

# Unprotected LM intervention

## Guideline for COMBAT

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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

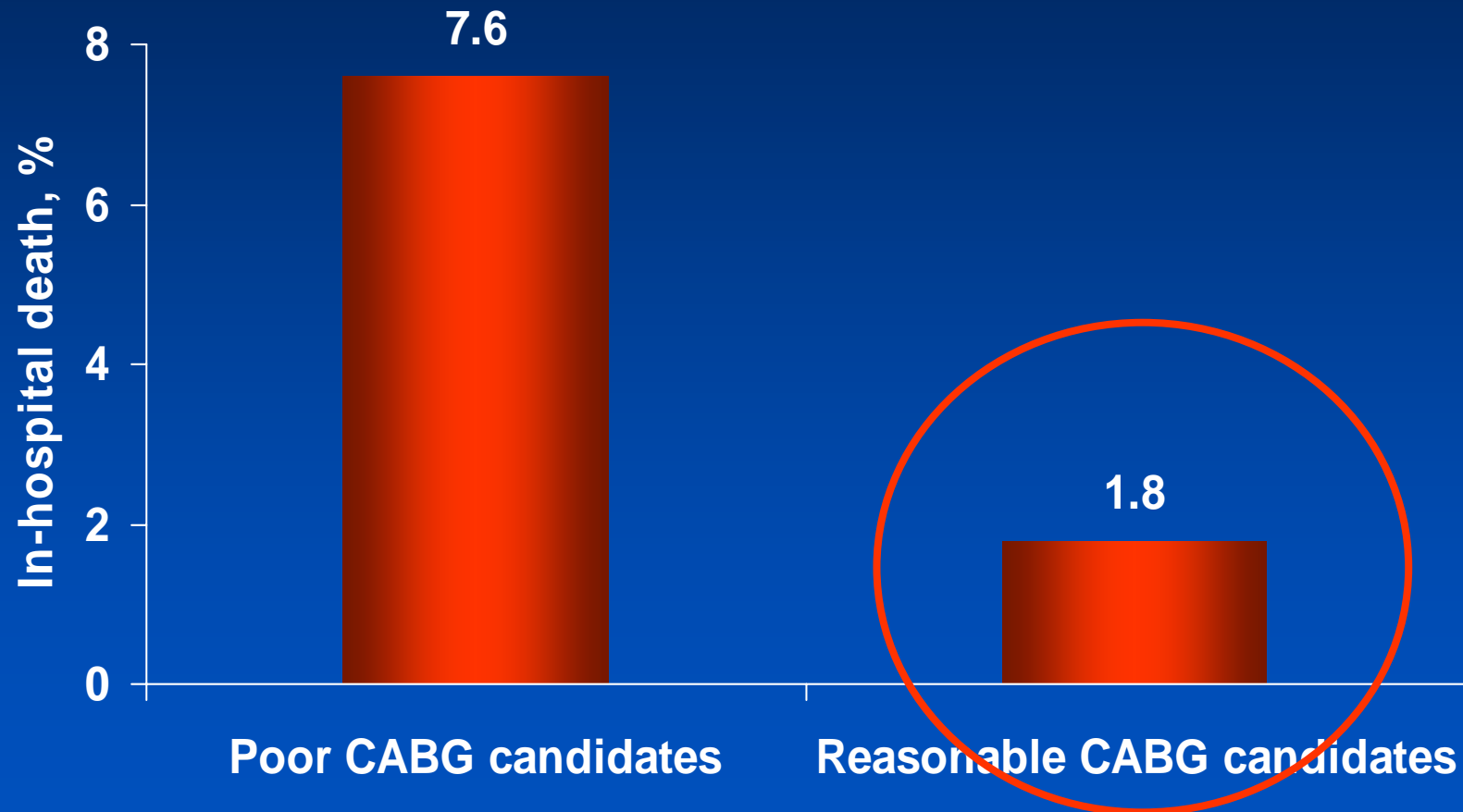
High Mortality in PCI ?

# 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%
More than 1,300 patients were included				
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%

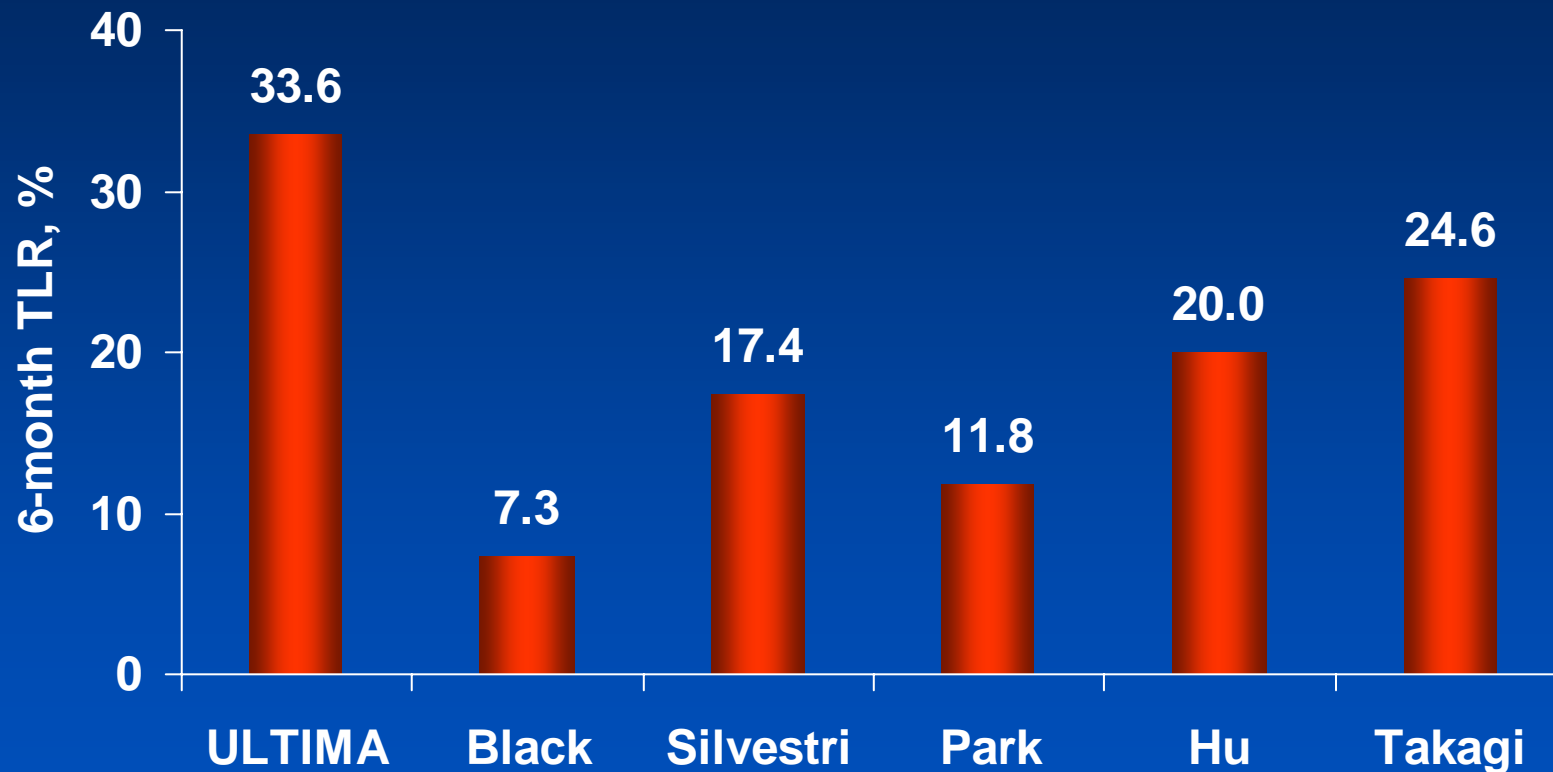
# Low in-Hospital Mortality for good candidate for Surgery



