CARDIOVASCULAR SUMMIT
TCTAP 2015

Unprotected Left main Coronary Disease:

Thoughtful Insights

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Tuesday 28th April 2015
9:08 AM – 9:16 AM
Coronary Theater, Level 1

Disclosure Statement of Financial Interest

Patrick W. Serruys, MD, PhD

☒ I have no relevant financial relationships

Scope of the talk

- Patients selection:
  - PCI vs. CABG, risk score
  - MSCT, IVUS for evaluation severity of Left main disease, FFR-CT
- Long term follow up in clinical trial
- Technical perspective
- Antiplatelet management
  (old vs. new potent P2Y12)

Current Status of LMCA stenting in guideline

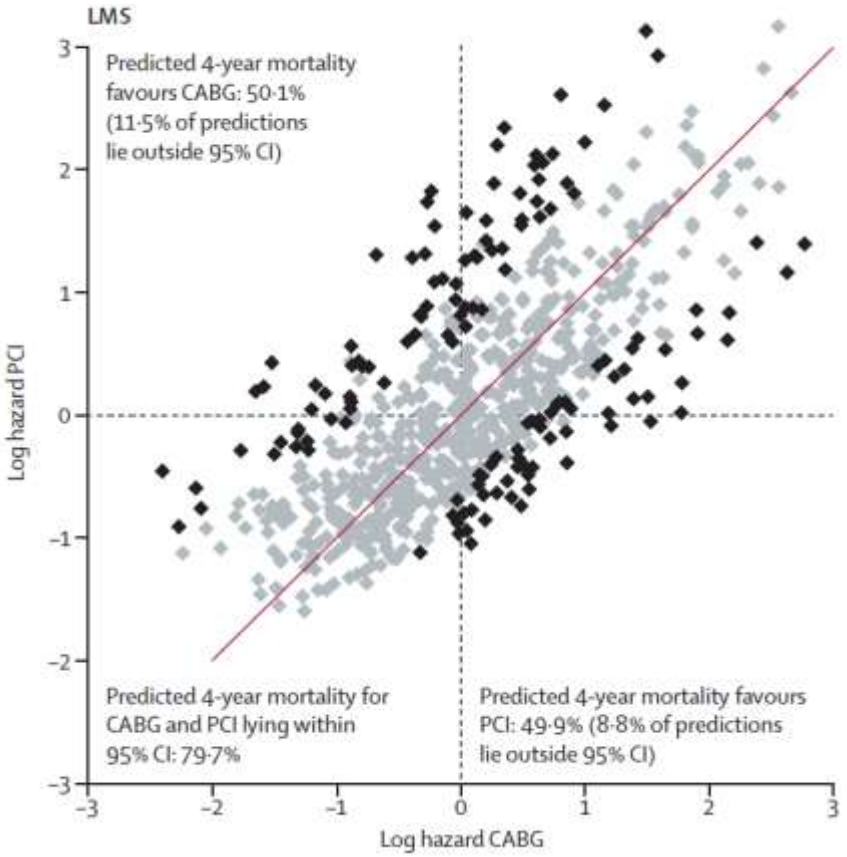
2014 ESC guidelines

Recommendations according to extent of CAD	CABG		PCI	
	Class[a]	Level[b]	Class[a]	Level[b]
Left main disease with a SYNTAX score ≤ 22.	I	B	I	B
Left main disease with a SYNTAX score 23–32.	I	B	IIa	B
Left main disease with a SYNTAX score >32.	I	B	III	B

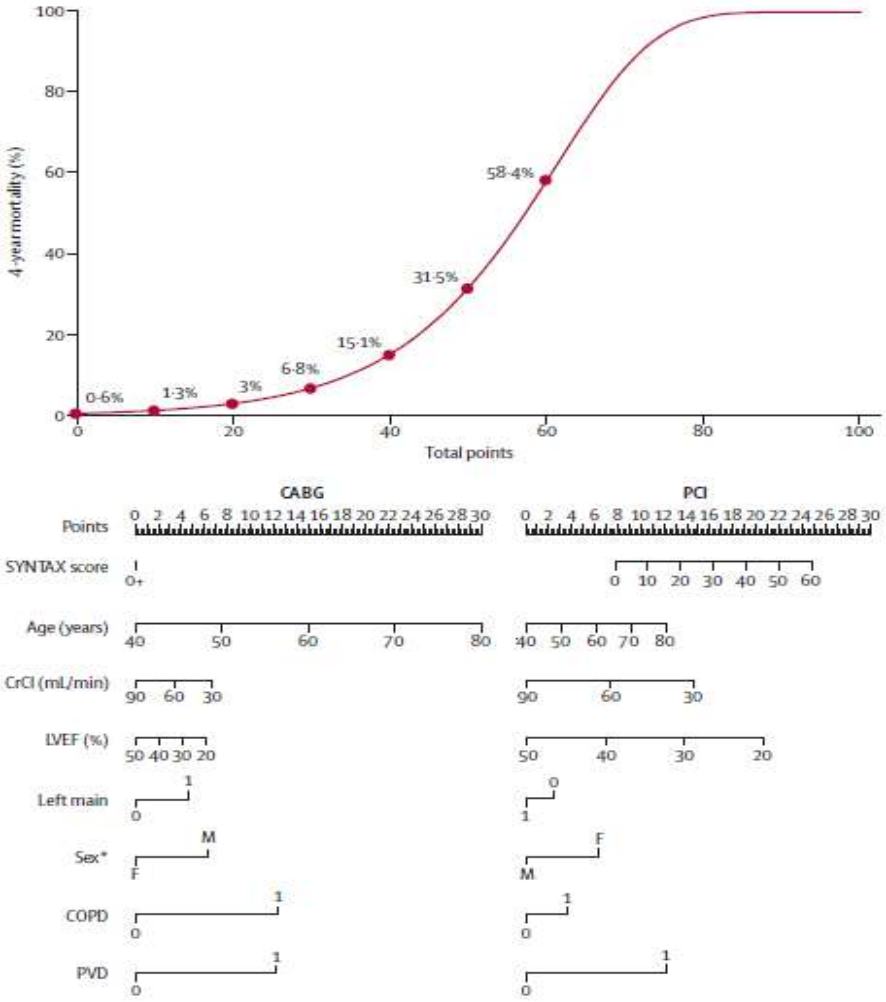
Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Mortality predictions for CABG versus PCI for each individual patient in the randomized SYNTAX trial



