

PCI for In-Stent Restenosis



ISR of BMS

Patterns of In-Stent Restenosis

Pattern I : Focal



Type IA: Articulation / Gap



Type IB: Marginal



Type IC: Focal body



Type ID: Multifocal

Pattern II,III,IV : Diffuse



Pattern II : Intra-stent



Pattern III: Proliferative

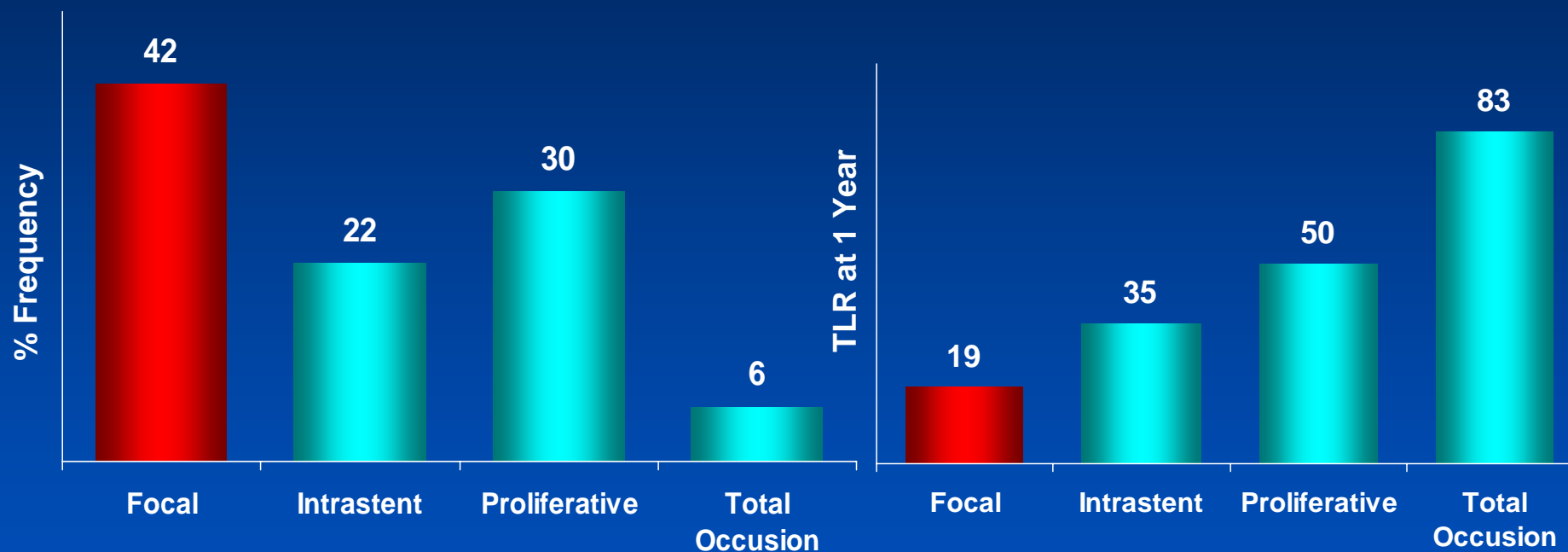


Pattern IV : Total occlusion

Mehran R. Circulation 1999;100:1872 -8

Patterns of ISR

282 Lesions



Predictors of TLR: diabetes, previous ISR and ISR patterns

Mehran R. Circulation 1999;100:1872-8



Treatment of BMS-ISR

- Balloon angioplasty
- Cutting balloon angioplasty
- Rotabating atherectomy
- Repeat stenting
- **Intracoronary brachytherapy**
- **Drug-eluting stent**

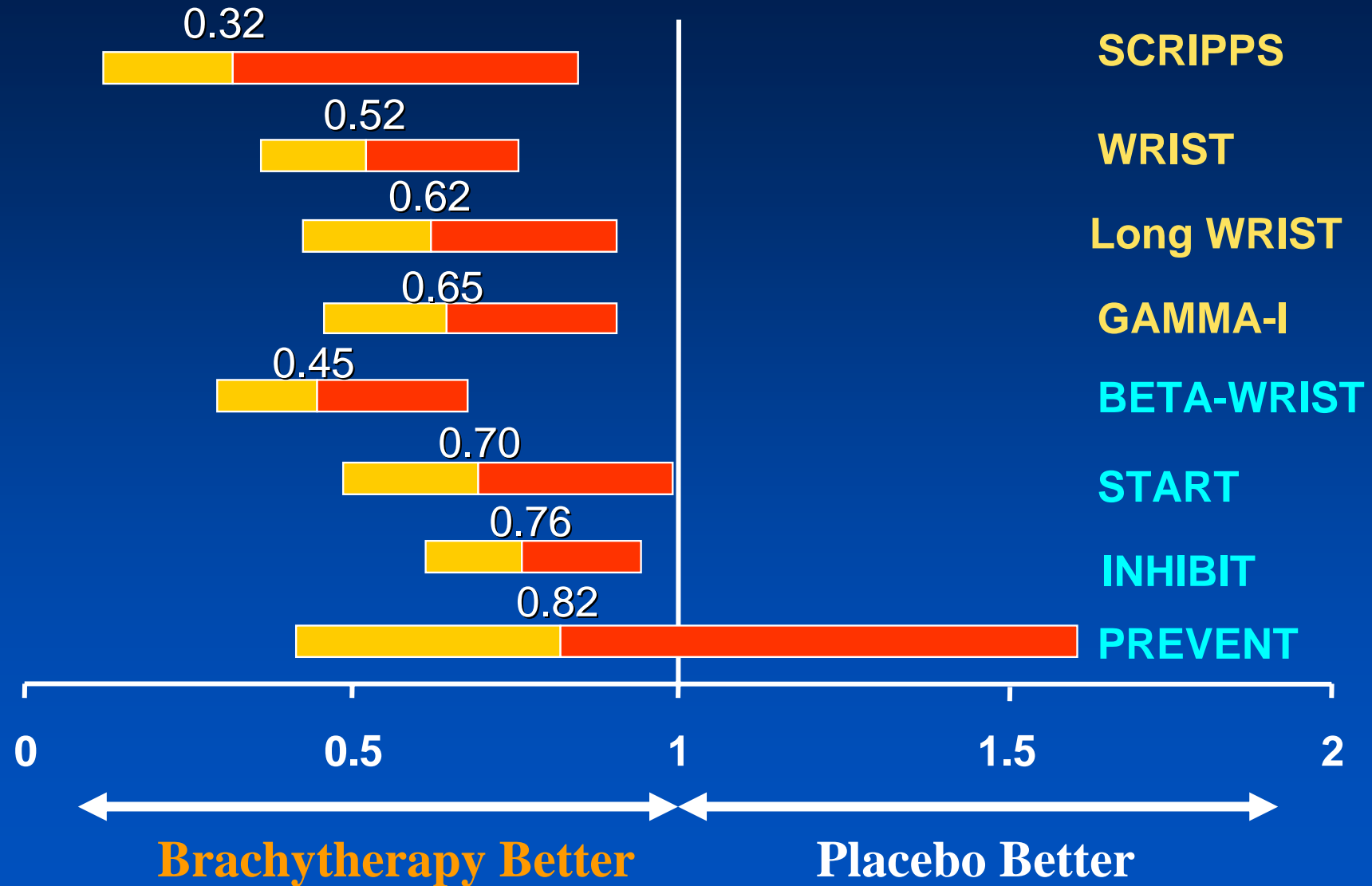
Not
encouraging
in diffuse ISR

Intracoronary Brachytherapy

- Most effective therapy of in-stent restenosis before development of DES
- Use of source train or balloon with beta or gamma radiation
- Inhibition of neo-intimal growth



Risk Reduction of Brachytherapy



Brachytherapy

Reported Clinical Trials for ISR

Trials	Source	Length (mm)	Pts (n)	Restenosis (%)	
				Placebo	Treated
SCRIPPS	192Ir	15.3	35	70.5	11.1
WRIST	192Ir	23.7	130	58.3	19.0
GAMMA 1	192Ir	20.2	252	50.5	21.6
GAMMA 2	192Ir	19.0	125		23.0
LONG WRIST	192Ir	32.0	120	71.0	32.0
B-WRIST	90Y	20.6	50		22.0
START	Sr/90	17.0	476	42.2	14.2
INHIBIT	P32	17.0	332	48.0	16.0
BRITE	P32	17.0	26		0

Paclitaxel-Coated Balloon for ISR

PACCOATH ISR Study

From December 2003 to July 2004

Bare metal ISR (n=52)

Randomization (1:1)

**Coated with Paclitaxel
(n=26, coated-balloon
group)**

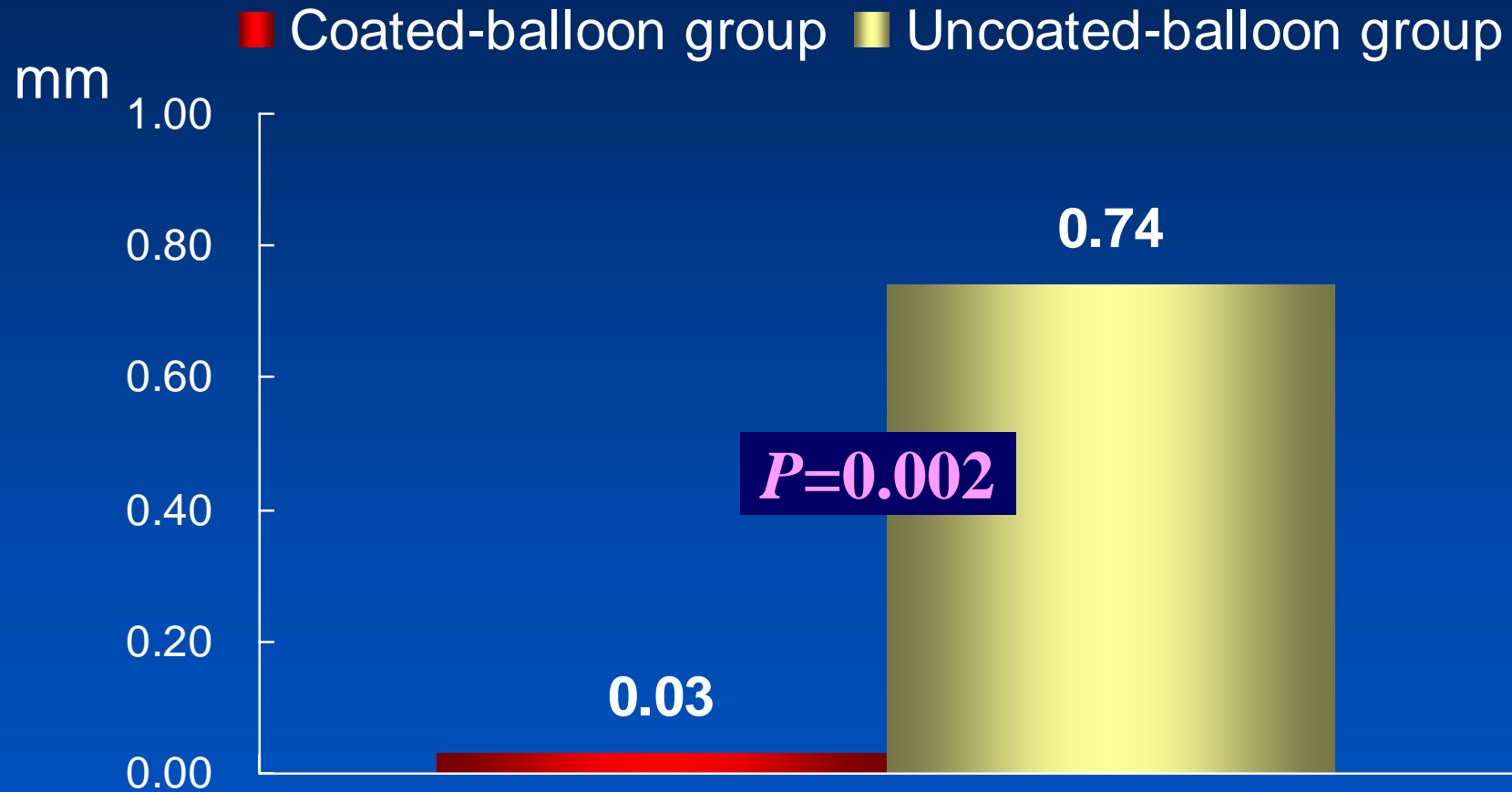
**Uncoated balloon catheter
(n=26, uncoated-balloon
group)**

6-month angiographic late luminal loss
12-month rates of restenosis & MACE including TLR,
MI, stroke, and death

