DEB Strategy for In-Stent Restenosis

2018. 11. 29
Eun-Seok Shin MD/PhD

Division of Cardiology
Ulsan Medical Center
Ulsan, Korea

Presenter disclosure information

Presenter: Eun-Seok Shin, MD/PhD

Title: DEB Strategy for In-Stent Restenosis

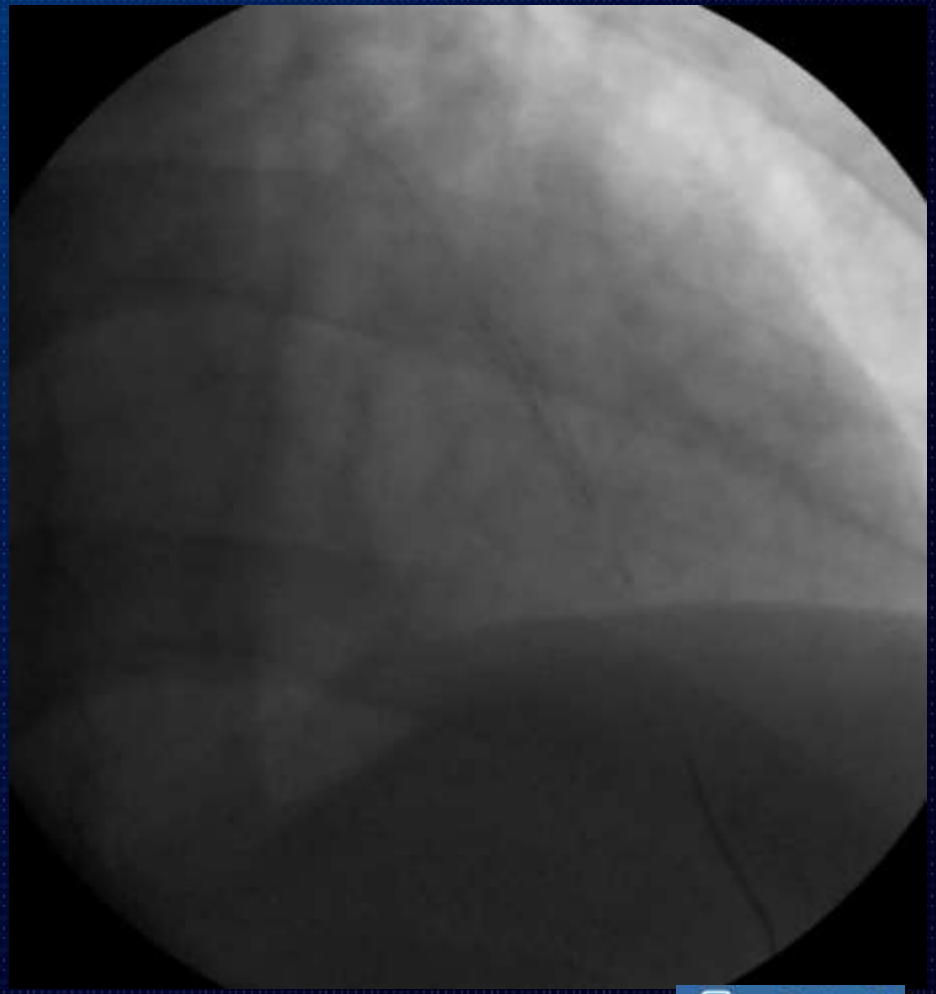
No relationships to disclose
No industry sponsorship

울산병원
ULSAN MEDICAL CENTER

62/M, after 6 months (1st ISR)

Focal DES-ISR with angina

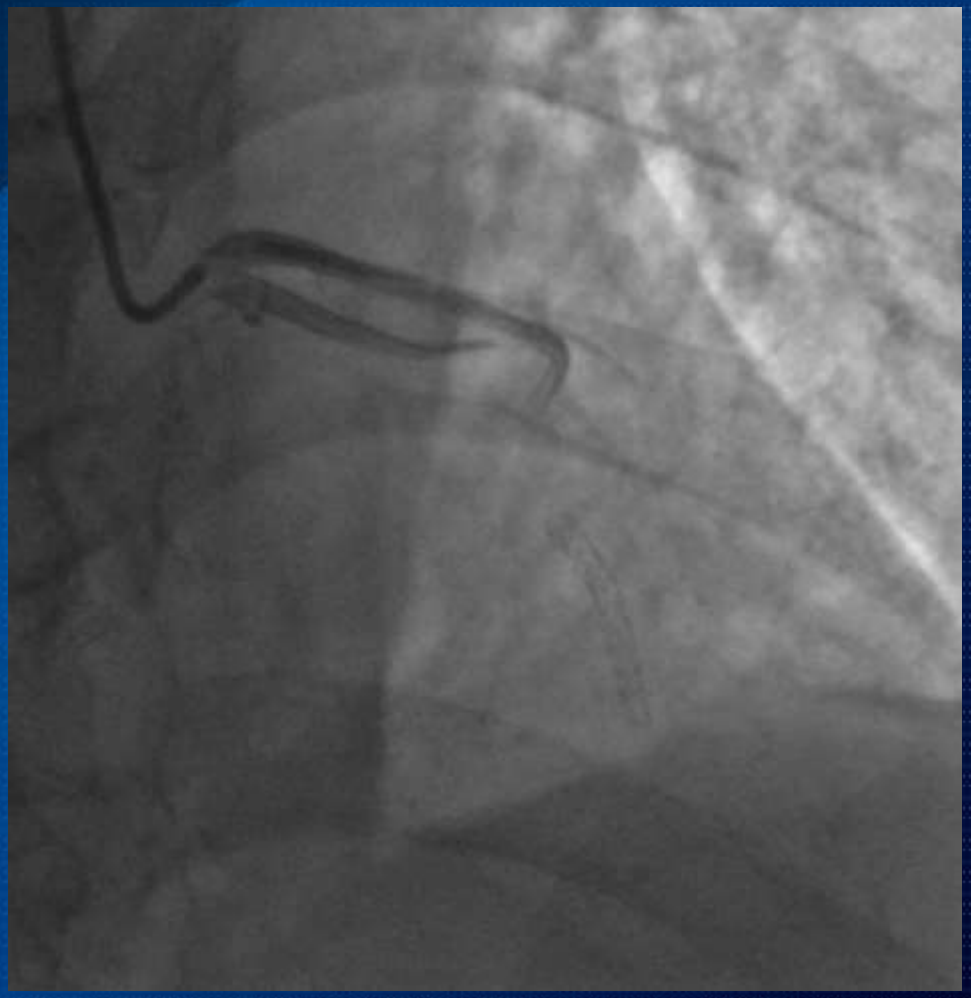
POBA



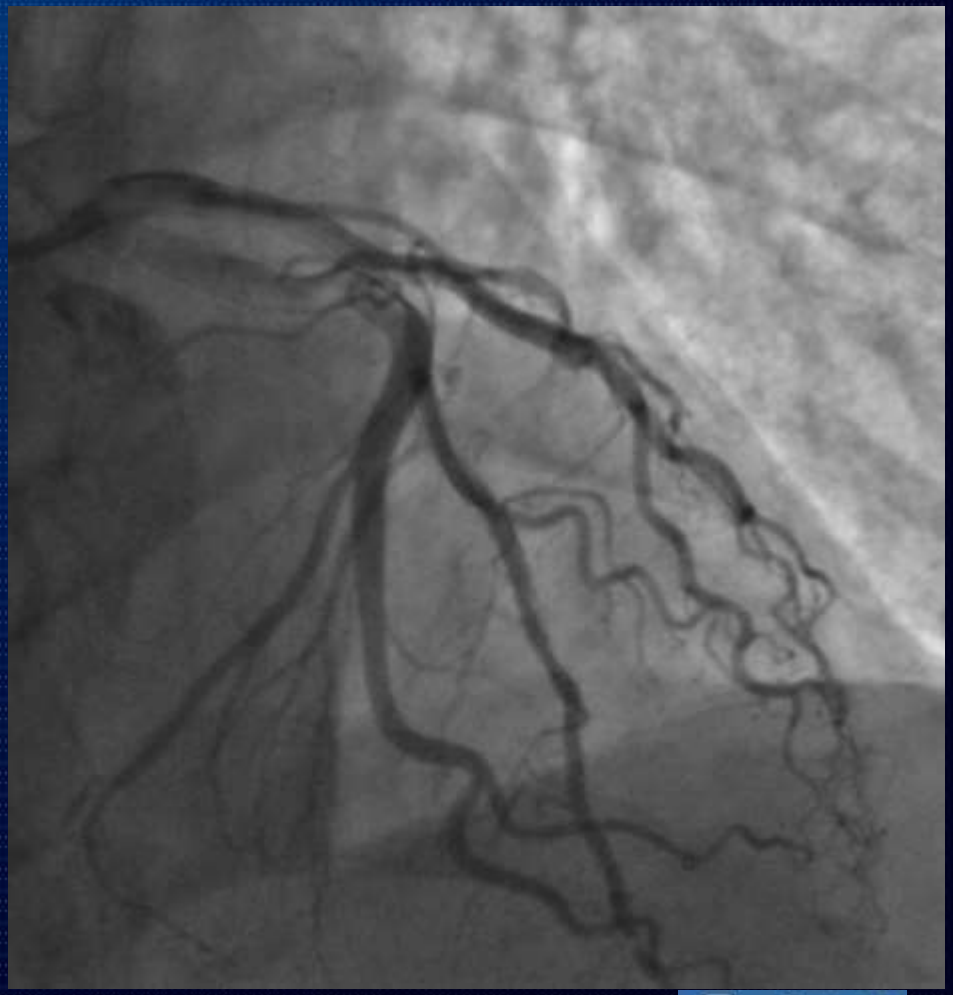
울산병원

After 10 months (2nd ISR)

2nd ISR with angina



Cutting balloon



울산병원
ULSAN MEDICAL CENTER

After 7 months (3rd ISR)

