Current Treatment Option for DES Failure

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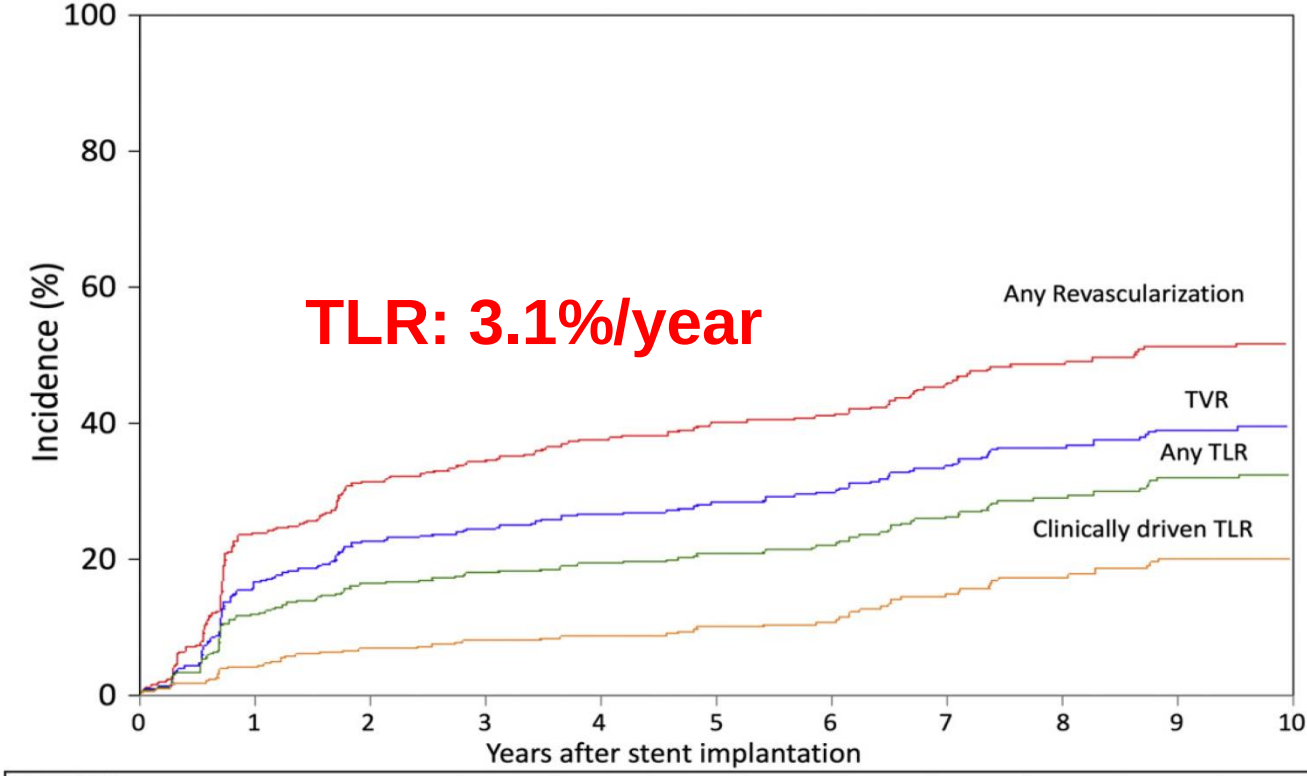
Gachon University
Gil Medical Center

Content

DES failure: Still challenging

SES Long term f/u

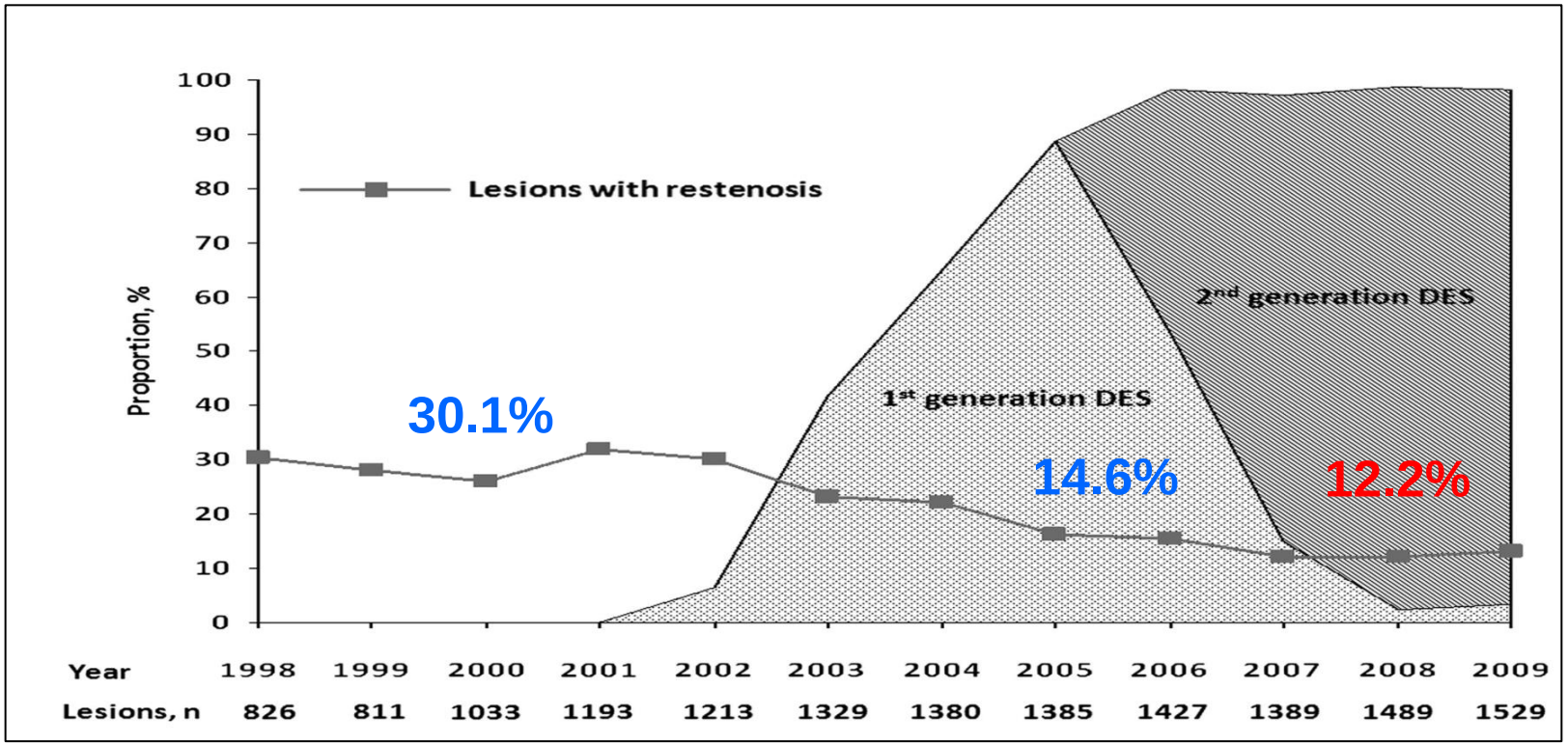


Interval (Year)		1	2	3	4	5	6	7	8	9	10
Any revascularization	Cumulative incidence	18.9	27.8	30.8	34.6	37.1	38.2	41.4	46.8	49.1	49.7
	N of patients at risk	269	222	209	188	173	161	146	119	108	67
TVR	Cumulative incidence	11.1	18.3	20.0	22.7	24.8	26.7	30.2	33.9	36.7	37.3
	N of patients at risk	295	253	243	255	211	190	173	150	136	87
Any TLR	Cumulative incidence	8.7	14.0	15.3	17.0	18.8	20.3	23.8	27.4	30.6	31.1
	N of patients at risk	303	267	258	243	230	211	192	169	149	96
Clinical driven TLR	Cumulative incidence	3.3	6.7	7.4	8.1	9.7	10.6	14.1	17.3	20.0	20.0
	N of patients at risk	303	267	258	243	230	211	192	169	149	96

Miura K, et al. Am H J 2016;175:47

DES ISR is Still Challenging

- Although DES have drastically reduced the incidence of ISR, **treatment of DES-ISR is particularly challenging.**



Cassese S, et al. Heart 2014;100:153-9

DES ISR is differ from BMS ISR

Table 1 Comparison of Principal Features of Restenotic Tissue After Bare-Metal and Drug-Eluting Stent Implantation

	Bare-Metal Stent Restenosis	Drug-Eluting Stent Restenosis
Imaging features		
Angiographic morphology	Diffuse pattern more common	Focal pattern more common
Optical coherence tomography tissue properties	Homogeneous, high-signal band most common	Layered structure or heterogeneous most common
Time course of late luminal loss	Late loss maximal by 6–8 months	Ongoing late loss out to 5 years
Histopathological features		
Smooth muscle cellularity	Rich	Hypocellular
Proteoglycan content	Moderate	High
Peri-strut fibrin and inflammation	Occasional	Frequent
Complete endothelialization	3–6 months	Up to 48 months
Thrombus present	Occasional	Occasional
Neoatherosclerosis	Relatively infrequent, late	Relatively frequent, accelerated course

- Drug resistance
- Hypersensitivity
- Stent under-expansion
- Stent strut fracture
- Non-uniform stent strut coverage
- Gap in stent coverage
- Residual uncovered atherosclerotic lesion
- geographic miss

Alfonso et al. JACC 2014;63:2659-73.

Treatment of DES ISR had poor outcomes than in BMS ISR

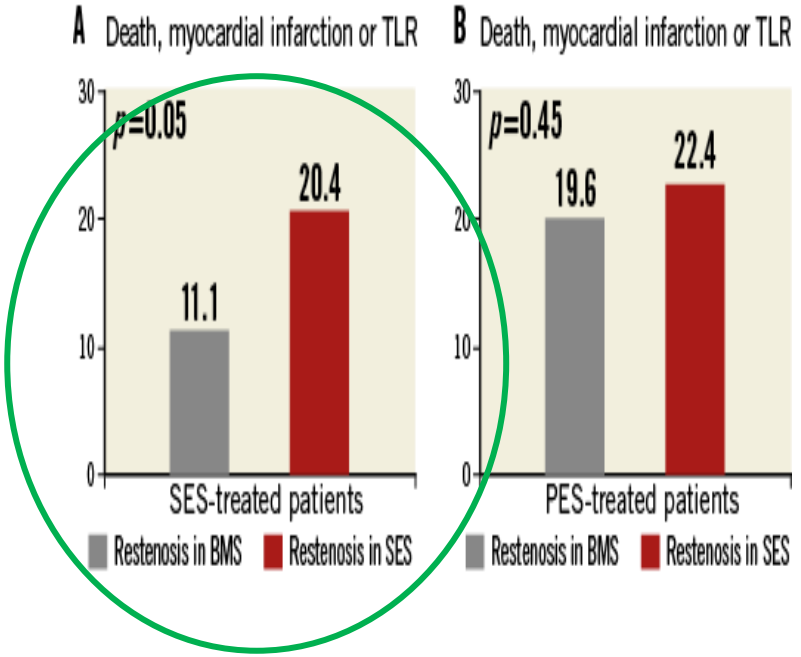
Angiographic outcomes

Table 2. Angiographic outcomes at 6-8 months: SES-treated and PES-treated patients.

