Ischemic coronary disease without significant coronary lesions. What are the options?

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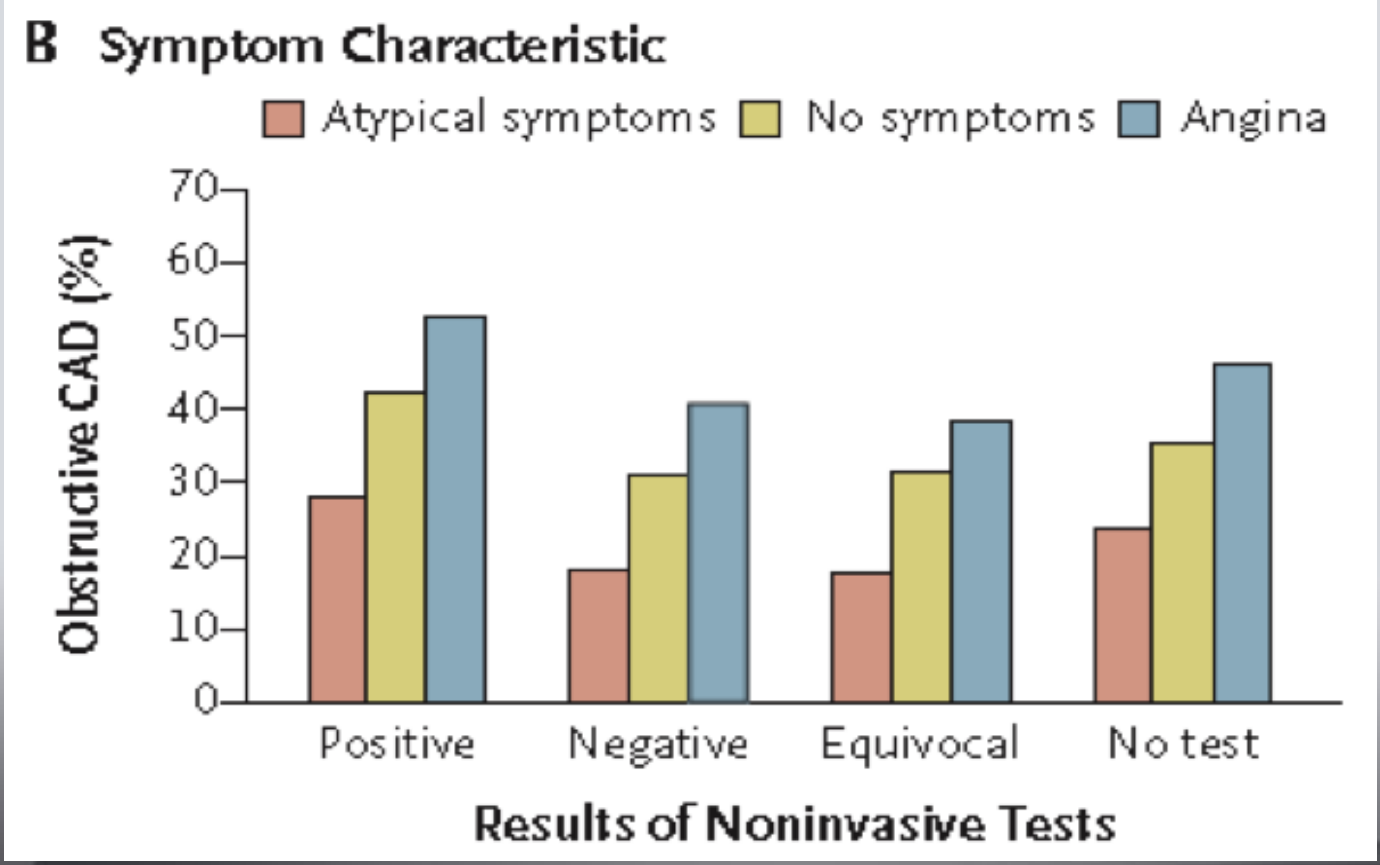
- Coronary angiography timing in stable coronary disease?
- Angiography without significant lesions. Are they all the same?
- Non-invasive ischemia testing. Do we perform it?
- Additional invasive procedures. Which tool for which problem?
- PCI indications. Recommendation and what is the current practice?

When to perform angiography?

- For diagnostic purposes
  - confirmation of the disease: rare
    - impossible to perform non-invasive testing
    - typical angina and reduced EF
    - in special indication (exclusion of coronary disease in pilots etc.)
  - evaluation of disease extent
    - after non-invasive ischemia testing
- For potential therapy other than medical (PCI or CABG)

When to perform angiography?

Risk stratification : clinical evaluation



Patel MR. N Engl J Med 2010;362:886-95

When to perform angiography?

Risk stratification: stress testing, coronary anatomy

Exercise stress ECG[b]	High risk Intermediate risk Low risk	CV mortality >3%/year. CV mortality between 1 and 3%/year. CV mortality <1%/year.
Ischaemia imaging	High risk Intermediate risk Low risk	Area of ischaemia >10% (>10% for SPECT; limited quantitative data for CMR – probably ≥2/16 segments with new perfusion defects or ≥3 dobutamine-induced dysfunctional segments; ≥ 3 segments of LV by stress echo). Area of ischaemia between 1 to 10% or any ischaemia less than high risk by CMR or stress echo. No ischaemia.
Coronary CTA[c]	High risk Intermediate rick Low risk	Significant lesions of high risk category (three-vessel disease with proximal stenoses, LM, and proximal anterior descending CAD). Significant lesion(s) in large and proximal coronary artery(ies) but not high risk category. Normal coronary artery or plaques only.

Eu Heart J 2013:doi:10.1093/eurheartj/eht296

When to perform angiography?

Risk stratification: ventricular function

A resting transthoracic echocardiogram is recommended in all patients for: a) exclusion of alternative causes of angina; b) identification of regional wall motion abnormalities suggestive of CAD; c) measurement of LVEF for risk stratification purpose; d) evaluation of diastolic function.	I	B

