DCB Current Status and Perspectives

2018. 12. 8
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Drug-Coated Balloon – Clinical Applications

1. Endovascular

2. Coronary Artery

    1) In-Stent Restenosis
    2) De-novo lesions

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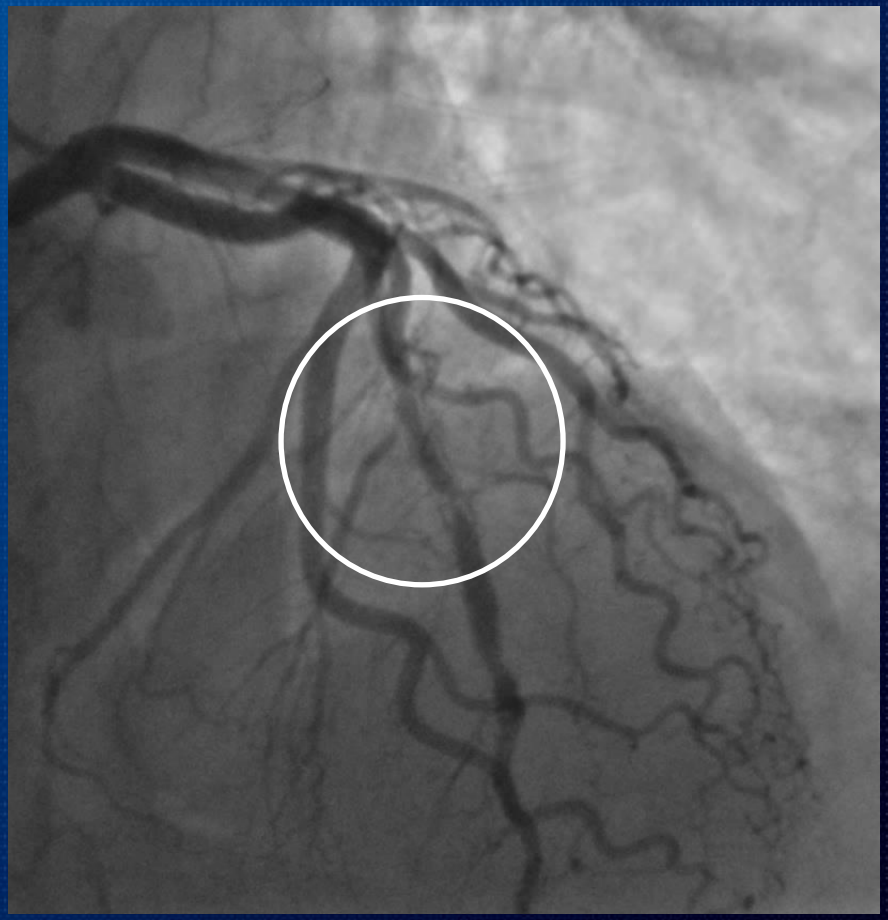
In-Stent Restenosis



? Treatment: CABG, POBA, DES, DCB

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RCT results of ISR treatment

ISR	Intervention	Angiographic result	Clinical outcome
BMS	PCB vs BA	PCB>BA	PCB>BA
	PCB vs PES	PCB>PES	PCB=PES
	PCB vs EES	PCB=EES	PCB=EES
DES	PCB vs BA	PCB>BA	PCB>BA
	PCB vs PES	PCB=PES	PCB=PES
	PCB vs EES	PCB≤EES	PCB≤EES

PCB = Paclitaxel-coated balloon
BA = Balloon angioplasty
PES = Paclitaxel-coated stent
EES = Everolimus-coated stent

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2018 ESC/EACTS Guidelines on myocardial revascularizatio

Restenosis		
DES are recommended for the treatment of in-stent restenosis of BMS or DES.[373,375,378,379]	I	A
Drug-coated balloons are recommended for the treatment of in-stent restenosis of BMS or DES.[373,375,378,379]	I	A
In patients with recurrent episodes of diffuse in-stent restenosis, CABG should be considered by the Heart Team over a new PCI attempt.	IIa	C
IVUS and/or OCT should be considered to detect stent-related mechanical problems leading to restenosis.	IIa	C

European Heart Journal (2018) 00, 1–96

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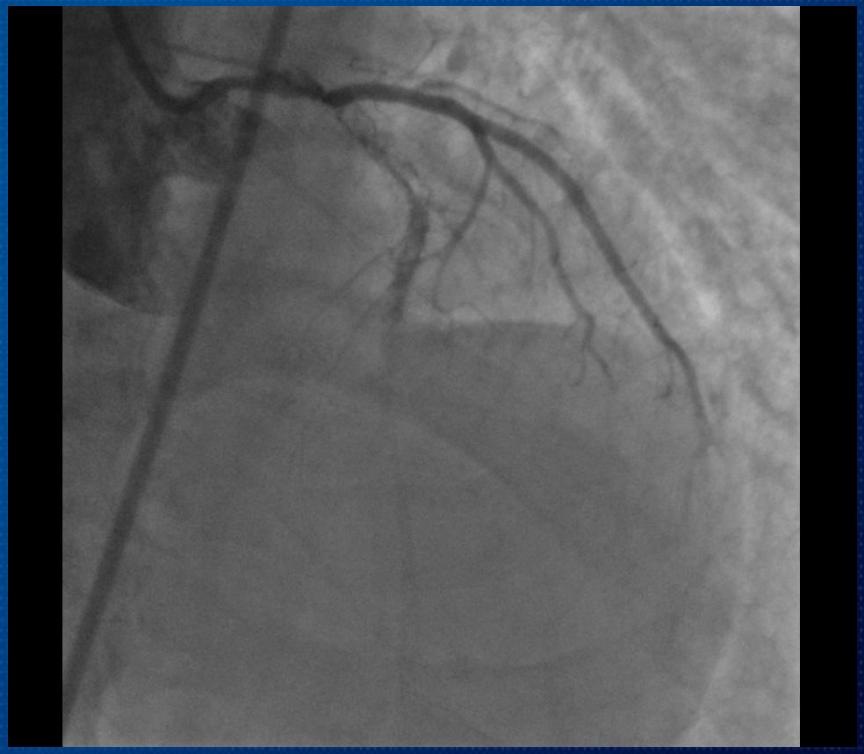
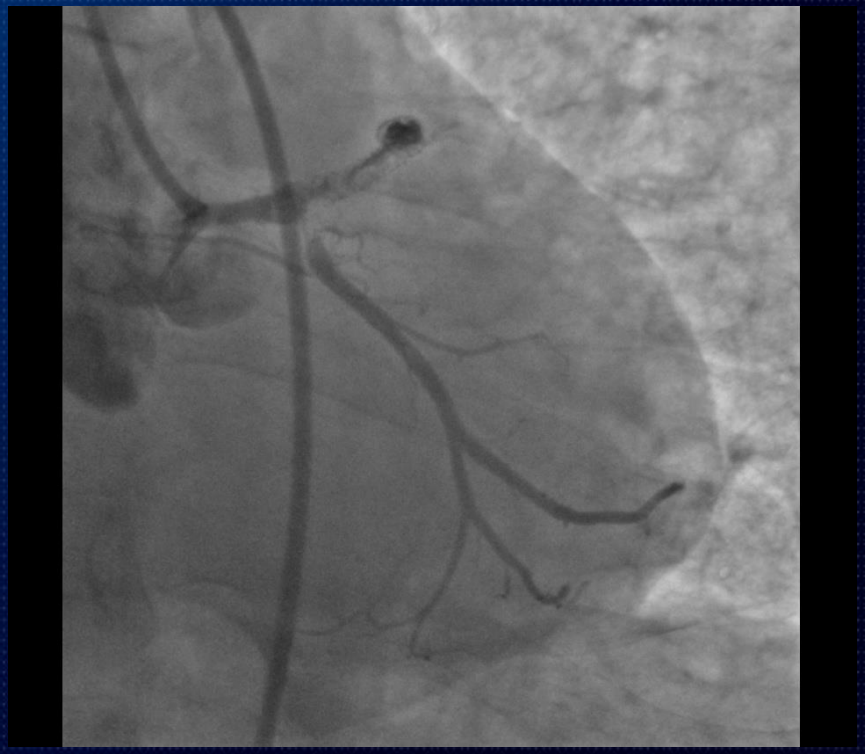
Late stent failure

Stop aspirin for 5 days

AMI & SCD





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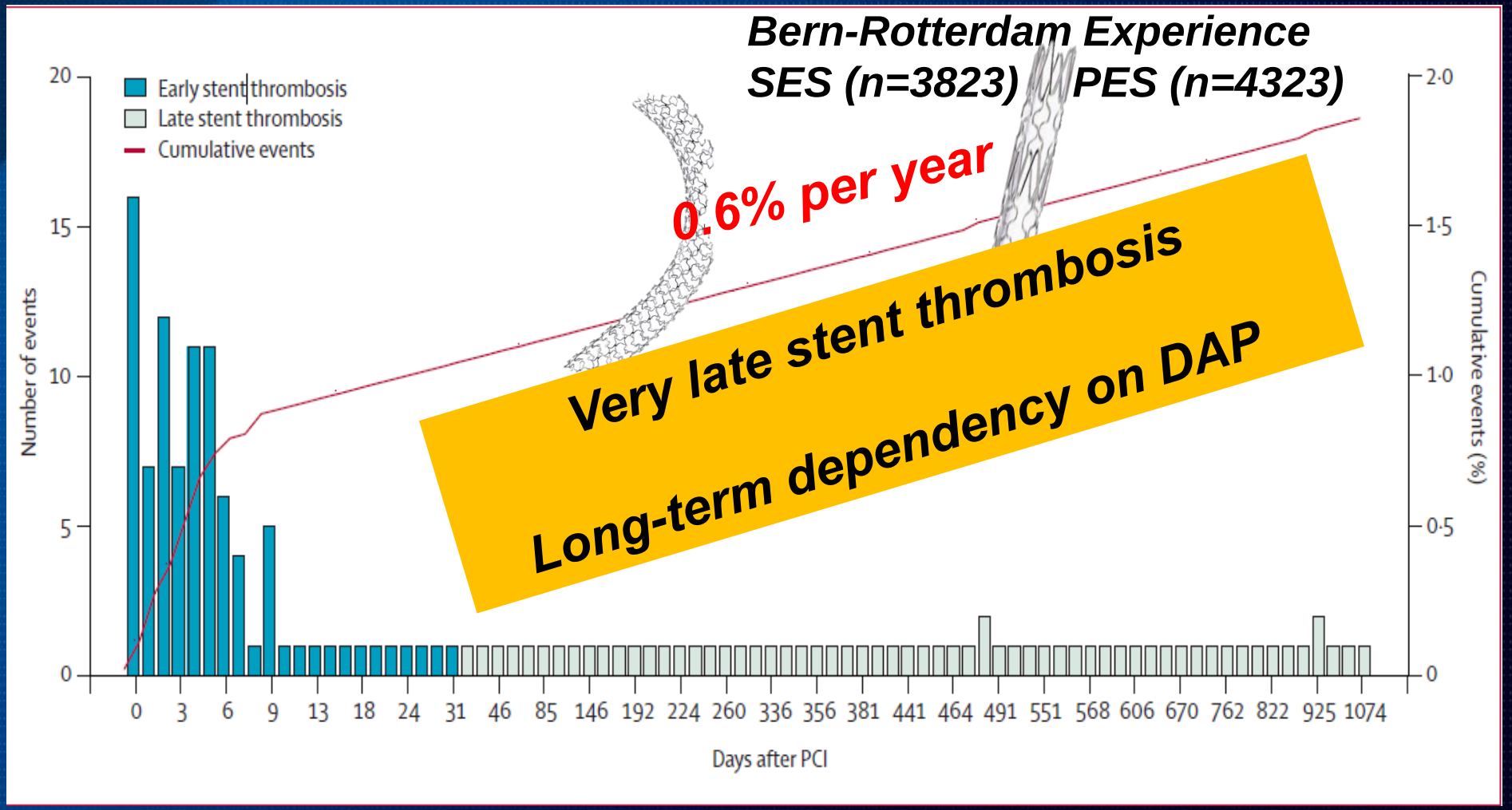
Frequency of DES Thrombosis

Cumulative Incidence of Definite ST in 8,146 Patients
During a 4-Year Follow-Up Period



Eamen J et al. Lancet 2007 Feb 24;369(9562):667-78.