SYNTAX Score II nomogram for bedside application



Farooq V, Serruys PW, et al. Lancet 2013;381(9867):639-50

European Heart Journal
doi:10.1093/eurheartj/ehu518

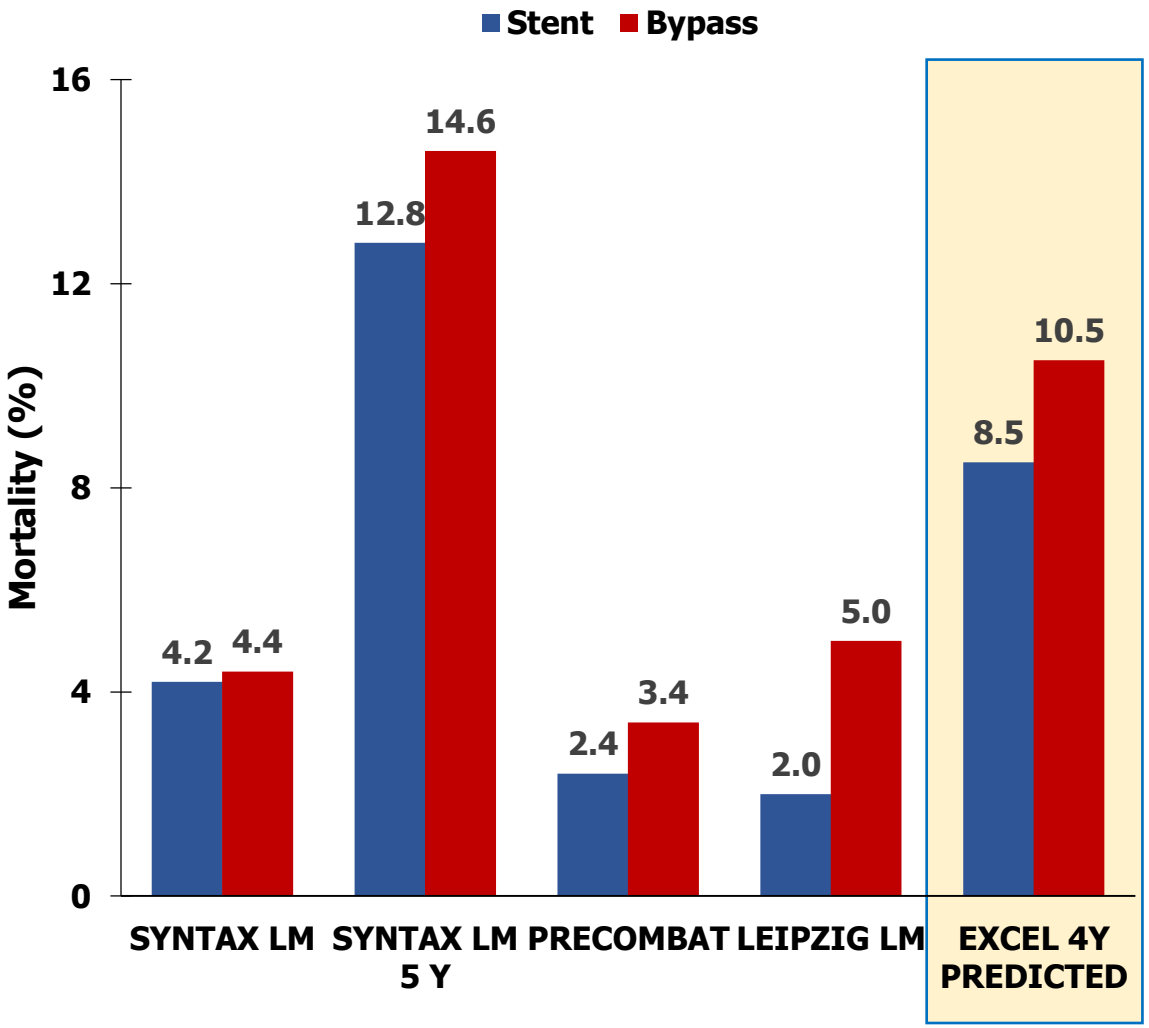
FASTTRACK CLINICAL RESEARCH
Coronary artery disease

Long-term forecasting and comparison of mortality in the Evaluation of the Xience Everolimus Eluting Stent vs. Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial: prospective validation of the SYNTAX Score II

Carlos M. Campos[1,2†], David van Klaveren[1†], Vasim Farooq[3], Charles A. Simonton[4], Arie-Pieter Kappetein[1], Joseph F. Sabik III[5], Ewout W. Steyerberg[1], Gregg W. Stone[6,7], and Patrick W. Serruys[1,8*], On Behalf of the EXCEL Trial Investigators

Campos CM, Serruys PW. Eur Heart J. 2015 Jan 12.[Epub ahead of print]

Prognosis after revascularization for UPLM: Mortality of patients with UPLM treated with DES vs. CABG in RCT with predicted mortality based on the SYNTAX Score II from the ongoing EXCEL randomized trial



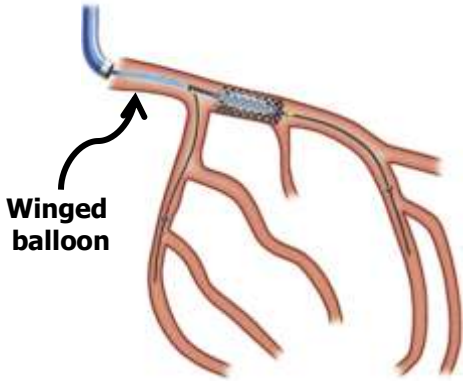
SYNTAX Score II

- Age
- Gender
- Creatinine Clearance
- Ejection Fraction
- COPD
- Peripheral vascular disease
- Unprotected LMCA disease
- Anatomical complexity (SYNTAX Score)

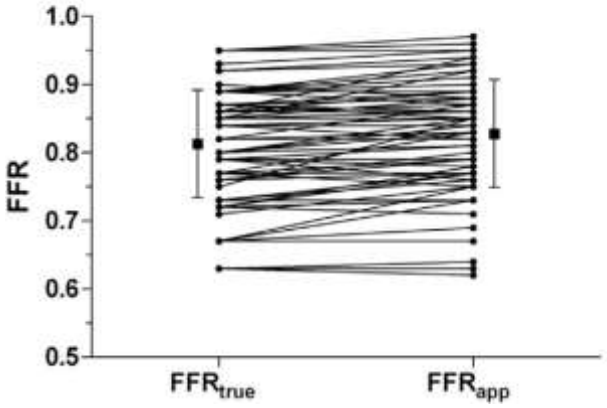
Byrne RA, Kastrati A. Eur Heart J. 2015 Mar 16 [Epub ahead of print]

The impact of Downstream Coronary Stenosis on FFR Assessment of Intermediate Left Main Coronary Artery Disease: Human Validation

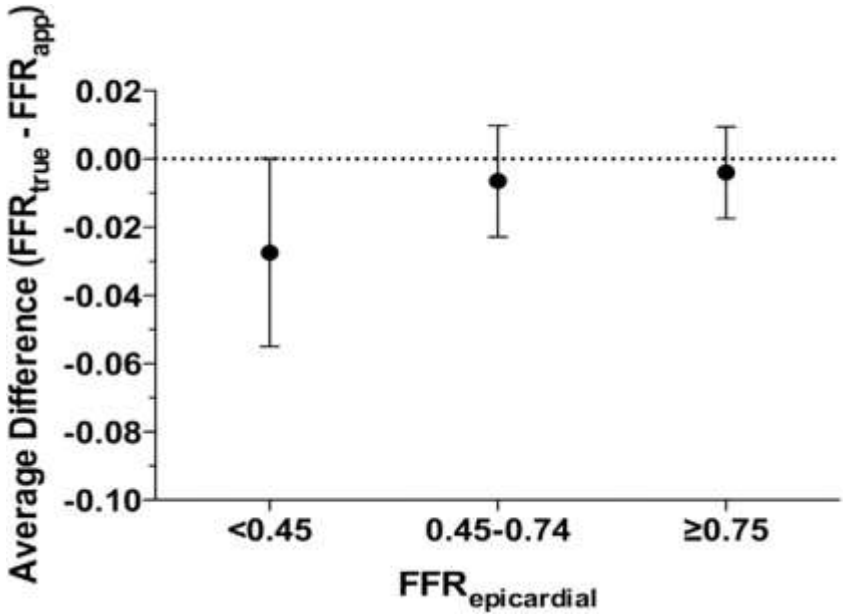
Effect of downstream disease on LMCA FFR



0.81±0.08 vs. 0.83± 0.08, *P*<0.001 (n=91)



The difference between FFR$_{true}$ and FFR$_{app}$ correlated with the severity of the downstream disease



In all cases in which the FFRapp was >0.85, the FFRtrue was >0.80. Only 6 cases in which the FFRapp was >0.05 FFRtrue; the average FFRepi = 0.24, and all FFR ≤ 0.45, indicating that the downstream stenosis was essentially occlusive.

