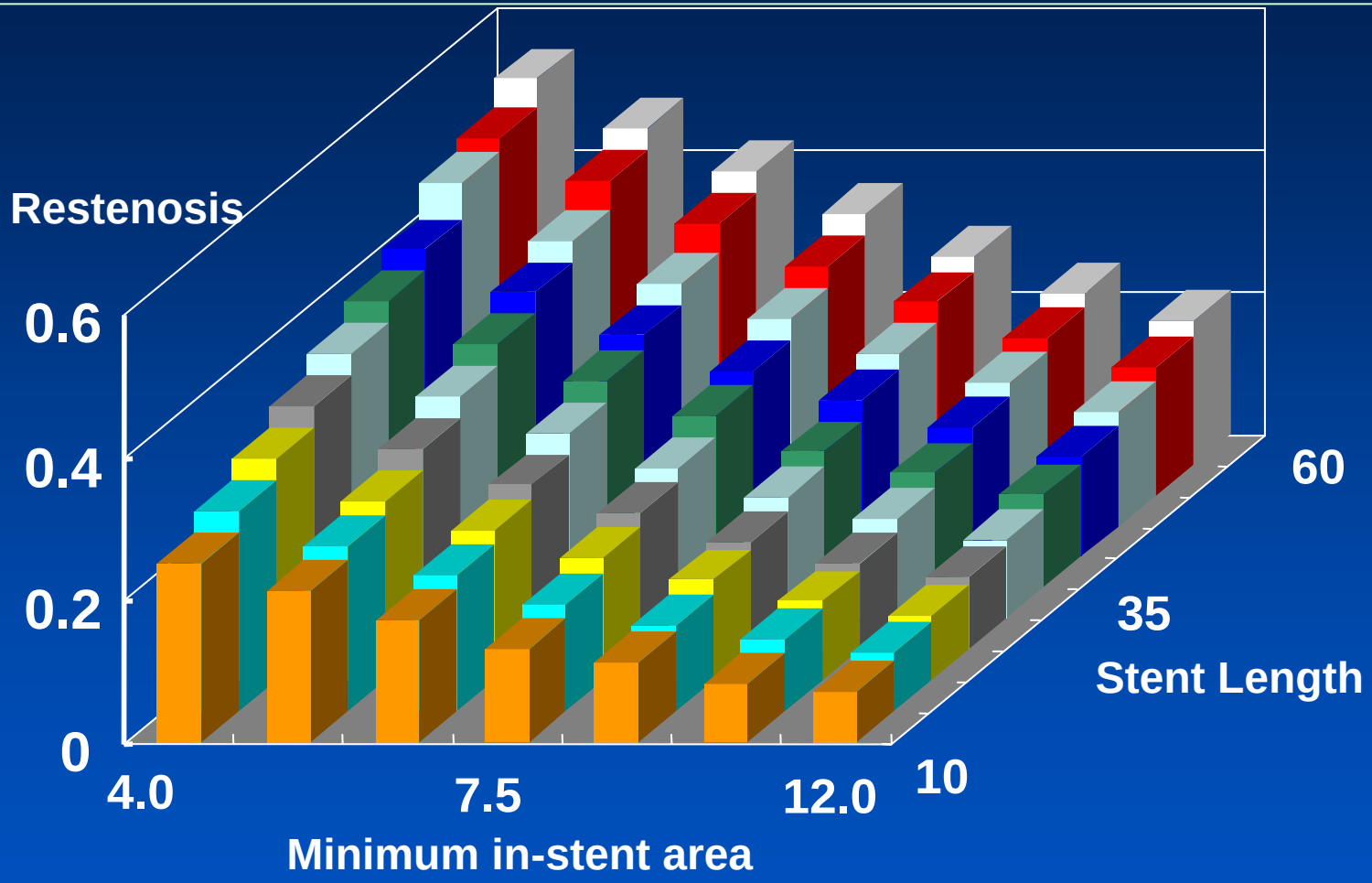
PCI for
Long Coronary Lesion

In the Bare Metal Stent Era

Higher Restenosis Rate With Increasing Stent Length and Decreasing Stent Area

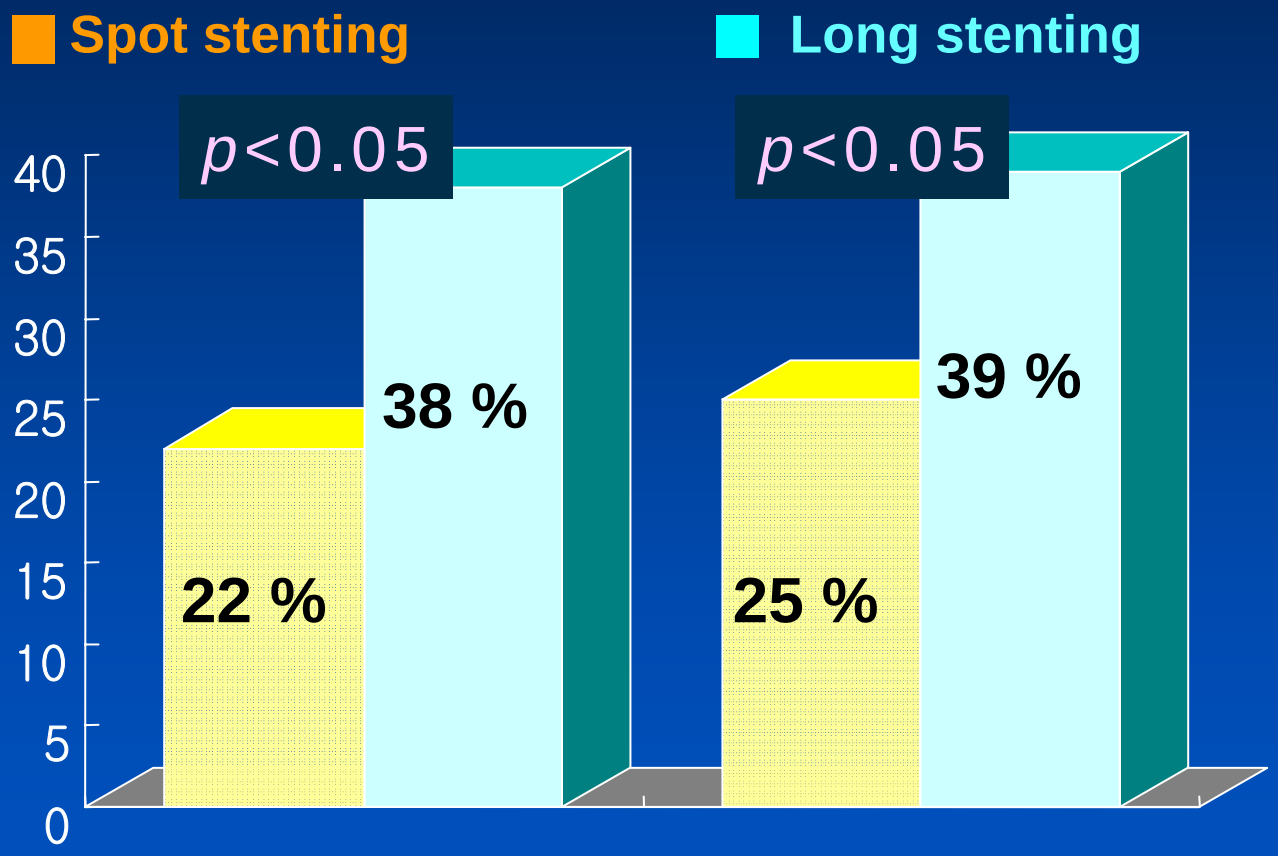


De Feyter. Circulation 1999; 100:1777-83

Spot Stenting vs. Long Stenting

6 Months MACE

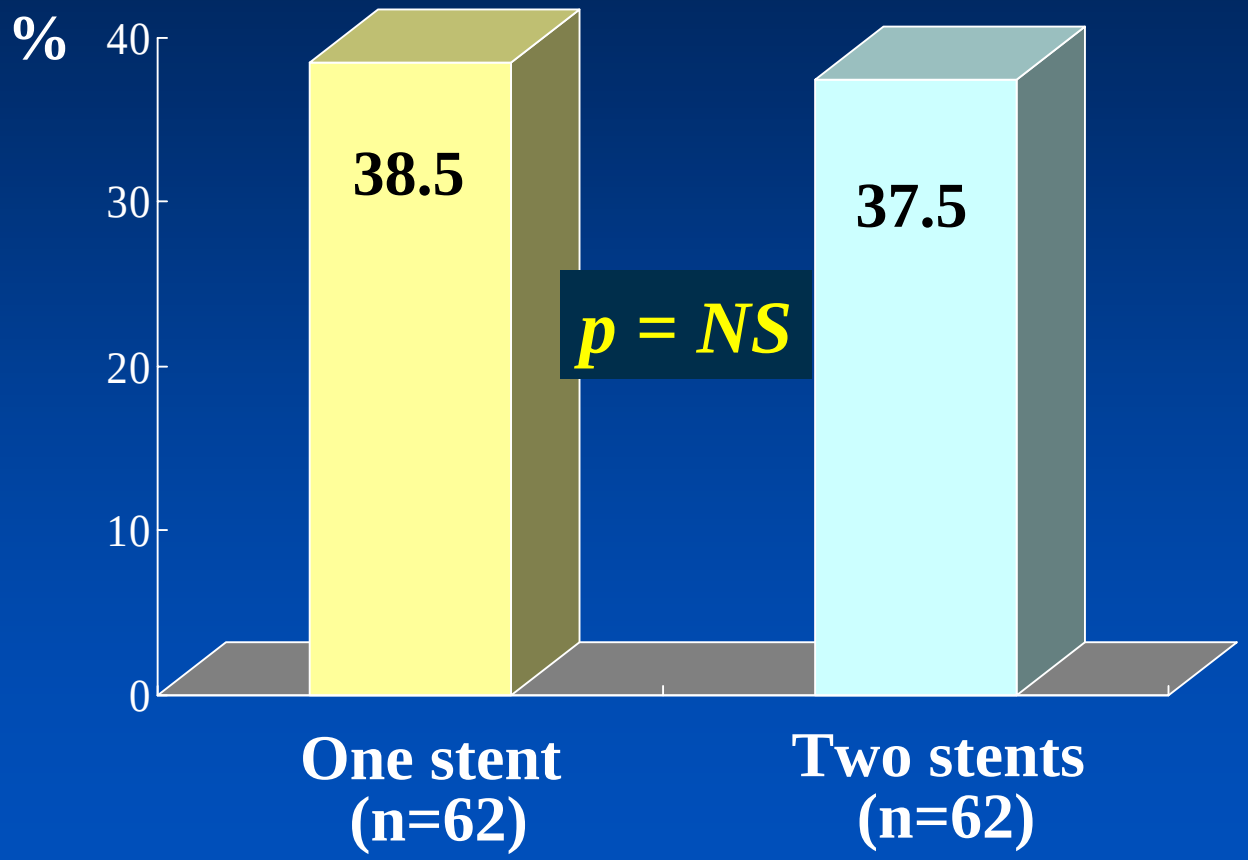
Restenosis Rate



Colombo A et al, J Am Coll Cardiol 2001;38:1427-33

Single Stent vs. Multiple Stents

Restenosis Rate

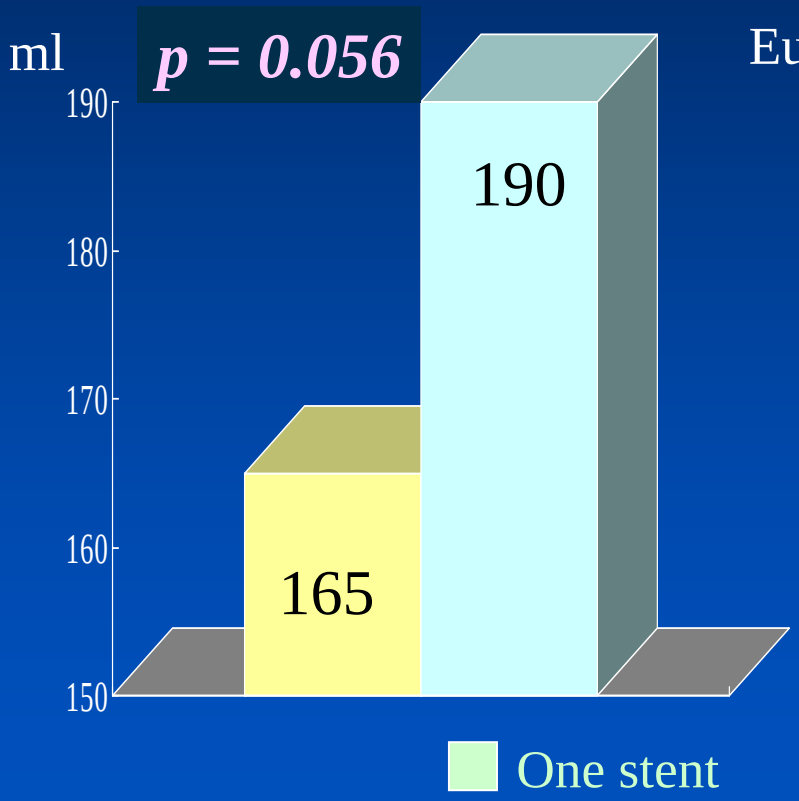


Hoffmann R et al. Am J Cardiol 2002:90:460-464

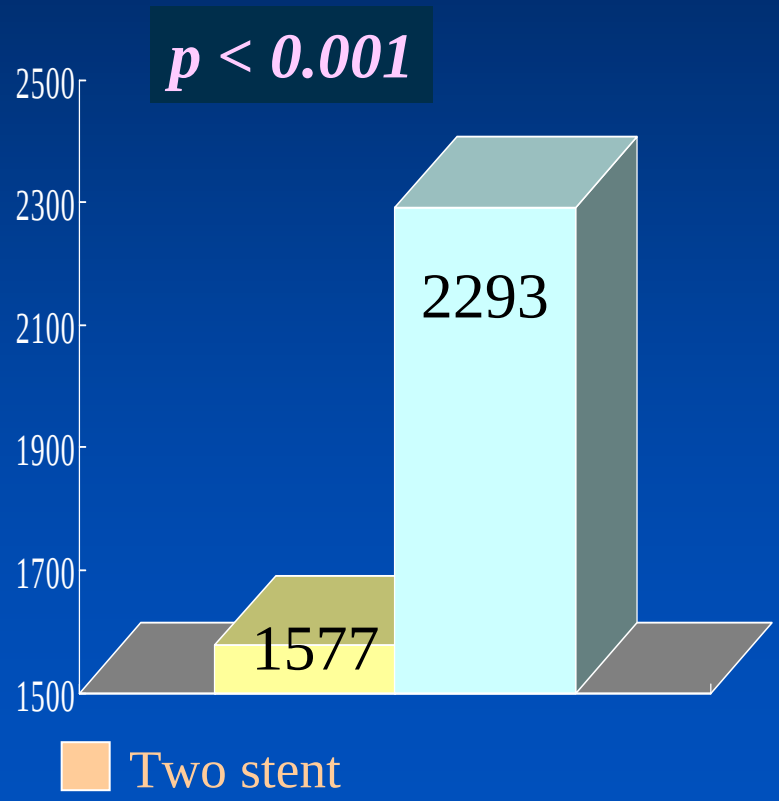
Single Stent vs. Multiple Stents

Cost-Effectiveness

Contrast agent



Intervention Cost



One stent Two stent

Hoffmann R et al. Am J Cardiol 2002:90:460-464

Stenting with Bare Metal Stent for Long Coronary Lesion