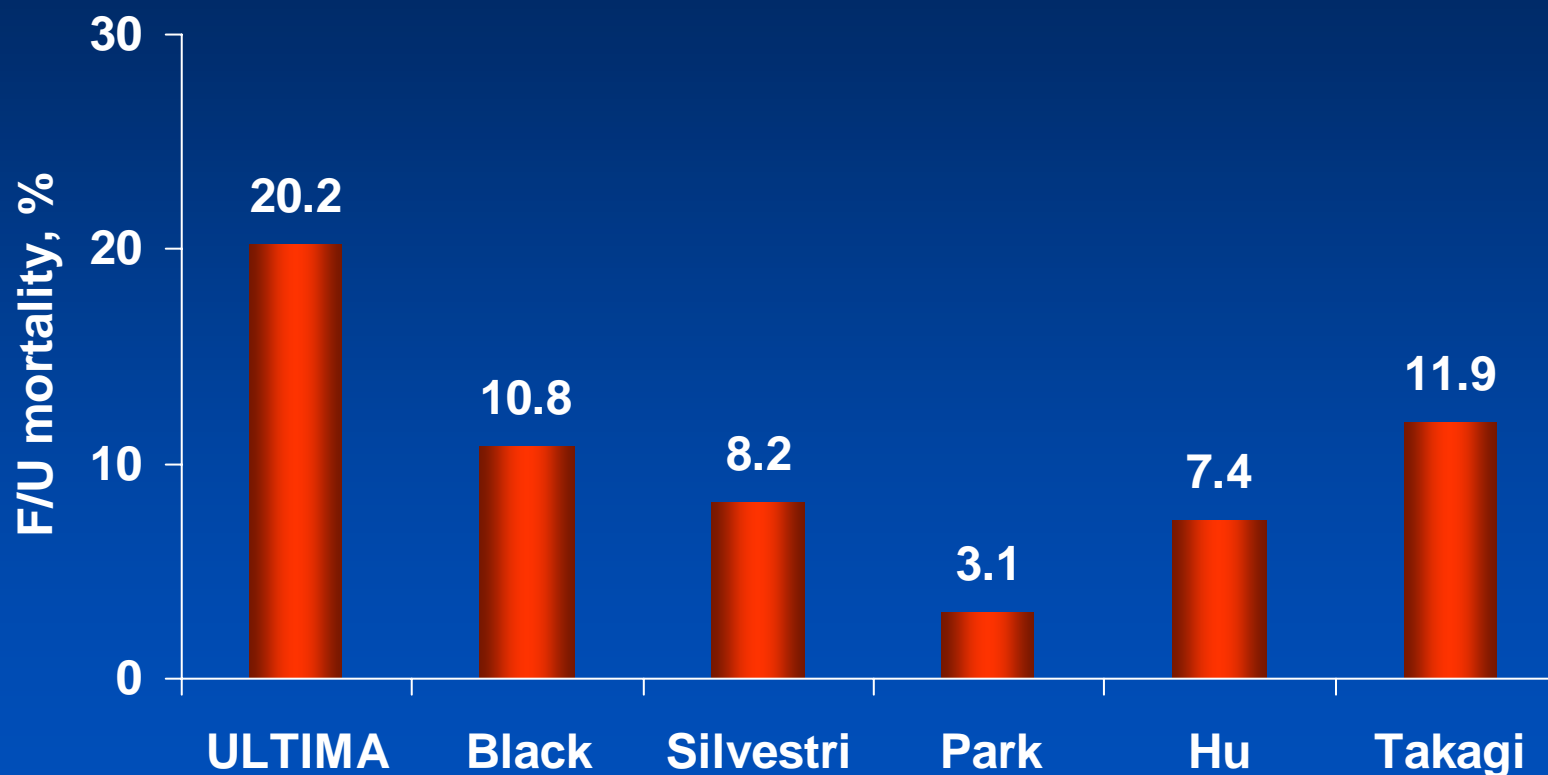
*Black et al, JACC, 2001.*

# 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

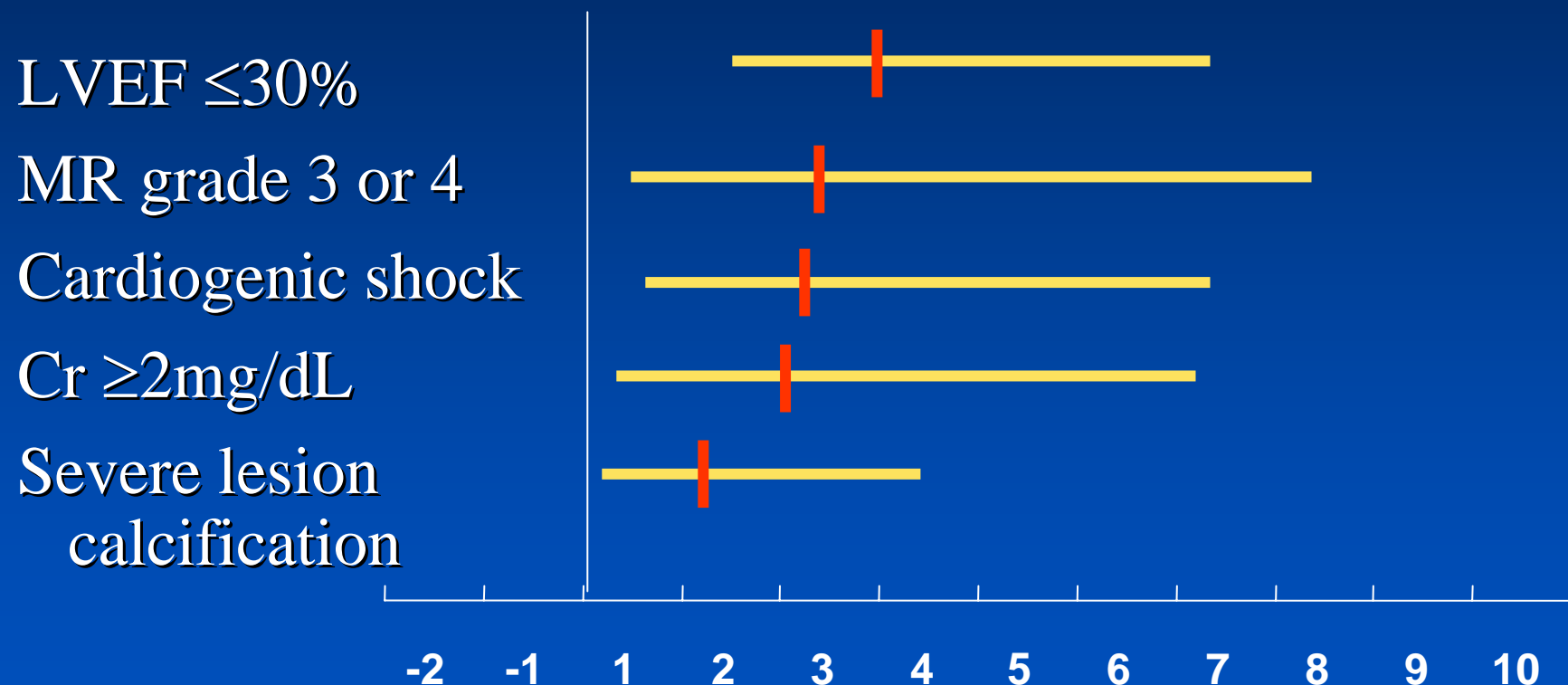
25.5

6

31



# Multivariate Predictors of All-Cause Mortality: ULTIMA Registry



*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 ( $\geq 6$ )	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,<sup>a,f</sup> William Wijns, MD, PhD,<sup>b</sup> Patrick W. Serruys, MD, PhD,<sup>a</sup> Ulrich Sigwart, MD,<sup>c</sup> Marcus D. Flather, MBBS,<sup>d</sup> Rodney H. Stables, DM, FRCP,<sup>e</sup> William W. O'Neill, MD,<sup>f</sup> Alfredo Rodriguez, MD,<sup>g</sup> Pedro A. Lemos, MD, PhD,<sup>a</sup> Whady A. Hueb, MD,<sup>h</sup> Bernard J. Gersh, MB, ChB, DPhil,<sup>i</sup> Jean Booth, MSc,<sup>d</sup> and Eric Boersma, PhD<sup>a</sup>

*The Journal of Thoracic and Cardiovascular Surgery* • August 2005

## *Included trials:*

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

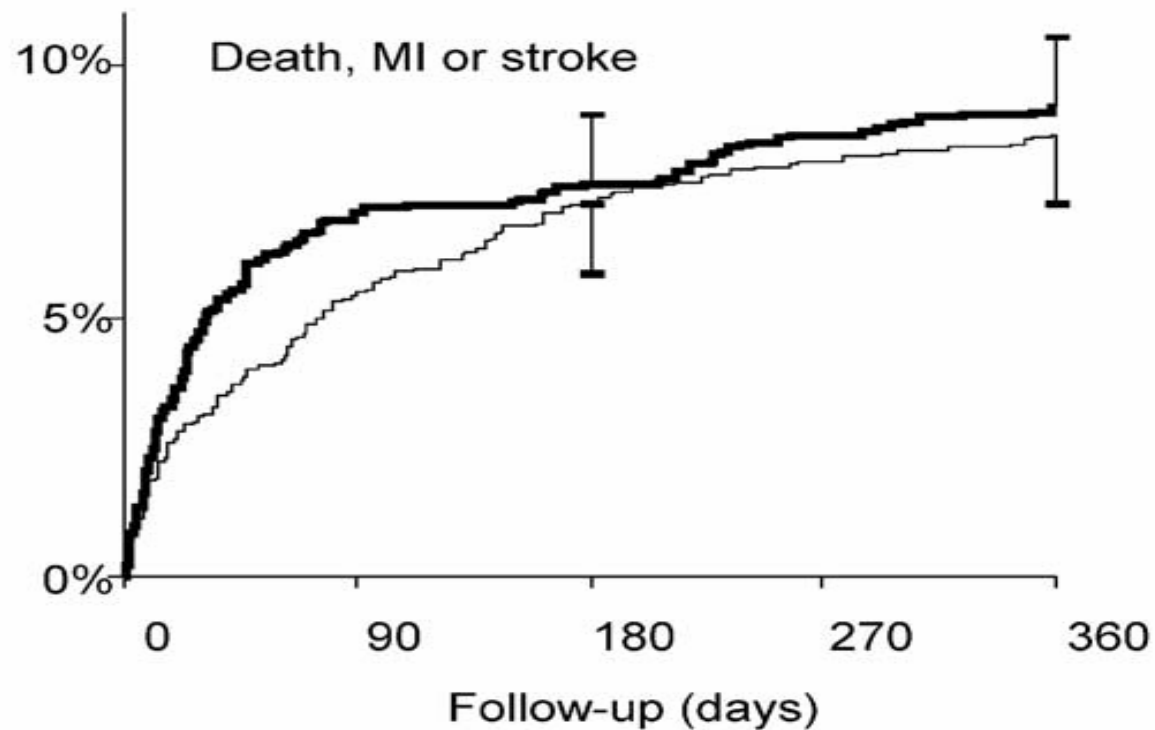
# Four CABG vs. Stent Assisted PCI trials

