

How to Optimize Long lesion Intervention with DES

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Long Coronary Lesion

Why is it complex ?

- Association with multivessel disease
- Association with diabetes mellitus
- Extended to the small distal vessel
- Involvement of bifurcation lesion
- Long treated segment
- Stent overlapping
- High incidence of periprocedural complications
- Poor long-term outcome
- Increased cost

Long lesion PCI in the era of DES

1. Safety Concerns
2. Efficacy Concerns

We have very limited data yet.

Perspective

Stent Thrombosis Redux — The FDA Perspective

Andrew Farb, M.D., and Ashley B. Boam, M.S.

As compared with on-label use, off-label use is associated with increased risks of stent thrombosis and death or myocardial infarction

NEJM 2007;356:10



Off-label Use :
Very long lesion stenting
with DES

More Prone to Stent Thrombosis ?

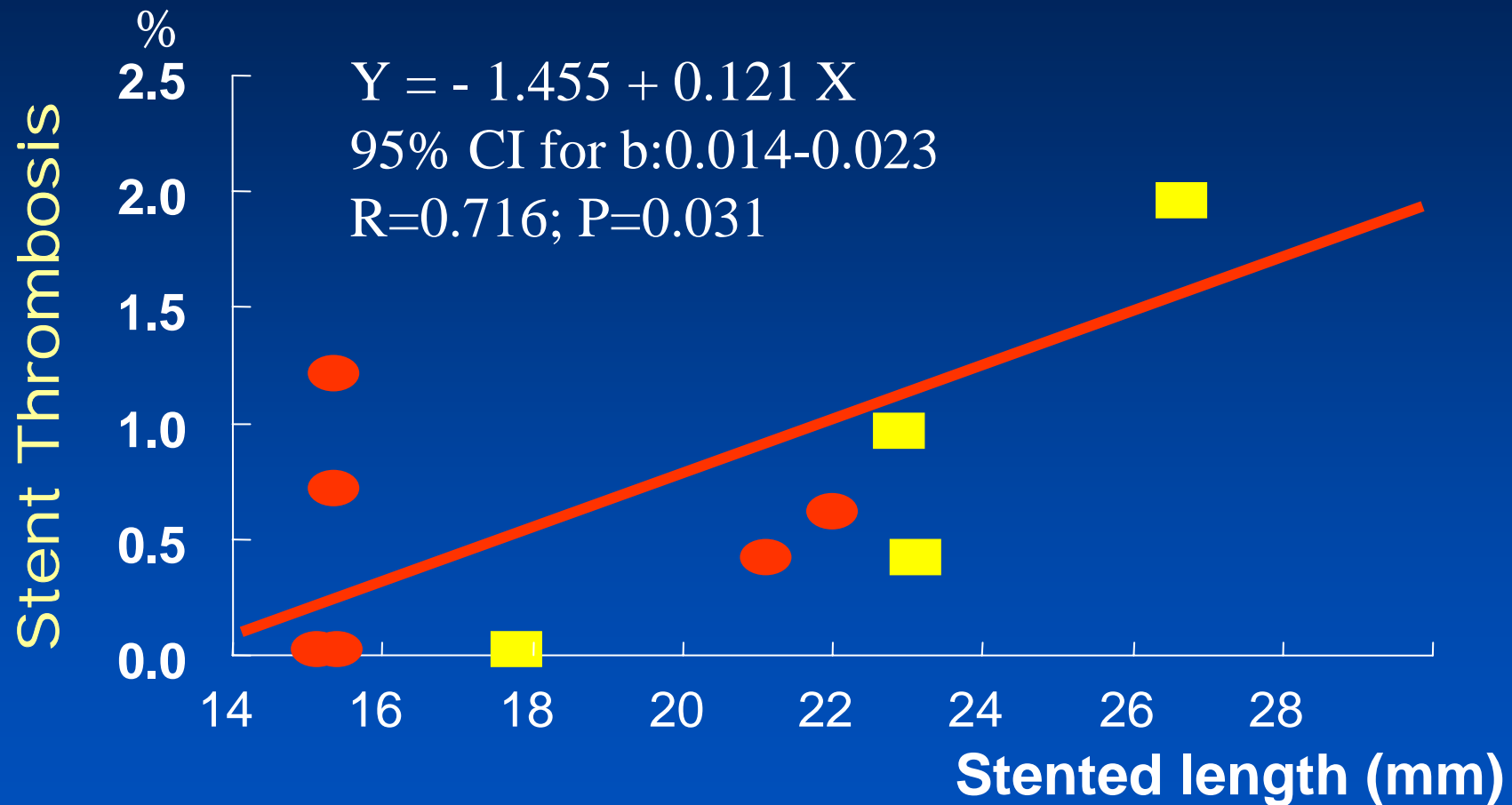
Independent Predictors of Subacute Stent Thrombosis

Analysis of 2229 patients treated with DES

Variables	Hazard Ratio (95% CI)	P value
Premature antiplatelet discontinuation	161.17 (26.03-997.94)	<0.001
Renal failure	5.96 (1.90-18.68)	<0.001
Bifurcation lesion	5.96 (1.90-18.68)	0.002
Diabetes	5.84 (1.74-19.56)	0.004
LVEF per 10% decrease	1.12 (1.06-1.19)	<0.001
Stent length per 1mm increase	1.03 (1.00-1.05)	0.01

Iakovou I et al. JAMA 2005;293:2126

Stent thrombosis rate increased with increased Stented segment length by meta-analysis



Moreno R et al. J Am Coll Cardiol 2005;45:954

Independent Predictors of ST Multivariate Analysis

Variables	(95% CI)	P
Acute / subacute stent thrombosis		
• Primary stenting in acute MI	74.22 (5.89-861.45)	0.001
• Total stent length	1.04 (1.01-1.08)	0.048
Late stent thrombosis		
• Premature interruption of antiplatelet therapy	24.79 (7.51-81.84)	<0.001
• Renal failure	8.40 (1.81-39.09)	<0.001
Total stent thrombosis		
• Premature interruption of antiplatelet therapy	19.21 (5.63-65.51)	<0.001
• Primary stenting in acute MI	12.24 (1.67-89.71)	0.014
• Total stent length	1.02 (1.001-1.04)	0.037

Park, DW. AJC 2006;98:353-356

Safety concerns...

Long Lesion PCI

- Total stent thrombosis rate was 0.8% (early stent thrombosis 0.2%, late stent thrombosis rate 0.6%), which was quite low rather than we expected for 2 year follow up period.
- Total stented length was independent risk factor for early stent thrombosis.
- Premature interruption of antiplatelet therapy and renal failure were independent risk factor for late stent thrombosis.

Long lesion PCI in the era of DES

1. Safety Concerns
2. Efficacy Concerns

Long lesion PCI in the era of DES

Very long lesions
> 30mm

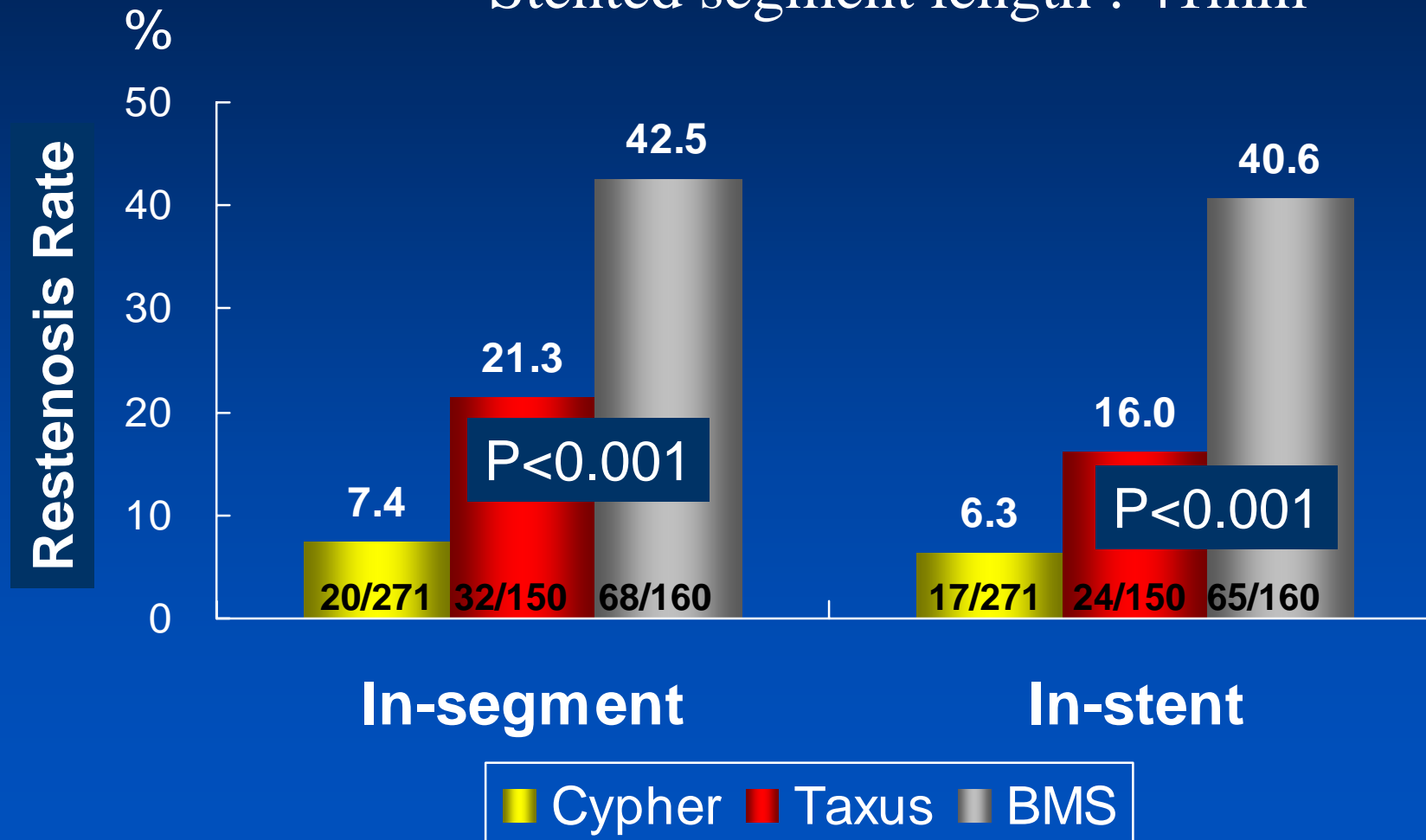
We have limited data.

