Defining Lesion Severity
(by Angiography, Physiology & IVUS)

Jung-Min Ahn, MD.

Division of Cardiology, Asan Medical Center,
University of Ulsan College of Medicine, Seoul, Korea

My Thought

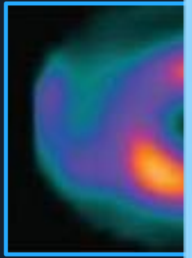
"The determination of coronary stenosis severity to decide on coronary revascularization should be evaluated from the perspective of myocardial perfusion."

"It is necessary to demonstrate that reduced myocardial perfusion is due to coronary stenosis.."

How To Detect Objective Ischemia

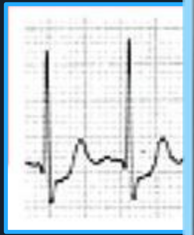
- During **Stress** Flow To Induce

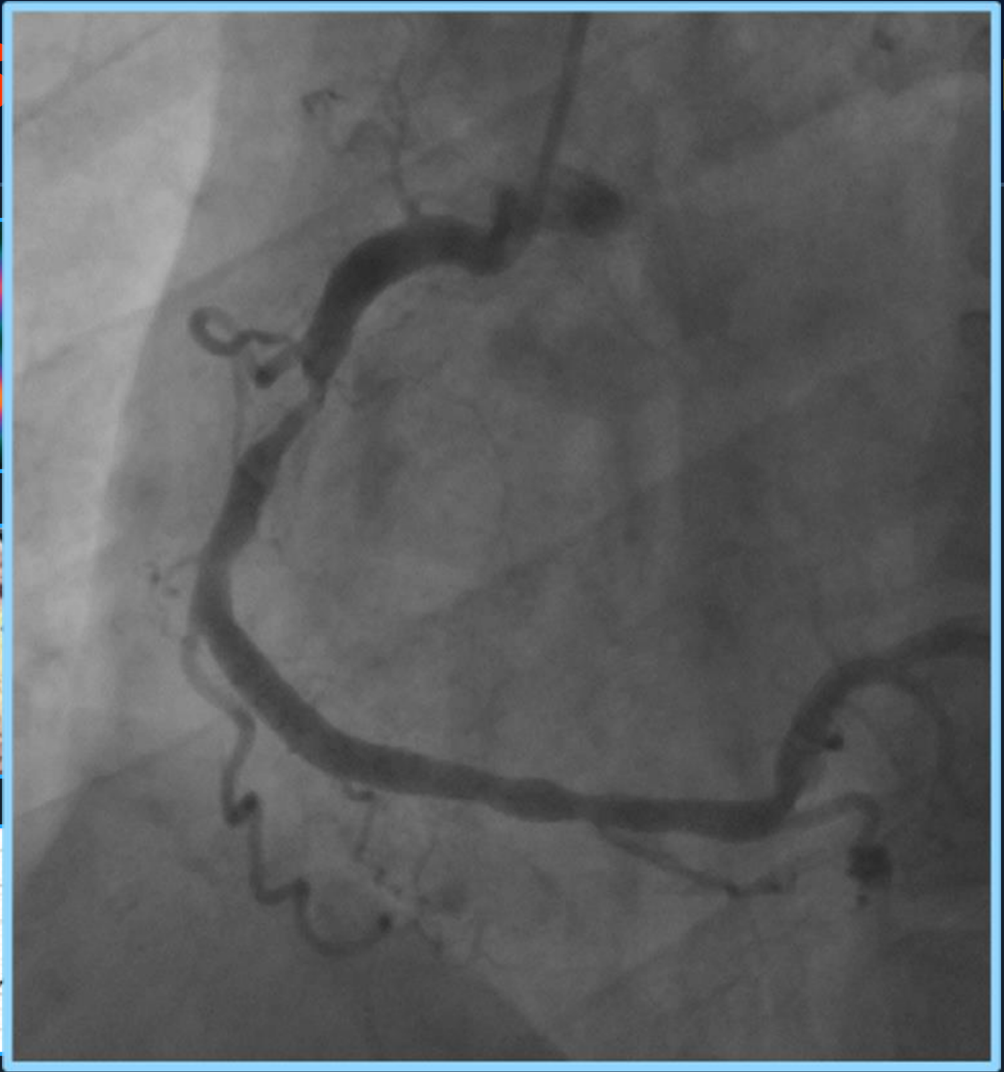
Myocardial Perfusion Imaging



Stress Echo

Treadmill Test

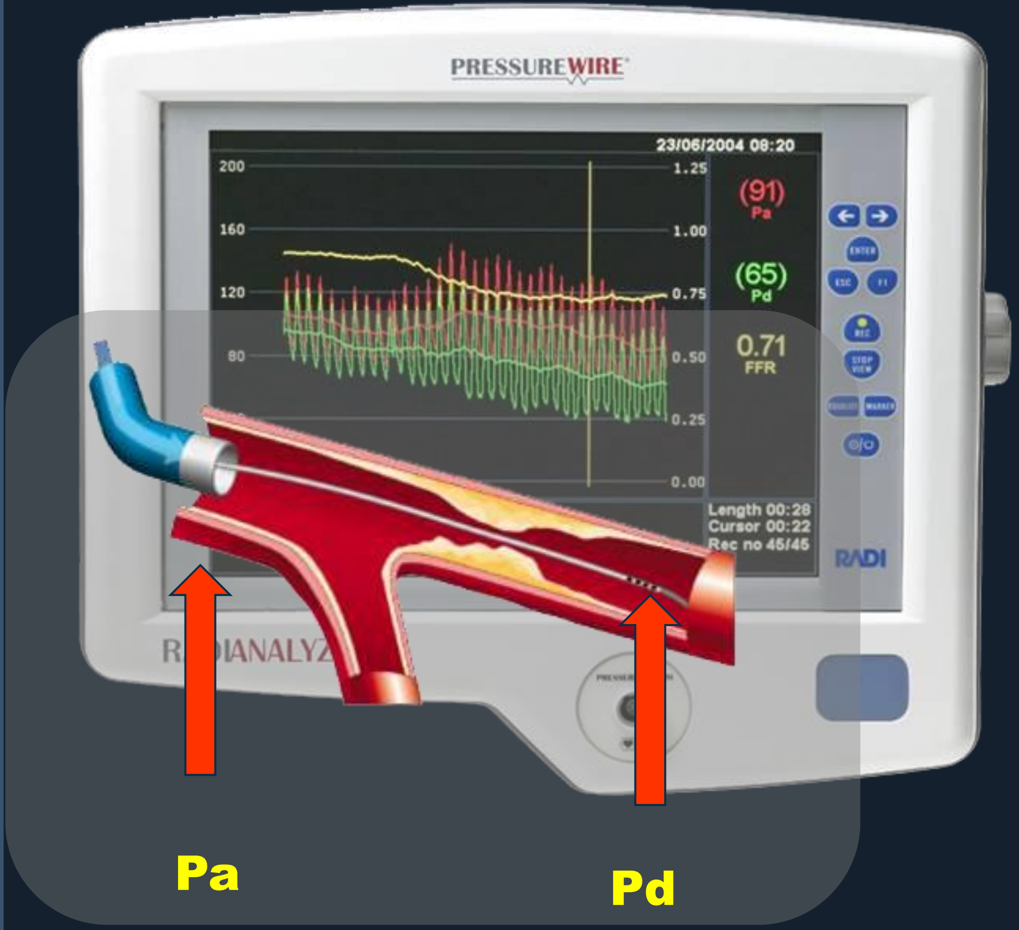




Direct Evidence of Ischemia

Fractional Flow Reserve

- FFR is a simple, reliable, pressure-derived index



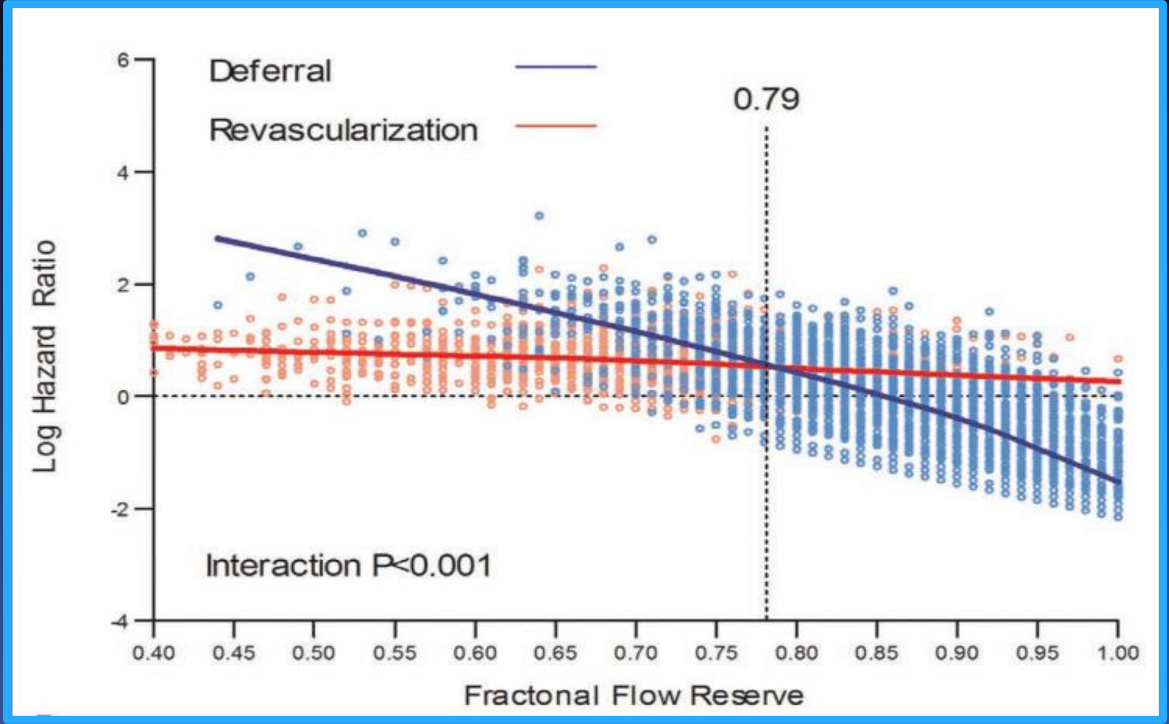
$$FFR = \frac{Q_S^{max}}{Q_N^{max}}$$

Hyperemia

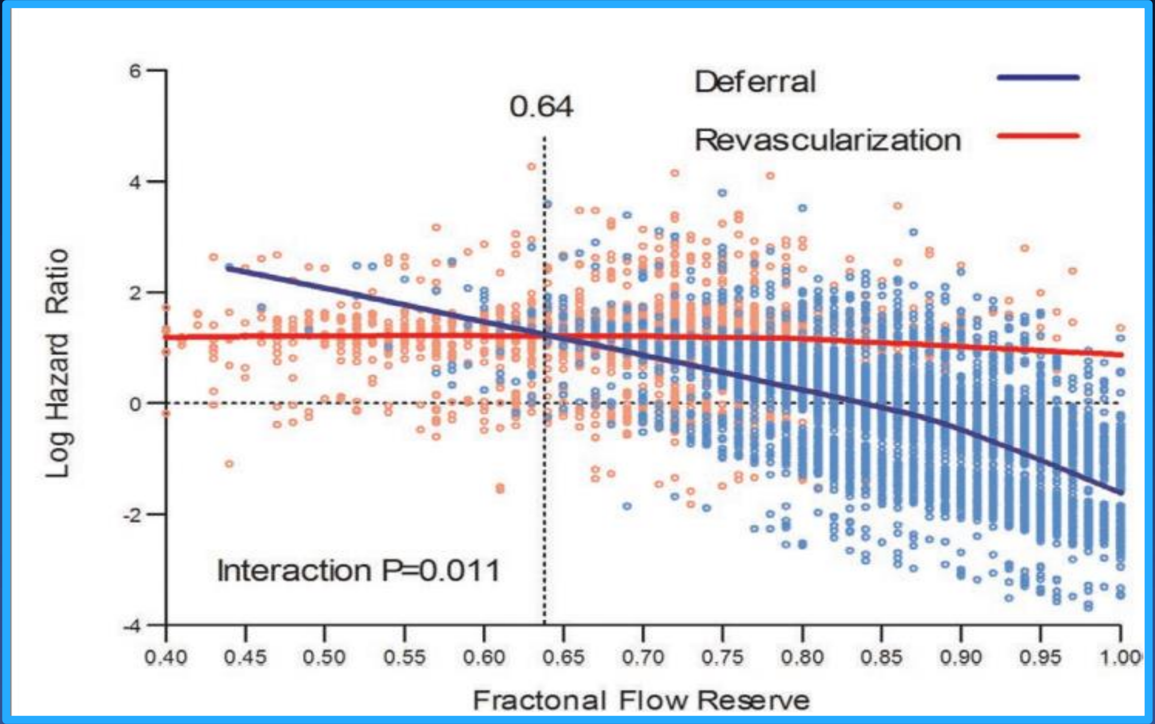
$$= \frac{Pd}{Pa}$$

IRIS-FFR Registry

Cardiac Death, MI, and TVR

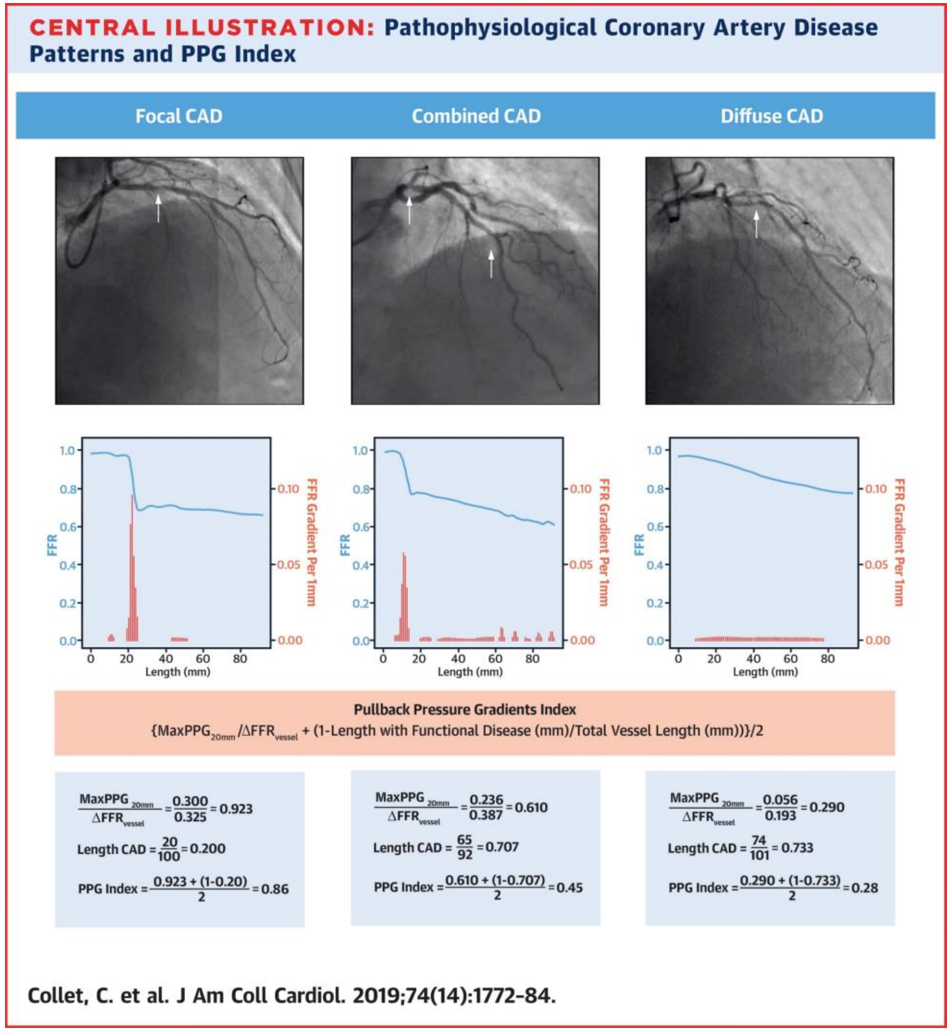


Cardiac Death, and MI



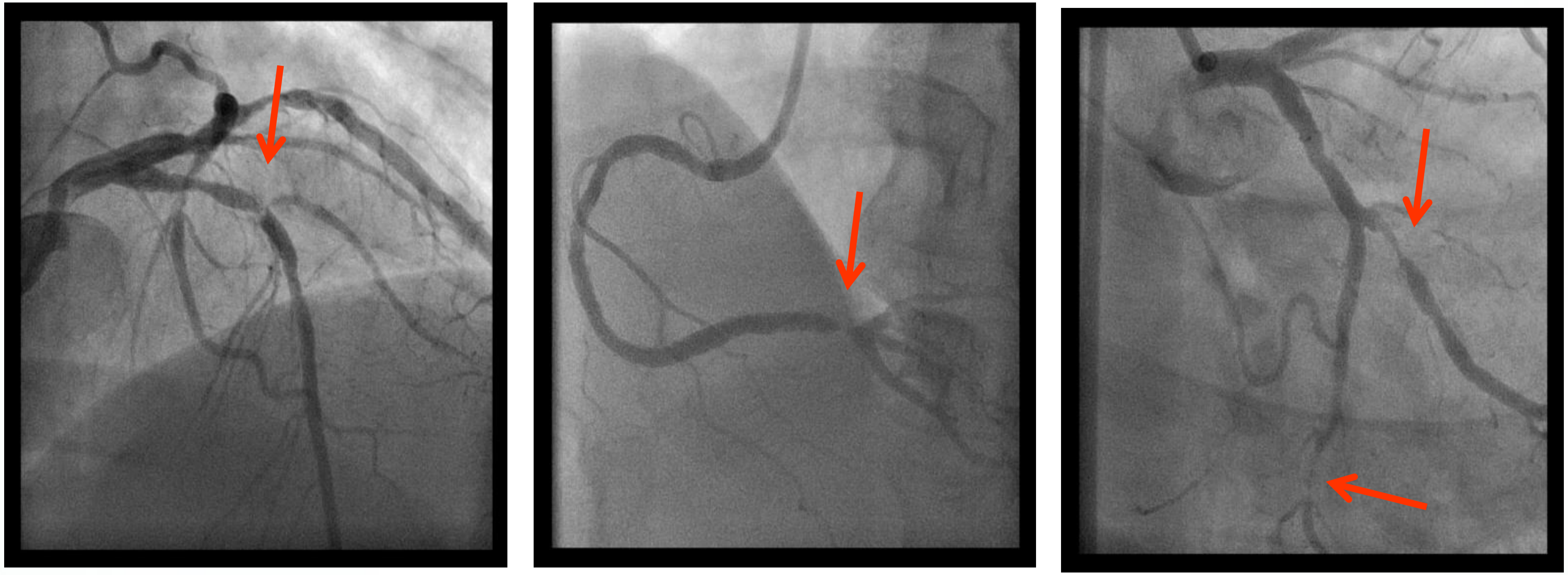
Ahn JM, Park SJ et al. Circulation 2017 Jun 6;135(23):2241-2251