Downstream epicardial disease **does affect** FFR value ***but*** the effect on FFR is small and clinically irrelevant, unless the downstream disease is severe.

Fearon F, et al. J Am Coll Cardiol Intv 2015;8:398–403

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Summary of Studies Using IVUS to Determine the significance of ULMCA Disease

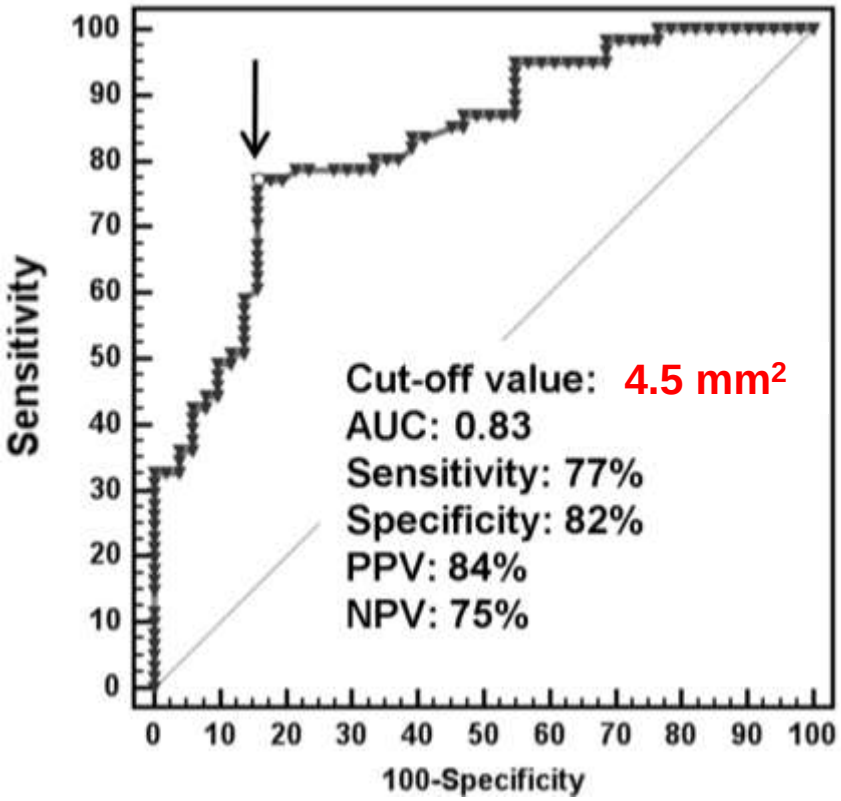
First Author	N	FU (Months)	Outcome	IVUS Criterion for Significance	Comment
Abizaid et al	**122**	**12**	**MACE**	**MLD**	No specific cutoff suggested. LMCA MLD >3 mm portends incremental risk, also determined by comorbidities and coronary artery disease in other territories
Ricciardi et al.	**107**	**29**	**MACE**	**MLA**	No specific cutoff suggested. MLA was a predictor of cardiac events
Legutko et al.	**44**	**44**	**Ischemia**	**MLD, MLA**	**MLA <8 mm²** and MLD <2.8 mm correlated with FFR <0.75 and ischemia on 99Tc-Mibi-Spect
Jasti et al.	**51**	**11**	**Ischemia**	**MLD, MLA**	**MLA <5.9 mm²** and MLD <2.8 mm. FFR of <0.75 used as gold-standard reference
Fassa et al.	**214**	**40**	**MACE**	**MLA**	**MLA <7.5 mm²**
de la Torre Hernandez et al.	**354**	**24**	**MACE**	**MLA**	**MLA <6 mm²**
Kang et al.	**55**	**NA**	**Functional**	**FFR**	IVUS-derived **MLA of <4.8 mm²** correlated with FFR <0.80

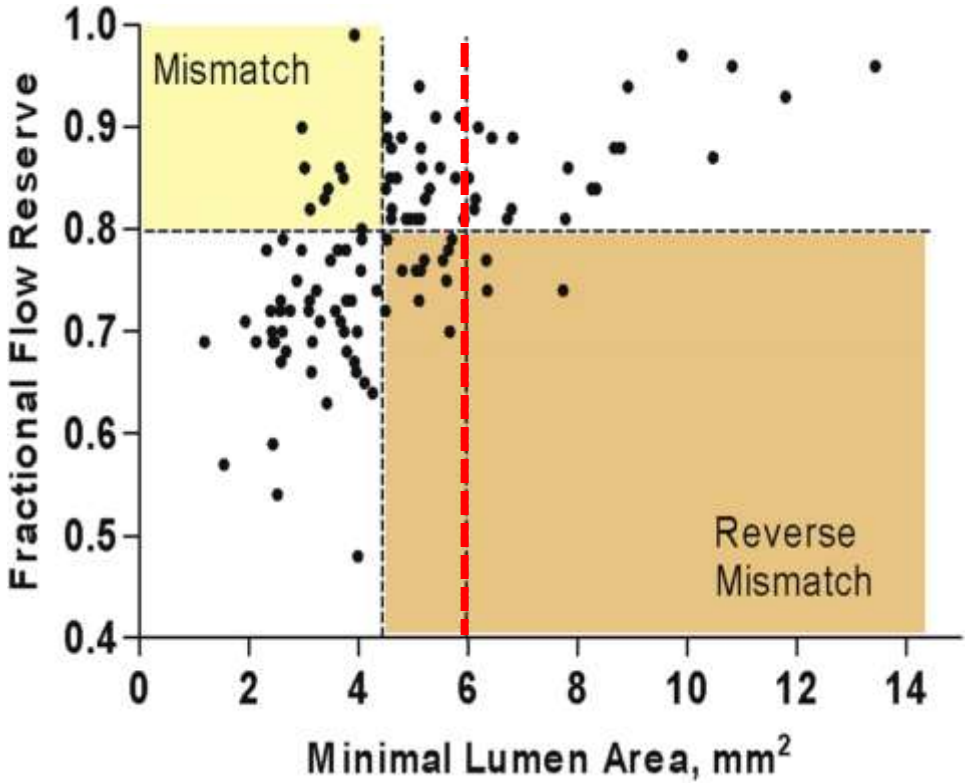
Puri R, et al. J Am Coll Cardiol Intv. 2012;5(7):697-707

IVUS-Derived MLA Criteria for Functionally Significant Left Main Coronary Artery Stenosis

112 patients with isolated ostial and shaft intermediate LMCA stenosis (angiographic diameter stenosis of 30% to 80%) who underwent IVUS and FFR measurement.