SES-treated patients	SES for SES restenosis	SES for BMS restenosis	*p*-value
Patients	190	91	
Minimal luminal diameter, in-segment, mm	1.95±0.73	2.07±0.69	0.16
Stenosis, in-segment, %	34.0±20.9	27.6±19.4	0.015
Late loss, in-stent, mm	0.41±0.66	0.21±0.59	0.007
Recurrent binary restenosis	37 (19.5)	13 (14.3)	0.29
PES-treated patients	**PES for SES restenosis**	**PES for BMS restenosis**	***p*-value**
Patients	191	92	
Minimal luminal diameter, in-segment, mm	1.96±0.67	1.94±0.72	0.78
Stenosis, in-segment, %	32.7±18.6	33.5±22.2	0.75
Late loss, in-stent, mm	0.39±0.59	0.48±0.71	0.47
Recurrent binary restenosis	38 (19.9)	20 (21.7)	0.72

Data shown as patient level analysis and presented as means±SD or number (percentage).
BMS: bare metal stent; PES: paclitaxel-eluting stent; SES: sirolimus-eluting stent

MACE



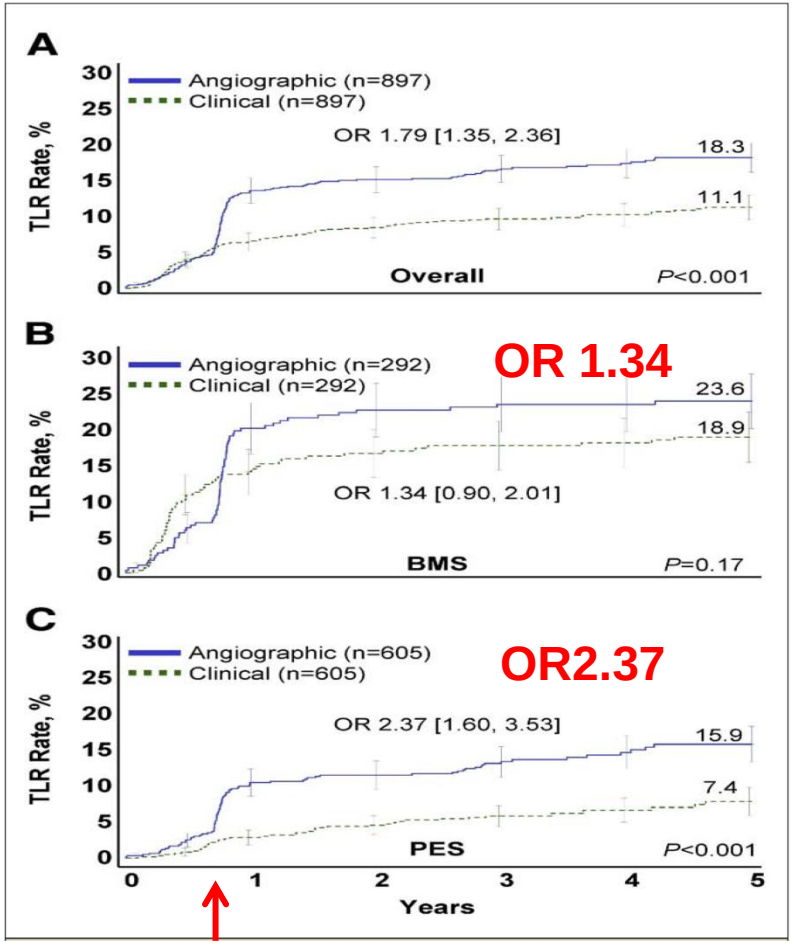
Pooled analysis of ISAR-DESIRE and ISAR-DESIRE 2 trials

Byrne RA, et al. EuroIntervention 2013;9:797-802

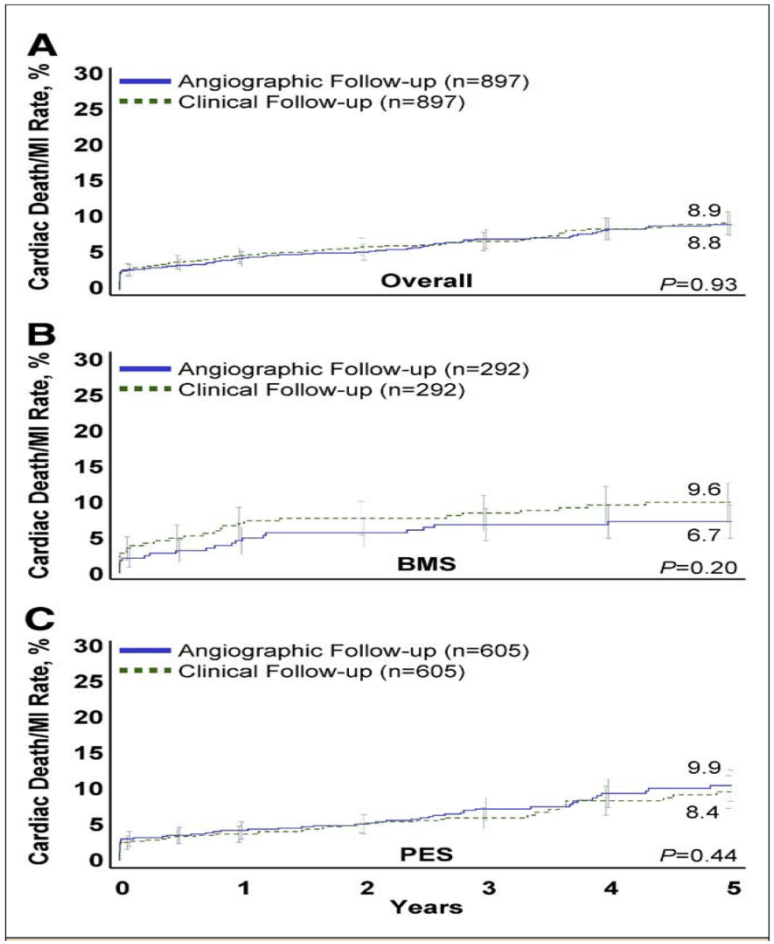
Content

Avoid Oculo-stenotic reflex

TLR Rates, %



Cardiac Death/MI Rates, %



Pooled analysis taxus IV, V and liberte

Uchida T et al. JACC int 2010;3:403-11

FFR Guided Treatment of ISR Lesions

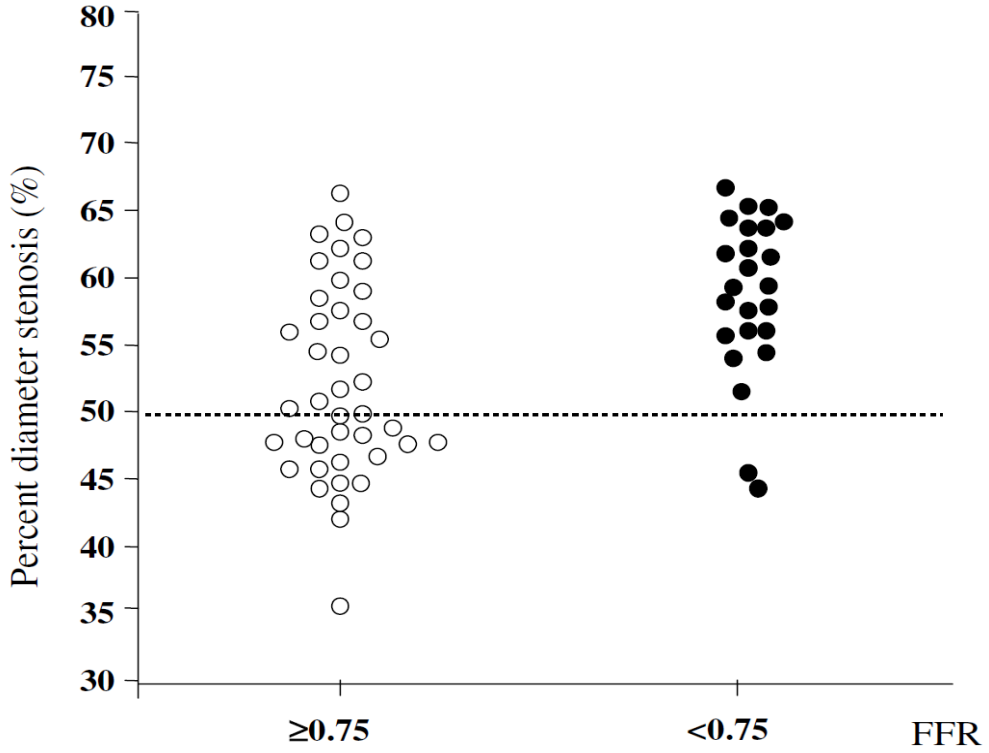


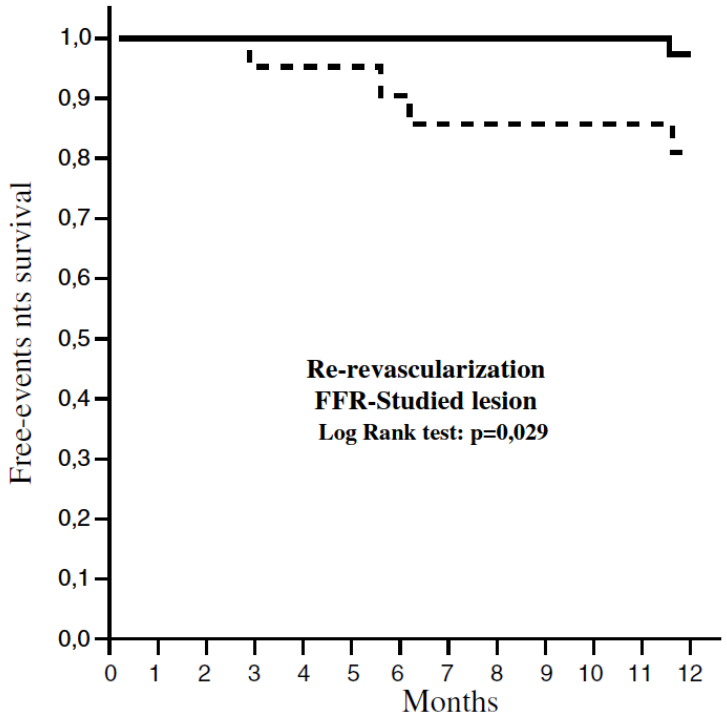
Fig. 2 Distribution of lesions according to percentage of diameter stenosis and significance of fractional flow reserve. (Shaded circles: re-revascularized lesions. White circles: medically treated lesions.)

