Is DES an Alternative to Bypass Surgery for Left Main Stenosis ?

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Efficacy Concern…

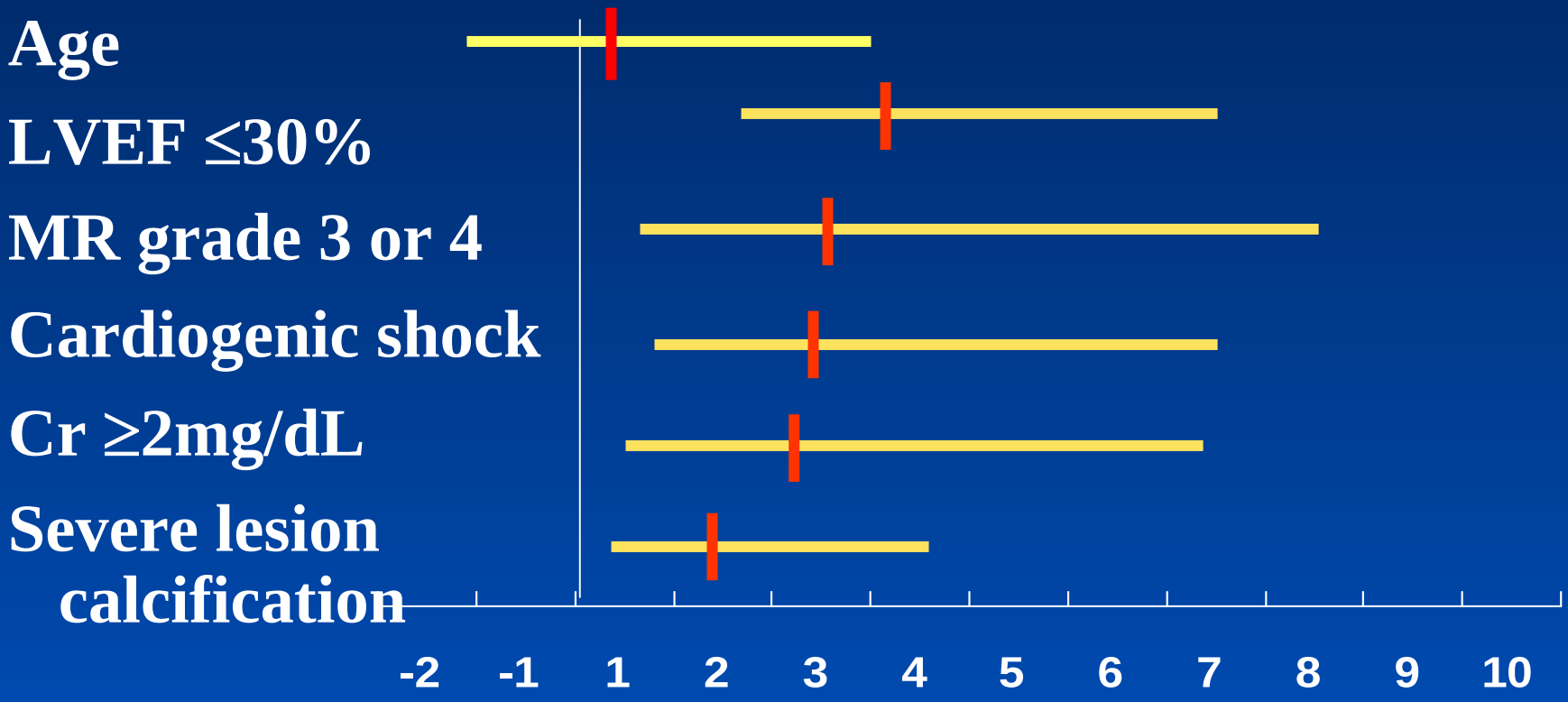
Issue in the era of BMS

for Unprotected LM stenting

High Mortality ?

Relative Risk of Mortality in LMCA Stenting

ULTIMA Registry (279 pts)



Nalysnyk L, Heart 2003, 89:767,

Relative Risk of Mortality in LMCA Stenting

However…
Relative risk mortality were mainly related with clinical variables such as LV dysfunction, degree of mitral regurgitation, renal impairment and cardiogenic shock rather than lesion morphology, lesion site and different treatment strategy

What we have learned...

Unprotected Left main stenting

Patients selection is important for lower mortality and good clinical outcomes

In-hospital Outcomes

AMC

310 pts, Elective Unprotected left main stenting in highly selected groups of patients who have normal left ventricular function (mea age 56 yrs)

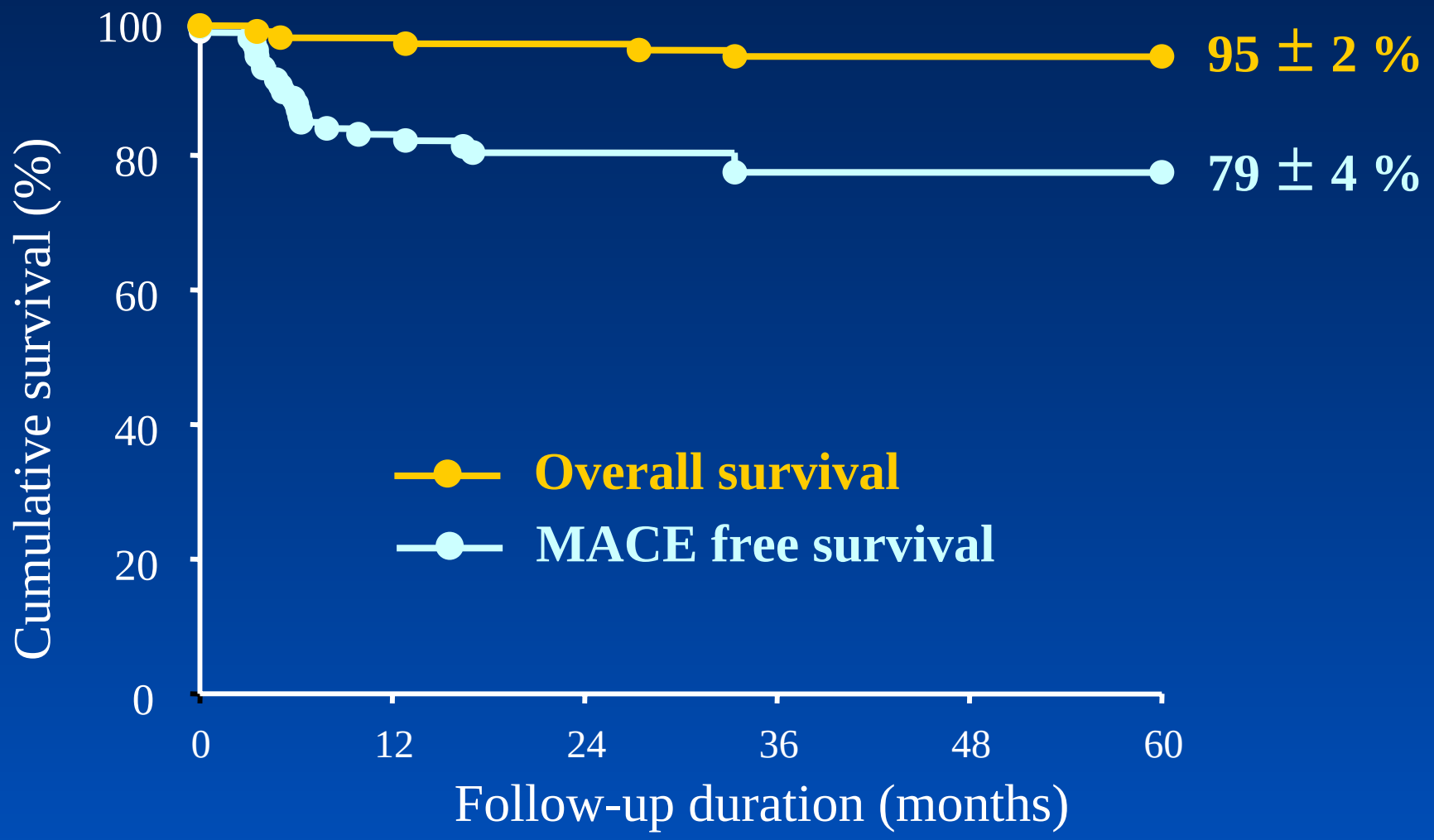
Procedural Success Rate: 99%

Acute closure	**0**
Subacute thrombosis	**1 (0.5%)**
Death	**0**
Q-MI	**0**
Emergent CABG	**0**

Park SJ, Am J Cardiol 2003

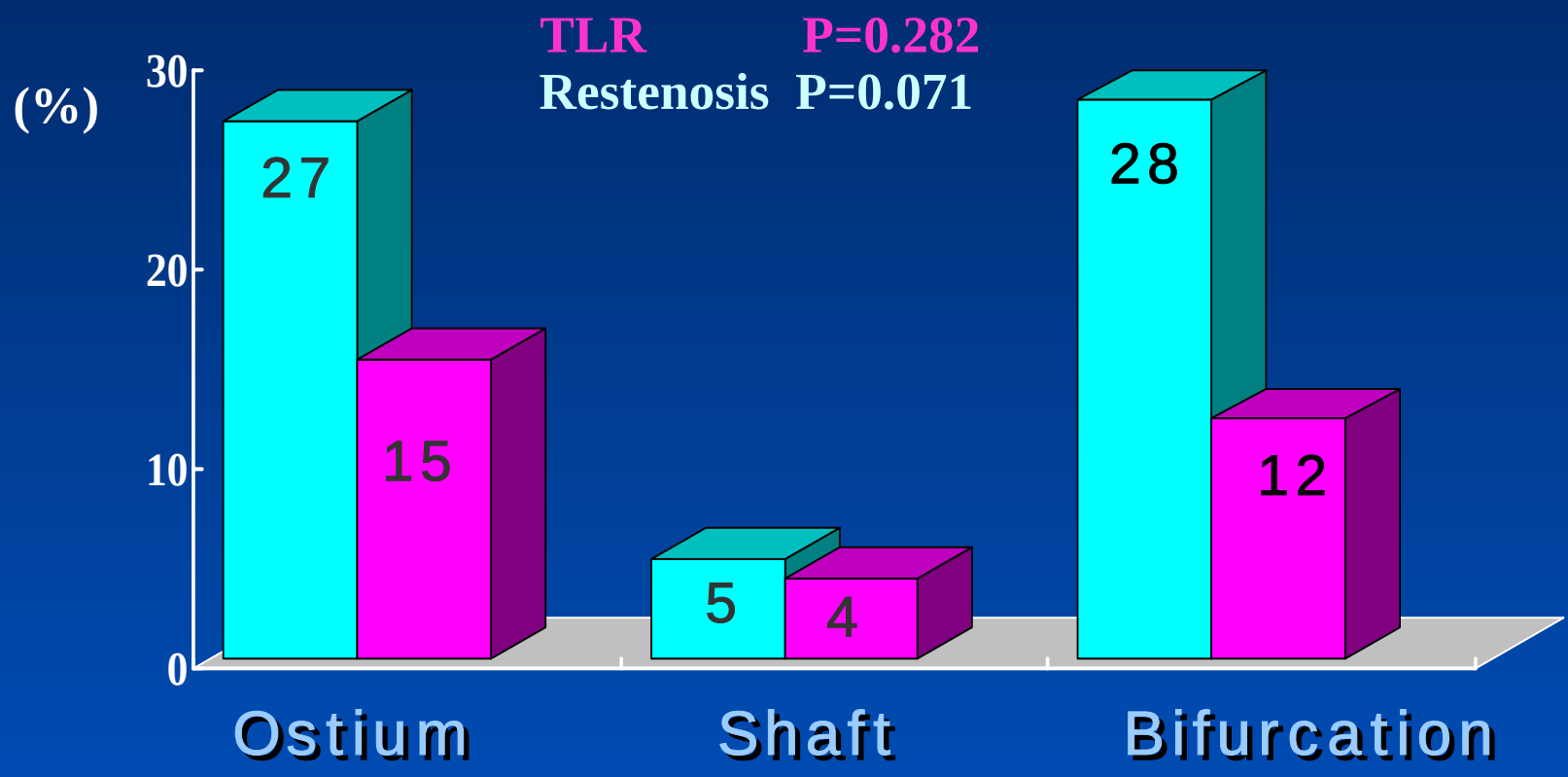
Survival for 5 years

AMC



Major Concerns in BMS era…

Restenosis and TLR



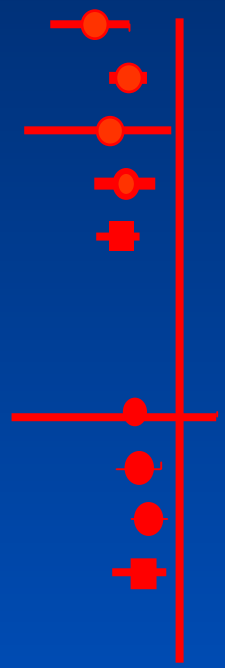
In the era of DES…

Efficacy of DES

Evidenced in Large Randomized Trials

Meta-analysis of MACE

Trial	DES n/N	BMS n/N	Odds ratio (95% Crl)
Sirolimus			
RAVEL	7/120	35/118	0.16 (0.06 to 0.33)
SIRIUS	38/533	99/525	0.33 (0.22 to 0.49)
C-SIRIUS	2/50	9/50	0.23 (0.03 to 0.81)
E-SIRIUS	14/175	40/177	0.30 (0.15 to 0.56)
Pooled	61/878	183/870	0.28 (0.17 to 0.41)
Paclitaxel, polymeric			
TAXUS I	1/31	3/30	0.39 (0.03 to 2.41)
TAXUS II	27/260	57/263	0.42 (0.25 to 0.68)
TAXUS VI	56/662	98/652	0.52 (0.37 to 0.74)
Pooled	84/953	158/945	0.47 (0.25 to 0.71)