It Provides the Physiologic Anatomy of Coronary Artery with Single Number



Coronary Angiogram

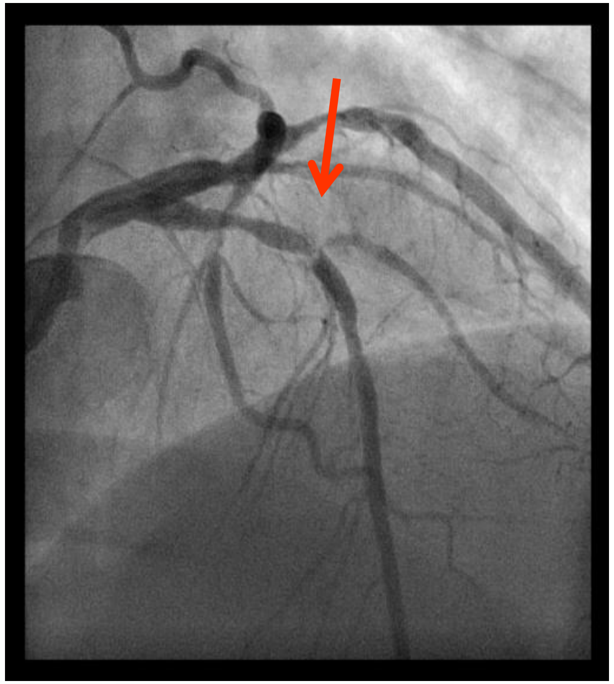
Angiographically 3 VD



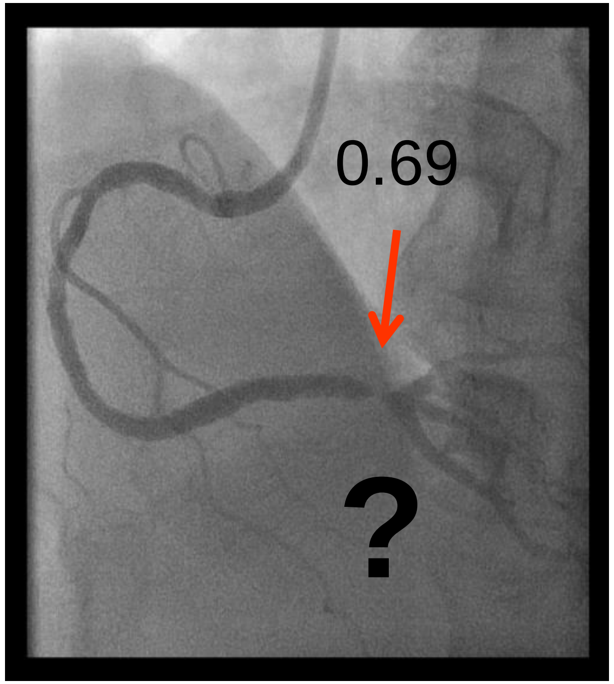
Thallium: large perfusion defect at LAD territory

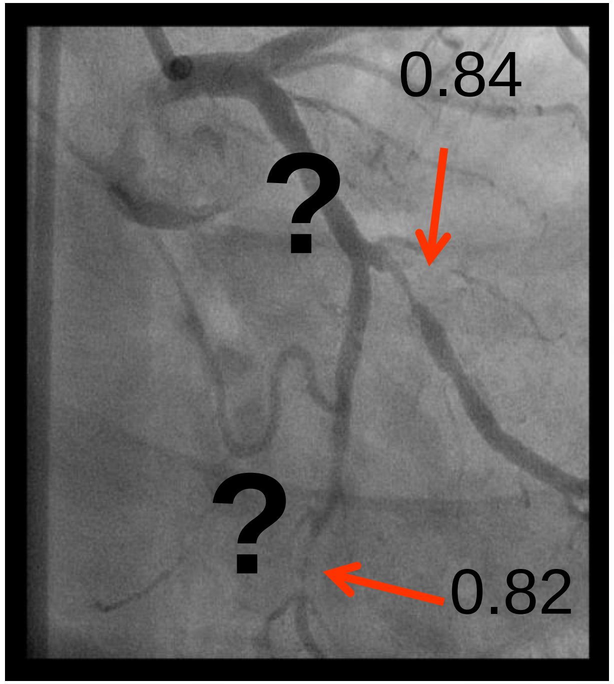
Fractional Flow Reserve

Functionally 2 VD



Not Done

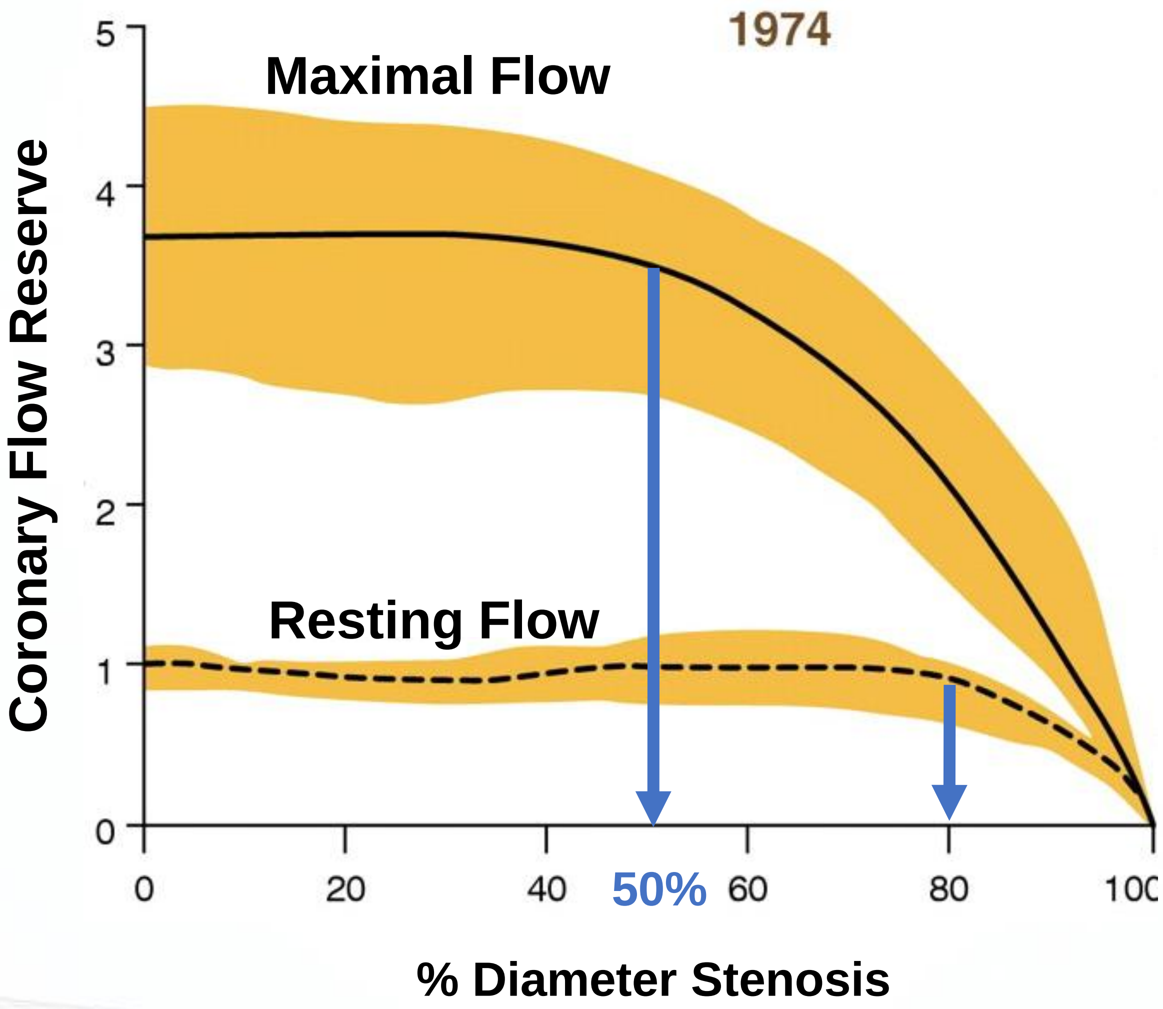




Thallium: large perfusion defect at LAD territory

Angiographic Significant Stenosis

Diameter Stenosis > 50%



Gould KL Am J Cardiol 1974;34:48-55

Critical Stenosis

CRITICAL CORONARY STENOSIS—GOULD ET AL.

serve independent of arteriographic interpretation. Our approach was used initially to determine critical coronary stenosis in dogs and to establish experimentally the relation between severity of constriction, resting and maximal coronary blood flow and regional flow distribution. Critical coronary stenosis is defined here as a constriction sufficient to prevent an increase in flow over resting values in response to increased myocardial oxygen demands; as subsequently shown, this constriction also corresponds to the point at which resting coronary flow values start to decrease. With appropriate instrumentation

Gould KL Am J Cardiol 1974;34:48-55

Relation between Myocardial Blood Flow and the Severity of Coronary-Artery Stenosis

Table 2. Regional Myocardial Blood Flow and Coronary Vasodilator Reserve in the Study Groups in Relation to the Degree of Stenosis.

Group	No. of Subjects	Myocardial Blood Flow			Coronary Vasodilator Reserve	
		base line	base line, corrected*	during hyperemia	uncorrected	corrected†
		ml/min/g of tissue				
Controls (no stenosis)	21	1.13±0.26	1.19±0.32	3.37±1.25	3.16±1.47	3.00±1.36
Patients						
<40% stenosis	8	0.96±0.19	0.94±0.28	3.44±1.47	3.75±1.85	3.71±1.22
40–59% stenosis	11	1.25±0.34	1.27±0.52	2.07±0.83‡§	1.83±1.06‡§	1.89±1.11§¶
60–79% stenosis	12	1.23±0.57	1.16±0.43	1.51±0.37‡§	1.49±0.79‡§	1.55±0.90‡§
≥80% stenosis	4	0.92±0.33	1.23±0.50	1.22±0.36‡§	1.43±0.54§¶	1.07±0.29‡§

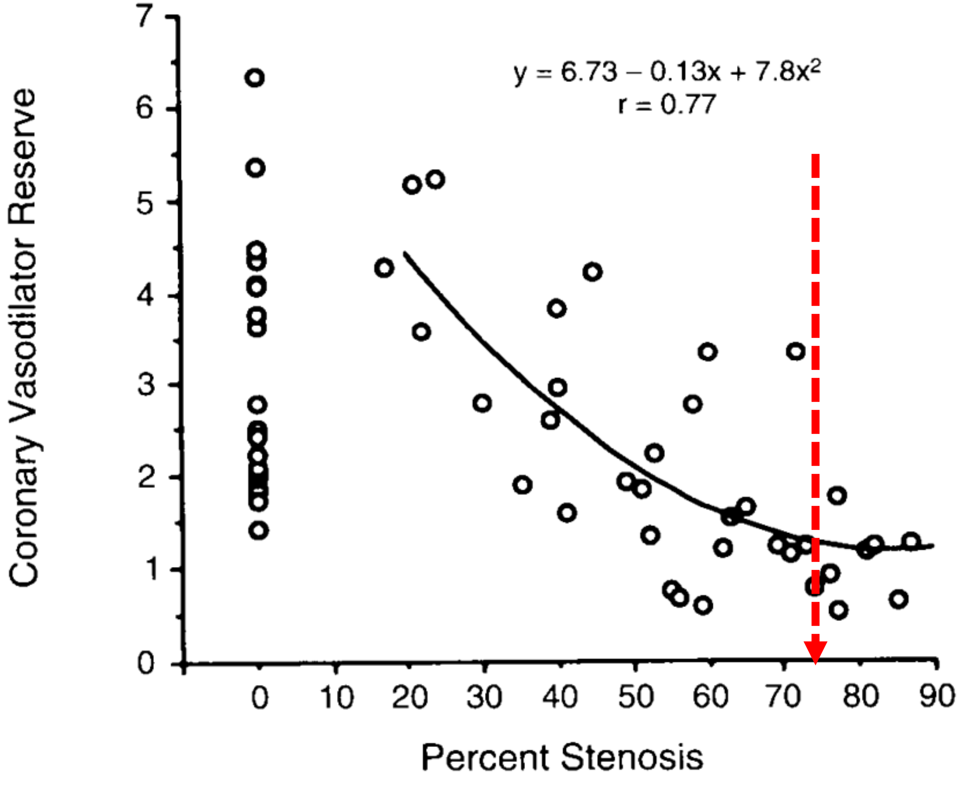
*Corrected for the rate–pressure product.

†Corrected by dividing the myocardial blood flow during hyperemia by the flow at base line corrected for the rate–pressure product.

‡P<0.01 for the comparison with the controls.

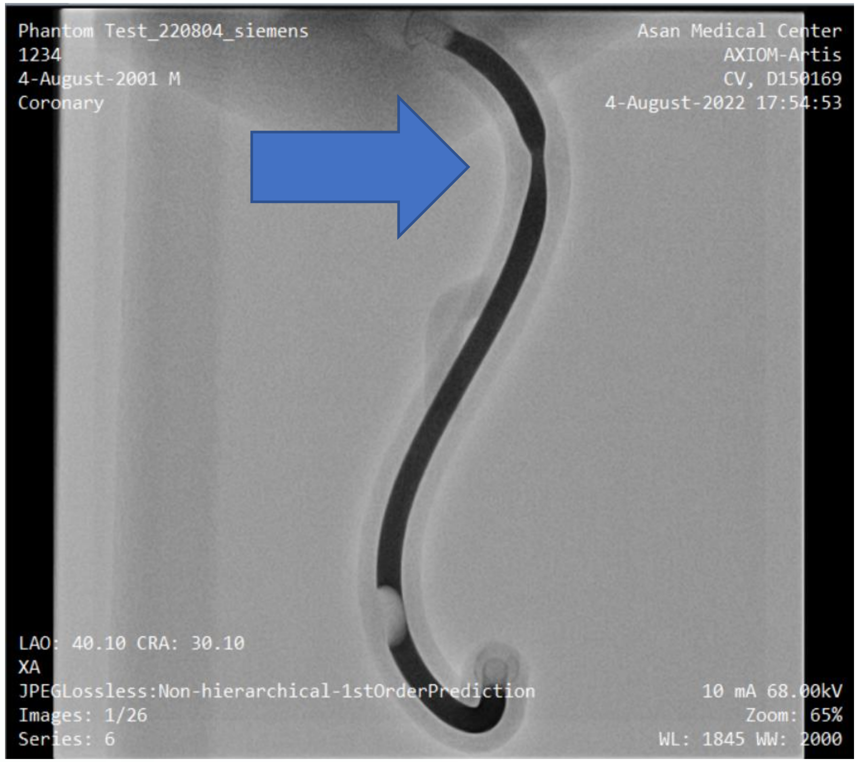
§P<0.01 for the comparison with the patients with stenosis of less than 40 percent.

¶P<0.05 for the comparison with the controls.