Eu Heart J 2013:doi:10.1093/eurheartj/eht296

Angiography without significant lesions

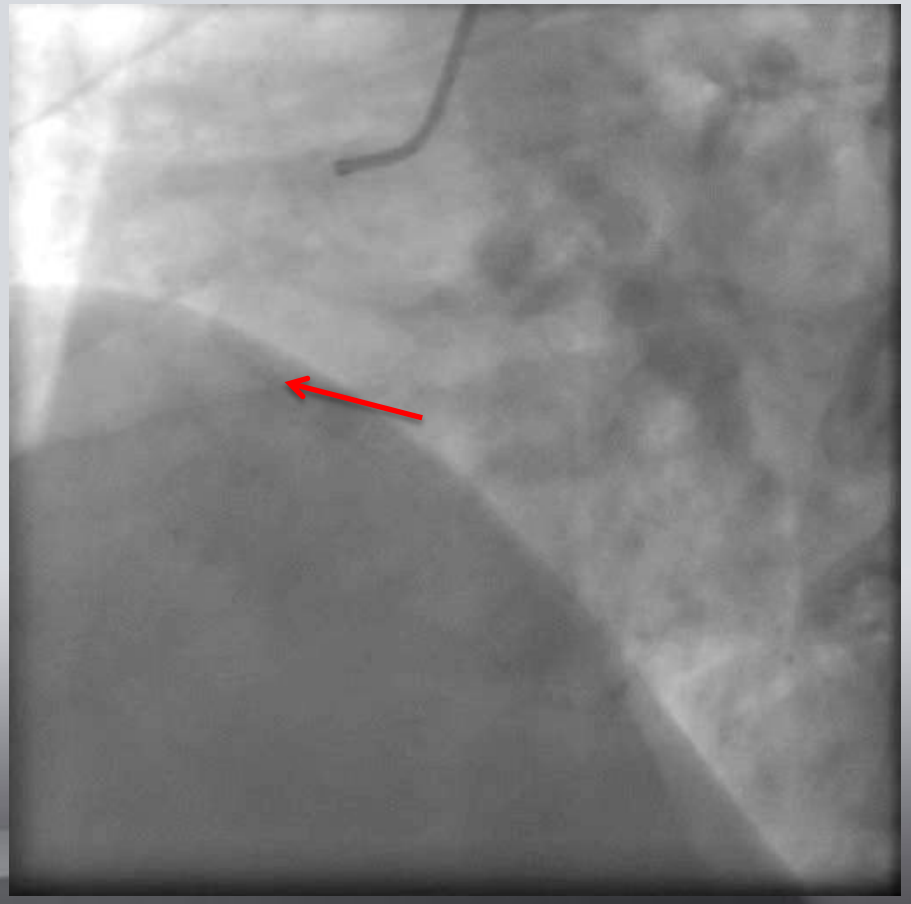
- Case 1

- Case 2

Angiography without significant lesions

- Case 3

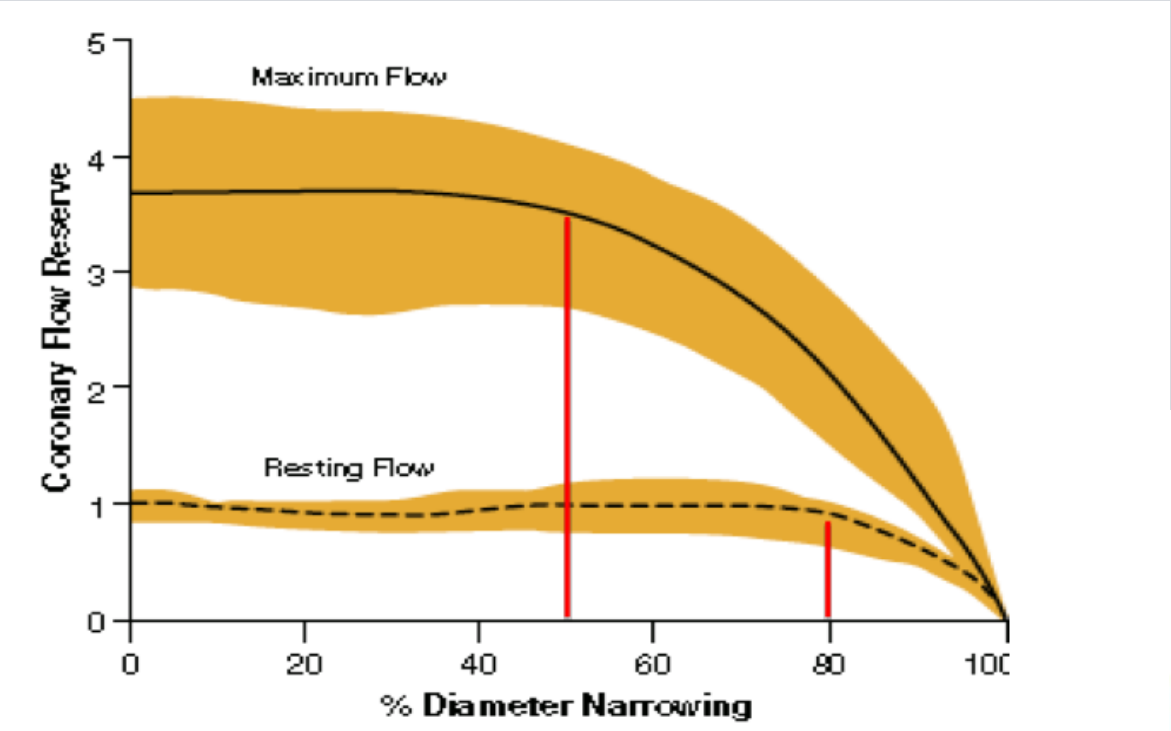
- Case 4

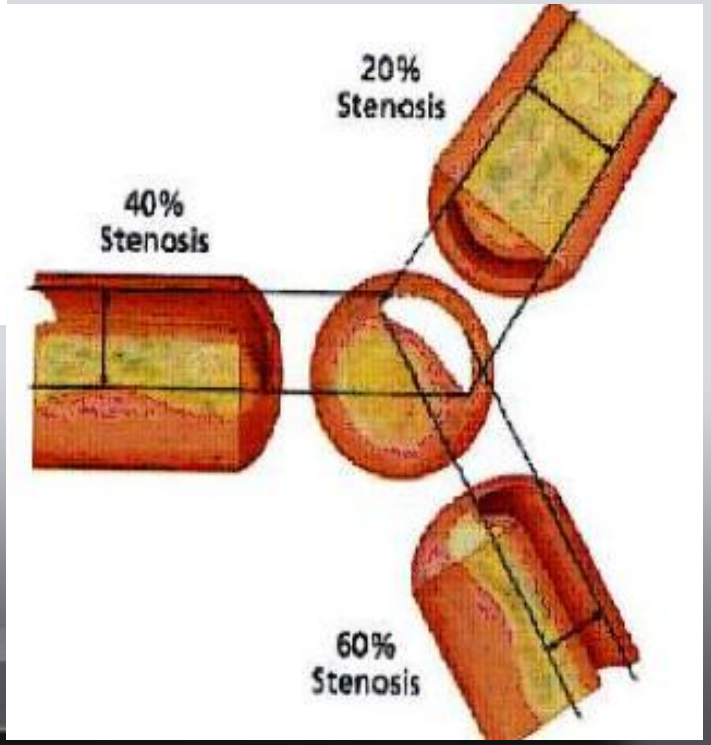


Angiography without significant lesions

- Macro vascular lesions < 50%
- Micro vascular disease
  - in 20% of patients co-exist with macro vascular disease
- Vaso-spastic disease
  - more in the area of instable angina

Angiographic stenosis and ischemia





Non-invasive ischemia testing

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

Results In the United States, 44.5% (n=10 629) of patients underwent stress testing within the 90 days prior to elective PCI. There was wide regional variation among

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

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

Non-invasive ischemia testing

	Diagnosis of CAD	
	Sensitivity (%)	Specificity (%)
Exercise ECG [a, 91, 94, 95]	45–50	85–90
Exercise stress echocardiography[96]	80–85	80–88
Exercise stress SPECT[96-99]	73–92	63–87
Dobutamine stress echocardiography[96]	79–83	82–86
Dobutamine stress MRI[b, 100]	79–88	81–91
Vasodilator stress echocardiography[96]	72–79	92–95
Vasodilator stress SPECT[96, 99]	90–91	75–84
Vasodilator stress MRI[b, 58, 100-102]	67–94	61–85
Coronary CTA[c, 103-105]	95–99	64–83
Vasodilator stress PET[97, 99, 106]	81–97	74–91

Eu Heart J 2013:doi:10.1093/eurheartj/eht296

Can CT angiography replace invasive approach?

Recommendations	Class [a]	Level [b]
Coronary CTA should be considered as an alternative to stress imaging techniques for ruling out SCAD in patients within the lower range of intermediate PTP for SCAD in whom good image quality can be expected.	IIa	C
Coronary CTA should be considered in patients within the lower range of intermediate PTP for SCAD after a non conclusive exercise ECG or stress imaging test or who have contraindications to stress testing in order to avoid otherwise necessary invasive coronary angiography if fully diagnostic image quality of coronary CTA can be expected.	IIa	C
Coronary calcium detection by CT is not recommended to identify individuals with coronary artery stenosis.	III	C
Coronary CTA is not recommended in patients with prior coronary revascularization.	III	C
Coronary CTA is not recommended as a 'screening' test in asymptomatic individuals without clinical suspicion of coronary artery disease.	III	C

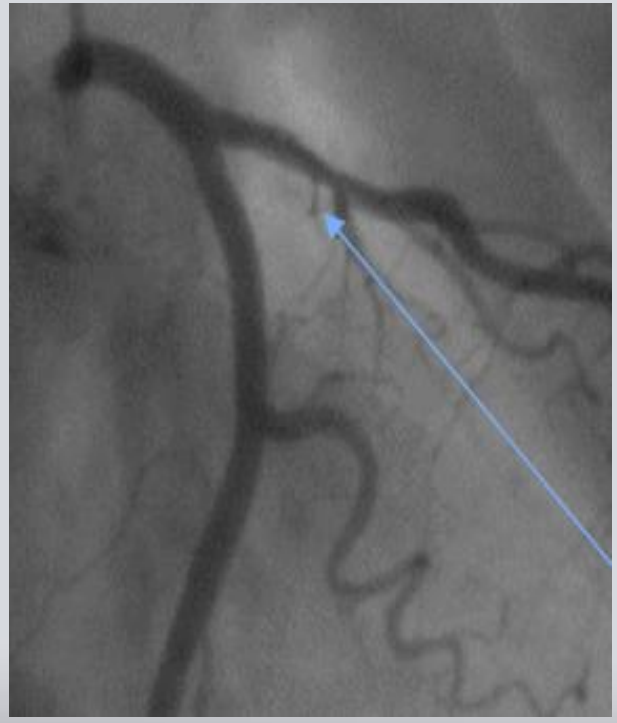
Still not, in majority of patients

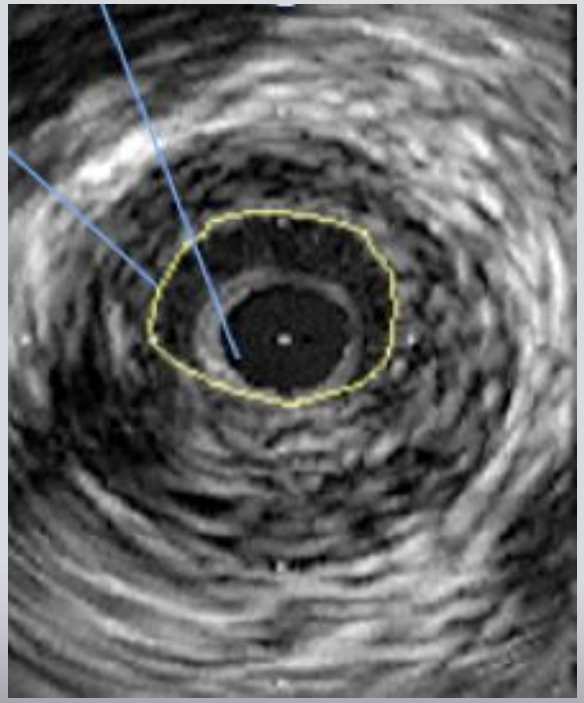
Eu Heart J 2013:doi:10.1093/eurheartj/eht296

Non angiographic invasive evaluation of stenosis

- Intra vascular ultrasound- IVUS
- Virtual histology-VH
- Optical coherence tomography –OCT and Near Infrared spectroscopy-NIRS
- Fractional flow reserve-FFR

Lesion assessment with IVUS





In proximal LAD, RCA and CX cut off value for significant stenosis MLA less than 3mm2

For LMCA MLA less than 6mm2 cause ischemia and must be treated

Tagaki et al Circulation 1999;100:250-5

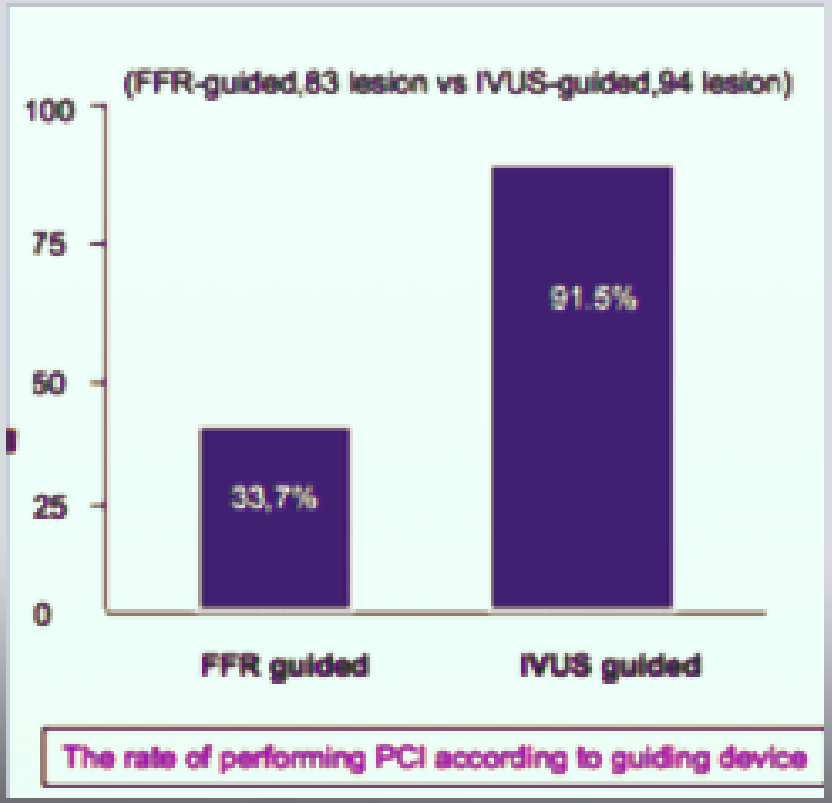
How could IVUS help?