Scheller B. NEJM 2006;355:2113-24

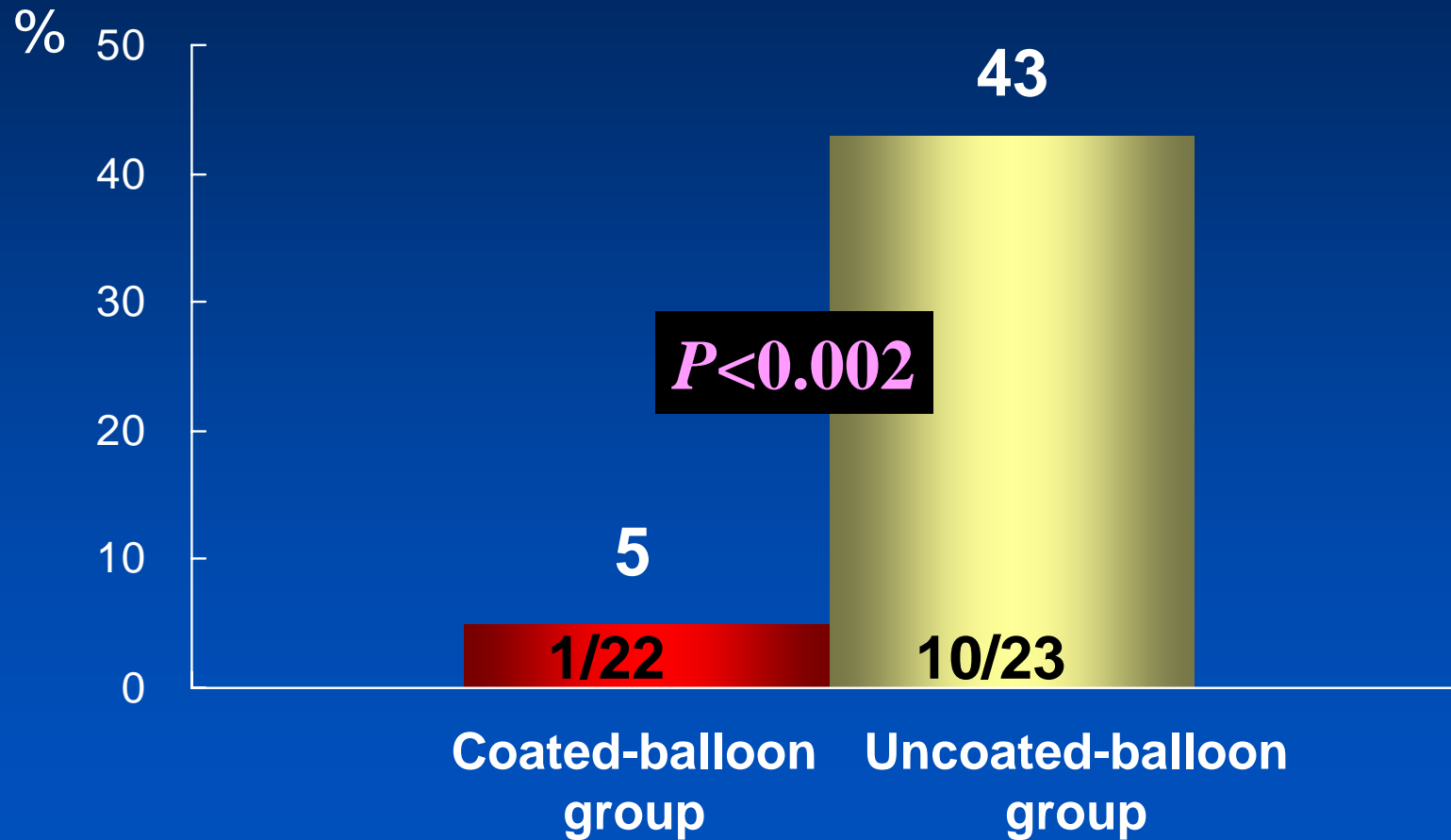


In-segment Late Loss at 6 months



Scheller B. NEJM 2006;355:2119

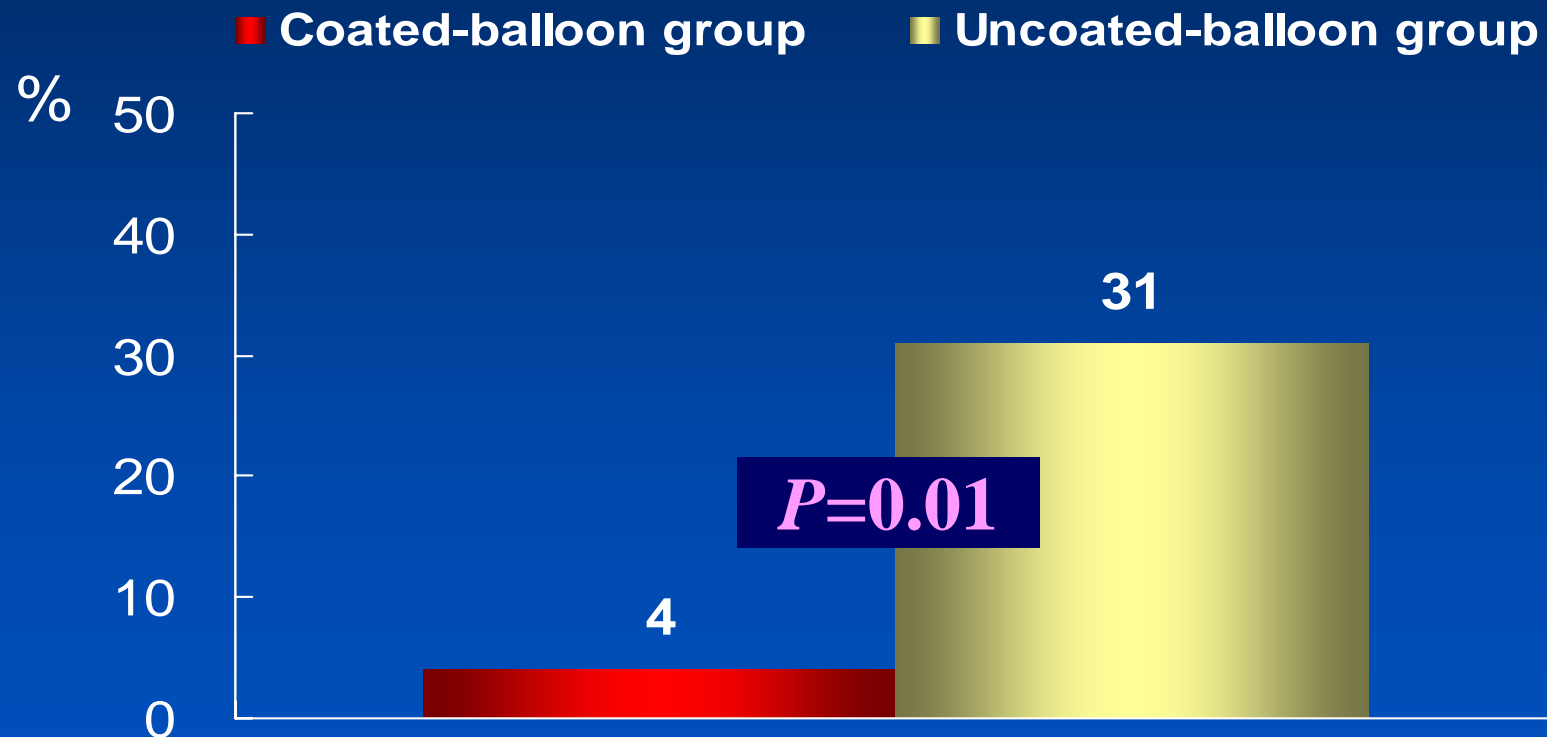
Restenosis Rate at 6 months



Scheller B. NEJM 2006;355:2119

12-month Clinical Outcomes

MACE including death, MI, TLR, stroke

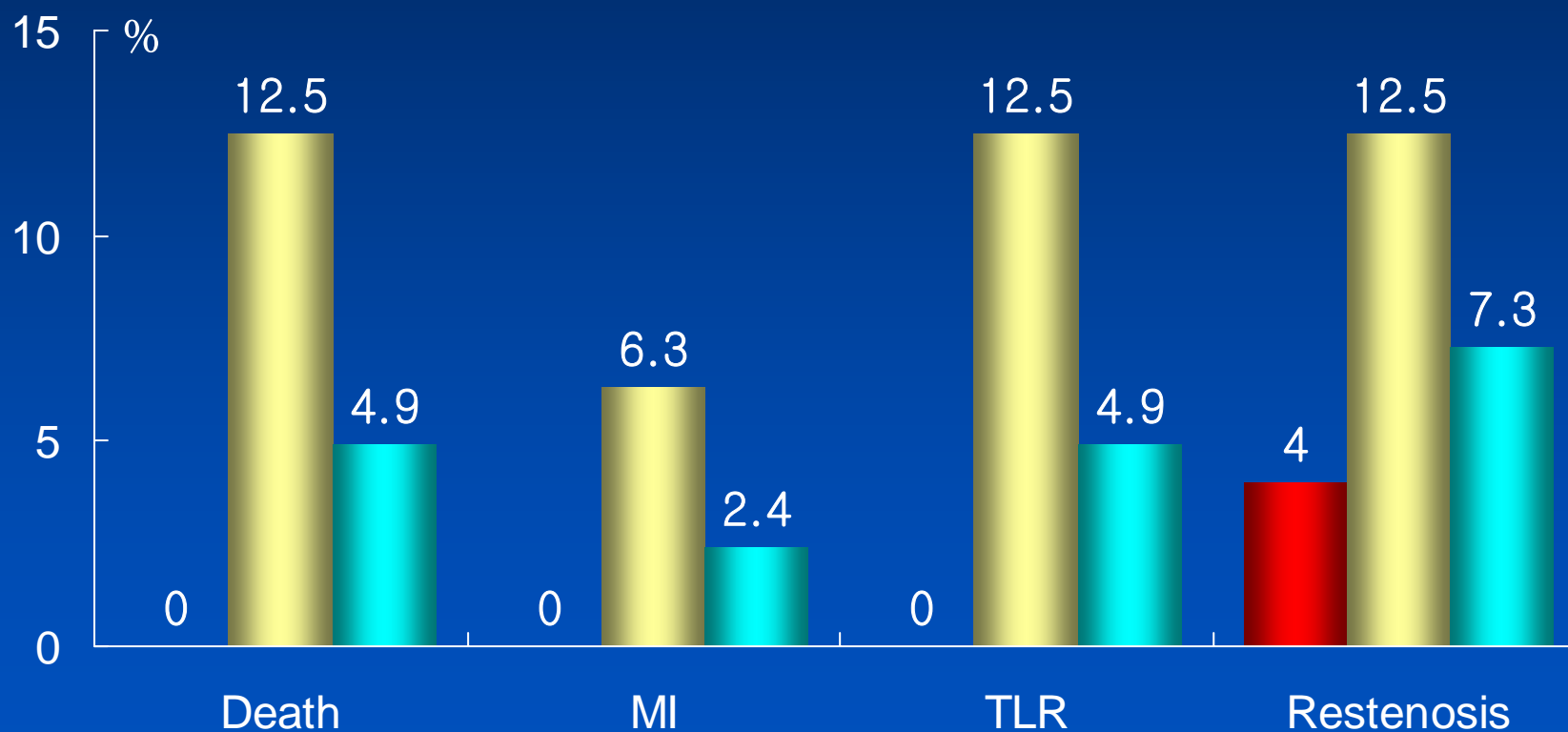


Scheller B. NEJM 2006;355:2119

First Study with SES

1-Year Clinical Event

■ Brazil (n=25) ■ Rotterdam (n=16) ■ Pooled data (n=41)

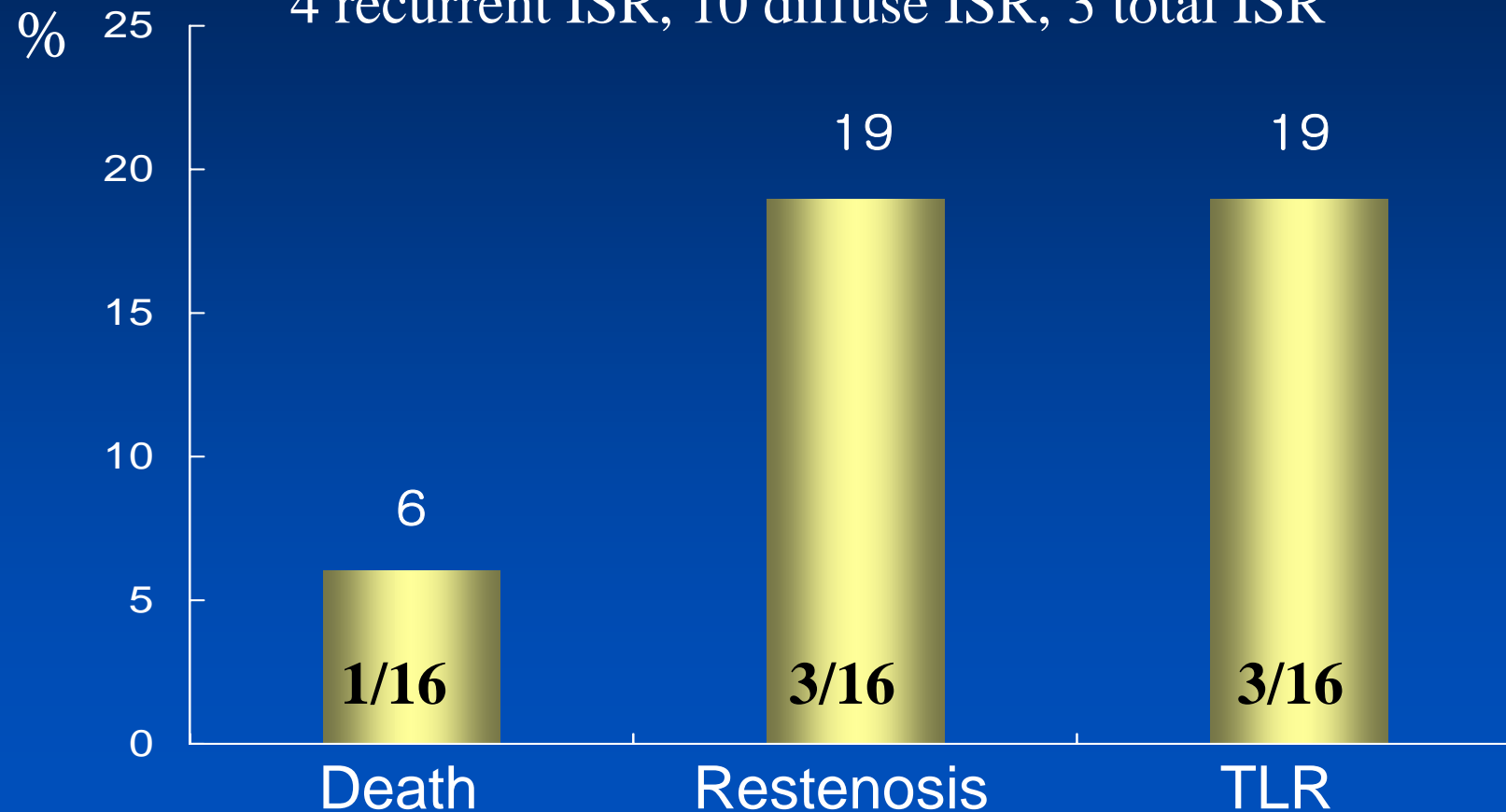


Tanabe K. Circulation 2003;107

SES for Very Complex ISR

9-Month Results in 16 patients

4 recurrent ISR, 10 diffuse ISR, 3 total ISR



Degertekin M. JACC 2003;41:184

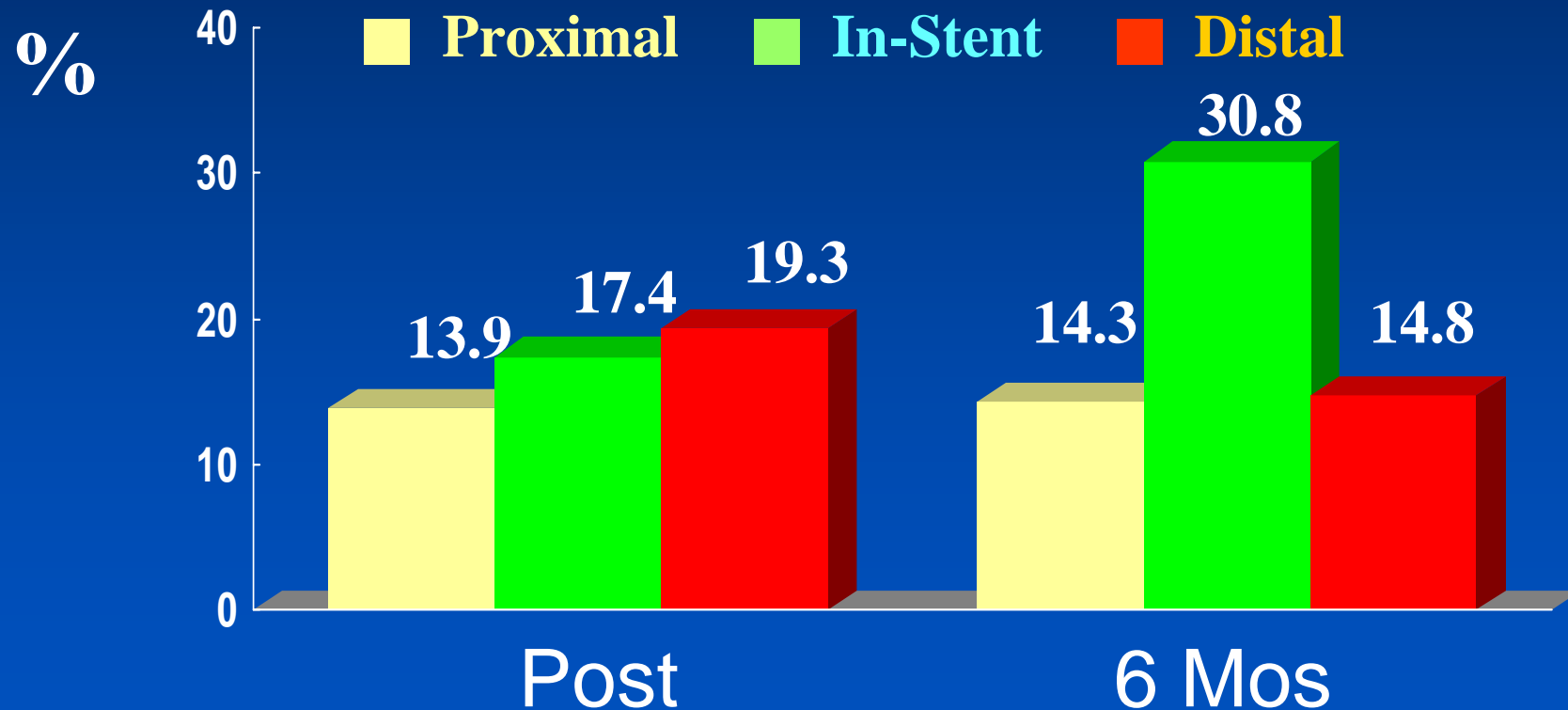


TAXUS III for ISR

2 Clinical Centers (n=28 pts)

Re-Restenosis = 4 / 25 (16%)

Percent diameter stenosis



Tanabe K. Circulation 2003;107



ISR of BMS

DES vs. Brachytherapy

Treatment of IN-stent restenosis with Drug-Eluting stent versus intracoronary bEta-raDiation

INDEED Study

Seung-Jung Park,¹ Seong-Wook Park,¹ Young-Hak Kim,¹
Seung-Whan Lee,¹ Cheol Whan Lee,¹ Myeong-Ki Hong,¹
Jae-Joong Kim,¹ Bon Kwon Koo,² Myoung Mook Lee,²
for the INDEED Study investigators

¹ Asan Medical Center, University of Ulsan College of Medicine

² Seoul National University Hospital

Study Algorithm

From March 2003 to July 2004

Diffuse ISR (n=129)

Randomization (1:1)

Cutting balloon angioplasty

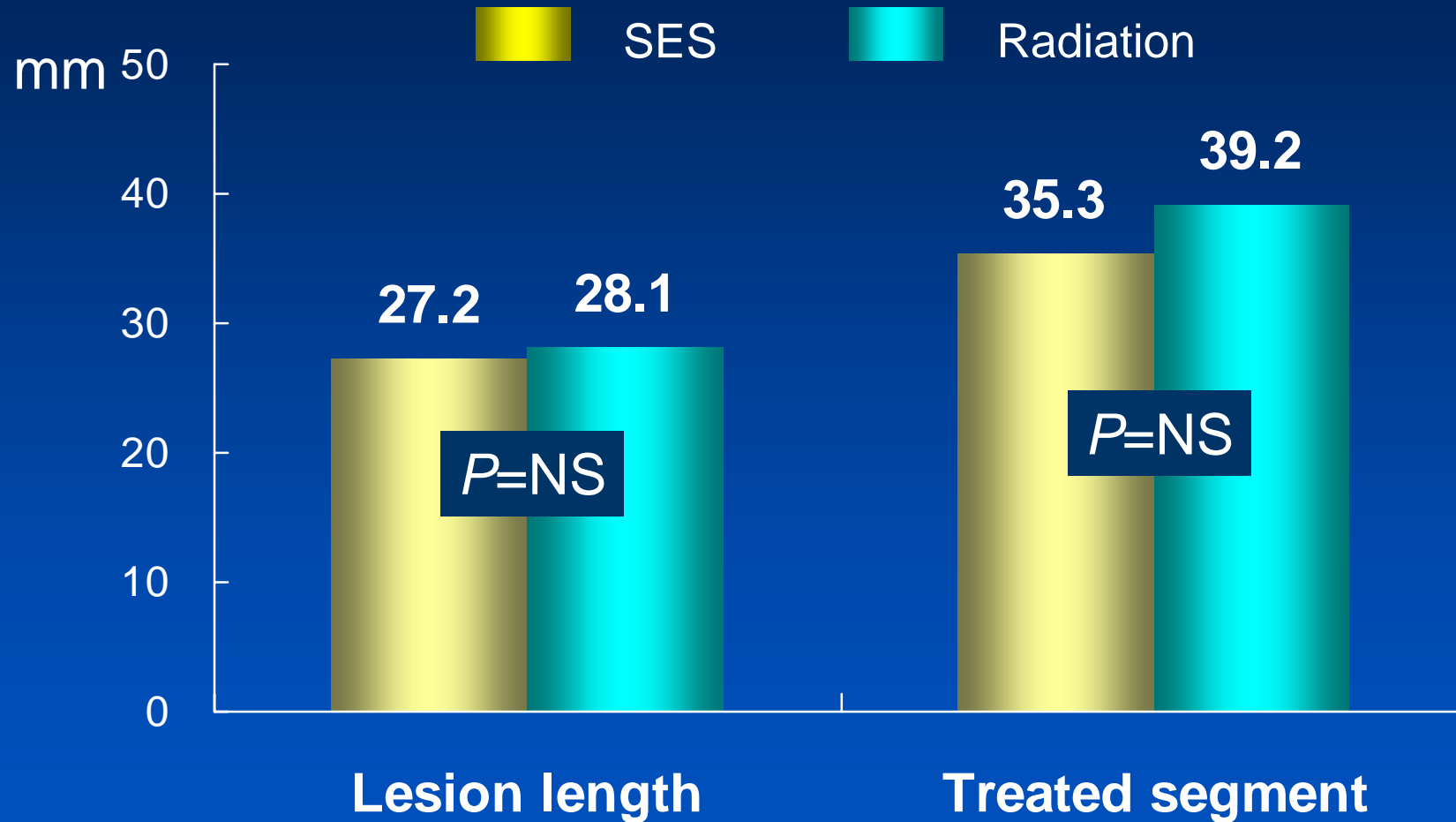
**Sirolimus-Eluting Stent
(n=65, SES group)**

* **Coronary Brachytherapy
(n=64, RT group)**

6-month angiographic and
1-year clinical follow-up

* One patient failed to receive RT due to isotope spillage before RT

Lesion Length & Treated Segment



QCA Analysis, Postprocedure

	SES (n=65)	RT (n=64)	P-value
MLD, mm			
Proximal Edge	2.86±0.49	2.86±0.56	0.959
In-stent	2.49±0.47	2.20±1.47	<0.001
Distal edge	2.58±0.60	2.52±0.57	0.561
In-segment	2.30±0.55	2.10±0.48	0.034
Acute gain			
In-stent	1.72±0.57	1.39±0.49	<0.001
In-segment	1.52±0.59	1.29±0.50	0.017

Values are given as n(%) and mean±SD

In-Hospital Outcomes

	SES (n=65)	RT (n=64)	P-value
Death	0	0	1.0
Myocardial Infarction	1 (1.5)	2 (3.1)	0.619
Q-MI	0	0	
Non Q-MI	1 (1.5)	2 (3.1)	
Stent thrombosis	0	0	1.0
TLR	0	0	1.0