It was suggested that…

- Spot stenting
- Single stent

What is changing ?

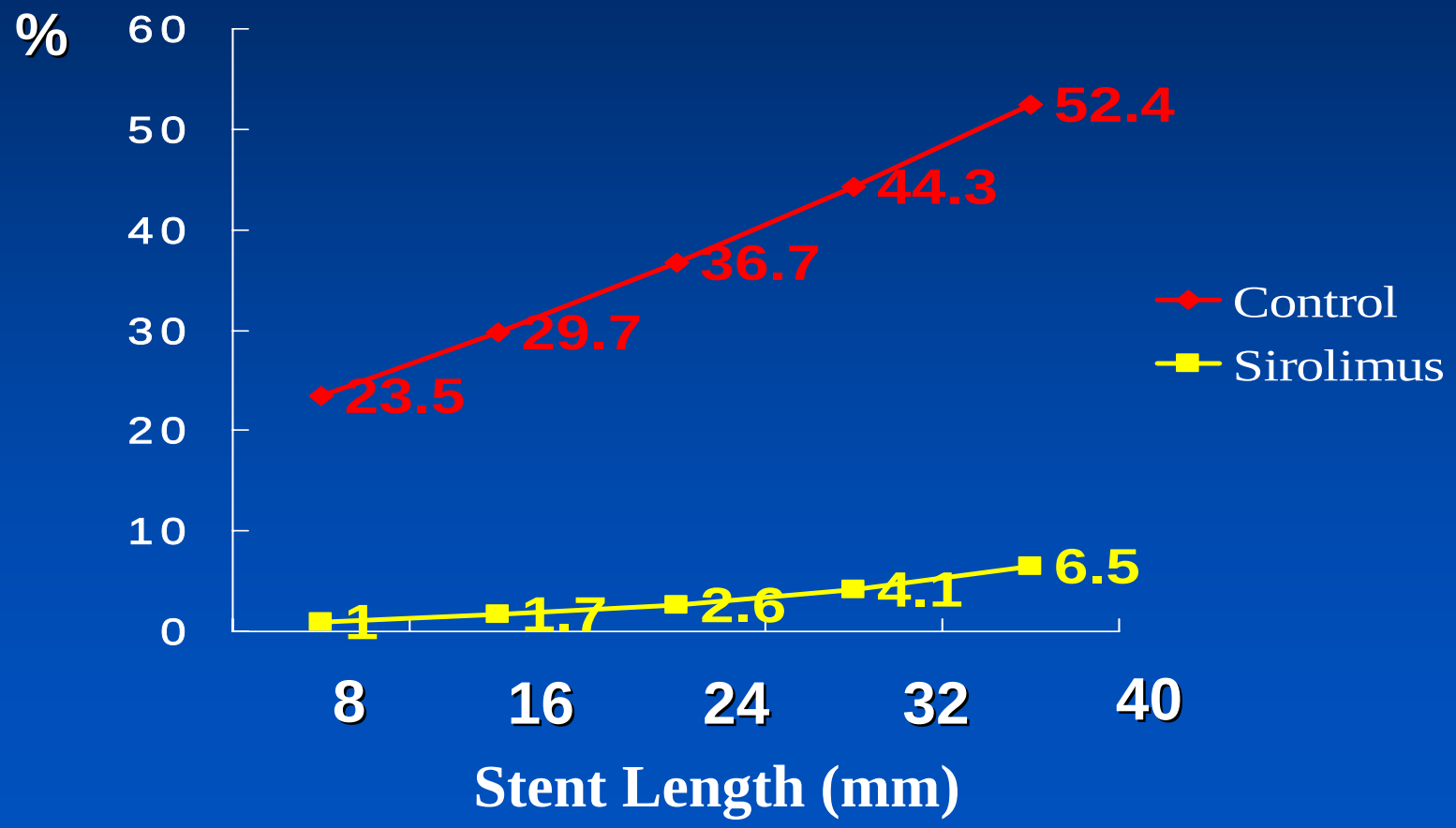
In the Era of Drug Eluting Stent

DES vs. BMS

In the Era of Drug Eluting Stent

Sirolimus-Eluting Stent in SIRIUS

Minimal Increase of Restenosis With Increasing stent length

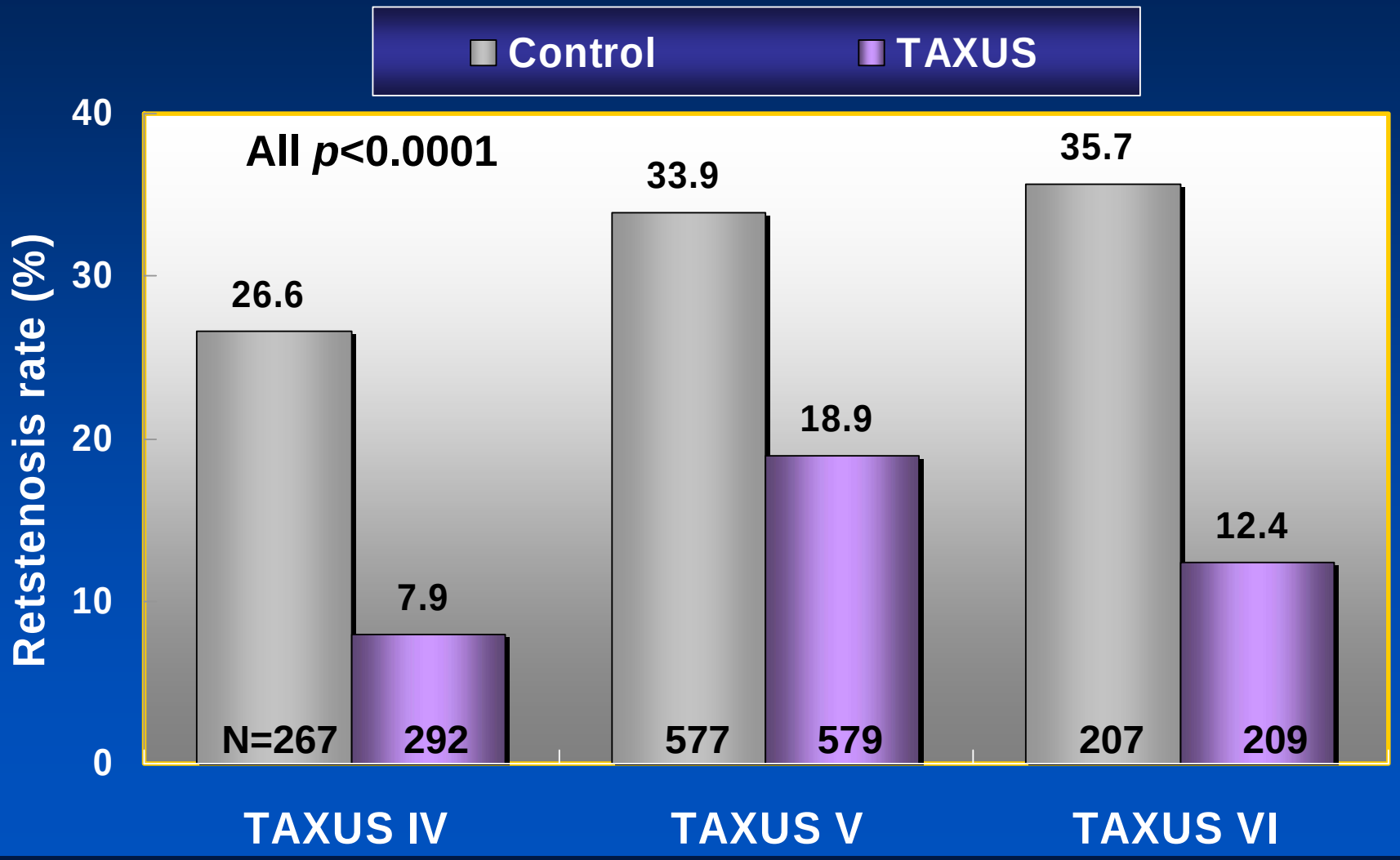


Paclitaxel-Eluting Stent in TAXUSs

More involvement of long lesions

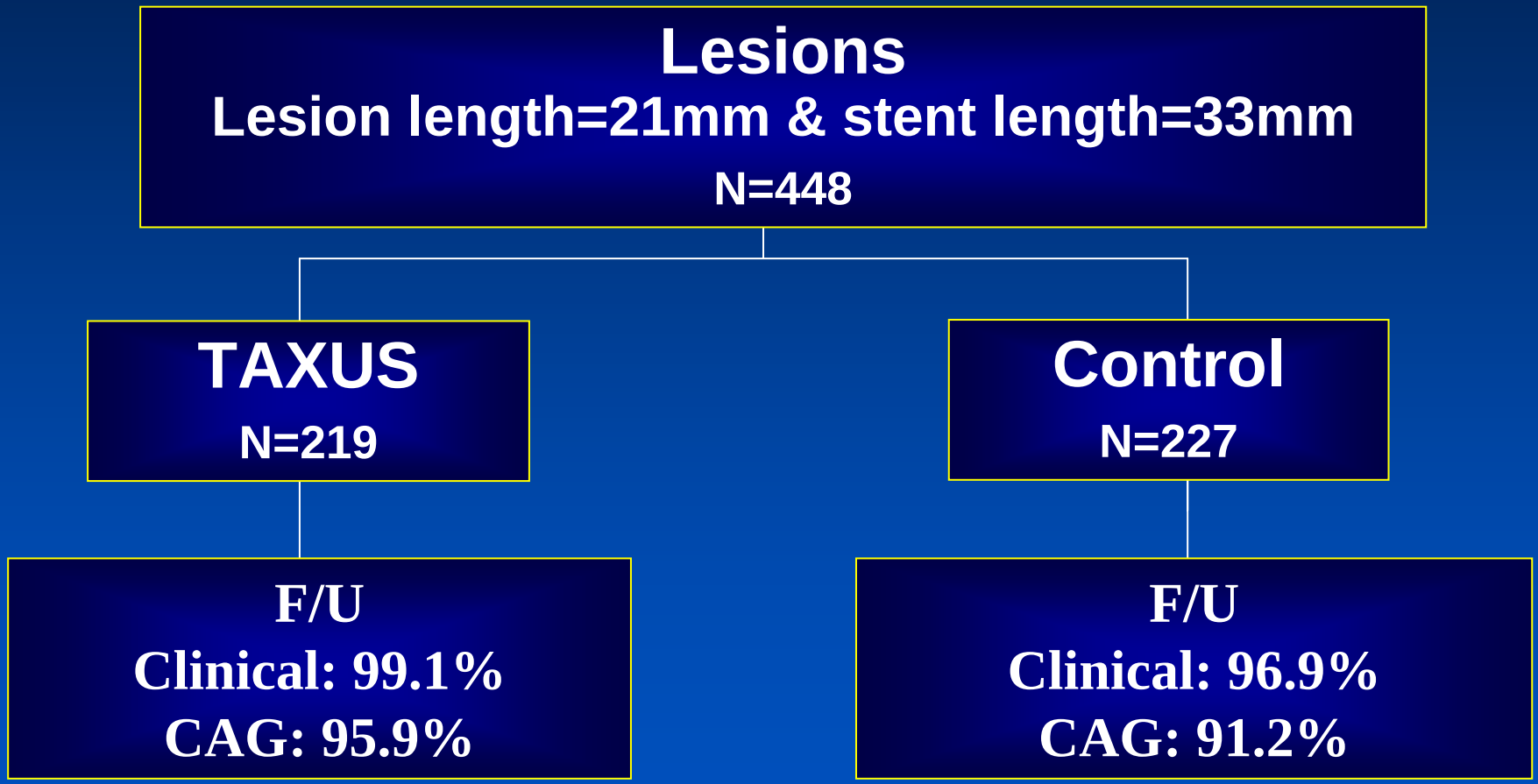
	TAXUS IV	TAXUS V	TAXUS VI
No of patients	1,314	1,156	446
Lesion length (mm)	14.4	17.3	20.6
Stent length (mm)	21.9	28.7	33.4
AHA/ACC type C lesions (%)	20.3	36.8	55.6
Small vessels (<2.5mm) (%)	32.1	18.7	27.8
Overlapping stent (%)	Not permit	29.1	27.8
Non-target vessel intervention (%)	20.8	NA	23.5
Diabetes mellitus (%)	23.4	31.7	20.0

