FFR-Guided vs. Angiography-Guided PCI in Patients with Left Main Coronary Artery Disease: FATE-MAIN Trial

Duk-Woo Park, MD

**Asan Medical Center, Ulsan University College of Medicine,
Seoul, Korea**

Disclosure

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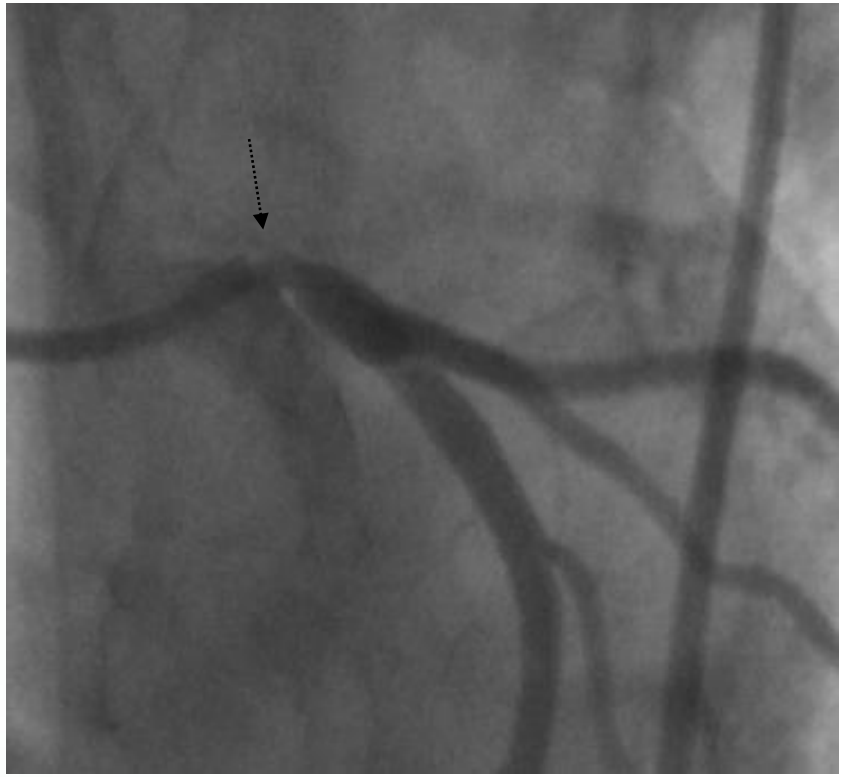
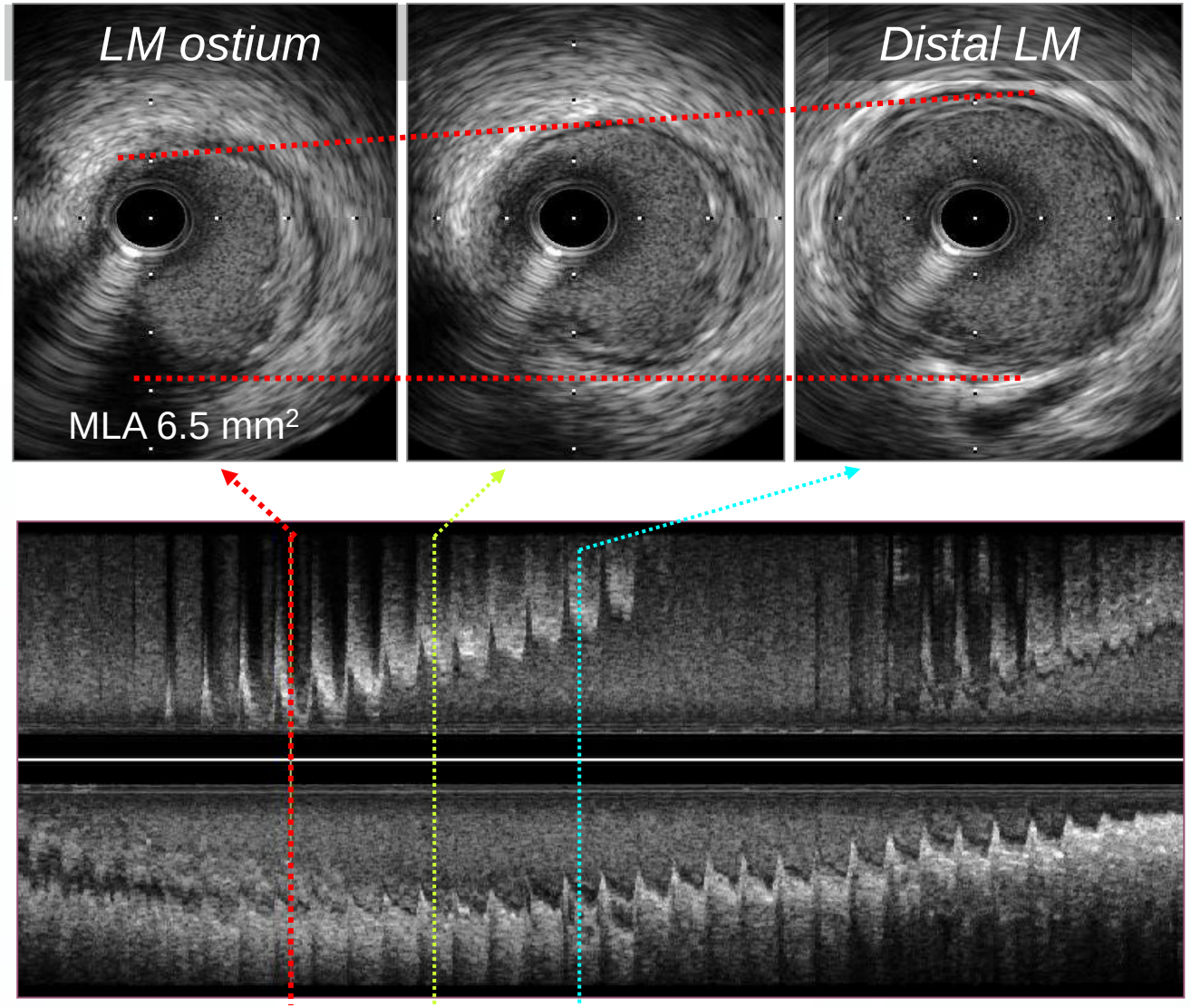
Why FFR for Left Main Disease?

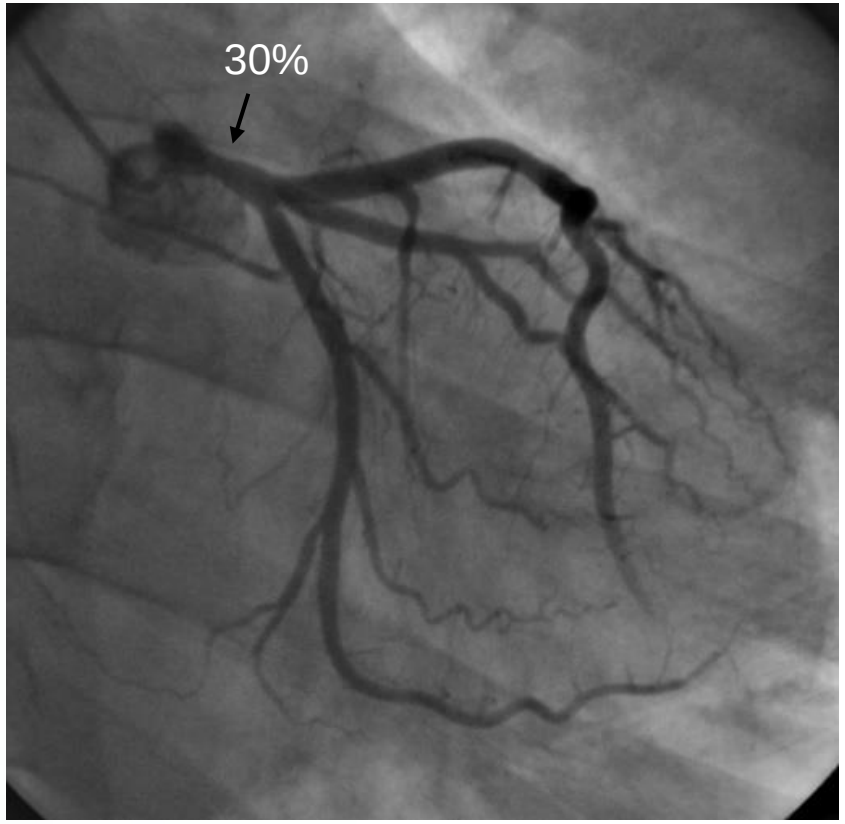
Significant Stenosis,
Negative FFR, 0.80