3rd ISR with angina

DES stenting

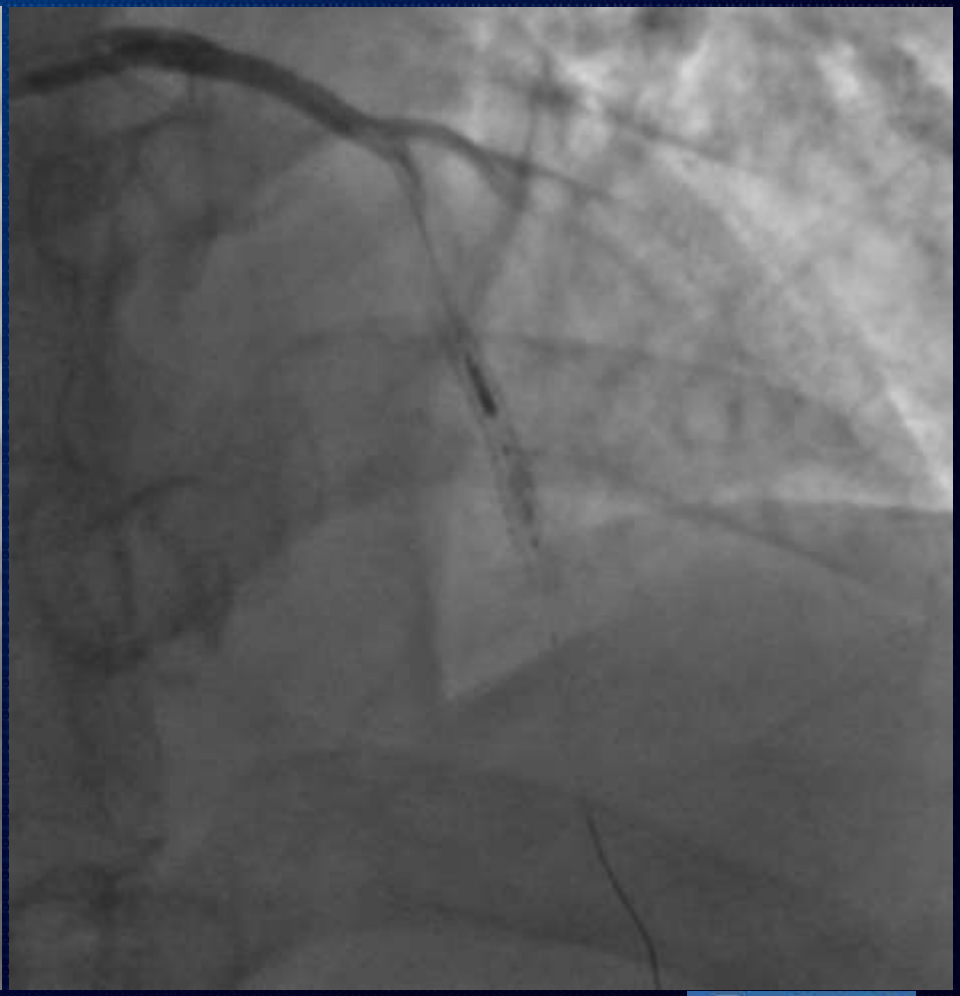
sandwich technique

울산병원

After 8 months (4th ISR)

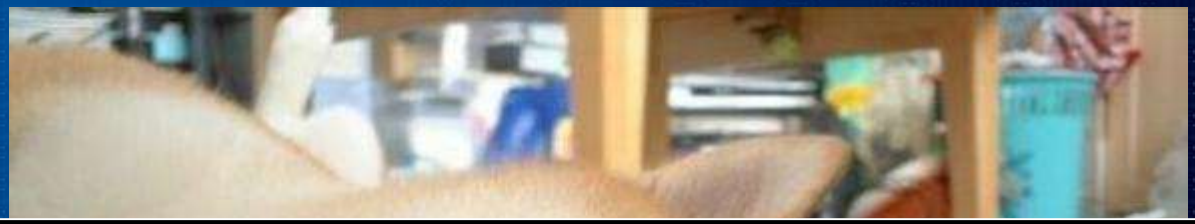
4th ISR with angina

IVUS could not passage



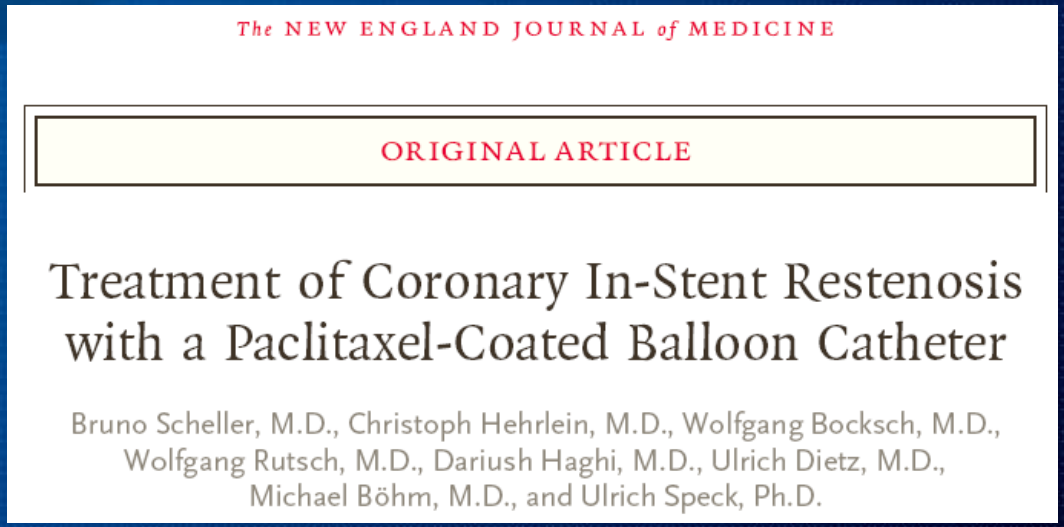
울산병원

What should I do!



Restenotic lesion remains a challenging!

울산병원
ULSAN MEDICAL CENTER



Primary endpoint (late lumen loss in-segment)

