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# Management of Left Main Restenosis

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# The longlasting challenge in PCI : In-Stent-Restenosis

- **BMS: -20-30% (up to 40% in high- risk subsets)**
- **DES: -pivotal trials: < 6%**
- **Real world trials: 10-15%**
- **BVS : (6-10%) ?**

## *Clinical Presentation*

- **DES & BMS:**
  - ✓ **up to 60% presenting with ACS**
  - ✓ **up to 20% presenting with acute MI**
  - ✓ **50% in need for TVR**

# In-Stent-Restenosis .*Predictors & Mechanisms*

**Table 3** Predictors/mechanisms of drug-eluting stent restenosis

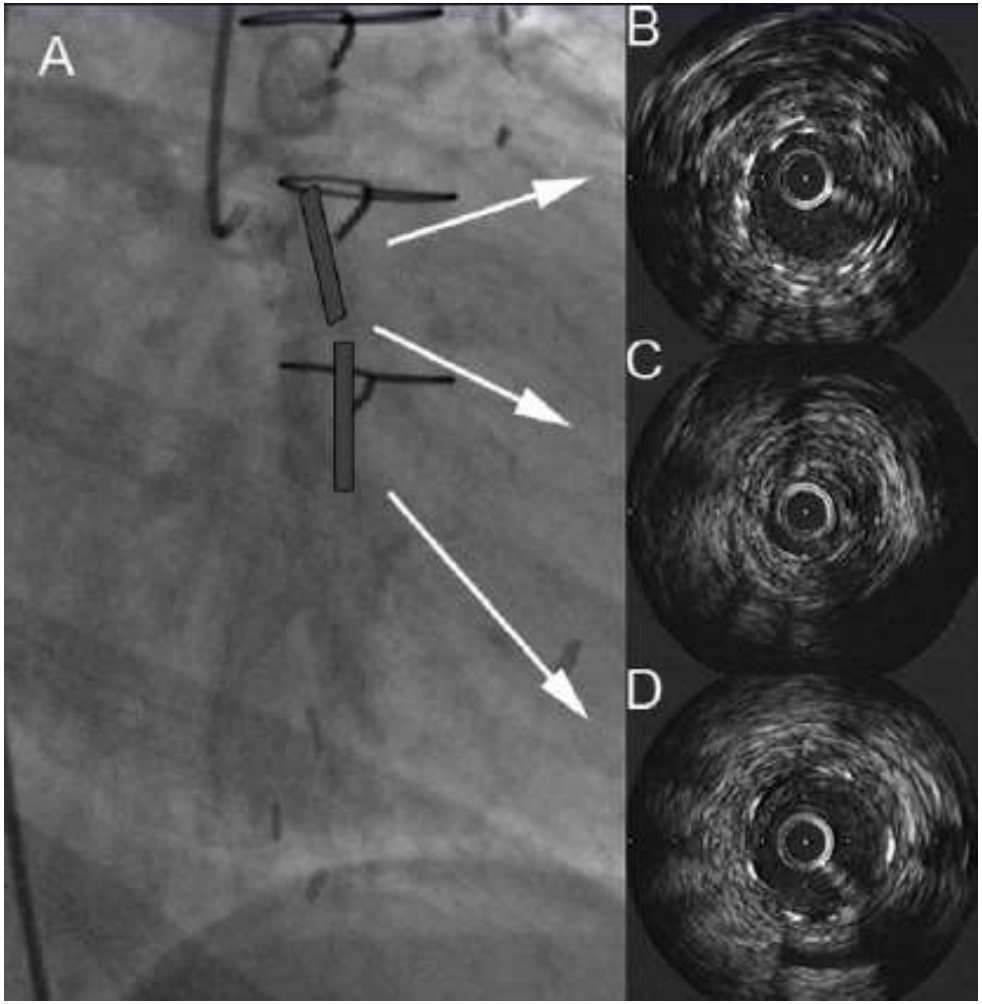
| Patient factors | Vessel factors | Procedure factors |
|---|---|---|
| Female gender | Chronic occlusion | Smaller poststent MLD |
| Diabetes mellitus | In-stent restenosis | Stent under expansion |
| Chronic renal failure on hemodialysis | Bifurcation lesion | Over dilation of an undersized stent |
| Prior MI | Lesion location = LAD | Stent fracture |
| Prior PCI | Small vessel (diameter < 2.75 mm) | Nonuniform stent expansion (i.e., nonuniform drug depostio |
| Drug resistance or hypersensitivity | Long lesion (length > 20 mm) | |
| | Severe calcification or tortuosity | |
| | Ostial location | |
| | Type C lesion | |

MI, myocardial infarction; PCI, percutaneous coronary intervention.

**Similar in BMS & DES..**

*Kim MS. et al, Cardiovasc Ther 2011;29:190-8*

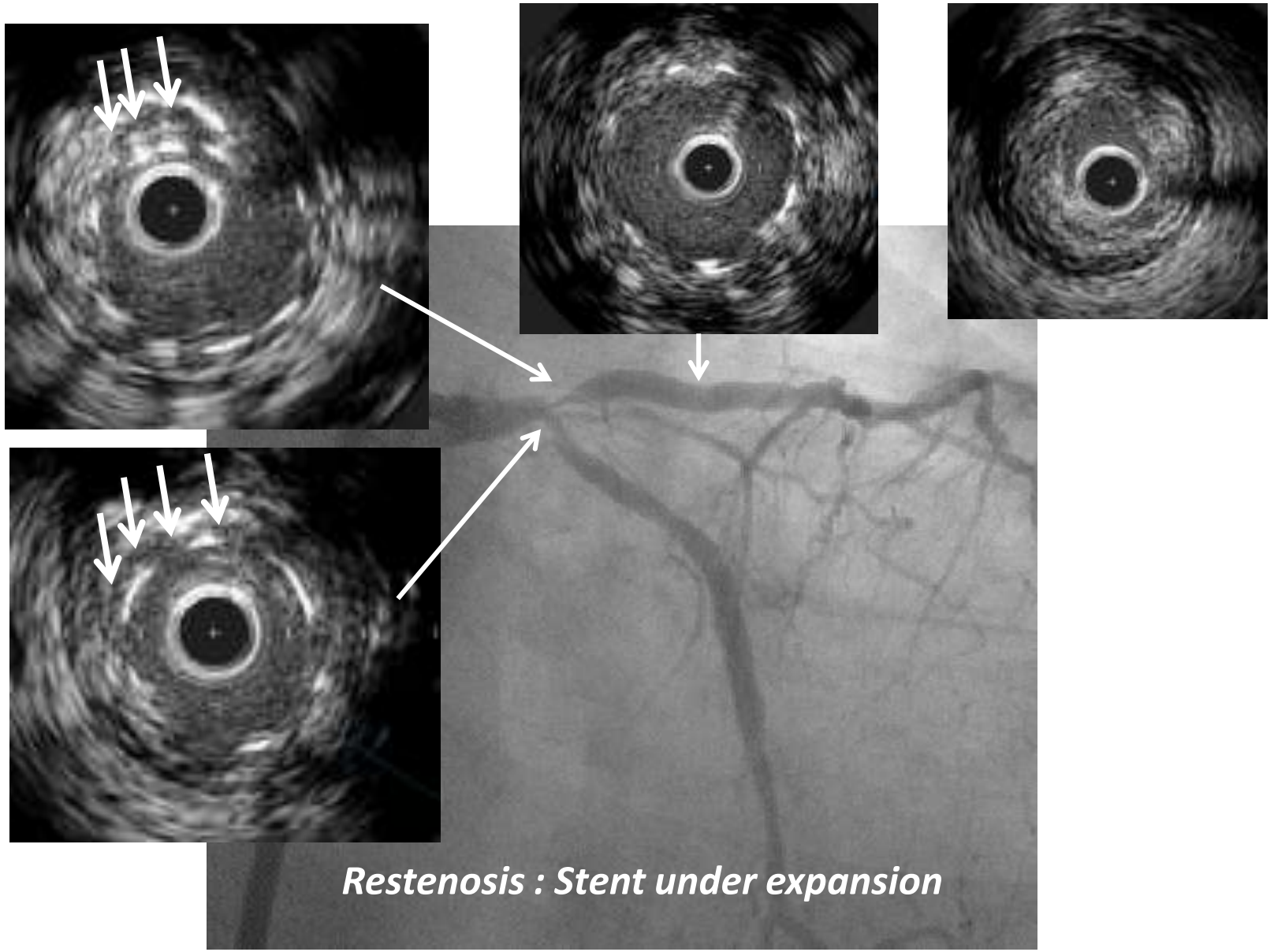
# In-Stent-Restenosis : *Stent Fracture*




