How would latest theory change my practical approach

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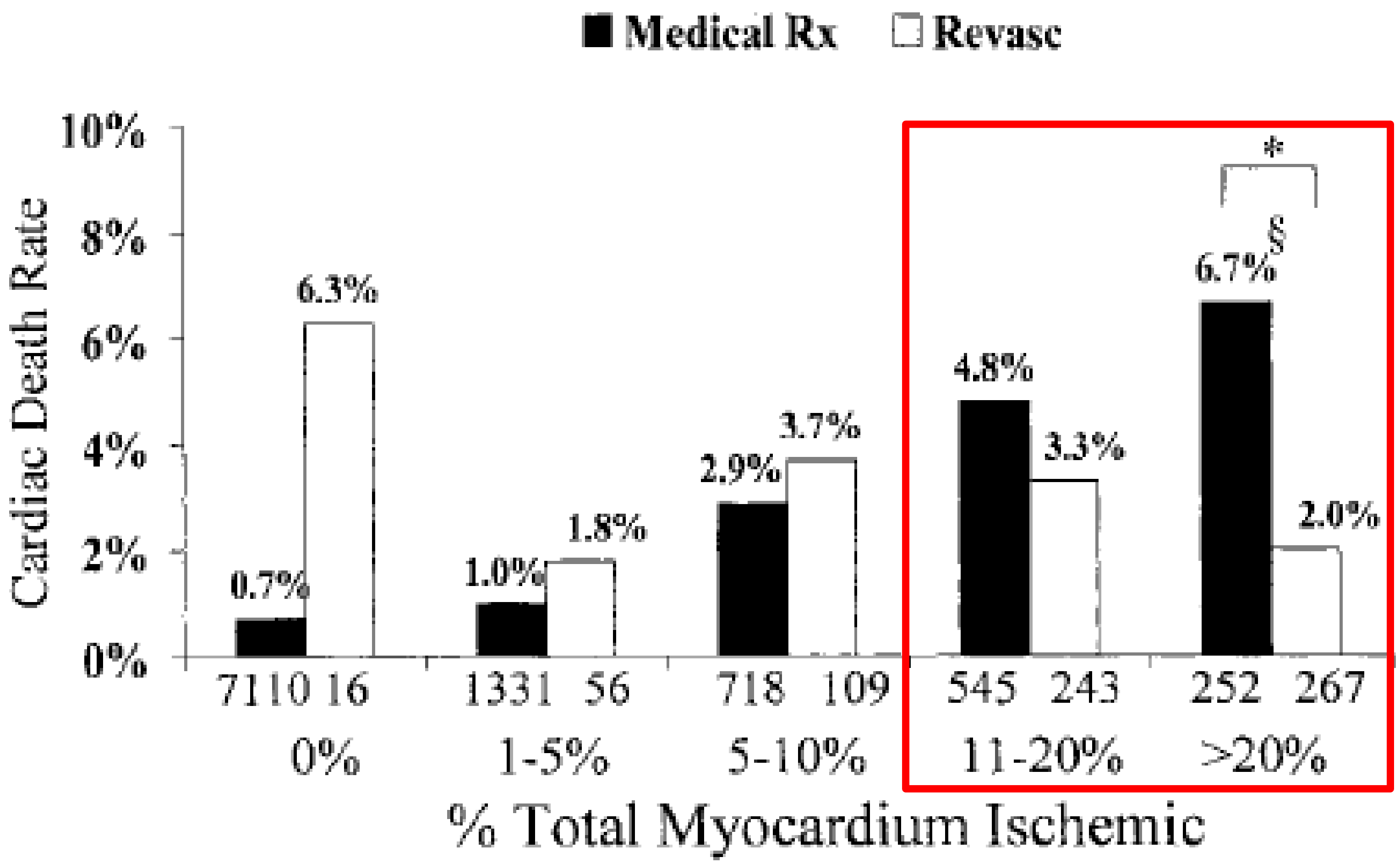
9 ¾ Bulgarian Bifurcation and Complex Coronary Intervention Course
23-24 January 2021

RAMSAY GÉNÉRALE DE SANTÉ

I, Yves Louvard, have no conflict of interest to disclose

New coronary bifurcation lesion definition

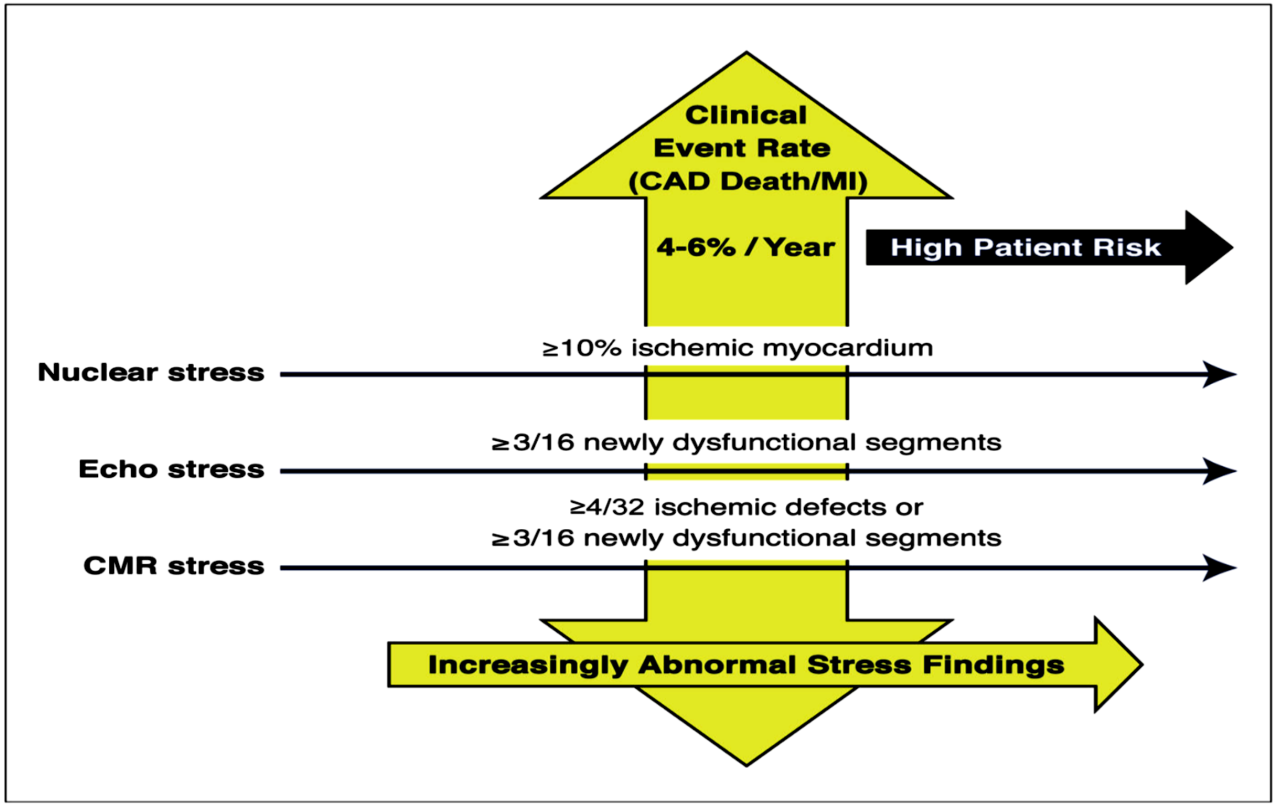
PCI better than medical treatment when ischemia is more than 10% of myocardium



Hachamovitch, Circulation 2003

Comparative definitions for moderate-severe ischemia in stress nuclear, echocardiography, and magnetic resonance imaging

Definitions of Moderate-Severe Ischemia



Comparable multimodality estimates of moderate-severe ischemia using risk-based thresholds of CAD death or MI rates of 4% to 6%/year

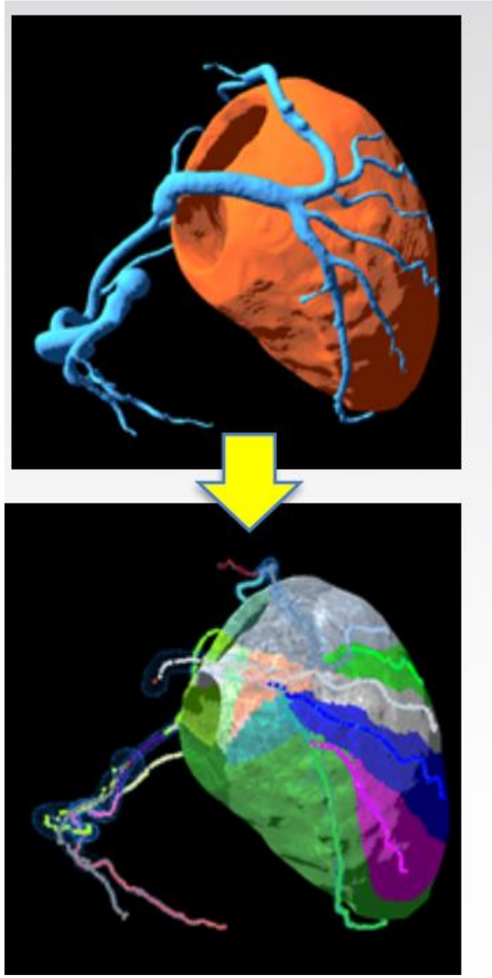
Shaw, JACC Cardiovasc Imaging. 2014 June ; 7(6): 593–604

Can we adapt this concept to bifurcation SB?

- Can we measure which amount of ischemia is depending of SB ? **No** (excepted 0,0,1)

- MMAR (myocardial mass at risk) and FMM (fractional myocardial mass) can be used as surrogates for ischemia volume which is always smaller than MMAR / FMM

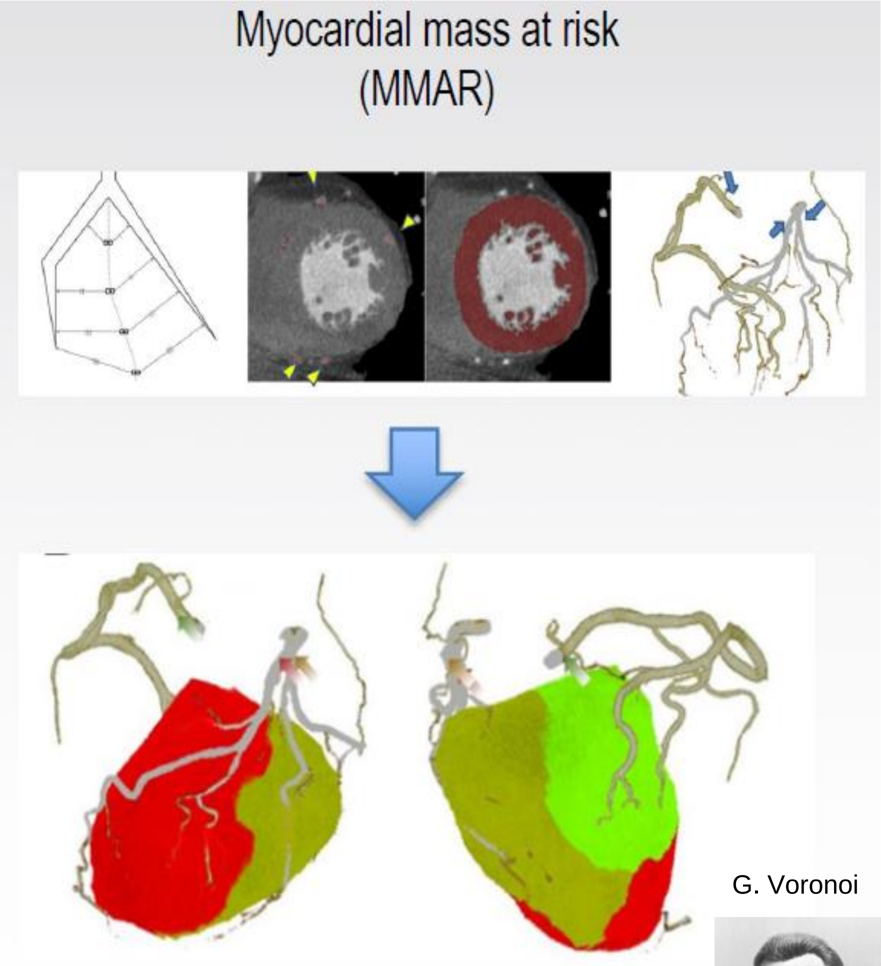
Myocardial segmentation techniques with CT scan