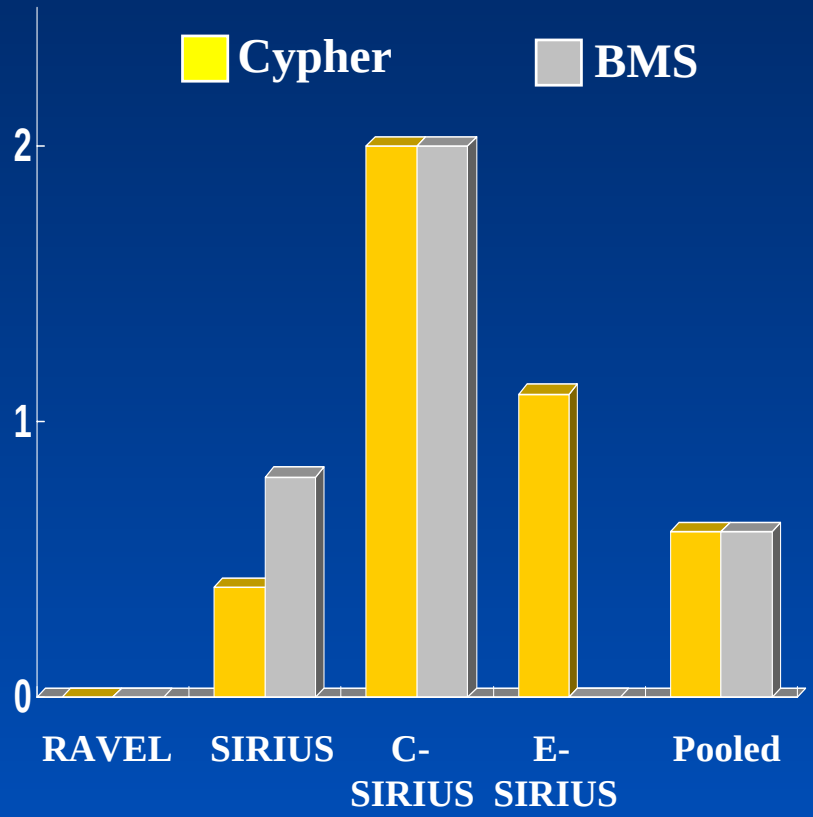


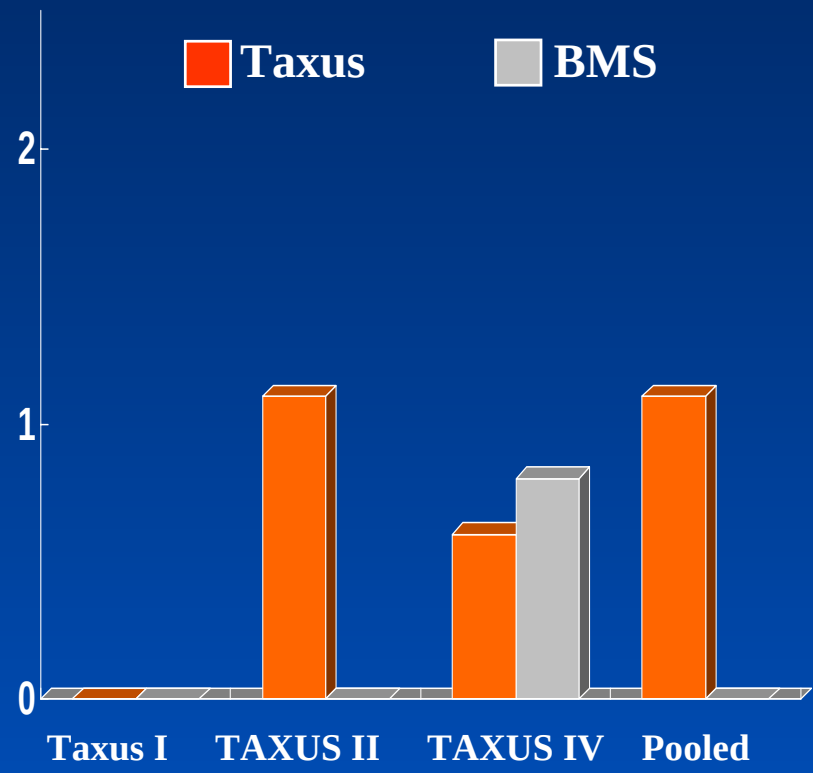
Babapulle MN et al. lancet 2004;364:583

Safety of DES

Evidenced in Large Randomized Trials

Meta-analysis of SAT





Babapulle MN et al. lancet 2004;364:583

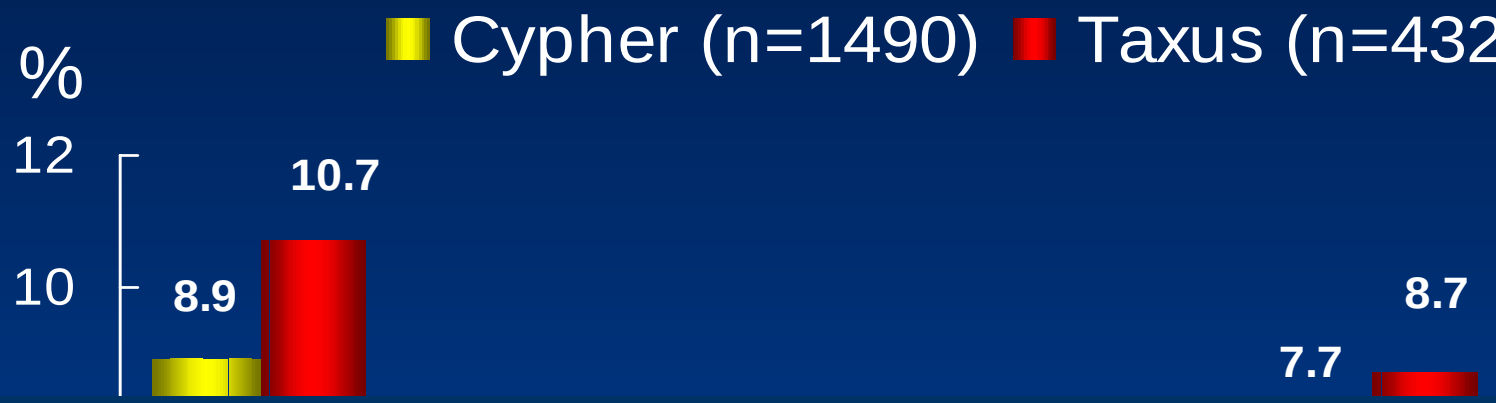
In real world practice…

DES Experience
(Feb, 2003 - April, 2005)

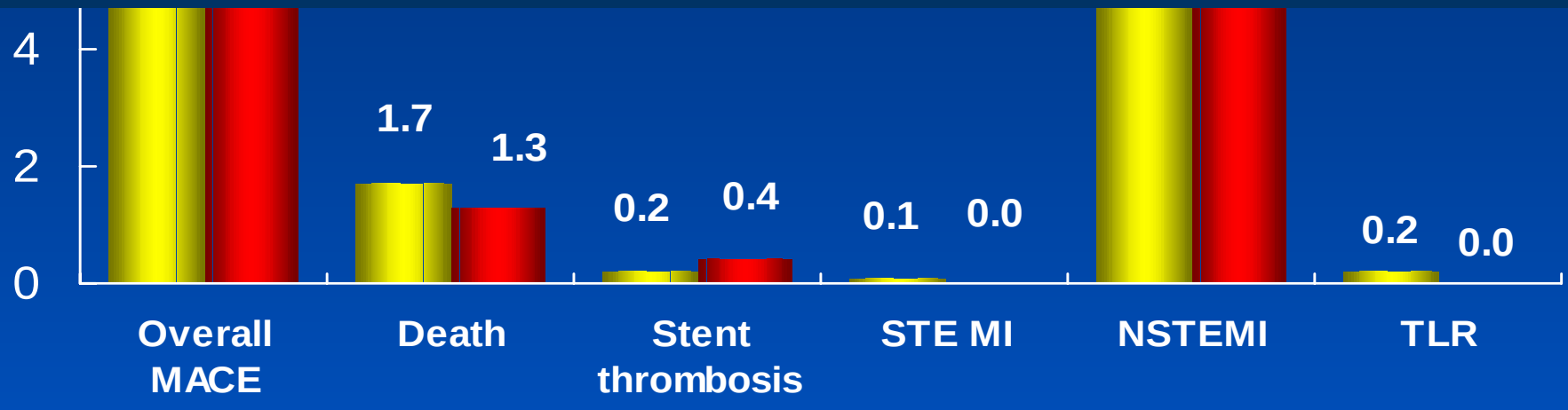
2,833 patients
3,563 lesions
4,600 stents

We treated more complex patients and lesion subsets…

In-Hospital Events

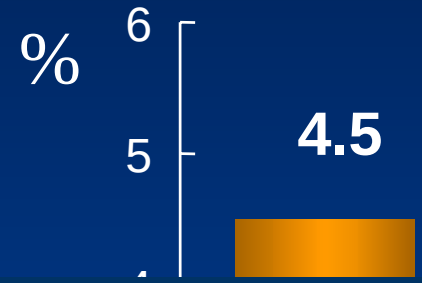


Acceptable SAT rate < 0.5%

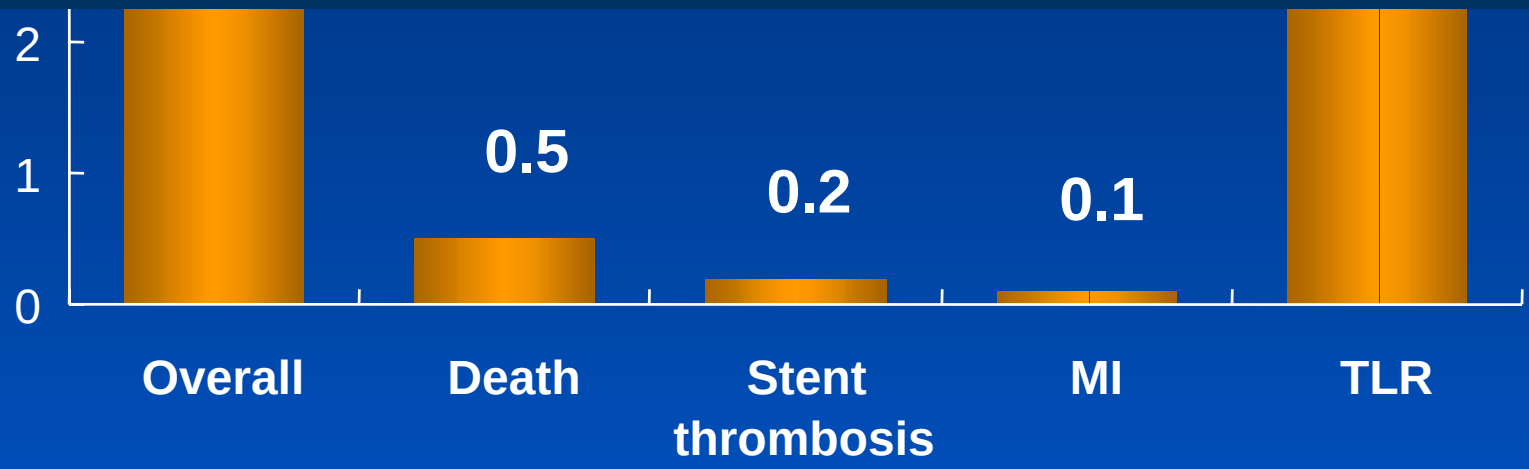


6-Month TLR

1958 patients with Cypher or Taxus implantation & 6-month F/U



Very Low TLR rate : 2.7%



DES in 2005
Safety and Efficacy Proven

DES is safe and effective...

Left main stenting with DES

Not enough data

Outcome of Elective DES Implantation

First author	RESEARCH (preliminary)	Colombo A	Park SJ	RESEARCH
Number	16	85	102	95 (15 protected)
Technical success (%)	100	100	100	99
In-hospital				
Cardiac death	0	0	0	1 (1%)
MI (Q and Non-Q)	1 (6%)	5 (5.9%)	7 (6.9%)	1 (1%)
CABG	0	0	0	0
Long-term	1-Yr	6-Mo	1-Yr	1-Yr
Cardiac death	0	3 (3.5%)	0	13 (14%)
MI	0	0	0	4 (4%)
TLR	1 (6%)	12 (14.1%)	2 (2.0%)	6 (6%)

DES Implantation from RESEARCH and T-RESEARCH

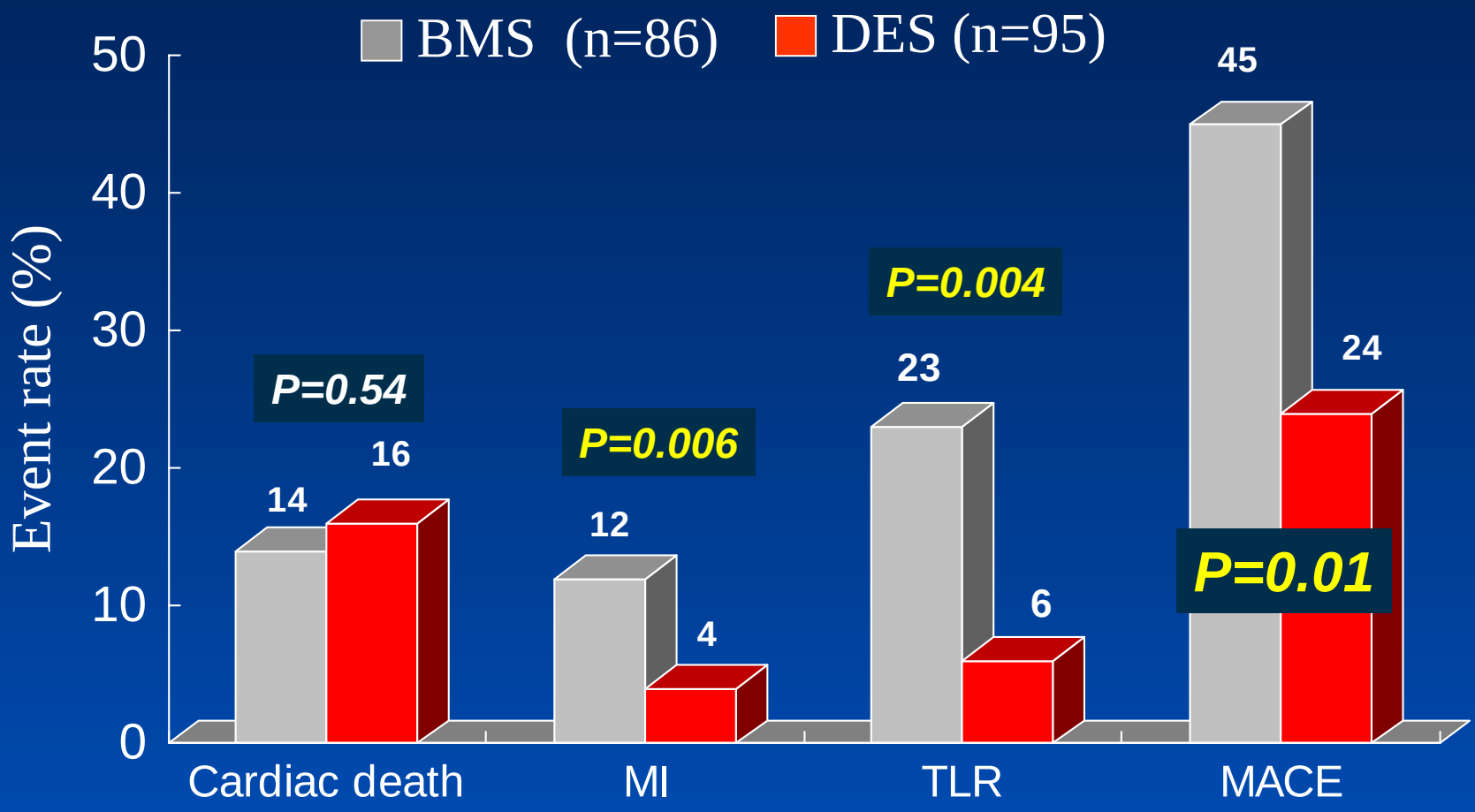
86 BMS (19 protected) vs.
95 DES (15 protected, 52 SES and 43 PES)

	BMS	DES	P value
Distal location, %	66	65	0.9
LM plus more than 2 vessel disease	71	83	< 0.001
Total stent length per pt, mm	20±9	24±13	0.02
Debulking atherectomy, %	6	0	0.007
Bifurcation stenting	10	26	0.02
Culotte	11	36	0.4
T technique	88	44	0.35
Crush	0	12	0.56
Kissing technique	0	8	0.91

Valgimigli M et al. Circulation 2005;111:1383

One-year Clinical Outcomes

DES vs. BMS in RESEARCH



Valgimigli M et al. Circulation 2005;111:1383

SES Implantation from Milan

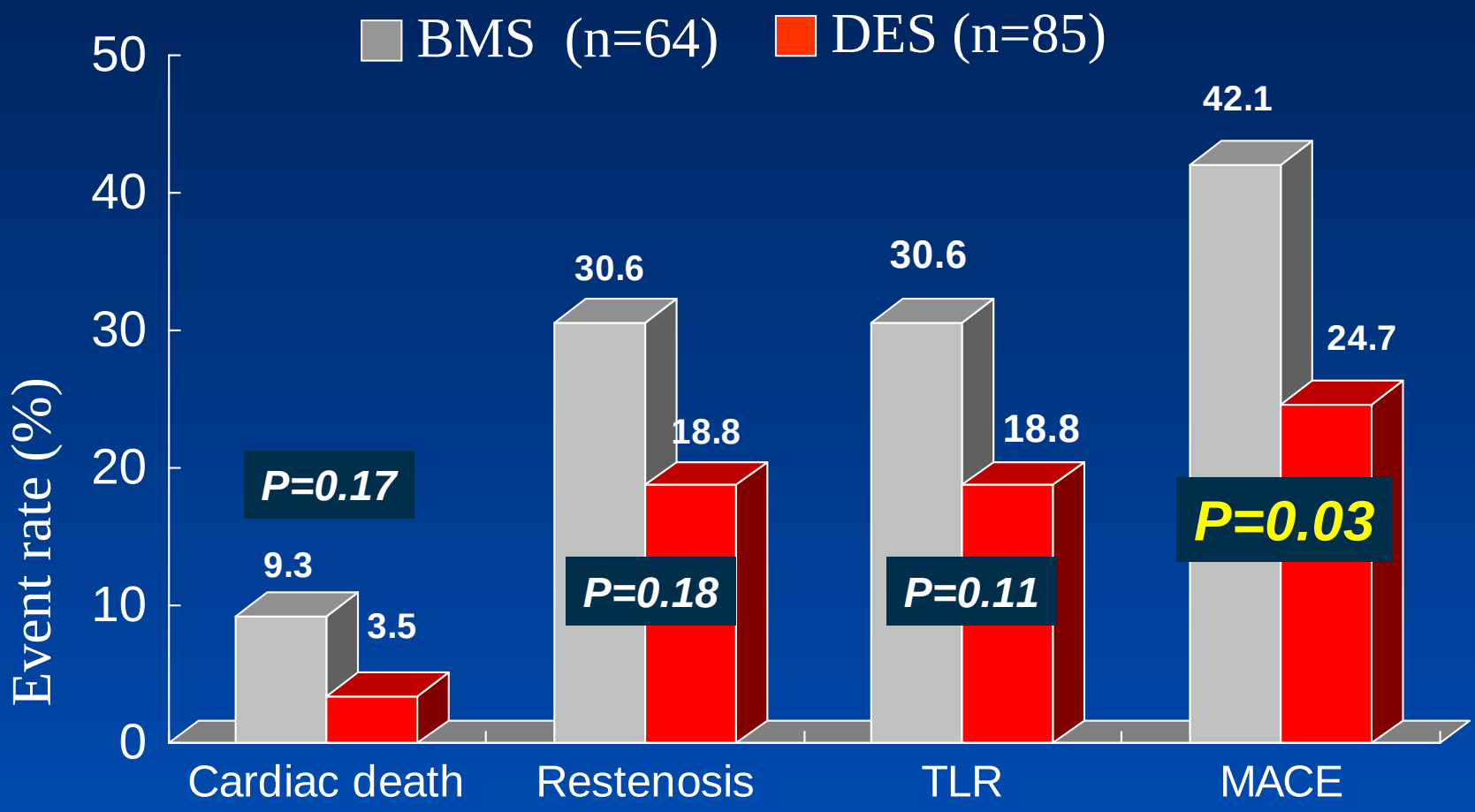
85 BMS unprotected vs. 64 SES unprotected