- *Incidence: 1% to 8%*
- *Need for TLR: 15% to 60%*

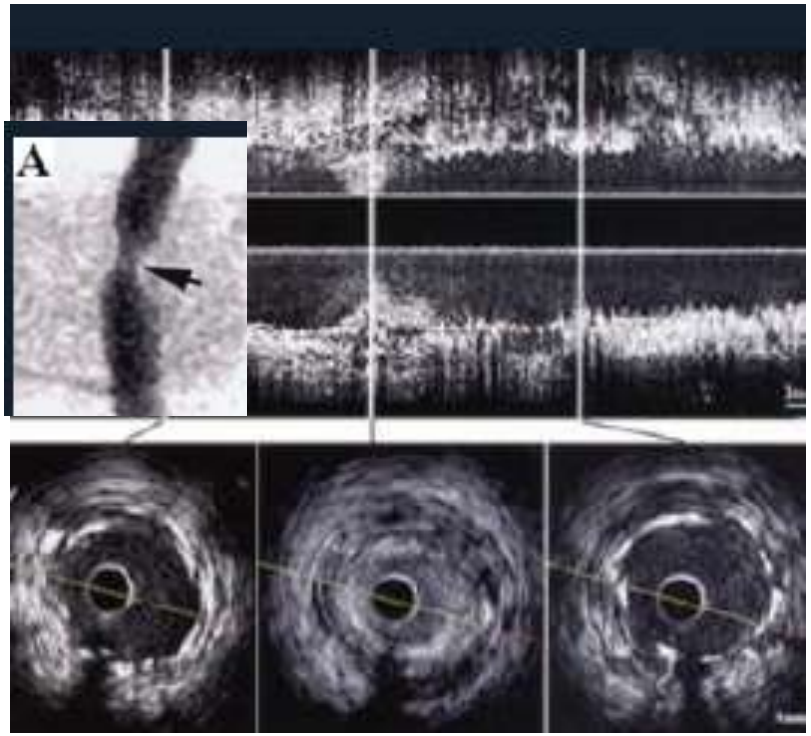
*Dangas GD. et al, JACC 2010;56:1897-907*

# Management of Left Main Restenosis

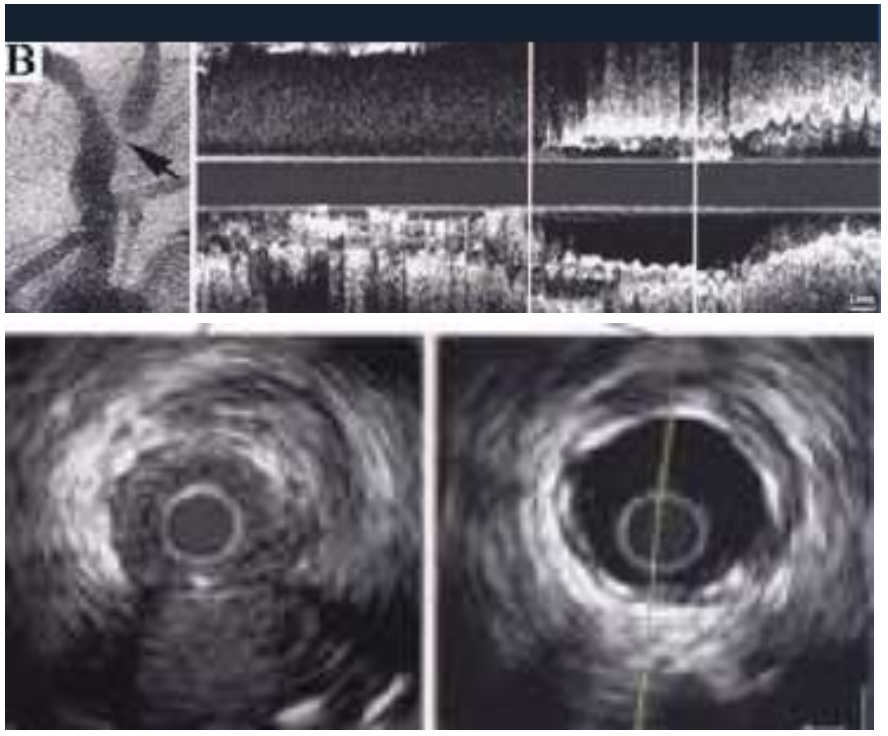


# Technical factors

**Gap between two stents**




**Incomplete stent coverage**




**Stent edge restenosis**: local trauma outside the stent.

**In-stent restenosis** : a localized lesion, associated with a discontinuity in stent coverage

*Lemos A. et al. Circulation 2003; 108: 257-60*

# Management of Left Main Restenosis

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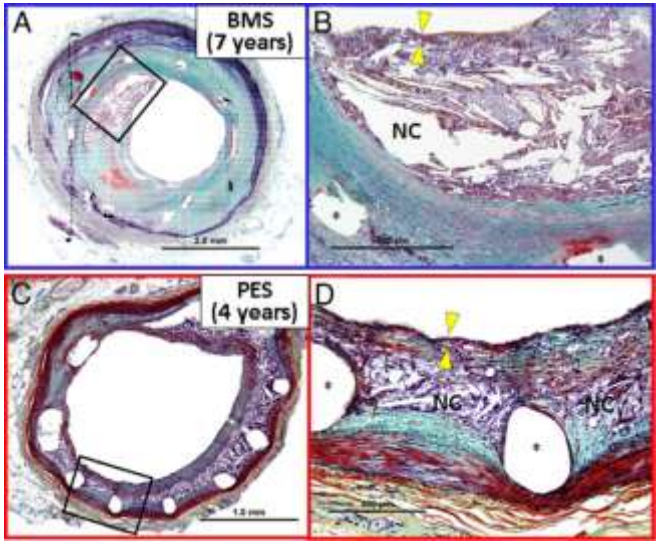
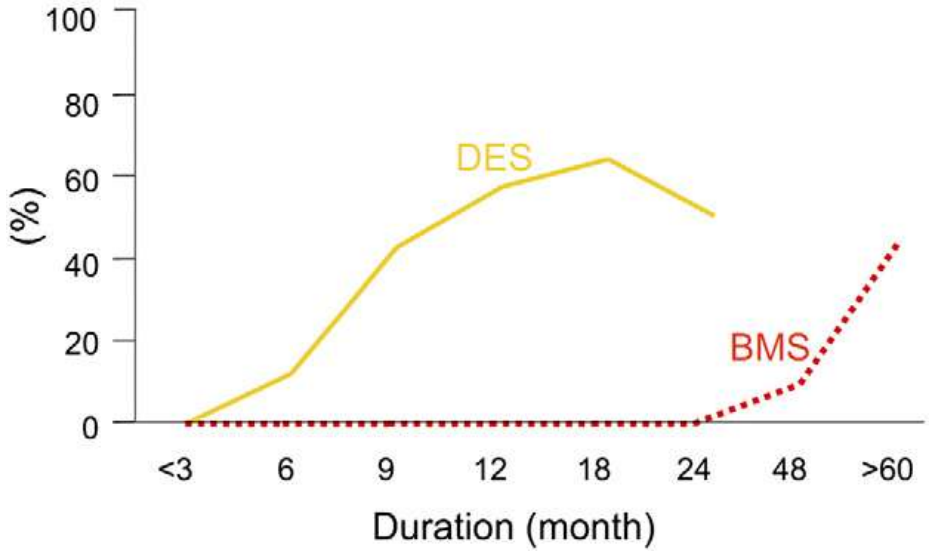
**STATE-OF-THE-ART PAPER**

## In-Stent Neoatherosclerosis

### A Final Common Pathway of Late Stent Failure

Seung-Jung Park, MD, PHD,* Soo-Jin Kang, MD, PHD,* Renu Virmani, MD,†
Masataka Nakano, MD,† Yasunori Ueda, MD‡
*Seoul, South Korea; Gaithersburg, Maryland; and Osaka, Japan*

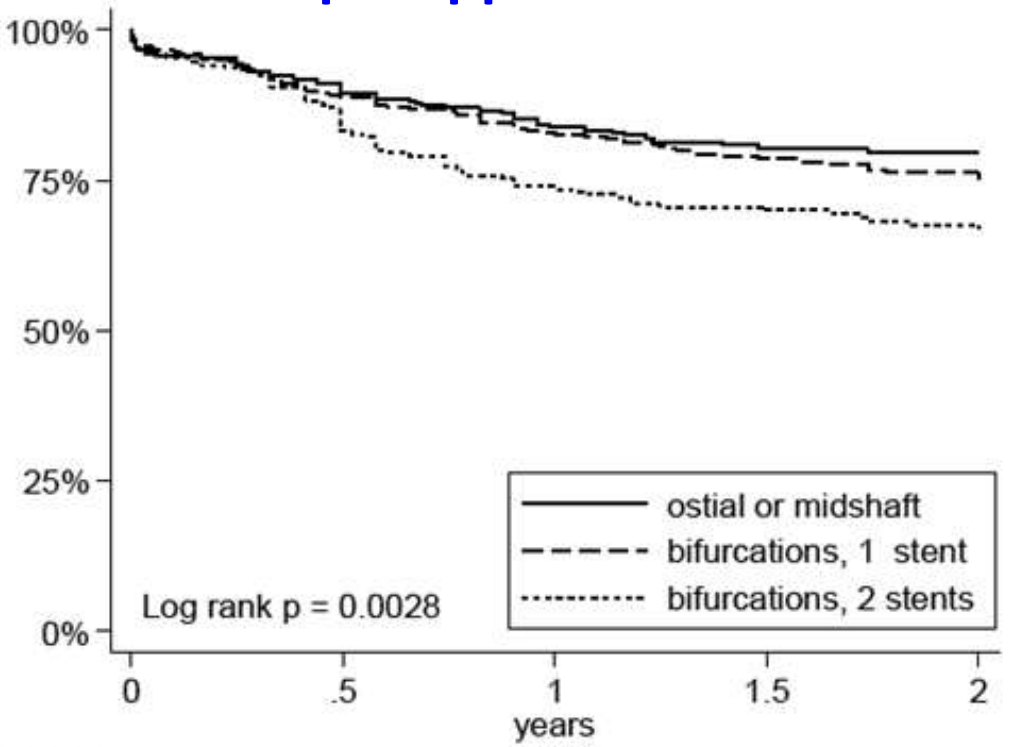



**Conclusions**

Emerging evidence suggests in-stent neoatherosclerosis as an important substrate for both ISR and LST, especially in the extended phase. In light of the rapid progression in DES, early detection of neoatherosclerosis may be beneficial to improving long-term outcome of patients with DES implants. Although angioscopy and multimodal images have consistently supported de novo atherosclerotic changes of neointima for both BMS and DES, the methodologies should be more validated to clarify the clinical implications.