Uncoated balloon	DCB
0.74 ± 0.86 mm	0.03 ± 0.48 mm

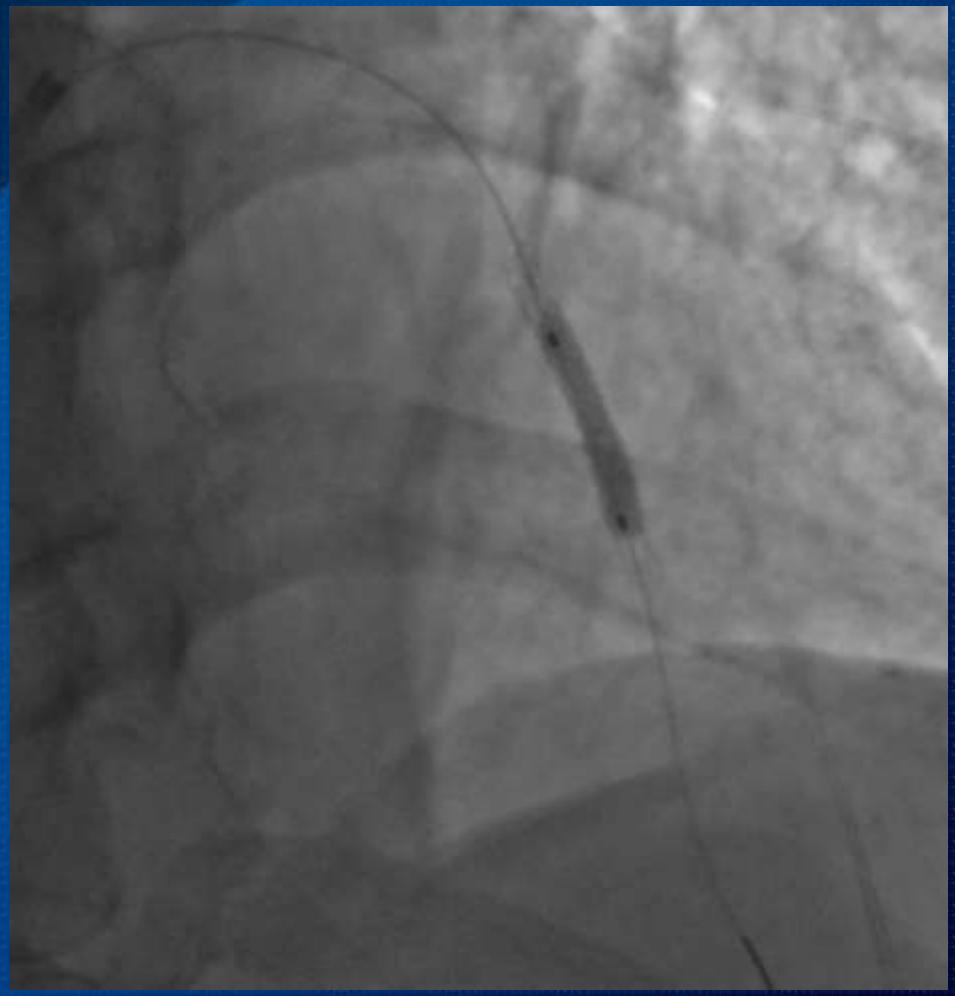
52 patients with in-stent restenosis

New Engl J Med 2006, 355: 2113-24

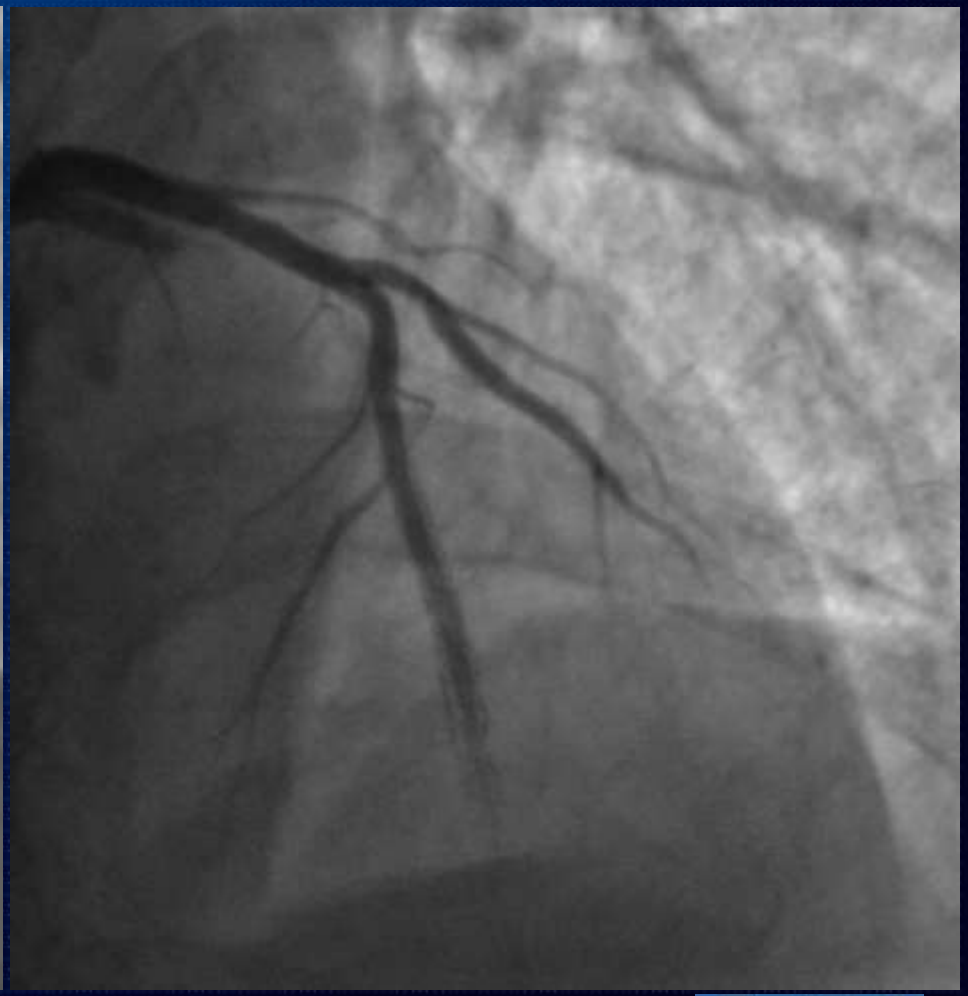
울산병원

4th ISR treated by DCB

DCB apply



Final CAG



울산병원

Drug-coated balloon

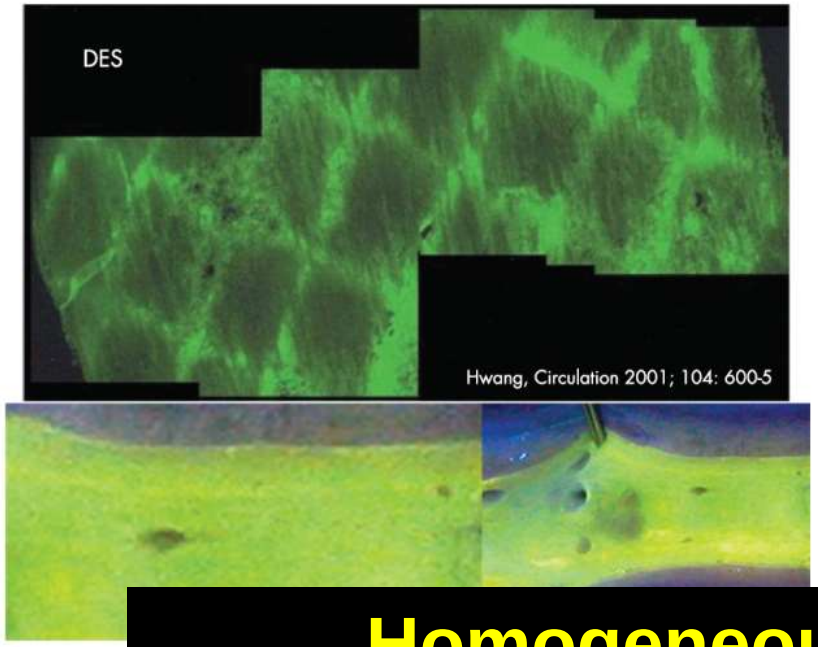


Figure 1 Inhomogeneous drug distribution from luminal surface after implantation of a drug-eluting stent (DES) (reprinted with permission from Hwang CW, Wu D, Edelman ER. Physiological transport forces govern drug distribution for stent-based delivery. *Circulation* 2001;104:600–5).[11] Homogeneous drug distribution from luminal surface after an inflation of 60 s with a drug-coated balloon (porcine coronary artery, experiments done by Nicola Kaufels, Berlin, Germany).

Drug Eluting Stent

- Slow release
- Persistent exposure
- ~ 100 - 200 µg dose
- Polymer
- Stent mandatory

Drug Coated Balloon

- Immediate release
- Short-lasting exposure
- ~ 300 - 600 µg dose
- No polymers
- Premounted stent optional

Homogeneous drug delivery
Immediate drug release without polymer
No foreign material left behind
Reducing anti-platelet therapy
Lower restenosis rates

Circulation 2004; 110: 810-4
Heart 2007, 93: 539-41

울산병원

DCB for coronary artery

1. In-stent restenosis

2. De-novo lesions

울산병원
ULSAN MEDICAL CENTER

DCB for coronary artery

1. In-stent restenosis

2. De-novo lesions

울산병원

12 RCTs for ISR lesions

ISR	Intervention	N	End point	Study
BMS	PCB-POBA	108	In-segment LLL	PACCPCATH ISR
	PCB-PES	131	In-segment LLL	PEPCAD 2 ISR
	PCB-EES	189	In-segment MLD	RIBS V
	PCB-EES	136	LLL	ISR study
DES	PCB-POBA	110	LLL	PEPCAD-DES
	PCB-POBA	208	TVF	Habara et al
	PCB-POBA	50	In-segment LLL	Habara et al
	PCB-PES	402	In-segment DS	ISAR-DESIRE 3
	PCB-PES	220	In-segment LLL	PEPCAD-ISR-China
	PCB-EES	309	In-segment MLD	RIBS IV
	PCB-EES	172	In-segment LLL	RESTORE
	PCB-EES	278	In-segment MLD	DARE

울산병원

12 RCTs for ISR lesions

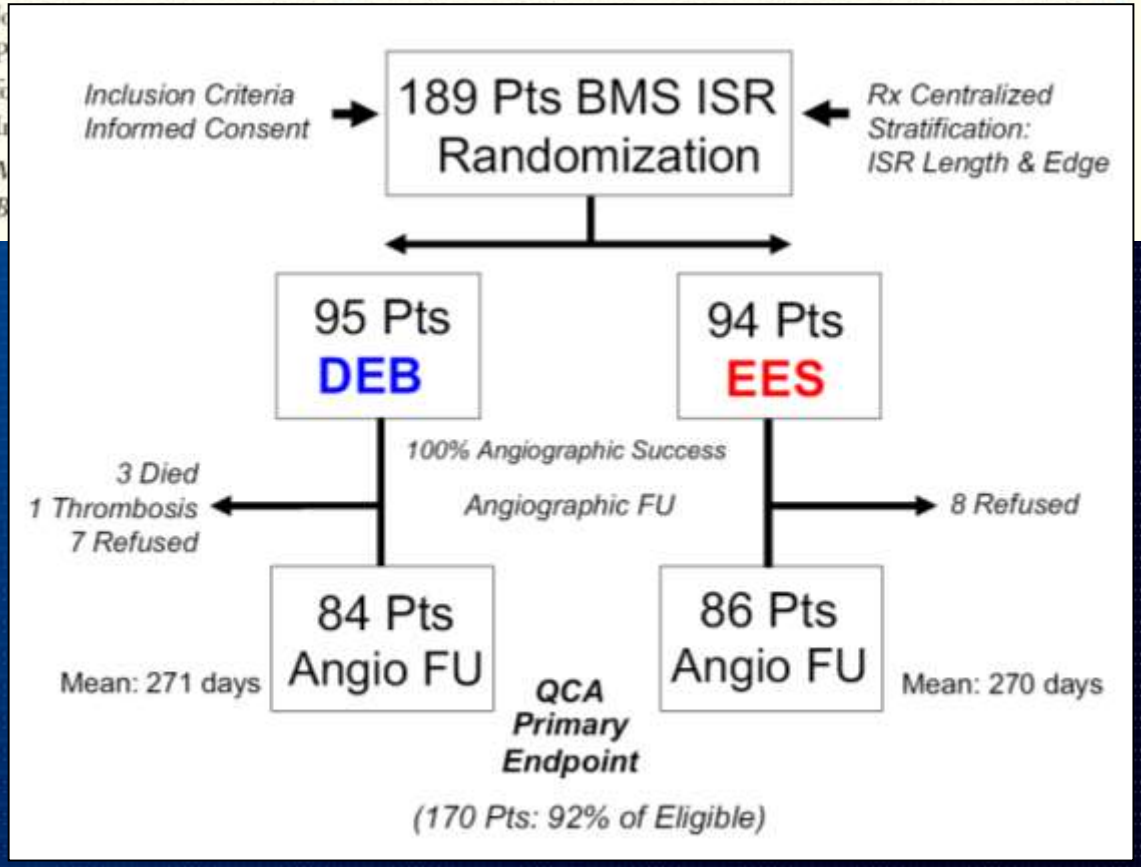
ISR	Intervention	N	End point	Study
BMS	PCB-POBA	108	In-segment LLL	PACCPCATH ISR
	PCB-PES	131	In-segment LLL	PEPCAD 2 ISR
	PCB-EES	189	In-segment MLD	RIBS V
	PCB-EES	136	In-segment LLL	ISR study
DES	PCB-POBA	110	In-segment LLL	PEPCAD-DES
	PCB-POBA	208	TVF	Habara et al
	PCB-POBA	50	In-segment LLL	Habara et al
	PCB-PES	402	In-segment DS	ISAR-DESIRE 3
	PCB-PES	220	In-segment LLL	PEPCAD-ISR-China
	PCB-EES	309	In-segment MLD	RIBS IV
	PCB-EES	172	In-segment LLL	RESTORE
	PCB-EES	278	In-segment MLD	DARE

울산병원

A Randomized Comparison of Drug-Eluting Balloon Versus Everolimus-Eluting Stent in Patients With Bare-Metal Stent–In-Stent Restenosis

The RIBS V Clinical Trial (Restenosis Intra-stent of Bare Metal Stents: Paclitaxel-eluting Balloon vs. Everolimus-eluting Stent)

