

Percutaneous Intervention for Unprotected Left Main Stenosis

Where we are,
Where we are going...

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Current Recommendation for unprotected LMCA Stenosis

- Class IIb C in ESC guideline (2005) and Class III in ACC guideline (2006) in patients eligible for CABG
- Class III is the conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/ effective and in some cases may be harmful.

Compare to Surgery,

Limited Data

High Mortality in PCI ?

In the era of BMS...

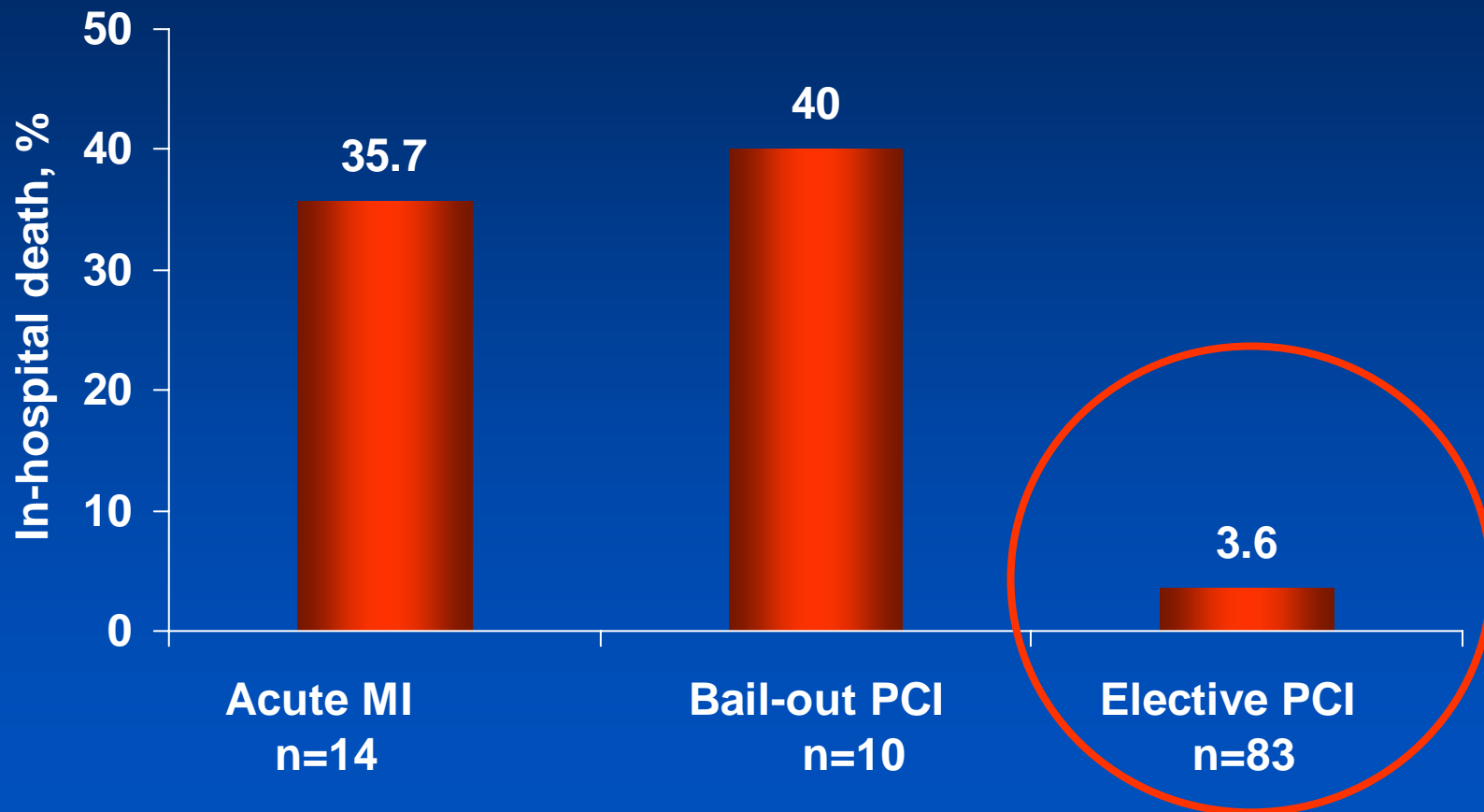


Procedural Success (BMS) in Left Main PCI Series

Study	Site(s)	Years	Pts #	Procedure success
Park et al, 1998	Asan Medical Center & WHC	1995-1997	42	100%
Silvestri et al	Marcielle, France	1993-1998	140	100%
Park et al	Asan Medical Center & WHC	1995-1997	42	98.9%
<p>More than 1,300 patients were included</p>				
Brueren et al	Nieuwegein, Netherlands	1991-2001	71	94.4%
Takagi et al	Columbus Hospital and San Raffaele Hospital, Milan	1993-2001	67	91%
Ellis et al	16 hospitals (ULTIMA Registry)	1994-1996	107	98%