HY Kim, JACC
Cardiovasc Interv 2017

Fractional Myocardial Mass (FMM)

- Myocardial mass supplied by a specific vessel
- **Calculated from vessel length in CT**
- FMM was computed using stem and crown model based on allometric system

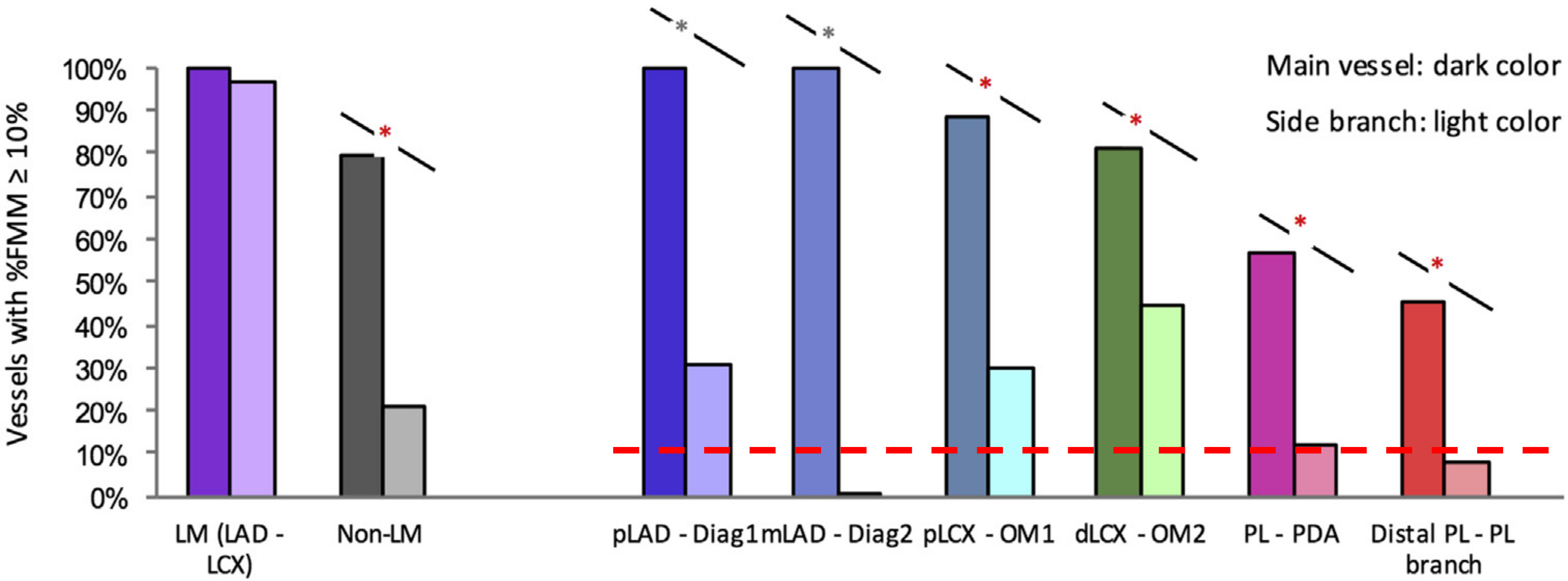


Sumitsuji, Cardiovasc Interv and Ther 2015

G. Voronoi

Identification of coronary artery SB supplying myocardial mass that may benefit from revascularization

Frequency of side branch supplying %FMM ≥10%



Only 1 out of every 5 non-LM SB supplies %FMM ≥10%

HY Kim, JACC Cardiovasc Interv 2017

Modified SNUH score (Diagonal branches)

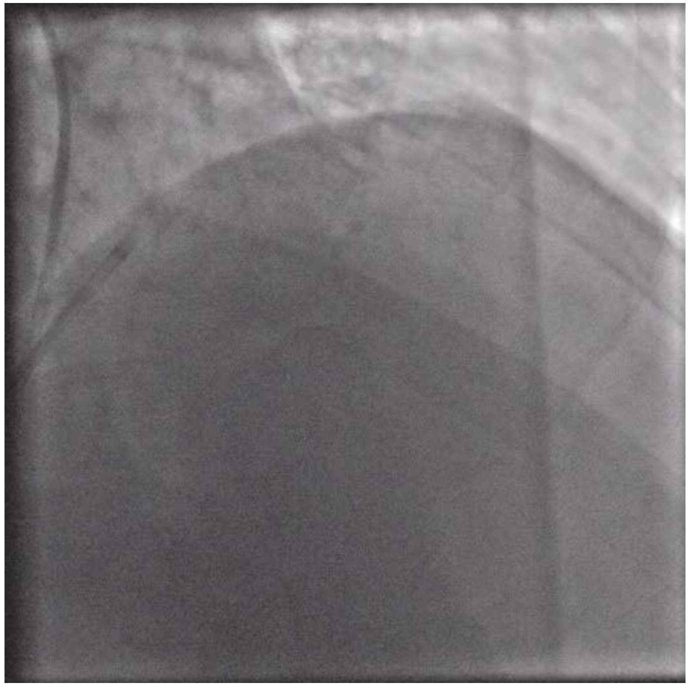
Variables	Description	Score
Size	Vessel diameter ≥ 2.5mm	1
	Number of diagonal branches = 1	2
Number	Number of diagonal branches = 2	1
	Number of diagonal branches ≥ 3	0
Ubiety	Left dominant or Apical area reaching OM branch	-1*
Highest	No branch below the target branch in proximal to mid LAD	1

*If total score is 0, then -1 is not added (The lowest total score is 0

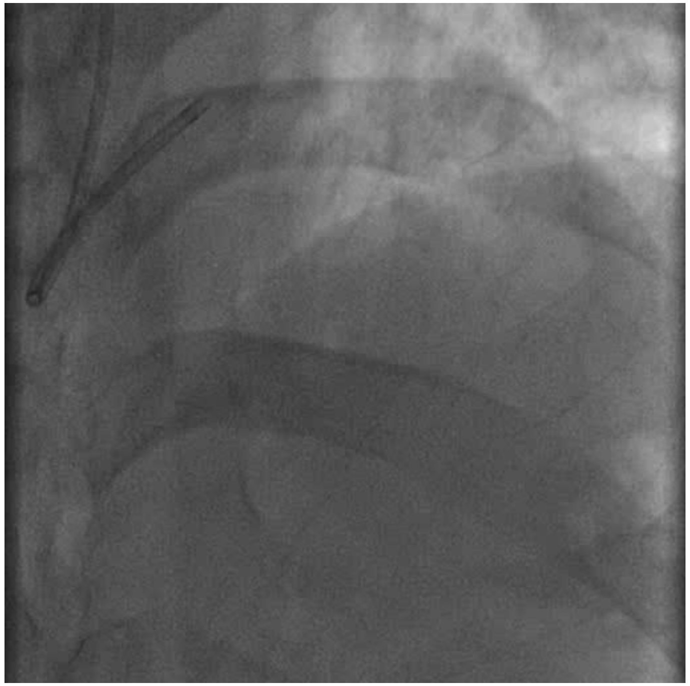
Courtesy of BK Koo

Relevant SB ?

No



No



Yes

Minor bifurcation
(non clinically relevant SB)