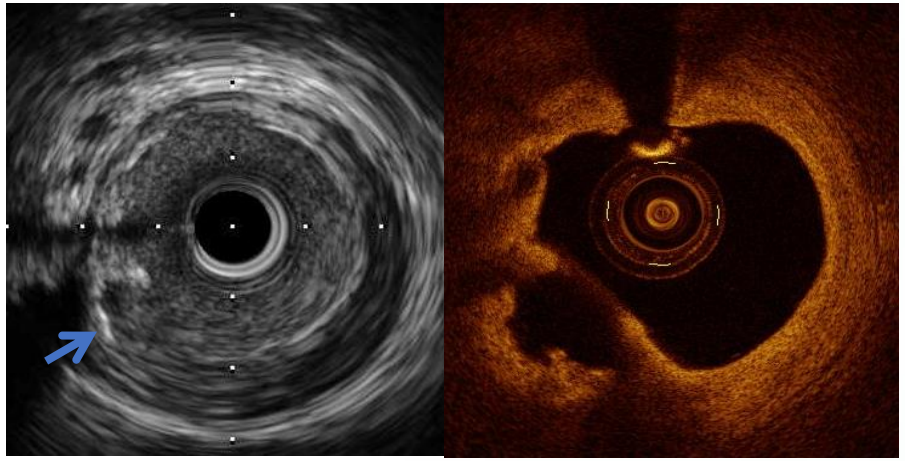


Negative Remodeling



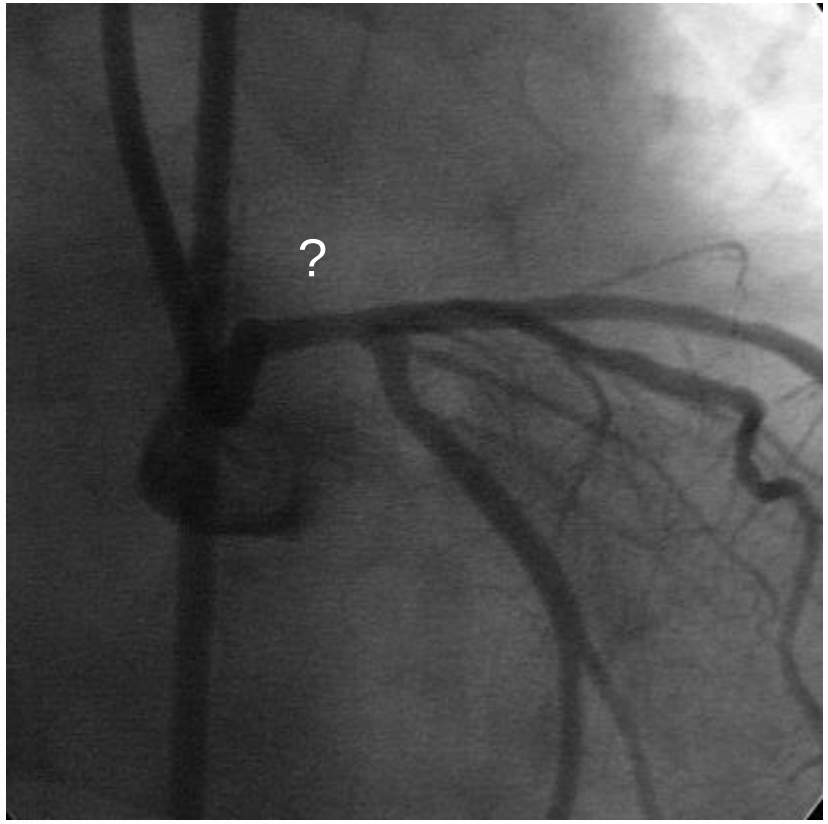
Insignificant Stenosis, *Positive FFR, 0.70*