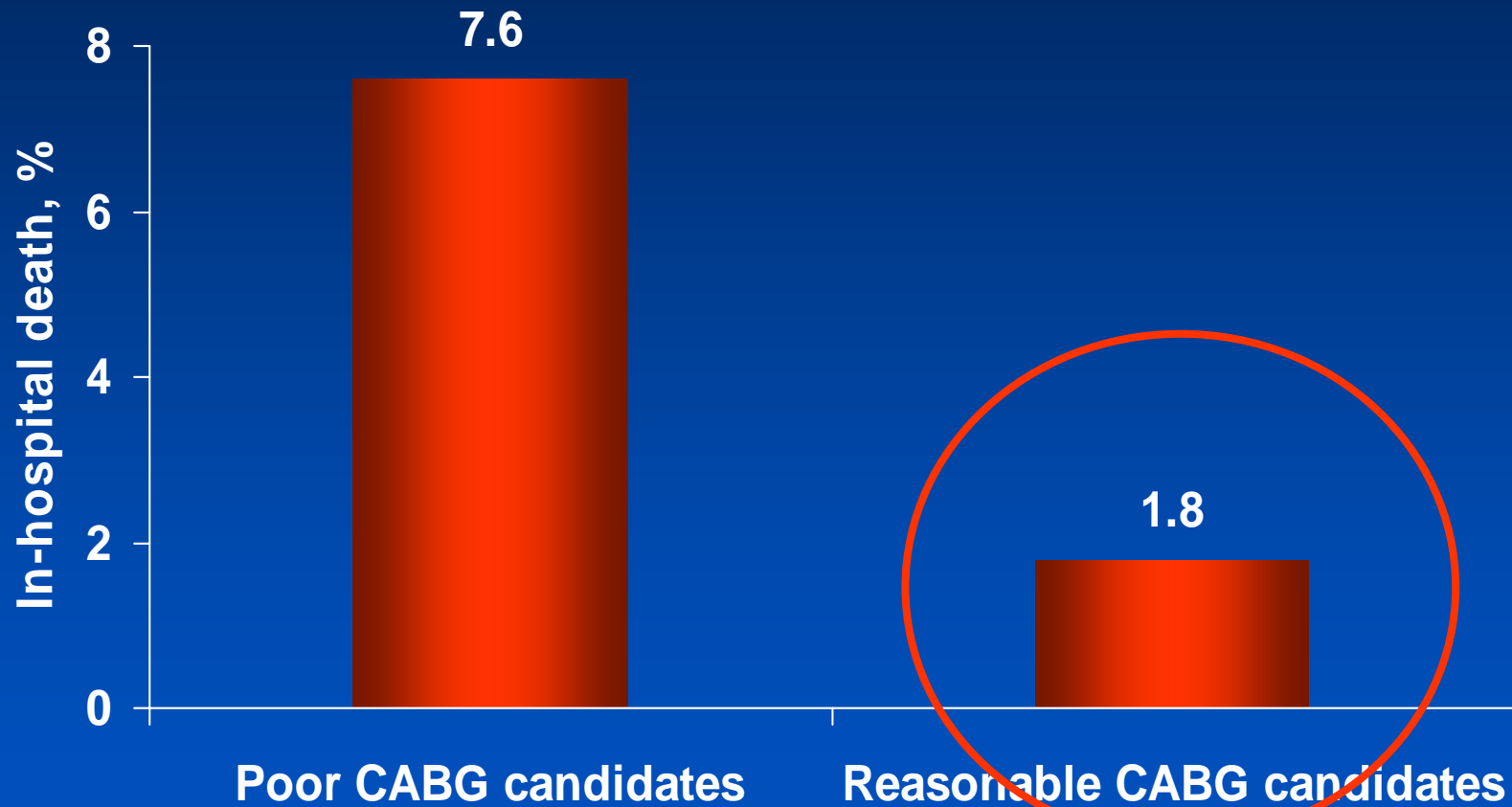
In-Hospital Mortality

In High-Risk vs. Low-Risk Patients



Kosuga et al, AJC, 1999

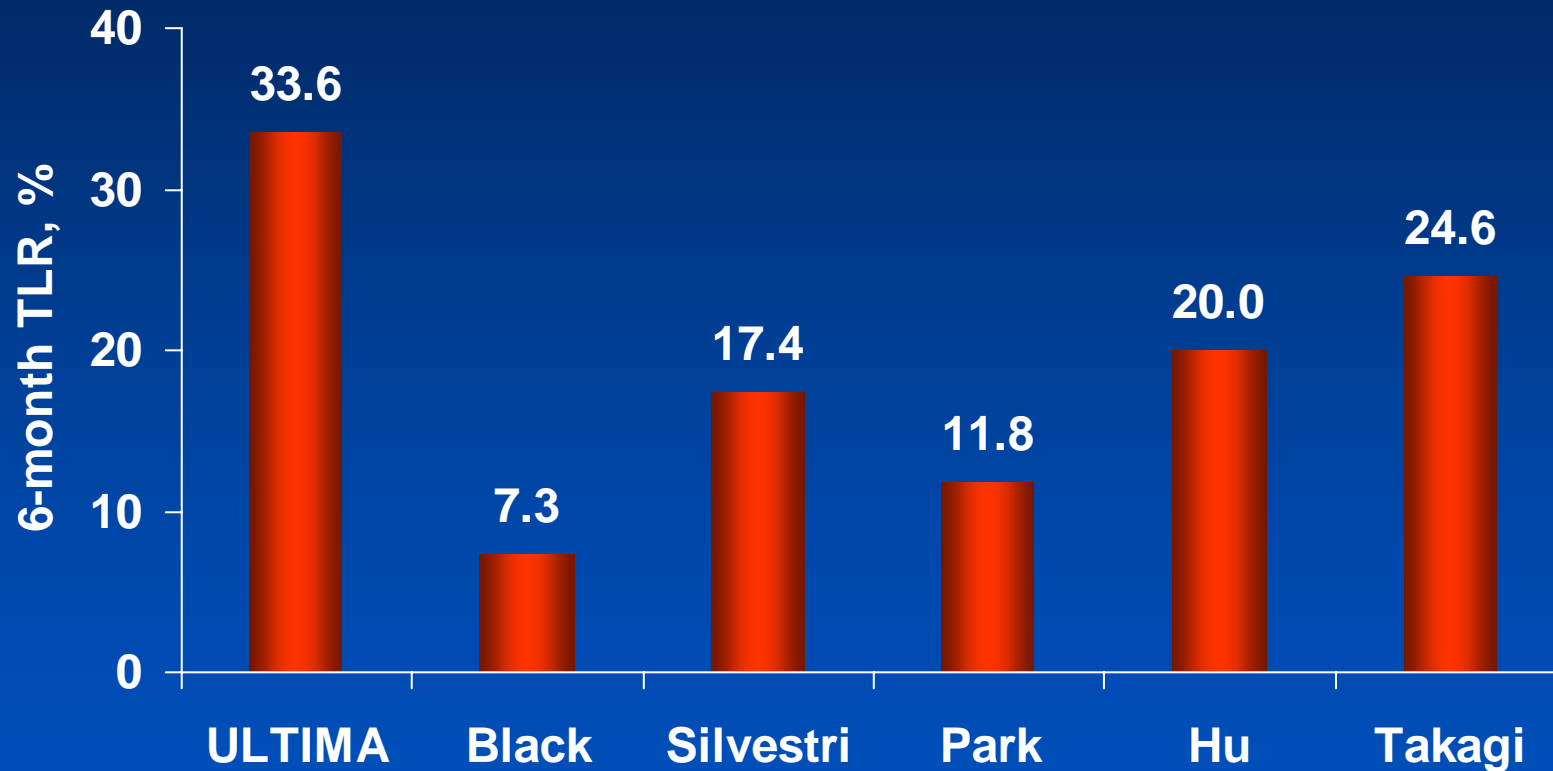
Low in-Hospital Mortality for good candidate for Surgery



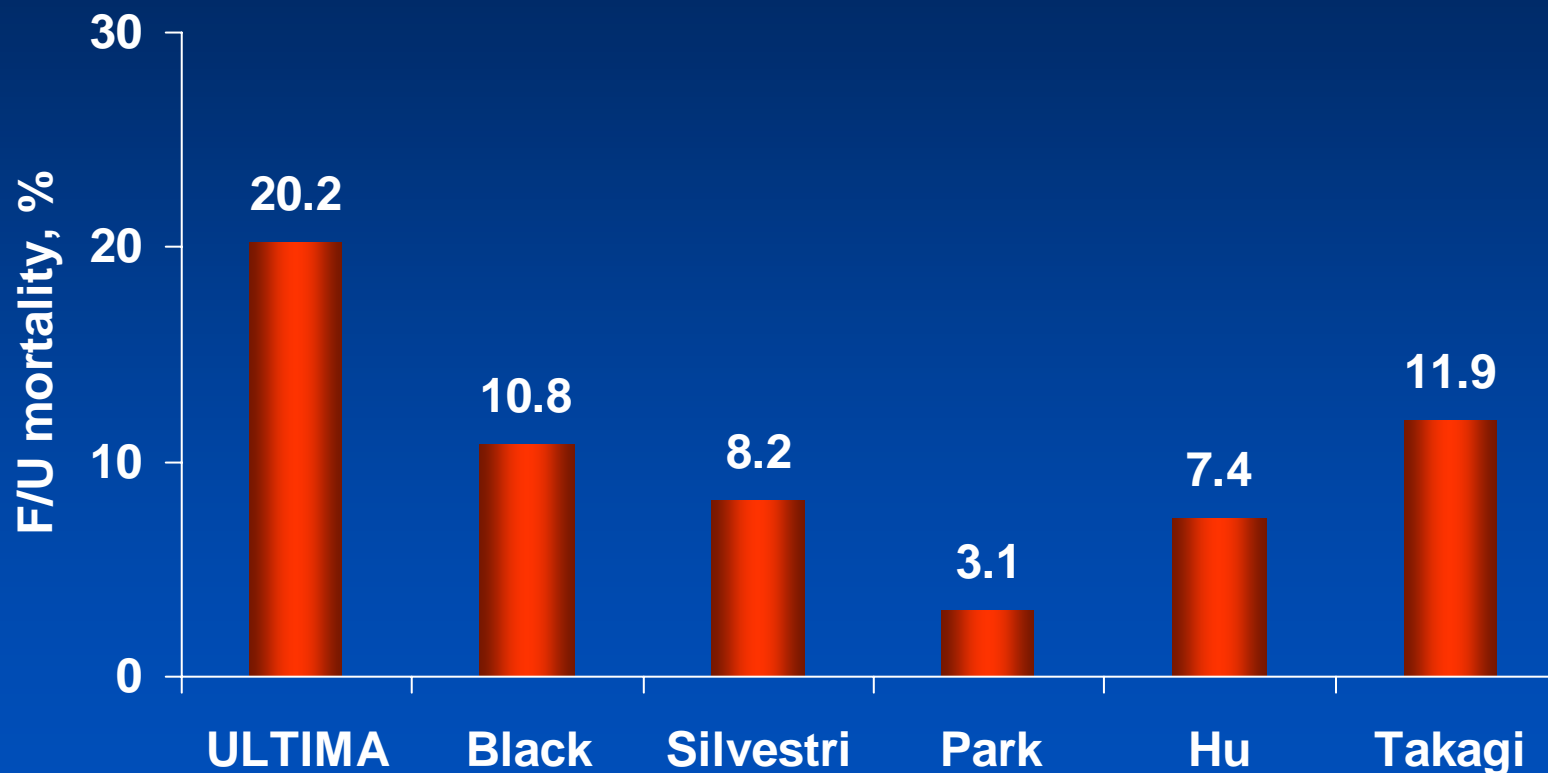
Black et al, JACC, 2001.

Six-Month TLR

in PCI Series on Unprotected LM



Long-term Mortality at Follow-up in PCI Series on Unprotected LM



F/U duration,
mean (months)

12

7.3

12

25.5

6

31

Multivariate Predictors of All-Cause Mortality: ULTIMA Registry

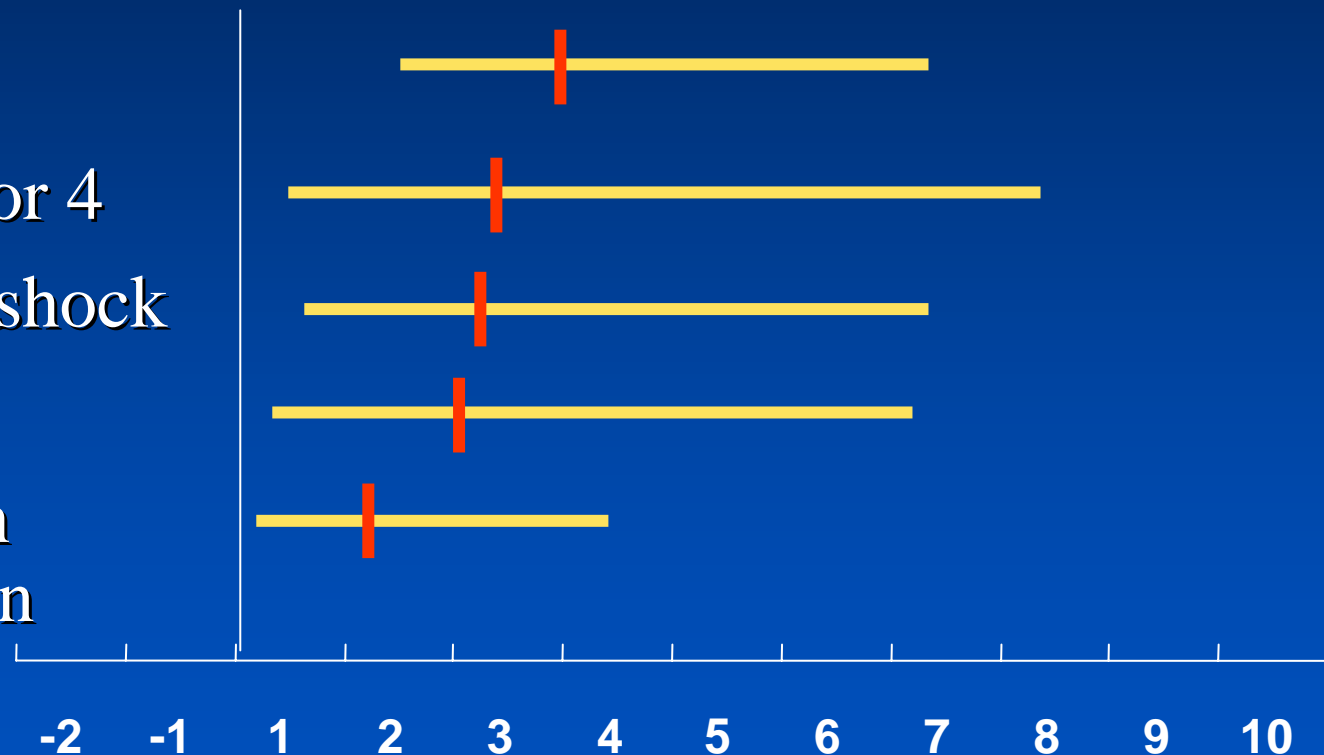
LVEF $\leq 30\%$

MR grade 3 or 4

Cardiogenic shock

Cr $\geq 2\text{mg/dL}$

Severe lesion
calcification



Tan et al, Circulation, 2001

Multivariate Predictors of All-Cause MI /Death : AMC data

324 patients who underwent elective coronary stenting for the treatment of unprotected LMCA

	Hazard ratio	95% CI	P value
High EuroSCORE (≥ 6)	3.362	1.181 – 9.574	0.023
No. of total used stents	1.792	1.021 – 3.146	0.042
Use of GP IIb/IIIa inhibitor	8.640	2.722 – 27.418	<0.001

Unpublished AMC data, 2006

Lessons from data of PCI on unprotected LM (BMS)

- In the reviewed series, outcomes of PCI are highly correlated with pre-procedure clinical risk profile of the patient (low mortality in low risk patients)
- Good candidate for surgery is good candidate for PCI

Compare to Surgery,

Efficacy concerns...