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To overcome the limitations,

- No inflammation
- No restenosis
- Normal healing
- No thrombosis (esp. late/very late)
- No prolonged DAPT

Leaving Nothing Behind

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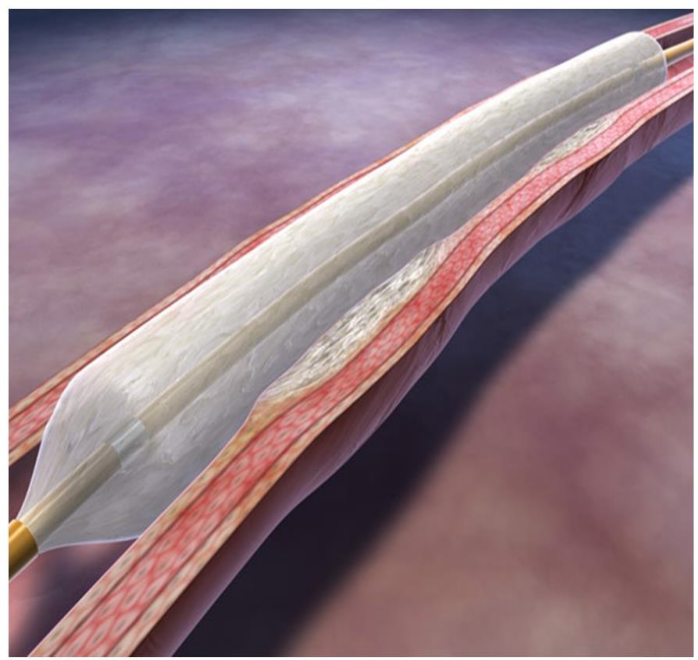
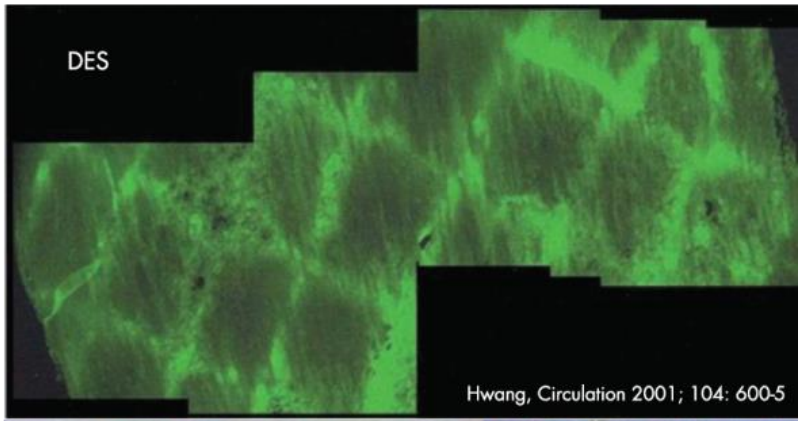
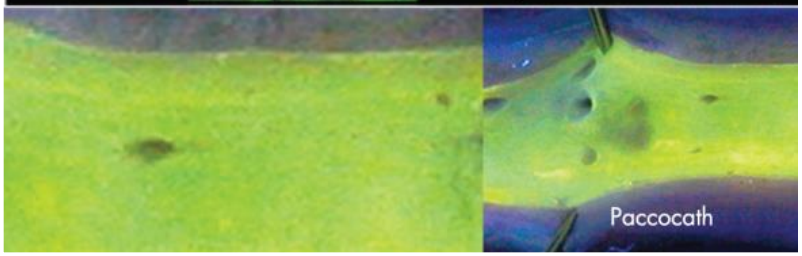
New Paradigm of PCI







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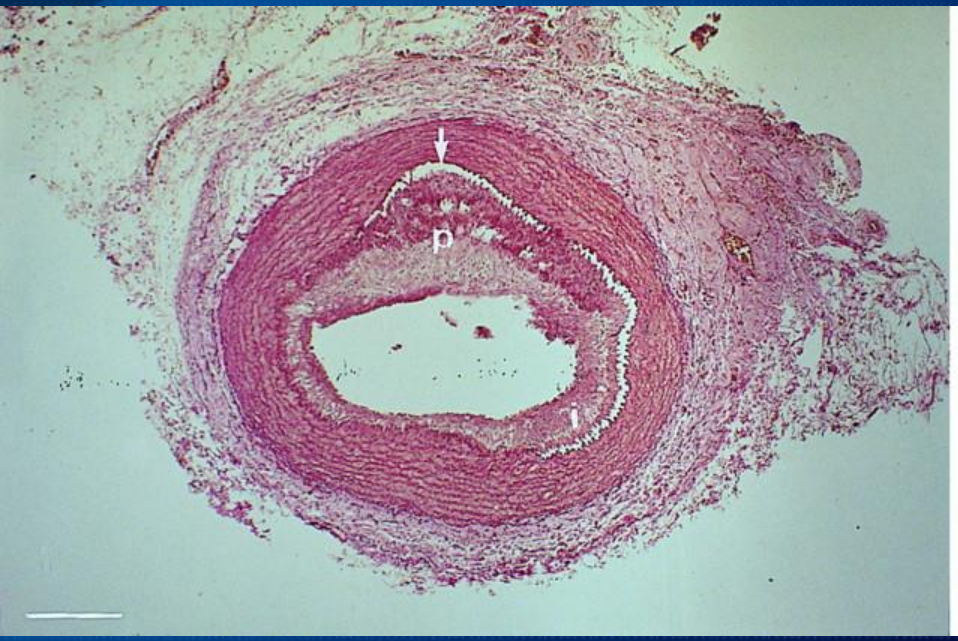
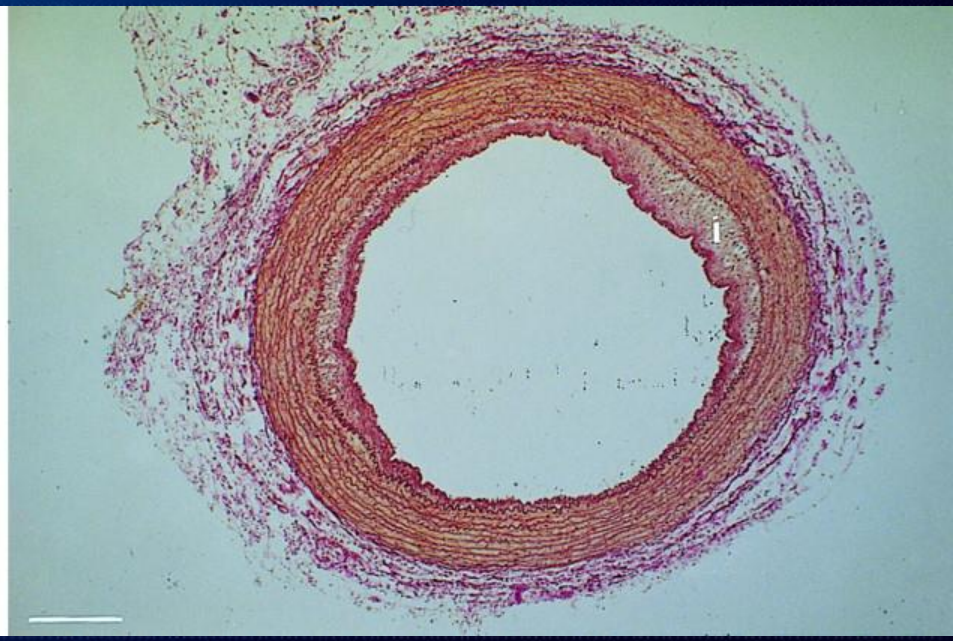
Paclitaxel inhibits smooth muscle cell proliferation and migration in vitro and in vivo



untreated control animal



paclitaxel-treated animal

Circulation. 1997;96:636

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RCT in small coronary artery lesions

Drug-coated balloons for small coronary artery disease (BASKET-SMALL 2): an open-label randomised non-inferiority trial

Raban V Jeger, Ahmed Farah, Marc-Alexander Ohlow, Norman Mangner, Sven Möbius-Winkler, Gregor Leibundgut, Daniel Weilenmann, Jochen Wöhrle, Stefan Richter, Matthias Schreiber, Felix Mahfoud, Axel Linke, Frank-Peter Stephan, Christian Mueller, Peter Rickenbacher, Michael Coslovsky, Nicole Gilgen, Stefan Osswald, Christoph Kaiser, Bruno Scheller, for the BASKET-SMALL 2 Investigators

Summary

Background Drug-coated balloons (DCB) are a novel therapeutic strategy for small native coronary artery disease. However, their safety and efficacy is poorly defined in comparison with drug-eluting stents (DES).

Methods BASKET-SMALL 2 was a multicentre, open-label, randomised non-inferiority trial. 758 patients with de-novo lesions (<3 mm in diameter) in coronary vessels and an indication for percutaneous coronary intervention were randomly allocated (1:1) to receive angioplasty with DCB versus implantation of a second-generation DES after successful predilatation via an interactive internet-based response system. Dual antiplatelet therapy was given according to current guidelines. The primary objective was to show non-inferiority of DCB versus DES regarding major adverse cardiac events (MACE; ie, cardiac death, non-fatal myocardial infarction, and target-vessel revascularisation) after 12 months. The non-inferiority margin was an absolute difference of 4% in MACE. This trial is registered with ClinicalTrials.gov, number NCT01574534.

Findings Between April 10, 2012, and February 1, 2017, 382 patients were randomly assigned to the DCB group and 376 to DES group. Non-inferiority of DCB versus DES was shown because the 95% CI of the absolute difference in MACE in the per-protocol population was below the predefined margin (–3·83 to 3·93%, p=0·0217). After 12 months, the proportions of MACE were similar in both groups of the full-analysis population (MACE was 7·5% for the DCB group *vs* 7·3% for the DES group; hazard ratio [HR] 0·97 [95% CI 0·58–1·64], p=0·9180). There were five (1·3%) cardiac-related deaths in the DES group and 12 (3·1%) in the DCB group (full analysis population). Probable or definite stent thrombosis (three [0·8%] in the DCB group *vs* four [1·1%] in the DES group; HR 0·73 [0·16–3·26]) and major bleeding (four [1·1%] in the DCB group *vs* nine [2·4%] in the DES group; HR 0·45 [0·14–1·46]) were the most common adverse events.

Interpretation In small native coronary artery disease, DCB was non-inferior to DES regarding MACE up to 12 months, with similar event rates for both treatment groups.

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See Online/Comment
http://dx.doi.org/10.1016/S0140-6736(18)31926-3

University Hospital Basel, University of Basel, Basel, Switzerland (Prof R V Jeger MD, F-P Stephan MD, Prof C Mueller MD, Prof P Rickenbacher MD, M Coslovsky PhD, N Gilgen MD, Prof S Osswald MD, Prof C Kaiser MD); **Knappschaftskrankenhaus, Klinikum Westfalen, Dortmund, Germany** (A Farah MD); **Central Clinic, Bad Berka, Germany** (Prof M-A Ohlow MD, S Richter MD, M Schreiber MD); **Herzzentrum Dresden, Technische Universität Dresden, Dresden, Germany** (N Mangner MD, Prof A Linke MD); **Heart Center Leipzig, University Hospital, Leipzig, Germany** (N Mangner,

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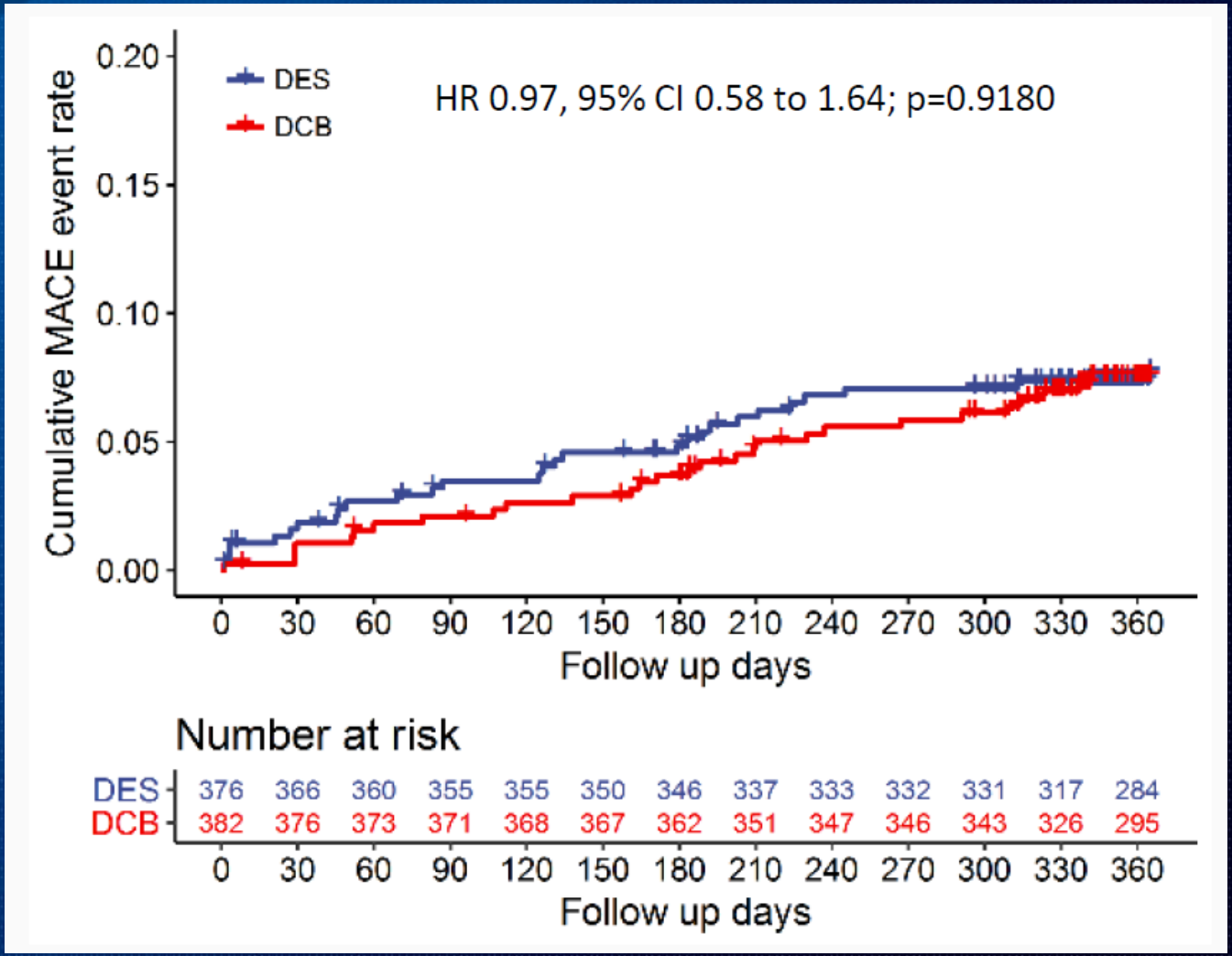
DCB is non-inferior to DES in small native coronary artery



Lancet. 2018 Sep 8;392(10150):849-856.