We cannot conduct RCTs

Long DES-I

Lesion length :36 mm

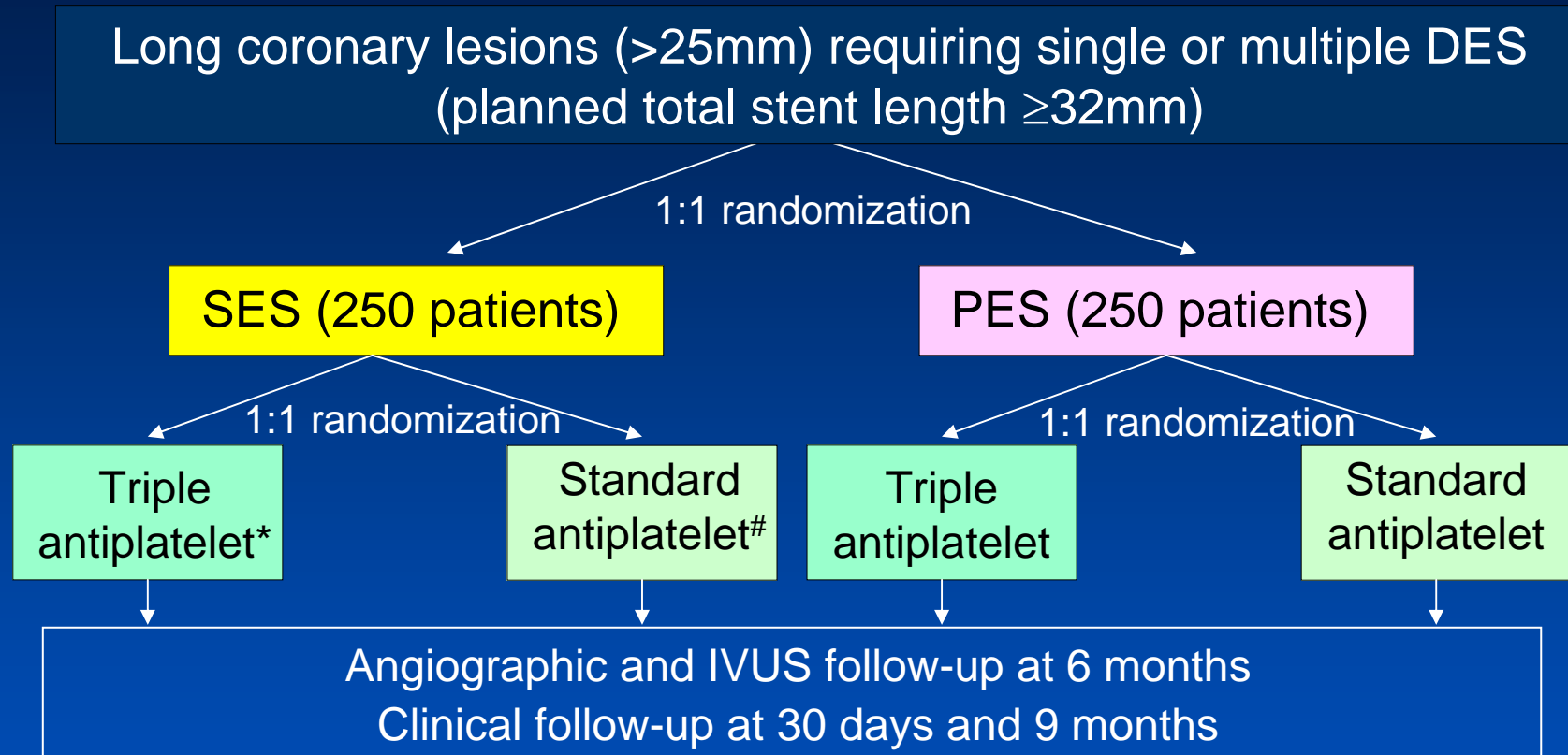
Stented segment length : 41mm



Kim YH et al, *Catheter Cardiovasc Interv* 2006;67:181-7

Long-DES II

Prospective,
Randomized
Multicenter trials



Primary endpoint:

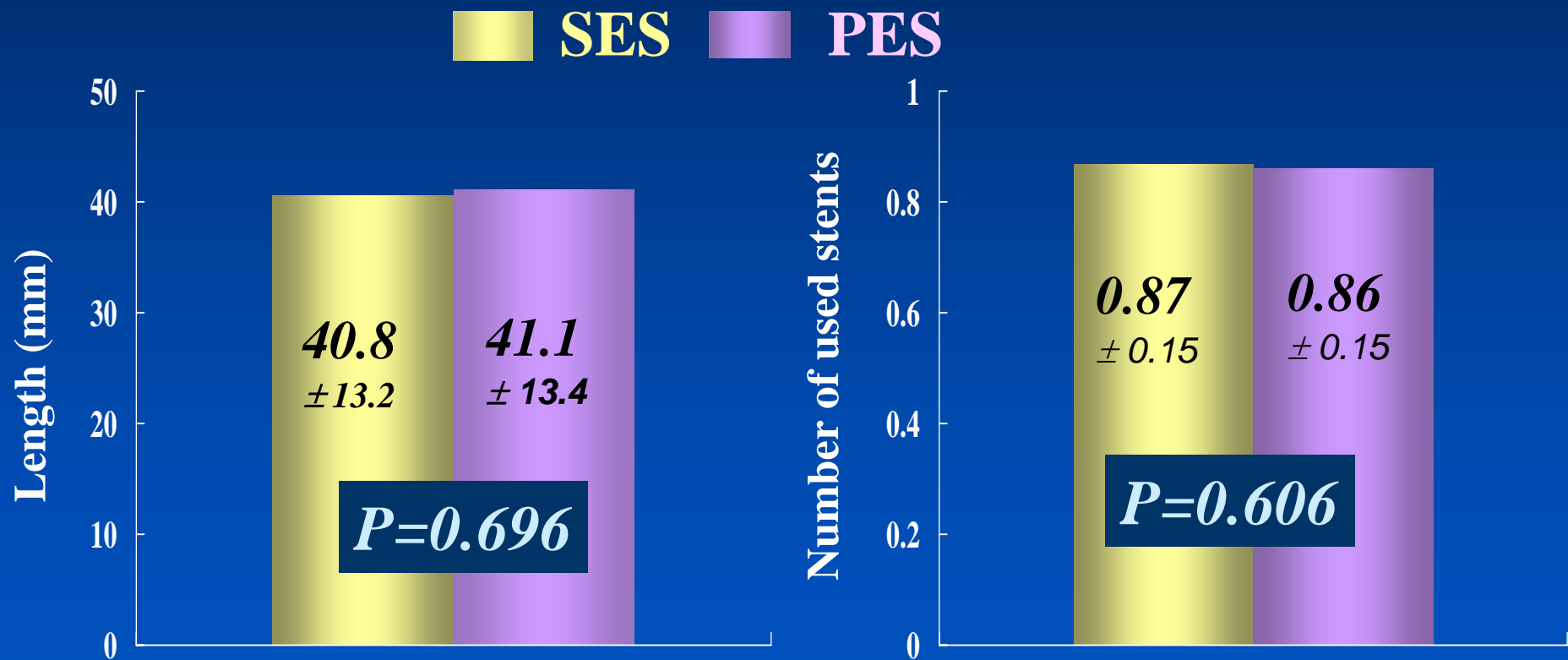
1. Comparison of SES or PES: binary in-segment restenosis at 6 months
2. Comparison of triple and standard antiplatelet: in-stent late loss at 6 months