Values are given as n(%)

QCA Analysis, Follow-up

	SES (n=49)	RT (n=54)	P-value
F/U rate	75%	84%	
MLD, mm			
Proximal edge	2.83±0.44	2.62±0.58	0.147
In-stent	2.29±0.63	1.78±0.75	<0.001
Distal edge	2.64±0.61	2.25±0.65	0.002
In-segment	2.17±0.68	1.53±0.70	<0.001

Values are given as n(%) and mean±SD

QCA Analysis, Follow-up

	SES (n=49)	RT (n=54)	P-value
DS, %			
Proximal edge	17.55±10.65	18.32±19.69	0.828
In-stent	20.55±17.60	32.27±27.66	0.011
Distal edge	13.35±12.98	18.35±21.18	0.152
In-segment	25.26±16.75	41.20±26.42	<0.001

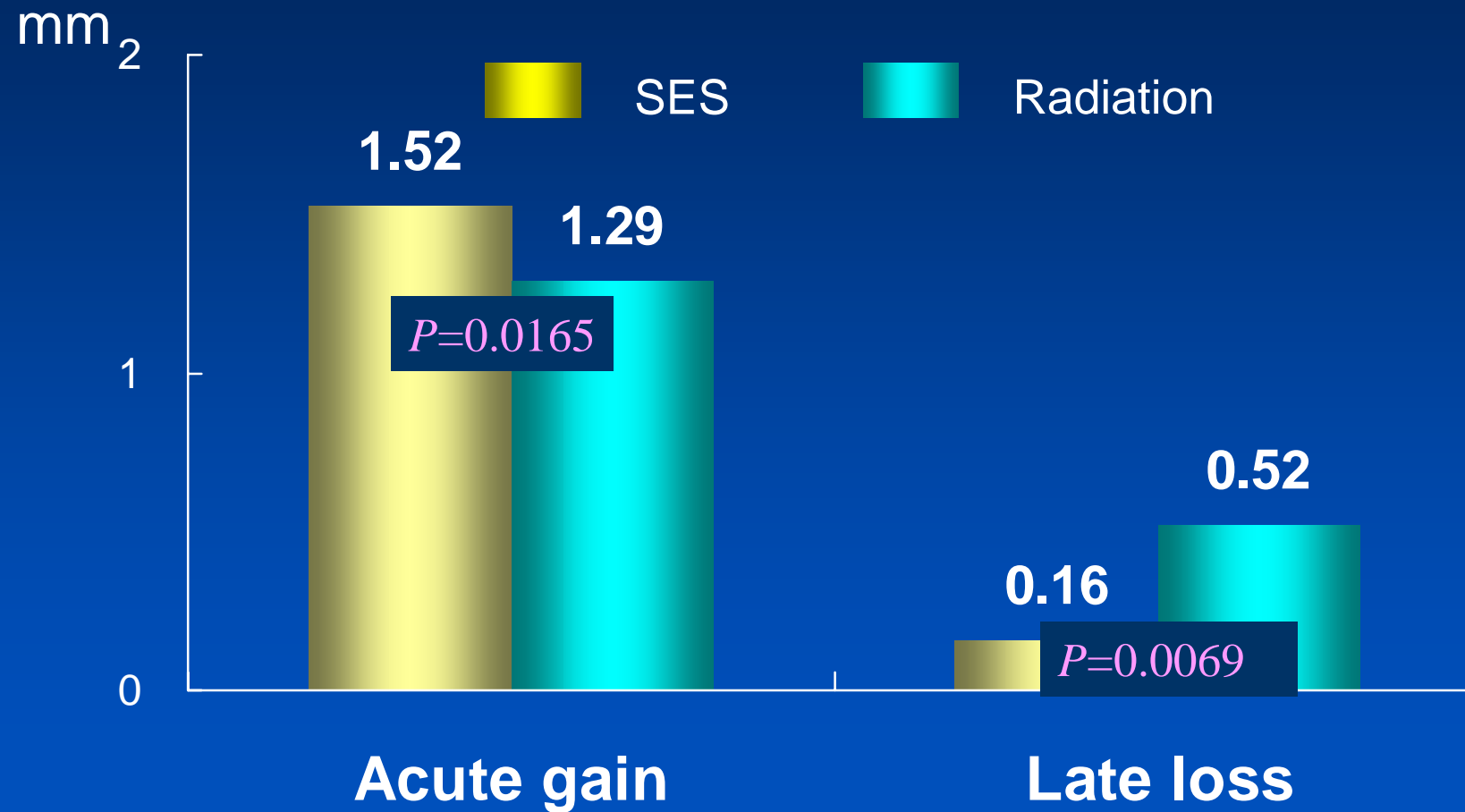
Values are given as n(%) and mean±SD

QCA Analysis, Follow-up

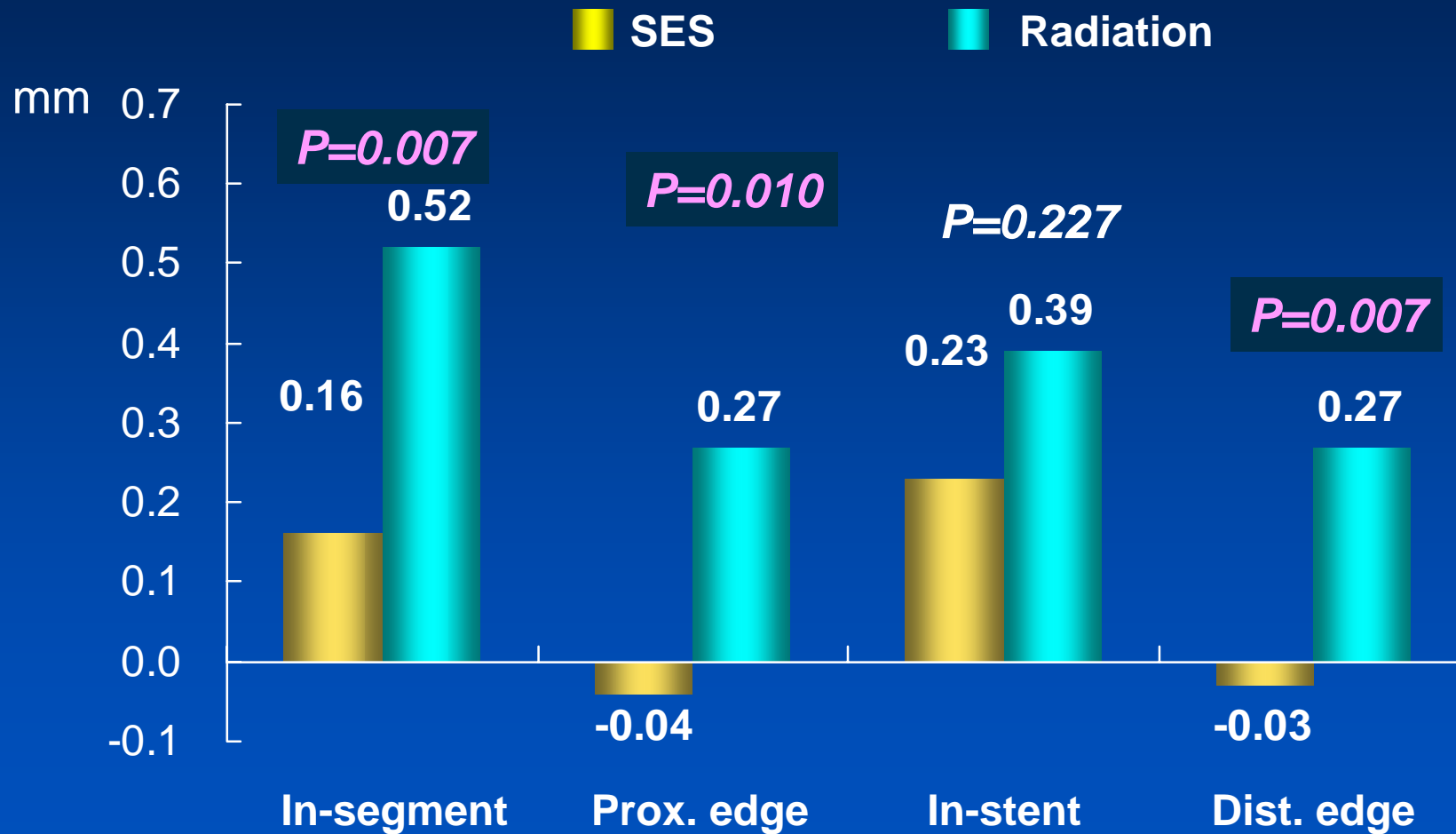
	SES (n=49)	RT (n=54)	P-value
Late loss, mm			
Proximal edge	-0.04±0.34	0.27±0.65	0.010
In-stent	0.23±0.60	0.39±0.72	0.227
Distal edge	-0.03±0.42	0.27±0.64	0.006
In-segment	0.16±0.57	0.52±0.70	0.007
Loss index, In-segment	0.13±0.60	0.43±0.82	0.032
Loss index, In-stent	0.12±0.35	0.30±0.82	0.148

Values are given as n(%) and mean±SD

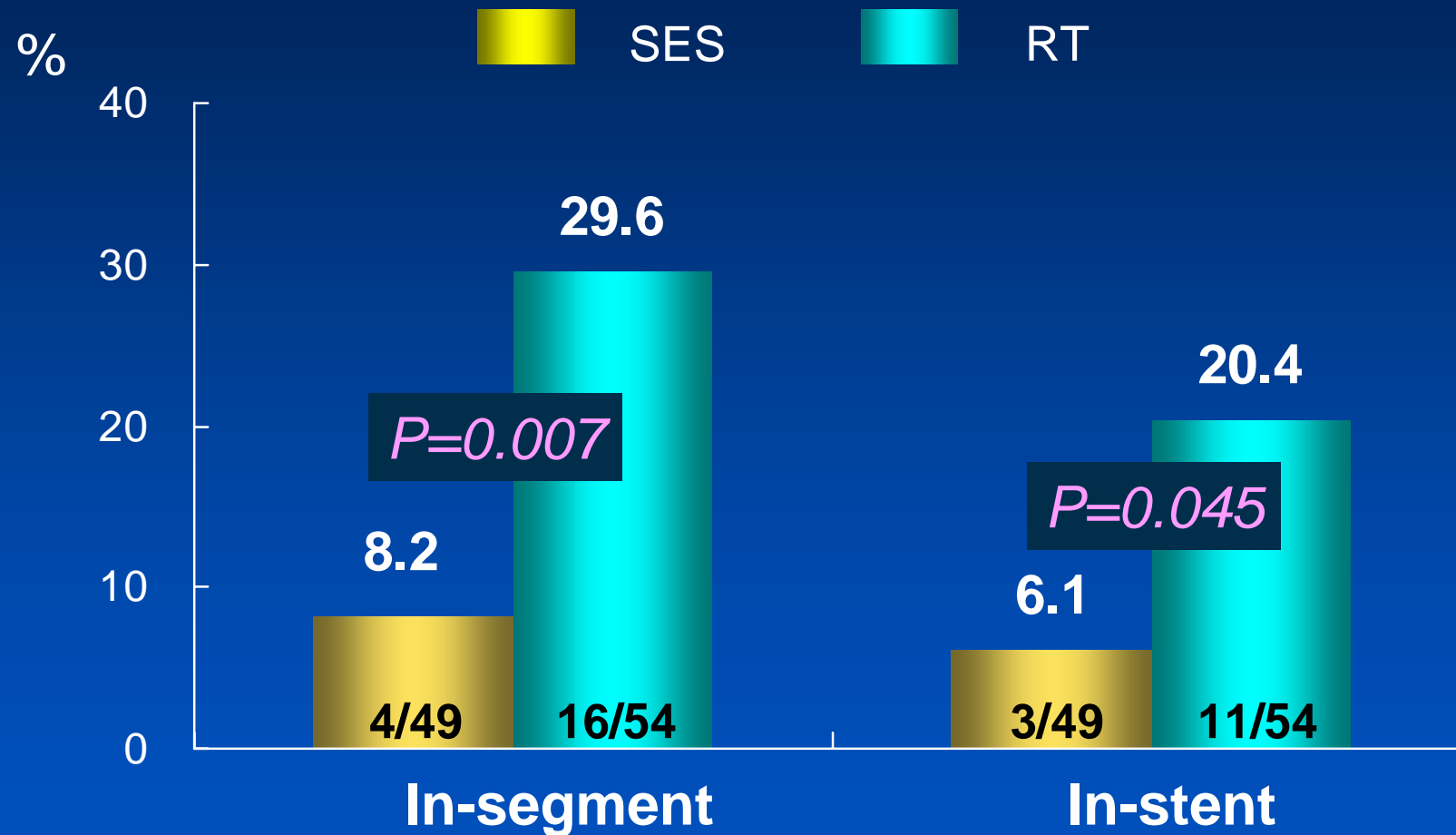
Acute Gain & Late Loss In-segment



Late Loss at 6 Months



Restenosis Rates at 6 Months



Clinical Outcomes at 1 Year

	SES (n=65)	RT (n=64)	P-value
Death	2 (3.1)	0	0.496
Cardiac	1 (1.5)	0	
Non-cardiac	1 (1.5)	0	
MI	1 (1.5) *	0	1.0
Stent thrombosis	1 (1.5) **	0	1.0
TLR	3 (4.6)	12 (18.8)	0.014
Cardiac death, MI, and TLR	5 (7.7)	12 (18.8)	0.073

* Acute STEMI due to the occlusion of non-target vessel

** Late stent thrombosis, 6 months after the index procedure

SES vs. RT

SISR Study

From Feb 2003 to July 2004

Bare metal ISR (n=374)

Randomization (2:1)

Cutting balloon angioplasty

**Sirolimus-Eluting Stent
(n=259, SES group)**

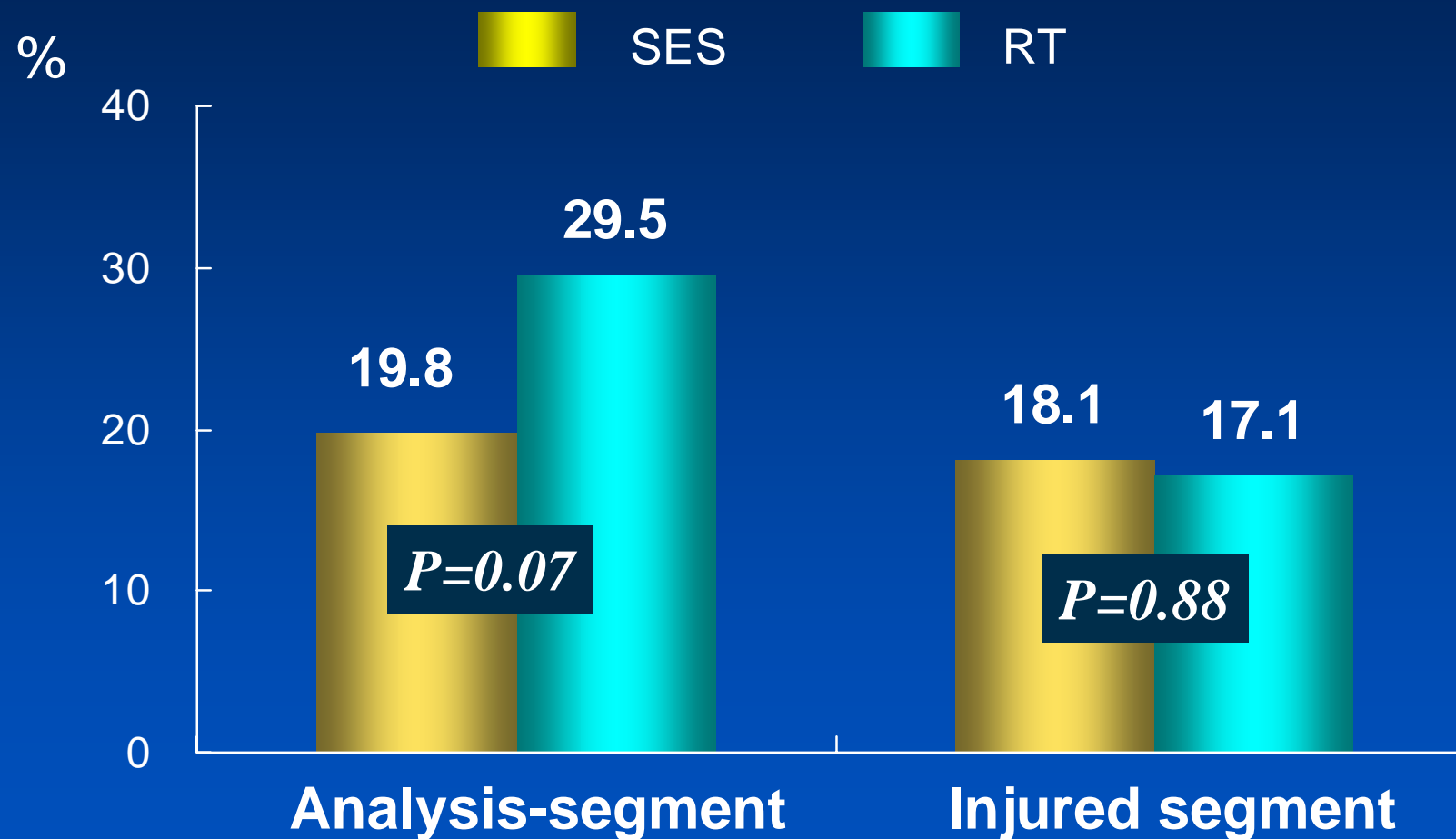
**Coronary Brachytherapy
(n=125, RT group)**

9-month target vessel failure (cardiac death,
myocardial infarction, target vessel revascularization)

Holmes D. JAMA 2006;295:1307-9



Restenosis Rates at 6 Months



Holmes D. JAMA 2006;295:1307-9

9-Month Clinical Outcomes



Holmes D. JAMA 2006;295:1307-9

Six-Month Angiographic and Long-Term Outcomes after Sirolimus-Eluting Stent Implantation for Diffuse In-Stent Restenosis: Comparison with Brachytherapy

Comparison of the 6-month and 2-year outcomes of sirolimus-eluting stent implantation versus β -radiation therapy with $^{188}\text{Re-MAG}_3$ - filled balloon for diffuse ISR in a prospective manner.