One-year outcomes of coronary artery bypass graft surgery versus percutaneous coronary intervention with multiple stenting for multisystem disease: A meta-analysis of individual patient data from randomized clinical trials

Nestor Mercado, MD, PhD,^{a,f} William Wijns, MD, PhD,^b Patrick W. Serruys, MD, PhD,^a Ulrich Sigwart, MD,^c Marcus D. Flather, MBBS,^d Rodney H. Stables, DM, FRCP,^e William W. O'Neill, MD,^f Alfredo Rodriguez, MD,^g Pedro A. Lemos, MD, PhD,^a Whady A. Hueb, MD,^h Bernard J. Gersh, MB, ChB, DPhil,ⁱ Jean Booth, MSc,^d and Eric Boersma, PhD^a

The Journal of Thoracic and Cardiovascular Surgery • August 2005

Included trials:

- ARTS
- SoS
- ERACI-2
- MASS-2

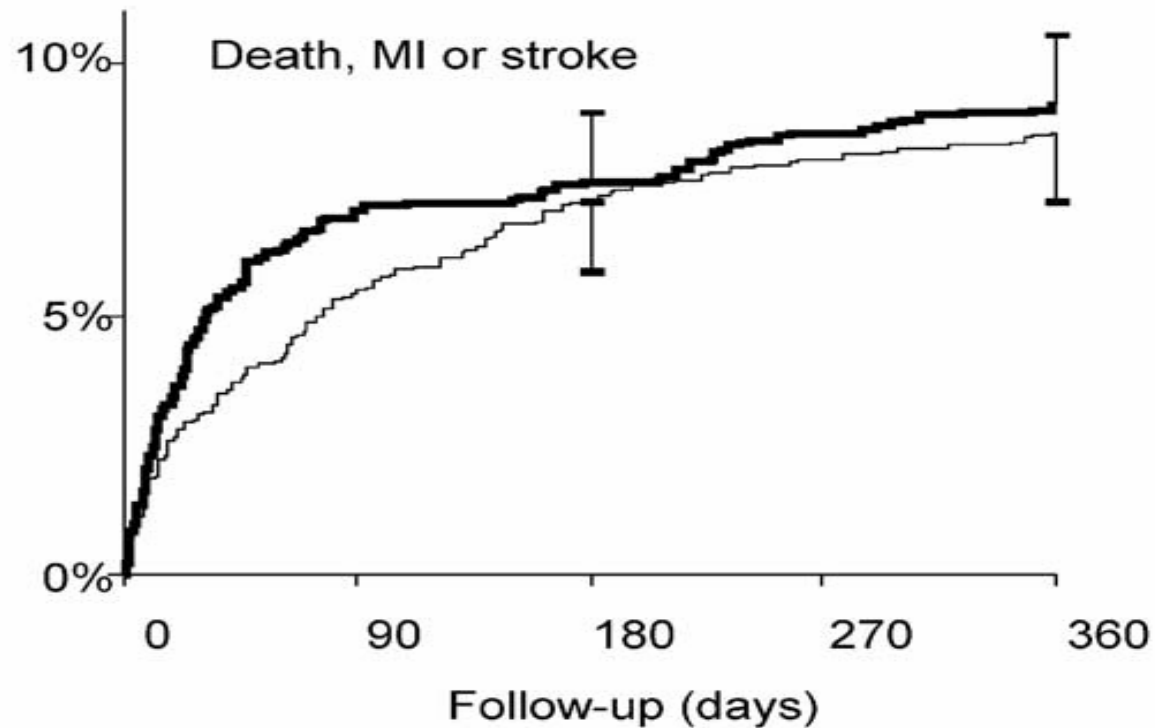
Four CABG vs. Stent Assisted PCI trials

	ARTS	SoS	ERACI-2	MASS-2
Enrollment period	1997-1998	1996-1999	1996-1998	1995-2000
Number of screened pts	NA	NA	2,759	18,692
Number of eligible pts	NA	NA	1,076	2,076
Number of randomized pts	1,076	1,076	1,076	2,076
Primary endpoint	12-month MACCE free survival	Repeat revascularization	MACE within 30 days and need for repeat revascularization at 30 days	Composite of cardiac death, MI, and angina requiring revascularization
Exclusion criteria	<ul style="list-style-type: none"> LMCA stenosis Transmural MI within previous week 	<ul style="list-style-type: none"> MI within 48 hours 	<ul style="list-style-type: none"> MI within 48 hours 	<ul style="list-style-type: none"> LMCA stenosis

More than 3,000 patients were randomized

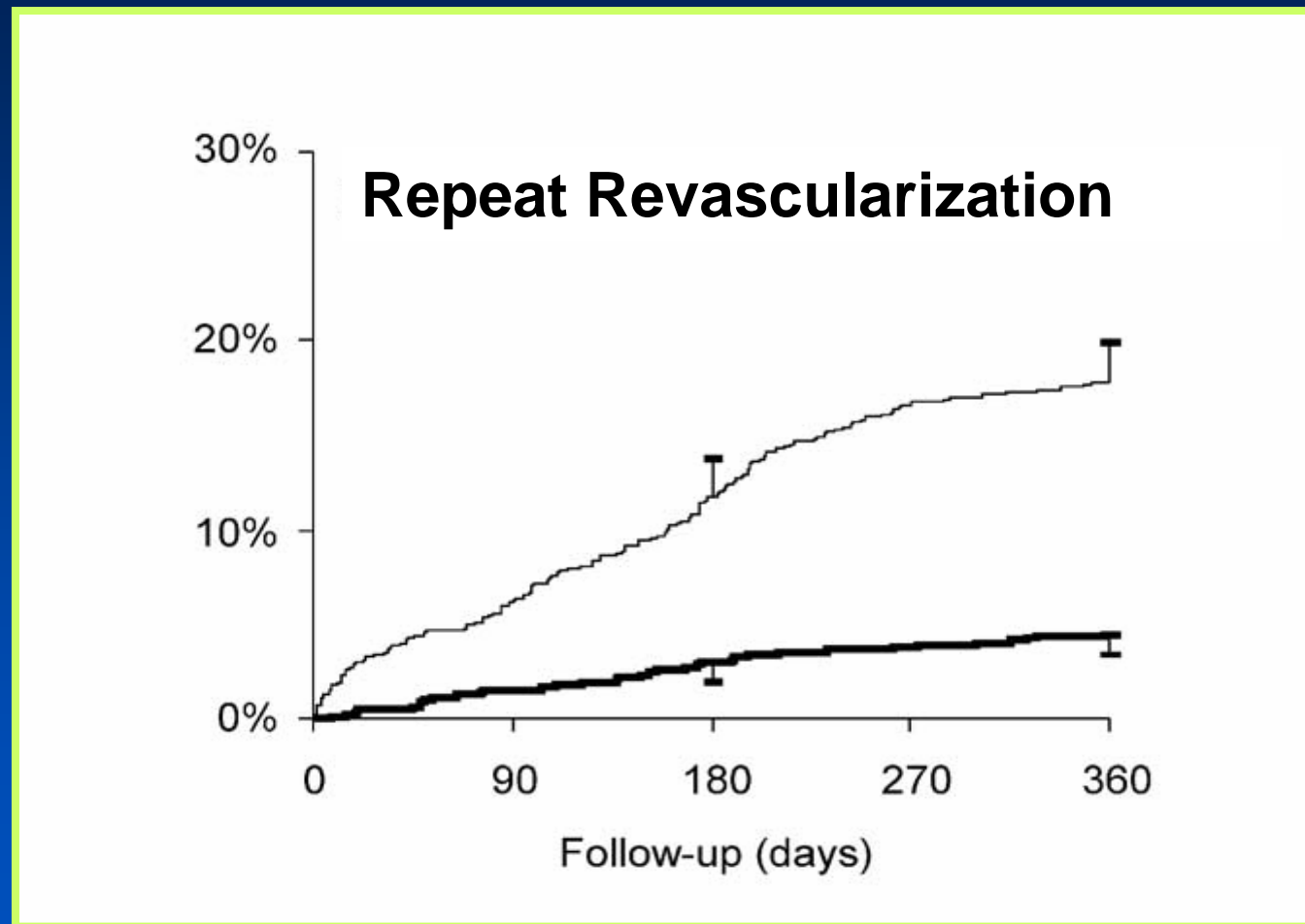
Mercado et al, J thoracic Cardiovasc Surg, 2005

One-year Rates of Death, MI or Stroke in 4 CABG vs. Stent Assisted PCI Trials



Mercado et al, J thoracic Cardiovasc Surg, 2005

One-year Rates of Repeat Revascularization in 4 CABG vs. Stent Assisted PCI Trials



Mercado et al, J thoracic Cardiovasc Surg, 2005

Efficacy concerns of PCI (BMS) for LM disease

Compare to surgery

- PCI have comparable clinical outcomes at least one year follow-up period. There is no difference in rates of death, MI or stroke.
- Repeat revascularization is the only problem in PCI

In the era of DES...

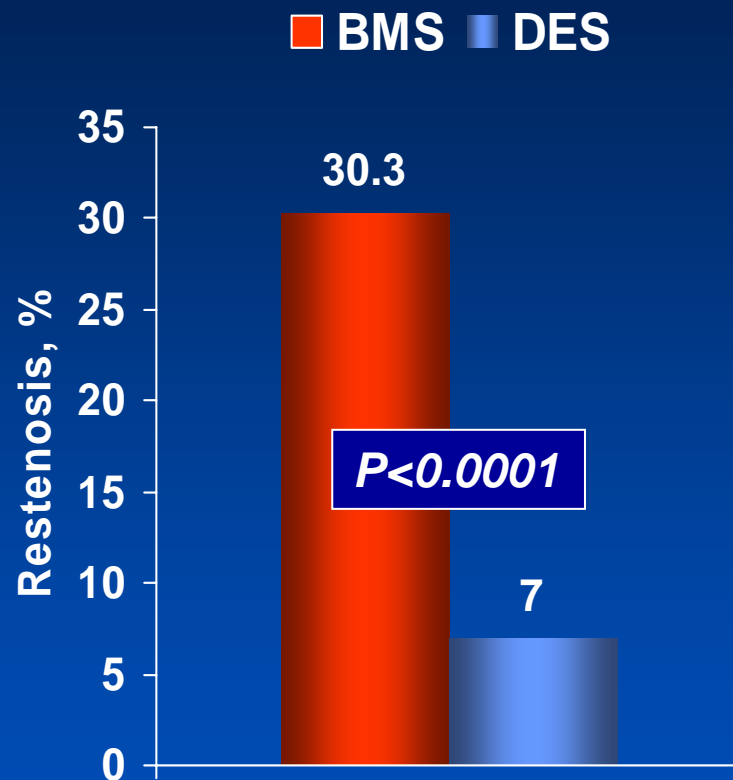


In-Hospital Outcomes: DES in Left Main PCI Series

Series	Procedure success	Death
Park et al	100%	0
Chieffo et al	100%	0
Valcin et al		1.0%
More than 1,000 patients were included		
Gersmick et al	100%	0
Lefevre et al*	96.9%	0.8%
Costa et al*	100%	0
Nakamura et al*	100%	0
Di Salvo et al*	98.7%	0