Kim YH, Long DES-II investigator, Circulation, 2006;114:2148-2153

Stented Segment

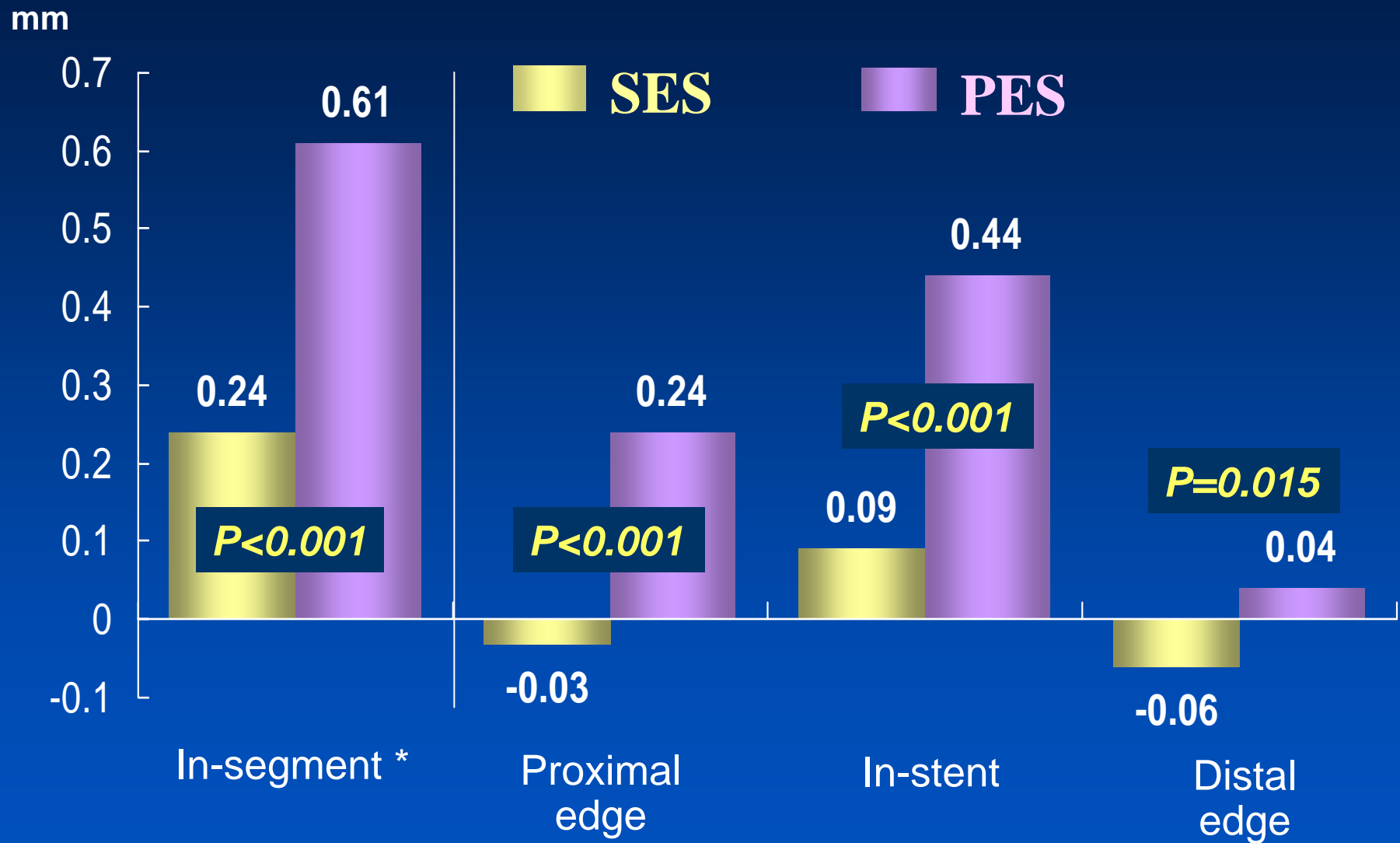
Angiographic Length of stented segment

Ratio of Length of Stent / Lesion



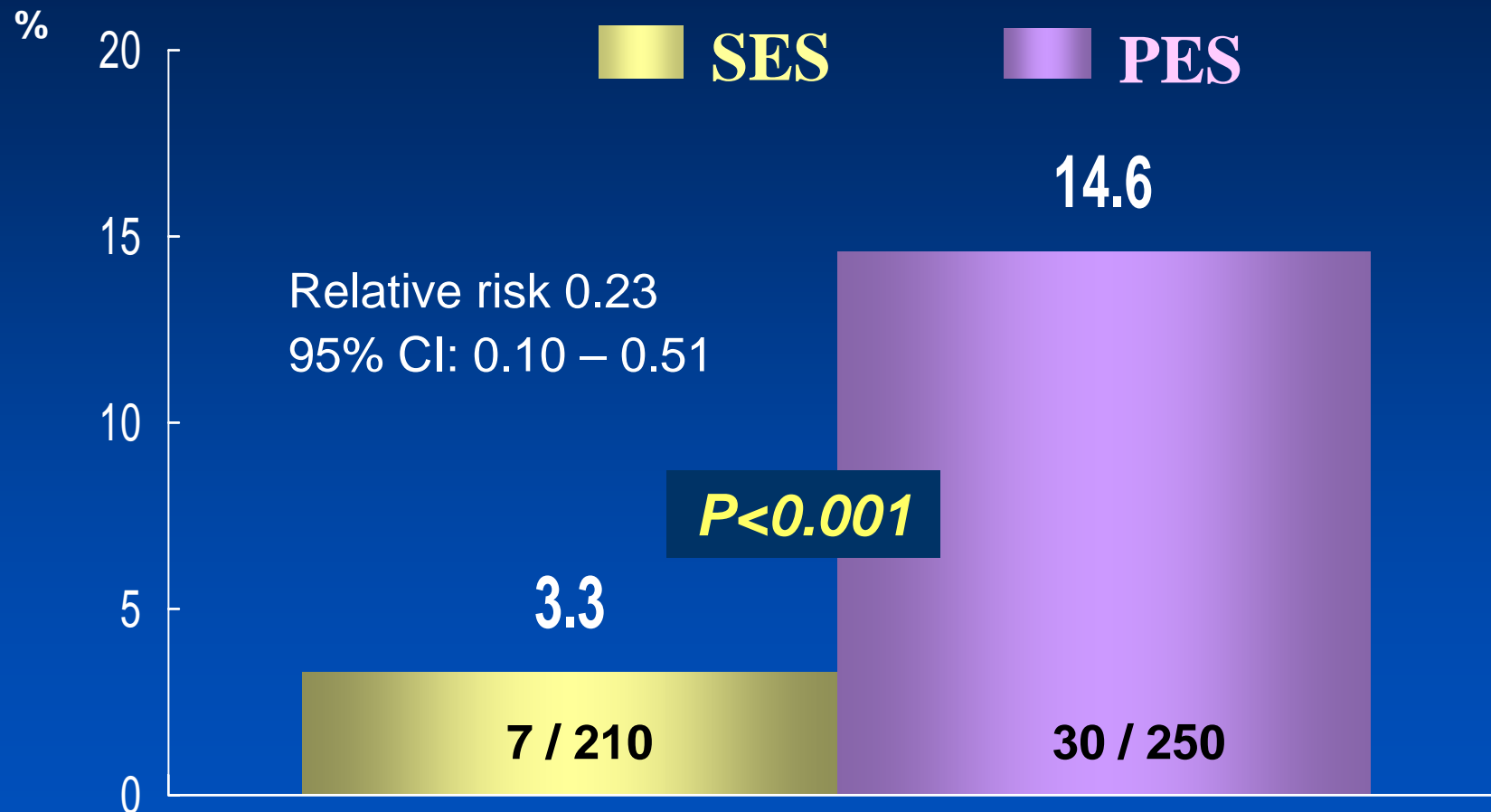
Kim YH, Long DES-II investigator, *Circulation*, 2006;114:2148-2153

Late Loss



* Maximal regional late loss, $(-0.01 \pm 0.37$ in SES and 0.31 ± 0.53 in PES ($p < 0.001$) if subtracted from the whole segment)

Primary Study End Point In-Segment Restenosis Rate



Kim YH, Long DES-II investigator, *Circulation*, 2006;114:2148-2153

Pattern of Restenosis

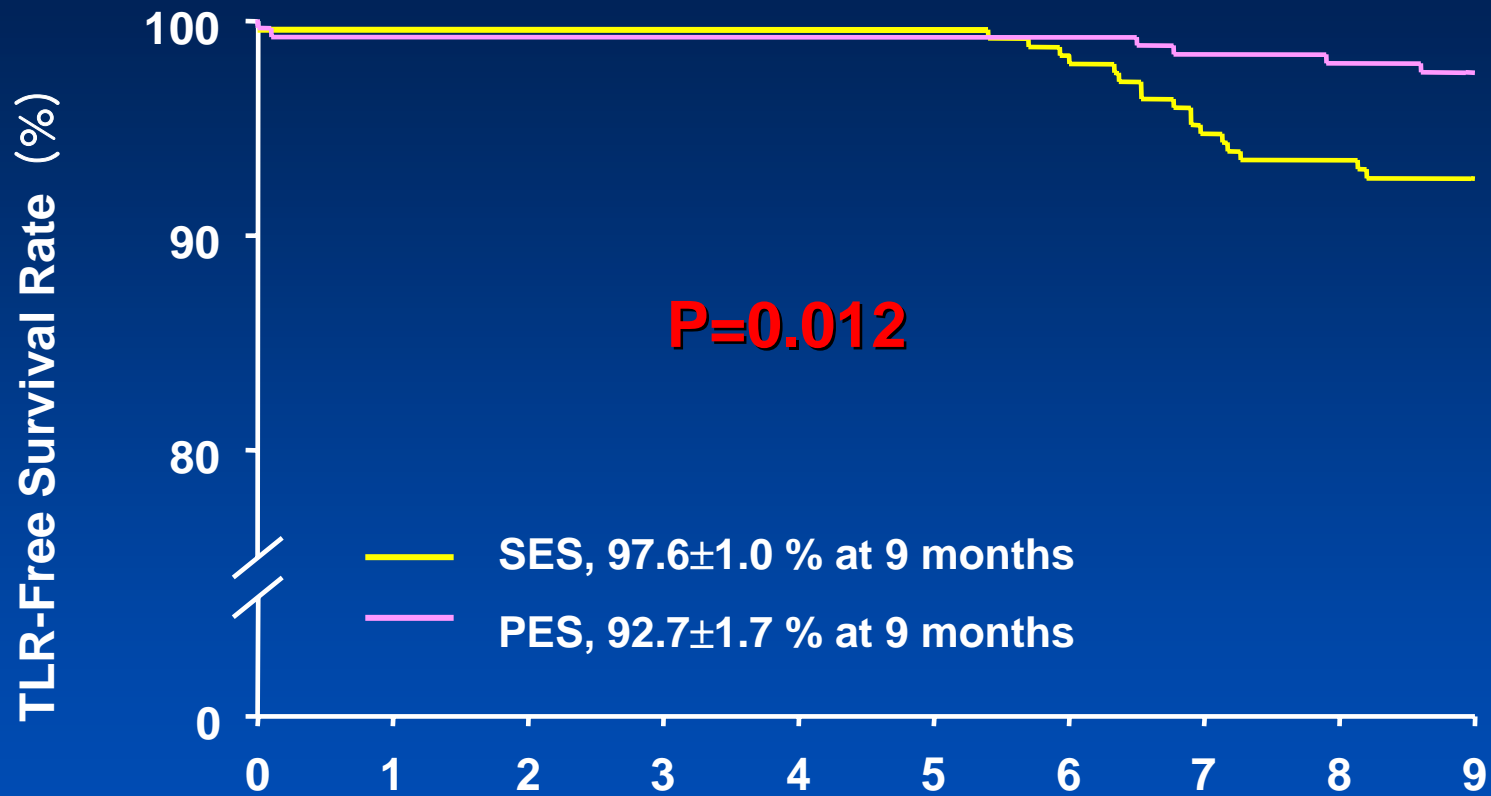
Variable	SES (N=7)	PES (N=30)	P
Focal	7 (100%)	16 (53.3%)	0.031
IA (Articulation or gap)	0	0	1.000
IB (Margin)	0	6 (20.0%)	0.571
IC (Focal body)	✓ 6 (85.7%)	8 (26.7%)	0.007
ID (Multifocal)	1 (14.3%)	2 (6.7%)	0.477
Diffuse	0	14 (46.7%)	0.031
II (Intra-stent)	0	9 (30.0%)	0.160
III (Proliferative)	0	0	1.000
IV (total occlusion)	0	5 (16.7%)	0.560
Length of in-stent restenosis, mm	5.5±3.1	11.6±7.1	0.016

Clinical Outcomes at 9 Mo

Variable	SES (N=250)	PES (N=250)	<i>p</i>
Death	2 (0.8%)	0	0.499
Cardiac	1 (0.4%) *	0	1.000
Non-cardiac	1 (0.4%)	0	1.000
MI	22 (8.8%)	27 (10.8%)	0.452
Non-Q	21 (8.4%)	27 (10.8%)	0.362
Q	1 (0.4%) *	0	1.000
TLR	6 (2.4%)	18 (7.2%)	0.012
TVR	8 (3.2%)	19 (7.6%)	0.030
Stent thrombosis	2 (0.8%)	0	0.499
Composite of death, MI, and TLR	28 (11.2%)	42 (16.8%)	0.071
Composite of death, MI, and TVR	30 (12.0%)	43 (17.2%)	0.100

* The patient was dead by Q-MI without angiographic documentation.

TLR-Free Survival Curves



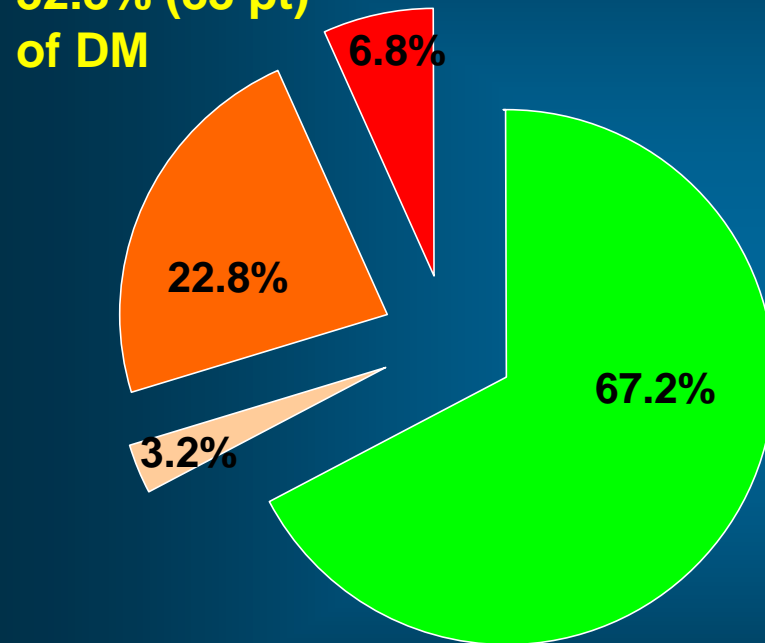
No. at Risk	Months of Follow-up									
	0	1	2	3	4	5	6	7	8	9
SES	250	249	249	247	247	247	247	244	243	241
PES	250	250	250	250	250	250	246	236	232	227

Impact of DM

Diabetes Mellitus

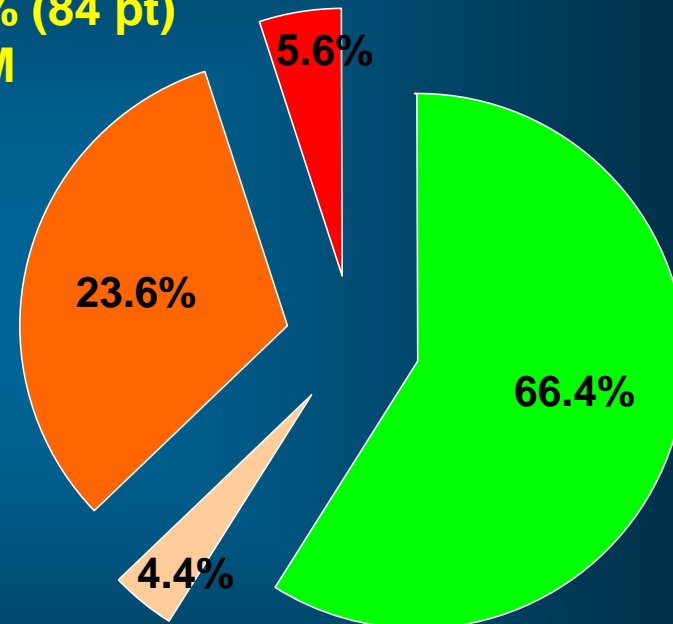
SES
(N=250)

32.8% (83 pt)
of DM



PES
(N=250)

