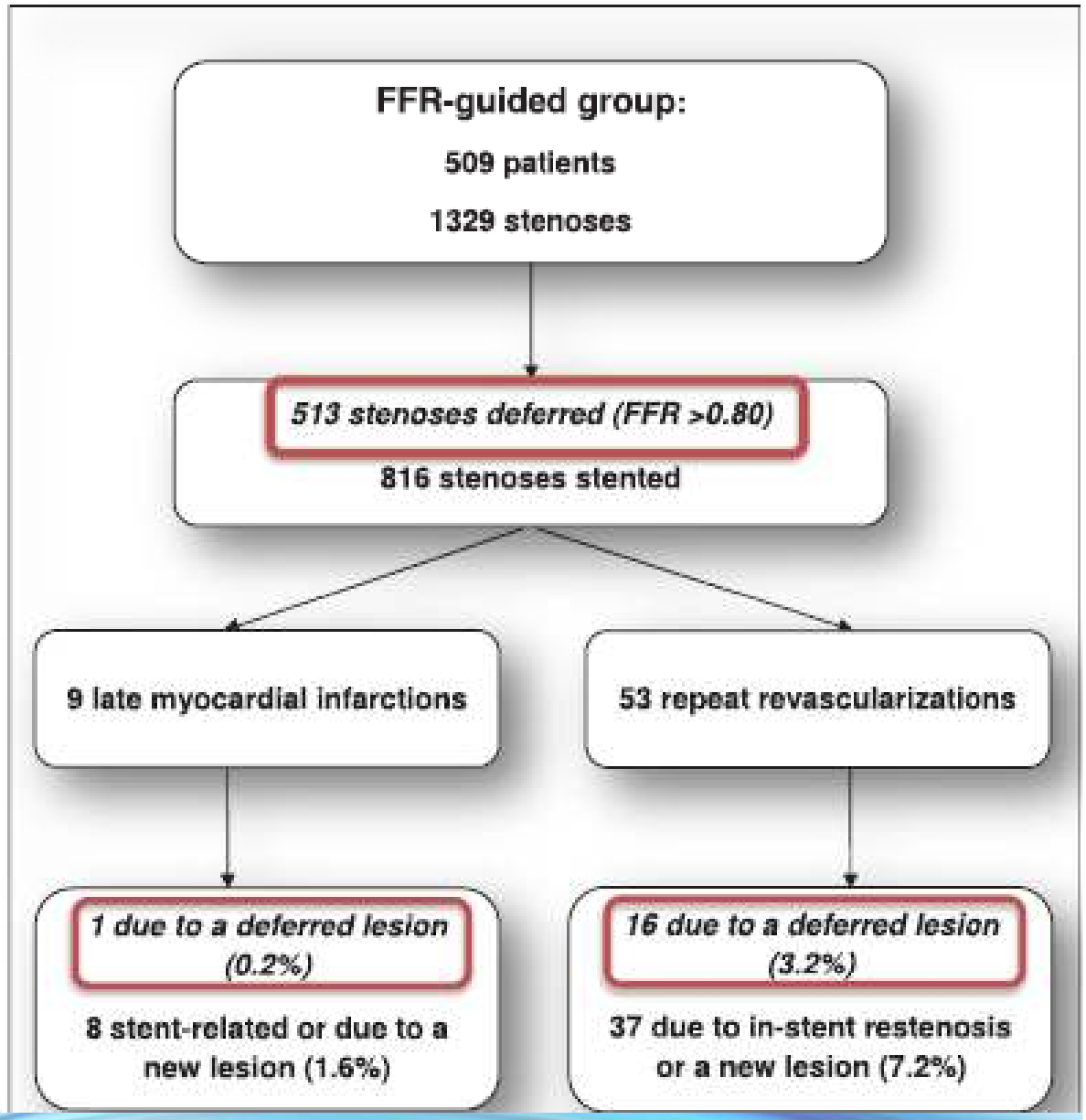
Pijls, et al. J Am Coll Cardiol 2007;49:2105-11

Safety of Deferring PCI Based on FFR

FAME Trial: 2-Year Outcome of Deferred Lesions

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

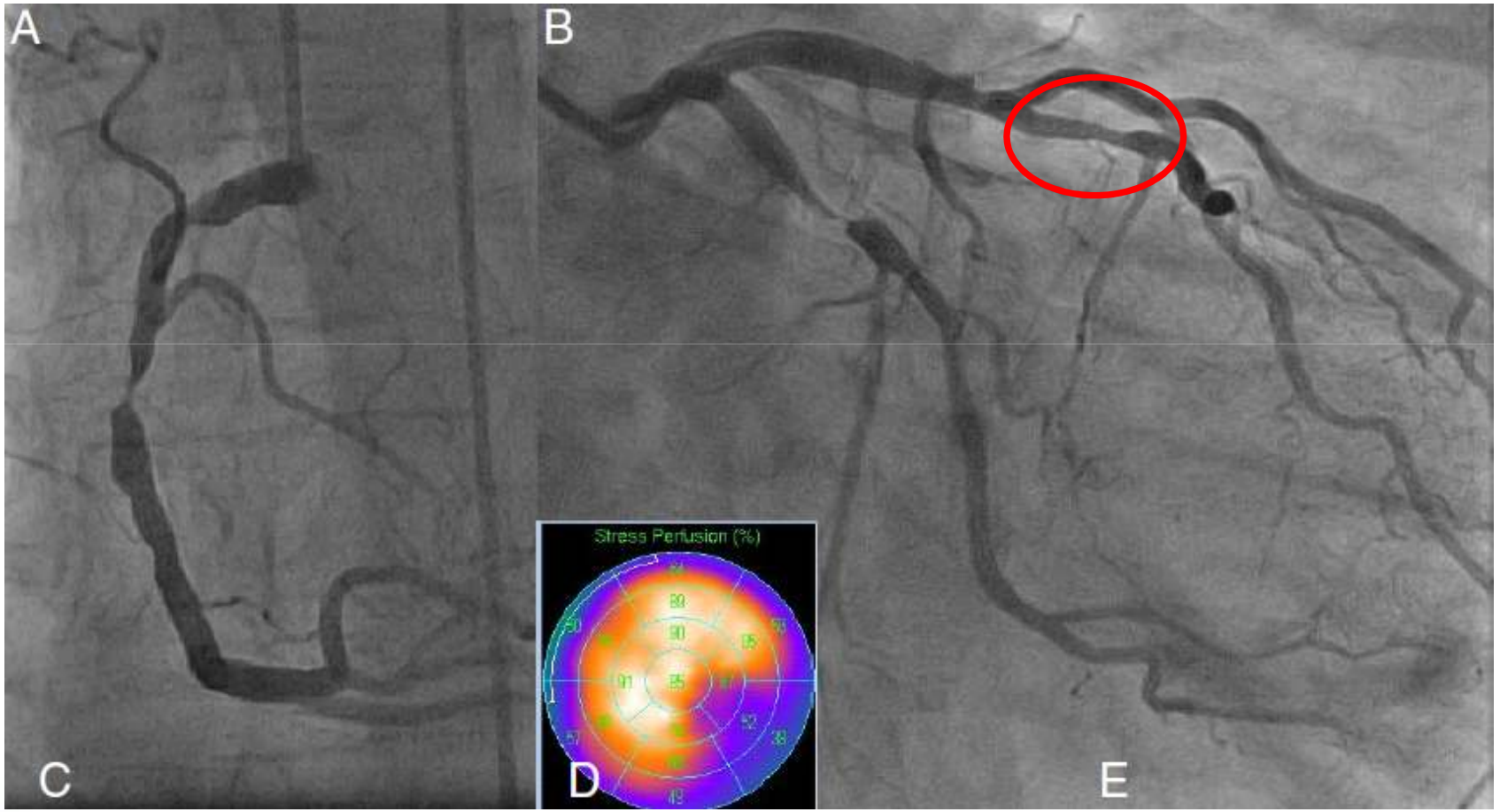
Fearon W. TCT 2011



Safety of Deferring PCI Based on FFR

These results strongly support the use of FFR measurements *as a guide for decision making about the need for revascularization in intermediate lesions*.

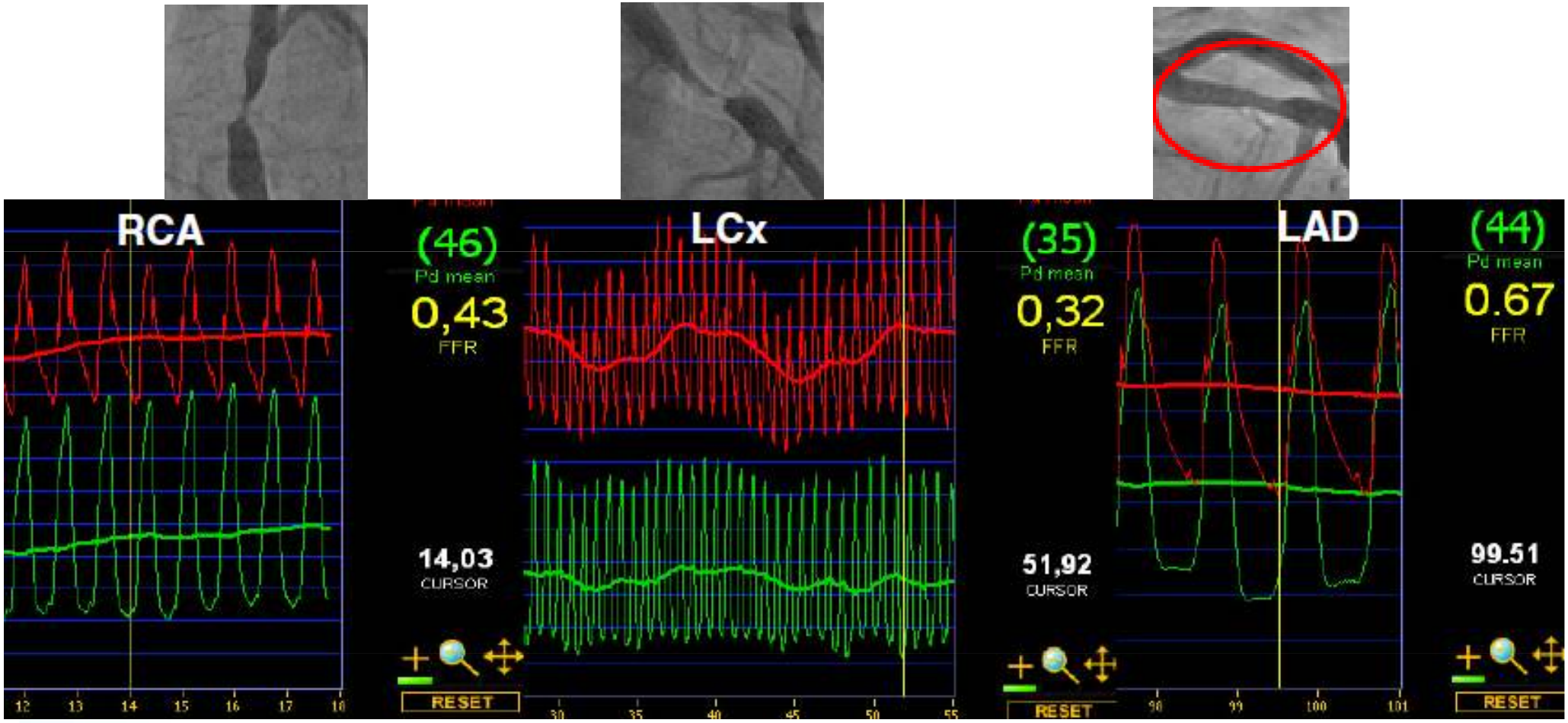
A 69-Year-Old Man With Severe Angina



This mid LAD stenosis, was considered non-significant on the angiogram

- **Myocardial perfusion imaging showed a reversible defect in the inferolateral segments**

However, the mid left descending artery (LAD) stenosis, considered non-significant on the angiogram, *appears to be hemodynamically significant.*



By nuclear scintigraphy, the significant defect in the anterior wall is masked by the more severe defects in the other areas.

FFR & multivessel disease

✓**Patients with "multi-vessel disease" actually represent a very heterogeneous population .**

- All the *angiographically multi-vessel diseases are not functionally equivalent.*

✓**What we should treat is ischaemia, not lesions.**

- **In patients with multi-vessel disease, determining which lesion(s) warrant stenting and which do not can be difficult if one chooses to use non-invasive imaging modalities.**

- **Systematically measuring FFR can maximize the benefit of PCI by accurately discriminating those lesions for which revascularisation will provide the most benefit from those for which PCI may only increase the risk.**

Fractional Flow Reserve

versus

Angiography for

Multivessel

Evaluation

Angio-guided group:

"anatomical complete revascularization"

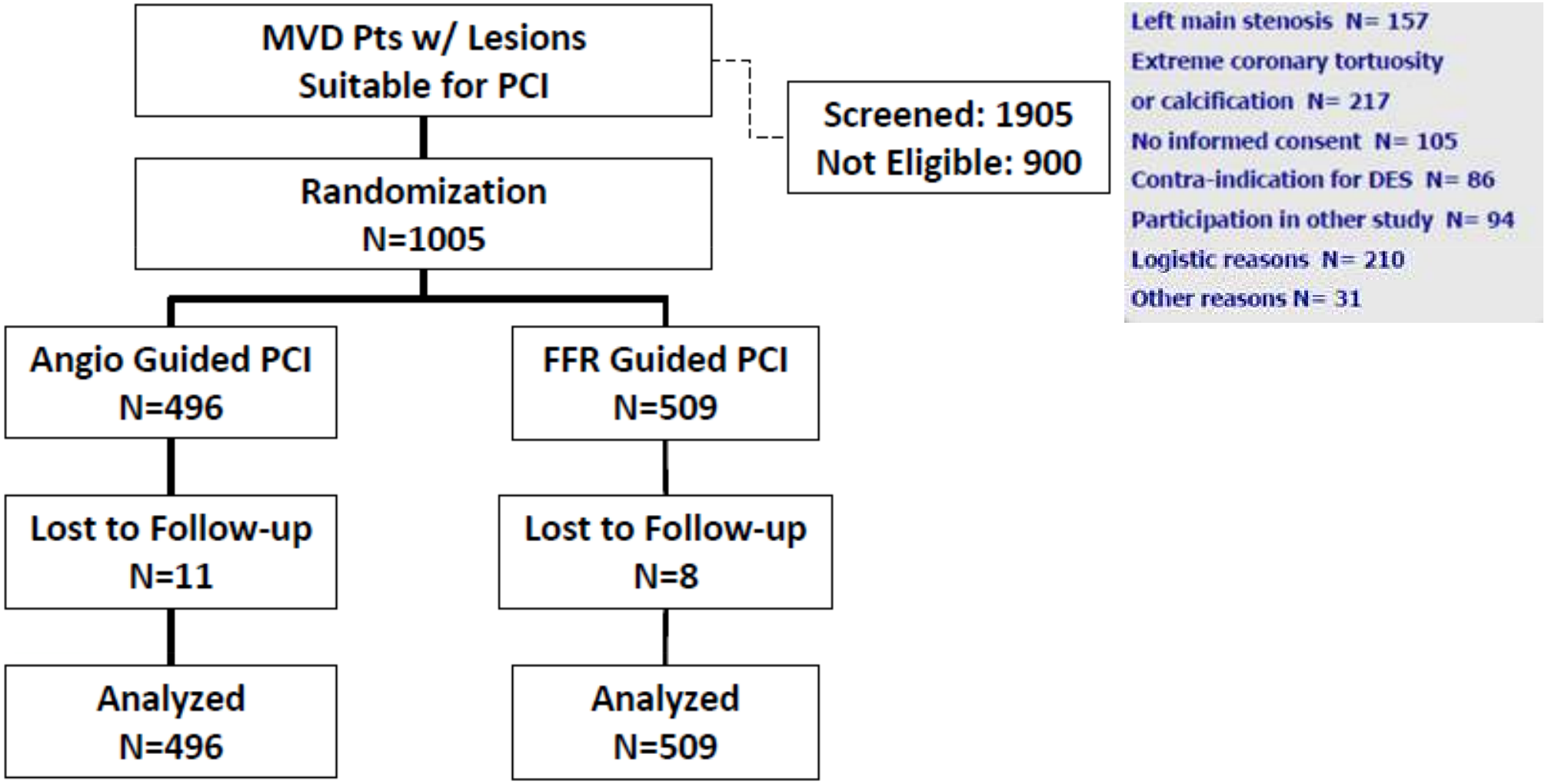
Stenting all lesions >50% on the angiogram

FFR-guided group:

"functionally complete revascularization"

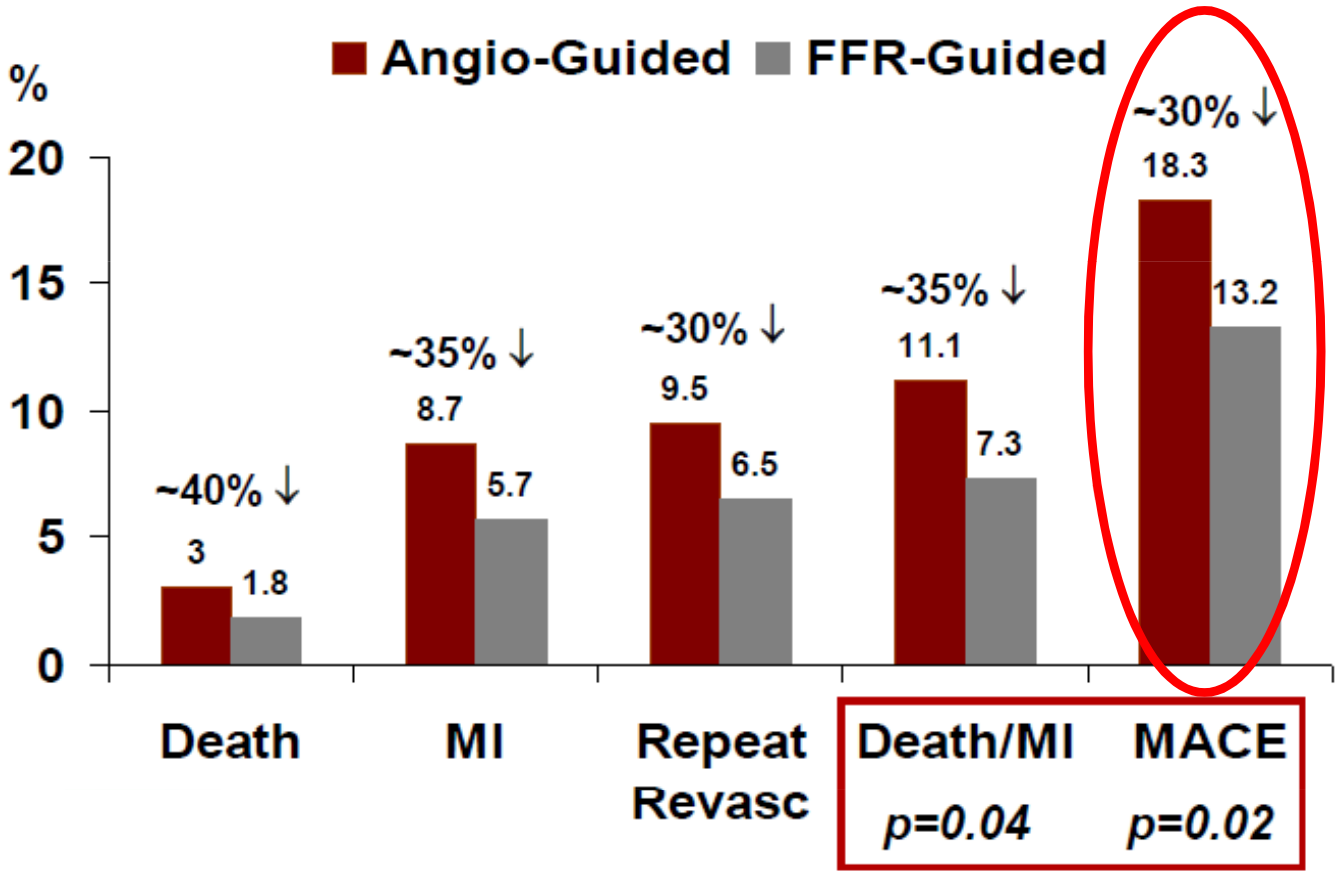
Stenting isschemic lesions only (FFR<0.80)

FAME Trial: Study Flowchart



Tonino PA, et al. NEJM 2009;360:213–24

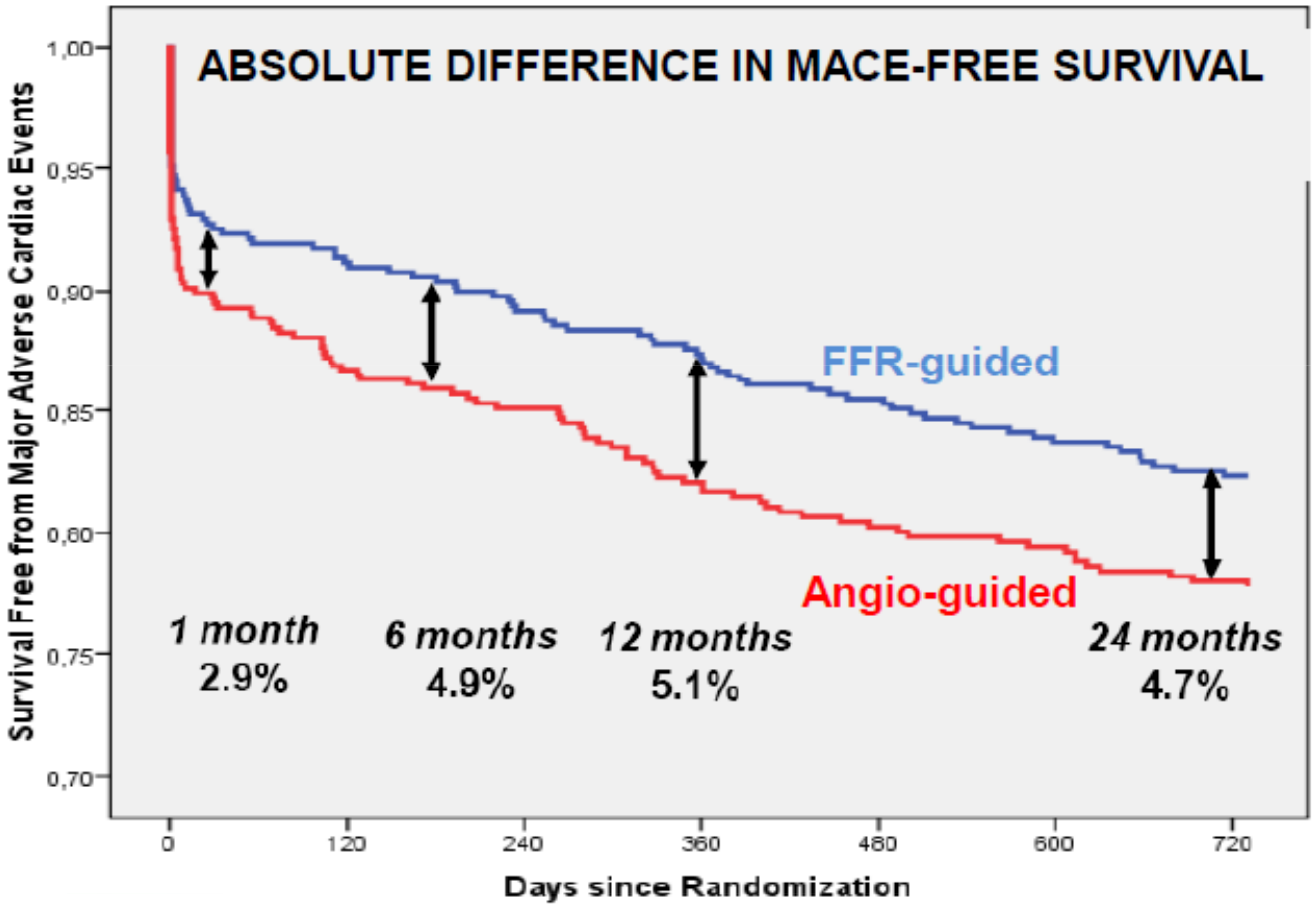
FAME Trial: One Year Outcomes



It was demonstrated that all types of adverse events **were decreased by 30%** in the first year after PCI in multivessel disease

Tonino, et al. New Engl J Med 2009;360:213-24.

