"Long Cypher" Multicenter Prospective non-Randomized Registry study for DES in Very Long Lesion ;

-Preliminary Data-

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Background

- Sirolimus eluting stent implantation has been demonstrated to dramatically diminish in-stent restenosis in elective patients with relatively simple coronary lesions.
- However, the impact of sirolimus eluting stent for very long coronary lesions is not well documented.

Objective

- The present study was performed to evaluate the safety and efficacy of the sirolimus eluting stent (Cypher™ stent; Cordis) for very long coronary lesion.
- And it was compared with a control group composed of patients with long coronary lesions treated with long bare metal stents in the same period.

Investigating Centers (10 centers)

Coordinating center : Asan Medical Center, *Seung-Jung Park*

Collaborating centers

Ajou University Medical Center,	*SJ Tahk*
Catholic University of Korea, St Mary's Hospital,	*KB Seung*
Chonnam Nat'l University Hospital,	*MH Jeong*
Keimyung University Dongsan Medical Center,	*KS Kim*
Korea University Kuro Hospital,	*DJ Oh*
Samsung Medical Center,	*HC Gwon*
Seoul National University Hospital,	*Lee MM, Koo BK*
Yonsei University Severance Hospital,	*YS Jang*
Yonsei University Wonju Christian Hospital,	*JH Yoon*

Inclusion Criteria

- The treated vessels were of 2.5-4.0 mm in diameter with ≥ 50% diameter stenosis, and had a lesion length ≥ 24 mm that could be covered by a single stent or multiple stents (total contiguous stent length ≥ 28 mm).

Exclusion Criteria

- Contraindication to antiplatelet agents
- Left main coronary artery stenosis
- Grafted lesions
- In-stent restenotic lesions
- Primary angioplasty in AMI
- Left ventricular dysfunction (EF< 40%)
- An inability to follow the protocol

March 2003 - February 2004

Enrollment

De-novo Lesions (≥ 24mm)

487 patients, 597 lesions

Cypher stent (≥ 28mm)

338 patients, 424 lesions
Mean stent length : 41mm
(28- 92 mm)

BMS stent (≥ 28mm)

149 patients, 173 lesions
Mean stent length : 37mm
(28 – 73 mm)

Study End Point

Primary end point

The incidence of major adverse cardiac events including death, nonfatal MI, target lesion revascularization.

Secondary end point

The restenosis rate and late loss at angiographic follow-up

Follow Up

- Data were collected with a standardized case-report forms completed by the research coordinator at each site.
- All clinical events were monitored.
- Angiographic follow-up is being routinely performed at six months or earlier if a patient shows symptoms of recurrence.

Antiplatelet Regimens

Bare Metal Stent

- **Aspirin** indefinitely
- **Clopidogrel**

  300 mg loading, before intervention

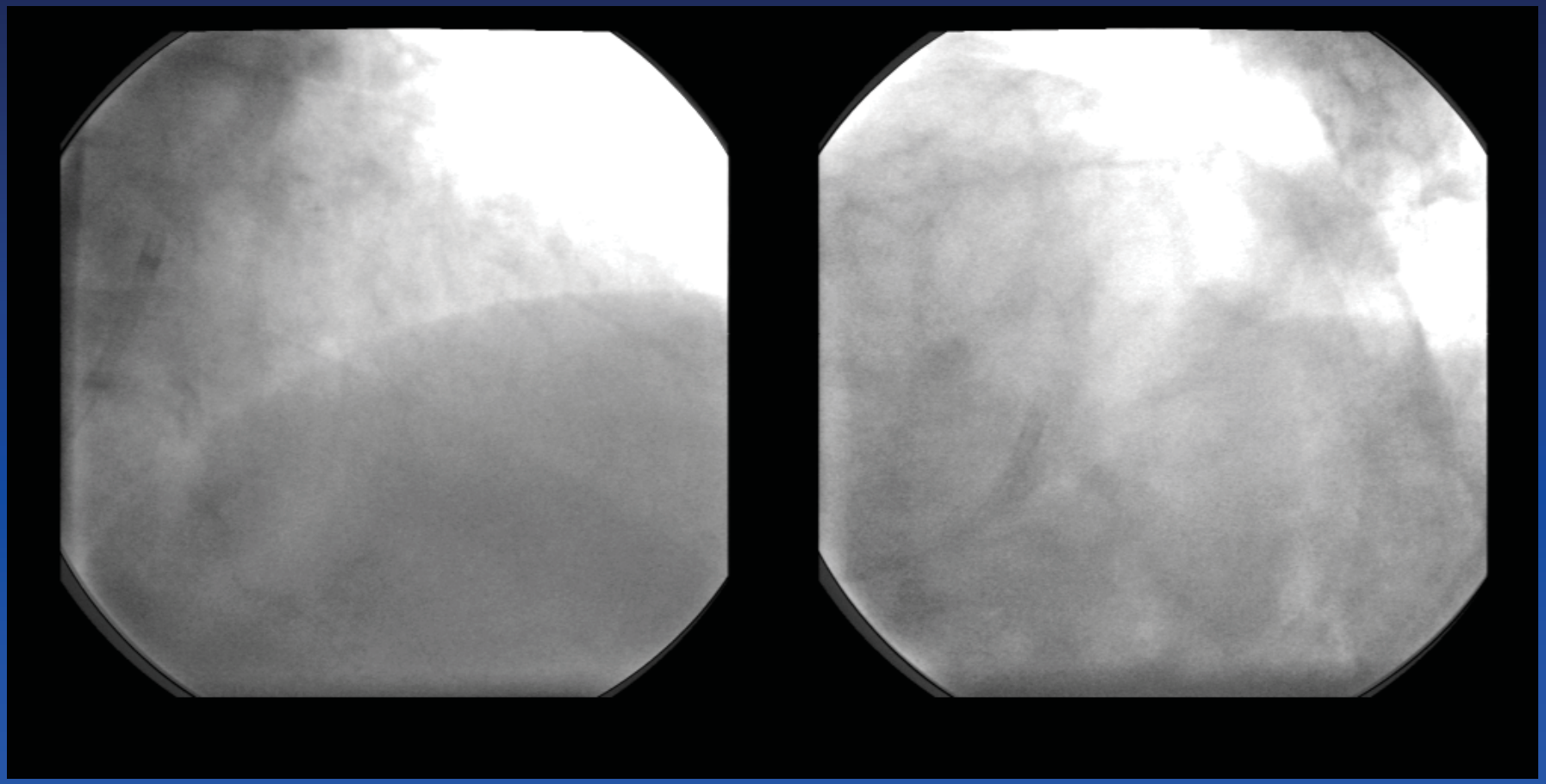
  75 mg maintenance, for 1 month

Antiplatelet Regimens

Cypher stent

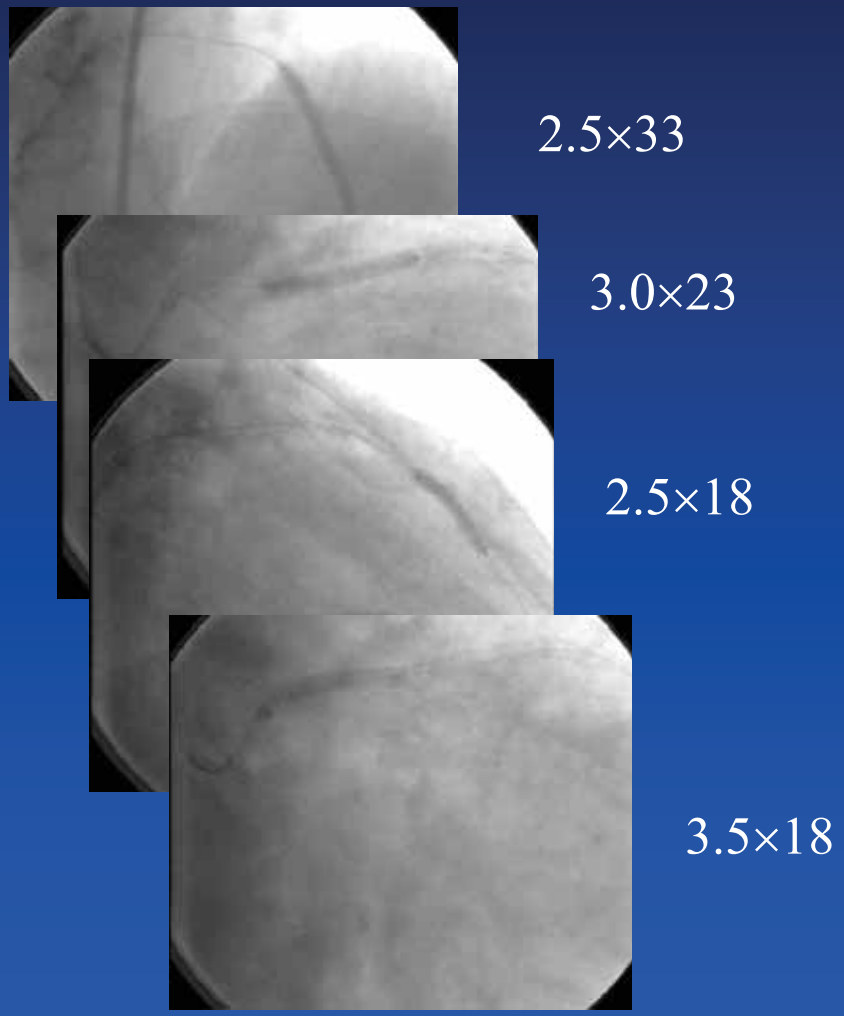
Initial 100 patients	Following 238 patients
Aspirin lifelong	**Aspirin** lifelong
Clopidogrel	**Clopidogrel**
75mg QD for 6 months (300mg loading)	75mg QD for 6 months (450mg loading)
Cilostazol	
100mg BID for 1 month (200mg loading)	

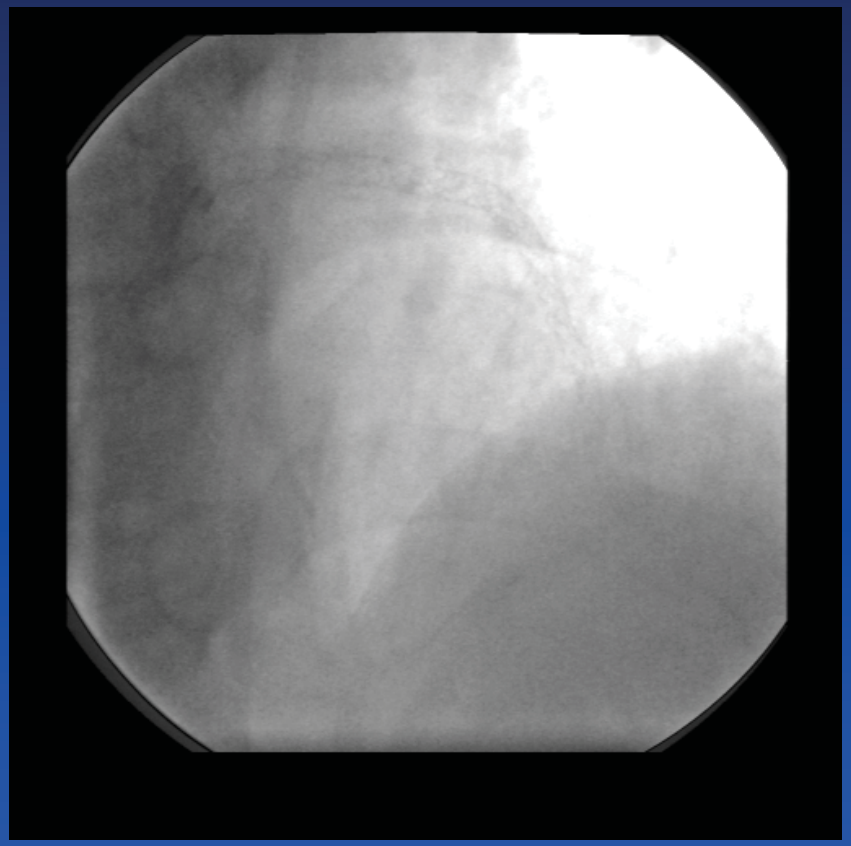
What a Big Changes !