SES vs. Brachytherapy

Diffuse ISR (n=362)

Cutting or Rotablation or
simple balloon

Sirolimus-Eluting Stent
(n=120, SES group)

Historical control

*
Coronary Brachytherapy
(n=242, RT group)

Radiation dose of *15, 18 Gy at a
depth of 1.0 mm* into the vessel wall

Six-month Angiography follow-up
2-year Clinical follow-up including death, MI, TLR

QCA Analysis, Baseline

	SES (n=120)	RT (n=242)	P-value
Reference diameter, mm	2.98±0.52	2.91±0.43	0.154
Lesion length, mm	25.1±14.2	24.5±10.4	0.150
MLD, mm	0.74±0.61	0.73±0.40	0.380
DS, %	75.1±13.9	74.9±13.5	0.280

QCA Analysis, Postprocedure

	SES (n=120)	RT (n=242)	P-value
MLD, mm	2.97±0.50	2.64±0.43	<0.001
DS, %	-0.5±14.3	8.32±14.0	<0.001
Acute gain, mm	2.23±0.62	1.91±0.54	<0.001

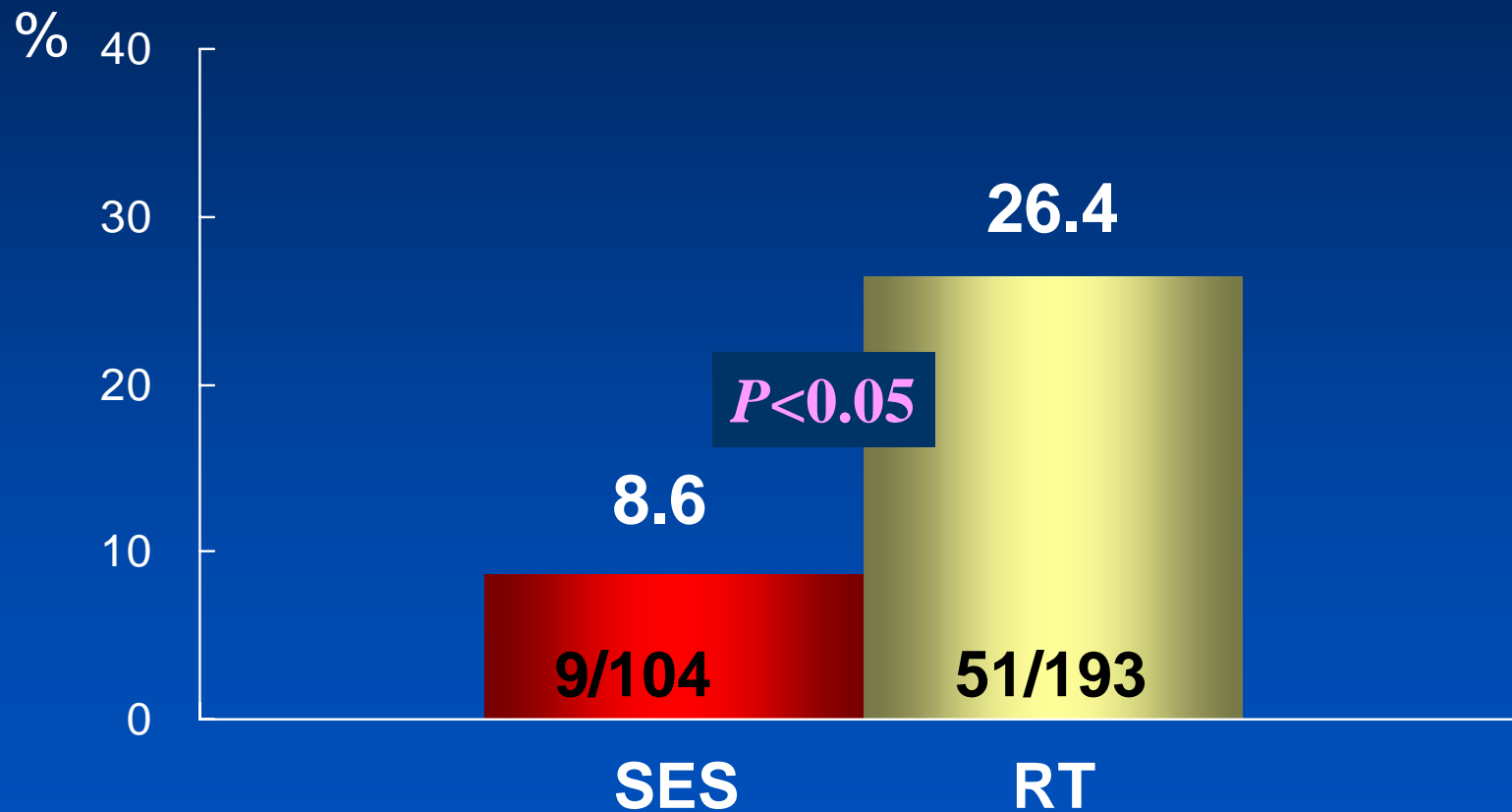
In-Hospital Outcomes

	SES (n=120)	RT (n=242)	<i>P</i> -value
Angiographic success	100 (100)	242 (100)	1.0
Death	0	0	1.0
Myocardial infarction	1 (0.8)	1 (0.4)	1.0
Q-MI	0	0	
Non Q-MI	1 (0.8)	1 (0.4)	
Stent thrombosis	0	0	1.0
TLR	0	0	1.0

QCA Analysis, Follow-up

	SES (n=120)	RT (n=242)	P-value
Angio F/U rate	104/120(86%)	193/242(80%)	
Reference, mm	2.98±0.52	2.91±0.43	0.154
MLD, mm	2.48±0.77	1.97±0.79	<0.001
DS, %	16.34±24.9	31.34±28.64	<0.001
Late loss, mm	0.50±0.55	0.67±0.81	0.042

Restenosis Rate at 6 Months

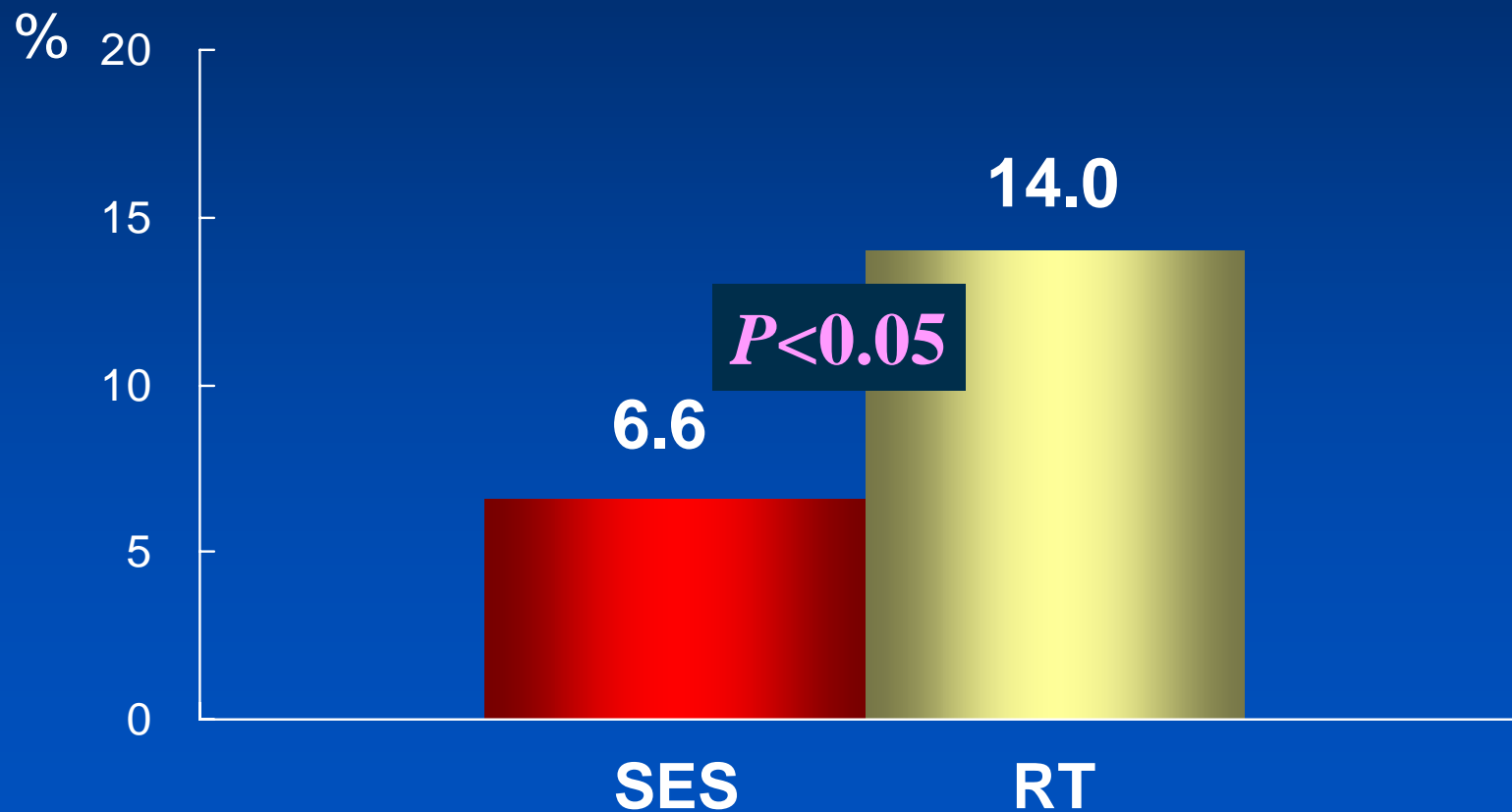


Clinical Outcomes at 2 years

	SES (n=120)	RT (n=242)	P-value
Death	0.8%	0.4%	NS
MI	0.8%	0.4%	NS
TLR	4.6%	13.2%	<0.05
One-year	4.6%	9.9%	<0.05
Two-year	4.6%	13.2%	<0.05

Two-Year Clinical Outcomes

MACE including death, MI, TLR



PES vs. RT

TAXUS V ISR Study

From June 2003 to July 2004

Bare metal ISR (n=396)

Randomization (1:1)

Cutting balloon angioplasty

**Paclitaxel-Eluting Stent
(n=195, PES group)**

**Beta radiation
(n=201, RT group)**

9-month ischemia driven target vessel revascularization

Stone GW. JAMA 2006;295:1253-1263

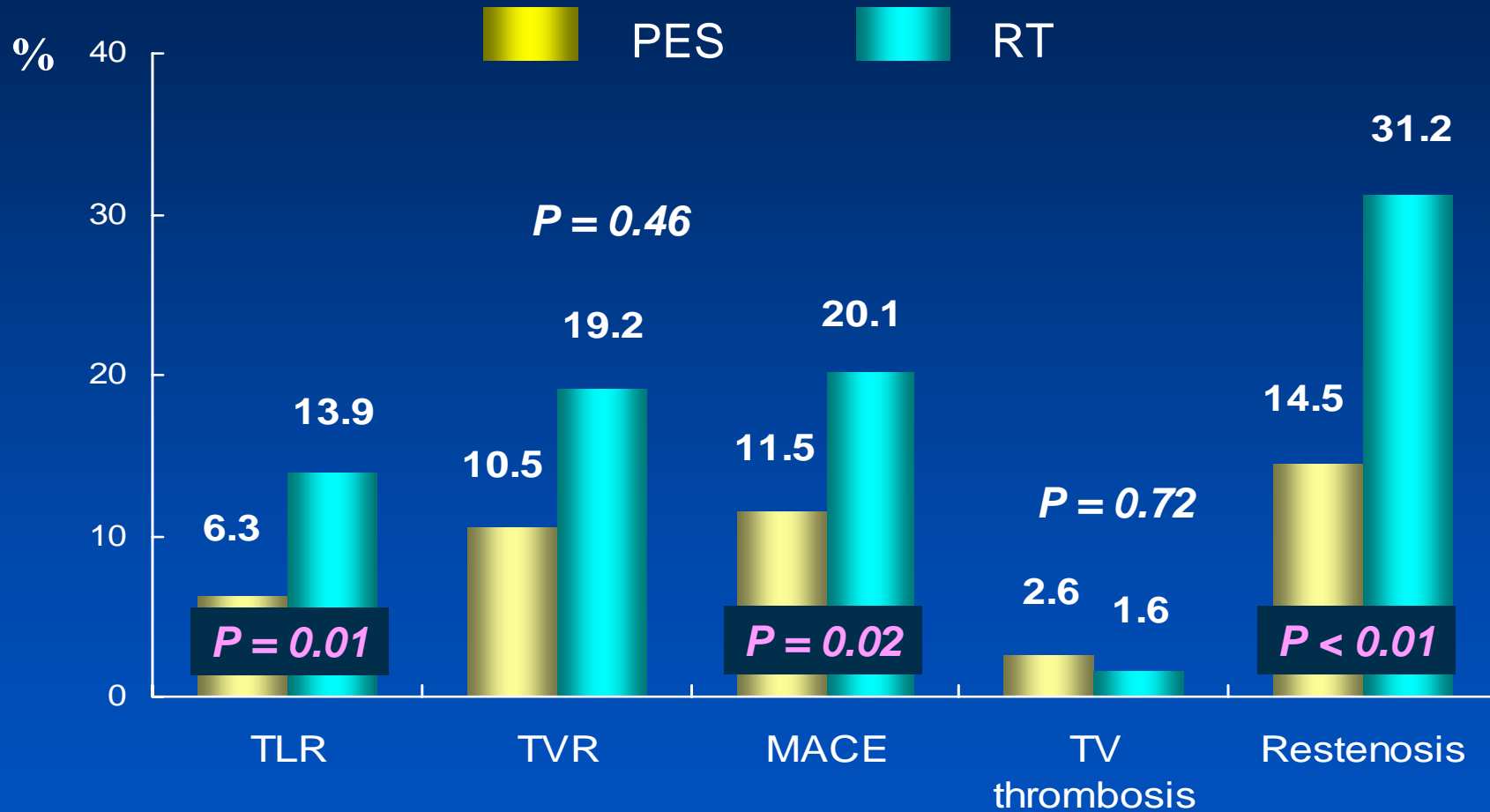


Baseline Characteristics

	TAXUS (n=195)	RT (n=201)	P-value
Reference vessel, mm	2.58	2.61	0.290
Lesion length, mm	15.9	15.0	0.140
LAD lesion (%)	39.2	33.3	0.230
Type C lesion (%)	2.07	2.52	0.910
ISR pattern (%)			
- Focal	18.6	29	0.015
- Diffuse	60.8	47	0.006
- Proliferative	19.1	23.5	0.280
- Total occlusion	1.0	0.5	0.620