FFR and IVUS guided PCI

in 167 patients with intermediate coronary stenosis

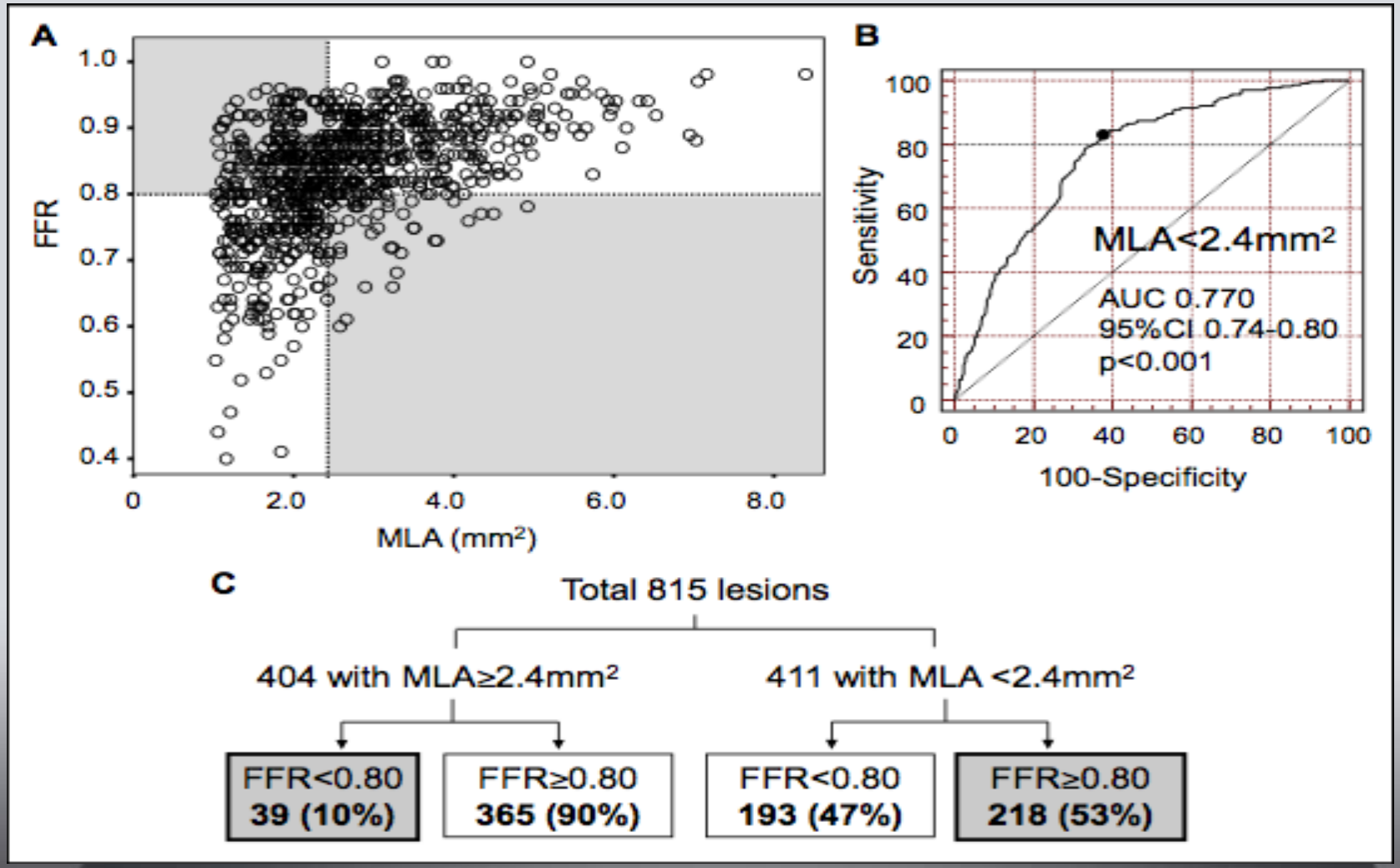
	FFR 0,80	IVUS 4mm2
N	83	94
Stenosis	51%	52%
Lenght	24 mm	24mm
Revascularisation	33,7%	91,3%
MACE	3,6%	3,2%

p= 0,001



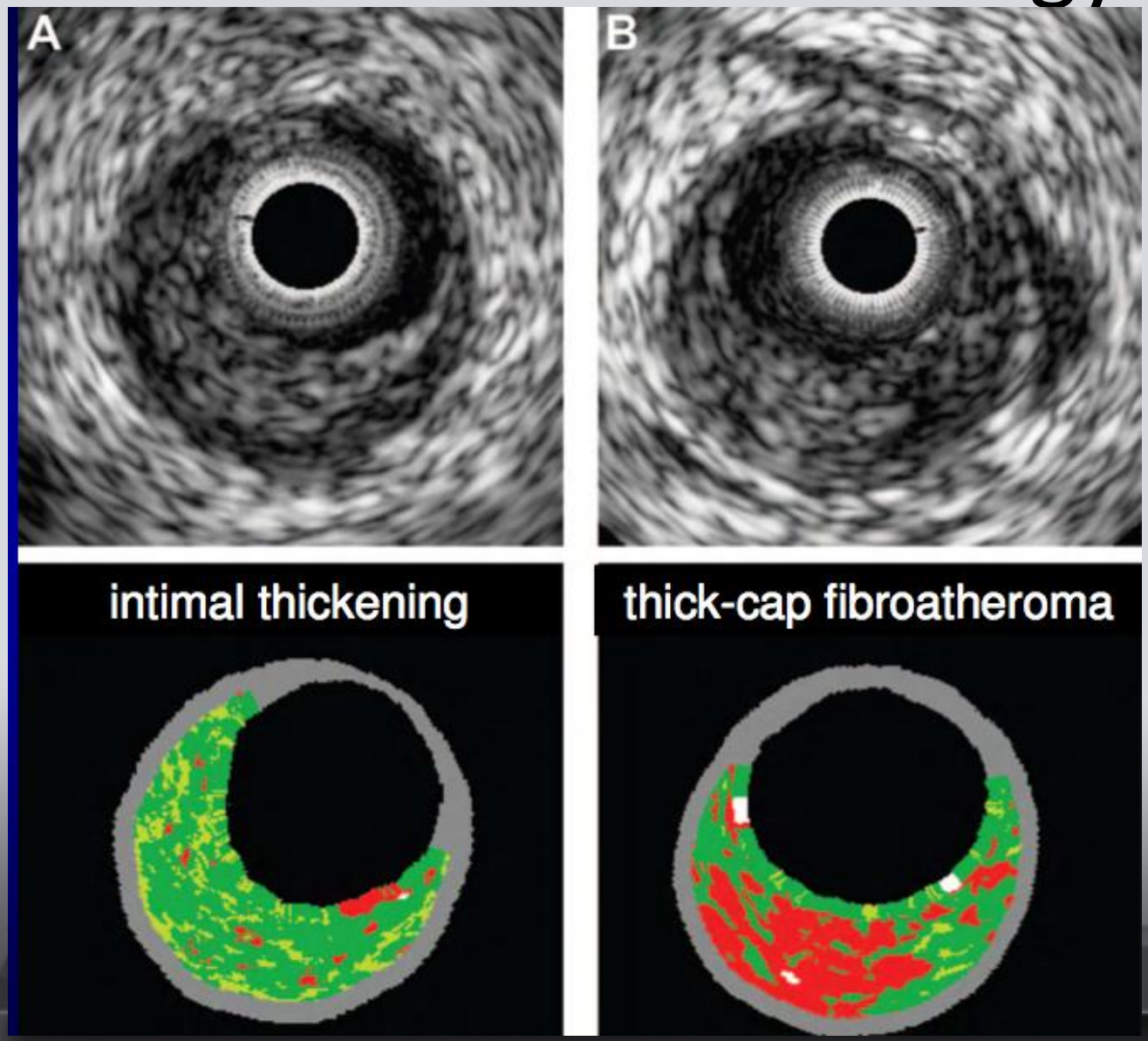
Nam CW et al JACC 2010 Aug;3(8):812-7

IVUS versus FFR



Kang SJ. **Am J Cardiol 2012;109:947–953**

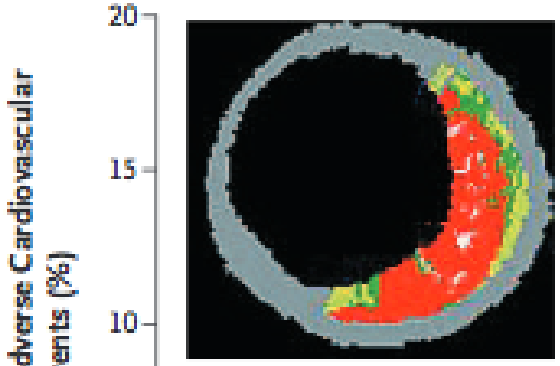
IVUS and virtual histology (VH)



VH-IVUS (radiofrequency) plaque composition, especially detection of the lipid-rich necrotic core

