10th Angioplasty Summit 2005
April 28th -30th 2005

Abciximab Eluting Stent in Acute Coronary Syndrome

Myung Ho Jeong, MD, PhD, FACC, FESC, FSCAI

The Heart Center of Chonnam National University Hospital,
Applied Chemical Engineering of Chonnam National University

Gwangju, Korea

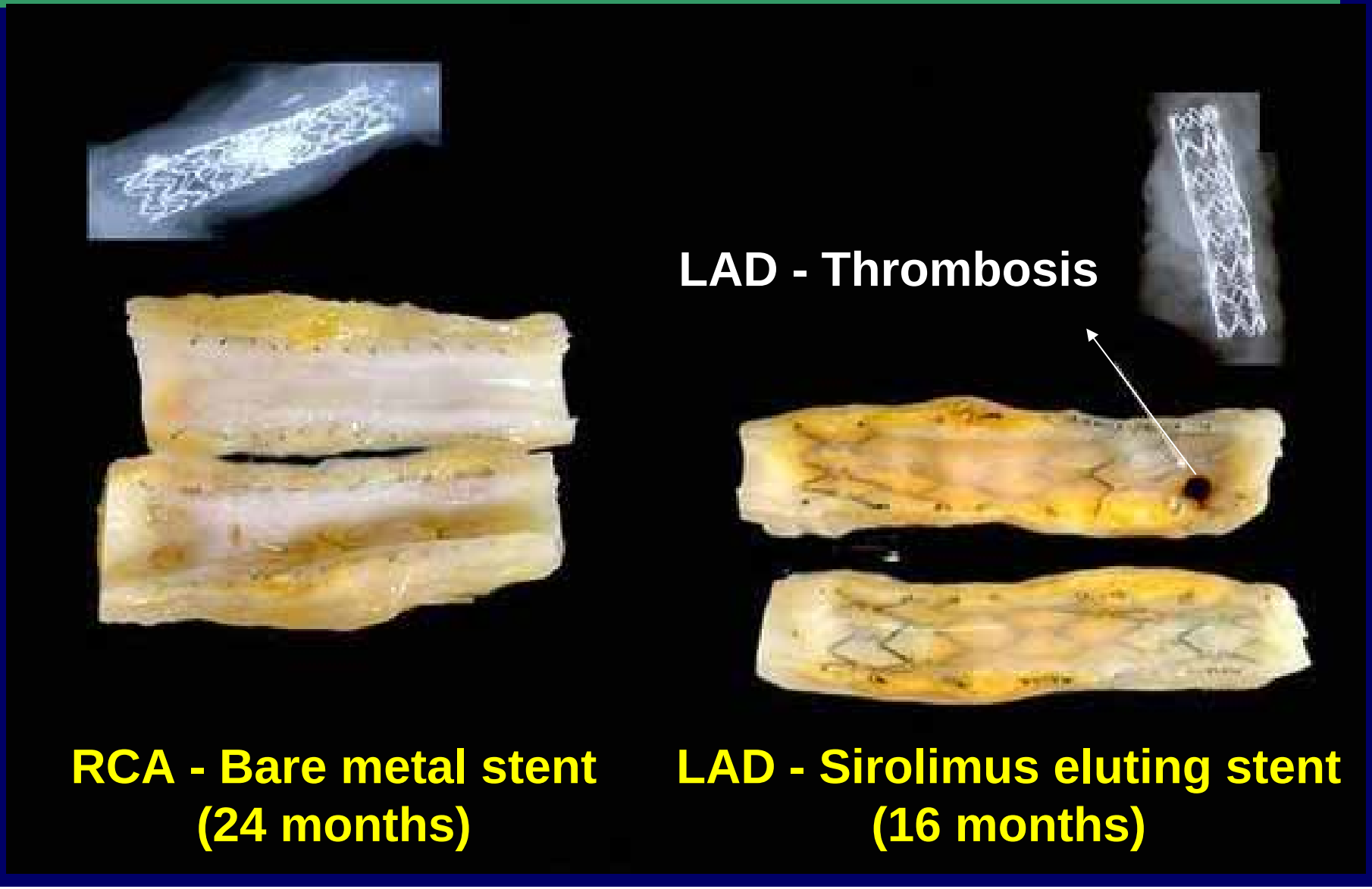
Drug Eluting Stent

PTCA	BMS	DES

RS → 30~40% → 15~30% → 0~9%

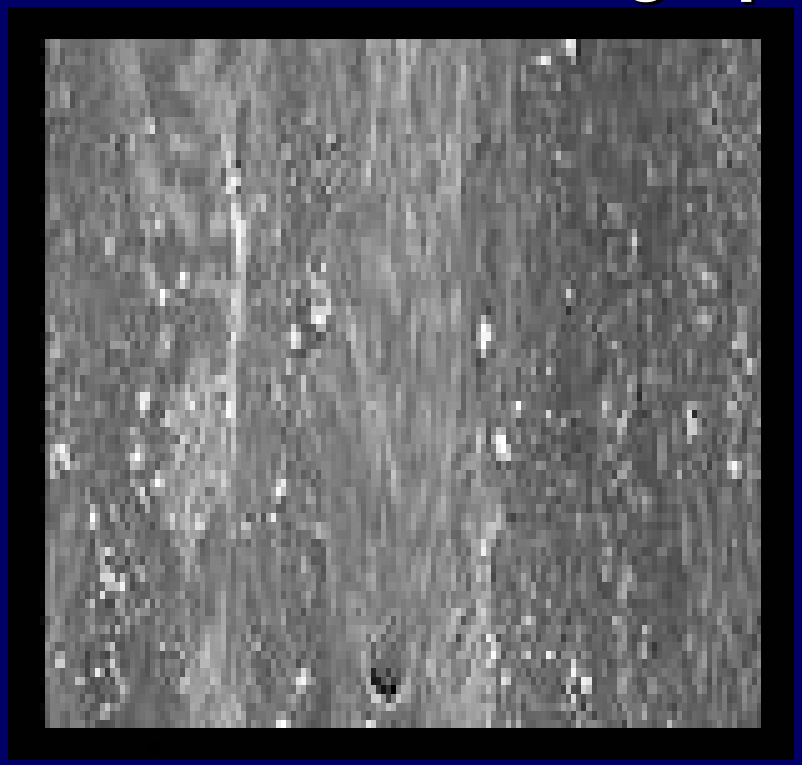
DES: Very promising, NOT perfect !