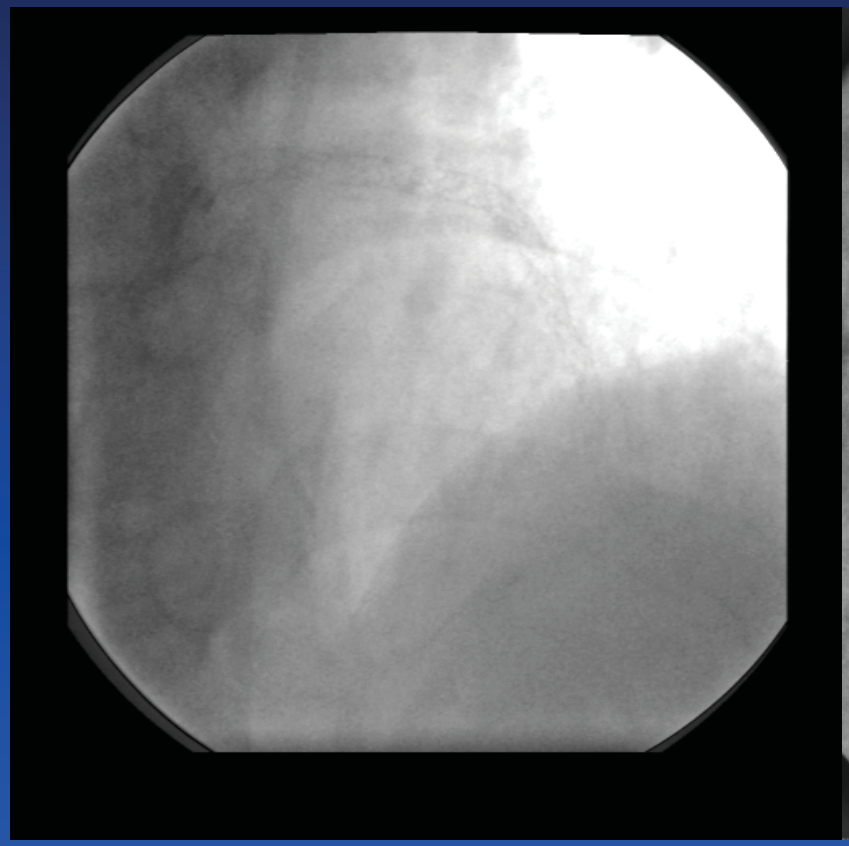
Very long and LAD lesion from ostium

Consecutive 4 Cyphers
(Total stent length 92 mm)

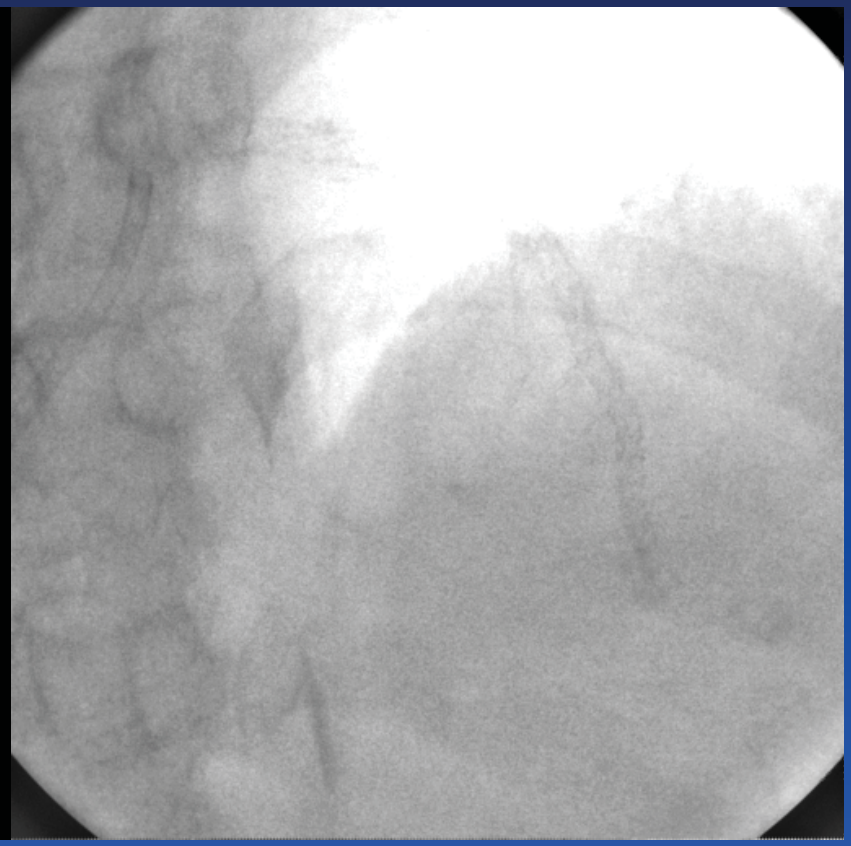




Can You Discriminate ?



Post-intervention



At 6-month

Diabetic patients : 36%

	Cypher (n=338)	Control (n=149)	P value
Age (years)	60 ± 10	60 ± 10	0.950
Man	243 (72%)	112 (75%)	0.614
Hypertension	193 (57%)	79 (53%)	0.488
Hypercholesterolemia	91 (27%)	31 (21%)	0.194
Diabetes mellitus	122 (36%)	43 (29%)	0.106
Smoking	108 (32%)	73 (49%)	0.001

Unstable Angina : 44%

	Cypher (n=338)	Control (n=149)	P value
LV ejection fraction (%)	60 ± 10	56 ± 9	<0.001
Prior PCI	37 (11%)	21 (14%)	0.323
Prior CABG	3 (2%)	0 (0%)	0.268
Clinical diagnosis			0.220
Stable angina	155 (46%)	70 (47%)	
Unstable angina	149 (44%)	55 (37%)	
Acute MI	34 (10%)	24 (16%)	

Multivessel disease : 70%

	Cypher (n=338)	Control (n=149)	P value
No of diseased vessels			0.176
1 vessel	118 (35%)	41 (28%)	
2 vessel	124 (37%)	55 (37%)	
3 vessel	96 (28%)	53 (36%)	

LAD : 61%

	Cypher (n=424)	Control (n=173)	P value
Lesion location			<0.001
LAD	259 (61%)	72 (42%)	
LCX	59 (14%)	25 (20%)	
RCA	110 (26%)	53 (39%)	
Chronic total occlusion	38 (9%)	22 (13%)	0.166
Infarct related artery	20 (5%)	14 (8%)	0.106

Overlapping : 46%

	Cypher (n=424)	Control (n=173)	P value
Used No of stents	1.55 ± 0.68	1.29 ± 0.54	<0.001
Overlapping	196 (46%)	44 (25%)	<0.001
✓Contiguous stent length (mm)	40.8 ± 15.0	36.6 ± 12.4	0.001
Maximal inflation pressure (atm)	15.4 ± 3.6	11.7 ± 3.3	<0.001
Maximal balloon size	3.31 ± 0.38	3.41 ± 0.51	0.008
Balloon-to-artery ratio	1.11 ± 0.16	1.06 ± 0.14	<0.001
IVUS guidance	303 (72%)	71 (41%)	<0.001
Use of Abciximab	11 (3%)	7 (4%)	0.492

Pre and Post QCA data

	Cypher (n=424)	Control (n=173)	P value
Lesion length (mm)	33.0 ± 13.1	29.9 ± 12.7	0.012
Proximal reference (mm)	3.02 ± 0.46	3.27 ± 0.55	<0.001
Distal reference (mm)	2.63 ± 0.47	2.81 ± 0.59	<0.001
MLD (mm), Pre	0.72 ± 0.46	0.78 ± 0.52	0.146
Post	2.72 ± 0.43	2.92 ± 0.54	<0.001
Diameter stenosis (%), Pre	74.2 ± 16.3	74.0 ± 16.7	0.898
Post	2.7 ± 14.9	5.3 ± 14.4	0.062
Acute gain	2.00 ± 0.61	2.13 ± 0.68	0.022

In-Hospital Outcomes
SAT : 0 %

	Cypher (n=338)	Control (n=149)	P value
Procedural success *	97.8%	94.8%	0.051
Death	0	1 (0.7%) **	1.000
MI	29 (9%)	18 (12%)	0.228
Q wave	0	0	
Non-Q wave ***	29 (9%)	18 (12%)	
Stent thrombosis	0	0	1.000
TLR	0	0	1.000
TVR	0	0	1.000

* Final TIMI flow ≥ 2 and residual diameter stenosis ≤ 30%
** No reflow after multivessel PCI , *** CK-MB ≥ 3 times normal value

30 days Outcomes

	Cypher (n=338)	Control (n=149)	P value
Death	1 (0.3%) *	1 (0.7%)	0.519
Non-cardiac	1 (0.3%)	0	
Cardiac	0	1 (0.7%)	
MI	0	0	1.000
Q wave	0	0	
Non-Q wave	0	0	
Sent thrombosis	0	0	1.000
TLR	0	0	1.000
TVR	0	0	1.000

* Due to intracranial hemorrhage, 5 days after intervention

6 months Outcomes

Clinical follow-up in all patients (100%)

- SES : 338 pts
- BMS : 149 patients

Angiogrpahic follow-up (ongoing ….)

