Incidence, mechanism, predictors, and long-term prognosis of late stent malapposition after bare-metal stent implantation in 992 coronary lesions.

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Background

In the era of brachytherapy and drug-eluting stents, unusual IVUS findings have included late stent malapposition (LSM) suggesting that these findings are more common than after bare metal stent (BMS) implantation.

Background

Incidence: One study reported LSM in 4-5% (9 / 206 patients) of BMS implantation (Shah VM, et al. *Circulation*. 2002;106: 1753–1755).

Mechanism - Regional remodeling: Previous IVUS studies suggested that the main cause of LSM is an increase in EEM out of proportion to the increase in peri-stent intimal hyperplasia (Mintz GS, *Circulation*. 2003;107: 2660–2663).

Purpose

However, the predictors *of LSM* and long-term prognosis *after detection of LSM* in BMS implantation have not been reported.

The aim of the current study was to evaluate the incidence, mechanism, predictors, and long-term prognosis of LSM after BMS implantation.

Study Population

From the Asan Medical Center clinical and core IVUS laboratory database, we identified 881 patients with 992 native lesions who underwent BMS implantation into *de novo* lesions with IVUS imaging at index and 6 months follow-up (mean interval: 6.3±2.8 months).

Definition of study end-point

Death: cardiac vs. non-cardiac.

Myocardial infarction (MI): elevation of CK-MB to a value 3 times the upper limit of the normal range.

Target lesion revascularization (TLR): repeat percutaneous or surgical intervention of the stented lesion.

Major adverse cardiac events (MACE): death of cardiac origin, MI, and TLR.

Antithrombotic Therapy

- Aspirin 200 mg/day and ticlopidine 500 mg/day or cilostazol 200 mg/day before stenting.

- Ticlopidine or cilostazol was given for 1 month after stenting, but aspirin was administered indefinitely.

- No additional antiplatelet agents except aspirin were administered to the patients with LSM after the 6-month follow-up angiogram.