Sustained Reduction of In-segment Restenosis



TAXUS-VI

for Long Lesion Involvement



Dawkins KD et al, Circulation 2005;112:3306-13

Angiographic Outcomes

TAXUS-VI

	TAXUS (n=219)	Control (n=227)	*p value*
Baseline reference, mm	2.81±0.49	2.77±0.46	0.41
MLD, mm			
Before procedure	0.84±0.35	0.87±0.33	0.39
After procedure	2.58±0.41	2.57±0.36	0.68
9-month	2.20±0.60	1.58±0.66	<0.0001
Diameter stenosis, %			
Before procedure	70.2±10.7	68.6±10.7	0.12
After procedure	8.3±10.4	7.7±10.1	0.60
9-month	22.2±19.2	42.8±20.9	<0.0001

Dawkins KD et al, Circulation 2005;112:3306-13

Angiographic Outcomes

TAXUS-VI

	TAXUS (n=219)	Control (n=227)	*p value*
Binary restenosis			
In-stent	9.1% (19/209)	32.9% (68/207)	<0.0001
Analysis segment	12.4% (26/210)	35.7% (74/207)	<0.0001
Late loss, mm			
In-stent	0.39±0.56	0.99±0.59	<0.0001
Analysis segment	0.24±0.57	0.66±0.62	<0.0001
Proximal edge	0.16±0.54	0.33±0.53	0.0019
Distal edge	-0.02±0.41	0.11±0.37	0.0013

Dawkins KD et al, Circulation 2005;112:3306-13

9-Month Clinical Outcomes

TAXUS-VI

	TAXUS (n=219)	Control (n=227)	*p value*
MACE, overall	16.4% (36)	22.5% (51)	0.12
Cardiac death	0 (0)	0.9% (2)	0.50
MI	8.2% (18)	6.2% (14)	0.46
TVR, overall	9.1% (20)	19.4% (44)	0.0027
TLR, overall	6.8% (15)	18.9% (43)	0.0001
TVR, nontarget lesion	3.2% (7)	0.9% (2)	0.10
TVF	16.0% (35)	22.0% (50)	0.12

Dawkins KD et al, Circulation 2005;112:3306-13

Registries with DES

In the Era of Drug Eluting Stent

One-Year Clinical Outcomes In RESEARCH

Stented length of 79mm (64-168)

	All (n=122)	SES (n=81)	PES (n=41)	*p value*
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 Overlapping in AMC

352 lesions (266 SES, 86 PES)

- Reference vessel diameter: 2.82±0.40mm
- Diameter stenosis(%): 70.2±10.7
- Target lesion length: 68.5±13.5mm
- Stented segment : 71.9± 13.7(≥60)mm

Lee CW et al, Am J Cardiol (In submission)

Angiographic Outcome at 6 Mo

234 of 352 lesions (70.1% F/U)

	Pre-procedure	Post-procedure	Follow-up
MLD	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			0.52±0.67
Restenosis			37%
SES			11.1% (20/180)
PES			22.2% (12/54)

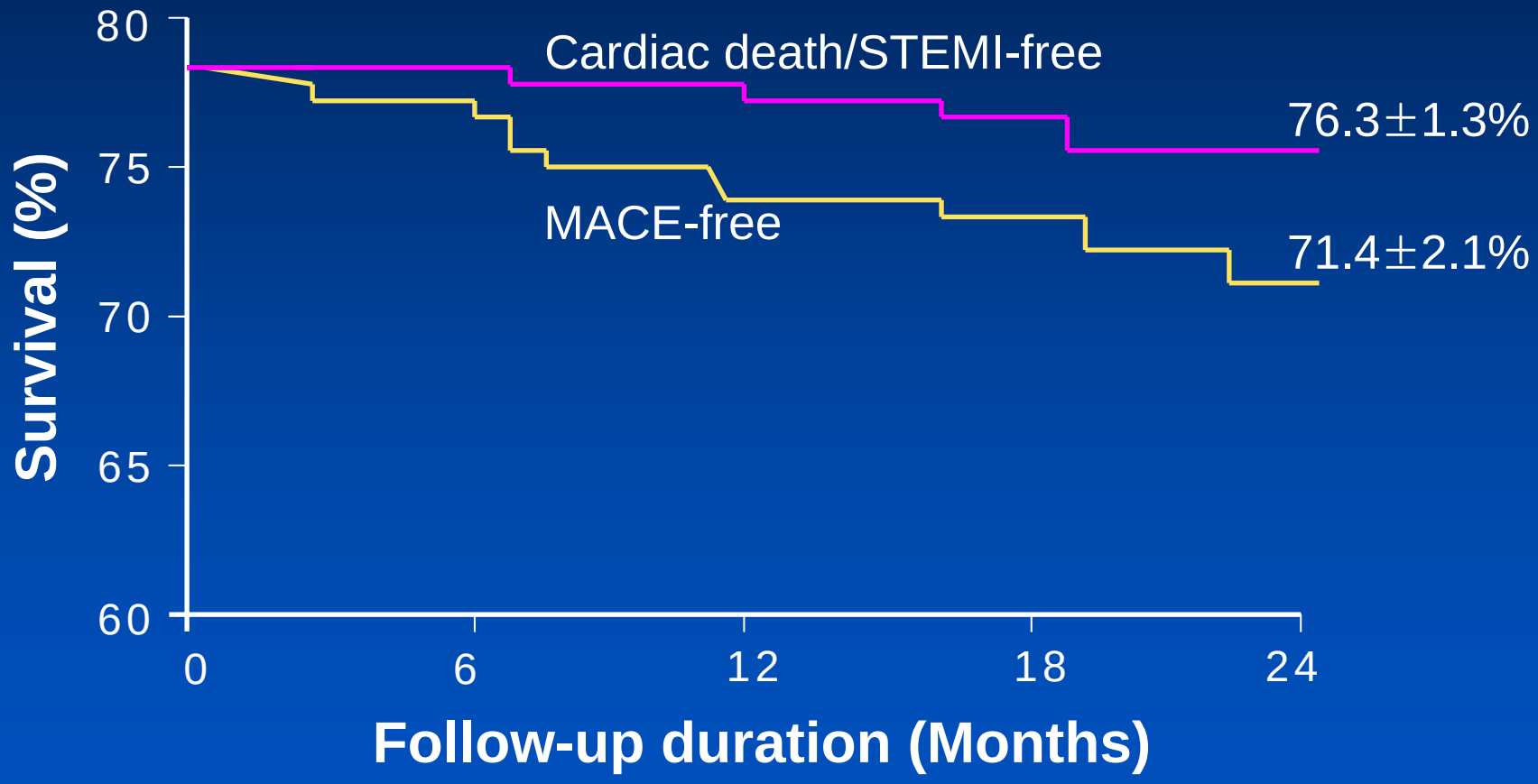
Lee CW et al, Am J Cardiol (In submission)

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
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 (In submission)

Kaplan-Meyer Survival Curves



Lee CW et al, Am J Cardiol (In submission)

Multiple Overlapping DES in LAD

Milan Experience

66 patients (27 PES, 39 SES)

- Reference vessel diameter: 2.53±0.6mm
- Diameter stenosis(%): 68.5±19.3
- Stented segment : 64±18(≥60)mm
- Glycoprotein IIb/IIIa inhibitors: 47%

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

Angiographic Outcome at 6 Mo

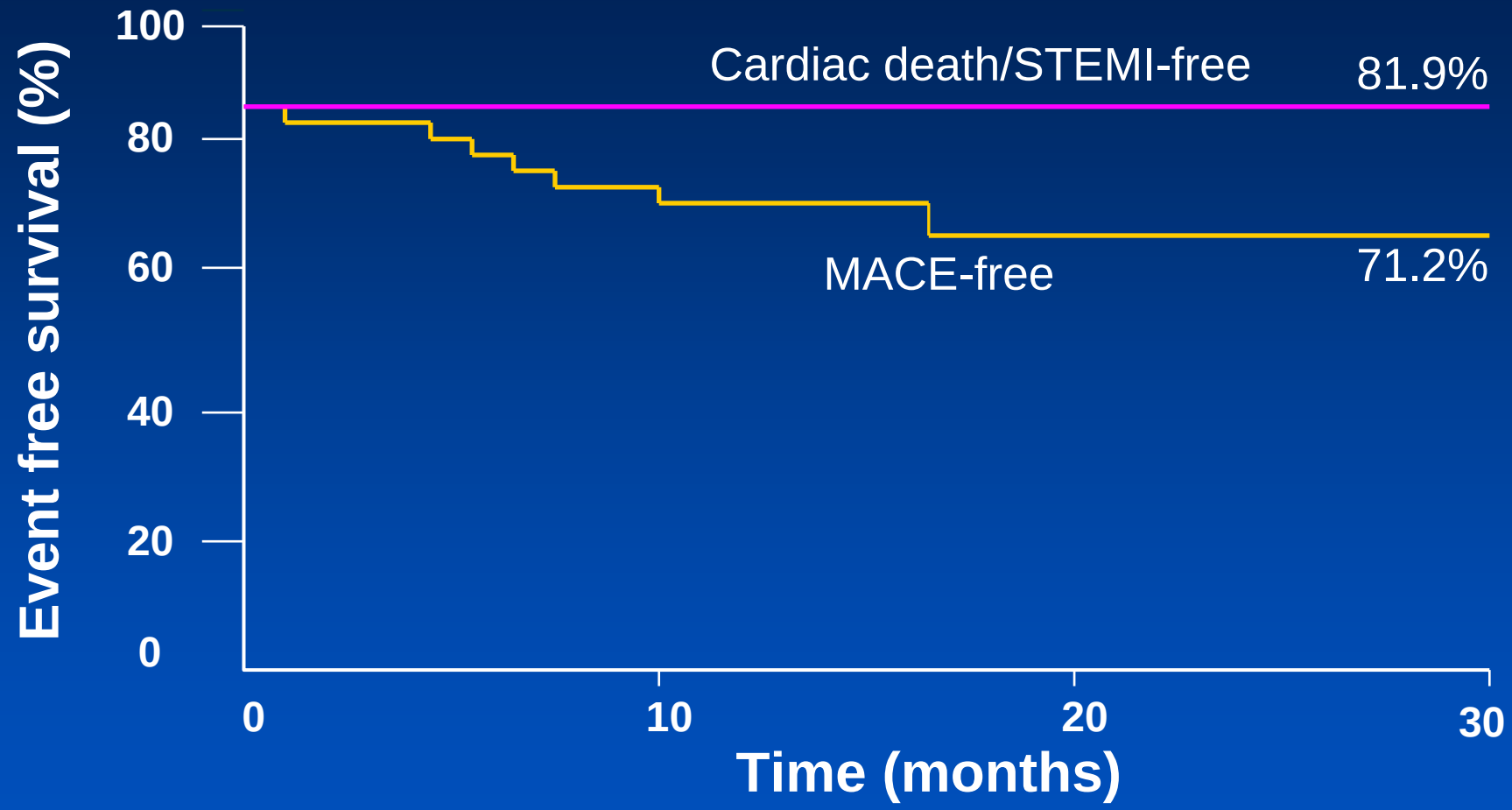
DES (n=52)	Baseline	After procedure	Follow-up
RVD	2.43±0.6	2.86±0.48	2.88±0.56
MLD	0.76±0.5	2.54±0.5	2.22±0.86
% diameter stenosis	68.5±19.3	11.4±7.8	24.2±22.8
Late lumen loss			0.44±0.77

Binary restenosis rate : 19.6%

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

Milan

Kaplan-Meyer Curve



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

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

SES vs. PES

In the Era of Drug Eluting Stent

Clinical Outcomes at 6 Mo

Stented Segment ≥ 60mm

	SES (n=69)	PES (n=52)	*p value*
6 month			
TVR-MACE (%)	9(19)	6(16)	0.76
TLR-MACE(%)	8(17)	5(14)	0.69
TVR(%)	6(13)	5(14)	1.00
Death(%)	3(6)	1(3)	0.63
Late thrombosis	0	0	-

Mishra et al, AHA 2005

Long DES-I Registry Study

From March 2003 - to February 2004

De-novo Lesions
(≥ 24mm)