FAME Trial: Two Year Outcomes



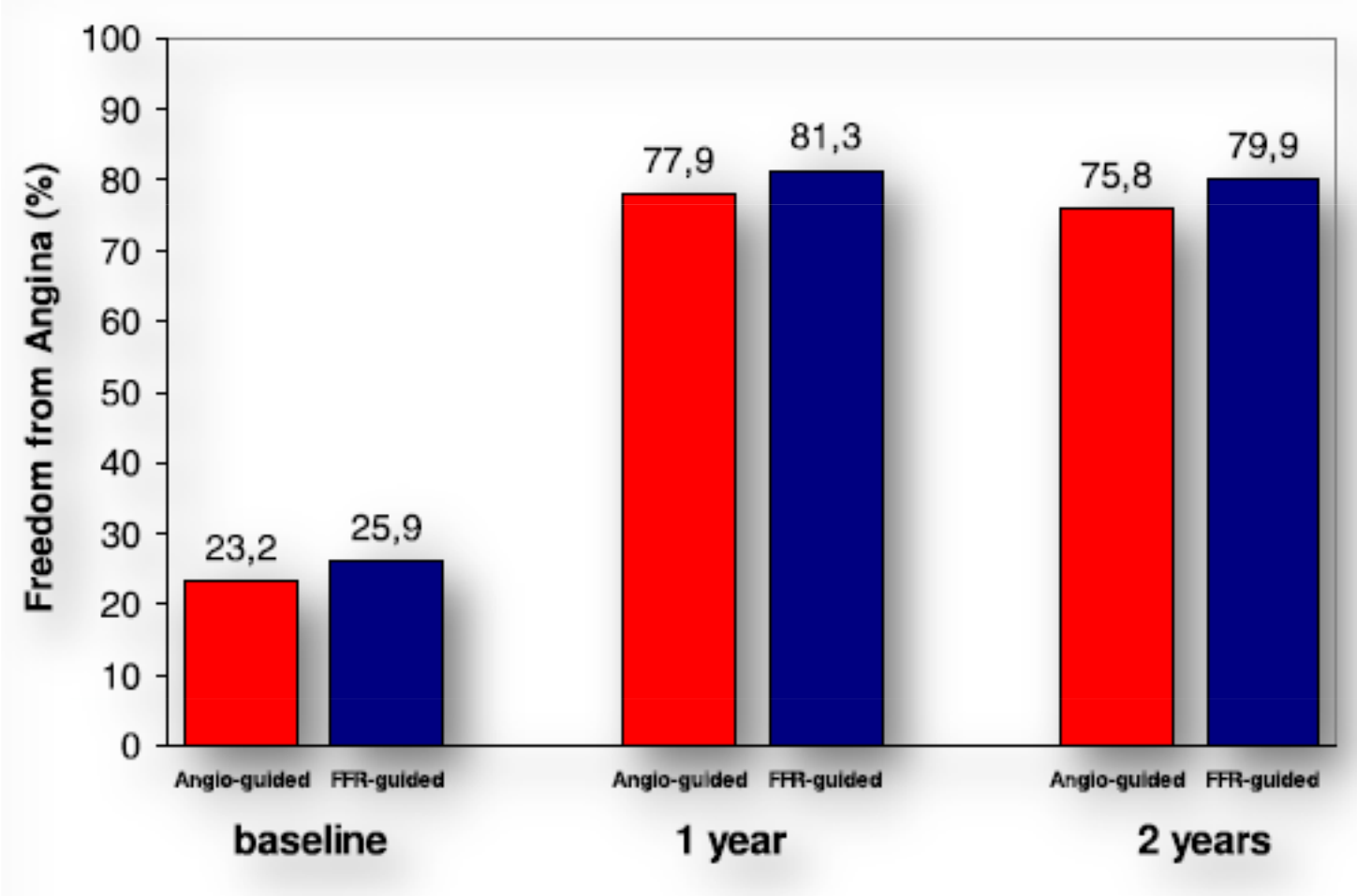
Death/MI was significantly reduced from 12.9% to 8.4% (p=0.02)

Very little risk with deferral of stenting in patients with lesions with an FFR >0.80

- ✓***MI rate of 0.2 %(1 late MI) and***
- ✓***Revascularization rate of 3.2 % (16 late PCIs),***

FAME Trial: Two Year Outcomes

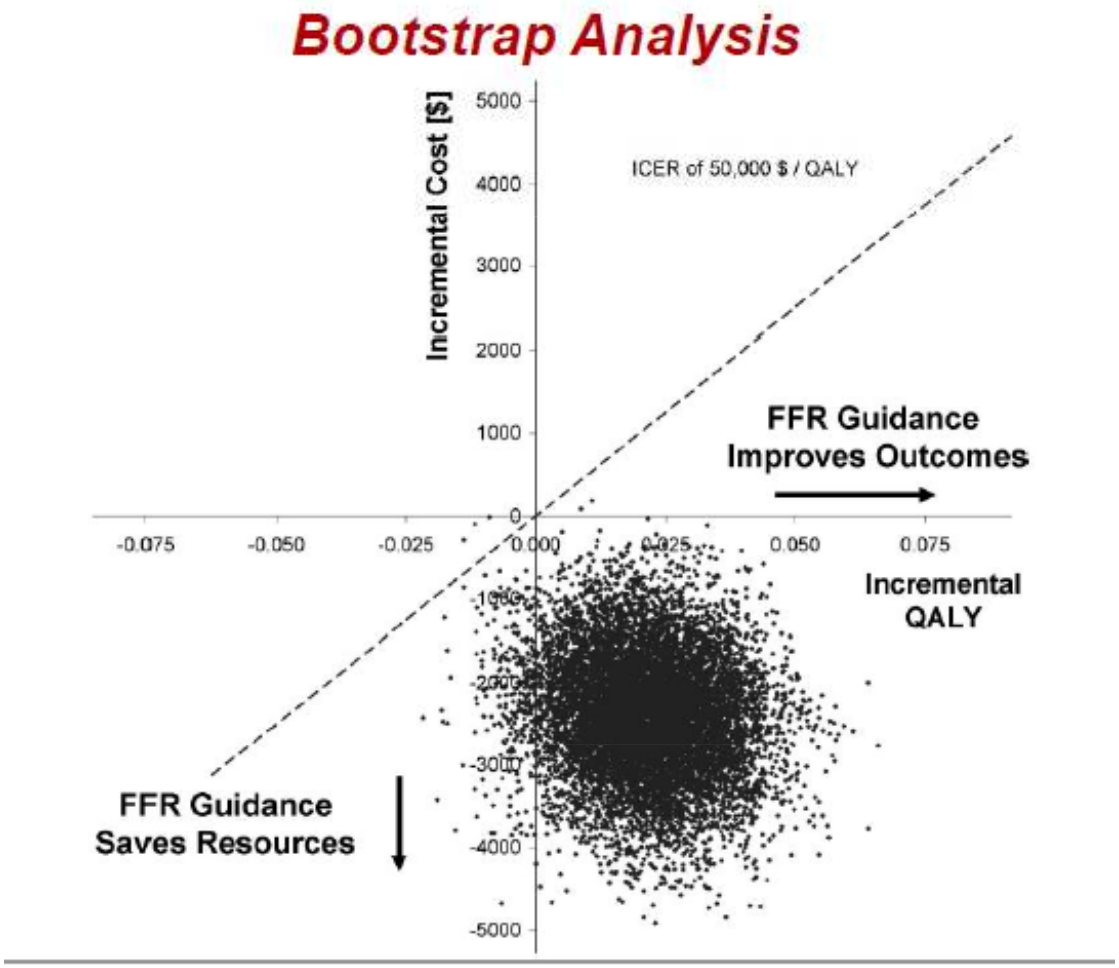
NO DIFFERENCE IN SYMPTOM OUTCOME



Angina in FFR-guided patients was relieved at least as effectively

FAME: Economic Evaluation

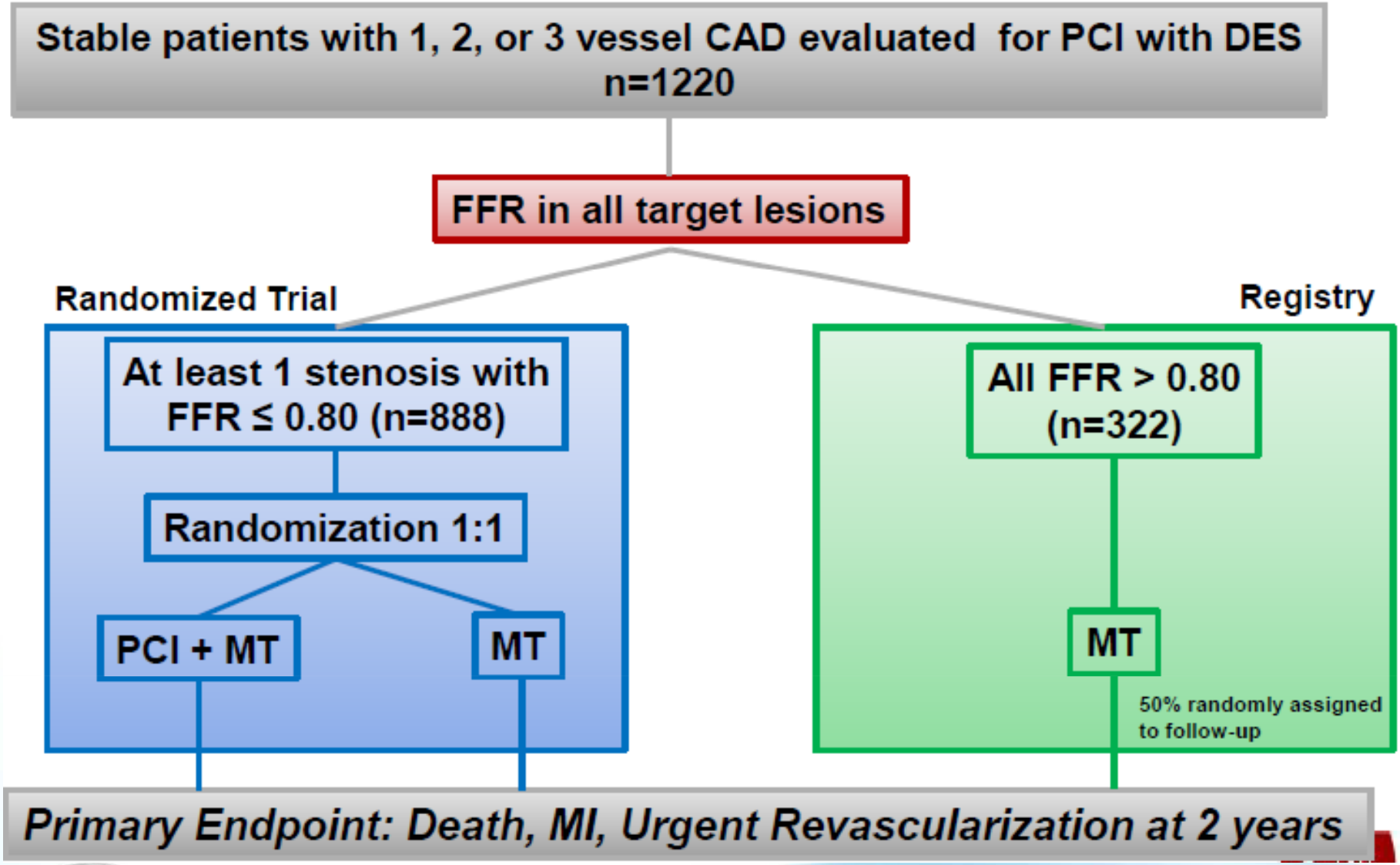
The FAME trial showed **improved patient outcomes with FFR-guided PCI.** This was achieved ***at a lower cost and without prolonging the interventional procedure***



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

Circulation 2010;122:2545-50.

FAME 2 : Flow Chart

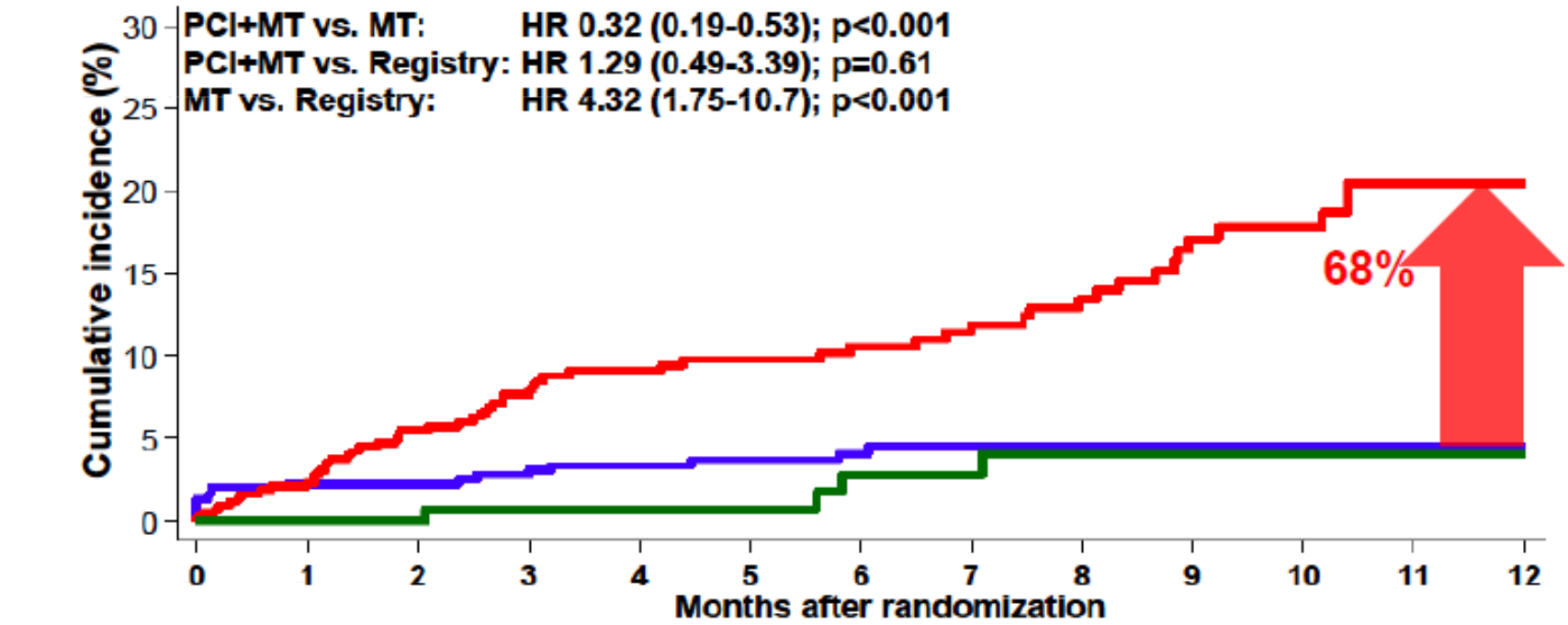


***Recruitment for the FAME 2 study was halted in January 2012*, when an independent Data and Safety Monitoring Board (DSMB) recommended early termination of the study.**

The preliminary results were considered so compelling that research was stopped so patients with FFR <0.80 randomized to optimal medical therapy only *could also receive the benefits of PCI*

In patients with stable coronary artery disease, FFR guided PCI improves patient outcome and is cost effective when compared to medical therapy alone

Death, MI, or Urgent Revascularization

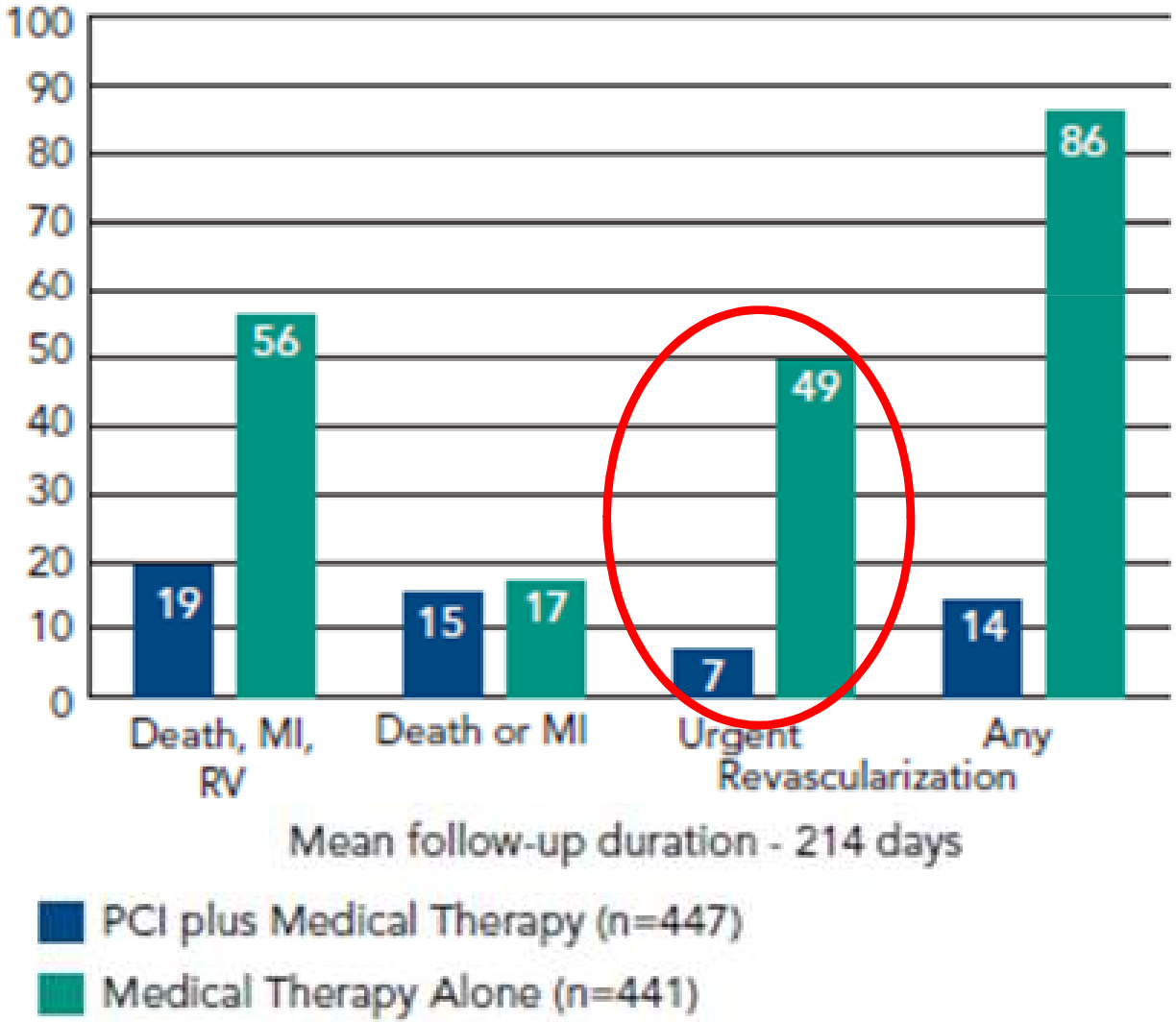


No. at risk

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

De Bruyne, et al. New Engl J Med 2012;367:991-1001

FAME 2 : FFR-Guided PCI versus Medical Therapy in Stable CAD



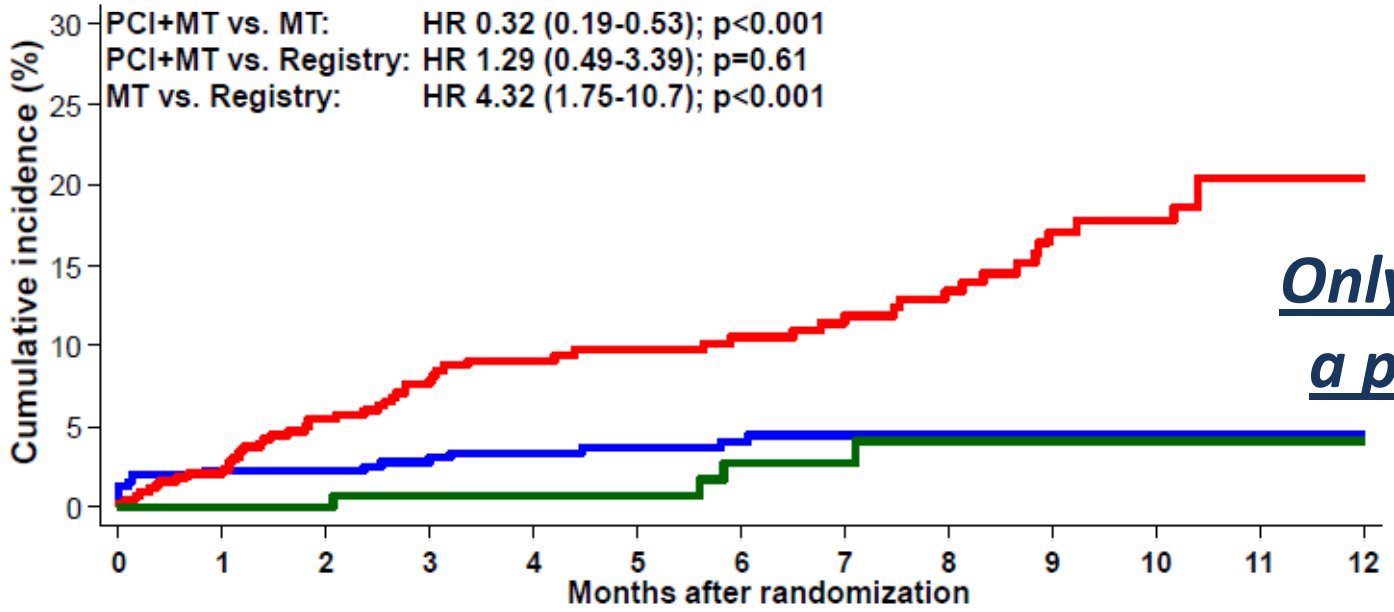
✓**This improvement is driven by a dramatic decrease in the need for *urgent revascularization* for ACS.**

✓**Neither the rate of *death* from any cause nor the rate *of myocardial infarction* differed significantly between the PCI group and the medical-therapy group**

FAME 2 : FFR-Guided PCI versus Medical Therapy in Stable CAD

Among patients with stenoses that were not functionally significant (25%), the best available medical therapy alone resulted in an excellent outcome, regardless of the angiographic appearance of the stenoses.