33.6% (84 pt)
of DM



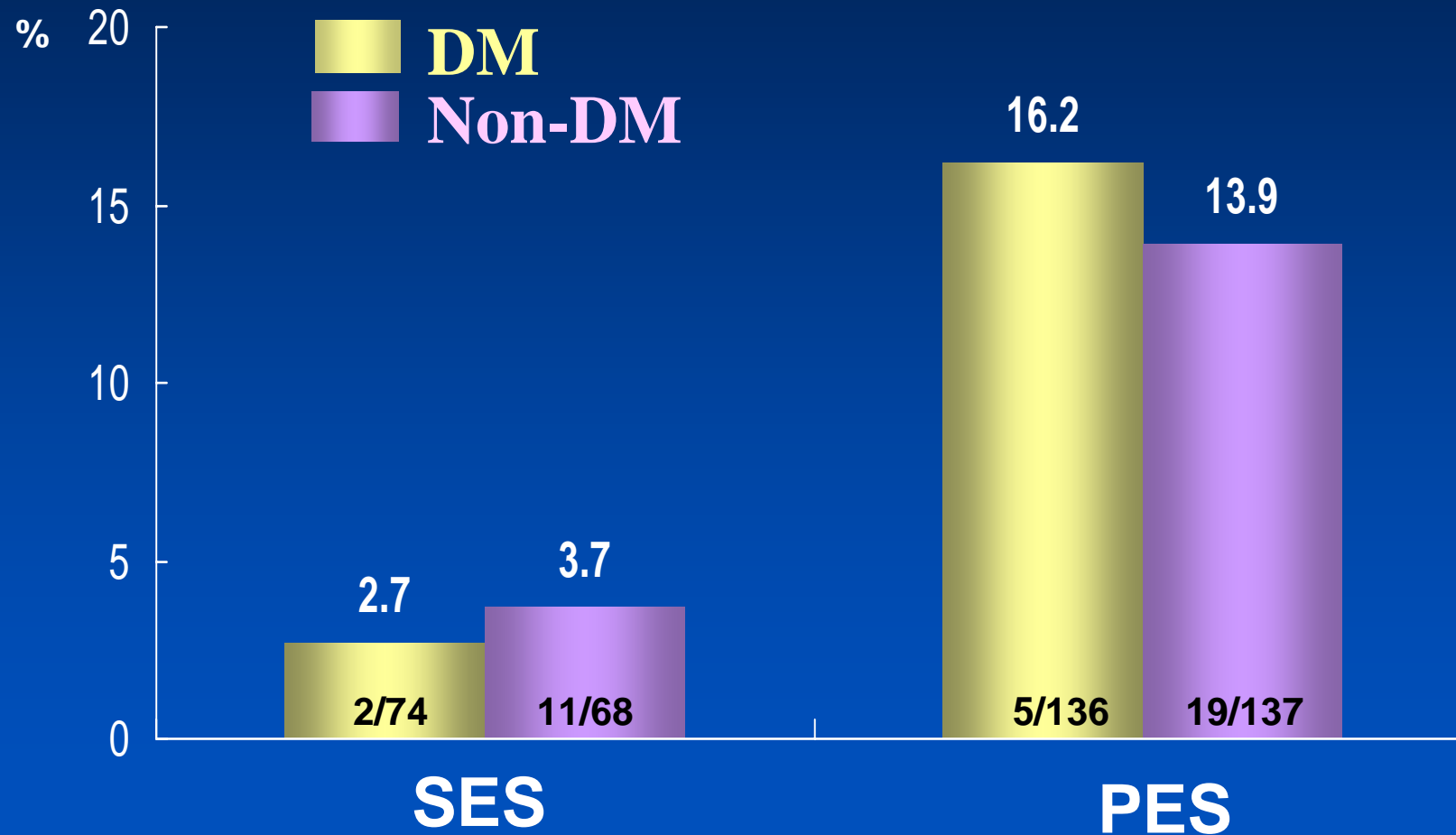
■ Non-DM

■ DM on diet

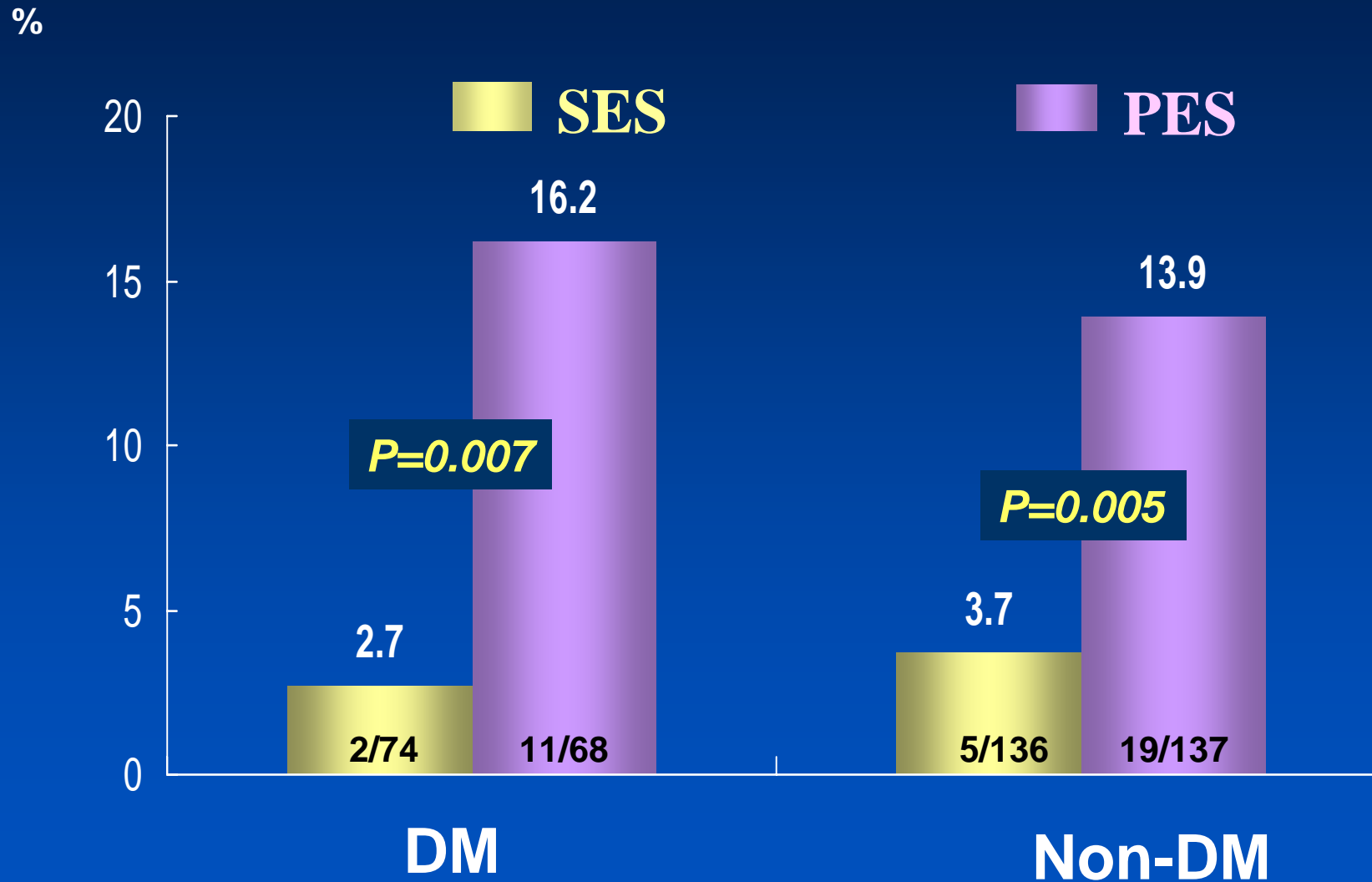
■ DM on oral agent

■ DM on insulin

Impact of Diabetes Mellitus In-segment Restenosis

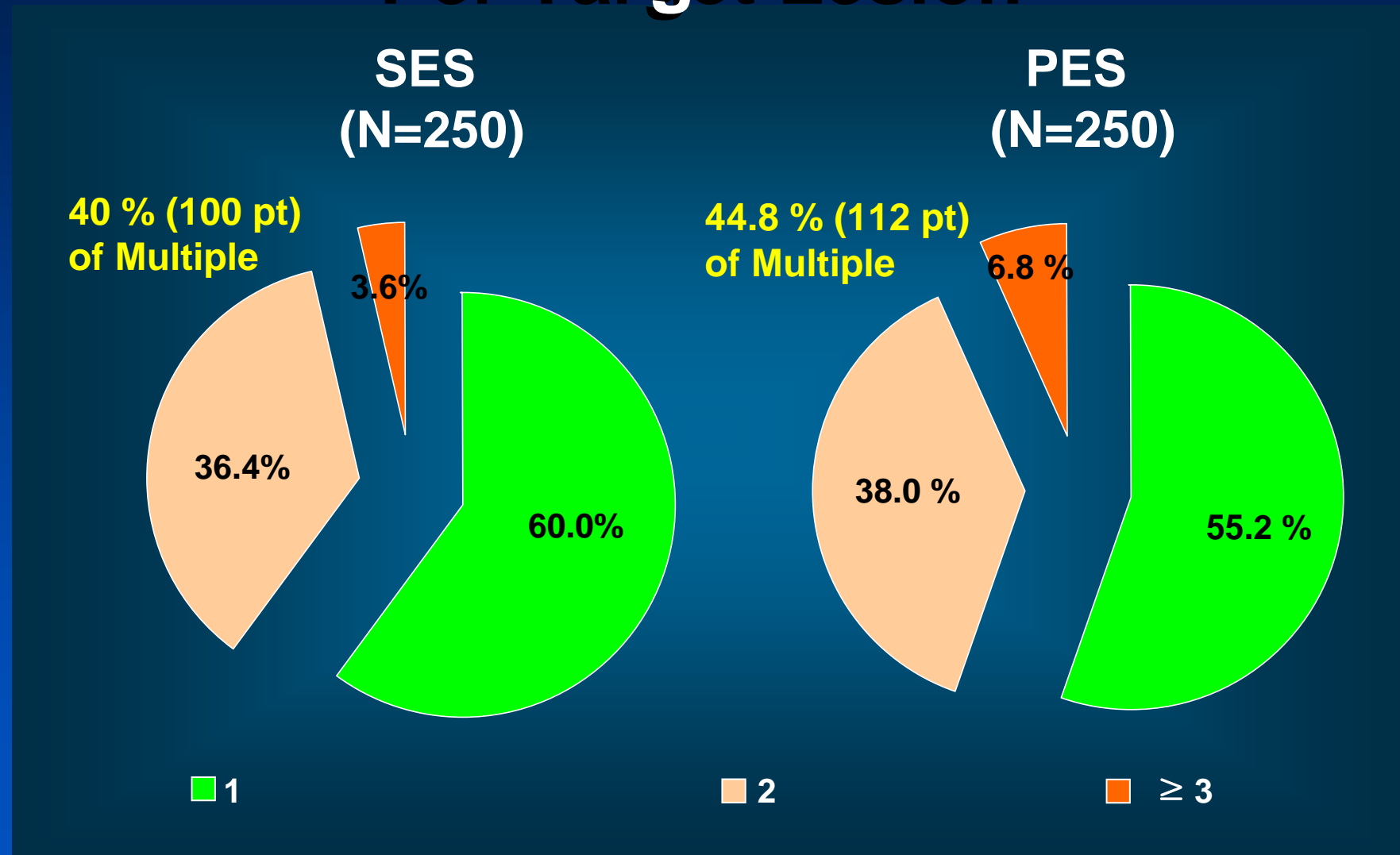


Impact of Diabetes Mellitus In-segment Restenosis



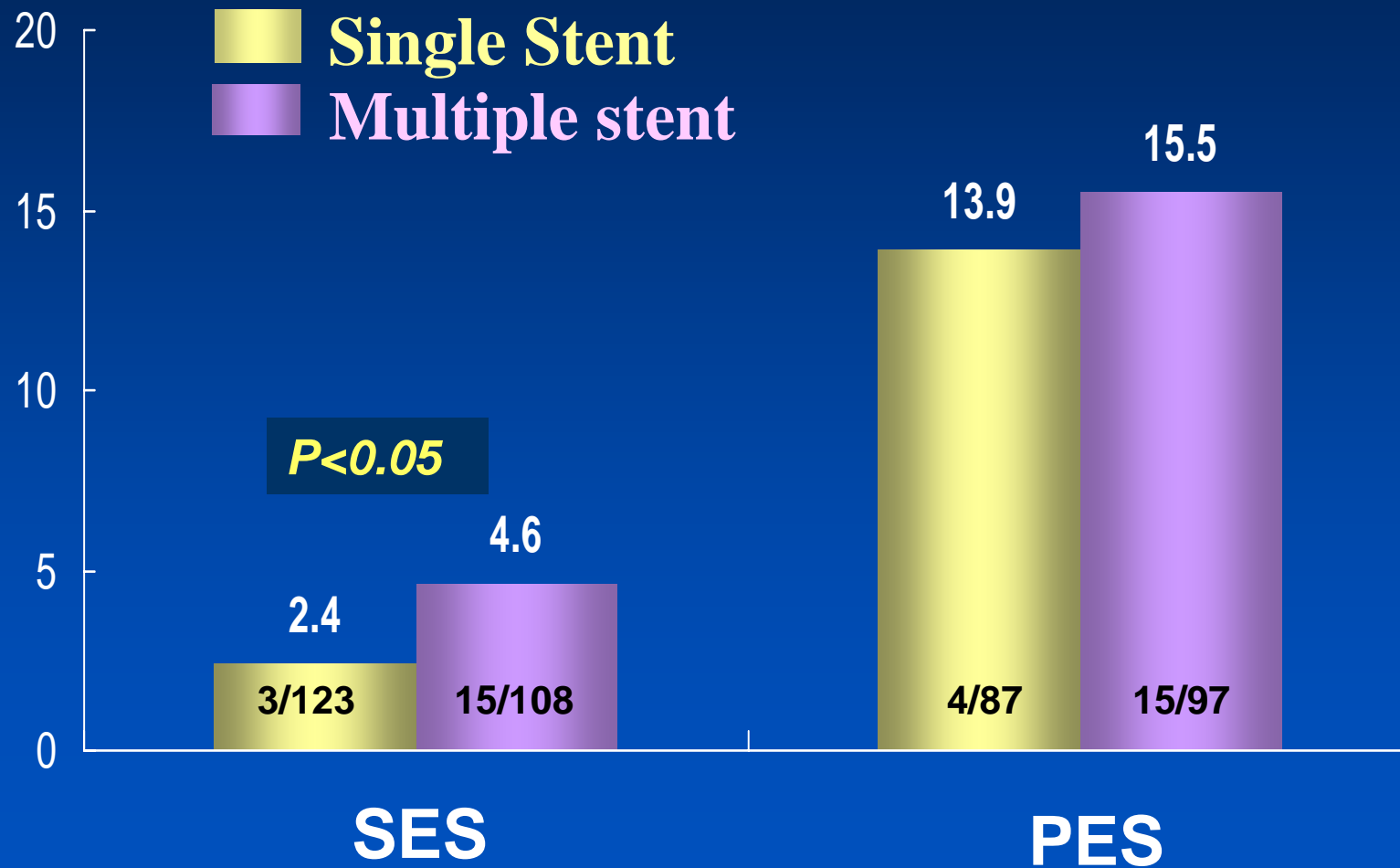
Impact of Multiple Stent

No. of Used Stents Per Target Lesion

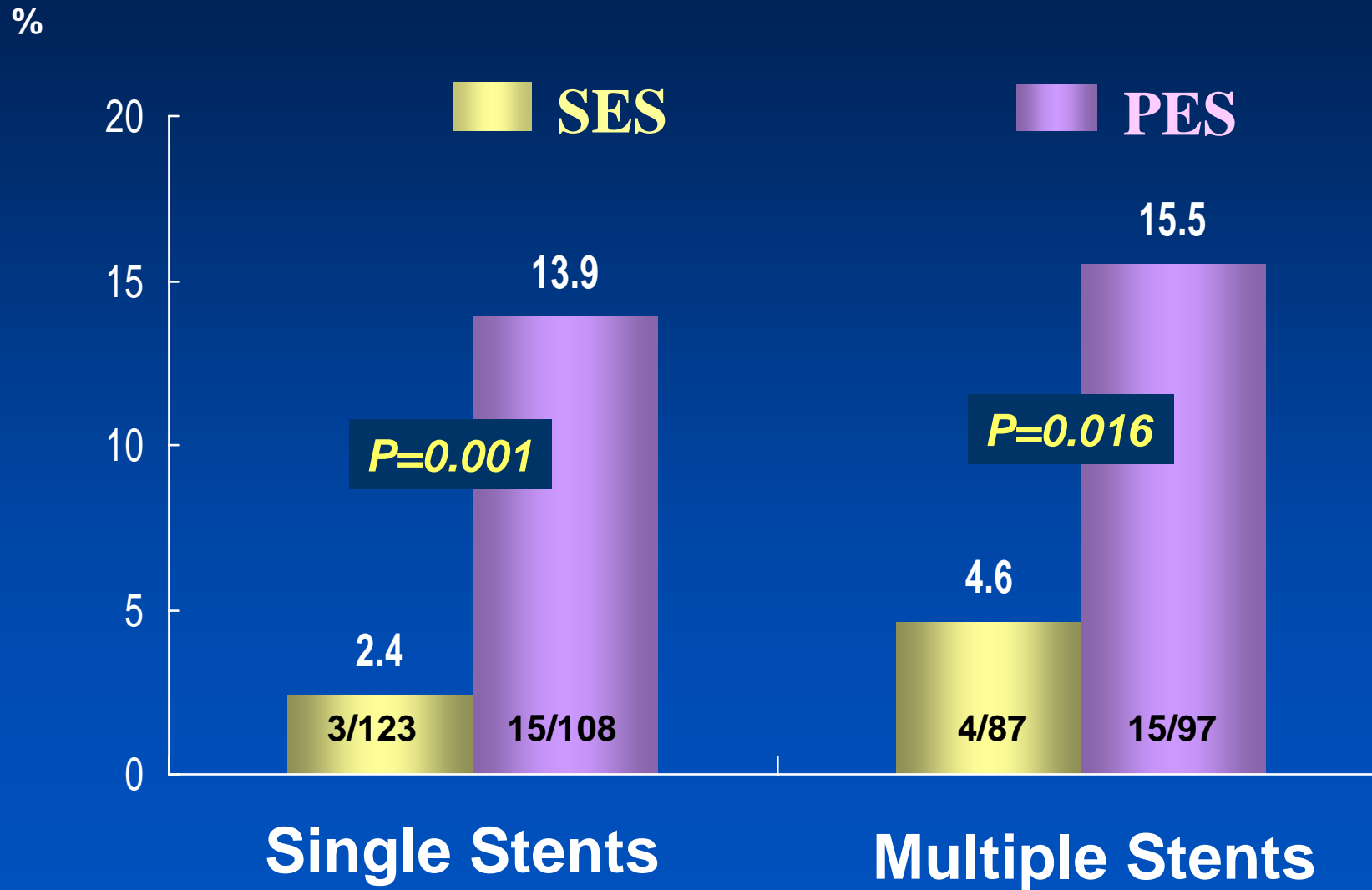


Impact of Multiple Stents In-segment Restenosis

%



Impact of Multiple Stents In-segment Restenosis



Impact of Cilostazol

*Drug-Eluting stenting followed by
Cilostazol treatment reduces LAte Restenosis
in Patients with LONG native Coronary Lesions*

Long-DECLARE

Long-DES II

Prospective,
Randomized
Multicenter trials