IVUS Imaging Protocol

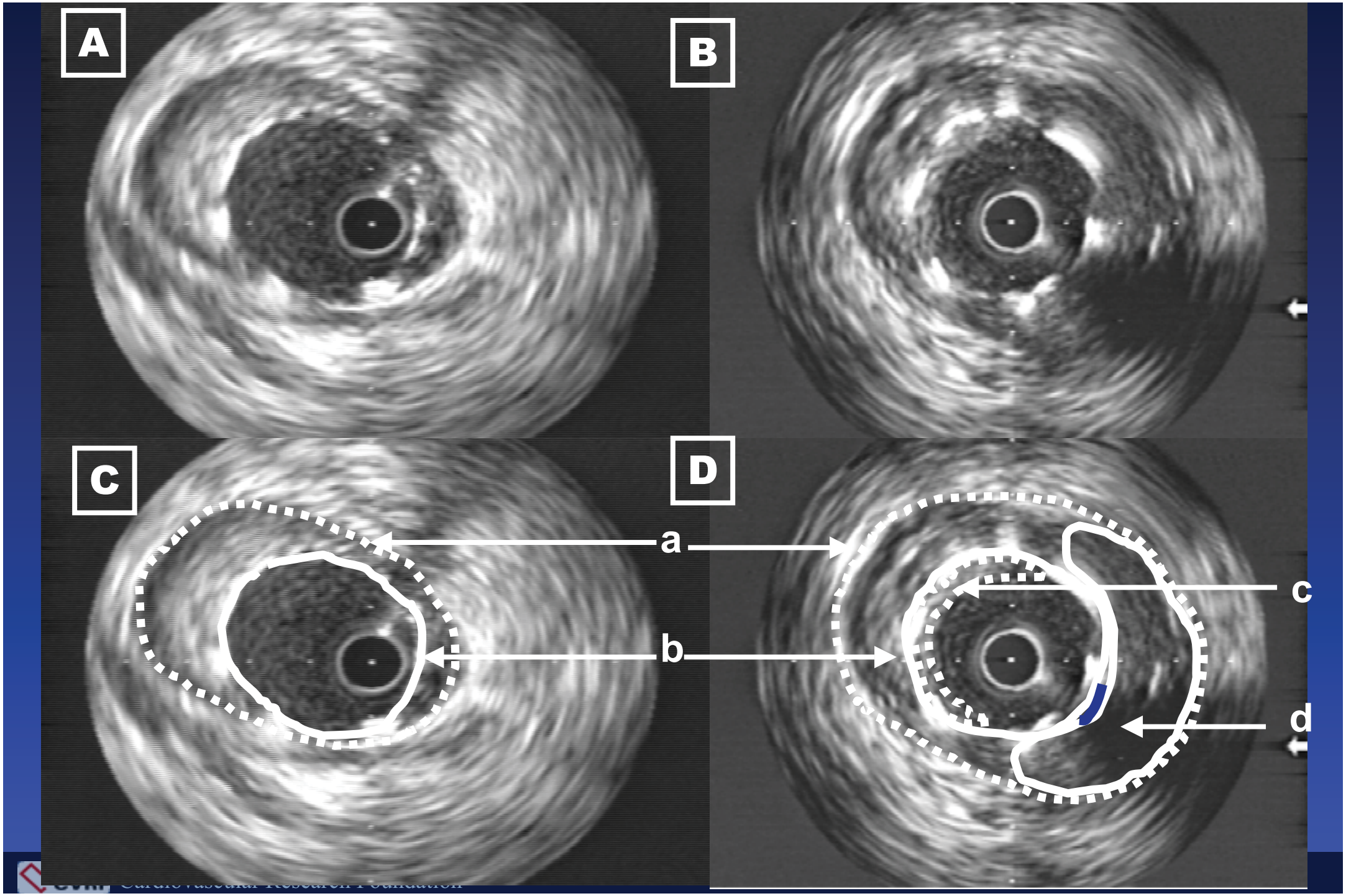
- Post-intervention and 6- month follow-up IVUS in identical fashion
- Automatic transducer pullback device (0.5 mm/sec)
- After intracoronary administration of 0.2mg NTG
- From more than 10 mm beyond the lesion segment to aorto-ostial junction
- CVIS system: 1,800 rpm, 3.2F IVUS catheter

IVUS analysis

Definition of LSM: a separation of at least 1 stent struts from the intimal surface of the arterial wall that was not overlapping a side branch, was not present at post-stent implantation, and had evidence of blood flow (speckling) behind the strut (Shah VM, et al. *Circulation*. 2002;106: 1753–1755).

Quantitative IVUS analysis:

- at LSM sections as well as stented segments with complete late apposition and reference segments.
- EEM, lumen, and stent CSA at stented and reference segments
- EEM, stent, P&M, intra-stent lumen, IH, and LSM CSA at LSM sections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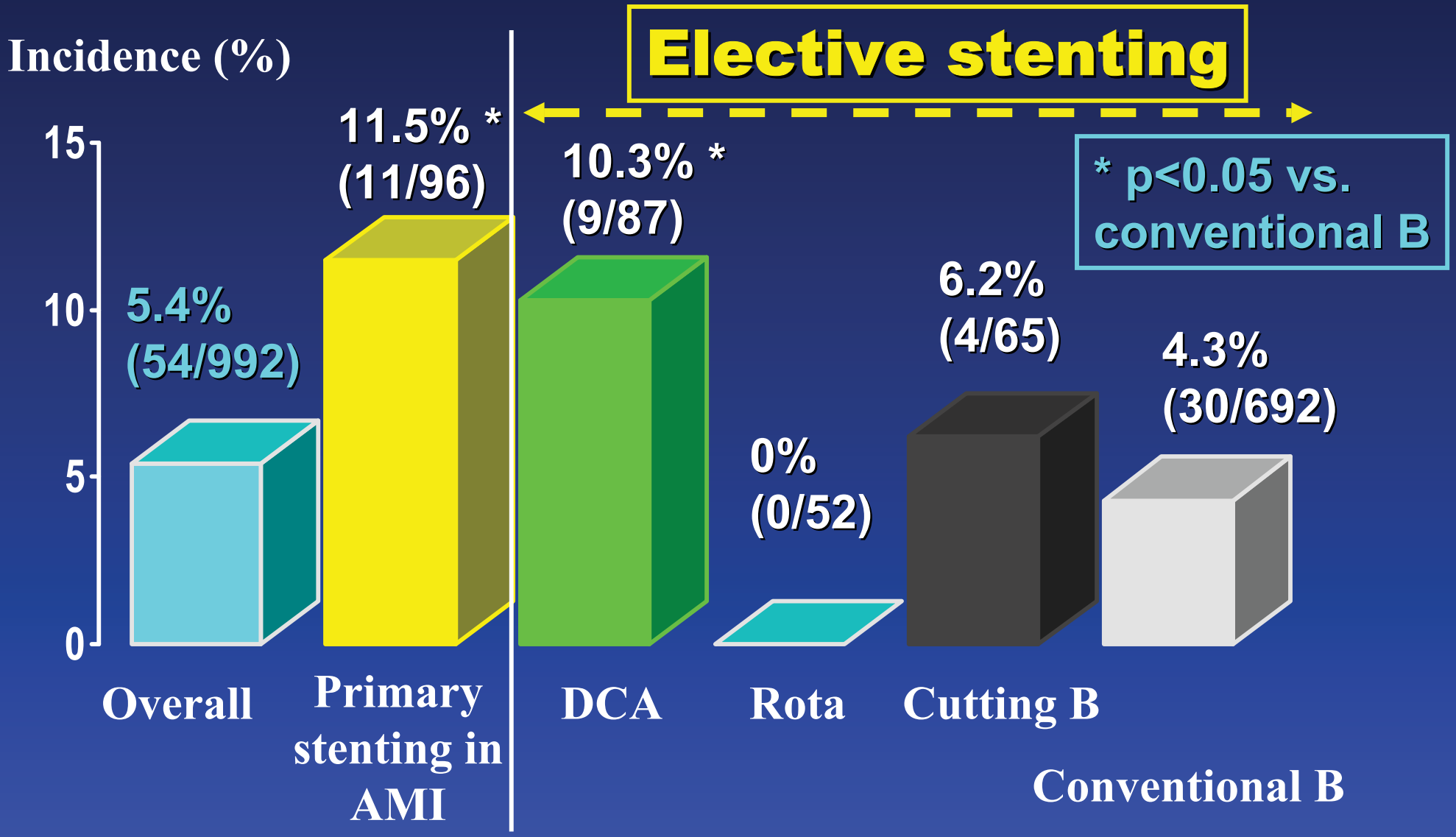
Incidence of LSM



Baseline clinical characteristics

	LSM	Non-LSM	P-value
No. of patients	54	827	
Age (years)	56±10	56±9	0.8
Male, # (%)	40 (74)	622 (75)	1.0
Hypertension, # (%)	20 (37)	283 (34)	0.8
Diabetes mellitus, # (%)	8 (15)	122 (15)	0.9
Smoking, # (%)	28 (52)	465 (56)	0.6

Baseline clinical characteristics

	LSM	Non-LSM	P-value
No. of patients	54	827	
Number of disease vessels			0.9
1, # (%)	40 (74)	595 (72)	
2, # (%)	10 (19)	166 (20)	
3, # (%)	4 (7)	66 (8)	
Clinical presentation			0.5
Stable angina, # (%)	16 (30)	196 (24)	
Unstable angina, # (%)	24 (44)	437 (52)	
Acute MI, # (%)	14 (26)	194 (24)	