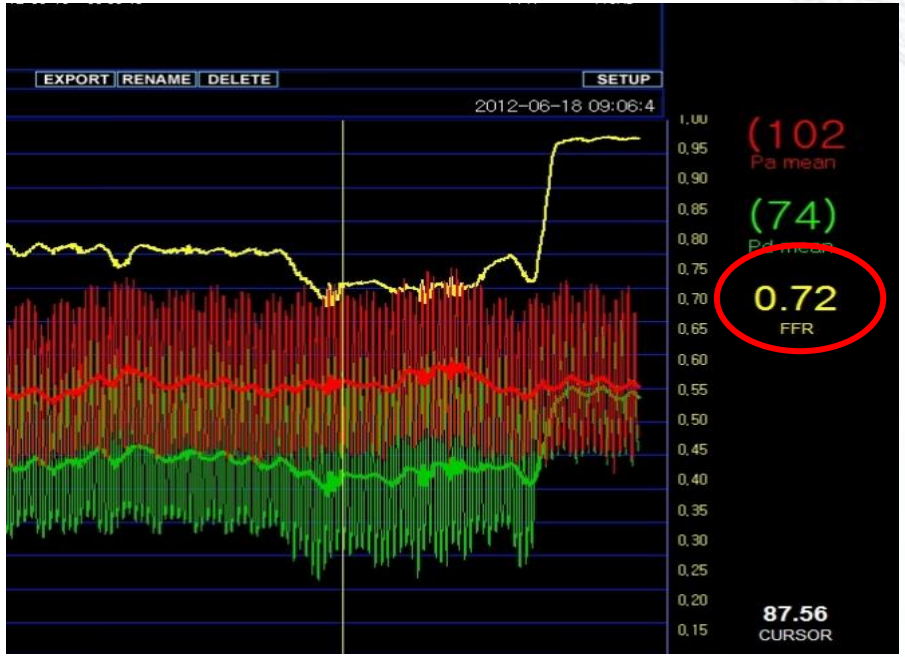


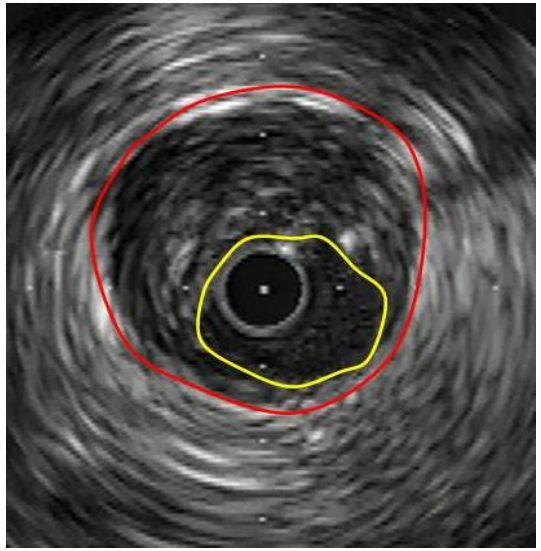


Plaque Rupture
MLA 6.2mm²

Insignificant Stenosis, *Positive FFR, 0.72*



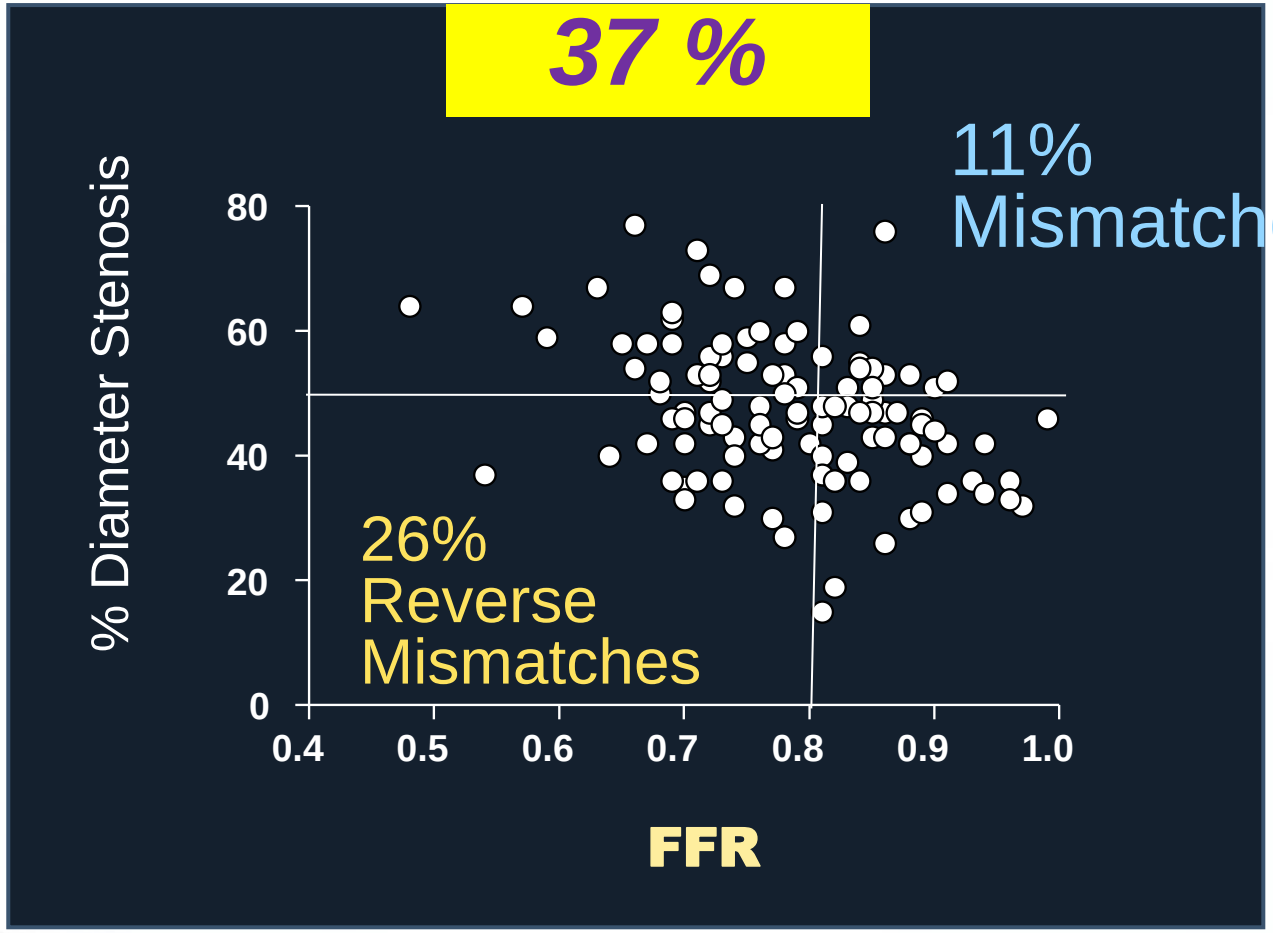




Diffuse Disease
MLA 4.0 mm²

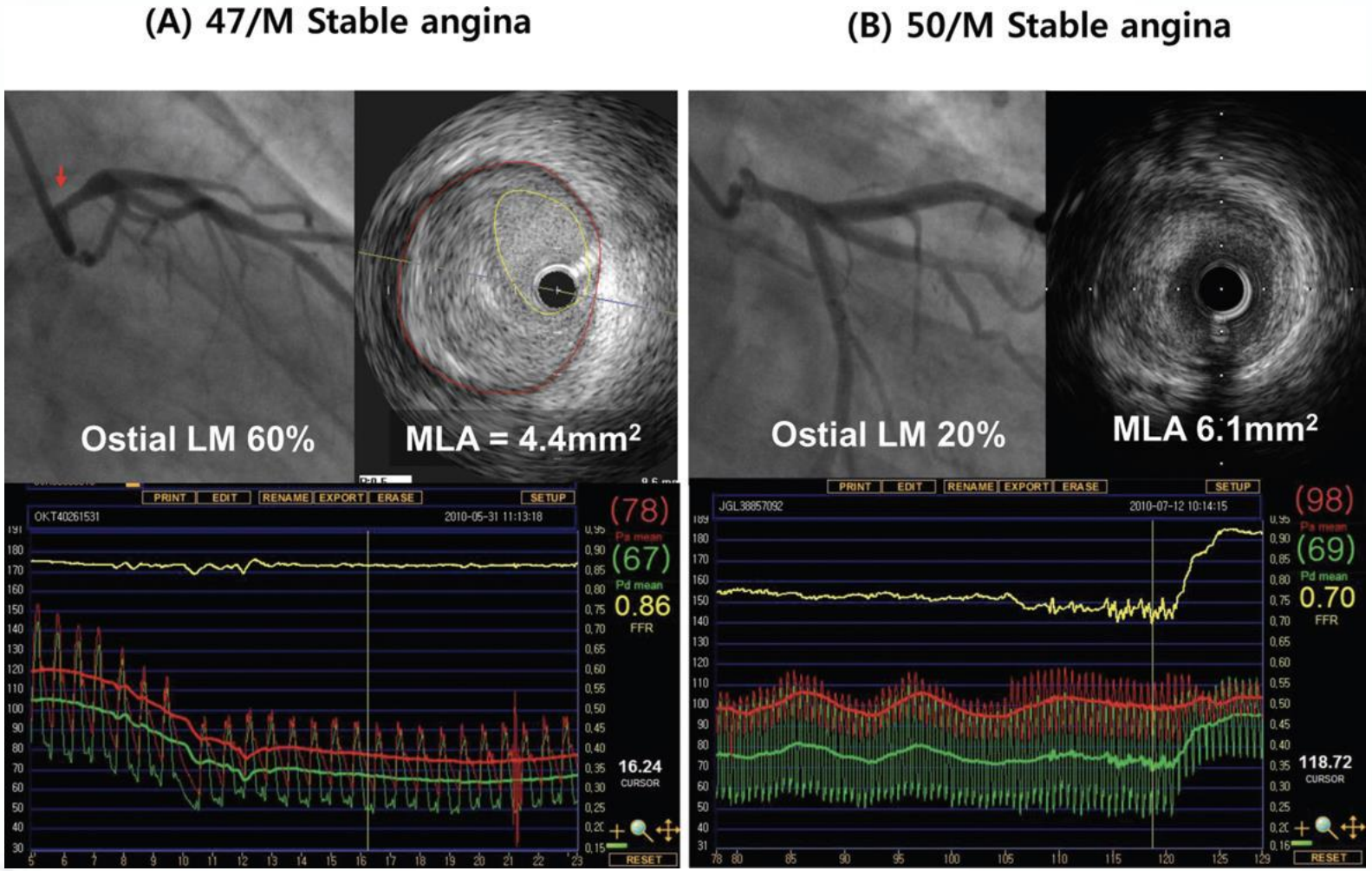
Intermediate LM Disease, Os/Shaft

Mismatches



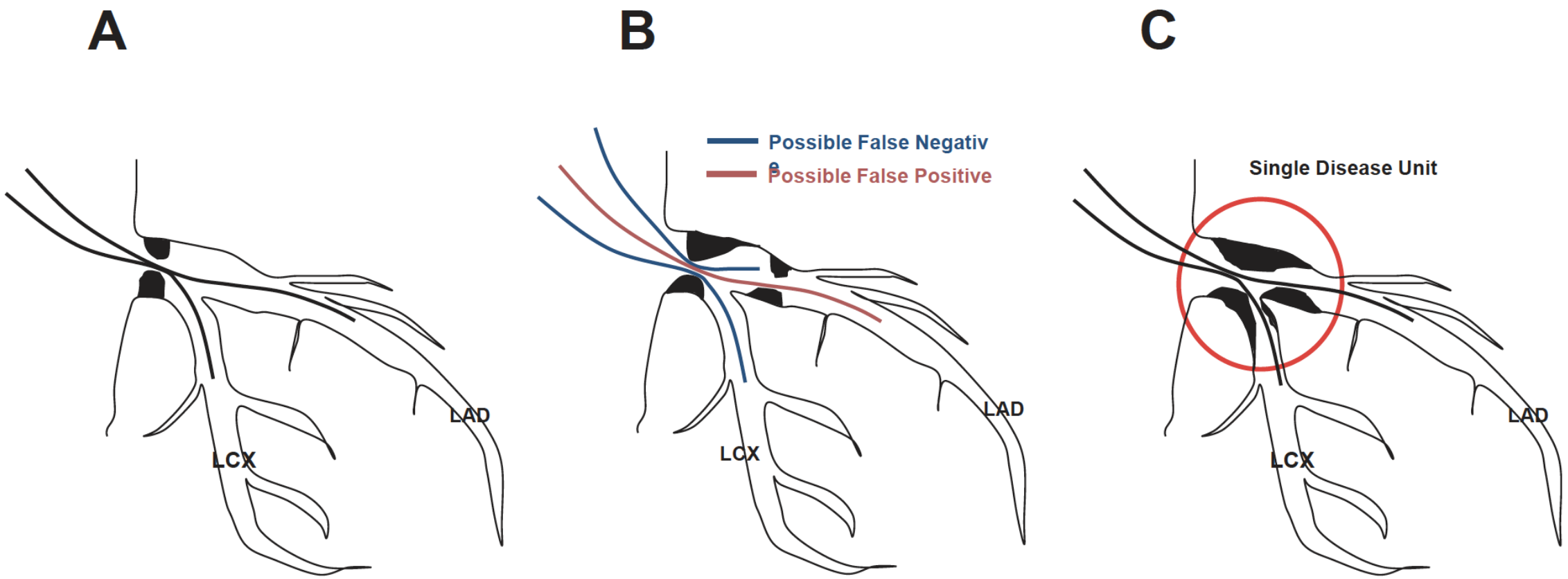
Park SJ et al. *JACC Interv, 2014;7(8):868-874*