	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 patients randomized	1,000	1,000	1,076	2,076
Exclusion criteria	<ul style="list-style-type: none"> <li>• LMCA stenosis</li> <li>• Transmural MI within previous week</li> </ul>	<ul style="list-style-type: none"> <li>• MI within 48 hours</li> </ul>	<ul style="list-style-type: none"> <li>• MI within 48 hours</li> </ul>	<ul style="list-style-type: none"> <li>• LMCA stenosis</li> <li>• Presence of ischemia</li> </ul>
Primary endpoint	<ul style="list-style-type: none"> <li>• 12-month MACCE free survival</li> </ul>	<ul style="list-style-type: none"> <li>• Repeat revascularization</li> </ul>	<ul style="list-style-type: none"> <li>• MACE within 30 days and need for repeat revascularization at 30 days</li> </ul>	<ul style="list-style-type: none"> <li>• Composite of cardiac death, MI, and angina requiring revascularization</li> </ul>

More than 3,000 patients were randomized

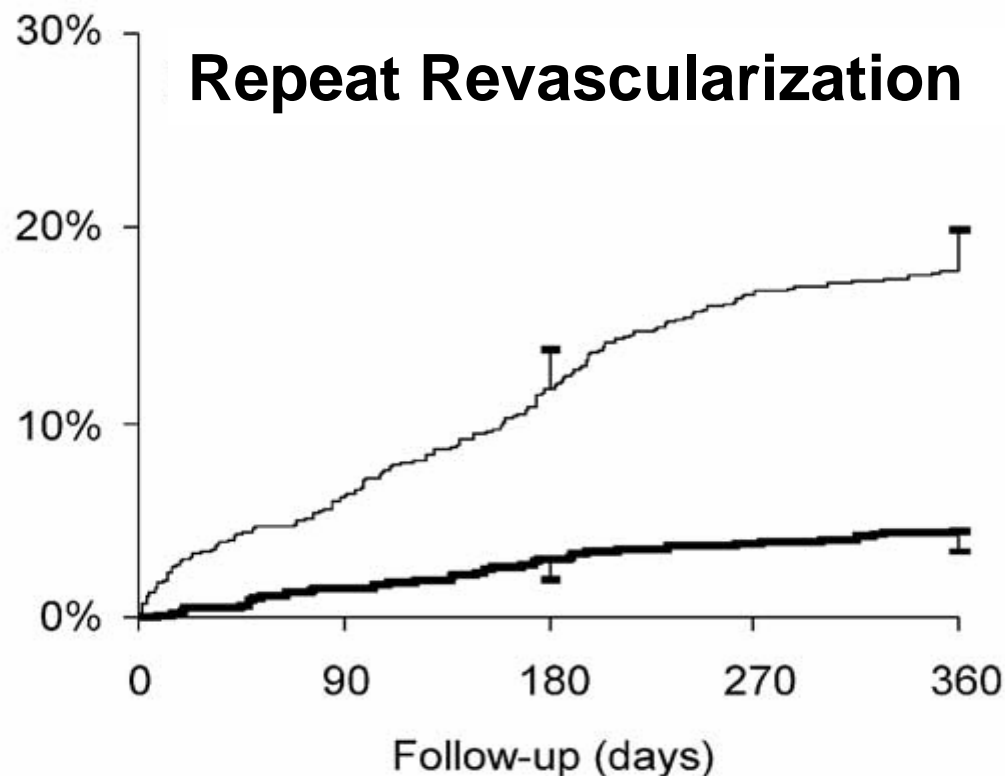
Mercado et al, J thoracic Cardiovasc Surg, 2005

# 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

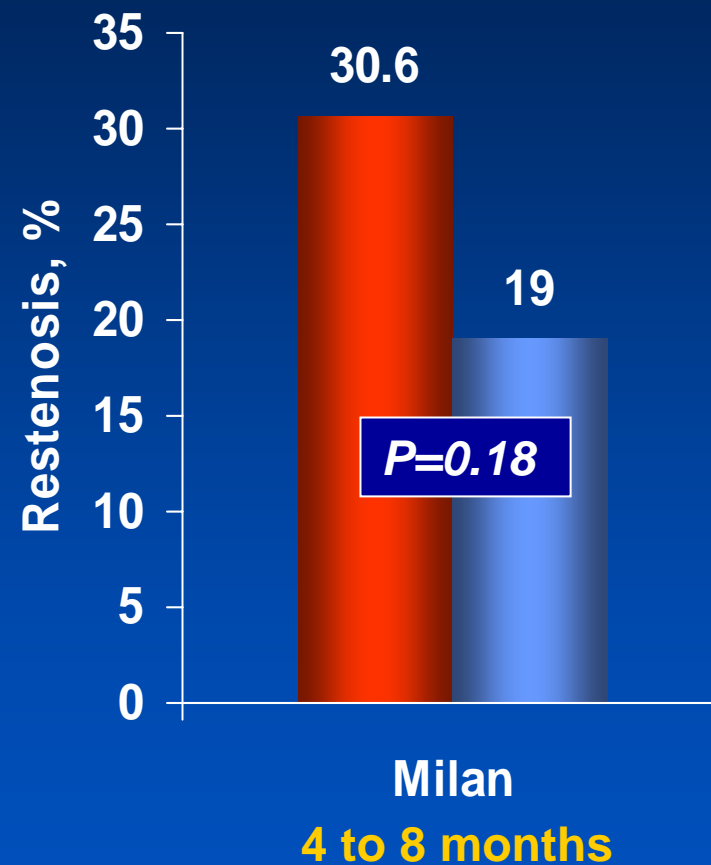
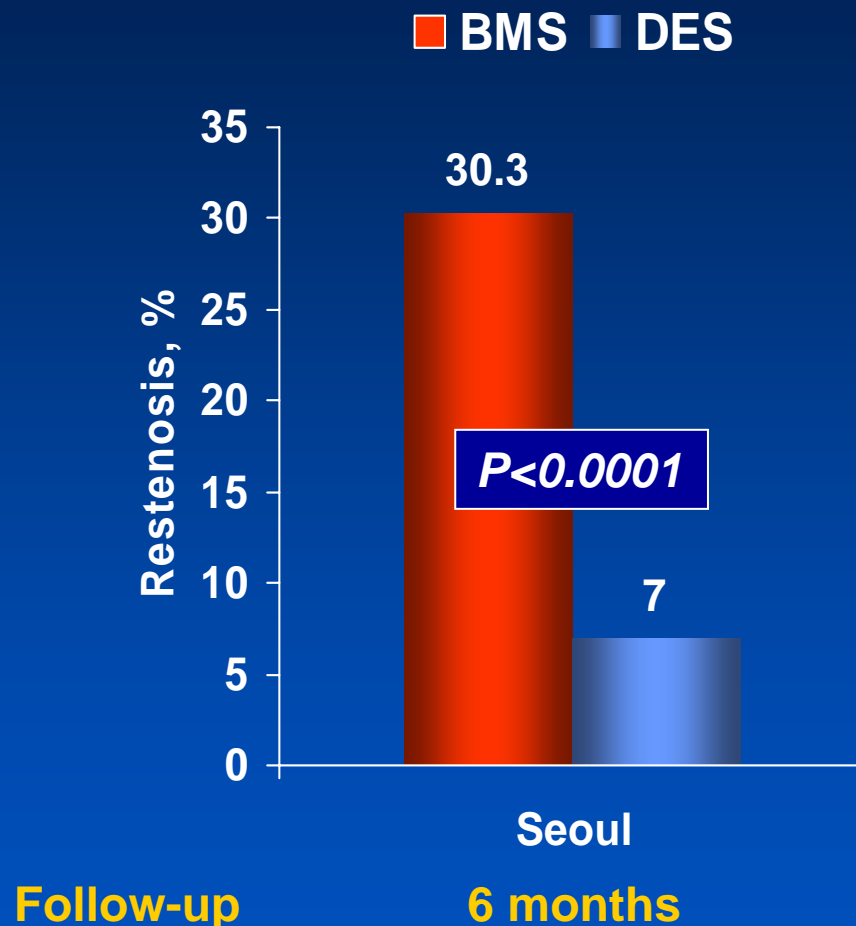
# In the era of DES...