- SES : 117 / 182 eligible lesions (63%)
- BMS : 97 / 147 eligible lesions (66%)

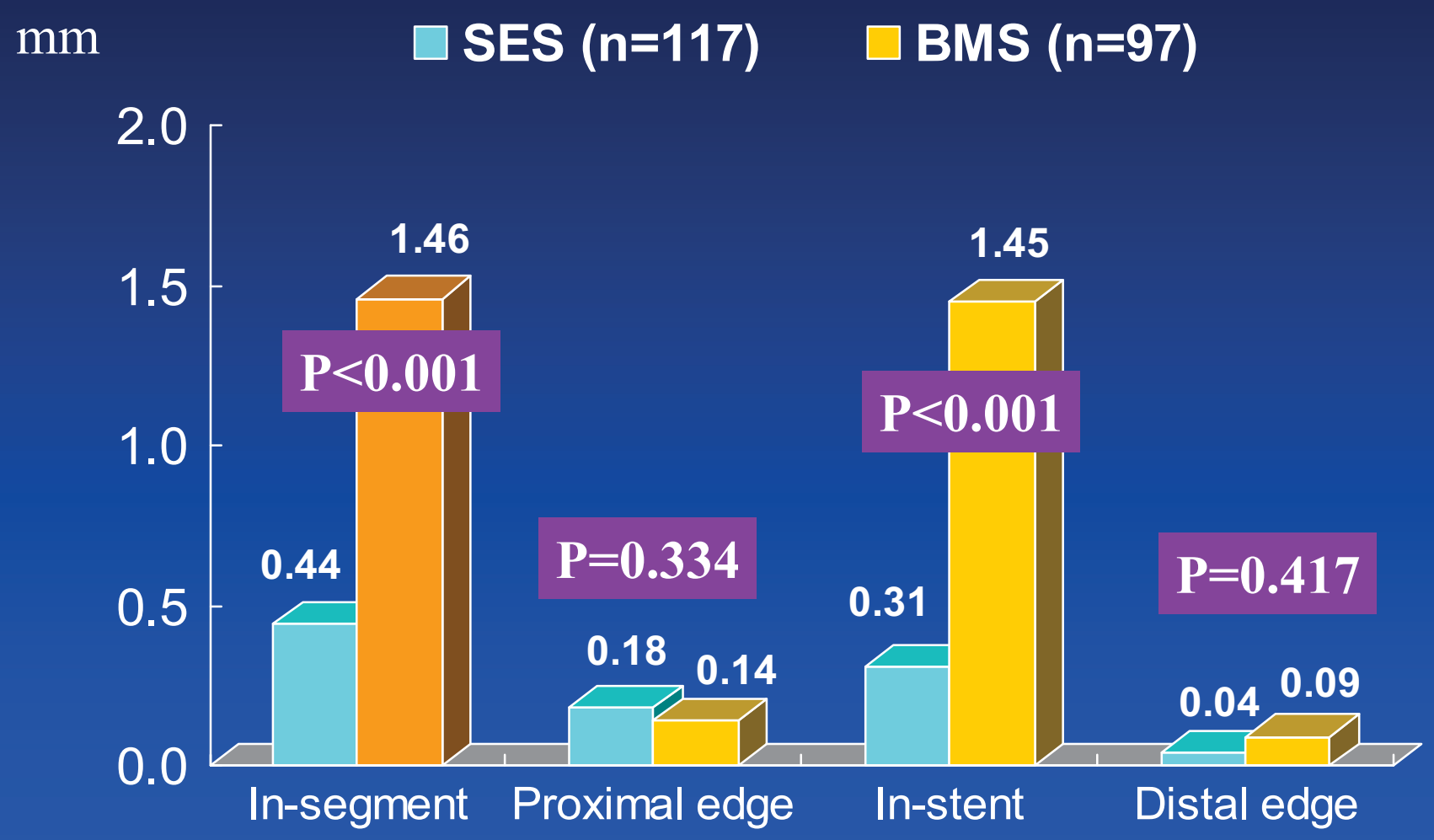
TLR : 0.6 %

	Cypher (n=162)	Control (n=127)	P value
Death	1 (0.6%)	1 (0.8%)	1.000
Non-cardiac	1 (0.6%)	0	
Cardiac	0	1 (0.8%)	
MI	0	0	1.000
Q wave	0	0	
Non-Q wave	0	0	
Stent thrombosis	0	0	1.000
TLR	1 (0.6%)	18 (14.2%)	<0.001
Repeat PCI	0	16	
CABG	1	2	
MACE	2 (1.1%)	19 (15.0%)	<0.001

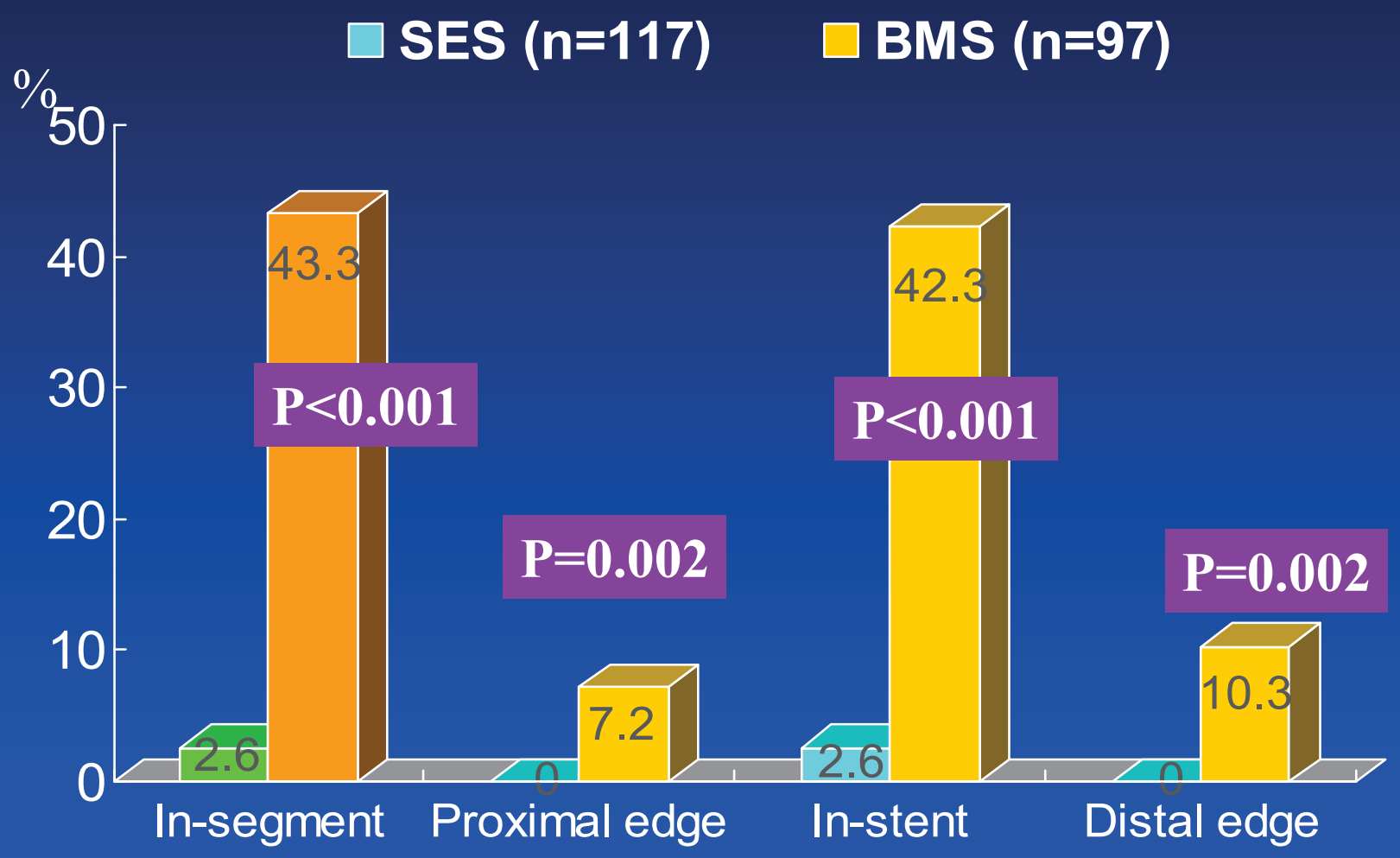
Restenosis Rate : 2.6 %

	Cypher (n=117)	Control (n=97)	P value
Proximal reference (mm)	3.00 ± 0.49	3.64 ± 0.45	0.172
Distal reference (mm)	2.60 ± 0.43	2.69 ± 0.58	0.241
MLD (mm)	2.54 ± 0.53	1.53 ± 0.76	<0.001
Diameter stenosis (%)	9.3 ± 17.4	48.0 ± 22.2	<0.001
Late loss (mm)	0.31 ± 0.57	1.45 ± 0.72	<0.001
Restenosis	3 (2.6%)	42 (43.3%)	<0.001

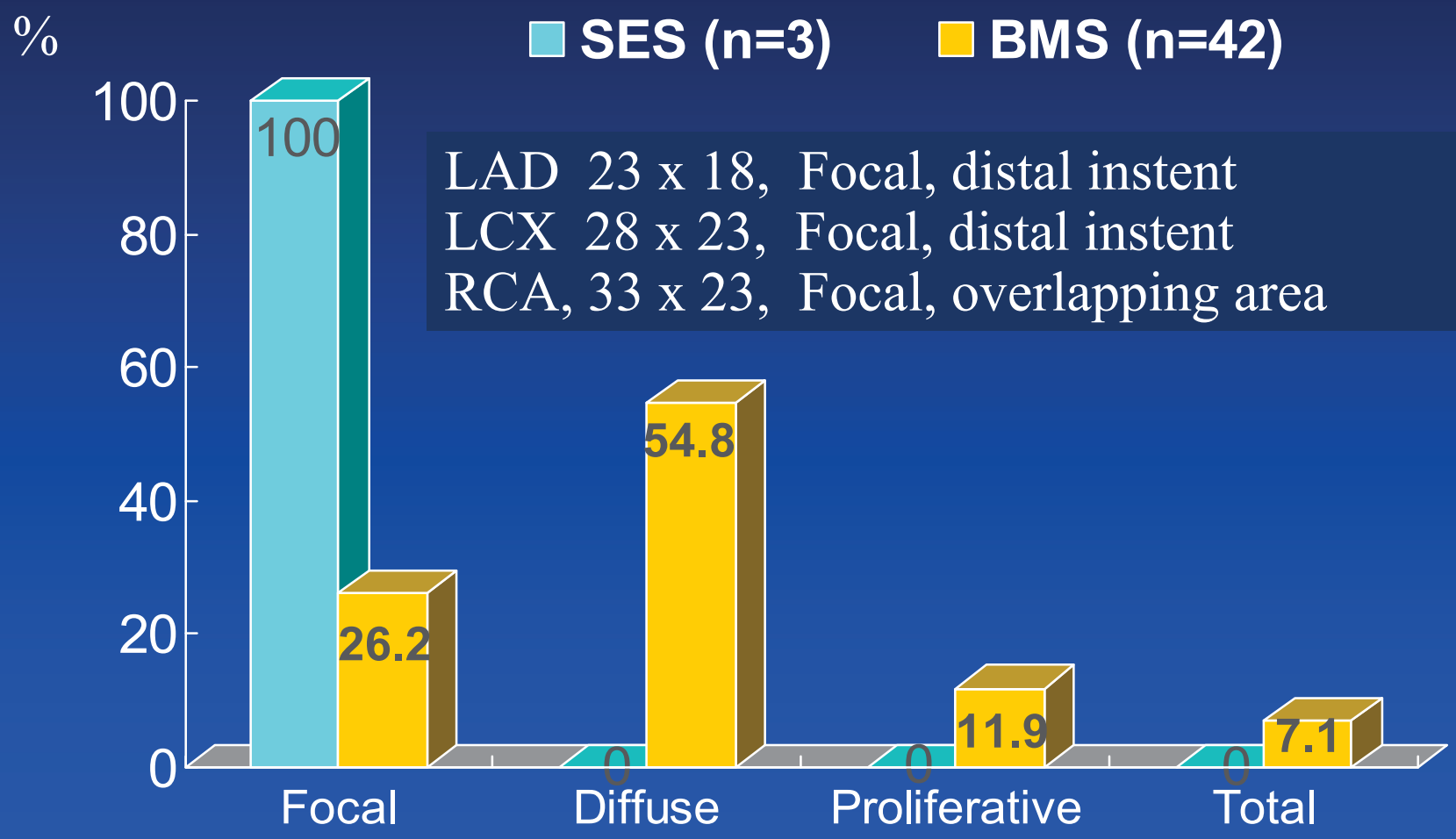
Late Loss


mm
SES (n=117)
BMS (n=97)
2.0
1.5
1.0
0.5
0.0
0.44
1.46
P<0.001
0.18
0.14
P=0.334
0.31
1.45
P<0.001
0.04
0.09
P=0.417
In-segment
Proximal edge
In-stent
Distal edge