Death, MI, or Urgent Revascularization



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Registry	166	156	145	133	117	106	93	74	64	52	41	25	13

Only 3 % experienced a primary endpoint

Guidelines on myocardial revascularization

ESC/EACTS GUIDELINES 2010

Recommendations for specific percutaneous coronary intervention devices and pharmacotherapy

	Class[a]	Level[b]	Ref.[c]
FFR-guided PCI is recommended for detection of ischaemia-related lesion(s) when objective evidence of vessel-related ischaemia is not available	I	A	15, 28

FFR-guided PCI is recommended for detection of ischaemia-related lesion(s) when objective evidence of vessel-related ischaemia is not available

FFR in left main coronary artery stenosis. Why?

✓The presence of a significant stenosis in the left main stem is of critical prognostic importance.

✓The left main is among the most difficult segments to assess by angiography

✓Noninvasive testing is often noncontributive in patients with a left main stenosis.

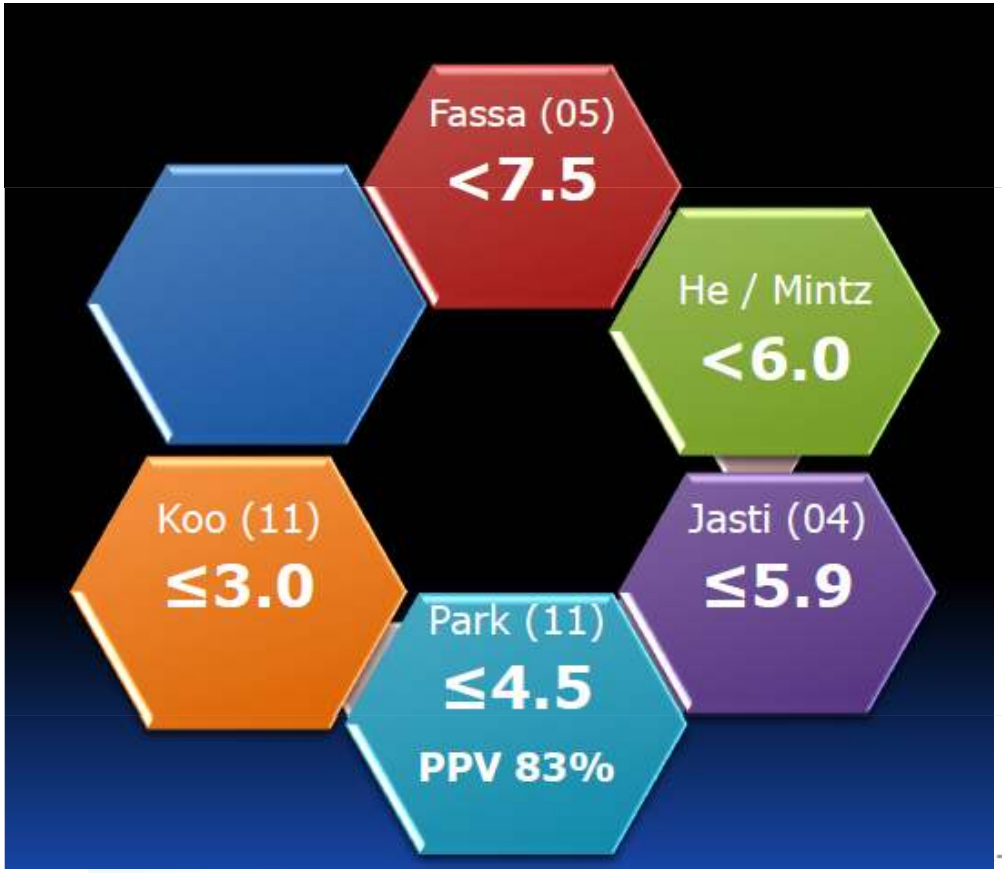
✓Furthermore, revascularization of a non-significant stenosis in the left main may lead to early occlusion of the conduits, especially when internal mammary arteries are used .

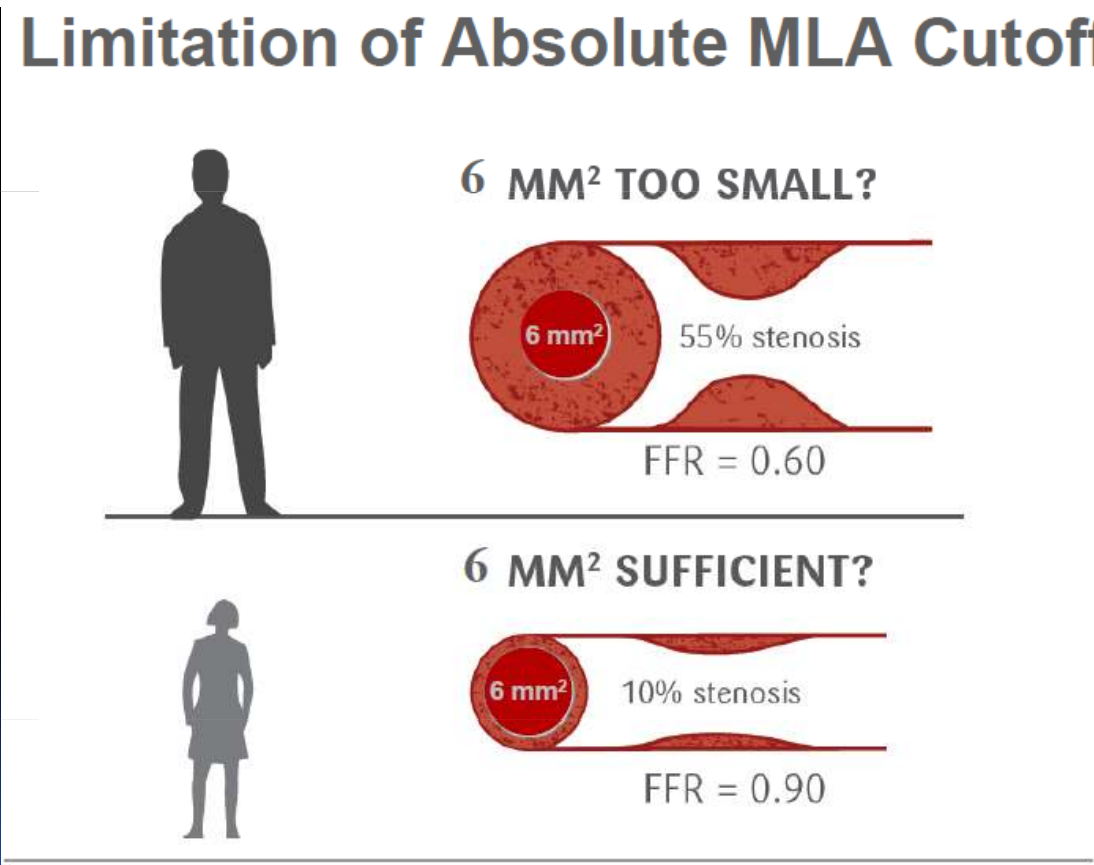
✓Consequently ambiguous LMCA disease sometimes results in considerable uncertainty when deciding on the best therapeutic strategy for the patient

✓In most of the cases, therapeutic decision for its treatment is based on the angiographic appearance of the lesion

What LM MLA is ischemic?

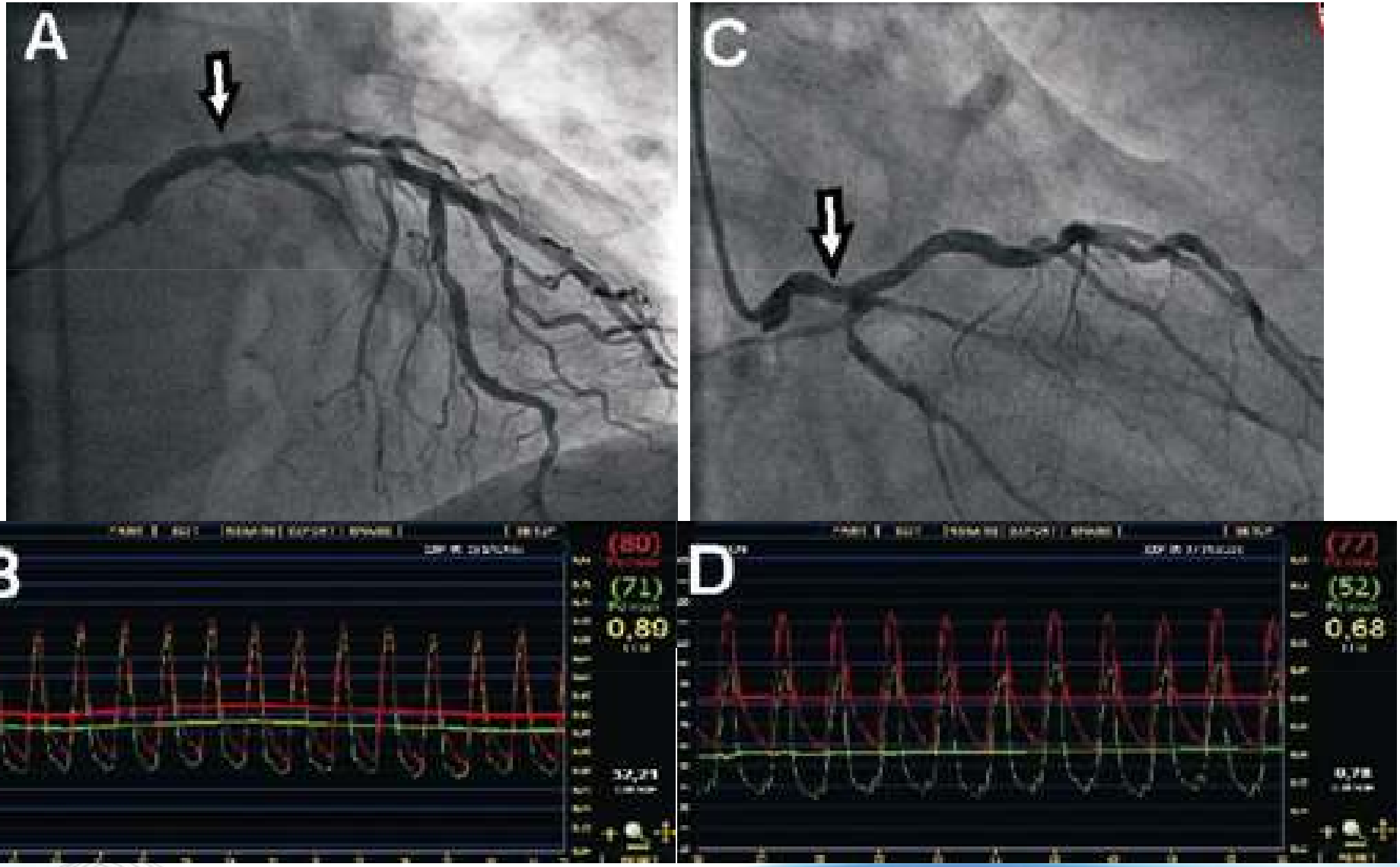
- FFR can be applied in LM stenosis as usual, with similar cut-off value





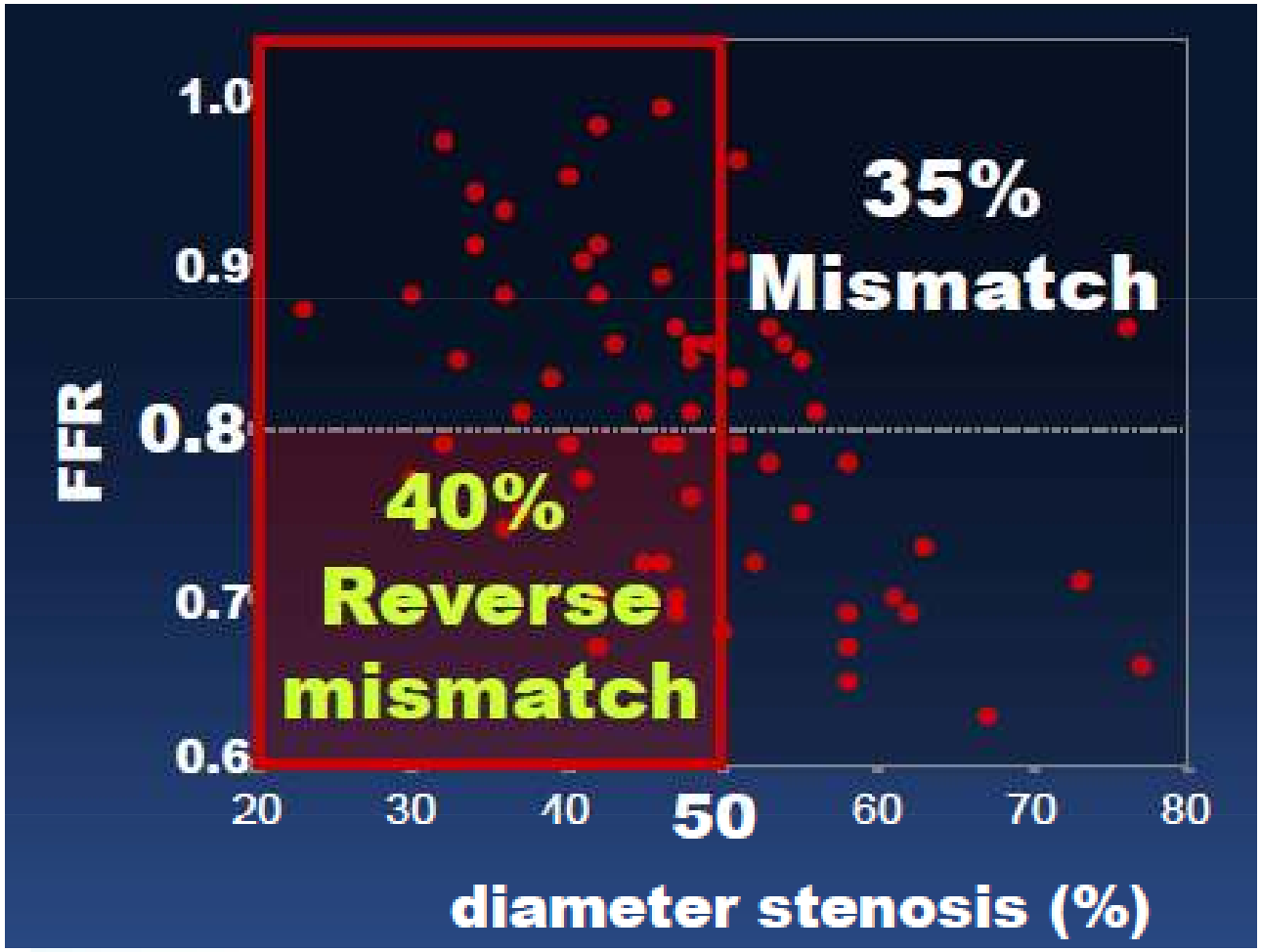
Fassa JACC, 2005:204-211, Jasti Circulation 2004;2831-6, Koo JACC 2011 8033-11,

Does these left main stenoses need revascularization?



QCA-FFR Discordance in Left Main Stem Stenoses

Park et al. 2012 JACC Interv



In 35% of patients with LM stenosis >50%, FFR was >0.80

In 40% of patients with LM stenosis <50%, FFR was <0.80

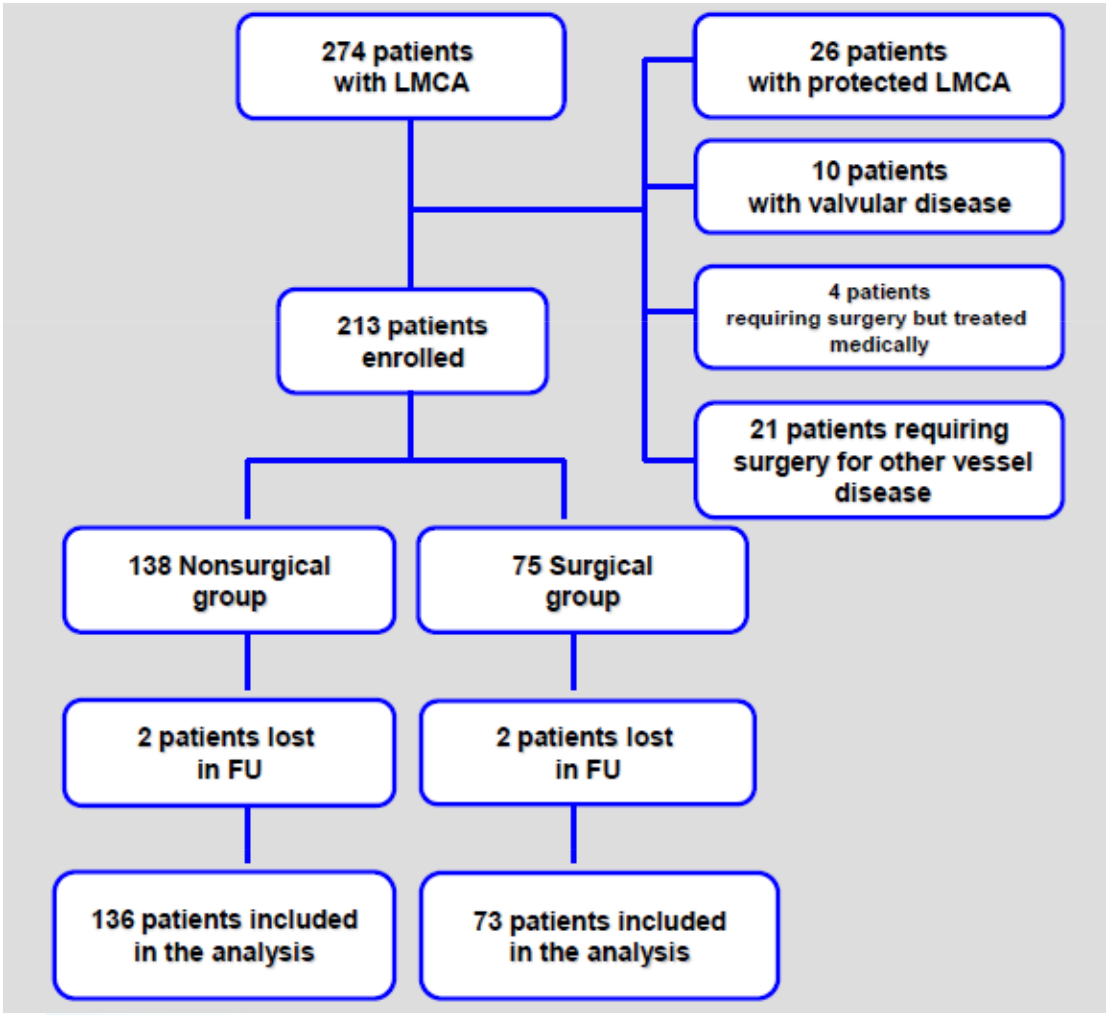
Does this left main stenosis need revascularization?

Can you really leave lesions that looks significant to your eyes ……. but have negative FFR?