	BMS	DES	P value
Distal location, %	58	81	0.003
Lesions treated, n (%)	2.25±1.3	2.94±1.6	0.004
Total stent length per pt, mm	15.8±8.6	24.3±12	0.0001
Debulking atherectomy, %	20.3	2.3	0.0005
Bifurcation stenting		74	
Culotte		9	
T technique		7	
Crush		59	
V stenting		25	

Chieffo A et al. Circulation 2005;111:791

Six-month Follow-up Results

DES vs. BMS in Milan



Chieffo A et al. Circulation 2005;111:791

Asian Multicenter Registry Data

	BMS	Cypher	Taxus	P value
Patients	88	94	90	
Prior MI, %	9.1	8.5	7.8	NS
LV EF, %	**55.8**	**47.5**	**45.8**	**0.01**
Three vessels, %	29.5	35.1	42.2	NS
Proximal ref., mm	3.5	3.5	3.4	NS
Lesion length, mm	**13.5**	**20.4**	**21.8**	**0.05**
Bifurcation, %	43.2	55.3	61.1	NS
Unstable angina, %	29.5	19.1	11.1	NS

Nakamura S et al. ACC 2005

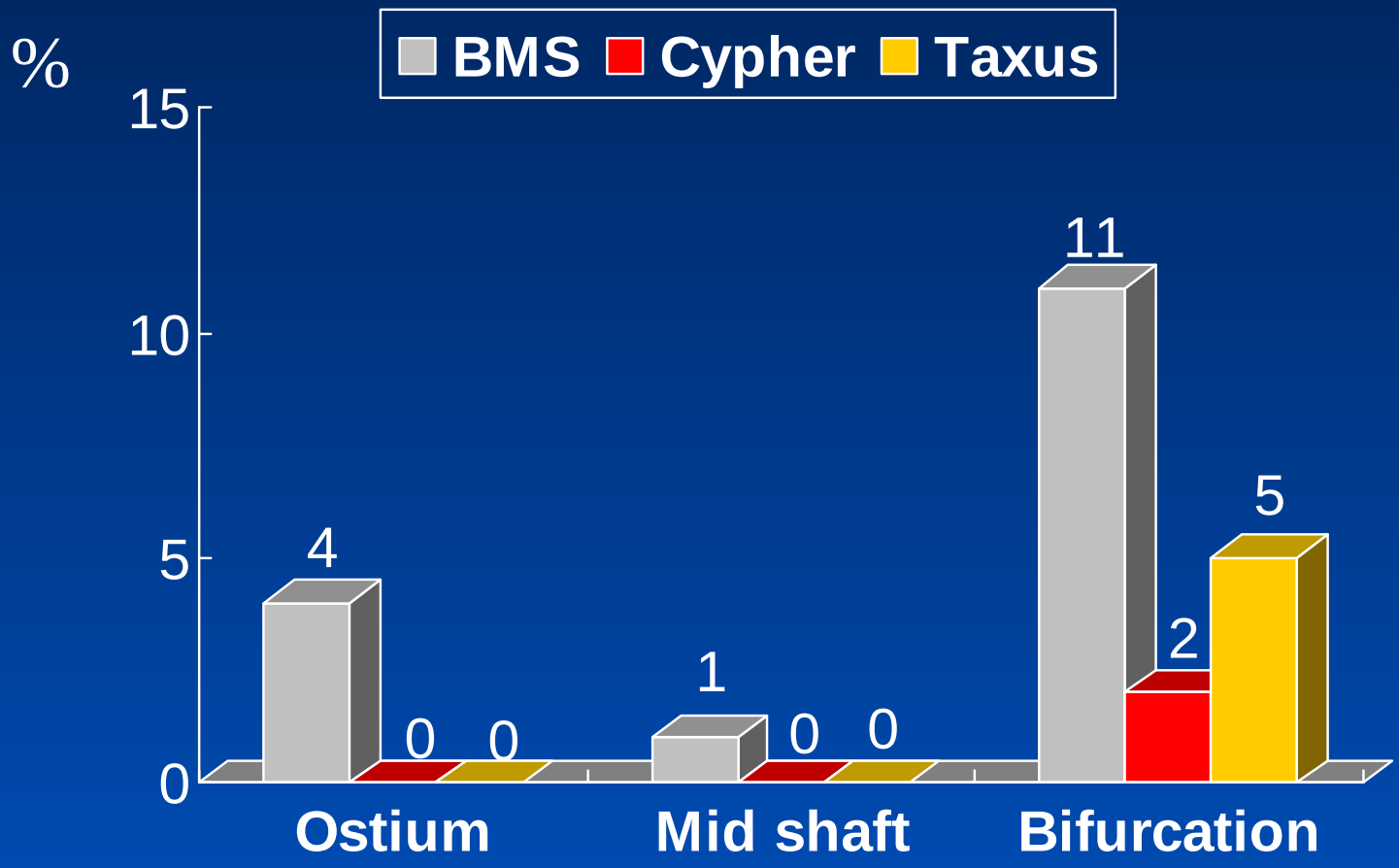
Asian Multicenter Registry Data

In-hospital Outcomes

	BMS (n=88)	Cypher (n=94)	Taxus (n=90)	P value
Angiographic success, %	100	100	100	NS
Clinical success, %	98.9	100	100	NS
MACE, n				
Death	0	0	0	NS
Q MI	1	0	0	NS
Urgent CABG	**0**	**0**	**0**	NS
Urgent PCI	1	0	0	NS
Vascular hematoma, %	4.5	5.3	5.6	NS

Nakamura S et al. ACC 2005

Asian Multicenter Registry Data
Restenosis Rate



Nakamura S et al. ACC 2005

Unprotected LMCA Cypher in AMC

From Feb 2003 till April 2005

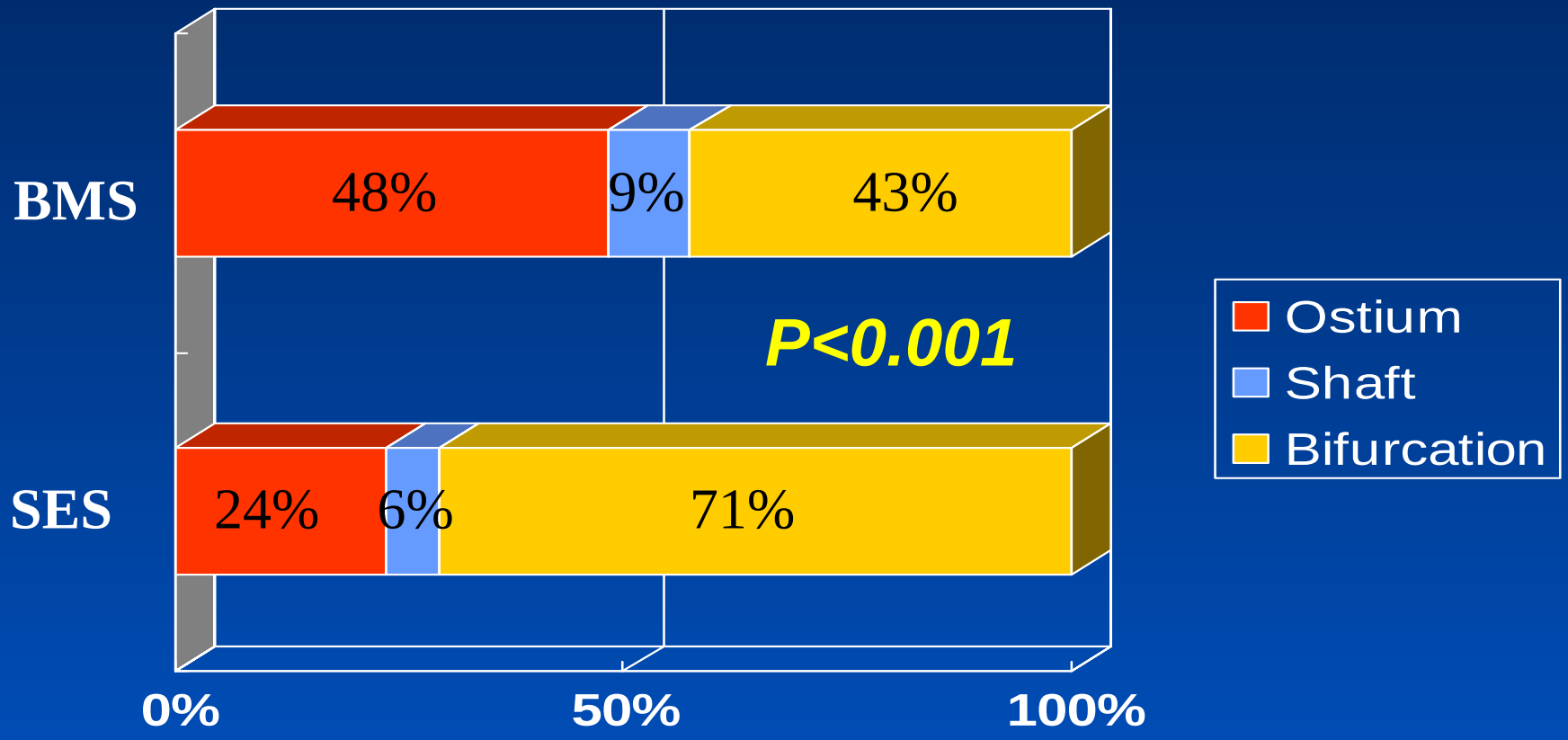
Total 201 patients

Proximal involvement	**52 (26 %)**
Ostium	**44**
Shaft	**8**
Distal involvement	**149 (74 %)**

Matched Comparison with BMS

More LM Bifurcation stenting...

149 pts with SES (Feb 2003-Sep 2004)
121 pts with BMS (Feb 2001-Jan 2003)



Park SJ et al, J Am Coll Cardiol 2005;45:351

Multiple & Longer Stents

	SES	BMS	P
Reference diameter, mm	3.46±0.65	3.98±0.69	<0.001
Stents per patient	2.1±1.0	1.6±0.7	<0.001
Stents per lesion	1.6±0.9	1.1±0.4	<0.001
Total stent length, mm	26.6±18.1	13.3±5.5	<0.001
Final balloon size, mm	3.90±0.44	4.39±0.55	<0.001
Inflation pressure, mm	18.5±2.8	14.0±2.6	<0.001
Balloon/Artery ratio	1.1±0.3	1.1±0.2	0.290

Park SJ et al, J Am Coll Cardiol 2005;45:351

Fewer Debulking, More Direct Stenting

	SES	BMS	P
Patients	149	121	
Multivessel PCI	63 (42.3)	42 (34.7)	0.254
Direct stenting	67 (45.0)	21 (17.4)	<0.001
Debulking atherectomy	3 (2.0)	40 (33.1)	<0.001
IVUS guidance	129 (86.6)	91 (75.2)	0.039
GP IIb/IIIa inhibitor	10 (6.7)	6 (5.0)	0.376
IABP support	6 (4.0)	5 (4.1)	0.782

Park SJ et al, J Am Coll Cardiol 2005;45:351

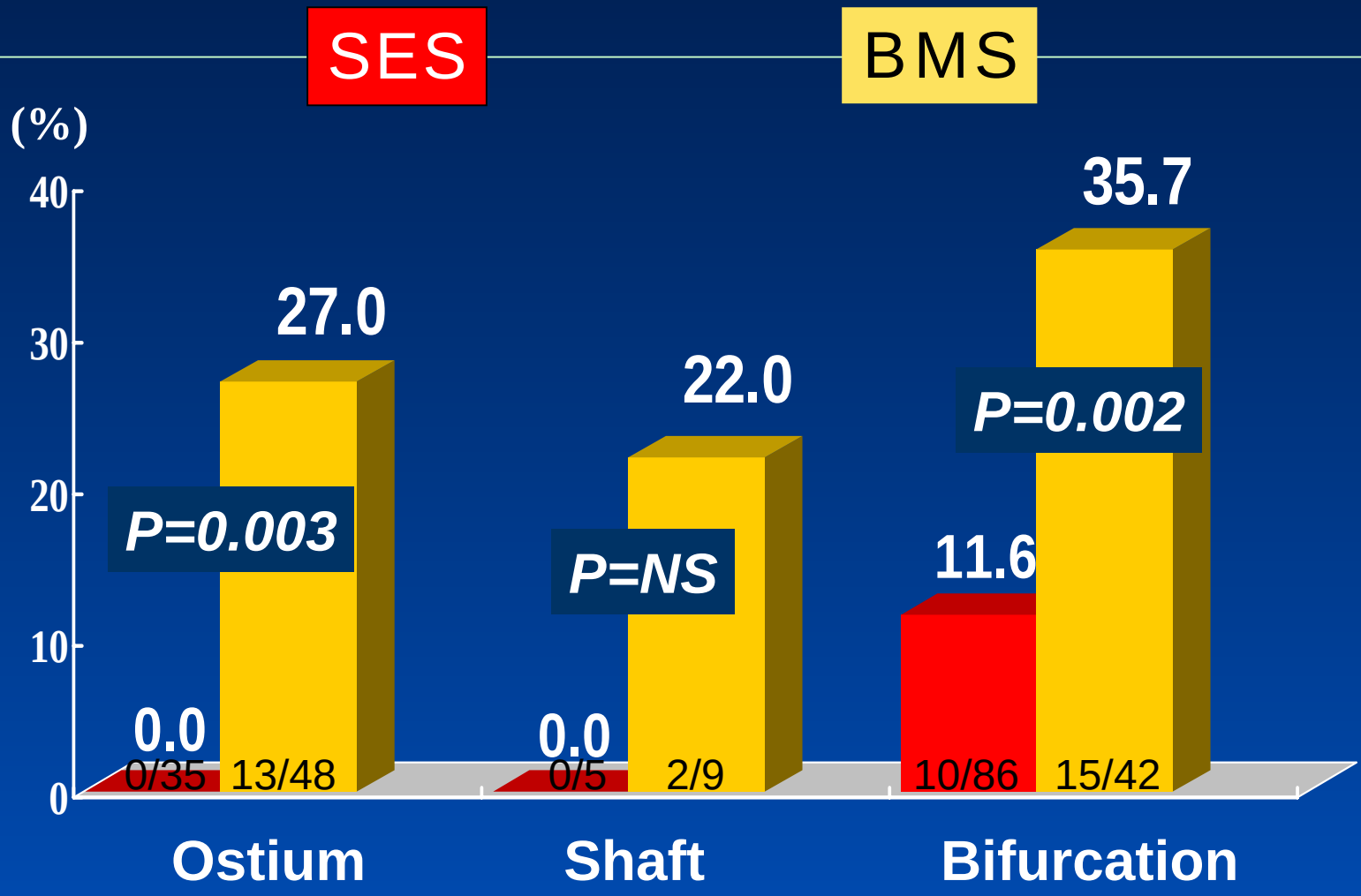
In-Hospital Outcomes

	BMS N=121	SES N=149
Procedure Success (%)	**100**	**100**
Death	**0**	**0**
Q MI	**0**	**0**
Non-QMI	**10 (8.3%)**	**11 (7.4%)**
SAT	**0**	**0**
Emergent CABG	**0**	**0**
Repeat PCI	**0**	**0**