Long coronary lesions (>25mm) requiring single or multiple DES
(planned total stent length \geq 32mm)

1:1 randomization

SES (250 patients)

PES (250 patients)

1:1 randomization

1:1 randomization

Long-DECLARE

Angiographic and IVUS follow-up at 6 months
Clinical follow-up at 30 days and 9 months

Primary endpoint:

1. Comparison of SES or PES: binary in-segment restenosis at 6 months
2. Comparison of triple and standard antiplatelet: in-stent late loss at 6 months

Kim YH, Long DES-II investigator, Circulation, 2006;114:2148-2153

Long-DECLARE

Triple Regimen :

Aspirin 100mg/d + Clopidogrel 75mg/d
+ Cilostazol 200mg/d for 6 months

Standard dual antiplatelet therapy :

Aspirin 100mg/d + Clopidogrel 75mg/d
for at least 6 months

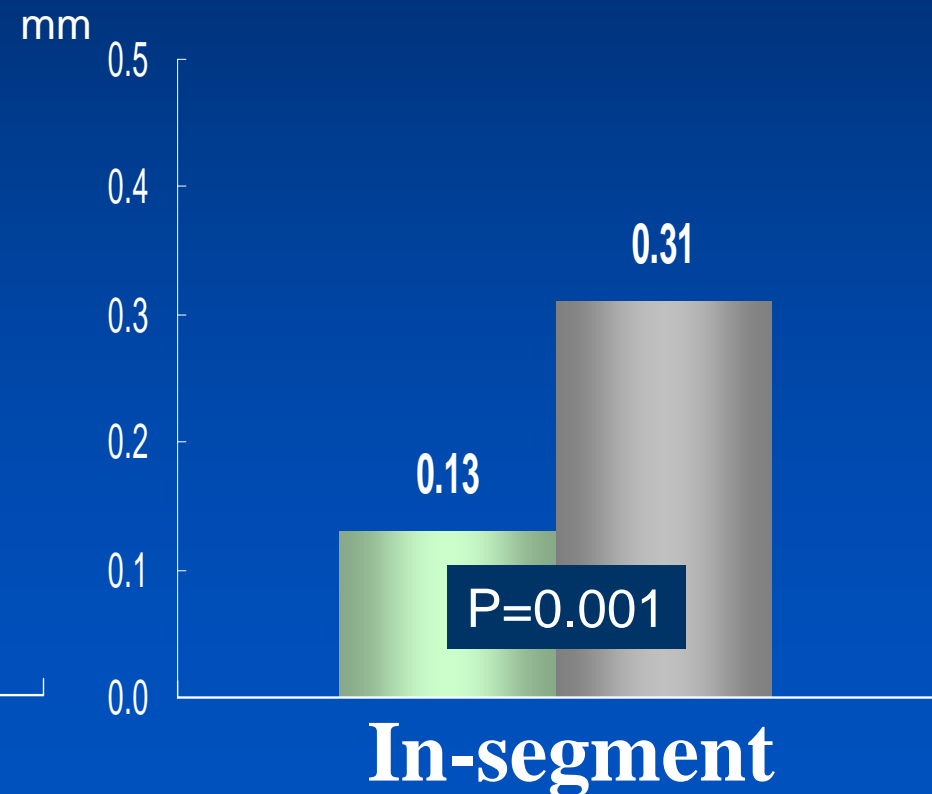
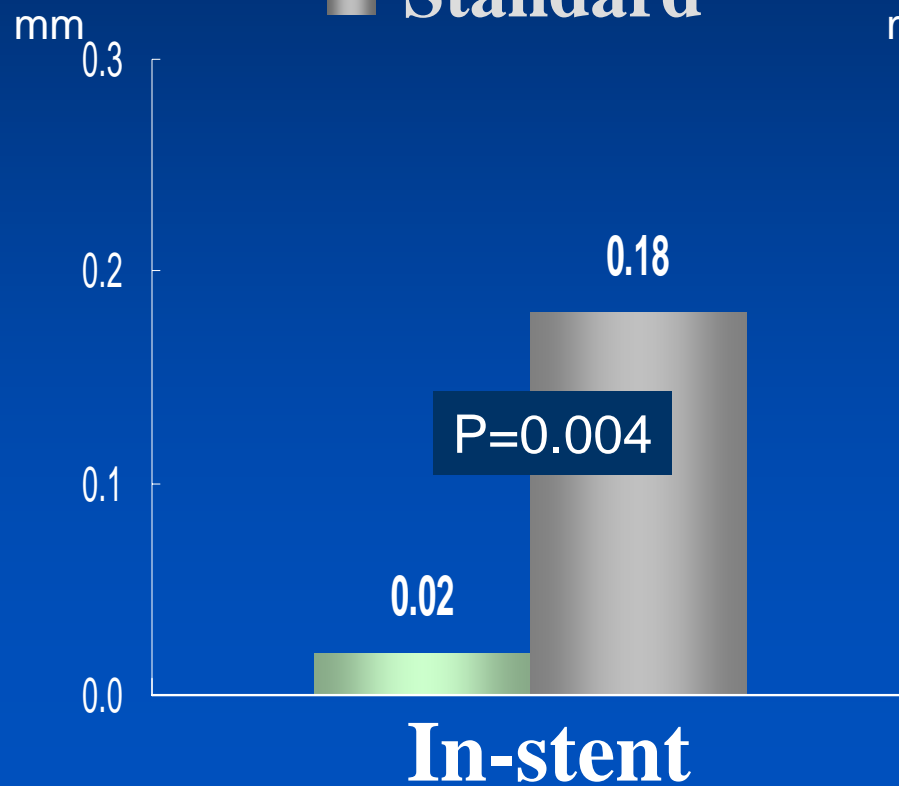
QCA at 6 months F/U