Representative case of visual–functional mismatch in LMCA stenosis



Park SJ et al. JAHA 2012 Dec;1(6):e004556

Practical approach for the evaluation of functional significance of LMCA disease



Park SJ et al. JAHA 2012 Dec;1(6):e004556

EXCEL Trial Inclusion Criteria

Inclusion criteria (all must be present)
1a. Unprotected LMCAD with angiographic diameter stenosis ≥70% (visually estimated), or with angiographic diameter stenosis ≥50% but <70% with one or more of the following present: a. Non-invasive evidence of ischaemia referable to a haemodynamically significant left main lesion, and/or b. IVUS MLA ≤6.0 mm^2, and/or c. FFR ≤0.80

EuroIntervention 2016;12:861-872

EXCEL Main QCA data

Table S5. Baseline angiographic core laboratory assessment

	PCI (N=948)	CABG (N=957)
Qualifying left main lesion*		
- Left main coronary segment	919/942 (97.6%)	908/936 (97.0%)
- Left main equivalent disease**	11/942 (1.2%)	14/936 (1.5%)
- Neither	12/942 (1.3%)	14/936 (1.5%)
Bifurcation or trifurcation disease of the distal left main segment	771/942 (81.8%)	741/936 (79.2%)
Number of diseased non-left main coronary arteries*		
- 0	163/942 (17.3%)	167/936 (17.8%)
- 1	292/942 (31.0%)	292/936 (31.2%)
- 2	325/942 (34.5%)	295/936 (31.5%)
- 3	162/942 (17.2%)	182/936 (19.4%)
SYNTAX score	26.9 ± 8.8	26.0 ± 9.8
- Low (≤22)	294/914 (32.2%)	364/926 (39.3%)
- Intermediate (23-32)	391/914 (42.8%)	345/926 (37.3%)
- High (≥33)	229/914 (25.1%)	217/926 (23.4%)

*Diameter stenosis ≥50% by quantitative coronary angiography (among 1878 analyzable angiograms received in the core laboratory). **Diameter stenosis of both the ostial left anterior descending and ostial left circumflex coronary arteries ≥50% by quantitative coronary angiography, without ≥50% left main diameter stenosis. There were no significant differences between groups, except for the mean SYNTAX score by angiographic core laboratory assessment (P=0.005).

NEJM 2016;375:2223-2235

EXCEL Substudy QCA data

TABLE 2 Baseline Angiographic and Procedural Characteristics

	Lesion Location		
	Ostial/Shaft Only (n = 293)	Distal Bifurcation (n = 1,559)	p Value
Ostial or shaft diameter stenosis ≥50%	293 (100.0)	730/1,534 (47.6)	<0.0001
Ostial diameter stenosis ≥50%	268 (91.5)	402/1,534 (26.2)	<0.0001
Shaft diameter stenosis ≥50%	107 (36.5)	652/1,534 (42.5)	0.057
Distal left main bifurcation	0 (0.0)	1,559 (100.0)	–
Distal left main trifurcation	0 (0.0)	642 (41.2)	–
Left main diameter stenosis, %	65.9 ± 10.8	64.4 ± 12.1	0.03
Number of non-left main diseased vessels			
0	70 (23.9)	259/1,559 (16.6)	0.003
1	96 (32.8)	483/1,559 (31.0)	0.55
2	86 (29.4)	522/1,559 (33.5)	0.17
3	41 (14.0)	295/1,559 (18.9)	0.04
SYNTAX score	19.8 ± 7.5	27.9 ± 9.0	<0.0001
Vessels stented or bypassed			
Left anterior descending	186 (63.5)	1,200 (77.0)	<0.0001
Left circumflex	150 (51.2)	1,002 (64.3)	<0.0001
Right coronary artery	86 (29.4)	514 (33.0)	0.22
>1 Stent used in left main*	24/133 (18.0)	342/781 (43.8)	0.0006
≥1 Arterial conduits†	146/146 (100.0)	732/743 (98.5)	0.23
≥2 Arterial conduits†	31/146 (21.2)	247/743 (33.2)	0.004
≥1 Venous conduits†	114/146 (78.1)	555/740 (75.0)	0.43
≥2 Venous conduits†	43/146 (29.5)	269/740 (36.4)	0.11

J Am Coll Cardiol Intv 2018;11:1224–33

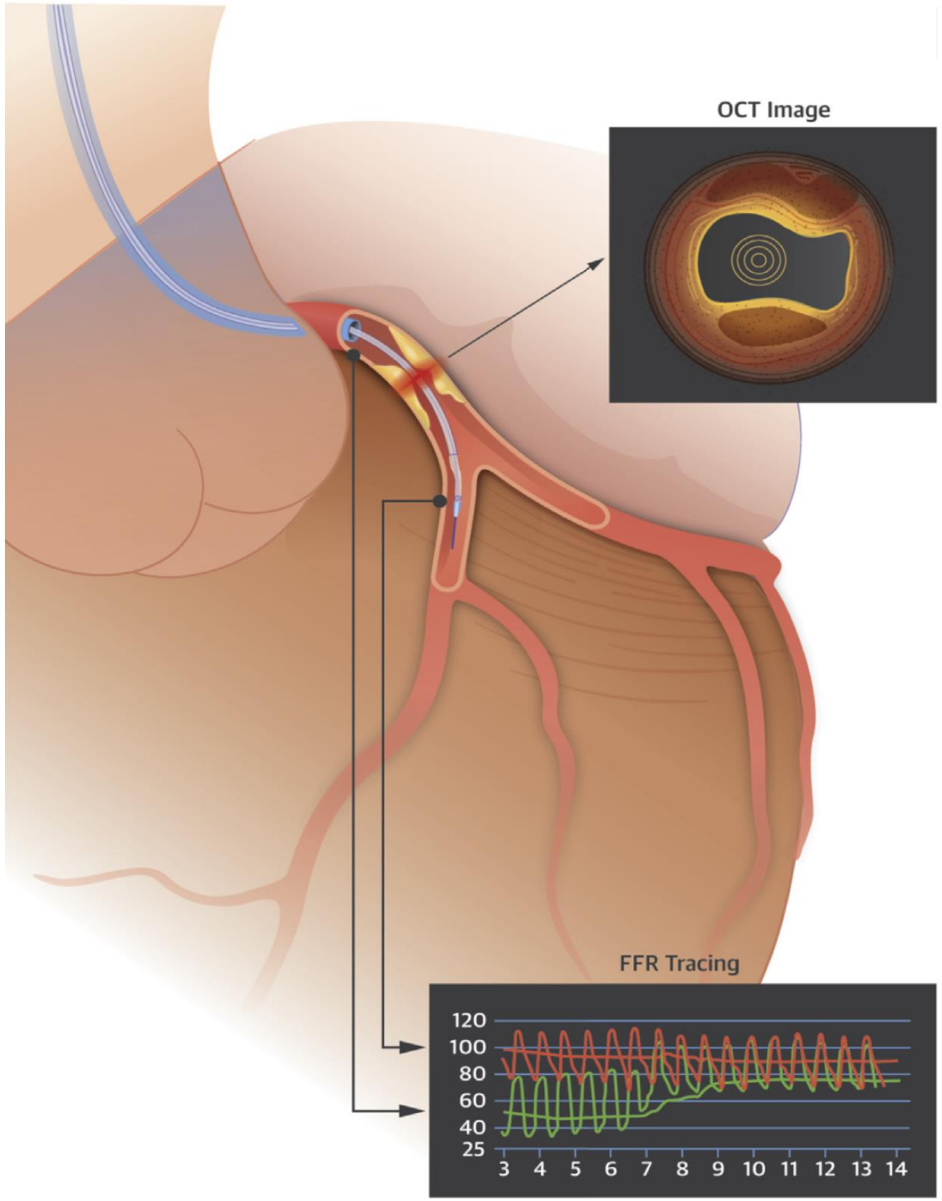
PRECOMBAT QCA data

Supplemental Table 2. Baseline Angiographic Characteristics of the Patients, According to Study Group. *