51.2% of angiographic restenosis (DS ≥ 50%) presented a FFR ≥ 0.75

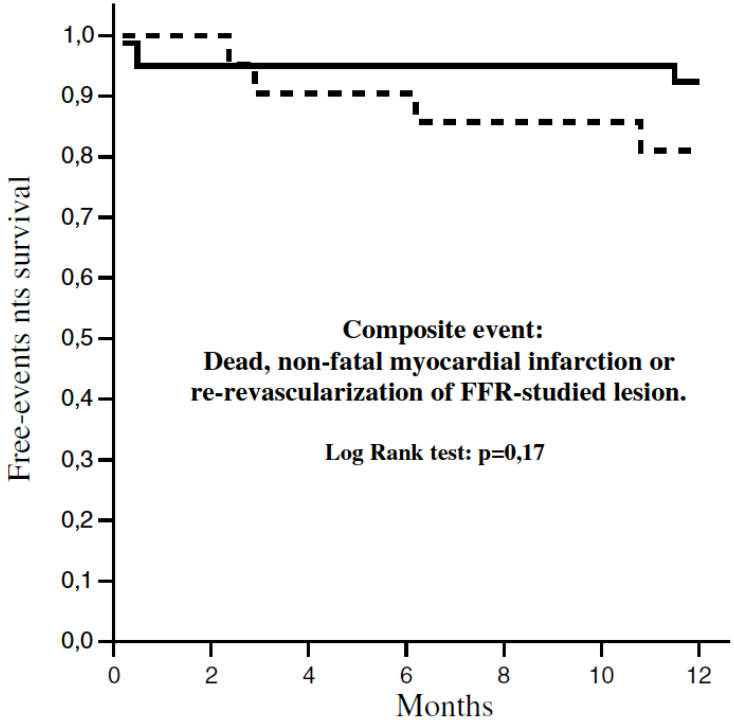
Lopez-Palop R et al. EHJ 2004;25:2040-7

FFR Guided Treatment of ISR Lesions

Revascularization



Composite end points



Patients with non-treated lesions (FFR≥0.75)

Patients with treated lesions (FFR<0.75)

Lopez-Palop R et al. EHJ 2004;25:2040-7

FFR Guided Treatment of DES ISR Lesions

MACE

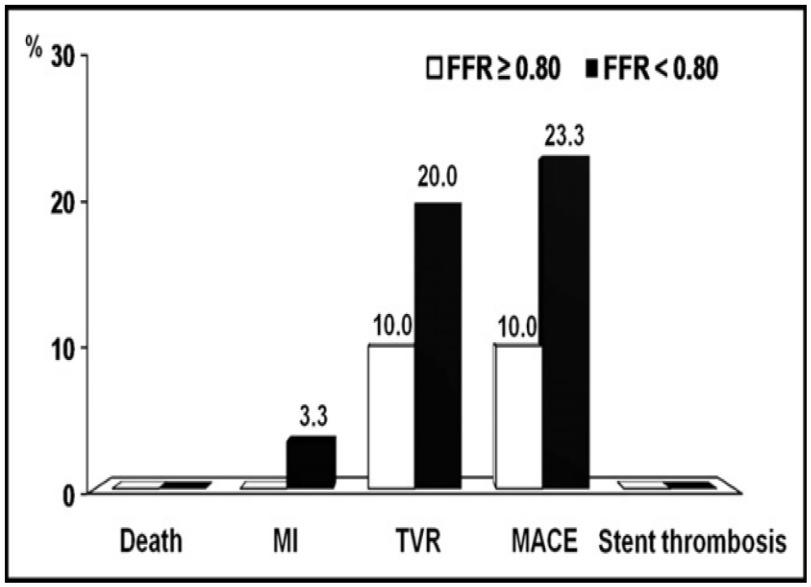


Figure 2. Twelve-month clinical outcomes of restenotic lesions after DES implantation according to FFR. Deferred lesions (FFR ≥0.80) demonstrated tendency toward lower incidence of major adverse cardiac events. All p values >0.05.

Event free survival

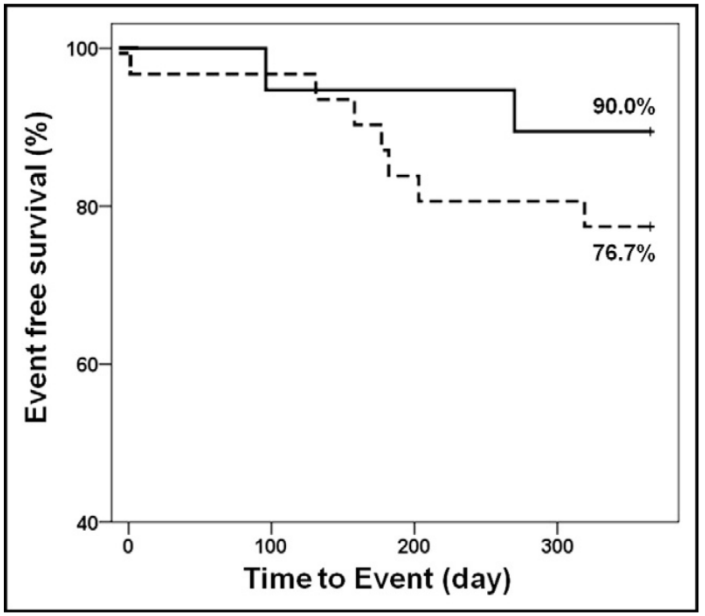


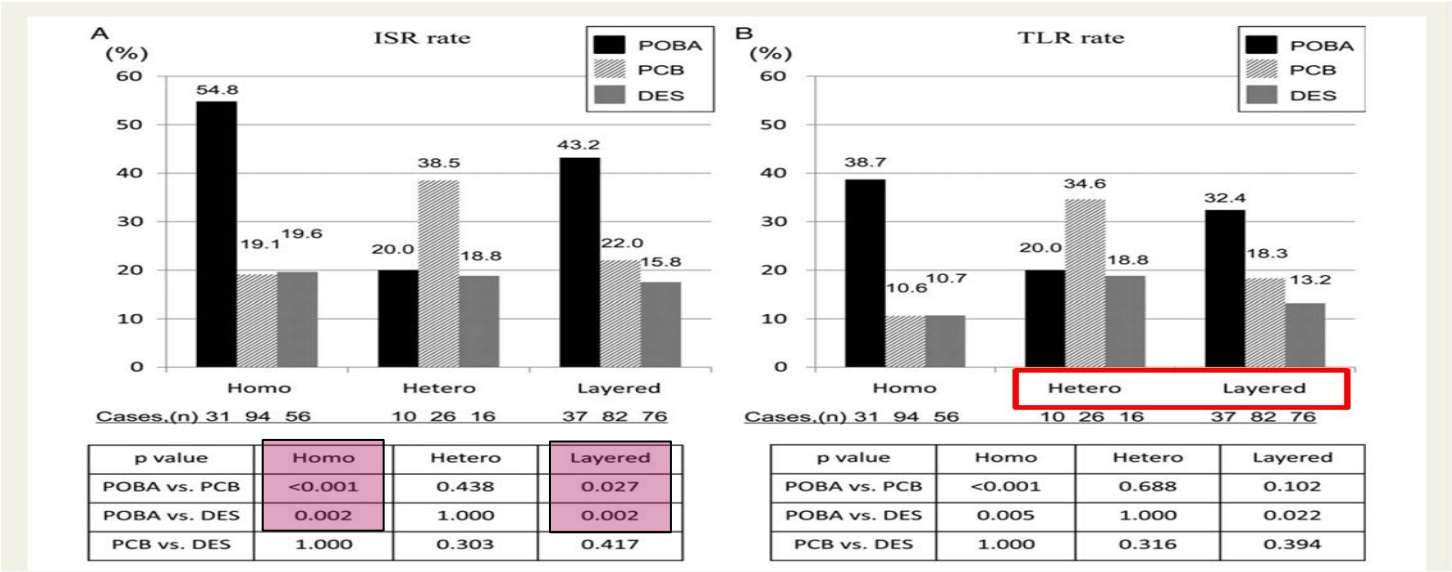
Figure 3. Kaplan-Meier estimates of cumulative freedom from composite cardiac events, including death, myocardial infarction, TVR, and stent thrombosis during 12-month follow-up in patients with restenotic lesions after DES implantation, for whom interventional procedure was deferred *(solid line)* or in whom an additional intervention was performed *(dotted line)* according to FFR (<0.80). p >0.05.

Nam CW, et al. Am J Cardiol 2011;107:1783-6

Role of Intravascular Imaging

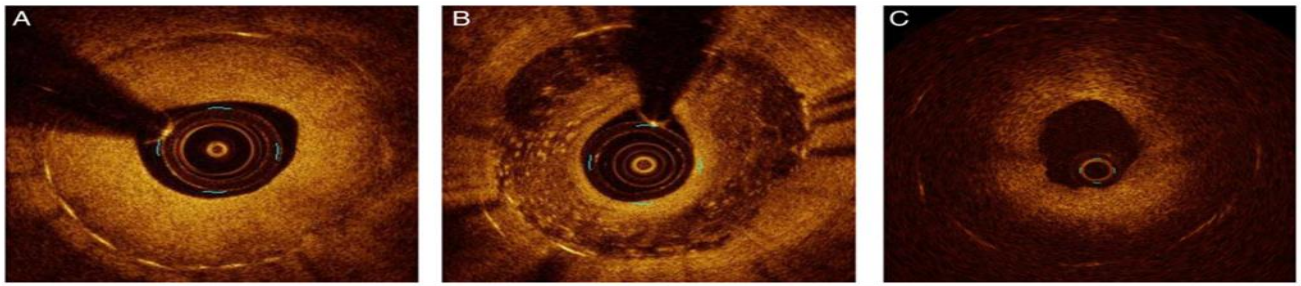
- Detect the presence of neointimal hyperplasia, device under-expansion, or edge problems, EEM

- OCT: pattern of neointimal hyperplasia, neoatherosclerosis, plaque rupture, intracoronary thrombus



p value	Homo	Hetero	Layered
POBA vs. PCB	<0.001	0.438	0.027
POBA vs. DES	0.002	1.000	0.002
PCB vs. DES	1.000	0.303	0.417

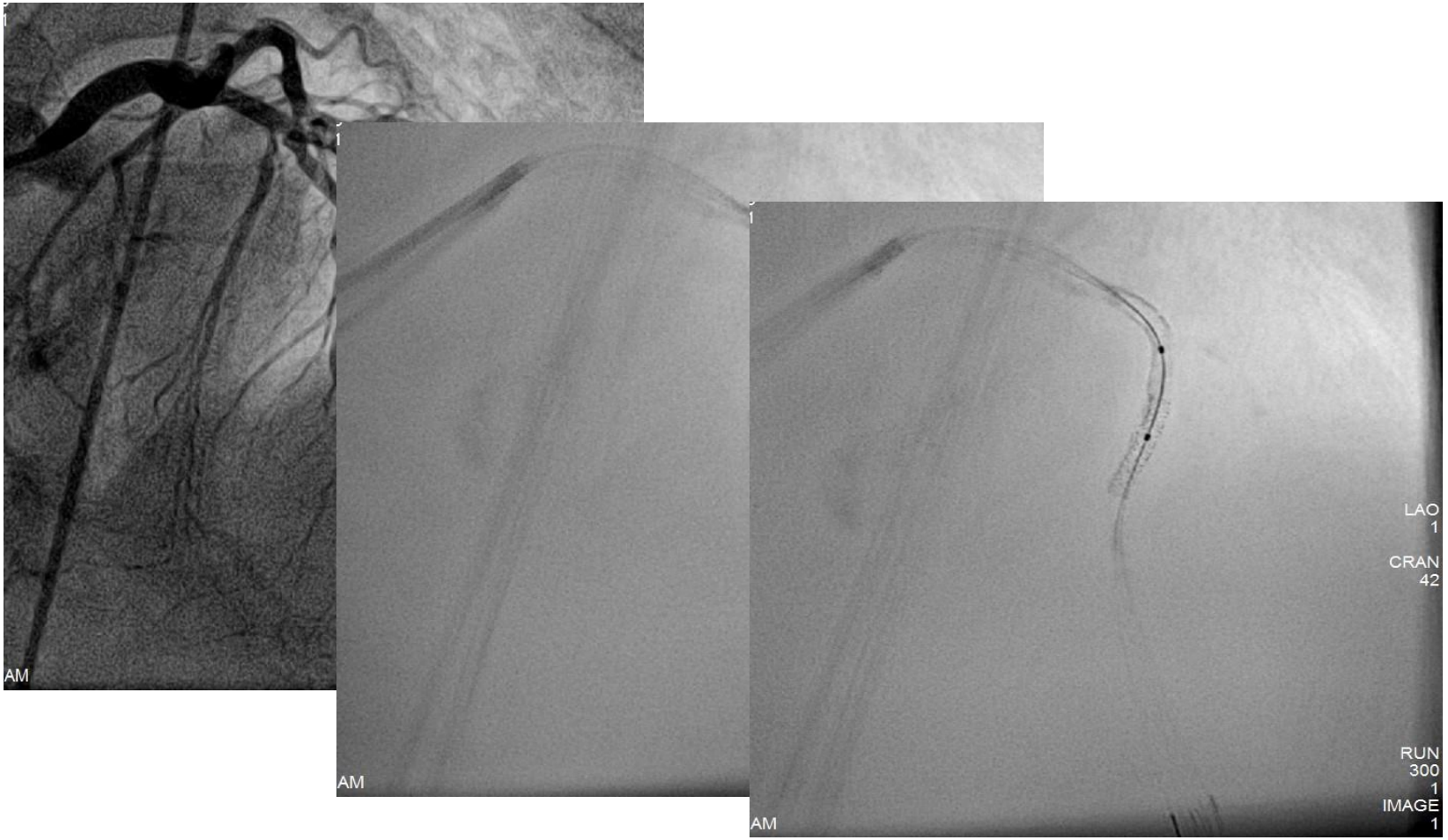
p value	Homo	Hetero	Layered
POBA vs. PCB	<0.001	0.688	0.102
POBA vs. DES	0.005	1.000	0.022
PCB vs. DES	1.000	0.316	0.394