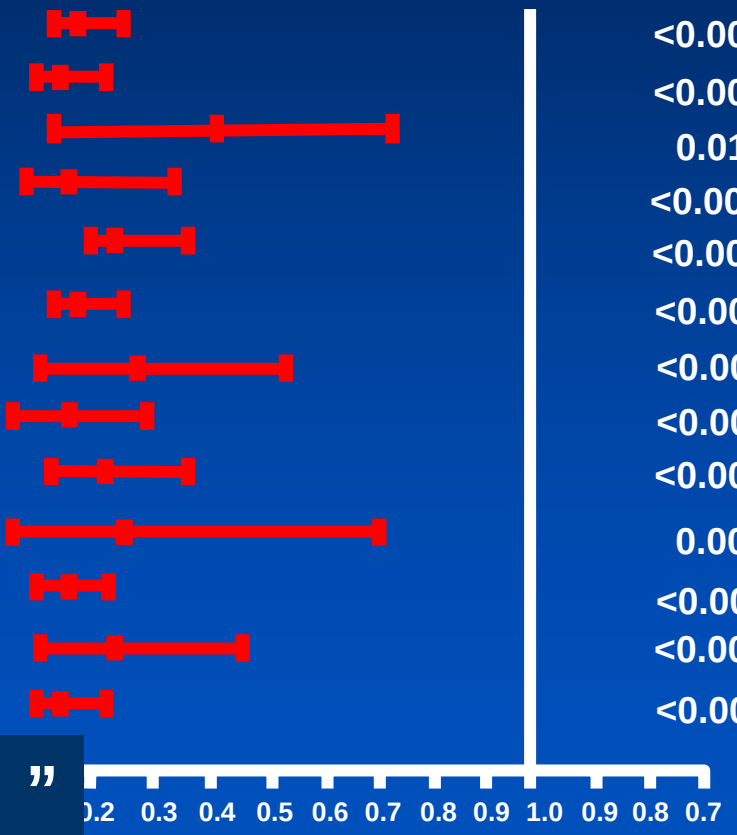
637 patients, 739 lesions

CYPHER (≥ 28mm)	TAXUS (≥ 28mm)	Bare Metal (≥ 28mm)
294 patients 344 lesions	166 patients 194 lesions	177 patients 201 lesions

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

Angiographic Restenosis : DES vs. BMS

	DES	BMS	P-value
Overal	12.4	42.5	<0.0001
Male	12.1	45.6	<0.0001
Female	13.9	31.4	0.019
Diabetes	15.2	52.7	<0.0001
No Diabetes	11.1	37.1	<0.0001
LAD	10.3	45.9	<0.0001
Non-LAD	14.8	34.7	<0.0001
Small Vessel (≤2.75)	15.0	56.6	<0.0001
Large Vessel	10.1	35.5	<0.0001
Stent length>45mm	18.4	44.0	0.004
Stent length≤45mm	8.5	42.2	<0.0001
Multiple stent	15.8	45.2	<0.0001
Single	8.5	41.5	<0.0001

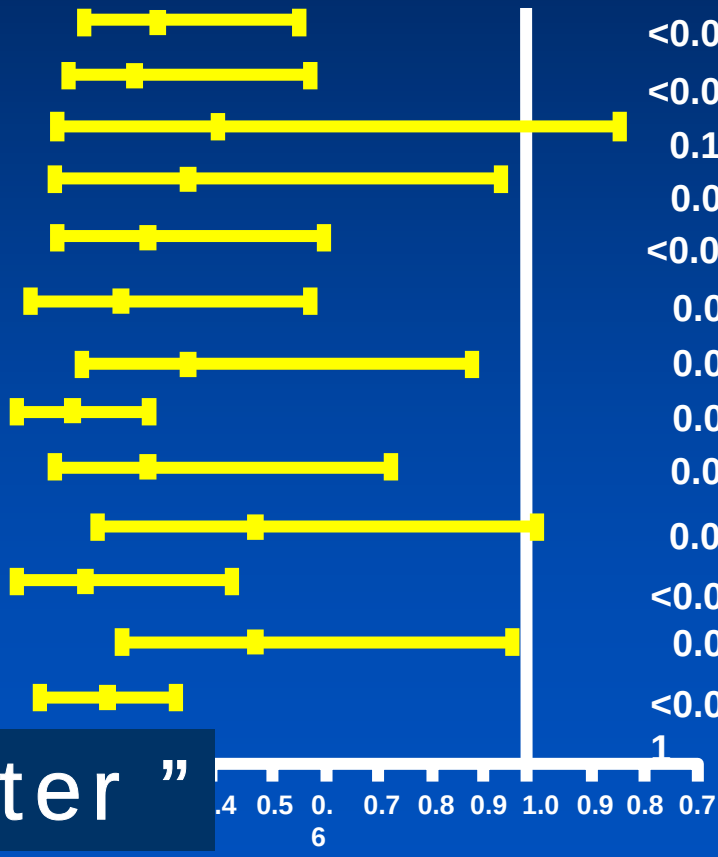


" DES Better "

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

Angiographic Restenosis : Cypher vs. Taxus

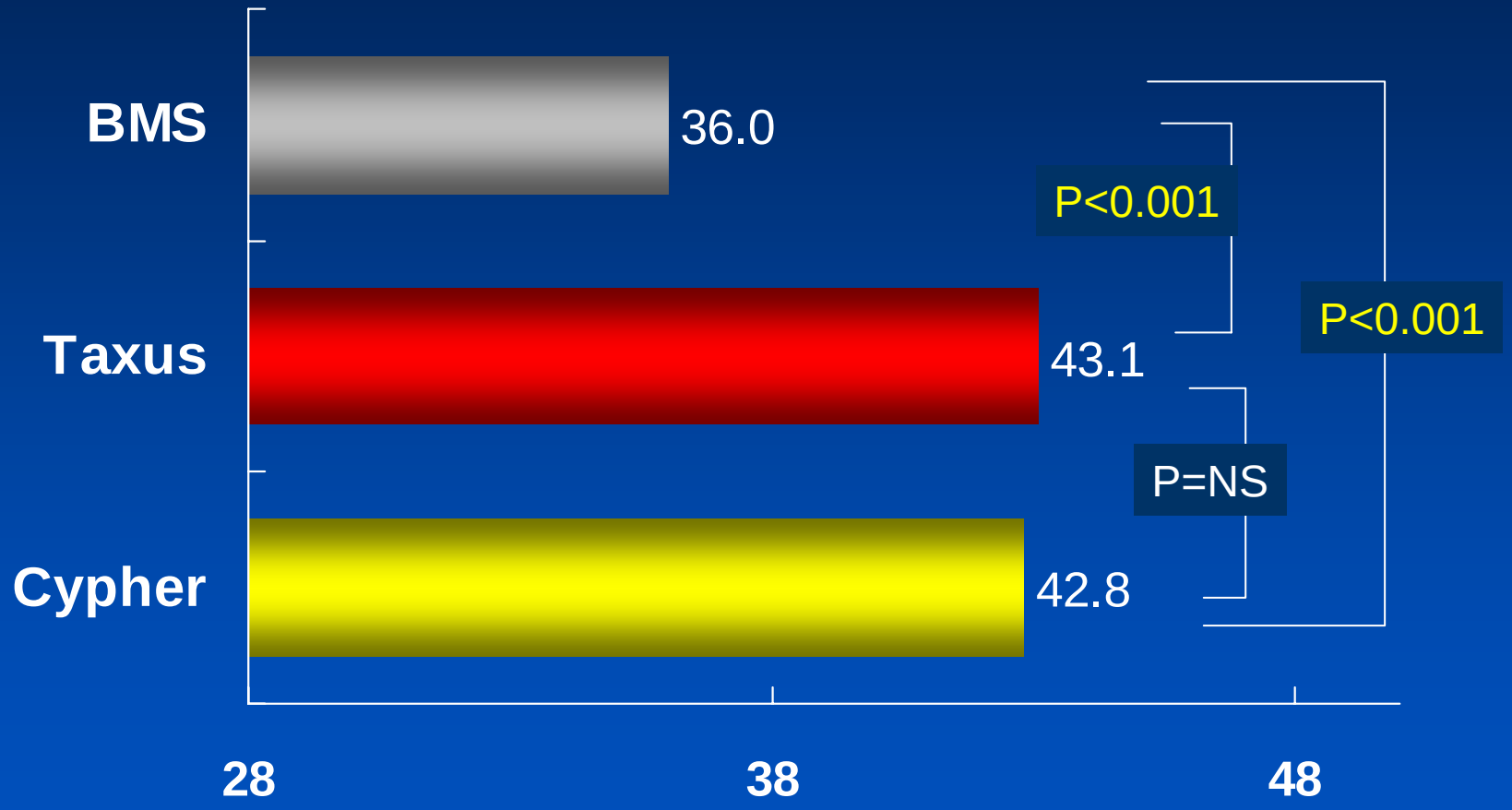
	Cypher	Taxus	P-value
Overall	7.4	24.3	<0.0001
Male	6.6	21.3	<0.0001
Female	10.5	21.9	0.119
Diabetes	9.9	23.5	0.033
No Diabetes	6.3	20.2	<0.0001
LAD	5.7	20.5	0.001
Non-LAD	9.8	22.1	0.020
Small Vessel (≤2.75)	9.2	27.0	0.001
Large Vessel	5.7	17.2	0.005
Stent length>45mm	13.9	25.8	0.056
Stent length≤45mm	3.5	18.2	<0.0001
Multiple stent	12.1	22.5	0.041
Single	2.3	20.0	<0.000 1



" Cypher Better "

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

Total Stent Length Treated



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

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Procedural Characteristics

	Cypher (n=337)	Taxus (n=194)	Control (n=201)	P value
Used stents	1.65±0.71 #	1.63±0.70 **	1.28±0.49	**<0.001**
Overlapping	179 (53) #	100 (52) **	52 (26)	**<0.001**
Maximal pressure, (atm)	16.0±3.6 * #	13.2±3.9 **	12.0±3.3	**<0.001**
Maximal device diameter, (mm)	3.35±0.37 *	3.40±0.41	3.47±0.52	**0.014**
IVUS guidance	266 (79) #	144 (74) **	96 (48)	**<0.001**
Use of Abciximab	8 (3)	2 (1)	7 (4)	0.266

Between groups: * p<0.025 Cypher vs Taxus; # p<0.025 Cypher vs BMS;**, p<0.025 Taxus vs. BMS

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

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In-Hospital Outcomes

	Cypher (n=294)	Taxus (n=166)	Control (n=177)	P value
Angiographic success (%)	329 (98)	191 (99)	193 (96)	0.296
Death	0 (0)	0 (0)	1 (0.6)	0.422
MI				
Q wave	0 (0)	0 (0)	1 (0.6)	0.272
Non-Q wave	26 (8.8)	16 (9.6)	14 (7.9)	0.852
Stent thrombosis	0 (0)	0 (0)	1 (0.6)	0.272
TLR	0 (0)	0 (0)	1 (0.6)	0.272
MACE	26 (8.8)	16 (9.6)	15 (8.5)	0.928

Between groups: * p<0.025 Cypher vs Taxus; # p<0.025 Cypher vs BMS;**, p<0.025 Taxus vs. BMS