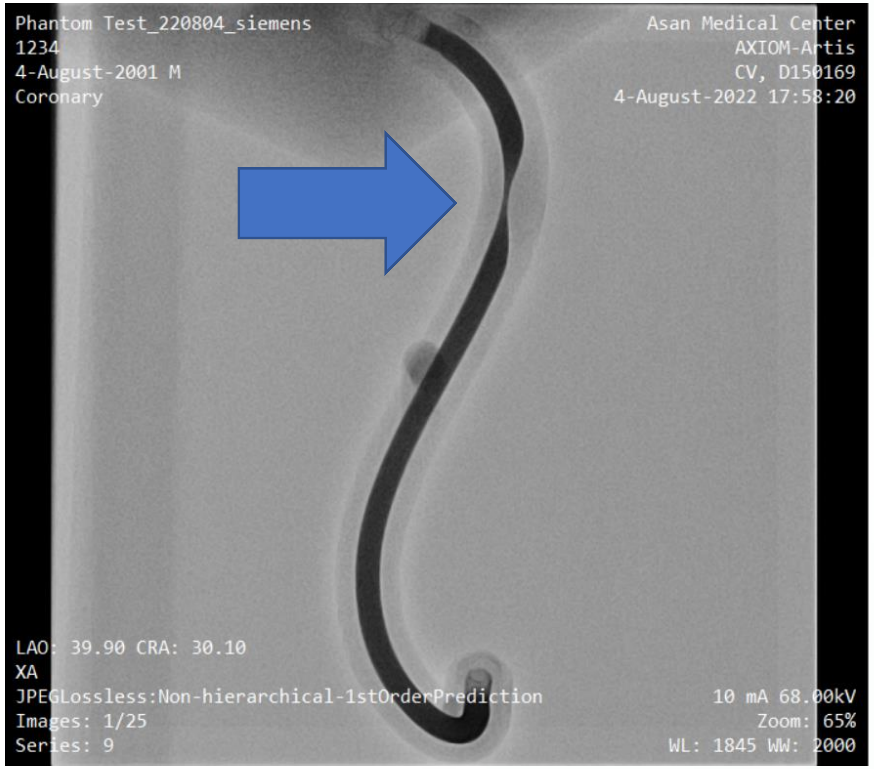


N Engl J Med 1994; 330:1782-1788

Stenosis Model (Silicon Tube)



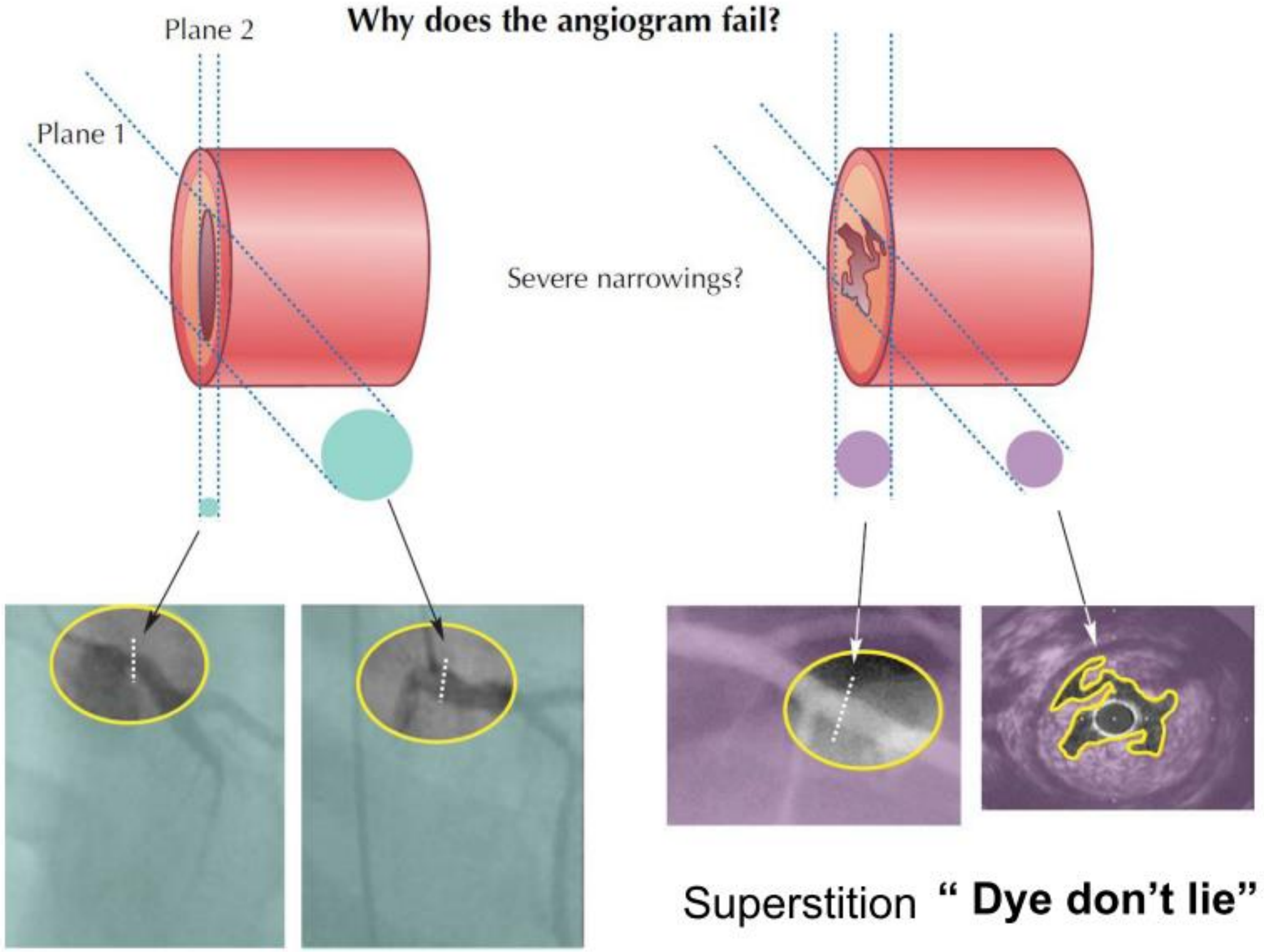
DS 50%



DS 70%

Diameter Stenosis ?

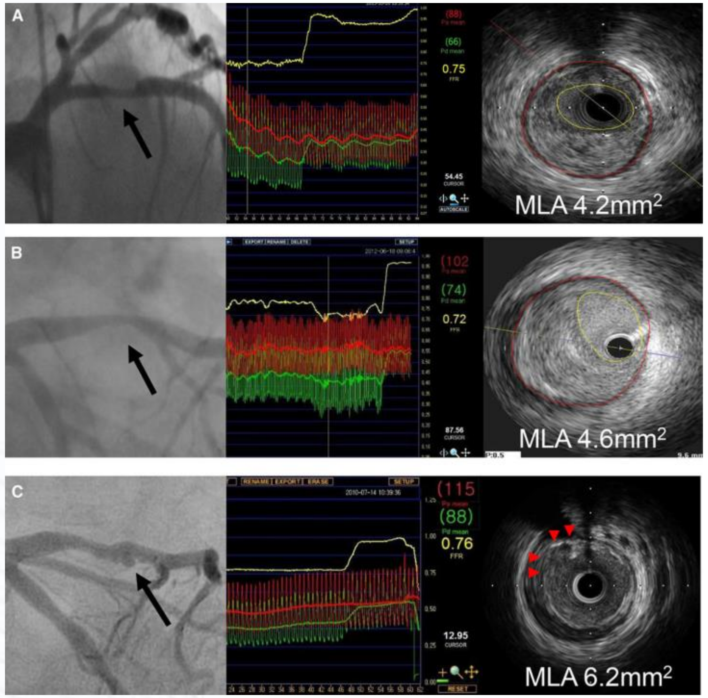
Inaccuracy of CAG

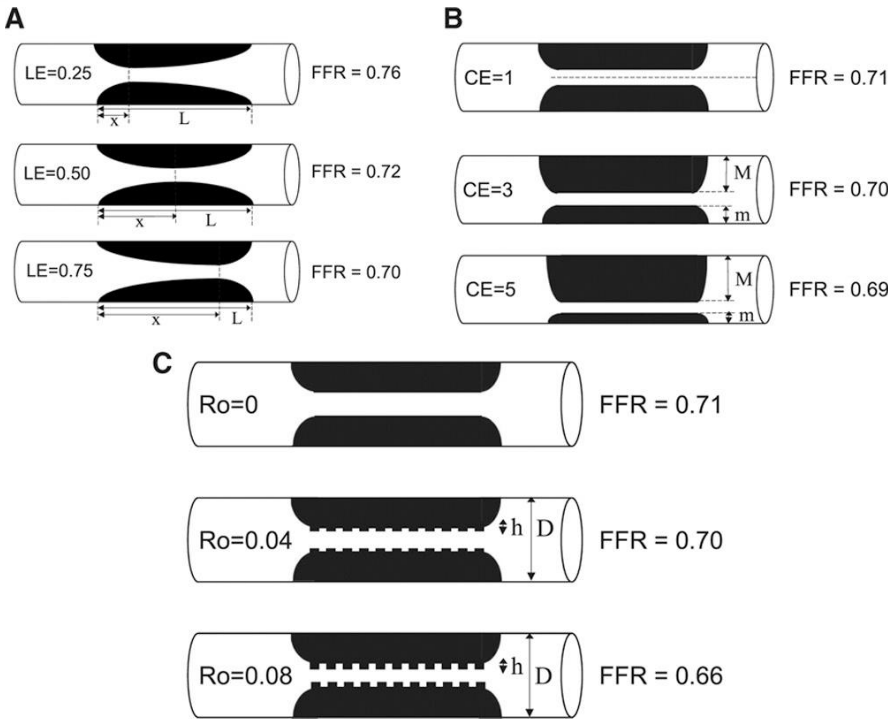


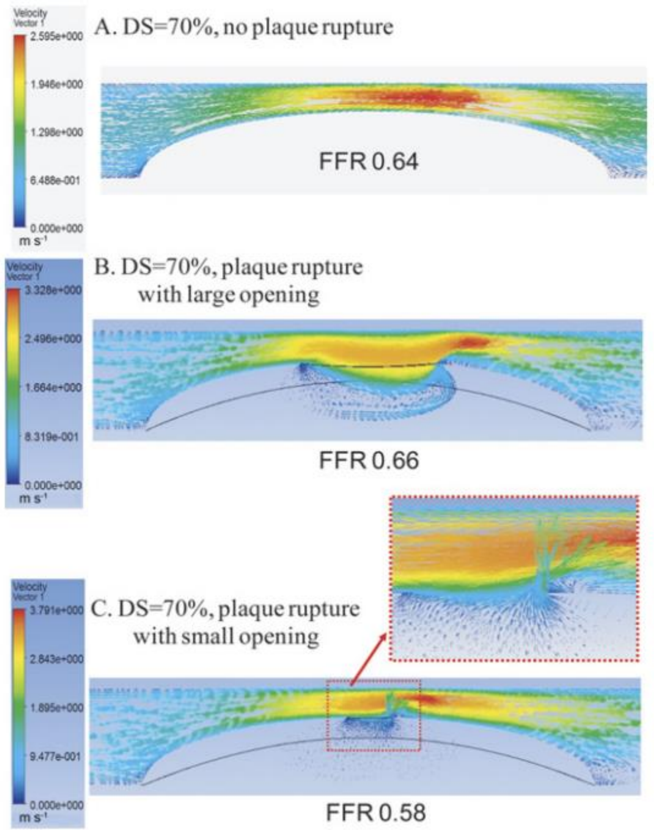
Superstition **" Dye don't lie"**

Kern MJ et al. JACC 2010;55:173-185

Impact of Coronary Lesion Geometry on Fractional Flow Reserve





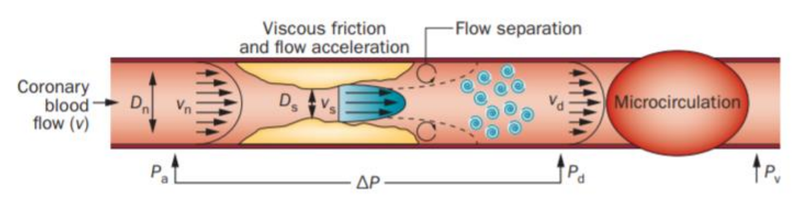


Circ Cardiovasc Imaging . 2018 Jun;11(6):e007087.

J Am Coll Cardiol Intv 2012;5:1029 –36

Why? Determinants of FFR

Stenosis



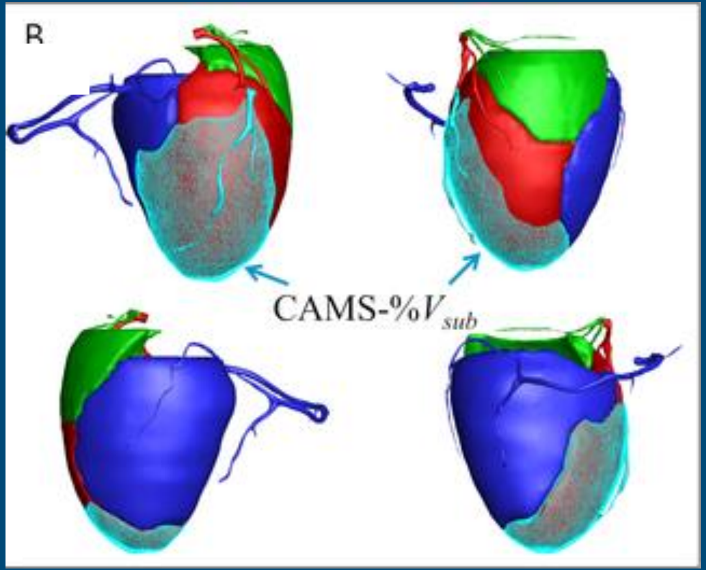
The pressure gradient across a stenosis is determined by the sum of viscous and separation losses.

$$\Delta P = Av + Bv^2$$

The most-important geometric parameter is the minimum diameter of the stenosis

Nat. Rev. Cardiol. 10, 439–452 (2013)

Myocardium



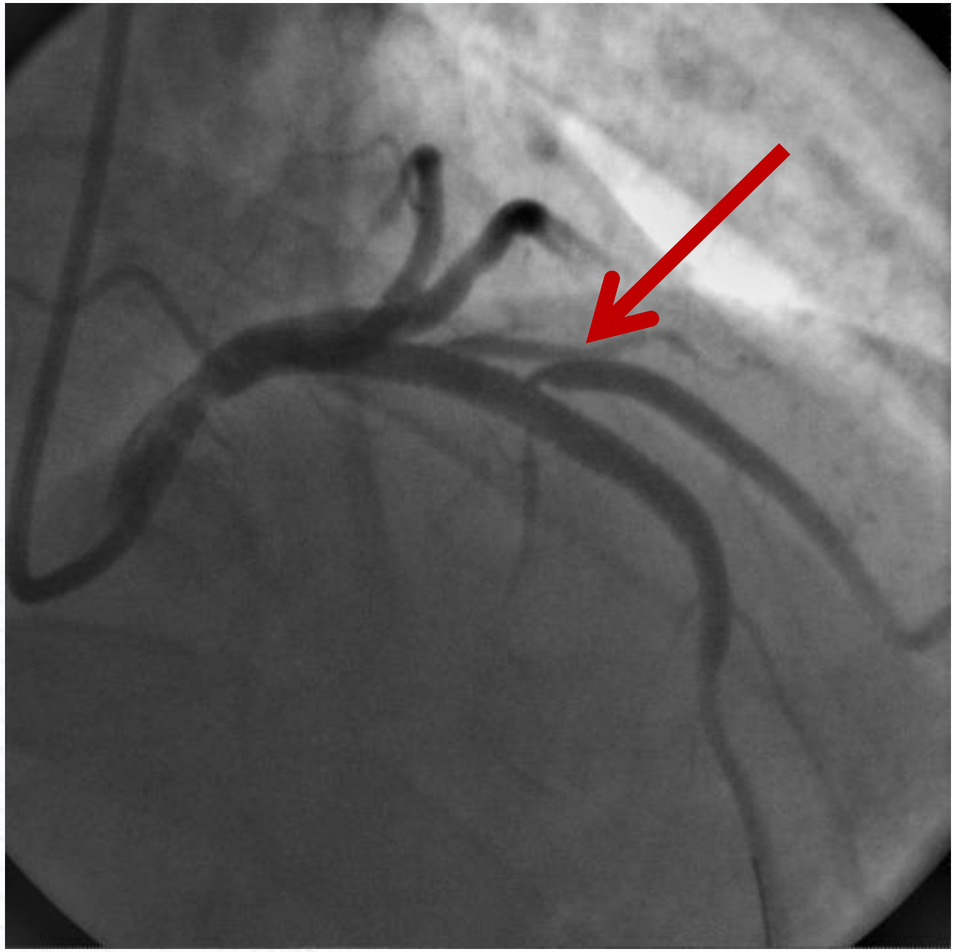
- Vascular territory on the FFR value
- Any given stenosis,