	Triple (n=168)	Standard (n=164)	<i>p</i>
Ref vessel (mm)	2.77±0.52	2.77±0.46	0.977
MLD (mm)			
In-stent	2.28±0.59	2.17±0.55	0.089
In-segment	2.17±0.50	1.92±0.53	0.010
Diameter stenosis (%)			
In-stent	16.1±21.0	20.2±18.5	0.061
In-segment	22.7±14.7	28.3±16.4	0.001
Late loss (mm)			
In-stent	0.21±0.47	0.33±0.48	0.021
In-segment	0.32±0.48	0.48±0.48	0.003

Late loss

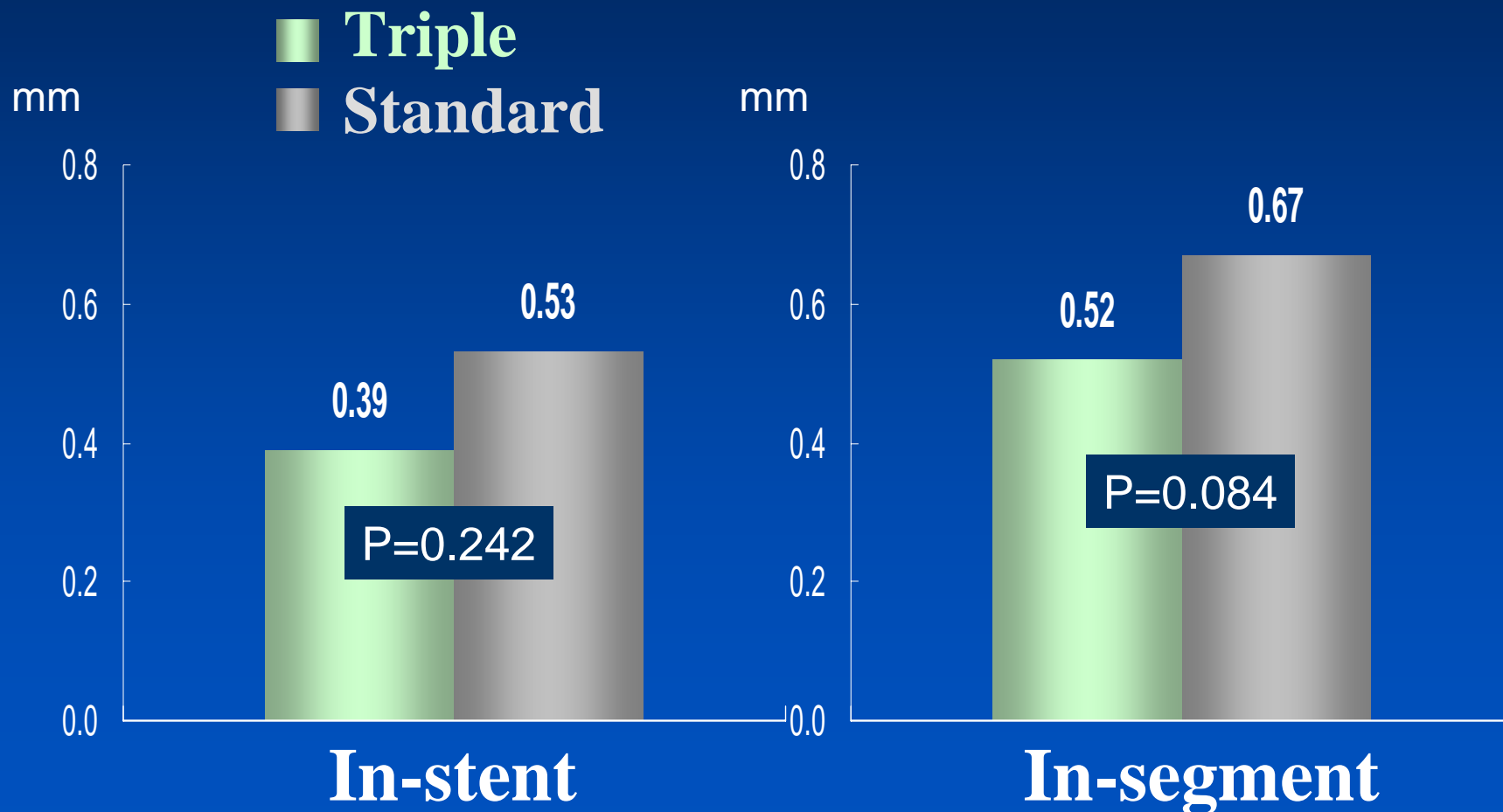
SES

■ Triple
■ Standard

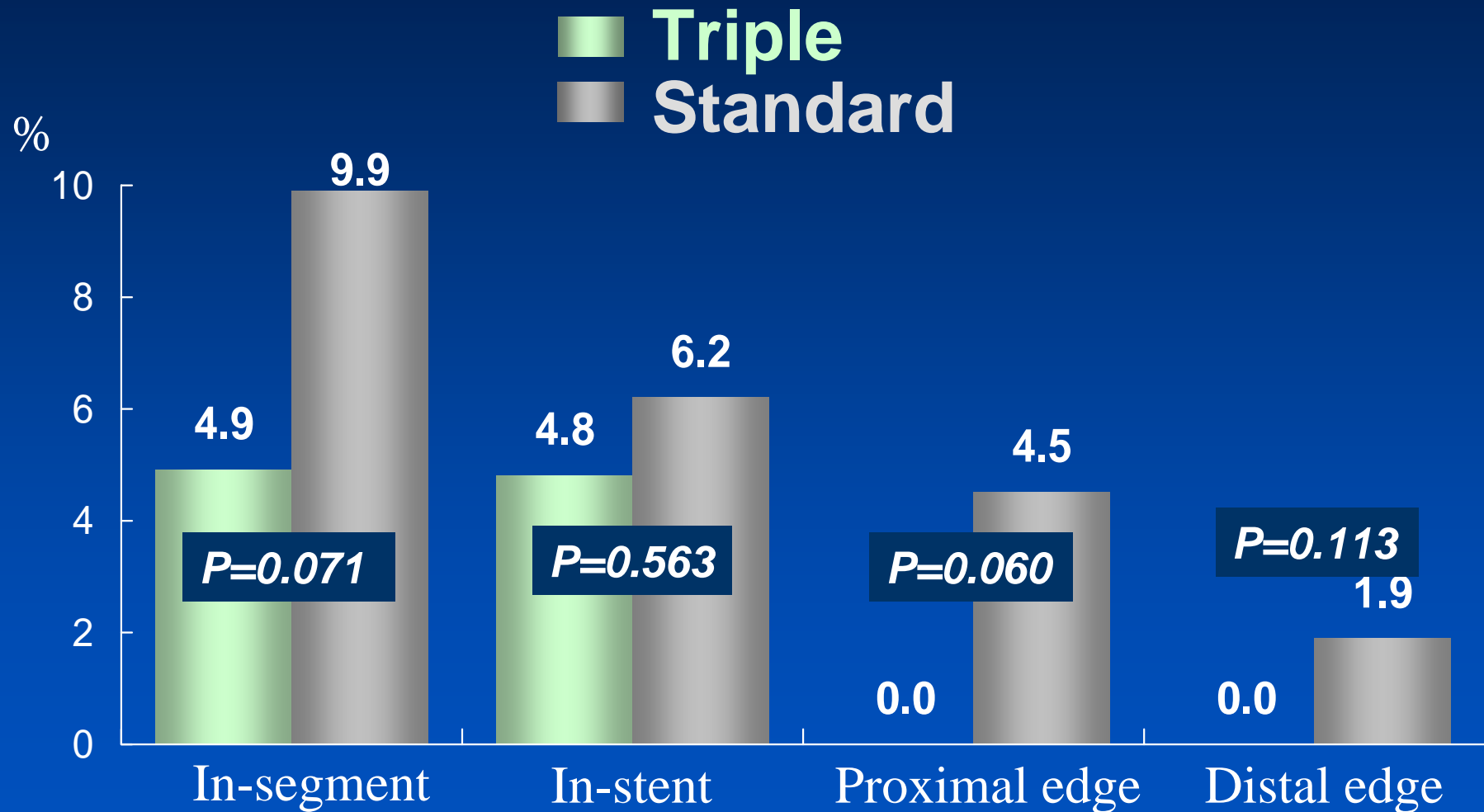


Late loss

PES

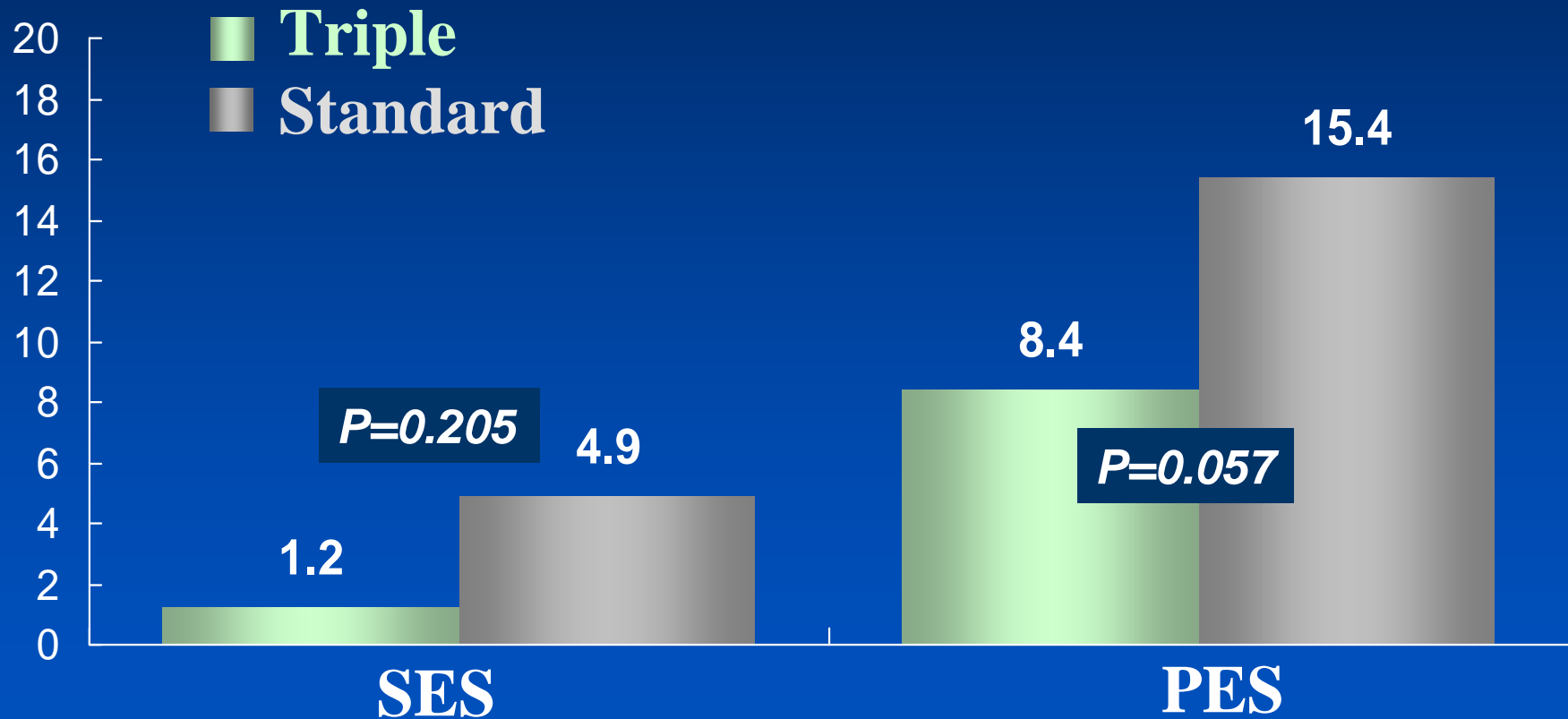


Angiographic Restenosis



Angiographic Restenosis SES vs. PES

%



Clinical Outcomes at 9 Months

	Triple	Standard	P
Patients	206	200	
Death	0	1 (0.5%)	0.493
Cardiac	0	1 (0.5%)	
Non-cardiac	0	0	
MI	1 (0.5%)*	1 (0.5%)**	0.242
Stent thrombosis	1 (0.5%)	1 (0.5%)	1.0
Acute	0	0	
Subacute	1	0	
Late	0	1**	
TLR	5 (2.4%)	16 (8.0%)	0.014
MACE	5 (2.4%)	17 (8.5%)	0.007

* This patient had subacute stent thrombosis and underwent TLR.

** This patient was presented with STEMI and cardiogenic shock 3 months after the index procedure. Before emergent revascularization, this patient was dead.

Long lesion PCI in the era of DES

(Full Metal Jacket)

Very long lesions
> 60mm

We have limited data.

We cannot conduct RCTs

Clinical Outcomes at 1 year of Very Long Lesions in RESEARCH

Stented length of 79mm (64-168)

	All (n=122)	SES (n=81)	PES (n=41)	<i>p value</i>
Death (%)	4.1	2.5	7.3	0.2
MI (%)	10.0	11.2	7.4	0.53
TVR (%)	7.5	7.5	7.6	0.96
MACE (%)	18.0	18.5	17.1	0.87

Aoki J et al, Am Heart J 2005;150:994-9



Multiple Stenting with DES for Long LAD Lesions in Milan

66 patients with ≥ 60 mm stent
(27 PES, 39 SES)

- Reference vessel diameter: 2.53 ± 0.6 mm
- Diameter stenosis: 68.5 ± 19.3 %
- Stented segment : 64 ± 18 mm
- Glycoprotein IIb/IIIa inhibitors: 47%
- Restenosis Rate : 19.6 %

Tsagalou E et al, J Am Coll Cardiol 2005;45:1570-3

Very Long Lesion Clinical Outcomes at 1 year

	In-hospital (n=66)	Follow-up (n=66)
Death	0	0
Q wave	0	0
Non-Q wave	11 (16.6%)	1 (1.5%)
Thrombosis	1 (1.5%)	0