Stone GW. JAMA 2006;295:1253-1263

9-Month Clinical Outcomes



Stone GW. JAMA 2006;295:1253-1263

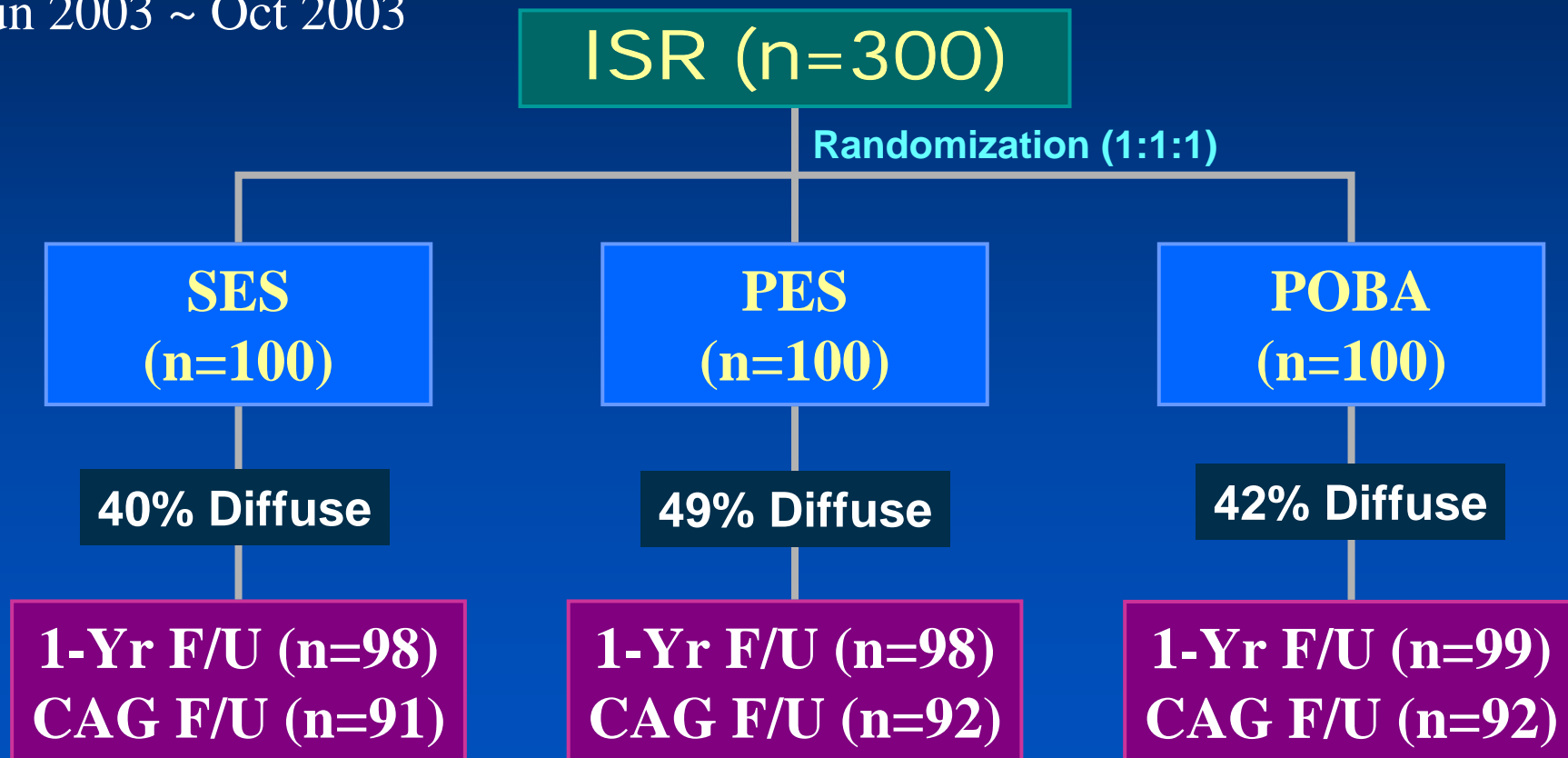
ISR of BMS

SES vs. PES

SES vs PES vs POBA for ISR

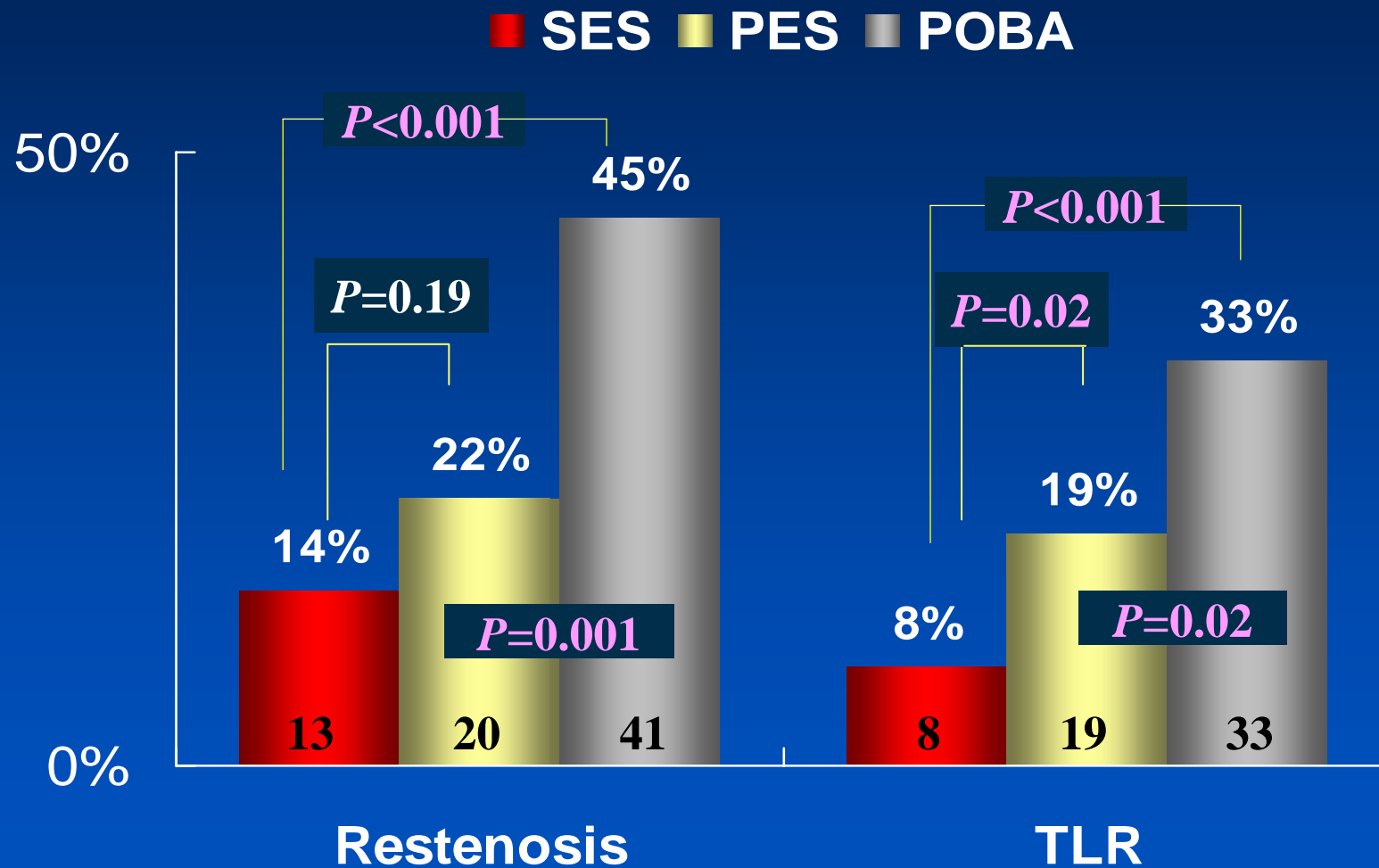
ISAR-DESIRE study

Jun 2003 ~ Oct 2003



Kastrati A. JAMA 2005;293:165

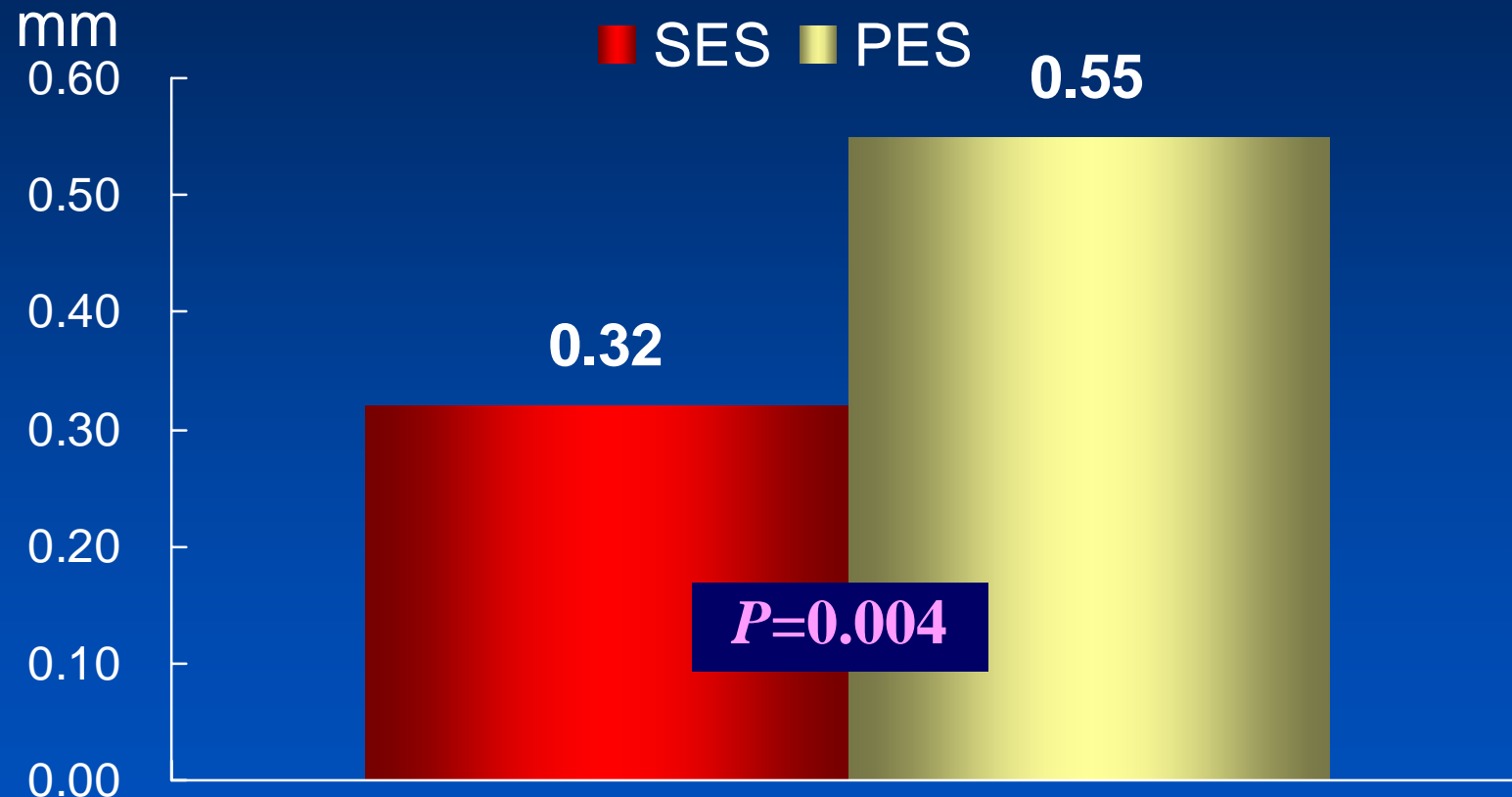
Restenosis and TLR Rates



Kastrati A. JAMA 2005;293:165

SES vs PES

In-segment Late loss of SES and PES

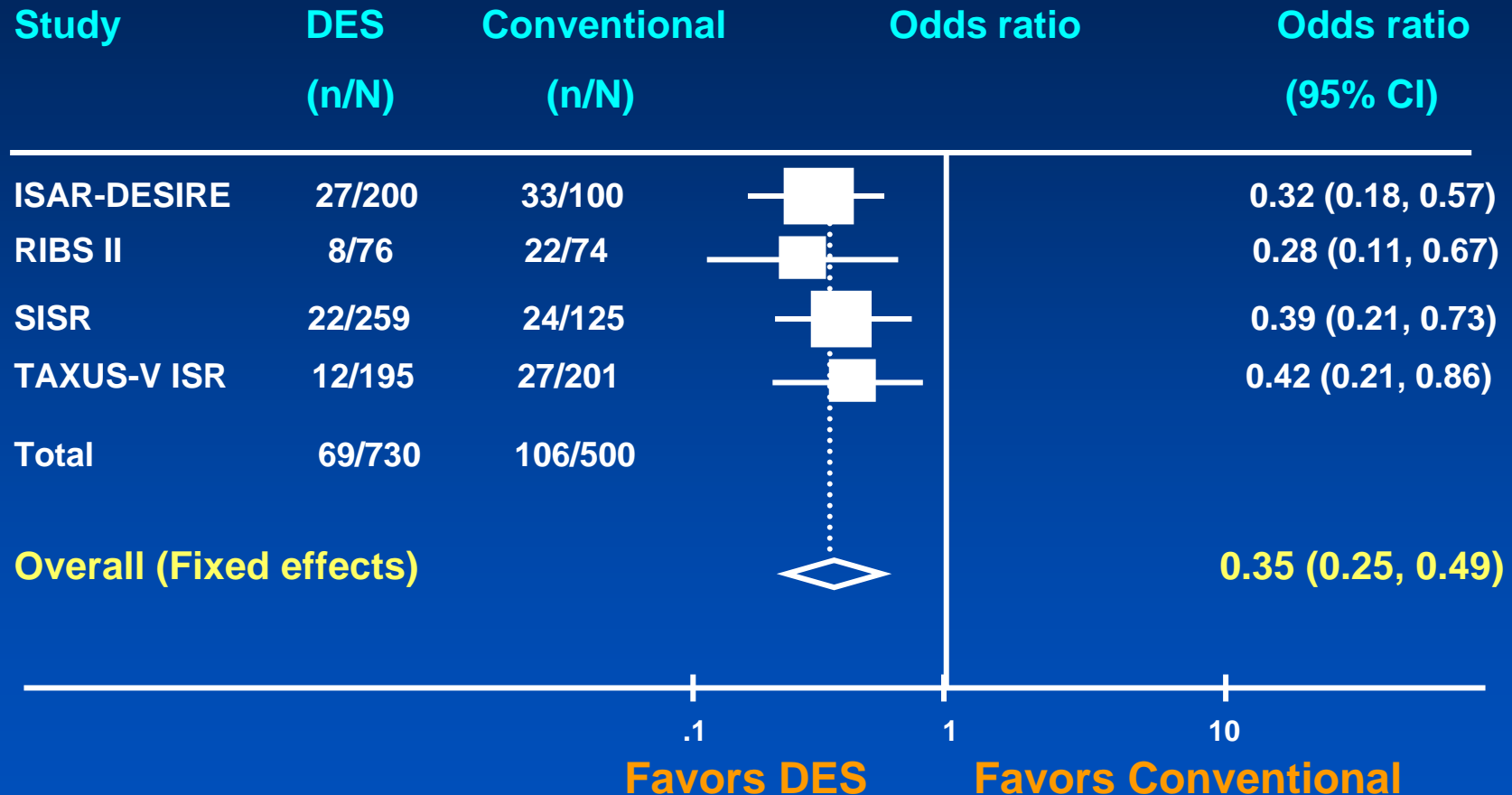


Late loss

Kastrati A. JAMA 2005;293:165

DES for BMS ISR

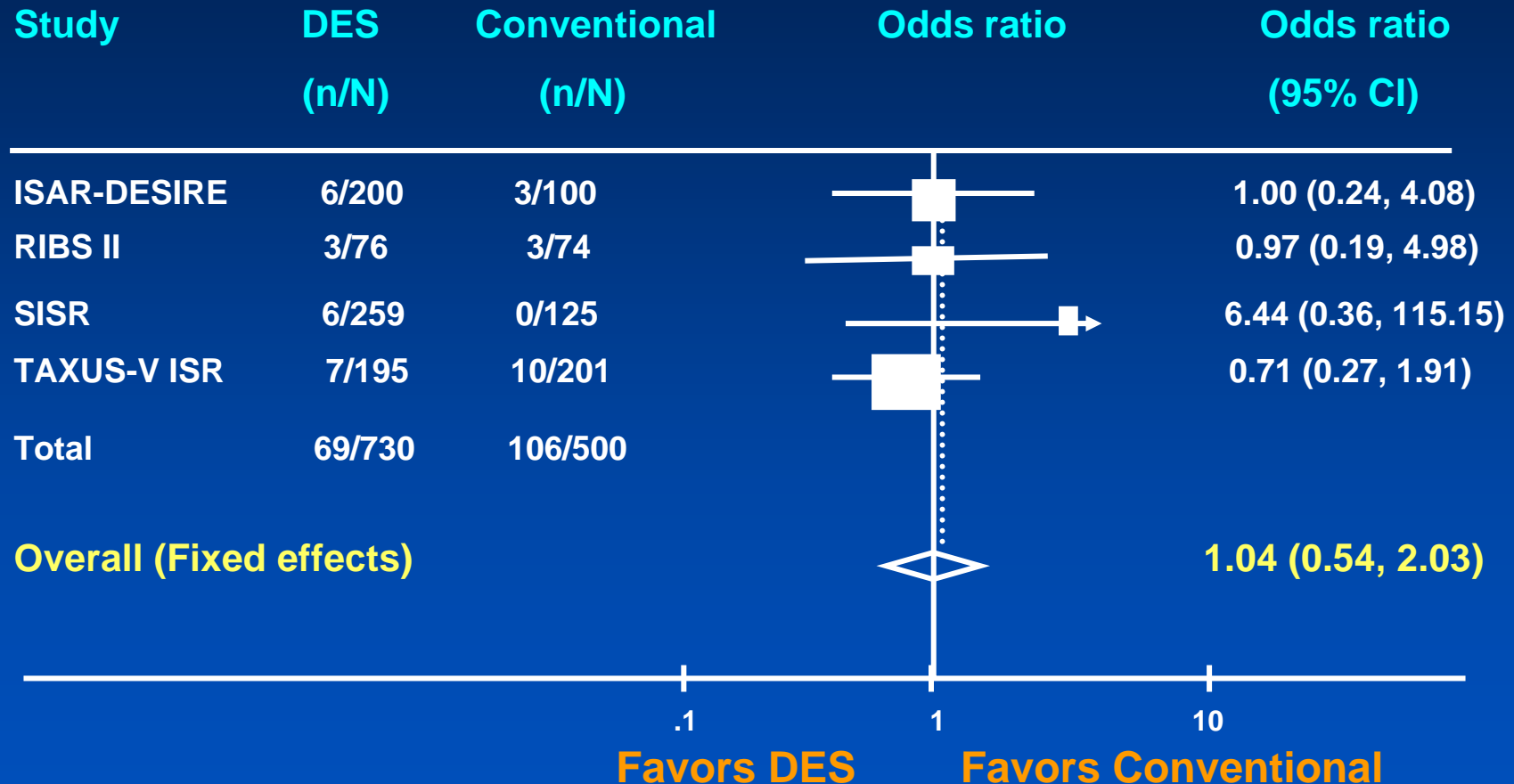
TLR in DES vs. Conventional



Dibra A. JACC 2007;49:616-23

DES for BMS ISR

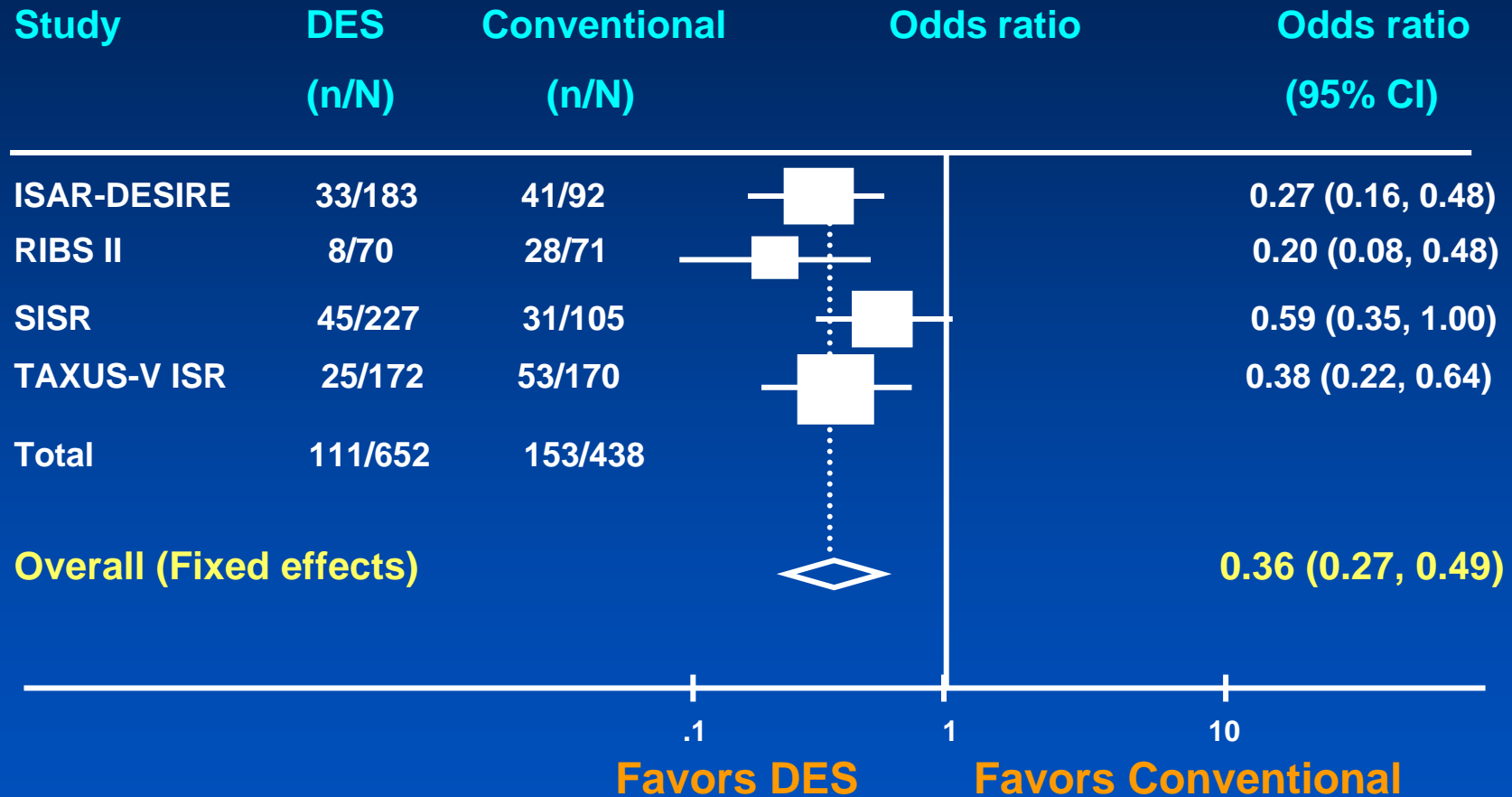
Composite of Death or MI



Dibra A. JACC 2007;49:616-23

DES for BMS ISR

Angiographic Restenosis



Dibra A. JACC 2007;49:616-23

Conclusions

- The superiority of DES for bare-metal ISR is derived from the greater acute gain and similar to or lower late loss than that of brachytherapy.
- Drug-eluting stent has become the first-line therapy for bare-metal ISR replacing the brachytherapy.