* Abstracts

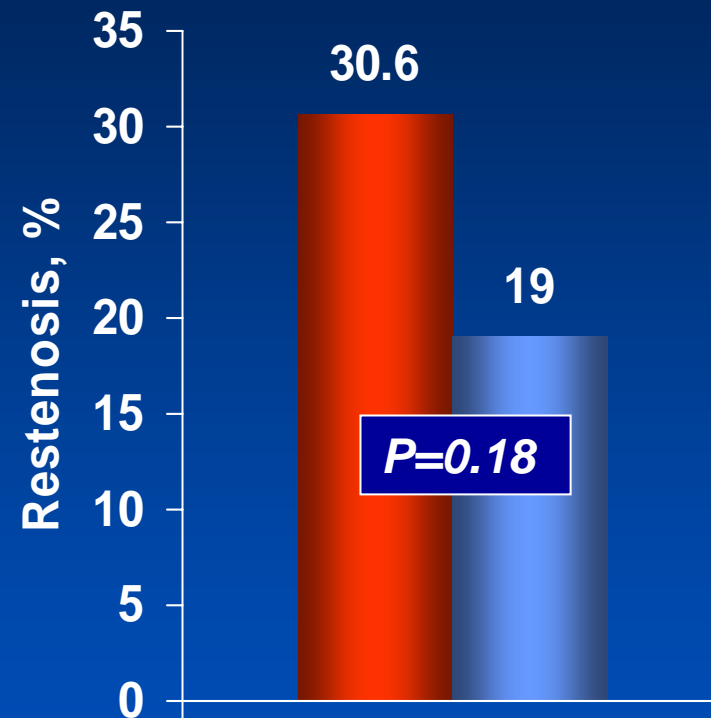
Angiographic Restenosis in Two DES vs. BMS Left Main PCI Series



Seoul

Follow-up

6 months



Milan

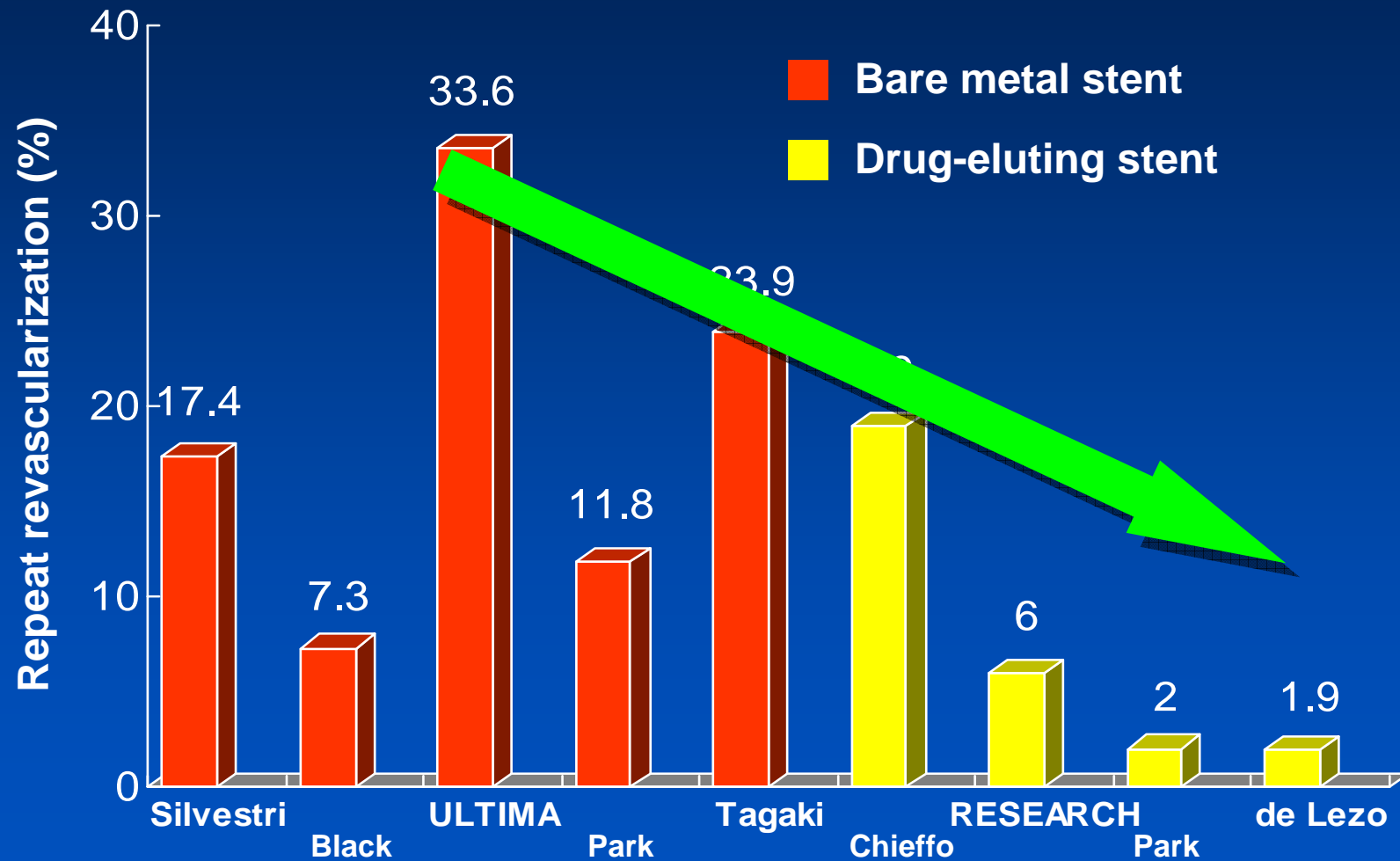
4 to 8 months

Park et al, JACC 2005

Chieffo et al, Circulation 2005

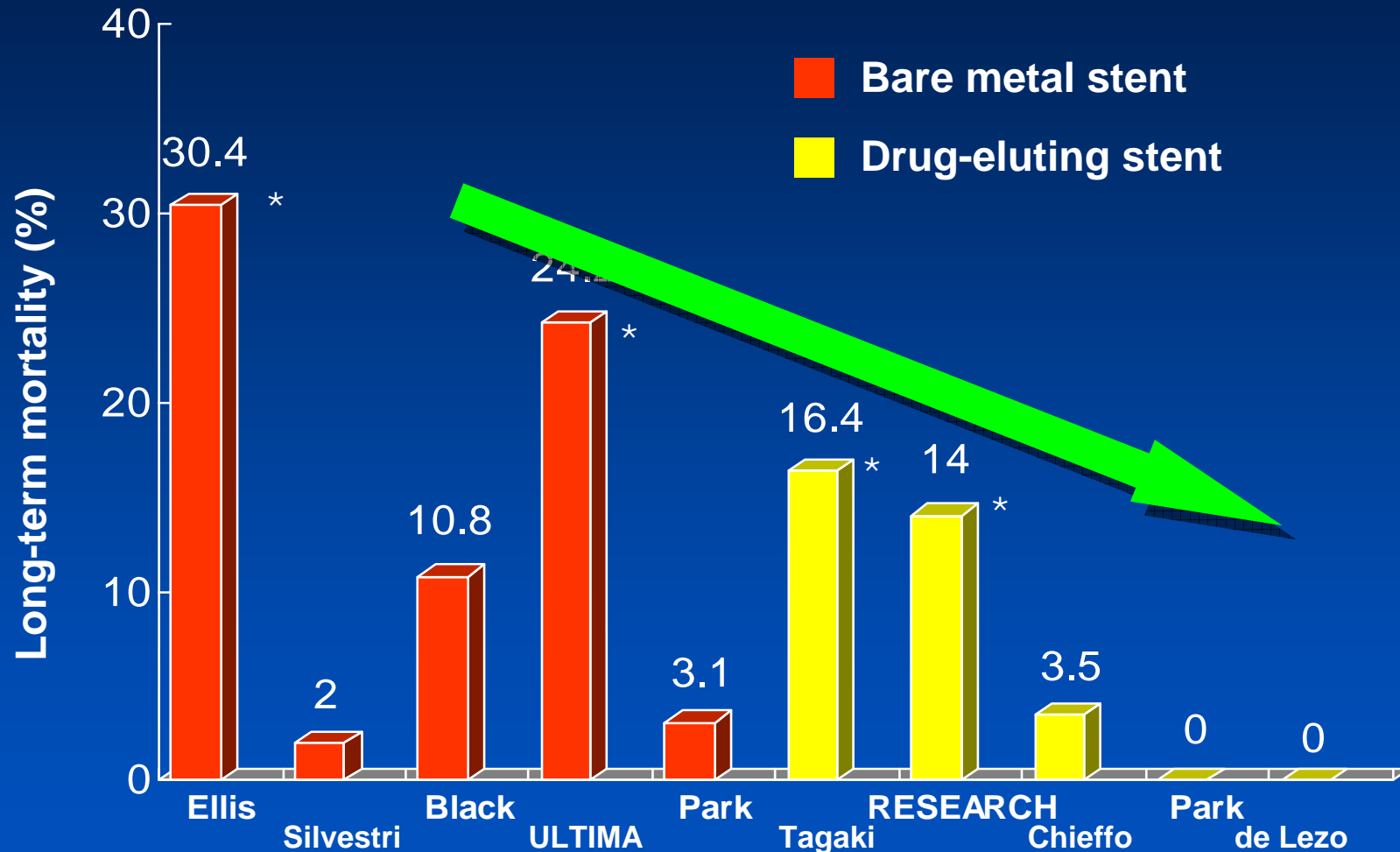
Significant Reduction of TLR with DES

Unprotected Left main stenting



Long-term Mortality (after 6 Mo)

Acceptable in the patients at a low risk !



* High-risk surgical candidates

Current data suggested...

DES are safe in the treatment of LM stenosis

While treatment of unprotected LMCA stenosis with PCI remains controversial, improved outcome through reduced recurrence rates may influence opinion away from the surgical towards the percutaneous approach.

DES for Ostial or Shaft LMCA Stenosis ?