# In-Hospital Outcomes: DES in Left Main PCI Series

Series	Procedure success	Death
Park et al	100%	0
Chieffo et al	100%	0
Valicenti et al		1.0%
More than 1000 patients were included		
Gershnick 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

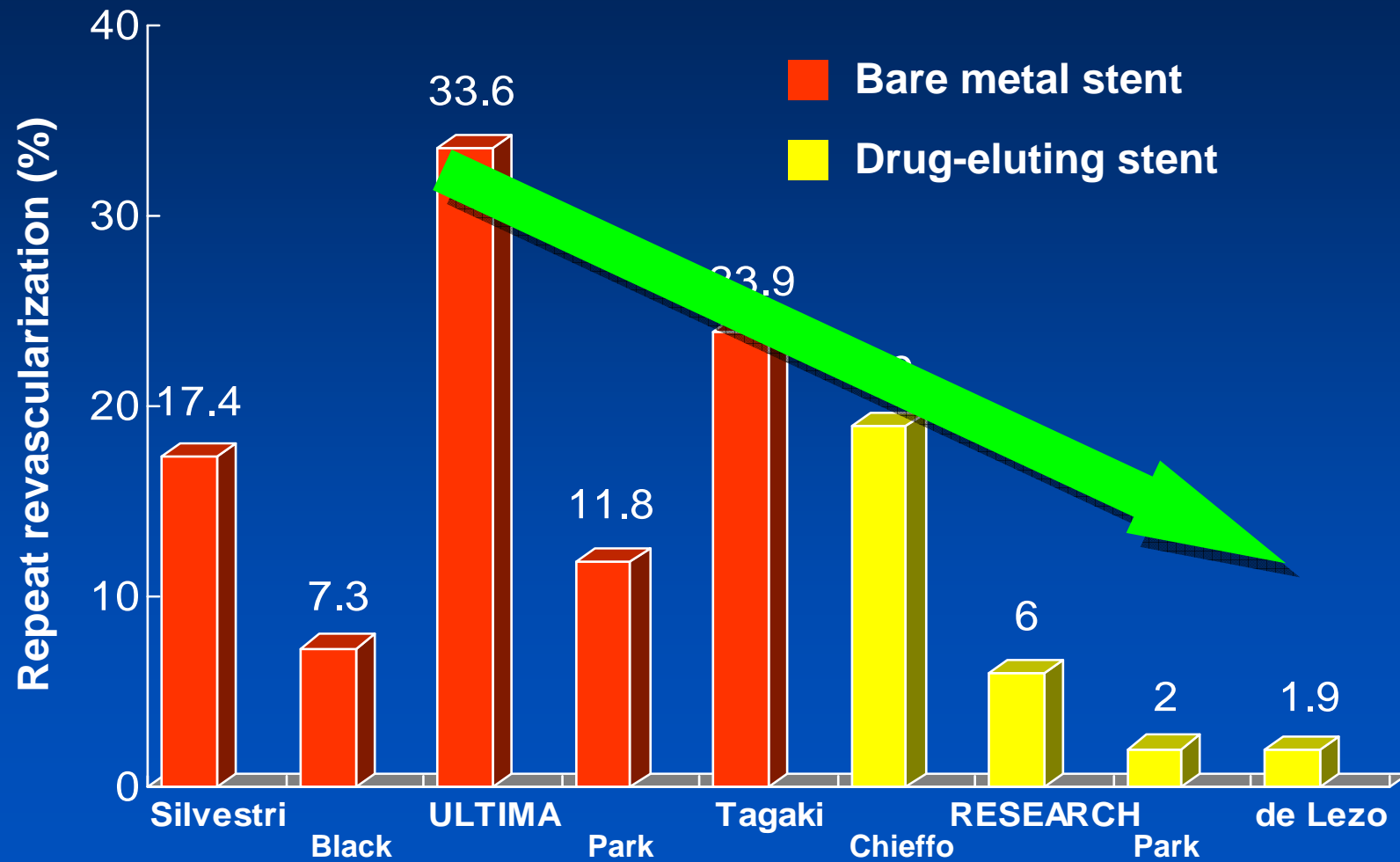
# Angiographic Restenosis in Two DES vs. BMS Left Main PCI Series



*Park et al, JACC 2005*  
*Chieffo et al, Circulation 2005*

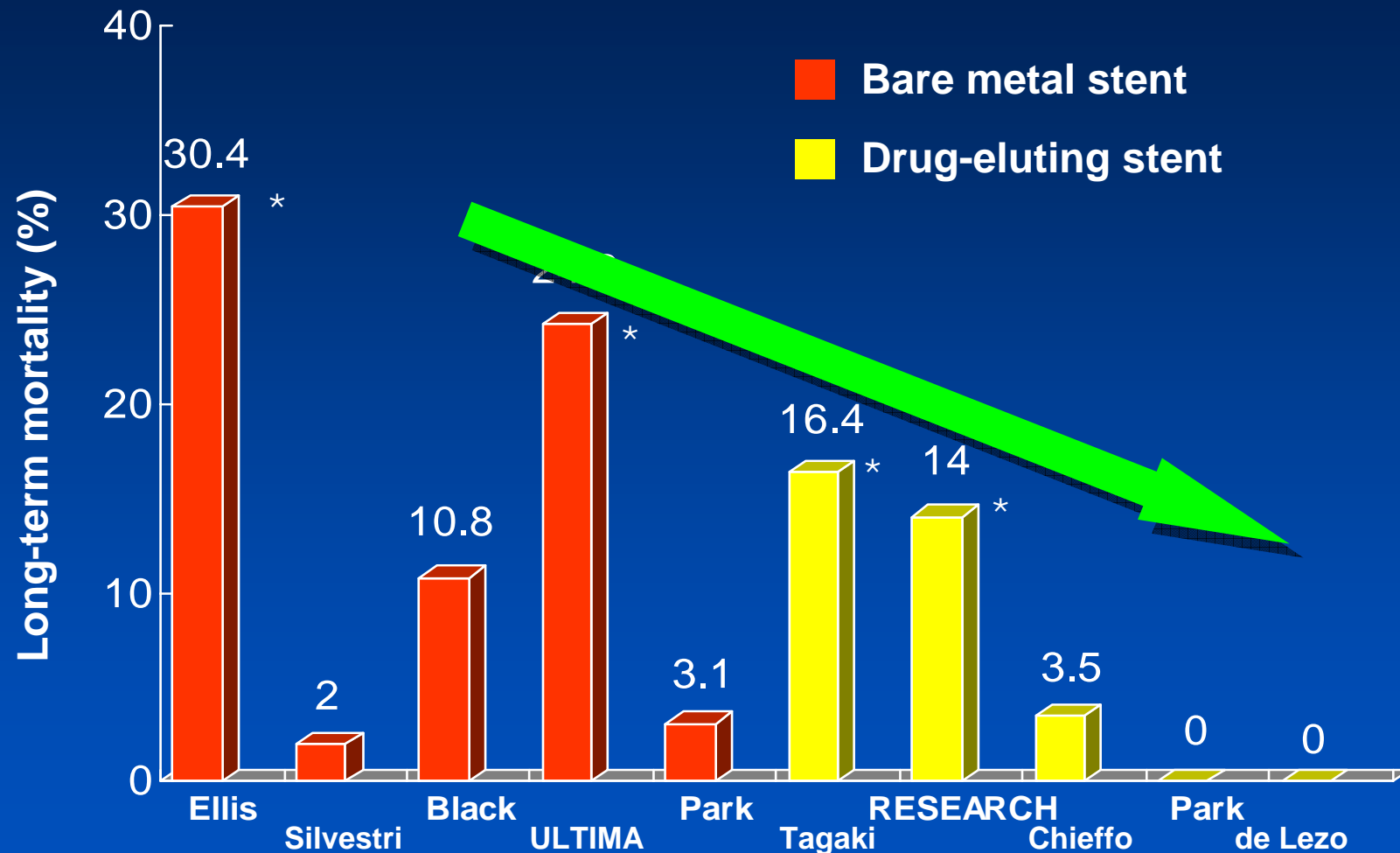
# Significant Reduction of TLR with DES

## Unprotected Left main stenting



# Long-term Mortality (after 6 Mo)

Acceptable in the patients at a low risk !