# Procedural Factors : Complex approach vs Simple approach

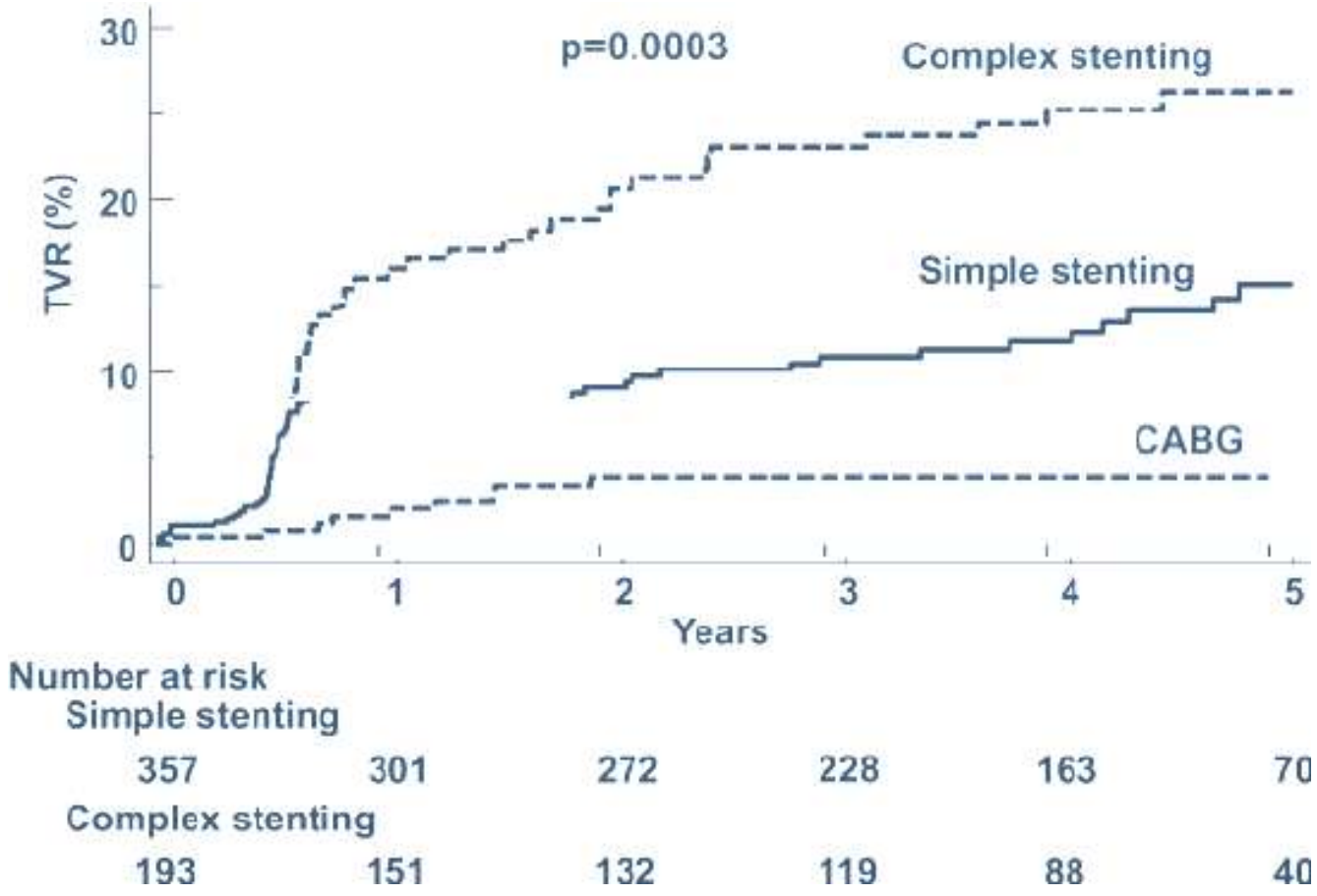



| At-risk | | | | | |
|---|---|---|---|---|---|
| ostial or midshaft | 334 | 259 | 194 | 125 | 100 |
| bifurcations, 1 stent | 456 | 358 | 269 | 180 | 134 |
| bifurcations, 2 stents | 317 | 227 | 164 | 121 | 102 |

*Palmerini et al Eur Heart J 2009*

# Procedural Factors: Complex approach vs Simple approach

**TVR**



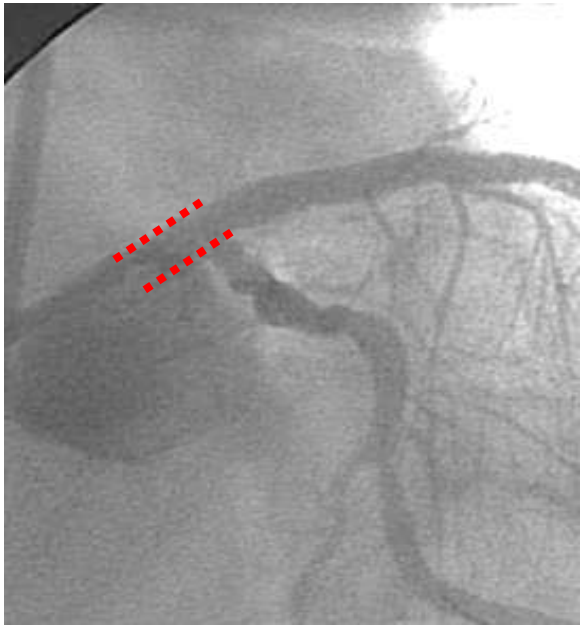

*Chang et al. Heart 2011*

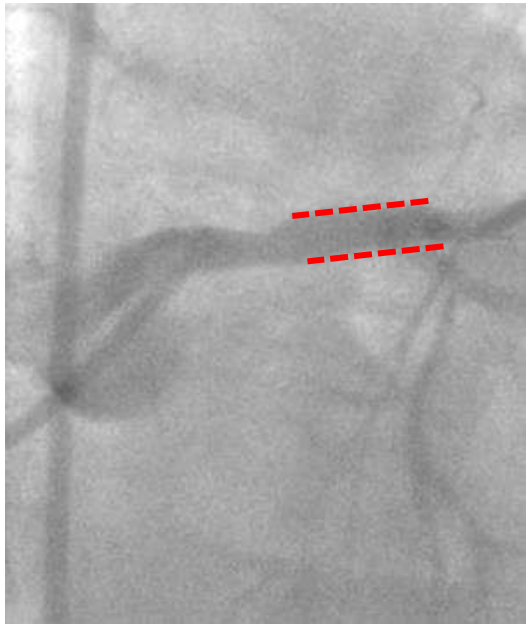
# Management of Left Main Restenosis

## Procedural Factors :

:

***From MITO Registry ( Milan and New-TOkyo )***
***Full cover approach (Ostial LM cover)***
***FCA strategy: 252 patients vs No FCA strategy: 127patients***





***Overall MB-ISR 4.8% in FCA vs. 12.6% in no FCA***

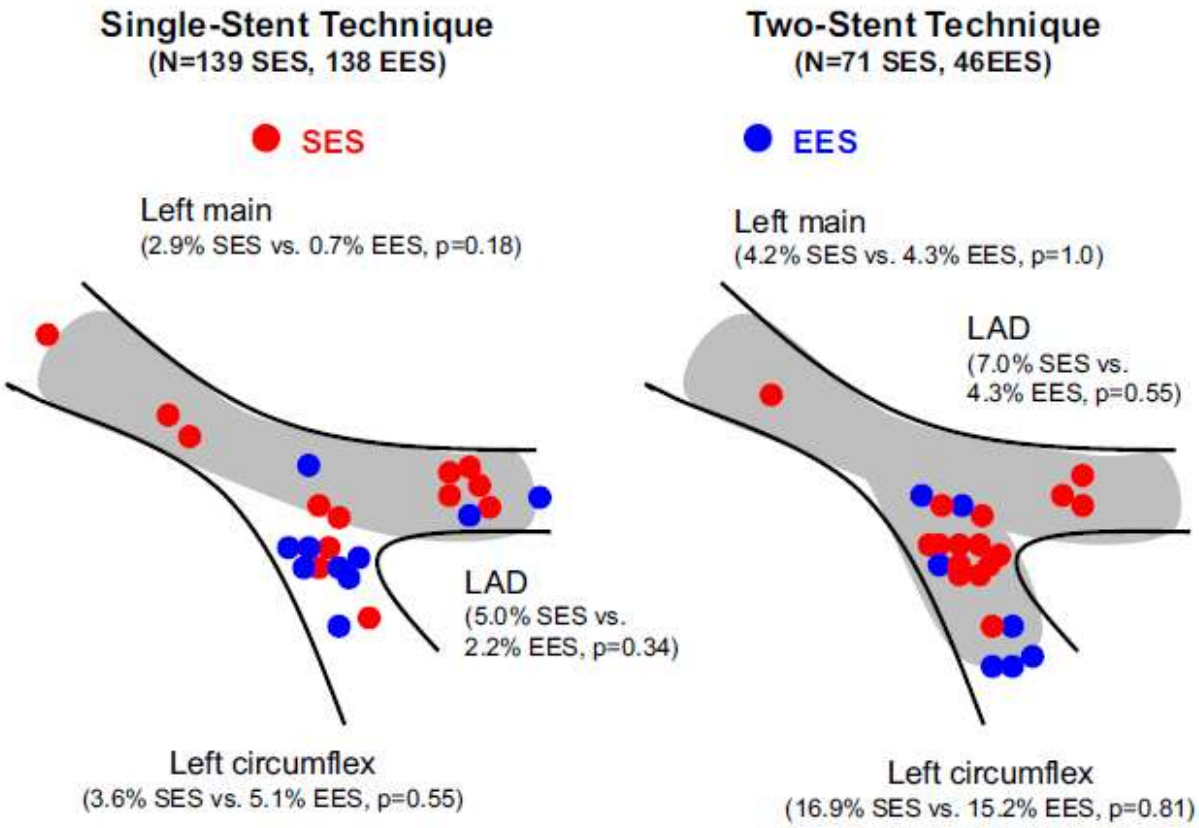
***MB ostial ISR 0.4% in FCA vs. 6.4% in no FCA***