Minimal Lumen area



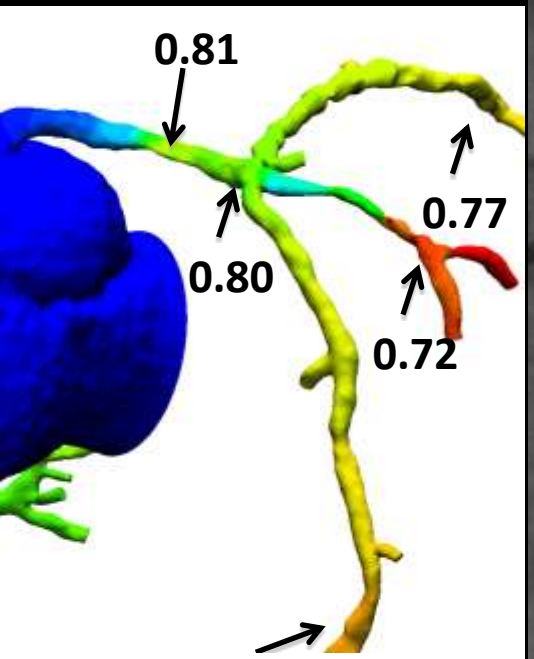


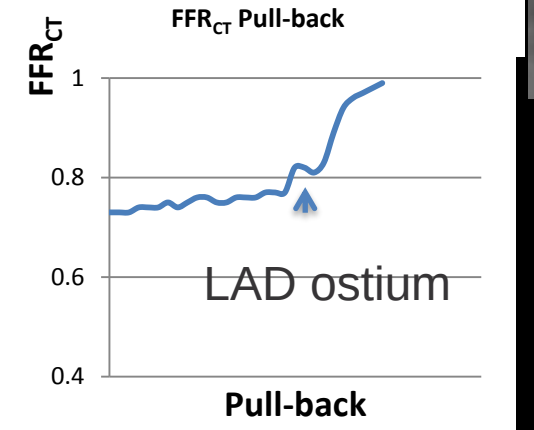
Park SJ et al, JACC Cardiovasc Interv. 2014;7:868-74

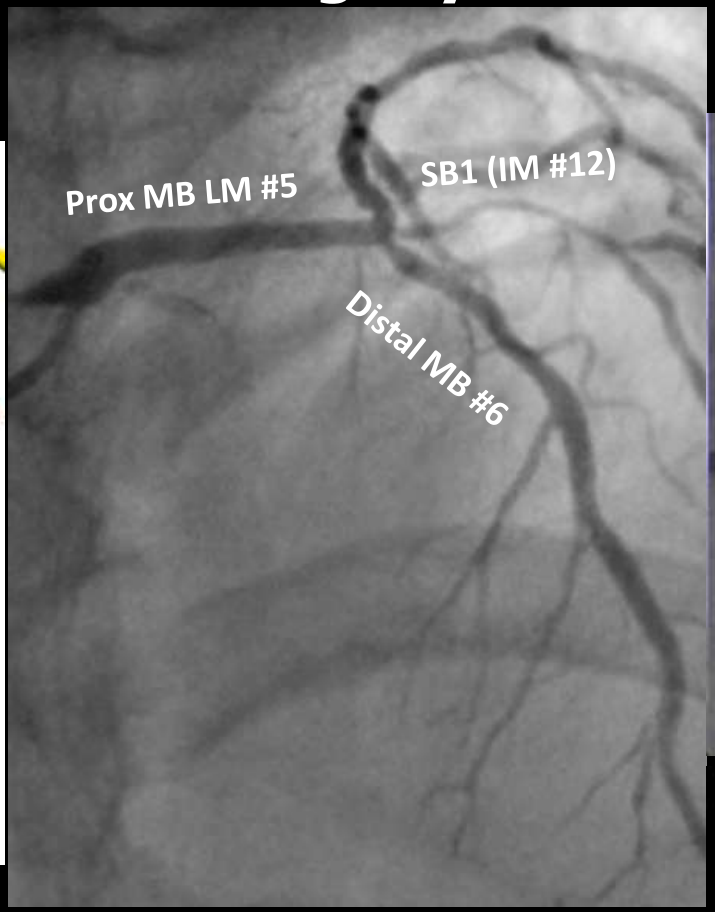
Which lesion is causing myocardial ischemia?

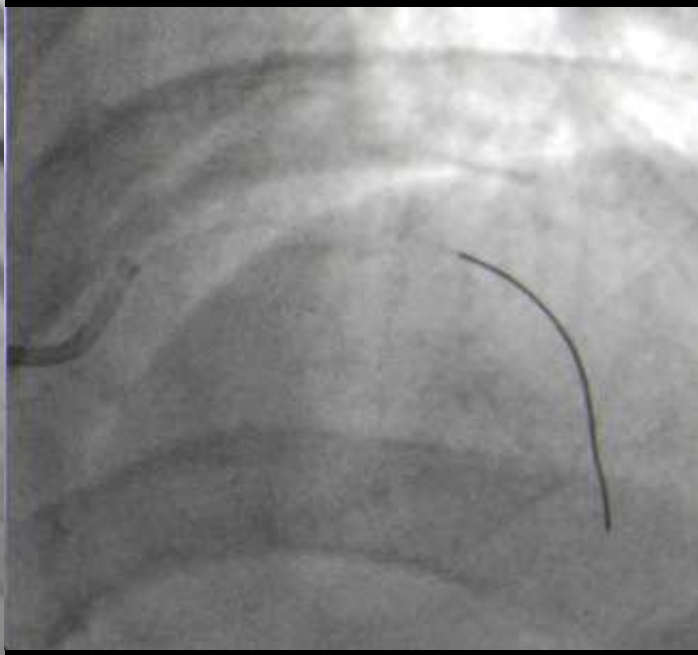
Angiography

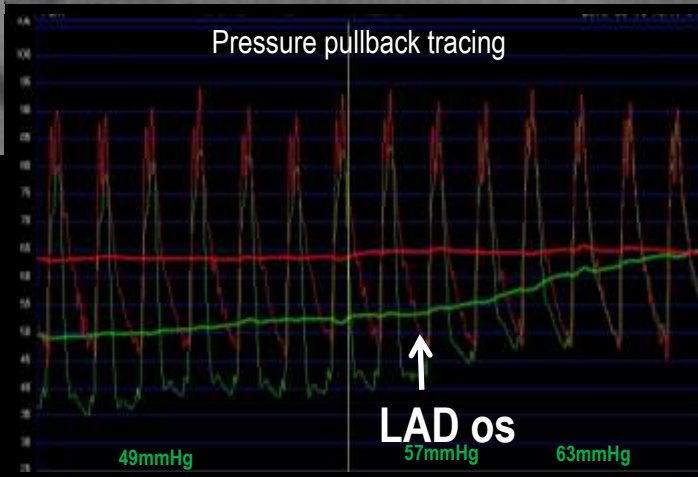
Which lesion is causing myocardial ischemia?