Maehara A
Circ Cardiovasc Intervent.
2009:2:482-9

Virtual hystology

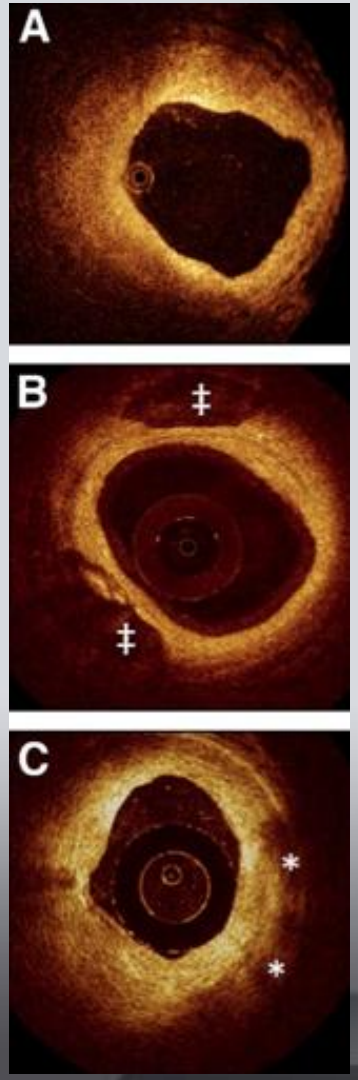


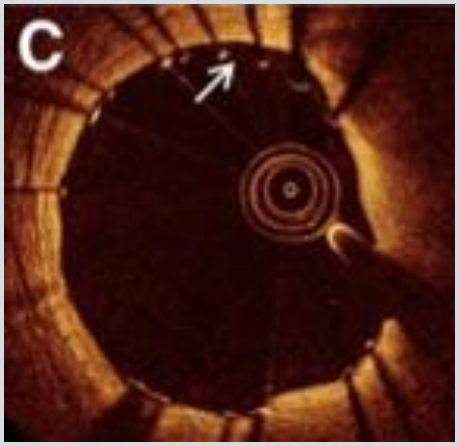
Lesion hazard ratio (95% CI)	3.90 (2.25–6.76)	6.55 (3.43–12.51)	10.83 (5.55–21.10)	11.05 (4.39–27.82)
P value	<0.001	<0.001	<0.001	<0.001
Prevalence (%)	46.7	15.9	10.1	4.2

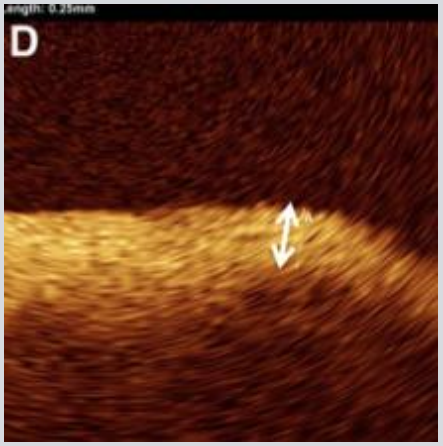
PROSPECT study

Stone GW Engl J Med 2011;364:226-35.

OCT and IVUS differences



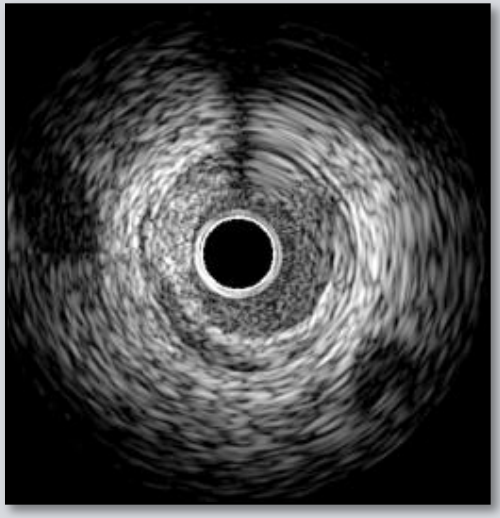


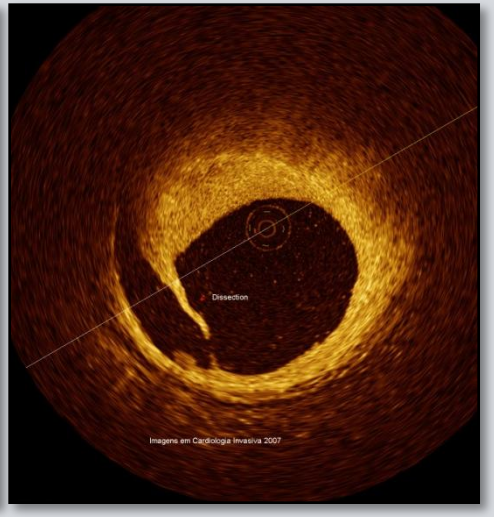


	OCT	IVUS
Resolution	15 µm	100 µm
Penetration*	2 mm	10 mm

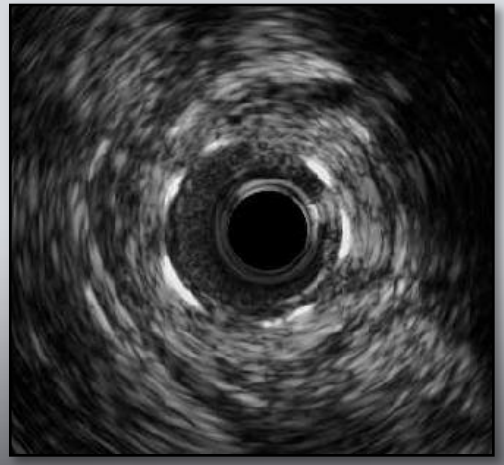
Hiram G J Am Coll Cardiol Intv, 2009; 2:1035-1046,

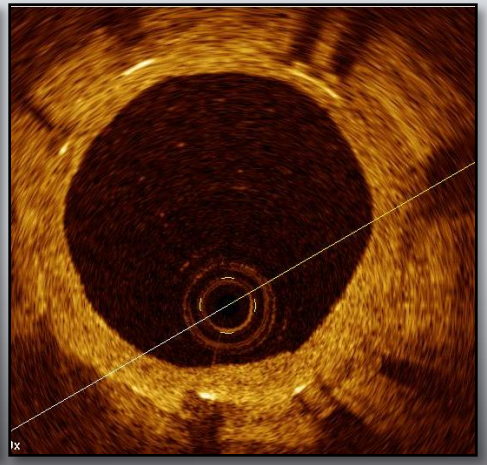
IVUS and OCT comparison





- Edge dissection during stent implantation





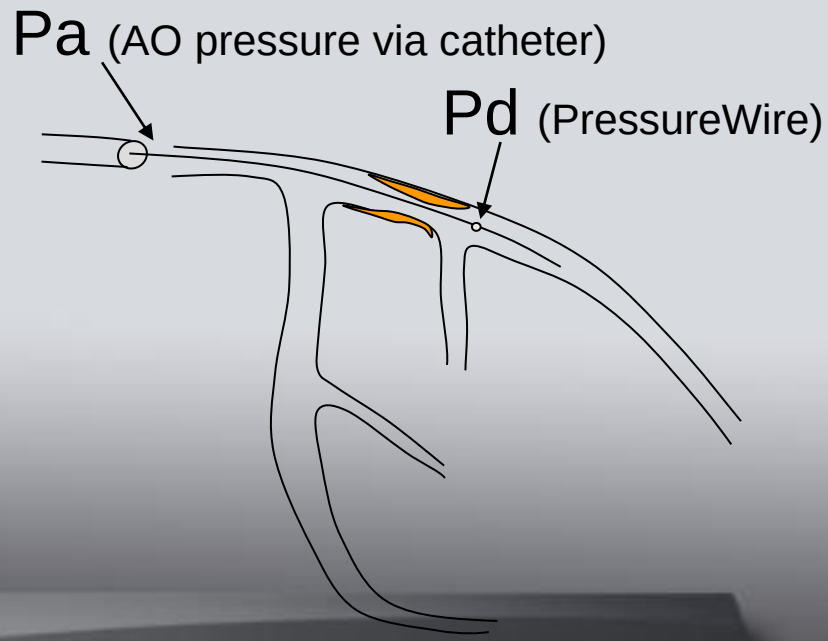
- Neointimal growth on previously implanted stent at follow-up

Fractional flow reserve /FFR

Definition of FFR
“Maximum achievable blood flow in stenotic coronary artery divided by
Maximum blood flow in the same artery without stenosis”