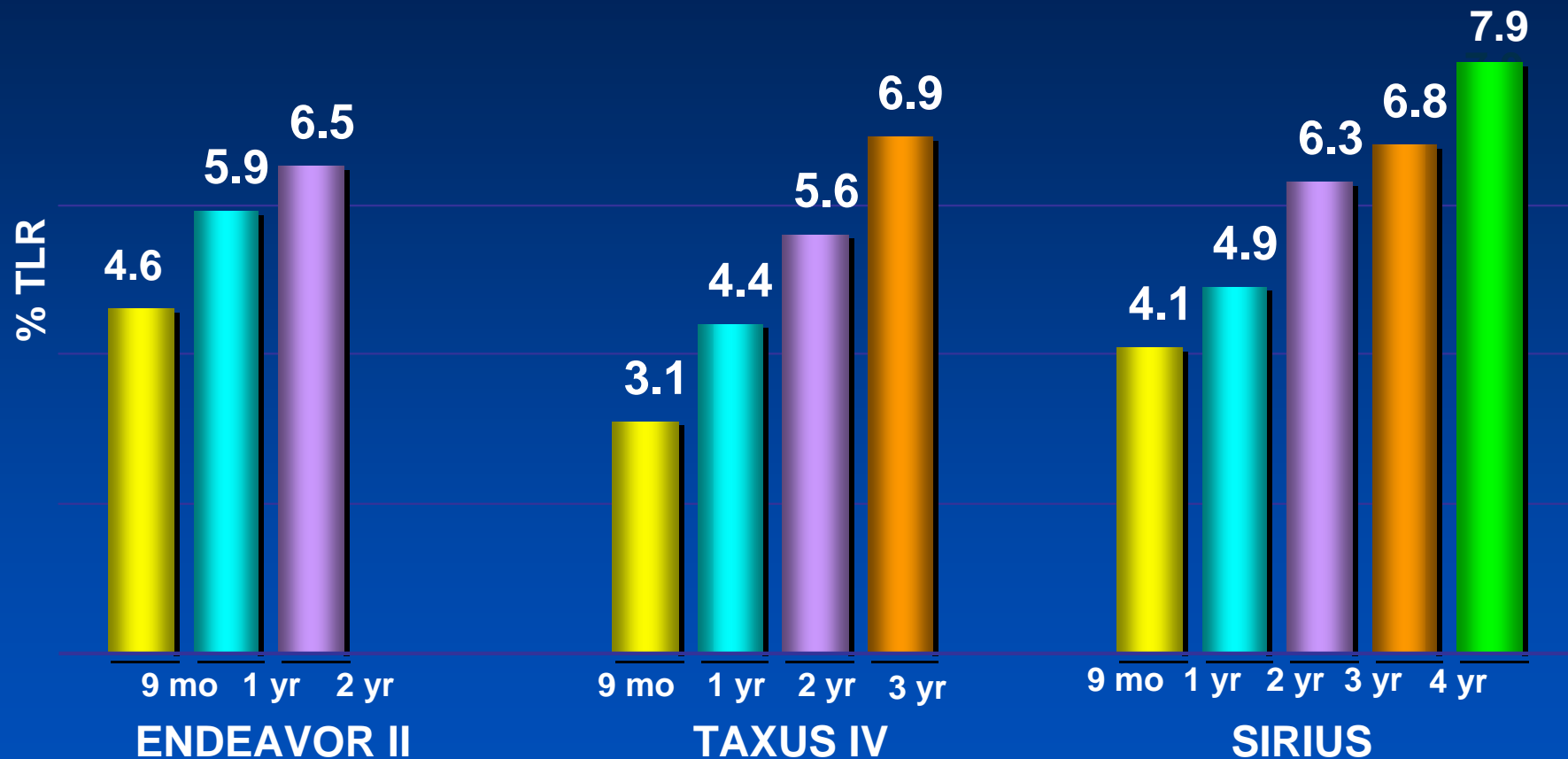
Conclusions

- Among the DESs, the SES may be more effective in reducing the recurrent restenosis and improving clinical outcomes in treatment of bare-metal ISR.
- The superiority of SES over brachytherapy for treatment of bare-metal ISR was maintained to 2 years.

ISR of DES



TLR Rates of DES



1 year Outcomes in the Sirius Trial, Holmes et al, Circulation 2004 1 Year Clinical Results of TAXUS IV, Stone et al, Circulation 2004
2 year Outcomes in the Sirius Trial, Leon, ACC 2004 2 Year Clinical Results of TAXUS IV, Stone, TCT 2004
3 year Outcomes in the Sirius Trial, Leon, TCT 2005 3 Year Clinical Results of TAXUS IV, Stone, ACC 2005
4 year Outcomes in the Sirius Trial, Leon, TCT 2006



Possible Causes of DES ISR

- Stent under-expansion
- Asymmetric strut distribution
- Stent fracture
- Polymer disruption
- Peri-stent vessel wall injury
- Drug failure or resistance
- Polymer hypersensitivity
- Drug hypersensitivity

Morphology Patterns of ISR

SIRIUS

	Cypher (n=31)	Control (n=128)	P-value
I - focal	87.0% (27)	42.2% (54)	<0.001
II/III – diffuse or proliferative	6.5% (2)	50.0% (64)	<0.001
IV - total occlusion	6.5% (2)	7.8% (10)	0.895

Moses JW. NEJM 2003;349:1315-23

Patterns of Cypher Restenosis

SIRIUS

	Cypher (n=31)	BMS (n=128)	P-value
Focal	26 (84%)	55 (43%)	<0.001
Diffuse	1 (3.2%)	46 (35.9%)	<0.001
Proliferative	2 (6.5%)	17 (13.3%)	0.372
Total	2 (6.5%)	10 (7.8%)	1.00
Length of ISR, mm	9.1	14.8	<0.001
Aneurysm	2 (0.6%)	4 (1.1%)	0.686

Popma JJ. Circulation 2004;110:3773

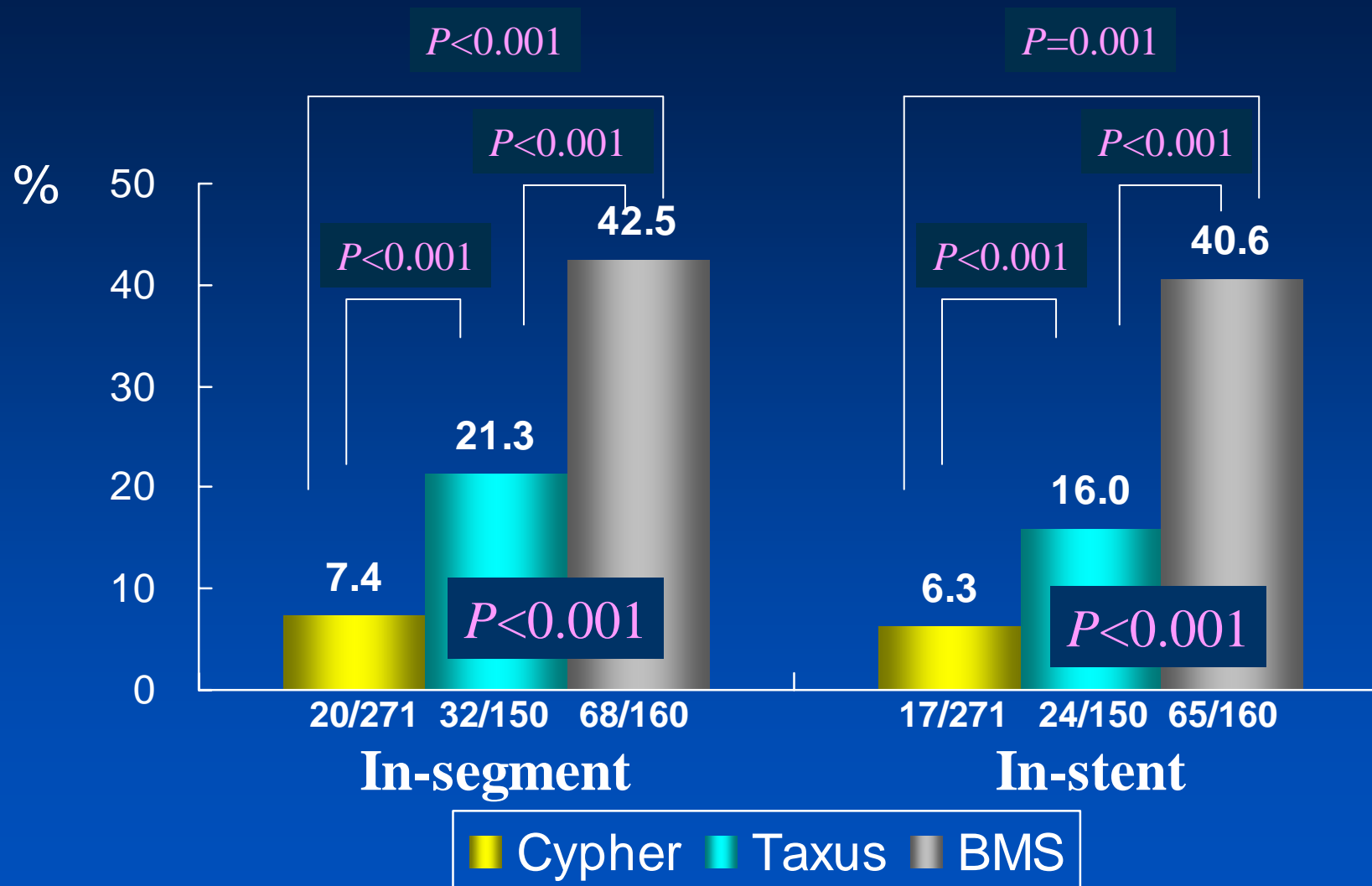
Patterns of Taxus Restenosis

TAXUS-IV

	Taxus (n=16)	BMS (n=65)	P-value
Focal	63 %	31 %	0.04
Diffuse	19 %	58 %	<0.001
Proliferative	6 %	8 %	0.11
Total	13 %	3 %	1.00
Length of ISR, mm	9.8	15.3	0.01

Stone GW. NEJM 2004;350:221

Restenosis Rate



Kim YH. 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. Catheter Cardiovasc Interv 2006;67:181-7

Predictors of Restenosis

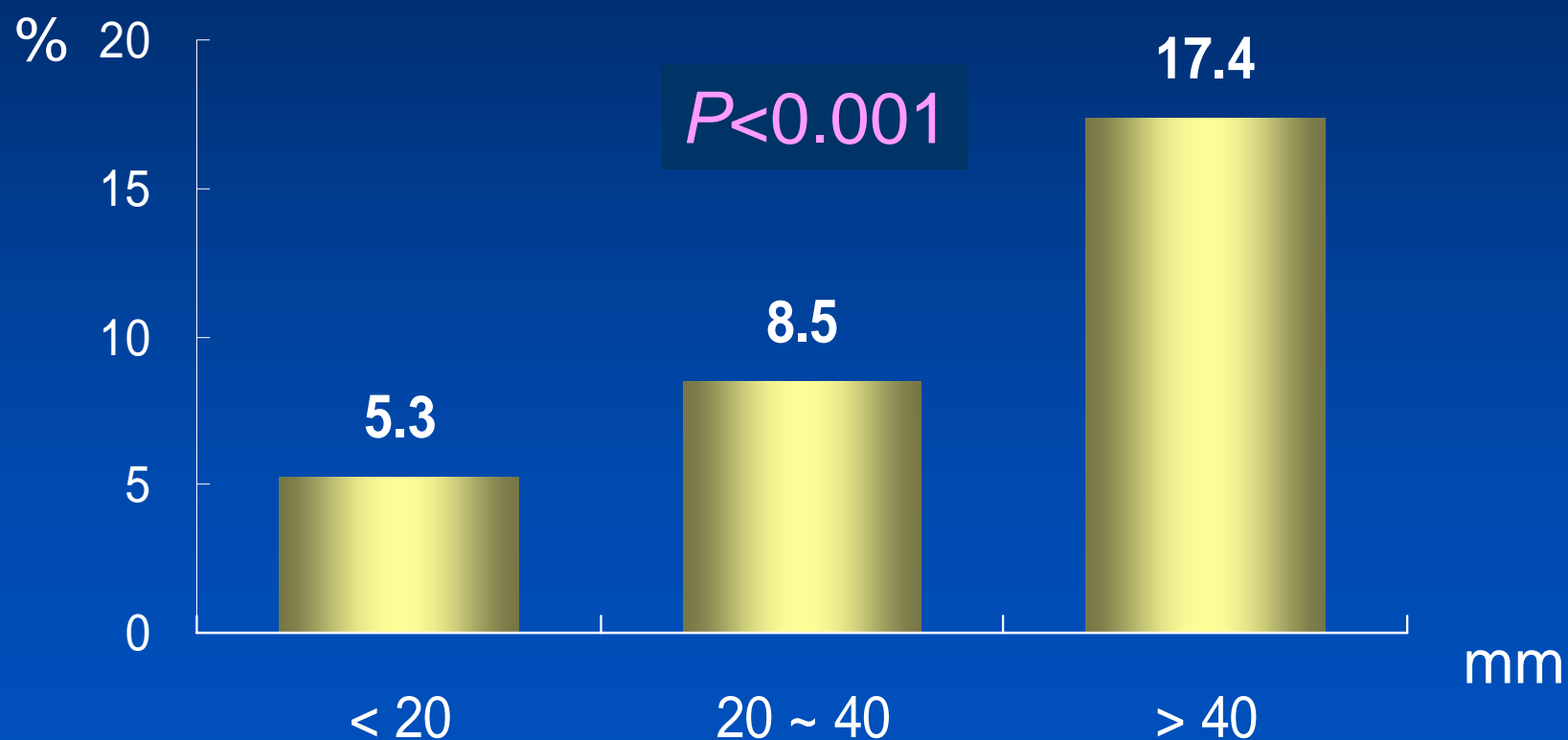
Cypher or Taxus subgroup

		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. Catheter Cardiovasc Interv 2006;67:181-7

Restenosis Rate According to Lesion Length

From Asan Medical Center



Lee CW. Am J Cardiol 2006;97:506-11

Drug-Eluting Stent Restenosis

The Pattern Predicts the Outcome

Cosgrave J, et al.
JACC 2006;47:2399

Patterns of DES ISR

- Of total 250 lesions in 203 patients (66.4% with SES, 33.6% with PES)
 - Focal ($\leq 10\text{mm}$): 65.2%
 - Diffuse ($> 10\text{mm}$): 24.3%
 - Proliferative : 2.4%
 - Obstructive: 8%
- Pattern of restenosis associated with occurrence of ISR (OR 5.1, 95% CI 1.1~23, $P=0.03$) and TLR (OR 3.6, 95% CI 1.2~10.9, $P=0.02$)

Cosgrave J. JACC 2006;47:2399-404



Patterns of DES ISR

	Focal (n=132)	Nonfocal (n=71)	P-value
Risk factors			
Family history	43.8%	46.4%	0.76
Hypertension	63.4%	67.6%	0.64
Hypercholesterolemia	71.8%	71.4%	1.0
Current smoker	16.2%	11.6%	0.53
Diabetes	25.4%	47.9%	0.002
Details of DES			
SES	69.9%	59.8%	0.122
PES	30.1%	40.2%	0.122
Stent diameter	2.9±0.30	2.9±0.34	0.99
Stent length	29.56±12.6	35.74±18.25	0.002

Cosgrave J. JACC 2006;47:2399-404



Treatment DES ISR

	Focal (n=132)	Nonfocal (n=71)	P-value
Treatment			
Repeat DES implantation	57.1%	69%	0.043
POBA	30.1%	40.2%	0.043
Max balloon diameter (mm)	3.15±0.42	3.01±0.43	0.012
Max inflation pressure (mmHg)	16.35±4.7	16.21±3.9	0.8
IVUS	30.7%	34.5%	0.57

Cosgrave J. JACC 2006;47:2399-404



Clinical Events

Patterns of DES ISR

	Focal (n=132)	Nonfocal (n=71)	<i>P</i> -value
Procedural/ in-hospital death	0	0	-
Procedural/ in-hospital CABG	0	0	-
Periprocedural MI	1.5% (2)	0	0.54
Clinical follow-up (days)	447±218	447±214	0.99
MACE	18.9% (25)	29.6% (21)	0.11
Cardiac death	3% (4)	4.2% (3)	0.69
MI at follow-up	0	2.8% (2)	0.12
TVR (per patient)	15.9% (21)	22.5% (16)	0.25
TLR (per patient)	11.4% (15)	22.5% (16)	0.04
TVR (per lesion)	14.7% (24)	23.0% (20)	0.12
TLR (per lesion)	9.8% (16)	23.0% (20)	0.007

Cosgrave J. JACC 2006;47:2399-404



Treatment of DES failure

Very little information about the results of ...