* All procedure related, CK-MB ≥ 3 times normal value

Park SJ et al, J Am Coll Cardiol 2005;45:351

Overall Restenosis Rate : 7.9 %



Park SJ et al, J Am Coll Cardiol 2005;45:351

Left main stenting with DES

Ostial and Shaft lesions intervention

LM ostial or shaft lesions

Total 47 patients	
Age	61 ± 13
Male	28 (60%)
Hypertension	17 (36%)
Diabetes	12 (26%)
Smoking	11 (23%)
Hypercholesterolemia	10 (21%)
Previous PCI	10 (21%)
Acute coronary syndrome	27 (57%)
LV EF (%)	60 ± 10

Procedural Findings

Used stent	Single in all pts
IVUS guidance	38 (81%)
Stent size	
3.0 mm	10 (21%)
3.5 mm	37 (79%)
Mean stent length, mm	13.6±5.3
Maximal device diameter, mm	4.0±0.4
Cutting balloon	1 (2.1%)
Use of reopro	1 (2.1%)
Debulking atherectomy	1 (2.1%)

Angiographic Analysis

Lesion length, mm	9.3 ± 5.4
Reference, mm	3.49 ± 0.53
Minimal lumen diameter, mm	
Before procedure	1.37 ± 0.6
After procedure	3.55 ± 0.37
At follow-up	3.53 ± 0.35
Acute gain, mm	2.18 ± 0.66
Late loss, mm	0.02 ± 0.23
Restenosis	0 (0%)

Clinical Outcome

Mean F/U duration, months	13.1 ± 6.8
Death	0
Myocardial infarction	
Q-wave	0
Non-Q-wave *	2 (4.3%)
Stent thrombosis	0
Target lesion revascularization	0

* procedure-related, no event after discharge

DES for Ostial and Shaft LMCA stenosis

No Mortality

No Restenosis

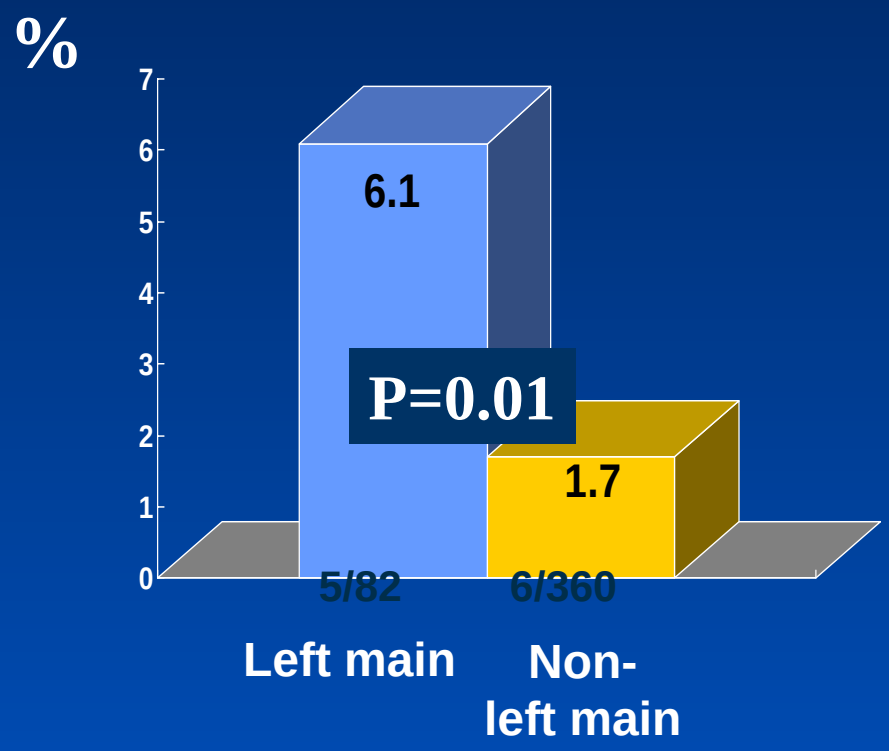
No TLR

Do you still prefer surgery ?

In-hospital mortality of CABG for LMCA stenosis was 6 %

Left main was a predictor of in-hospital mortality

OP mortality



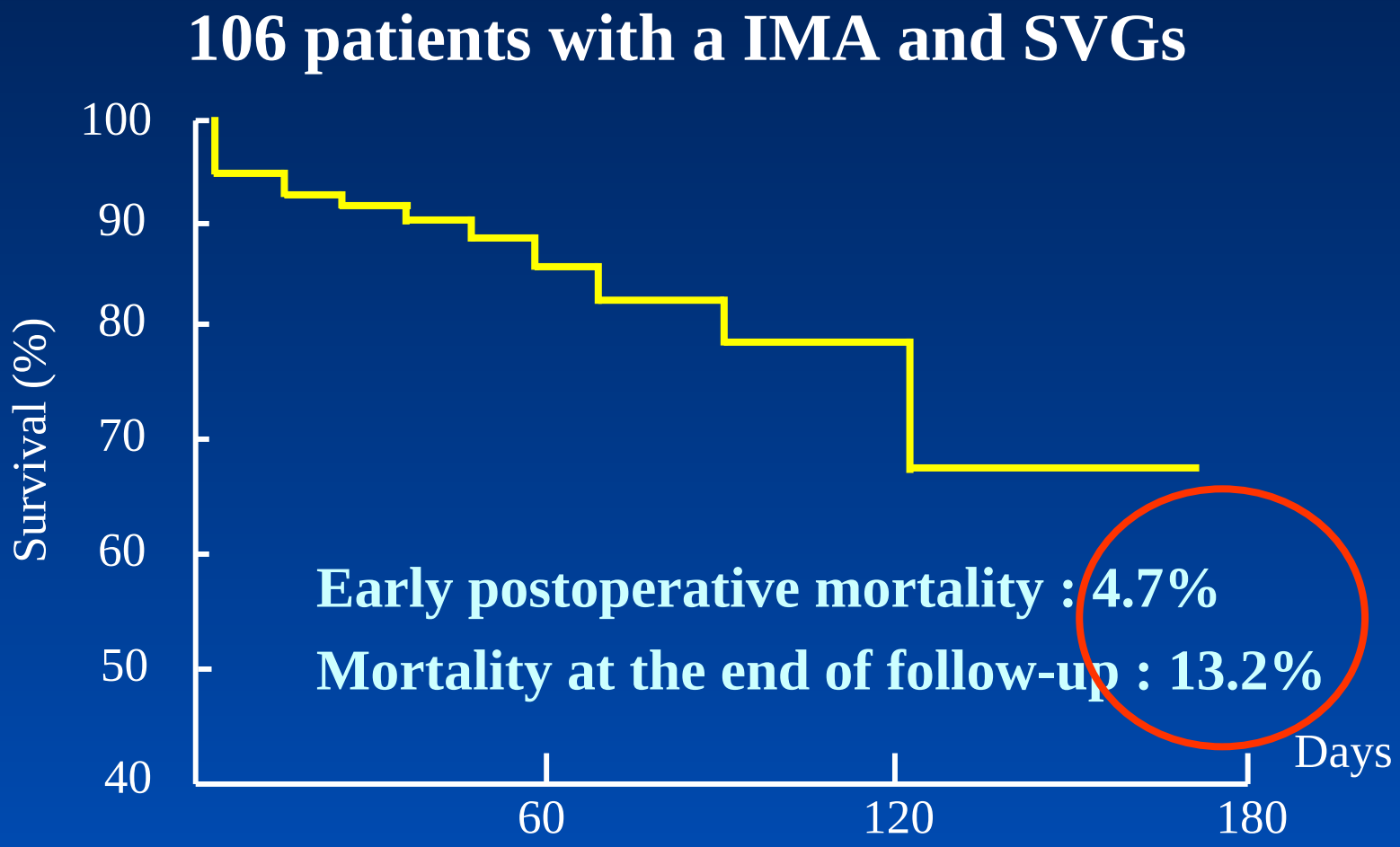
Circulation 1980;62:I-84

Independent predictors of OP mortality (CASS)

Variables	Regression Coefficient
Age	0.05
Male	1.11
Left main stenosis	2.61
Angina class	0.16

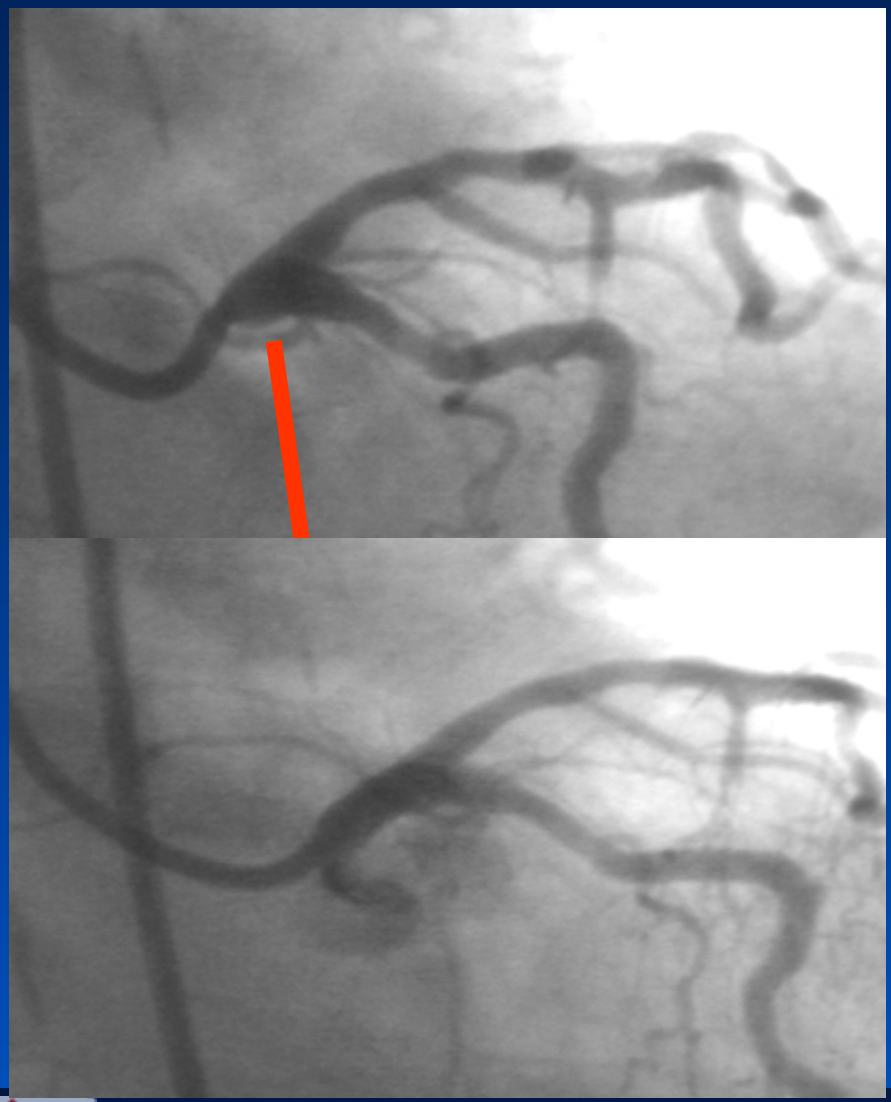
J Thoac Cardiovasc Surg 1980;80:876

Higher mortality of CABG with multiple grafts for isolated LMCA stenosis

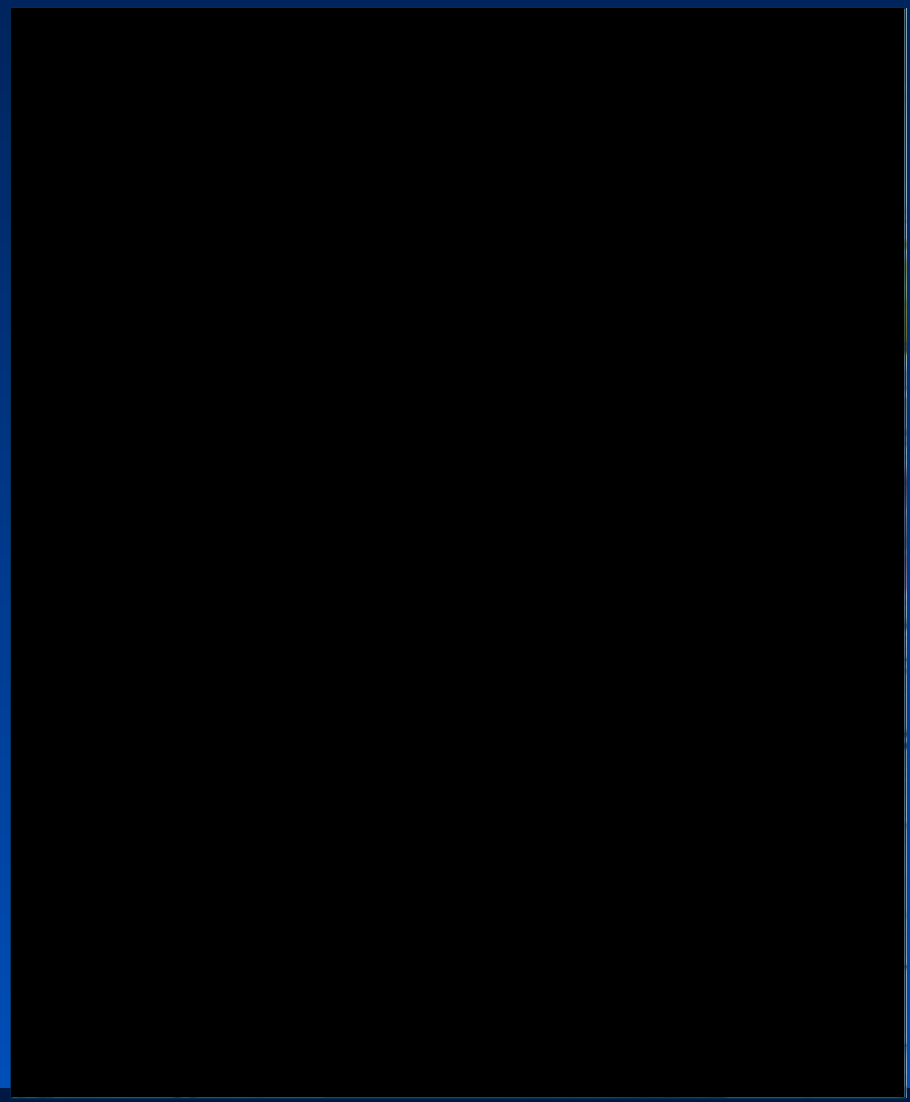


d'Allonnes et al. Heart 2002;87:544

Just 5-minute work !