AMC data, 2006

Ostial and Shaft LM PCI

51 patients

Lesion length, mm	9.3 ± 5.4
Reference, mm	3.49 ± 0.53
Used stent	Single in all pts
IVUS guidance	41 (80%)
Acute gain, mm	2.18 ± 0.66
Late loss, mm	0.10 ± 0.23
Restenosis	1/38 (2.6%)
TLR	1 (2.0%)
Stent thrombosis	0

AMC data, 2006



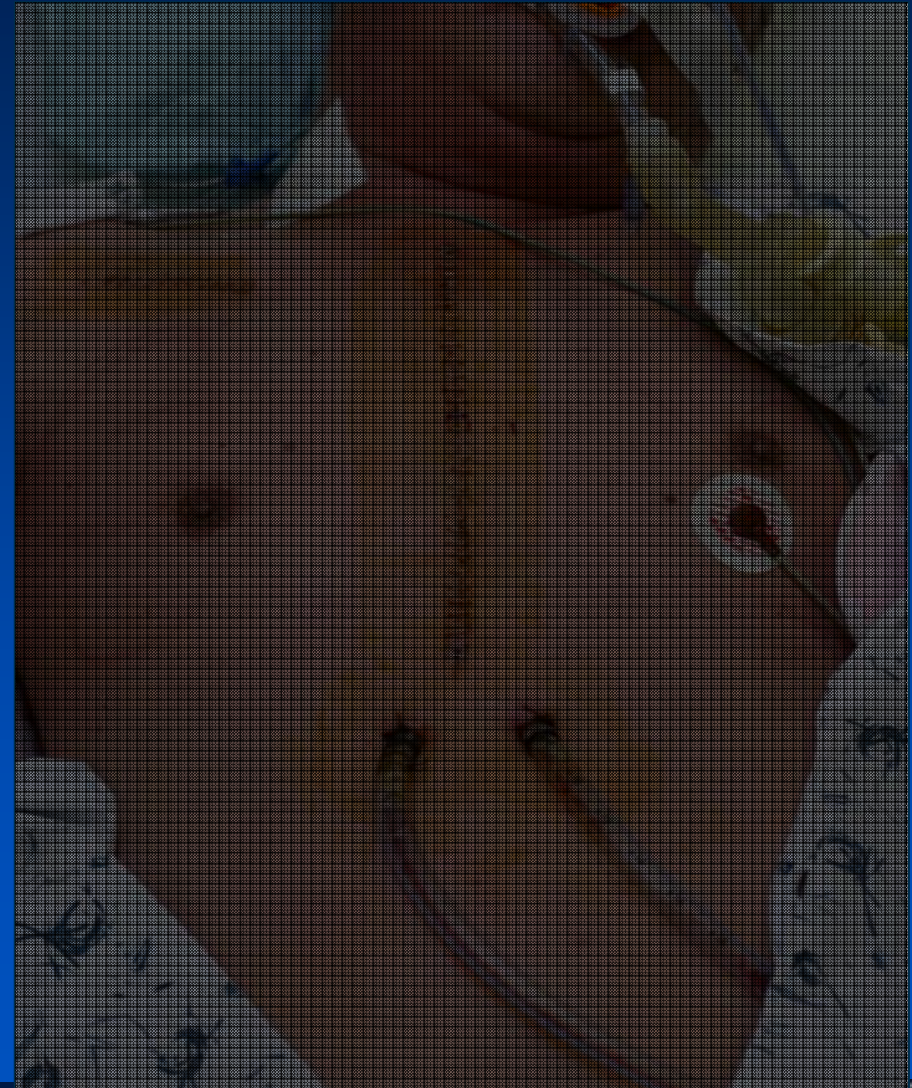
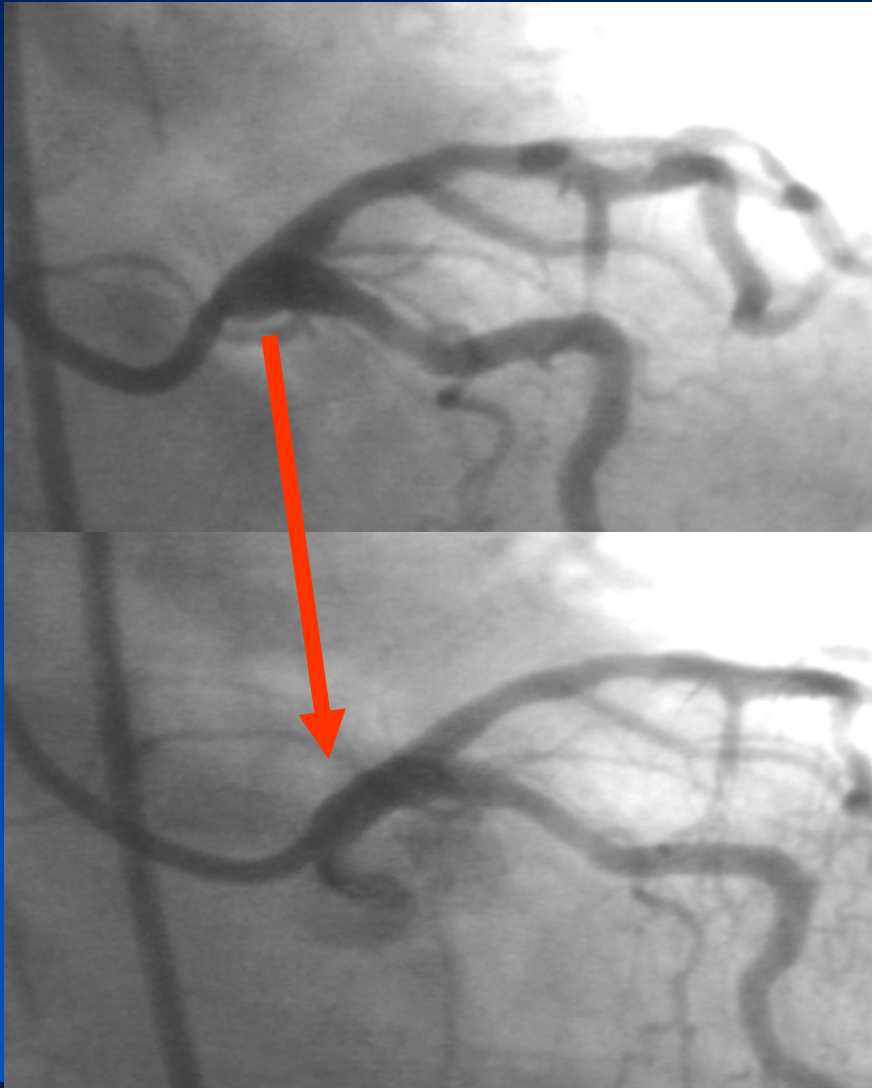
DES for Ostial or Shaft LMCA Stenosis

No Mortality
2.6% Restenosis
2% TLR

Would be an effective alternative and
even better compare to surgery...

**Just 1-minute
work !**

**Do you still prefer
surgery ?**



What about DES for Bifurcation LMCA Stenosis ?

More challenging issue

Different treatment strategy for LM bifurcation lesion

	Colombo A	Serruys PW	Park SJ
Distal location	69 (81.2%)	65%	72 (70.6%)
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%)
TLR	12 (14.1%)	6 (6%)	2 (2.0%)

Makes diverse TLR rates

Recommended Treatment Strategy for LMCA bifurcation lesions

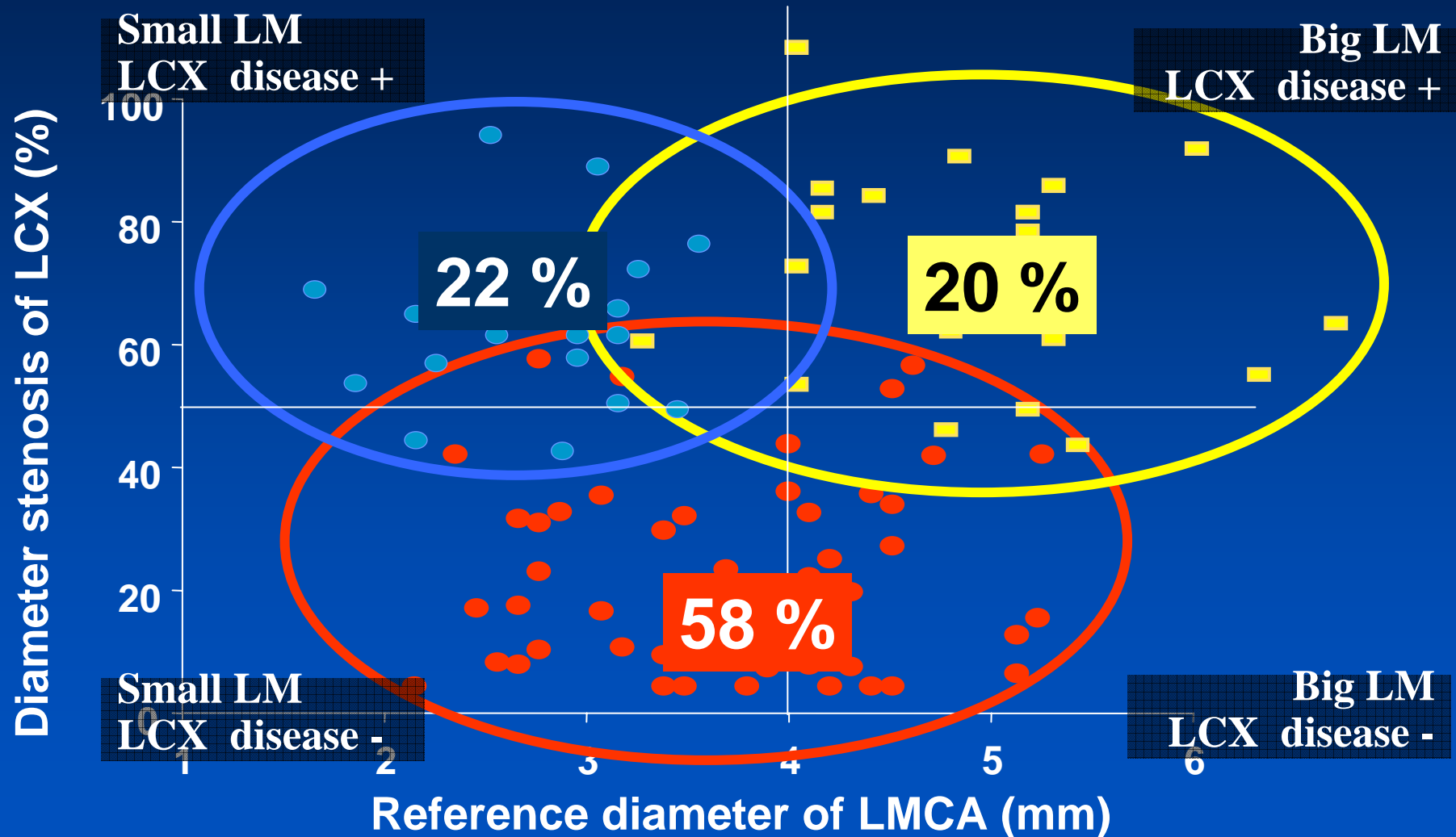
Stenting Cross-over
(provisional T stenting)