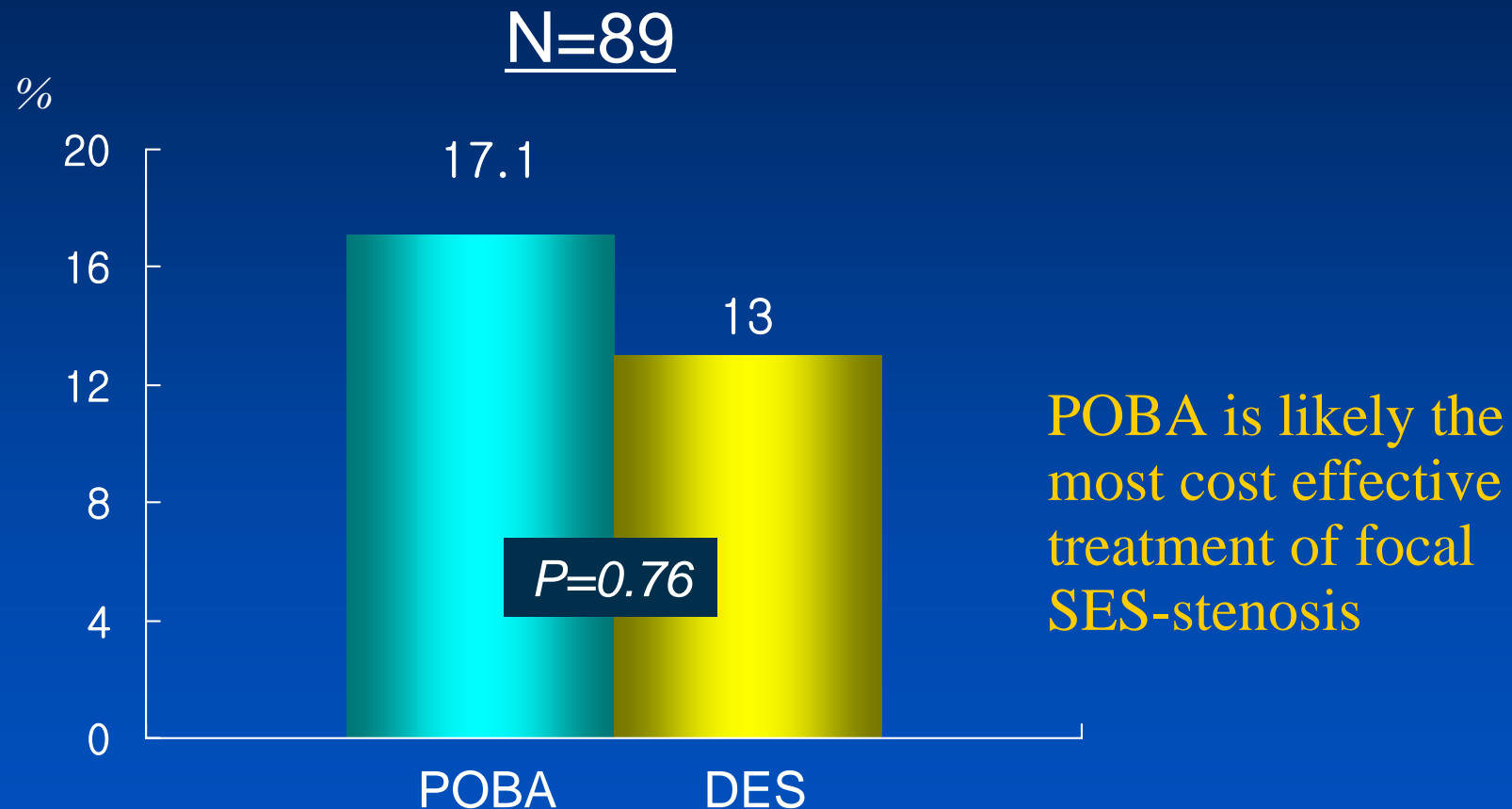
0 Published data on randomized trials

0 Registry data including more than 100 patients

- Balloon angioplasty
- Cutting balloon angioplasty
- Repeat stenting
- Debulking
- Intracoronary brachytherapy
- Drug eluting stent

Focal SES Restenosis

Target lesion revascularization



Melzi G. Am J Cardiol 2005;96(suppl 7A): 188H

Brachytherapy for DES Restenosis

RESCUE registry

6-month clinical follow-up

All MACE	2 (4.0%)
Death	0 (0)
Q-wave MI	0 (0)
Non Q-wave MI	2 (4.0%)
TVR	2 (4.0%)
TLR	2 (4.0%)
Subacute thrombosis	0 (0)
Late thrombosis	0 (0)

RT as adjunct therapy to PCI for ISR of a DES is safe.

Torguson R. Circulation 2005;112 (Suppl 17): II-519



Repeated DES for DES ISR

Variable	Same DES (n=107)	Different DES (n=94)	P-value
Pattern of Restenosis			
Focal	72.9% (78)	50% (47)	0.001
Nonfocal	27.1% (29)	50% (47)	0.001
Diffuse	19.6% (21)	34% (32)	
Proliferative	5.6% (6)	0	
Occlusive	1.9% (2)	16% (15)	
Treatment of DES restenosis			
SES implantation	72% (77)	48.9% (46)	-
PES implantation	28% (30)	51.1% (48)	-
DCA	3.7% (4)	7.4% (7)	0.35
IVUS	25.2% (27)	42.6% (40)	0.01
Cutting balloon	6.5% (7)	2.1% (2)	0.18
Stent length (mm)	22.17±12.3	25.8±12.9	0.04

Cosgrave J. Am Heart J 2007;153:354-9



Repeated DES for DES ISR

Clinical Events

Variable	Same DES (n=96)	Different DES (n=78)	P-value
Procedural MI	2.1% (2)	1.3% (1)	1.0
Acute thrombosis	0	0	-
Follow-up			
Total death	3.1% (3)	0	0.25
Cardiac death	3.1% (3)	0	0.25
MI	1% (1)	0	1.0
TLR (per patient)	16.7% (16)	16.7% (13)	1.0
TVR (per patient)	20.8% (20)	17.9% (14)	0.7
Major adverse cardiac events	26% (25)	17.9% (14)	0.27
CABG	1% (1)	0	1.0
Angiographic follow-up	68.1% (64)	67.5% (52)	1.0

Cosgrave J. Am Heart J 2007;153:354-9



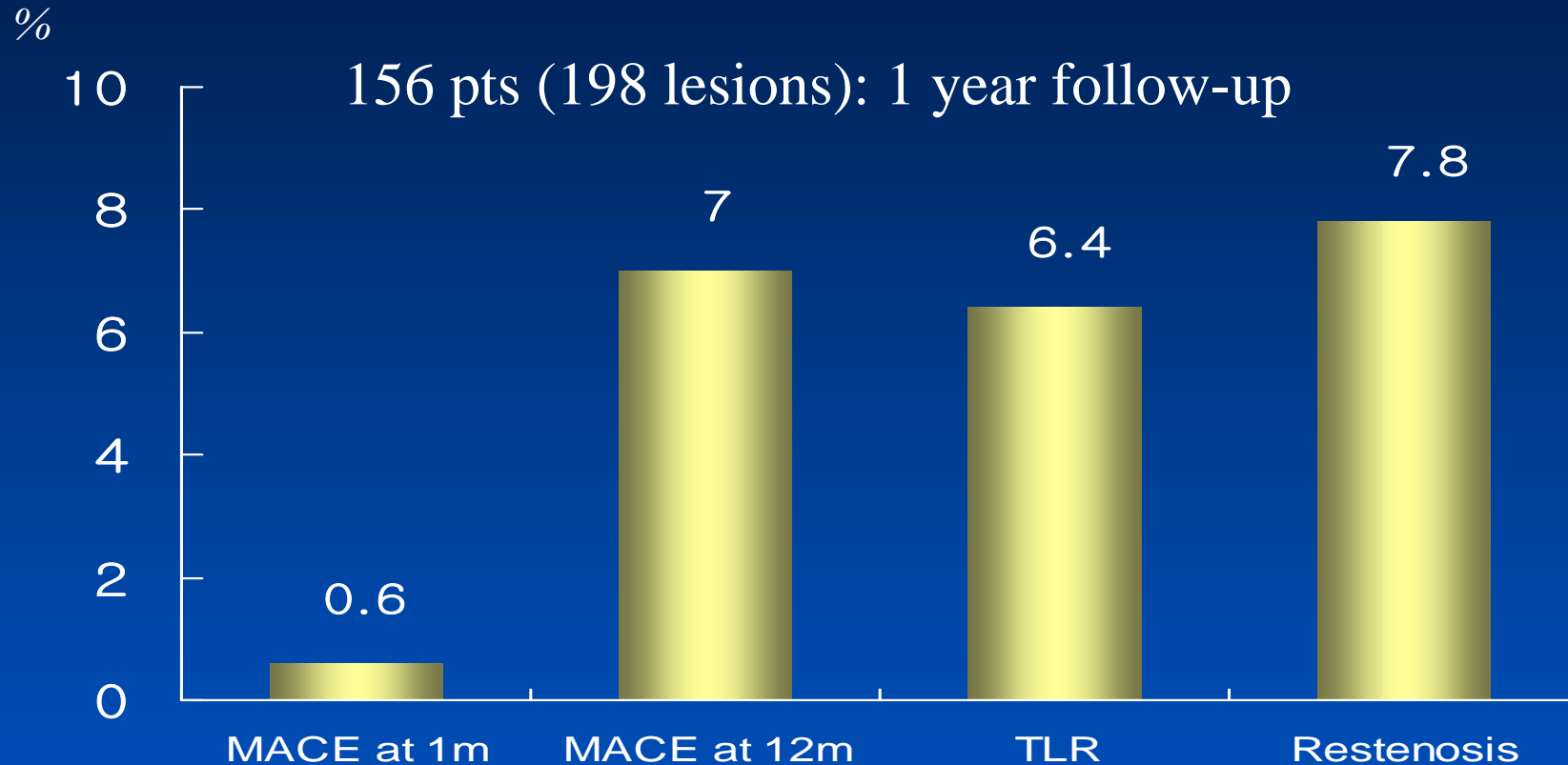
Repeated DES for DES ISR

Variable	Same DES (n=107)	Different DES (n=94)	P-value
Focal DES restenosis	78	47	
Diabetes mellitus	26.9% (21)	17% (8)	0.28
Angio follow-up lesions	71.4% (55)	78.3% (36)	0.53
TLR (per lesion)	12.8% (20)	8.5% (4)	0.57
TVR (per lesion)	19.2% (15)	12.8% (6)	0.46
Restenosis	20% (11)	13.9% (5)	0.58
Nonfocal DES restenosis	29	47	
Diabetes mellitus	58.6% (17)	31.9% (15)	0.03
Angio follow-up lesions	60.7% (17)	63.8% (30)	0.81
TLR (per lesion)	24.1% (7)	23.4% (11)	1.0
TVR (per lesion)	24.1% (7)	23.4% (11)	1.0
Restenosis	47.1% (98)	40% (120)	0.76

Cosgrave J. Am Heart J 2007;153:354-9

SES for SES Restenosis

Asian Multicenter Registry



The use of SES in SES-ISR was safe with low complication and low incidence of restenosis.

Nakamura S. Circulation 2005;112(Suppl 17A): II-736



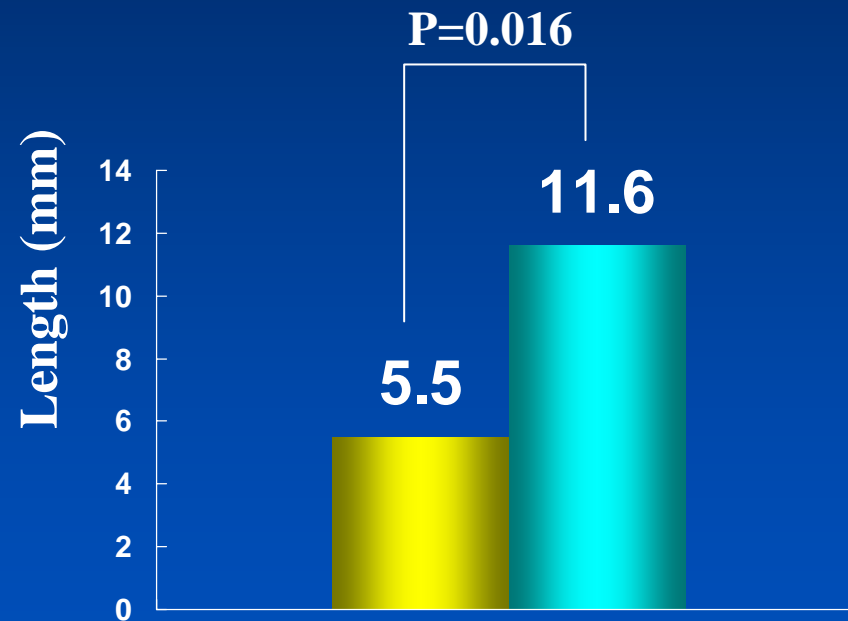
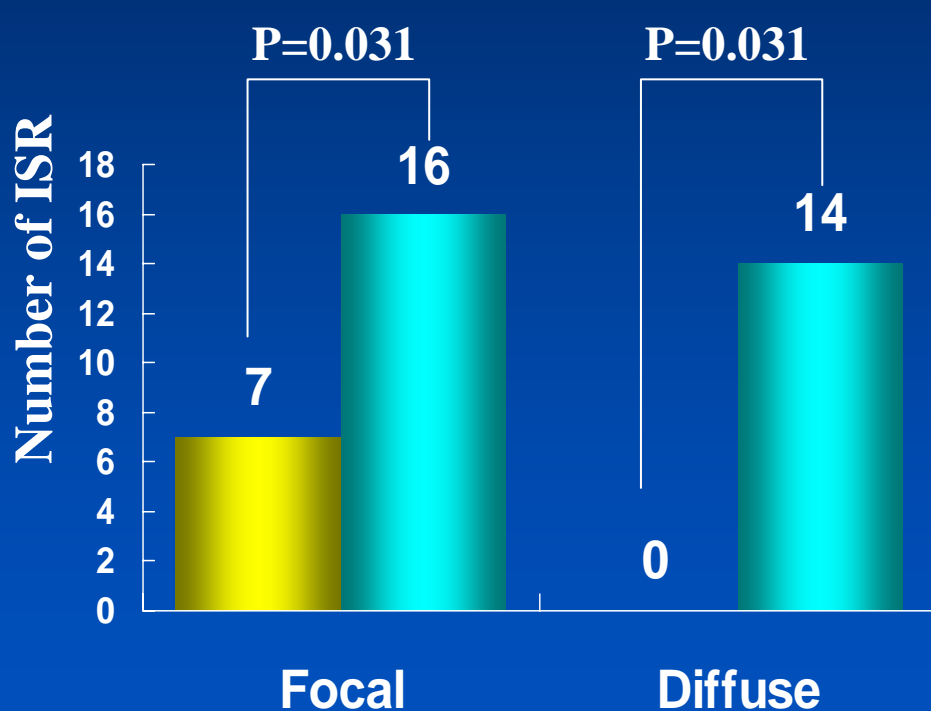
Angiographic Restenosis

No. of ISR

Length of ISR

 SES

 PES



Kim YH. Circulation 2006;114:2148-53

TLR for SES Restenosis in SIRIUS

27 TLRs (5%) from 533 patients

Bypass surgery	4 (14.8%)
Repeat PCI	23 (85.2%)
BMS	20 (87.0%)
Balloon	2 (8.7%)
Brachytherapy	1 (4.3%)
Recurrent TLR for 2 years	6 (26%)
BMS	2
Balloon	1
Brachytherapy	3

Moses JW. Am J Cardiol 2004;supple 6A:130E



Registry of Repeat PCI for SES Restenosis

Lesion characteristics at index procedure

	24 pts (27 lesions)
De novo lesion	70%
Balloon restenosis	4%
In-stent restenosis	15%
Brachytherapy failure	11%

Lemos PA. Circulation 2004;109: 2500-2



Registry of Repeat PCI for SES Restenosis Methods of PCI

	24 pts (27 lesions)
Balloon dilatation	11%
Bare-metal stenting	4%
Repeated SES implantation	44%
PES implantation	41%
Mean lesion length, mm	11.2 (6.6-17.1)
Total length of repeat stenting, mm	17(8-30)

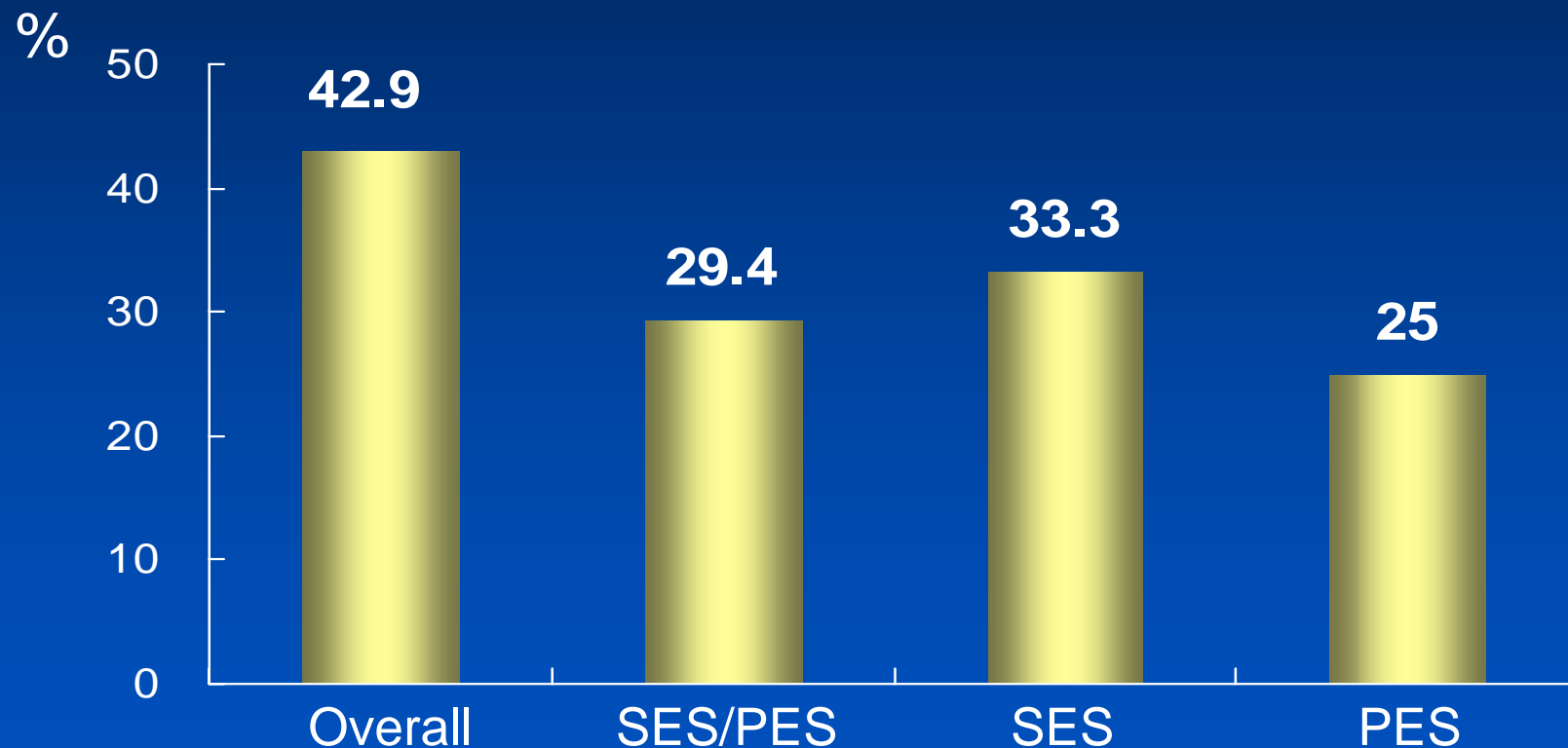
Lemos PA. Circulation 2004;109: 2500-2



Registry of Repeat PCI for SES Restenosis

Restenosis Rates (median 281 days)

(TLR: 20.8%, Event-free survival : 70.2% during 279 days)