Angiographic Characteristics	PCI (N=300)	CABG (N=300)	P value
Diseased vessels, N (%)			0.68
Left main only	27 (9.0)	34 (11.3)	
Left main plus single vessel disease	50 (16.7)	53 (17.7)	
Left main plus double vessel disease	101 (33.7)	90 (30.0)	
Left main plus triple vessel disease	122 (40.7)	123 (41.0)	
Bifurcation left main involvement	200 (66.9)	183 (62.2)	0.24
Heavy calcification of left main	17 (5.7)	14 (4.7)	0.58
Diameter stenosis of left main, N (%)			0.12
> 50% and ≤ 70%	160 (53.3)	141 (47.0)	
> 70%	140 (46.7)	159 (53.0)	
Right coronary artery disease, N (%)	149 (49.7)	159 (53.0)	0.41
Restenotic lesion, N (%)	1 (0.3)	2 (0.7)	0.56
Chronic total occlusion, N (%)	2 (0.7)	2 (0.7)	1.0
SYNTAX score, mean±SD §	24.4±9.4	25.8±10.5	0.09
SYNTAX score by tertiles, N (%)			0.75
Score ≤ 19	95 (32.9)	85 (31.6)	
Score > 19 and ≤ 29	105 (36.3)	93 (34.6)	
Score > 29	89 (30.8)	91 (33.8)	

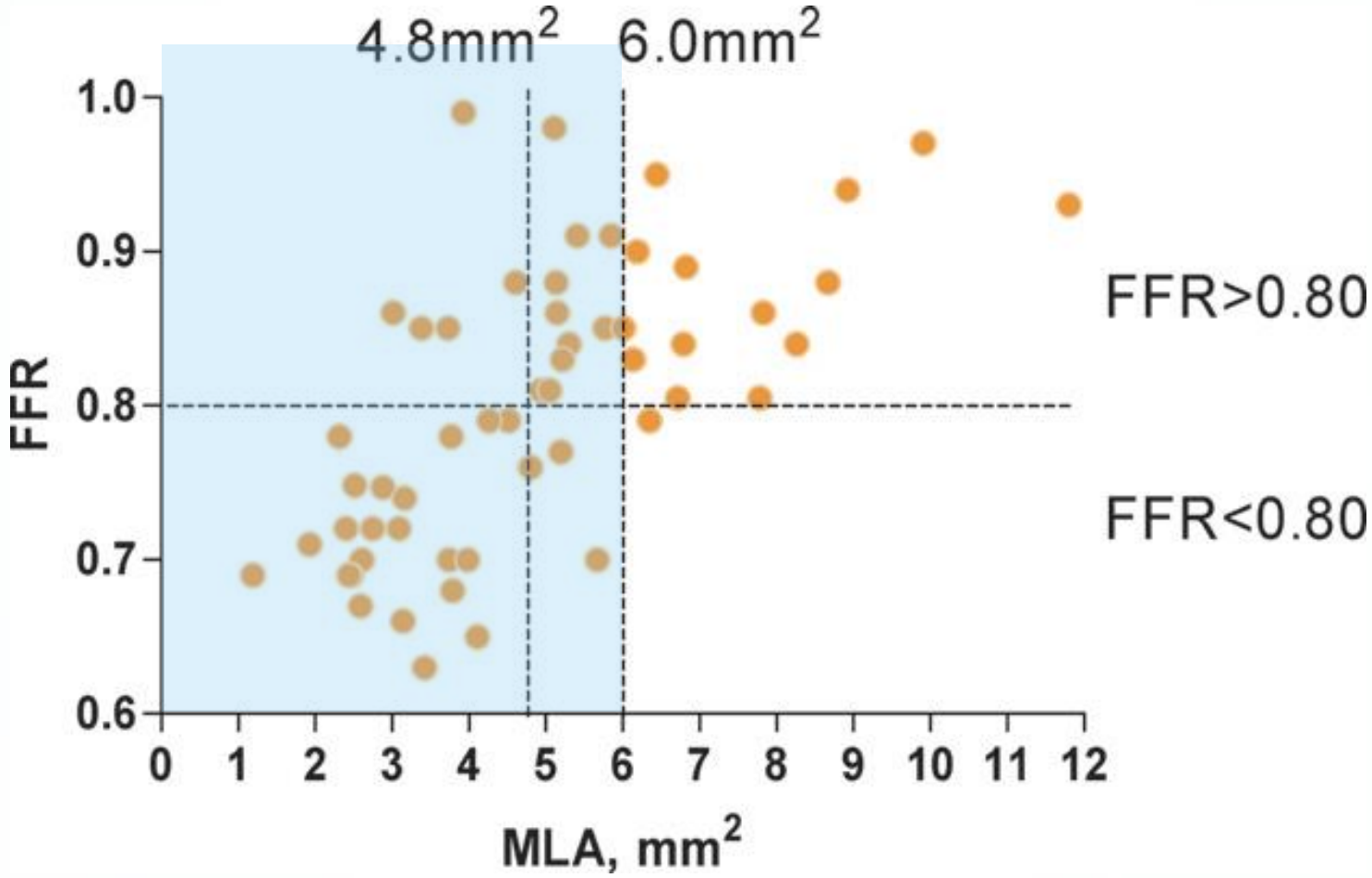
NEJM 2011;364:1718-27

CENTRAL ILLUSTRATION **OCT/FFR Evaluation of Moderate LMCA Lesion**



Bing, R. et al. J Am Coll Cardiol Intv. 2015; 8(12):1529–39.

Correlation between MLA (IVUS) and FFR in intermediate LMCA disease



Park SJ et al. JAHA 2012 Dec;1(6):e004556

Integrated use of FFR and IVUS in left main PCI

Park SJ et al. JAHA 2012 Dec;1(6):e004556

Intermediate LMCA stenosis (DS* 30-70%)

Ostial or Shaft Stenosis

- **Whether to Treat or Not: FFR guidance**
  - FFR measurement is crucial
- **How to Treat: IVUS guidance**
  - Pre-intervention IVUS evaluation
    Evaluate minimal lumen diameter, reference vessel diameter, lesion length, plaque burden and distribution.
  - Pre-intervention IVUS optimization
    MSA‡ >8.2mm^2 is important

Bifurcation Stenosis

- **Whether to Treat or Not: FFR guidance**
  - FFR measurement is important
    Consider a bifurcation stenosis as a single unit of disease (see Figure 2.)
  - IVUS can assist the functional evaluation of bifurcation stenosis
    MLA†>4.8mm^2 (sensitivity 89%, specificity 83%) and plaque burden>72% (sensitivity 73%, specificity 79%) to predict FFR≤0.80 (see Figure 3.)
- **How to Treat: IVUS guidance**
  - Pre-intervention IVUS evaluation
    Evaluate anatomic features favoring single stent cross over stenting (see Table 4.)
  - Post-intervention IVUS optimization
    Evaluate MSA in every segment of LMCA (see Figure 5.)