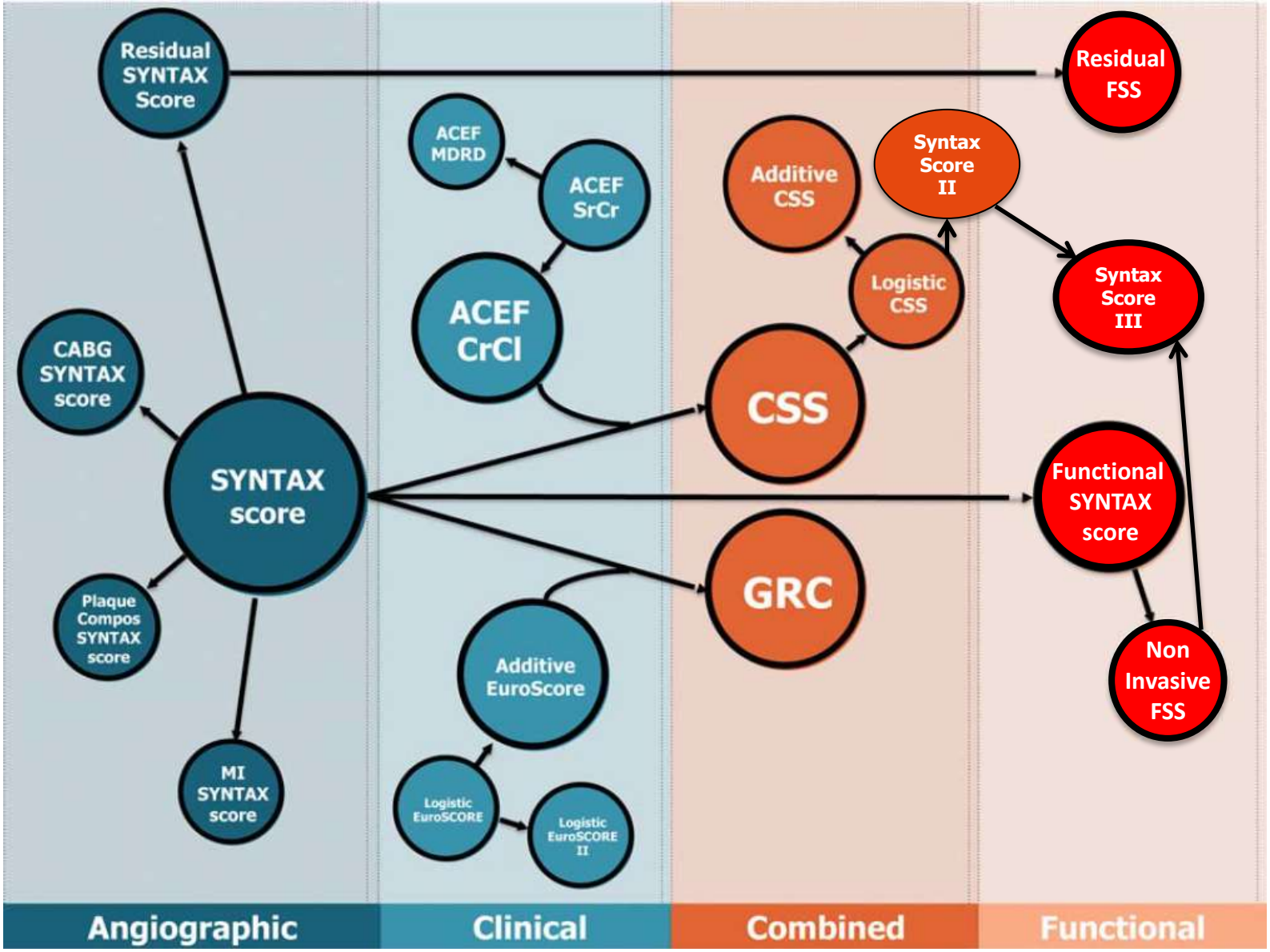








The Syntax Family...
But missing the personalized and comparative approach



Cappodano D. Eur Heart J. 2012 Dec;33(24):3008-10

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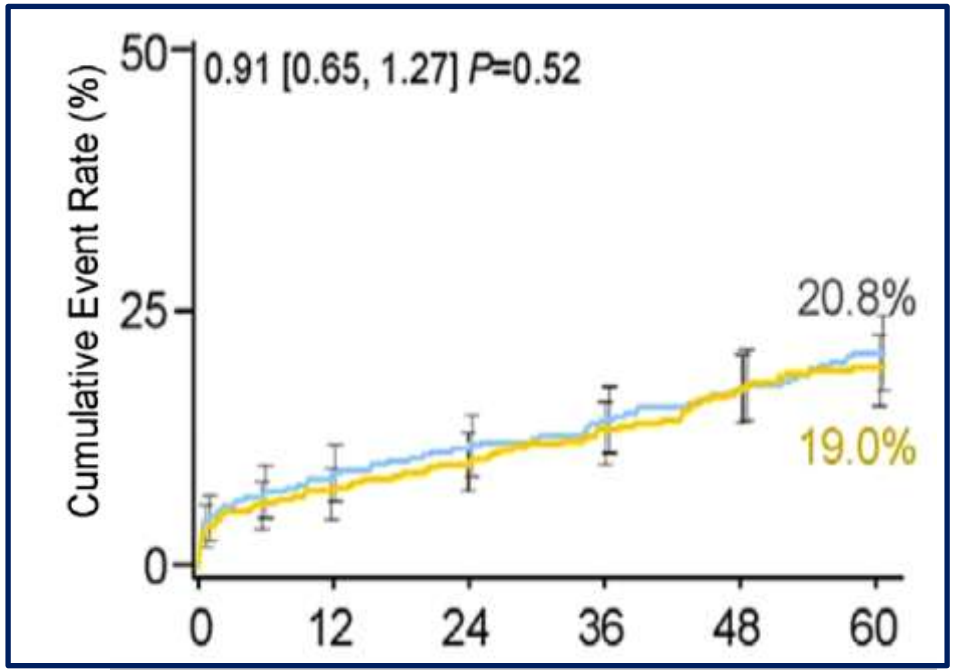
5-Year outcome of trial of Stents vs. Bypass Surgery for left main coronary Artery Disease

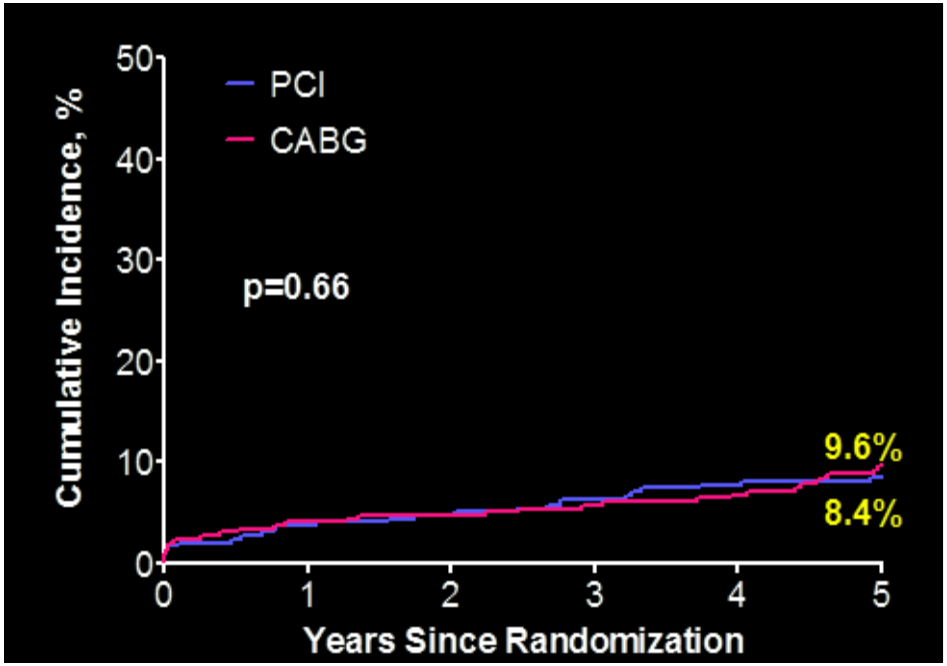
Event at 5 Year		MACCE (%)	All-cause death (%)	MI (%)	Stroke (%)	ID-TVR (%)
Milan	PCI =107	NA	18.3	0.9	0.9	18.7
	CABG =142	NA	15.9		4.2	8.4
	HR	NA	NA	NA	NA	NA
SYNTAX	PCI=357	36.9	12.8	8.2	1.5	26.7
	CABG=348	31.0	14.6	4.8	4.3	15.5
	HR	1.23	0.88	1.67	**0.33**	**1.82**
Pre combat	PCI=300	17.5	5.7	2.0	0.7	13.0
	CABG=300	14.3	7.9	1.7	0.7	7.3
	HR	1.27	0.73	0.76	0.99	**1.86**

Five-year outcomes in patients with left main disease treated with either PCI or CABG in SYNTAX trial vs. PRECOMBAT trial

Death/MI/Stroke



SYNTAX



PRECOMBAT

Morice MC, et al. Circulation. 2014;129:2388-2394.