Tada T, et al. EHJ CV imaging 2015;16:1101-11

Adequate Pre-dilation is crucial

- Lesion pre-dilation with or without noncompliant balloon remains important to treat potential underlying stent under-expansion

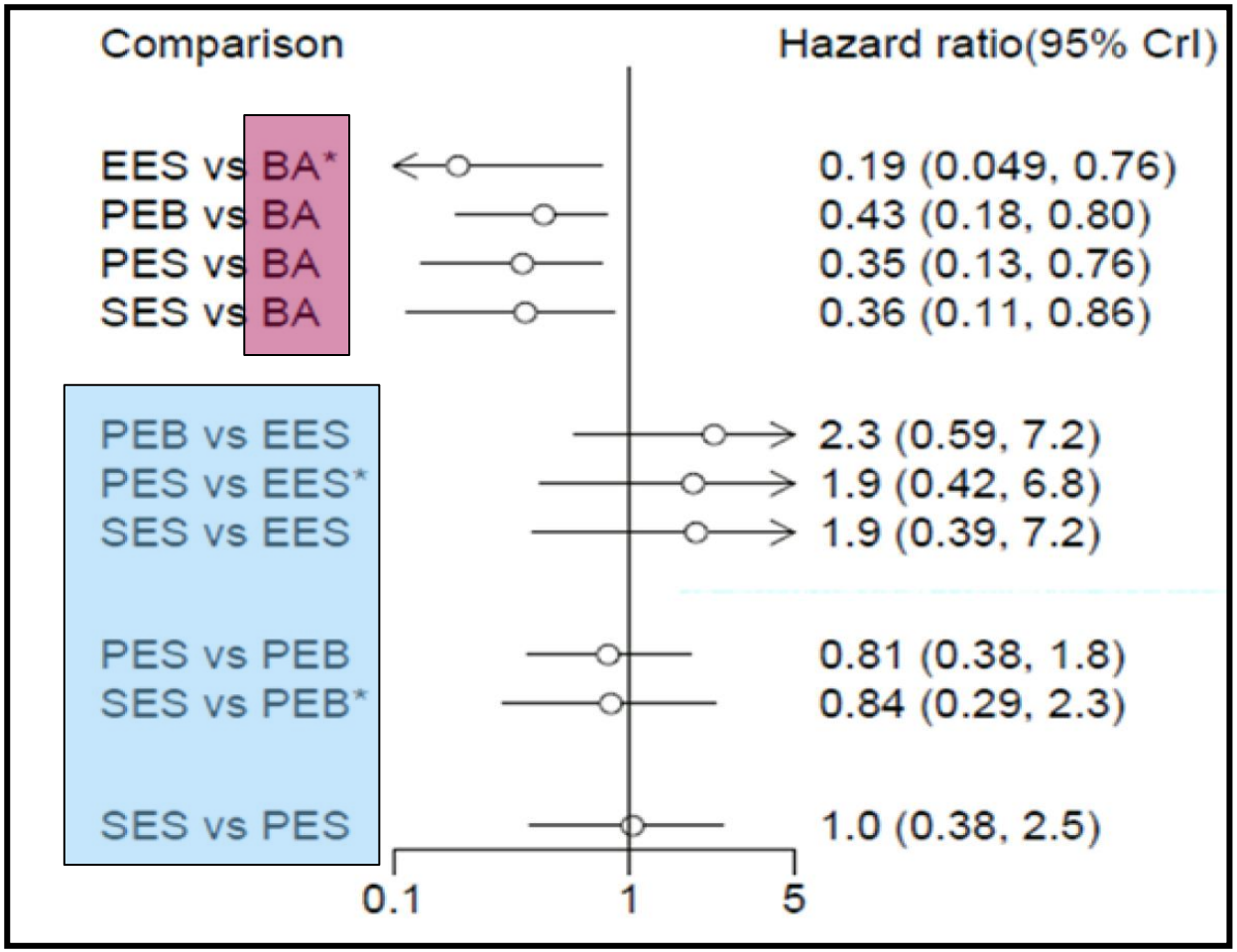


Content

Network Meta analysis of Randomized Controlled Trials

8 studies, 326 TVR over 1718 patient-years f/u in DES-ISR lesions

TVR



P<0.05

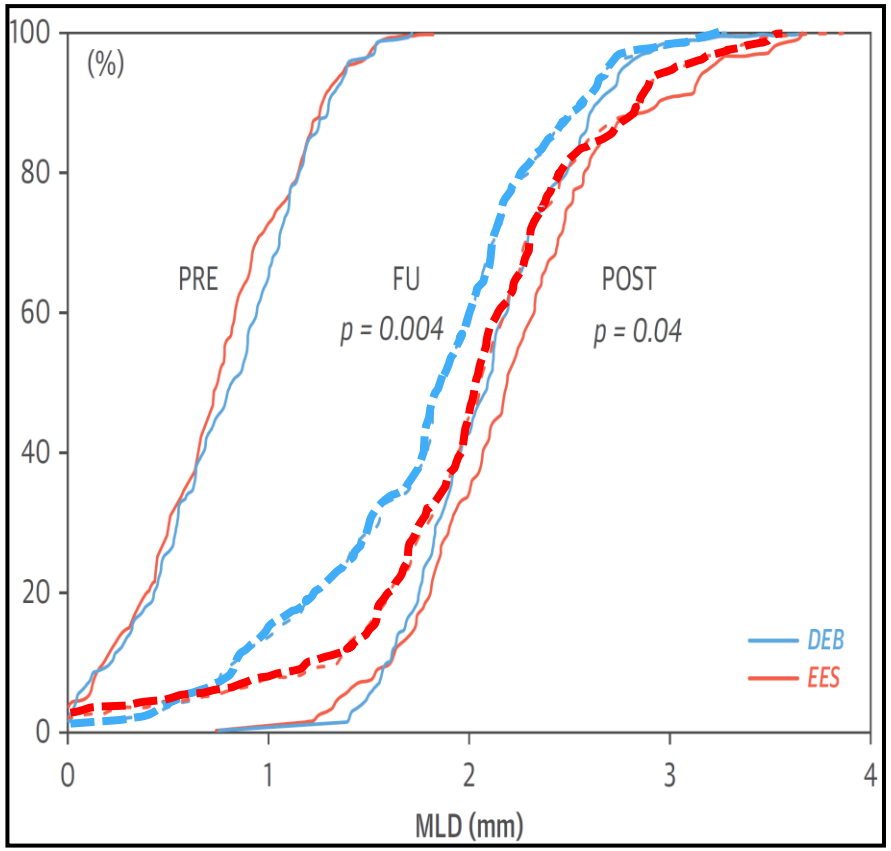
P=NS

Sethi A, et al. Circ Cardiovasc Interv 2015;8:e002778

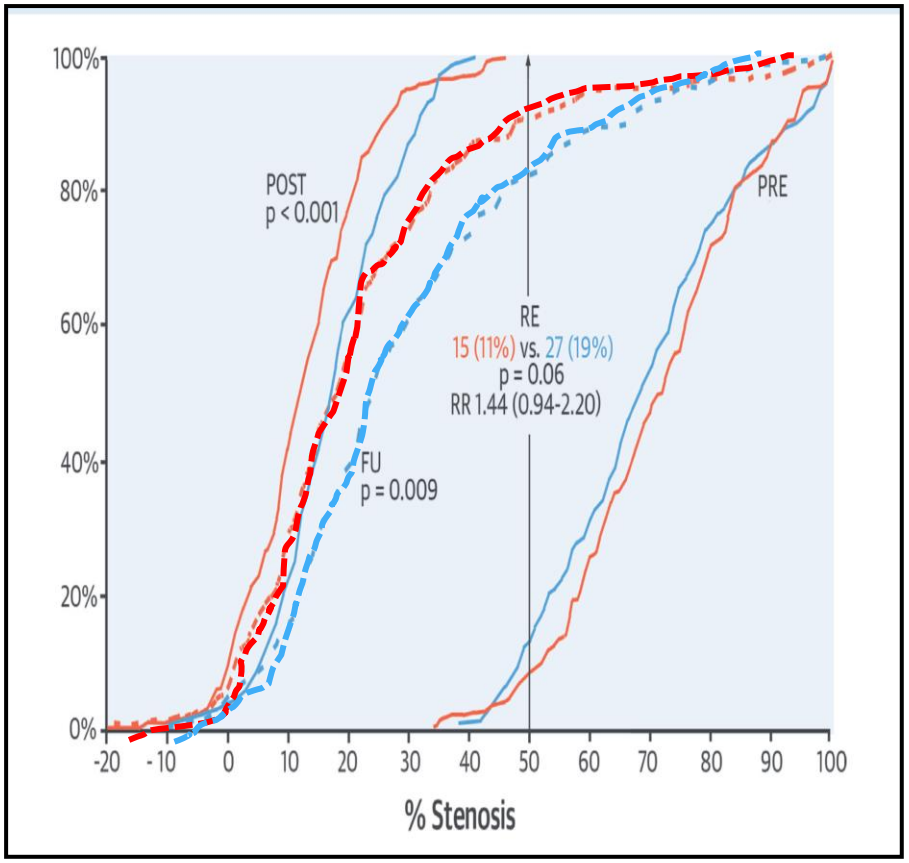
RIBS IV

PEB (n=154) vs. EES (n=155) in DES ISR
Multicenter, randomized clinical trial

MLD



% DS



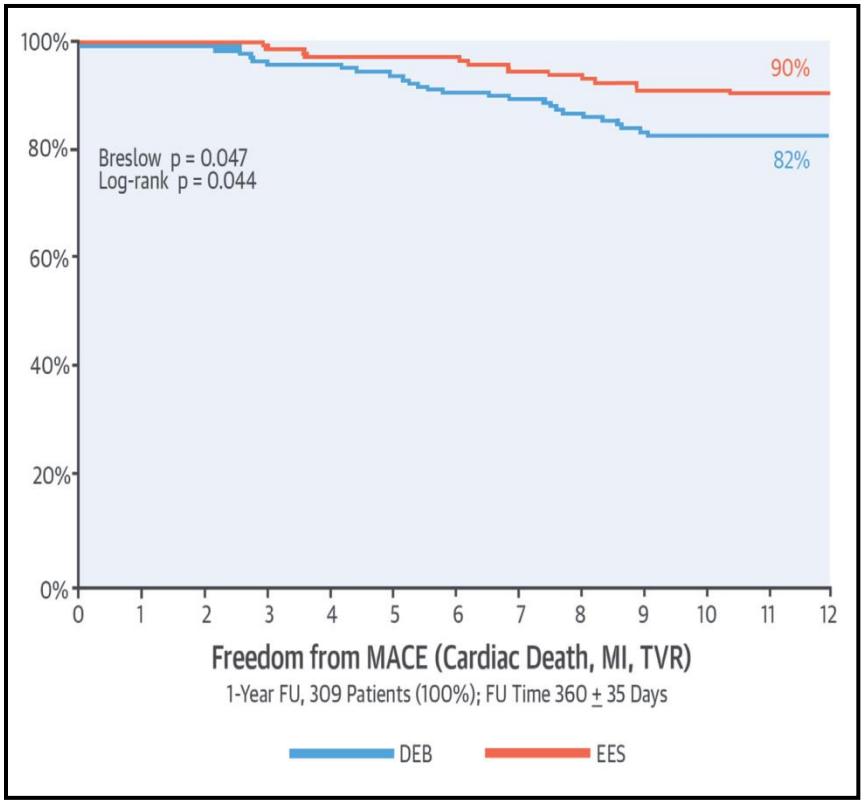
Alfonso F, et al. JACC 2015;66:23-33

RIBS IV

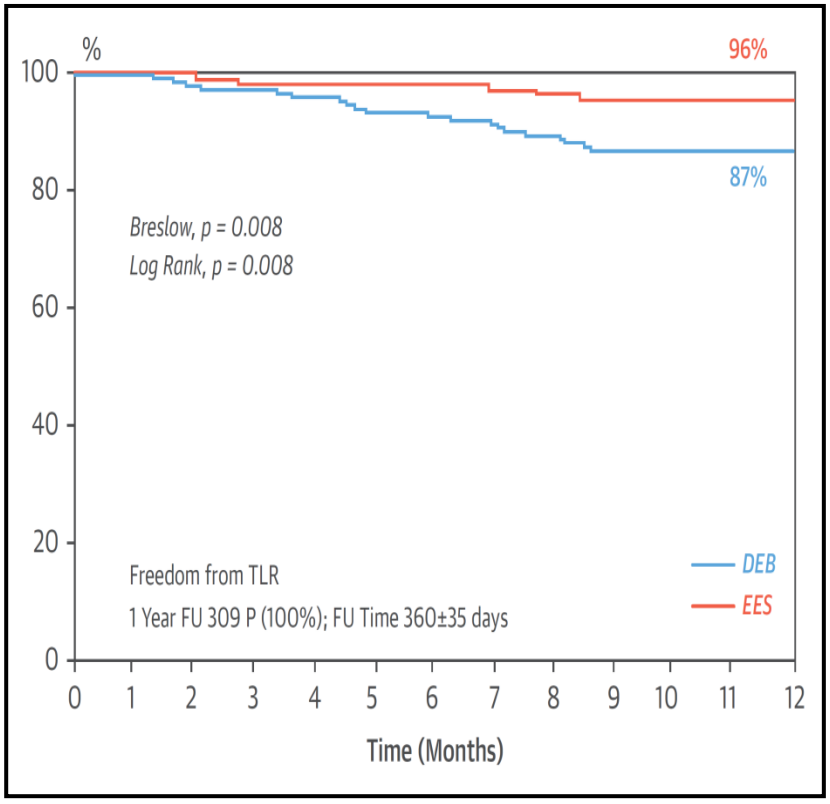
PEB (n=154) vs. EES (n=155) in DES ISR

Multicenter, randomized clinical trial

MACE



TLR



Alfonso F, et al. JACC 2015;66:23-33

Meta-analysis

% DS

	EES	DCB	SES	PES	VBT	BMS	BA	ROTA
EES	99·6 (0·98)	-9·0% (-15·8 to -2·2)	-9·4% (-17·4 to -1·4)	-10·2% (-18·4 to -2·0)	-19·2% (-28·2 to -10·4)	-23·4% (-36·2 to -10·8)	-24·2% (-32·2 to -16·4)	-31·8% (-44·8 to -18·6)

Binary restenosis

	EES	DCB	SES	PES	VBT	BMS	BA	ROTA
EES	98·5 (0·92)	0·60 (0·30-1·19)	0·44 (0·19-0·99)	0·42 (0·19-0·92)	0·20 (0·09-0·45)	0·11 (0·04-0·28)	0·10 (0·05-0·22)	0·06 (0·02-0·16)

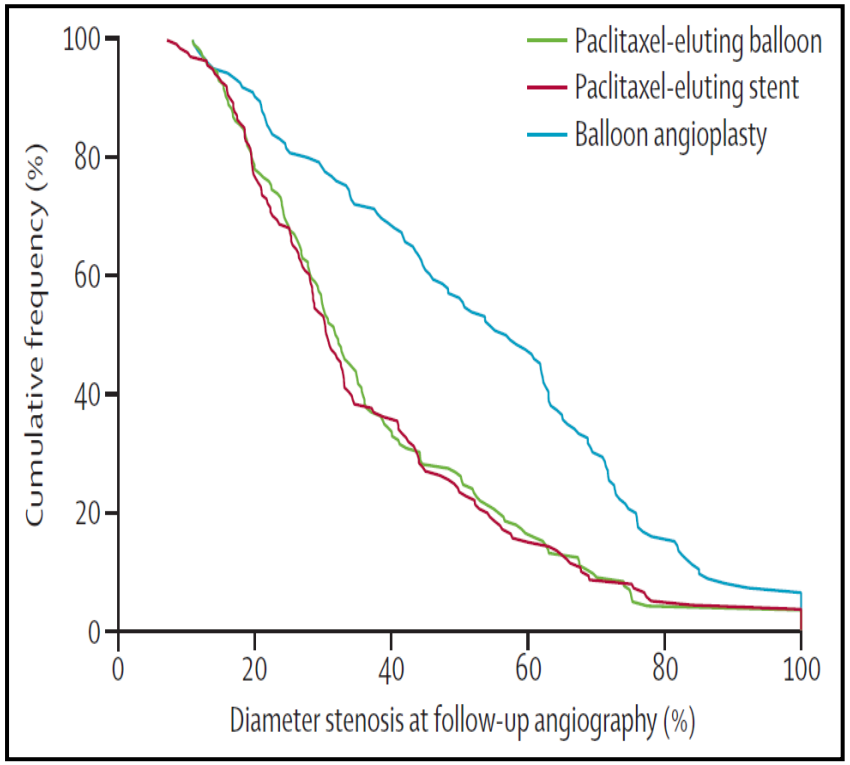
TLR

	EES	DCB	PES	SES	VBT	BMS	ROTA	BA