Lemos PA. Circulation 2004;109: 2500-2



Registry of Repeat PCI for SES Restenosis

Predictors of recurrent restenosis

Hypercholesterolemia	69% vs. 0%, $P<0.01$
Previous angioplasty at index procedure	67% vs. 11%, $P=0.02$
Failed brachytherapy	100% vs. 33%, $P=0.06$
SES failure treated with balloon dilatation	100% vs. 33%, $P=0.06$
Needing treatment before 6 months from index procedure	100% vs. 25%, $P<0.01$

Lemos PA. Circulation 2004;109: 2500-2



Repeated PCI for DES ISR

AMC Registry

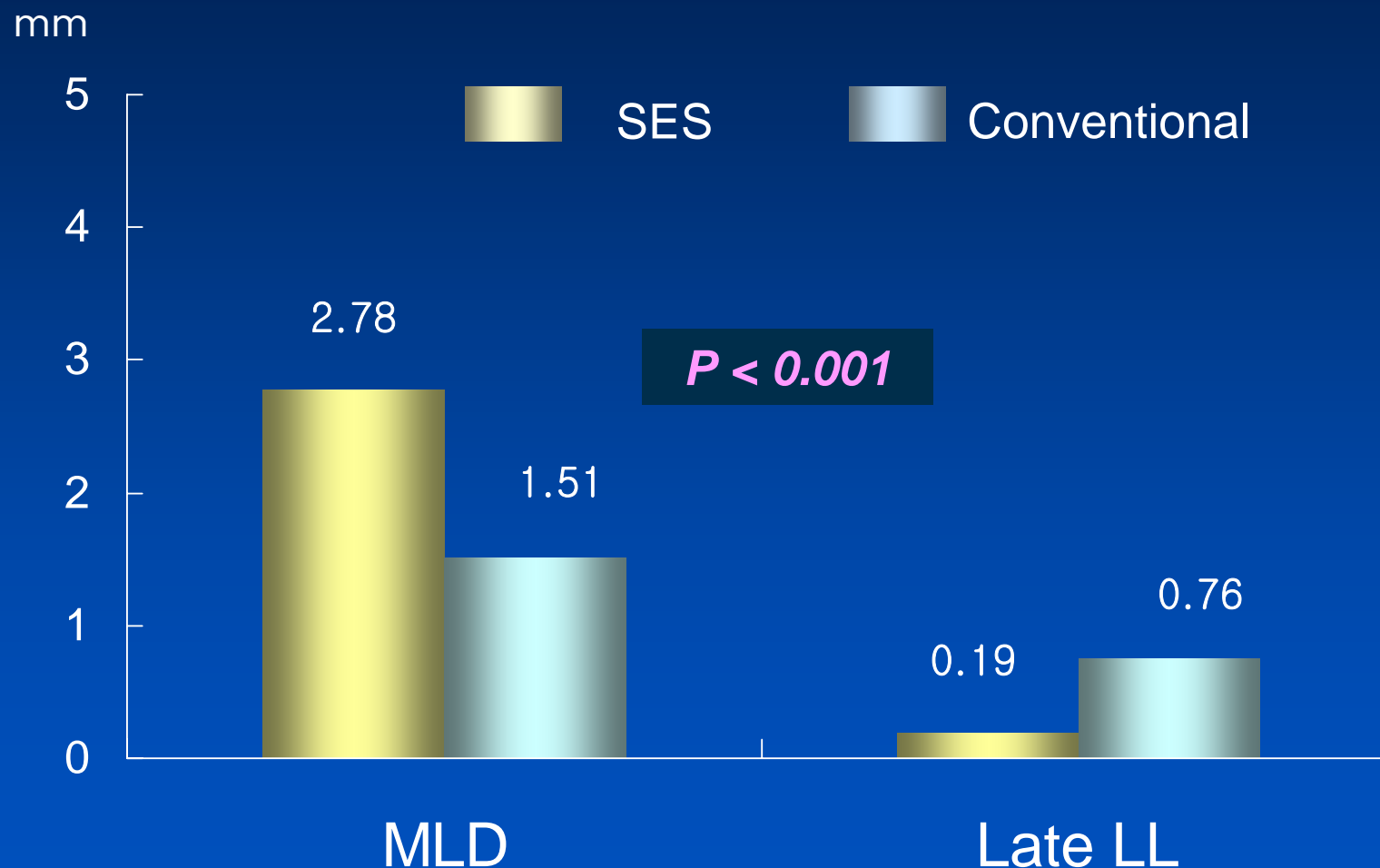
	SES (n=33)	Conventional (n=25)	P-value
CTO (> 3m)	2.60	2.57	1.000
ISF of BMS	12.4	12.3	0.690
Ostial	0.91	0.95	0.222
Bifurcation stenting	2.52	2.07	0.387
Use of SES	14 (42.4%)	13 (52%)	0.596
Location			0.801
LM	2 (6.1%)	1 (4.0%)	
LAD	23 (69.7%)	15 (60.0%)	
LCX	1 (3.0%)	1 (4.0%)	
RCA	7 (21.2%)	8 (32.0%)	
Total stent length (mm)	32.2 ± 15.6	40.2 ± 20.4	0.107

Conventional treatment: cutting balloon in 11 lesions and brachytherapy in 14 lesions

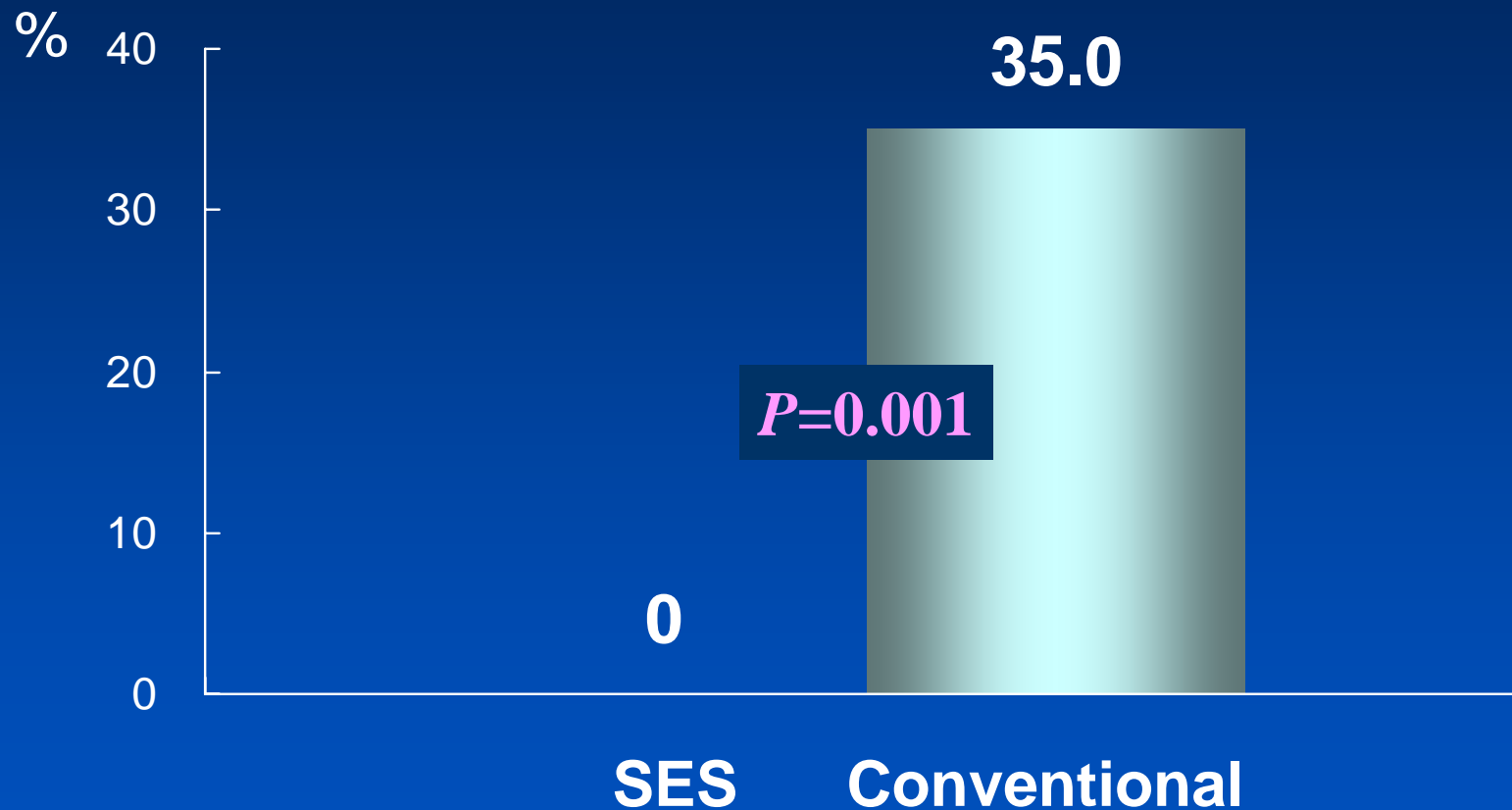
Angiographic Characteristics

	SES (n=33)	Conventional (n=25)	P-value
ISR classification			
Focal	18 (54.9%)	9 (36.0%)	0.161
Diffuse	5 (15.2%)	8 (32.0%)	0.203
Proliferative	7 (21.2%)	7 (28.0%)	0.550
Total	3 (9.1%)	1 (4.0%)	0.627
Location of restenosis			
Edge	25 (75.8%)	9 (36.0%)	0.002
Intra-stent	17 (51.5%)	25 (100.0%)	< 0.001
LL, mm	14.0 ± 8.2	15.3 ± 10.8	0.606
RVD, mm	2.92 ± 0.45	2.81 ± 0.31	0.300
MLD, mm			
Before procedure	0.95 ± 0.43	0.98 ± 0.42	0.800
After procedure	2.93 ± 0.45	2.21 ± 0.31	< 0.001
Acute gain, mm	1.98 ± 0.50	1.22 ± 0.48	< 0.001

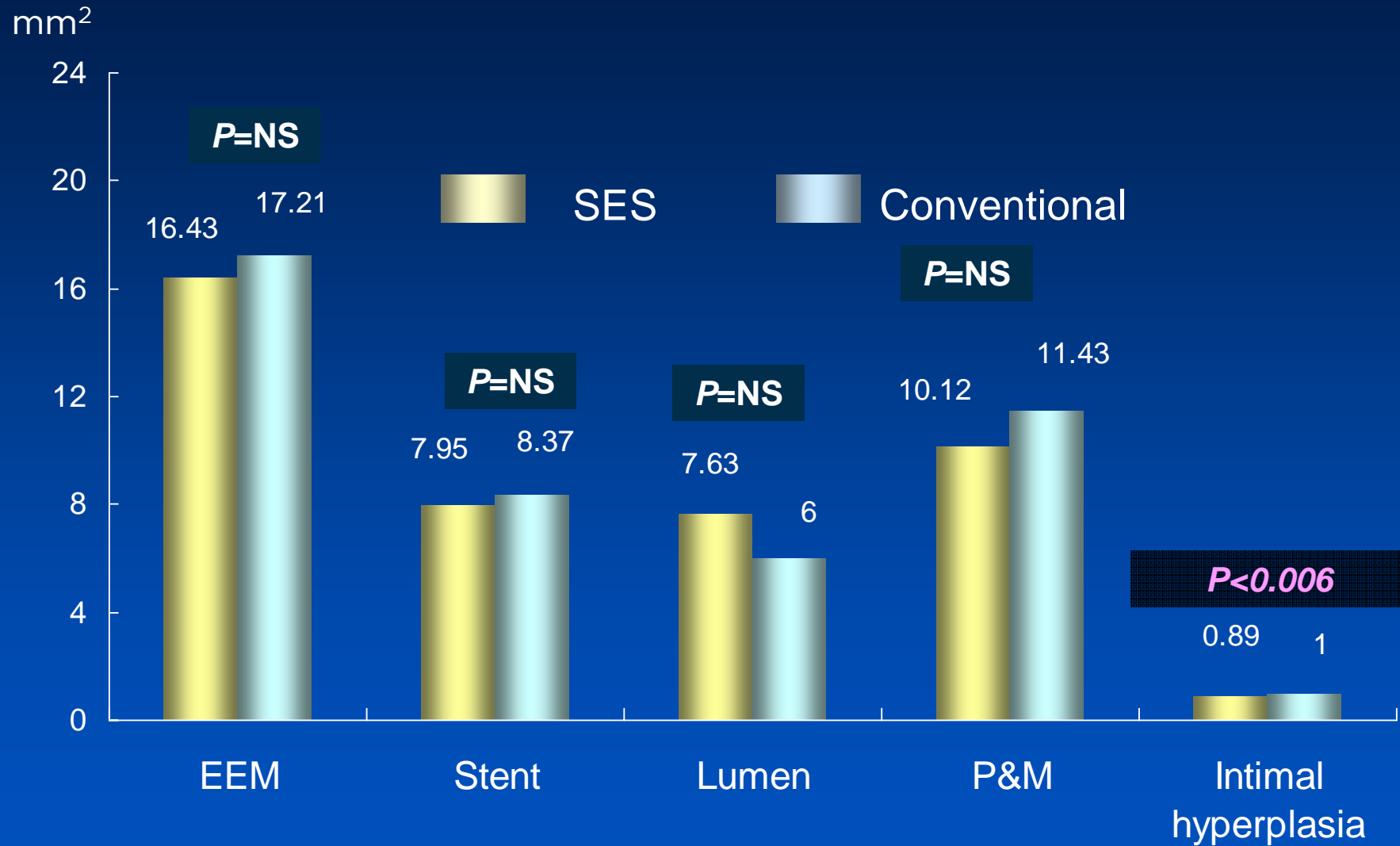
Follow-up MLD and Late Loss



Restenosis Rate at 6 Months



Outcomes of IVUS Follow-up



Subgroup Analysis of Recurrent Restenosis Rates

Variables	SES	Conventional	P-value
Used stent at the index procedure			
Sirolimus-eluting	0/12 (0%)	2/11 (18.2%)	0.217
Paclitaxel-eluting	0/15 (0%)	5/9 (55.6%)	0.003
Location of restenosis			
Edge	0/22 (0%)	4/7 (57.1%)	0.001
Intra-stent	0/12 (0%)	7/20 (35.0%)	0.029
Pattern of restenosis			
Type I	0/16 (0%)	3/8 (37.5%)	0.028
Type II, III, and IV	0/11 (0%)	4/12 (33.3%)	0.093

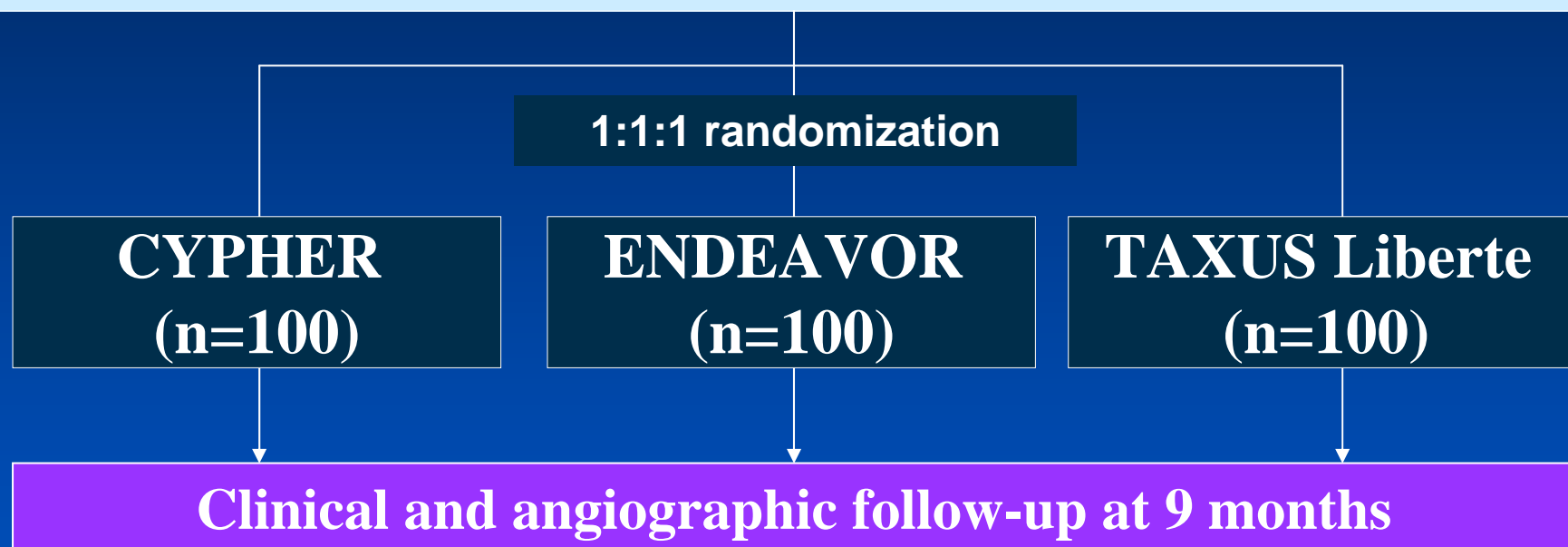
Randomized Trials of ISR



**DIFFUSE Type In-Stent Restenosis
after Drug-Eluting Stents
Implantation Treated by Additional
Drug-Eluting Stents: **Sirolimus-
Eluting Stent vs. Paclitaxel-Eluting
Stent and vs. Zotarolimus-Eluting
Stent****

DIFFUSE-ISR 3 Trial

Diffuse Type In-Stent Restenosis (Lesion Length \geq 10mm) After Drug-Eluting Stent Implantation
(Total 300 patients)



Primary end point: (1) Binary angiographic restenosis at 9 months

**FOcal In-stent Restenosis after
Drug-Eluting Stent Implantation
Treated by Cutting Balloon
Angioplasty versus Sirolimus-
Eluting Stent**

FOCUS Trial

Focal In-Stent Restenosis (Lesion Length \leq 10mm) After Drug-Eluting Stent Implantation
(Total 200 patients)

1:1 randomization

Sirolimus-Eluting Stent
(n=100)

Cutting balloon
(n=100)

Clinical and Angiographic follow-up at 9 months

Primary end point: (1) Binary angiographic restenosis at 9 months

Conclusions

- The effective treatment of ISR within DES has not been sufficiently studied.
- Up to now, the effectiveness of conventional angioplasty for the focal ISR after DES may be acceptable and comparable to repeat DES implantation.

Conclusions

- Repeat DES treatment with same or different antiproliferative agents appears to be effective treatment option for DES failure
- Further larger trial is needed for delineating the role of DES, conventional treatment or brachytherapy for treatment of DES failure.

Recommended Strategy to Treat DES ISR