Kissing Stenting
Stent Crushing

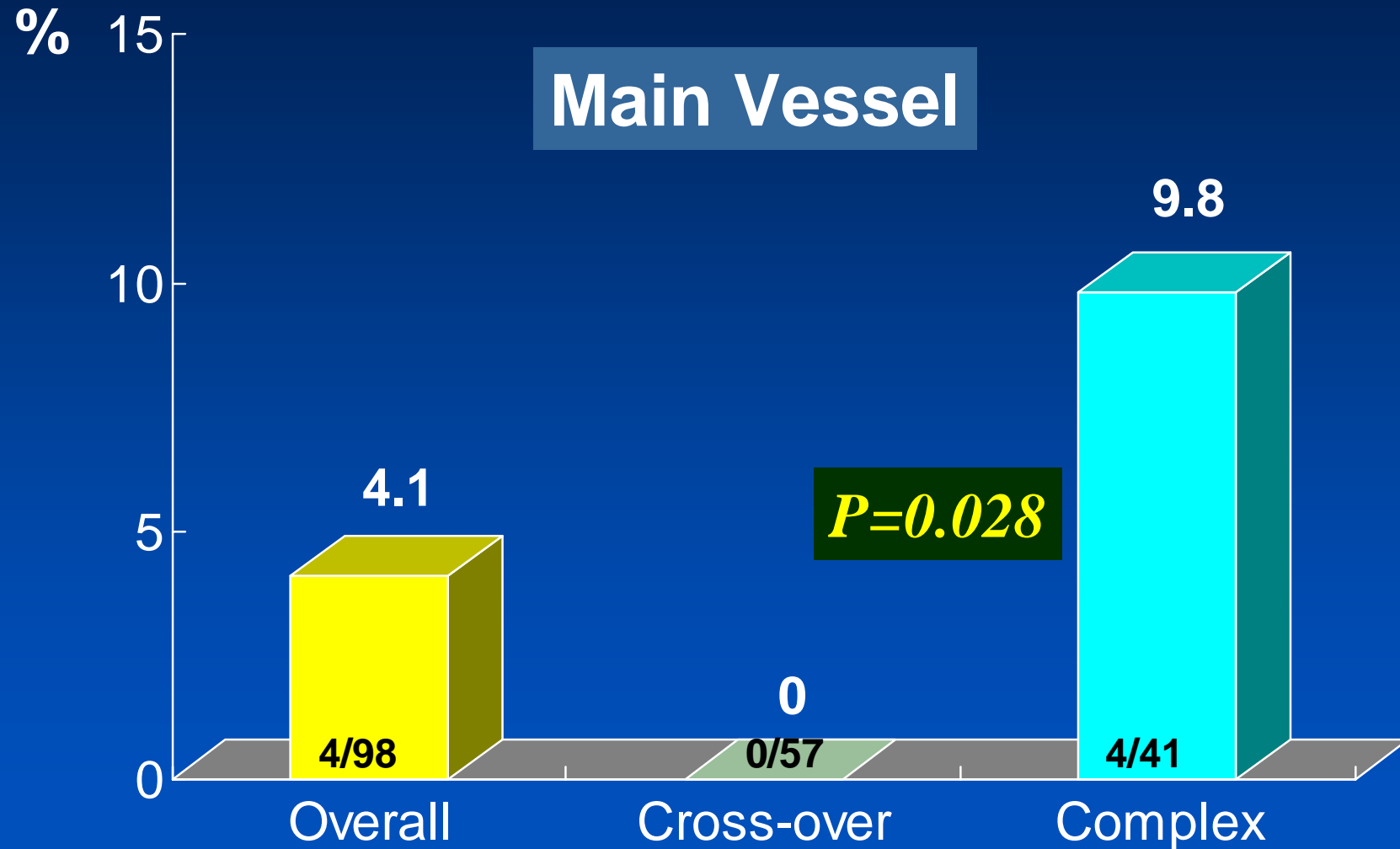
Different Treatment Strategy

According to LM size and LCX involvement

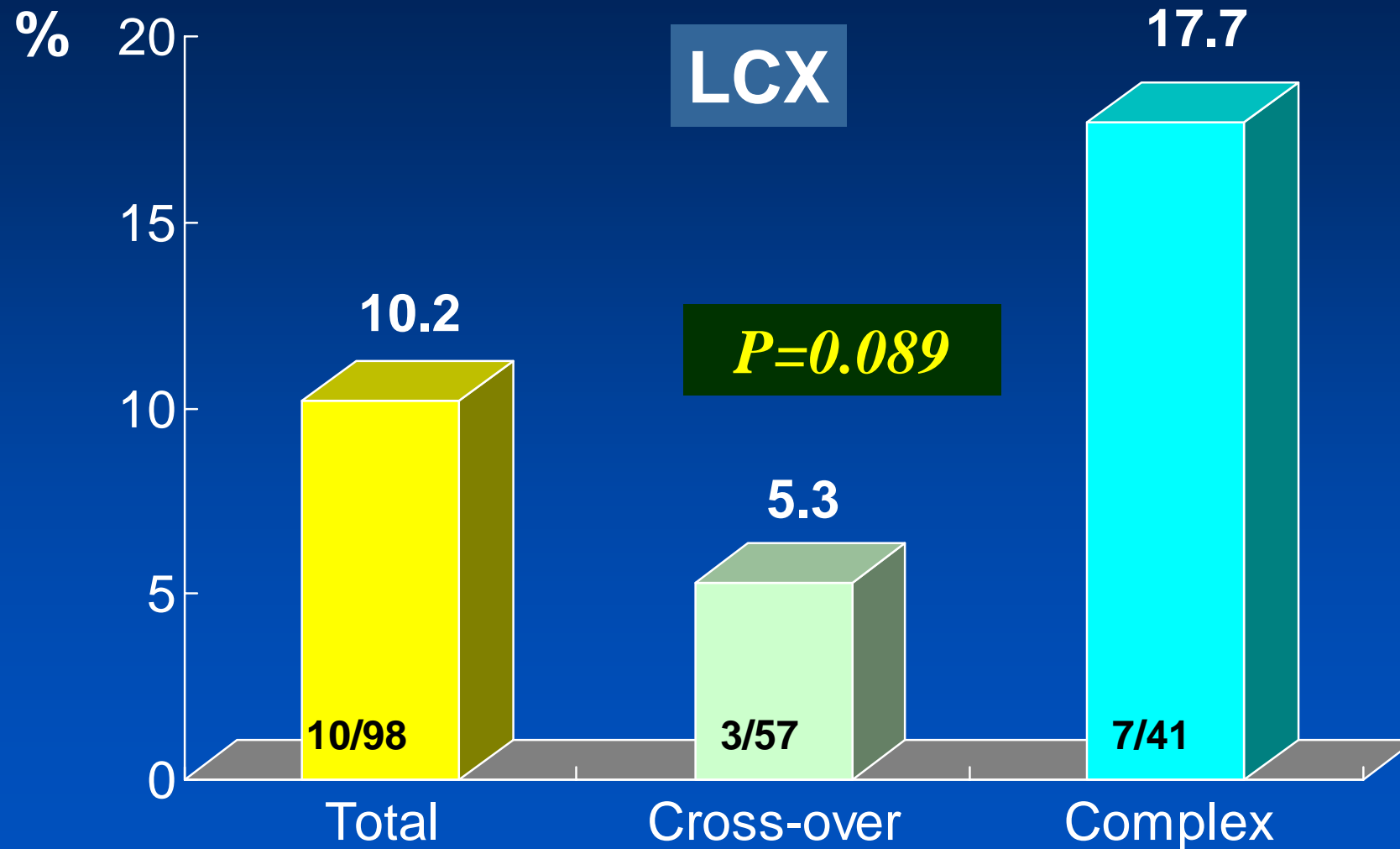
- Across LCX
- Crush
- Kissing



Restenosis Rate of 124 LM Bifurcation PCI

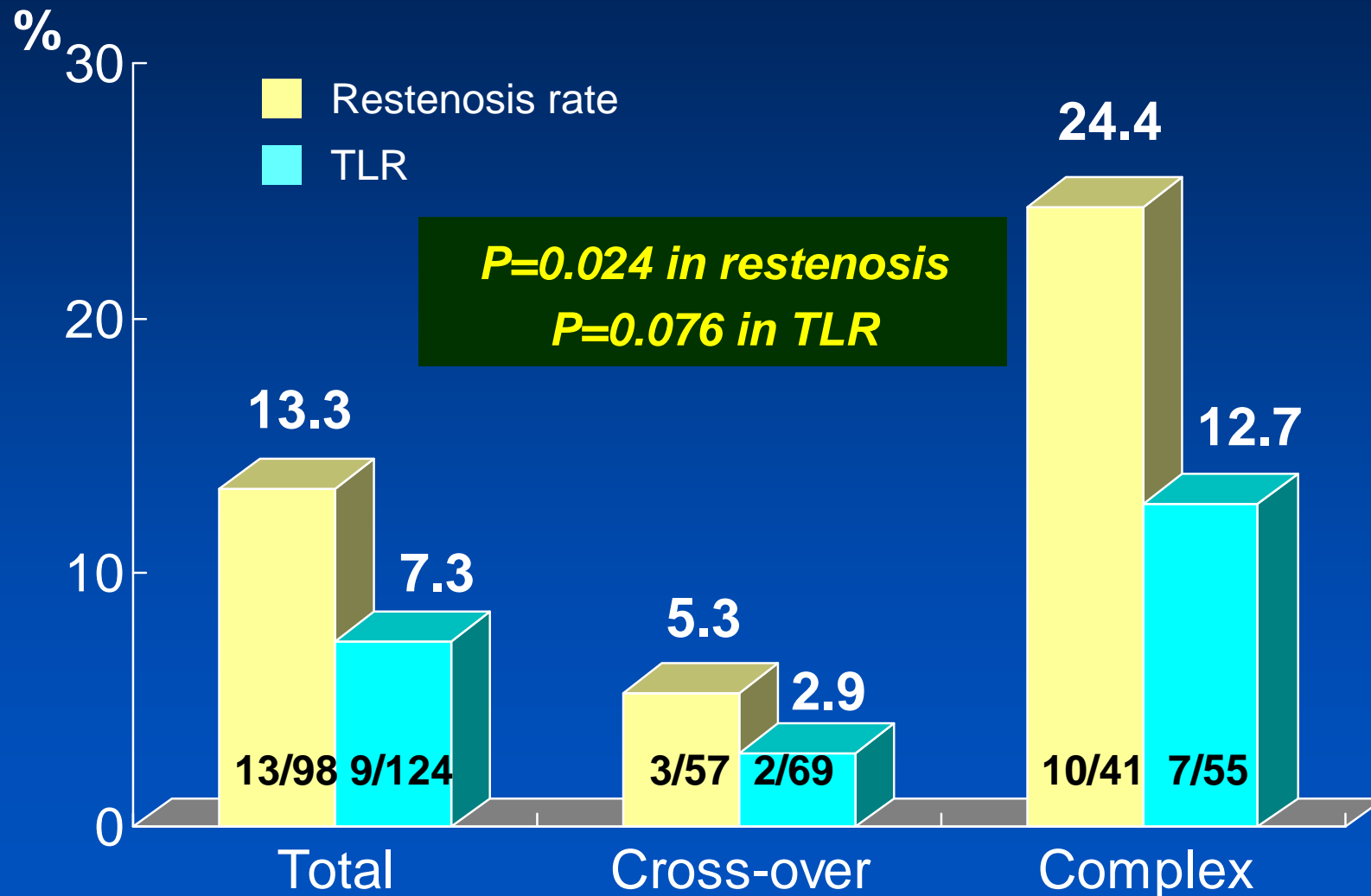


Restenosis Rate of 124 LM Bifurcation PCI



Restenosis Rates and TLR

Overall LM bifurcation PCI



Two Different Complex Strategies

Kissing vs. Stent Crushing

QCA at Main Vessel

	Kissing stenting	Stent Crushing	<i>p</i>
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
Restenosis	3 (15.0)	1 (4.8)	1.000

YH Kim, Am J Cardiol 2006 (in press)



QCA at LCX

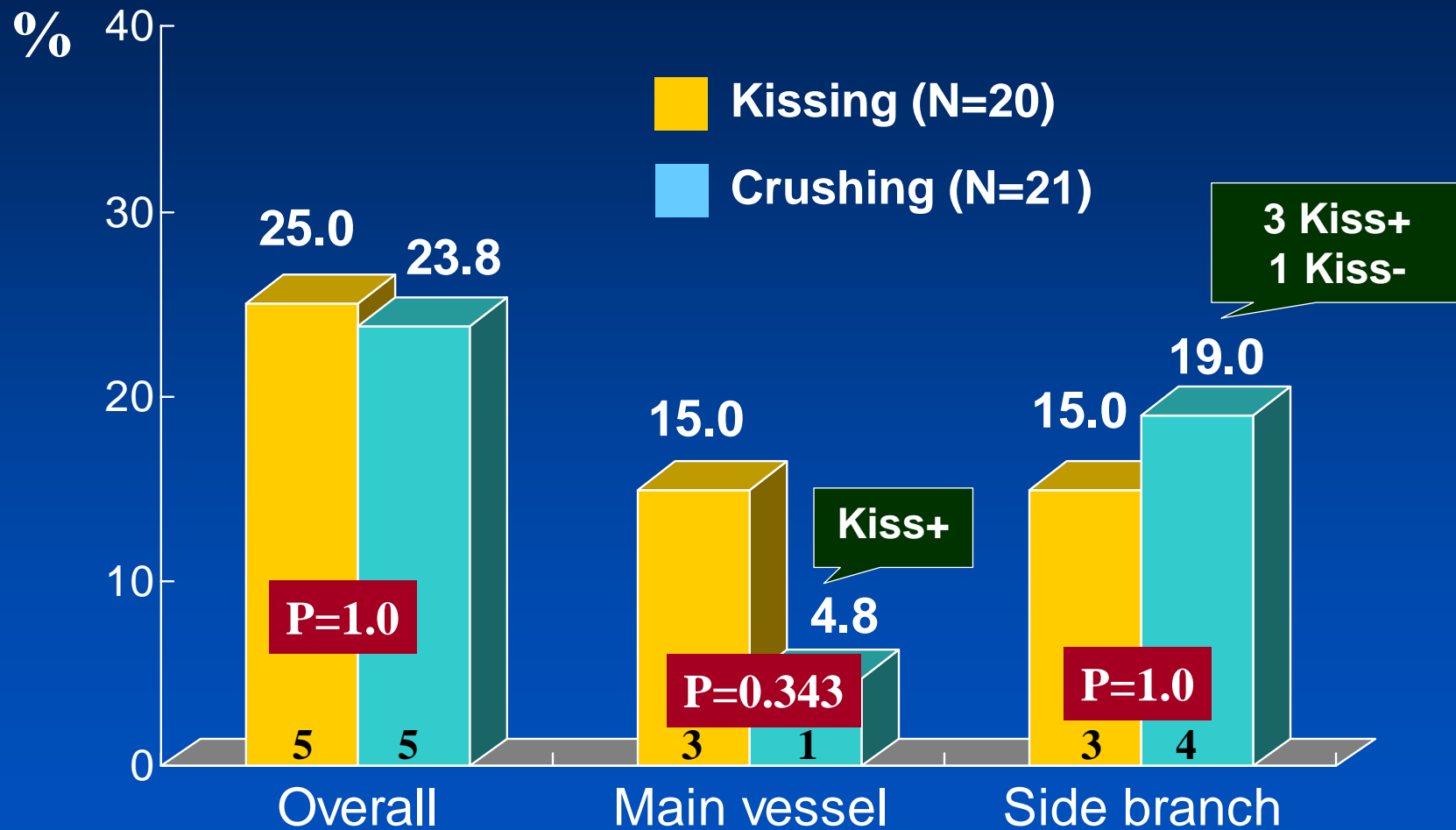
	Kissing stenting	Stent Crushing	<i>p</i>
Patients	24	25	
Follow-up CAG	20 (83)	21 (84)	
Distal RVD, mm	2.73±0.56	2.56±0.40	0.229
MLD, mm			