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   1) In-Stent Restenosis

De Novo large epicardial coronary artery?

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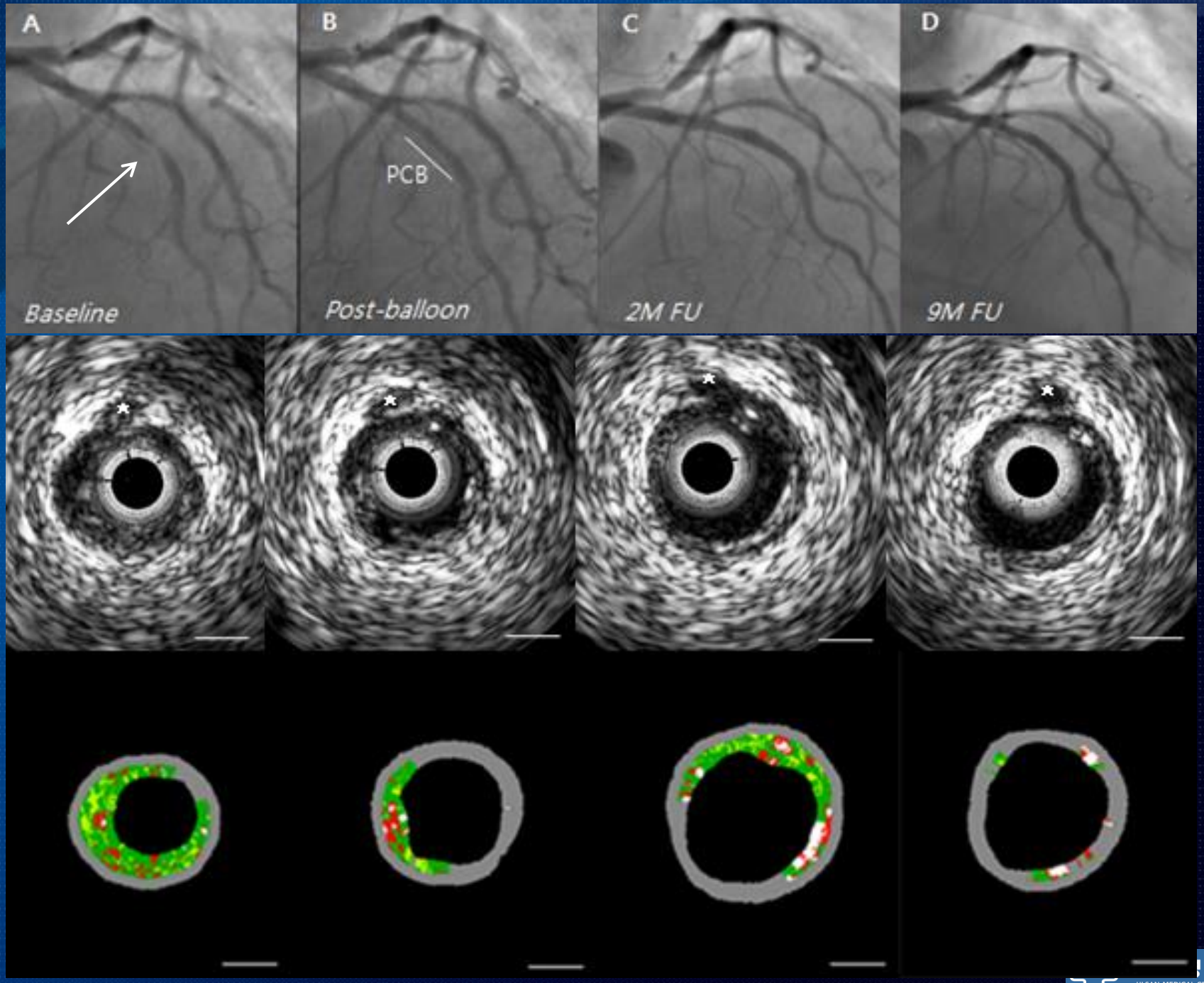
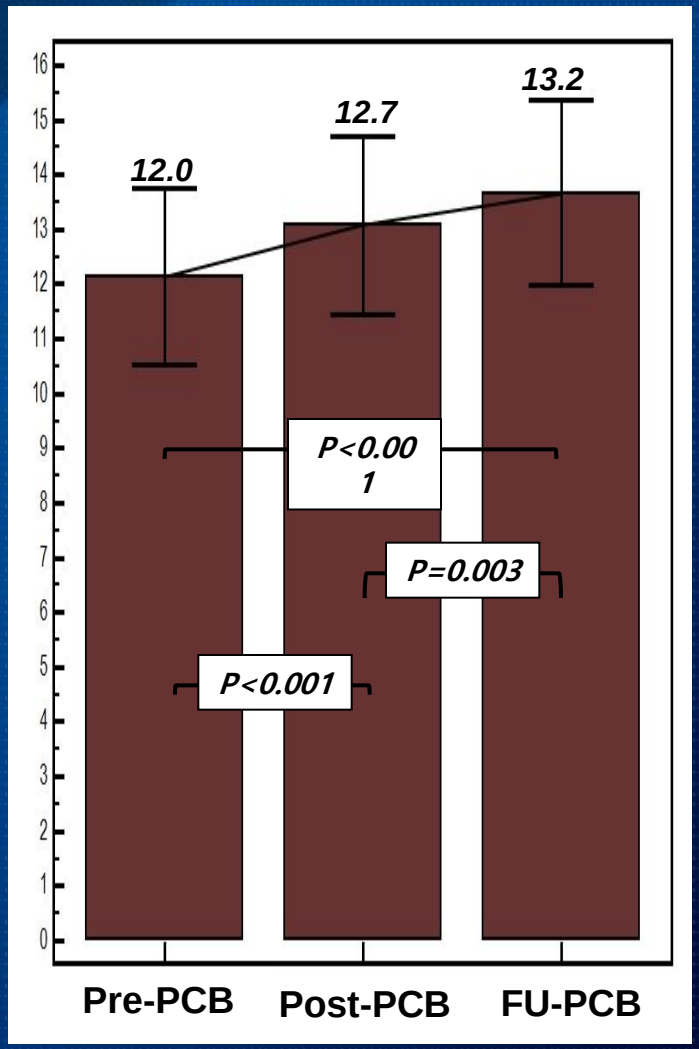
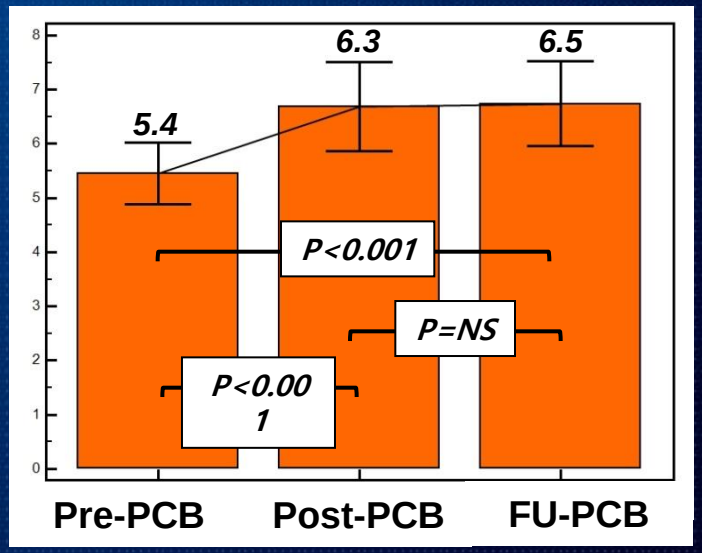

A
B
C
D
PCB
Baseline
Post-balloon
2M FU
9M FU

Changes of mean Area of Vessel /Lumen /Plaque

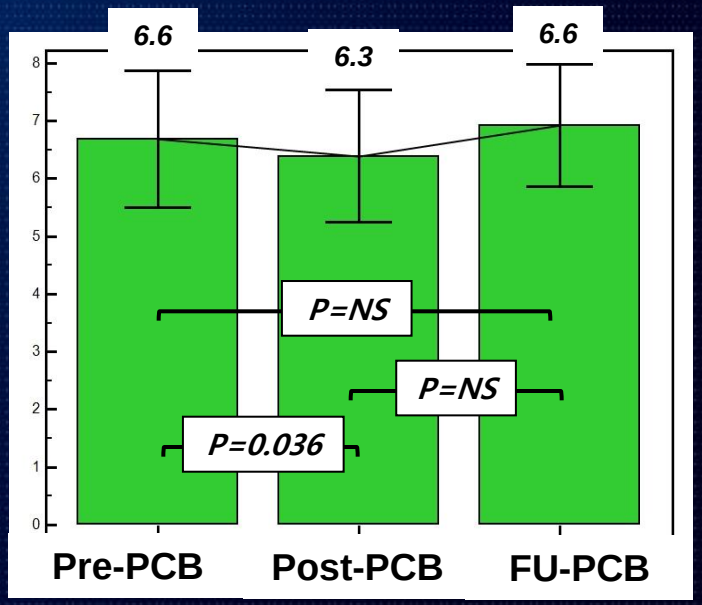
Vessel



Lumen



Plaque



PLOS ONE | DOI:10.1371/journal.pone.0147057 January 29, 2016

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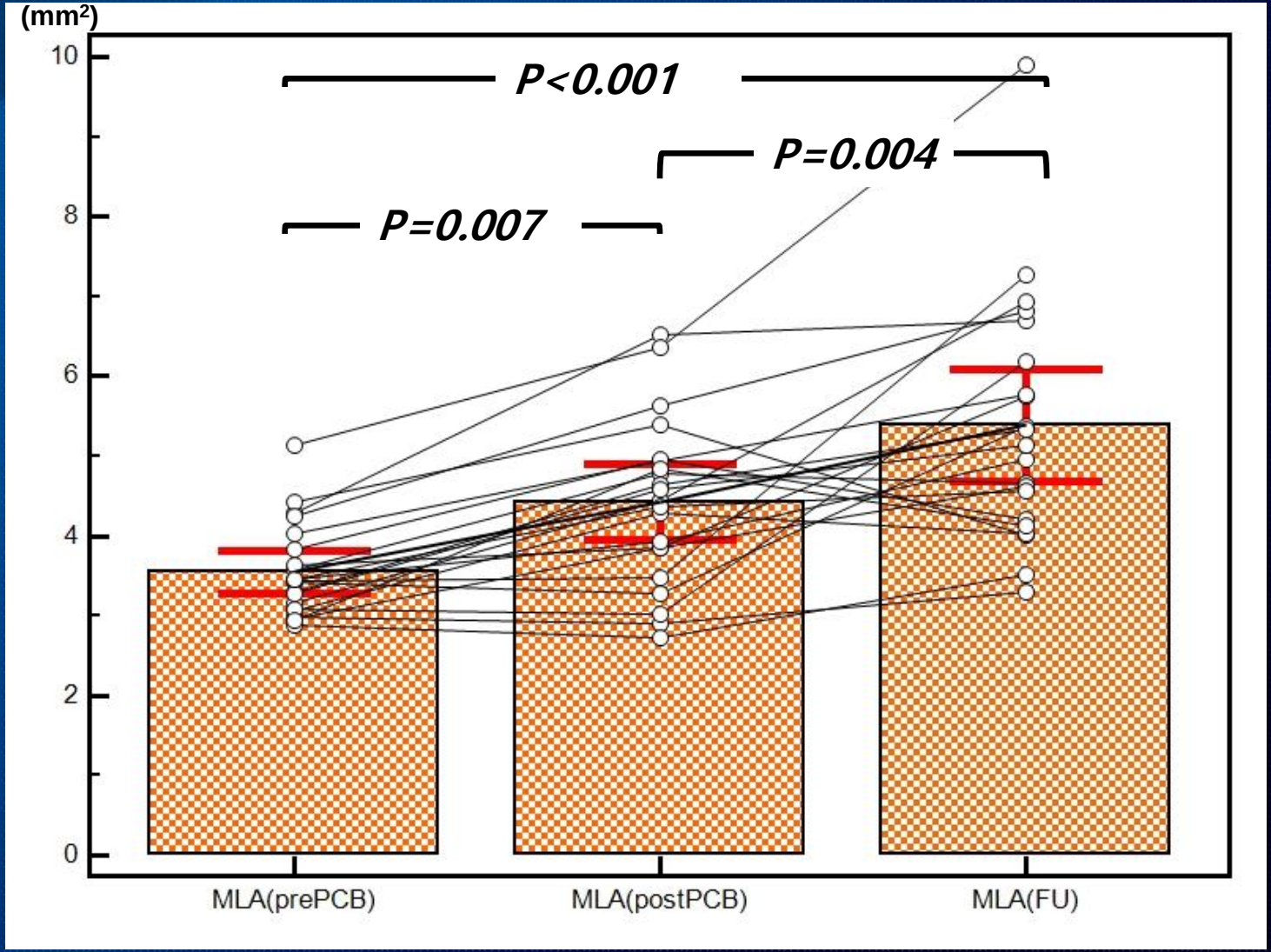
Changes in Minimal Lumen Area