Angiographic characteristics

	LSM	Non-LSM	P-value
No. of lesions	54	938	
Coronary artery dilated			0.9
LAD	34 (63%)	606 (65%)	
LCX	5 (9%)	100 (11%)	
RCA	15 (28%)	232 (25%)	
Stent length (mm)	18.9±7.2	18.7±6.1	0.8
Ref. diameter (mm)	3.5±0.5	3.4±0.6	0.11
MLD (mm)			
Pre-intervention	0.6±0.5	0.8±0.5	<0.001
Post-intervention	3.4±0.5	3.4±0.6	0.5
Pressure (atm)	13.5±2.0	13.1±3.2	0.4
Balloon-to-artery ratio	1.16±0.14	1.14±0.13	0.4

IVUS data: post-intervention

	LSM	Non-LSM	P-value
Distal reference			
EEM CSA (mm^2)	15.0±4.3	13.9±4.5	0.088
Lumen CSA (mm^2)	9.1±2.7	8.5±2.9	0.095
Stented segment			
Stent CSA (mm^2)	8.2±1.8	7.9±2.5	0.3
Proximal reference			
EEM CSA (mm^2)	18.0±4.2	16.4±4.1	0.019
Lumen CSA (mm^2)	10.7±2.9	9.7±3.1	0.047

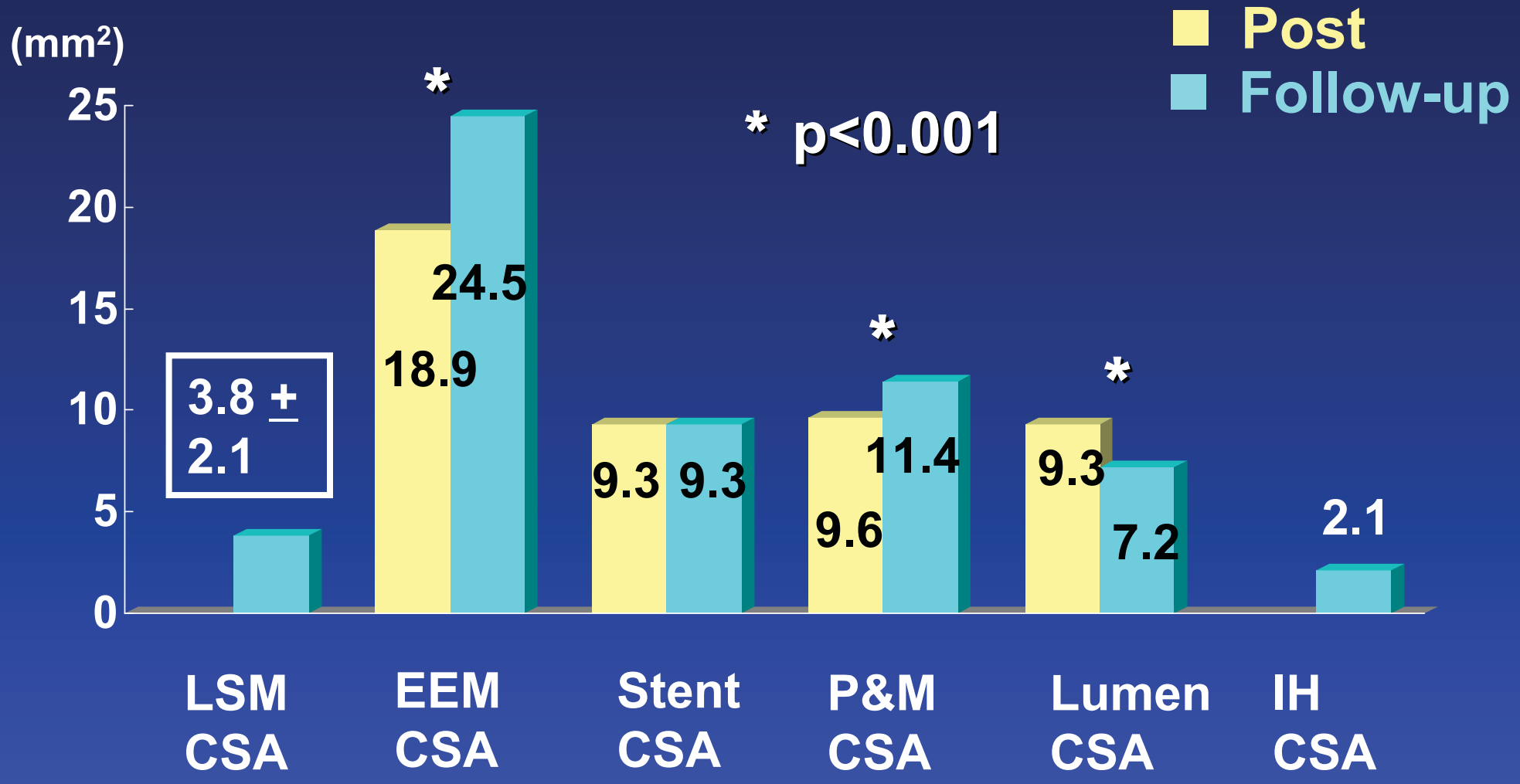
Angiographic characteristics in subgroup with stenting after conventional balloon predilation