Nakamura et al . ***EuroPCR. 2012***

## Left Main ISR Distribution

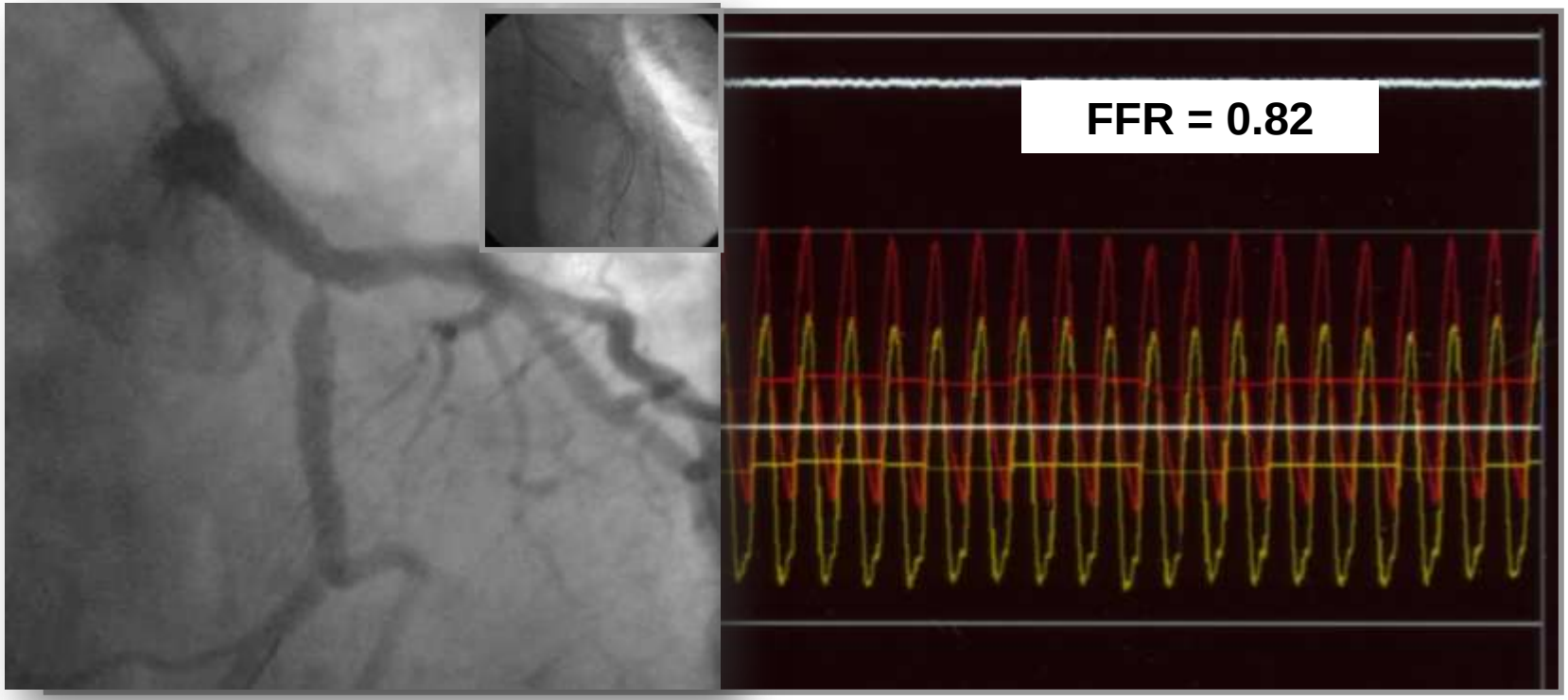
**PRECOMBACT 2**

**Angiographic Restenosis in the Subgroups Stratified By Stenting Technique**




KIM YH et al ; J A C C CardioVac Interv 2012: 708-717

# Ostial LCX compromised ?




Angio vs FFR (FFR <0.75 = ischemia) : to treat or not treat

- FFR reflects both degree of stenosis and myocardial territory

Bon-Kwon Koo, MD

## In-Stent-Restenosis *Treatment Options*

- **POBA**
- **Cutting Balloon**
- **Scoring Balloon**
- **Laser, Rotablation**
- **DEB**
- **DES (same vs. different)**
- **VBT**
- **CABG**

# Management of Left Main Restenosis

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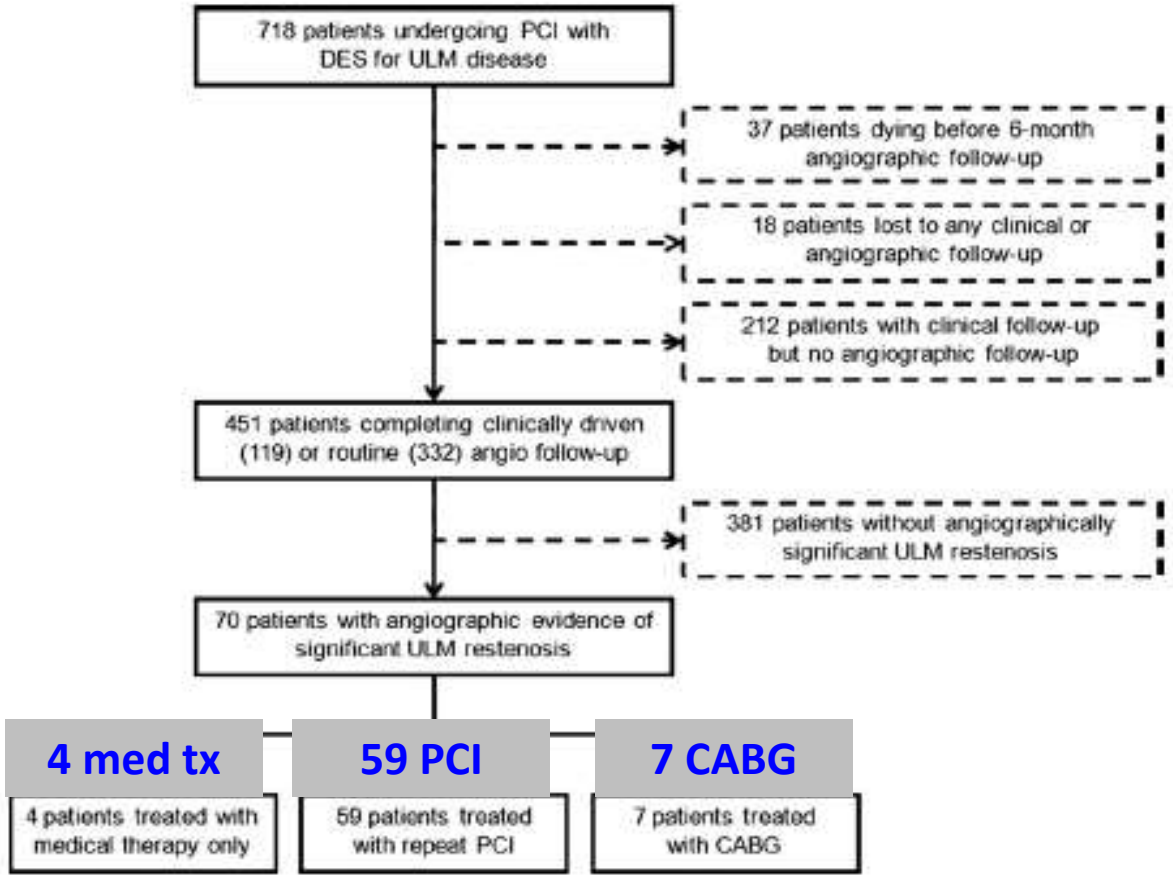
CLINICAL RESEARCH — Interventional Cardiology

## Incidence and Management of Restenosis After Treatment of Unprotected Left Main Disease With Drug-Eluting Stents

70 Restenotic Cases From a Cohort of 718 Patients: FAILS (Failure in Left Main Study)

Imad Sheiban, MD,* Dario Sillano, MD,* Giuseppe Biondi-Zoccai, MD,* Alaide Chieffo, MD,†