Before procedure	1.48±0.78	1.30±0.47	0.332
After procedure	2.70±0.36	2.60±0.44	0.387
At follow-up	2.03±0.78	1.91±0.85	0.646
Acute gain, mm	1.22±0.72	1.30±0.46	0.645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

YH Kim, Am J Cardiol 2006 (in press)



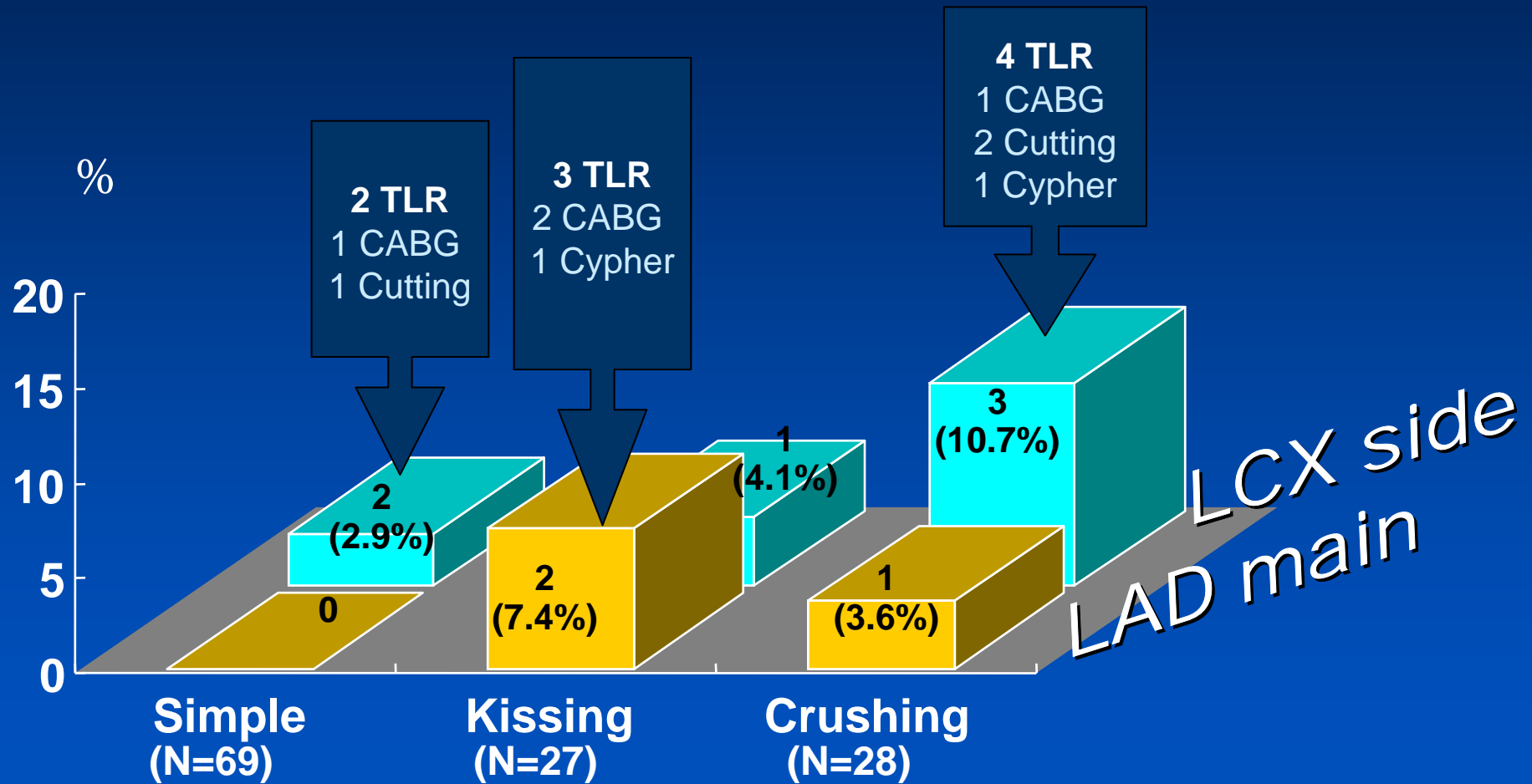
Kissing vs. Crush

Restenosis Rate



TLR : 7.3% in LM Bifurcation PCI

9/124 patients



Lessons from AMC data for LM Bifurcation PCI

- Both the presence of ostial LCX disease (diameter stenosis $\geq 50\%$) and the LMCA size by angiographic and IVUS examinations were two important considerations in selecting the stenting strategy.
- Compared to the complex stenting approach, the simple approach (stenting cross-over) was technically easier and appeared to be more effective in improving long-term outcomes for lesions with normal or diminutive LCX.