	LSM	Non-LSM	P-value
No. of lesions	30	662	
Stent length (mm)	18.8±7.6	18.6±4.3	0.5
Ref. diameter (mm)	3.3±0.4	3.3±0.8	1.0
MLD (mm)			
Pre-intervemtion	0.6±0.4	0.9±0.5	<0.001
Post-intervention	3.3±0.5	3.3±0.6	0.9
Pressure (atm)	13.5±1.8	13.1±3.2	0.5
Balloon-to-artery ratio	1.21±0.15	1.14±0.13	0.019

IVUS data: post-intervention in subgroup with stenting after conventional balloon predilation

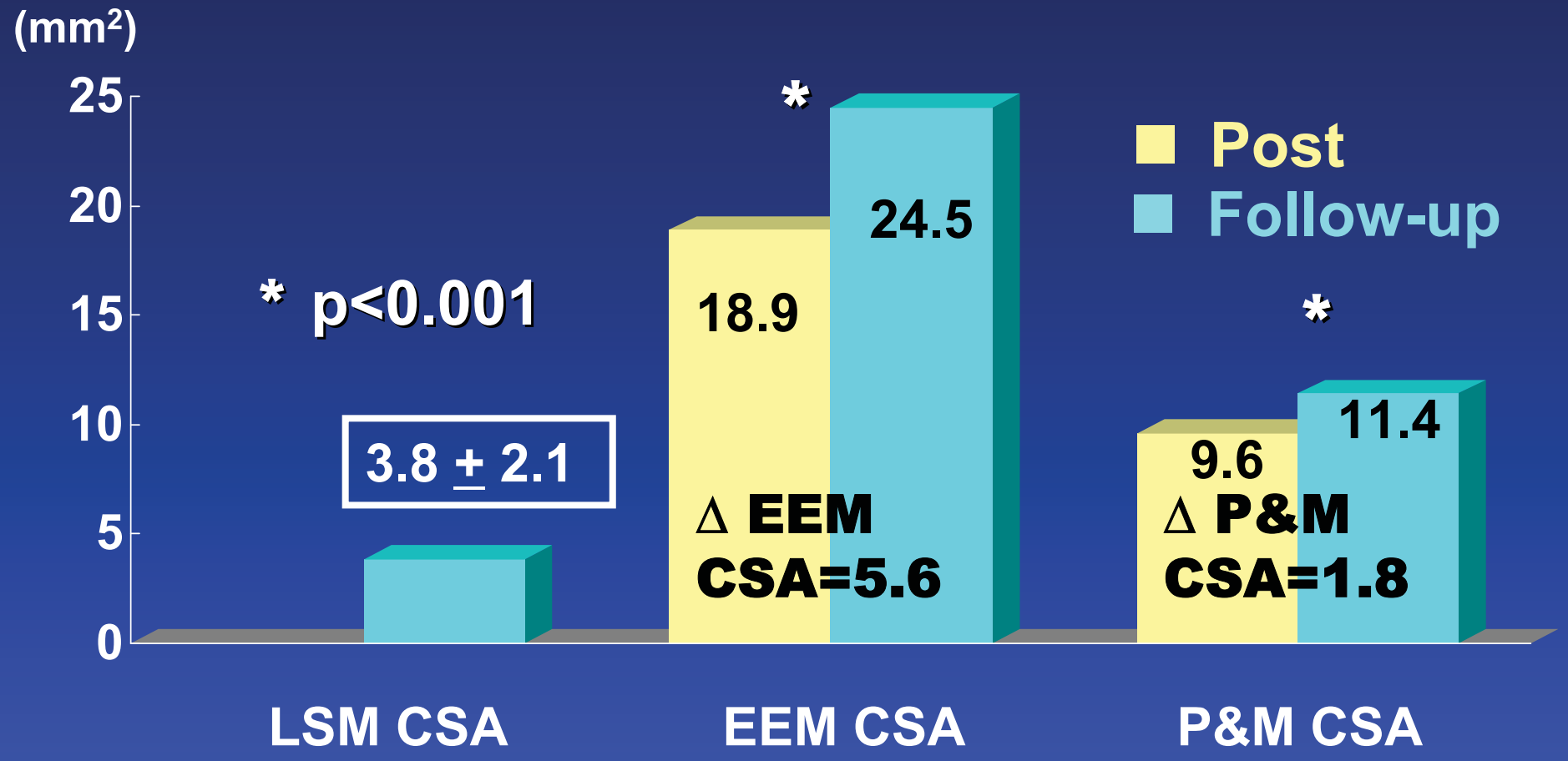
	LSM	Non-LSM	P-value
Distal reference			
EEM CSA (mm^2)	14.5±4.1	13.6±4.5	0.3
Lumen CSA (mm^2)	8.7±2.7	8.3±2.9	0.4
Stented segment			
Stent CSA (mm^2)	8.1±1.7	7.6±2.4	0.19
Proximal reference			
EEM CSA (mm^2)	17.8±4.3	16.2±4.2	0.11
Lumen CSA (mm^2)	10.5±3.2	9.6±3.1	0.18

Post-intervention and follow-up IVUS at LSM segment



Mechanism of LSM- vascular remodeling:

The increase in EEM was greater than the increase in P&M ($p<0.001$).