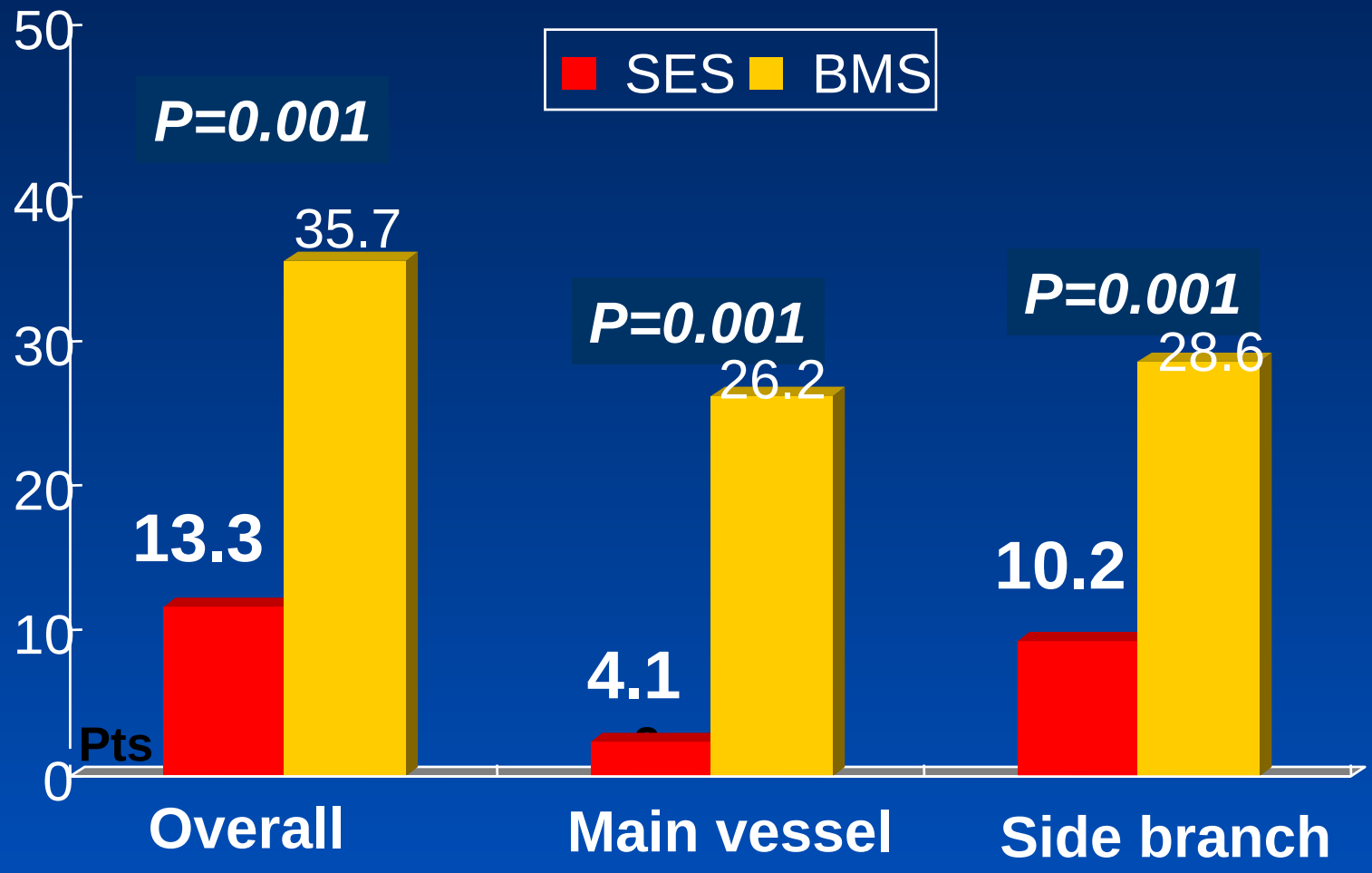
Do you still prefer surgery ?



Left main stenting with DES

Bifurcation lesions intervention

Restenosis Rate of LM Bifurcation in AMC
DES vs BMS



However, reported TLRs are different !

First author	Colombo A	Serruys PW	Park SJ
Number	85	95 (15 protected)	102
DES used	Cypher	Cypher+Taxus	Cypher
Technical success (%)	100	99	100
In-hospital			
Cardiac death	0	1 (1%)	0
MI (Q and Non-Q)	5 (5.9%)	1 (1%)	7 (6.9%)
CABG	0	0	0
Long-term	6-Mo	1-Yr	1-Yr
Cardiac death	3 (3.5%)	13 (14%)	0
MI	0	4 (4%)	0
TLR	12 (14.1%)	6 (6%)	2 (2.0%)

Comparison of three major papers
70-80% of distal location

	Colombo A	Serruys PW	Park SJ
Patient	85	95	102
Age	63.2±11.7	64±12	60.3±11.1
Male	70 (84.3%)	66%	87 (71.9%)
Diabetes mellitus	18 (21.2%)	30%	29 (84.4%)
Ejection fraction, %	51.1±11	41±14	60.4±8.4
Acute MI	NA	17%	10 (9.8%)
Cardiogenic shock	NA	9%	0
Multivessel involvement	NA	80%	59 (58.4%)
Distal location	69 (81.2%)	65%	72 (70.6%)

Comparison of three major papers

More bifurcation stenting in Colombo's study

	Colombo A	Serruys PW	Park SJ
Reference diameter, mm	3.73±0.6	3.25±0.5	3.46±0.65
MLD, pre, mm	1.34±0.5	1.09±0.44	1.31±0.57
Treated lesions or multi-vessel PCI	2.9±1.6	NA	43 (42.2%)
Stent length, mm	24.3±12	24±13	26.6±18.1
DCA, mm	2 (2.3%)	0	3 (2.9%)
MLD, post, mm	3.3±0.6	2.83±0.49	3.36±0.47
Bifurcation stenting	51 (74%)	40%	29 (41%)
Culotte	5 (10%)	36%	0
T technique	4 (8%)	44%	1 (3%)
Crush	30 (59%)	12%	11 (38%)
Kissing	12 (24%)	8%	17 (59%)

Relatively a high TLR rate might be influenced by more frequent use of complex stentings

	Colombo A	Serruys PW	Park SJ
Number	85	95	102
Technical success (%)	100	99	100
In-hospital			
Cardiac death	0	1 (1%)	0
MI (Q and Non-Q)	5 (5.9%)	1 (1%)	7 (6.9%)
CABG	0	0	0
Long-term	6-Mo	1-Yr	1-Yr
Cardiac death	3 (3.5%)	13 (14%)	0
MI	0	4 (4%)	0
TLR (all bifurcation)	12 (14.1%)	6 (6%)	2 (2.0%)

LMCA Bifurcation Stenting with DES

- The remarkable efficacy of DES in inhibiting intimal growth makes the LMCA lesion an inviting target of percutaneous coronary intervention.

- However, as contrasted with the treatment of proximal unprotected LMCA (ULMCA), stenting with DES at the LMCA bifurcation remains challenging because of the technical complexity and relatively high recurrence rate.

- The current registry data showed that the long-term outcomes of LMCA bifurcation stenting with DES might be associated with the stenting technique used.