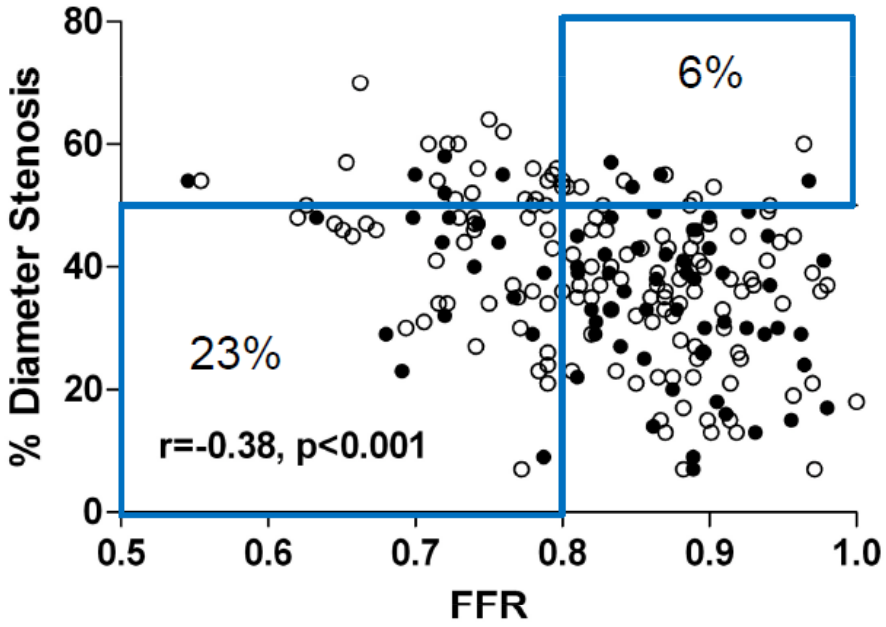
Several small studies and one larger study, published recently, showed that an FFR-aided strategy for equivocal LMCA lesions is safe and related to a favorable clinical outcome.

Publication	Journal	Pts	Defer	Surg	FU	EFS (Def)	EFS (Surg)	Surviv (Def)	Surviv (Surg)
Bech et al	Heart 2001	54	24	30	29	76	83	100	97
Jasti et al	Circulation 2004	51	37	14	25	90	100	100	100
Jiminez et al	J Invas Card 2004	27	20	7	26	90	86	100	86
Legutko et al	Kardiol Pol 2005	38	20	18	24	90	89	100	89
Suemaru et al	Heart Vessels 2005	15	8	7	33	100	71	100	100
Linsdtaedt et al	Am Heart J 2006	51	24	27	29	69	66	100	81
Courtis et al	Am J Cardiol 2009	142	82	60	14	87	93	96	95
Hamilos et al	Circulation 2009	213	138	75	36	74	83	90	85

Is it safe to differ revascularization on LM lesions with FFR>0.80?



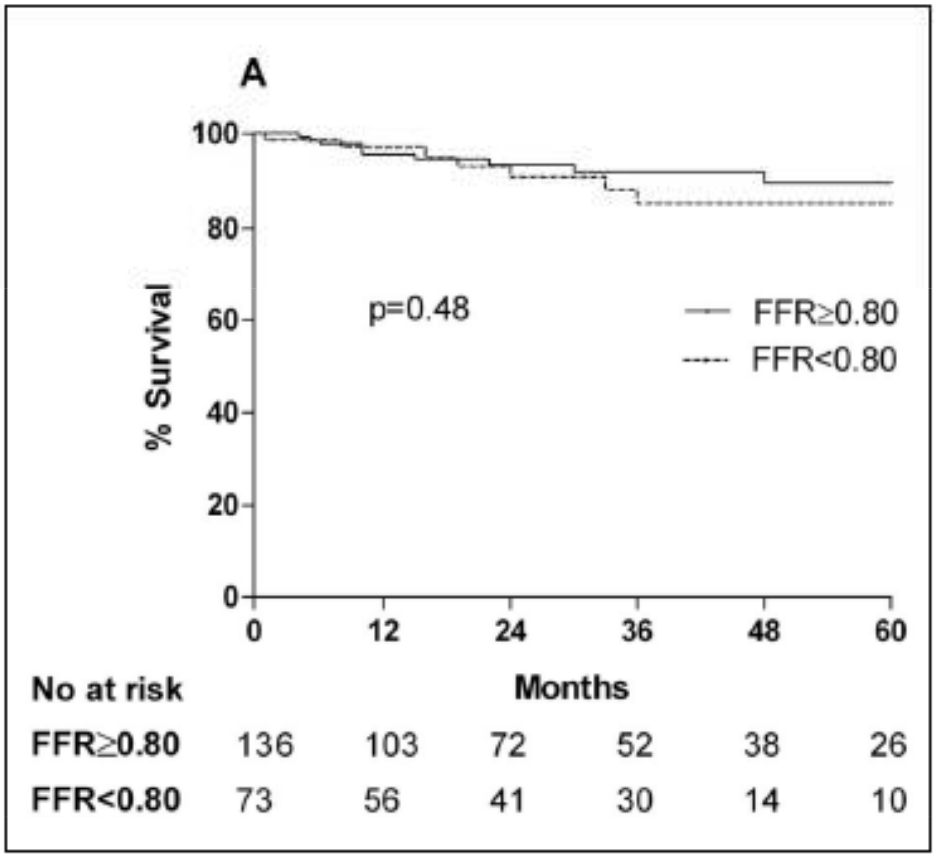
In 23% of patients with LM stenosis <50%, FFR was <0.80



Hamilos et al., Circulation 2009;120:1505

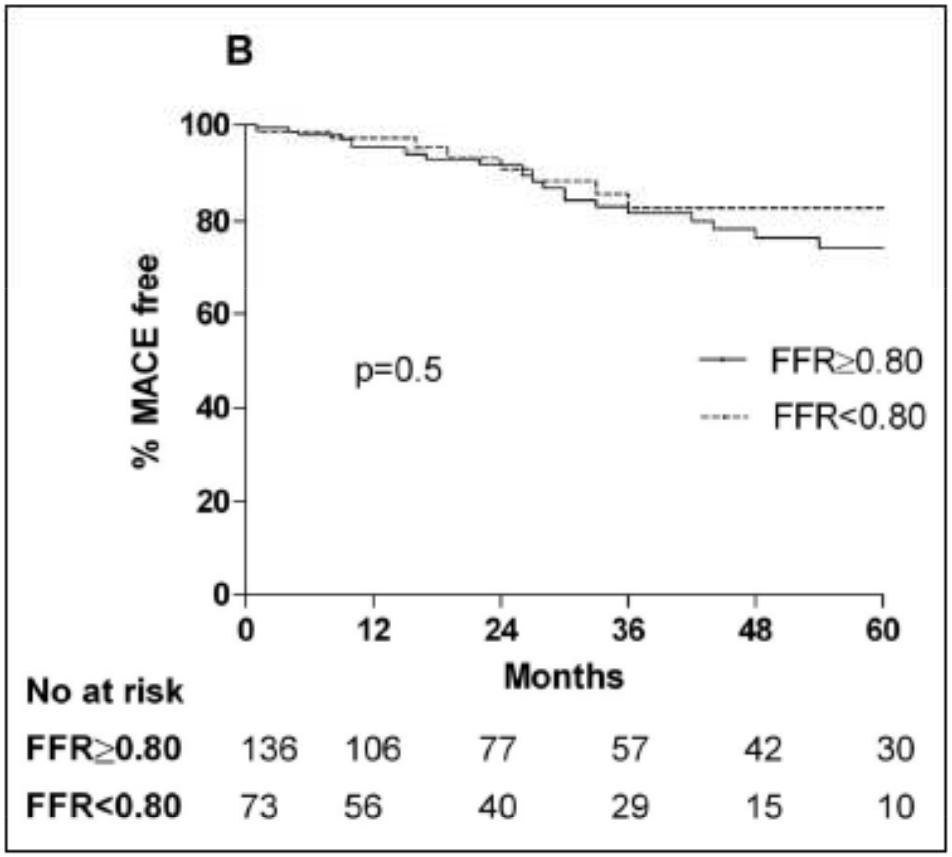
Is it safe to differ revascularization on LM lesions with FFR>0.80?

Survival at long term follow-up



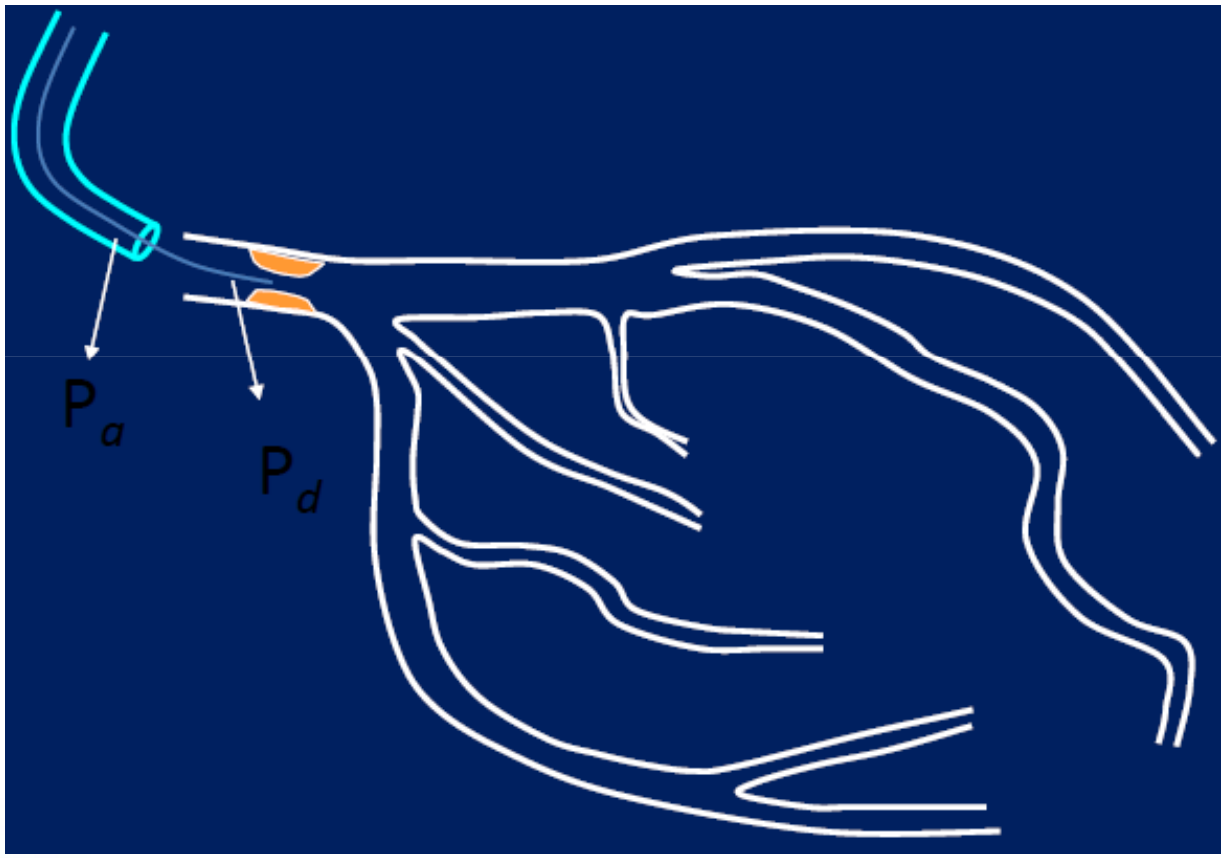
No at risk						
FFR≥0.80	136	103	72	52	38	26
FFR<0.80	73	56	41	30	14	10

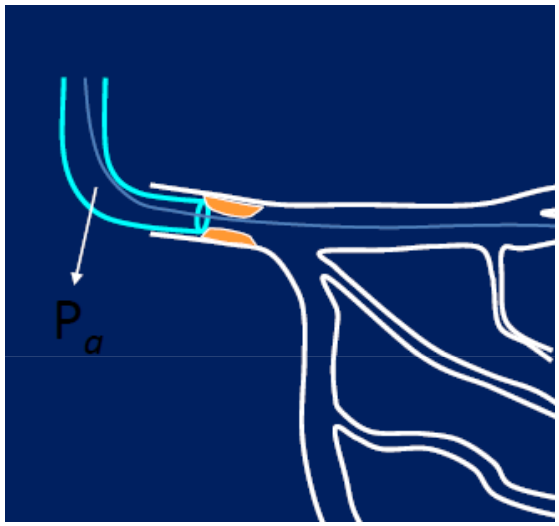
MACE free-survival

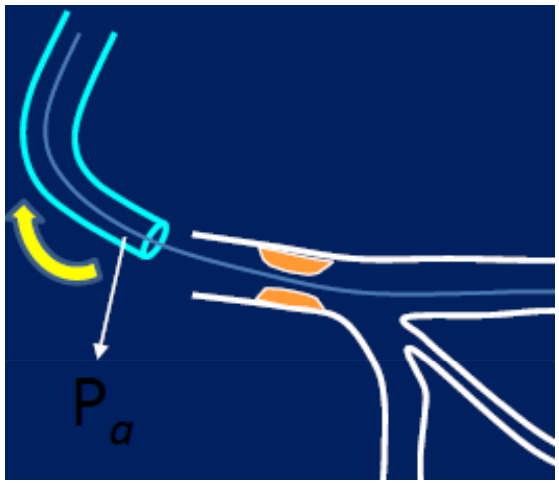


No at risk						
FFR≥0.80	136	106	77	57	42	30
FFR<0.80	73	56	40	29	15	10

FFR in the LMCA: Practical Aspects



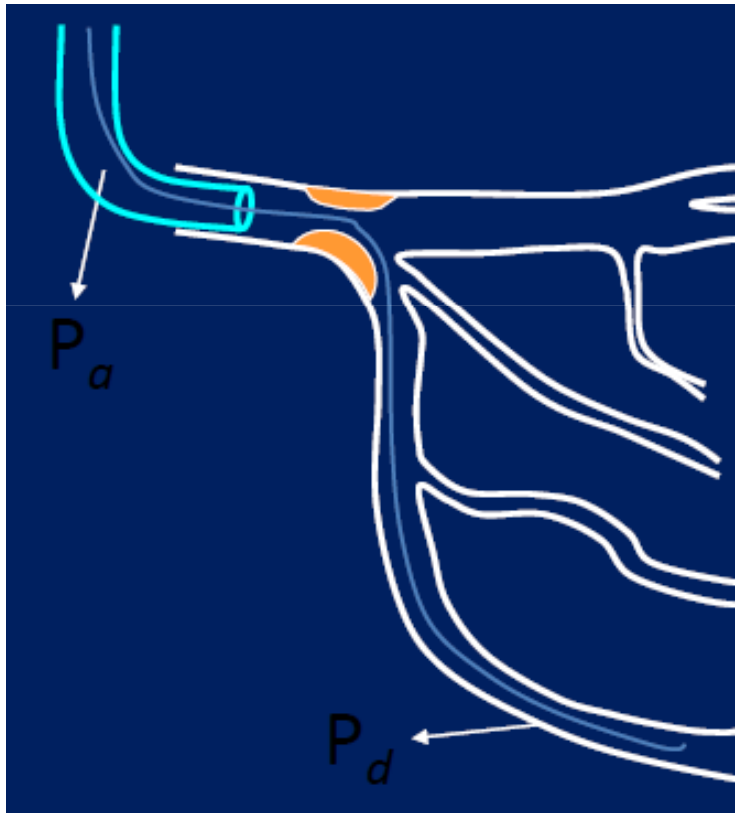




Equalization of 2 pressures (guiding catheter [P_a] and PW [P_d]):
to be perfomed with the GC disengaged !

Hyperemia with IV Adenosine infusion is strictly recommended !

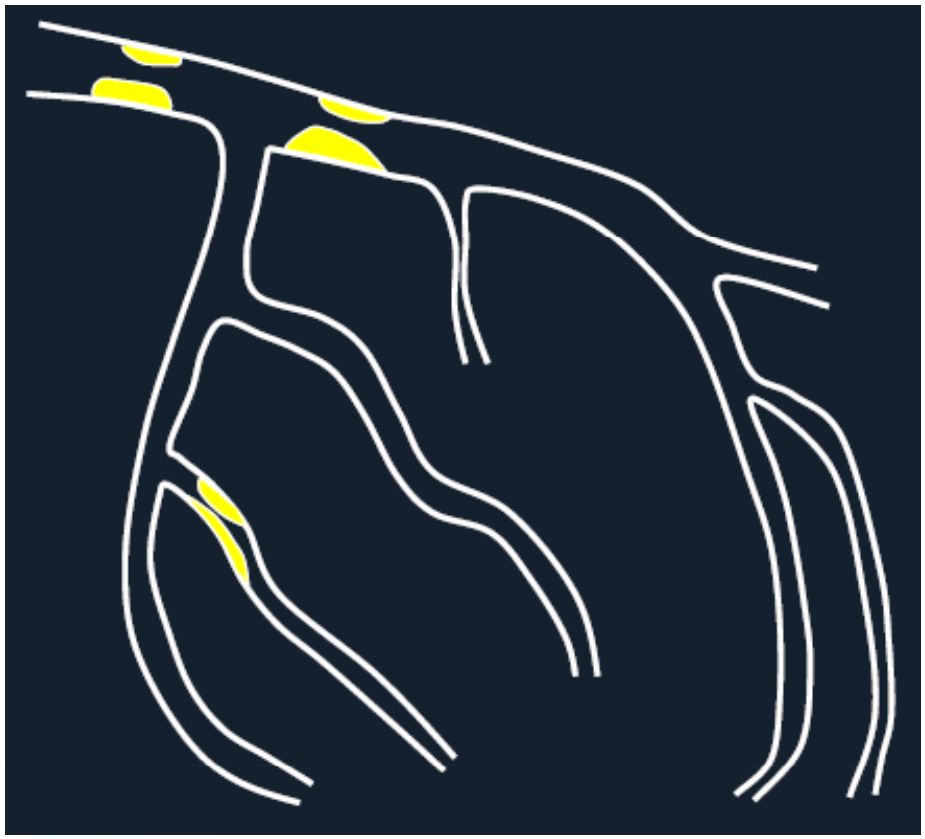
FFR in the LMCA: Practical Aspects



With distal stenosis, FFR should be measured in both LAD and Cx

Left Main Stem Stenoses are Rarely Isolated

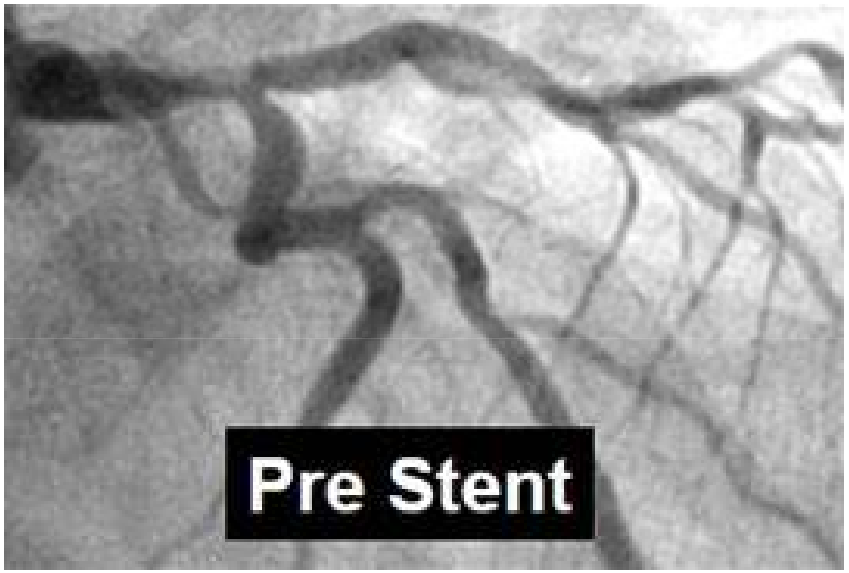
When tight stenoses are present in the LAD or in the LCx the presence of these lesions *will tend to increase the FFR measured across the left main.*

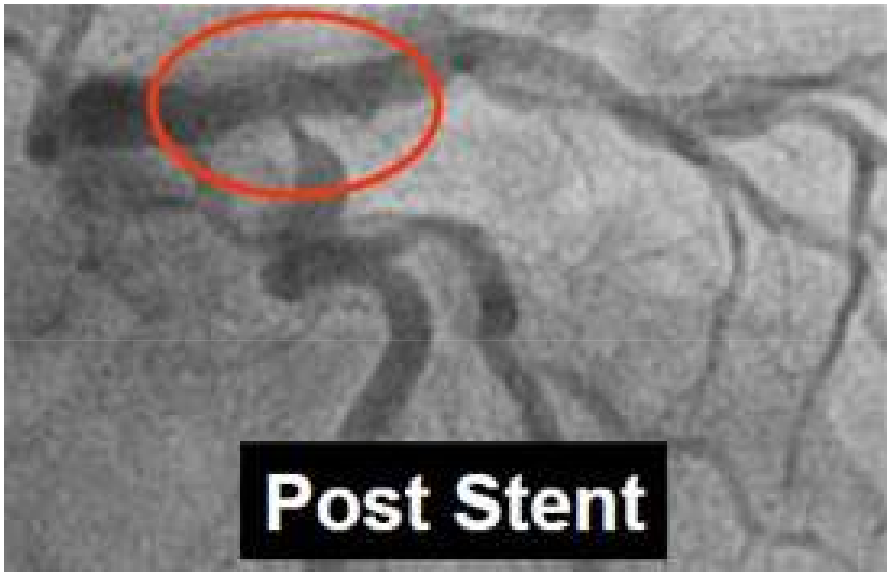


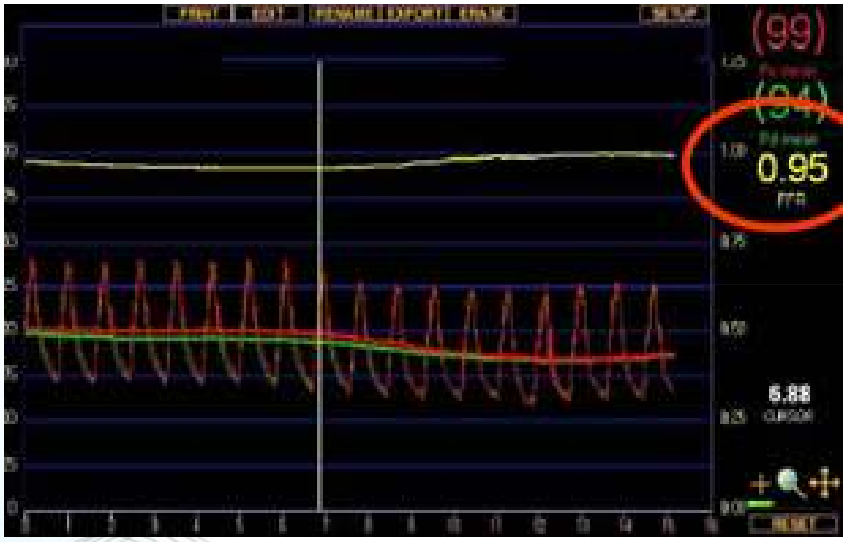
Influence of proximal LAD lesion will be more pronounced than a stenosis of a small marginal branch