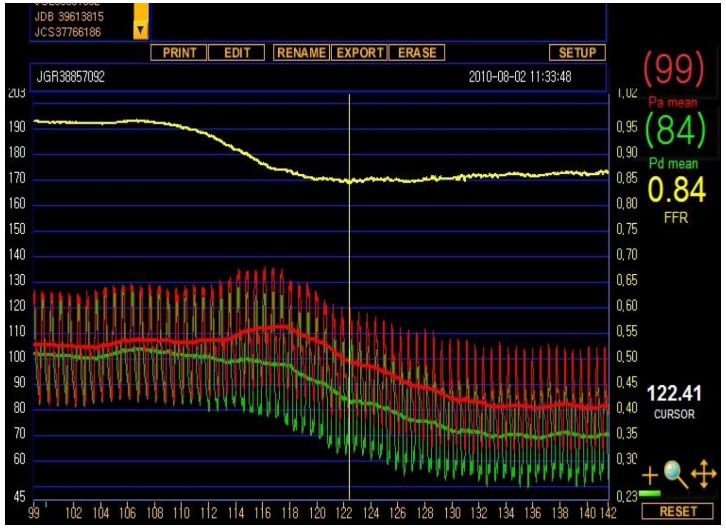
  Vascular territory ↑ FFR ↓

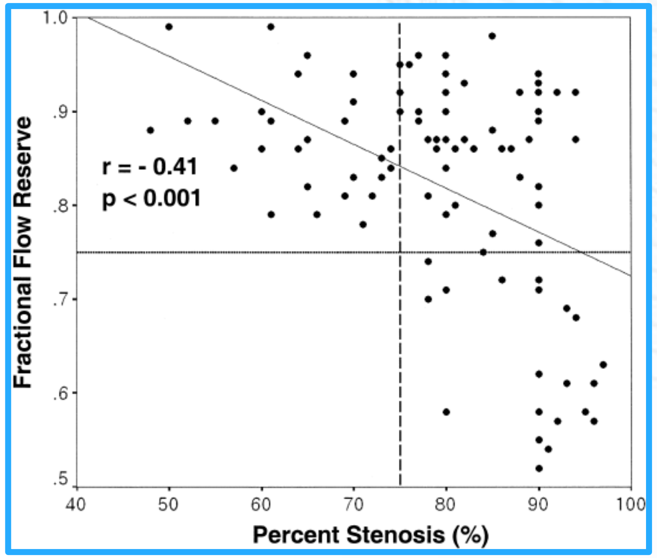
  Vascular territory ↓ FFR ↑

PLoS Med 15(11): e1002693

Jailed Side Branch



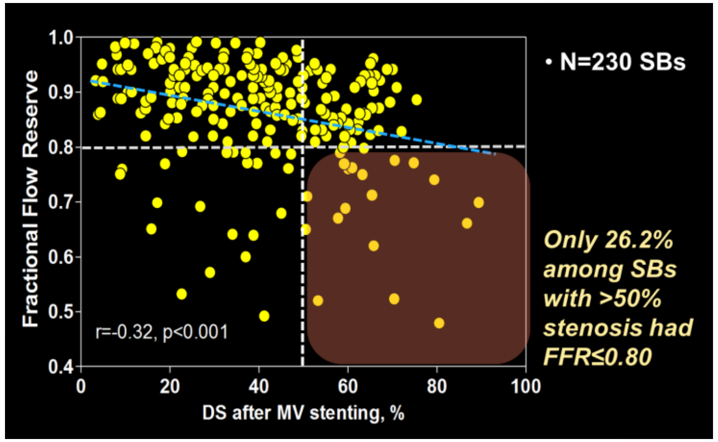




Koo BK et al. J Am Coll Cardiol 2005;46:633–7.

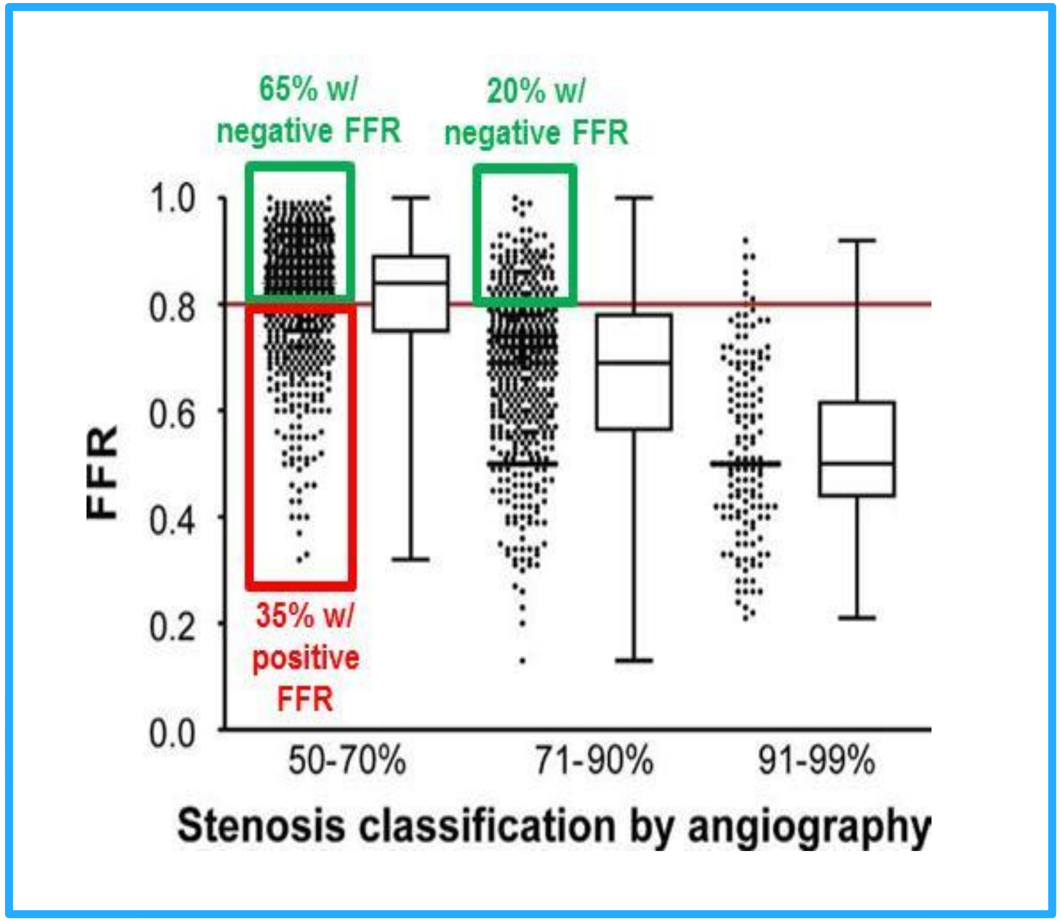
FFR 0.84

Leave it alone.



SJ Park, Ahn JM et al. JACC Cardiovasc Interv. 2012 Feb;5(2):155-61

"Obstructive" CAD Identified by Angiography Correlates Poorly with invasive FFR

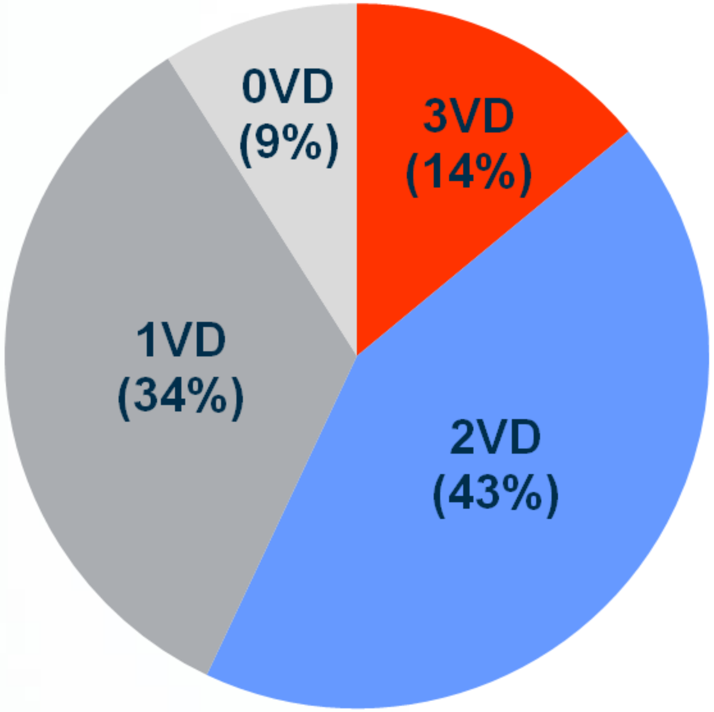


Tonino et al., J Am Coll Cardiol 2010;55:2816–21

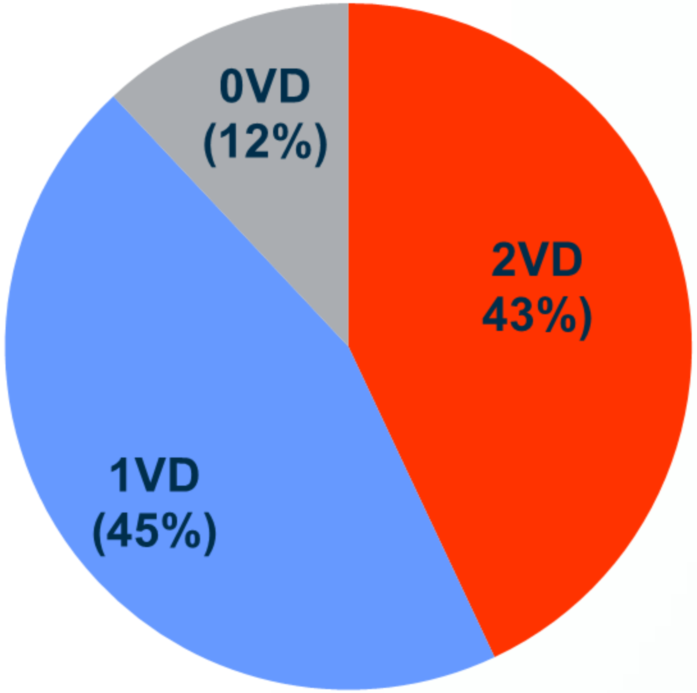
Visual-Functional Mismatch

From FAME Study

Functionally Diseased Coronary Arteries



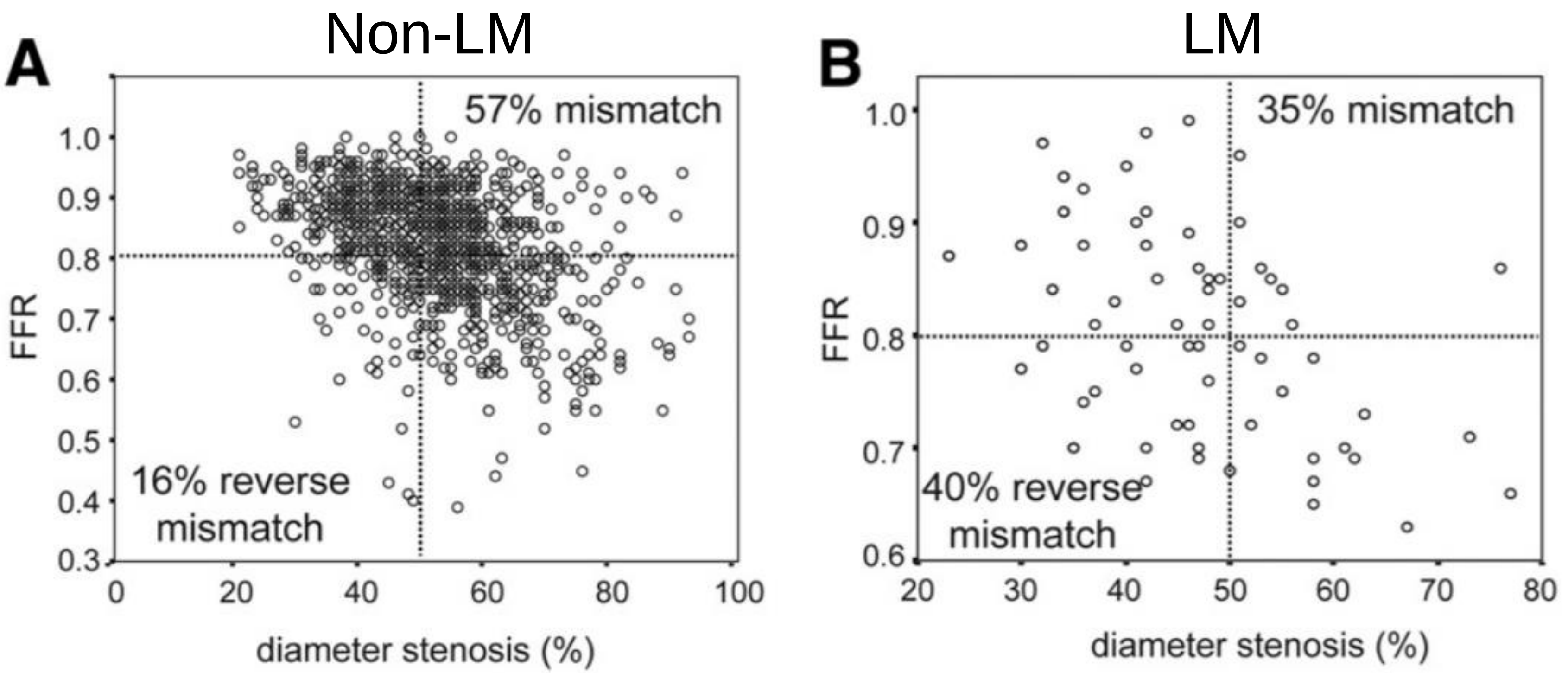
Angiographic 2VD



Angiographic 3VD

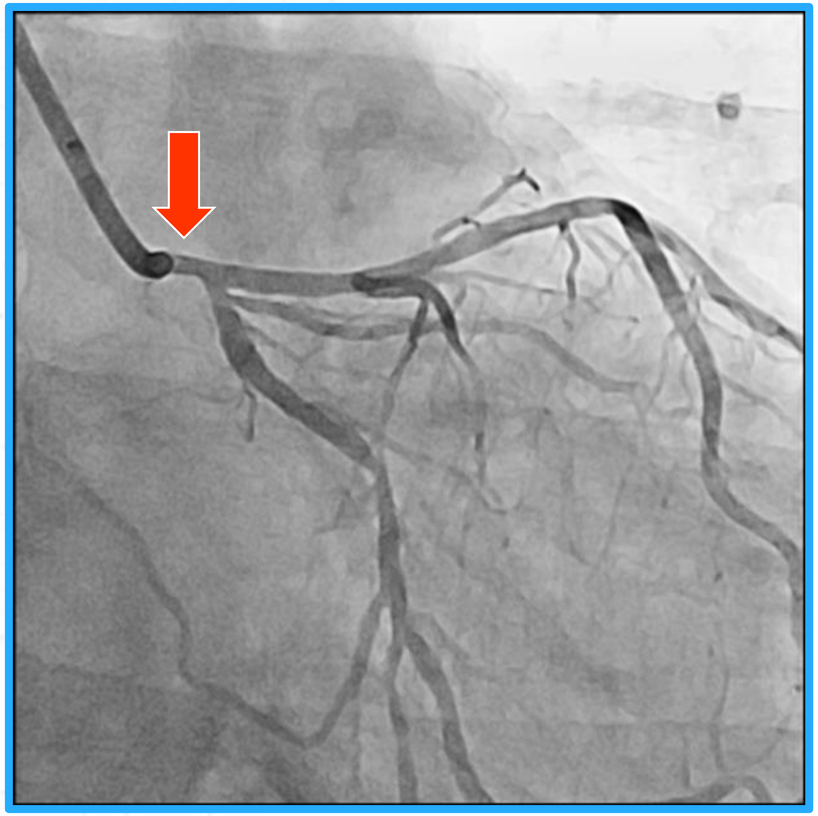
Tonino et al., J Am Coll Cardiol 2010;55:2816–21

Visual Functional Mismatch – Coronary Angiography

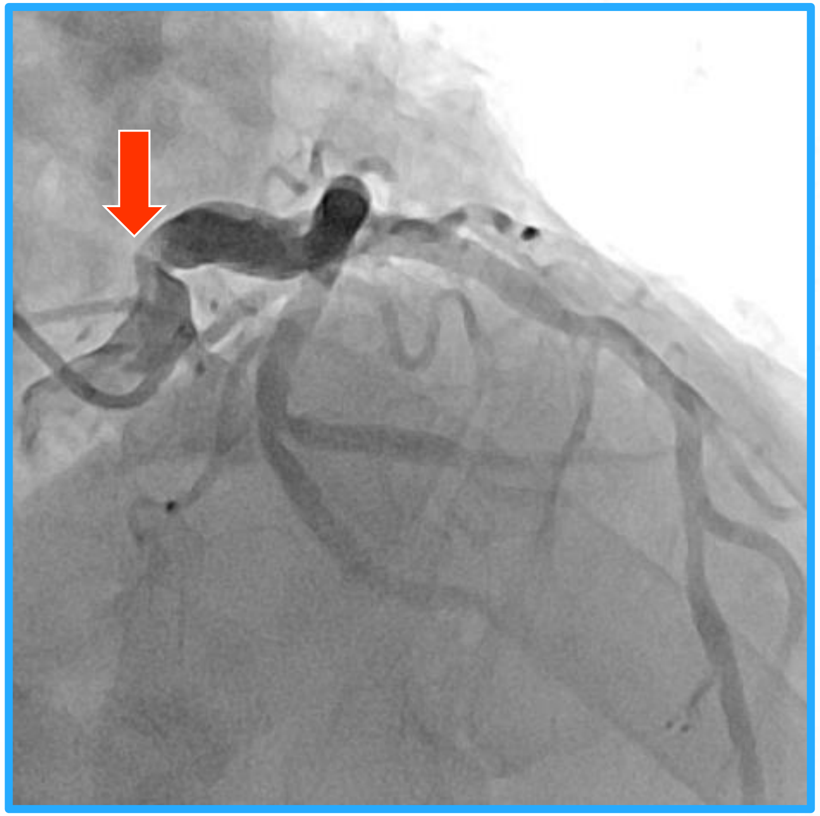


Park SJ, Kang SJ et al. J Am Coll Cardiol Intv 2012;5:1029 –36

Which is a Significant Stenosis ?