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

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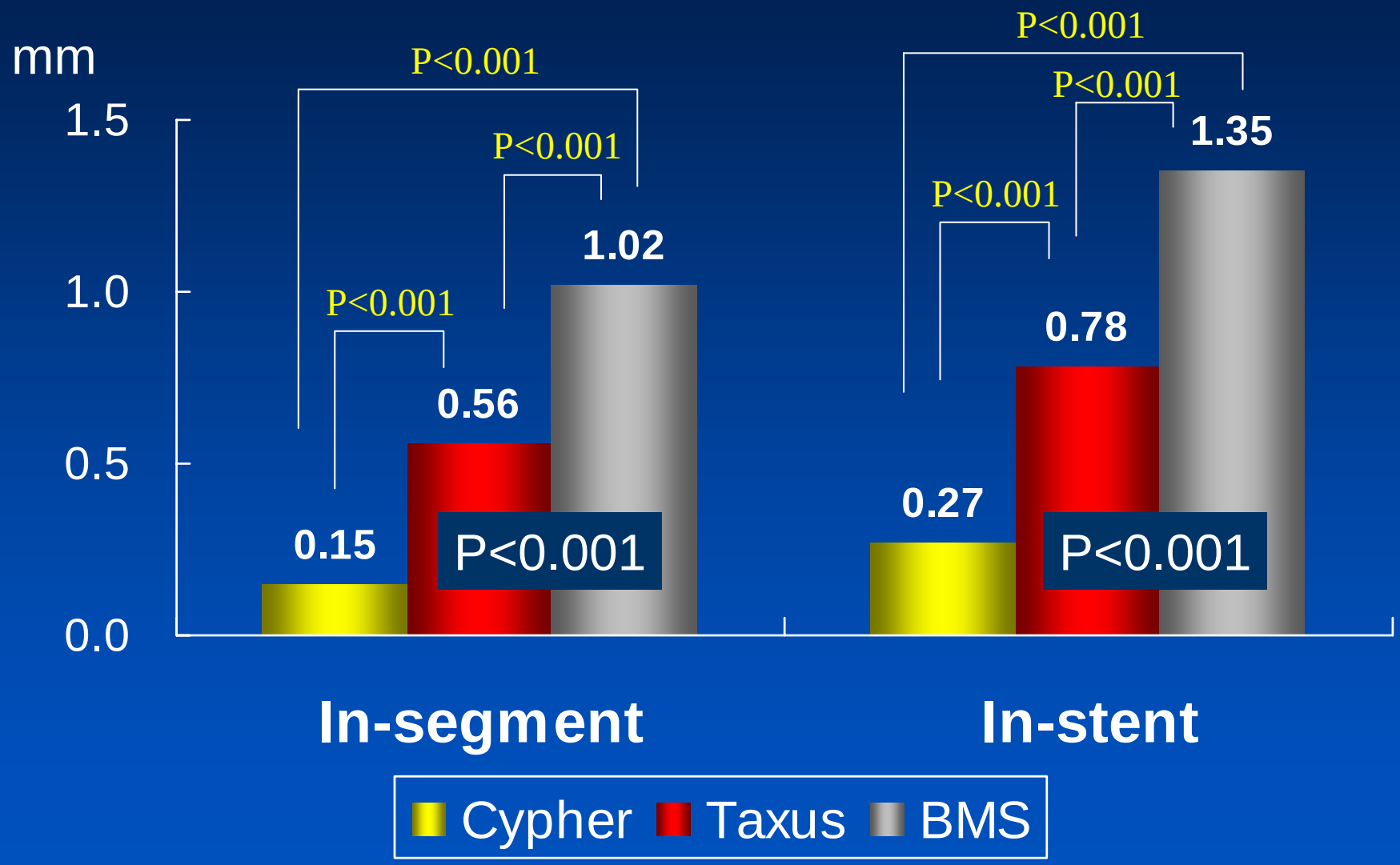
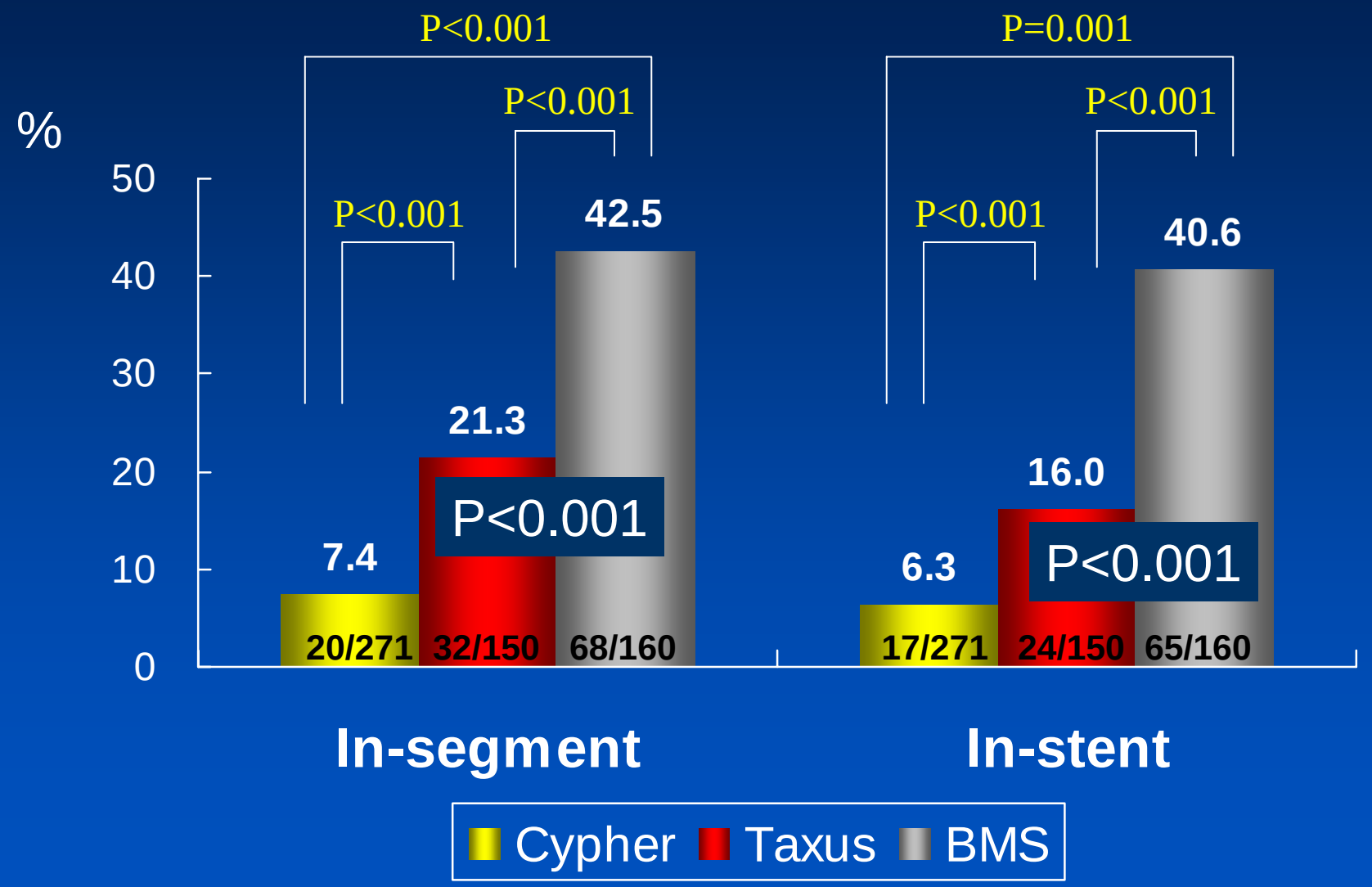
Late Loss



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

Restenosis Rate

AMC



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

Predictors of Restenosis
Overall

Variables	Relative Risk	95% C.I.	P value
Bare metal stent	8.01	4.90-13.11	<0.001
Lesion length (10mm)	1.29	1.10-1.51	0.002
MLD after procedure (mm)	0.32	0.19-0.53	<0.001

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

Predictors of Restenosis
DES subgroup

Variables	Relative Risk	95% C.I.	P value
Taxus stent	3.65	1.96-6.79	<0.001
Lesion length (10mm)	1.31	1.08-1.60	0.006
MLD after procedure (mm)	0.29	0.13-0.61	0.001

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

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Predictors of Restenosis
Cypher or Taxus subgroup

		R.R	95% C.I.	P value
Cypher	▪ Multiples stent	5.62	1.60-19.68	0.007
Taxus	▪ MLD after procedure (mm)	0.19	0.05-0.57	0.004
	▪ Lesion length (10mm)	1.36	1.02-1.82	0.037
BMS	▪ MLD after procedure (mm)	0.31	0.15-0.64	0.001
	▪ Diabetes mellitus	2.00	1.01-3.98	0.048

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

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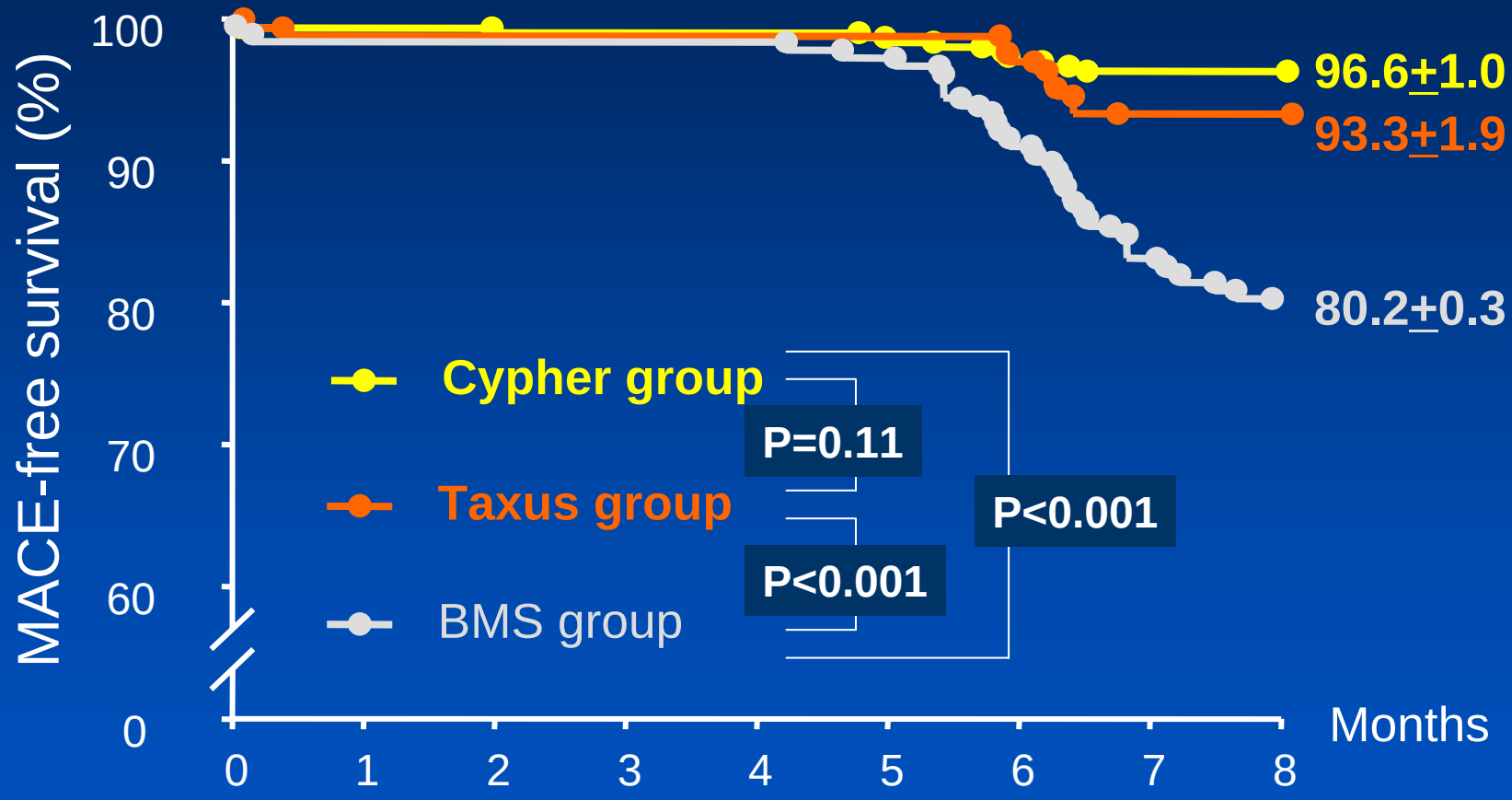
Nine-Month Outcomes

	Cypher (n=294)	Taxus (n=166)	Control (n=177)	P value
Death	2 (0.7)	1 (0.6)	1 (0.6)	0.987
MI	0 (0)	0 (0)	1 (0.6)	0.272
Q wave	0 (0)	0 (0)	1 (0.6)	
Non-Q wave	0 (0)	0 (0)	0 (0)	
Stent thrombosis	0 (0)	0 (0)	1 (0.6)	0.272
TLR	8 (2.7) #	10 (6.0) **	34 (19.2)	**<0.001**
Repeat PCI	7	7	32	
CABG	1	2	2	
MACE	10 (3.4) #	11 (6.6) **	35 (19.8)	**<0.001**

Between groups: * p<0.025 Cypher vs Taxus; # p<0.025 Cypher vs BMS;**, p<0.025 Taxus vs. BMS

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

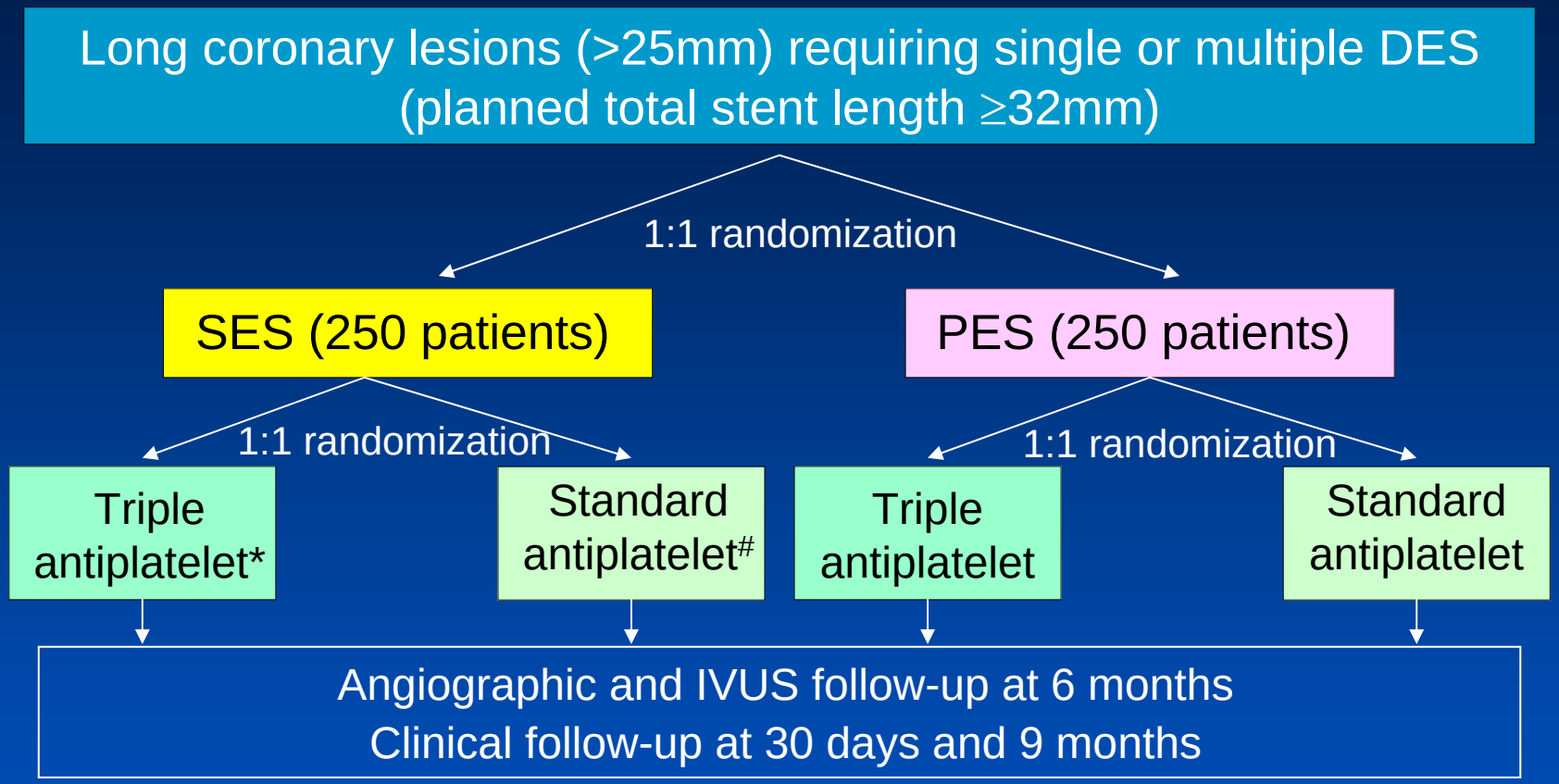
MACE-free Survival



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

Long-DES-II Study

AMC



* Triple antiplatelet : aspirin plus clopidogrel plus cilostazol for 6 months

\# Standard antiplatelet : aspirin plus clopidogrel for 6 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