PLOS ONE | DOI:10.1371/journal.pone.0147057 January 29, 2016

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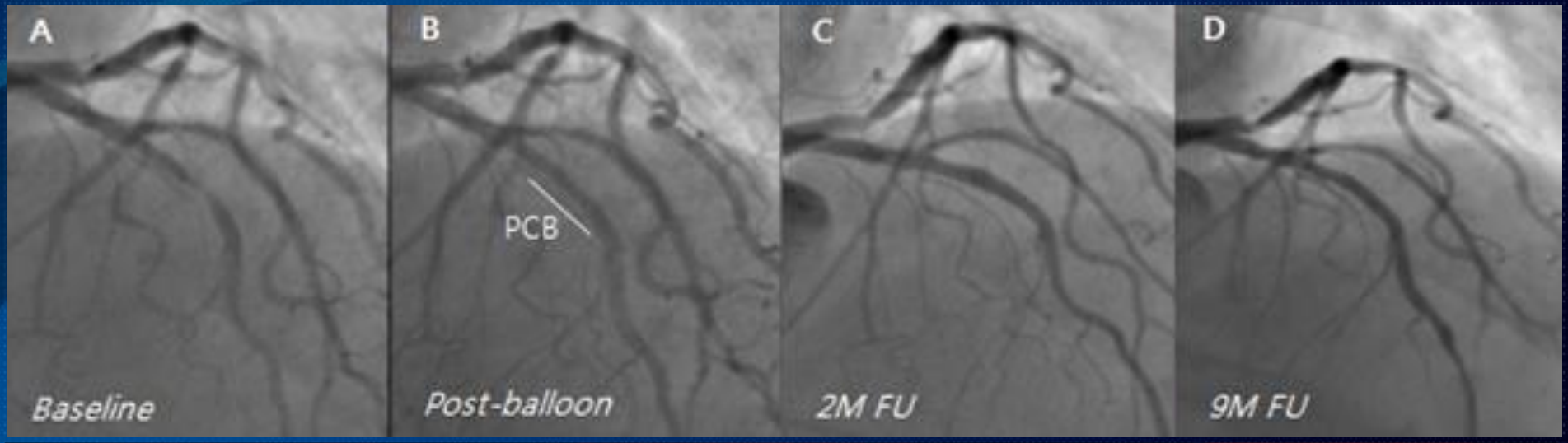

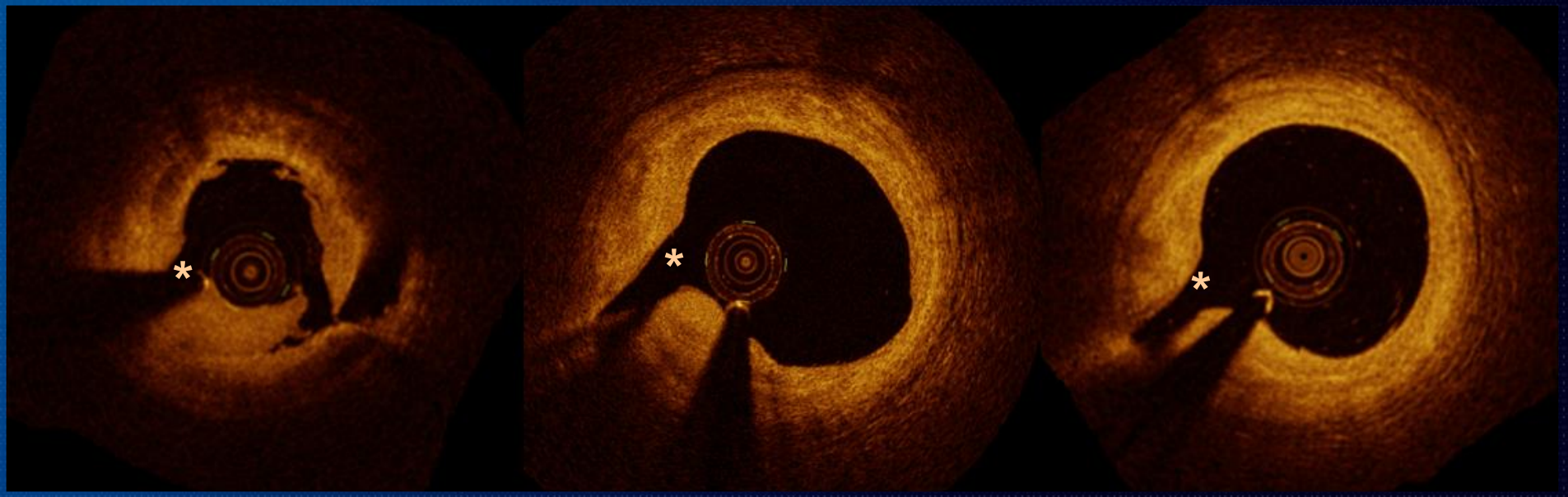

Rev Esp Cardiol 2016 Nov;69(11):1026-1032.

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Destiny of Dissection flap after DCB application

	Post-PCB	FU-PCB
Dissection Flap, n(%)	**21 (100%)**	**7 (33.3%)**
Maximal thickness (mm)	0.67±0.29	0.44±0.21
Maximal length (mm)	1.34±0.71	0.68±0.33
Longitudinal length (mm)	11.9±8.7	1.8±1.5

Rev Esp Cardiol 2016 Nov;69(11):1026-1032.

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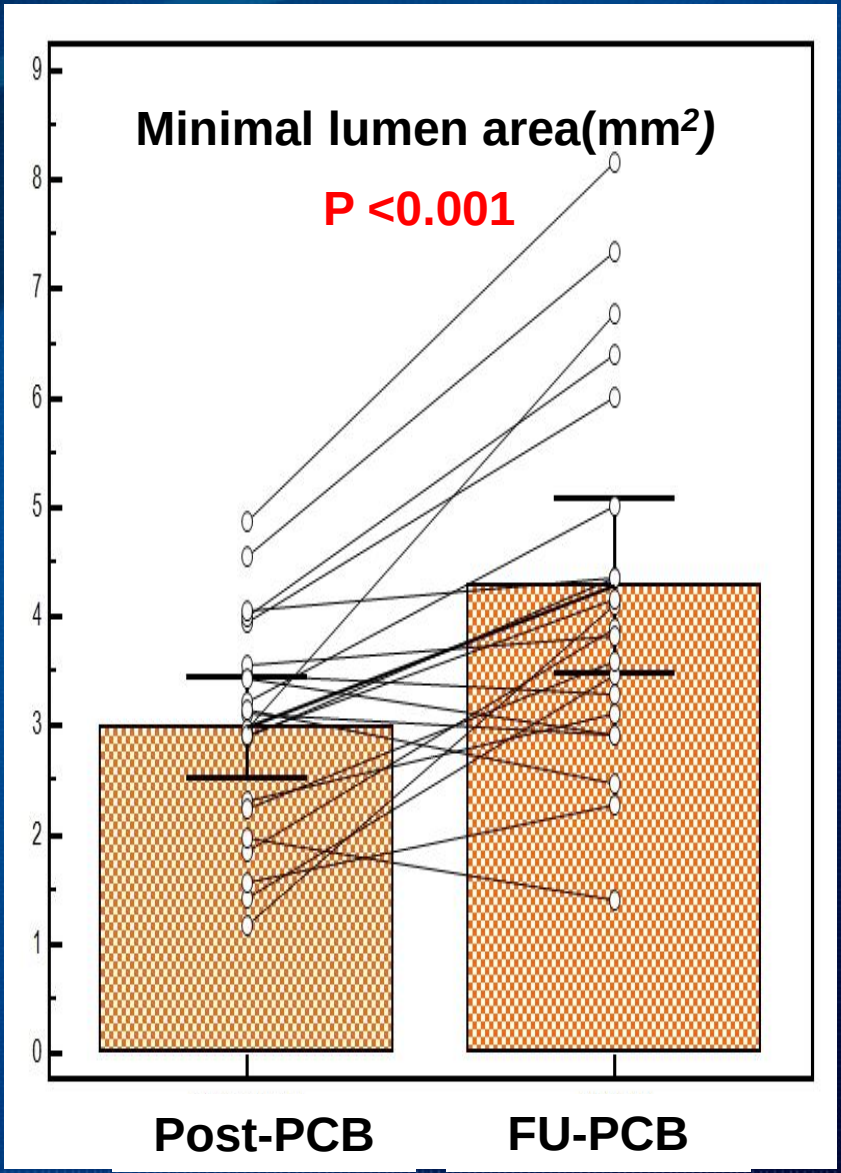

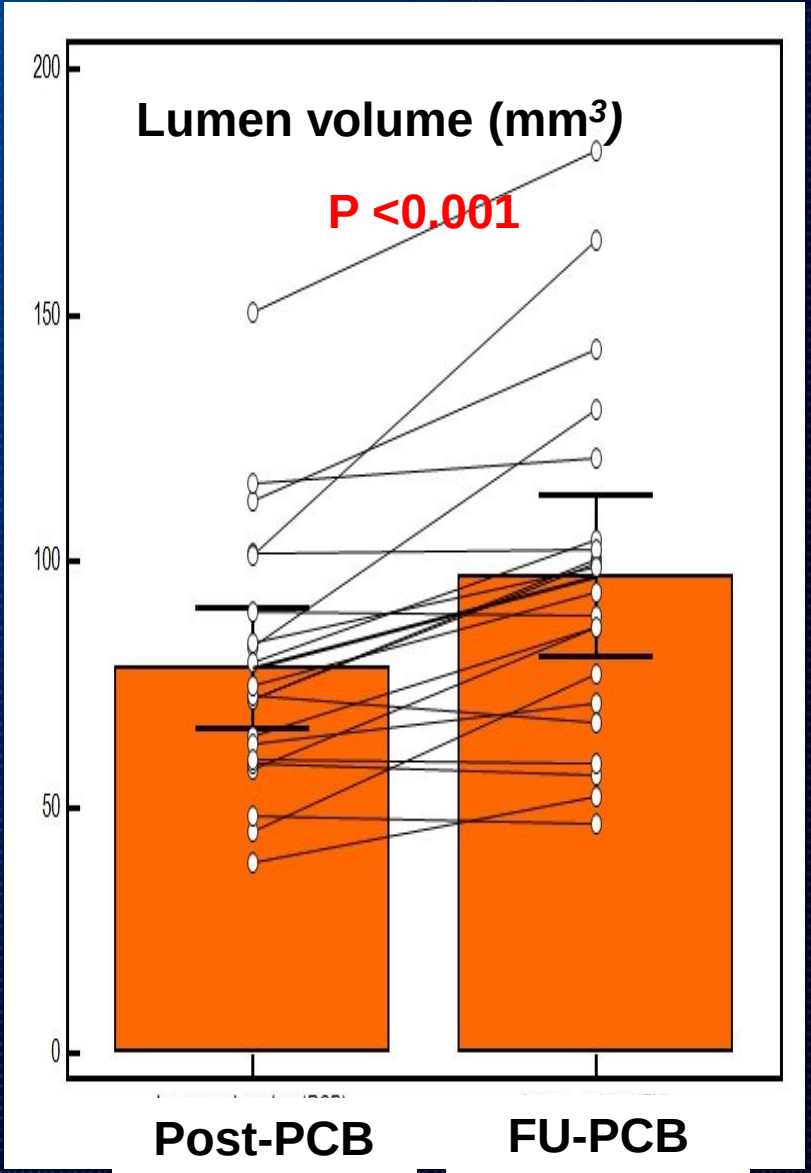

Rev Esp Cardiol 2016 Nov;69(11):1026-1032.