The influence of a LAD/left circumflex coronary artery (LCx) lesion on the FFR value of the left main *will depend on the severity* of this distal stenosis but, even more, on the *vascular territory supplied by this distal stenosis*

FFR of “Jailed” Left Circumflex

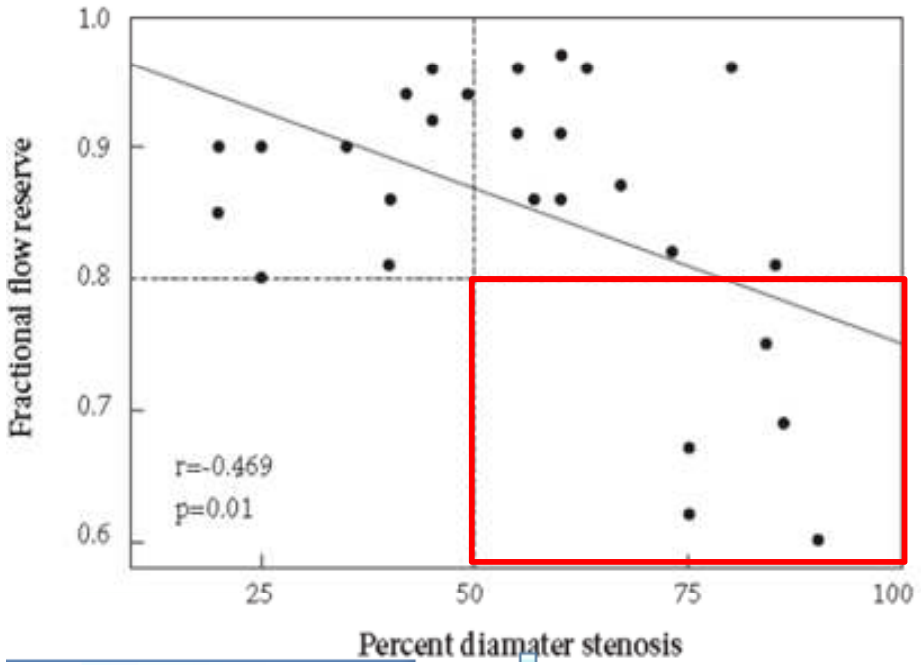






FFR of "Jailed" Left Circumflex

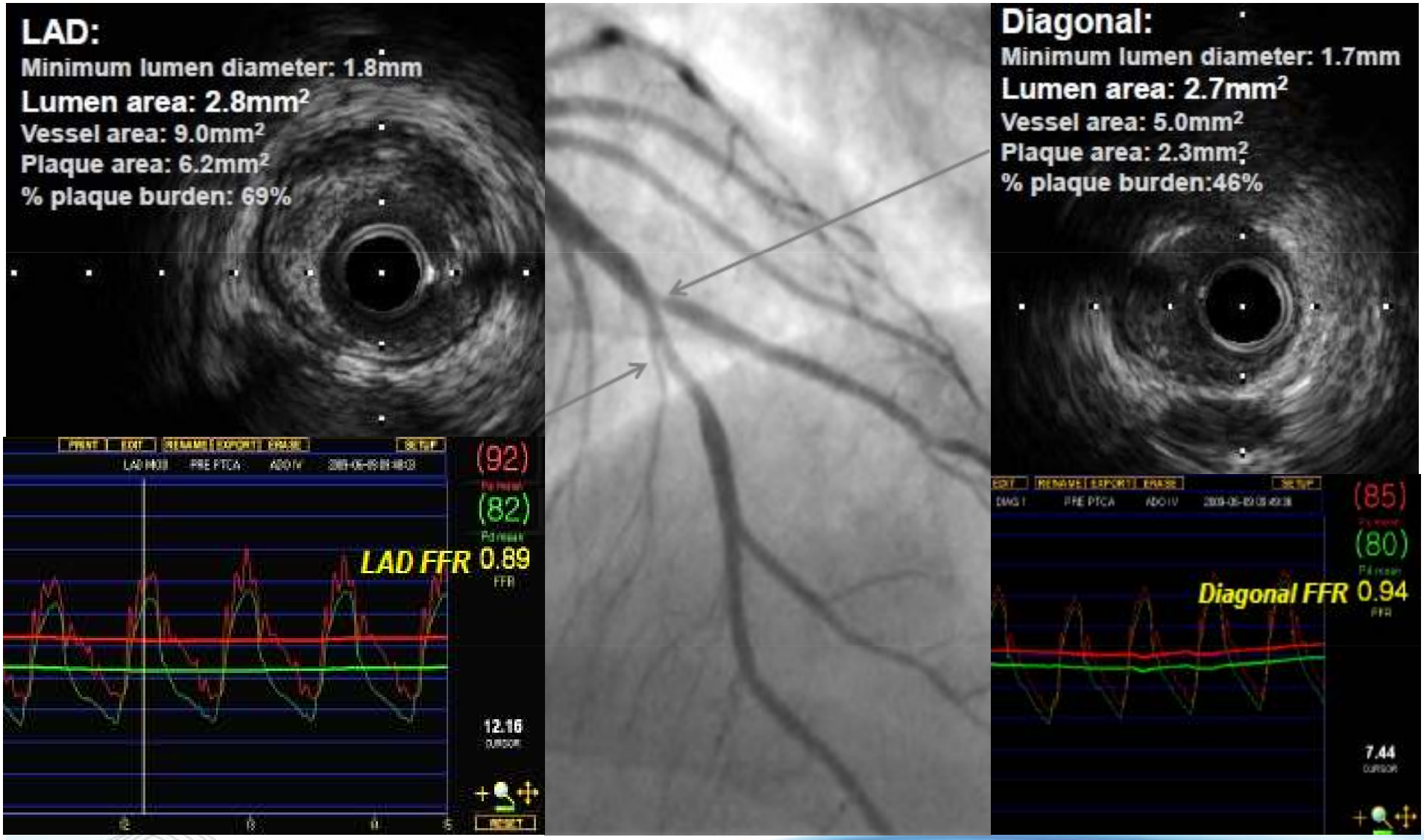
29 patients with LM/LAD crossover stenting with FFR of "jailed" Cx



Mean 20 month follow-up	Defer group n = 24	PCI group n = 5
Death, n	0	1
Myocardial Infarction, n	0	0
TLR, n	3	1
Stent Thrombosis, n	0	0
Total Events, n	3	2

Nam CW, et al. Korean Circ J 2011;41:304-7.

Use and utility of FFR during Bifurcation PCI



Pre-intervention FFR

✓**Mainly to assess the functional significance of main branch lesion**

FFR of side branch lesion

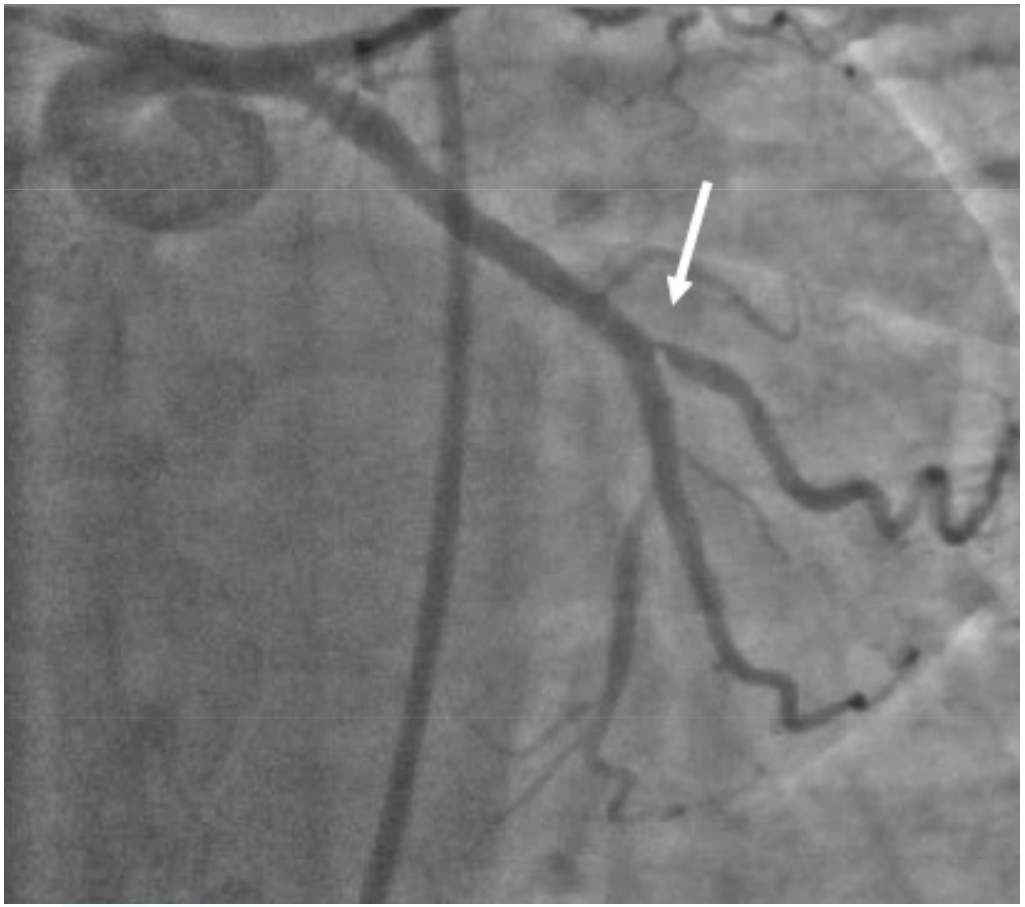
Practical tips you should know….

- FFR should be measured in a large SB. **FFR <0.75 does not always mean the clinical relevance of that side branch (SB) stenosis.**
- ***When SB FFR is measured, the influence of main branch stenosis should always be considered.***
- Pre-intervention SB FFR **is usually not helpful to predict the jailed SB FFR.**

To assess the functional significance of pure ostial SB lesion

Use and utility of FFR during Bifurcation PCI

After main branch stent implantation



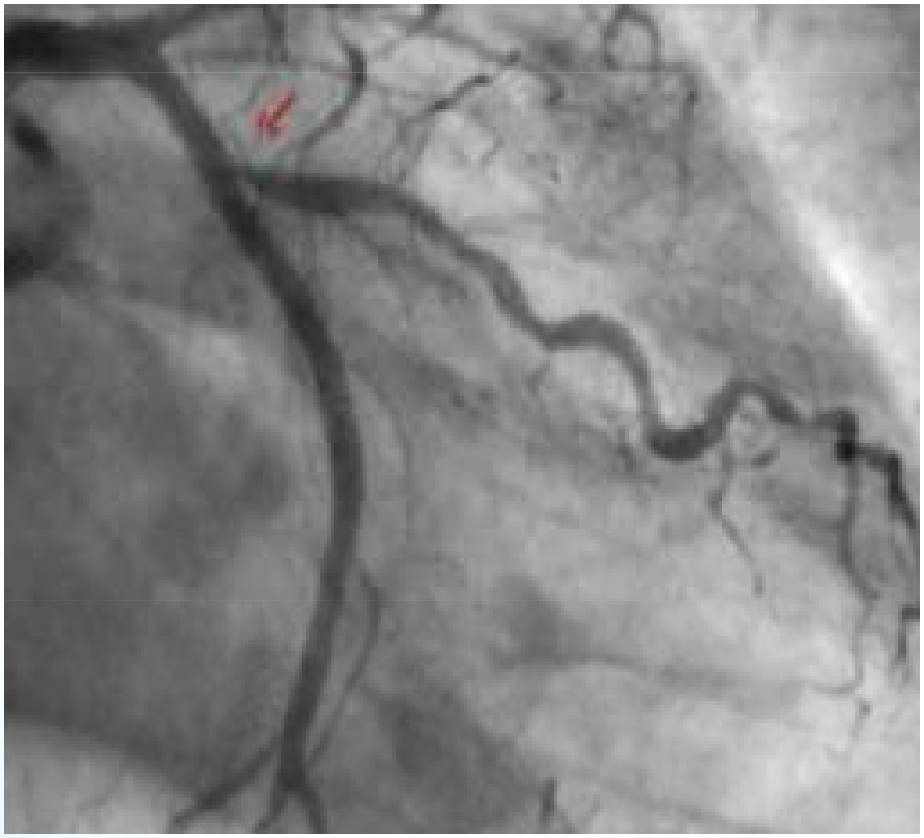
After stenting the main branch, the ostium of the side branch often looks pinched.

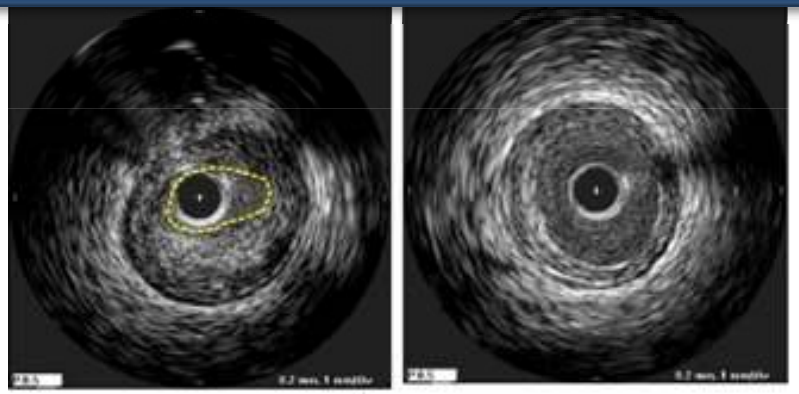
Yet such stenoses are grossly overestimated by angiography: few of these ostial lesions with a stenosis diameter 75% were found to have FFR< 0.75

Use and utility of FFR during Bifurcation PCI

After main branch stent implantation

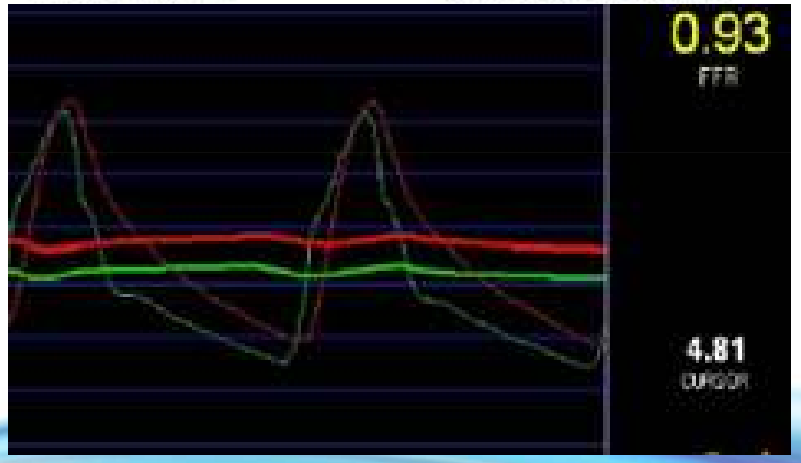
In Jailed side branch lesions,
Angiographic severity ≠ Presence of ischemia





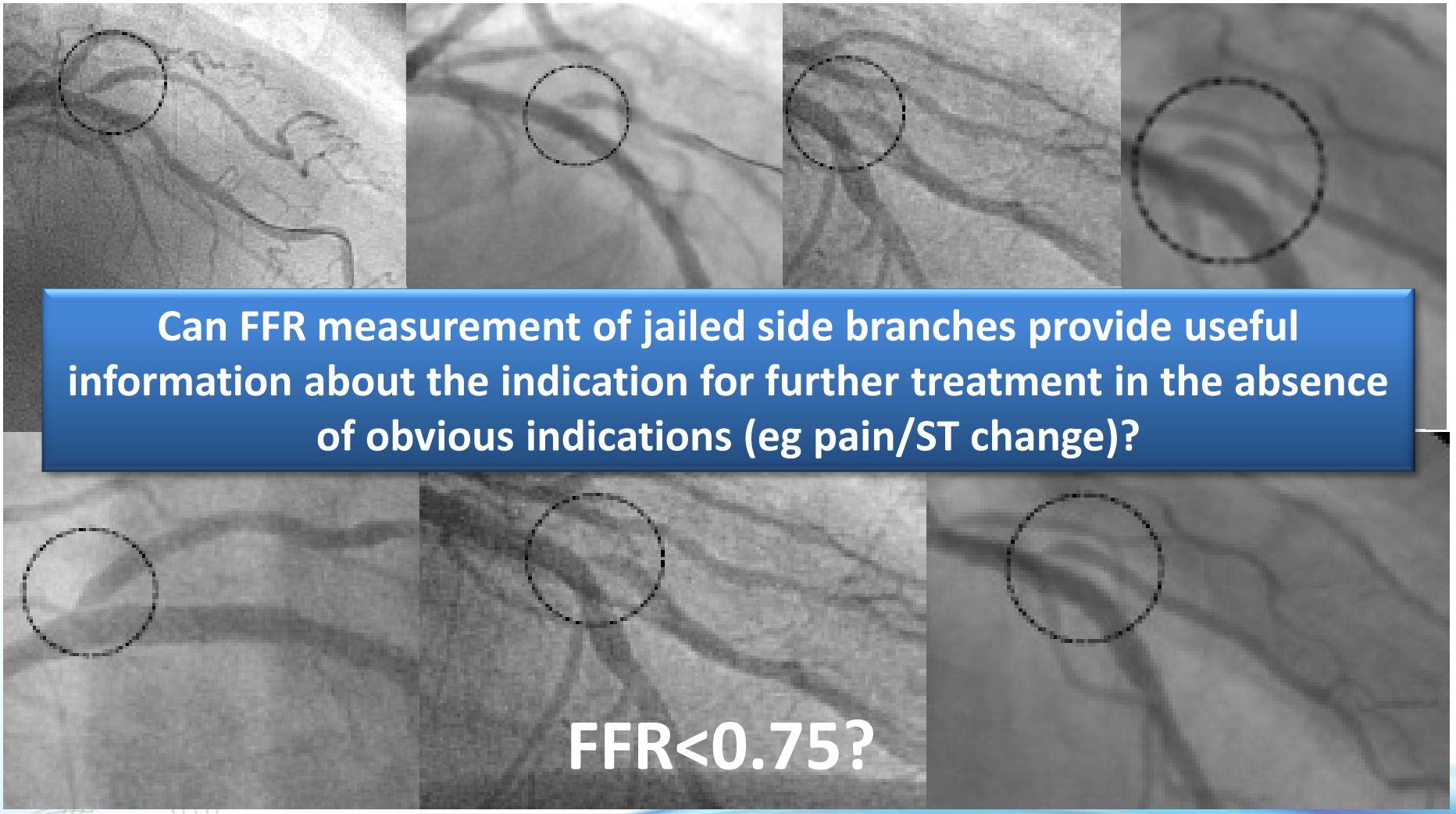
Lumen Area: 2.3mm^2
MLD: 1.2mm

Reference vessel diameter: 3.75mm



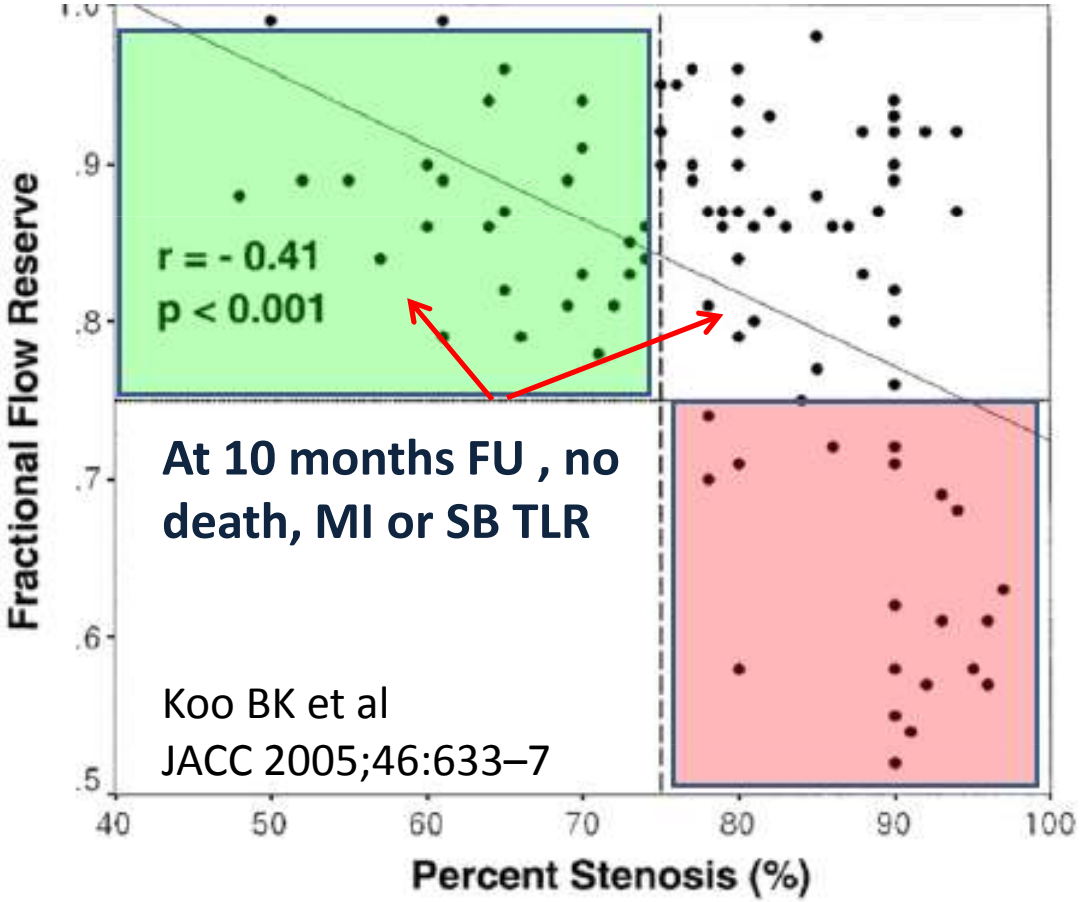
Use and utility of FFR during Bifurcation PCI

After main branch stent implantation



Correlation Between FFR and % Stenosis (QCA) in Jailed Side Branches

In Jailed side branch lesions,
Angiographic severity ≠ Presence of ischemia



FFR in 97 "Jailed" Side Branches

No lesion <75% (green) stenosis had FFR<0.75.