Preliminary Analysis

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

1:1 randomization

SES (250 patients)	PES (250 patients)
Angiographic F/U at 6 months	
168 patients (76.3%) of eligible patients	164 patients (75.2%) of eligible patients
Clinical F/U at 9 months	
200 patients (80%) of study population	206 patients (82%) of study population

QCA before Procedure

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	SES (n=250)	PES (n=250)	*p*
Reference vessel (mm)	2.82±0.42	2.76±0.46	0.230
Lesion length (mm)	34.1 ±11.8	34.8 ±12.3	0.554
MLD (mm)	0.69±0.48	0.69±0.45	0.902
Diameter stenosis (%)	70.4±13.7	70.1±12.0	0.826

Procedural Findings

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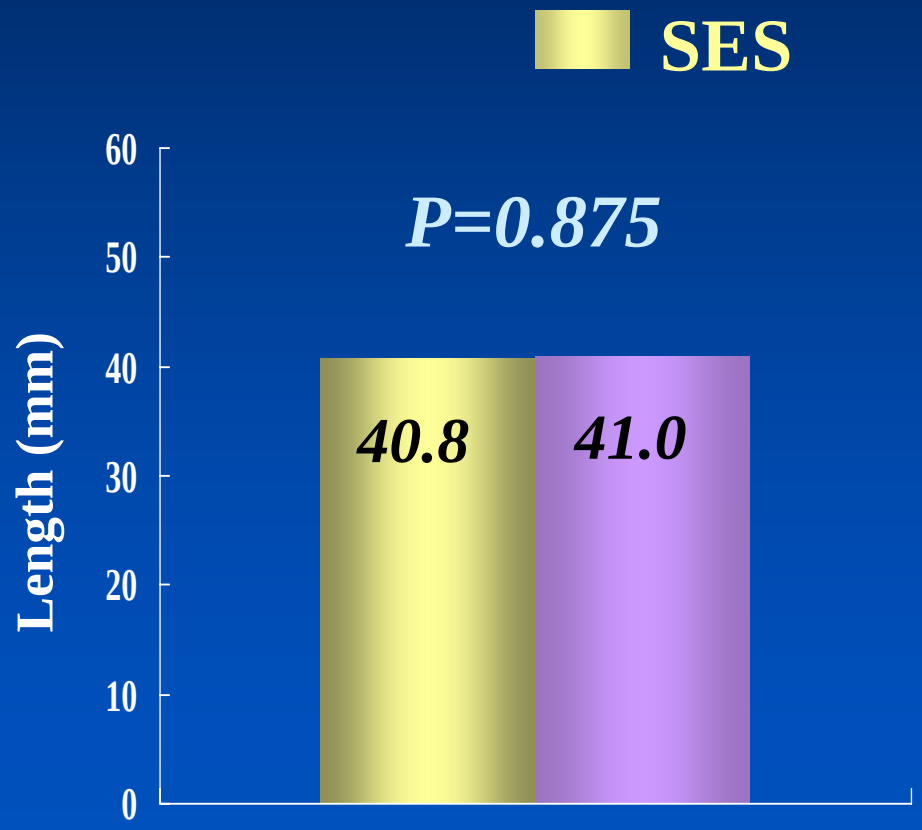
	SES (n=250)	PES (n=250)	*p*
Procedural success *	99.2%	98.8%	0.653
Maximal device diameter	3.5±0.4	3.6±0.3	0.084
(mm)	16.1±3.4	15.9±3.4	0.720
Maximal pressure (atm)	105	99	0.649
Use of IVUS	(42.0%)	(39.6%)	0.024
Use of GP IIb/IIIa inhibitor	2(0.8%)	9(3.6%)	

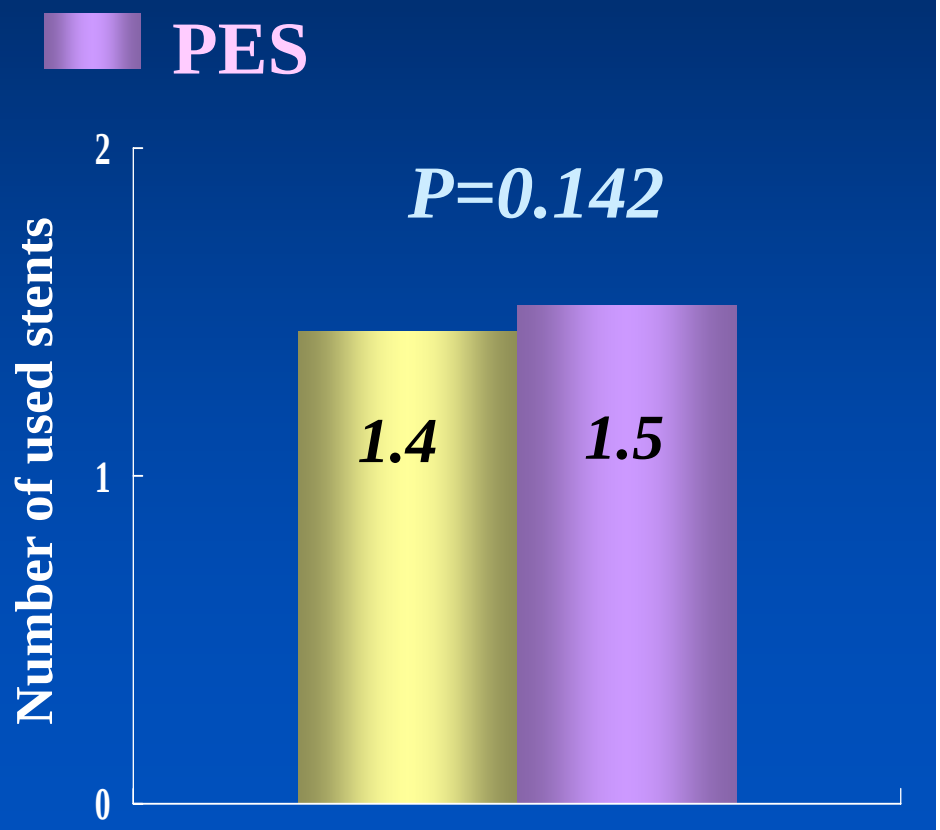
* Procedural success was defined as post-procedural DS in analysis segment <30% without death, Q-MI, or emergent revascularization during hospitalization

Length and No. of Used DESs

Length of stented segment



No. of stents per lesion



QCA after Procedure

AMC

	SES (n=250)	PES (n=250)	*p*
Reference vessel (mm)	2.70±0.50	2.69±0.55	0.614
MLD (mm)			
In-stent	2.47±0.41	2.49±0.40	0.599
In-segment	2.16±0.46	2.17±0.49	0.753
Acute gain (mm)			
In-stent	1.78±0.54	1.80±0.55	0.620
In-segment	1.46±0.60	1.48±0.61	0.732
Diameter stenosis (%)			
In-stent	6.5±15.9	5.0±16.7	0.325
In-segment	19.3±13.2	18.6±13.2	0.443

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Clinical Outcomes at 30 Days

	SES (n=250)	PES (n=250)	P
Peri-procedural CK-MB > 3 times normal	20 (8.0%)	27 (10.8%)	0.283
Death	0	0	1.0
Myocardial infarction	1(0.4%)*	0	0.500
Q-MI	1(0.4%)	0	
Non-Q MI	0	0	
Stent thrombosis	1(0.4%)*	0	0.500
TLR	1(0.4%)*	0	0.500
MACE	1(0.4%)*	0	0.500

* One patient underwent TLR for AMI due to subacute stent thrombosis 3 days after index procedure

QCA at Follow-up

AMC

	SES (n=168)	PES (n=164)	*p*
Reference vessel (mm)	2.79±0.48	2.74±0.55	0.339
MLD (mm)			
In-stent	2.39±0.46	2.04±0.65	<0.001
In-segment	2.17±0.50	1.92±0.53	<0.001
Diameter stenosis (%)			
In-stent	13.0±17.8	23.6±20.7	<0.001
In-segment	21.3±14.5	30.0±16.0	<0.001

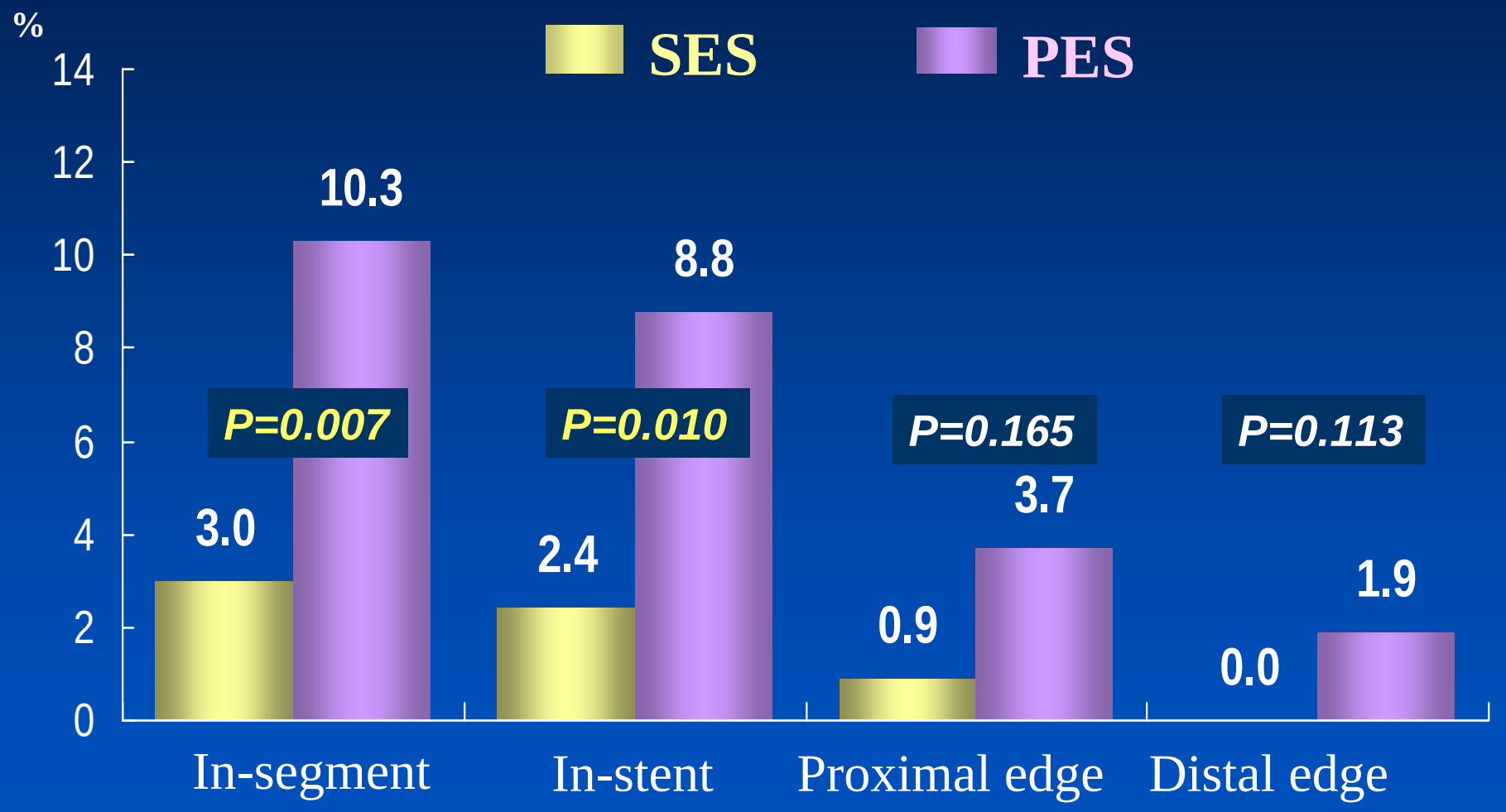
AMC

QCA at Follow-up

	SES (n=168)	PES (n=164)	*p*
Late loss (mm)			
In-stent	**0.10±0.34**	**0.43±0.54**	**<0.001**
In-segment	**0.22±0.36**	**0.59±0.53**	**<0.001**
Loss index			
In-stent	**0.05±0.22**	**0.25±0.35**	**<0.001**
In-segment	**0.17±0.36**	**0.49±0.69**	**<0.001**

Angiographic Restenosis

AMC



Clinical Outcomes at 9 Months

AMC

	SES	PES	P
Patients	**200**	**206**	
Death	**1 (1.0%)**	**0**	**0.493**
Cardiac	**1 (1.0%)**	**0**	
Non-cardiac	**0**	**0**	
MI	**2 (1.0%) ***	**0**	**0.242**
Stent thrombosis	**2 (1.0%)**	**0**	**0.242**
Acute	**0**	**0**	
Subacute	**1**	**0**	
Late	**1****	**0**	
TLR	**5 (2.5%)**	**16 (7.8%)**	**0.014**
MACE	**6 (3.0%)**	**16 (7.8%)**	**0.027**

* Both of them were related to subacute and late stent thrombosis
** This patient was presented with STEMI and cardiogenic shock 3 months after the index procedure. Before emergent revascularization, this patient was dead.