TVR	0	10 (15%)
CABG	0	1 (1.5%)

Tsagalou E et al, J Am Coll Cardiol 2005;45:1570-3

Multiple Stenting with DES for Long Lesions in AMC

352 lesions with ≥ 60 mm stent
(266 SES, 86 PES)

- Reference vessel diameter: 2.82 ± 0.40 mm
- Diameter stenosis: 70.2 ± 10.7 %
- Target lesion length: 68.5 ± 13.5 mm
- Stented segment : 71.9 ± 13.7 mm

Lee CW et al, Am J Cardiol 2006; 98 :918-922

Very Long Lesion

AMC

Angiographic Outcome at 6 Mo

234 of 352 lesions (70.1% F/U)

	Pre- procedure	Post- procedure	Follow-up
MLD, mm	0.66±0.53	2.66±0.40	2.14±0.68
% diameter stenosis	68.5±13.5	4.5±13.4	22.9±23.8
Late lumen loss, mm			0.52±0.67
Restenosis			13.7%
SES (N=180)			11.1%
PES (N=54)			22.2%

Lee CW et al, Am J Cardiol 2006; 98 :918-922

Clinical Outcomes at 1 year

	In-hospital (n=347)	Follow-up (n=346)
Death	1 (0.3%)	9 (2.6%)
Cardiac	1 (0.3%)	6 (1.7%)
Noncardiac	0	3 (0.9%)
Myocardial infarction	70 (20.2%)	1 (0.3%)
Q wave	2 (0.6%)	1 (0.3%)
Non-Q wave	68 (19.6%)	0
Stent Trombosis	2 (0.6%)	3 (0.86%)
TLR	2 (0.6%)	13 (3.8%)
PCI	2 (0.6%)	12 (3.5%)
CABG	0	1 (0.3%)

Lee CW et al, Am J Cardiol 2006; 98 :918-922

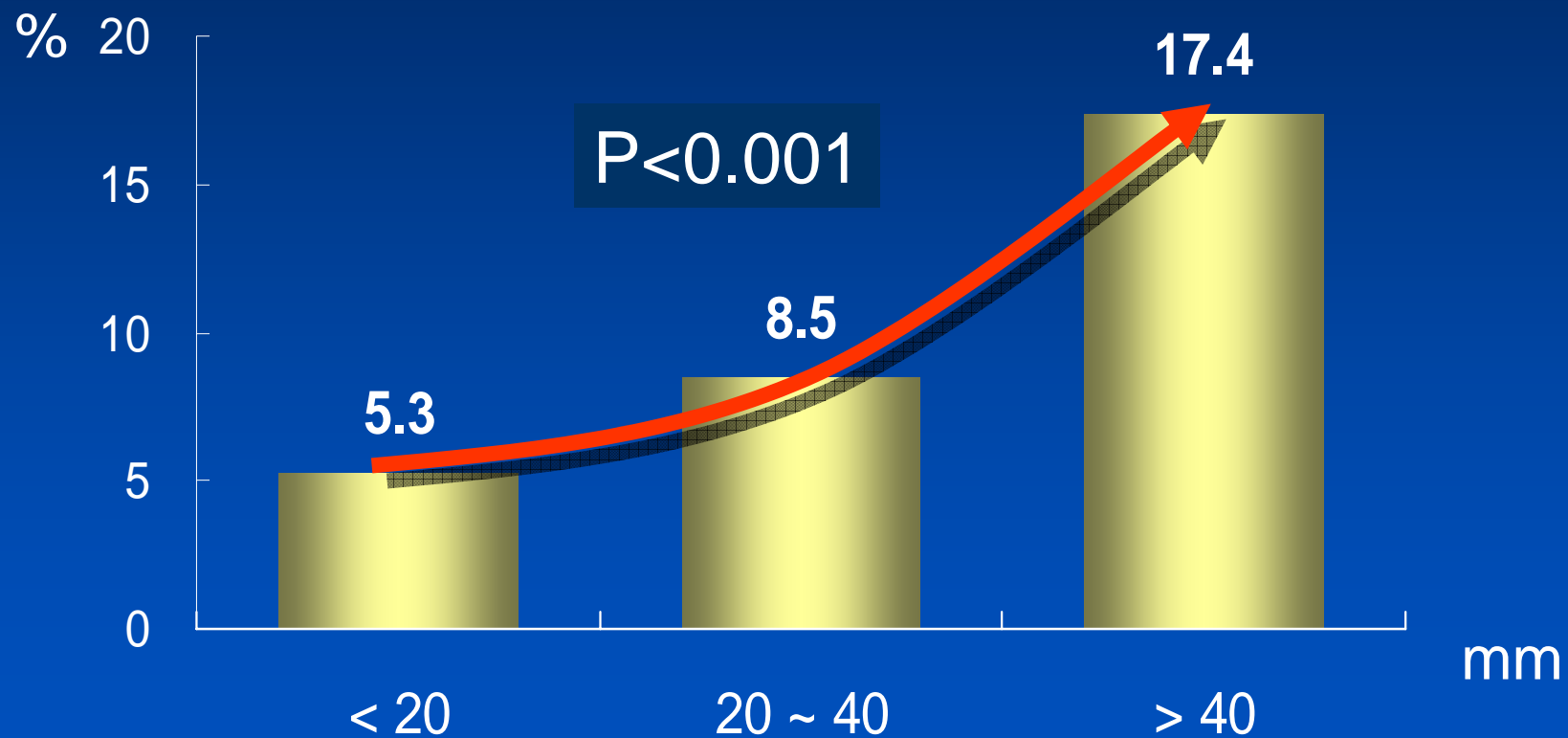
Predictors of Angiographic Restenosis

“Multivariable Analysis”

Variables	OR	95%CI	p Value
Ref. vessel diameter	0.05	0.01-0.33	0.002
Use of TAXUS stent	2.88	1.03-8.04	0.043

Lee CW et al, Am J Cardiol 2006; 98 :918-922

Restenosis Rate According to Stented Segment Length In Asan Medical Center



Lee CW et al. Am J Cardiol 2006;97:506-511

Long lesion remains a predictor of restenosis.

DES Registry in Asan Medical Center

	OR	95% CI	p
Lesion length, mm	1.023	1.010-1.035	<0.001
Post-stent MLD, mm	0.319	0.202-0.503	<0.001
Use of TAXUS stent	4.637	2.899-6.579	<0.001

Lee CW et al. Am J Cardiol 2006;97:506-511

Efficacy concerns...

Long Lesion PCI

Overall angiographic restenosis rate and TLR rate of long lesion intervention with DES were quite acceptable. However, long stented segment is still independent predictor of angiographic restenosis.

Long Lesion PCI

How to optimize ?