Restenosis Rate



3 Restenosis : Focal, In-Stent

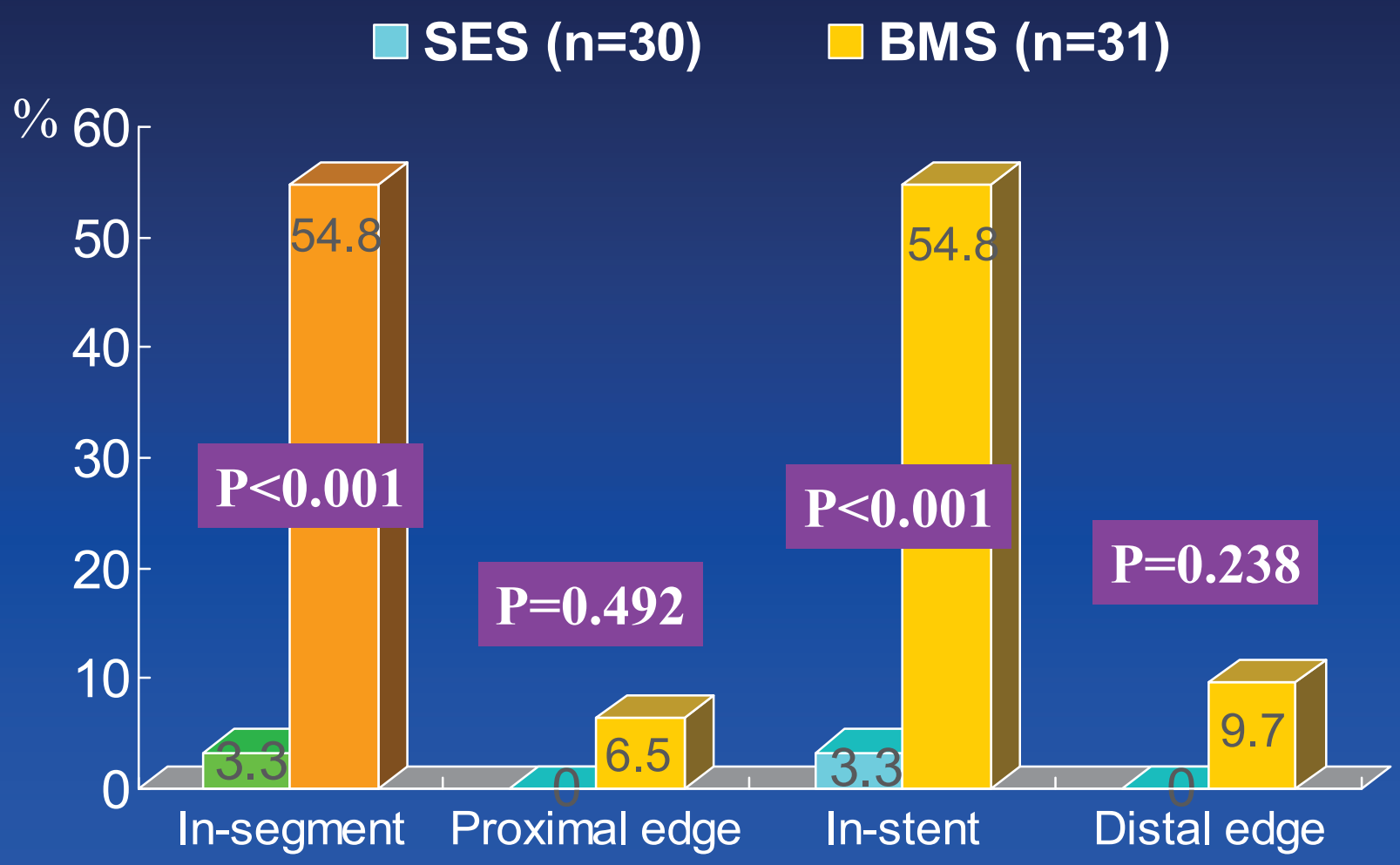


LAD 23 x 18,	Focal, distal instent	54%
LCX 28 x 23,	Focal, distal instent	56%
RCA, 33 x 23,	Focal, overlapping area	82%

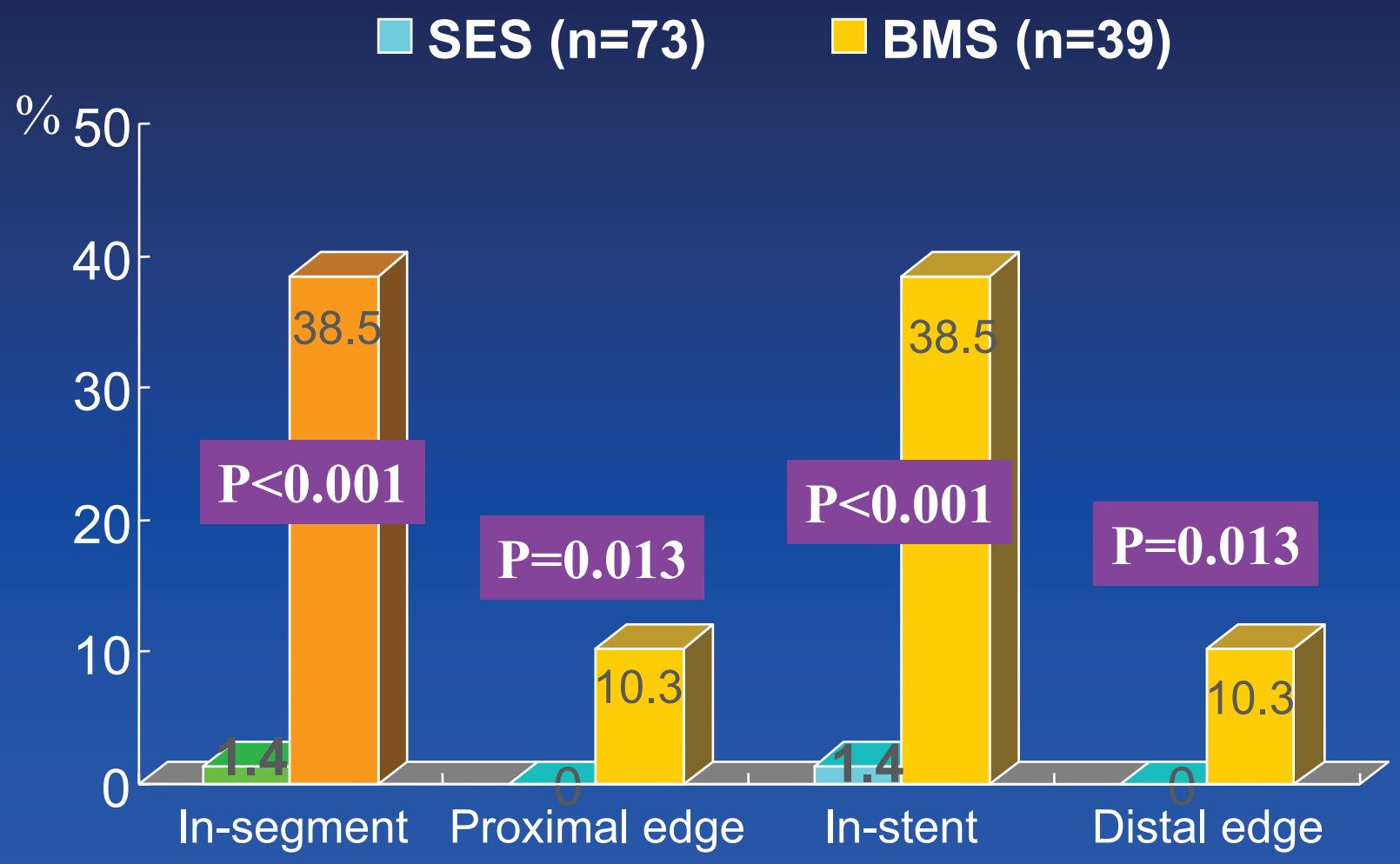
"Long Cypher"