Impact of Lesion Length

In the Era of Drug Eluting Stent

Multivariate Predictors of In-Segment Restenosis after SES

RESEARCH Registry

	OR	95% CI	p
ISR	4.16	1.63-11.01	<0.01
Ostial lesion	4.84	1.81-12.07	<0.01
DM	2.63	1.14-6.31	0.02
Stent length	1.42	1.21-1.68	<0.01
Ref diameter	0.46	0.24-0.87	0.03
LAD	0.30	0.10-0.69	<0.01

Lemos PA et al. Circulation 2004;109:1366-1370

Multivariate Predictors of In-Segment Restenosis after DES

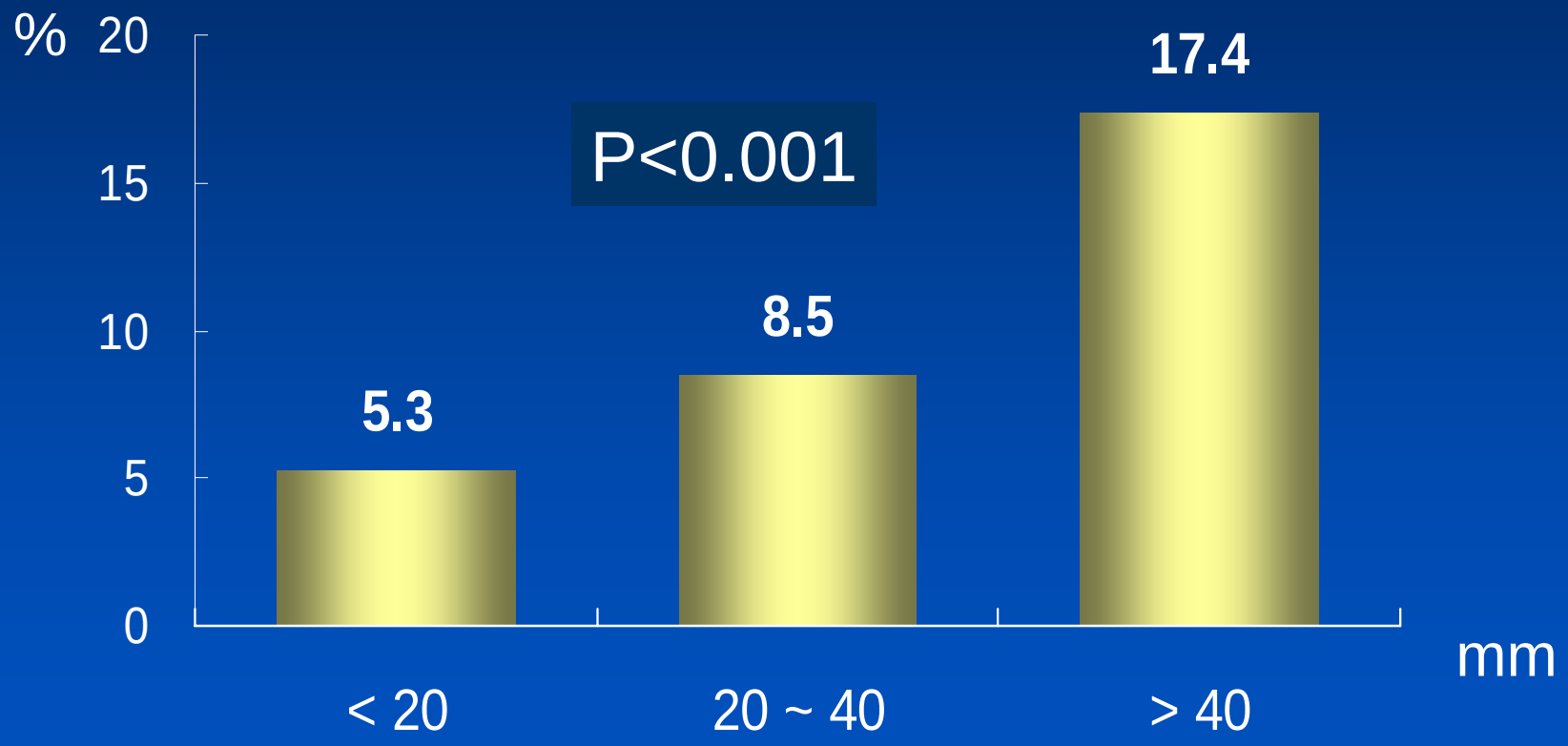
From Asan Medical Center

	OR	95% CI	p
Lesion length, mm	1.023	1.010-1.035	<0.001
Post-intervention 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

Restenosis Rate According to Lesion Length

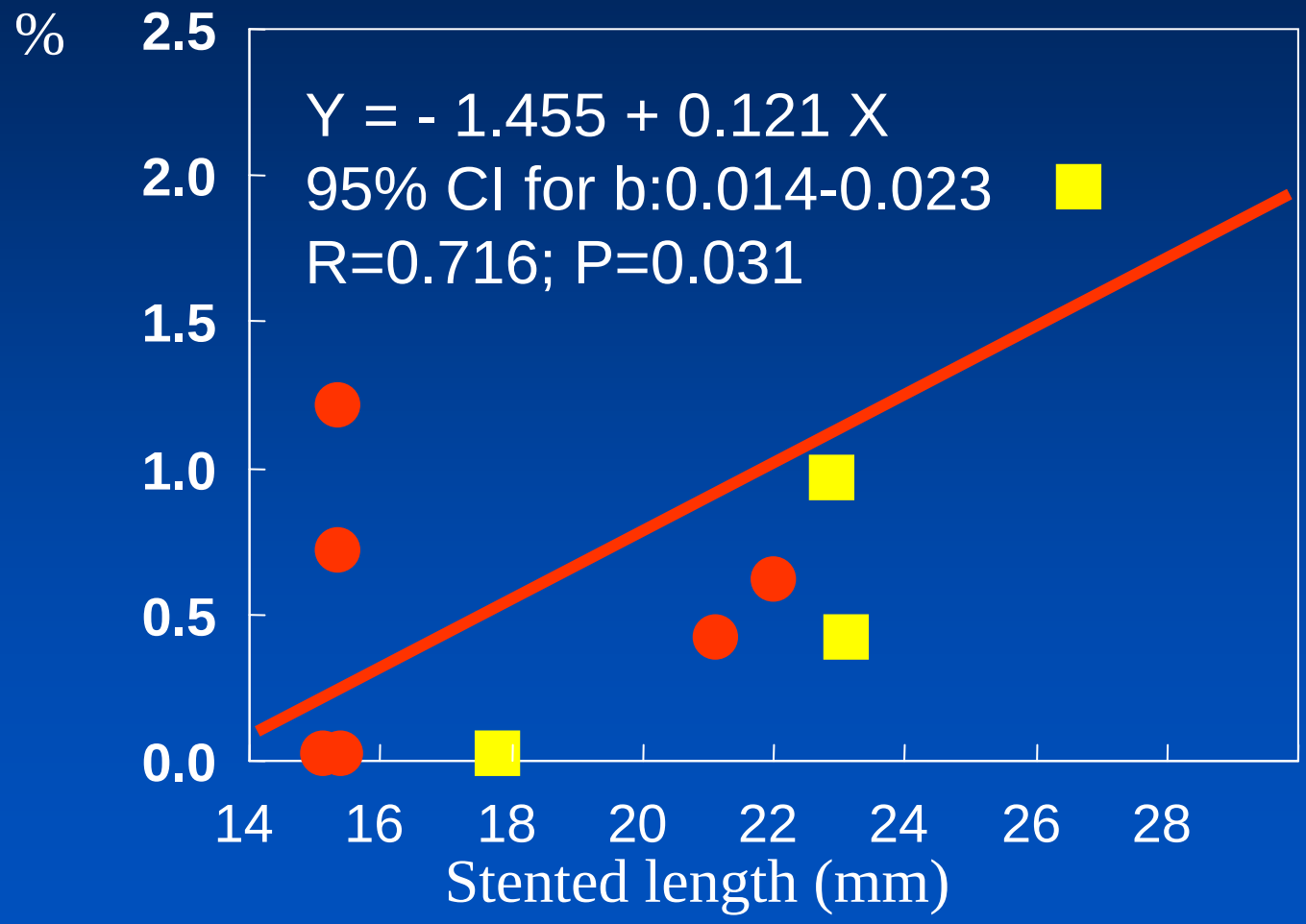
From Asan Medical Center



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

Stented Length and Thrombosis

Stent thrombosis rate by meta-analysis



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

Independent Predictors of Subacute Stent Thrombosis

Analysis of 2229 patients treated with DES

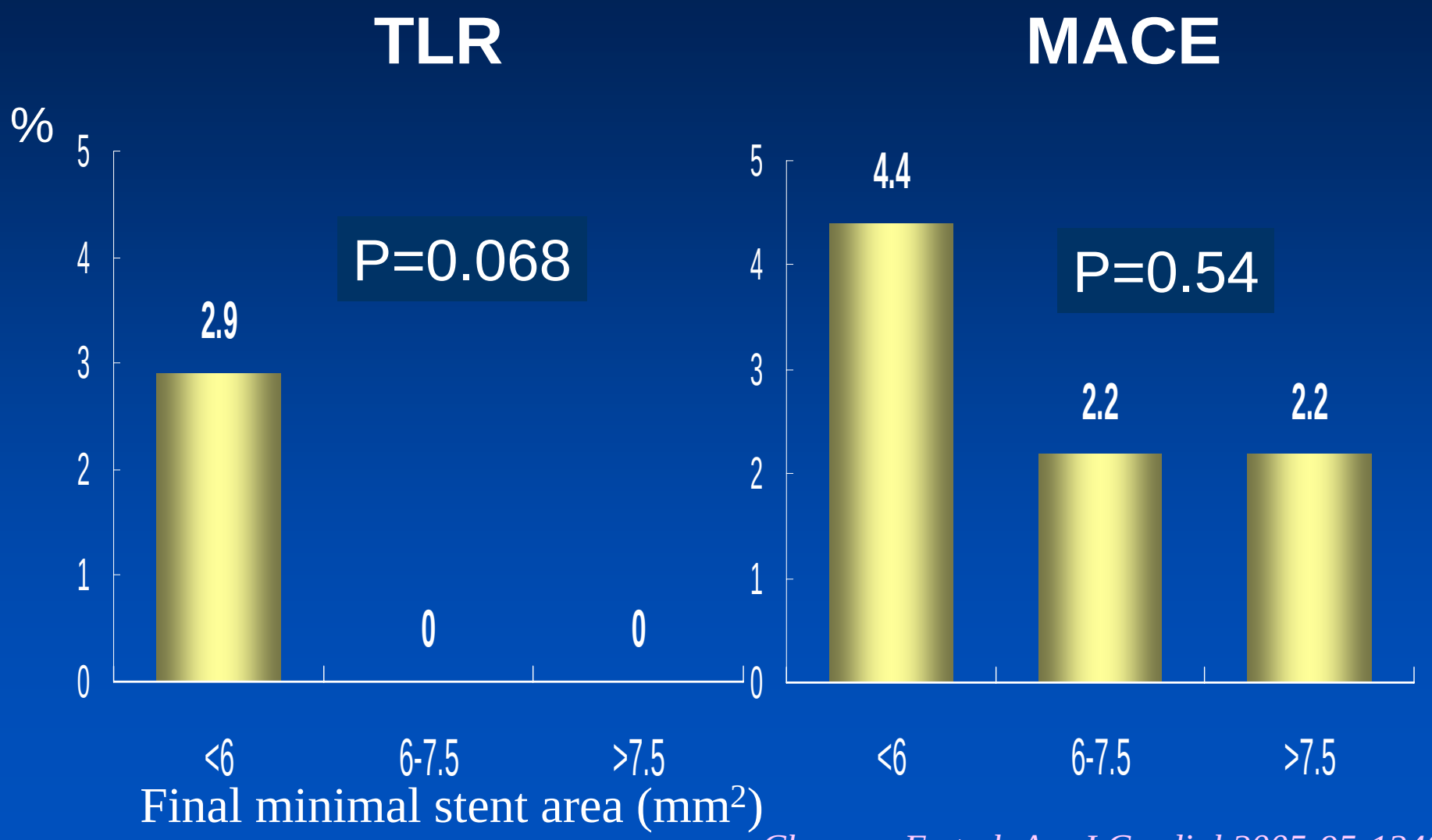
Variables	Hazard Ratio (95% CI)	P value
Premature antiplatelet discontinuation	161.17 (26.03-997.94)	<0.001
Renal failure	5.96 (1.90-18.68)	<0.001
Bifurcation lesion	5.96 (1.90-18.68)	0.002
Diabetes	5.84 (1.74-19.56)	0.004
LVEF per 10% decrease	1.12 (1.06-1.19)	<0.001
Stent length per 1mm increase	1.03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

Iakovou I et al. JAMA 2005;293:2126

How to do ?