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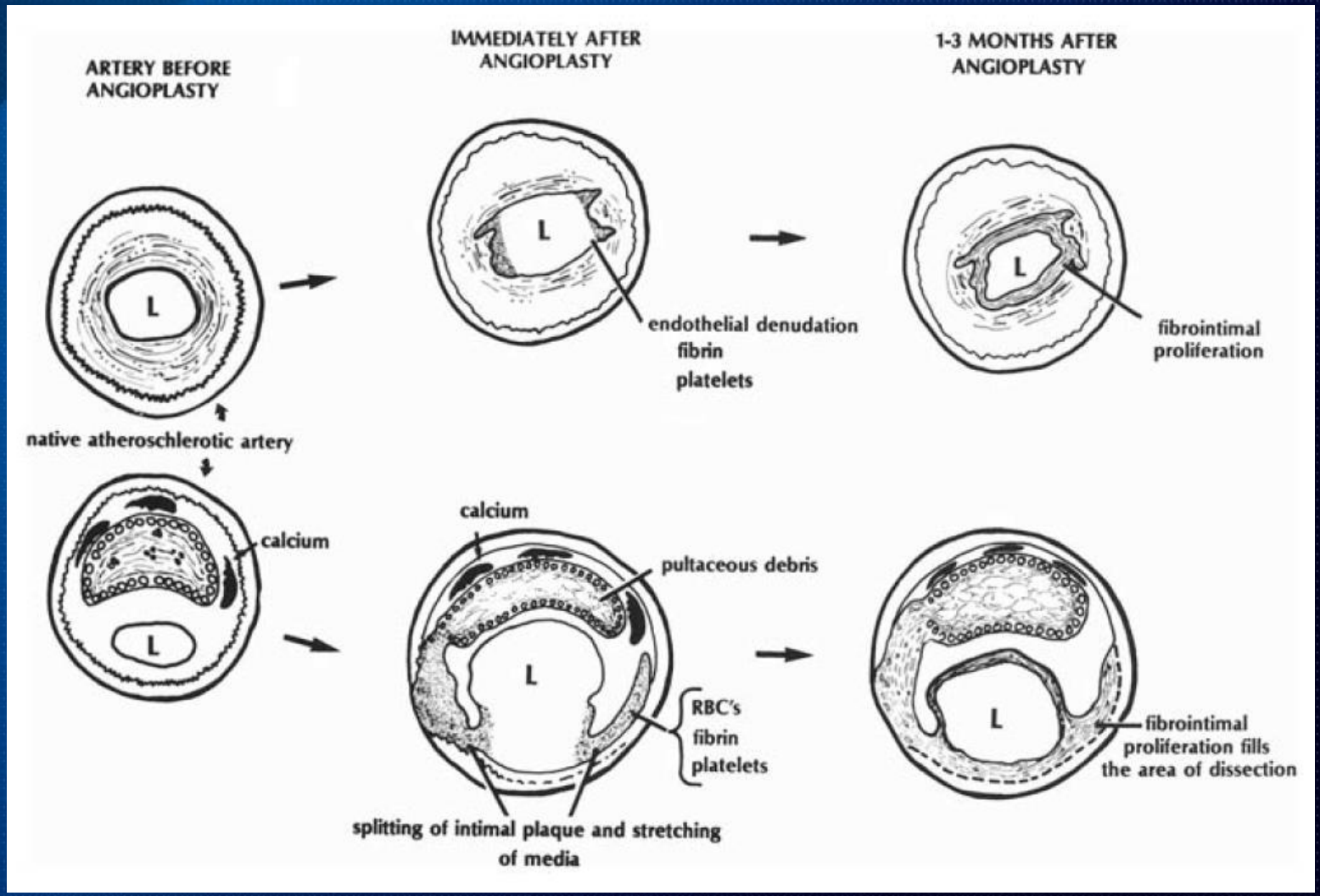
Successful BA



J Am Coll Cardiol 1990 :16:1421-9

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How can we predict the adverse events of dissection after BA?

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Original Studies

Fractional Flow Reserve-guided Paclitaxel-coated Balloon Treatment for De Novo Coronary Lesions

Eun-Seok Shin,[1*] MD, PhD, Soe Hee Ann,[1] MD, Gillian Balbir Singh,[1] MBCHB, FRACP, Kyung Hun Lim,[1] MD, Franz X. Kleber,[2] MD, and Bon-Kwon Koo,[3] MD, PhD

Objectives: To assess the safety and efficacy of fractional flow reserve (FFR) guided paclitaxel-coated balloon (PCB) treatment for de novo coronary artery lesions. Background: There is limited data on PCB treatment for de novo lesions especially of major epicardial coronary arteries. Methods: Sixty-six patients with 67 de novo lesions who underwent successful plain old balloon angioplasty (POBA) were included. If POBA-FFR was favorable (≥ 0.85), PCB was applied and if POBA-FFR was <0.85, stent implantation was preferred over PCB. Results: Forty-five lesions were treated with PCB (67.2%) and 22 lesions with stents (32.8%). Dual antiplatelet therapy duration was 6 weeks. Late luminal loss with PCB was significantly less than stent (0.05 ± 0.27 mm vs. 0.40 ± 0.54 mm, $P = 0.022$). The baseline FFR of target lesions was 0.69 ± 0.16 in PCB and 0.60 ± 0.11 in stent group ($P = 0.015$), however, the FFR at 9 months was not different between groups (0.85 ± 0.08 in PCB vs. 0.85 ± 0.05 in stent group, $P = 0.973$). At 1 year, one myocardial infarction and one target lesion revascularization related to in-stent restenosis were detected, both in the stent group. Conclusion: POBA-FFR-guided PCB treatment is safe and effective for de novo coronary lesions with good anatomical and physiological patency at mid-term follow-up. © 2015 Wiley Periodicals, Inc.

Key words: paclitaxel-coated balloon; fractional flow reserve; plain old balloon angioplasty; de novo lesion; late luminal loss

Catheter Cardiovasc Interv. 2015 Oct 1.

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What is the FFR-guided DCB treatment?

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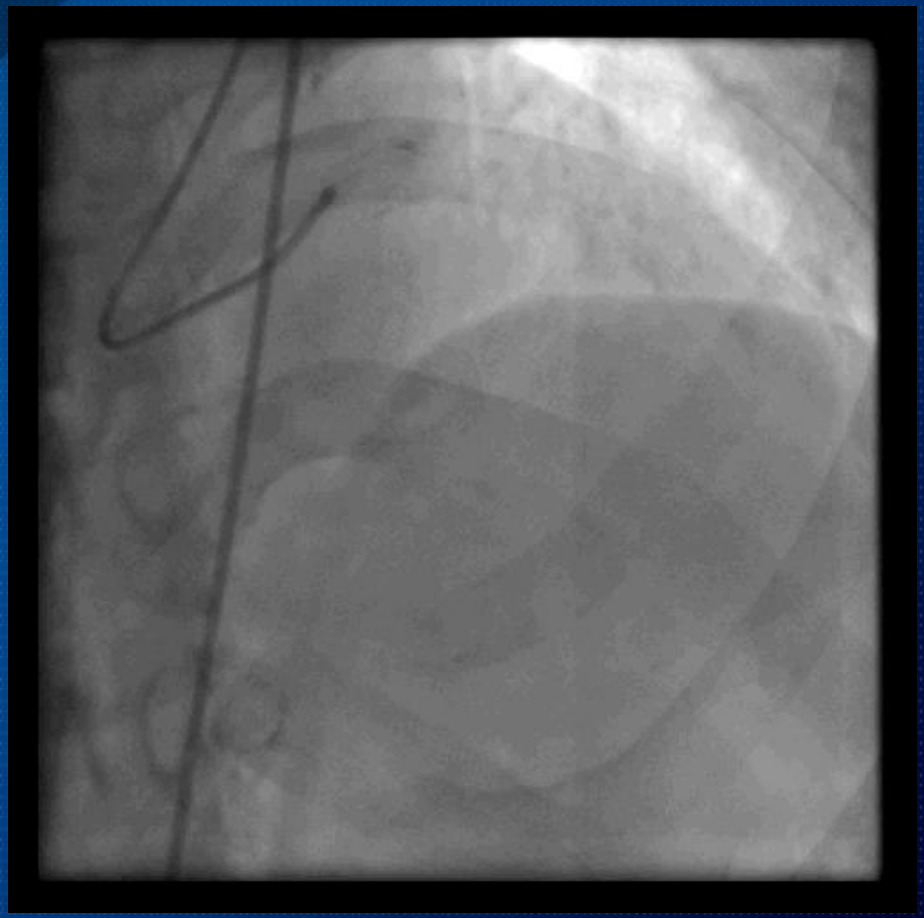
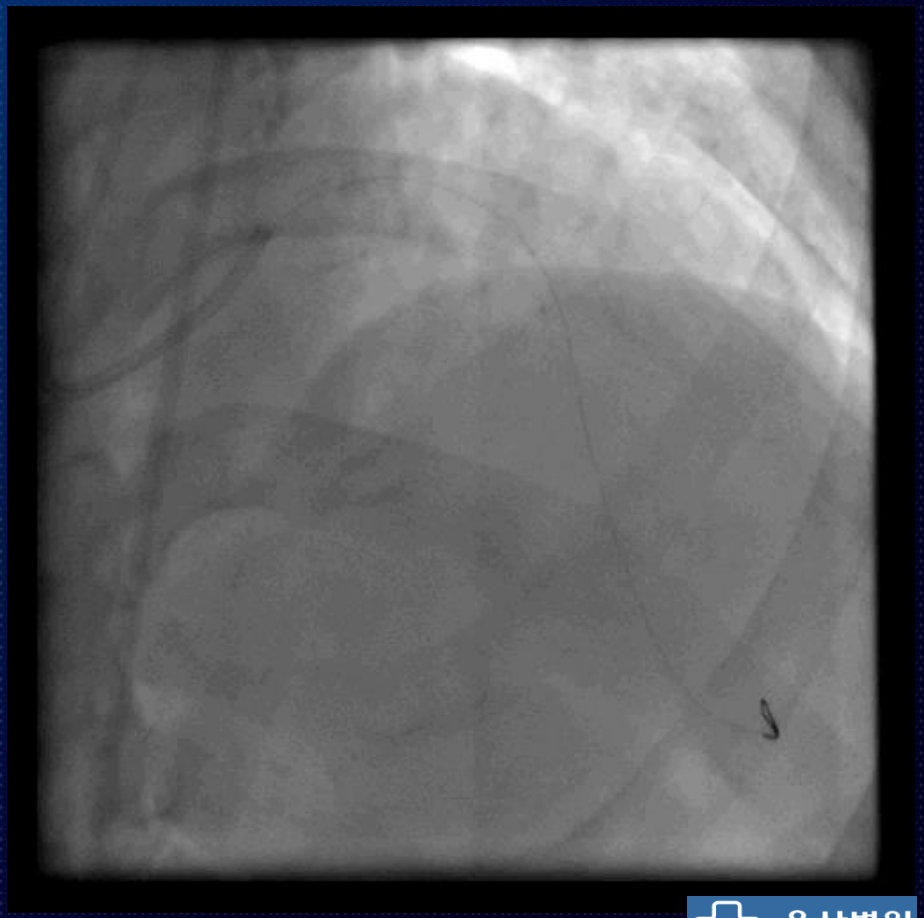
Functionally adequate after BA → DCB treatment