## 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

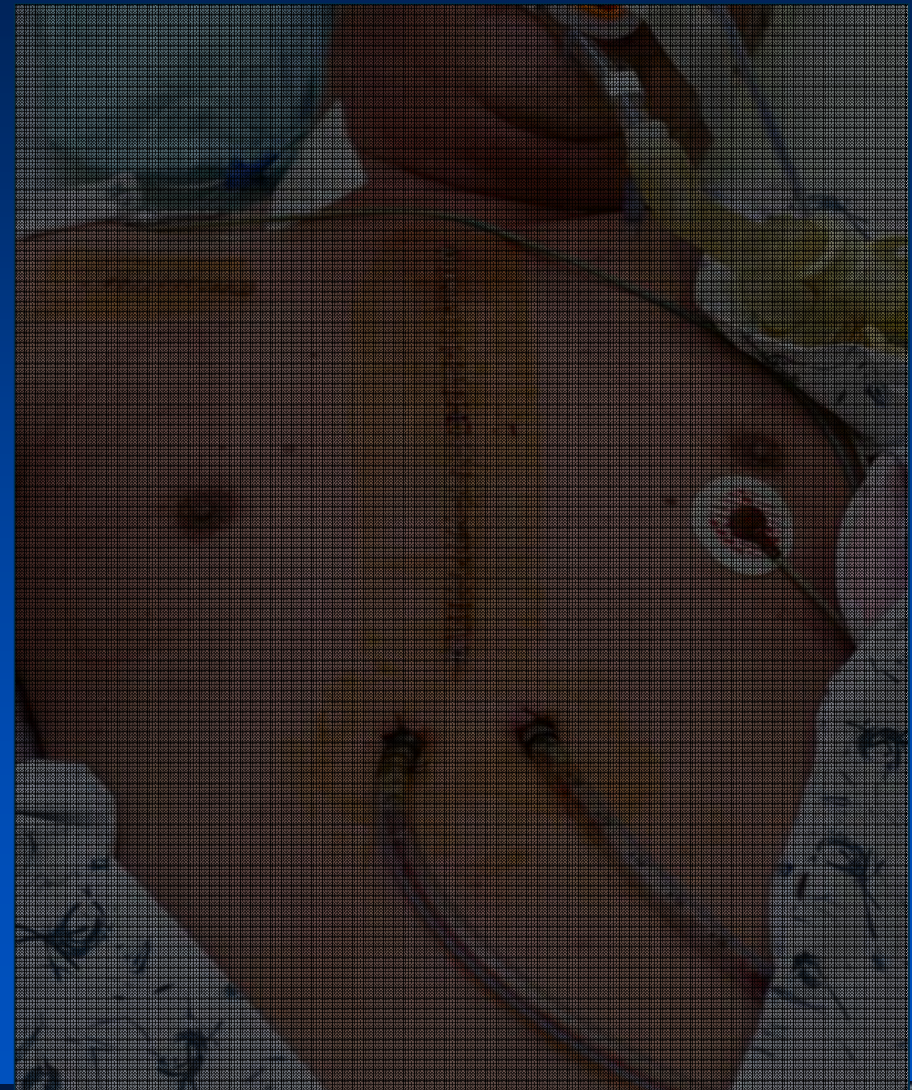
No	Mortality
2.6%	Restenosis
2%	TLR

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



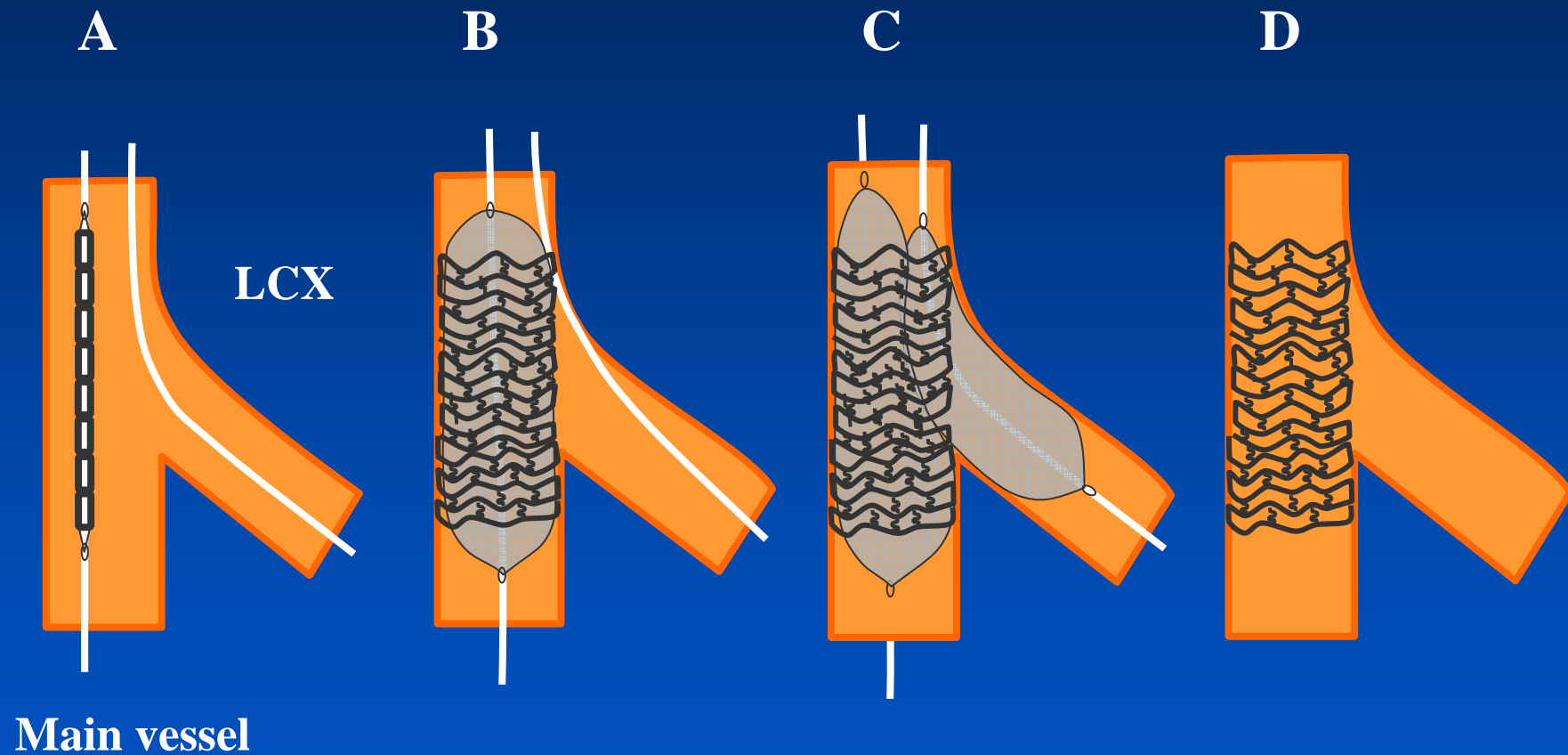
# Recommended Treatment Strategy for LMCA bifurcation lesions

Stenting Cross-over  
(provisional T stenting)