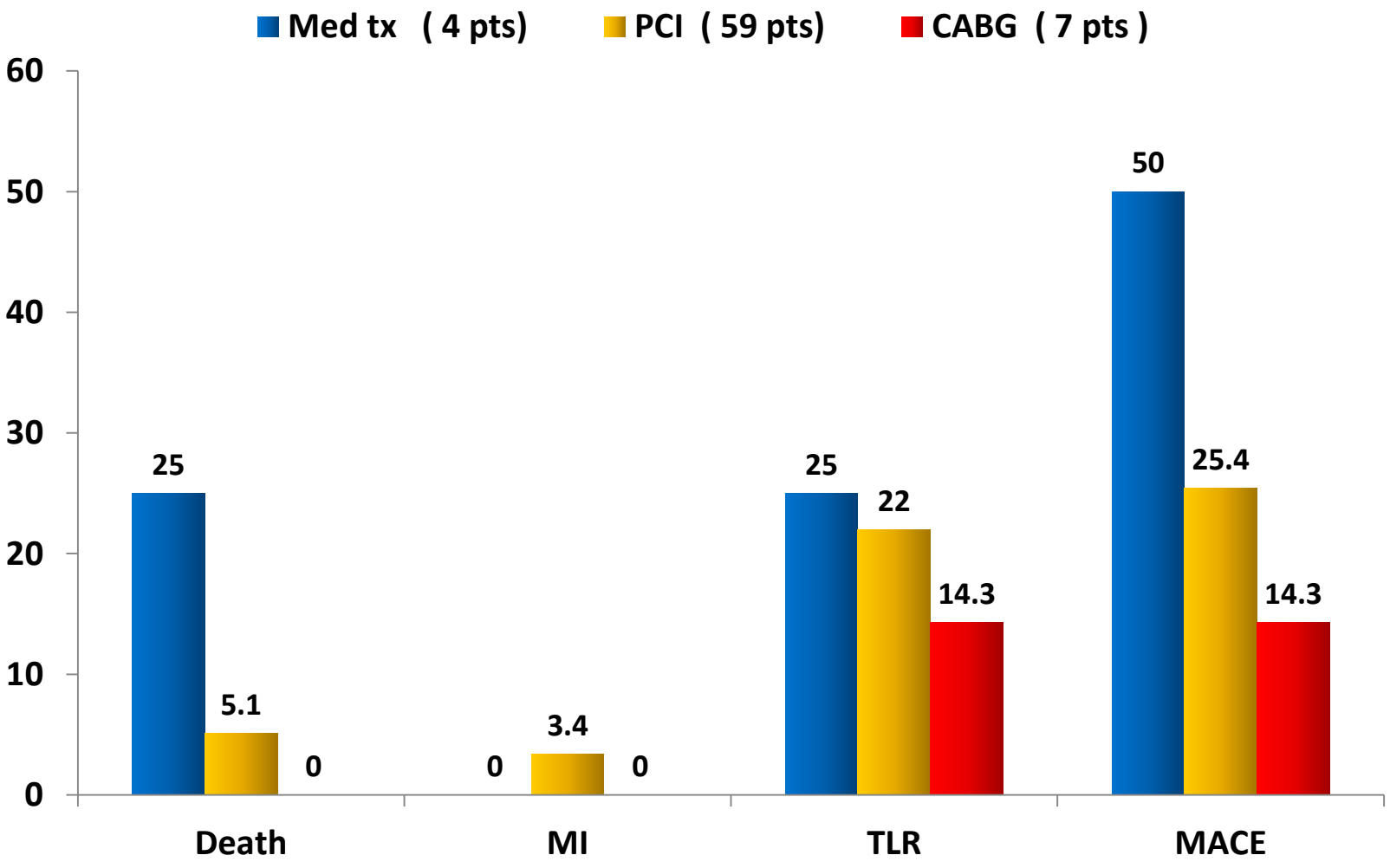



*Sheiban et al , JACC , 2009*

# Management of Left Main Restenosis

## DES In-Stent Restenosis in Left Main ( n = 70 )

*FU : 25,6 ± 16,3 months*




*Sheiban et al , JACC , 2009*

## DES vs. POBA : RIBS II: 150 patients with BMS-restenosis: SES vs. POBA

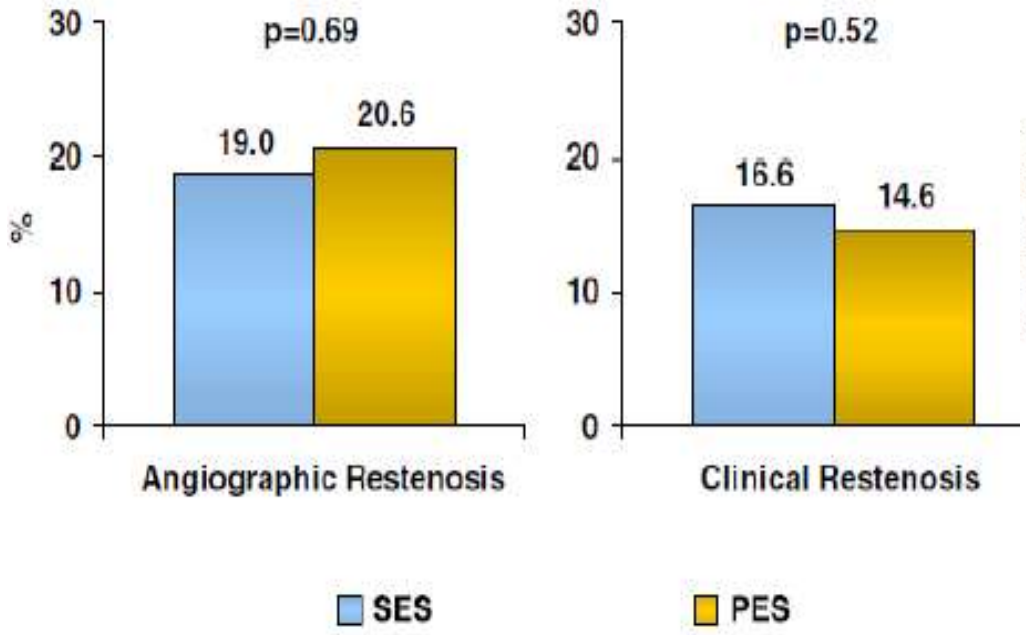
**Table 3.** In-Hospital and One-Year Clinical Events

| Event | SES Group (n = 76) | BA Group (n = 74) | p Value | HR (95% CI) |
|---|---|---|---|---|
| Hospital events, n (%) | | | | |
| Death | 1 (1.3) | 0 (0) | 0.49 | — |
| Myocardial infarction | 0 (0) | 0 (0) | 1 | 1 |
| Target vessel revascularization | 0 (0) | 0 (0) | 1 | 1 |
| Coronary angioplasty | 0 (0) | 0 (0) | 1 | 1 |
| Coronary surgery | 0 (0) | 0 (0) | 1 | 1 |
| Any major hospital event | 1 (1.3) | 0 (0) | 0.49 | — |
| Events at 9 months, n (%) | | | | |
| Death | 3 (3.9) | 1 (1.4) | 0.32 | 0.34 (0.03–3.27) |
| Myocardial infarction | 2 (2.6) | 1 (1.4) | 0.57 | 0.51 (0.05–5.61) |
| Target vessel revascularization | 3 (3.9) | 10 (13.5) | 0.03 | 3.56 (0.98–12.9) |
| Coronary angioplasty | 2 (2.6) | 7 (9.5) | 0.08 | 3.65 (0.76–17.5) |
| Coronary surgery | 1 (1.3) | 3 (4.1) | 0.54 | 2.06 (0.19–22.7) |
| Any major event at 9 months | 4 (5.3) | 11 (14.9) | 0.05 | 2.93 (0.93–9.20) |
| Events at 1 year, n (%) | | | | |
| Death | 3 (3.9) | 3 (4.1) | 0.98 | 1.02 (0.21–5.05) |
| Myocardial infarction | 2 (2.6) | 2 (2.7) | 0.99 | 1.01 (0.14–7.17) |
| Target vessel revascularization | 8 (10.5) | 22 (29.7) | 0.003 | 3.16 (1.40–7.09) |
| Coronary angioplasty | 7 (9.2) | 18 (24.3) | 0.01 | 2.83 (1.18–6.76) |
| Coronary surgery | 1 (1.3) | 4 (5.4) | 0.16 | 4.12 (0.46–36.9) |
| Any major event at 1 year | 9 (11.8) | 23 (31.1) | 0.004 | 2.90 (1.34–6.28) |

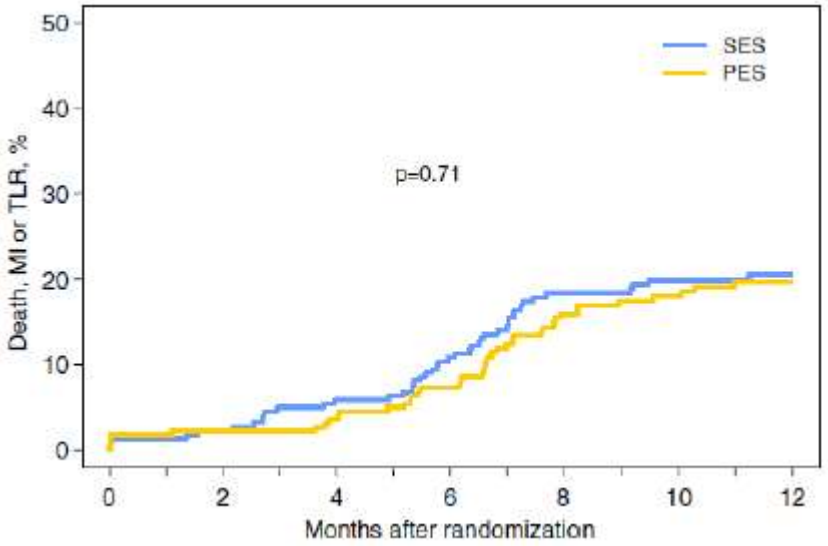
Patients with more than one event are counted only once for the composite clinical end points, although each event is listed separately in the corresponding category. p values from Cox analysis.
CI = confidence intervals; HR = hazard ratio; — = undefined; other abbreviations as in Table 1.