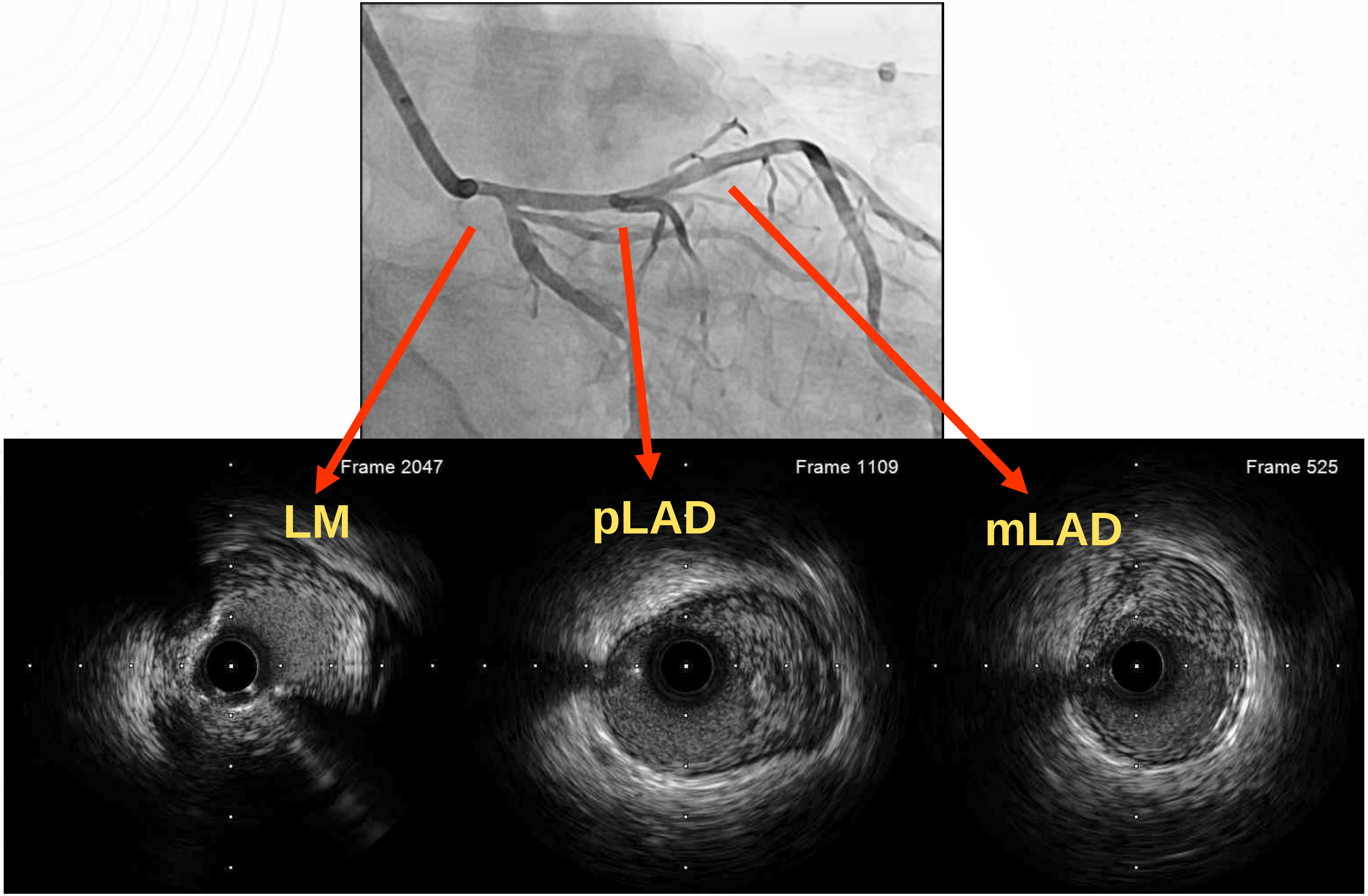


FFR 0.71

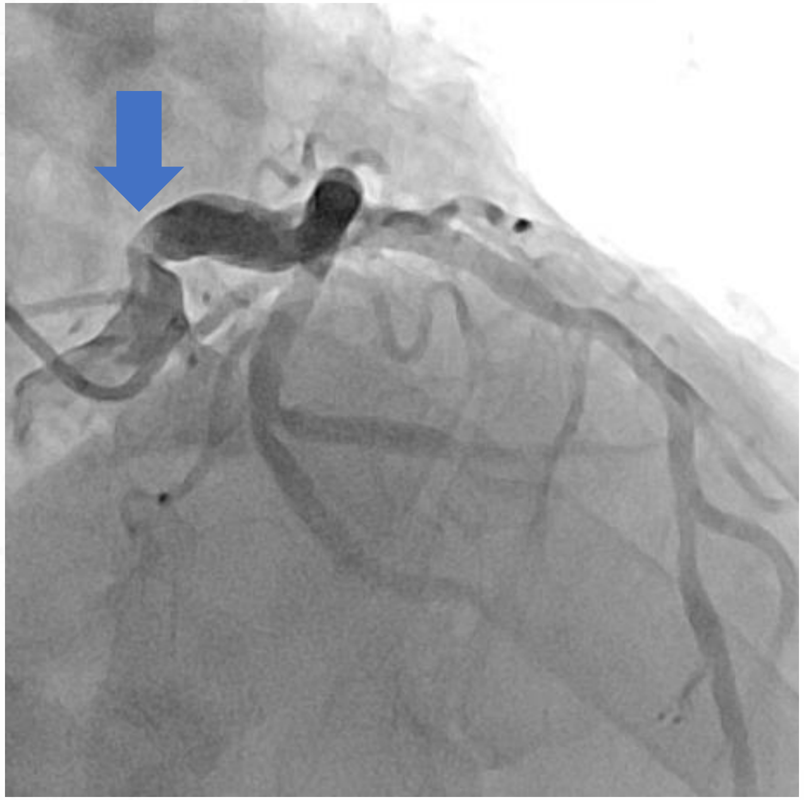


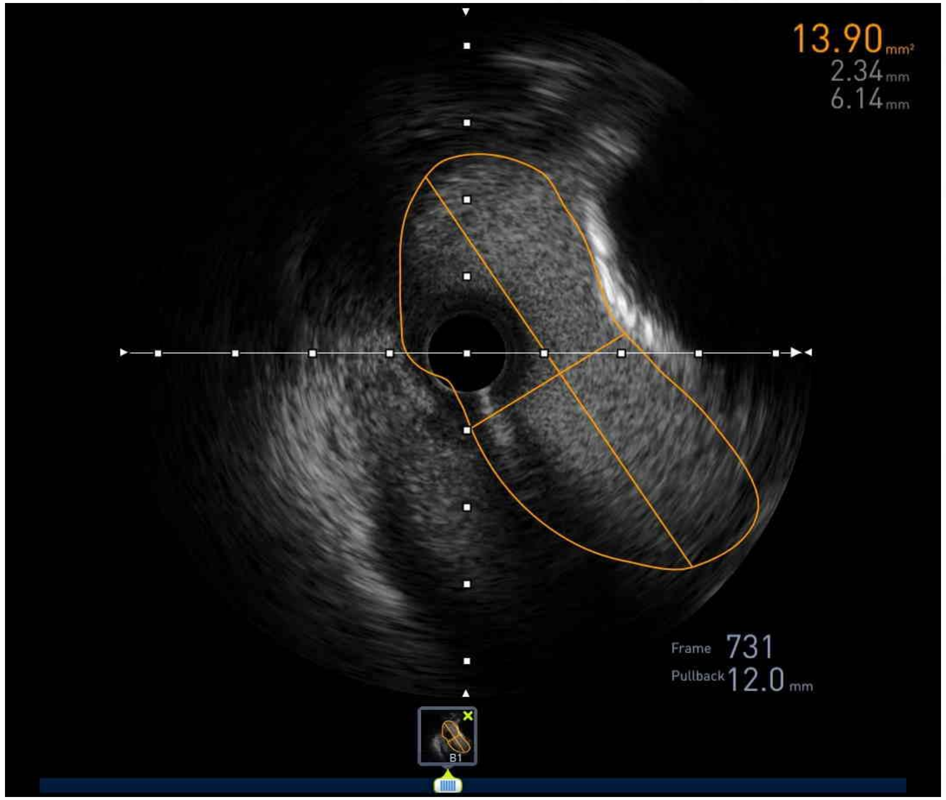
FFR 0.89

Diffuse Atherosclerosis



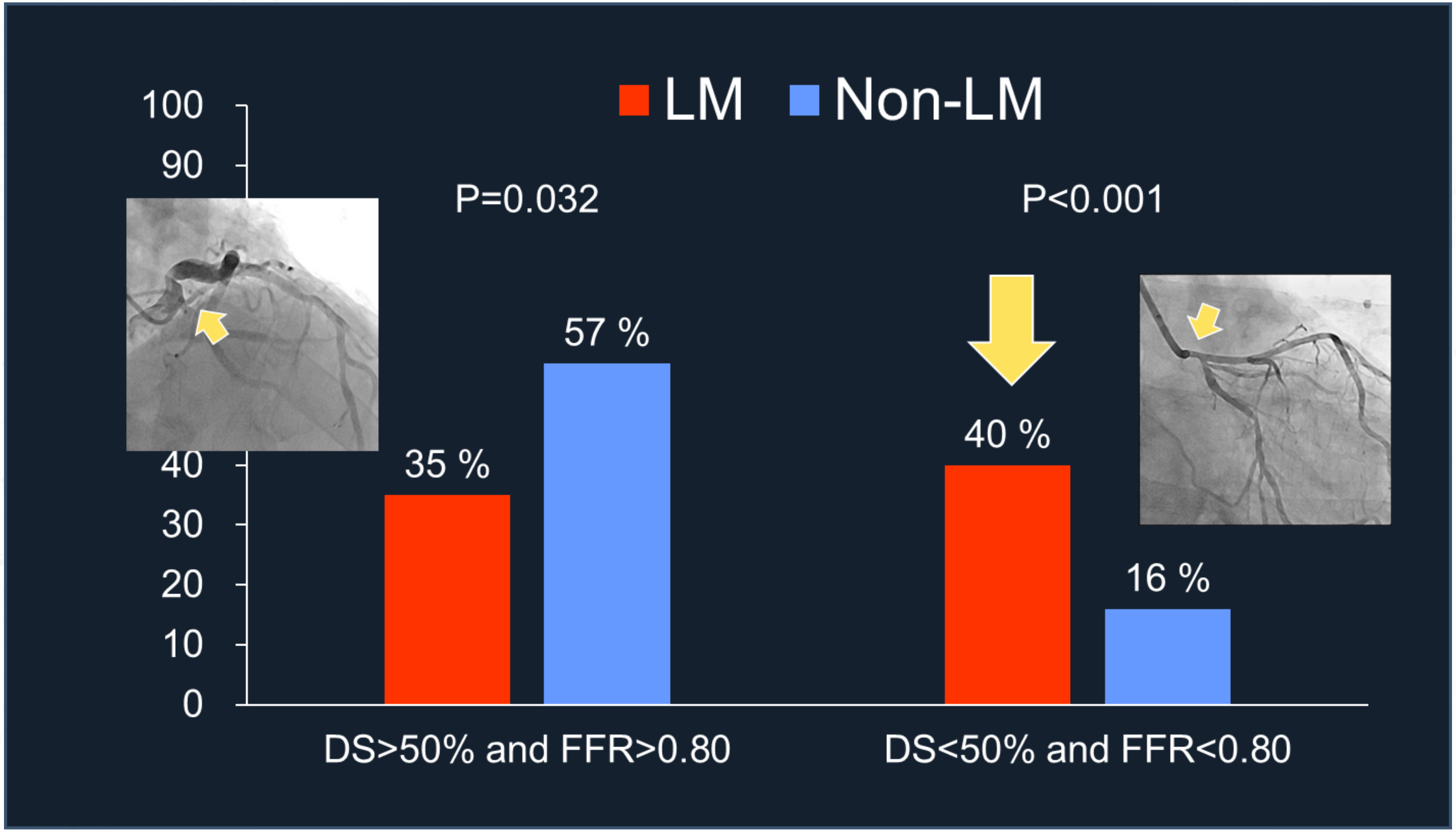
MLA 8.8-13.9mm^2





Left Main Supplies Large Myocardium

In symptomatic patients, ambiguous LM stenosis should be evaluated by FFR



Park SJ et al JACC Cardiovasc Interv. 2012;5:1029-36

Decision Making Outcome

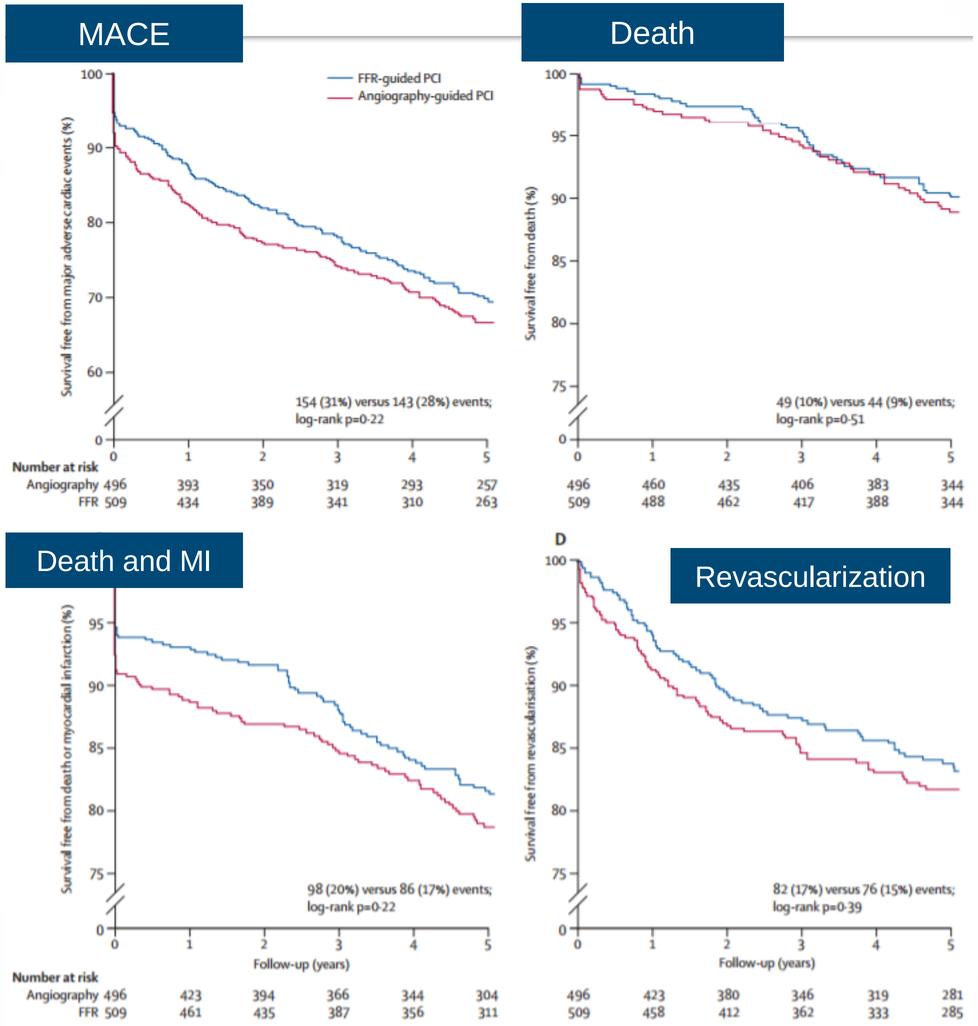
Changes in Practice: “Less Treatment by FFR”

26-44%

Trial (Year) (Ref. #)	Subjects	PW Assessment	Change in Management Strategy
DEFINE REAL (2018) (6)	Multivessel disease	FFR and/or iFR Intermediate lesions	26.9% (130 of 484 patients)
POST-IT (2016) (7)	FFR in ≥1 vessel	FFR Operator's discretion	44.2% (406 of 918 patients)
FAMOUS-NSTEMI (2015) (8)	NSTEMI	FFR All lesions with ≥30% stenosis	21.6% (38 of 176 patients)
R3F (2014) (9)	Ambiguous stenosis +	FFR Angiographically 35% to 65% stenosis	43.2% (464 of 1,075 patients)
RIPCORD (2014) (10)	Stable chest pain	FFR All coronary arteries ≥2.25 mm	26.5% (53 of 200 patients)