Kissing Stenting  
Stent Crushing

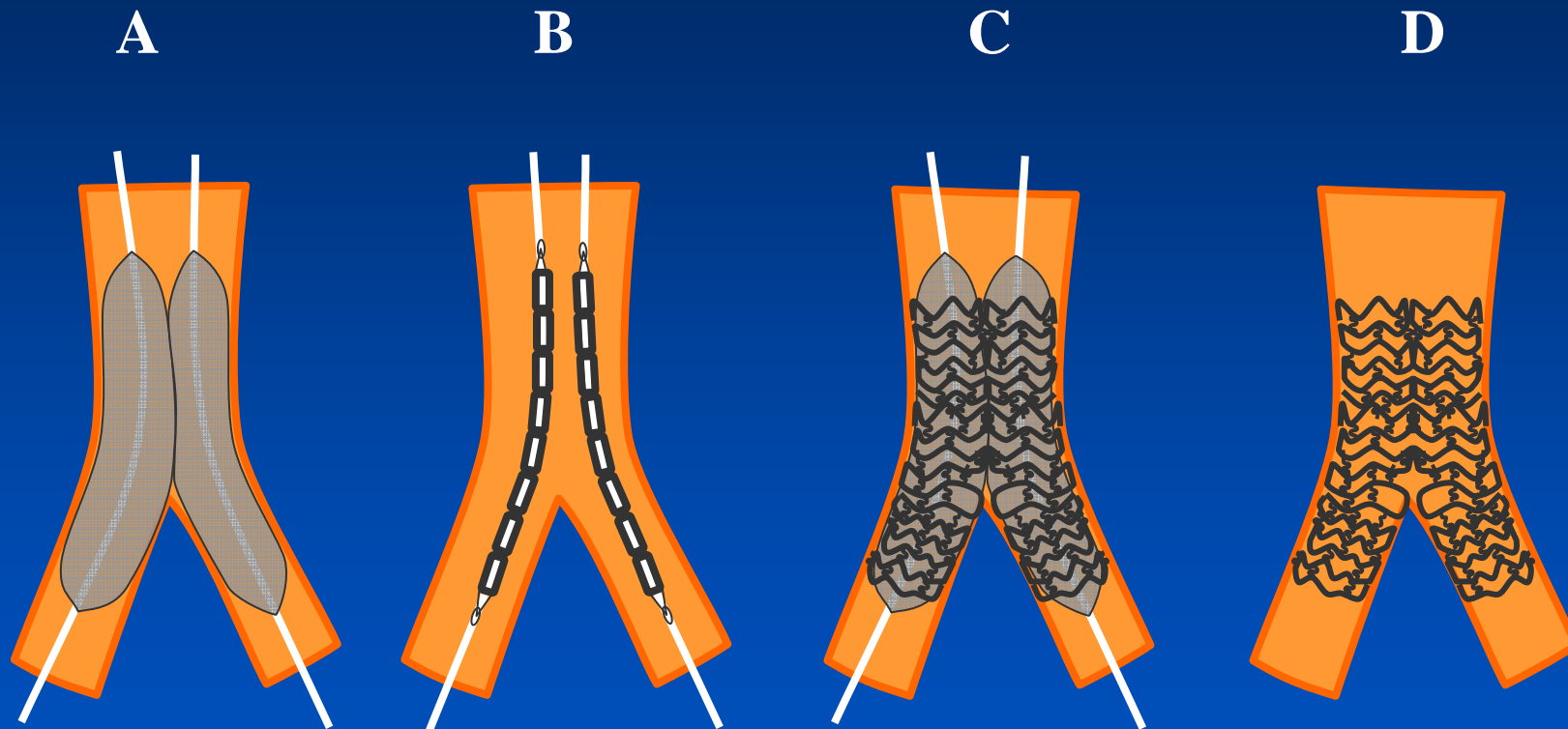
# Stenting Cross-over

## In lesions with normal LCX



# Kissing Stenting

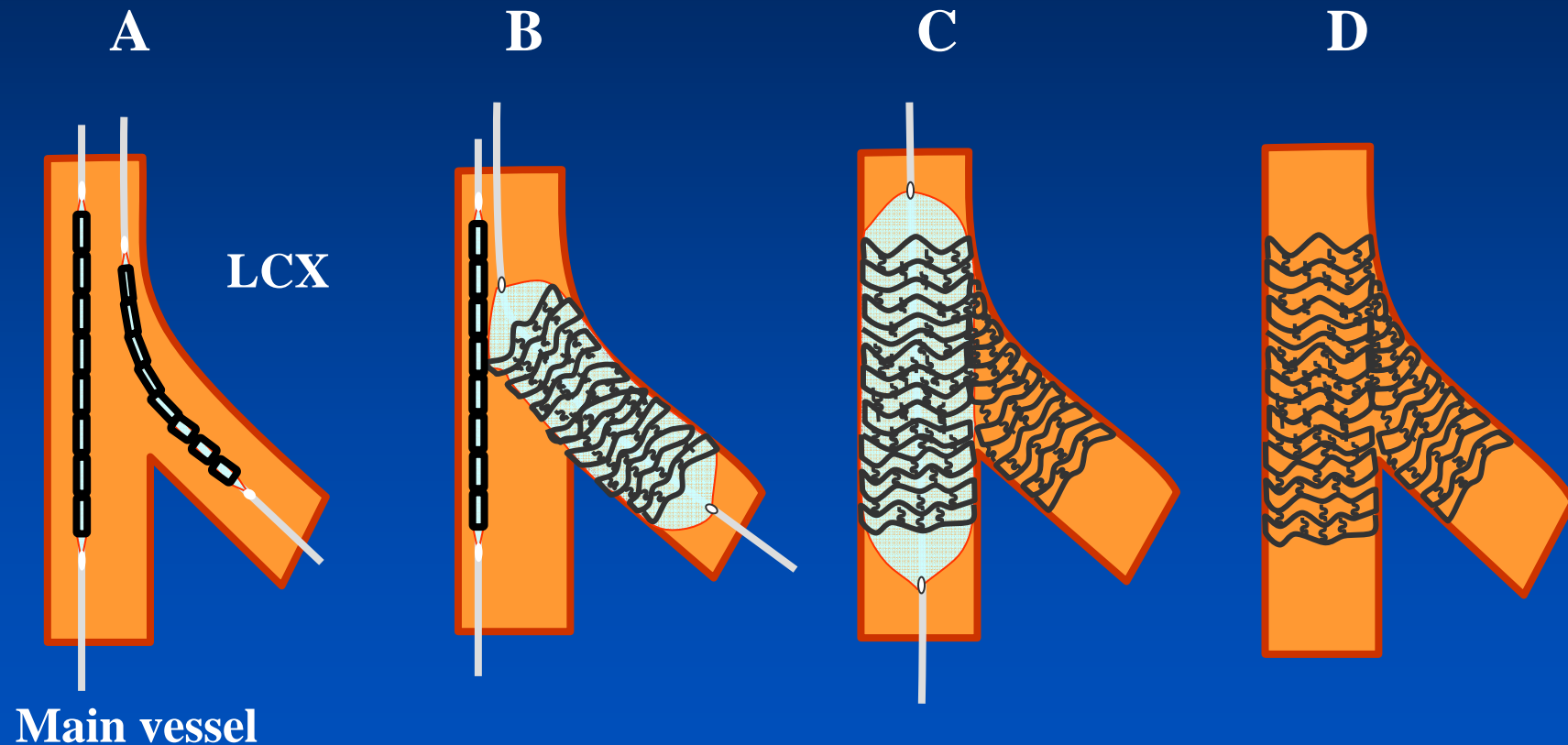
Lesions with large LM and diseased LCX





# Stent Crushing

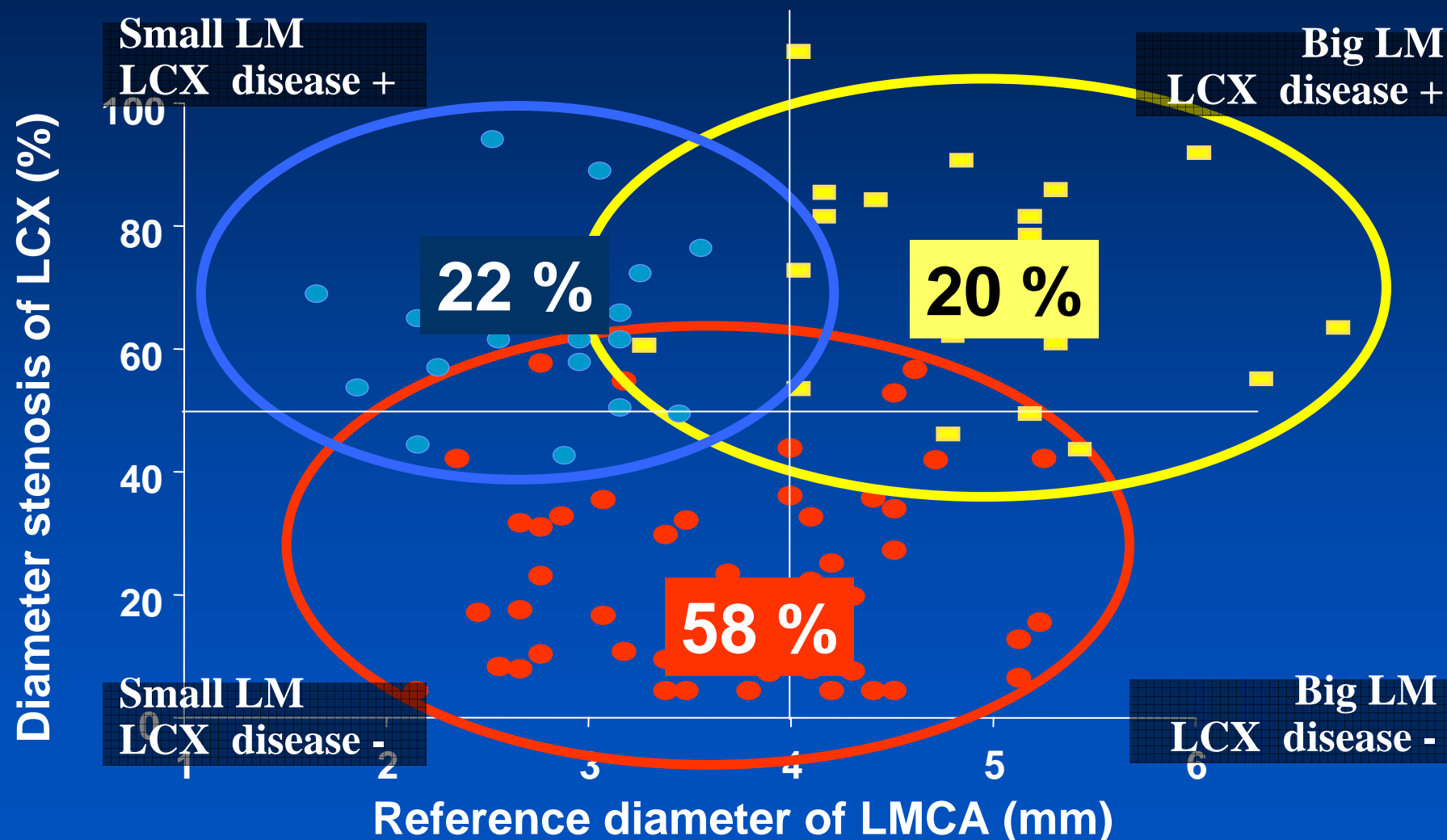
In moderate sized LM and diseased LCX



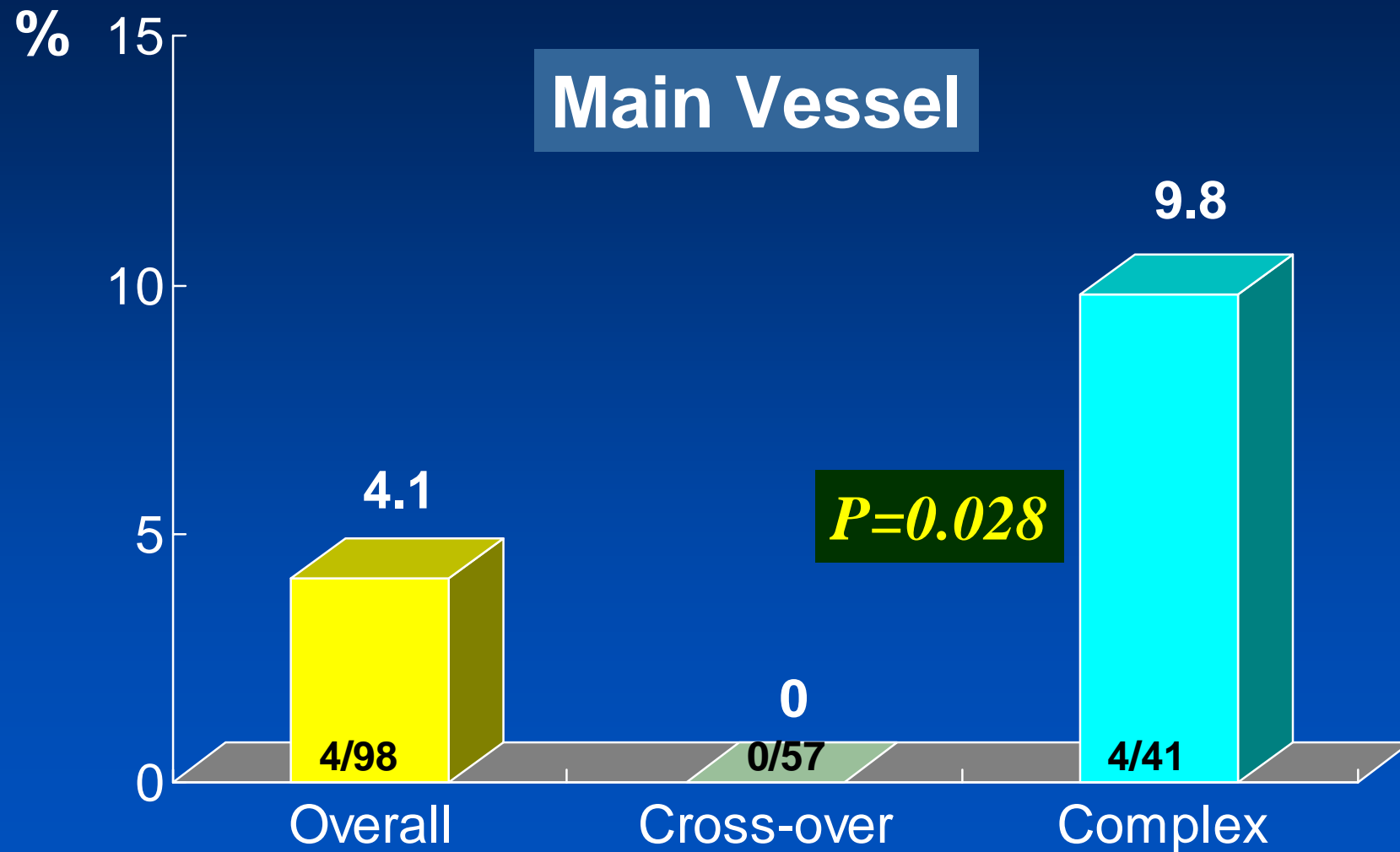
# Different Treatment Strategy

According to LM size and LCX involvement

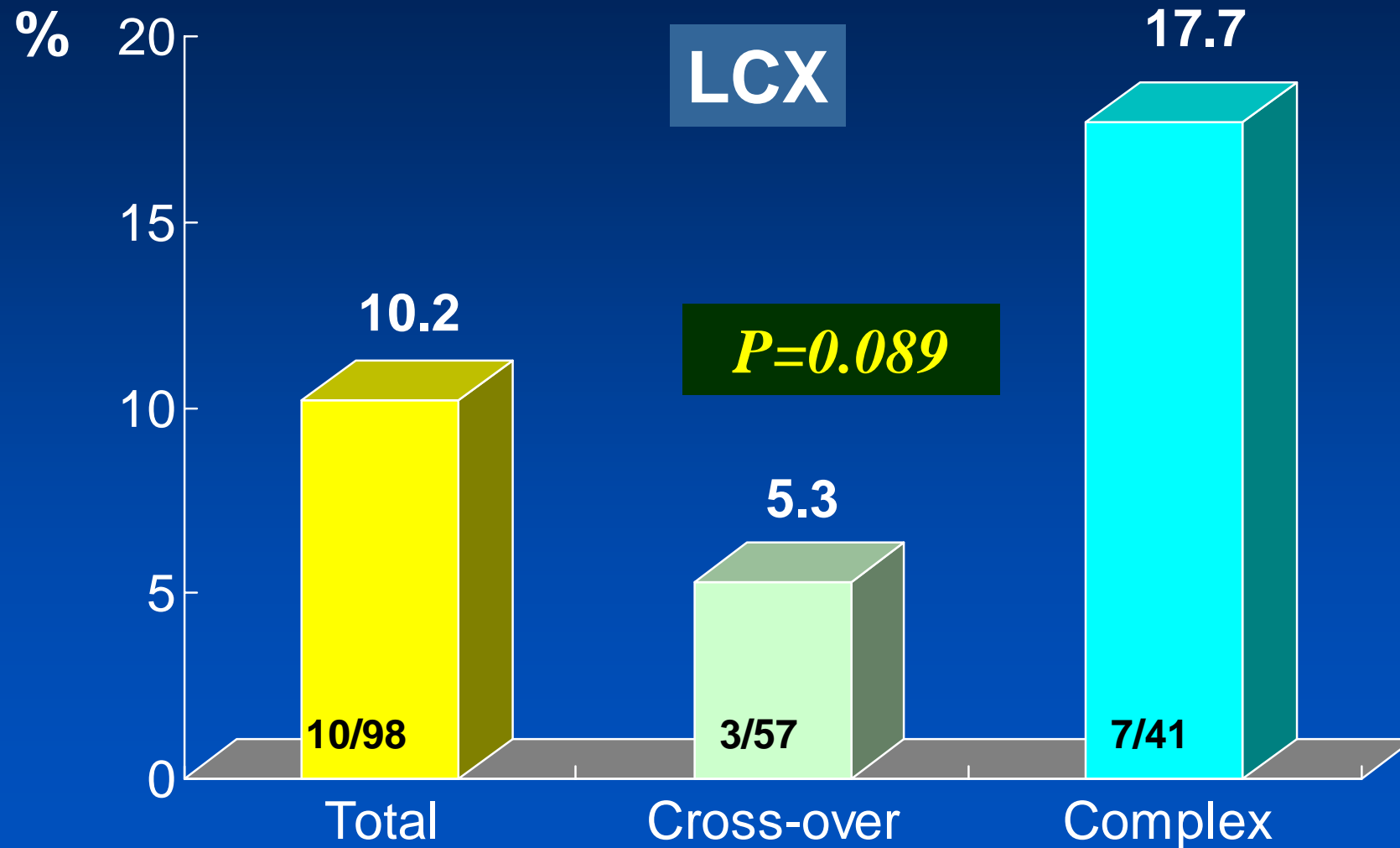