Alfonso F. et al, JACC 2006;56:2152-60

# ISAR-DESIRE: 450 patients with SES-restenosis: SES vs. PES




**Angiographic Restenosis at 6 to 8 months and Clinical Restenosi t 1 year**




**Composite MACE : Death / MI / TLR**

*Mehilli J. et al, JACC 2010;55: 2710-6*

# Management of Left Main Restenosis

**DEB vs. POBA PEPCAD-DES :110 patients with DES-restenosis: Paclitaxel-eluting balloon vs POBA (SES & PES)**

**Clinical Outcome at 6 Months**

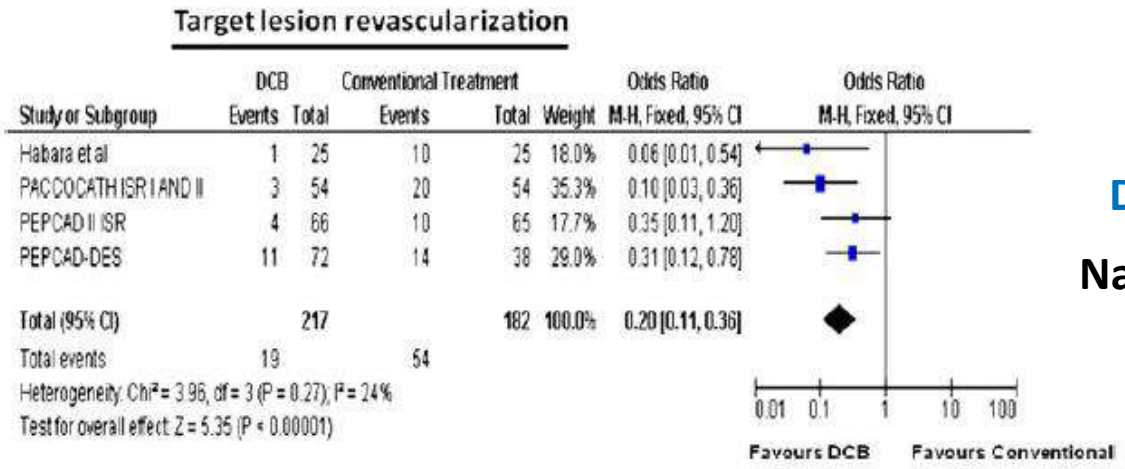
| | Drug-Coated Balloon (n = 72) | Uncoated Balloon (n = 38) | p Value |
|---|---|---|---|
| Target lesion revascularization | 11 (15.3%) | 14 (36.8%) | 0.005 |
| Myocardial infarction | 0 (0.0%) | 1 (2.6%) | 0.35 |
| Cardiac death | 1 (1.4%) | 4 (10.5%) | 0.048 |
| MACE | 12 (16.7%) | 19 (50.0%) | <0.001 |
| Stent thrombosis | | | |
| Definite | 0 | 0 | |
| Possible | 1 (1.4%) | 4 (10.5%) | 0.048 |

**Angiographic Outcome at 6 Months according to type of restenotic stent**

| | Drug-Coated Balloon | Uncoated Balloon | p Value |
|---|---|---|---|
| Non-PES | 56 | 31 | |
| Late lumen loss, mm | 0.41 ± 0.65 | 0.90 ± 0.65 | 0.004 |
| PES | 16 | 7 | |
| Late lumen loss, mm | 0.46 ± 0.50 | 1.58 ± 1.03 | 0.021 |

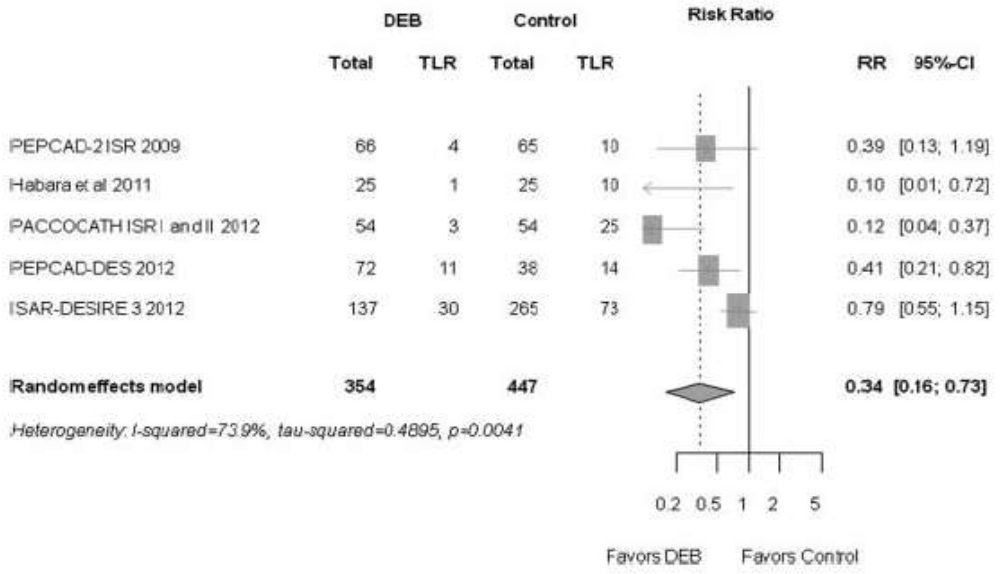
*Rittger H. et al, JACC 2012;*

# Management of Left Main Restenosis




## DEB vs POBA

**Navarese et al. *Clin Res Cardiol* 2013**




## DEB vs DES

**Indermuehle et al. *Heart*2013**

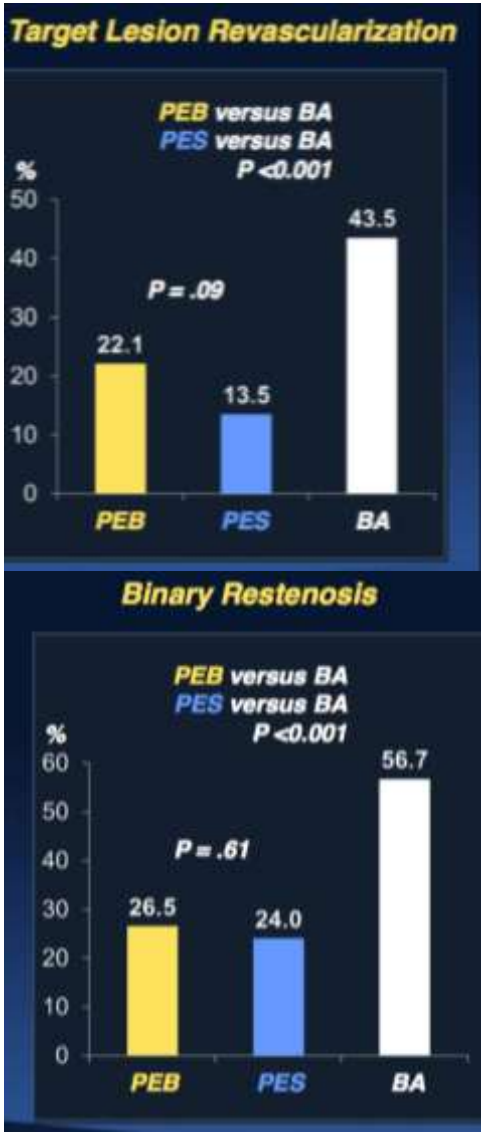
# Management of Left Main Restenosis

## DES restenosis: ISAR DESIRE 3

| | PEB | PES | Balloon angioplasty | p values | | |
|---|---|---|---|---|---|---|
| | | | | PEB vs PES | PEB vs balloon angioplasty | PES vs balloon angioplasty |
| Death | 3 (2·2%) | 6 (4·6%) | 7 (5·3%) | 0·27 | 0·17 | 0·80 |
| Myocardial infarction | 3 (2·1%) | 3 (2·4%) | 2 (1·5%) | 0·92 | 0·70 | 0·63 |
| Q wave myocardial infarction | 1 (0·7%) | 1 (0·8%) | 0 | 0·95 | 0·34 | 0·32 |
| Target lesion thrombosis | 1 (0·7%) | 1 (0·8%) | 0 | 0·97 | 0·33 | 0·31 |
| Target lesion revascularisation | 30 (22·1%) | 17 (13·5%) | 56 (43·5%) | 0·09 | <0·0001 | <0·0001 |
| Target vessel revascularisation | 33 (24·2%) | 21 (16·6%) | 58 (45·1%) | 0·18 | 0·0001 | <0·0001 |
| Death or myocardial infarction | 6 (4·4%) | 9 (6·9%) | 9 (6·8%) | 0·35 | 0·36 | 0·97 |
| Death, myocardial infarction, or target lesion revascularisation | 32 (23·5%) | 25 (19·3%) | 61 (46·2%) | 0·50 | <0·0001 | <0·0001 |

Data are n (%). Percentages are Kaplan-Meier estimates. PEB=paclitaxel-eluting balloon. PES=paclitaxel-eluting stent.