116 LMCA bifurcation patients in AMC

Different Treatment Strategy

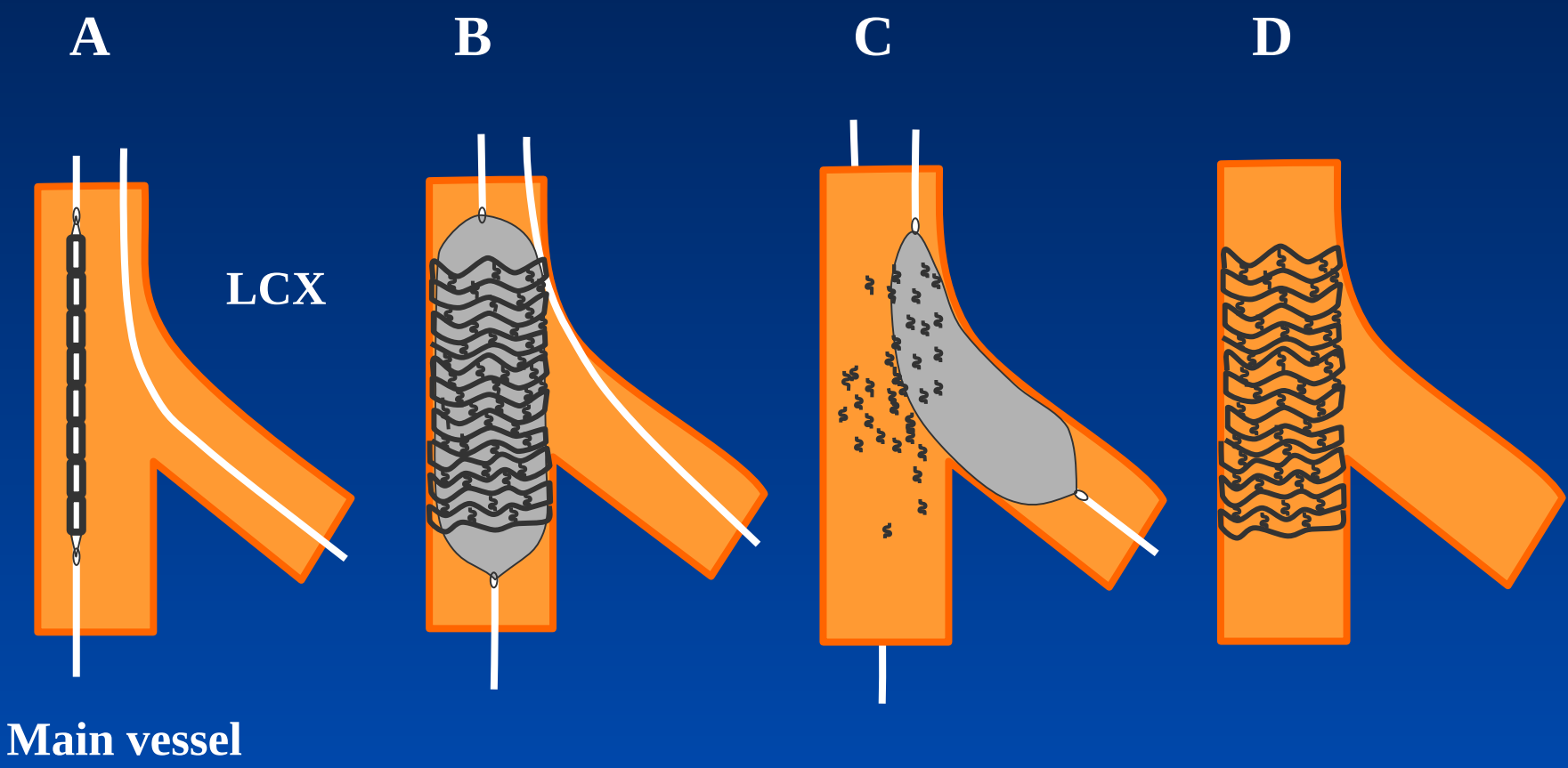
Stenting Cross Over

Kissing Stenting

Stent Crushing

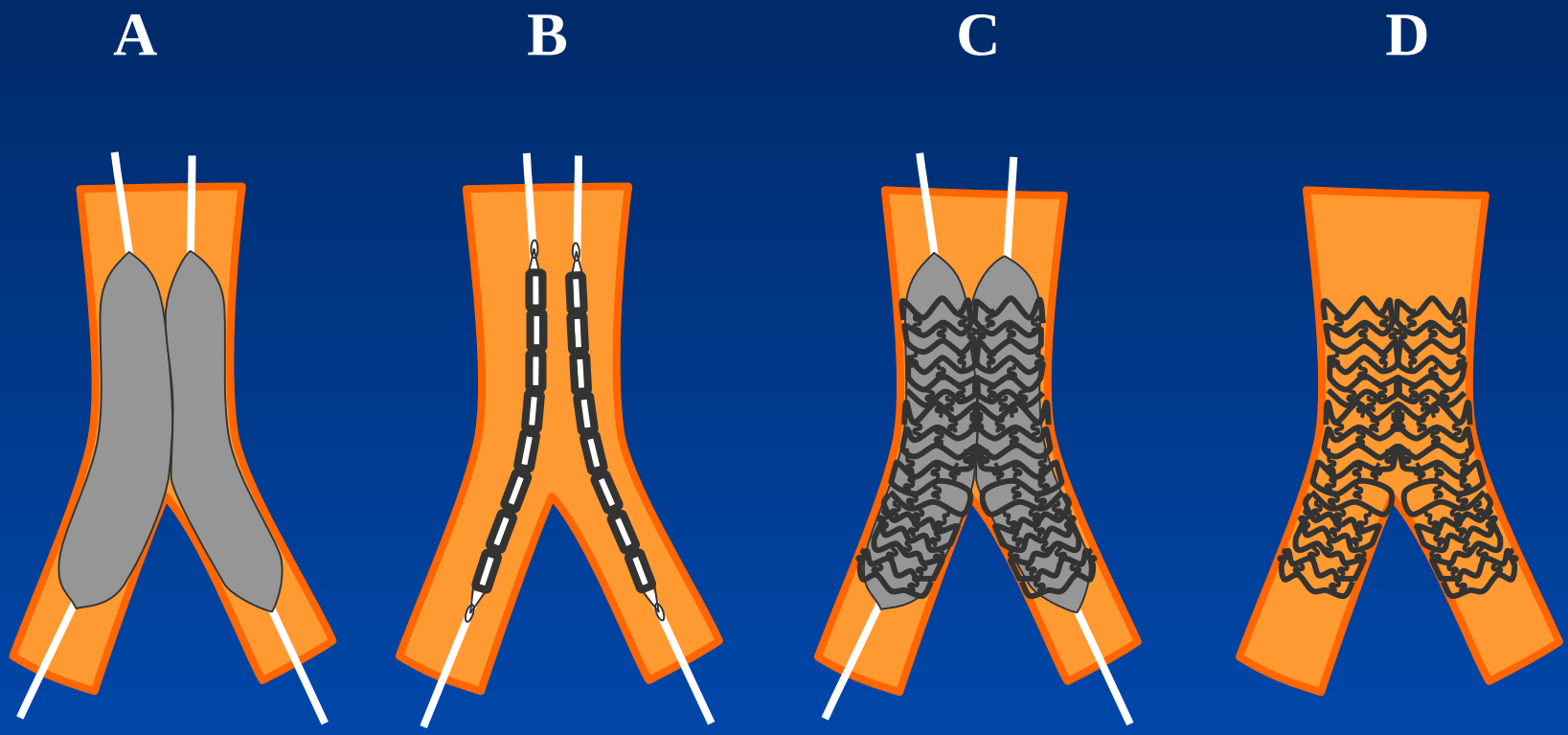
Stenting Cross-over

In lesions with normal LCX



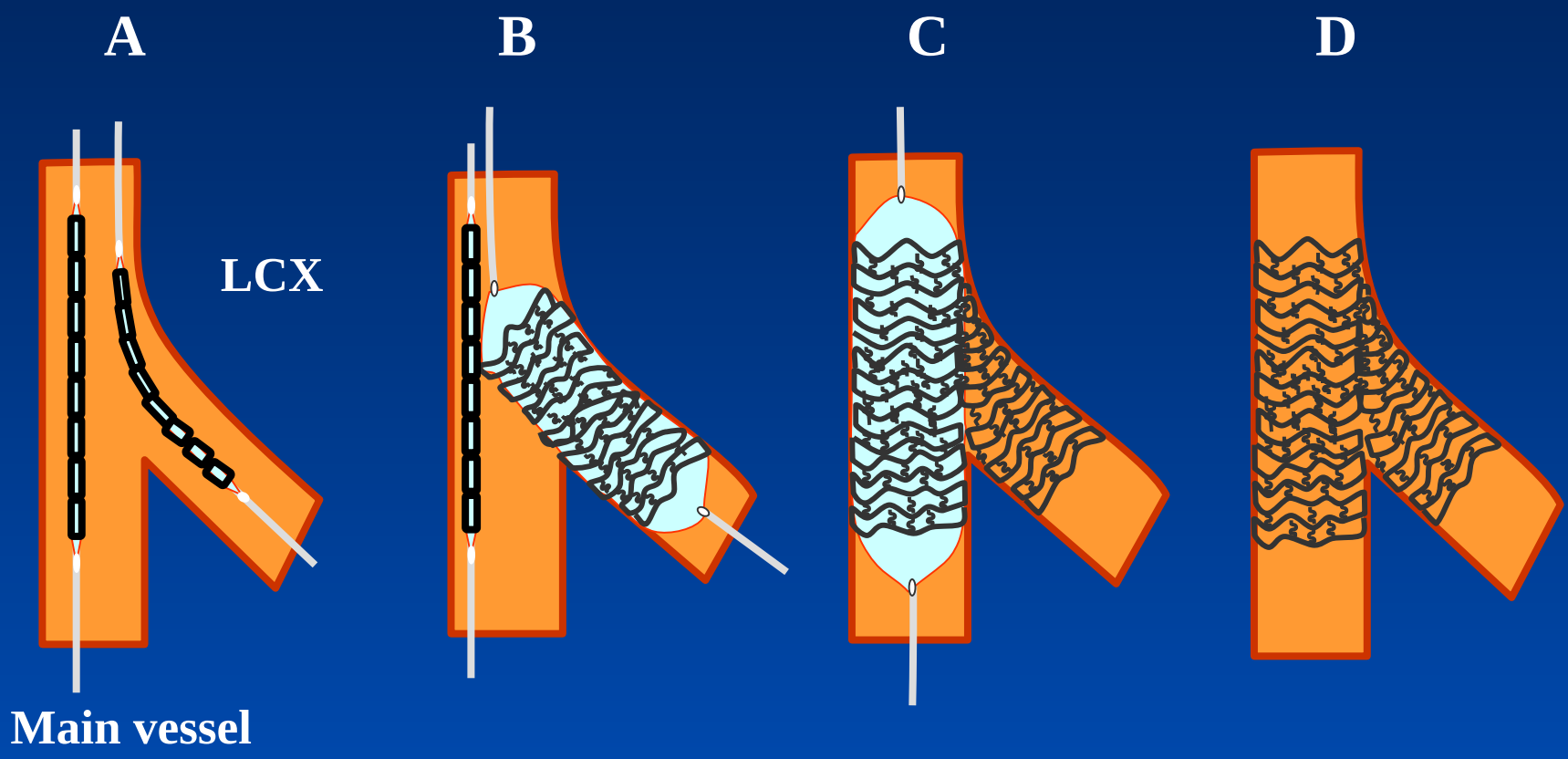
Kissing Stenting

Lesions with large LM and diseased LCX



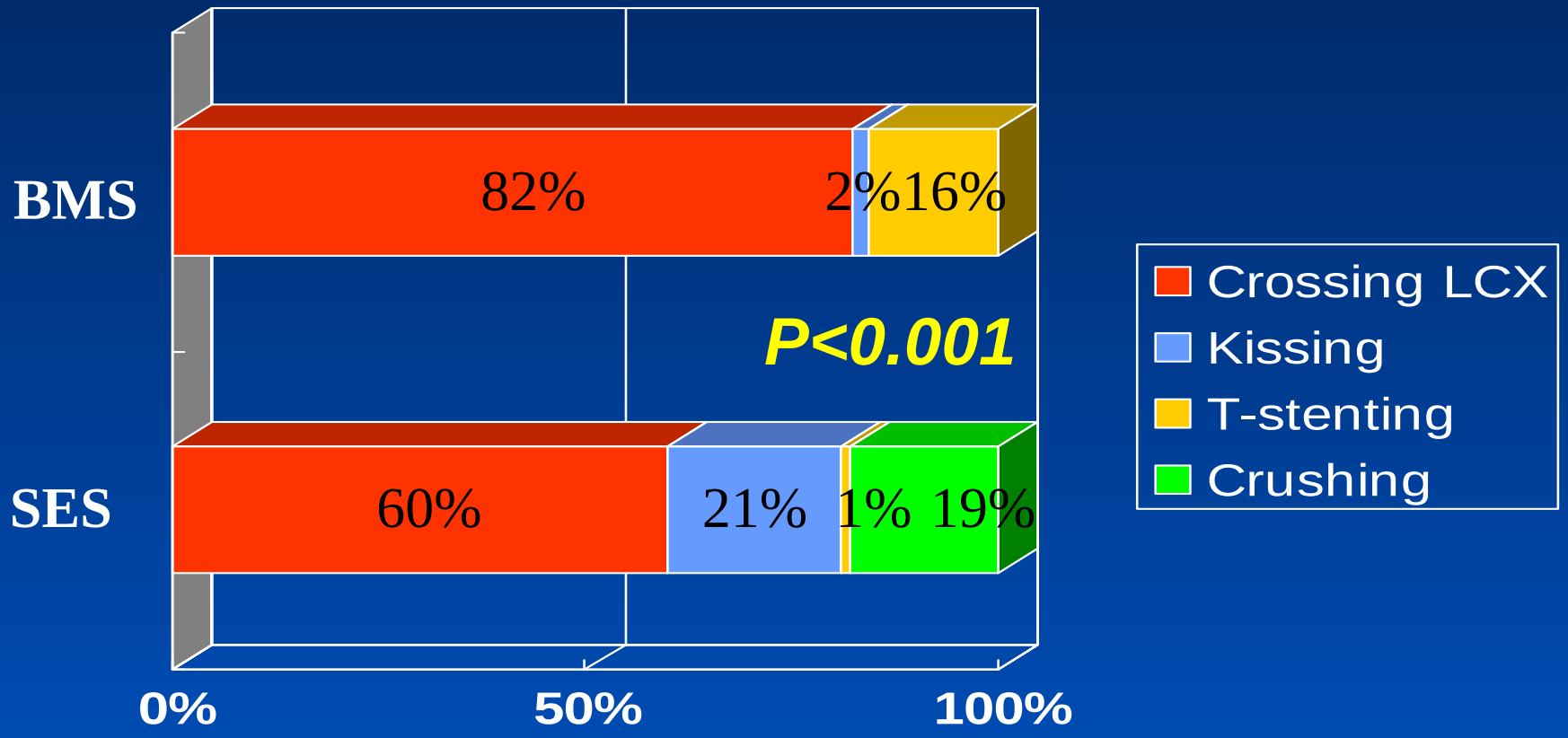
Stent Crushing

In moderate sized LM and diseased LCX



More Complex LM Bifurcation Stenting

116 pts with SES vs. 51 pts with BMS for bifurcation LM disease

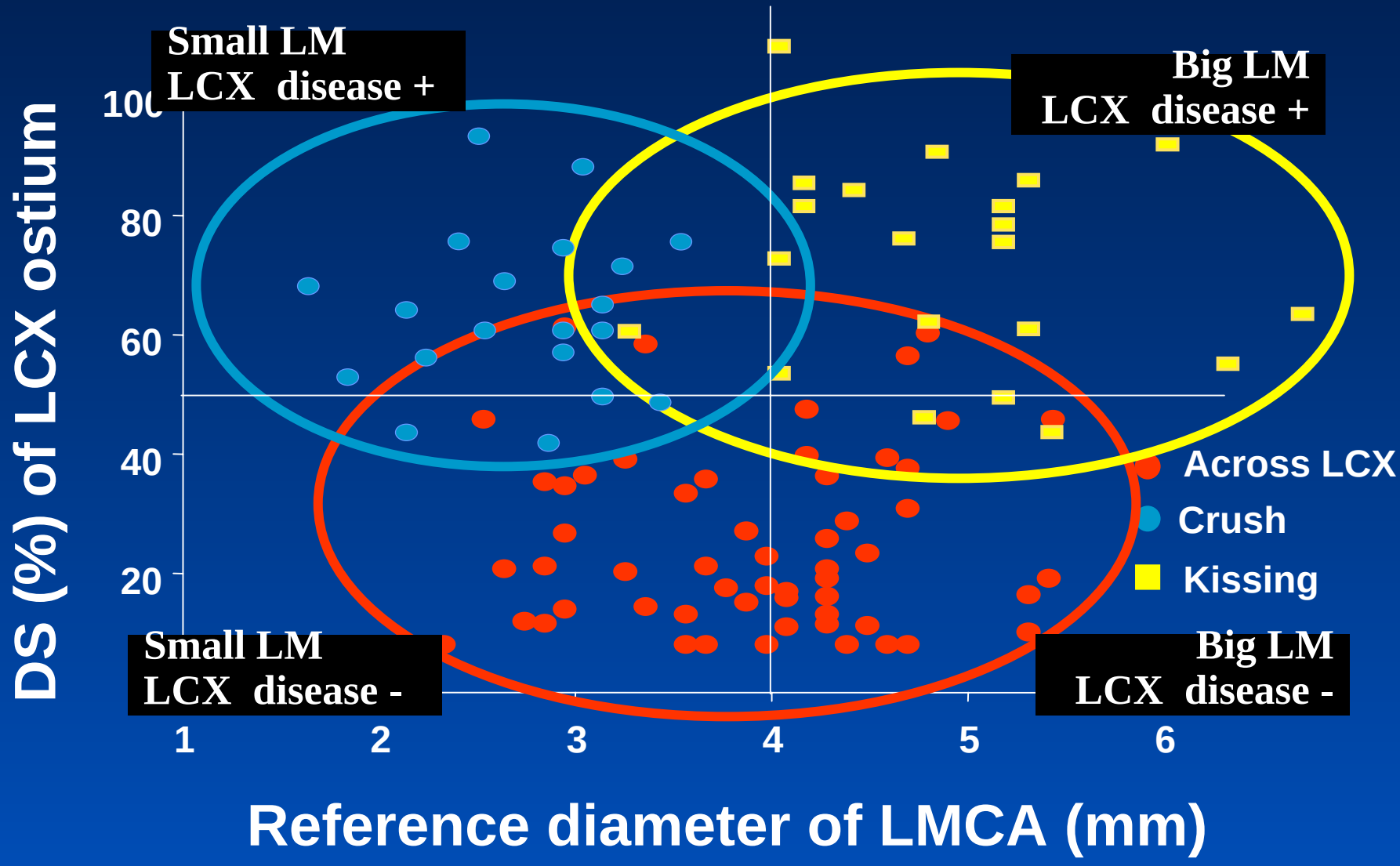


Park SJ et al, J Am Coll Cardiol 2005;45:351

116 LMCA bifurcation patients

Different treatment strategies can be applied according to LM reference vessel size and the existence of LCX ostial disease

Different Stenting Techniques



Comparison Data

Simple technique

Vs

Stenting Cross-over

Complex technique

Kissing Stenting
Stent Crushing

Baseline Data

Characteristic	Stent Cross-over	Complex tech.	P value
Patients	67	49	
Age, yr	59.6±12.0	60.6±8.5	0.604
Males	48 (71.6)	38 (77.6)	0.473
Cardiac risk factors			
Hypertension	34 (50.7)	17 (34.7)	0.085
Diabetes mellitus	24 (35.8)	11 (22.4)	0.121
Hypercholesterolemia	17 (25.4)	8 (16.3)	0.242
Current smoking	13 (19.4)	15 (30.6)	0.163
Previous PCI	8 (11.9)	9 (18.4)	0.334
ACS	34 (50.7)	29 (52.2)	0.368
Multivessel involvement	46 (68.7)	42 (85.7)	0.047
Left ventricular EF, %	59.2±8.0	61.5±7.3	0.110

Procedural Data

Characteristic	Cross-over.	Complex tech.	P value
Patients	67	49	
Multiple lesion intervention	25 (37.3)	18 (36.7)	0.949
Debulking atherectomy	4 (6.0)	3 (6.1)	0.973
Use of GP IIb/IIIa inhibitor	3 (4.5)	9 (18.4)	0.027
Intravascular ultrasound guidance	60 (89.6)	43 (87.8)	0.762
Stent length in main vessel, mm	31.8±19.3	35.4±18.3	0.314
Stents used per lesion	1.4±0.7	2.6±0.8	<0.001
Use of intra-aortic balloon pump	5 (7.5)	2 (4.1)	0.697

QCA Analysis: Main Vessel

	Cross-over	Complex tech.	*p*
Patients	67	49	
Follow-up CAG	57 (85)	41 (85)	
Proximal RVD, mm	3.61±0.72	3.77±0.74	0.240
Distal RVD, mm	2.81±0.60	2.75±0.45	0.557
MLD, mm			
Before procedure	1.11±0.47	1.01±0.47	0.269
After procedure	2.97±0.52	2.98±0.36	0.931
At follow-up	2.91±0.53	2.56±0.67	0.006
Lesion length, mm	25.8±17.1	26.2±14.5	0.918
Acute gain, mm	1.86±0.58	1.96±0.45	0.295
Late loss, mm	0.13±0.40	0.42±0.63	0.009

QCA Analysis: LCX

	Cross-over	Complex tech.	*p*
Patients	67	49	
Follow-up CAG	57 (85)	41 (85)	
Distal RVD, mm	2.78±0.66	2.64±0.49	0.209
MLD, mm			
Before procedure	2.25±0.76	1.39±0.64	<0.001
After procedure	2.21±0.77	2.65±0.40	<0.001
At follow-up	1.98±0.80	1.97±0.81	0.958
Acute gain, mm	-0.04±0.66	1.26±0.60	<0.001
Late loss, mm	0.20±0.59	0.69±0.72	<0.001

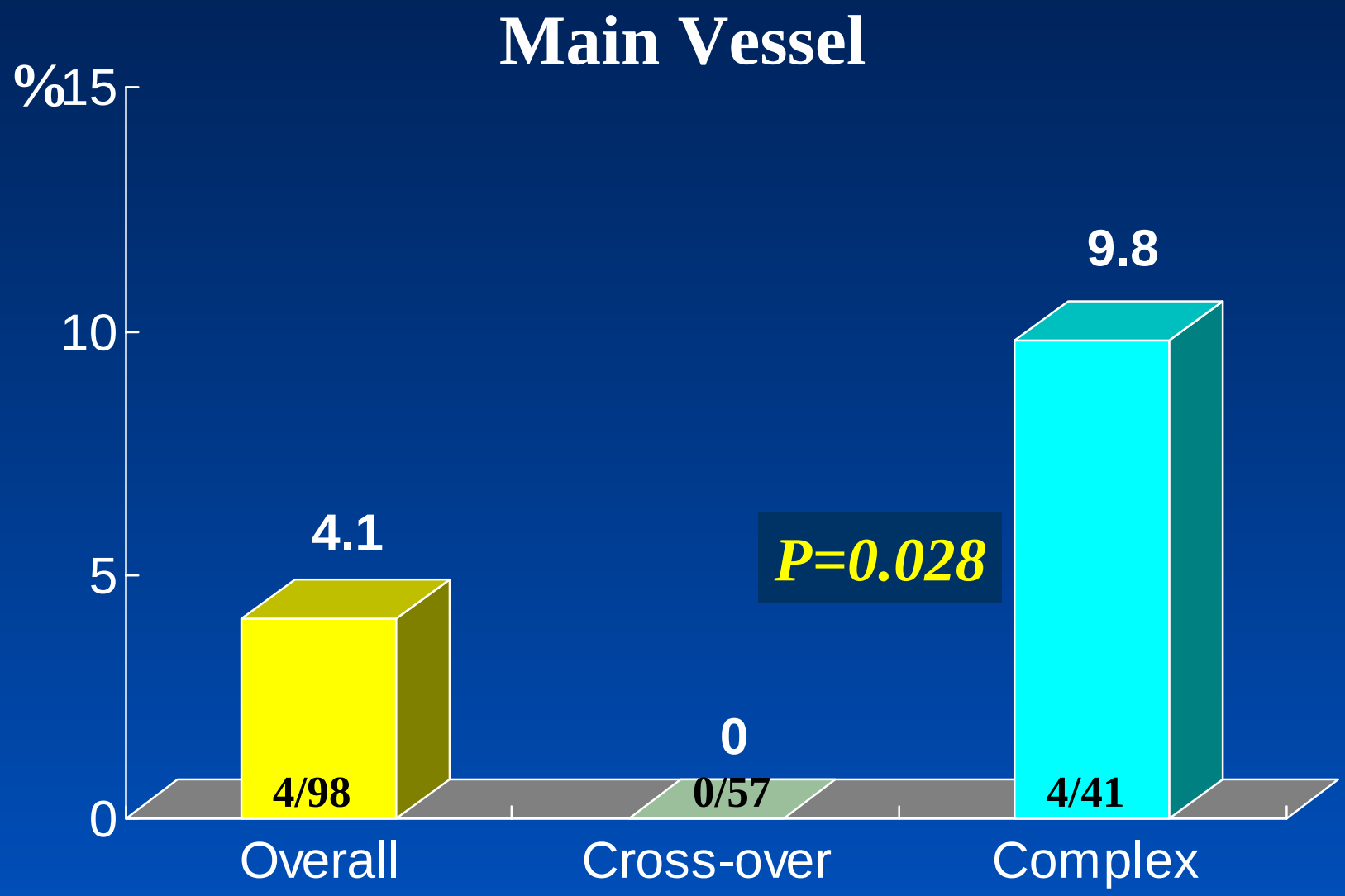
IVUS Analysis: Distal LM

	Cross-over	Complex tech.	*p*
Patients	46	39	
Before procedure			
EEM CSA, mm^2	21.7±6.0	20.6±4.0	0.391
Lumen CSA, mm^2	6.2±2.2	4.8±1.7	0.003
Plaque burden, %	70.8±8.9	76.1±9.1	0.012
After procedure			
EEM CSA, mm^2	23.9±5.7	24.0±3.9	0.905
Lumen CSA, mm^2	11.7±2.7	12.5±2.7	0.191
Plaque burden, %	50.2±8.4	47.7±8.8	0.184