Compare to Surgery,

Efficacy concerns of PCI with DES...



COMBAT Randomized Trial

COMparison of Bypass surgery and Angioplasty using sirolimus eluting stent in patients with left main coronary disease

Left Main disease with or without MVD

Up to 75 cardiac centers

Randomize over 1,776 (1:1)

Registry group
1,000

PCI with SES
N=888

CABG
N=888

CABG
PCI
Medication

Primary Endpoint: 2-year death, MI, and stroke

Key Secondary Endpoints: MACCE including primary end point and ischemia-driven TLR

PI: Seung-Jung Park, Martin B. Leon

Inclusion Criteria

- At least 18 years of age
- LM stenosis $> 50\%$ by visual estimate
- Patients with angina or documented ischemia, amendable to both stent-assisted PCI or bypass surgery
- Lesions outside LMCA potentially treatable with both PCI and CABG
- Agreement to informed written consent

Pre-COMBAT

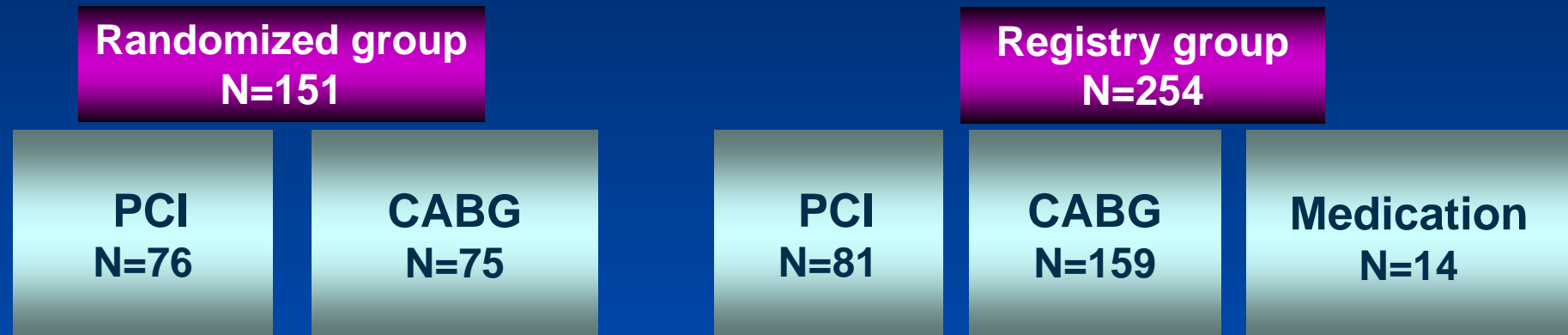
Preliminary analysis

**Data from
7 centers in Korea, for the last 12 months**

Pre-COMBAT

Run-in study

From December 2004 to December 2005



Randomization : Registry = 2 : 3

PCI in registry : CABG in registry = 1 : 2

Baseline Characteristics

	SES N=76	CABG N=75	P value
Age (years)	58±10	60±10	0.193
Men	54 (71%)	55 (73%)	0.857
Unstable angina	26 (34%)	30 (40%)	0.319
Past history			
Previous MI	3 (4%)	6 (8%)	0.320
Previous PCI	1 (1%)	5 (7%)	0.156
History of CVA	8 (11%)	3 (4%)	0.209
History of chronic lung disease	3 (4%)	2 (3%)	1.000
Renal insuff. (Cr ≥ 1.3mg/dL)	4 (5%)	5 (7%)	0.742

Baseline Characteristics

	SES N=76	CABG N=75	P value
Risk factors			
Hypertension	38 (50%)	43 (57%)	0.264
DM	23 (30%)	23 (31%)	0.865
Current smoking	30 (40%)	32 (43%)	0.582
Hypercholesterolemia	23 (30%)	23 (31%)	0.860
Family history of CAD	11 (15%)	9 (12%)	0.702
Peripheral vascular disease	1 (1%)	2 (3%)	0.513
LV ejection fraction (%)	63±7	60±9	0.156

Procedural Data

	SES N=76	CABG N=75	P value
Involvement of RCA	35 (46%)	36 (48%)	0.658
Lesion site			0.684
Ostium	19 (25%)	17 (23%)	
Shaft	9 (12%)	6 (8%)	
Bifurcation	48 (63%)	52 (69%)	
Days after randomization till OP	2.4±6.6	6.0±6.1	0.023
Use of IABP	2 (3%)	9 (12%)	0.027
Use of GP IIb/IIIa inhibitor	4 (5%)	1 (1%)	0.366

Procedural Data

	SES N=76	CABG N=75
Bifurcation stenting		
Stenting crossover circumflex	24 (50%)	
Provisional T stenting	1 (2%)	
Crush technique	10 (21%)	
Kissing stenting	11 (23%)	
Others	2 (4%)	
Number of used stents at LM	1.4±0.6	
Number of total used stents	2.5±1.4	
Extra-LM PCI	45 (59%)	
IVUS guidance	65 (86%)	
Use of off-pump		38 (51%)
Number of total conduits		2.5±1.4
Number of arterial conduits		2.2±0.9

In-hospital Outcome

	SES N=76	CABG N=75	P value
Death	0	1 (1%) ¹	0.478
Cardiac	0	0	
Non-cardiac	0	1 (1%)	
Myocardial infarction ²	5 (7%)	8 (11%)	0.387
ST elevation MI	0	3 (4%)	0.109
Non-ST elevation MI	5 (7%)	5 (7%)	1.000
Stroke	0	0	
Repeat revascularization	0	0	0.548
PCI	0	0	
CABG	0	0	
Stent thrombosis	0		
MACCE	5 (6.6%)	9 (12.0%)	0.192

¹ Pneumonia after CABG, ² CK-MB \geq 3 times normal in PCI and \geq 10 times normal in CABG

Additional MACCE at 9 months

	SES N=24	CABG N=25	P value
Death	0	0	
Cardiac	0	0	
Non-cardiac	1	0	
Myocardial infarction	0	0	
ST elevation MI	0	0	
Non-ST elevation MI	0	0	
Stroke	0	0	
Repeat revascularization	2 (8%)	1 (4%)	0.356
PCI	2	1	
CABG	0	0	
Stent thrombosis	0		

Registry Group

Primary reason of exclusion from randomization

	PCI group N=81	CABG group N=159
Patient's or doctor's preference	54 (67%)	21 (14%)
Complex lesion, not suitable for stenting	0	89 (57%)
Chronic total occlusion	3 (4%)	29 (19%)
Previous PCI within 1 year	7 (9%)	1 (1%)
Acute STEMI	5 (6%)	1 (1%)
Renal failure	4 (5%)	2 (1%)
Age more than 80 years	3 (4%)	0
Disabled CVA	1 (1%)	2 (1%)
Emergent CABG	0	4 (3%)
Bail-out PCI	1 (1%)	0
Patients who need major surgery	6 (4%)	1 (1%)

Baseline Characteristics

	SES N=81	CABG N=159	P value
Age (years)	63±11	64±8	0.682
Men	56 (69%)	123 (77%)	0.167
Unstable angina	20 (25%)	58 (36%)	0.043
Past history			
Previous myocardial infarction	9 (11%)	22 (14%)	0.528
Previous PCI	15 (19%)	18 (11%)	0.107
Previous CABG	1 (1%)	0	0.337
History of CVA	8 (10%)	16 (10%)	0.943
History of chronic lung disease	7 (9%)	11 (7%)	0.645
Carotid end arterectomy	0	1 (1%)	0.291
Renal insuff. (Cr ≥ 1.3mg/dL)	10 (12%)	19 (12%)	0.919

Baseline Characteristics

	SES N=81	CABG N=159	P value
Risk factors			
Hypertension	37 (46%)	85 (53%)	0.162
Diabetes	21 (26%)	57 (36%)	0.087
Current smoking	29 (36%)	72 (45%)	0.106
Hypercholesterolemia	18 (22%)	34 (21%)	0.890
Family history of CAD	7 (9%)	18 (11%)	0.488
Peripheral vascular disease	5 (6%)	4 (3%)	0.280
LV ejection fraction (%)	60.8±10.7	54.3±12.1	<0.001

Procedural Data

	SES N=81	CABG N=159	P value
Involvement of RCA	22 (27%)	124 (78%)	<0.001
Lesion site			<0.001
Ostium	26 (32%)	14 (9%)	
Shaft	8 (10%)	15 (9%)	
Bifurcation	47 (58%)	130 (82%)	
Days after random till OP	5.3±15.2	8.2±20.8	
Use of IABP	6 (7%)	14 (9%)	0.553
Use of GP IIb/IIIa inhibitor	0	5 (3%)	0.169

Procedural Data

	SES N=81	CABG N=159
Bifurcation stenting		
Stenting crossover circumflex	16 (34%)	
Crush technique	13 (28%)	
Kissing stenting	15 (32%)	
T stenting	1 (2%)	
Others	2 (4%)	
Number of used stents at LM	1.2±0.4	
Number of total used stents	2.2±1.1	
Extra-LM PCI	49 (60%)	
IVUS guidance	52 (64%)	
Use of off-pump		65 (41%)
Number of total conduits		3.1±0.9
Number of arterial conduits		2.5±0.9

In-hospital Outcome

	SES N=81	CABG N=159	P value
Death	2 (2%)	4 (3%)	0.992
Cardiac	2 (2%)	4 (3%)	
Non-cardiac	0	0	
Myocardial infarction	8 (10%)	35 (22%)	0.010
ST elevation MI	2 (3%)	7 (4%)	0.499
Non-ST elevation MI	6 (7%)	28 (18%)	0.019
Stroke	0	3 (2%)	0.553
Repeat revascularization	1 (1%)	0	
PCI	1 (1%)	0	
CABG	0	0	
Stent thrombosis	1 (1%) *		
MACCE	8 (9.9%)	38 (23.9%)	0.003

* Acute stent thrombosis after primary stenting for acute STEMI

Summary

of Pre-COMBAT Run-in Study

- About 2/5 of all LMCA patients has been randomized.
- Bifurcation lesions were included in 2/3 of all LMCA disease.
- Complex stenting techniques were used in a half of LMCA bifurcation PCIs .
- Arterial grafts were used in 2/3 of all grafts (LIMA in 98%)
- The initial outcomes of PCI and CABG appears to be comparable.
- Peri-operational MI tends to occur more commonly in the CABG group.