Subgroup Analysis

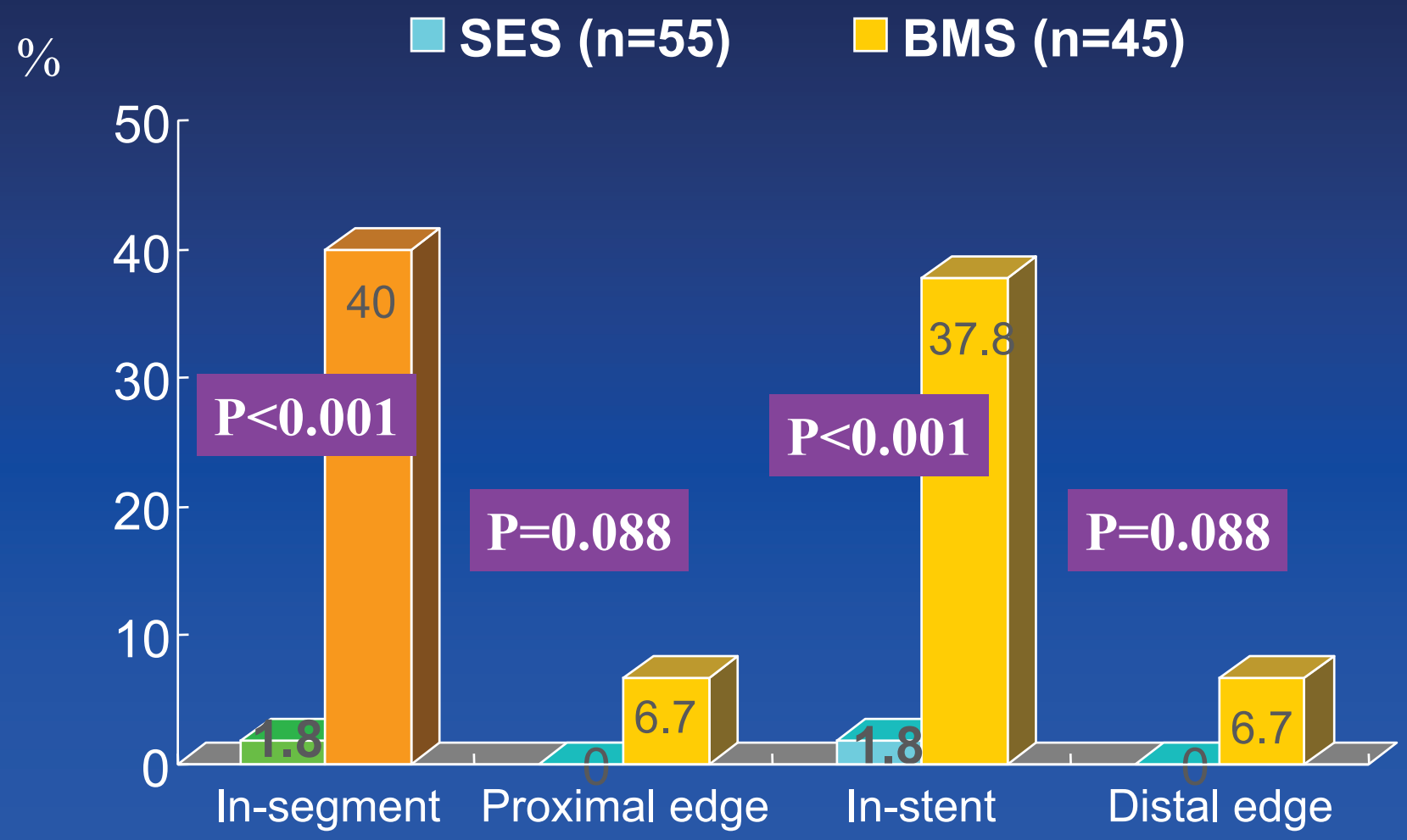
Restenosis Rate in DM : 3.3 %



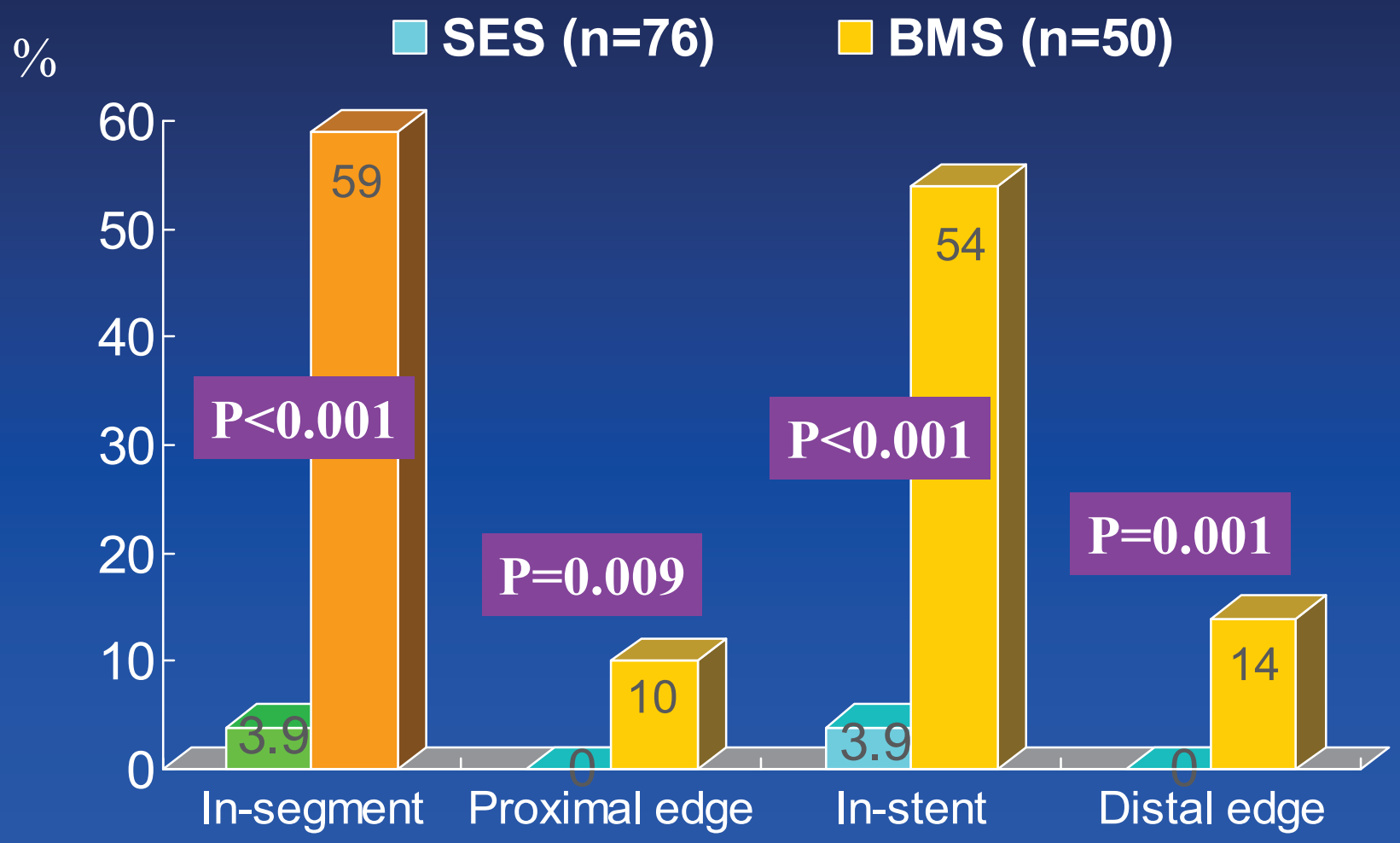
Restenosis Rate in LAD : 1.4 %



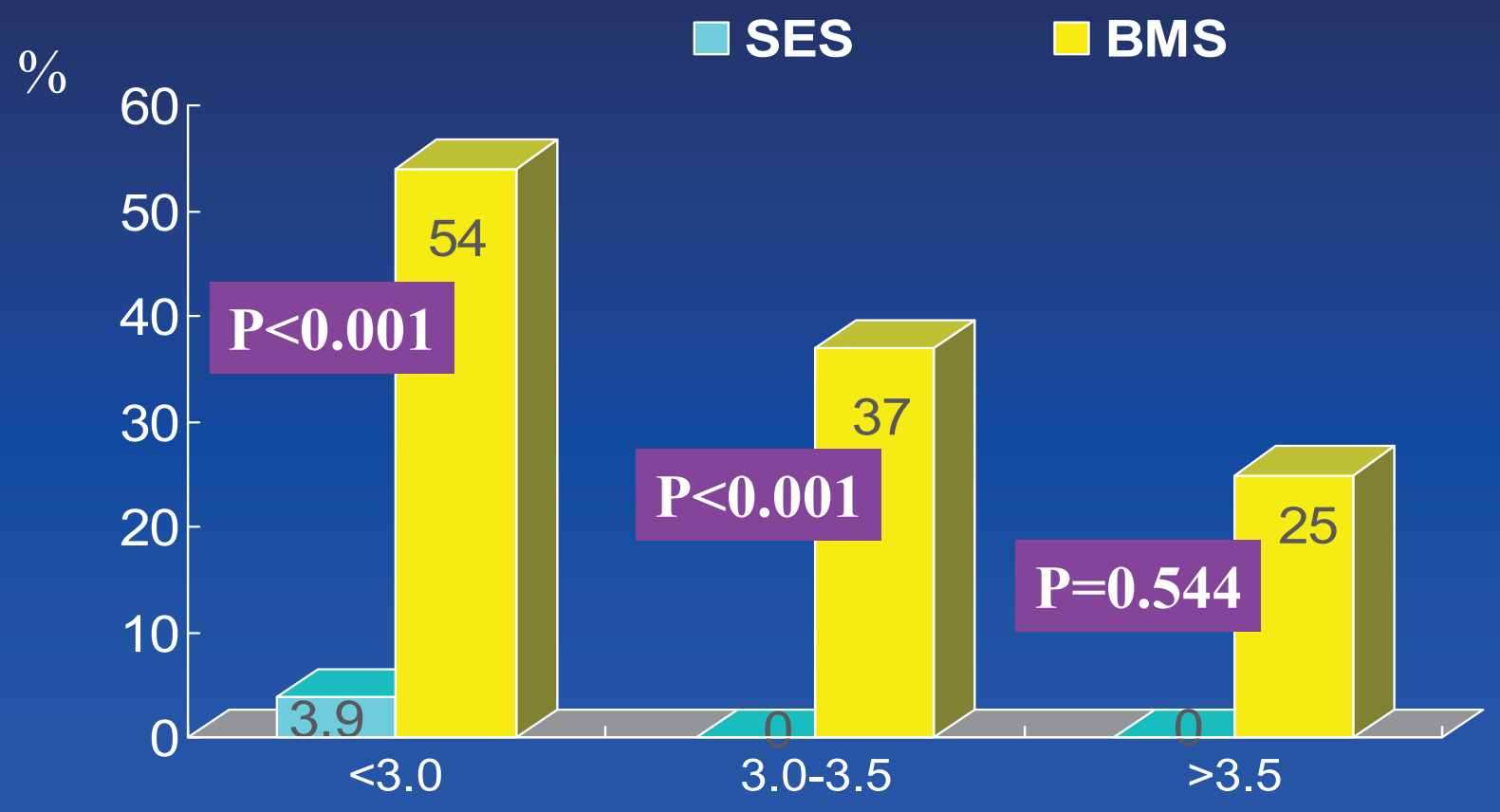
Restenosis Rate in Acute Coronary Syndrome : 1.8 %