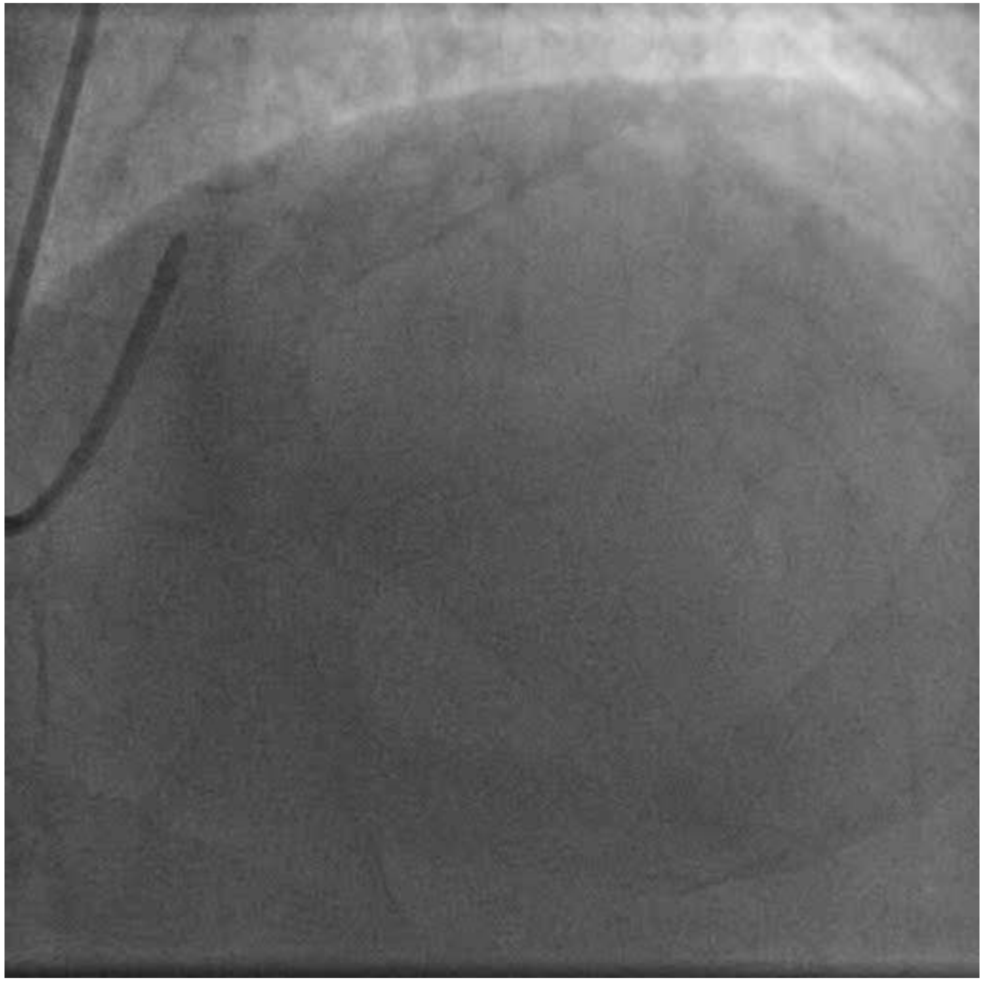
MADS*

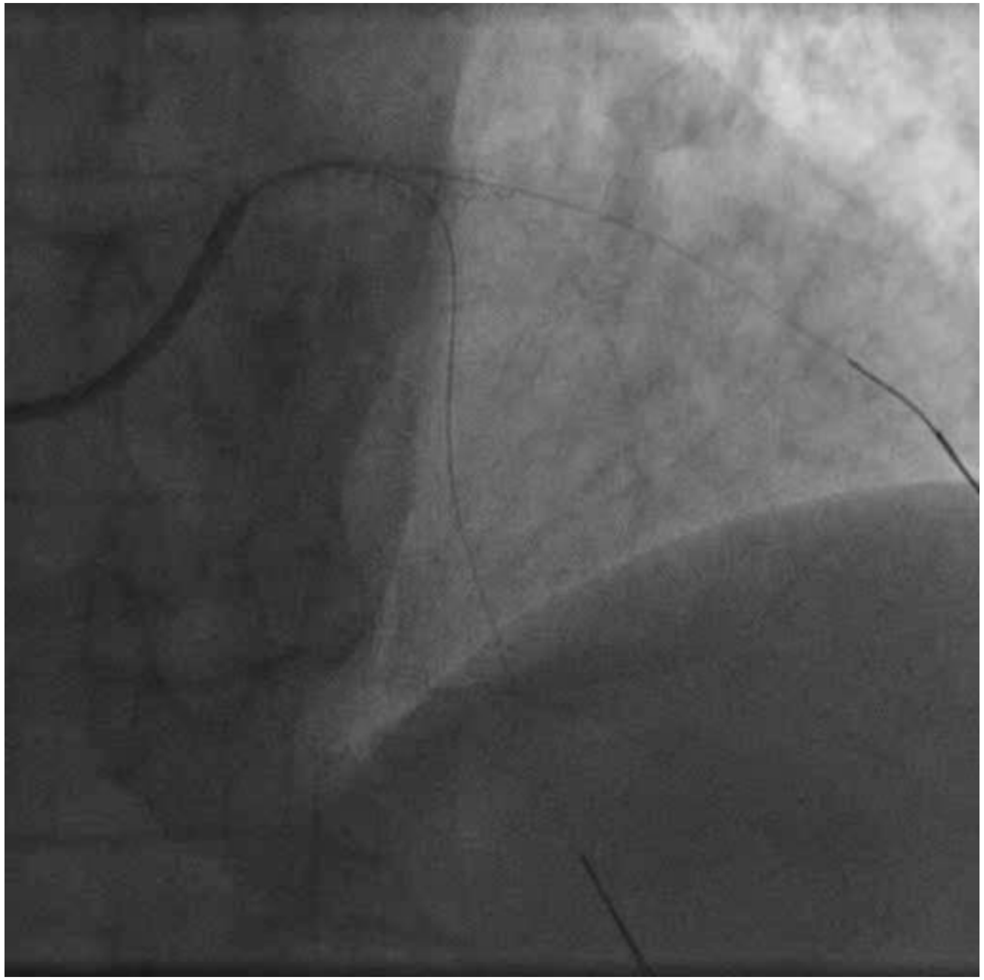
	M Main prox. first	A Main Across side first (Provisional)	D Double prox. lumen	S Side branch first
1st stent	PM stenting	MB cross-over stenting		SB ostial stenting
Ballooning	Skirt (K)	POT; Side-branch dilation; Kissing; S PS PK PSP PKP		S K; Balloon SB crush
2nd-3rd stent, (and further ballooning)	Extended skirt (K)	T; TAP; Culotte; K KP	V / SKS	Intentional T stenting; PK PKP; Step/DK crush
Dedicated Device:	Axxess	Bioss LIM, Xposition Stentys, Nile SIR		Capella Side-Guard

*(name from Kornowski)

Burzotta Louvard 2019

Inverted provisional strategy (LAD to Dg1)





3 years later: MSCT

LAD **Diagonal**

Major bifurcation
(clinically relevant SB)

Double stenting, main branch first: TAP

Courtesy of Yiannis Chatzizisis

Double stenting, side first: DK-Crush

Courtesy of Yiannis Chatzizisis

Treatment in DK Crush V

482 randomized patients

Provisional 242

Predilation
MB 83.9%
SB 39.7%
POT 98.8%

SB Stent 47.1%
(Simple 38.8%)
(complex 69.9%)

Final kissing 78.9%

DK Crush 240

Predilation
MB 75.4%
SB 68.3%
POT 99.2%

SB stent 100%

Final kissing 99.6%

SB lesion length (mm)

16.6±11.9 16.2±14

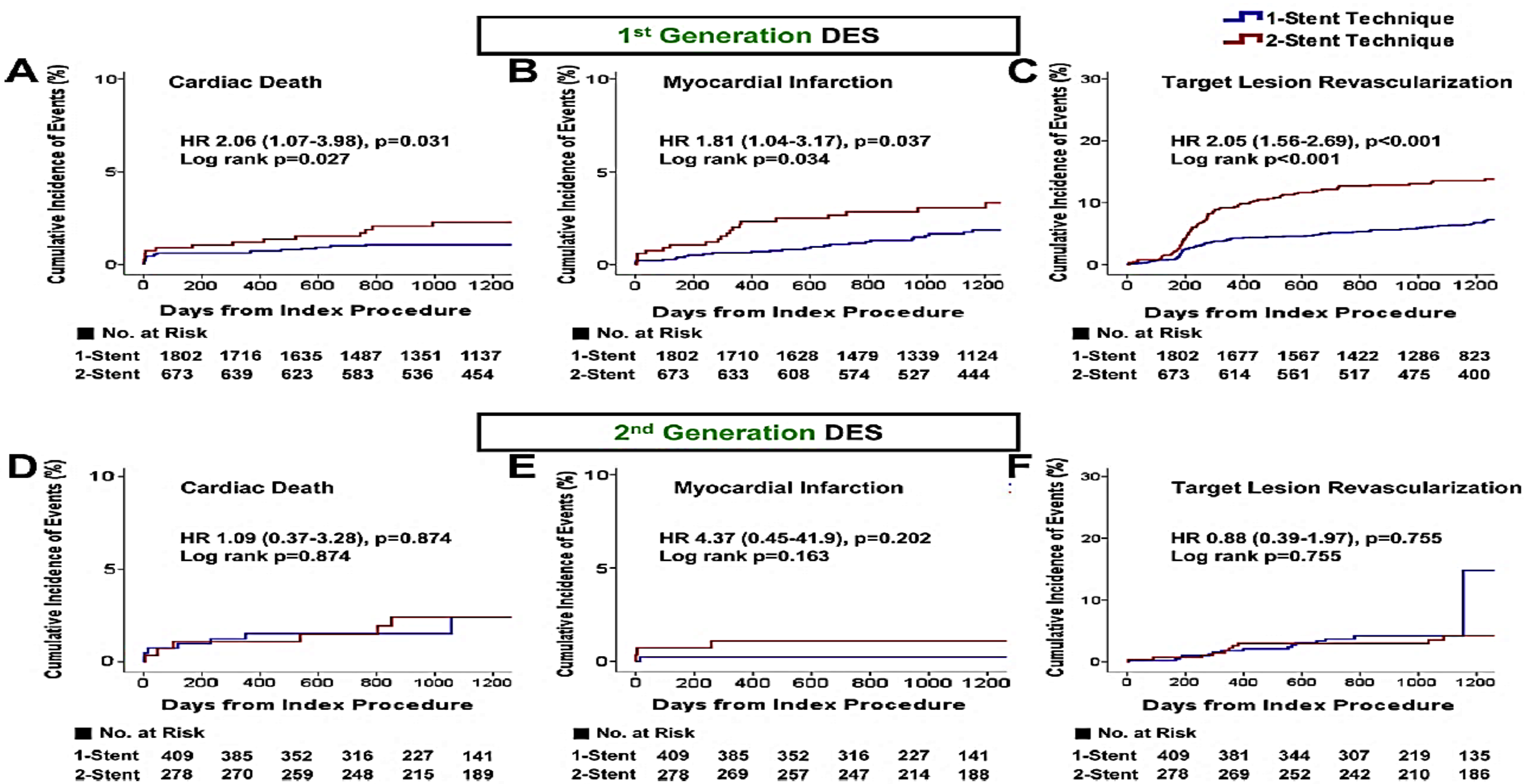
> 10 mm
42.9% 50%

Chen SL, J Am Coll Cardiol 2017;70:2605–17

Effect of complex procedures (double stenting) on ischemic outcomes

1st - and 2nd -Generation DES in Coronary Bifurcation Lesions: Patient-Level Analysis of the Korean Bifurcation Pooled Cohorts

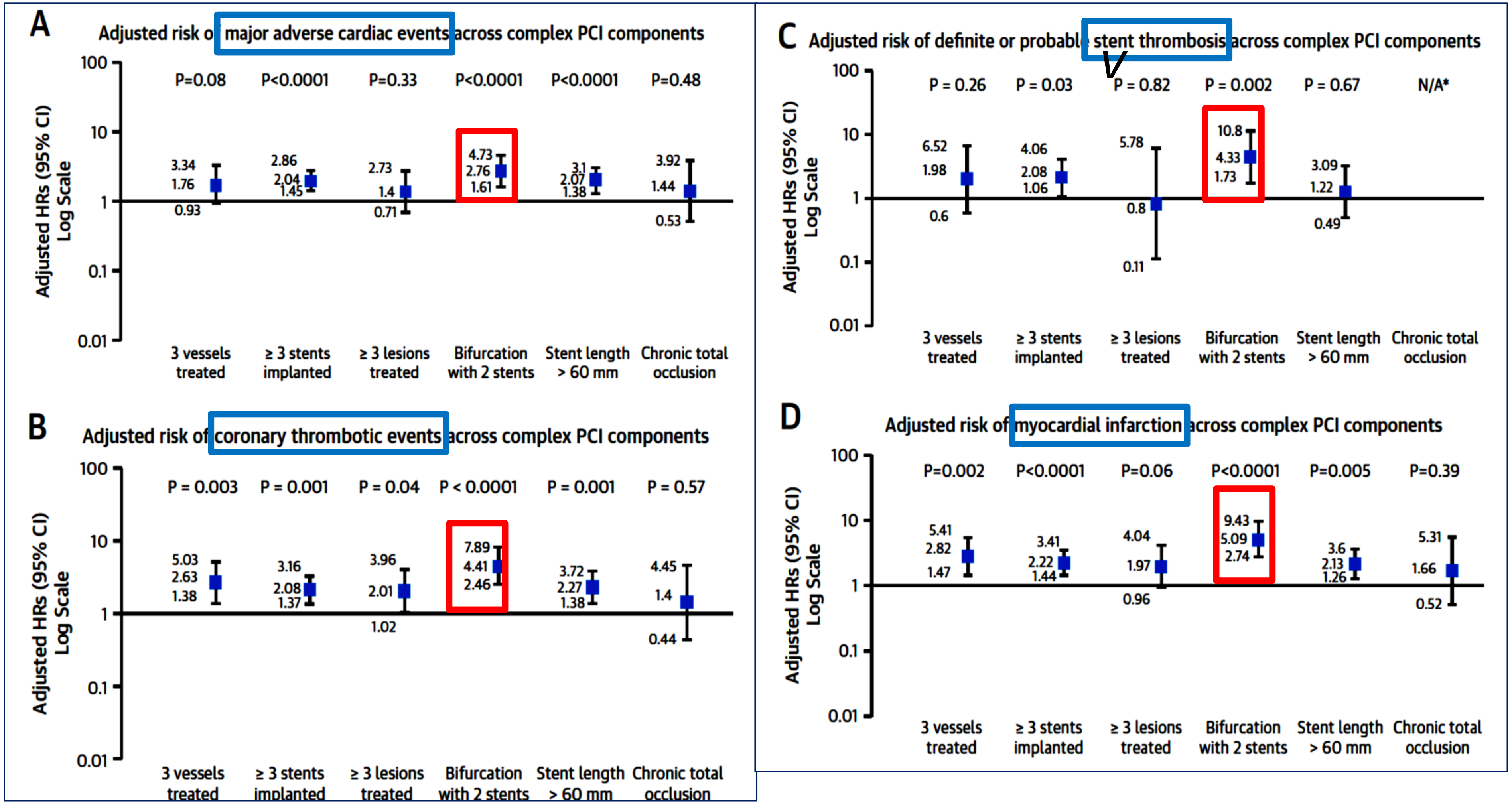
(A to C) Individual components of target lesion failure in 1st -generation DES. (D to F) Individual components of target lesion failure in 2nd generation DES