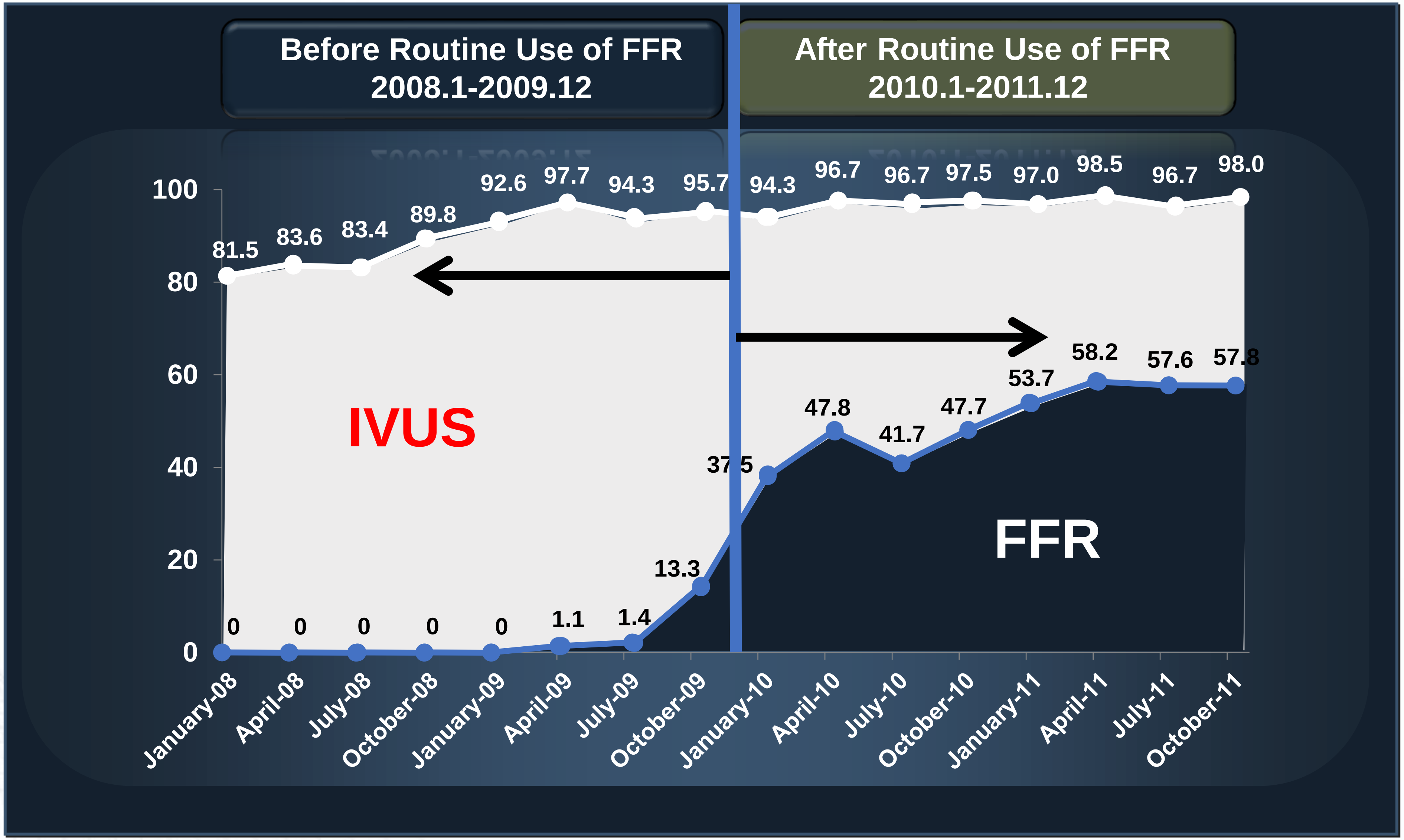
Koo BK, JACC: CARDIOVASCULAR INTERVENTIONS VOL. 11, NO. 4, 2018 FEBRUARY 26, 2018:366 – 8

FFR guided PCI in MV disease – FAME 1



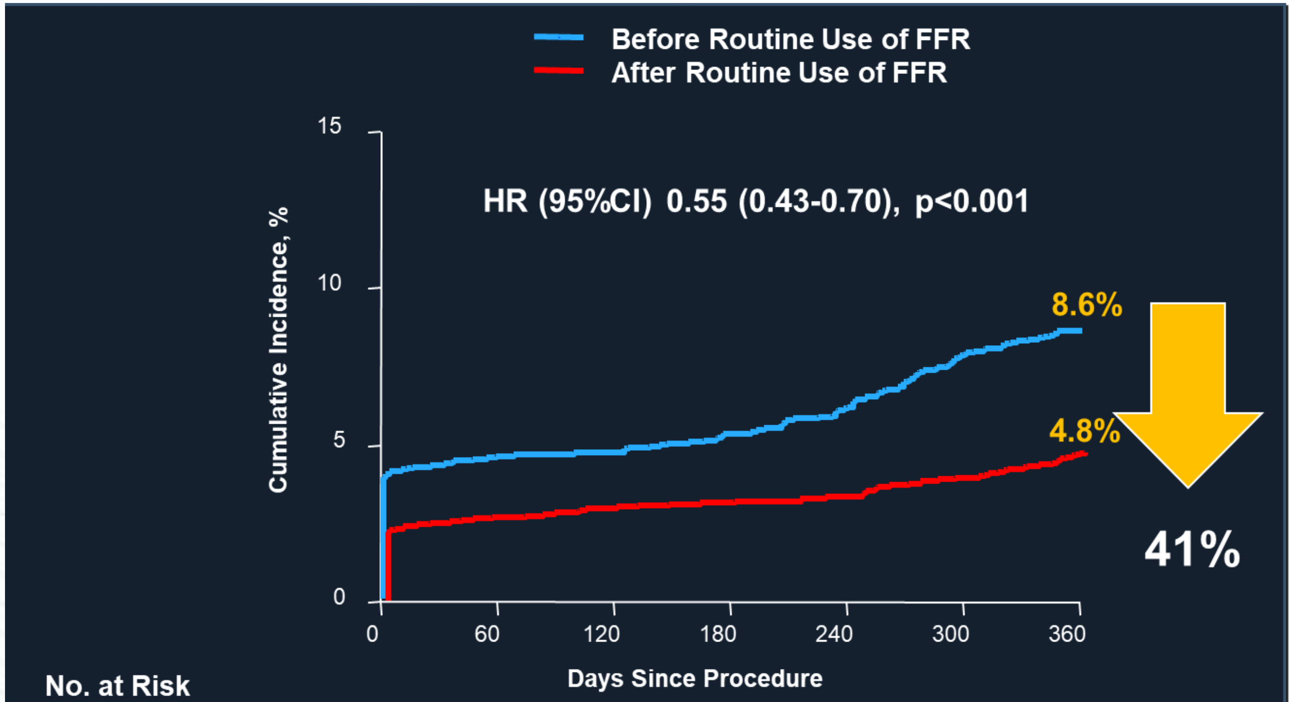
Lokien X van Nuen et al. LANCET 7–13 November 2015, Pages 1853–1860

Rate of FFR Use
in Asan Medical Center

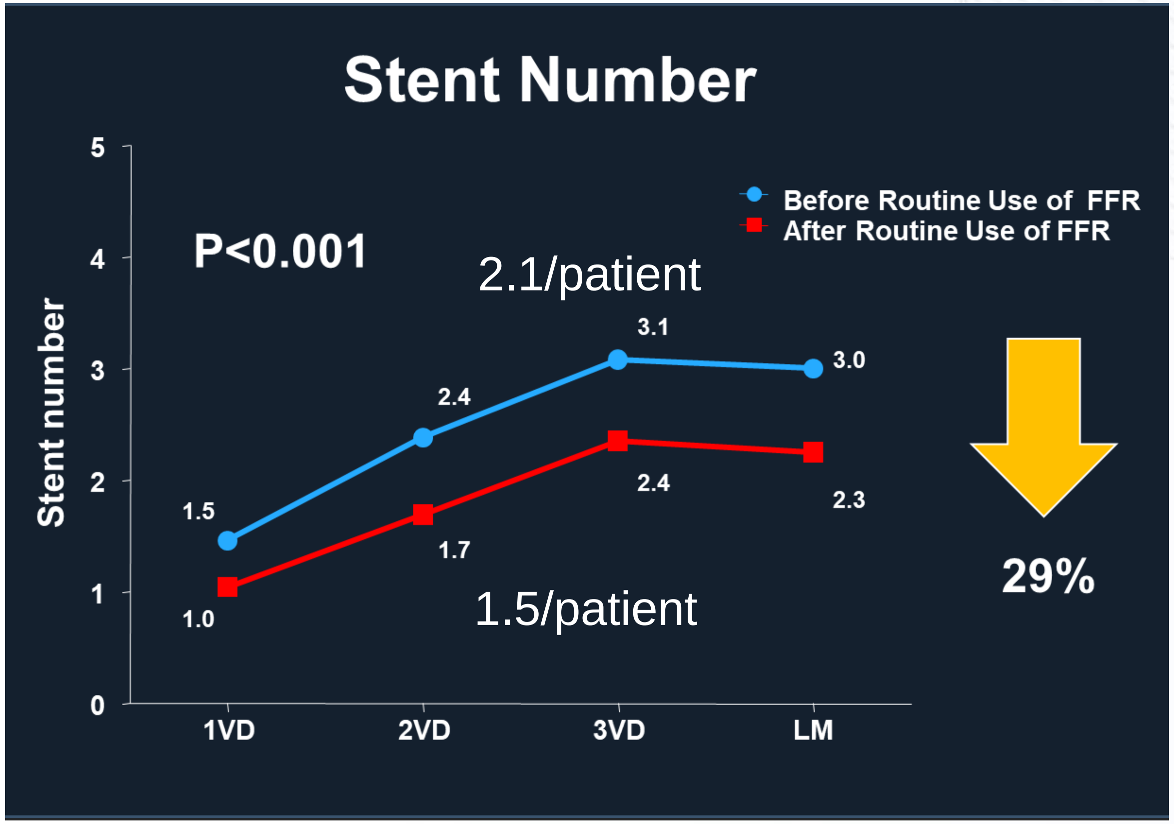


ASAN PCI Registry

Primary Endpoint: Death, MI, and Repeat Revascularization

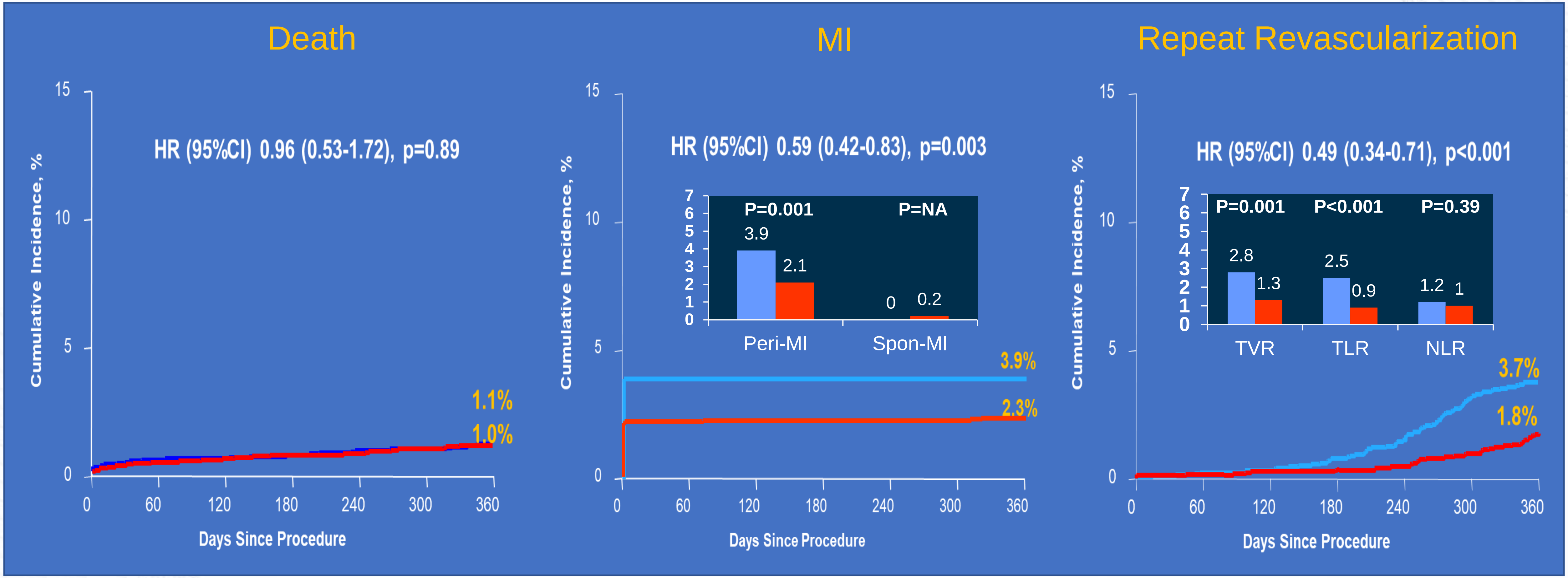


No. at Risk				
Before Routine Use	2178	2066	2011	1960
After Routine Use	2178	2092	2067	2037



Park SJ, Ahn JM et al. Eur Heart J. 2013 Nov;34(43):3353-61

ASAN PCI Registry



Park SJ, Ahn JM et al. Eur Heart J. 2013 Nov;34(43):3353-61

The Major Benefit of FFR(iFR) measurement

The benefit of FFR guided PCI is primarily due to

1) The reduced number of stents used per patient

2) Avoid unnecessary PCI, and

3) The subsequent decreased risk of

peri-procedural MI and (urgent) repeat revascularization

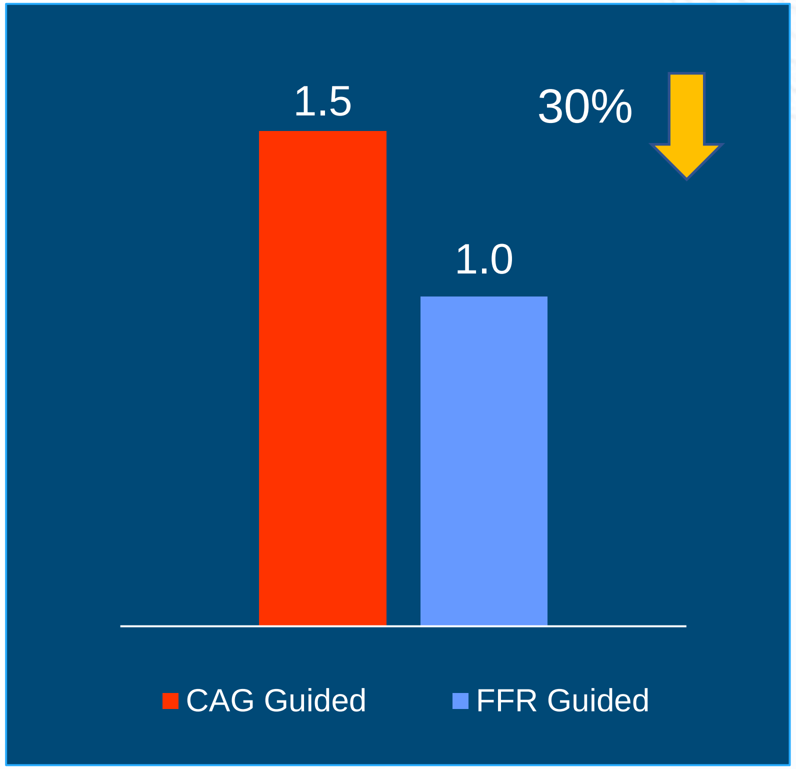
FLOWER-MI

Primary Endpoint

Death, nonfatal MI, or unplanned hospitalization

Outcomes	FFR-Guided Group (N=586)	Angiography-Guided Group (N=577)	Hazard Ratio or Difference (95% CI)†	P Value
Primary outcome				
Composite outcome — no. (%)‡	32 (5.5)	24 (4.2)	1.32 (0.78–2.23)	0.31
Death from any cause	9 (1.5)	10 (1.7)	0.89 (0.36–2.20)	
Nonfatal myocardial infarction§	18 (3.1)	10 (1.7)	1.77 (0.82–3.84)	
Unplanned hospitalization leading to urgent revascularization				
Patients with condition — no. (%)	15 (2.6)	11 (1.9)	1.34 (0.62–2.92)	
Treatment of target lesions in nonculprit artery by urgent revascularization — no./total no. (%)	8/15 (53.3)	3/11 (27.3)	—	