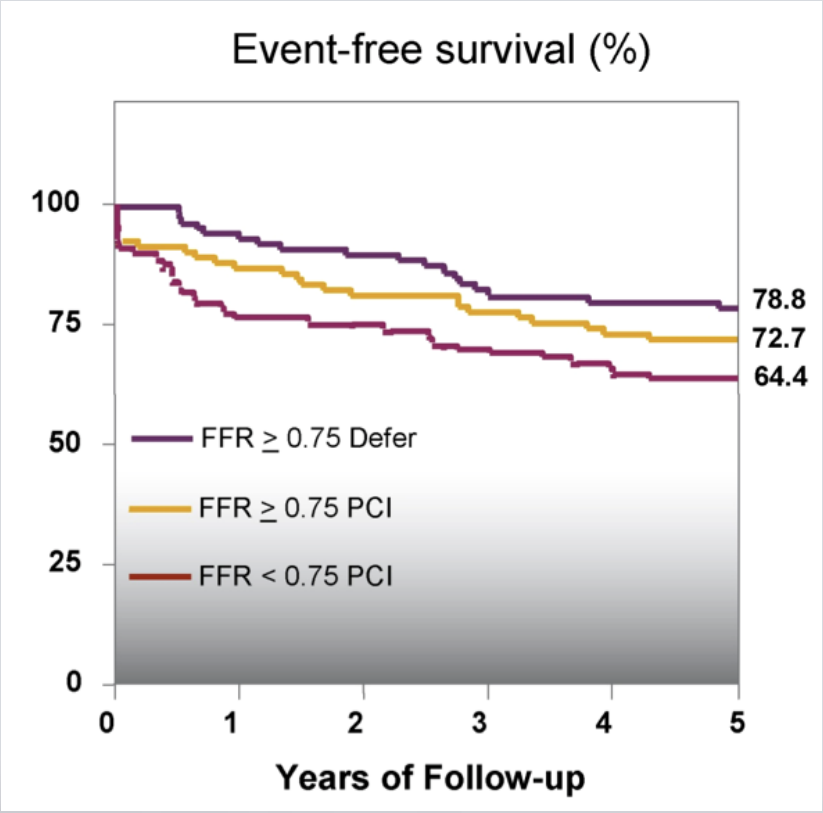
$$FFR = \frac{Pd}{Pa}$$

At maximum hyperemia



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

FFR: DEFER study

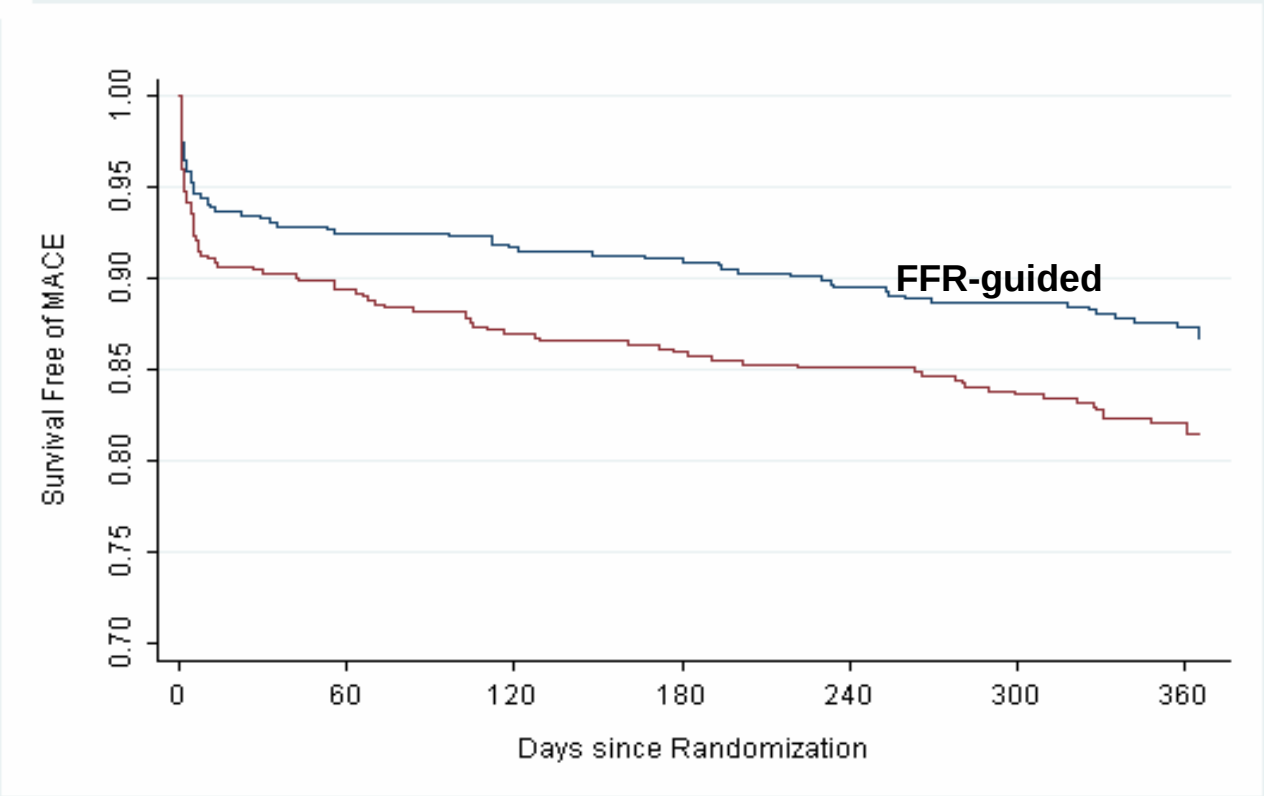


The risk of "non-significant" stenoses to cause death or AMI is < 1 % per year

In patients with one vessel disease and FFR more than 0.75, deferral of revascularization is at least as good as performance of an intervention.

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

FFR: FAME study



In patients with MVD, FFR significantly reduce death, MI, and repeat revascularization at 2 years (22,4% v 17,9%p=0,08)

Pijls et al. J Am Col. Cardiol 2010; 56: 177 - 184.

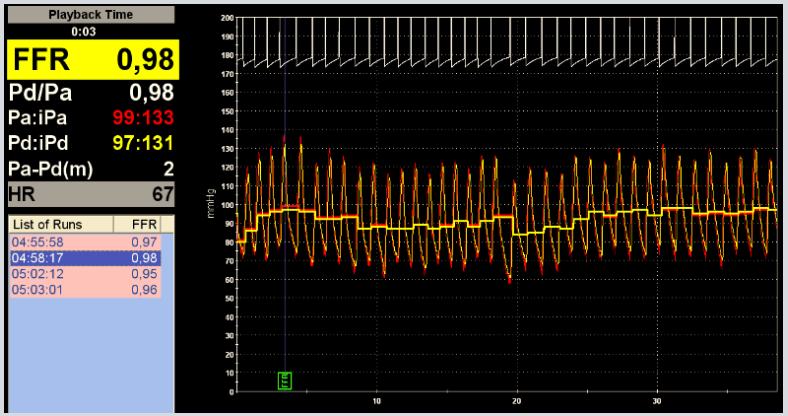
The FAME Study – Cost Savings Data

Improved Outcomes at Lower Costs

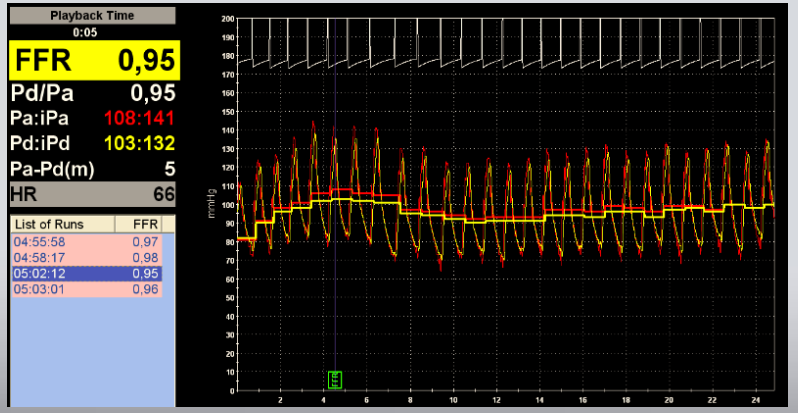
Bootstrap simulation indicated that the FFR-guided strategy was cost-saving in 99.8% and cost-effective in all 1,000 scenarios.

Tonino et al. N Engl J Med 2009; 360:213-224;

FFR



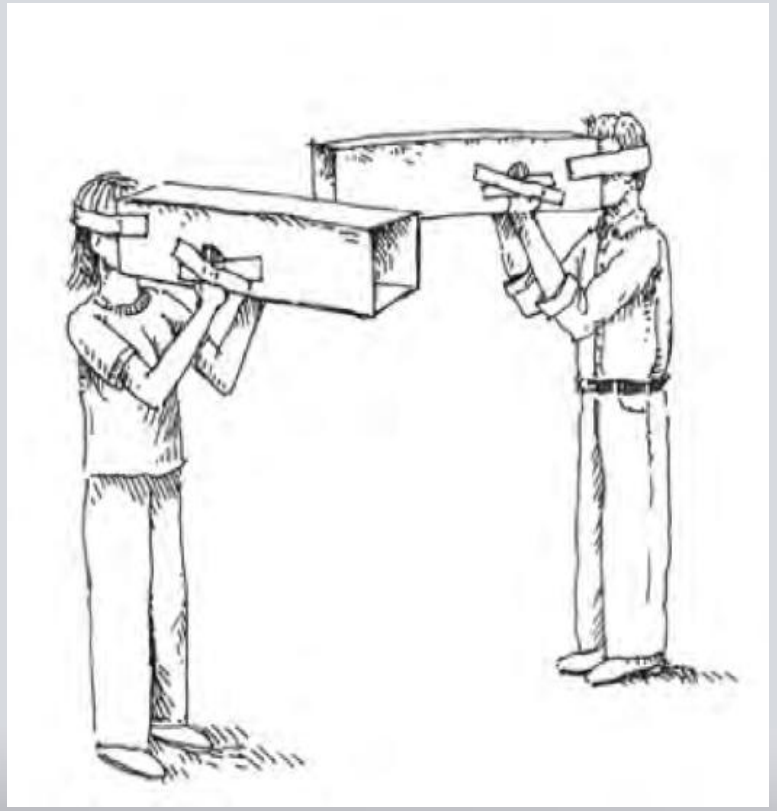
Proximal stenosis



Distal stenosis

FFR (100 and 120 mcg adenosin i.c. bolus)

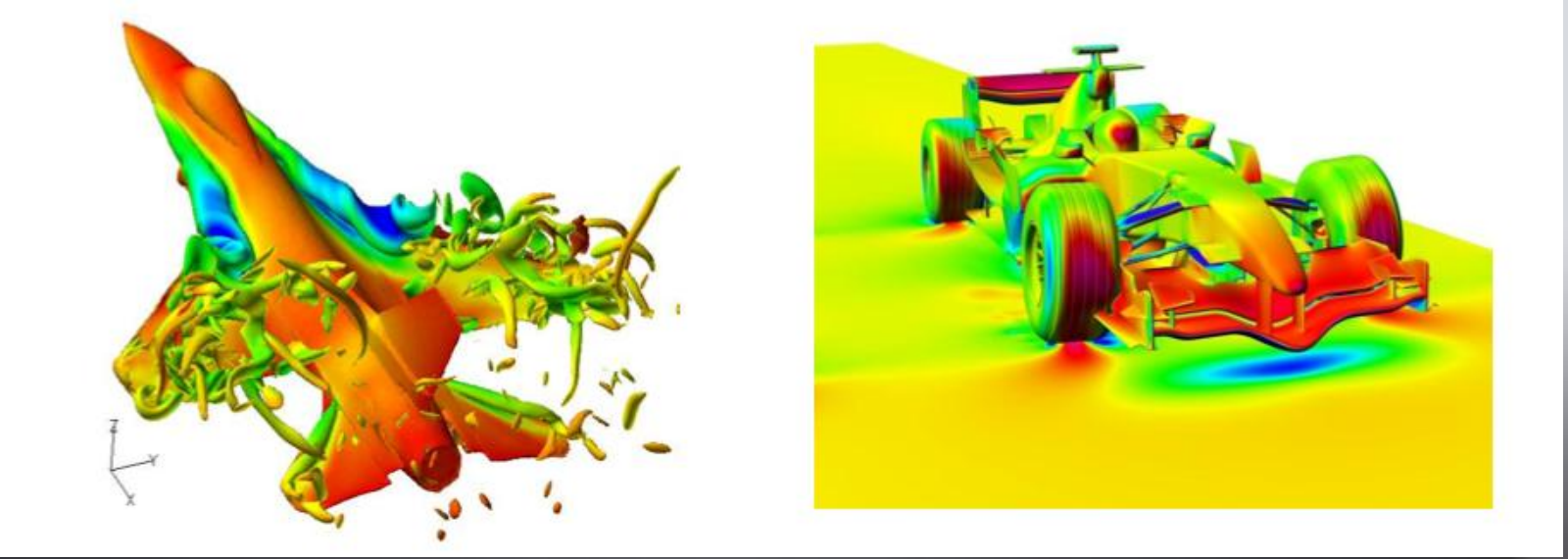
Recommendations	Class [a]	Level [b]
FFR is recommended to identify hemodynamically relevant coronary lesion(s) when evidence of ischaemia is not available.	I	A
Revascularization of stenoses with FFR <0.80 is recommended in patients with angina symptoms or a positive stress test.	I	B
IVUS or OCT may be considered to characterize lesions.	IIb	B
IVUS or OCT may be considered to improve stent deployment.	IIb	B
Revascularization of an angiographically intermediate stenosis without related ischaemia or without FFR <0.80 is not recommended.	III	B