* Visual estimated diameter stenosis; † Minimal lumen area; ‡Minimal stent area

DRIVING THE FUTURE of PRECISION MEDICINE

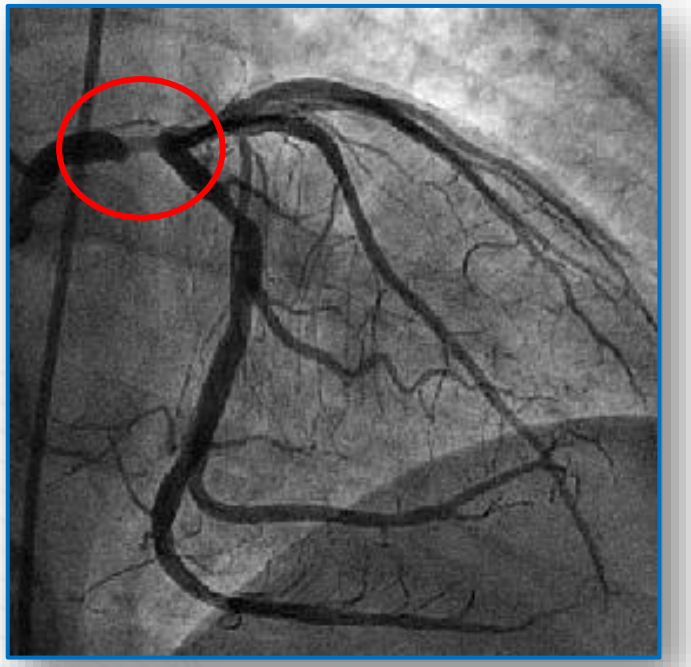
For LMCA PCI

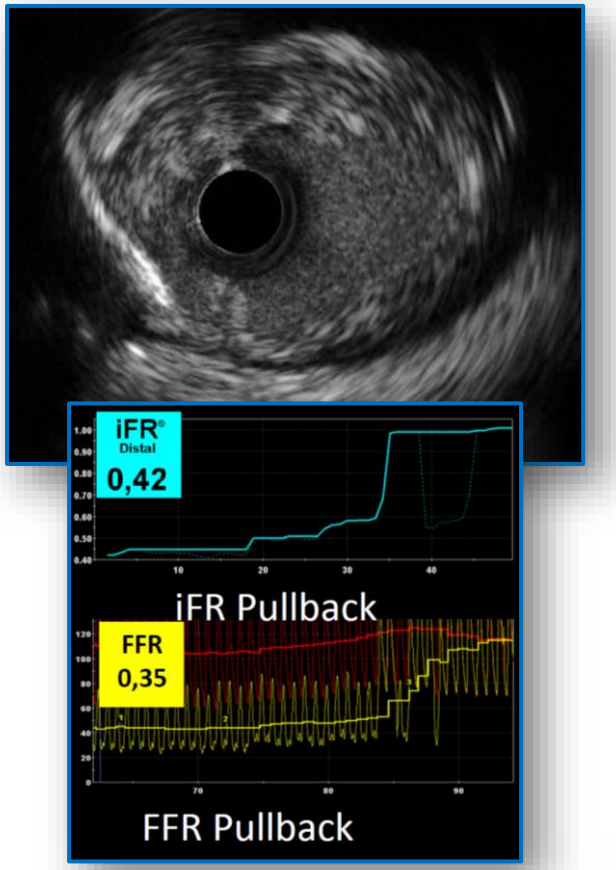
DIAGNOSIS

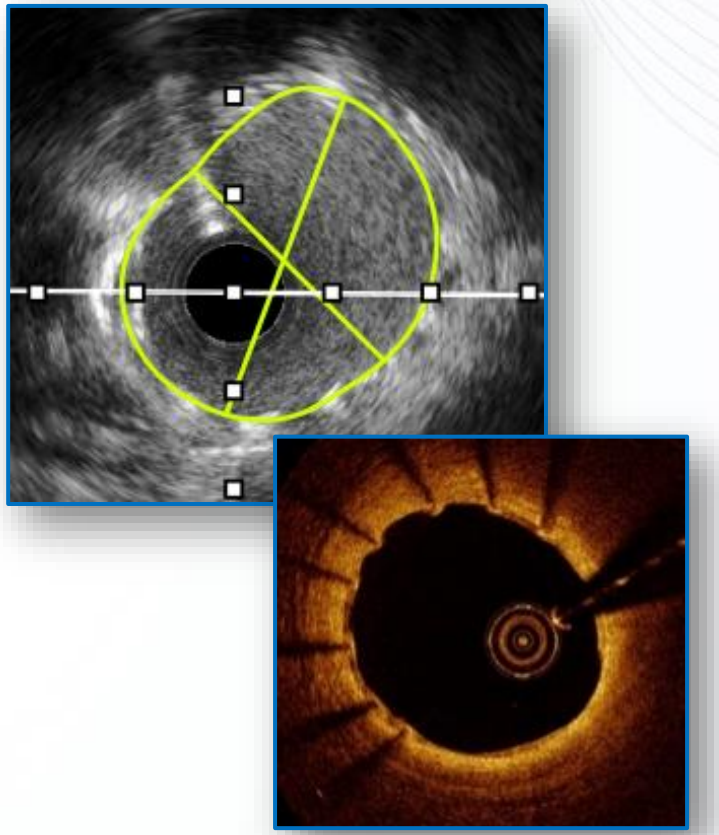
Assessment

INTERVENTION

Guidance Optimization







EDITORIAL

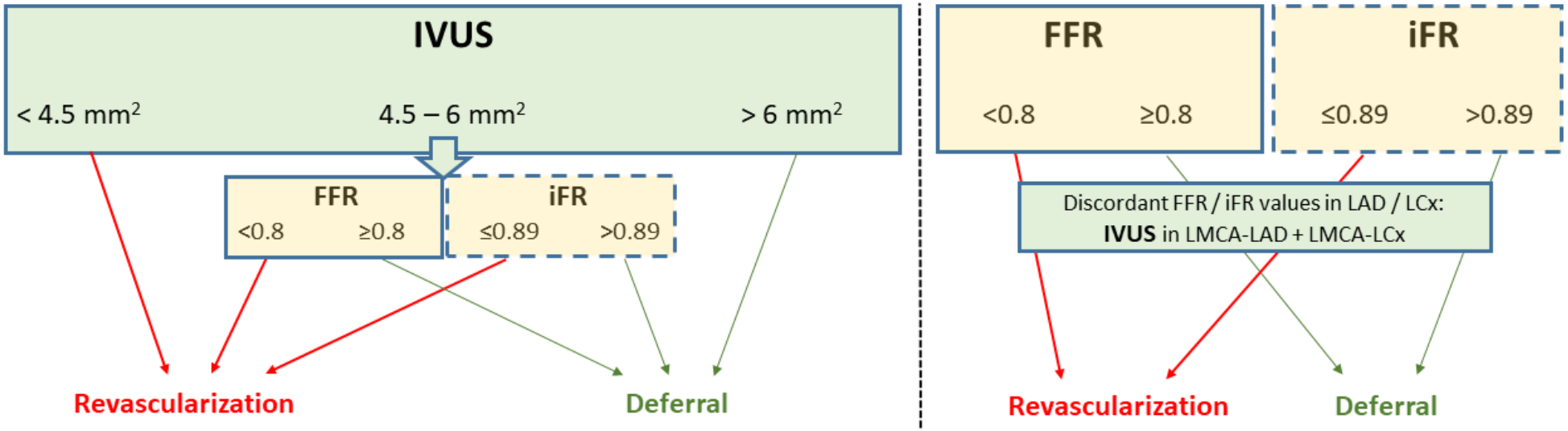
Imaging and Physiology Get Along in the Left Main Coronary Artey Disease

The Case for Intravascular Ultrasound and Instantaneous Wave-Free Ratio

Jose M. de la Torre Hernandez, MD, PhD

Circ Cardiovasc Interv. 2021;14(6):e010887

Left Main Coronary Artery intermediate stenosis



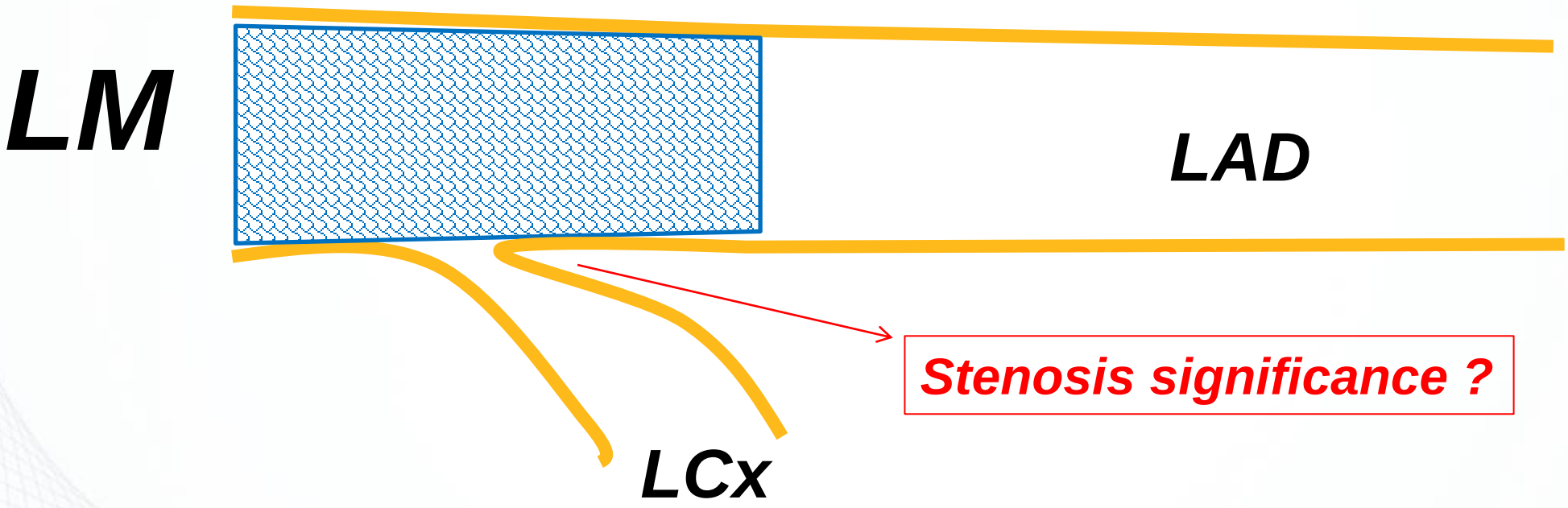
Pro-IVUS
- Mid-shaft LMCA lesion
- Distal LMCA lesion
- Lesions in LAD / LCx
- PCI-eligible if significant LMCA lesion

Always put IVUS/FFR/iFR data in context:
- Symptoms
- Electrocardiographic / echocardiographic findings
- LMCA lesion complexity
- Extension of coronary artery disease
- PCI / CABG eligible patient
- Patient profile (age, frailty, bleeding risk, comorbidities,…)

Pro-FFR / (iFR)
- Ostial LMCA lesion
- Ostial LAD / LCx involvement
- Akinesia (scar) LAD / LCx