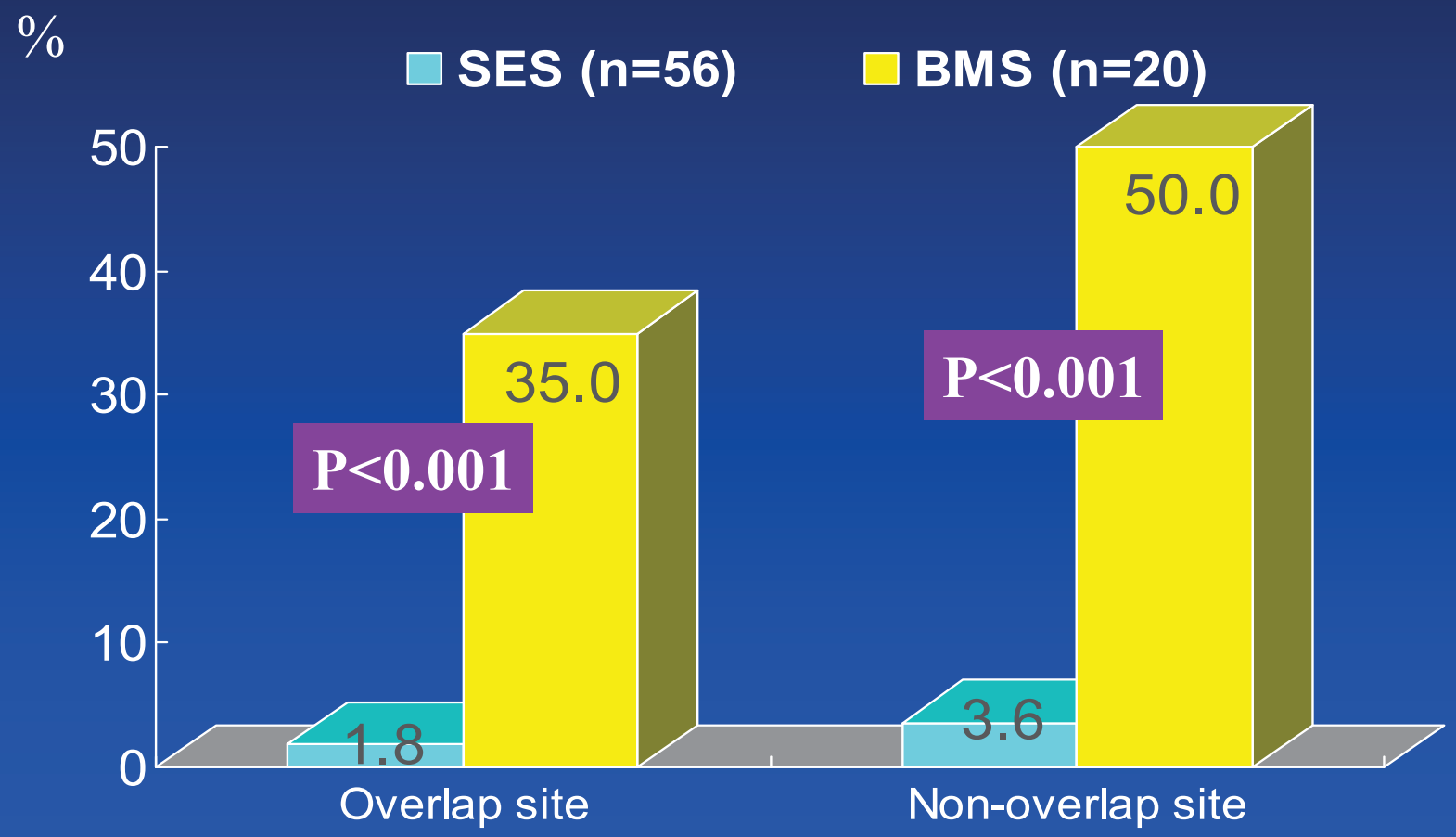
Restenosis Rate in Small Vessel (<3.0mm) : 3.9 %



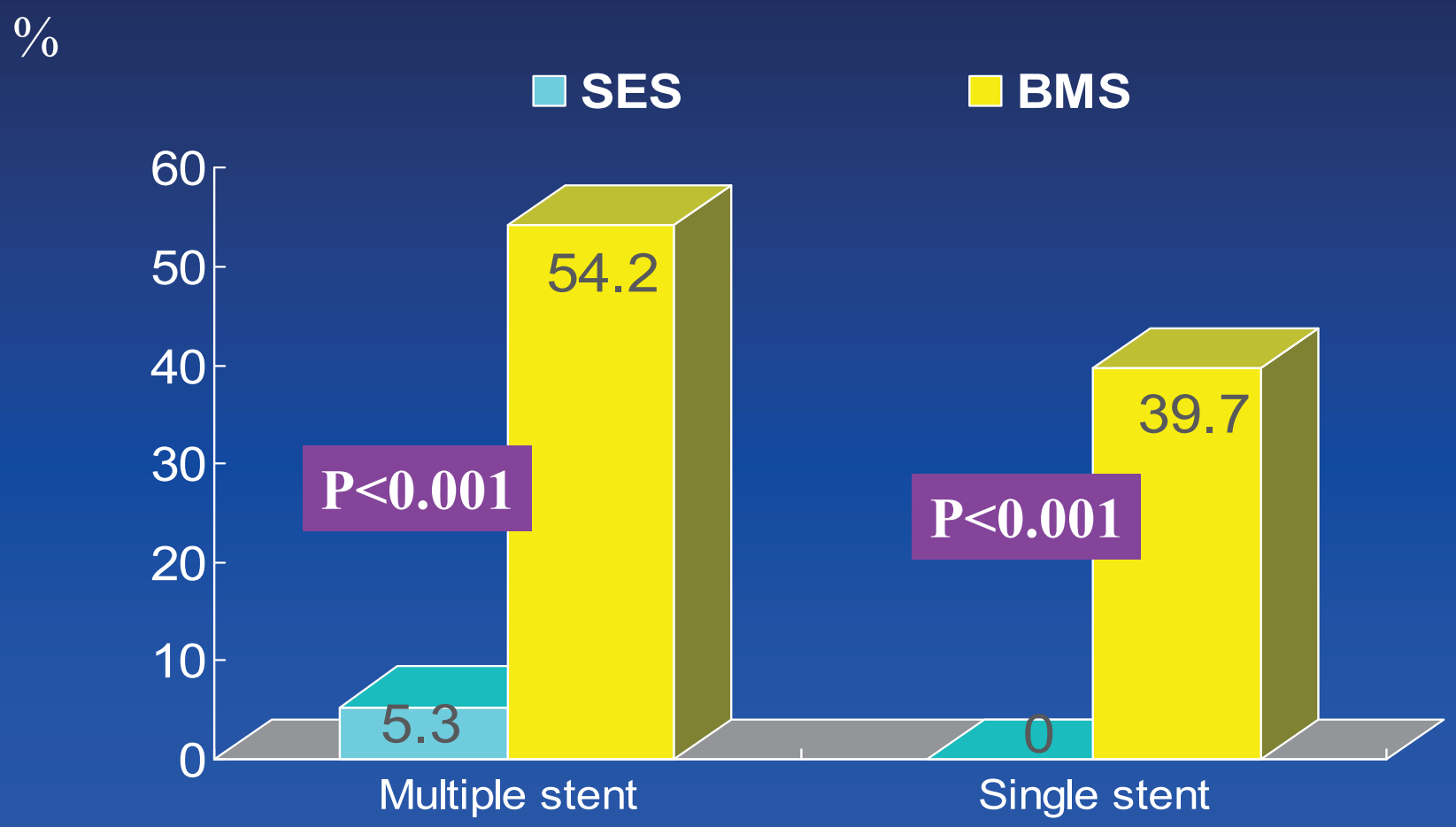
Restenosis Rate According to Reference Diameter



Restenosis Rate According to Stent Overlap : 1.8 %



Restenosis Rate According to Multiple Stenting : 5.3 %



Angiographic Restenosis : **"Cypher Better"**

	SES	BMS	P-value
Overall	2.7	46.8	<0.0001
Male	2.8	47.0	<0.0001
Female	4.3	46.2	0.0120
Diabetes	3.4	60.0	0.0001
No Diabetes	2.5	40.7	<0.0001
LAD	1.5	43.3	<0.0001
Non-LAD	4.8	49.0	<0.0001
Small Vessel (<2.75)	2.9	72.0	<0.0001
Large Vessel	2.7	35.2	<0.0001
ACS	2.0	42.5	0.0001
Non ACS	3.4	51.3	<0.0001
Overlap	5.4	55.0	<0.0001
No Overlap	0	44.1	<0.0001

"Long Cypher"
IVUS Analysis

Pre, Post-PCI and
6-month follow-up
in 67 lesions

Vulnerable plaques were frequently seen (55%) in long coronary lesions.

N	67 lesions
Thrombi	0
Lipid-pool like image	24 (36%)
Plaque rupture	13 (19%)

"Long Cypher" IVUS

Angiographically normal reference vessels actually had 28 - 38% plaque burden when seen by IVUS

Proximal reference (mm^2)	
EEM CSA (mm^2)	15.4 ± 3.6
Lumen CSA (mm^2)	9.6 ± 3.0
Plaque burden (%)	27.9 ± 6.7
Distal reference	
EEM CSA (mm^2)	9.4 ± 3.3
Lumen CSA (mm^2)	6.8 ± 2.5
Plaque burden (%)	37.9 ± 10.6

Post-Stent CSA

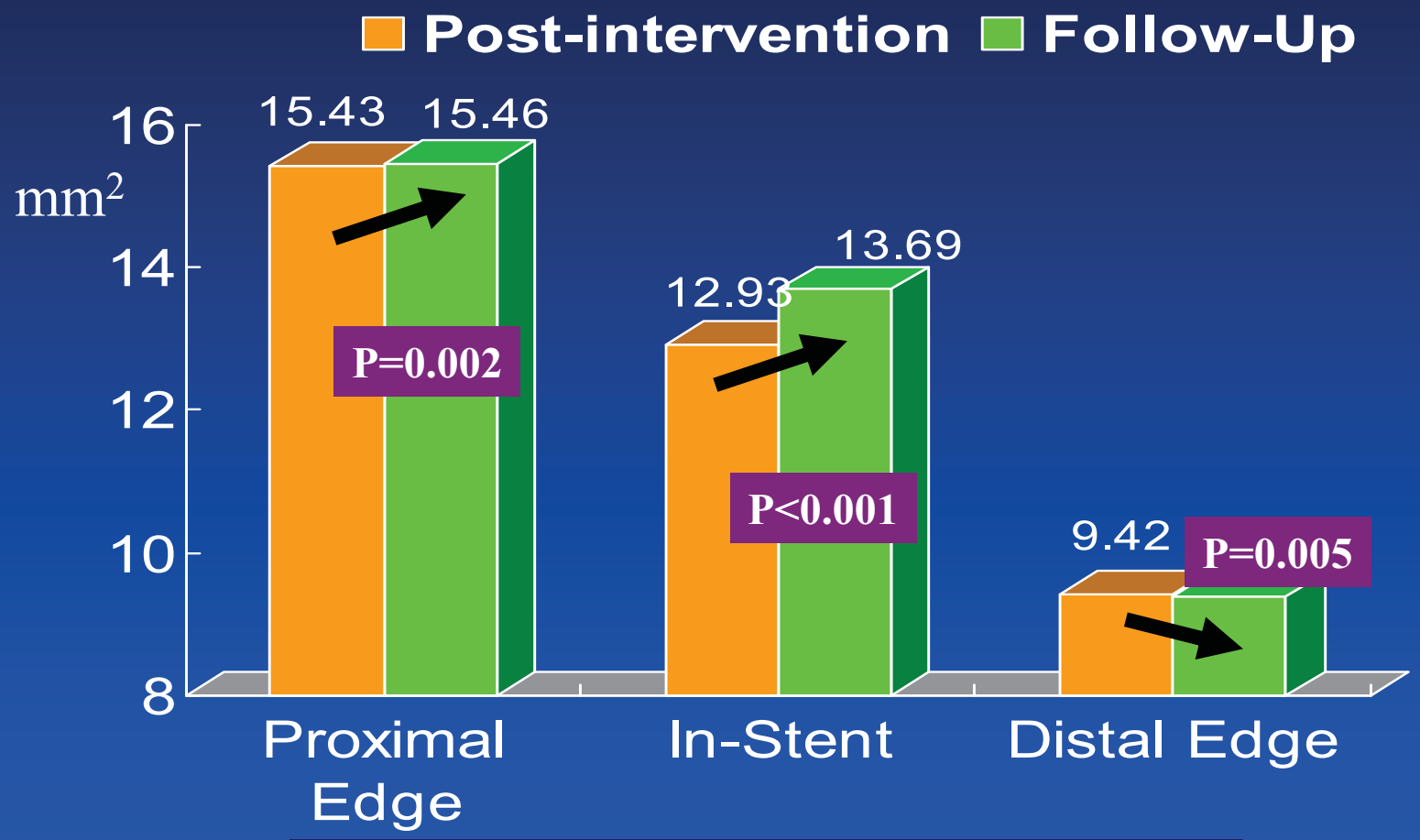
N	67 lesions
Stent (mm^2)	
EEM CSA	9.4 ± 3.3
Stent CSA	6.8 ± 2.5