*Table 4:* **Clinical results at 1 year by treatment group**




**RCT**

402 patients

137 (34%) were assigned to PEB

131 (33%) to PES

134 (33%) to balloon angioplasty

*Byrne AB et al. Lancet 2013*

# Management of Left Main Restenosis

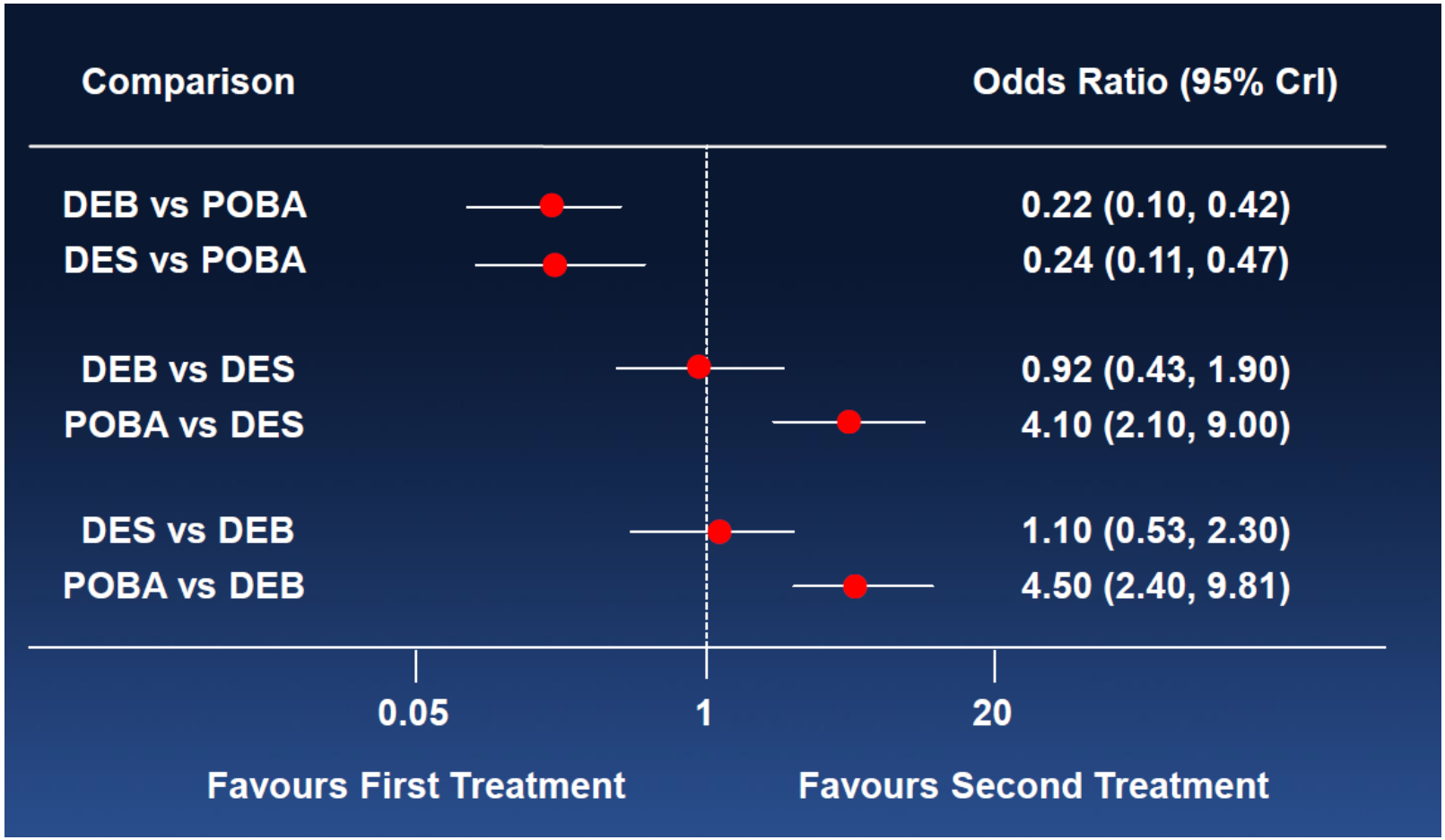
## Comparison Among Drug-eluting Balloon, Drug-eluting Stent, and Plain Balloon Angioplasty for Treatment of In-Stent Restenosis: A Network Meta-analysis of 11 Randomized Controlled Trials

**Total Pts = 2059 , Treatment : POBA = 557; DES = 808; DEB= 694**

| Trial (Year) | Age | Proportion of Co-morbidities | | | Pre-MLD (mm) | | Pre-DS (%) | | Lesion Length (mm) | | Post-MLD (mm) | | Post-DS (%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | HTN | DM | Dyslipid | Group1 | Group2 | Group1 | Group2 | Group1 | Group2 | Group1 | Group2 | Group1 | Group2 |
| ISAR-DESIRE (2005) | 64.3 | 54.3% | 27.7% | 56.7% | DES 0.94 | POBA 0.95 | DES 62.4 | POBA 61.8 | DES 11.95 | POBA 12.3 | **DES 2.54** | POBA 2.07 | **DES 9.35** | POBA 19.9 |
| RIBS-II (2008) | 64.0 | 54.7% | 34.7% | 61.3% | DES 0.74 | POBA 0.70 | DES 72.0 | POBA 74.0 | DES 16.9 | POBA 15.7 | **DES 2.69** | POBA 2.29 | **DES 8.0** | POBA 40 |
| PEPCAD-II (2009) | 64.8 | 81.7% | 29.8% | 74.8% | DEB 0.74 | DES 0.77 | DEB 73.9 | DES 72.8 | DEB 15.7 | DES 15.4 | DEB 2.30 | **DES 2.56** | DEB 19.5 | **DES 11.2** |
| Habara et al. (2011) | 69.4 | 64.0% | 62.0% | 62.0% | DEB 0.99 | POBA 0.92 | DEB 64.1 | POBA 68.4 | DEB 12.7 | POBA 13.2 | DEB 1.99 | POBA 2.00 | **DEB 25.7** | POBA 31.0 |
| ISAR-DESIRE 3 (2012) | 67.9 | 73.6% | 41.5% | 77.9% | DEB 0.97 | DES 0.93 | POBA 0.88 | DEB 64.4 | DES 66.7 | POBA 67.7 | DEB N/R | DES N/R | POBA N/R | **DEB 2.29** | **DES 2.53** | POBA 2.10 | **DEB 18.5** | **DES 12.8** | POBA 23.3 |
| PEPCAD-DES (2012) | 67.8 | 94.5% | 35.4% | 78.2% | DEB 0.66 | POBA 0.62 | DEB 72.1 | POBA 74.0 | DEB 11.2 | POBA 12.2 | DEB 2.15 | POBA 2.14 | DEB 12.6 | POBA 13.7 |
| PACCOCATH-ISR I&II Pooled Analysis (2012) | 65.9 | 81.5% | 26.9% | 75.0% | DEB 0.70 | POBA 0.63 | DEB N/R | POBA N/R | DEB 18.6 | POBA 18.3 | DEB 2.34 | POBA 2.43 | DEB N/R | POBA N/R |
| CRISTAL (2012) | 67.7 | 75.1% | 39.1% | 79.2% | DES 1.09 | POBA 1.18 | DES 58.8 | POBA 53.7 | DES 14.6 | POBA 13.4 | **DES 2.51** | POBA 2.12 | **DES 9.5** | POBA 18 |
| Habara et al. (2013) | 69.0 | 84.6% | 44.7% | 82.7% | DEB 0.86 | POBA 0.84 | DEB 65.6 | POBA 66.1 | DEB 12.8 | POBA 13.7 | DEB 1.97 | POBA 1.90 | DEB 21.9 | POBA 23.1 |
| PEPCAD China ISR (2014) | 61.9 | 68.4% | 36.7% | 34.0% | DEB 0.85 | DES 0.86 | DEB 68.3 | DES 68.4 | DEB 12.5 | DES 13.1 | DEB 2.39 | **DES 2.56** | DEB 10.5 | **DES 7.1** |
| RIBS V (2014) | 65.5 | 72.0% | 25.9% | 69.3% | DEB 1.02 | DES 0.93 | DEB 61.0 | DES 65.0 | DEB 13.7 | DES 13.8 | DEB 2.16 | **DES 2.38** | DEB 19.0 | **DES 11.0** |

JM Lee, TCT 2014

## Target Lesions Revascularization

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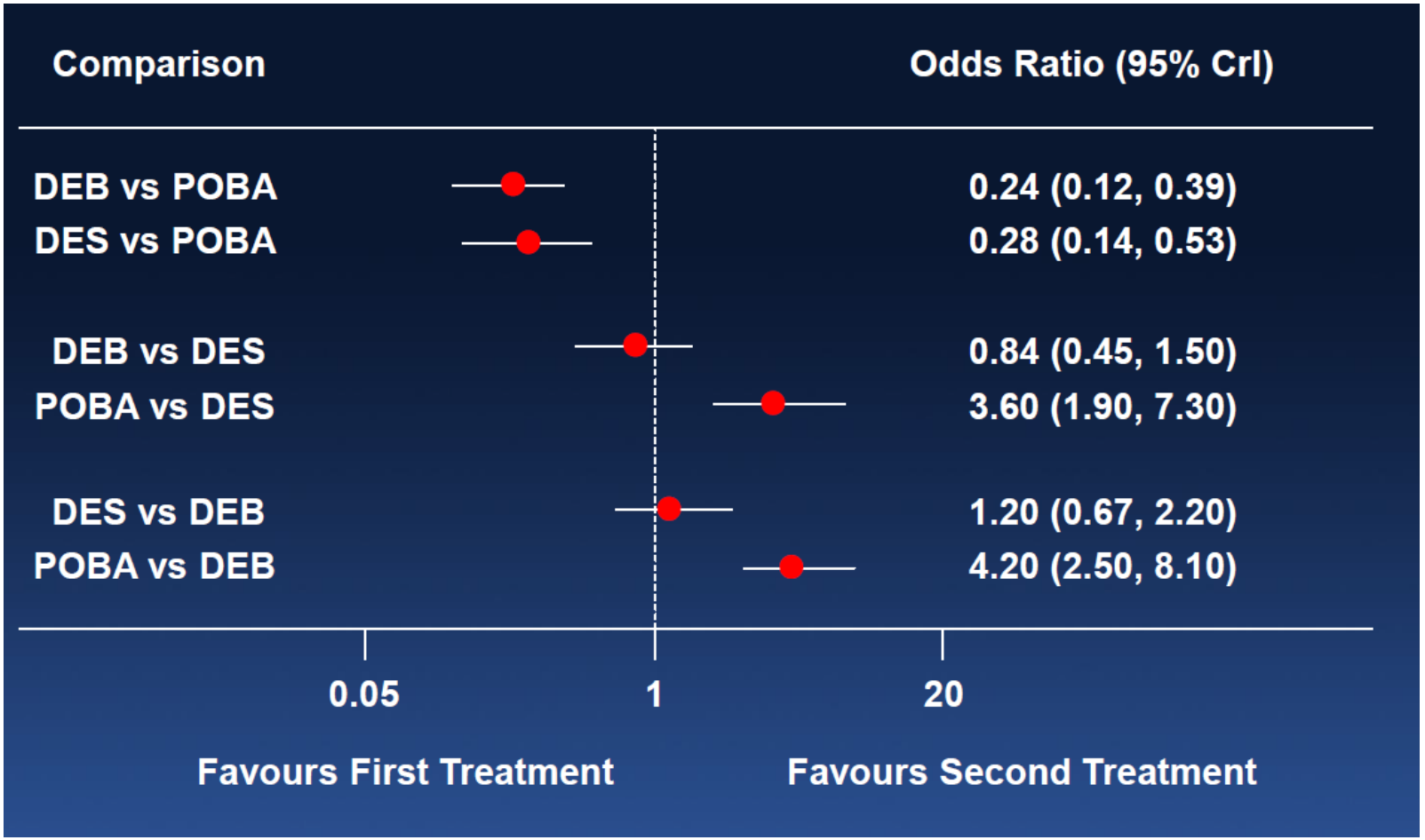
# MACE