Lee, J Am Coll Cardiol Intv 2015;8:1318–31

Efficacy and Safety of DAPT After Complex PCI (6 RCT investigating DAPT durations after PCI)

Effect of High-Risk Procedural Subsets on Ischemic Outcomes



Giustino, J Am Coll Cardiol

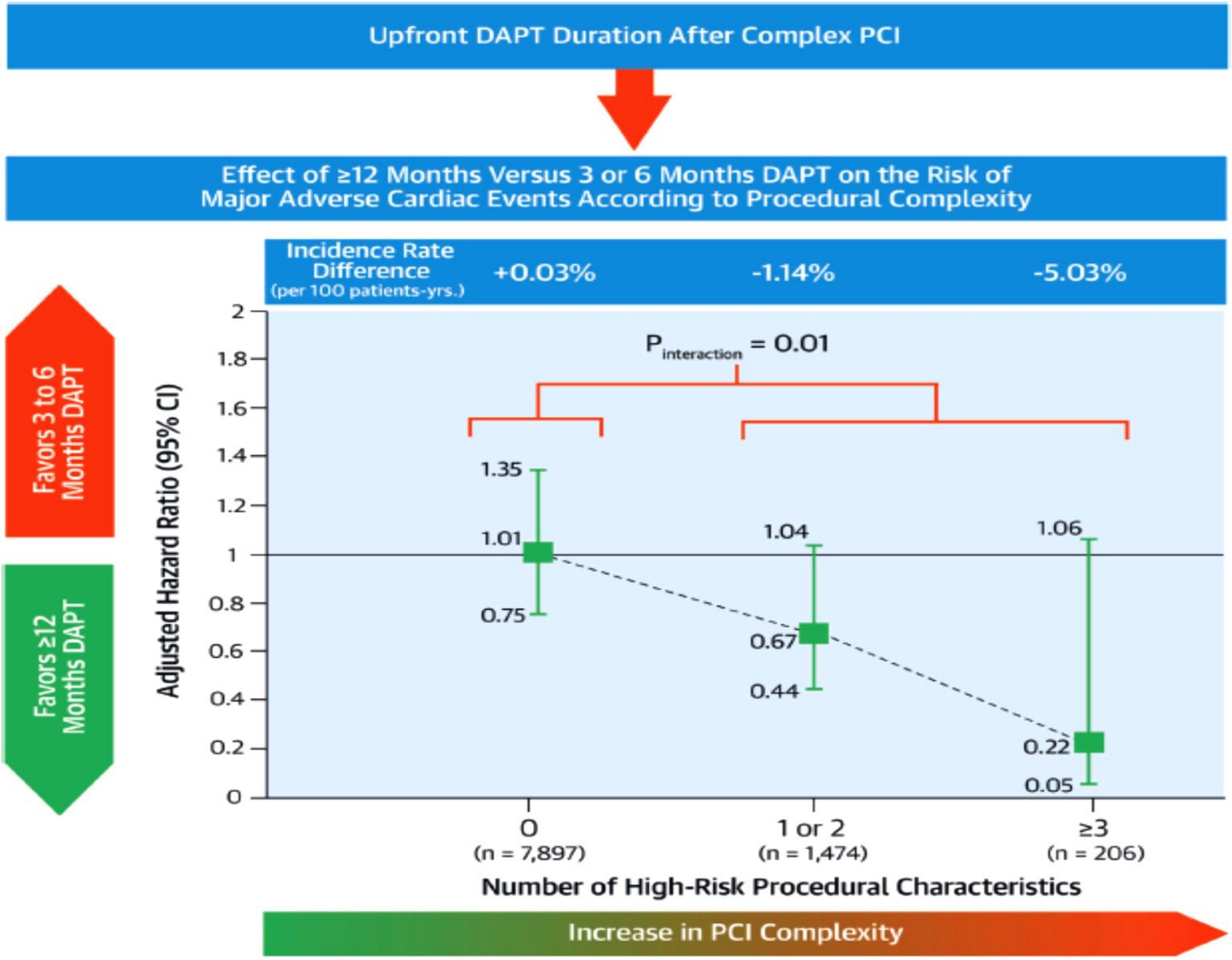
Efficacy and Safety of DAPT After Complex PCI (6 RCT investigating DAPT durations after PCI)

TABLE 4 Ischemic and Bleeding Outcomes in All Randomized Patients According to PCI Complexity and DAPT Duration

	Complex PCI (n = 1,680)			Noncomplex PCI (n = 7,897)			
	Longer DAPT (n = 854)	Shorter DAPT (n = 826)	Adjusted HR (95% CI)	Longer DAPT (n = 3,946)	Shorter DAPT (n = 3,951)	Adjusted HR (95% CI)	p Value for Interaction
MACE	35 (4.1)	56 (6.8)	0.56 (0.35-0.89)	116 (2.9)	114 (2.9)	1.01 (0.75-1.35)	0.01
Cardiac death	15 (1.8)	19 (2.3)	0.65 (0.30-1.41)	56 (1.4)	45 (1.1)	1.34 (0.86-2.09)	0.33
Myocardial infarction	25 (2.9)	40 (4.8)	0.60 (0.35-1.06)	71 (1.8)	72 (1.8)	0.90 (0.62-1.30)	0.08
Definite or probable stent thrombosis	7 (0.8)	13 (1.6)	0.37 (0.12-1.16)	20 (0.5)	21 (0.5)	0.95 (0.51-1.75)	0.08
CTE*	27 (3.2)	44 (5.3)	0.57 (0.33-0.97)	75 (1.9)	79 (2.0)	0.87 (0.61-1.25)	0.04
All-cause mortality	27 (3.2)	27 (3.3)	1.11 (0.60-2.04)	94 (2.4)	83 (2.1)	1.20 (0.87-1.67)	0.81
Noncardiac death	12 (1.4)	8 (1.0)	2.87 (0.91-9.03)	35 (0.9)	36 (0.9)	1.03 (0.62-1.70)	0.07
Target vessel revascularization	55 (6.4)	56 (6.8)	1.01 (0.68-1.49)	129 (3.3)	156 (3.9)	0.81 (0.64-1.02)	0.39
Stroke	7 (0.8)	3 (0.4)	2.67 (0.69-10.42)	25 (0.6)	24 (0.6)	1.04 (0.58-1.86)	0.32
Bleeding							
Major bleeding	11 (1.3)	6 (0.7)	1.81 (0.67-4.91)	32 (0.8)	18 (0.5)	1.75 (0.98-3.12)	0.96
Minor bleeding	11 (1.3)	7 (0.8)	1.51 (0.59-3.90)	44 (1.1)	35 (0.9)	1.25 (0.80-1.94)	0.68
Any bleeding	22 (2.6)	13 (1.6)	1.64 (0.83-3.26)	75 (1.9)	51 (1.3)	1.45 (1.02-2.07)	0.72

Giustino, J Am Coll Cardiol

Efficacy and Safety of DAPT After Complex PCI (6 RCT investigating DAPT durations after PCI)



Giustino, J Am Coll Cardiol

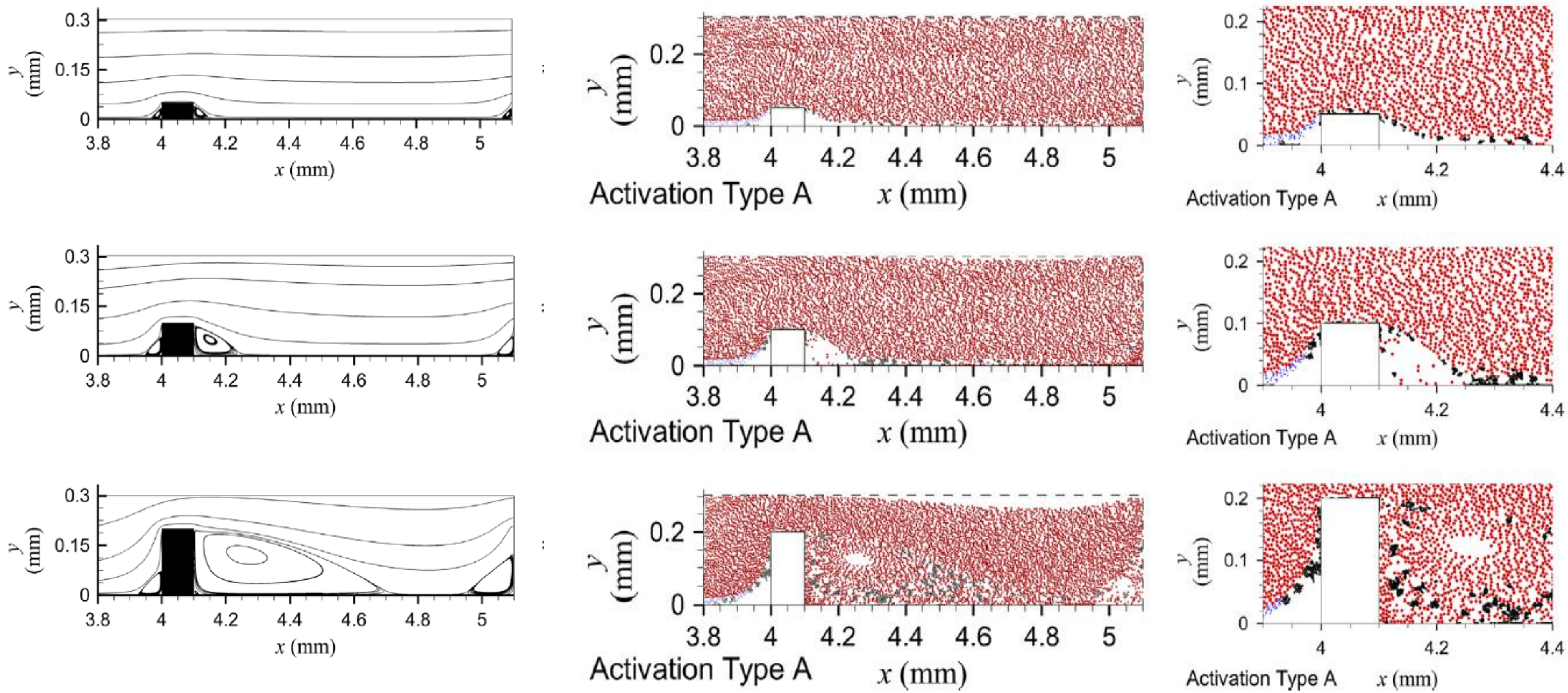
2017 ESC focused update on dual antiplatelet therapy in CAD developed in collaboration with EACTS