"Long Cypher" IVUS

"Long Cypher"

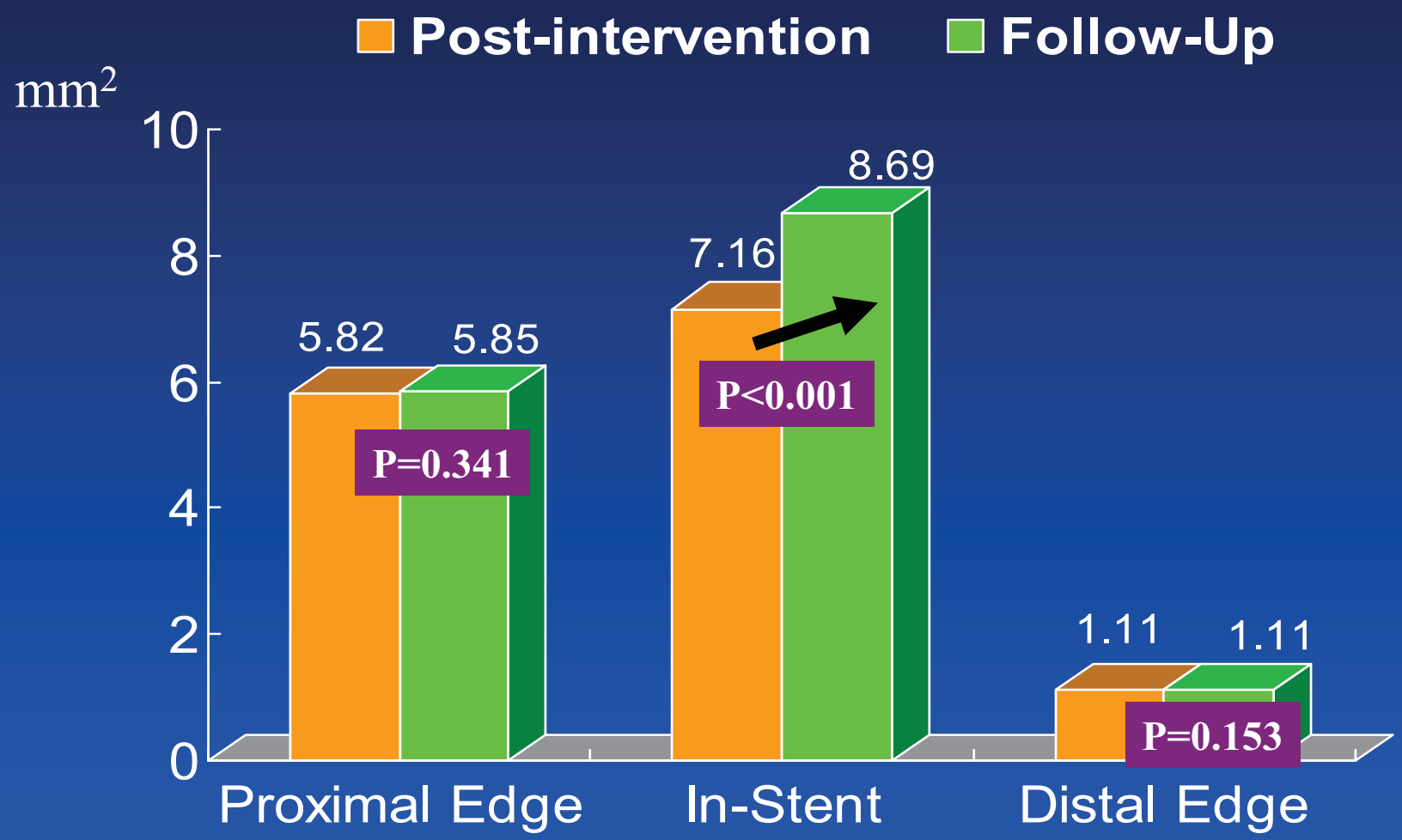
Stent Edge Analysis by IVUS

Positive vascular remodeling occurred in the proximal edge and the stented segment…