- Across LCX
- Crush
- Kissing



# Restenosis Rate of 124 LM Bifurcation PCI

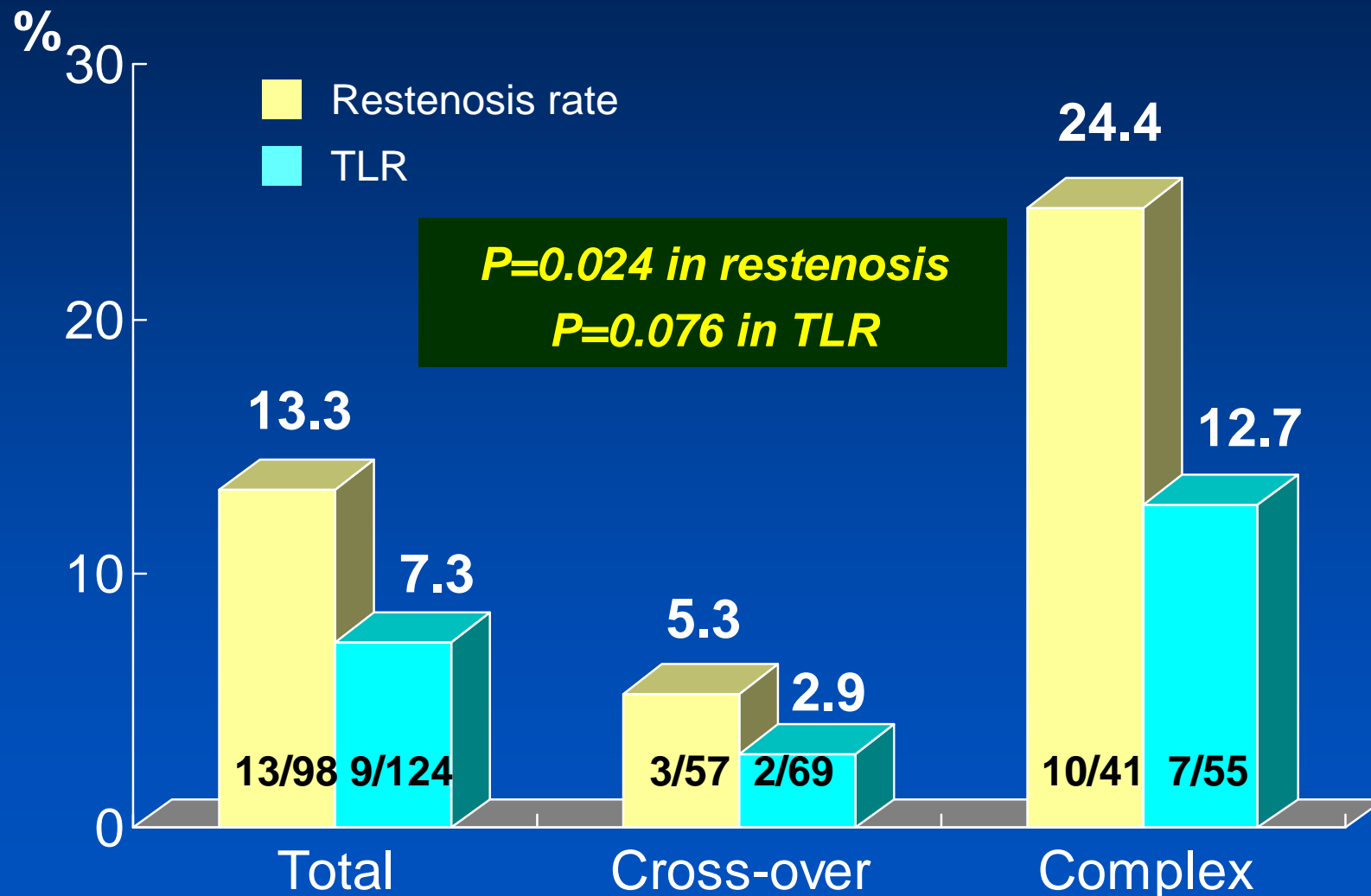


# Restenosis Rate of 124 LM Bifurcation PCI



# 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

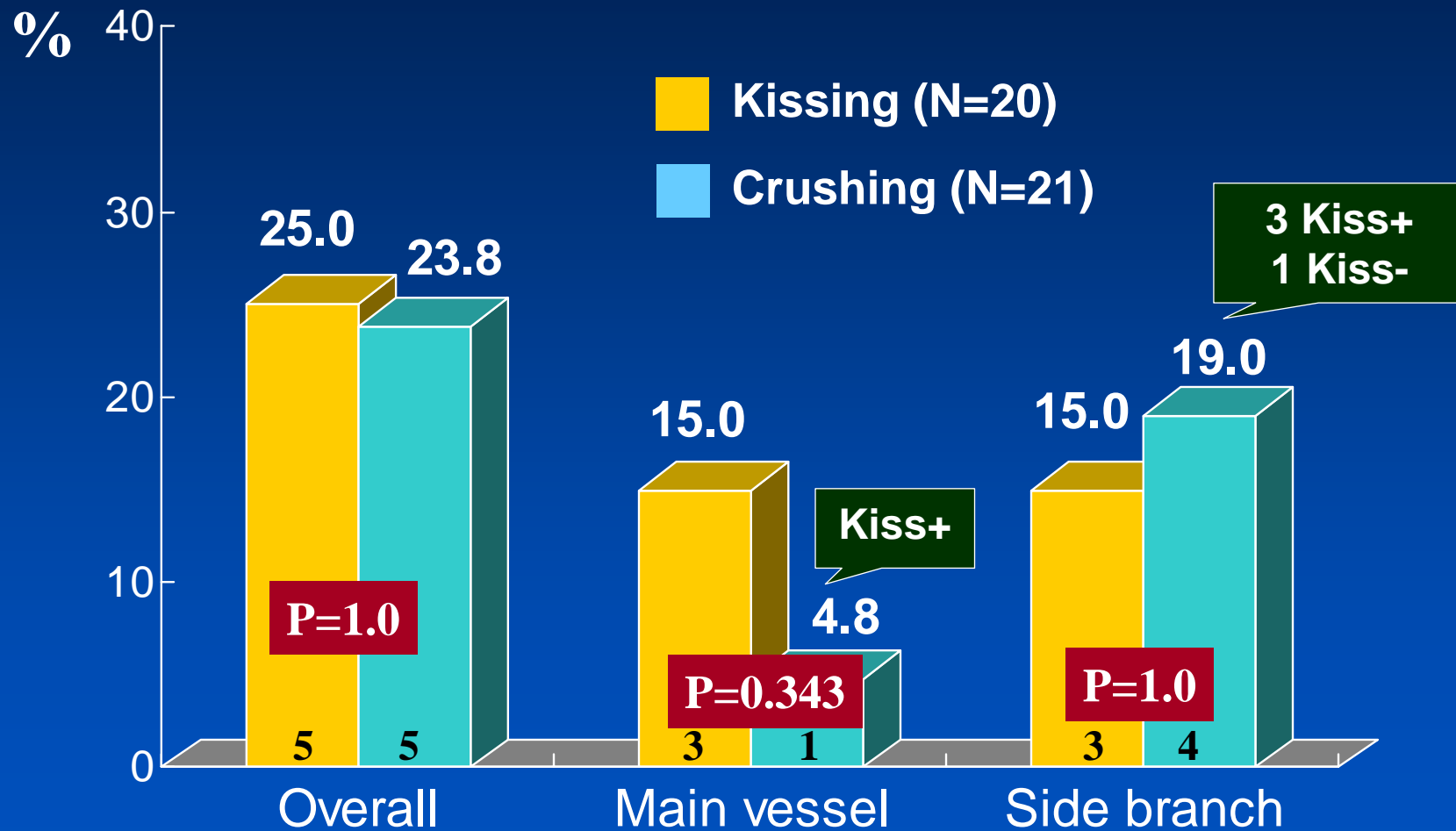
*YH Kim, Am J Cardiol 2006 (in press)*





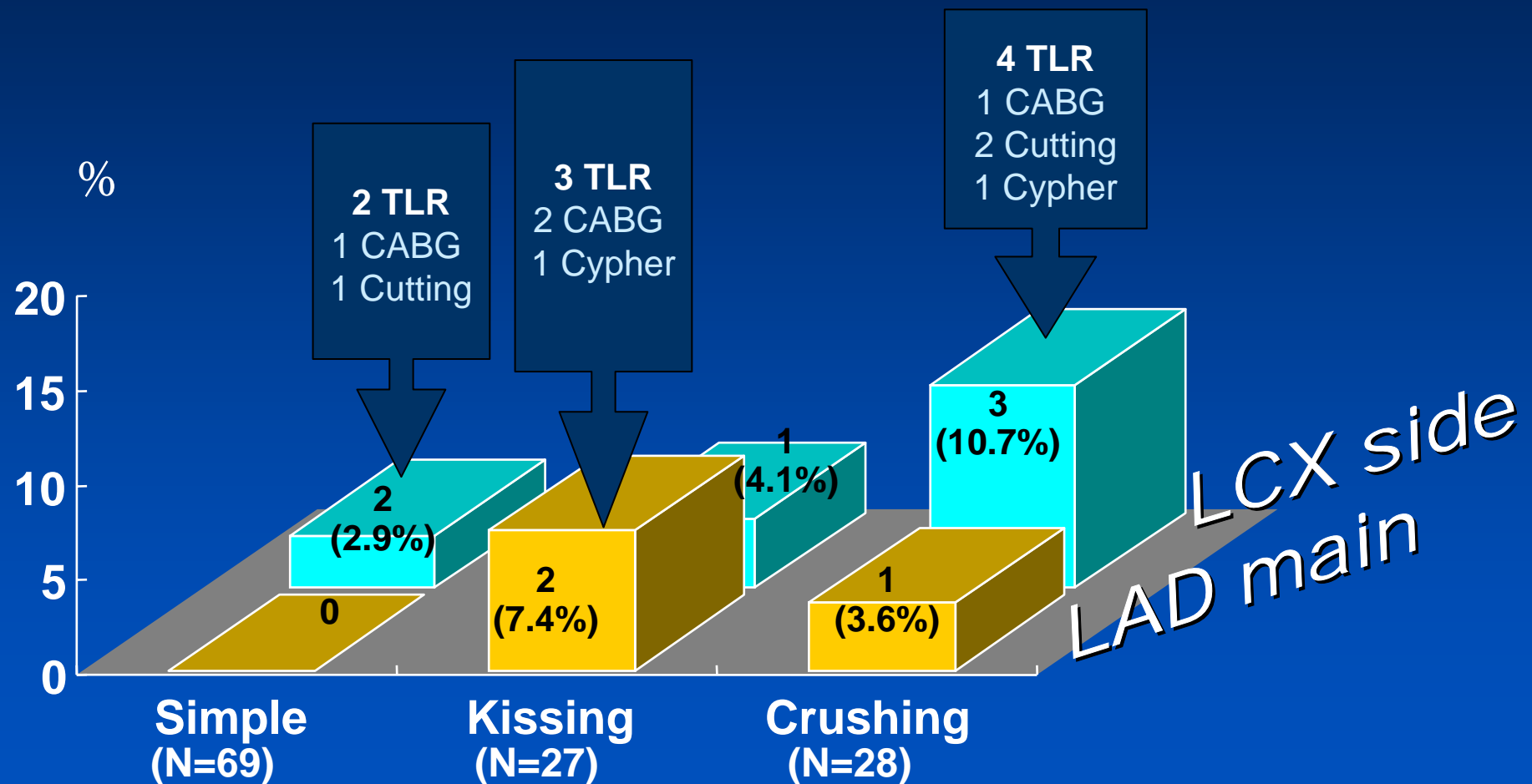
# Kissing vs. Crush

## 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)

**PCI with SES**  
N=888