Ahn JM, et al. J Am Coll Cardiol. 2015 Mar 10 [Epub ahead of print]

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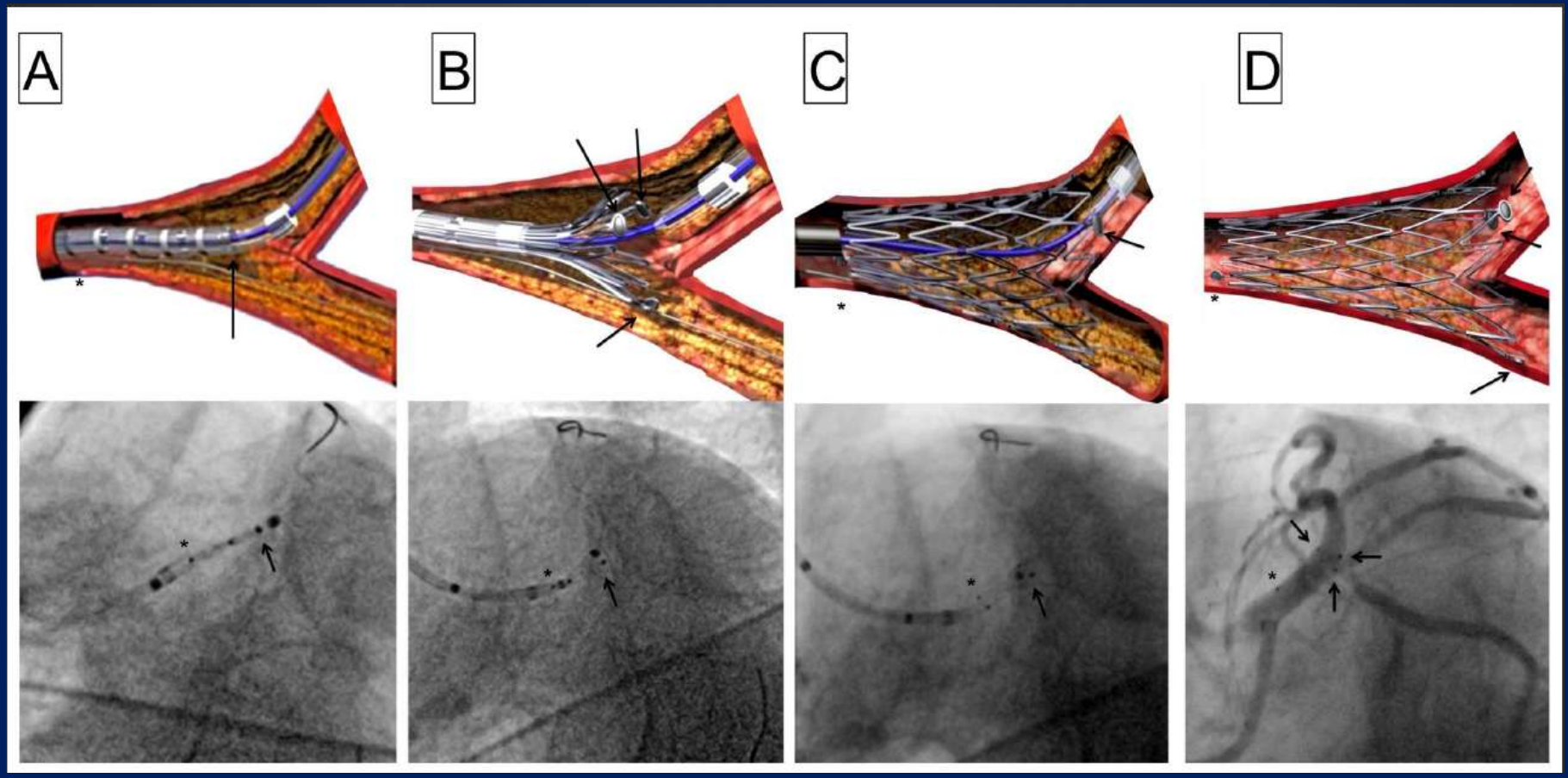
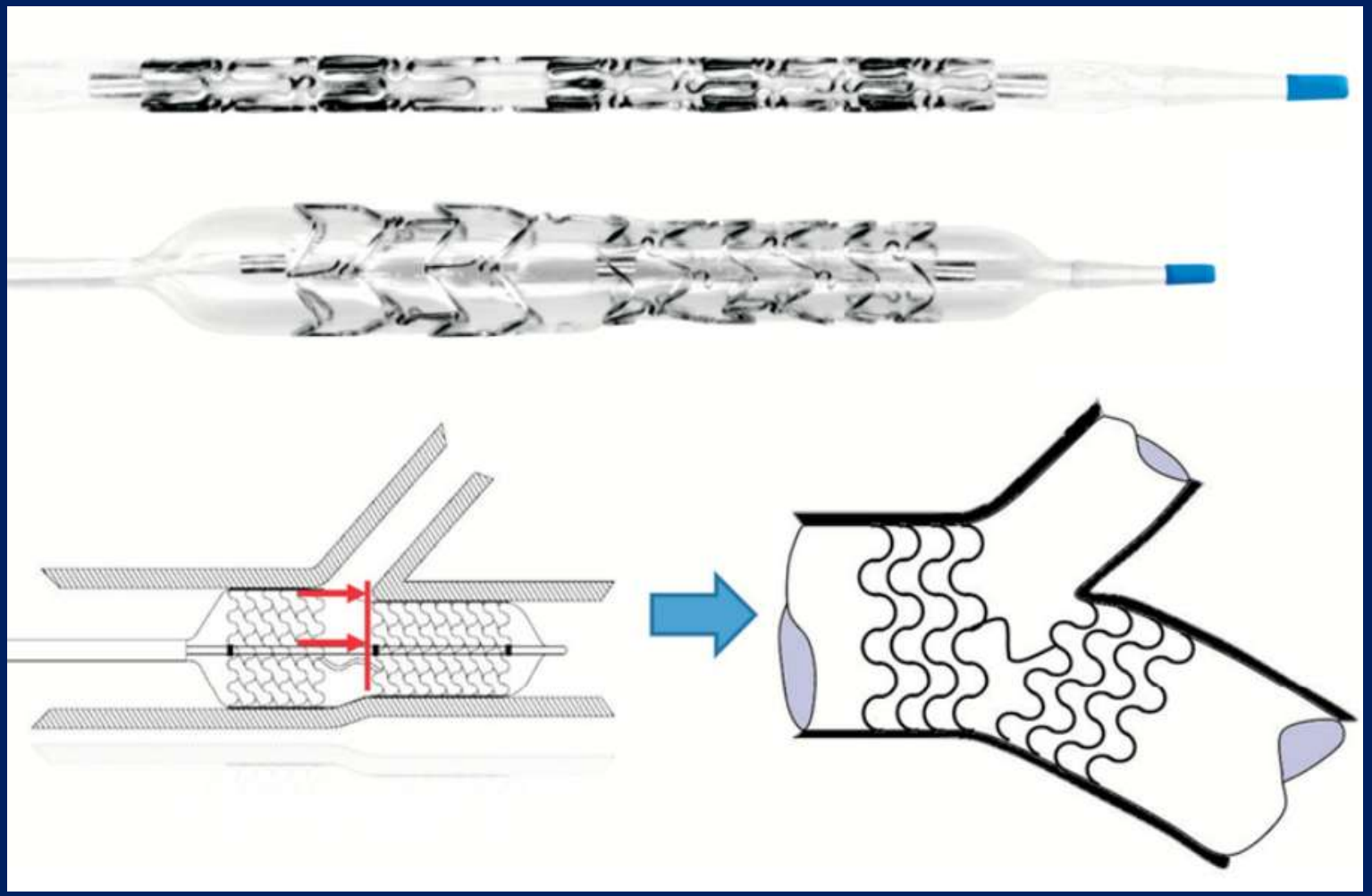
AXXESS PLUS Stent