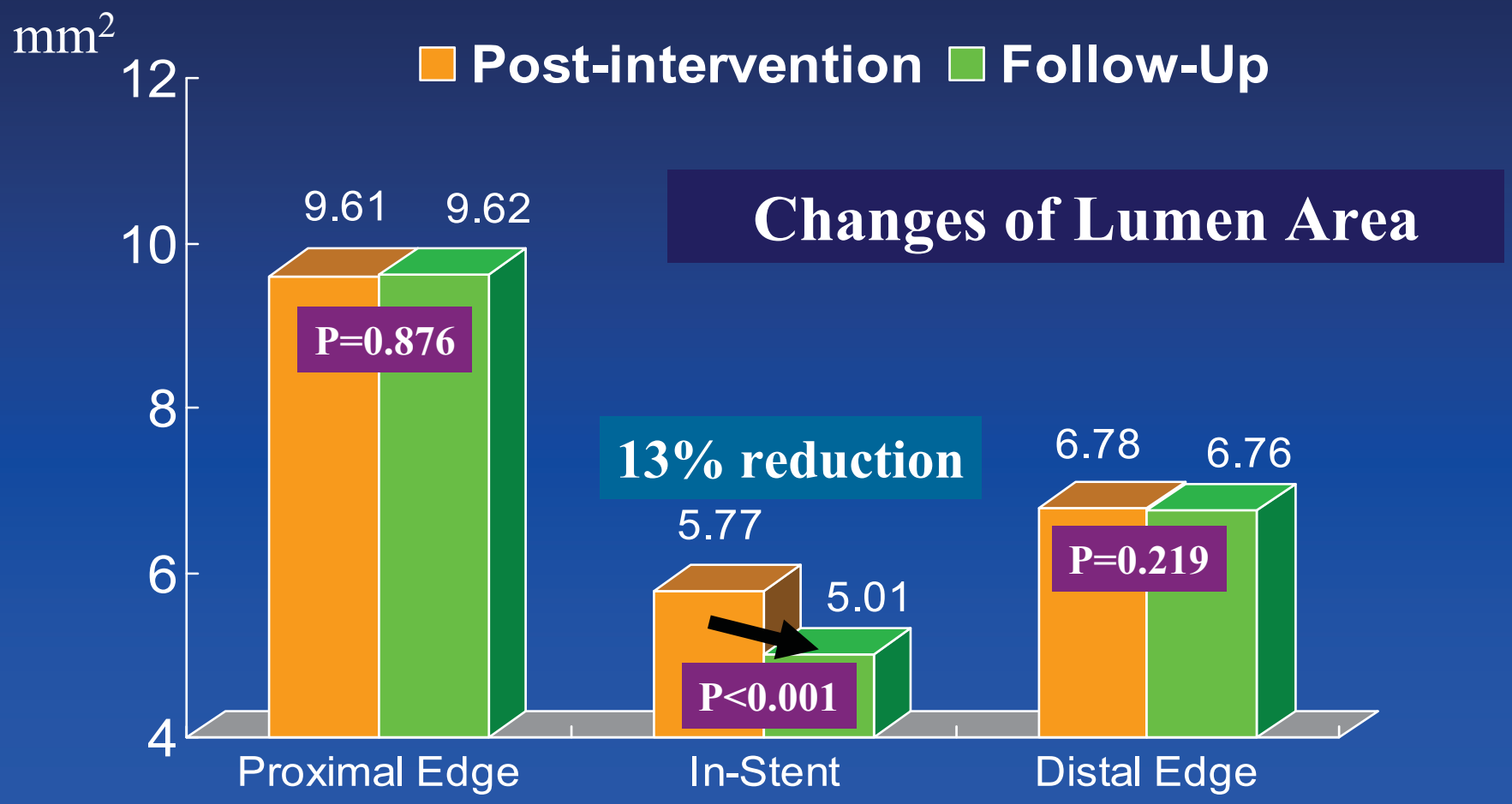
Changes of EEM Area

Plaque and media area increased in the stented segment,

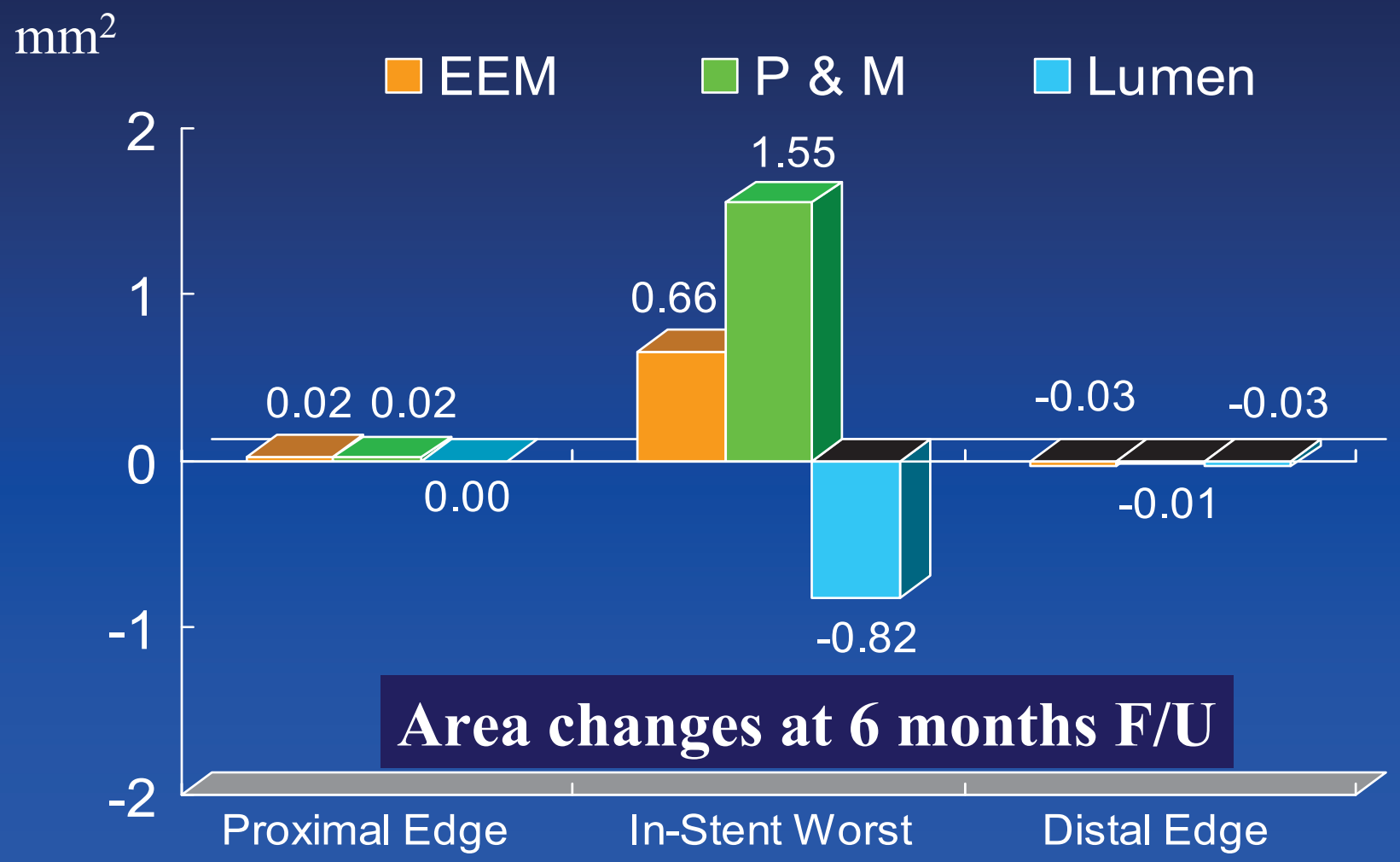


Changes of P & M Area

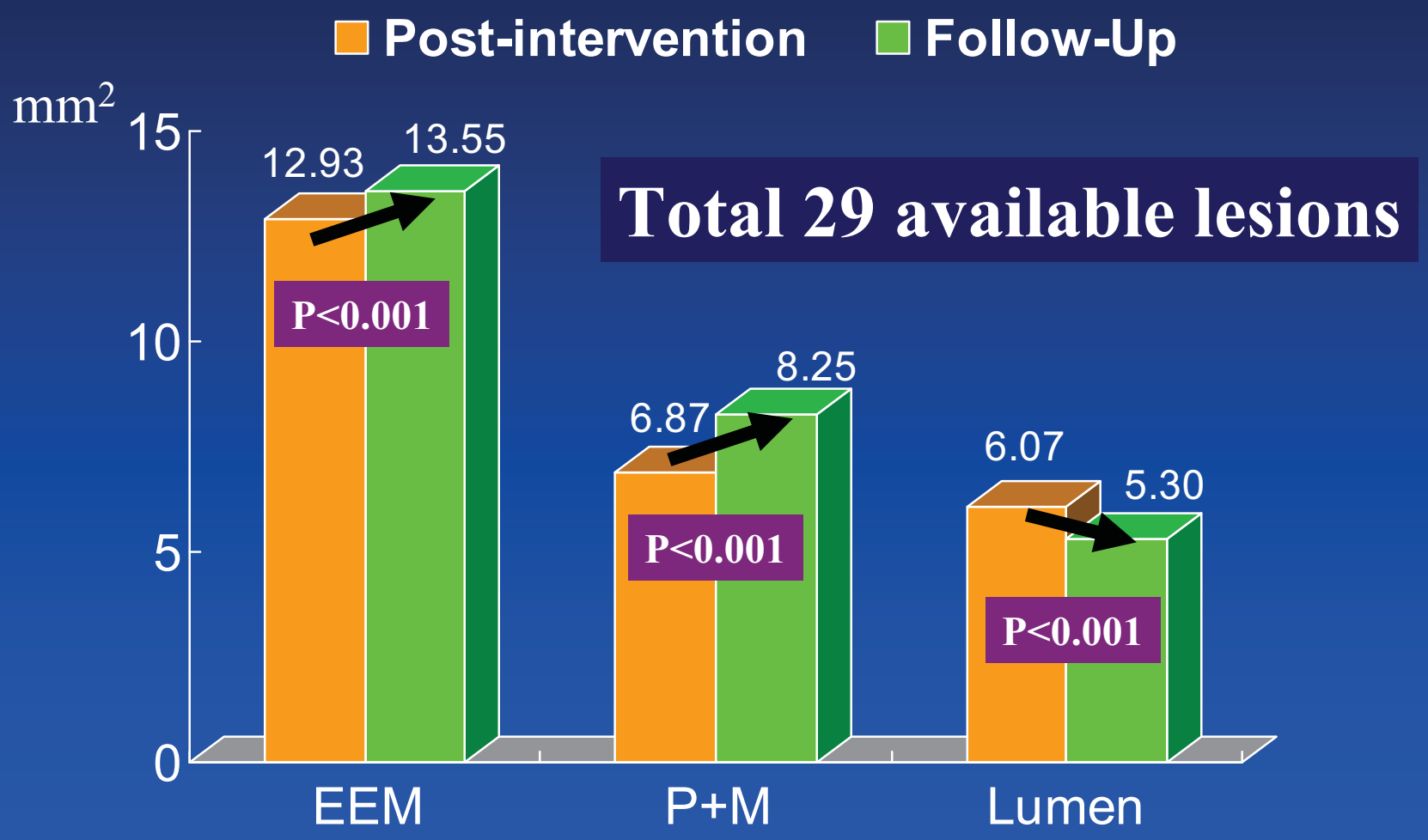
Lumen area was decreased only in stented segment…



No edge effect occurred in both stent edges

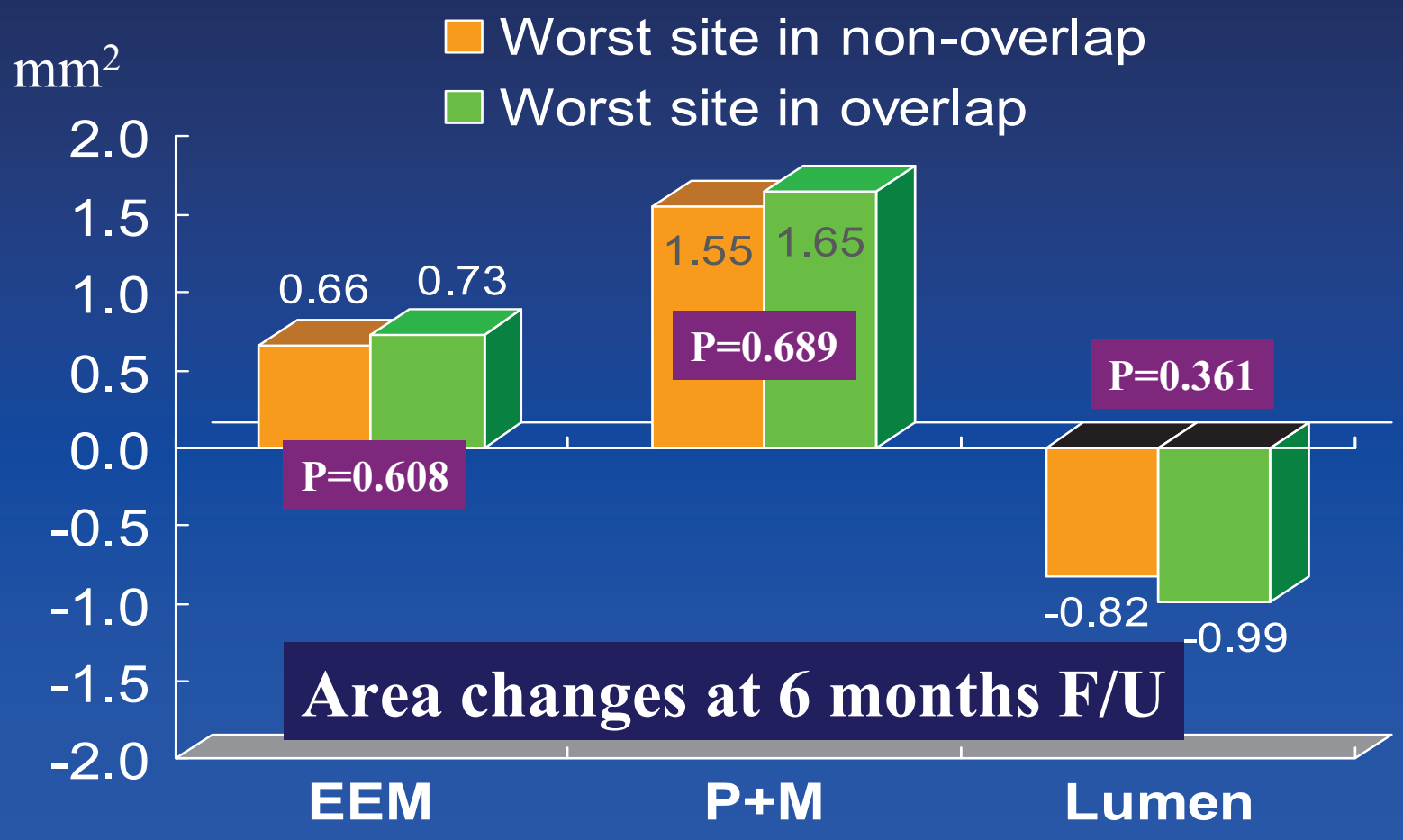


Area Change of Overlap Site



Total 29 available lesions

Stent-overlap did not show any difference



Late Stent Malapposition

(22%, 15/67 lesions) was not infrequently detected after long Cypher implantation at 6 month F/U IVUS study.

"Long Cypher" IVUS

Conclusions

- Compared with BMS, SES were more preferred in lesions at a high risk of restenosis, such as LAD lesions and very long lesions with small diameter.

“ Long Cypher ”

Conclusions

- SES implantation for very long coronary lesions was **safe with excellent early outcomes**
- Compared with BMS, SES remarkably **reduced in-stent neointimal formation and restenosis** and improved 6-month clinical outcome in patients with very long de novo coronary lesions.

“ Long Cypher ”

Conclusions

- **Edge restenosis** found in lesions with BMS implantation **was not observed in lesions with any SES implantation** at 6-month angiographic F/U.
- **Stent-overlap** did not increase adverse clinical outcomes or restenosis rate in SES implantation.
- **The superiority of SES over BMS** was consistently observed in all subgroups.

“ Long Cypher ”