Eu Heart J 2013:doi:10.1093/eurheartj/eht296

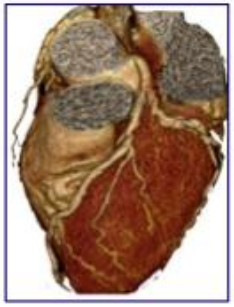
Computational fluid dynamics

- CFD quantifies fluid pressure and velocity based on physical laws, used in aerospace and auto industry for design and testing



CFD in coronary circulation

CCTA



3D Model

Physiologic conditions

- Coronary flow at rest
- Effect of hyperemia on microcirculation

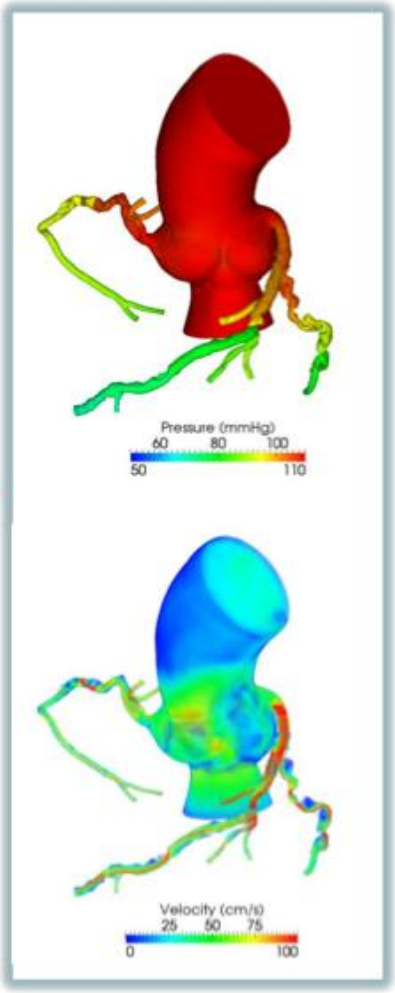
Equations of Blood Flow

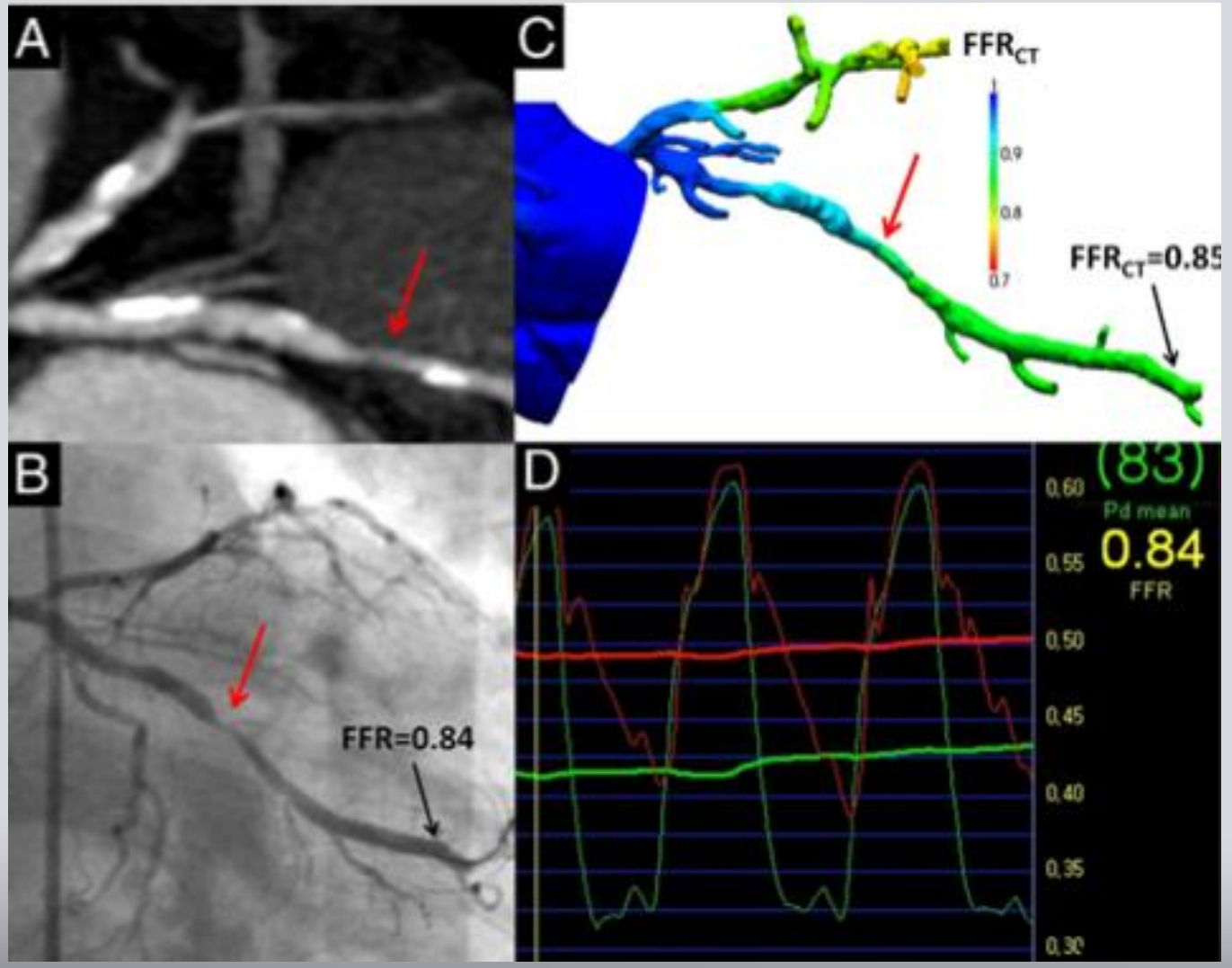
$$\rho v_{,t} + \rho v \nabla v = -\nabla p + \nabla \tau$$

$$\nabla v = 0$$

Supercomputer

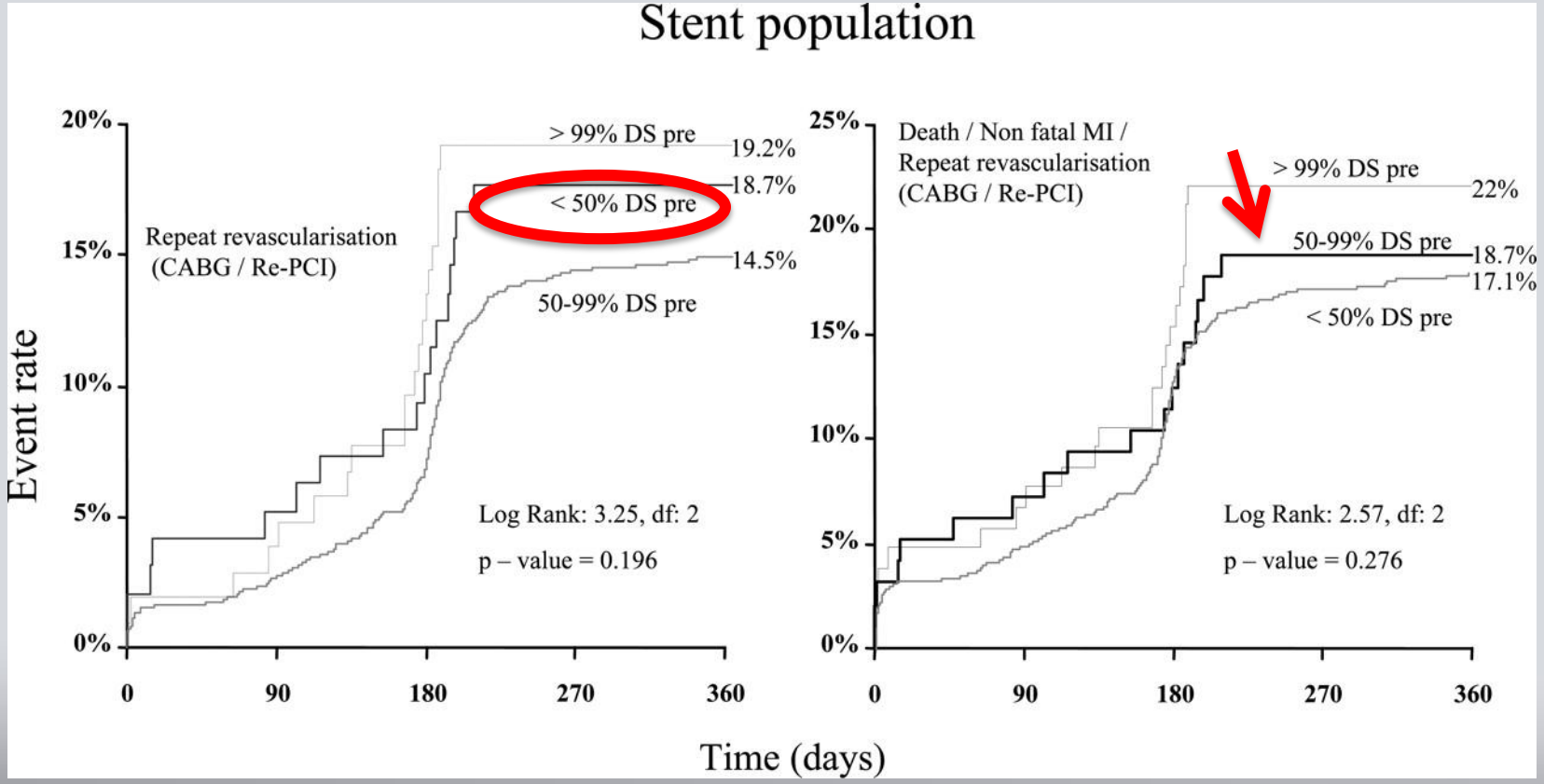
Simulated Hyperemic Blood Flow & Pressure