Gender considerations and special populations

Recommendations	Class[a]	Level[b]
Similar type and duration of DAPT are recommended in male and female patients.[26,240]	I	A
It is recommended to reassess the type, dose, and duration of DAPT in patients with actionable bleeding complications while on treatment.	I	C
Similar type and duration of DAPT should be considered in patients with and without diabetes mellitus.[145,242]	IIa	B
Prolonged (i.e. >12 months[c]) DAPT duration should be considered in patients with prior stent thrombosis, especially in the absence of correctable causes (e.g. lack of adherence or correctable mechanical stent-related issues).	IIa	C
Prolonged (i.e. >12 months) DAPT duration may be considered in CAD patients with LEAD.[140,246]	IIb	B
Prolonged (i.e. >6 months) DAPT duration[d] may be considered in patients who underwent complex PCI.[247]	IIb	B

Valgimigli, European Heart Journal (2018) 39,

Simulation of the microscopic process during initiation of stent thrombosis



Streamlines (left) for different strut heights, including 50, 100, and 200 µm, Cell locations at the final time for Activation Type A (blue: unactivated platelets; black: activated platelets; red: red blood cells)

J. Chesnutt, Computers in Biology and Medicine 56 (2015) 182–191

Correlates and outcomes of late and very late DES thrombosis: results from DESERT

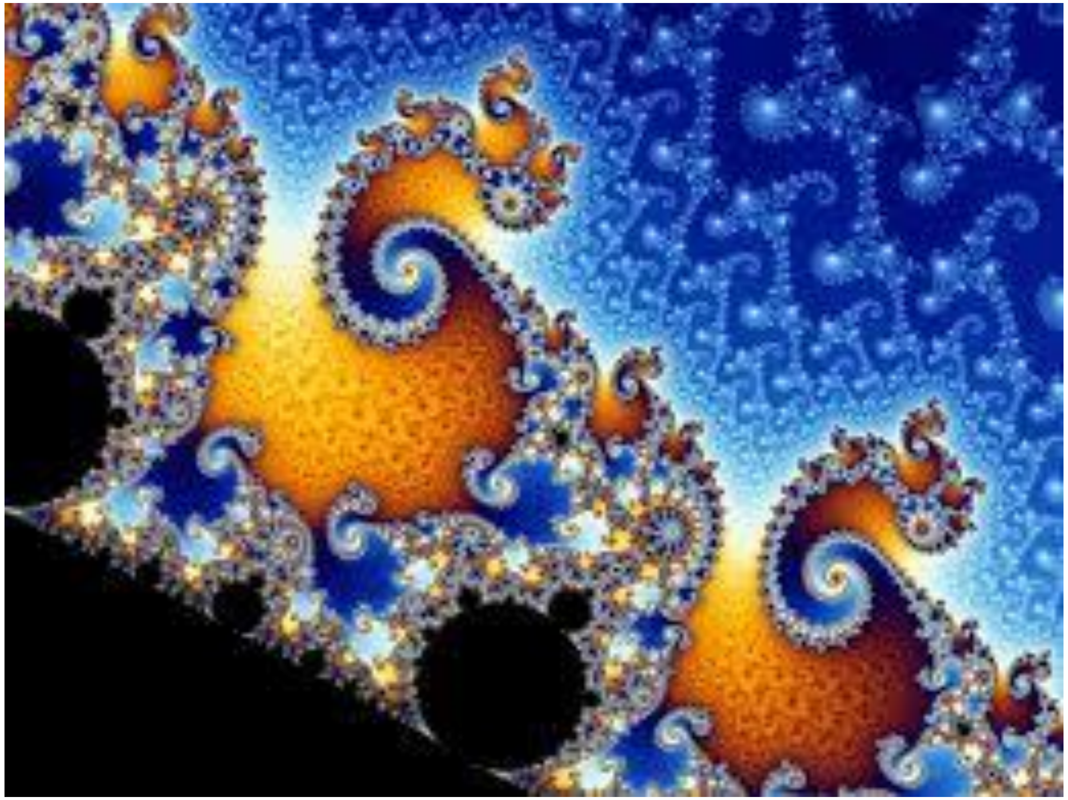
Clinical and Angiographic Correlates of Late/Very Late Stent Thrombosis

Variable	Clinical, OR (95% CI)	Angiographic	Combined, OR (95% CI)
Age	**0.964 (0.95–0.98)**	*	**0.793 (0.96–0.99)**
Hypertension	0.757 (0.51–1.12)	*	0.863 (0.56–1.34)
Body mass index	0.979 (0.95–1.01)	*	0.981 (0.95–1.01)
ACS/NSTEMI	1.084 (0.70–1.67)	*	0.831 (0.54–1.28)
Left anterior descending lesion	1.107 (0.77–1.59)	**1.671 (1.21–2.32)**	1.302 (0.87–1.96)
Current smoker	**1.890 (1.26–2.85)**	*	**1.633 (1.05–2.53)**
STEMI or thrombus (QCA)	1.059 (0.62–1.80)	**1.486 (1.03, 2.14)**	1.062 (0.66–1.71)
African American	**2.346 (1.21–4.54)**	*	1.612 (0.65–3.99)
Diabetes	0.915 (0.60–1.40)	*	1.021 (0.65–1.60)
Renal insufficiency	1.019 (0.50–2.09)	*	*
No. of diseased vessels	**1.313 (1.05–1.65)**	*	**1.712 (1.32–2.22)**
Type C lesion (QCA)	*	0.939 (0.54–1.63)	**2.188 (1.38–3.47)**
Final reference vessel diameter, mm	*	1.190 (0.77–1.85)	1.436 (0.84–2.44)
Acute gain, mm	*	0.982 (0.64–1.51)	1.013 (0.64–1.61)
Final in-stent diameter stenosis	*	**1.021 (1.00–1.04)**	1.014 (0.99–1.04)
Total stented length	**1.015 (1.00–1.03)**	1.022 (1.00–1.05)	**0.977 (0.97–0.99)**
Bypass graft lesion	**3.306 (1.18–9.27)**	**3.900 (1.55–9.84)**	1.997 (0.60–6.70)
Lesion length (QCA)	*	0.999 (0.97–1.03)	*
Overlapping stents	**1.757 (1.18–2.61)**	*	**2.220 (1.34–3.69)**

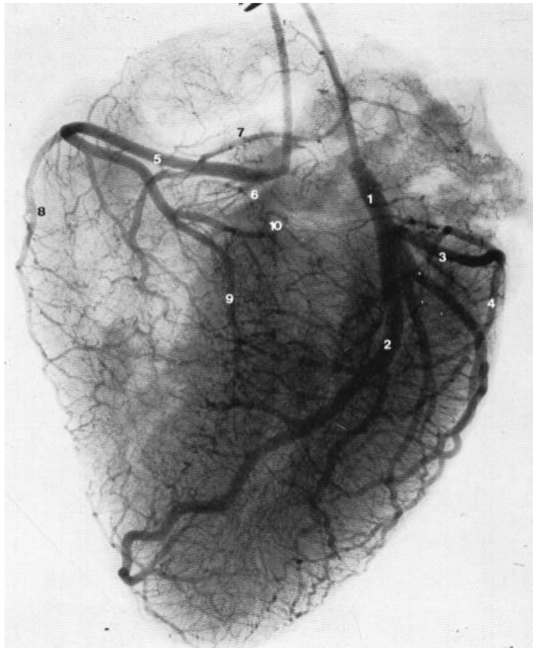
Waksman, J Am Coll Cardiol Intv 2014;7:1093–102