Independent predictors of LSM by multivariate analysis

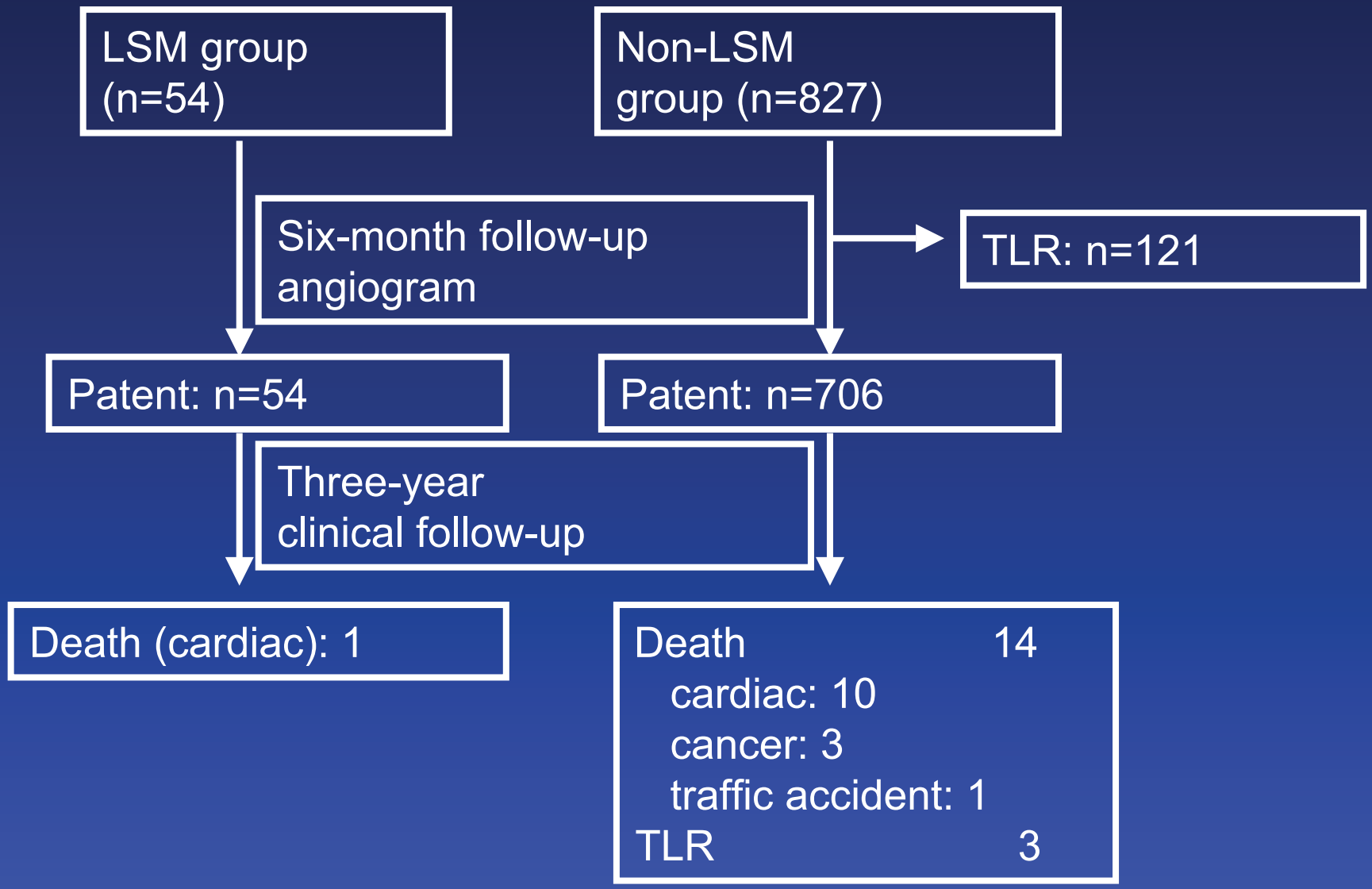
- Primary stenting in acute myocardial infarction (p=0.023, OR=2.55, 95% CI= 1.14-5.69)

- DCA before stenting (p=0.025, OR=3.02, 95% CI= 1.15-7.96).

Independent predictors of LSM by multivariate analysis in subgroup with conventional balloon predilation

Pre-intervention QCA MLD (p=0.003, OR=0.23, 95% CI= 0.09-0.60).