Fernando Alfonso, MD,*† Maria Jose Pérez-Vizcayno, MD,† Alberto Cárdenas, MD,† Bruno García del Blanco, MD,‡ Bernhard Seidelberger, MD,* Andrés Iñiguez, MD,§ Manuel Gómez-Recio, MD,‖ Mónica Masotti, MD,¶ M. Teresa Velázquez, MD,# Juan Sanchís, MD,** Arturo García-Touchard, MD,†† Javier Zueco, MD,‡‡ Armando Bethencourt, MD,§§ Rafael Melgares, MD,‖‖ Angel Cequier, MD,¶¶ Antonio Domínguez, MD,## Vicente Mainar, MD,***



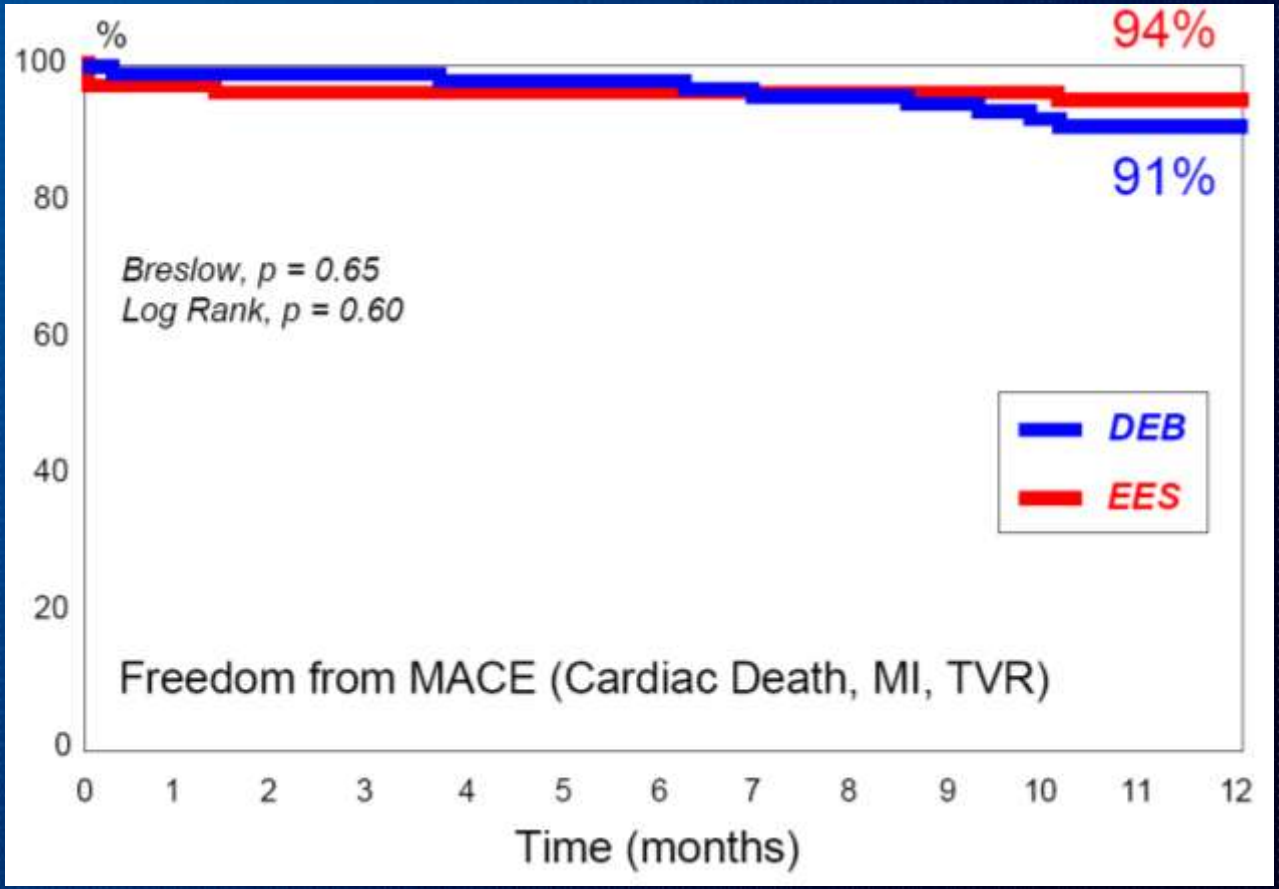
J Am Coll Cardiol 2014;63:1378–86

Primary endpoint: In-segment MLD at 9 months

	DCB (n=95)	EES (n=94)	p
MLD, mm	2.01 ± 0.6	2.36 ± 0.6	<0.001
DS, %	25 ± 20	13 ± 17	<0.001
Restenosis	8 (9.5)	4 (4.7)	0.22
Late luminal loss, mm	0.14 ± 0.5	0.04 ± 0.5	0.14

J Am Coll Cardiol 2014;63:1378–86

Kaplan-Meier estimates of event-free survival



J Am Coll Cardiol 2014;63:1378–86

Coronary Interventions

Comparison of the Efficacy of Paclitaxel-Eluting Balloon Catheters and Everolimus-Eluting Stents in the Treatment of Coronary In-Stent Restenosis

The Treatment of In-Stent Restenosis Study

Leos Pleva, MD; Pavel Kukla, MD; Pavlina Kusnierova, RNDr, PhD; Jana Zapletalova, MSc, PhD; Ota Hlinomaz, MD, PhD

Background—The aim of this prospective randomized noninferiority study was to compare the efficacy of paclitaxel-eluting balloon (PEB) catheters and everolimus-eluting stents (EES) in the treatment of bare metal stent restenosis.

Methods and Results—A total of 136 patients were enrolled in the study. Each treatment group included 68 patients with 74 in-stent restenotic lesions. The primary end point was in-segment late lumen loss (LLL) at 12 months. Secondary end

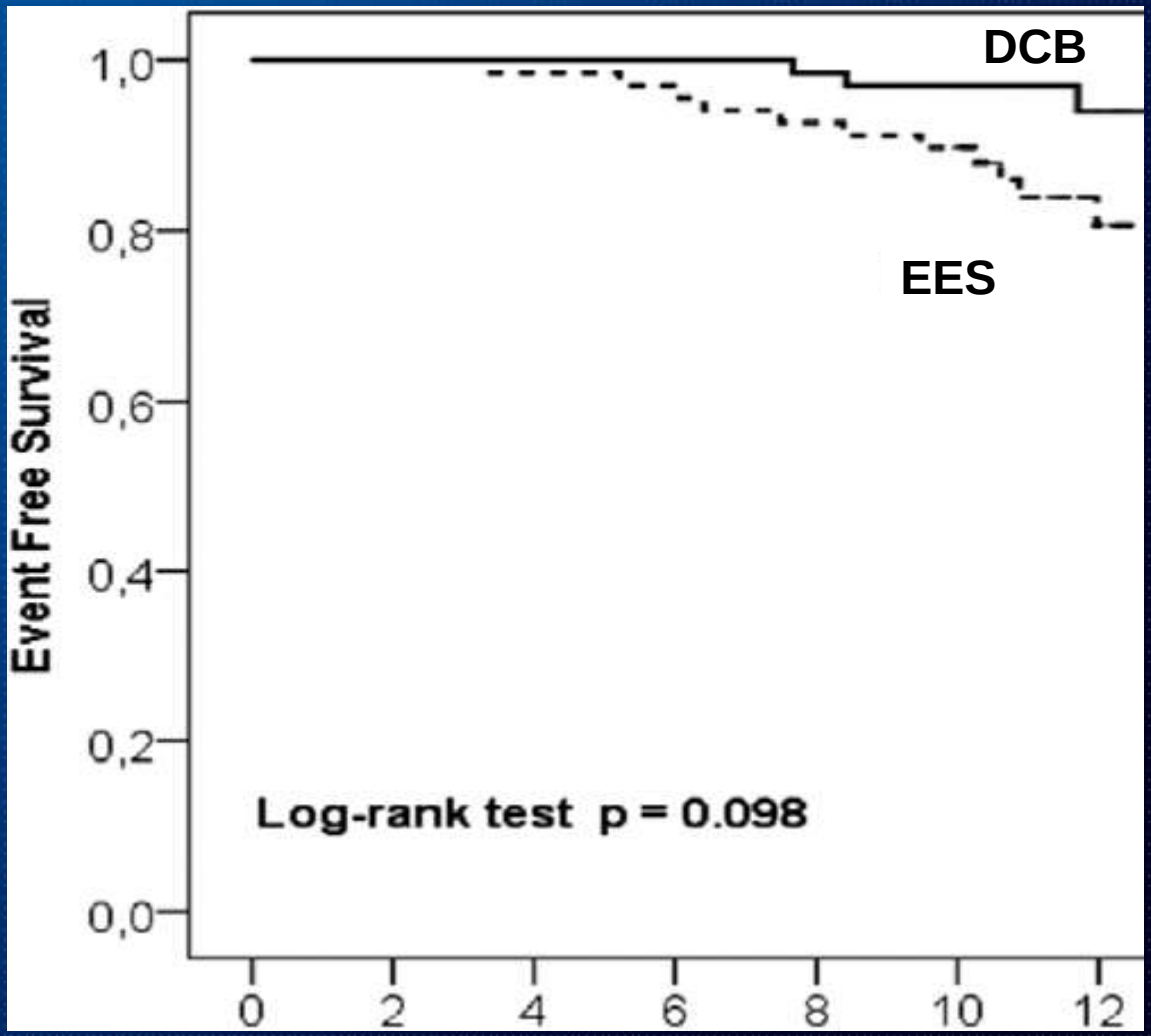
Primary end point: In-segment LLL at 12 months (n=136)

	DCB (n=63)	EES (n=62)	p
MLD, mm	2.09 ± 0.57	2.36 ± 0.6	0.481
DS, %	26.2 ± 18.0	30.9 ± 24.6	0.816
Restenosis	6 (8.7)	13 (19.1)	0.078
Late luminal loss, mm	0.02	0.19	0.0004

Circ Cardiovasc Interv. 2016;9:e003316.