Bifurcation functional anatomy

Benoit Mandelbrot (1924-2010): fractals

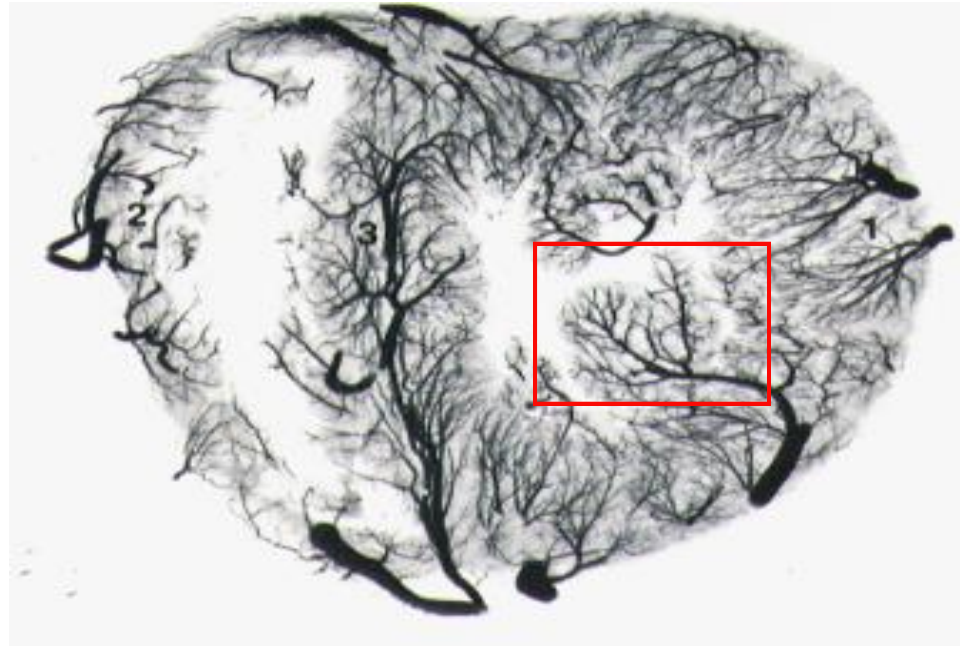


Coronary artery tree: pseudo-fractal object



X 1

X 0.75



X 4.5

X 10.5

X 90

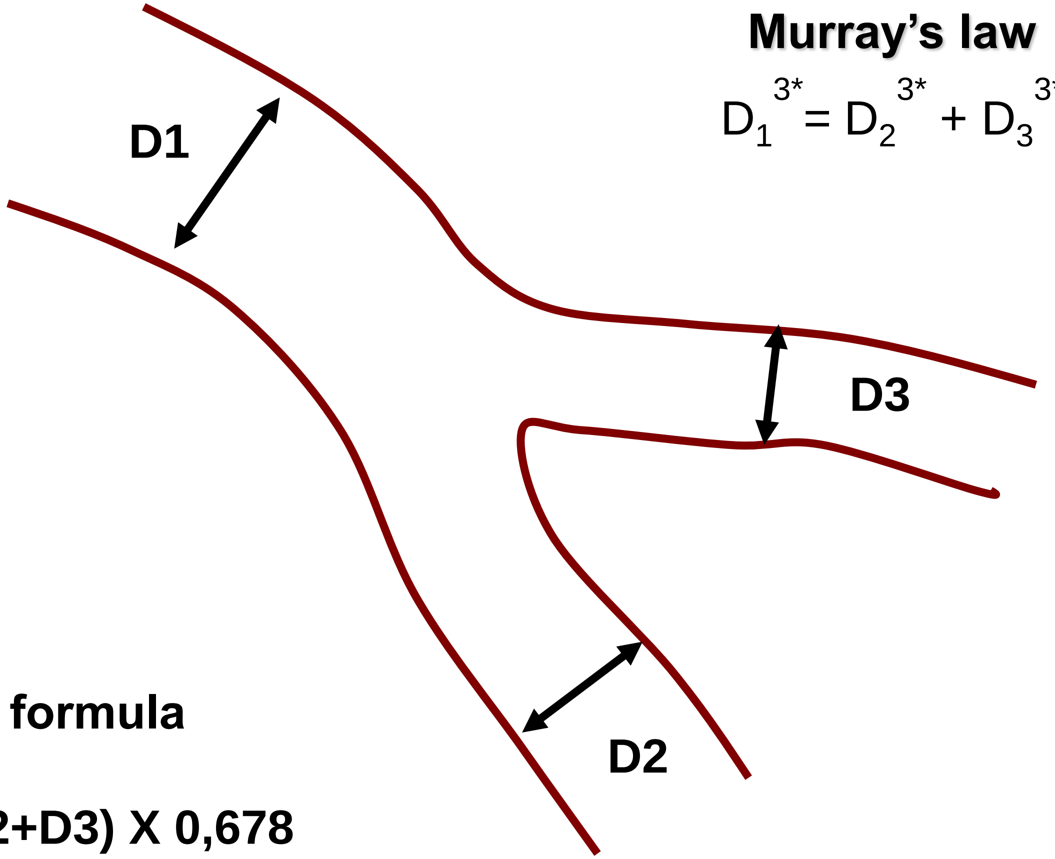
X 1100

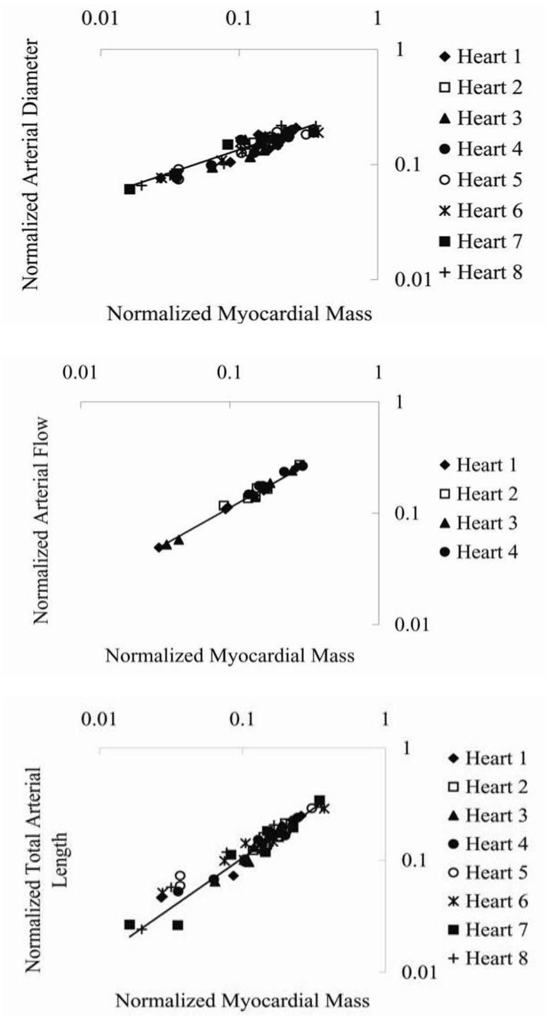
Finet et al. Eurointrevention 2007; 490-8

Structure-function scaling laws of vascular trees

Murray's law

$$D_1^{3*} = D_2^{3*} + D_3^{3*}$$





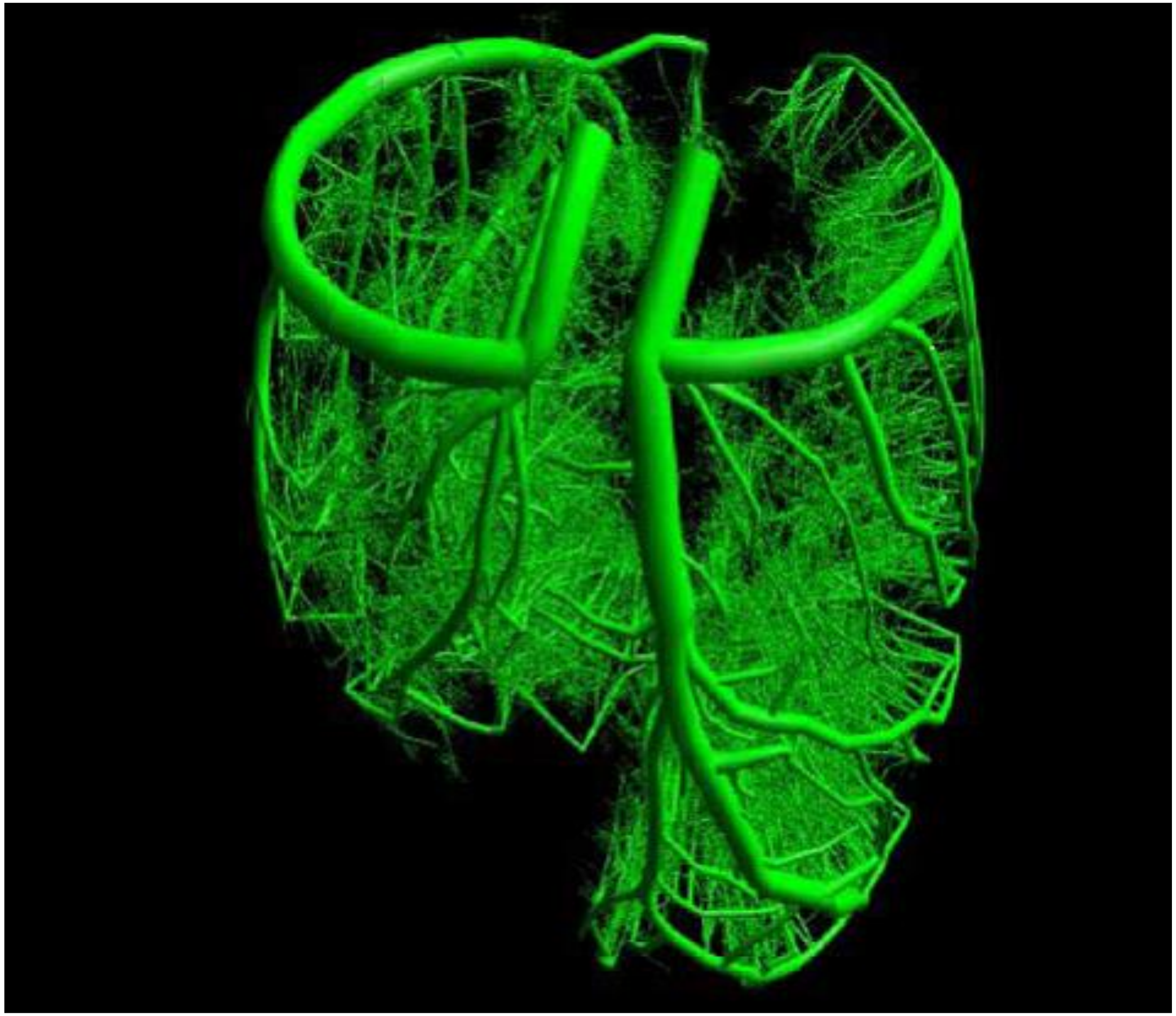
Finet's formula

D1= (D2+D3) X 0,678

* 2.3 **(Huo-Kassab)**

Adapted from G. Kassab

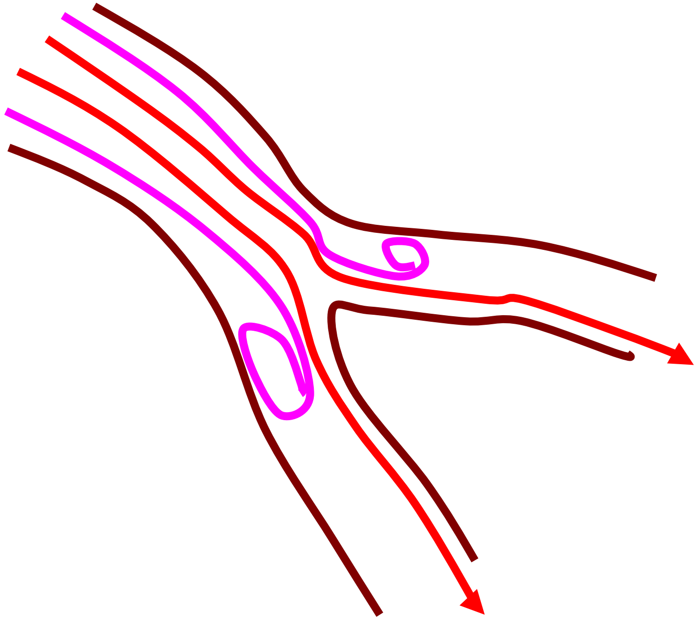
Mathematical model of coronary arterial tree

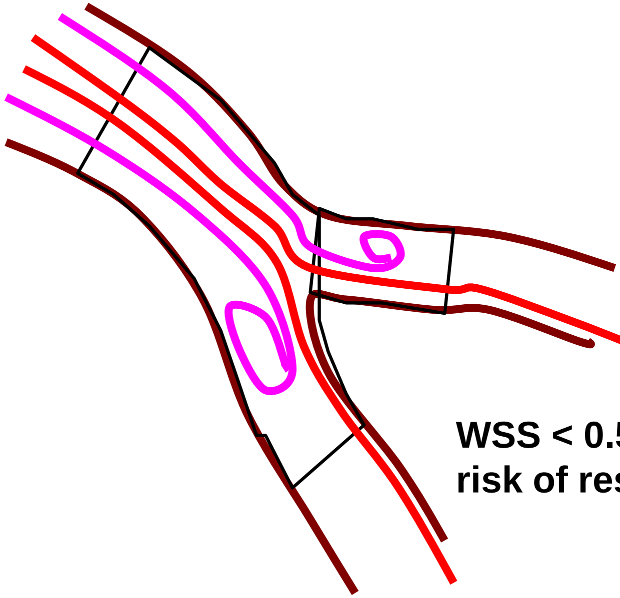


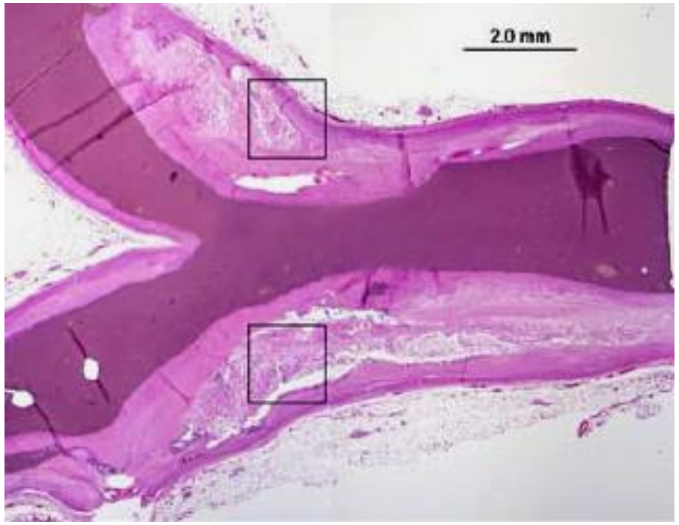
All along the epicardial branch the vascular surface is constant to preserve flow velocity and pressure