Base FFR = 0.35



POBA-FFR = 0.86



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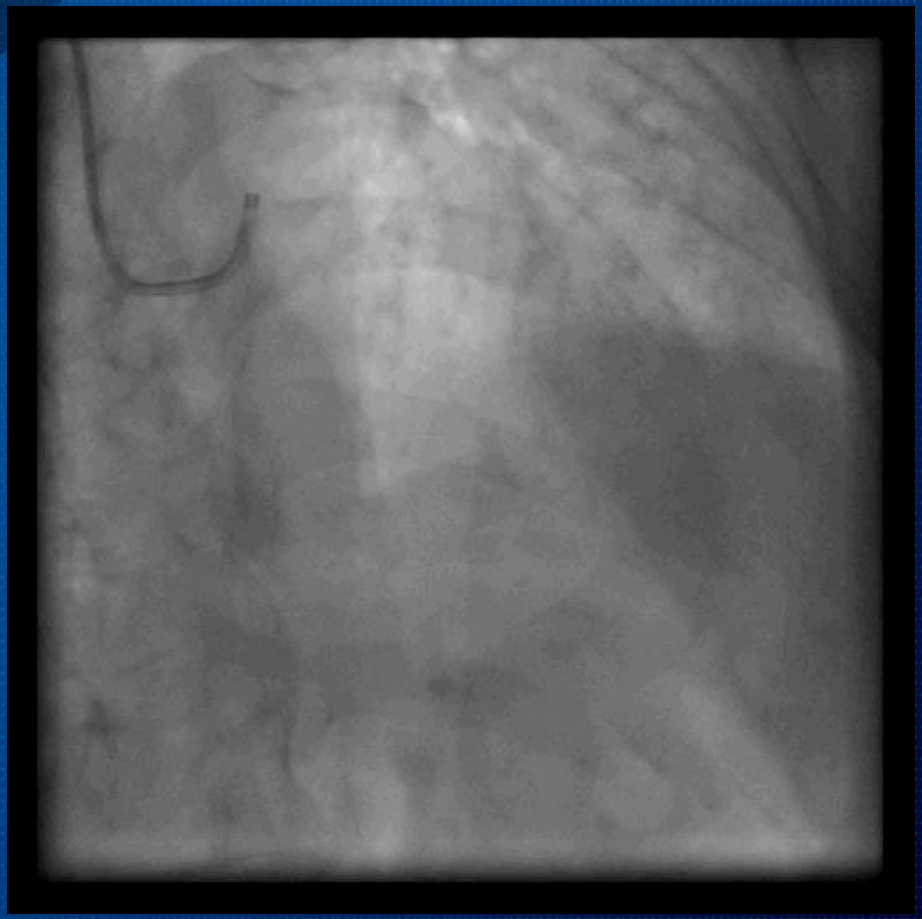
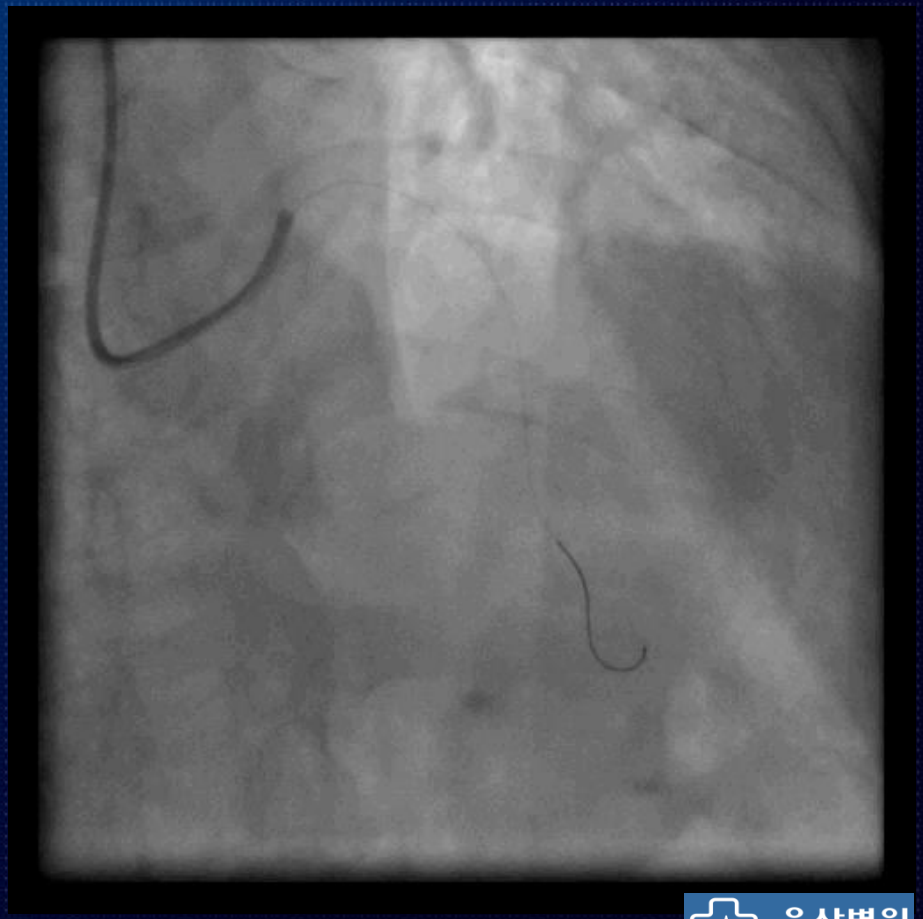
Functionally inadequate after BA → Stent treatment

Base FFR = 0.69



POBA-FFR = 0.63



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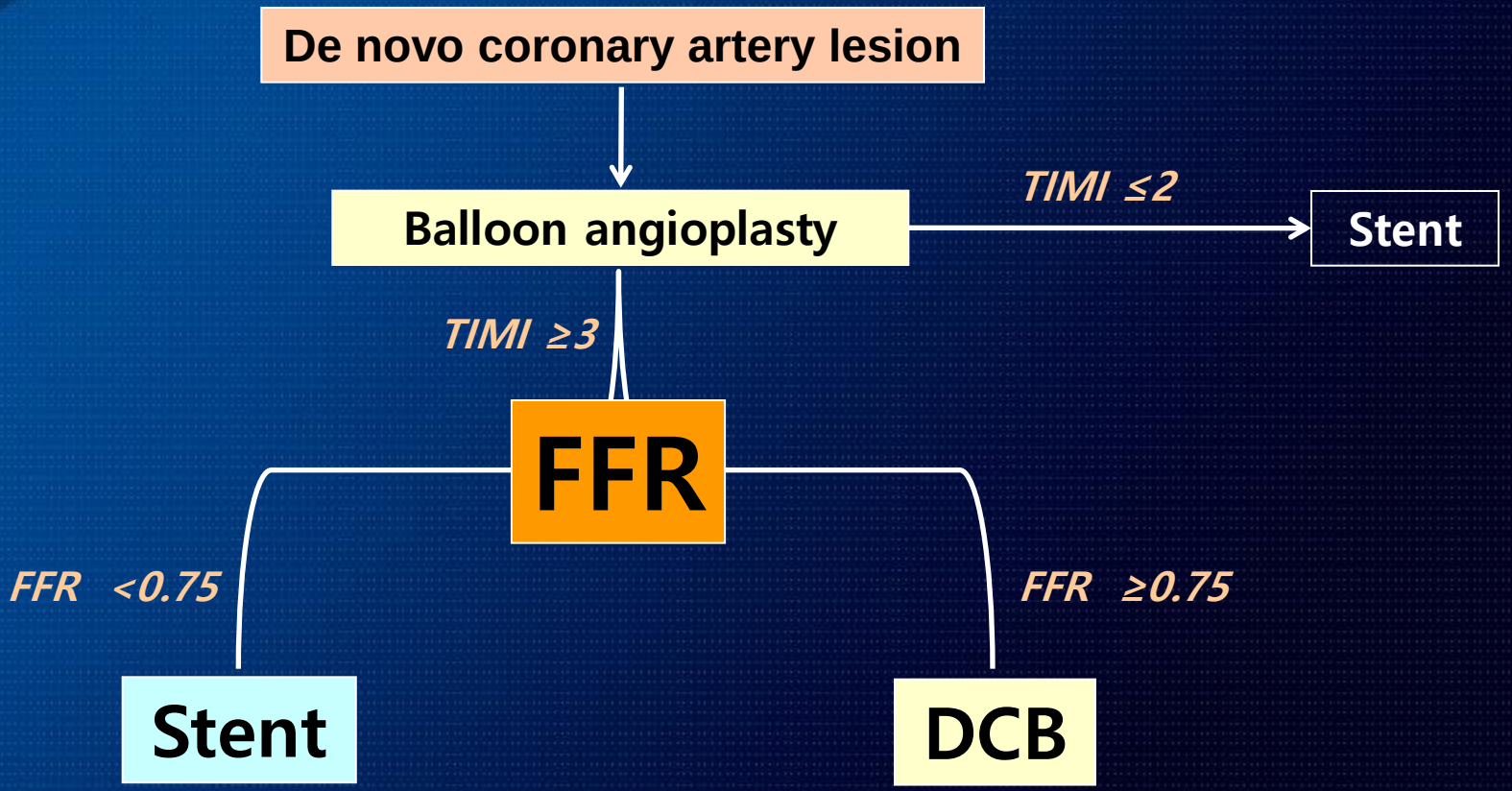
FFR-guided DCB treatment strategy



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Registry data

201 patients

95% FU CAG & FFR

100% clinical FU

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Study population

- 2012.6 ~ 2014.12
- Prospective registry study in Ulsan University Hospital

Inclusion criteria:

Major epicardial coronary a.

2.5 ≤ RD ≤ 3.5mm

Lesion length < 24mm

POBA with TIMI 3

Exclusion criteria:

ST-segment elevation MI

Left main coronary artery disease

Ostial or heavily calcified lesions

Contraindication to adenosine

Contraindication to stent

Life expectancy of <1 year

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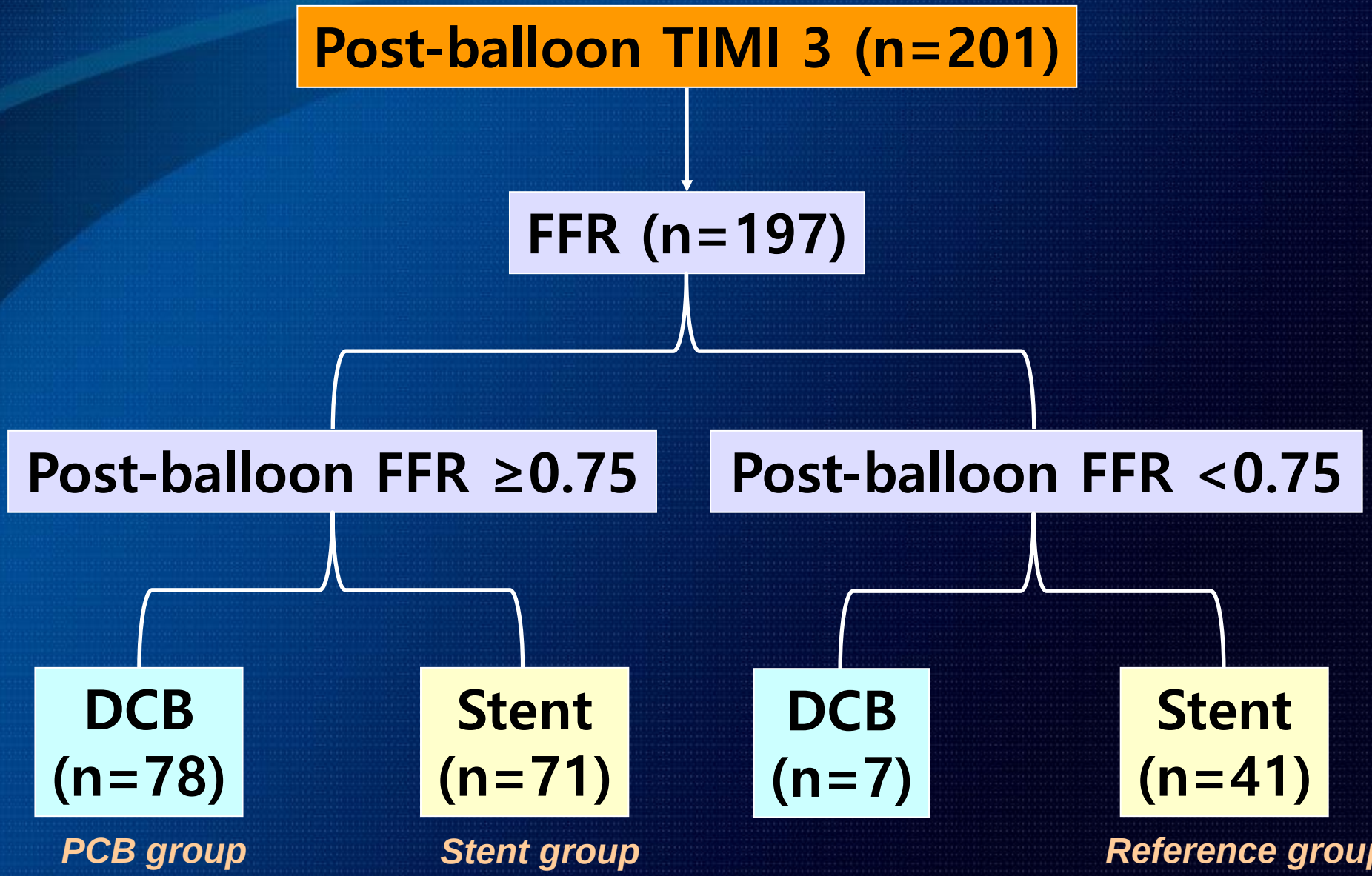