**IVUS guided procedure may be helpful
based on the AMC data ...**

IVUS predictors of angiographic restenosis in SES stent implantation

- Multivariate analysis -

Stent CSA

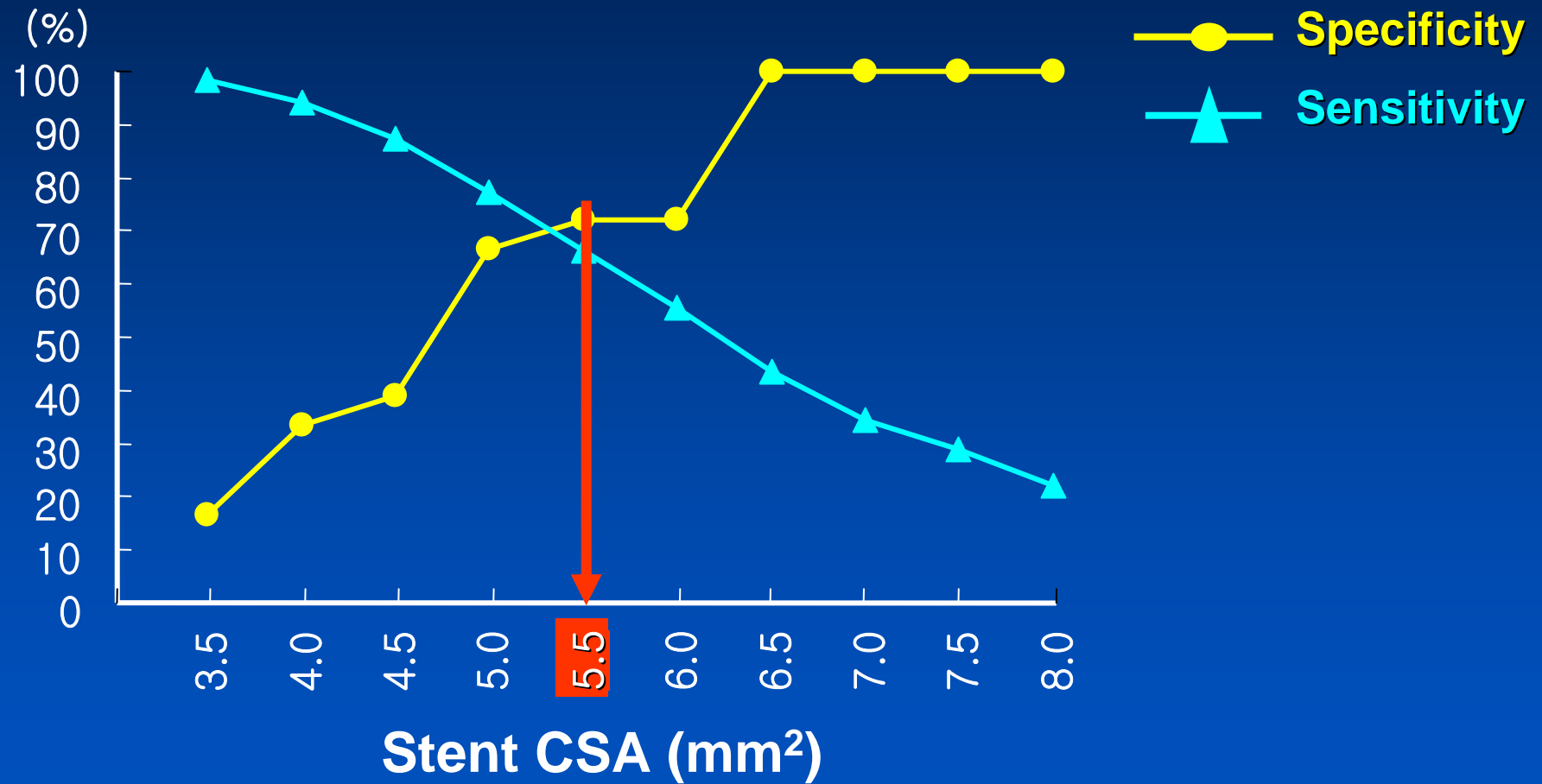
odds ratio=0.584, 95% CI
0.385–0.885, p=0.011

Total stent length

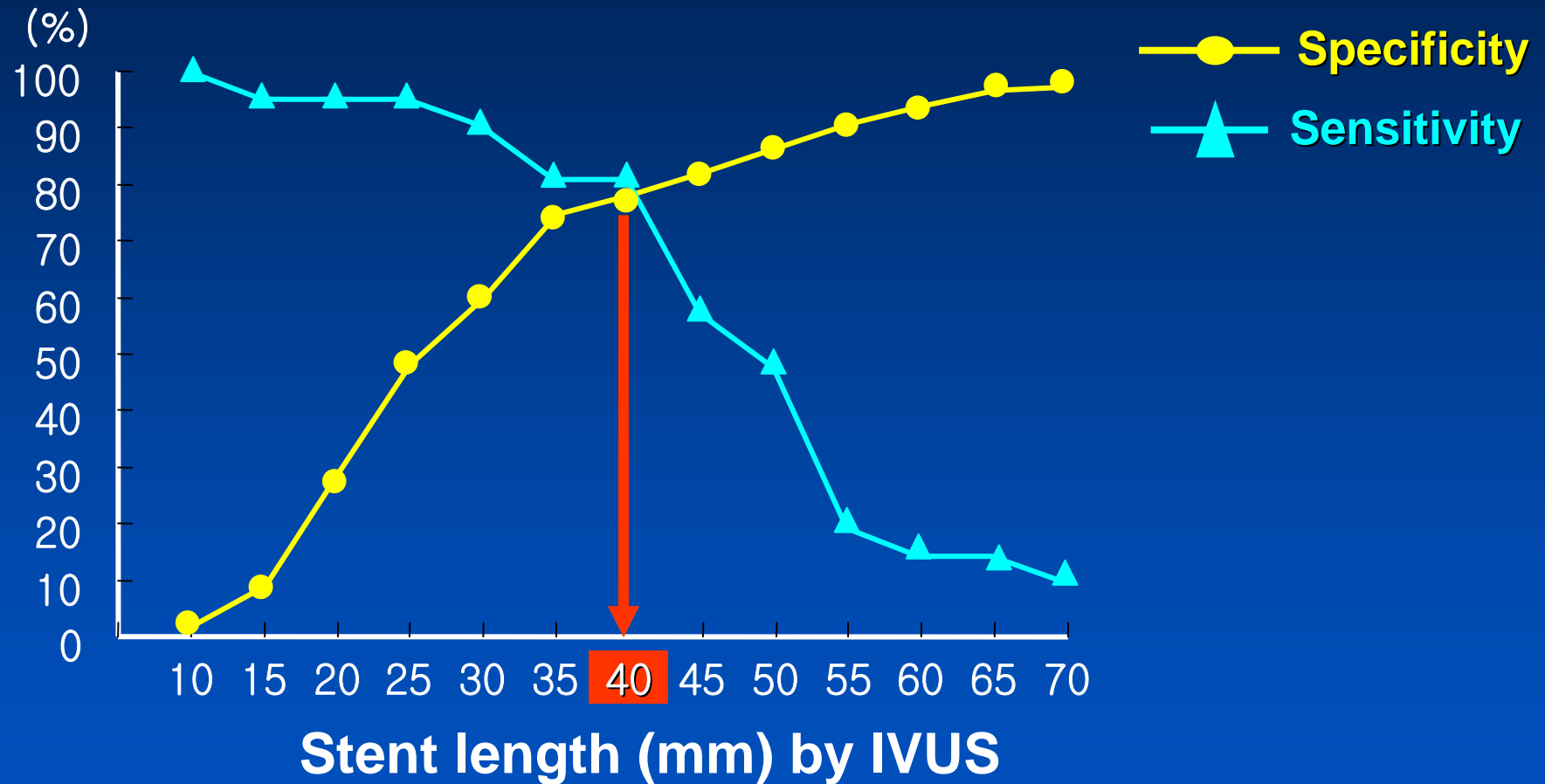
odds ratio=1.028, 95% CI
1.002–1.055, p=0.038

Hong MK, Eur Heart J, 2006 (in press)

Sensitivity and specificity curves to identify optimal cut-off values of stent CSA



Sensitivity and specificity curves to identify optimal cut-off values of total stent length



Restenosis Rate

According to Stent Length and Stent CSA by IVUS
SES Registry in Asan Medical Center

Stent length (mm)	Stent area (mm ²)	Restenosis rate	P value
≤ 40	≥ 5.5	1/284 (0.4%)	<i>P</i> < 0.001
≤ 40	< 5.5	3/127 (2.4%)	
> 40	≥ 5.5	6/70 (8.6%)	
> 40	< 5.5	11/62 (17.7%)	

How to Optimize for the long lesion PCI

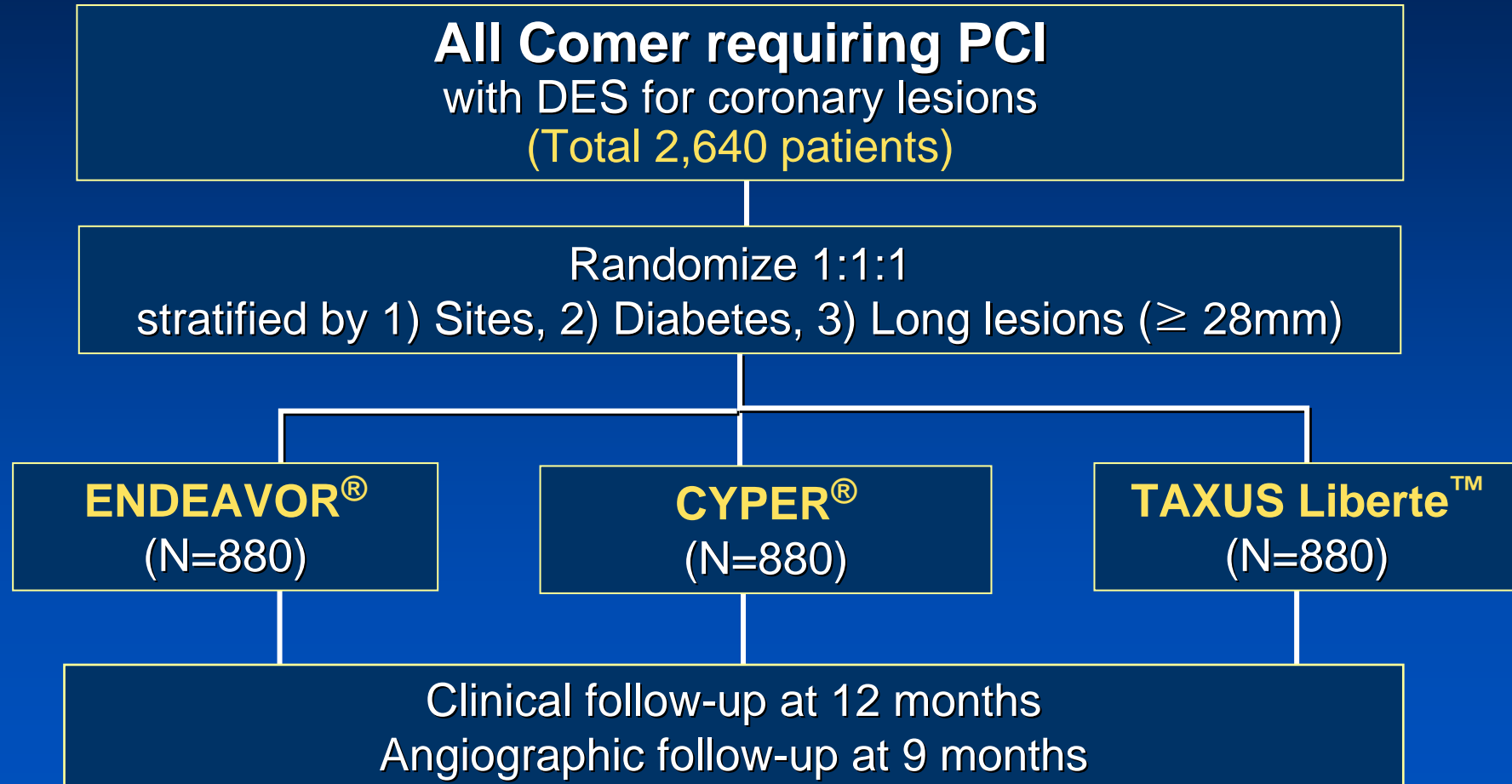
1. IVUS guided procedure may be helpful
2. Long coronary lesion is still independent predictor
Bigger the better, Shorter the better
Stented length <40mm, Stent CSA >5.5 mm²
3. Multiple overlapping would be OK
4. Triple antiplatelet therapy may be helpful to reduce the TLR and MACE

Which Stent is the Best for Long Lesion PCI ?

ZEST

(2006-2008)

Comparison of the Efficacy of Zotarolimus-Eluting Stent versus Sirolimus-Eluting Stent versus PacliTaxel-Eluting Stent for Coronary Lesions in 20 Centers of Korea



*Primary End-point: Target Vessel Failure (TVF) at 12 months