From G. Kassab

Flow Patterns and Spatial Distribution of Atherosclerotic Lesions





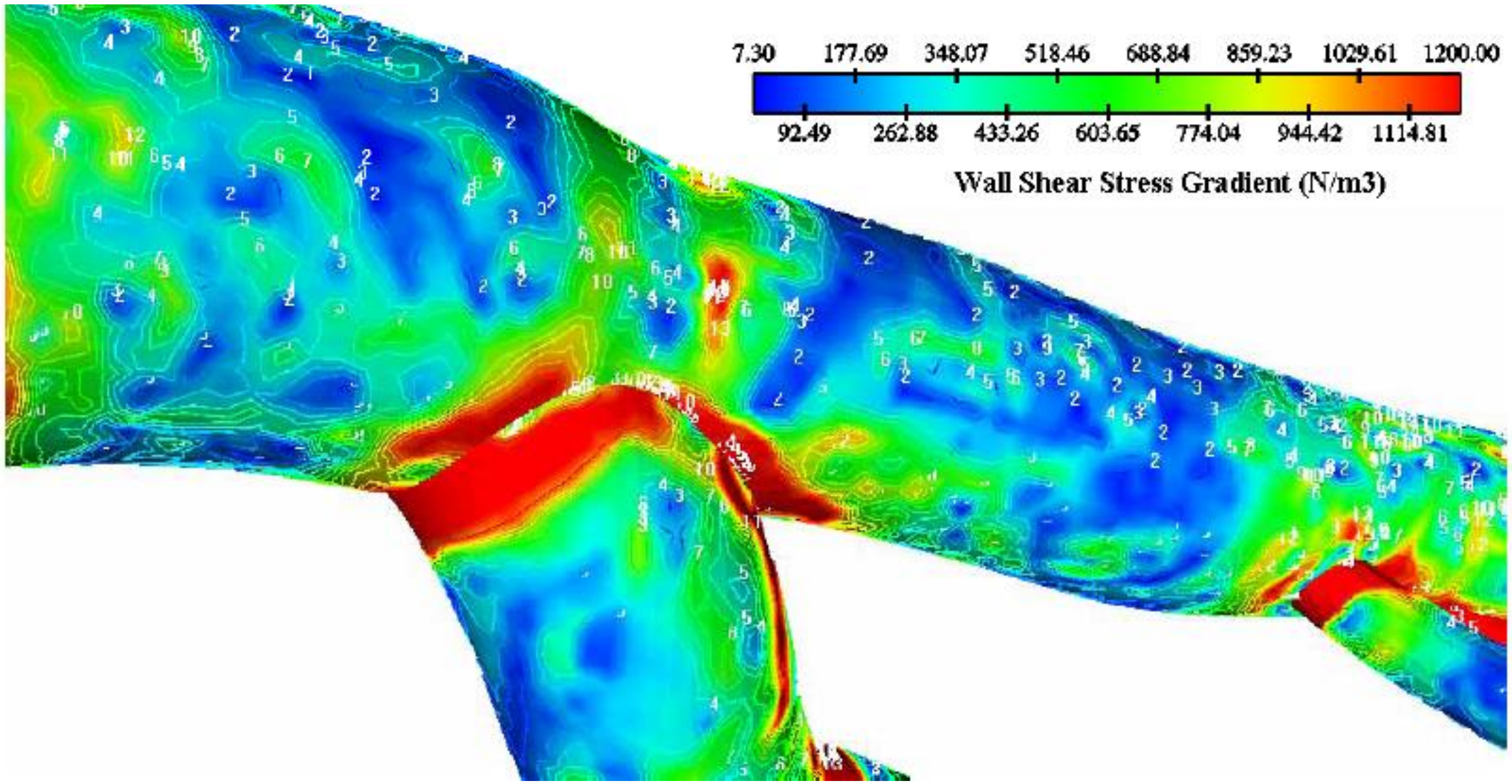


Flow mediated NIH and neo-atheroma

	Flow Divider	Lateral	p Value
Neointimal thickness (mm)	0.07 (0.03-0.15)	0.17 (0.09-0.23)	0.001
Fibrin deposition (% struts)	60 (21-67)	17 (0-55)	0.01
Uncovered struts (% struts)	40 (16-76)	0 (0-15)	0.001

Asakura, Virmani

The low WSS values distribution is in accordance with the frequent localization of atherosclerosis lesion



Soulis et al. J of Biomechanics 2006;39:742

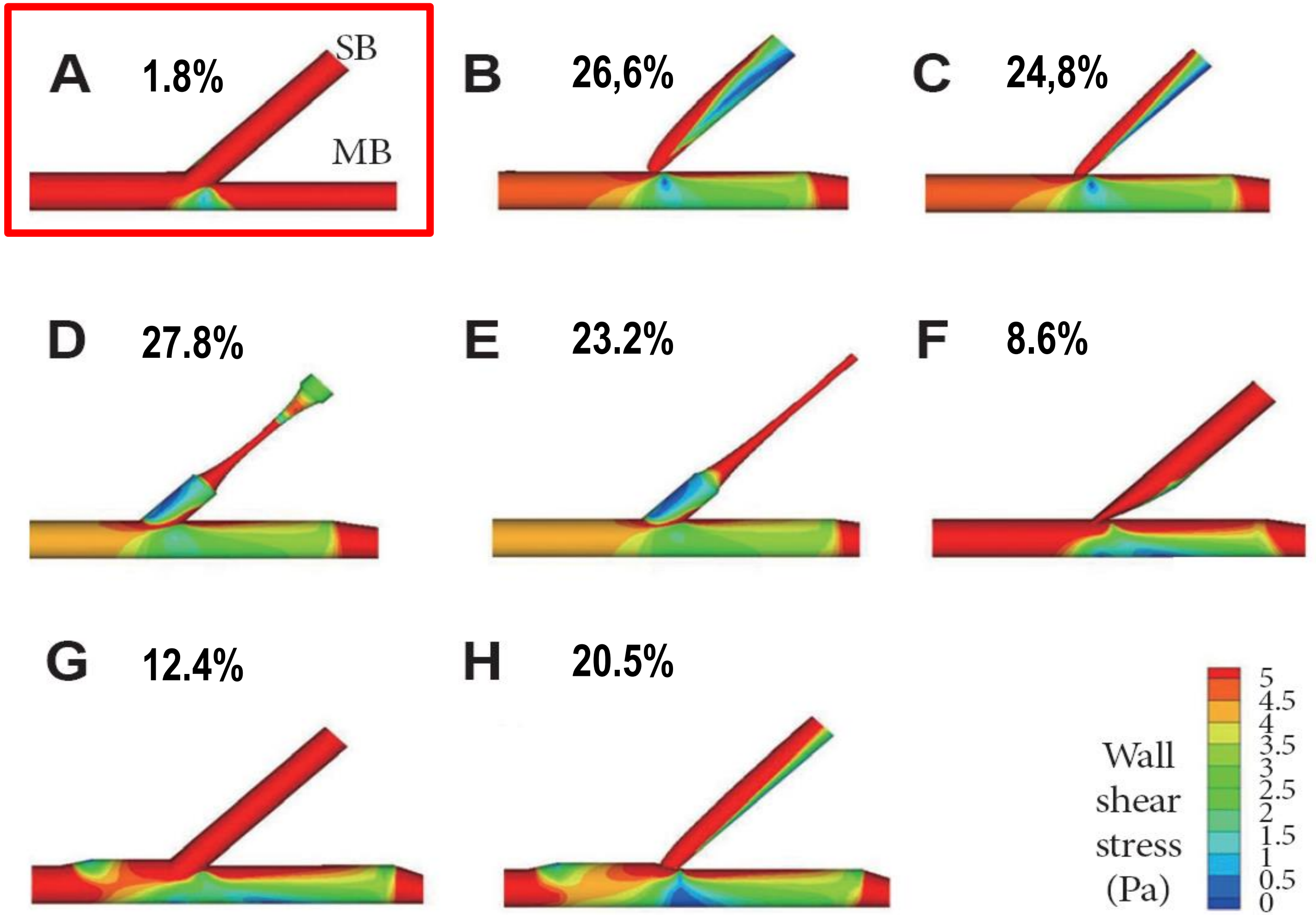
Pathological Findings at Bifurcation Lesions: Impact of Flow Distribution on Atherosclerosis and Arterial Healing After Stent Implantation

	DES (12 Lesions, 17 Stents)			BMS (14 Lesions, 18 Stents)			p Value for DES vs. BMS	
	Flow Divider	Lateral	p Value	Flow Divider	Lateral	p Value	Flow Divider	Lateral
Neointimal thickness (mm)	0.07 (0.03-0.15)	0.17 (0.09-0.23)	0.001	0.26 (0.16-0.73)	0.44 (0.17-0.67)	0.25	0.0002	0.004
Fibrin deposition (% struts)	60 (21-67)	17 (0-55)	0.01	8 (0-33)	3 (0-21)	0.21	0.008	0.19
Uncovered struts (% struts)	40 (16-76)	0 (0-15)	0.001	0 (0-21)	0 (0-0)	0.10	0.004	0.38

Nakazawa, Virmani, J Am Coll Cardiol 2010;55:1679–87

Local flow conditions in jailed SB lesions using computational fluid dynamics

Area of low WSS (<4 Pa) in 8-computational bifurcation models



SH. Na, BK. Koo, Korean Circ J 2011;41:91-96

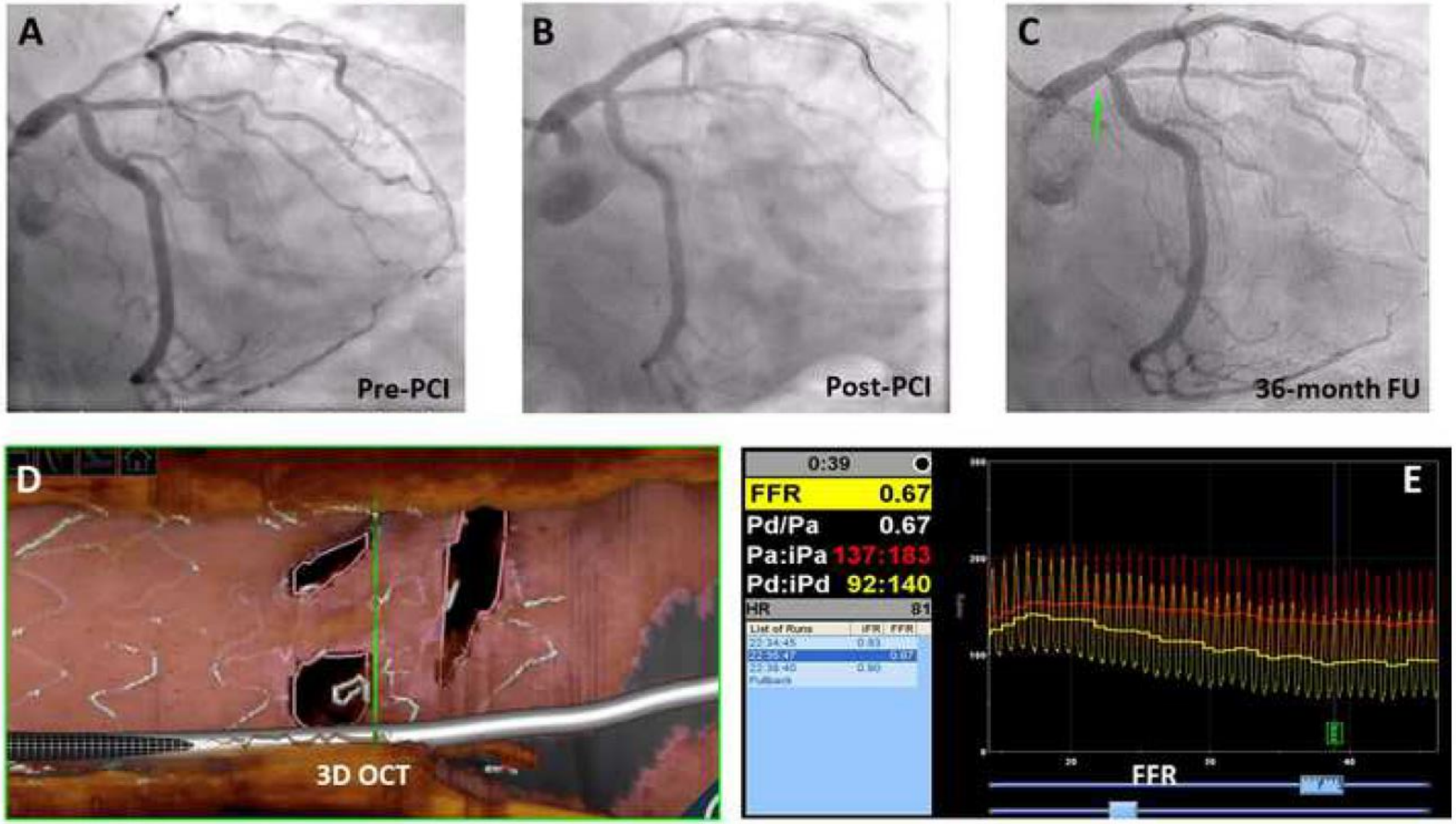
COBIS II POT Study: Clinical outcomes

- Patients with **SB diameter ≥ 2.5 mm in core-lab QCA (N=1,191)**
- Propensity score-matching population