Among 73 lesions with ≥75% stenosis, only 20 lesions (red) were functionally significant (PPV=27%)

while 53 (73%) were not (white)

Dilating >75% SB stenosis is approriate in 1 out of 4 patients (since 1 out of 4 will have FFR<0.75)

Use and utility of FFR during Bifurcation PCI

After main branch stent implantation:

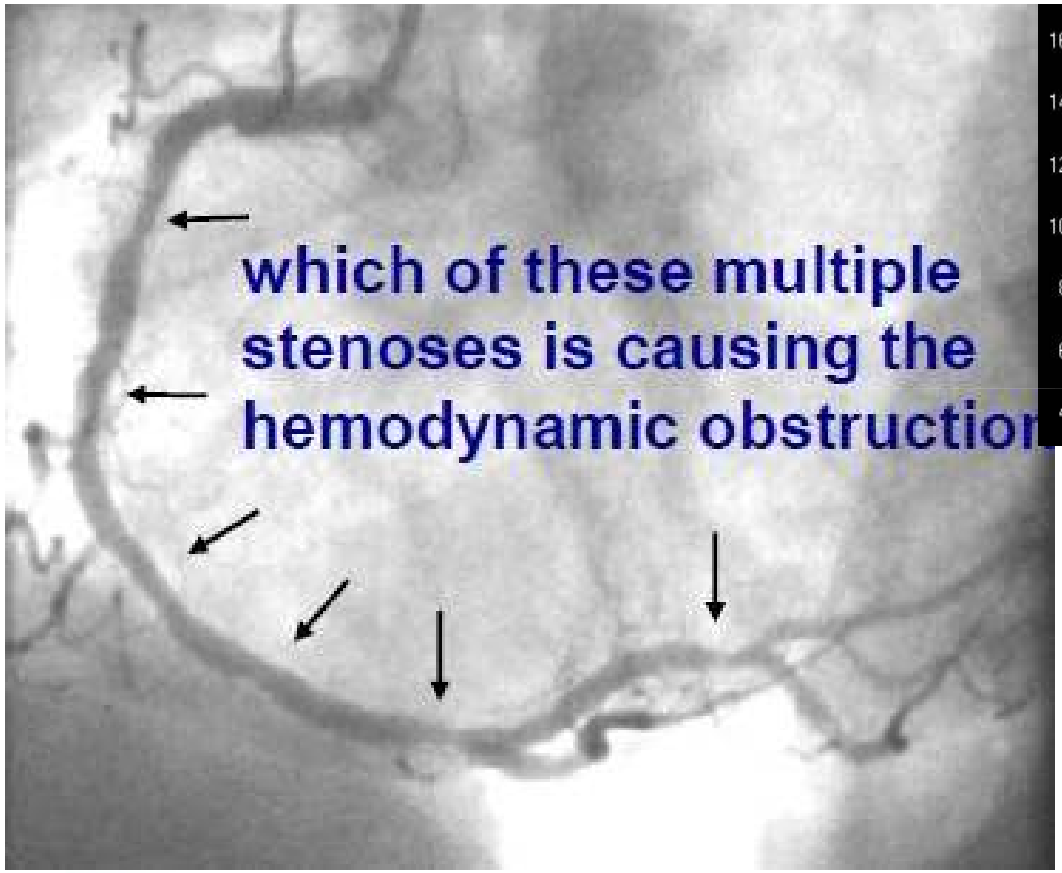
If FFR of the side branch is >0.75, the outcome is excellent without further intervention.

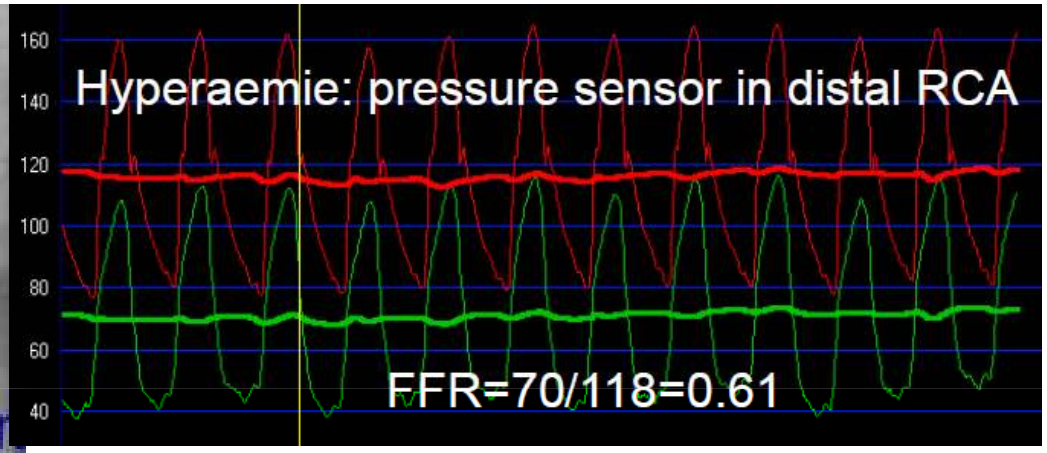
- **SB FFR is not recommended in very complicated SB lesions (severe tortuosity, heavy calcification, diffuse multiple stenosis…..).**

- **The pressure wire should not be jailed by a stent.**
-
- **SB FFR is not recommended in case of slow flow or severe dissection.**

- If you are intent on measuring the FFR of a “jailed” side branch, but cannot wire the vessel with a pressure wire, can wire with another wire and exchange over a transit catheter

FFR in sequential stenoses



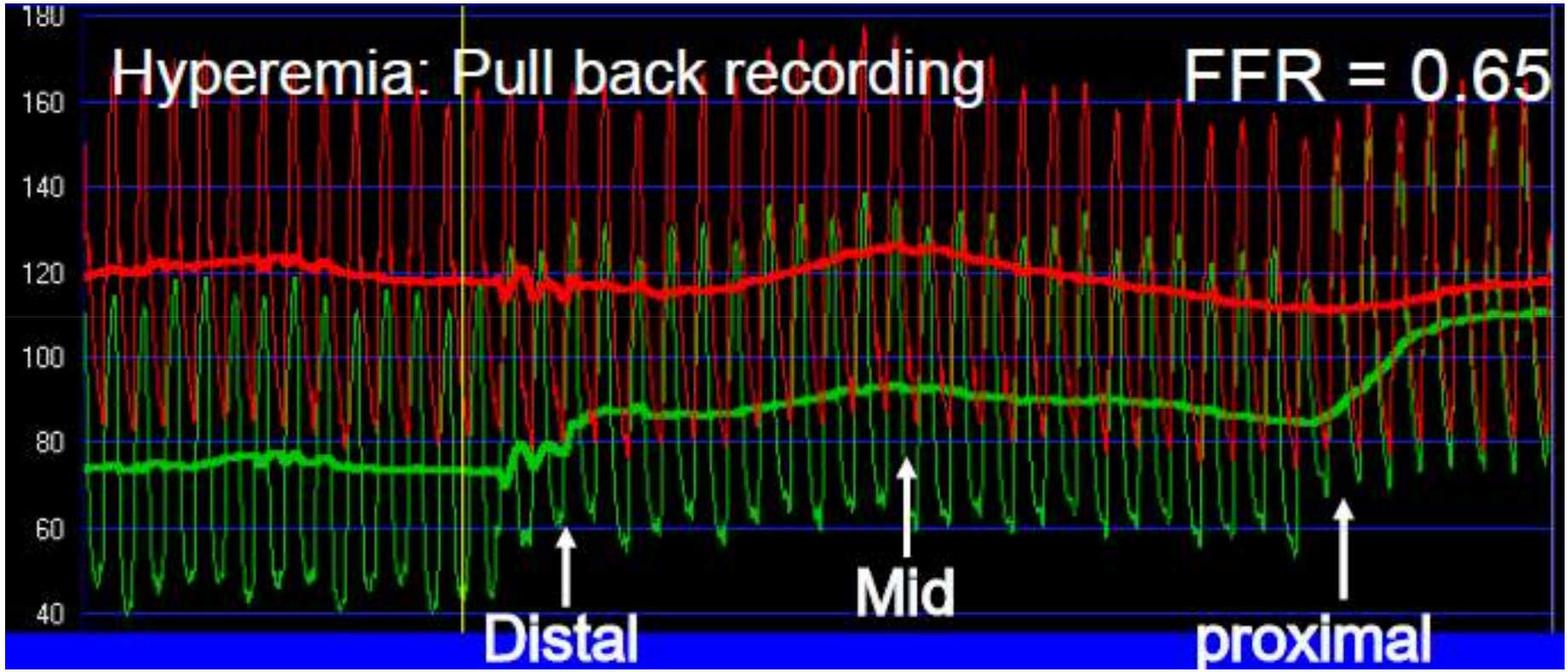


Practically *a pull-back maneuver under maximal hyperemia* is the best way to appreciate the exact location and physiologic significance of sequential stenoses and to guide the interventional procedure step-by-step

Place the *wire in the most distal part of the artery* *(at least distally to the most distal lesion of interest)*

- **Induce *hyperemia (i.v adenosine)*** *and determine FFR. If FFR < 0.75 – 0.80 , inducible ischemia related to this artery is established and PCI is appropriate.*

FFR in sequential stenoses

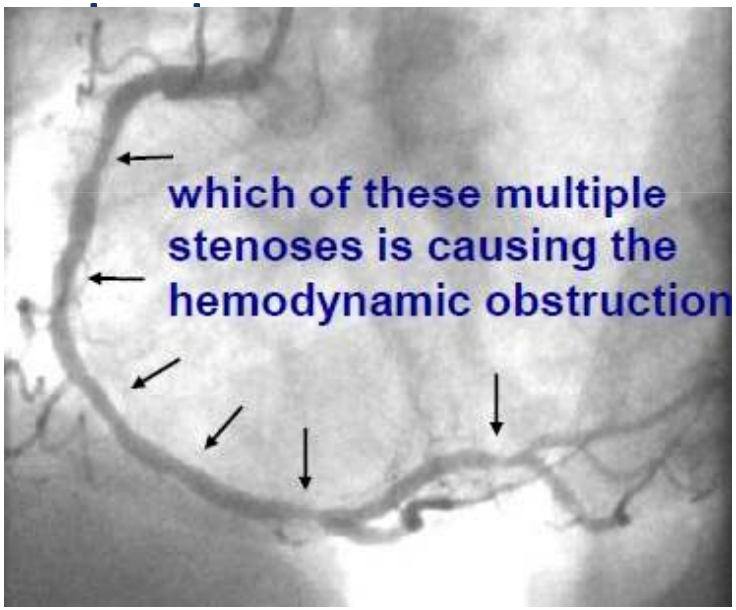


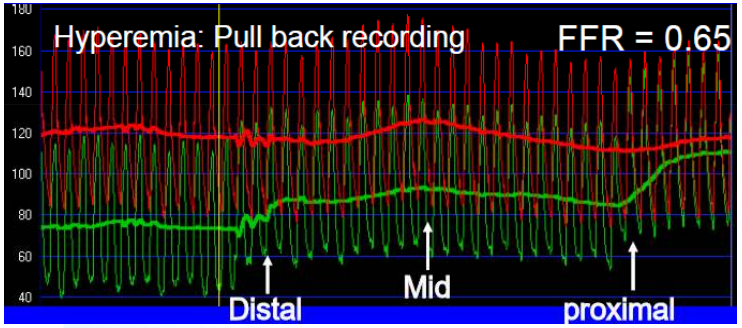
Start the *pull-back recording under fluoroscopy and establish those spots or segments with a sudden pressure drop.*

- **If local pressure drops ≥ 10 mmHg are present, stenting of those spots can be considered.**

FFR in sequential stenoses

Generally, the "most severe" spot (i.e., the stenosis with the largest gradient) is stented first and the *pull-back recording can be repeated thereafter to check the remaining lesions* and it can be decided whether and where a second stent should be



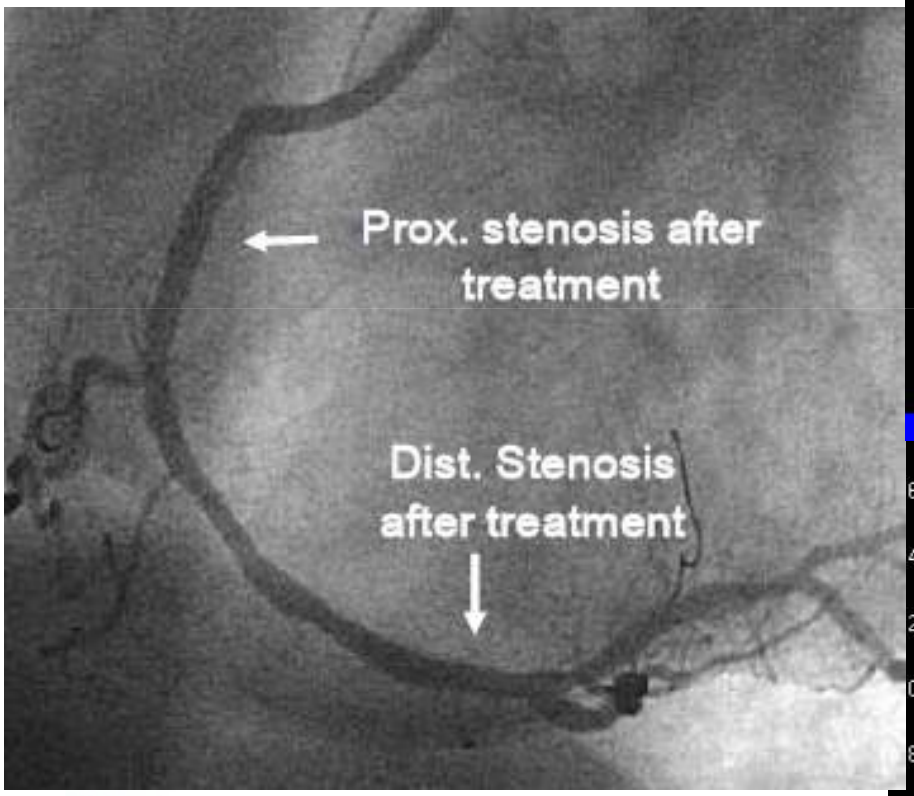


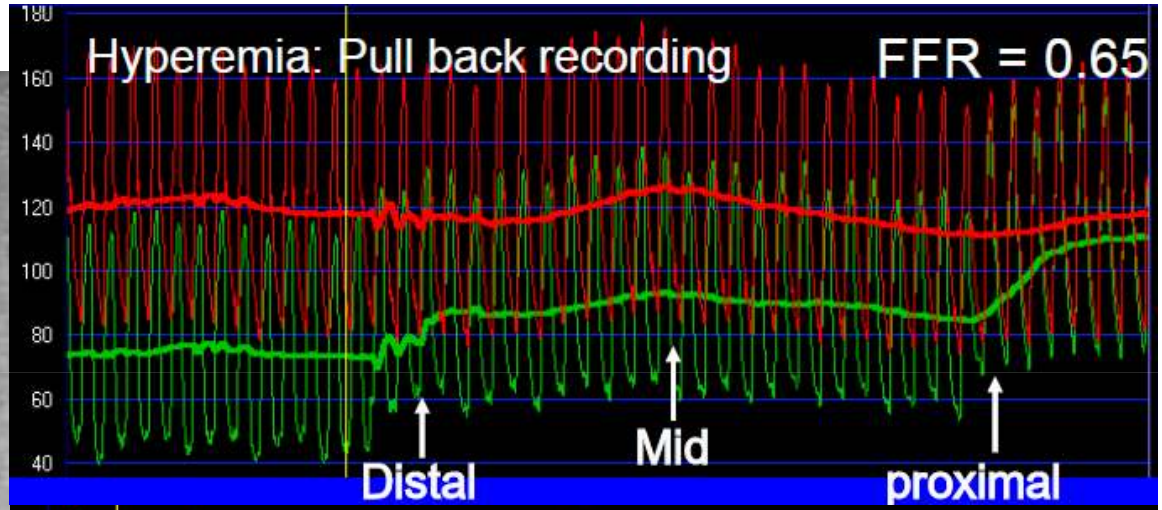
- **Sometimes, for technical reasons, the most distal lesion is stented first**, even if not the worst one

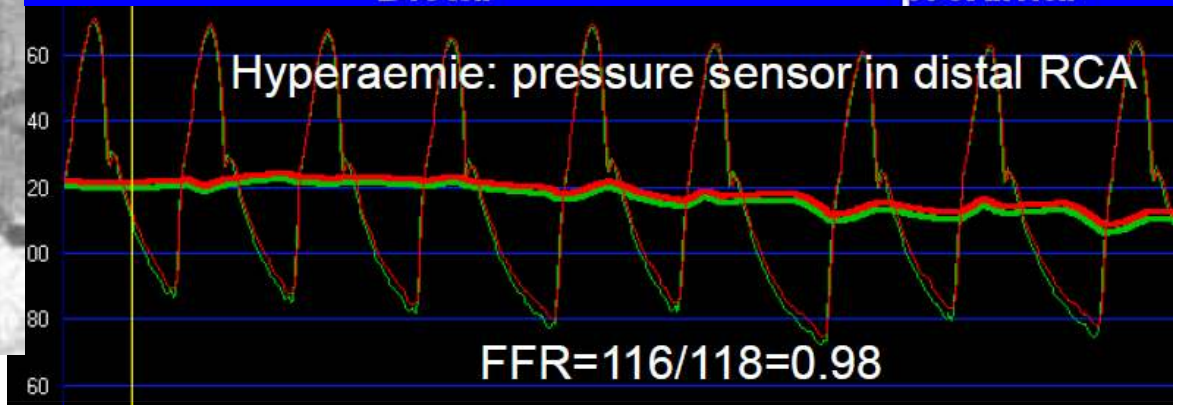
- Realize that – by stenting the most severe lesion – the gradient across the other lesion(s) may increase ***Rule of thumb: a severe distal lesion can mask the gradient across a proximal lesion much more than vice versa.***

- **Stenting spots or segments with a gradient < 10 mm, does not make much sense.**

FFR in sequential stenoses







Coronary pressure is unique in this respect and such detailed spatial information can not be obtained by any invasive or non-invasive method

FFR in diffuse disease

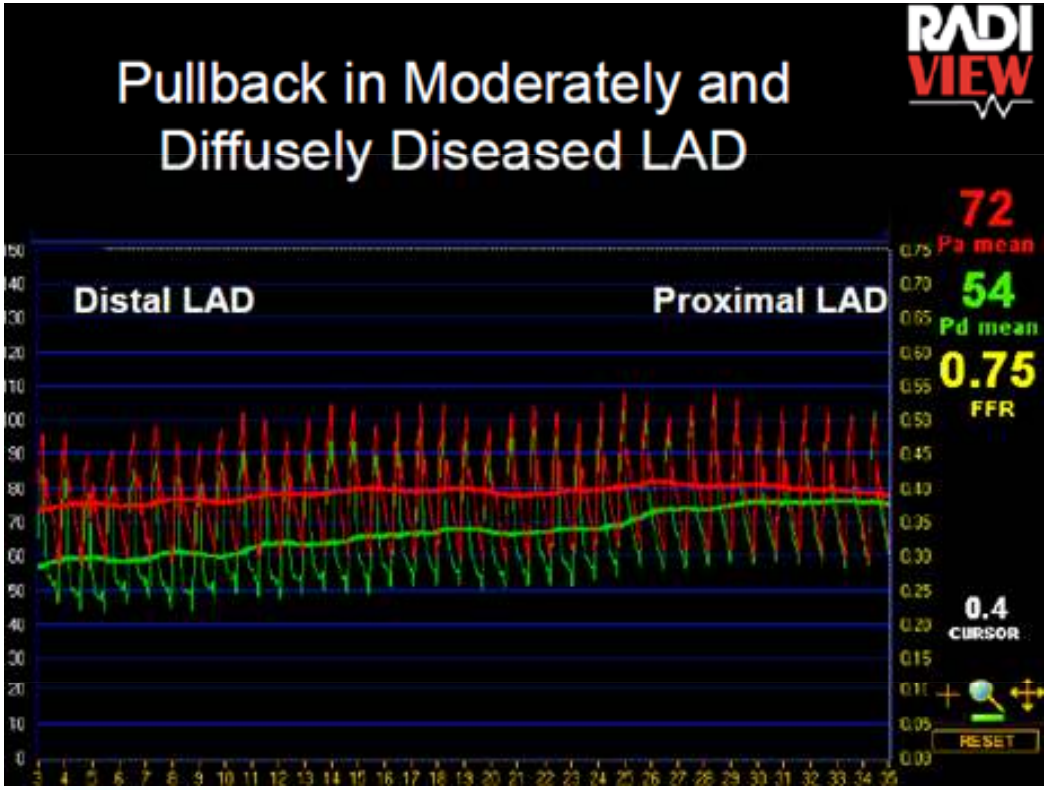
✓**The presence of diffuse disease is often associated with a progressive decrease in coronary pressure and flow, and this can often not be clearly assessed from the angiogram.** In contrast, this decrease in pressure correlates with the total atherosclerotic burden.