Self expanding and conical-shaped nickel-titanium stent coated with bioabsorbable polymer releasing Biolimus A9



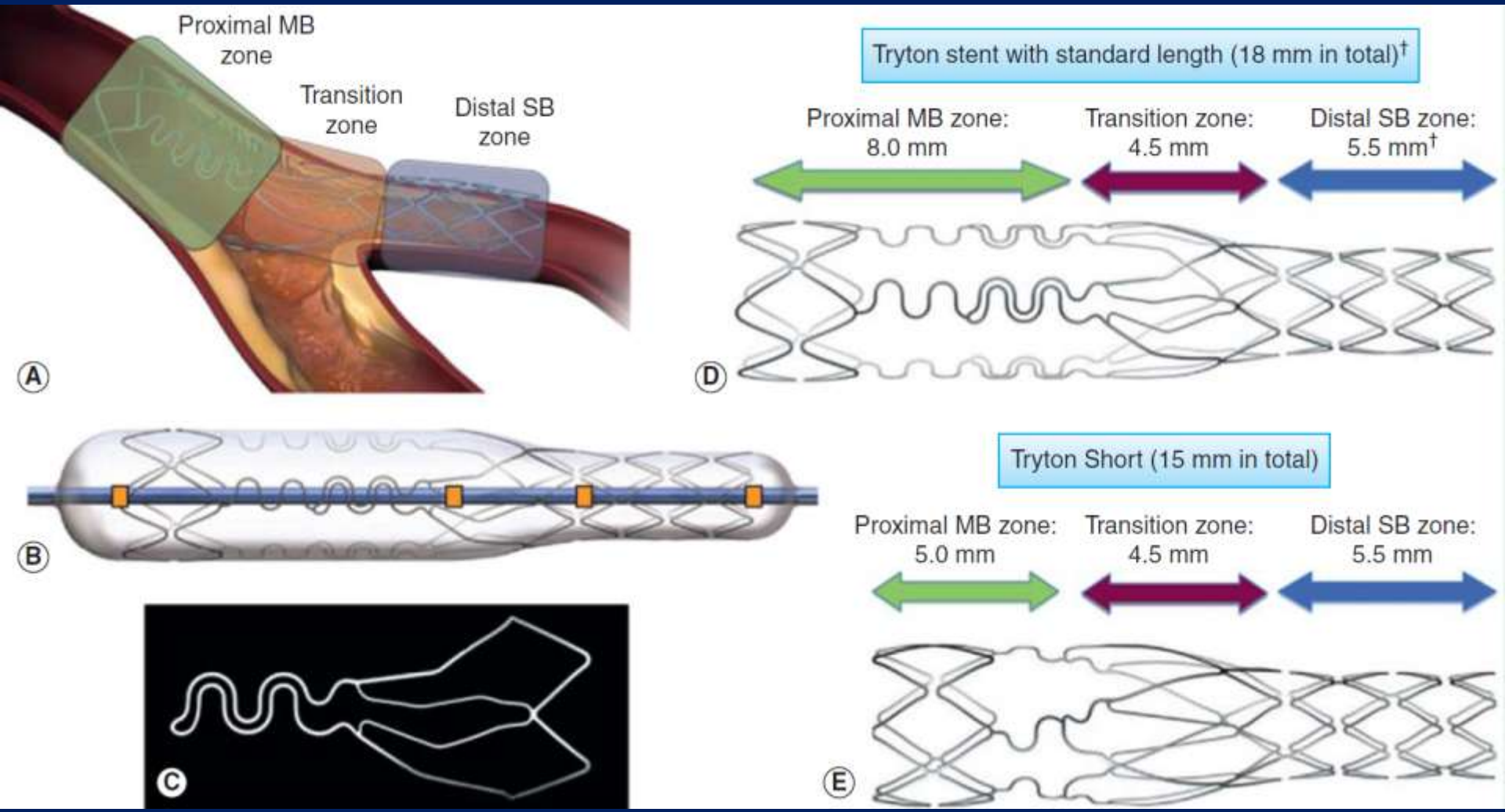
Garcia E, et al. J invasive Cardiol 2014;26:E45-7

The Bifurcation Optimisation Stent System (BiOSS®)



Gil et al. Eurointervention 2012;8:316-324

Tryton Side Branch Stent



Grundeken M, et al. Expert Rev. Med. Devices 2013;10:707-716

Dedicated bifurcation stent study in LM intervention

	AXXESS PLUS[1] N = 31	BiOSS Expert[2] N= 54	Tryton[3] N=52
Device description	BES, self expanding nitinol stent	PES, Balloon expandable 316L stainless steel	BMS, Balloon expandable Cobalt-Chromium
Patient setting	Stable CAD	NSTE-ACS or stable	All comers
Endpoint	Safety and efficacy endpoint	Cumulative rate of death, MI, TLR	Acute gain in 3 segment Major adverse cardiac events
Follow-up	12 month	12 month	6 month
SYNTAX score	NA	21.5±6.5	20±8
Medina class 1,1,1 (%)	41%	39%	63%
Main vessel diameter (mm)	3.91±0.34	4.15±0.32	3.4±0.4
MV diameter stenosis (%)	61.2±20.2	56±26	51±17
Final kissing, (%)	NA	66.7%	94%
Adverse events, (%)	MACE 19.4 % ISA 23.8% postprocedure but no late acquired ISA	Cumulative rate 9.3%	MACE 22%
Stent thrombosis, (%)	0	0	0
TLR/TVR, (%)	TLR 9.1%	TLR 9.3%	TVR 12%
Myocardial infarction,(%)	9.7%	0	10%
Death, (%)	0	0	0

1. Hosegawa T, et al. Catheter Cardiovasc Interv 2009;73:34-41 2. Bil J, et al. J Interv cardiol 2014;27:242-51
3. Magro M, et al. Eurointervention 2013;8:1259-69