EES	99·1 (0·97)	0·36 (0·14-0·94)	0·34 (0·12-1·00)	0·34 (0·12-0·97)	0·17 (0·06-0·51)	0·14 (0·04-0·47)	0·09 (0·03-0·31)	0·09 (0·03-0·25)

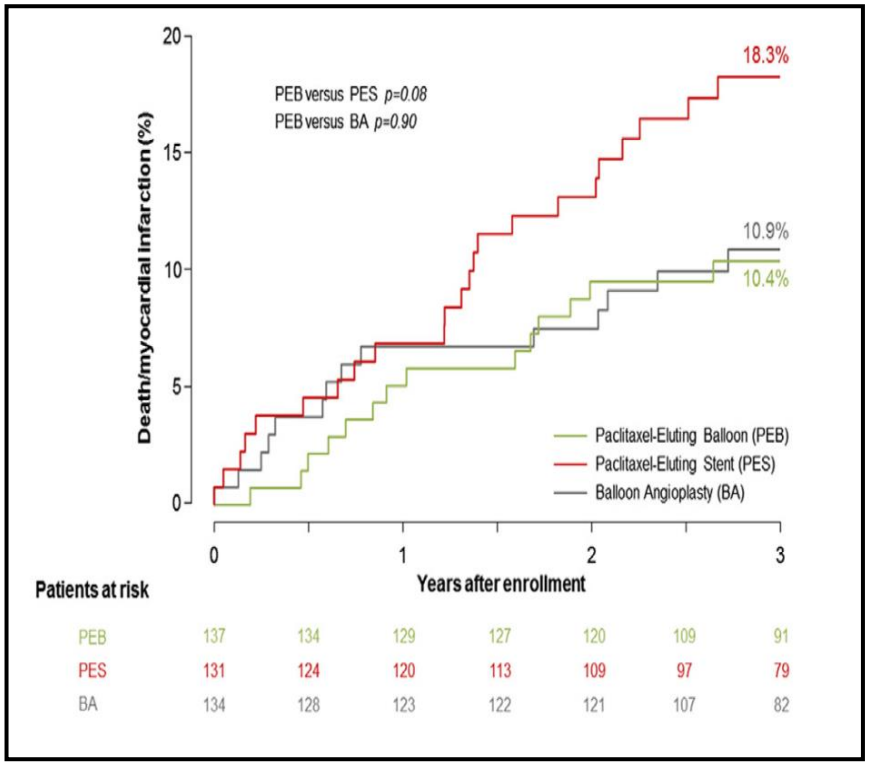
Siontis GC, et al. Lancet 2015;386:655

ISAR-DESIRE 3

Diameter Stenosis at 8 Months



Death/MI during 3 years



Kufner S, et al. JACC Cardiov Int 2015;8:877

Treatment of ISR in Real World Clinical Practice

ORIGINAL ARTICLE

Korean J Intern Med 2016;31:501-506
http://dx.doi.org/10.3904/kjim.2014.189

CrossMark
click for updates

KJIM

The efficacy and safety of drug-eluting balloons for the treatment of in-stent restenosis as compared with drug-eluting stents and with conventional balloon angioplasty

Pyung Chun Oh, Soon Yong Suh, Woong Chol Kang, Kyounghoon Lee, Seung Hwan Han, Taehoon Ahn, and Eak Kyun Shin

Clinical Outcomes

Table 3. Clinical outcomes during follow-up

Variable	DEB (n = 58)	DES (n = 54)	BA (n = 65)	*p*-value		
				DEB vs. DES	DEB vs. BA	DES vs. BA
Follow-up period, mon	17.2 ± 8.7	16.9 ± 13.4	15.4 ± 11.6	0.889	0.352	0.529
MACEs	5 (8.6)	5 (9.3)	9 (13.8)	1.000	0.407	0.571
Cardiac death	1 (1.7)	2 (3.7)	2 (4.1)	0.608	1.000	1.000
Myocardial infarction	0	2 (1.9)	0	0.230	-	0.204
TLR	4 (6.9)	1 (3.7)	7 (10.8)	0.365	0.537	0.070
Stent thrombosis	0	2 (3.7)	1 (1.5)	0.230	1.000	0.590

Values are presented as mean ± SD or number (%).

DEB, drug-eluting balloon; DES, drug-eluting stent; BA, conventional balloon angioplasty; MACE, major adverse cardiac event; TLR, target lesion revascularization.