**CABG**  
N=888

**Registry group**  
1,000

**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

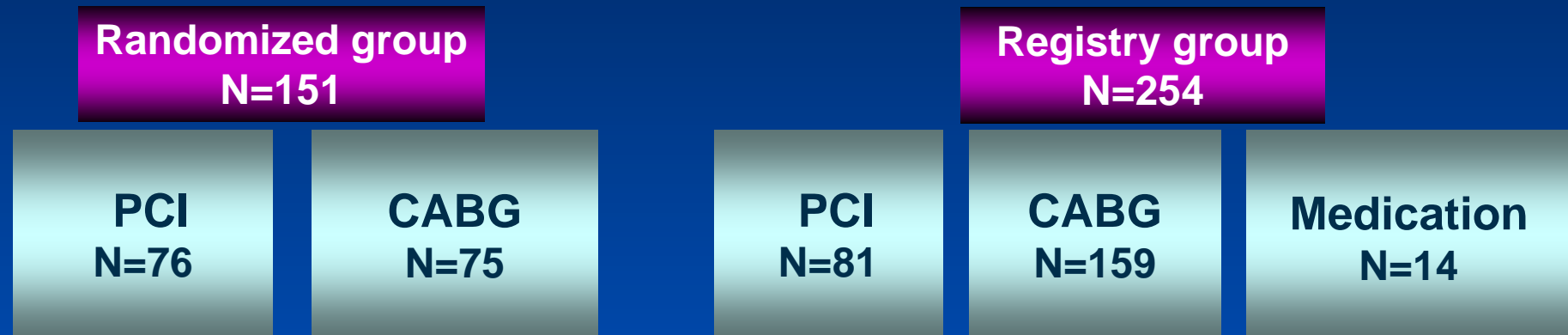
## Preliminary analysis

**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%) <sup>1</sup>	0.478
Cardiac	0	0	
Non-cardiac	0	1 (1%)	
Myocardial infarction <sup>2</sup>	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

<sup>1</sup> Pneumonia after CABG, <sup>2</sup> 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.