Number of stents per patient

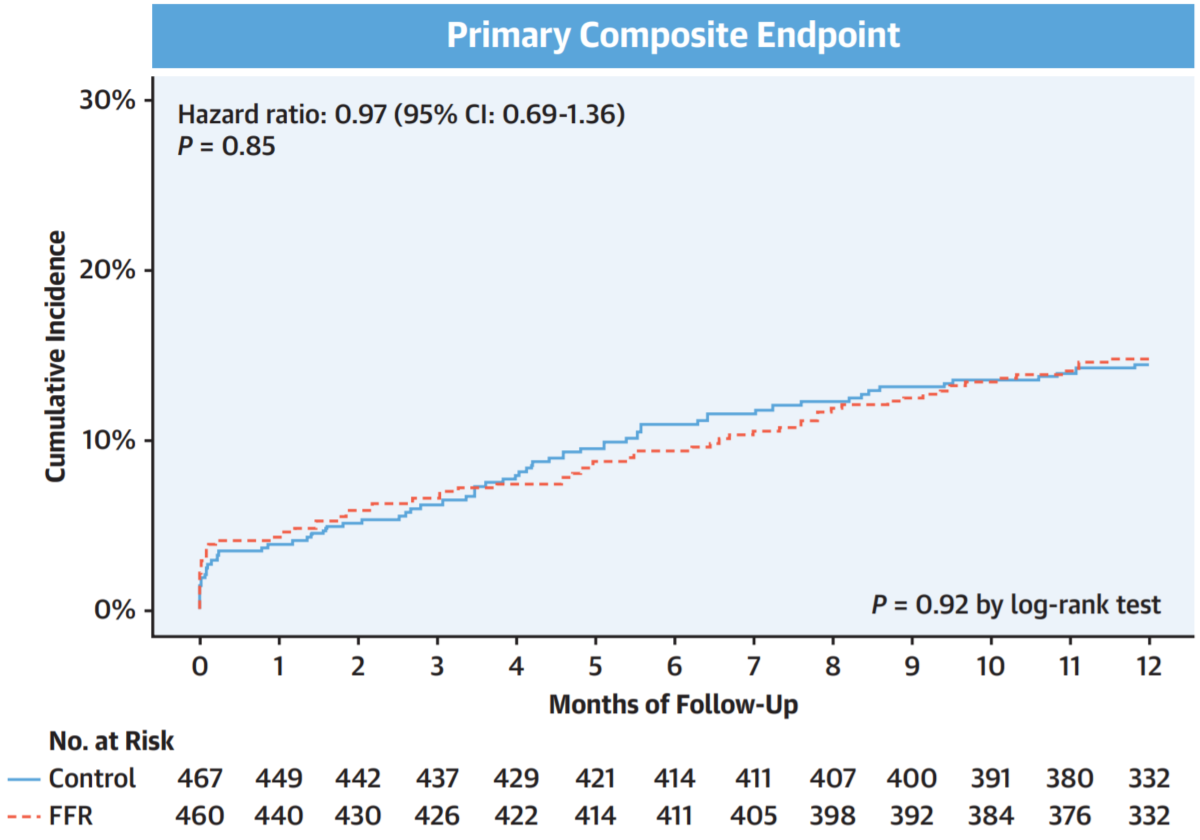


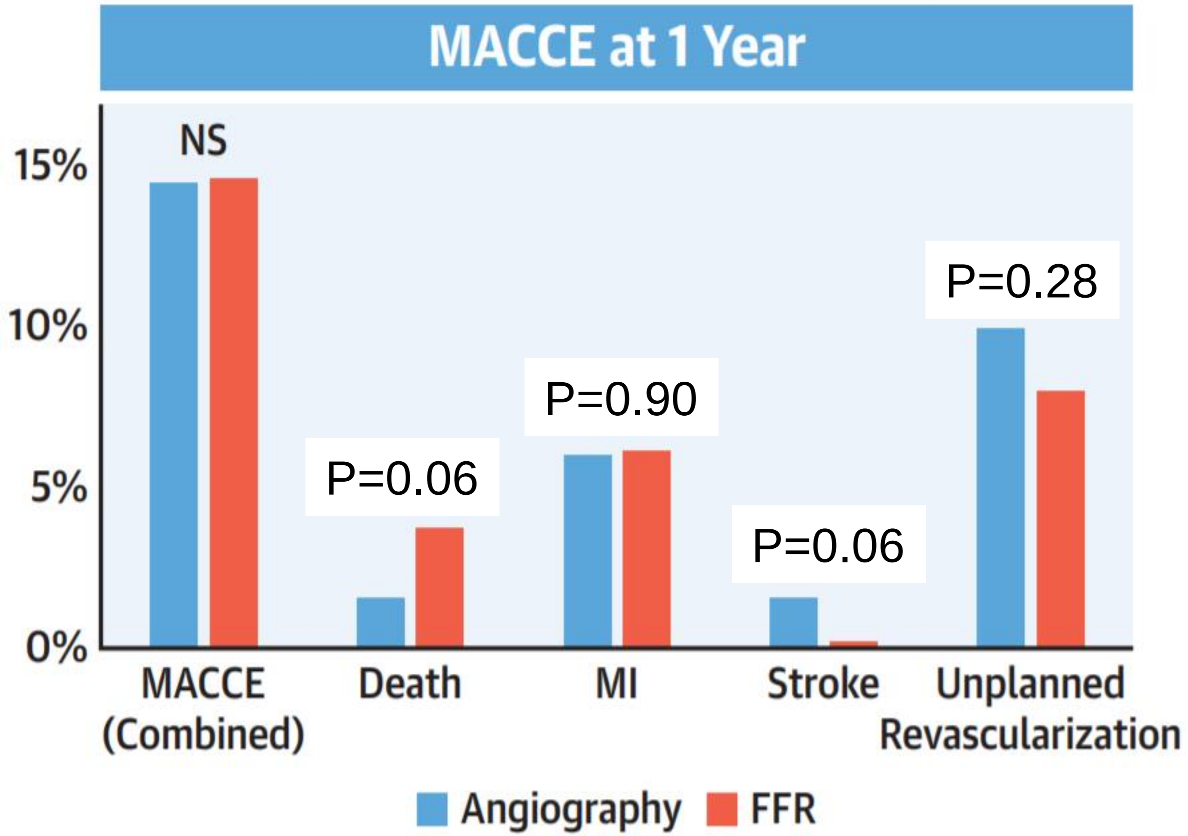
N Engl J Med 2021;385:297-308

FUTURE Trial

Primary Endpoint

Death, nonfatal MI, stroke or unplanned hospitalization





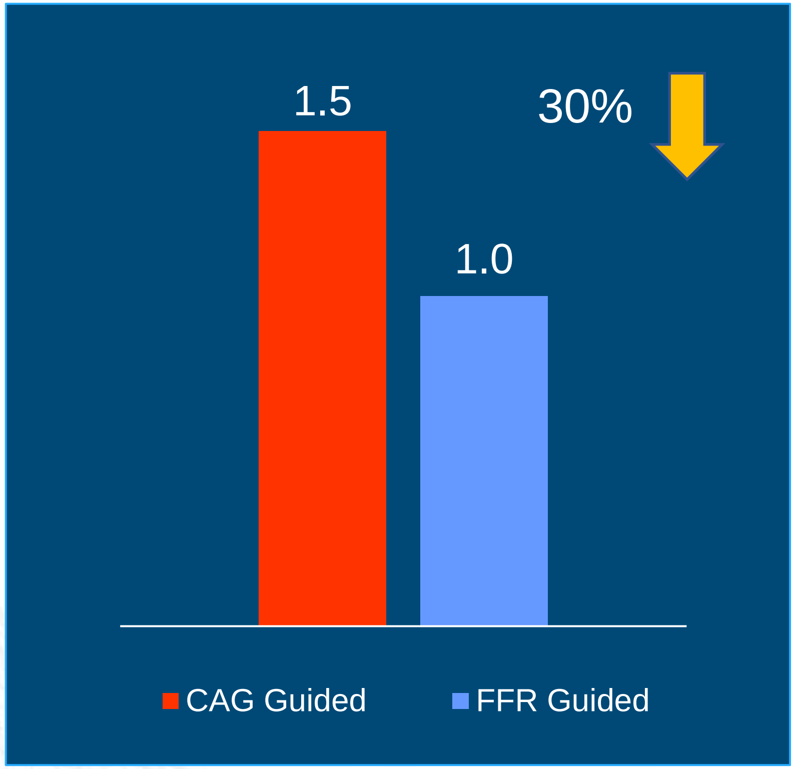
J Am Coll Cardiol 2021;78:1875–1885

Treatment Strategy

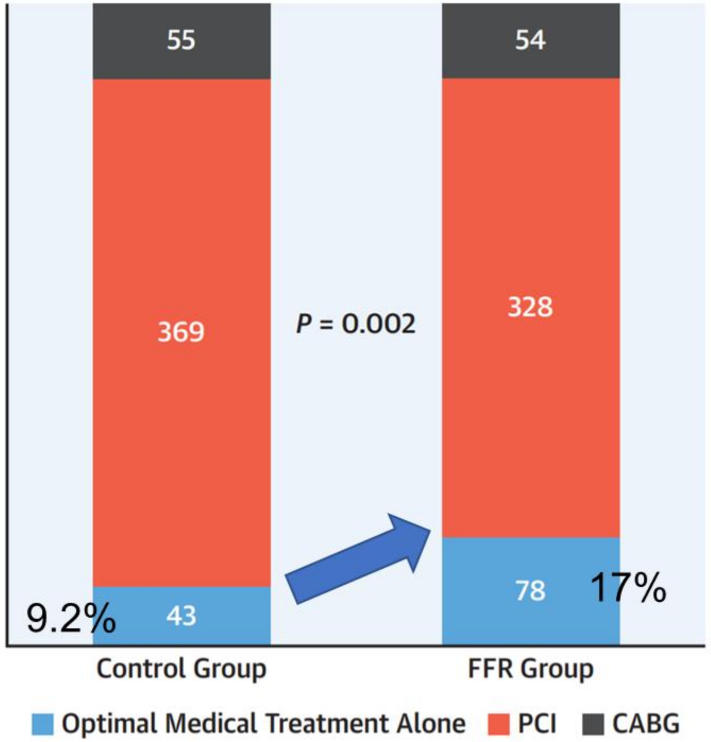
Reduced Stent Number and Increased Medical Treatment

FLOWER-MI

Number of stents per patient



FUTURE Trial



IVUS vs. FFR

Visual Functional
Mismatch (II)

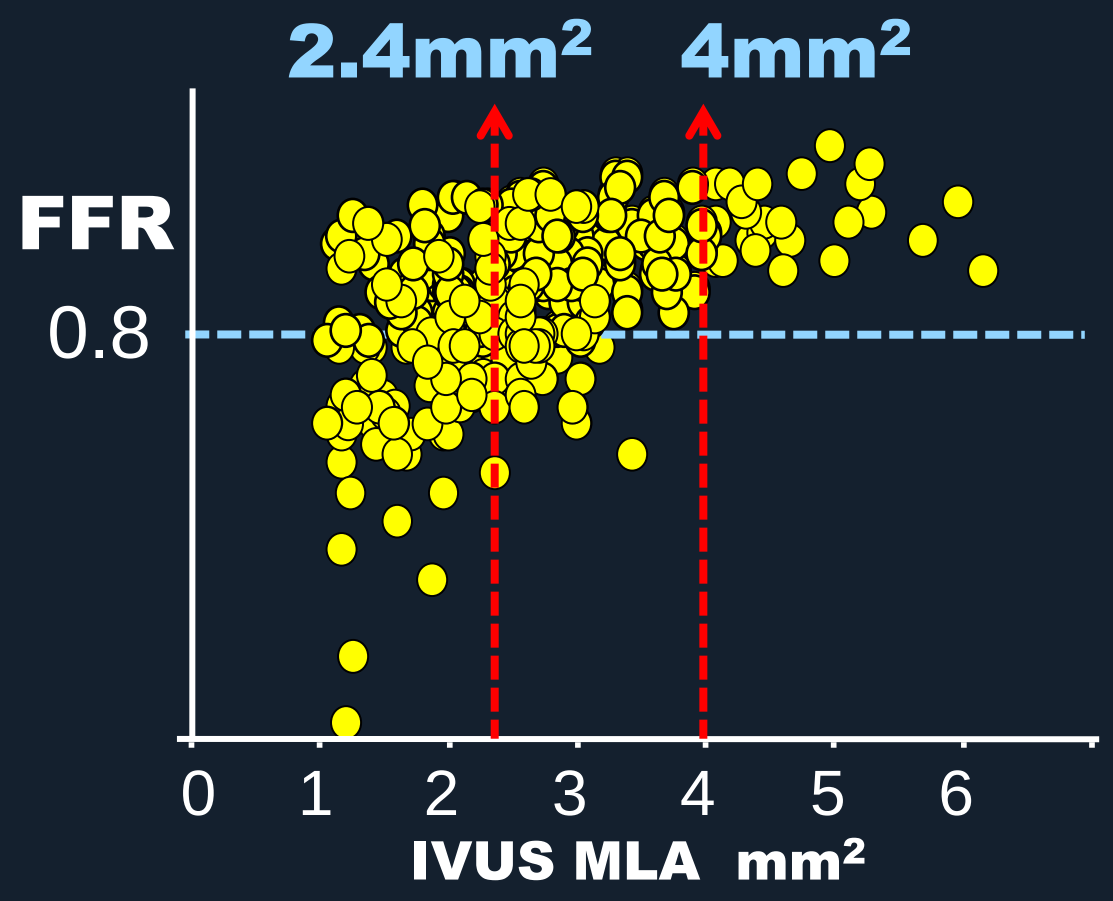
Meta-analysis: IVUS-MLA to Predict FFR (N=17 Studies)

MLA 2.3mm^2-4.0mm^2

Subgroups	Trials	Sensitivity	Specificity	Positive LR	Negative LR	Diagnostic OR	Summary ROC AUC/Q*	Diagnostic accuracy
FFR cut-off								
<0.75	4	0.84 (0.75-0.91)	0.77 (0.70-0.82)	3.80 (2.06-7.00)	0.21 (0.13-0.33)	21.61 (10.59-44.11)	0.8977/0.8287	0.790
<0.80	14	0.74 (0.72-0.76)	0.65 (0.64-0.67)	2.25 (2.00-2.53)	0.36 (0.28-0.45)	6.59 (4.62-9.39)	0.7496/0.6931	0.684
MLA (mm^2)								
<0.3	11	0.75 (0.72-0.77)	0.66 (0.64-0.68)	2.48 (2.10-2.92)	0.32 (0.24-0.44)	8.26 (5.16-13.22)	0.7996/0.7355	0.688
≥0.3	8	0.74 (0.70-0.79)	0.69 (0.65-0.72)	2.43 (1.93-3.07)	0.35 (0.26-0.48)	7.69 (4.48-13.19)	0.8026/0.7381	0.707
Ethnicity								
Asian	11	0.78 (0.76-0.81)	0.66 (0.63-0.68)	2.35 (2.09-2.64)	0.30 (0.23-0.39)	8.46 (5.92-12.10)	0.8046/0.7399	0.704
Western	7	0.69 (0.64-0.74)	0.69 (0.66-0.73)	2.29 (1.87-2.82)	0.46 (0.38-0.57)	5.37 (3.49-8.27)	0.7580/0.7001	0.669
QUADAS								
<7	10	0.73 (0.70-0.76)	0.66 (0.64-0.68)	2.30 (1.94-2.72)	0.36 (0.26-0.49)	6.80 (4.24-10.92)	0.7808/0.7193	0.684
≥7	7	0.79 (0.74-0.83)	0.66 (0.62-0.69)	2.39 (2.00-2.86)	0.30 (0.22-0.42)	8.76 (5.27-14.56)	0.7938/0.7304	0.700

IVUS: intravascular ultrasound, MLA: minimal lumen area, LR: likelihood ratio, OR: odds ratio, ROC: receiver operating characteristic, AUC: area under the curve, Q*: Q point, FFR: fractional flow reserve, QUADAS: quality assessment for studies of diagnostic accuracy

New IVUS MLA for FFR <0.80 In Epicardial Coronary Artery

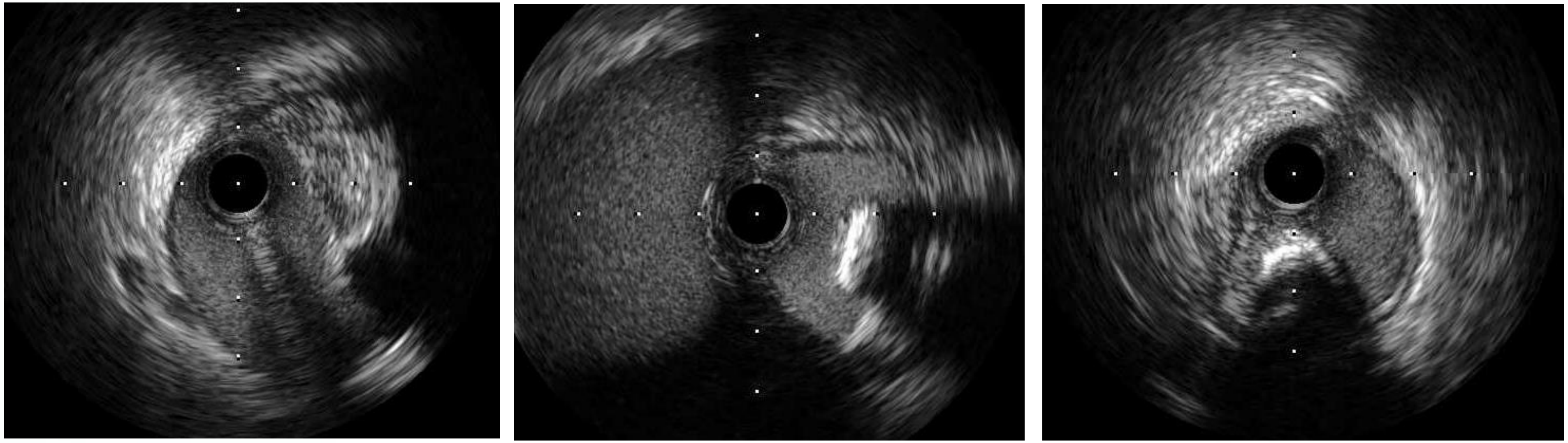


- 66% of analyzed lesions have MLA<4 mm² but FFR >0.80
- 30% of analyzed lesions had MLA <2.4mm² but FFR >0.80.
- Regardless of cutoff values, use of IVUS MLA criteria alone could not predict the result of FFR measurement