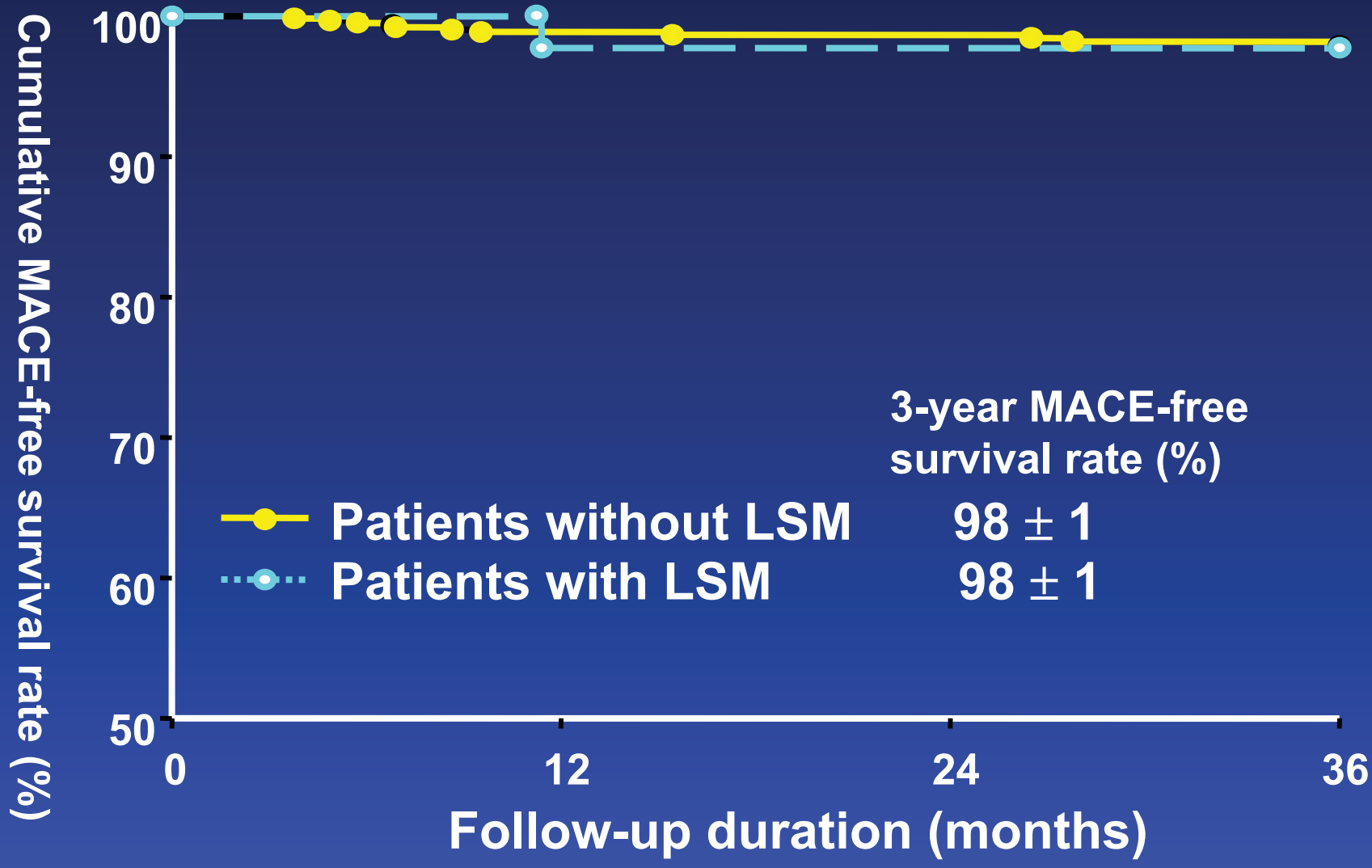
The flow diagram of long-term clinical follow-up



Long-term clinical follow-up: MACE after detection of LSM

- Mean duration after 6-month angiogram: 34.6±17.7 in LSM group and 35.3±15.0 months in non-LSM group.
- Death of cardiac origin: in 1 patient in LSM group and, 10 patients in non-LSM group.
- Late TLR in 3 patients in non-LSM group, but in none of the LSM group.
- No significant differences in MACE between LSM and non-LSM groups (1.9% vs. 1.8%, respectively, p=NS).

The cumulative (MACE) free survival curve



Conclusion

1) LSM occurs in approximately 5% after BMS implantation.

2) The predictors of LSM are primary stenting in AMI and DCA before stentng.

3) Compared with complete stent apposition at follow-up, LSM after BMS implantation is not associated with any MACE during 3-year follow-up after detection of LSM.