In the Era of Drug Eluting Stent

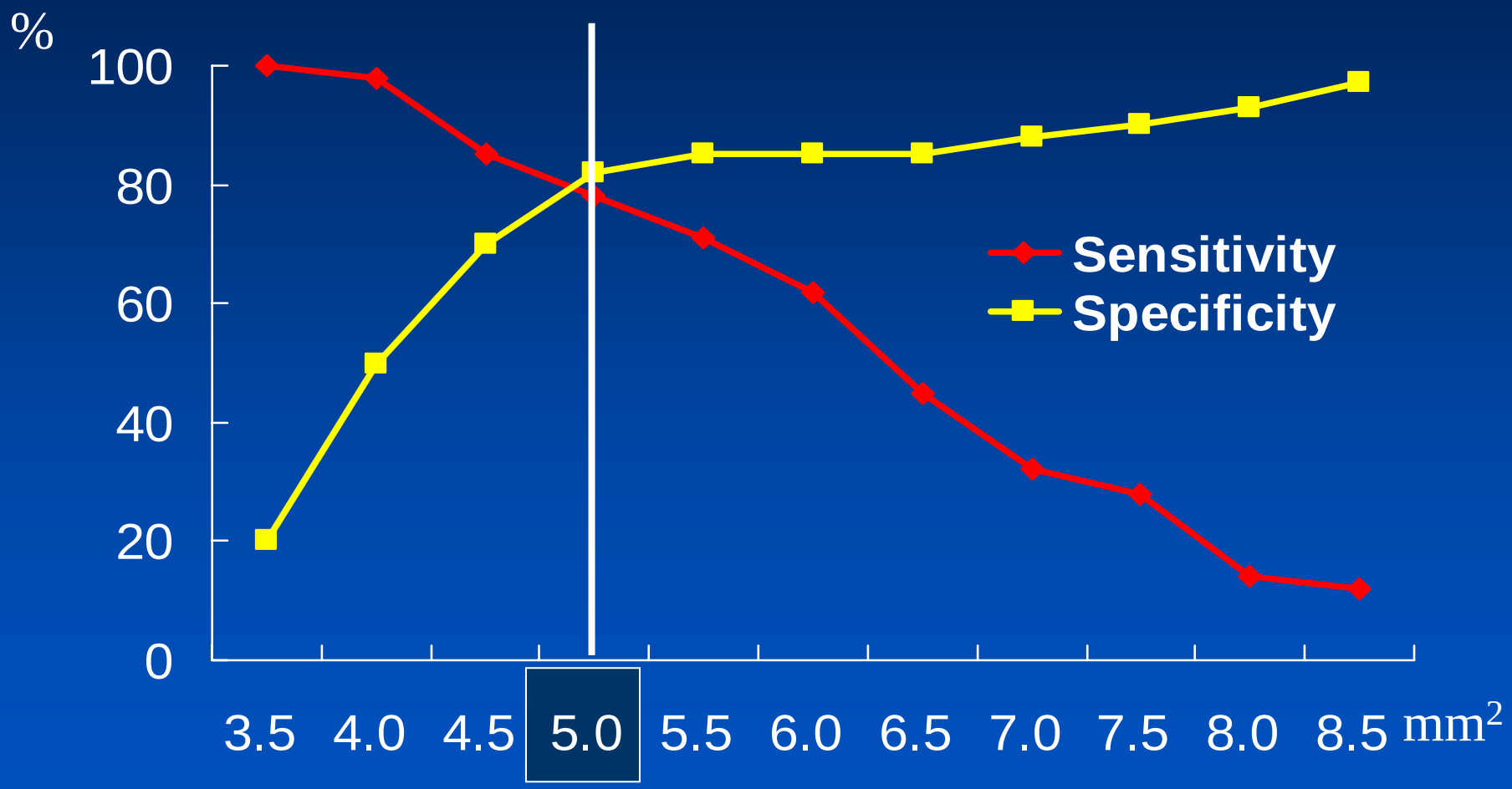
Optimal Stent Expansion



Cheneau E et al. Am J Cardiol 2005;95:1240

Final Stent Area for Prediction of F/U Stent Area

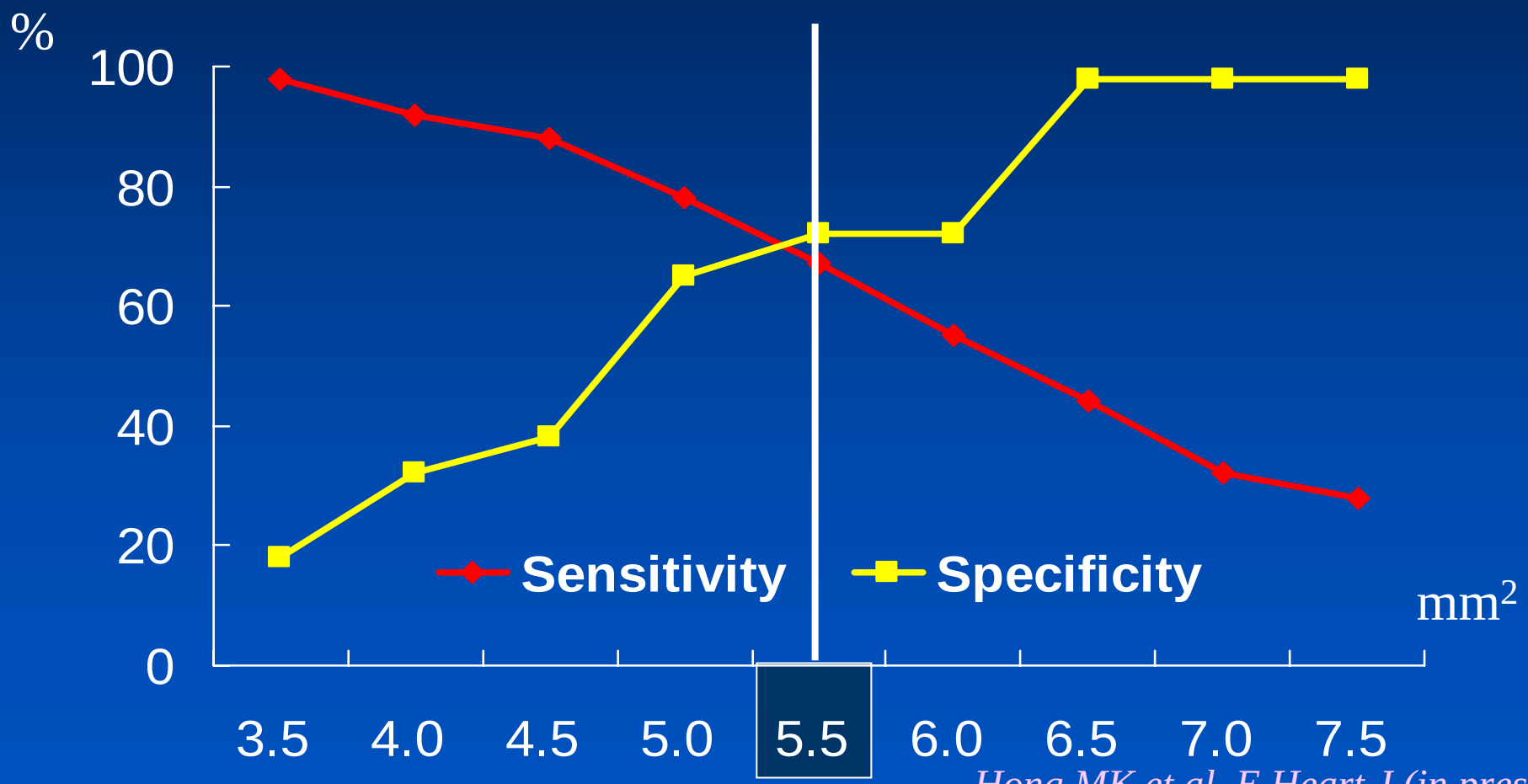
SES in SIRIUS Study



Sonoda S et al. J Am Coll Cardiol 2004;43:1959

Final Stent Area for Prediction of Restenosis

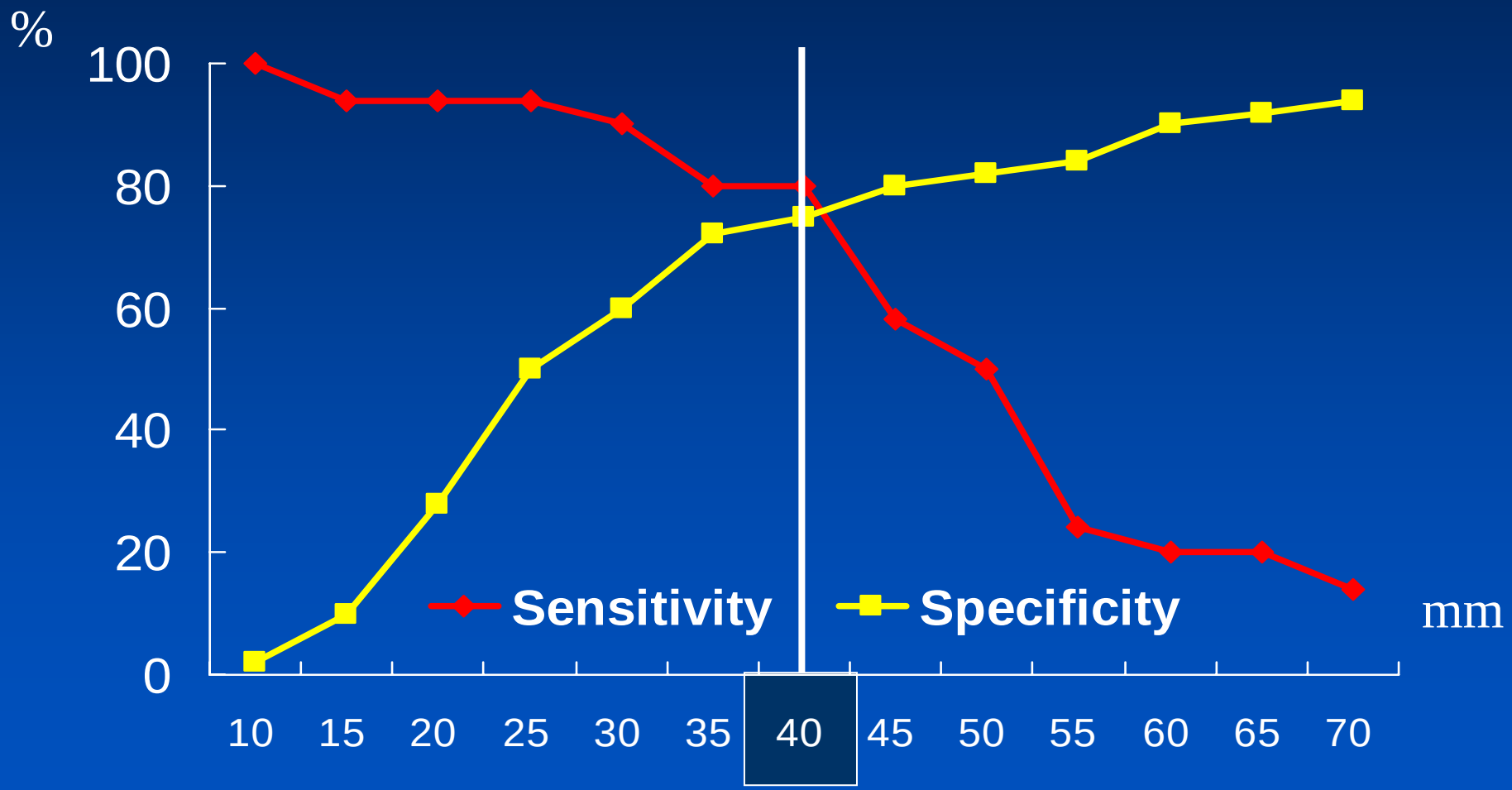
SES Registry in AMC



Hong MK et al. E Heart J (in press)

Stent Length for Prediction of Restenosis

SES Registry in AMC



Hong MK et al. E Heart J (in press)

Importance of Full-lesion Coverage

SES in SIRIUS Study

	Edge Stenosis		p
	Yes (n=6)	No (n=162)	
Reference area, mm^2	10.7±3.8	10.7±3.8	0.156
Reference plaque, mm^2	6.7±3.3	7.0±3.2	0.891
Reference minimum lumen area, mm^2	4.7±2.3	6.4±2.3	0.0498
Edge stent area, mm^2	6.8±3.2	7.3±2.1	0.358
Maximum reference plaque area, %	60.5±9.0	48.8±11.5	0.030
Step-up index	1.5±0.3	1.2±0.3	0.011
Edge teat or dissection	0	2 (1%)	1.000

Sakurai R et al. Am J Cardiol 2005;96:1251

Conclusions

- Angiographic and clinical benefits of DES compared to the BMS extended to the long coronary lesions.
- Recent registry data also showed that the need of repeat revascularization in very long coverage with DES was within the single digit.
- A multicenter registry and a randomized studies (Long-DES-I & -II) showed that the SES was more effective in reducing the restenosis rate as compared to the PES in long coronary lesions.

Conclusions

- In spite of the benefit of DES, long lesion and long stented segments remain predictors of adverse clinical outcomes such as relatively high incidence of angiographic resenosis, target lesion revascularization and stent thrombosis.
- Full lesion coverage and matching the stented segment properly to the adjacent segment using intravascular ultrasound guidance may improve DES implantation efficacy.
- The optimal cut-off values of final minimum IVUS stent area to predict angiographic restenosis has been reported as 5-6mm^2.