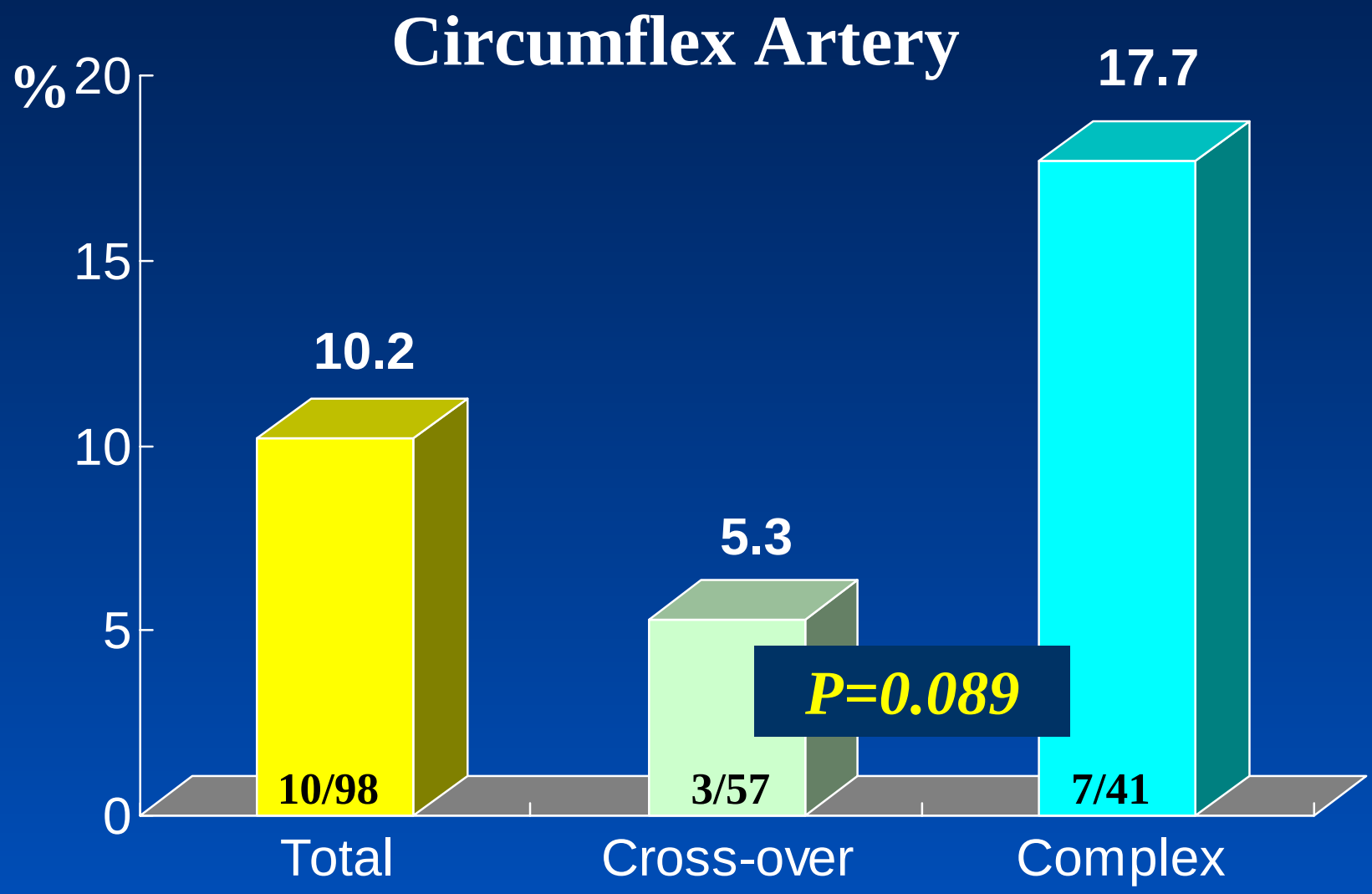
IVUS Analysis: Ostial LAD
Under-expansion in complex stenting

	Cross-over	Complex tech.	*p*
Patients	46	39	
Before procedure			
EEM CSA, mm^2	15.2±4.4	14.4±3.3	0.339
Lumen CSA, mm^2	4.5±2.0	4.2±1.8	0.548
Plaque burden, %	69.7±11.8	70.6±9.9	0.707
After procedure			
EEM CSA, mm^2	18.2±4.0	17.7±2.6	0.523
Lumen CSA, mm^2	9.7±2.0	8.0±1.7	<0.001
Plaque burden, %	45.8±10.2	54.8±7.5	<0.001

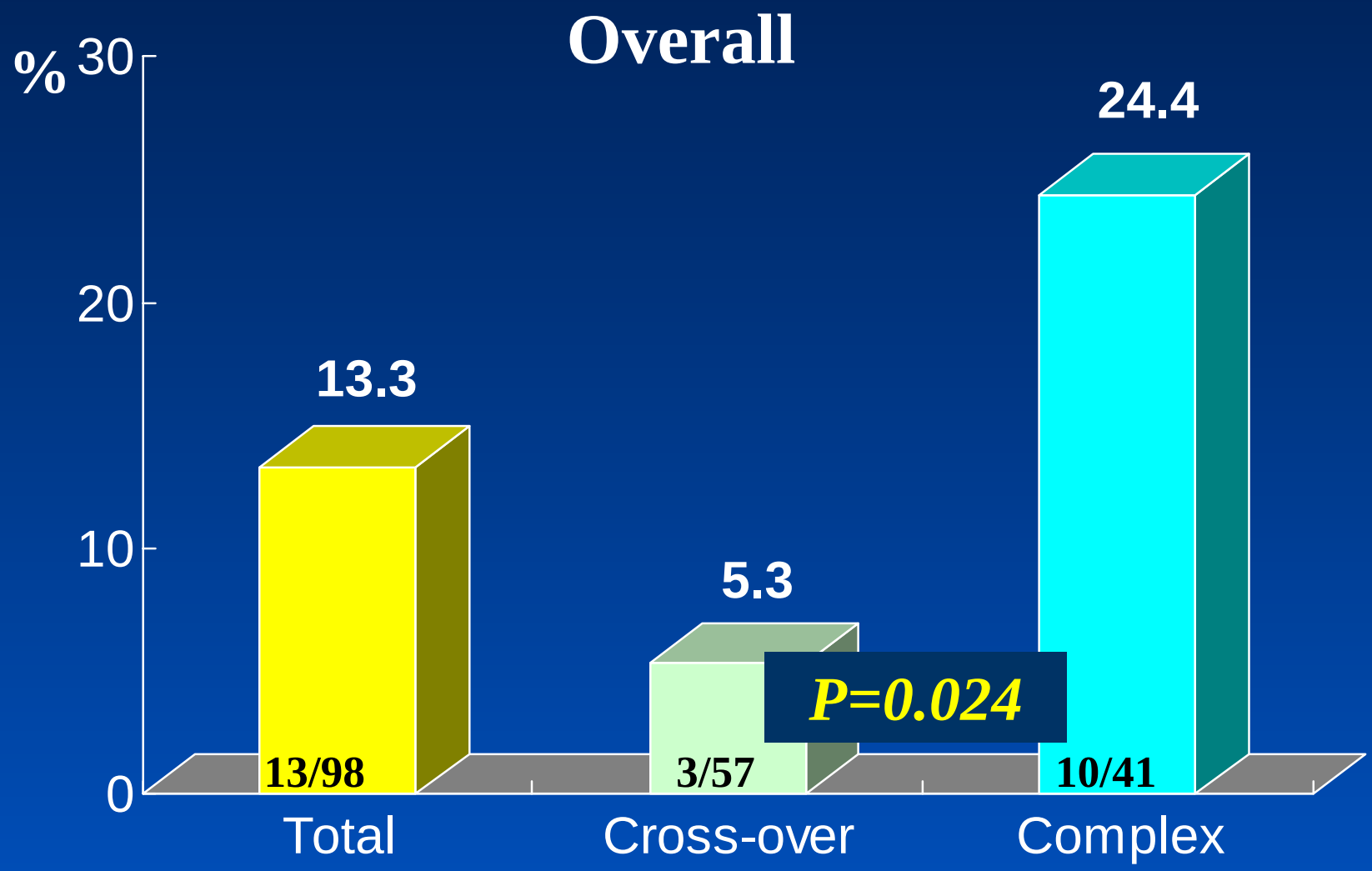
Restenosis Rate of Bifurcation



Restenosis Rate of Bifurcation

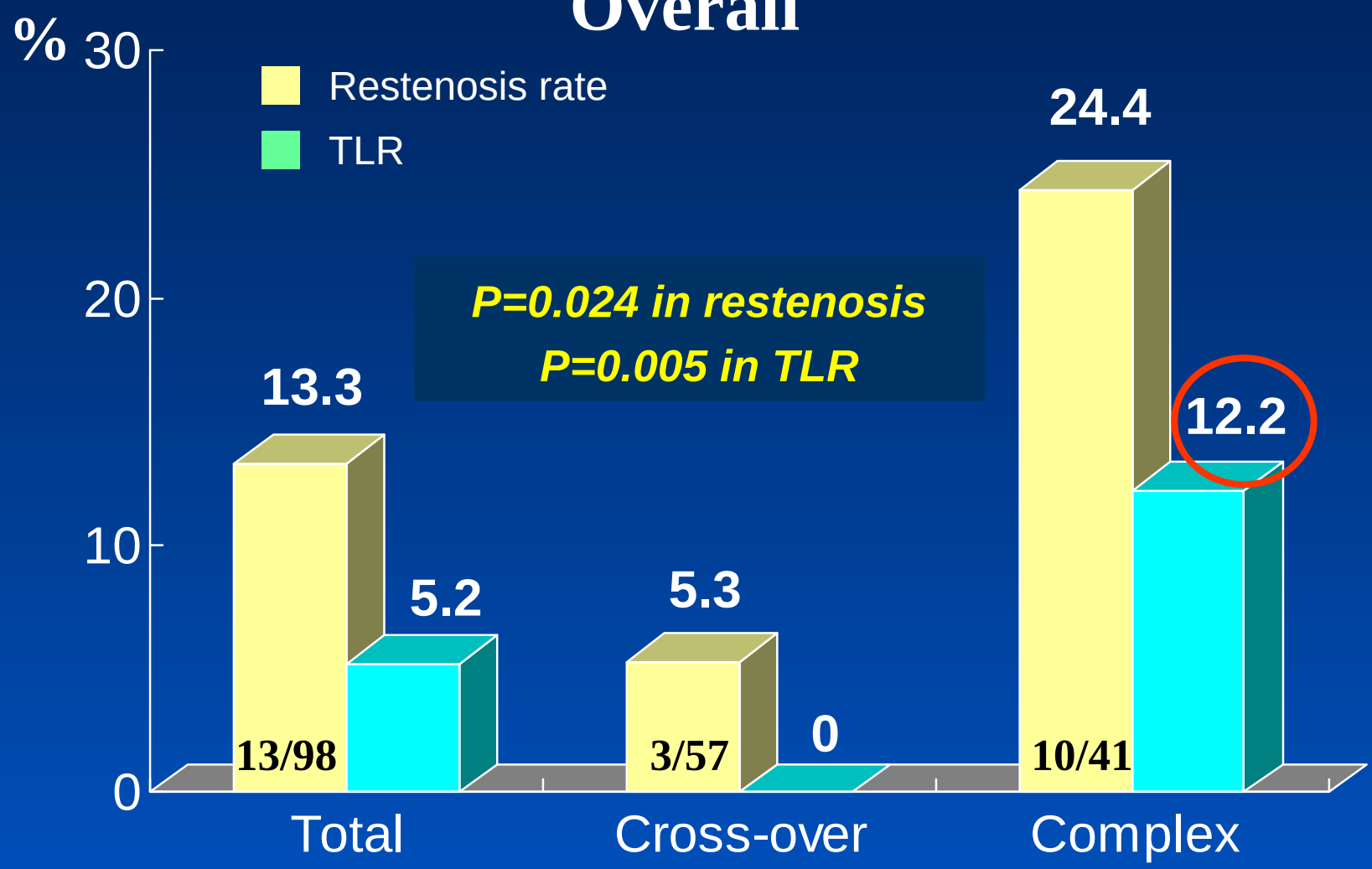


Restenosis Rate of Bifurcation



Rates of Restenosis and TLR of Bifurcation

Overall



Two Complex Strategies

Kissing Stenting

Vs.

Stent Crushing

QCA Analysis: Main Vessel

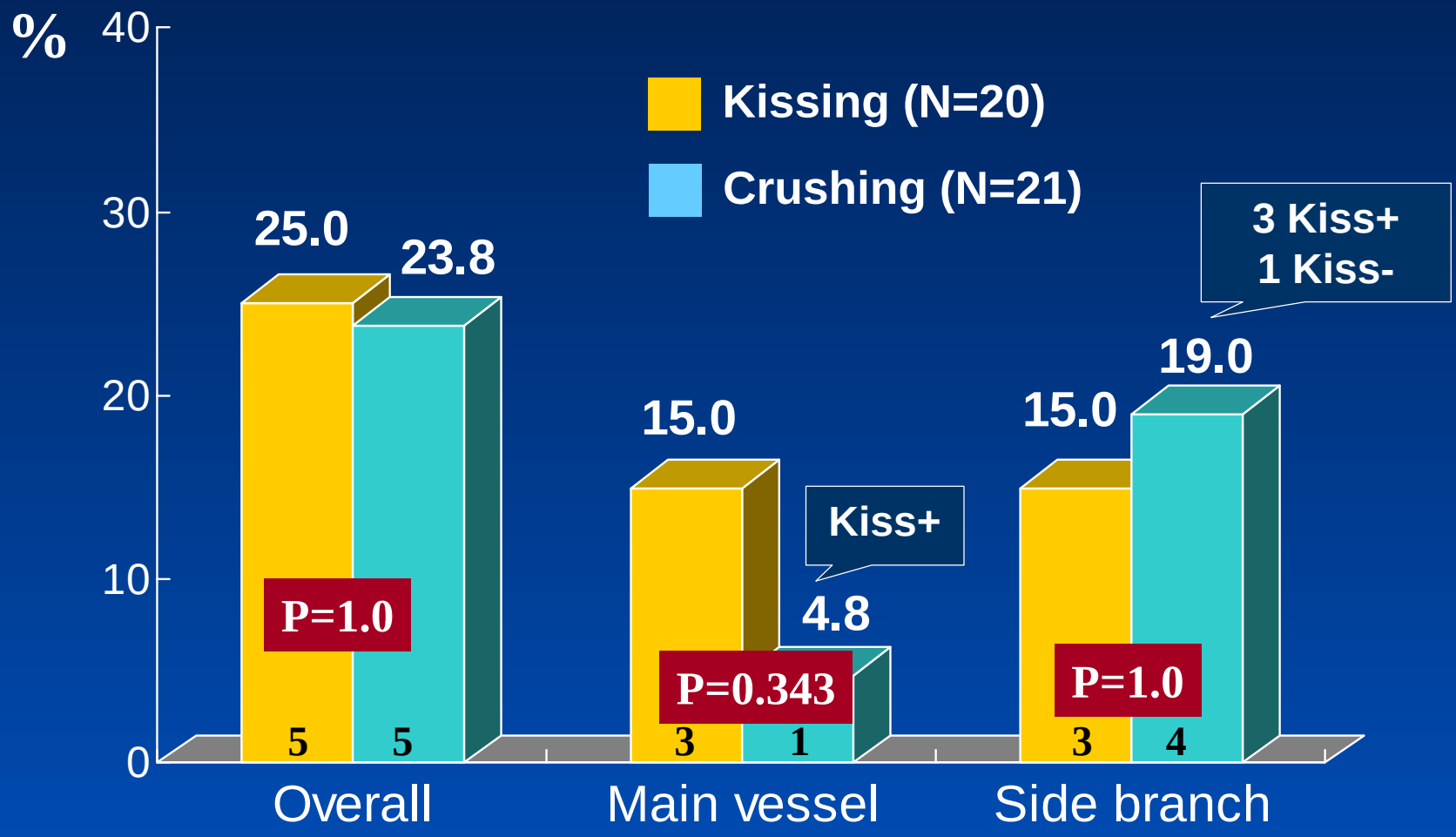
	Kissing stenting	Stent Crushing	*p*
Patients	24	25	
Follow-up CAG	20 (83)	21 (84)	
Proximal RVD, mm	4.09±0.69	3.46±0.65	0.002
Distal RVD, mm	2.92±0.42	2.59±0.42	0.009
MLD, mm			
Before procedure	0.91±0.52	1.12±0.40	0.111
After procedure	2.97±0.35	2.99±0.37	0.837
At follow-up	2.58±0.70	2.54±0.66	0.865
Lesion length, mm	23.7±13.3	28.6±15.4	0.253
Acute gain, mm	2.06±0.40	1.87±0.49	0.138
Late loss, mm	0.39±0.67	0.44±0.61	0.790