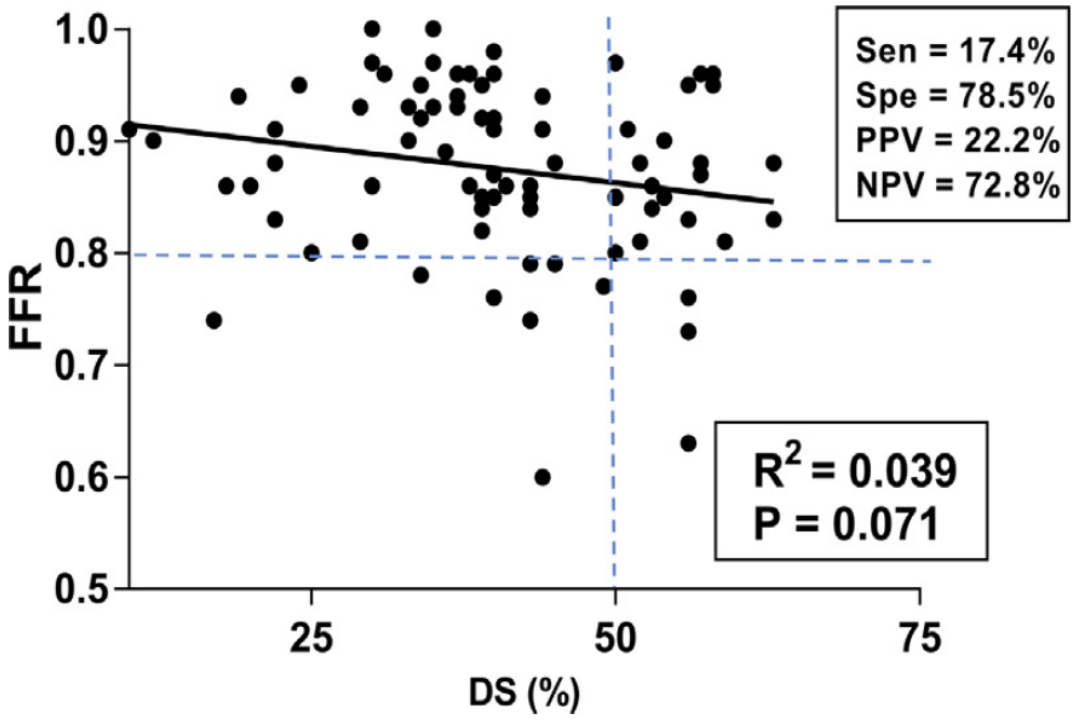
(pro-iFR)
- Lesions in LAD / LCx
- Severe LV hypertrophy

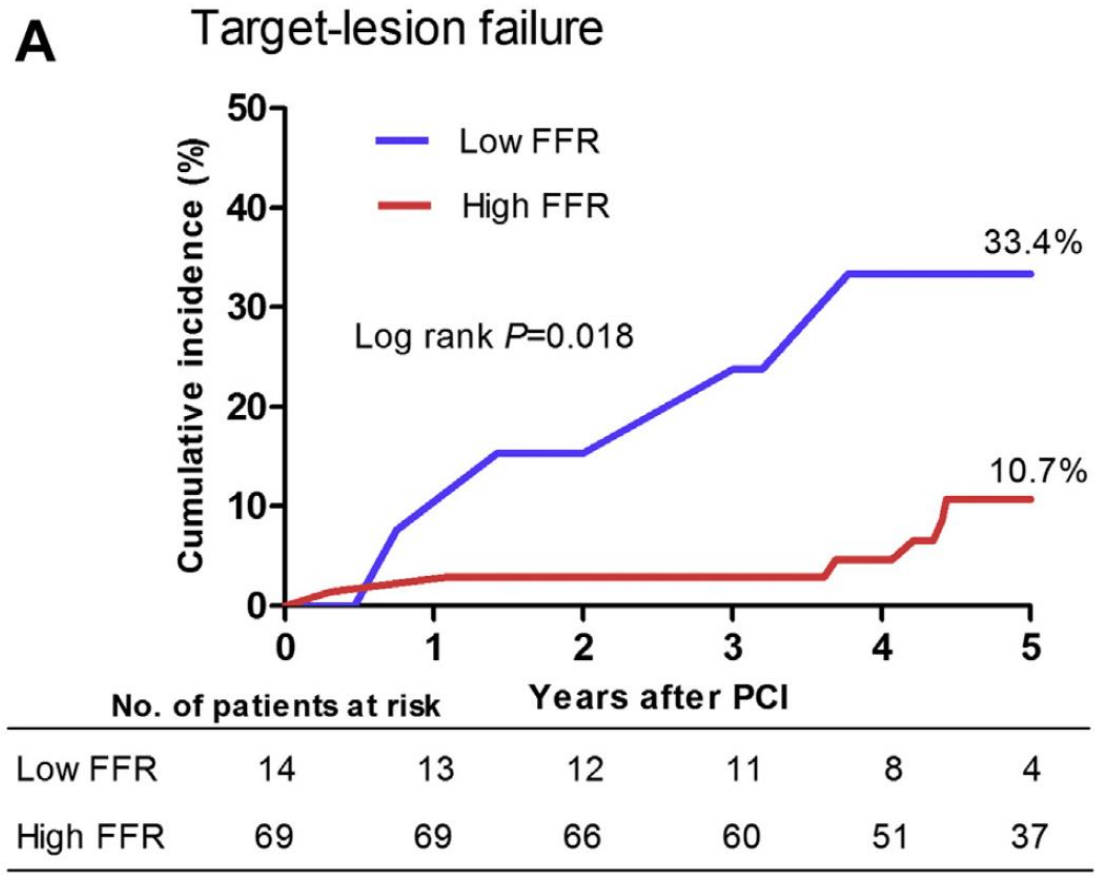
Use of the pressure guide to evaluate the compromise of LCx after stent implantation from LM to LAD in the provisional stenting approach



LCX Jailing and FFR Role in Left Main Cross-Over Stenting

FIGURE 1 Correlation Between FFR and % DS of Jailed LCx After LM Simple Crossover Stenting