JM Lee, TCT 2014

# In- BVS Restenosis

## Early (before 6 months), late (6-12 months) and very late (after 12 months) angiographic scaffold restenosis in the ABSORB Cohort B trial

Shimpei Nakatani[1], MD; Yoshinobu Onuma[1]*, MD; Yuki Ishibashi[1], MD, PhD; Takashi Muramatsu[1], MD, PhD; Javaid Iqbal[1], MRCP, PhD; Yao-Jun Zhang[1], MD, PhD; Robert-Jan van Geuns[1], MD, PhD; John A. Ormiston[2], MBChB, PhD; Patrick W. Serruys[1], MD, PhD; on behalf of the ABSORB Cohort B investigators

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GUEST EDITOR: Rafael Beyar, MD, DSc, MPH, Director; *Rambam Health Care Campus, Women's Division/Dr Philip and Sara Gottlieb Chair, Department of Medicine and Biomedical Engineering, Technion, Israel*

KEYWORDS
- bioresorbable scaffold
- everolimus
- intravascular imaging
- long-term follow-up
- restenosis

**Abstract**

**Aims:** The long-term follow-up of the first-in-man ABSORB Cohort B trial showed that angiographic binary restenosis can occur early, late or very late after implantation of the Absorb everolimus-eluting bioresorbable vascular scaffold (Absorb BVS). Since the mechanical support of the scaffold decreases during bioresorption, the mechanism of in-segment restenosis (ISR) of the Absorb BVS might be different from that of metallic stents. The objective of the current analysis was to review the multimodality imaging of cases with binary restenosis to elucidate the mechanism of ISR after Absorb BVS implantation.

**Methods and results:** The ABSORB Cohort B trial enrolled 101 patients with a maximum of two *de novo* coronary lesions. At the three-year imaging and clinical follow-up, there were six cases of in-segment binary restenosis: two early ISR (<6 months), one late ISR (6-12 months) and three very late ISR (>12 months). Three of these ISR cases seemed to be induced by anatomical or procedural factors. In the other three cases, intravascular imaging (IVUS/OCT) demonstrated that the main mechanism of restenosis was significant intra-scaffold tissue growth, while the structural circularity and diameter of the scaffold were not affected.

**Conclusions:** Early and late restenosis after implantation of the Absorb bioresorbable scaffold could be related to anatomical or procedural factors. In this small cohort of patients late or very late restenosis seems to be attributed to pure intra-scaffold tissue growth without extrinsic encroachment of the scaffold.

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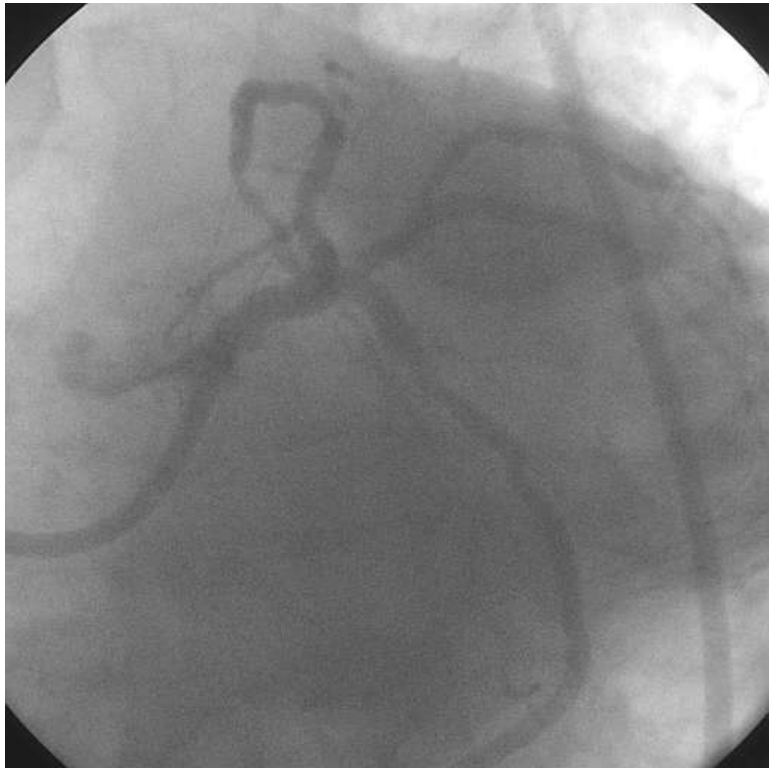
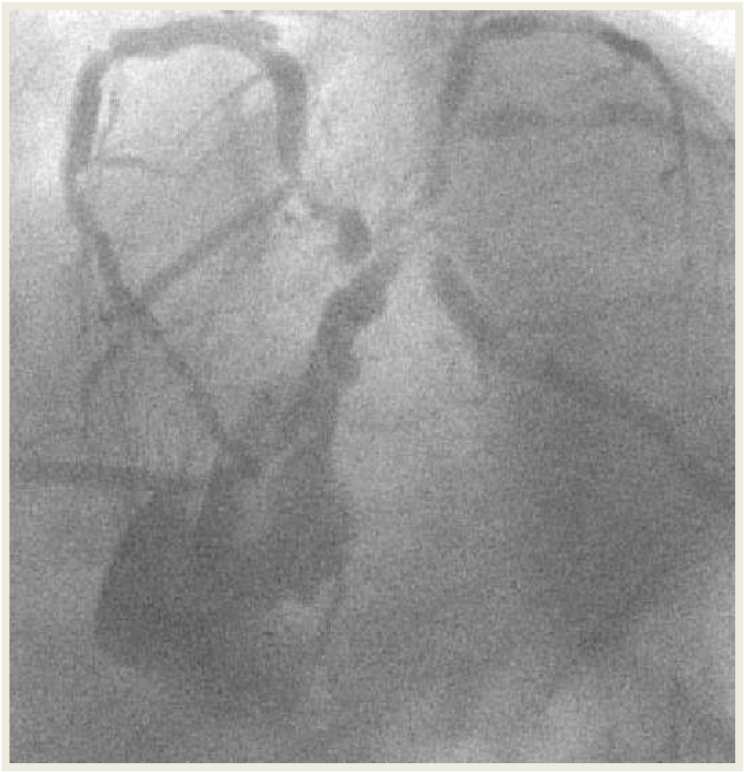
- **Total patients recieving BVS = 101**
- **In-BVS Restenosis = 6 (6%)**
- **Managment :**
  - **CABG = 1**
  - **DES = 5**

# Management of Left Main Restenosis

## Diffuse ISR : CABG could be the best option …



Post LM Trifurcation Stenting



After 5-month : diffuse ISR

# Management of Left Main Restenosis

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ESC/EACTS GUIDELINES

## 2014 ESC/EACTS Guidelines on myocardial revascularization

**The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)**

**Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI)**

| Restenosis | | |
|---|---|---|
| Repeat PCI is recommended, if technically feasible. | I | C |
| DES are recommended for the treatment of in-stent re-stenosis (within BMS or DES). | I | A |
| Drug-coated balloons are recommended for the treatment of in-stent restenosis (within BMS or DES). | I | A |
| IVUS and/or OCT should be considered to detect stent-related mechanical problems. | IIa | C |

# Final Remarks

- **POBA alone is not an effective treatment for ISR**
- **The results of clinical trials showed superior efficacy of DEB and DES, compared with POBA ,and similar efficacy between DEB and DES.**
- **DEB might be the suitable first line treatment option for both BMS and DES ISR, especially in patients who cannot tolerate long-term DAPT.**
- **CABG Should be considered in patient with diffuse and complex distal Left Main ISR**
- **Imaging (IVUS / OCT ) and functional ( FFR ) evaluation are extremely recommended for a more appropriate management**

# *Thanks for your attention*