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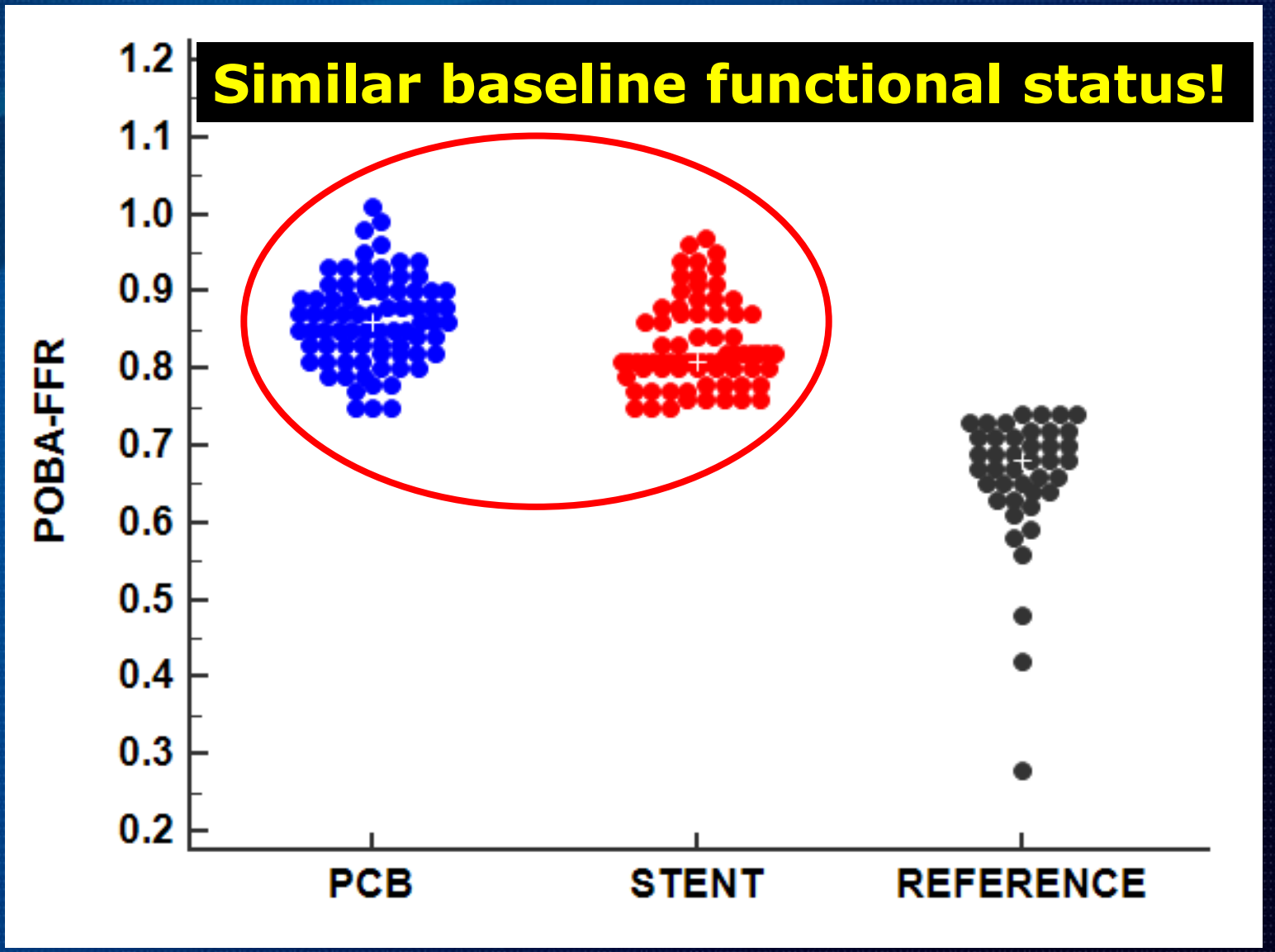

Post-balloon FFR ≥0.75 *Post-balloon FFR <0.75*

The International Journal of Cardiovascular Imaging (2018) 34:1339–1347

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Baseline characteristics

	Post-balloon FFR ≥0.75		Post-balloon FFR <0.75	
	DCB (n = 78)	Stent (n = 73)	Reference (n = 42)	DCB vs Stent p-value
Men	56 (71.8)	59 (80.8)	34 (81.0)	0.193
Age, years	58.6 ± 8.6	59.0 ± 8.7	59.2 ± 10.6	0.815
Cardiovascular risk factors				
Diabetes	25 (32.1)	16 (21.9)	9 (21.4)	0.162
Dyslipidemia	45 (57.7)	31 (42.5)	20 (47.6)	0.061
Hypertension	40 (51.3)	31 (42.5)	17 (40.5)	0.278
Current smoking	24 (30.8)	20 (27.4)	12 (28.6)	0.167
Previous myocardial infarction	6 (7.7)	4 (5.5)	0	0.747
Family history of coronary artery disease	10 (12.8)	10 (13.7)	5 (11.9)	0.874
Clinical manifestations				
Stable angina	38 (48.7)	29 (39.7)	12 (28.6)	0.266
Acute coronary syndrome	40 (51.3)	44 (60.3)	30 (71.4)	0.266
Ejection fraction, %	63.3 ± 6.7	62.3 ± 7.9	59.6 ± 9.0	0.405
Hospital stay, days	5.2 ± 6.9	4.7 ± 3.3	5.3 ± 3.2	0.551

Lesion and procedure characteristics

	Post-balloon FFR ≥0.75		Post-balloon FFR <0.75	
	DCB (n = 78)	Stent (n = 73)	Reference (n = 42)	DCB vs Stent p-value
Coronary artery				
Left anterior descending	35 (44.9)	42 (57.5)	32 (76.2)	0.120
Left circumflex	25 (32.0)	10 (13.7)	5 (11.9)	0.008
Right coronary	18 (23.1)	21 (28.8)	5 (11.9)	0.425
Lesion type				0.933
A, B1	24 (30.8)	22 (30.1)	9 (21.4)	
B2, C	54 (69.2)	51 (69.9)	33 (78.6)	
No. of diseased vessels	1.5 ± 0.7	1.4 ± 0.7	1.8 ± 0.8	0.175

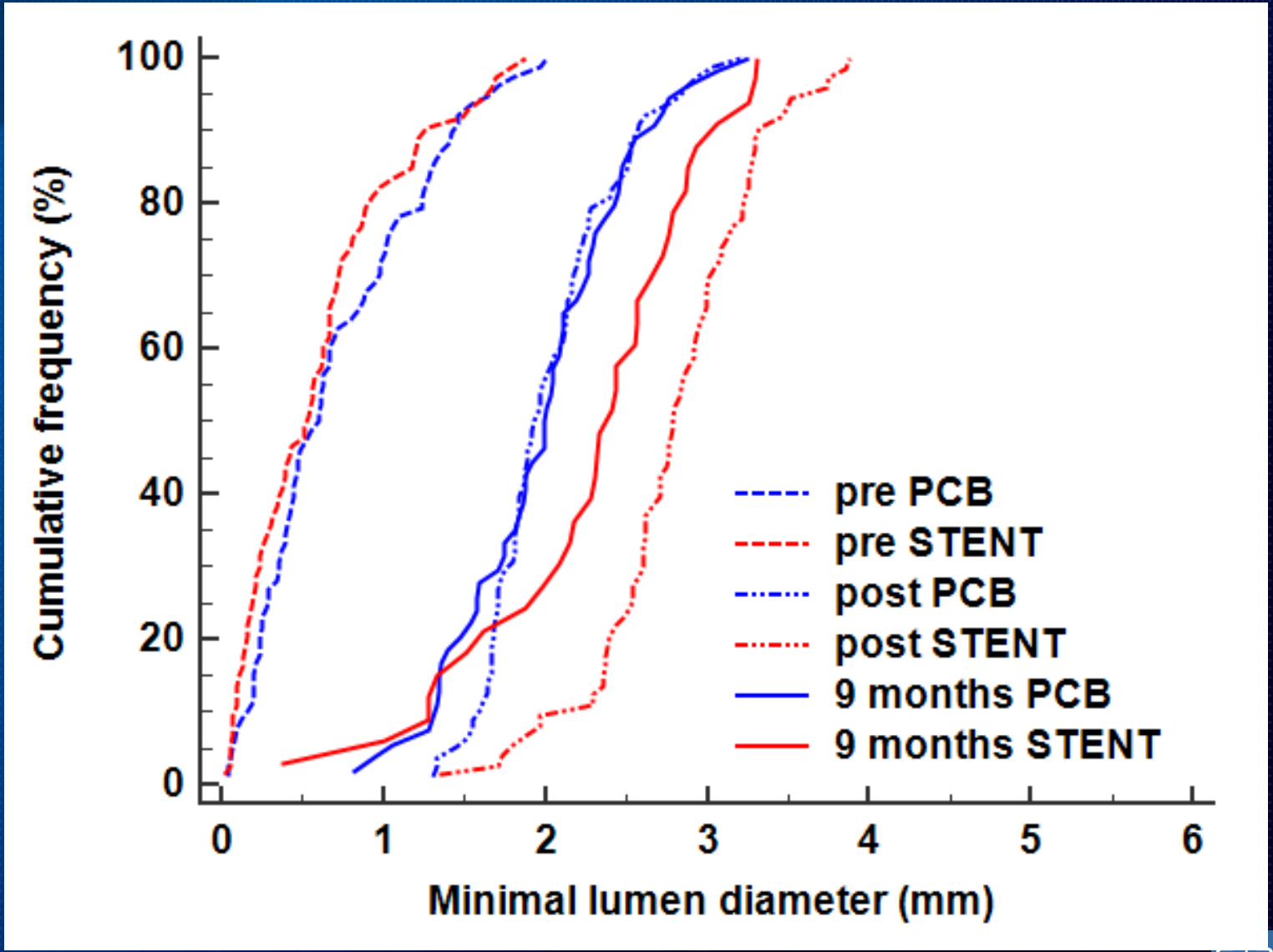
Before & after PCI: QCA & FFR

	Post-balloon FFR ≥0.75		Post-balloon FFR <0.75	
	DCB (n = 78)	**Stent (n = 73)**	**Reference (n = 42)**	DCB vs Stent p-value
Before procedure				
Lesion length, mm	20.0 ± 5.4	21.7 ± 6.4	24.7 ± 8.7	0.094
Reference diameter, mm	2.4 ± 0.5	2.6 ± 0.5	2.6 ± 0.5	0.002
Minimum lumen diameter, mm	0.70 ± 0.51	0.59 ± 0.48	0.58 ± 0.46	0.179
Diameter stenosis, %	71.8 ± 17.7	78.2 ± 16.0	78.9 ± 15.1	0.022
Pre-procedure FFR	0.65 ± 0.14	0.61 ± 0.16	0.62 ± 0.14	0.113
After procedure				
Reference diameter, mm	2.6 ± 0.5	3.1 ± 0.5	2.9 ± 0.4	<0.001
Minimum lumen diameter, mm	2.03 ± 0.41	2.80 ± 0.51	2.63 ± 0.48	<0.001
Diameter stenosis, %	21.7 ± 10.3	8.7 ± 10.6	9.8 ± 10.3	<0.001
Acute lumen gain, mm	1.32 ± 0.57	2.20 ± 0.68	2.05 ± 0.62	<0.001
Post-procedure FFR	0.87 ± 0.05	0.89 ± 0.06	0.82 ± 0.08	0.101

9-month QCA & FFR

	Post-balloon FFR ≥0.75		Post-balloon FFR <0.75	
	DCB (n = 78)	**Stent (n = 73)**	**Reference (n = 42)**	DCB vs Stent p-value
9 months follow up	n = 75	n = 71	n = 41	
Reference diameter, mm	2.5 ± 0.5	2.8 ± 0.5	2.8 ± 0.4	0.003
Minimum lumen diameter, mm	1.98 ± 0.53	2.28 ± 0.69	2.17 ± 0.84	0.024
Diameter stenosis, %	23.3 ± 13.0	20.0 ± 20.2	24.2 ± 25.6	0.405
Late lumen loss, mm	0.05 ± 0.33	0.59 ± 0.76	0.46 ± 0.76	<0.001
Net lumen gain, mm	1.20 ± 0.60	1.51 ± 0.91	1.43 ± 0.97	0.086
9 months-FFR	0.88 ± 0.08	0.88 ± 0.08	0.82 ± 0.07	0.852
FFR loss	0.01 ± 0.08	0.06 ± 0.09	0.15 ± 0.09	0.029
Net FFR gain	0.19 ± 0.17	0.22 ± 0.18	0.17 ± 0.15	0.472
Functional restenosis	3 (6.0)	2 (7.1)	2 (13.3)	>0.999