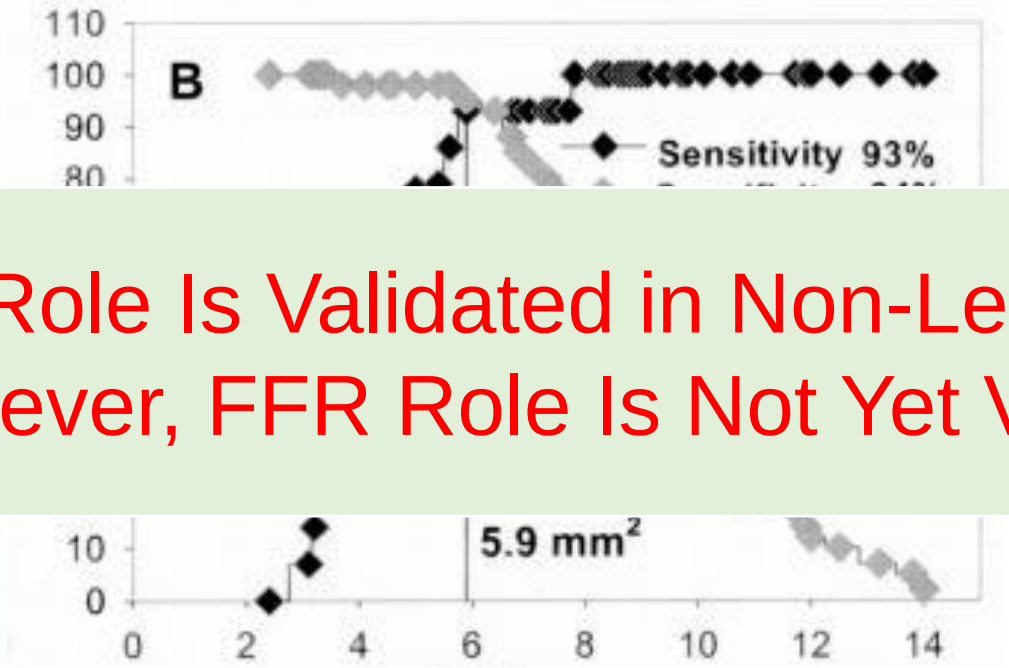




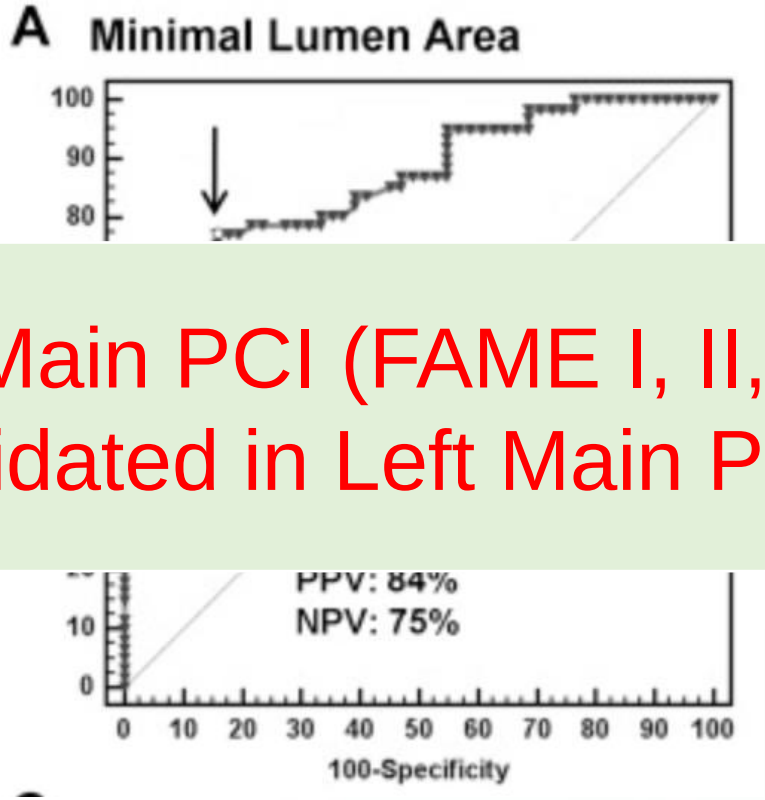
Lee CH et al. JACC Intv 2019;12:847-855

IVUS or FFR Assessment of LMCA Stenosis Severity : FFR-Matched IVUS Criteria

Western Cohort



Asian Cohort



FFR Role Is Validated in Non-Left Main PCI (FAME I, II, III)
However, FFR Role Is Not Yet Validated in Left Main PCI

MLA 5.9

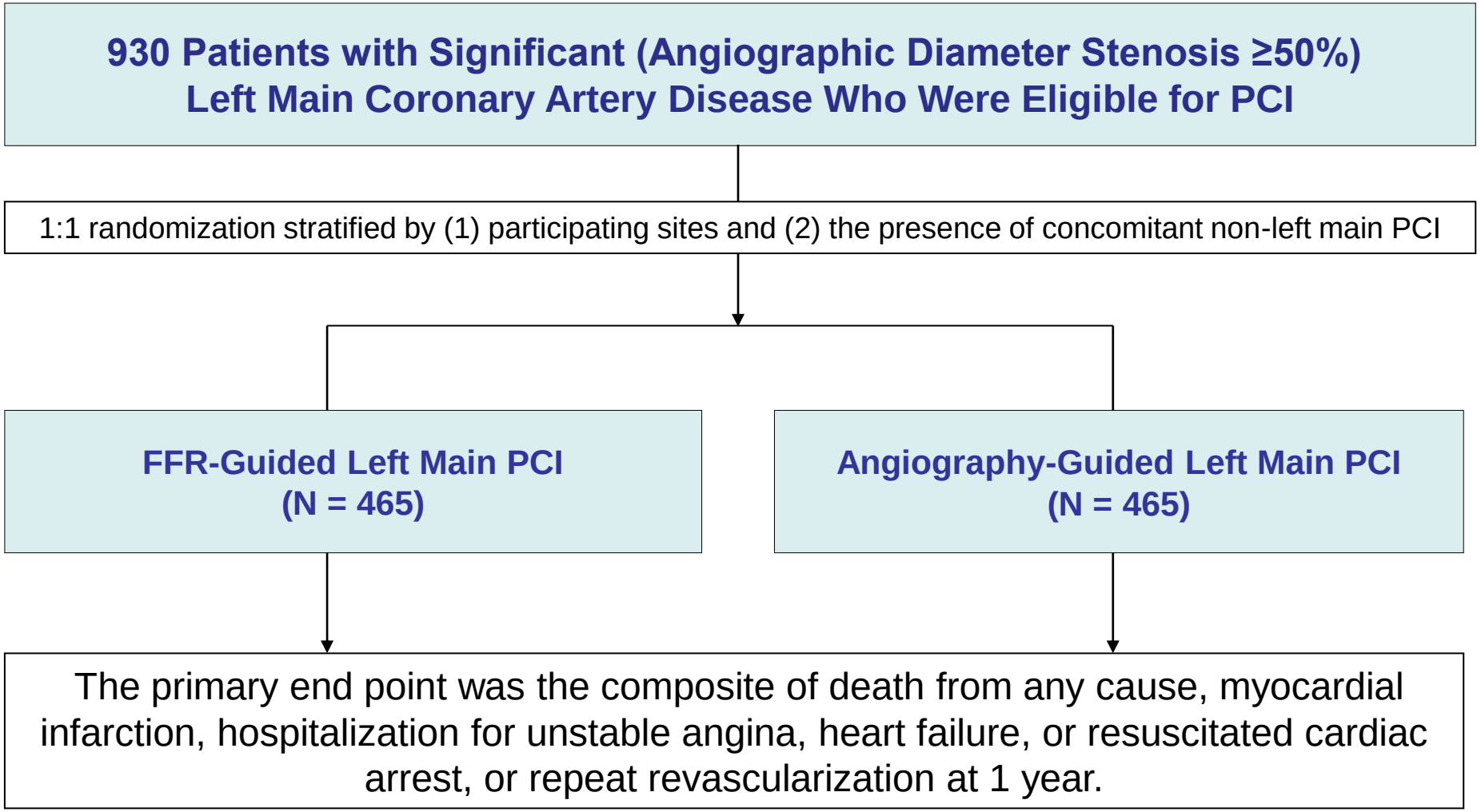
Jasti, et al. Circulation. 2004;110:2831–2836

MLA 4.5

Park, et al. JACC: CI. 2014, 7(8), 868-874

Fractional Flow Reserve versus Angiography for Treatment-Decision and Evaluation of Significant Left MAIN Coronary Artery Disease

FATE-MAIN Trial



Inclusion criteria

Inclusion Criteria: subject must have met all of the following criteria to be eligible for treatment in the study:

1. The subject must be ≥20 years of age with angina and/or evidence of myocardial ischemia
2. Significant de novo LMCA disease (defined as ≥ 50% diameter stenosis by visual estimation) with or without concomitant non-left main major epicardial CAD, amenable to PCI with DES implantation.
4. The patient or guardian agrees to the study protocol and the schedule of clinical follow-up, and provides informed, written consent, as approved by the appropriate Institutional Review Board/Ethical Committee of the respective clinical site.

Exclusion criteria

1. Extremely calcified or tortuous vessels precluding FFR measurement
2. The presence of complex coronary disease anatomy or lesion characteristics or other cardiac condition(s) which leads the participating interventional cardiologist to believe that PCI is not suitable (i.e. the subject should be managed with CABG or medical the rapy alone)
3. Recent STEMI (<7 days prior to randomization)
4. Cardiogenic shock and/or need for mechanical/pharmacologic hemodynamic support
5. Severe left ventricular dysfunction (ejection fraction <30%)
6. Requirement for other cardiac surgical procedure (e.g., valve replacement or aorta su rgery)
7. Contraindication or inability to take aspirin or P2Y12 inhibitors (clopidogrel, ticagrelor, or clopidogrel)
8. Prior PCI of the left main trunk
9. Prior CABG

Study endpoints

Primary

The primary outcome was the composite of death from any causes, MI, or hospitalization for unstable angina, heart failure, resuscitated cardiac arrest, or repeat revascularization at 12 months after randomization.

Secondary

Each individual component of primary composite outcome; Composite of death or MI; Stent thrombosis (ARC definition): Bleeding complications (Bleeding Academic Research Consortium [BARC] criteria); Procedure time; Amount of contrast agent used; Length of hospital stay; Rehospitalization (any, cardiac, or noncardiac causes); Functional class (assessed by the CCS Classification); Angina-related quality of life index (by SAQ); Health-related quality of life index (by the EQ-5D); Number of anti-anginal medications used at each time point

Key Messages

- In the contemporary clinical practice, the goal of PCI is to achieve complete functional revascularization of ischemic territories. Thus, theoretical and practical concept of physiology-guided PCI will also work even in left main PCI setting.

- For all “borderline or intermediate” LMCA, it is strongly recommended to confirm physiologic lesion significance before treatment using FFR evaluation and non-ischemia-producing lesions should not be treated.

- **In the FATE-MAIN trial,** we assume that the improved outcomes with FFR-guided PCI are likely a result of more judicious PCI whereby ischemia-producing LMCA lesions are revascularized and non-ischemia producing LMCA lesions are treated with OMT alone.