울산병원

Kaplan–Meier analysis of event-free survival (CV death, MI, TVR)

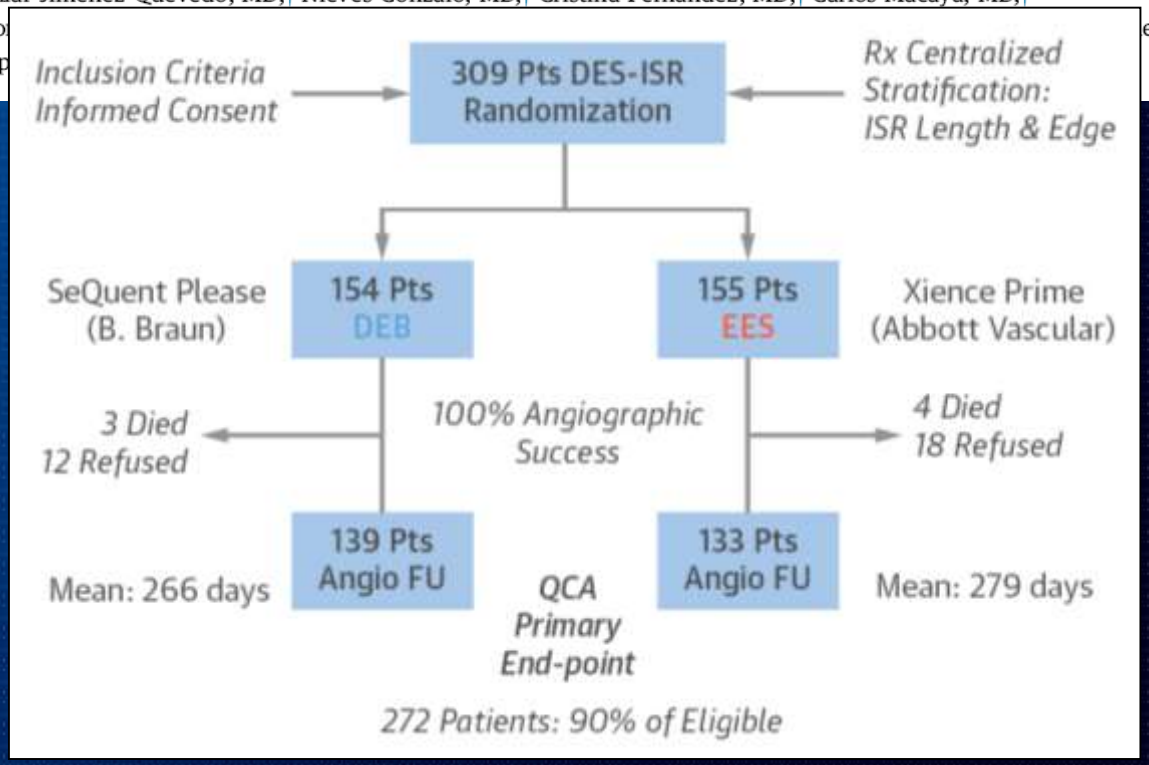


Circ Cardiovasc Interv. 2016;9:e003316.

A Prospective Randomized Trial of Drug-Eluting Balloons Versus Everolimus-Eluting Stents in Patients With In-Stent Restenosis of Drug-Eluting Stents

The RIBS IV Randomized Clinical Trial

Fernando Alfonso, MD,* María Jose Pérez-Vizcayno, MD,† Alberto Cárdenas, MD,† Bruno García del Blanco, MD,‡ Arturo García-Touchard, MD,§ José Ramón López-Minguéz, MD,‖ Amparo Benedicto, MD,* Mónica Masotti, MD,¶ Javier Zueco, MD,# Andrés Iñiguez, MD,** Maite Velázquez, MD,†† Raúl Moreno, MD,‡‡ Vicente Mainar, MD,§§ Antonio Domínguez, MD,‖‖ Francisco Pomar, MD,¶¶ Rafael Melgares, MD,## Fernando Rivero, MD,* Pilar Jiménez-Quevedo, MD,† Nieves Gonzalo, MD,† Cristina Fernández, MD,† Carlos Macaya, MD,† fo e Sp



J Am Coll Cardiol 2015;66:23–33

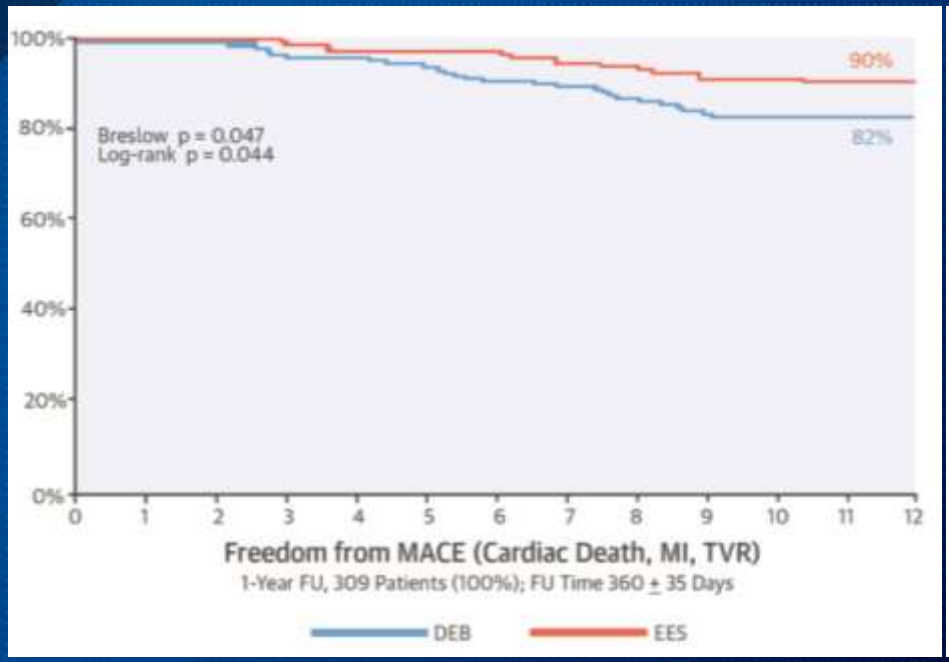
Primary endpoint: In-segment MLD at 6-9 months

	DCB (n=154)	EES (n=155)	p
MLD, mm	1.80 ± 0.6	2.03 ± 0.7	0.004
DS, %	30 ± 22	23 ± 22	0.009
Restenosis	27 (19)	15 (11)	0.06
Late luminal loss, mm	0.30 ± 0.6	0.18 ± 0.6	0.06

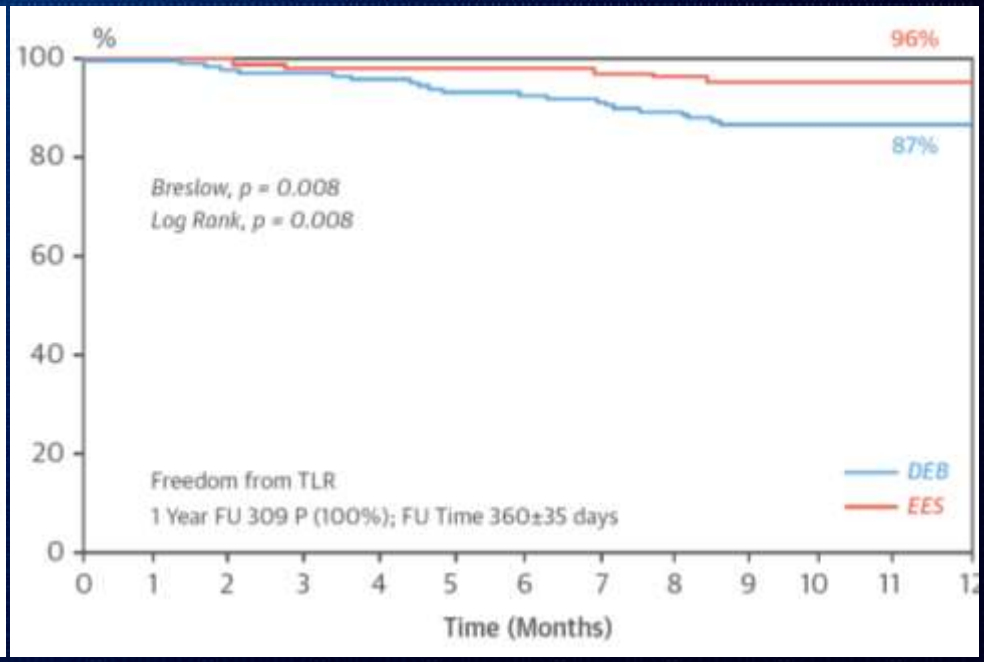
J Am Coll Cardiol 2015;66:23–33

Freedom from MACE & TLR

MACE (Cardiac death, MI, TVR)