Kang SJ, Park SJ, Circ Cardiovasc Interv. 2011;4: 65-71

Single Cut of Coronary Artery

IVUS MLA



Efforts to Improve the Accuracy of IVUS-MLA

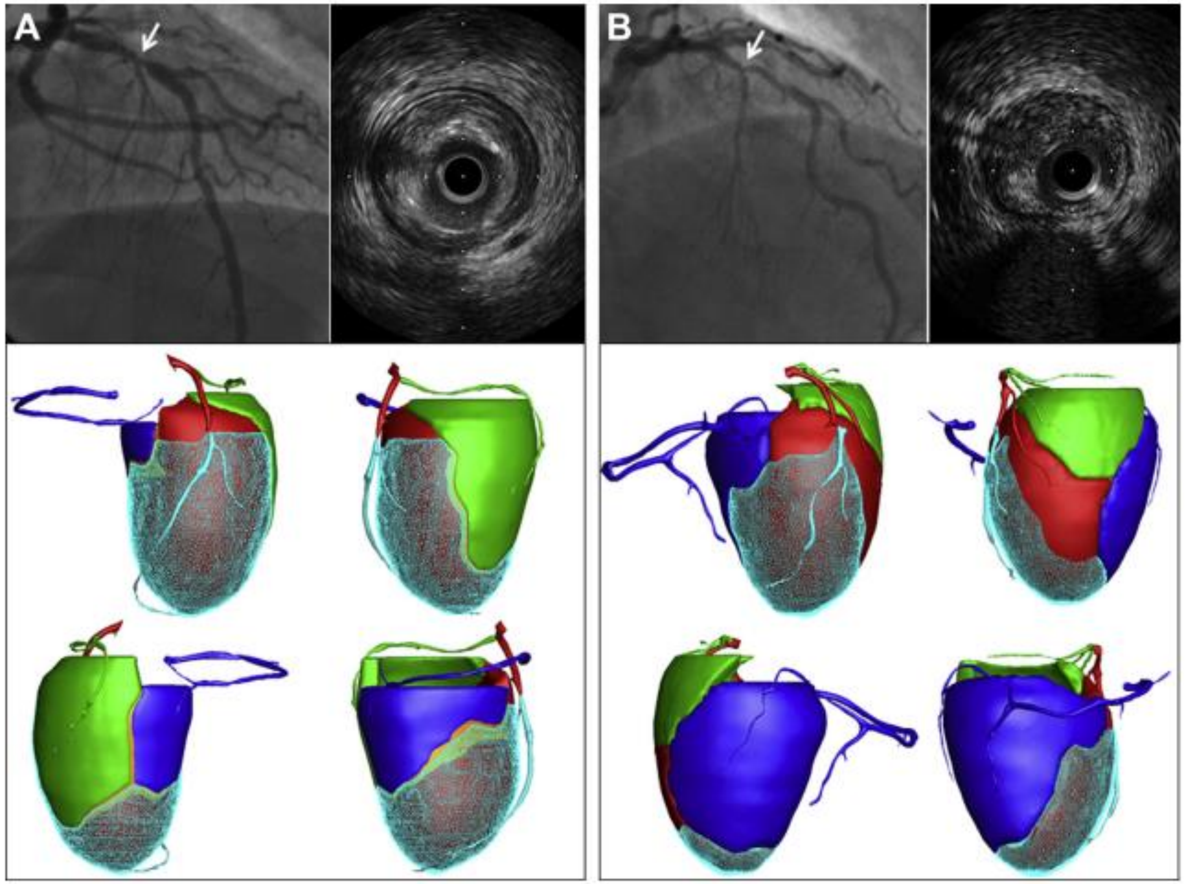
Mathematically Derived Criteria for Detecting Functionally Significant Stenoses Using Coronary Computed Tomographic Angiography—Based Myocardial Segmentation and Intravascular Ultrasound—Measured Minimal Lumen Area

Soo-Jin Kang, MD[a], Jihoon Kweon, PhD[a], Dong Hyun Yang, MD[b], June-Goo Lee, PhD[b], Joonho Jung, PhD[b], Namkug Kim, PhD[b], Gary S. Mintz, MD[c], Joon-Won Kang, MD[b], Tae-Hwan Lim, MD[b], Seong-Wook Park, MD[a], and Young-Hak Kim, MD[a,*]

The lack of practical method for quantifying myocardial territories has made it difficult to link anatomic lesion morphology to the hemodynamic significance of coronary artery stenosis. The aim of this study was to develop and validate mathematically derived morphologic criteria for predicting fractional flow reserve (FFR) <0.80 using intravascular ultrasound (IVUS) parameters and a coronary artery—based myocardial segmentation (CAMS) of the affected myocardial territory. Coronary computed tomography angiography, IVUS, and FFR data were analyzed in 103 non—left main intermediate coronary artery lesions (30% to 80% of angiographic stenosis). Using CAMS method, the total left ventricular myocardial volume and the myocardial volume subtended by a stenotic coronary segment (V_{sub}) were assessed. The morphologic criteria for detecting an FFR <0.80 using the IVUS and CAMS parameters were mathematically derived. Overall, an IVUS-measured minimal lumen area (MLA) <2.79 mm^2 predicted an FFR <0.80 with sensitivity of 76%, specificity of 78%, positive predictive value of 71%, and negative predictive value of 82%. A V_{sub}/MLA^2 >4.04 best predicted an FFR <0.80 (sensitivity 88%, specificity 90%, positive predictive value 86%, and negative predictive value 92%, area under curve = 0.944). There was a significant difference in the areas under the curves between IVUS-MLA versus V_{sub}/MLA^2 (difference = 0.068, p = 0.005). Conversely, adjusting for body or vessel size did not improve the diagnostic accuracy. (Am J Cardiol 2016;118:170—176)

Because revascularization treatment based on objective evaluation of ischemia improves clinical outcomes, frac-

main reasons is that supplied myocardial territories are variable,[11,12] and there is no reliable method to quantify the

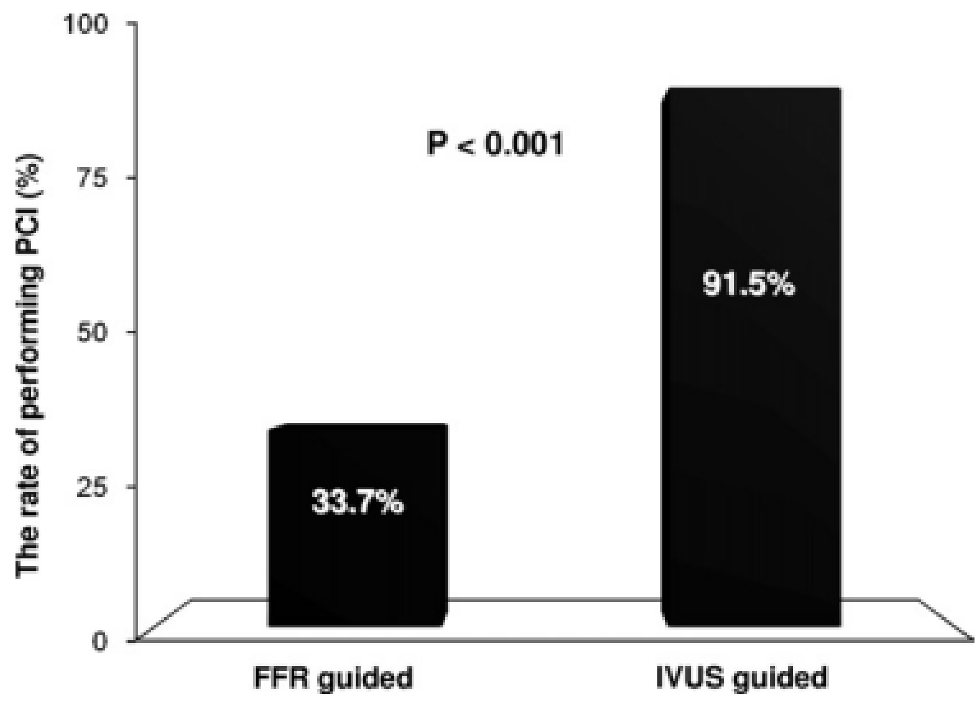


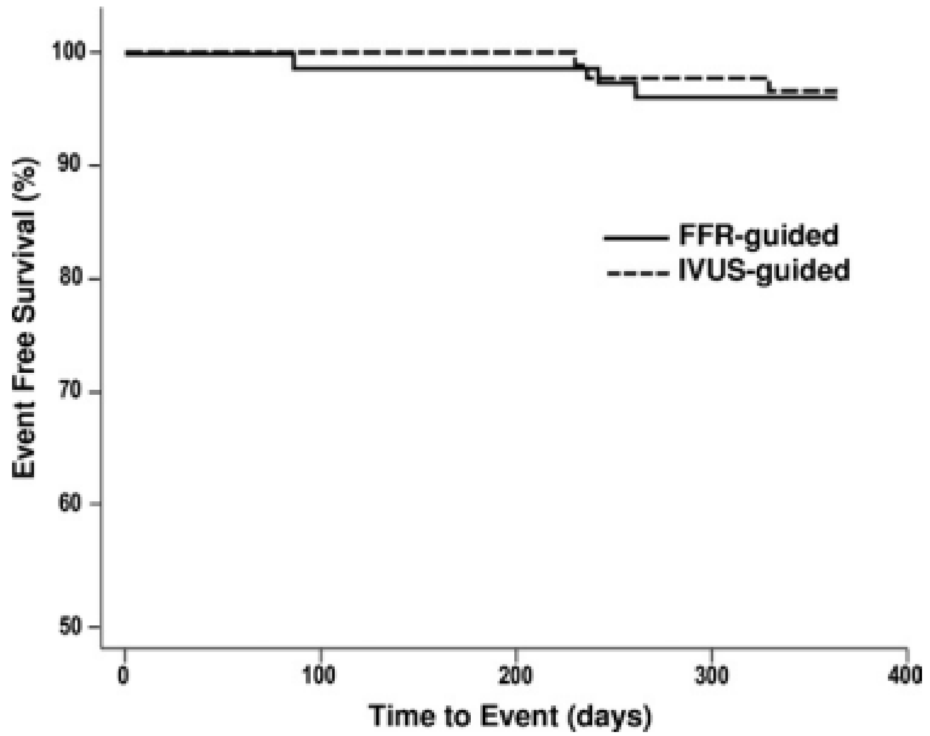
Am J Cardiol 2016;117:1282e1288

Decision Making Outcome

Registry Study: IVUS vs. FFR (N=177)

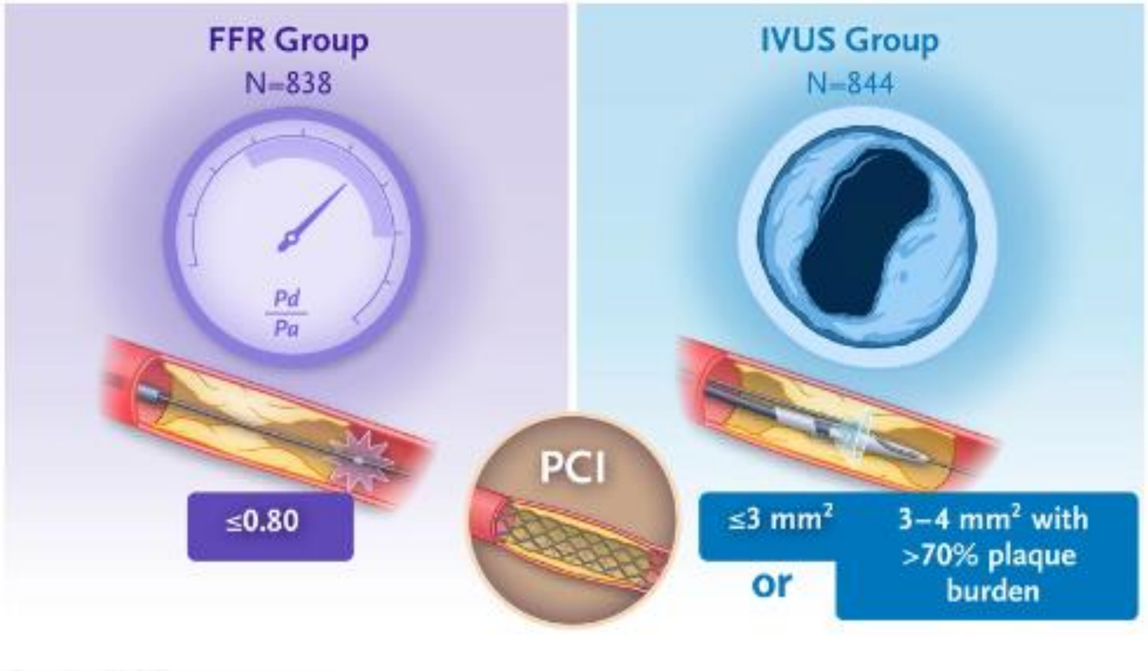
The cutoff value of FFR was 0.80, the cutoff value of MLA was 4.0 mm^2

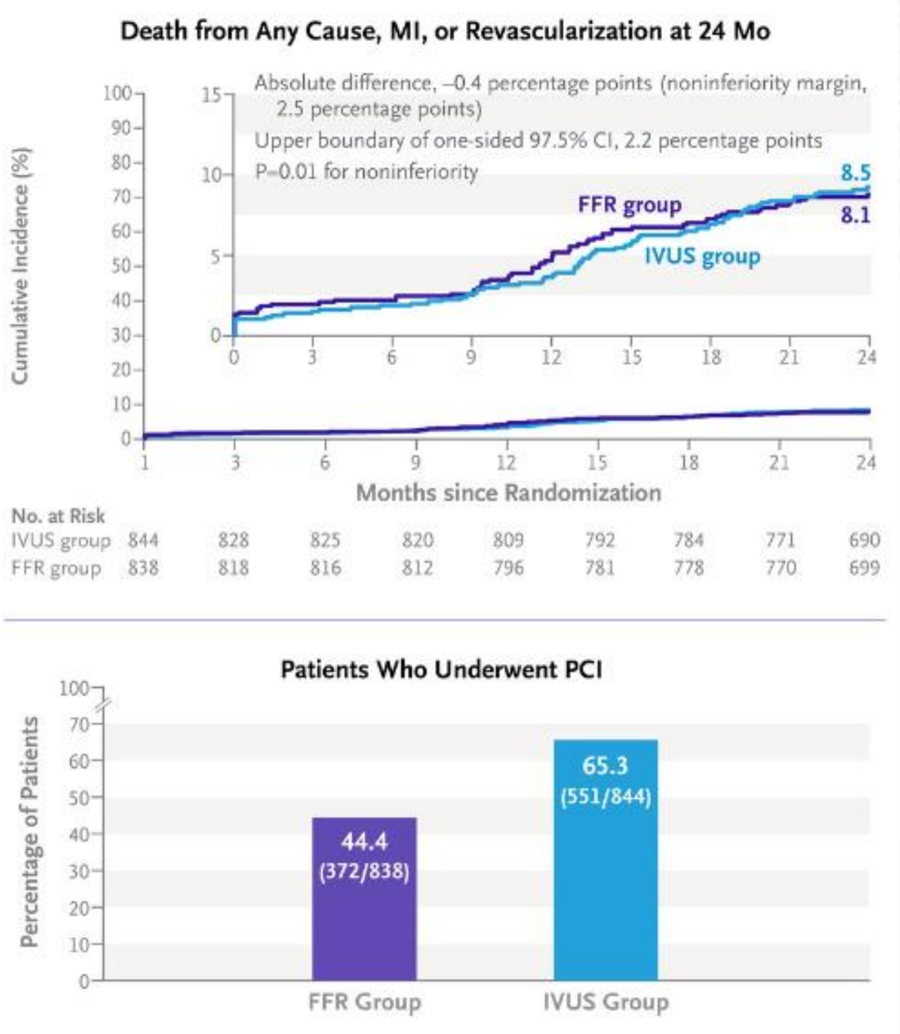




J Am Coll Cardiol Intv 2010;3:812–7

Randomized Study: IVUS vs. FFR





N Engl J Med. 2022 Sep 1;387(9):779-789

My Thought

"The determination of coronary stenosis severity to decide on coronary revascularization should be evaluated from the perspective of myocardial perfusion."

"It is necessary to demonstrate that reduced myocardial perfusion is due to coronary stenosis.."

My Thought

"Anatomical decision making, DS or IVUS increases the risk of unnecessary PCI."