Angiographically significant lesion , with FFR and CFD excluded significant ischemia

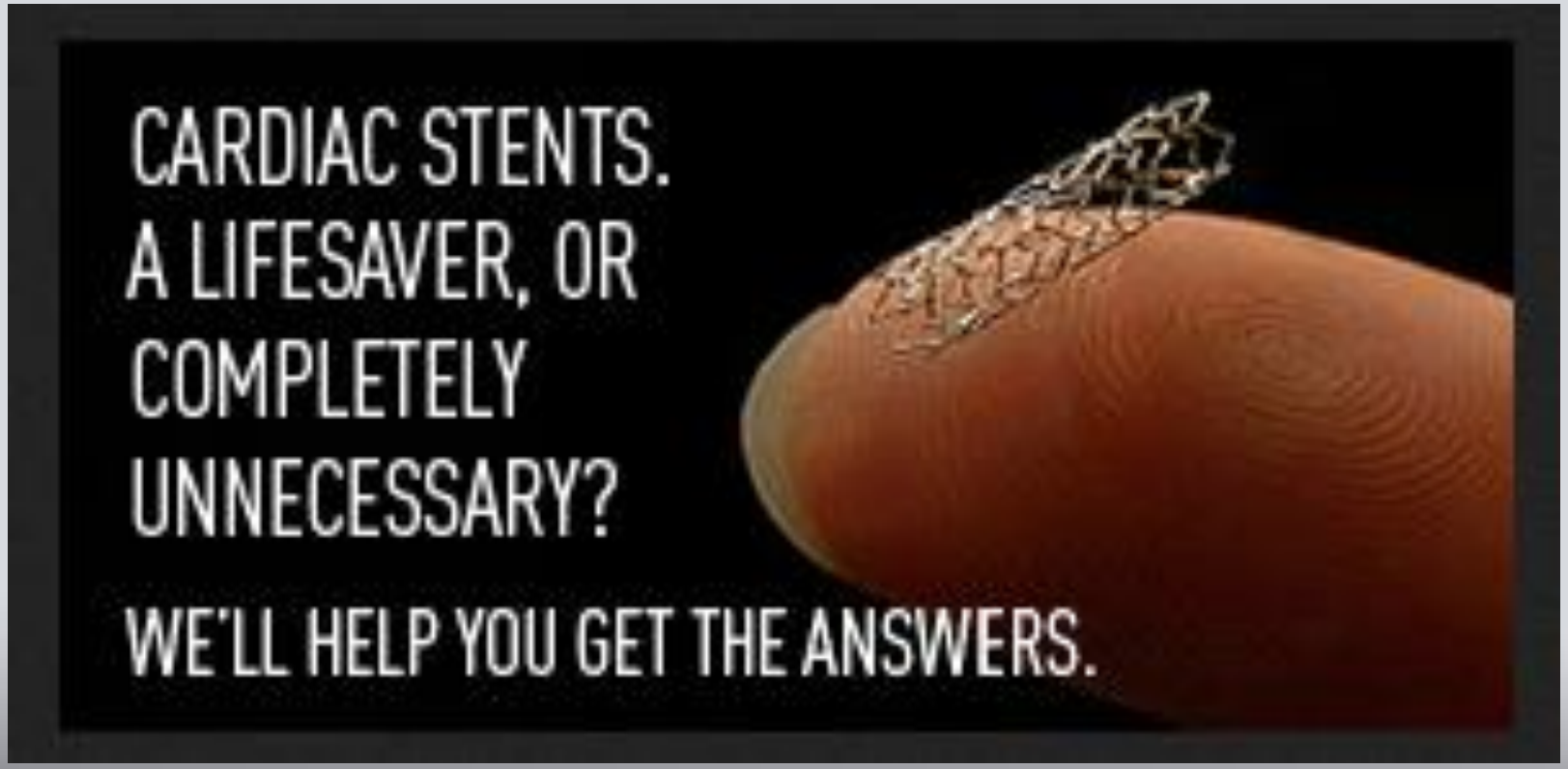
Angiographically non significant lesions and PCI



One-year event rate curves for patients treated with coronary stenting and varying degrees of stenosis severity measured by QCA.

Mercado N et al. Eur Heart J 2003;24:541-551

Angiographically non significant lesions and PCI



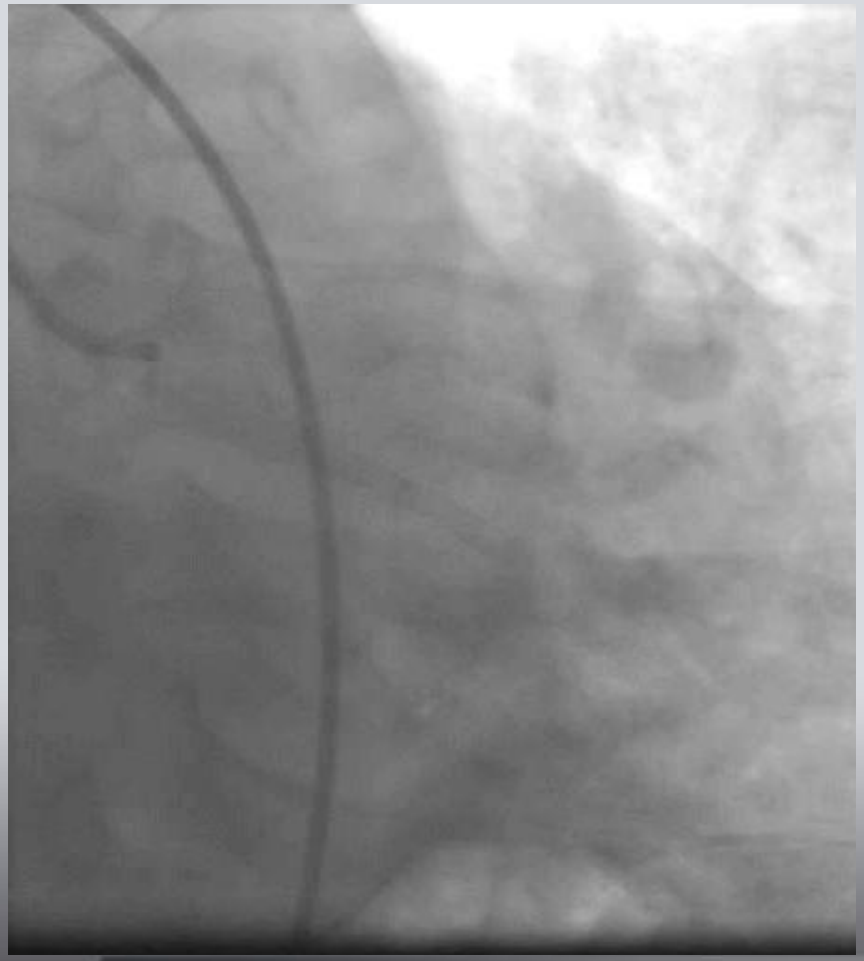
Inappropriate PCI

Variable	No. (%) Total (N = 144 737)	Procedural Appropriateness: Appropriate (n = 72 911)	Uncertain (n = 54 988)	Inappropriate (n = 16 838)	P Value
Angina					
No symptoms	20 607 (14.2)	4305 (5.9)	7239 (13.2)	9063 (53.8)	
CCS class					
I	17 709 (12.2)	4407 (6.0)	11 136 (20.3)	2166 (12.9)	<.001
II	48 853 (33.8)	13 606 (18.7)	29 890 (54.4)	5357 (31.8)	
III	45 486 (31.4)	39 636 (54.4)	5675 (10.3)	175 (1.0)	
IV	12 082 (8.3)	10 957 (15.0)	1048 (1.9)	77 (0.5)	
Noninvasive ischemia evaluation					
Low risk	29 665 (30.1)	7312 (14.0)	10 779 (35.6)	11 574 (71.6)	<.001
Intermediate risk	39 049 (39.6)	17 757 (34.0)	16 691 (55.1)	4601 (28.4)	
High risk	29 971 (30.4)	27 158 (52.0)	2813 (9.3)	0	
None performed[a]	46 052	20 684	24 705	663	
No. of antianginal medications					
0	40 549 (28.0)	15 726 (21.6)	17 697 (32.2)	7126 (42.3)	<.001
1	65 906 (45.5)	28 695 (39.4)	28 196 (51.3)	9015 (53.5)	
2	31 547 (21.8)	23 311 (32.0)	7629 (13.9)	607 (3.6)	
>2	6735 (4.7)	5179 (7.1)	1466 (2.7)	90 (0.5)	
Coronary artery stenoses					
1	72 219 (49.9)	29 851 (40.9)	31 849 (57.9)	10 519 (62.5)	<.001
2	47 792 (33.0)	24 469 (33.6)	18 030 (32.8)	5293 (31.4)	
3	24 726 (17.1)	18 591 (25.5)	5109 (9.3)	1026 (6.1)	
Presence of proximal LAD stenosis	38 564 (26.6)	28 168 (38.6)	9379 (17.1)	1017 (6.0)	<.001