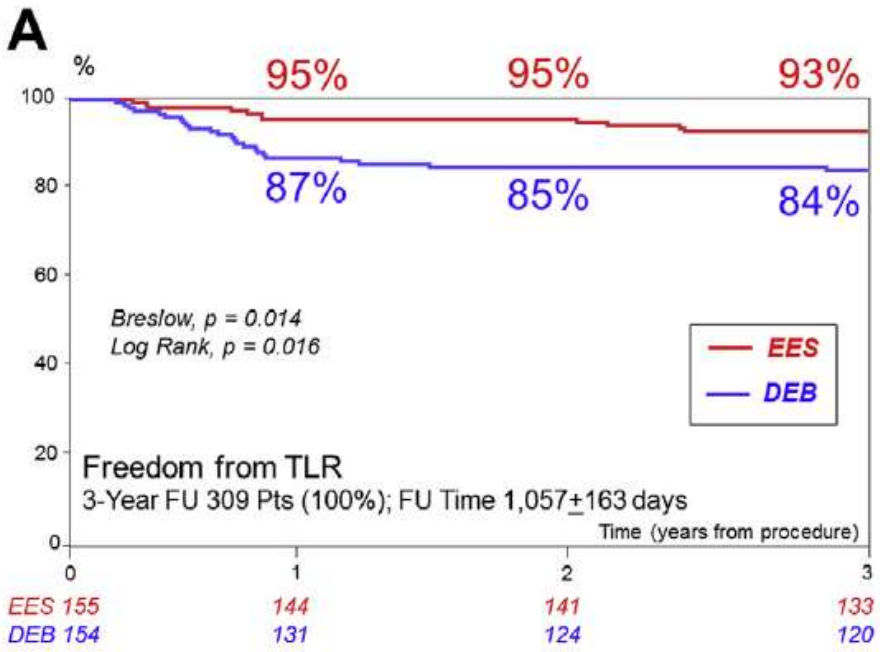
TVR



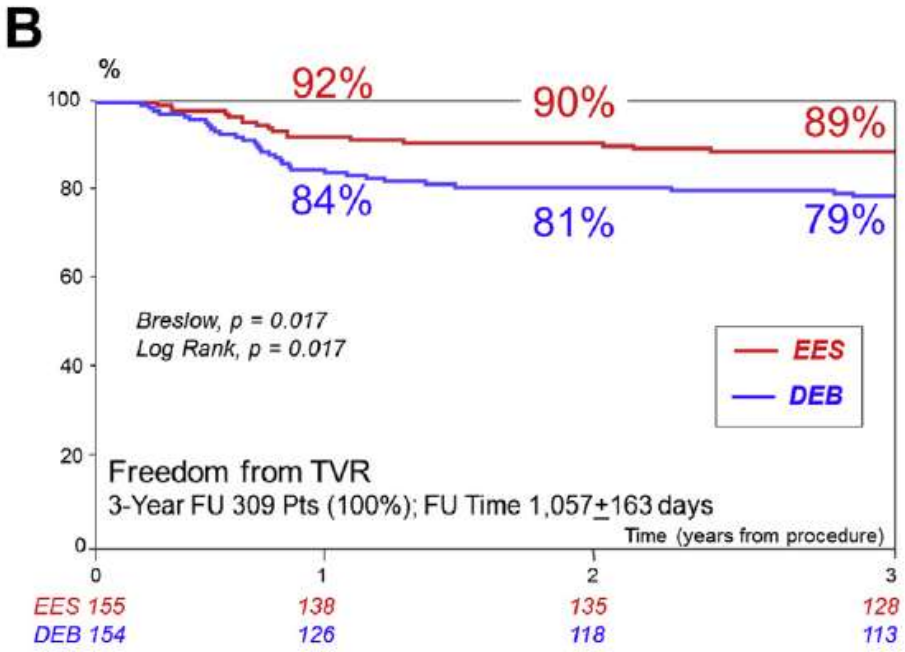
J Am Coll Cardiol 2015;66:23–33

Freedom From TLR and TVR

TLR



TVR

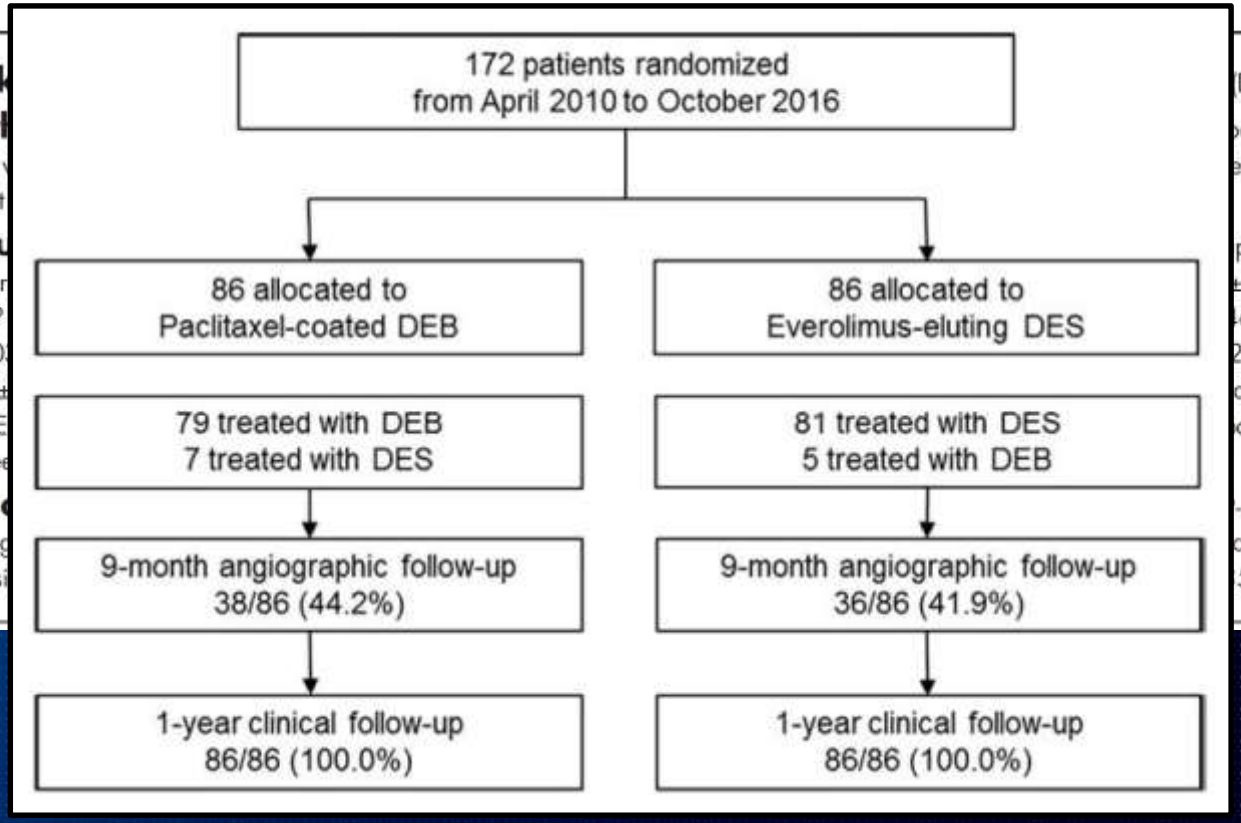


J Am Coll Cardiol Intv 2018;11:981–91

Comparison of drug-eluting stents and drug-coated balloon for the treatment of drug-eluting coronary stent restenosis: A randomized RESTORE trial

Yiu Tung Anthony Wong, MD,[a,1] Do-Yoon Kang, MD,[b,1] Jin Bae Lee, MD,[c] Seung-Woon Rha, MD,[d] Young Joon Hong, MD,[e] Eun-Seok Shin, MD,[f] Sung-Ho Her, MD,[g] Chang Wook Nam, MD,[h] Woo-Young Chung, MD,[i] Moo Hyun Kim, MD,[j] Cheol Hyun Lee, MD,[b] Pil Hyung Lee, MD,[b] Jung-Min Ahn, MD,[b] Soo-Jin Kang, MD,[b] Seung-Whan Lee, MD,[b] Young-Hak Kim, MD,[b] Cheol Whan Lee, MD,[b] Seong-Wook Park, MD,[b] Duk-Woo Park, MD, PhD,[b] and Seung-Jung Park, MD[b]

Hong Kong; Seoul, Daegu, Gwangju, Ulsan, Daejeon, and Busan, South Korea



Am Heart J 2018;197:35-42.

Primary endpoint: In-segment LLL at 9 months

	DCB (n=38)	EES (n=36)	p
MLD, mm	1.80 ± 0.69	2.09 ± 0.46	0.03
DS, %	34 ± 21	26 ± 15	0.05
Restenosis	8 (19.5)	2 (5.6)	0.65
Late luminal loss, mm	0.15 ± 0.49	0.19 ± 0.41	0.54

Am Heart J 2018;197:35-42.

Clinical outcomes at 1-year follow-up

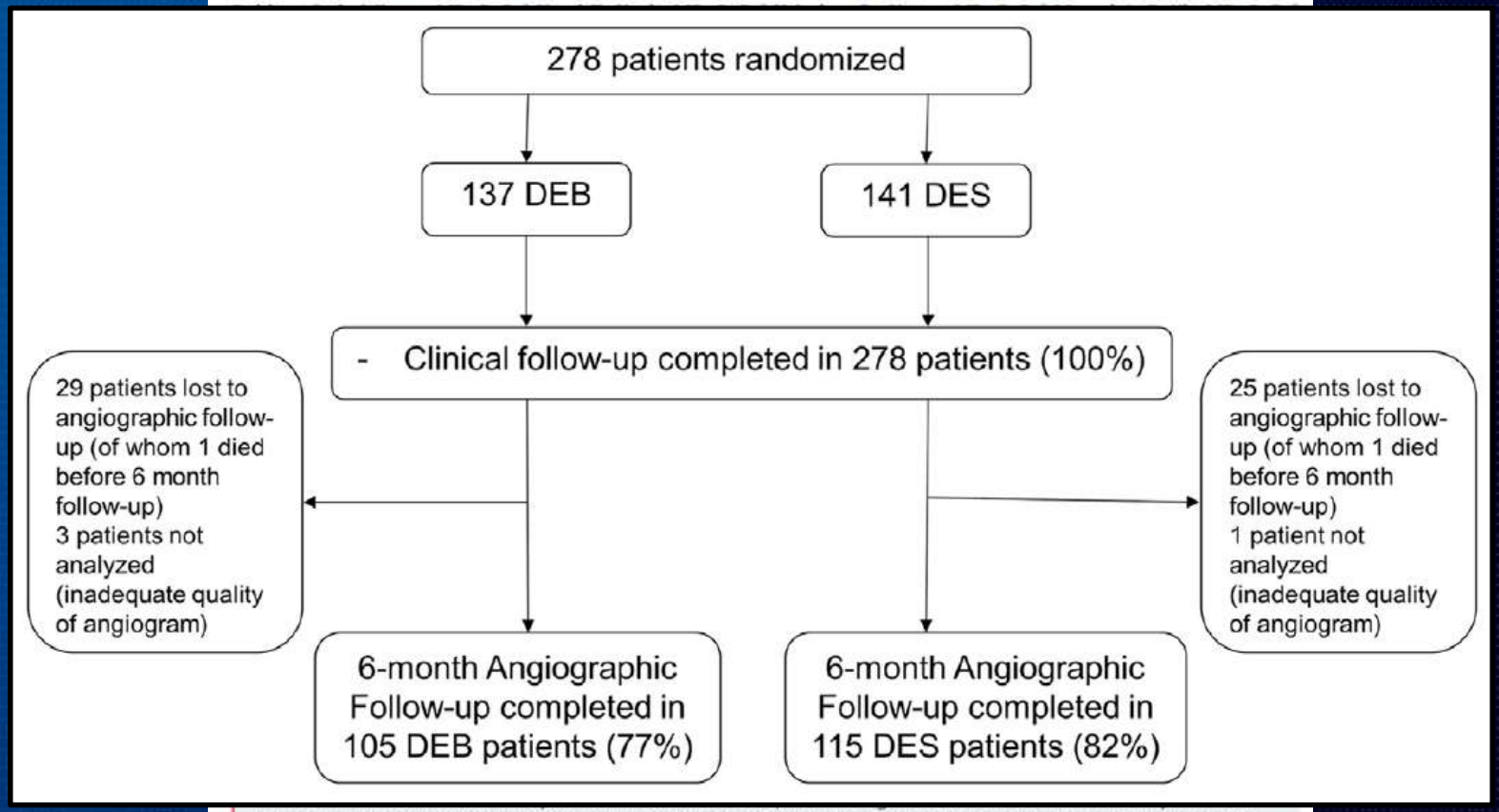
	DEB (n = 86)	DES (n = 86)	*P*
MACE	6 (7.0%)	4 (4.7%)	.51
Death	0 (0.0%)	0 (0.0%)	N/A
MI	1 (1.2%)	3 (3.5%)	.31
Death or MI	1 (1.2%)	3 (3.5%)	.31
Stent thrombosis	0 (0.0%)	0 (0.0%)	N/A
TVR	5 (5.8%)	1 (1.2%)	.10
TLR	5 (5.8%)	1 (1.2%)	.10
Stroke	0 (0.0%)	0 (0.0%)	N/A
Bleeding	18 (20.9%)	14 (16.3%)	.43

Am Heart J 2018;197:35-42.