✓**In approximately 10% of patients, this abnormal epicardial resistance may be responsible for reversible myocardial ischemia.**

✓**In these patients, chest pain is often considered noncoronary because no single focal stenosis is found, and the myocardial perfusion imaging is wrongly considered false positive**

FFR in diffuse disease

The only way to demonstrate the hemodynamic impact of diffuse disease is to perform a careful pull-back maneuver of the pressure sensor under steady-state maximal hyperemia



In a large multicenter registry of 750 patients, FFR was obtained after technically successful stenting. **A post-PCI FFR value of 0.9 was still present in almost one third of patients (despite the absence of a gradient across the stent), reflecting diffuse disease, and was associated with a poor clinical outcome.**

Patients with a very gradual decline of pressure along the artery (diffuse disease), fundamentally cannot be helped by PCI

FFR never lies?

“False” FFR readings

ALWAYS: error is on high side

Pitfalls and artifacts of fractional FFR measurement

If you know your enemy and yourself, you can win every battle

- ✓Insufficient hyperemia
- ✓Guide catheter problems
- ✓Pressure “drift”
- ✓Whipping
- ✓Spasm/accordion effect
- ✓Introducer in place
- ✓Cursor position

	IC Adenosine	IV adenosine	IC Papaverine
Peak effect	10 s	< 2 min	10 – 30 s
Duration of effect	20 s	Persists till < 2 min after D/C	45 – 60 s
Dose	40 – 60 mcg LCA; 20 – 40 mcg RCA	140 mcg/kg/min; higher dose if given peripherally	16 – 20 mg LCA 12 – 16 mg RCA
Side effects	AV block	AV block Bronchospasm Chest pain ↓ BP; ↑ HR	QT_c; Torsade de pointes / VT / VF
Main advantages	Easy, rapid	Steady-state hyperemia; Pull-back curve	Bolus; Rapid Pullback curve
Main disadvantages / Precautions	No pullback curve. Do not use guide with side-holes.	Central vein; Infusion pump; Time consuming	Torsades / VT / VF; Wait 5 min between measurements; ≤ 3 doses

Maximal Hyperemia is of paramount importance

Insufficient hyperemia

↓

Underestimation of gradient

↓

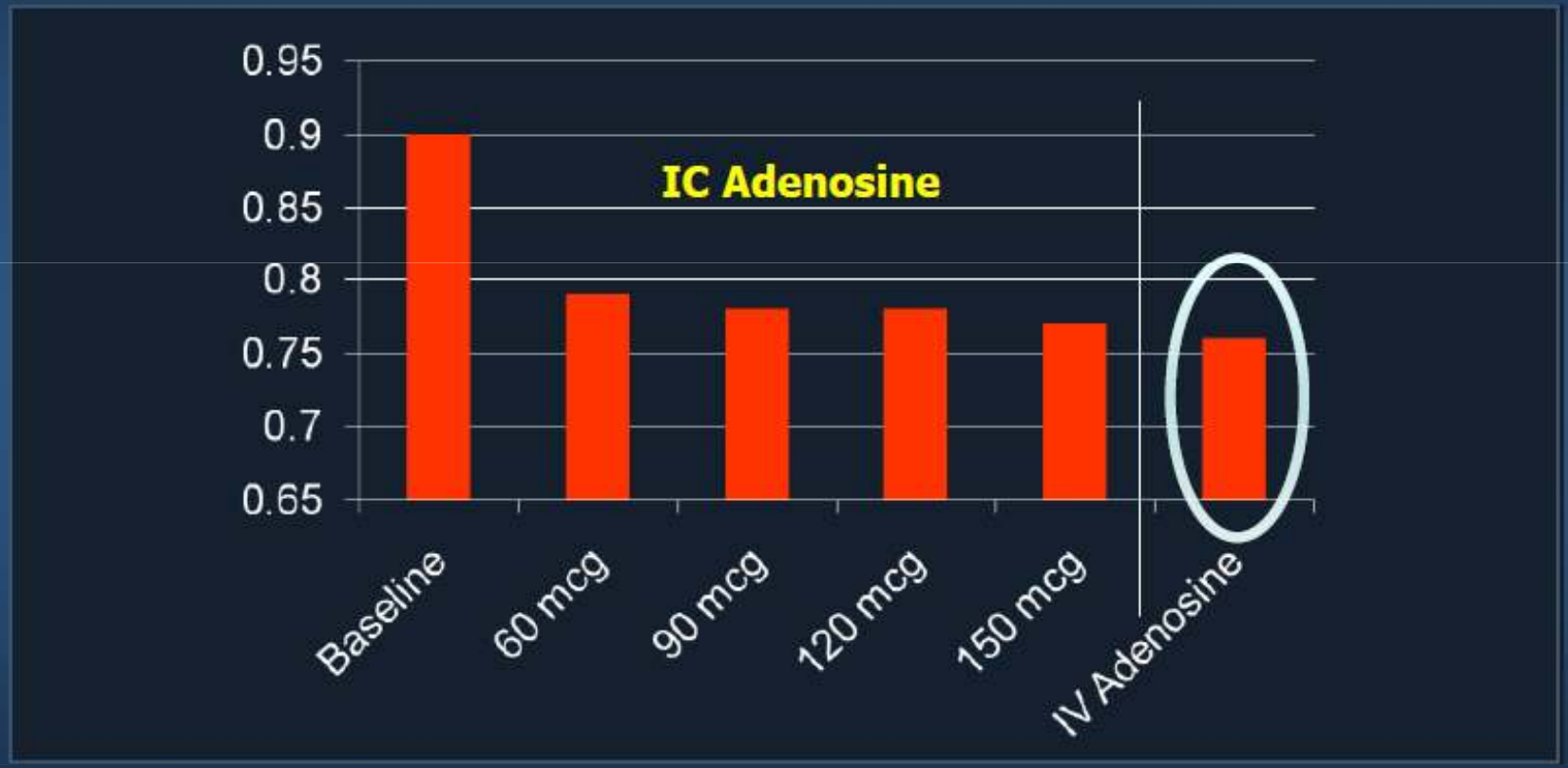
Overestimation of FFR

↓

Underestimation of stenosis severity

Intracoronary vs. Intravenous Adenosine

Higher IC Doses Produce More Hyperemia



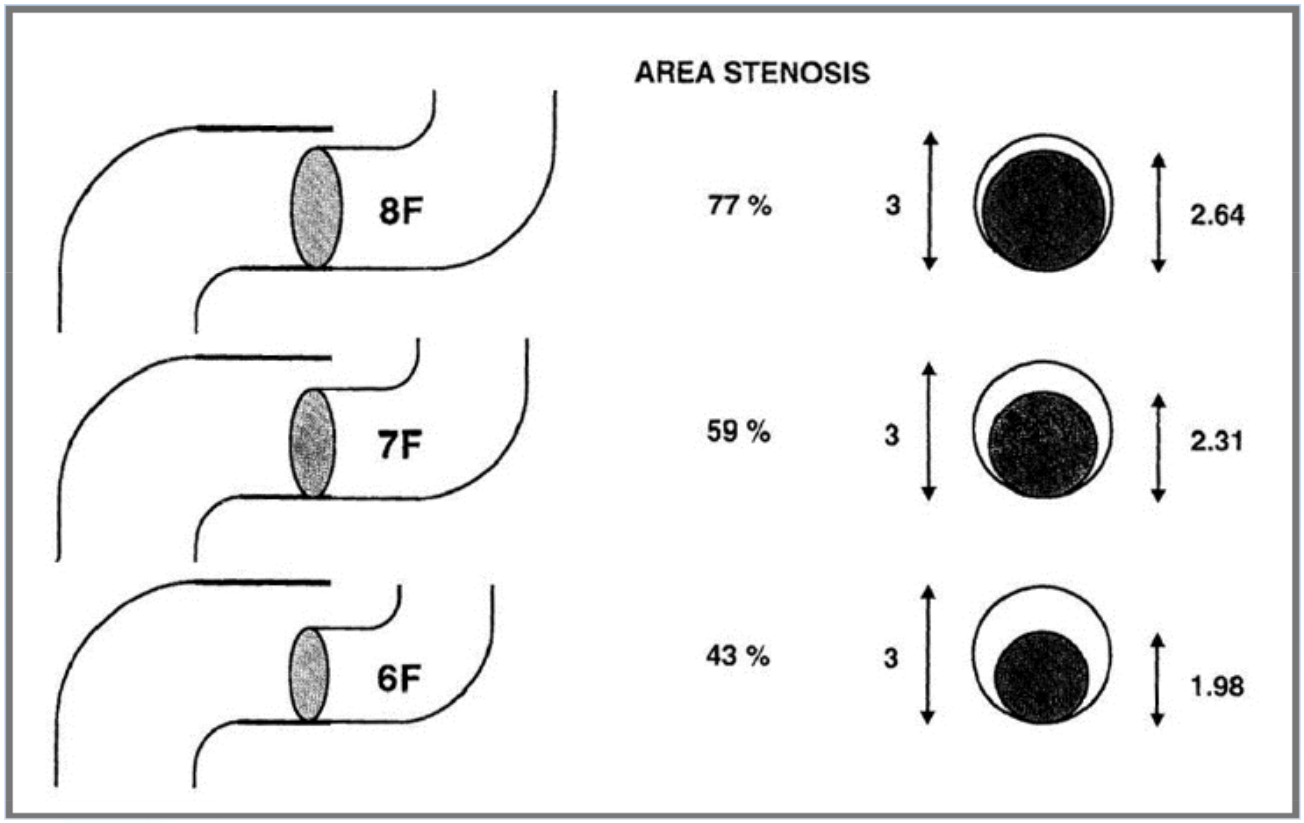
Casella et al, *Am Heart J* 2004

Intravenous Adenosine

Steady State: Maximum Hyperemia

Horizontal Pd/Pa line: Steady State and likely Maximum Hyperemia

Impact of Catheter Size on Hyperemic Flow

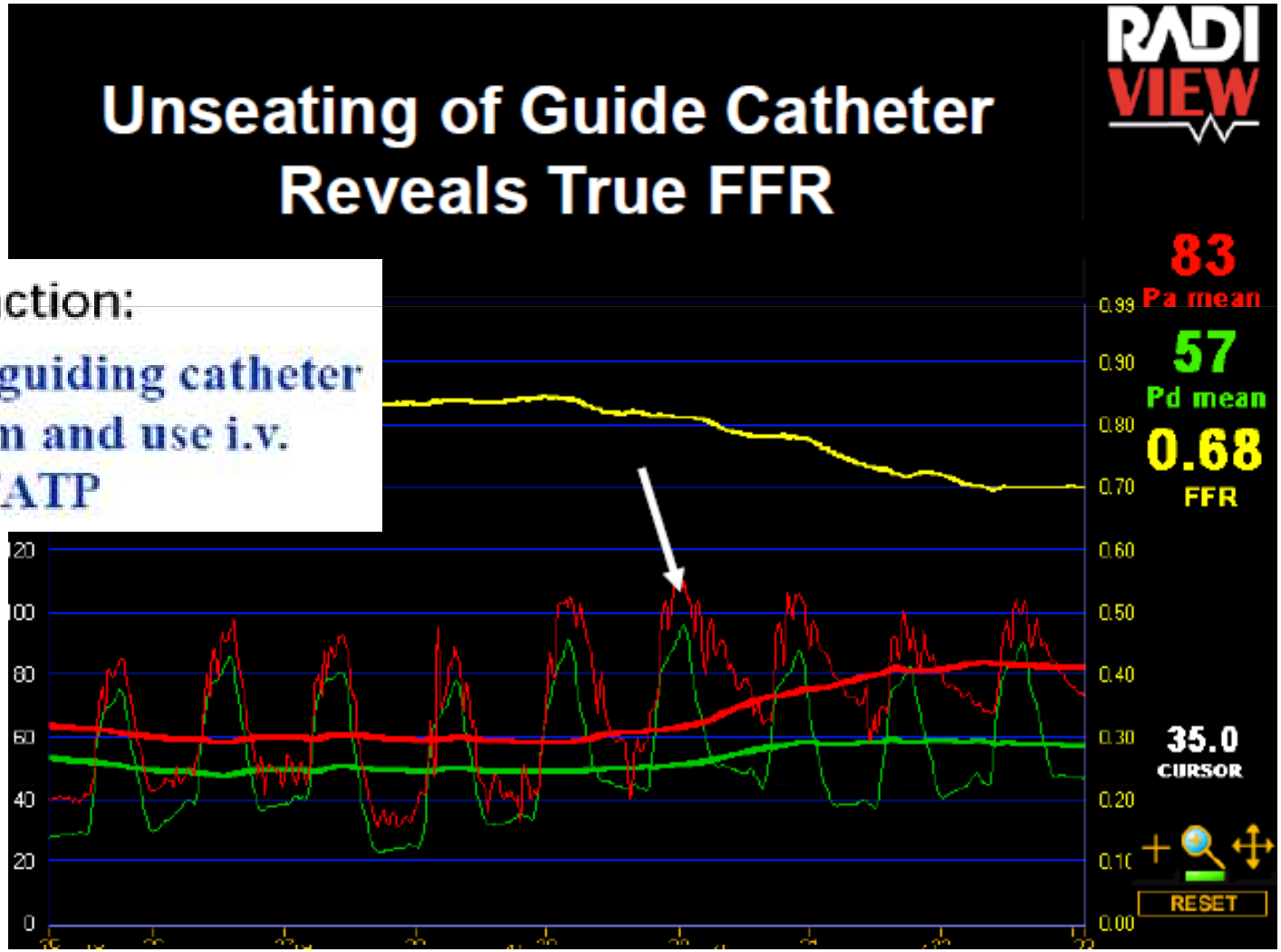


If the guiding catheter is too large, an additional stenosis is created by the catheter, reducing blood flow in the coronary artery

Underestimation of the pressure gradient across the stenosis

Overestimation of the FFR

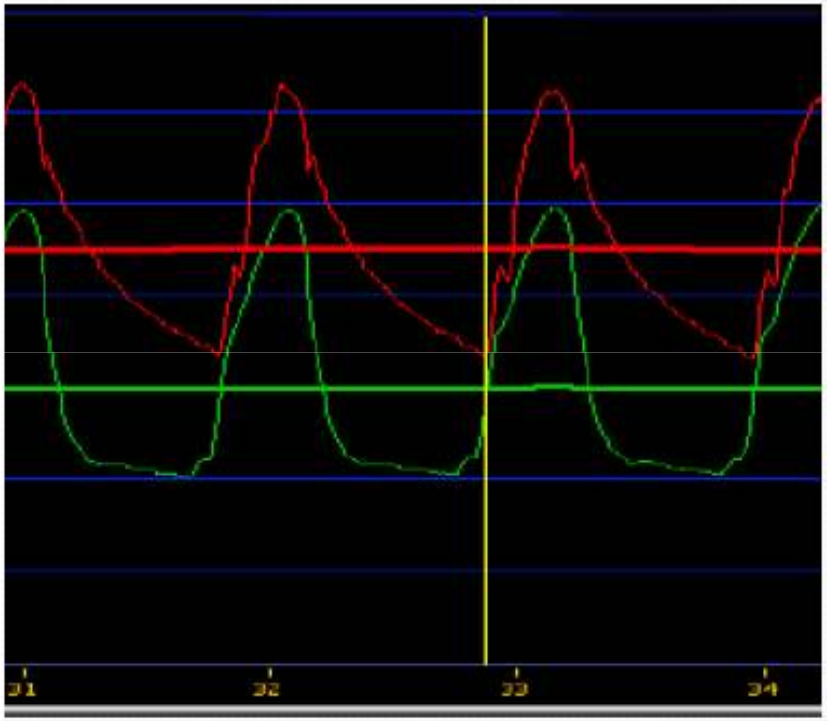
Recognize guiding catheter damping

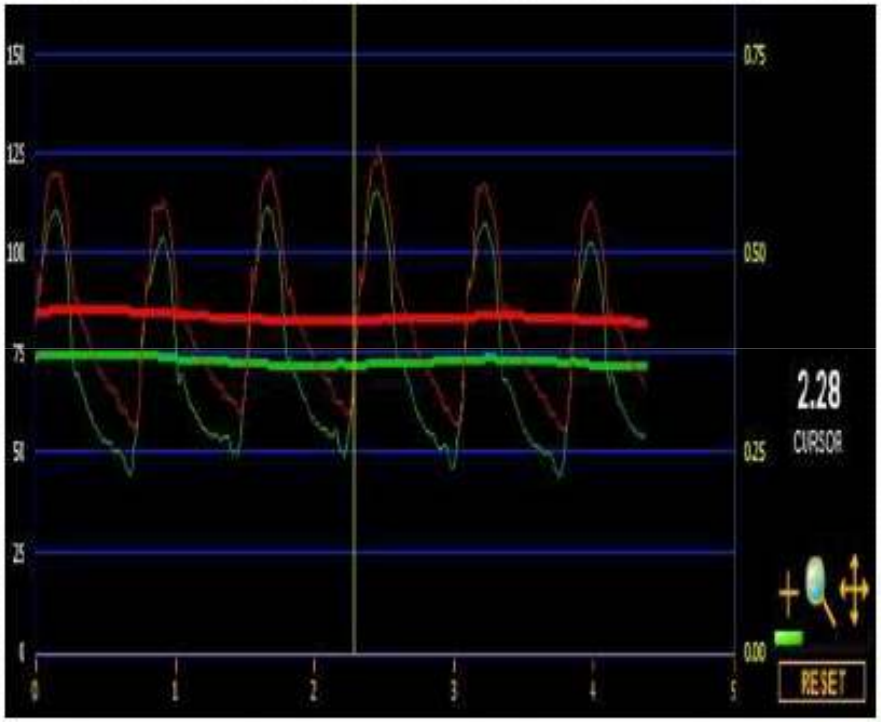


Best to avoid ....

- Using diagnostic catheter
  - more friction with guidewire
  - smaller inner lumen → pressure transmission may be dampened
  - in case of wire causing coronary dissection → will need to exchange for guiding catheter to perform emergency PCI

Recognise pressure "drift"

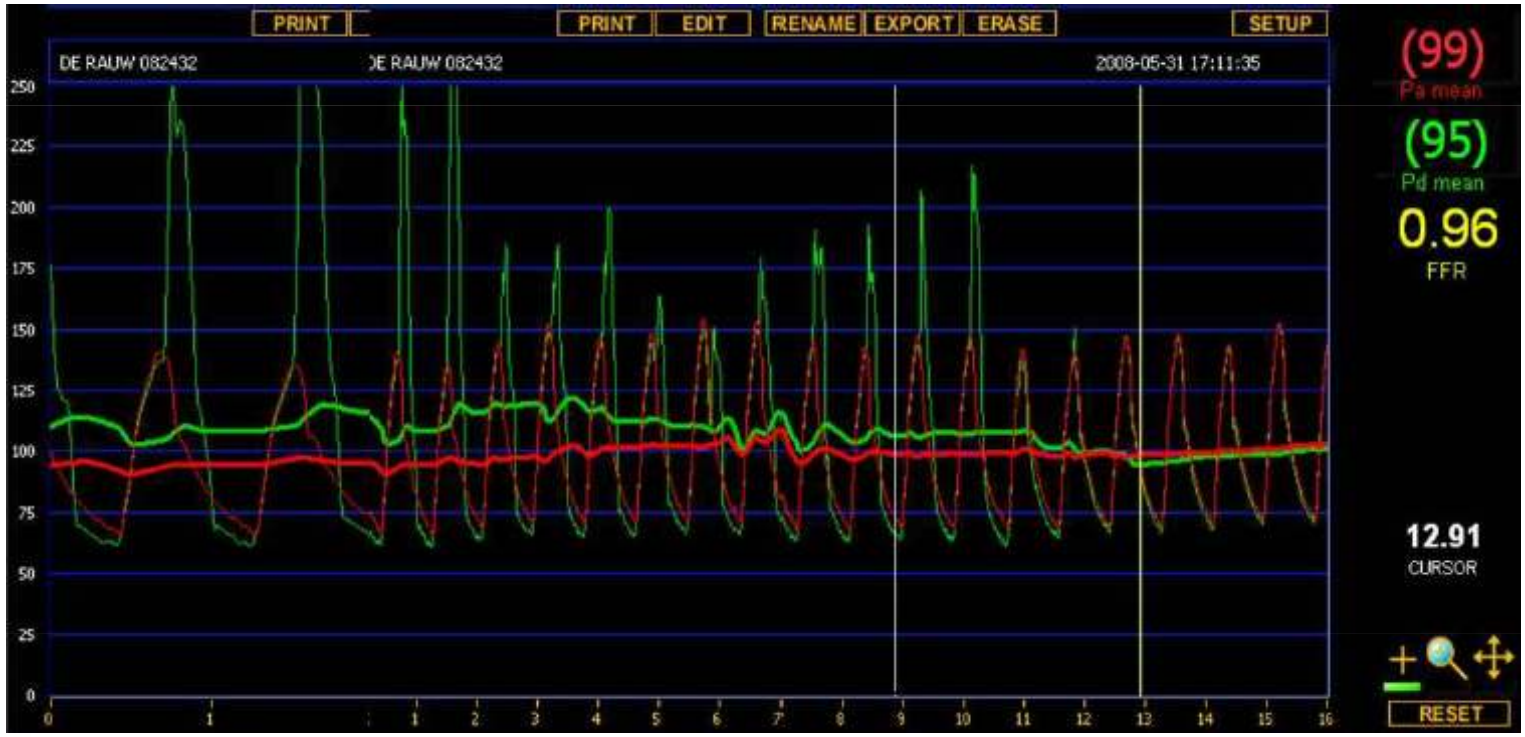




- When a **true gradient** is present the **distal pressure is "ventricularised"**.
- When the difference is due to **pressure drift**,
  - the two tracings have **similar shape**.
  - **Aortic notch** in distal curve (+)