QCA Analysis: LCX

	Kissing stenting	Stent Crushing	*p*
Patients	24	25	
Follow-up CAG	20 (83)	21 (84)	
Distal RVD, mm	2.73±0.56	2.56±0.40	0.229
MLD, mm			
Before procedure	1.48±0.78	1.30±0.47	0.332
After procedure	2.70±0.36	2.60±0.44	0.387
At follow-up	2.03±0.78	1.91±0.85	0.646
Acute gain, mm	1.22±0.72	1.30±0.46	0.645
Late loss, mm	0.72±0.56	0.67±0.85	0.824
Restenosis	3 (15.0)	4 (19.0)	1.000

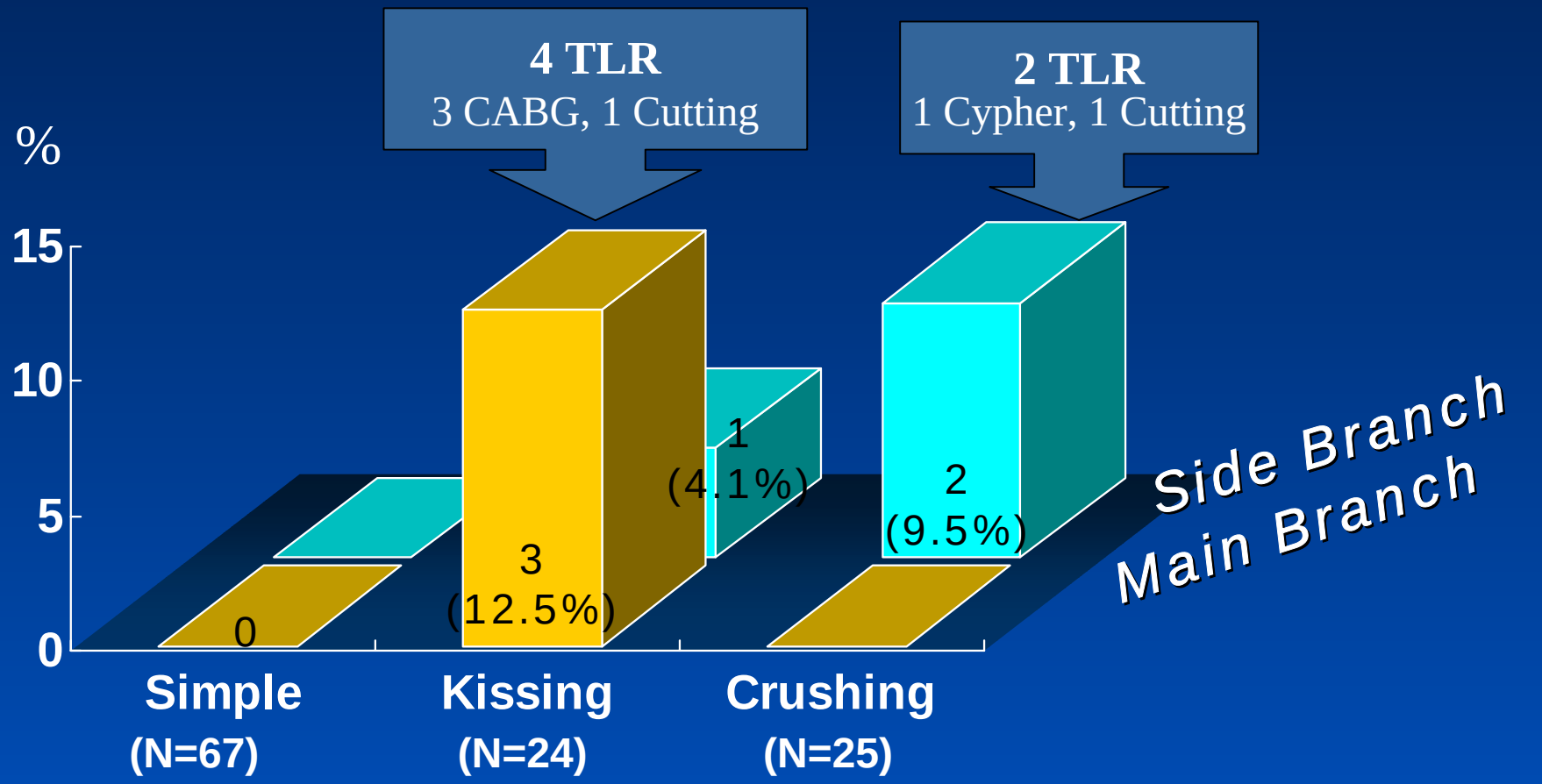
Kissing vs. Crush

Restenosis Rate



TLR : 5.2% in LM Bifurcation PCI

6/ 116 patients



What's different ?

Kissing Stenting	Crush Technique
TLR occurred mainly in Main vessel	TLR occurred mainly in LCX ostium, the side branch

Left main stenting with DES

Over-all

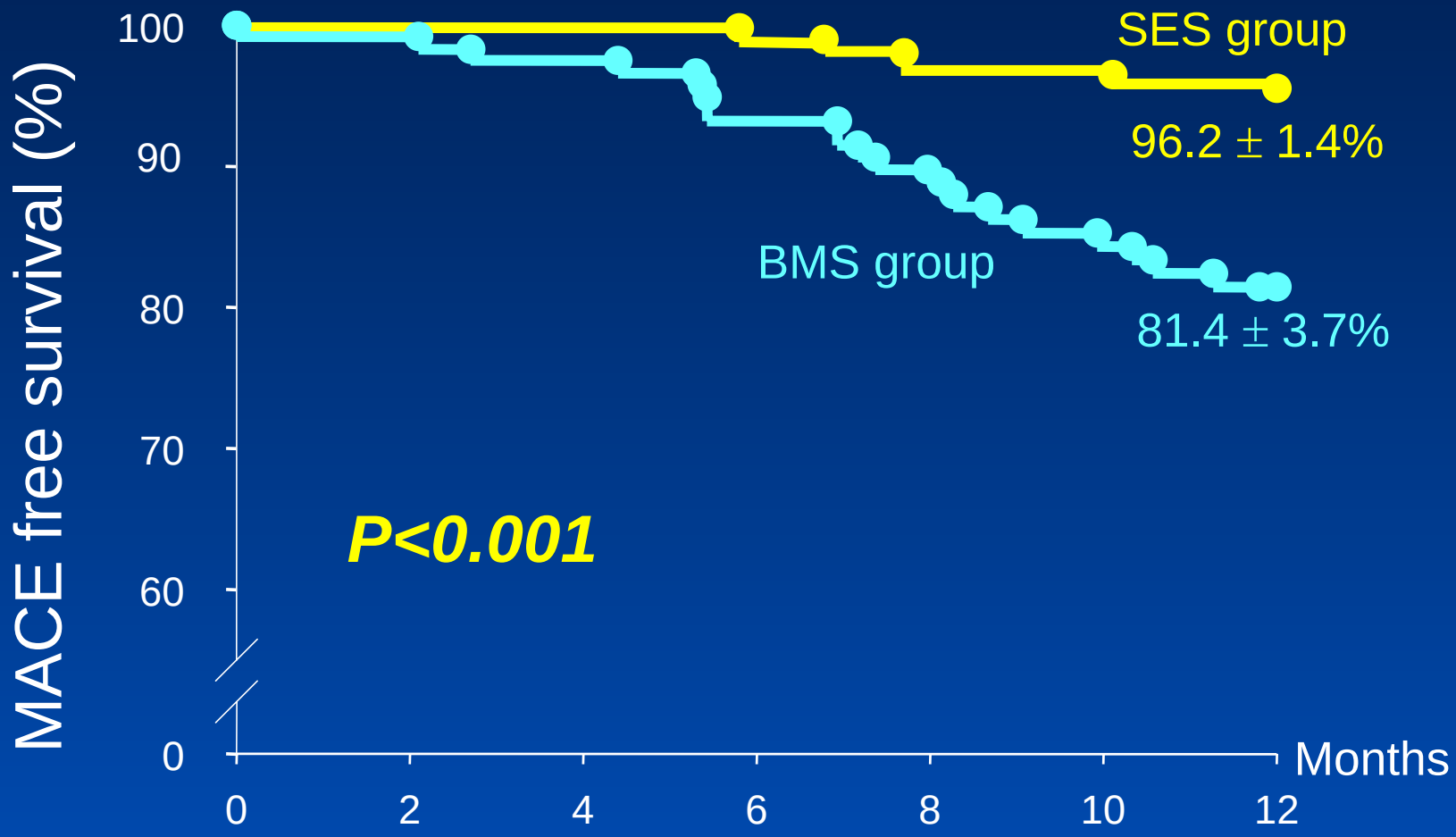
6-months Clinical Outcomes

	BMS N=121	SES N=163
Death	0	0
Q MI	0	0
Non-QMI	0	0
SAT	0	0
TLR *	24 (19.8%)	6 (3.7%)
CABG	13	2
PCI	11	0

* p<0.001

Park SJ et al, J Am Coll Cardiol 2005;45:351

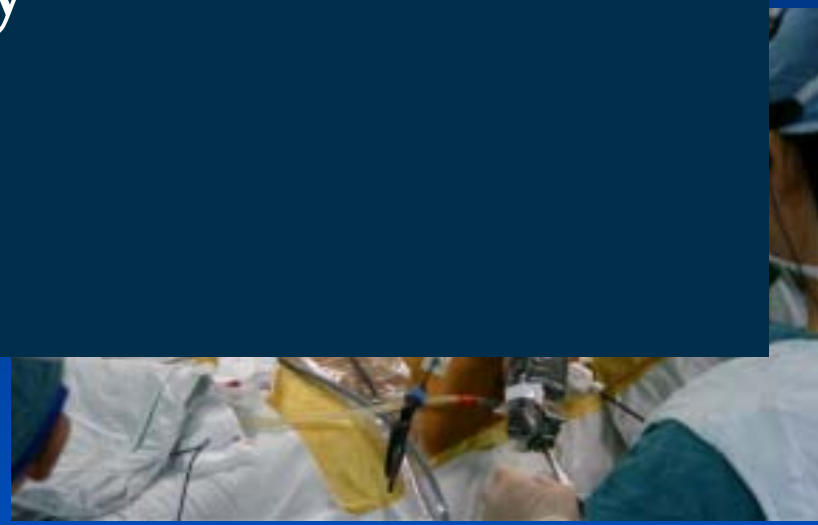
MACE free Survival at 1 year



Park SJ et al, J Am Coll Cardiol 2005;45:351

Bypass technique has improved !

- Use of arterial grafts
- Elimination of cardiopulmonary bypass
- Minimal invasive surgery
- Endoscopic approaches



In reality, Arterial grafts < 20%

No Restenosis
after stenting means…

It is working same as perfect multiple arterial grafts in CABG .

PCI for LMCA disease…

- Simple technique,
- Acceptable overall restenosis and TLR rate

PCI may be more effective alternative to bypass surgery if we could do appropriate treatment with DES

Restenosis and TLR rate in AMC data were acceptable

It is just the time

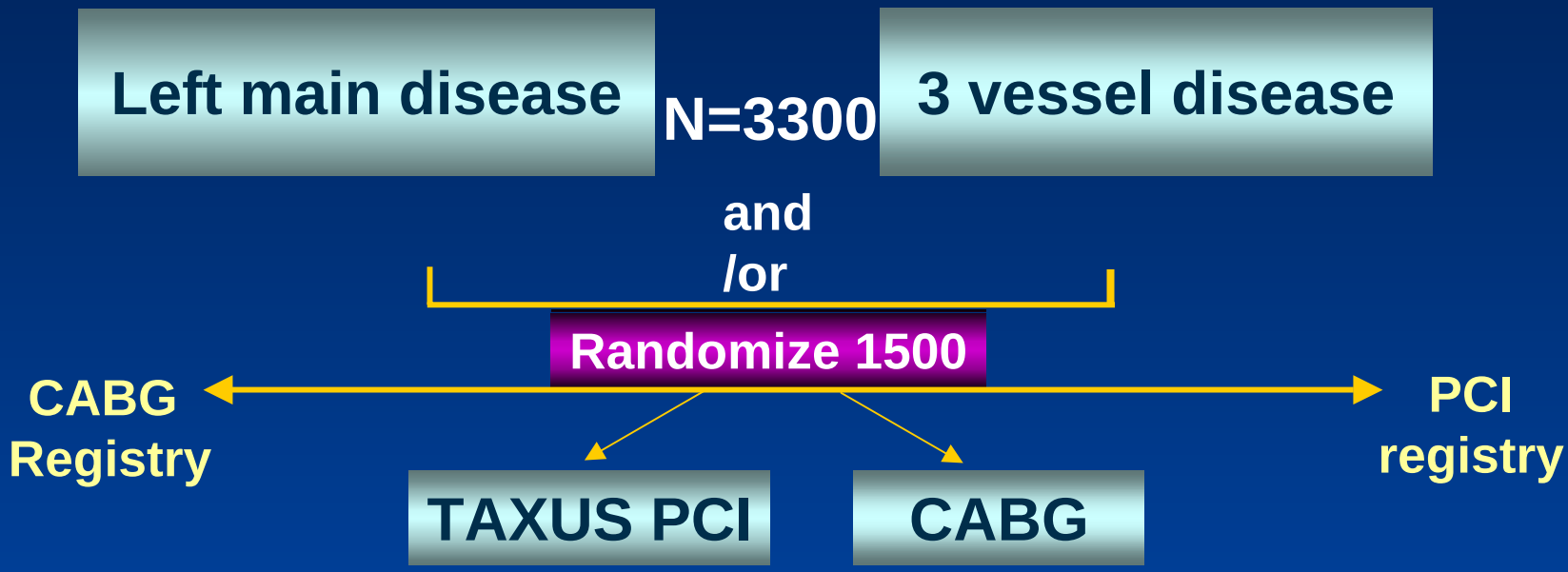
Comparison of DES with CABG

Large Randomized Studies

to find a more appropriate therapy for unprotected LM stenosis

SYNTAX Randomized Trial

De novo disease acceptable for revascularization



Primary NI endpiont – 1 year MACCE
All cause death, MI, cerebrovascular Event, repeat revascularization

Led by Patrick Serruys
And Frederick Mohr

COMBAT Trial

***COM*parison of *B*ypass surgery and *A*ngioplas*T*y using sirolimus electing stent in patients with left main coronary disease**

Eligibility LMCA stenosis patients with or without multivessel disease
Exclude: Patients with acute STEMI, CTO, CVA

50 Cardiac centers in 15 countries

Randomize over 1700 (1:1)

Cypher with optimal adjunctive medications

CABG with or without cardiopulmonary bypass

Registry group

CABG
PCI
Medication

PRIMARY Endpoint: 2-year death, MI, stroke
SECONDARY Endpoints: 6-mo, 2-yr CAG, QOL
PI: Seung-Jung Park, Martin B. Leon

11th

Angioplasty Summit 2006

TCT Asia Pacific

April 26 - 28, 2006

New Convention, WakerHill

Seoul,Korea

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