A Randomized Comparison of Paclitaxel-Eluting Balloon Versus Everolimus-Eluting Stent for the Treatment of Any In-Stent Restenosis

The DARE Trial

Jan Baan, Jr, MD, PhD,[a] Bimmer E. Claessen, MD, PhD,[a] Kirsten Boerlage-van Dijk, MD, PhD,[b] Jeroen Vendrik, MD,[a] René J. van der Schaaf, MD, PhD,[b] Martijn Meuwissen, MD, PhD,[c] Niels van Royen, MD, PhD,[d] A.T. Marcel Gosselink, MD, PhD,[e] Marleen H. van Wely, MD,[f] Atilla Dirkali, MD,[g] E. Karin Arkenbout, MD, PhD,[h]



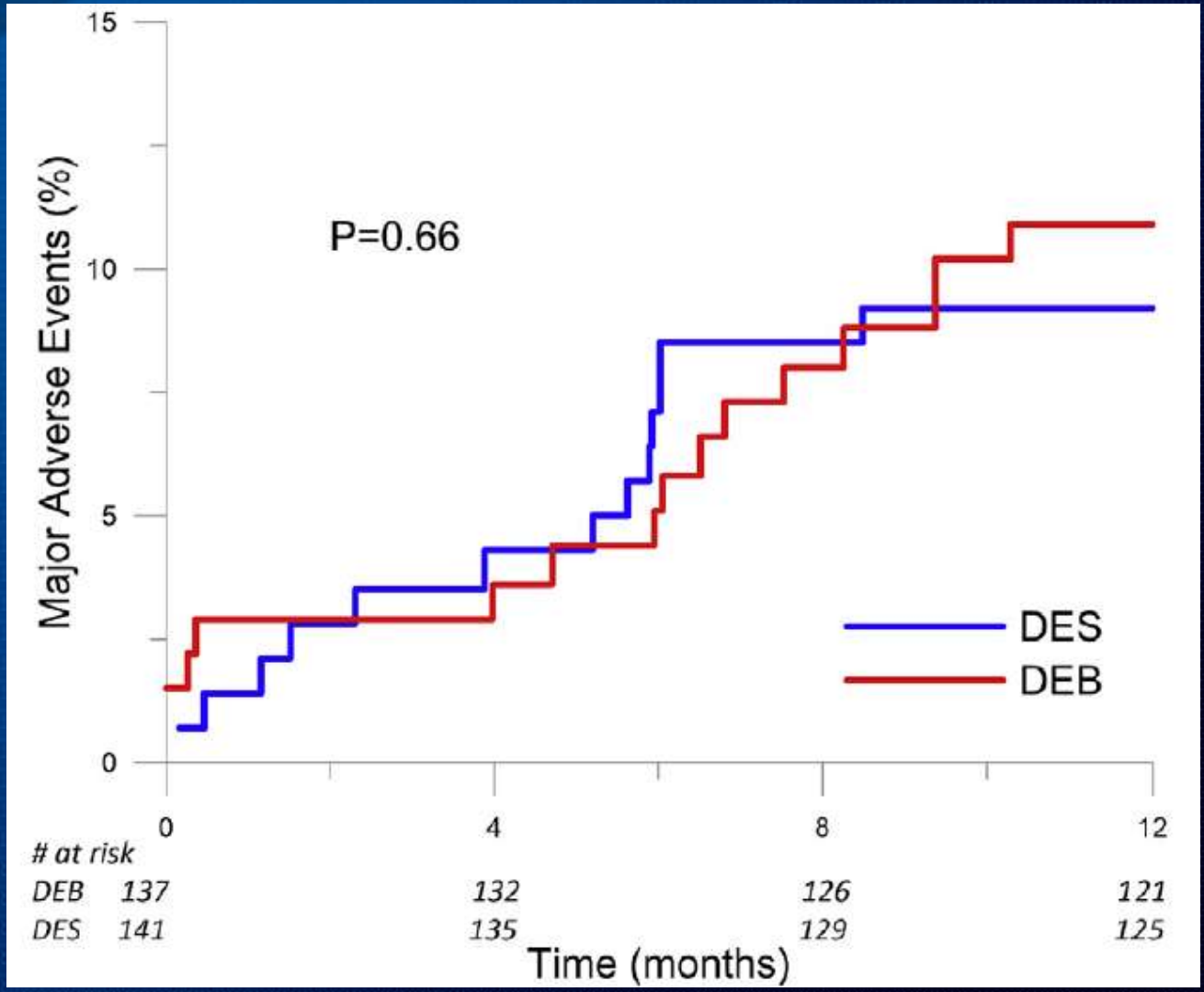
J Am Coll Cardiol Intv 2018;11:275–83

Primary endpoint: In-segment MLD at 6 months

	DCB (n=105)	EES (n=115)	p
MLD, mm	1.71 ± 0.51	1.74 ± 0.61	0.65
DS, %	36.1 ± 15.5	33.8 ± 18.6	0.32
Restenosis, %	18.1	20.9	0.60
Late luminal loss, mm	0.17 ± 0.41	0.45 ± 0.47	<0.001

J Am Coll Cardiol Intv 2018;11:275–83

Kaplan Meier Estimates of MACE at 12 months (death, TV-MI, TVR)



J Am Coll Cardiol Intv 2018;11:275–83

Summary

ISR	Intervention	Study	Angiographic Result (MLD/DS)	Clinical result
BMS	PCB vs. EES	RIBS V	PCB<EES	PCB=EES
	PCB vs. EES	ISR study	PCB=EES	PCB=EES
DES	PCB vs. EES	RIBS IV	PCB<EES	PCB<EES
	PCB vs. EES	RESTORE	PCB<EES	PCB=EES
	PCB vs. EES	DARE	PCB=EES	PCB=EES

울산병원

PCB vs. EES for DES-ISR

Study	N	Primary EP	ISR type	DAPT duration	Clinical result
RIBS IV	309	In-segment MLD	DES	EES: 1y PCB: 3m	PCB<EES PCB: ↑TLR / thrombotic event
RESTORE	172	In-segment LLL	DES	EES & PCB: 6m	PCB=EES
DARE	278	In-segment MLD	DES (55%) BMS (45%)	EES & PCB: 12m	PCB=EES

울산병원

Impact of Optimized Procedure-Related Factors in Drug-Eluting Balloon Angioplasty for Treatment of In-Stent Restenosis

Tae-Min Rhee, MD,[a,*] Joo Myung Lee, MD, MPH, PhD,[b,*] Eun-Seok Shin, MD, PhD,[c] Doyeon Hwang, MD,[a] Jonghanne Park, MD, PhD,[a] Ki-Hyun Jeon, MD,[d] Hack-Lyoung Kim, MD, PhD,[e] Han-Mo Yang, MD, PhD,[a] Jung-Kyu Han, MD, PhD,[a] Kyung Woo Park, MD, PhD,[a] Joo-Yong Hahn, MD, PhD,[b] Bon-Kwon Koo, MD, PhD,[a] Sang-Hyun Kim, MD, PhD,[c] Hyo-Soo Kim, MD, PhD[a]

ABSTRACT

OBJECTIVES The aim of this study was to investigate the impact of optimizing procedure-related factors during drug-eluting balloon (DEB) angioplasty on clinical outcomes of drug-eluting stent in-stent restenosis (ISR).

BACKGROUND Although DEB angioplasty is recommended as a reasonable option for ISR, recurrent target lesion failure (TLF) still occurs in many patients after DEB angioplasty.

METHODS Consecutive patients with drug-eluting stent ISR treated with DEB (SeQuent Please) were collected from 4 centers in Korea. The primary outcome was 2-year TLF. Procedure-related modifiable independent predictors for TLF and their best cutoff values were determined.