Oh PC, et al. KJIM 2016;31:501-6

Role of DEB in DES ISR lesions

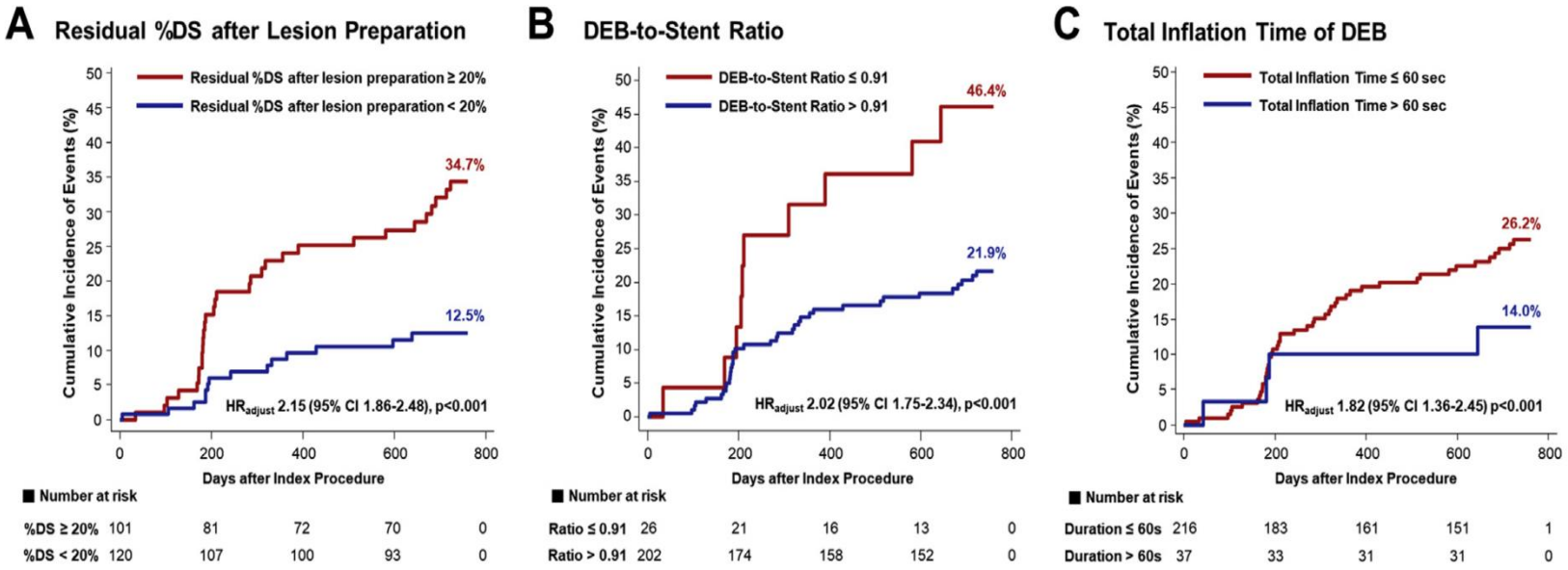
- Avoid multiple metal layers
- Save large side br
- Homogenous drug transfer to the arterial wall
- May be better in non-focal type ISR
- Avoid prolonged DAPT, suitable high bleeding risk

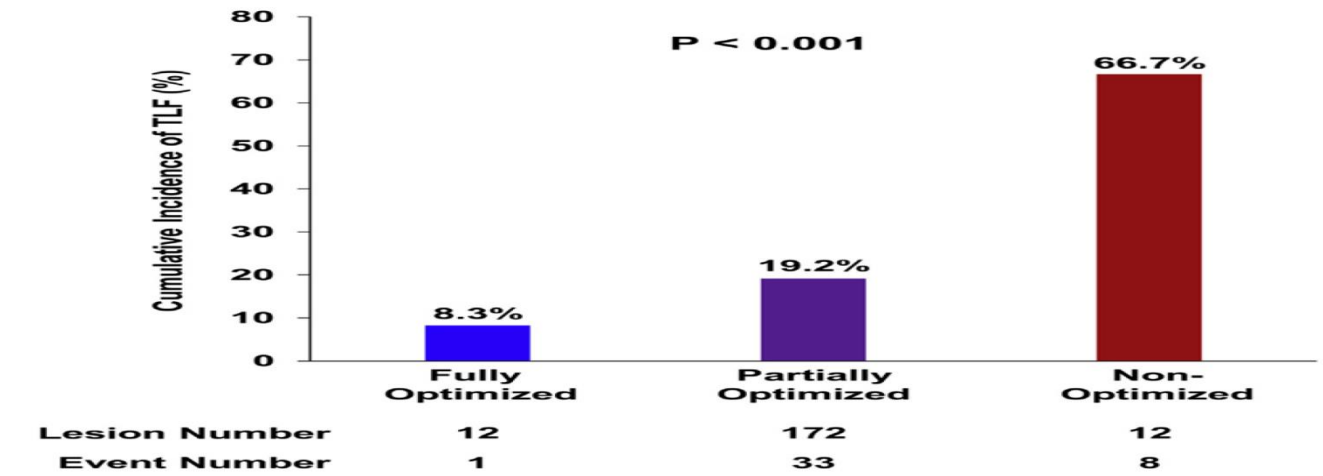
Role of DES in DES ISR lesions

- Suitable for stent fracture
- Suitable for restenosis extending outside the stent edge
- Suitable for suboptimal results after lesion pre-dilation
- EES are better in recurrent DEB failure ISR lesions.

How to perform DEB?

Factors for DEB failure in DES ISR lesion



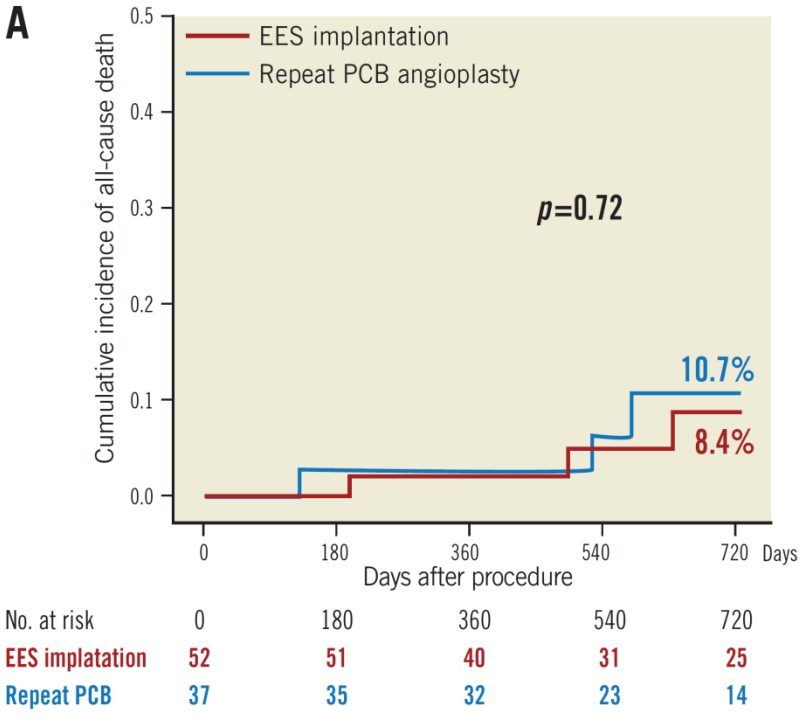


Rhee TM, et al. JACC CVInt 2018;11:969

Content

DEB (n=40) vs EES (n=53) in Recurrent DEB failure of ISR Lesions

All cause of death



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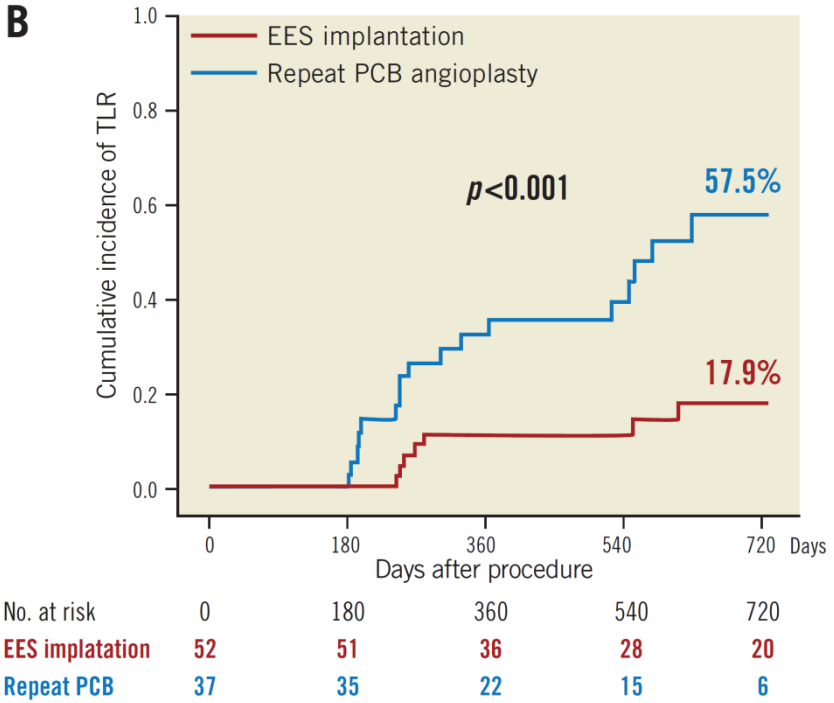
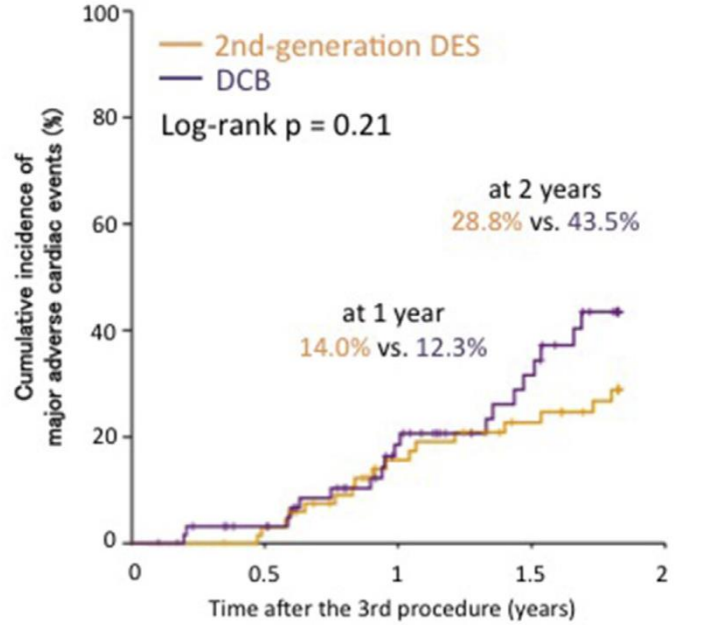


Kubo S, et al. EuroIntervention 2015;10:e1-8

DEB (n=89/68 pts) vs EES (n=82/65pts) in Recurrent Multimetal-layered ISR

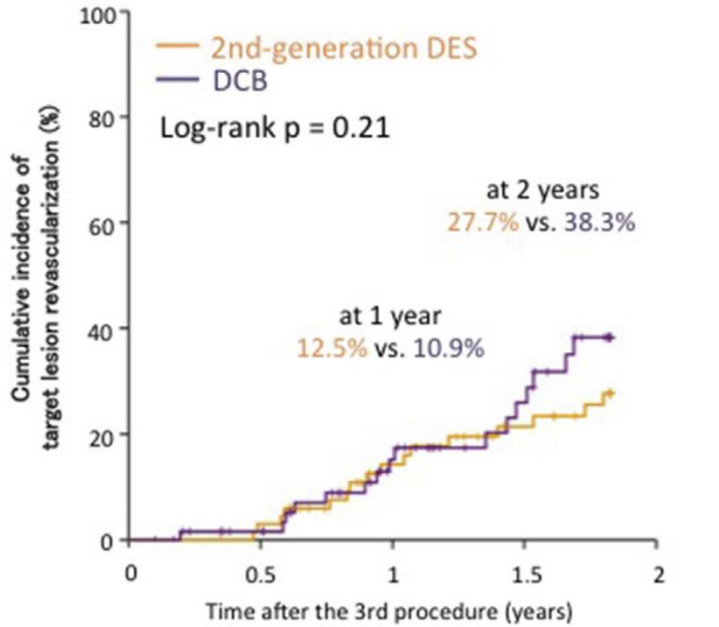
MACE (death, MI, TLR)



Number of events (number at risk)

DES	0 (68)	1 (67)	9 (51)	13 (43)	17 (33)
DCB	0 (65)	3 (57)	8 (45)	14 (28)	20 (13)

TLR



Number of events (number at risk)

DES	0 (68)	1 (67)	8 (51)	12 (43)	16 (33)
DCB	0 (65)	2 (57)	7 (45)	11 (29)	17 (14)

Kubo S, et al. EuroIntervention 2015;10:e1-8

Content

24 MAY 2017

MagicTouch™ sirolimus coated calloon: one year clinical outcomes

Insights from Nanolutè prospective registry

Titled "One year clinical outcomes of percutaneous treatment with world's first Sirolimus eluting balloons: Results from Nanolutè prospective registry" the article presents the results of analyses of patient-level data from the NANOLUTÈ clinical program, which enrolled a total of 408 patients who received a MagicTouch™ Sirolimus Coated Balloon as participants in study conducted in India.