*ARC definite stent thrombosis

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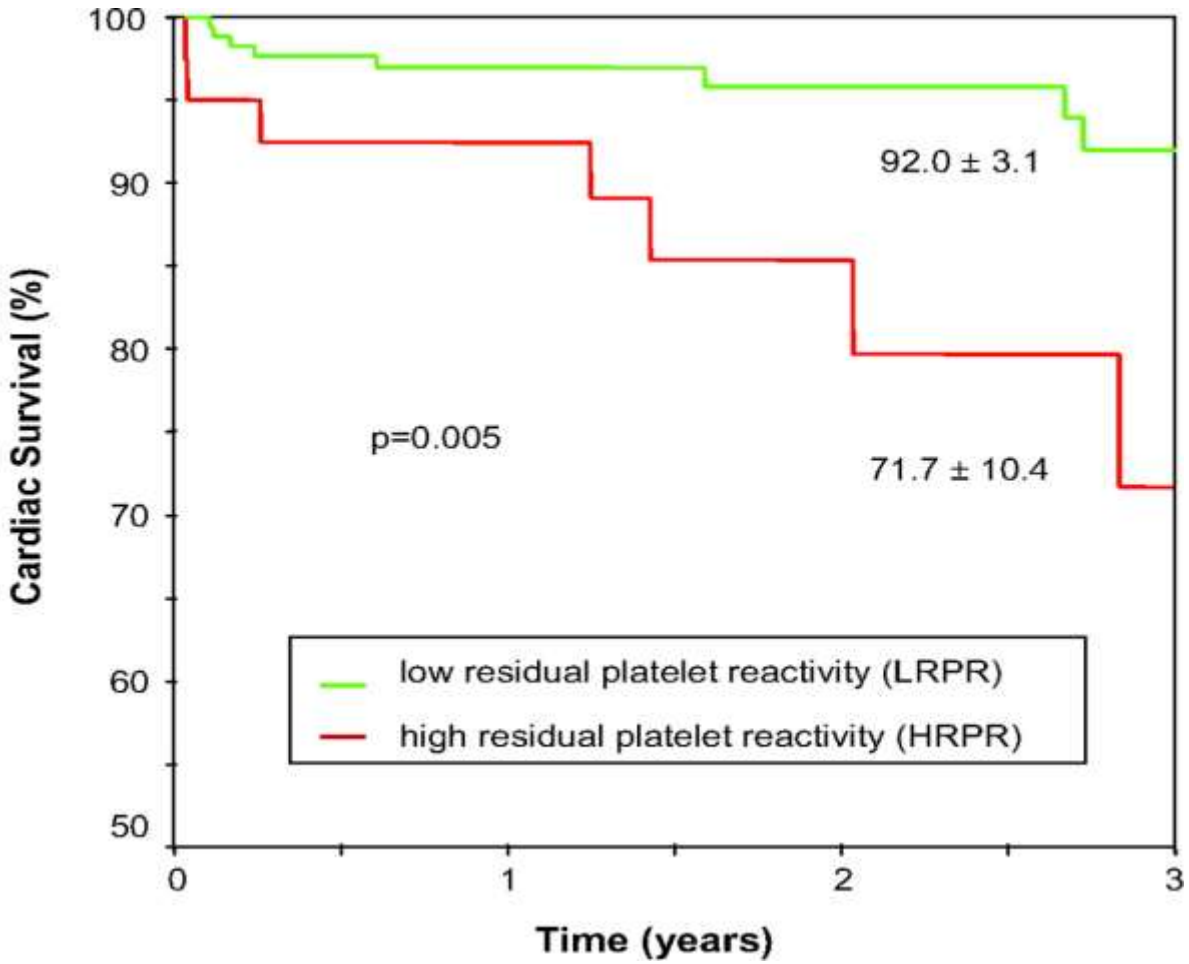
High residual platelet reactivity after clopidogrel loading and long-term clinical outcome after drug-eluting stenting for unprotected left main coronary disease. (n= 215)

Cardiac survival

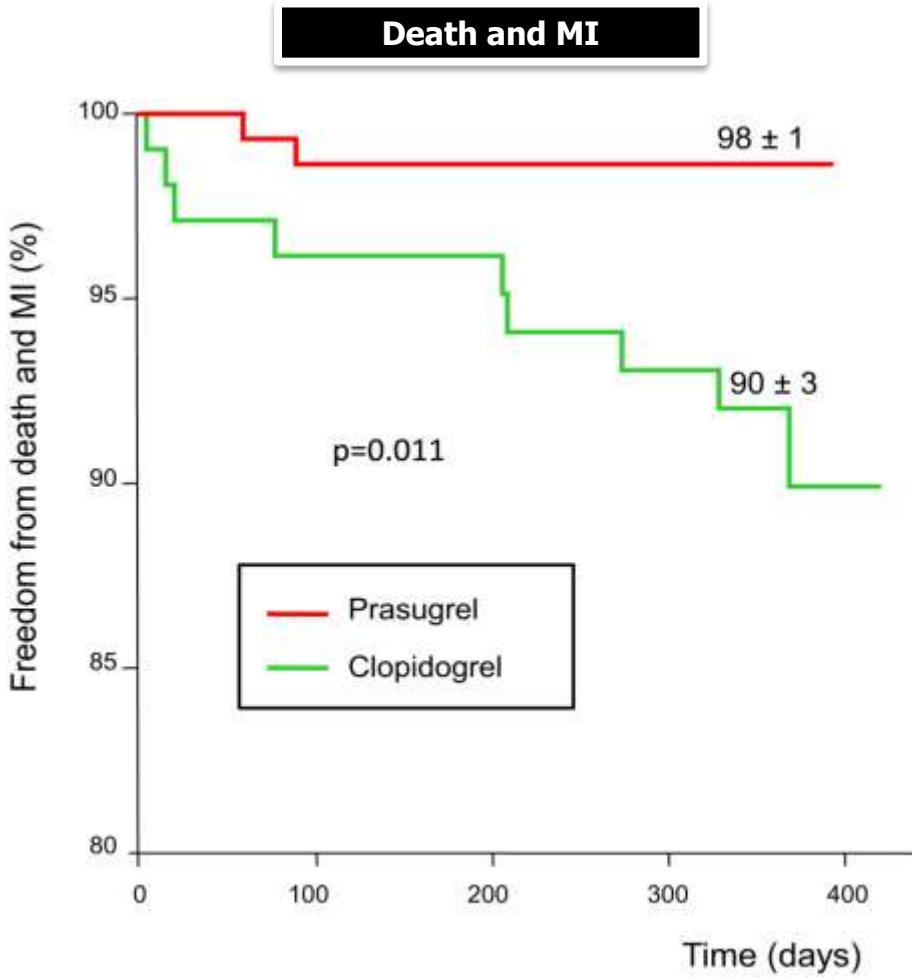
HRPR was defined as platelet aggregation by ADP ≥ 70%



Migliorini A et al. Circulation. 2009;120:2214-2221

Different antiplatelet regimens and clinical outcome

Comparison of the Degree of Platelet Aggregation Inhibition With *Prasugrel* Versus *Clopidogrel* and Clinical Outcomes in Patients With Unprotected Left Main Disease Treated With *Everolimus*-Eluting Stents (n= 252)



	Clopidogrel n=104	Prasugrel n=148	P-value
Cardiac death n (%)	8(7.7)	2(1.3)	0.11
Nonfatal MI n (%)	2(1.9)	0	0.09
Hemorrhagic Stroke n (%)	0	1(0.7)	0.40
Stent Thrombosis* n (%)	3 (2.9)	0	0.03
Major bleeding n (%)	2(1.9)	4(2.7)	0.68

*Possible stent thrombosis

Migliorini A et al. Am J Cardiol. 2013;112:1843-1848

Conclusion

- Treatment option for UPLM should be based on Heart team approach
- LMCA stenosis is usually associated with downstream epicardial vessels, thus it is mandatory to carefully review other coronary segments.
- Incidence of stent thrombosis is low and literature does not always report specificaly LM stent thrombosis but report stent thrombosis in stented LM patients.
- Low EF, Euroscore, high residual platelet reactivity and the use of two stents are the most frequently recognized determinant of LM stent thrombosis.
- Acute and subacute stent thrombosis are more dangerous than late and very late stent thrombosis.
- New potent antiplatelet might decrease risk of stent thrombosis

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