Cumulative frequency distribution of MLD



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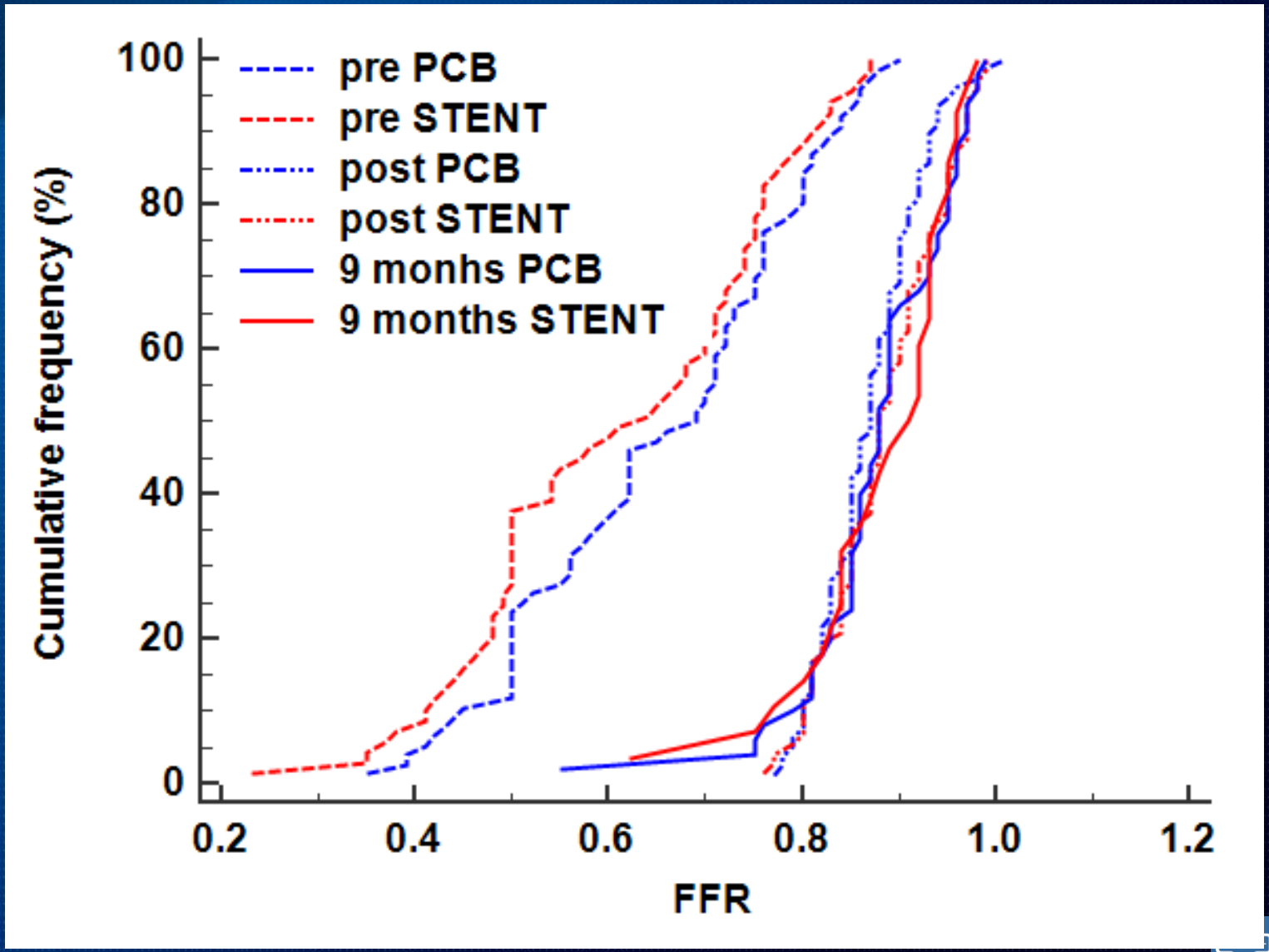
Cumulative frequency distribution of FFR



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Clinical outcomes during 12 months FU

	Post-balloon FFR ≥0.75		Post-balloon FFR <0.75	
	DCB (n = 78)	Stent (n = 73)	Reference (n = 42)	DCB vs Stent p-value
Cardiac death	0	1 (1.4)	0	0.483
Myocardial infarction	0	0	1 (2.4)	-
Target lesion thrombosis	0	0	0	-
Target lesion revascularization	1 (1.3)	3 (4.1)	3 (7.1)	0.354
Target vessel revascularization	2 (2.6)	3 (4.1)	4 (9.5)	0.673

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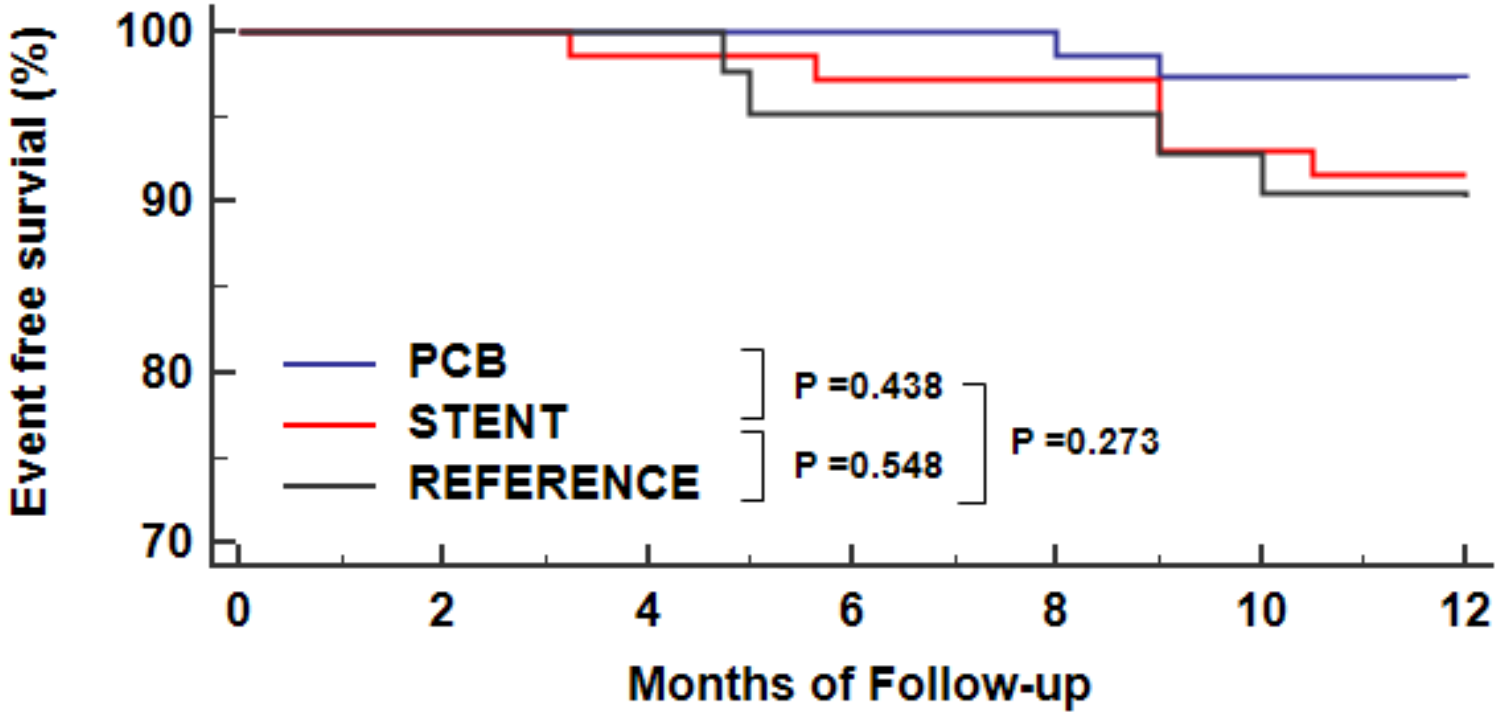
Event-free survival (%)



Number at risk

PCB	78	78	77	77	74	73	70
STENT	73	73	71	69	69	66	64
REFERENCE	42	42	42	40	40	38	36

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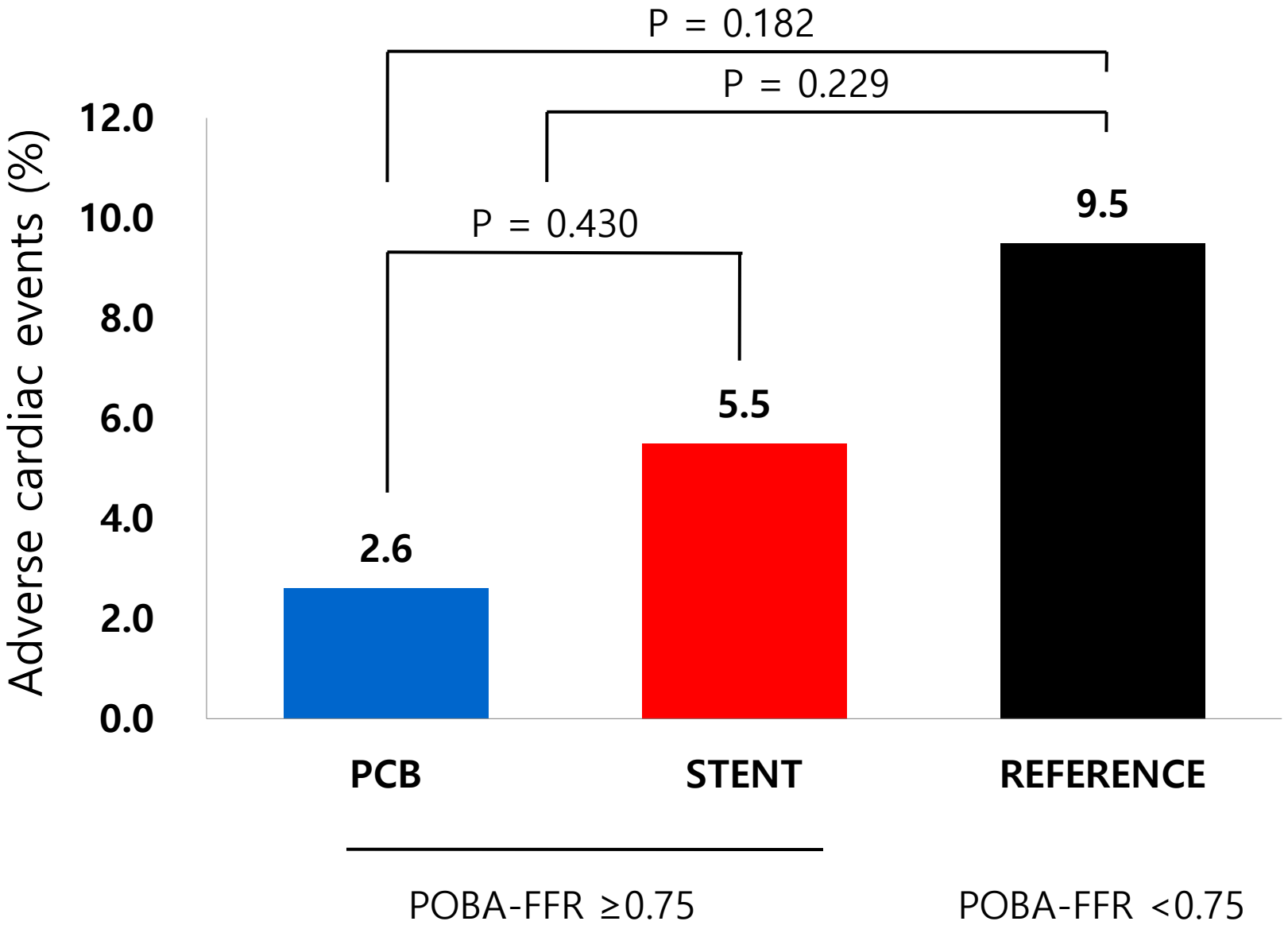
Cardiac death, MI, thrombosis, revascularization



Benefits of DCB

- DAPT 1 month due to rapid healing
- Poor drug compliance
- High-bleeding risk
- Chance of repeated revascularization

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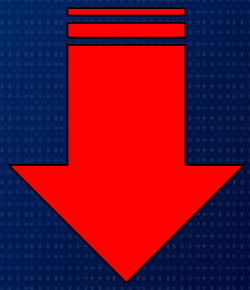
DCB

lesions not amenable to stent deployment

Too small vessels
Avoid jailing a major side-branch
Recurrent ISR



All stenotic lesions

Stent only for bail out after BA

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Take Home Messages

- DCB with highly lipophilic drugs, even short contact times between the balloon surface and the vessel wall are sufficient for effective drug delivery.
- DCB is strongly recommended to treat both BMS-ISR or DES-ISR lesions.
- In small native coronary artery disease, DCB was non-inferior to DES regarding MACE up to 1 year.

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Take Home Messages

- FFR-guided DCB application has a good safety and efficacy in de novo large CAD.
- Luminal gain and flow after DCB application is sustained without restenosis or any adverse clinical outcomes up to 1 year.
- FFR-guided DCB treatment will be a good option for de novo large coronary lesions beyond small vessels.
- DCB is a complementary to DES and will become one of treatment option in coronary intervention.

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