	POT (n=204)	No POT (n=665)	HR (95% CI)	p value
MACE	**6 (2.9)**	**78 (11.7)**	**0.25 (0.11-0.60)**	**0.002**
All-cause death	7 (3.4)	25 (3.8)	0.97 (0.41-2.33)	0.95
Cardiac death	1 (0.5)	9 (1.4)	0.37 (0.05-2.97)	0.35
Myocardial infarction	0	12 (1.8)	-	-
Stent thrombosis	2 (1.0)	8 (1.2)	0.98 (0.20-4.77)	0.98
TLR	5 (2.5)	61 (9.2)	0.27 (0.10-0.69)	**0.006**
MV, proximal	**3 (1.5)**	**40 (6.0)**	**0.25 (0.07-0.82)**	**0.02**
MV, distal	**4 (2.0)**	**47 (7.1)**	**0.28 (0.10-0.80)**	**0.02**
SB	4 (2.0)	35 (5.3)	0.37 (0.13-1.09)	0.07
Both vessels	5 (2.5)	48 (7.2)	0.34 (0.13-0.88)	**0.03**

Preliminary analysis:, HC. Gwon at EBC 2016

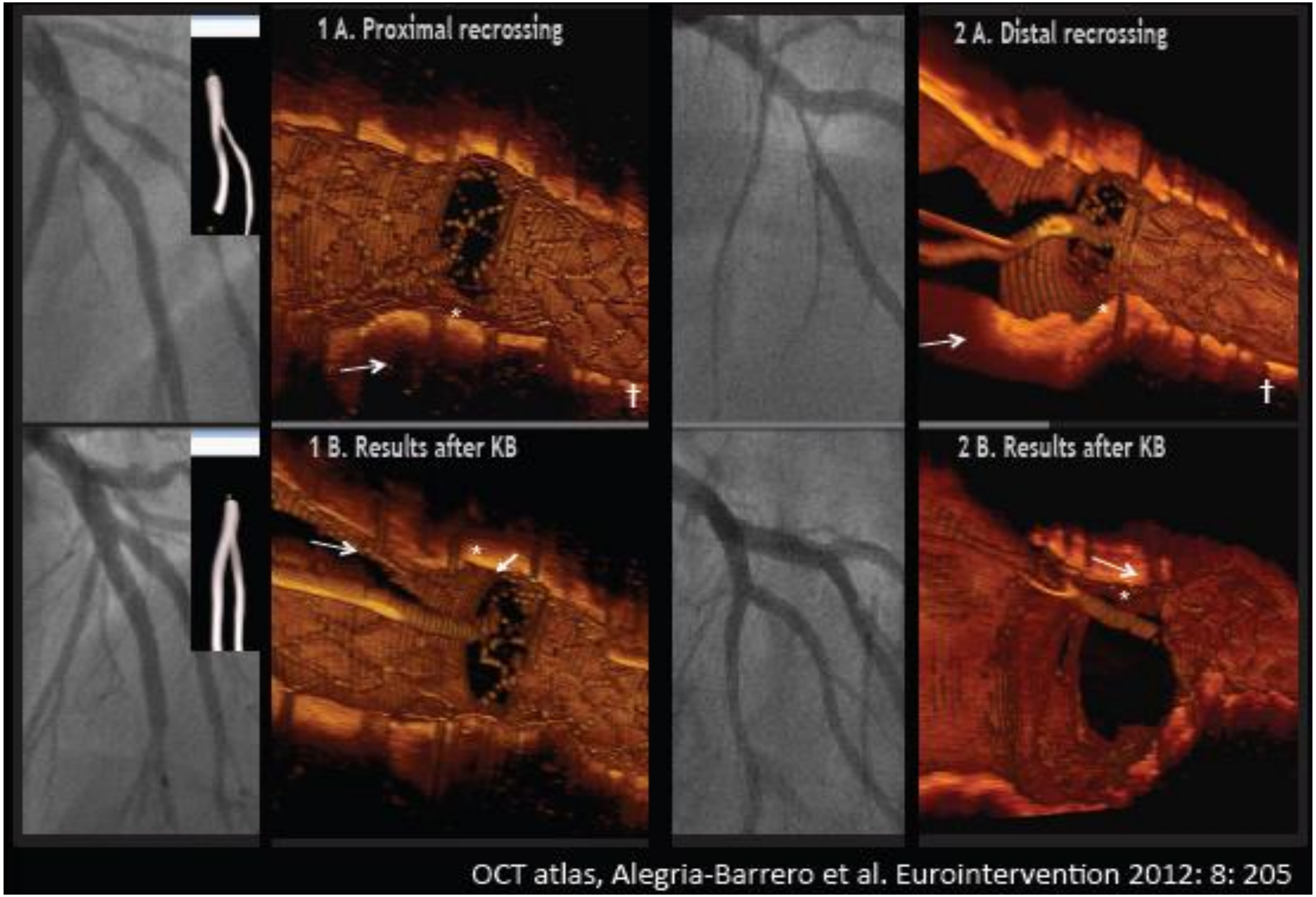
"Multiple-holes" restenosis after crossover stenting



A. Pre-PCI. **B.** After LM-LAD stent implantation and POT; **C.** 36-month FU: restenosis at LCX ostium; **D.** 3D OCT: neointima growth over the stent struts jailing the "splitted" in three holes; **E.** FFR documenting the significance of the restenosis.

courtesy of Rony Mathew Kadavil, EBC meeting 2019

Proximal vs distal recrossing toward side branch



Long-term Clinical outcomes of final KB in coronary bifurcation lesions treated with the 1-stent technique: results from the COBIS II registry

Clinical Outcomes in FKB Group Compared With Non-FKB Group in Propensity-Matched Population During FU Period

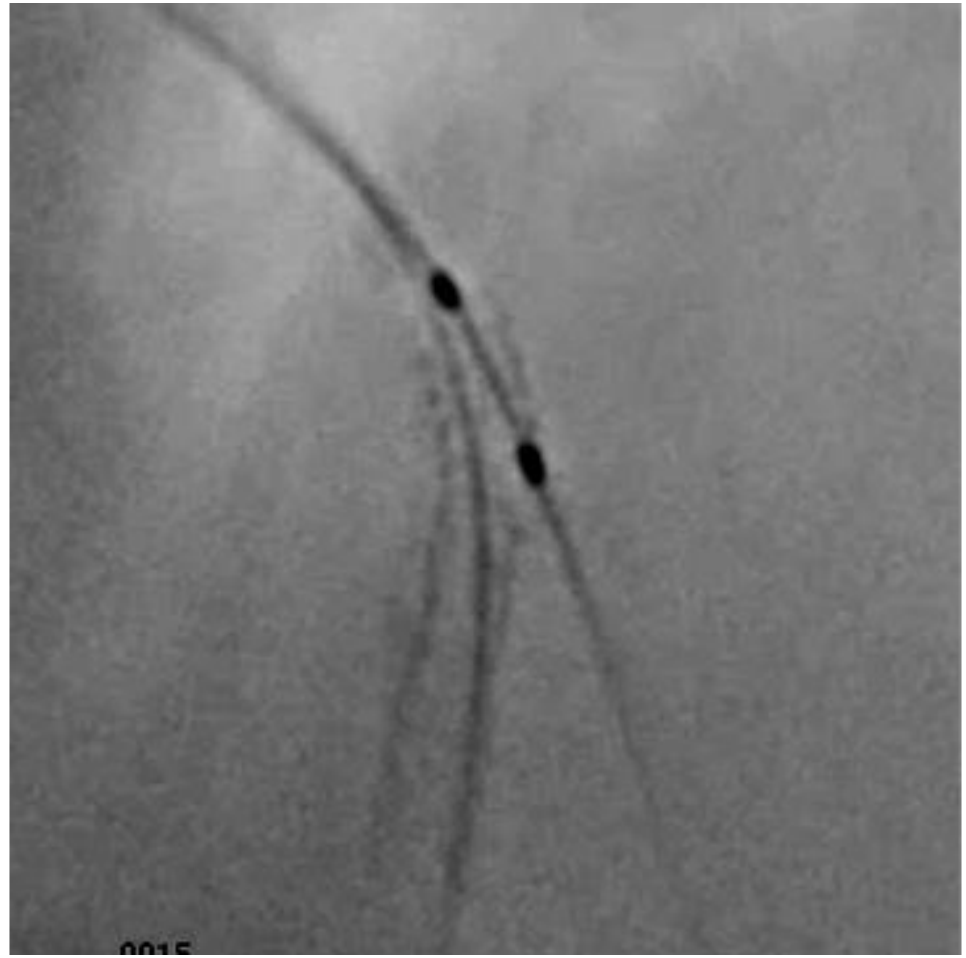
	FKB (n = 545)	Non-FKB (n = 545)	Unadjusted HR (95% CI)	p Value	Adjusted HR* (95% CI)	p Value
All-cause death	17 (3.1)	20 (3.7)	0.67 (0.30-1.48)	0.32	0.68 (0.28-1.63)	0.39
Cardiac death	3 (0.6)	8 (1.5)	0.43 (0.11-1.66)	0.22	0.50 (0.11-2.29)	0.37
MI	4 (0.7)	5 (0.9)	0.50 (0.09-2.73)	0.42	0.18 (0.01-20.36)	0.48
Stent thrombosis†	3 (0.6)	4 (0.7)	0.72 (0.16-3.23)	0.67	0.77 (0.17-3.45)	0.73
Target lesion revascularization	32 (5.9)	43 (7.9)	0.53 (0.30-0.94)	0.03	0.51 (0.28-0.91)	0.02
Main vessel	31 (5.7)	40 (7.3)	0.53 (0.30-0.96)	0.04	0.51 (0.28-0.93)	0.03
Side branch	12 (2.2)	18 (3.3)	0.57 (0.24-1.36)	0.21	0.57 (0.24-1.37)	0.21
Both vessels	23 (4.2)	38 (7.0)	0.47 (0.25-0.88)	0.02	0.47 (0.25-0.90)	0.02
MACE‡	37 (6.8)	53 (9.7)	0.54 (0.32-0.89)	0.02	0.50 (0.30-0.85)	0.01

*Adjusted covariates include hypertension, history of coronary artery bypass graft, and distal RD of SB

CW Yu, J Am Coll Cardiol Intv 2015;8:1297–307

T or TAP ? (stent boost)

T



TAP

Conclusion 1

How to translate science in practical approach

- Inspire / follow scientific activity: fundamental, bench, animal testing, case reports, simulation …
- Collect data on potential improvements and failures
- Exchange and share data, publish
- When feasible try to have clinical validation of practice: metaanalysis, RCT …
- Do it again …
- Be member of EBC

4 simple principles of bifurcation stenting

1. **Simple protection for non-relevant SB**
2. **Limit the stent number**
3. **Single stent layer well deployed well apposed**
4. **Restore/respect functional anatomy**