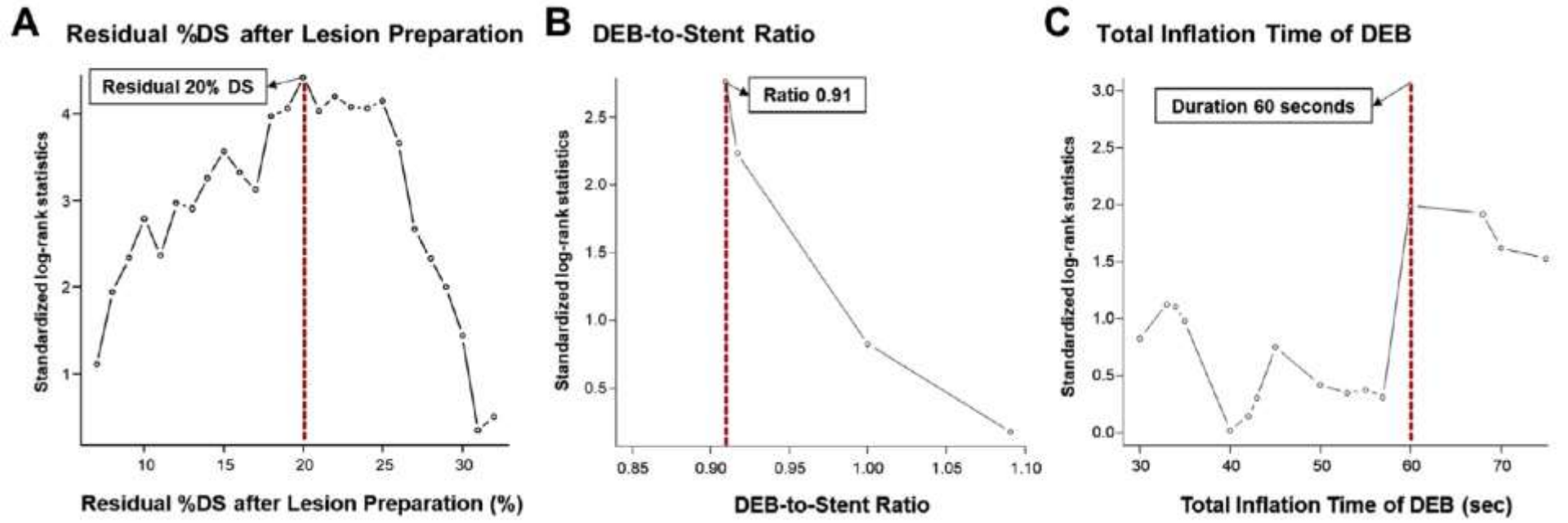
RESULTS In a total of 256 patients (309 lesions), TLF occurred in 52 patients (20.3%). Modifiable independent predictors of TLF among procedure-related factors were residual diameter stenosis after lesion preparation (residual percentage diameter stenosis [%DS]), DEB-to-stent ratio (BSR), and DEB inflation time ($T_{inflation}$), whose best cutoff values were 20%, 0.91, and 60 s, respectively. TLF rates were significantly higher in groups with residual %DS ≥20% (34.7% vs. 12.5%; adjusted hazard ratio: 2.15; 95% confidence interval: 1.86 to 2.48; $p < 0.001$), BSR ≤0.91 (46.4% vs. 21.9%; adjusted hazard ratio: 2.02; 95% confidence interval: 1.75 to 2.34; $p < 0.001$), and $T_{inflation}$ ≤60 s (26.2% vs. 14.0%; adjusted hazard ratio: 1.82; 95% confidence interval: 1.36 to 2.45; $p < 0.001$). When classifying ISR lesions by combination of procedure-related factors, TLF occurred in 8.3% in the fully optimized procedure group (residual %DS <20%, BSR >0.91, and $T_{inflation}$ >60 s) and 66.7% in the nonoptimized group (residual %DS ≥20%, BSR ≤0.91, and $T_{inflation}$ ≤60 s) ($p < 0.001$).

CONCLUSIONS Residual %DS after lesion preparation, BSR, and $T_{inflation}$ were the only modifiable procedure-related factors in DEB angioplasty. Fully optimized DEB angioplasty with optimal lesion preparation, prolonged inflation, and sufficient dilation may play an important role in reducing TLF after DEB angioplasty. (J Am Coll Cardiol Intv 2018;11:969–78)

J Am Coll Cardiol Intv 2018;11:969–78

울산병원

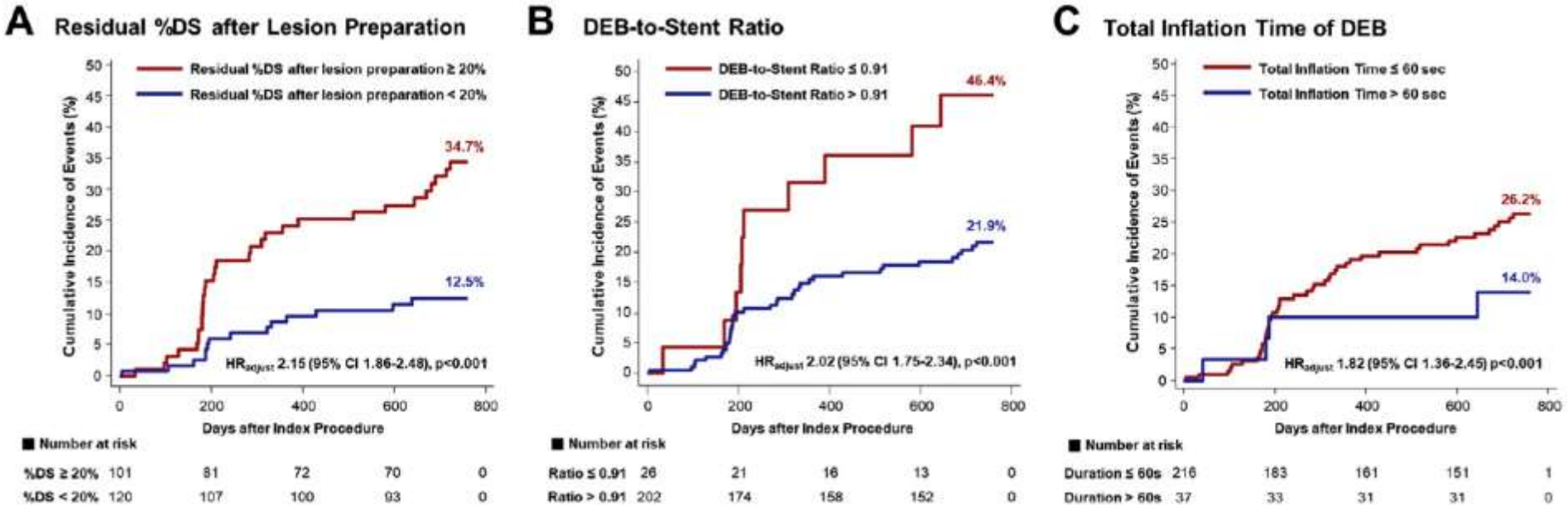
Optimal cutoff values for procedure-related factors



J Am Coll Cardiol Intv 2018;11:969–78

울산병원

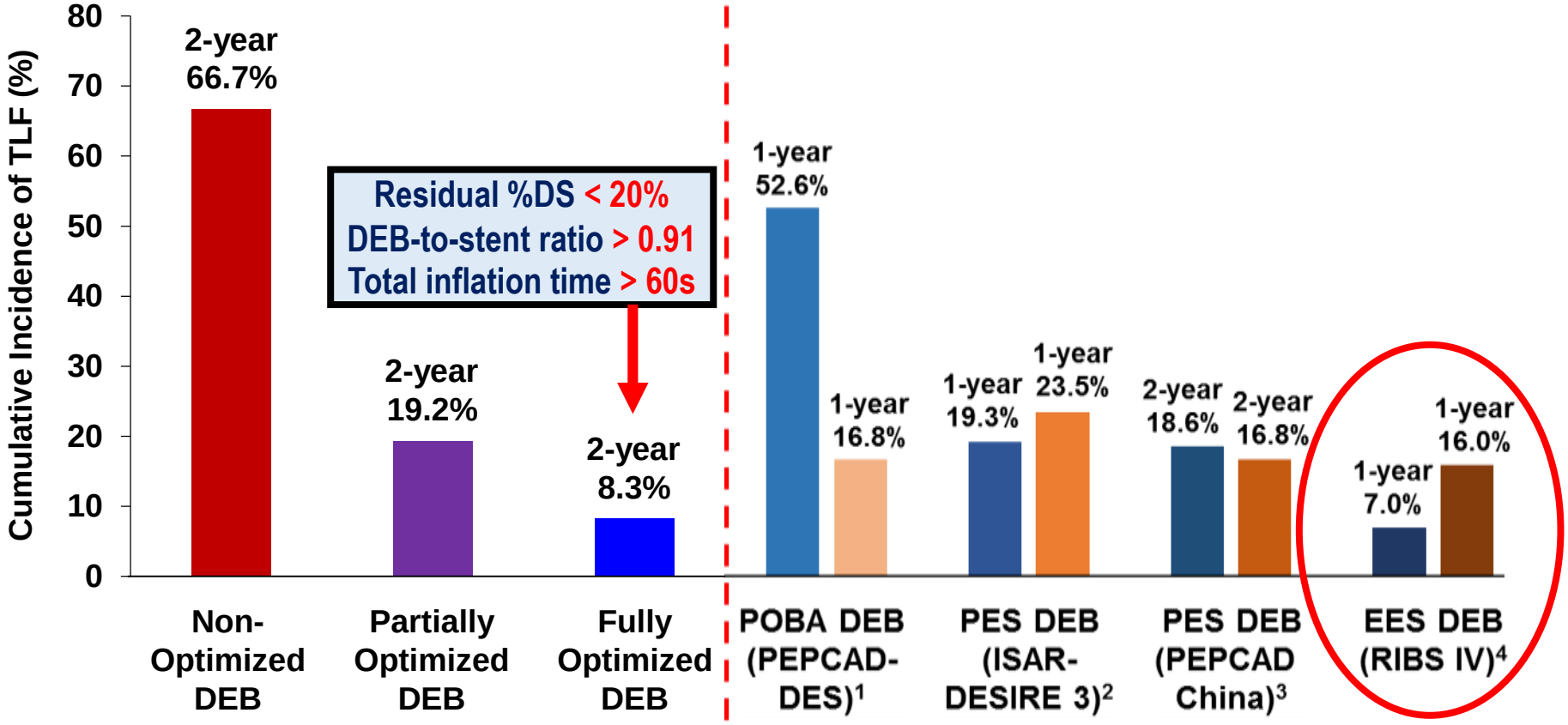
Cumulative incidence of TLF



J Am Coll Cardiol Intv 2018;11:969–78

울산병원

Incidence of TLF by combined procedure-related factors



2-year TLF rate in fully-optimized DEB group was 8.3%, Similar to or even better than 1st or 2nd generation DES groups in previous ISR trials

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

울산병원

Conclusions

- Currently, DCB is stronly recommended for the treatment of ISR (within BMS or DES) in the European guidelines (Class IA)
- There are important procedure-related factors that could independently predict future occurrence of TLF after DCB treatment for DES-ISR and would improve clinical outcomes comparable to 2nd gen DES.
- Despite the excellent performance of new-generation DES, there is a proper position for DCB, particularly for recurrent ISR lesions already covered with more metal layers.
- Further studies are required to determine appropriate DAPT duration after ISR treatment.

울산병원
ULSAN MEDICAL CENTER