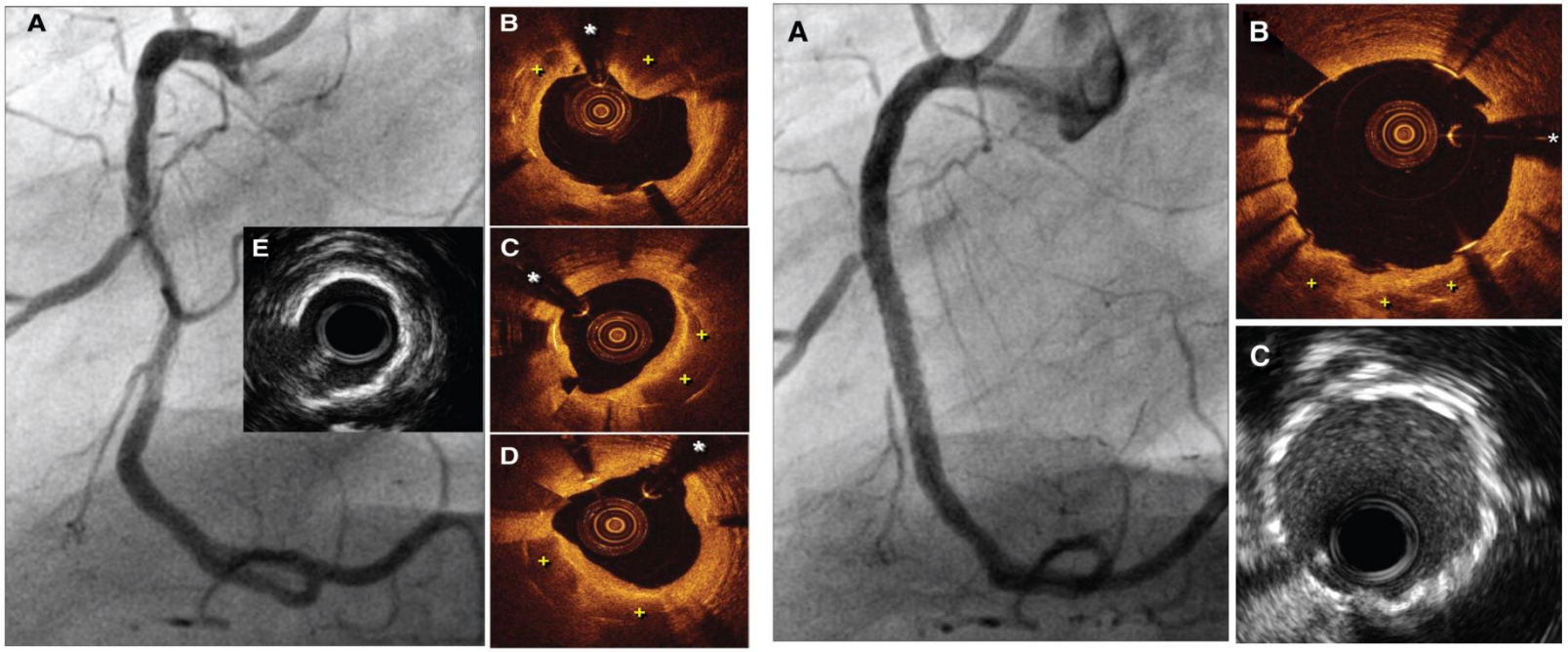
In NANOLUTÈ study, almost half of the patients presented with diabetes mellitus (44.36%) and acute coronary syndrome (47.55%). Results showed high procedural success rate of 99.51%. SCB-only strategy was employed in a great proportion of the cases (93.14%). There were no procedural deaths reported and the overall 12-month major adverse cardiac event (MACE) was 4.61% (14 cases of TLR, 1 case of myocardial infarction and 1 case of cardiac death).

Sirolimus coated balloon is indicated for lesions in small vessels, in-stent restenosis (ISR) and bifurcation lesions. Subgroup analyses for both small vessel and ISR groups were performed. Results revealed that MACE rate in small vessel group was 4.06% at 12 months with no myocardial infarction reported while in ISR group; MACE was reported as 6.17% at 12 months with no cardiac death reported. The strong performance of the MagicTouch SCB in patients with small vessels and ISR in real-world clinical practice advances the growing body of evidence that warranted the device's efficacy and safety.

Dr. Cortese concluded: "*SCB might constitute a new therapeutic option in the setting of complex coronary lesions, also considering the good deliverability and tractability of SCB. Good results were reported in complex patients like with SVD and ISR supports its efficacy*".

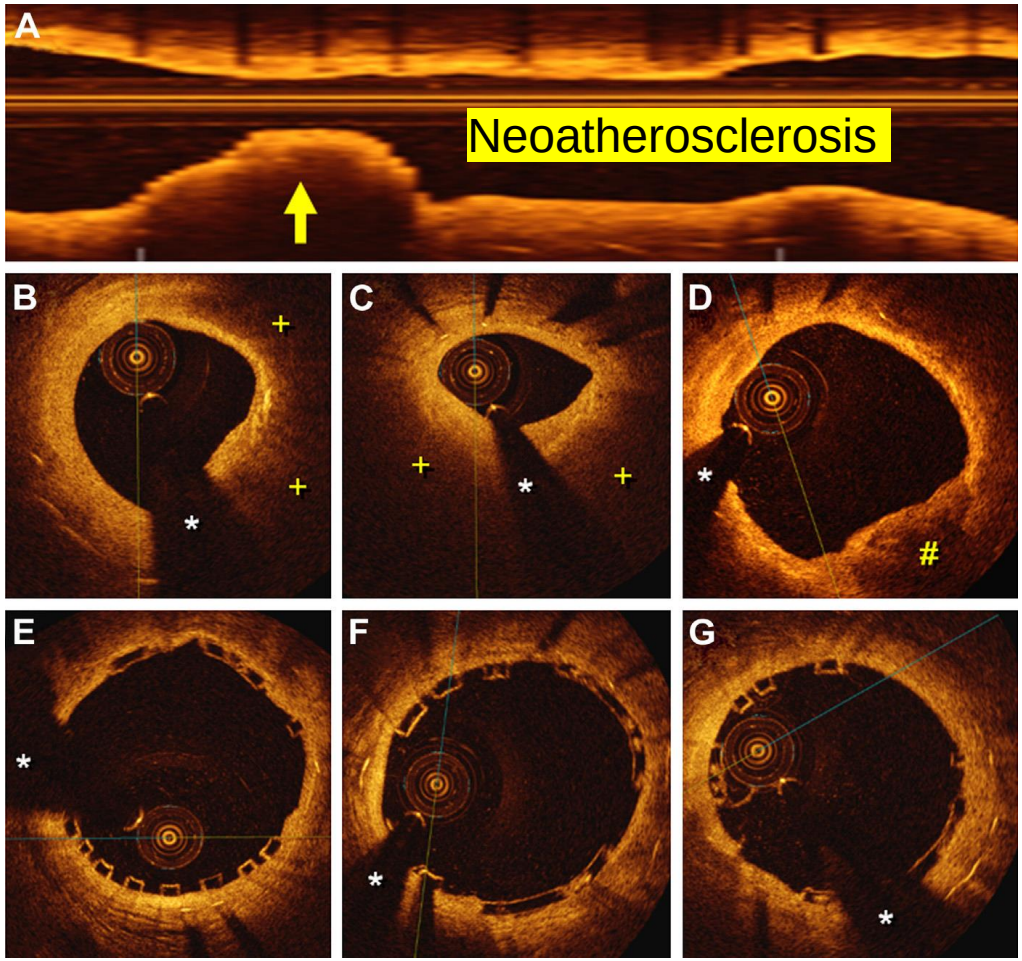
Rotational Atherectomy

- Failed to show benefit in ISR lesion compared to other tx
- RA may still be required as a **bailout strategy in patients with un-dilatable ISR lesions**
  - Severely under-expanded stents
  - Calcified intra-stent neoatherosclerosis



Kobayashi Y, et al. CCI 2001;52:208-11
Vales L, et al. Int J Angiol 2013;22:63-8
Alfonso F, et al. Circ Cardiovasc Interv

BRS for DES-ISR



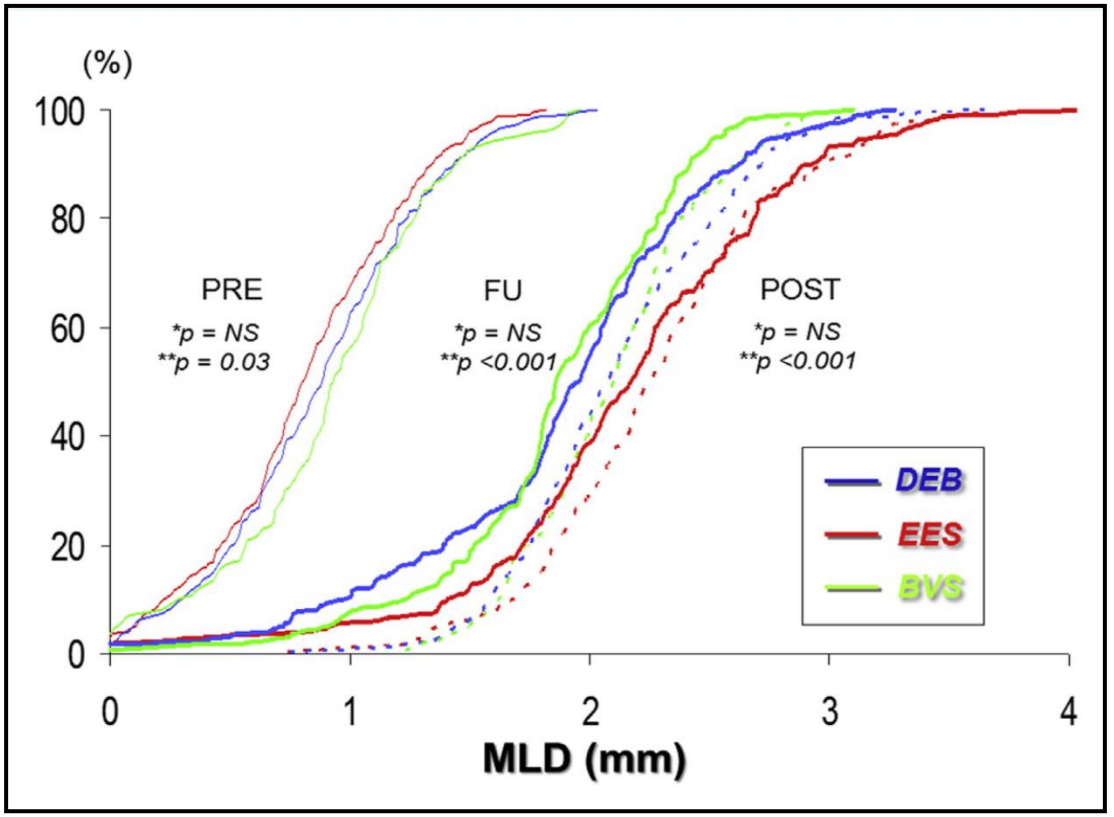
Alfonso F, et al. JACC 2014;63:2875

- Advantage: preventing early recoil, strong anti-proliferative property, device disappear, avoiding the presence of multiple stent layers (“onion-skin” phenomenon)