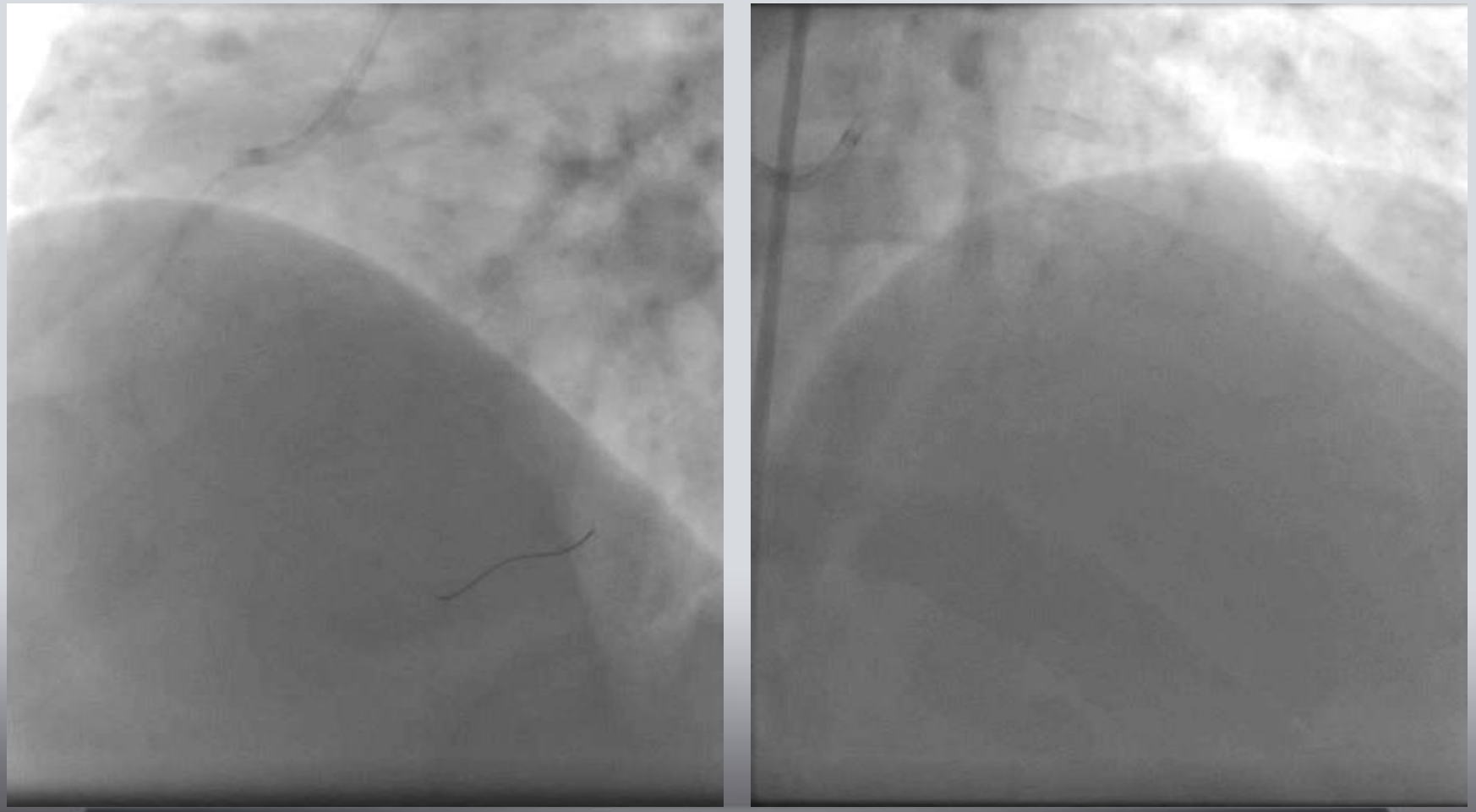
Abbreviations: CCS, Canadian Cardiovascular Society; LAD, left anterior descending artery.
[a] These percutaneous coronary interventions were matched to indications in the appropriate use criteria (18-21 or 46-47) that did not require prior noninvasive stress evaluation.

Chan PS *JAMA*. 2011;306(1):53-61

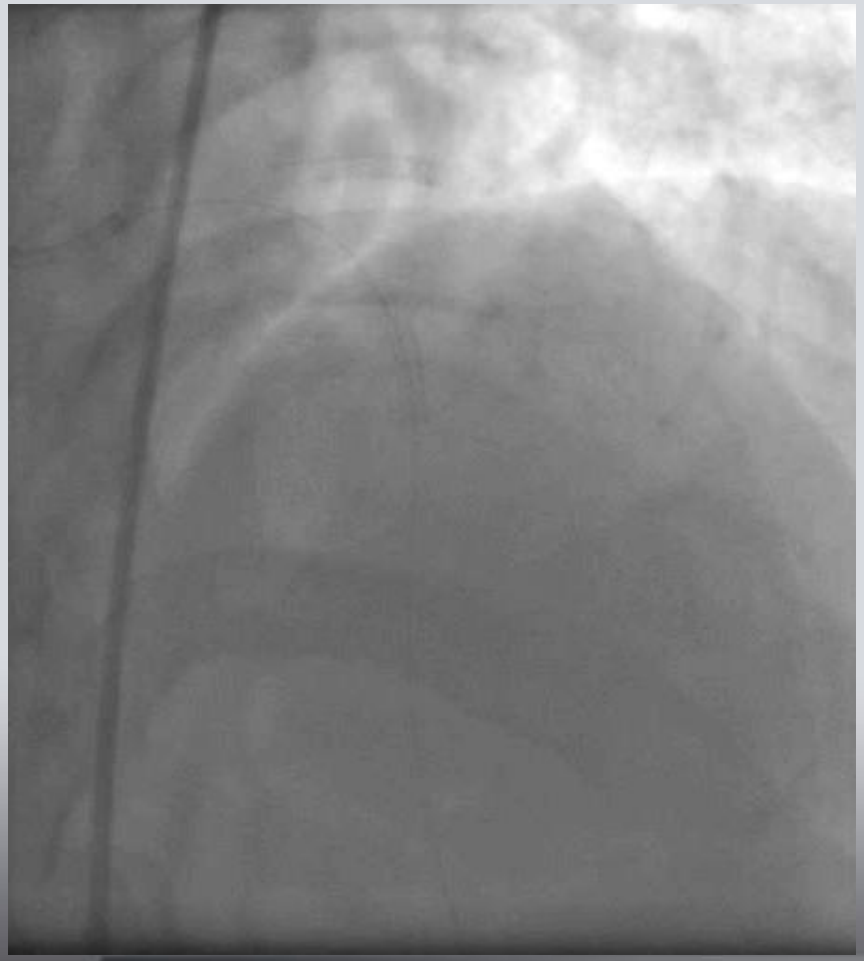
Inapropriate PCI?



Inapropriate PCI?



Inapropriate PCI?

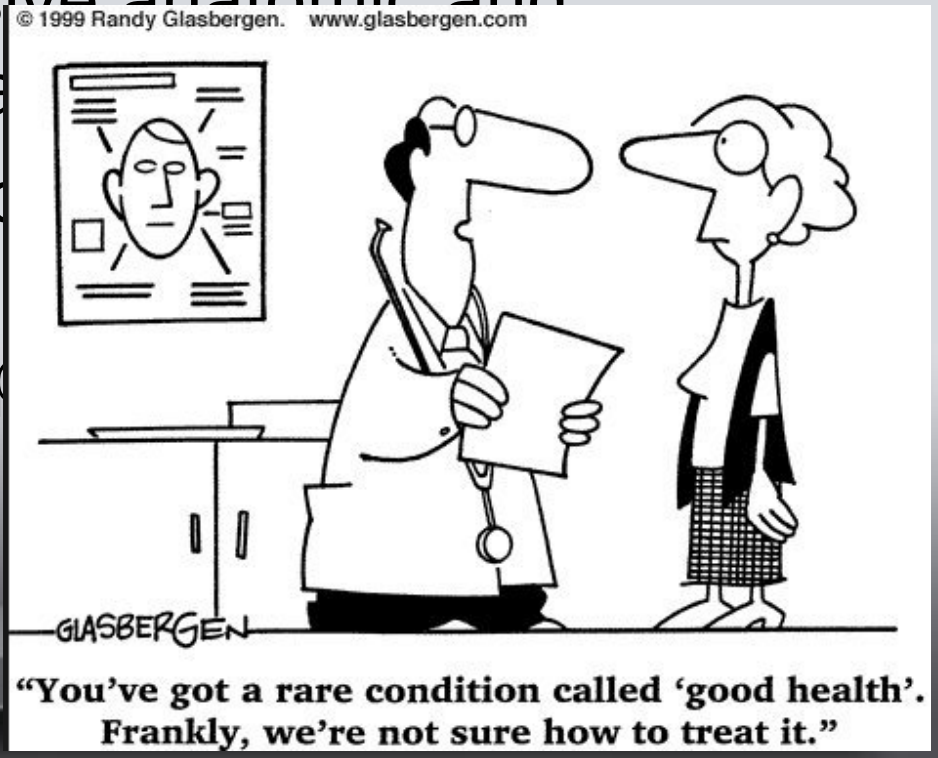


Conclusion

- Coronary angiography in stable coronary patients should be performed according risk stratification
- Non-invasive ischemia testing before invasive procedure is recommended
- Different non angiographic invasive technique can be used for improvement of diagnosis and treatment in CAD

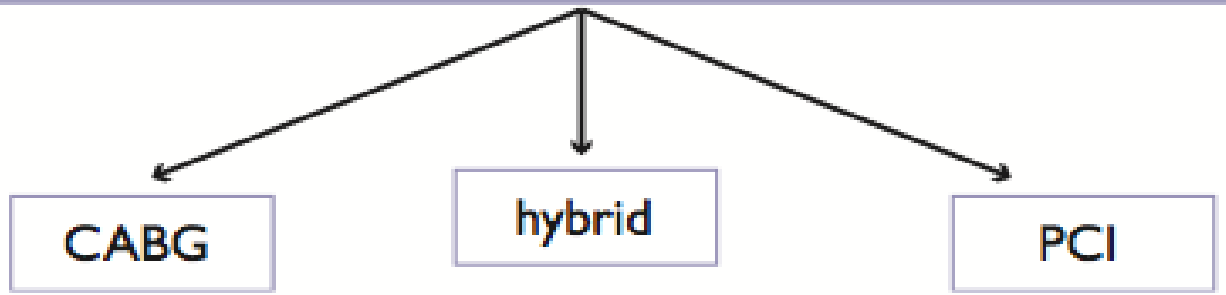
Conclusion

- The best tool for stenosis significance assessment is FFR (IVUS/OCT are beneficial specially in LCA interventions)
- In the future a CT FLOW, or non invasive FFR can give us non invasive anatomic and hemodynamic informa
- PCI of an angiographic intermediate stenosis or FFR <80 is inappro disease



If revascularization is appropriate

Anatomical factors	Single; multivessel disease; left main; last patent vessel; chronic total occlusion; proximal LAD; syntax score.
Clinical factors	Age; gender; diabetes; comorbilities; frailty; LV function; tolerance of meds; clinical scores.
Technical factors	Incomplete/complete revascularization; post CABG; post PCI; extensive tortuosity/calcifications.
Local factors	Volume/quality of center/operator; patient preference; local cost; availability; waiting lists.



Eu Heart J 2013:doi:10.1093/eurheartj/eht296