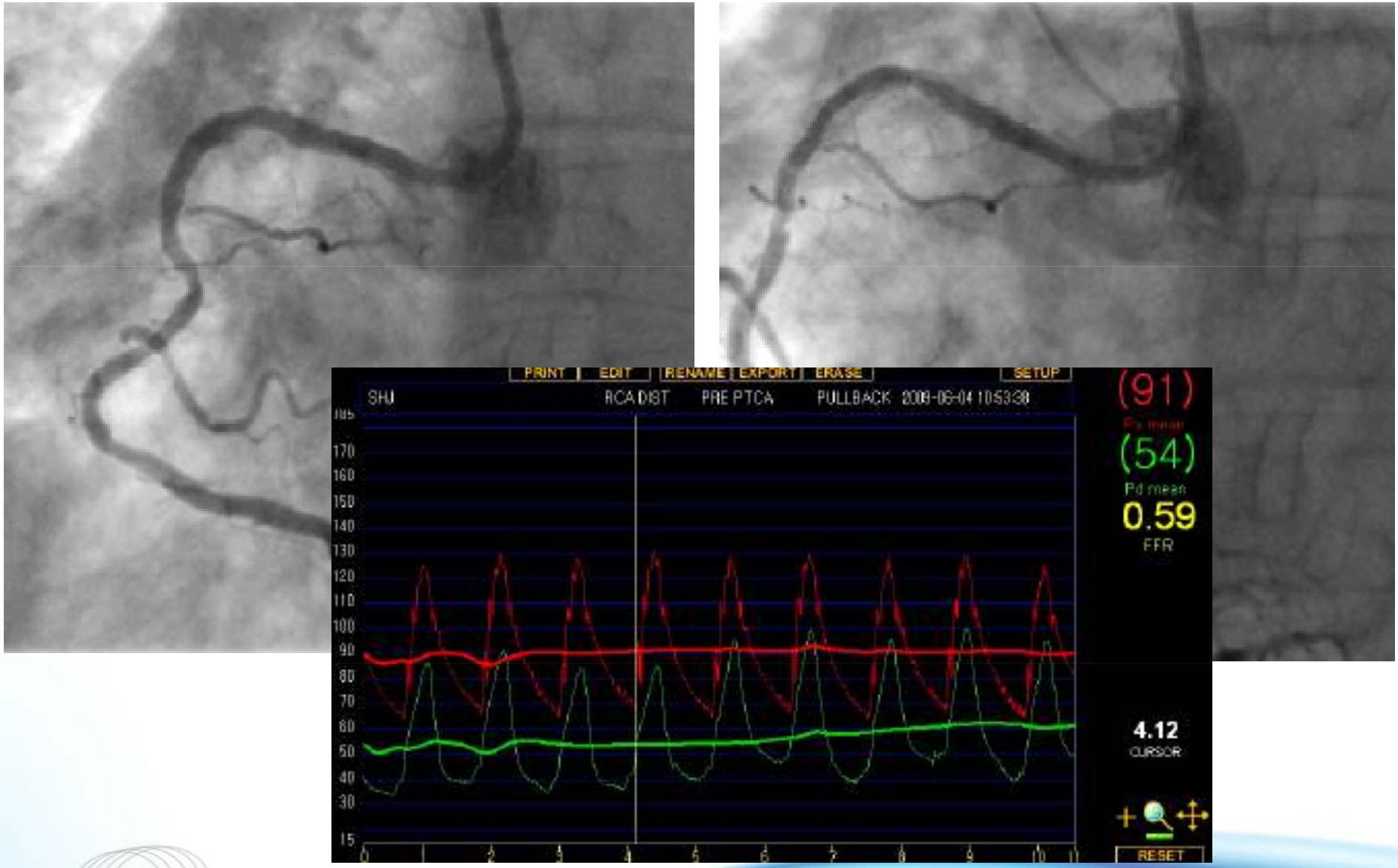
Aware of **“Whipping artifact”**

If the pressure wire sensor hits the coronary wall, “spikes” appear in the waveform - “Whipping"



SOLUTION: pull back or advance the wire 2-3mm

Aware of **“Accordion effect”**



CONCLUSIONS

In pts with stable CAD, presence and extent of myocardial ischemia is associated with the occurrence of adverse events and long-term prognosis.

In most cases, FFR will:

- ✓**Simplify and justify your procedure**
- ✓**Save money (cost-saving in some settings and cost-effective in others)**
- ✓**And most importantly, improve your patient's outcome!**

But……

FFR is a bare number only and this value may definitely determine the future life of our patient

The only guarantee on the validity is the

- Careful training on the steps of measurement (very simple)
- Awareness of the potential pitfalls and artifacts
- Continuous quality control of our FFR practice

- ***Know your patient***

(Symptoms ,Course of history , Ancillary testing)

Give the patient the benefit of the doubt

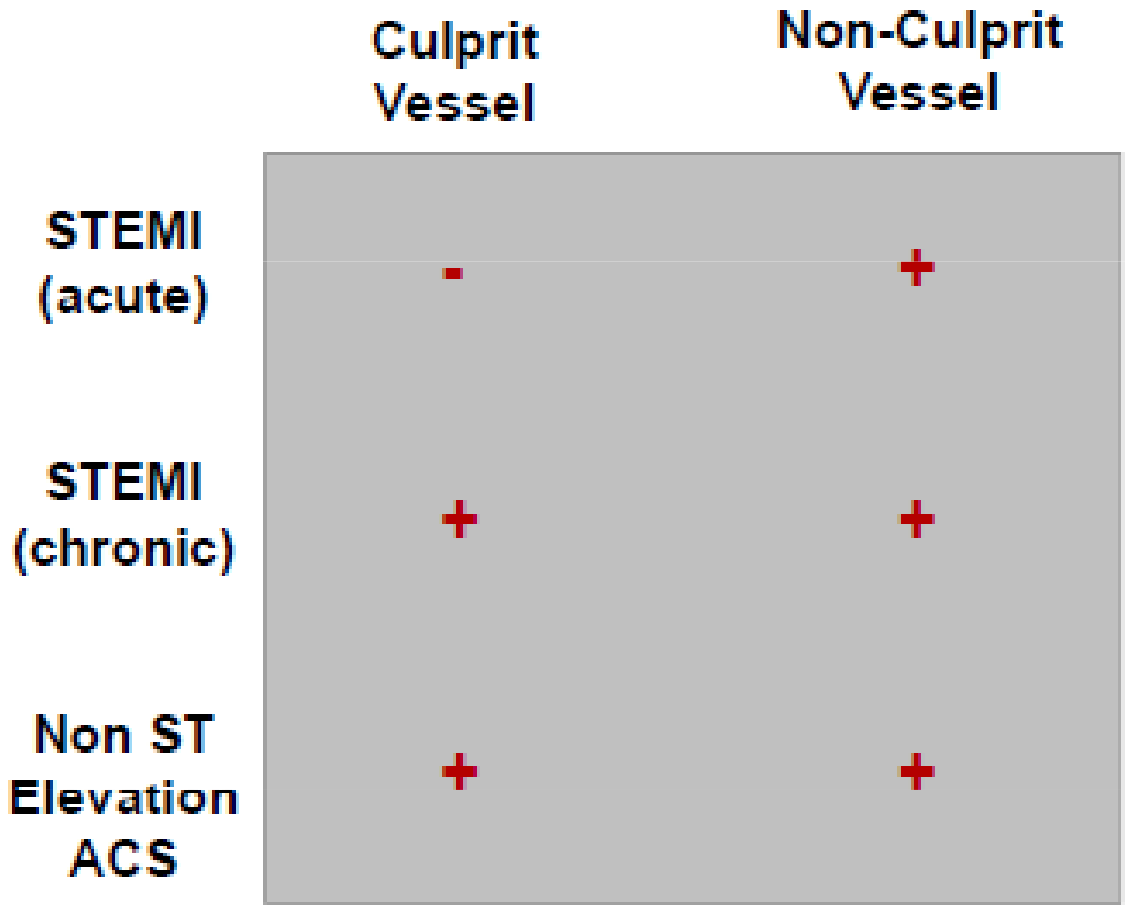
Thank you for your attention !!!!!!!!!

FFR in Acute Coronary Syndromes

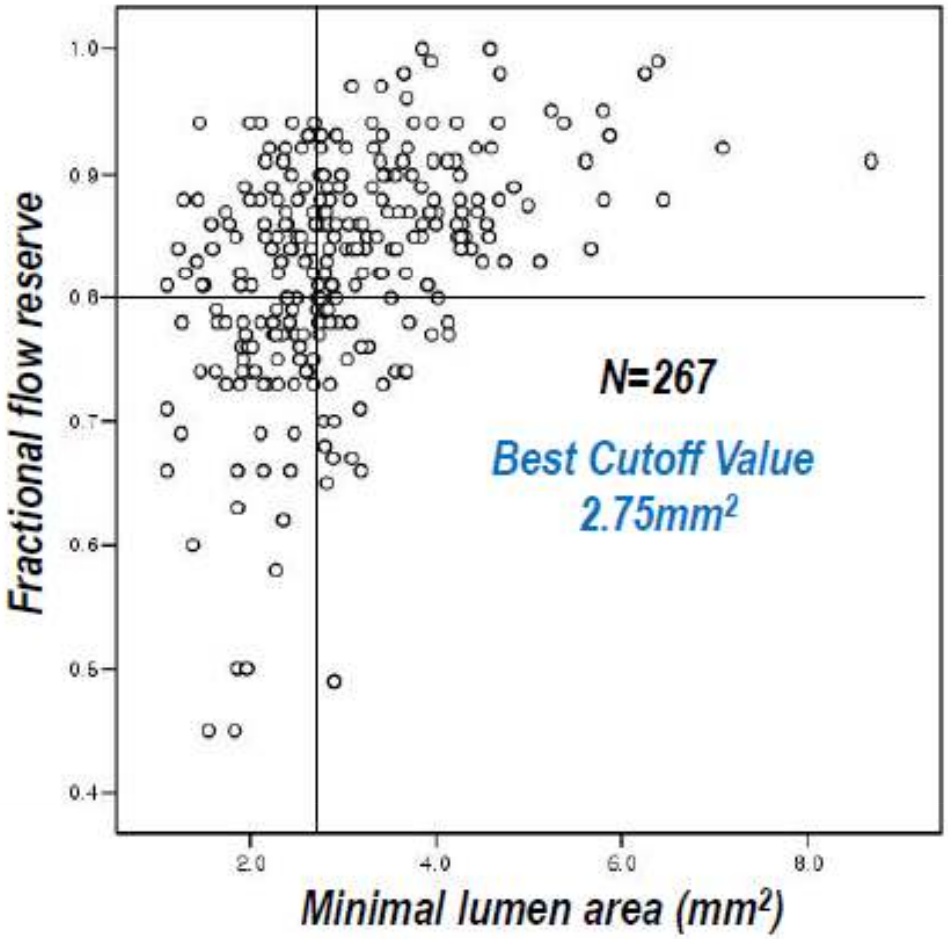
Take Home Messages:

- FFR of the culprit vessel may be unreliable in the setting of STEMI, but can be accurately measured in the non-culprit vessel
- In a less acute MI setting, once microvascular stunning has decreased, FFR at a cut-point of 0.75-0.80 remains accurate
- For a given stenosis, FFR correlates inversely with the mass of viable myocardium supplied
- FFR appears accurate and safe in the setting of NSTE ACS for both culprit and non-culprit vessels

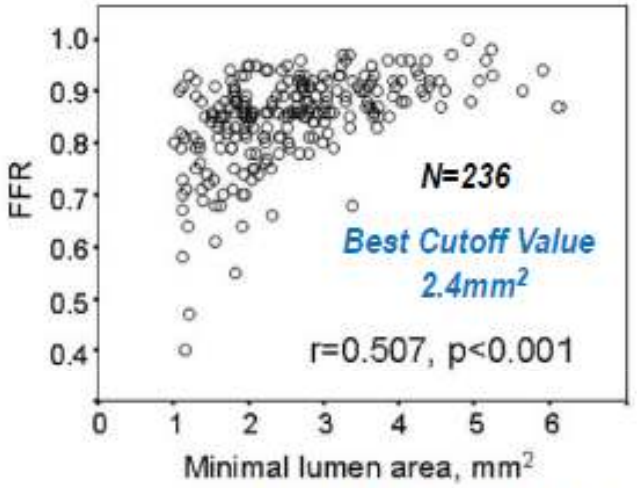
Indications for FFR in Acute Coronary Syndromes



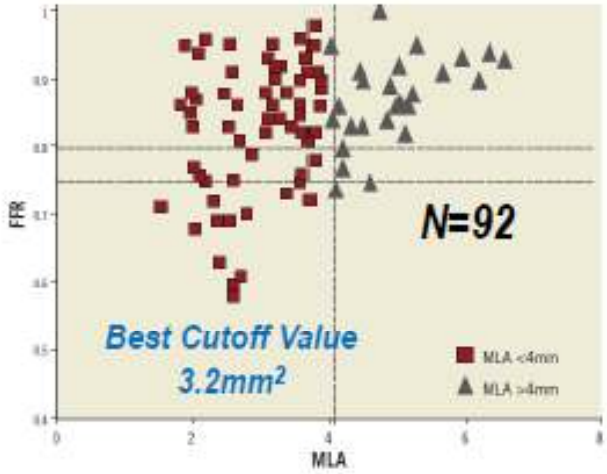
Minimal lumen area vs. Fractional flow reserve



Koo BK & Yang HM, et al. JACC Intv 2011



Kang SJ, et al., Circ CVI, 2011



Ben-Dor I, et al. EuroIntervention 2011

Morphometric Assessment of Coronary Stenosis Relevance With Optical Coherence Tomography

A Comparison With Fractional Flow Reserve and Intravascular Ultrasound

- 61 intermediate stenosis were assessed by FFR
- FFR less than 0.80 was considered significant
- OCT vs IVUS on these vessels for anatomic assessment
- In vessels less than 3 mm in diameter OCT was superior to IVUS in identifying functionally significant lesions
- MLA for IVUS was 2.36 mm^2/OCT 1.95 mm^2
- MLD for IVUS was 1.59 mm/OCT 1.34 mm

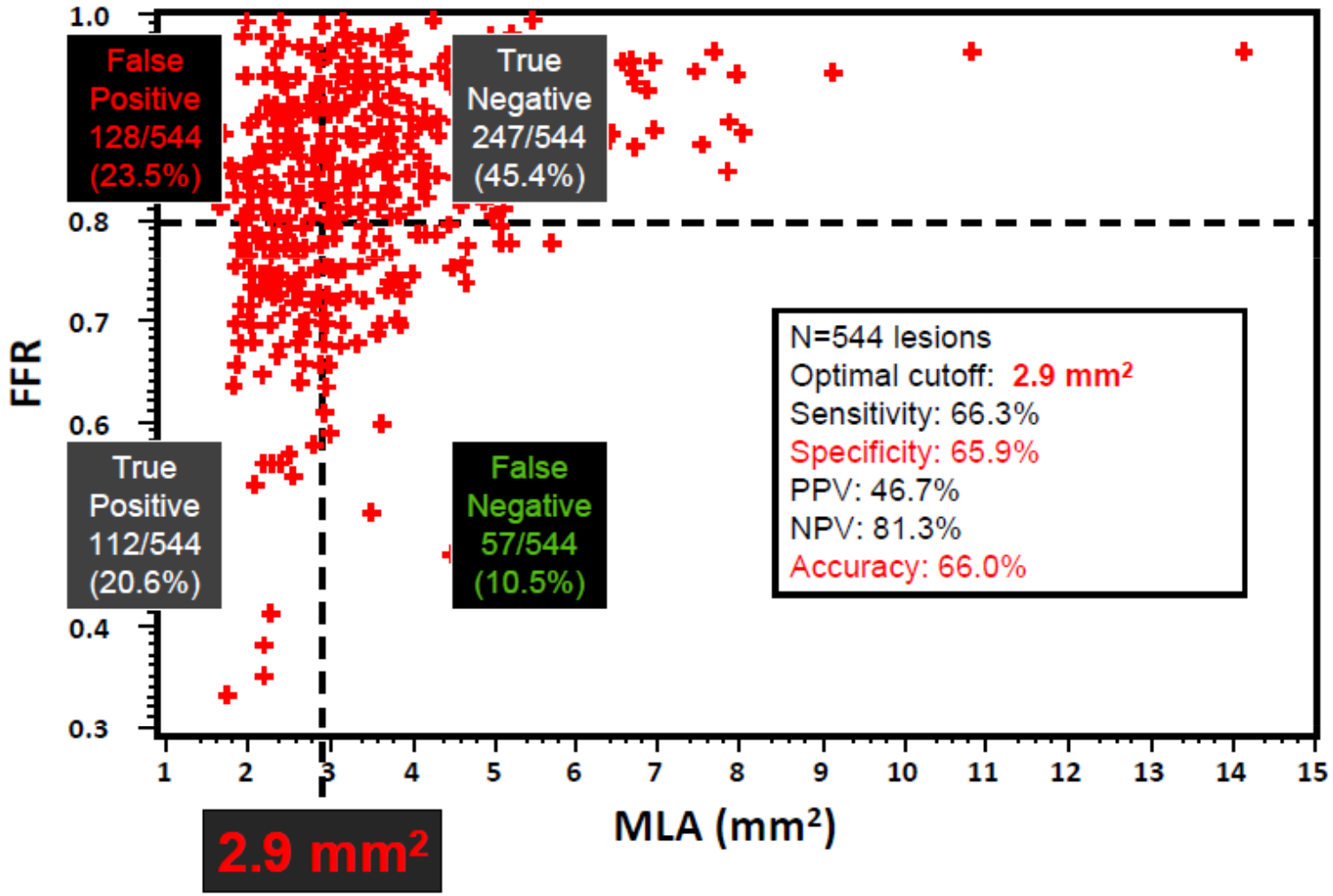
(J Am Coll Cardiol 2012;59:1080–9) © 2012

UCDAVIS

VERDICT

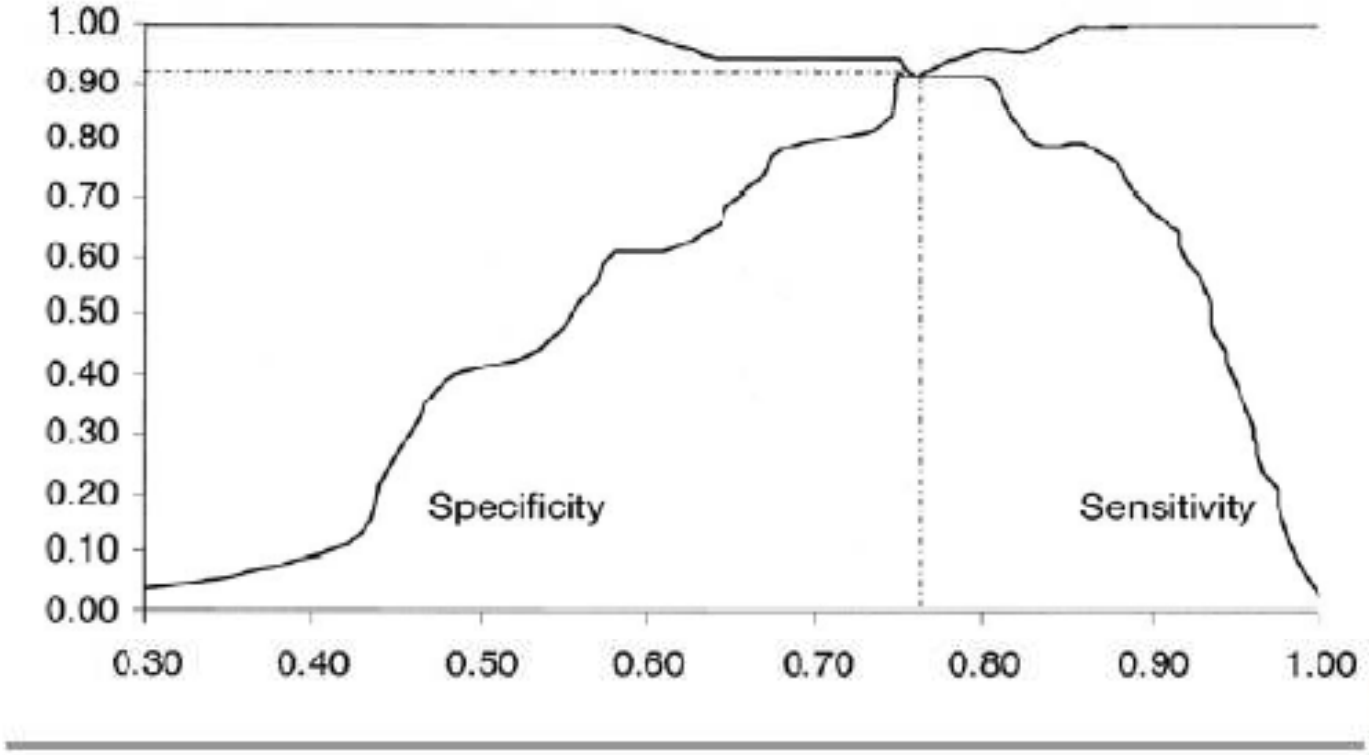
MLA vs. FFR Regression Plot

F1RST



FFR after Recent MI (Culprit Vessel)

Best FFR Cutoff is 0.78



Samady, et al. J Am Coll Cardiol 2006;47:2187-2193.