- **Potential limitations**: lumen crowding due to strut thickness (particularly in small vessels), device flexibility, questions regarding radial strength and recoil, risk for stent thrombosis

BVS vs DEB, EES in RIBS IV: MLD

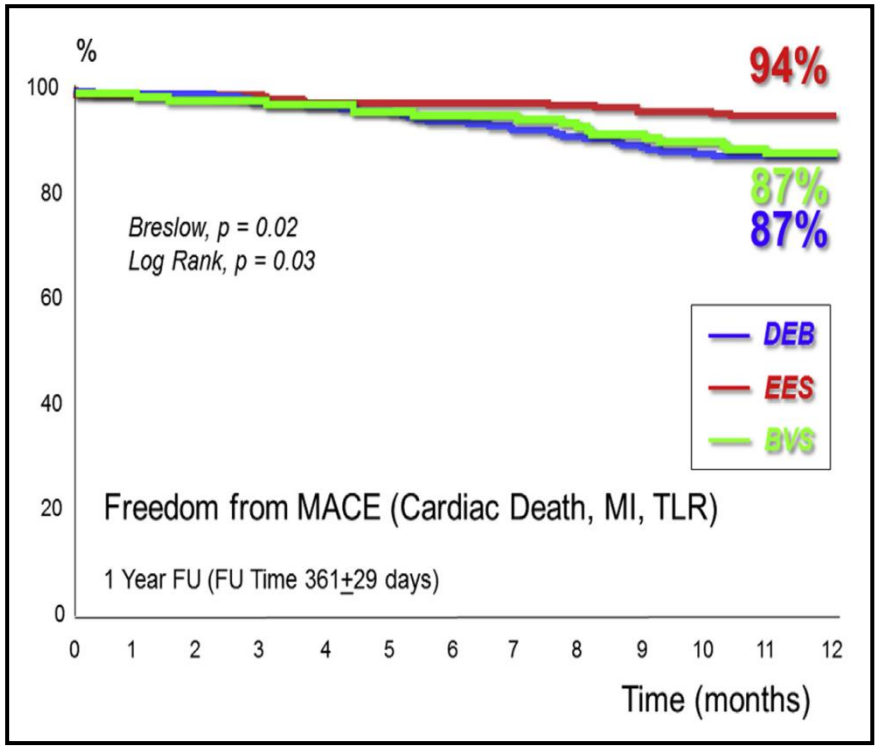
BMS and DES ISR
BVS: 141patients
DEB: 249
EES: 249



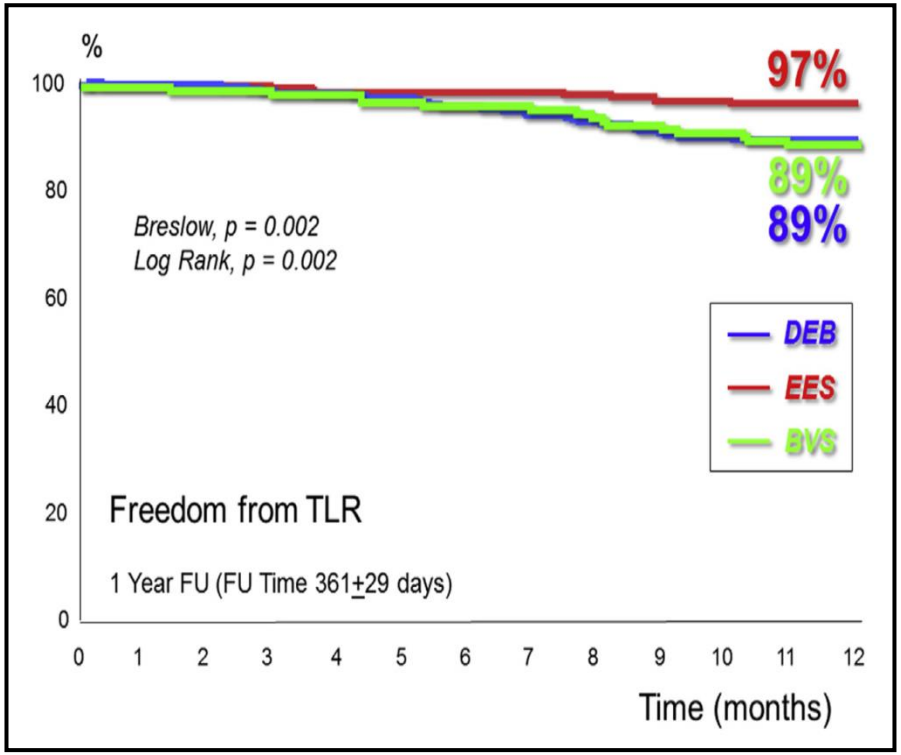
Alfonso F, et al. JACC Int 2017;10:1841

BVS vs DEB, EES in RIBS IV: MACE, TLR

MACE



TLR



BMS and DES ISR
BVS: 141
DEB: 249
EES: 249

Alfonso F, et al. JACC Int 2017;10:1841

DES ISR (%DS >50%)

- Avoid oculo-stenotic reflux
- FFR

If significant,

- IC imaging (especially OCT) guided PCI
- Lesion pre-dilation with NC balloon or scoring balloon

Patients with high bleeding risk	Stent fracture
Non-focal type ISR	Stent edge restenosis, dissection
Bifurcation lesion	Inadequate result of pre-dilation
DEB	2nd generation **DES**

If recurrent

EES → CABG ← DEB or EES ?

Thank you for attention !

DES in DES-ISR: Homo vs Hetero DES

- Hetero DES implantation in DES-ISR lesions might overcome drug resistance or specific polymer related problems.
- Overall, results remain inconclusive, and the evidence of favoring a switch strategy is weak. (ISAR-DESIRE 2 and RIBS III trials).

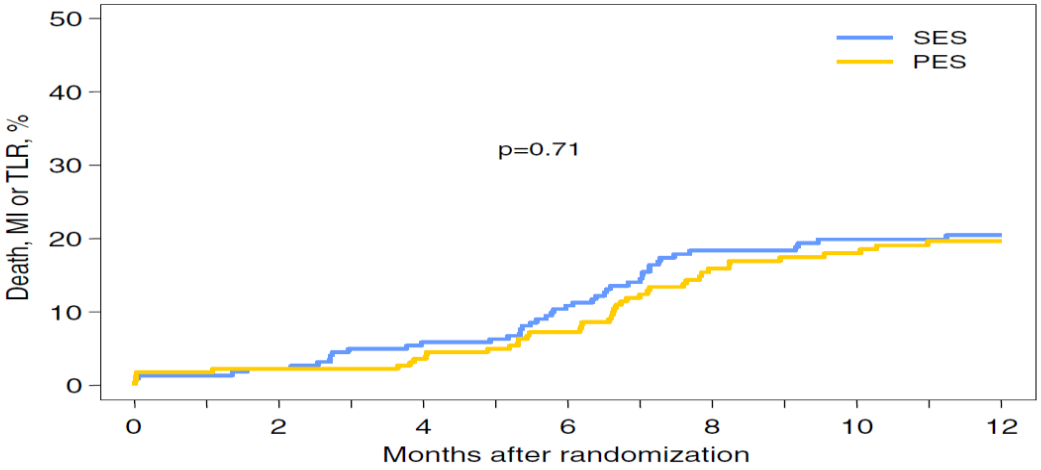


Figure 3 **Composite of Death, MI, or TLR**

The **gold line** indicates PES; the **blue line** indicates SES. MI = myocardial infarction; TLR = target lesion revascularization; other abbreviations as in Figure 1.

SES vs PES in SES-ISR lesions (ISAR-DESIRE2)

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

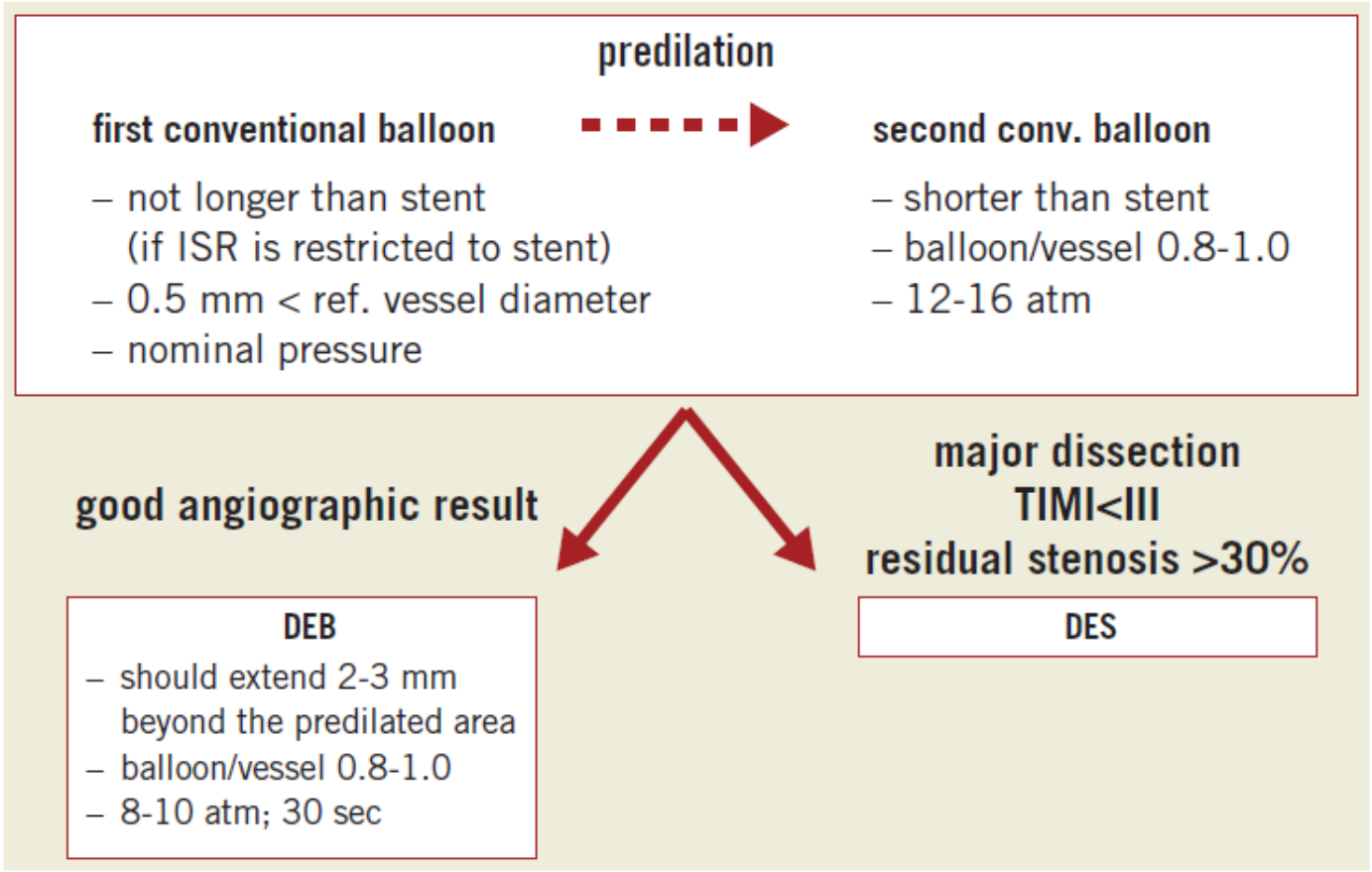


Figure 1. *Treatment recommendations for in- stent restenosis.*