Autopsy Findings Died of Stroke After BMS and DES

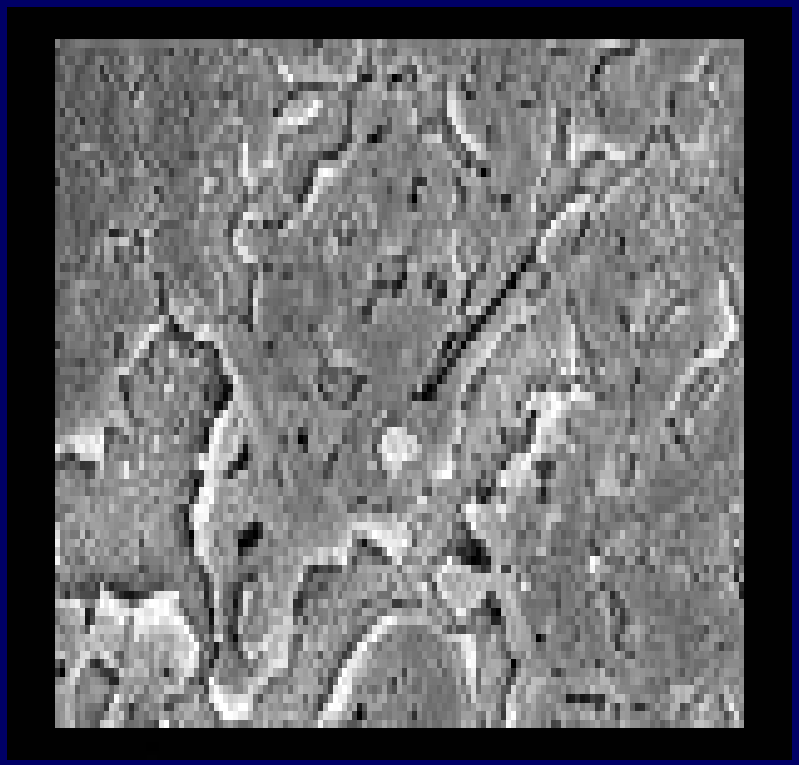


Delayed Endothelization and Platelet Deposition in DES

High power SEM



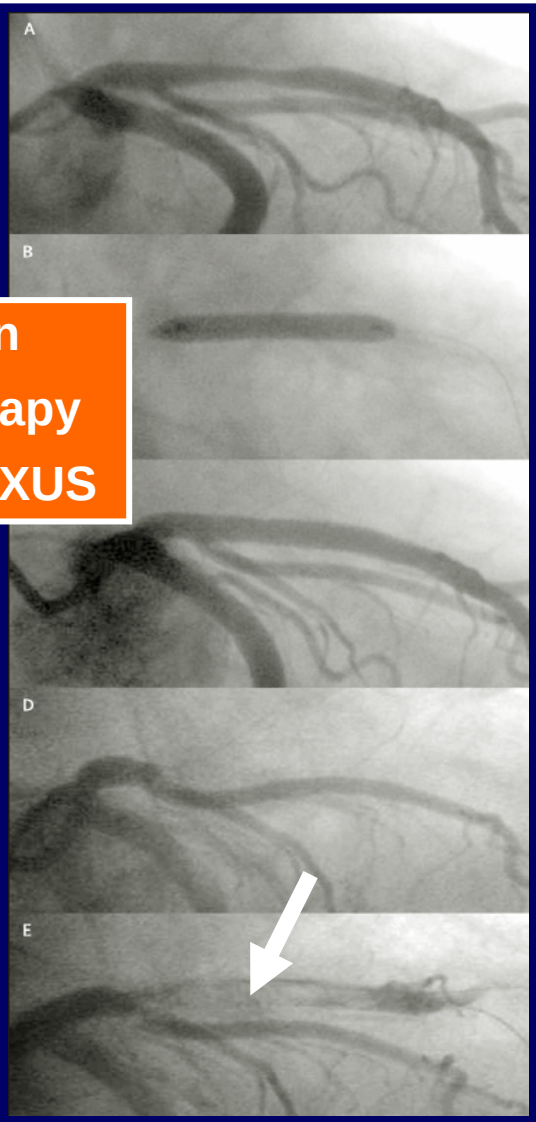
RCA -Bare metal stent : Confluent endothelial cells and few platelets

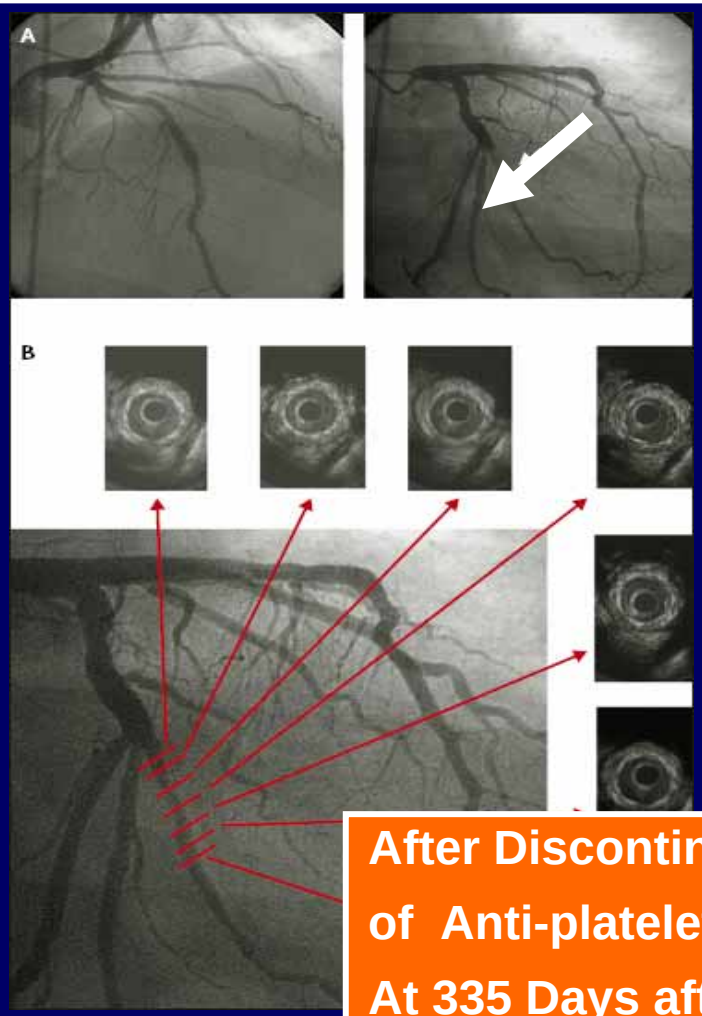


LAD-Sirolimus eluting stent : Non-confluent endothelial cells and multiple platelet thrombi

Late Stent Thrombosis in DES After Discontinuation of Anti-platelet Therapy

After Discontinuation of Anti-platelet Therapy At 343 Days after TAXUS





After Discontinuation of Anti-platelet Therapy At 335 Days after CYPHER

Thoraxcenter. Lancet 2004;364:1519-21

DES: *Things We Should Overcome…*

- Stent thrombosis - early or late
- Polymer-mediated inflammation
- Local hypersensitivity of Drug
- Availability of coating methods
- In specific lesion
  such as ISR, bifurcated lesion, CTO, DM,
  SVG, diffuse long lesion ….

Animal and Clinical Experiences of New Coronary Stents

1. **Bare Metal Stent**

   MAC stent, Freedom stent, Arthos (Carbon coated) stent

   PICO (Co-Cr) stent, Core stent

2. **Radioactive (Ho-166) stent**

3. **Drug-eluting stent**

   Heparin stent, Paclitaxel eluting on Carbon stent

   ReoPro® stent, Anti-oxidant (carvedilol) eluting *BiodyVisio* stent

   Echinomycin-heparin double coating on Co-Cr stent

   Phospholipid coating biocompatible stent

4. **Gene-coated stent**

   Natural polymer (LMWSC)-mediated gene coating stent

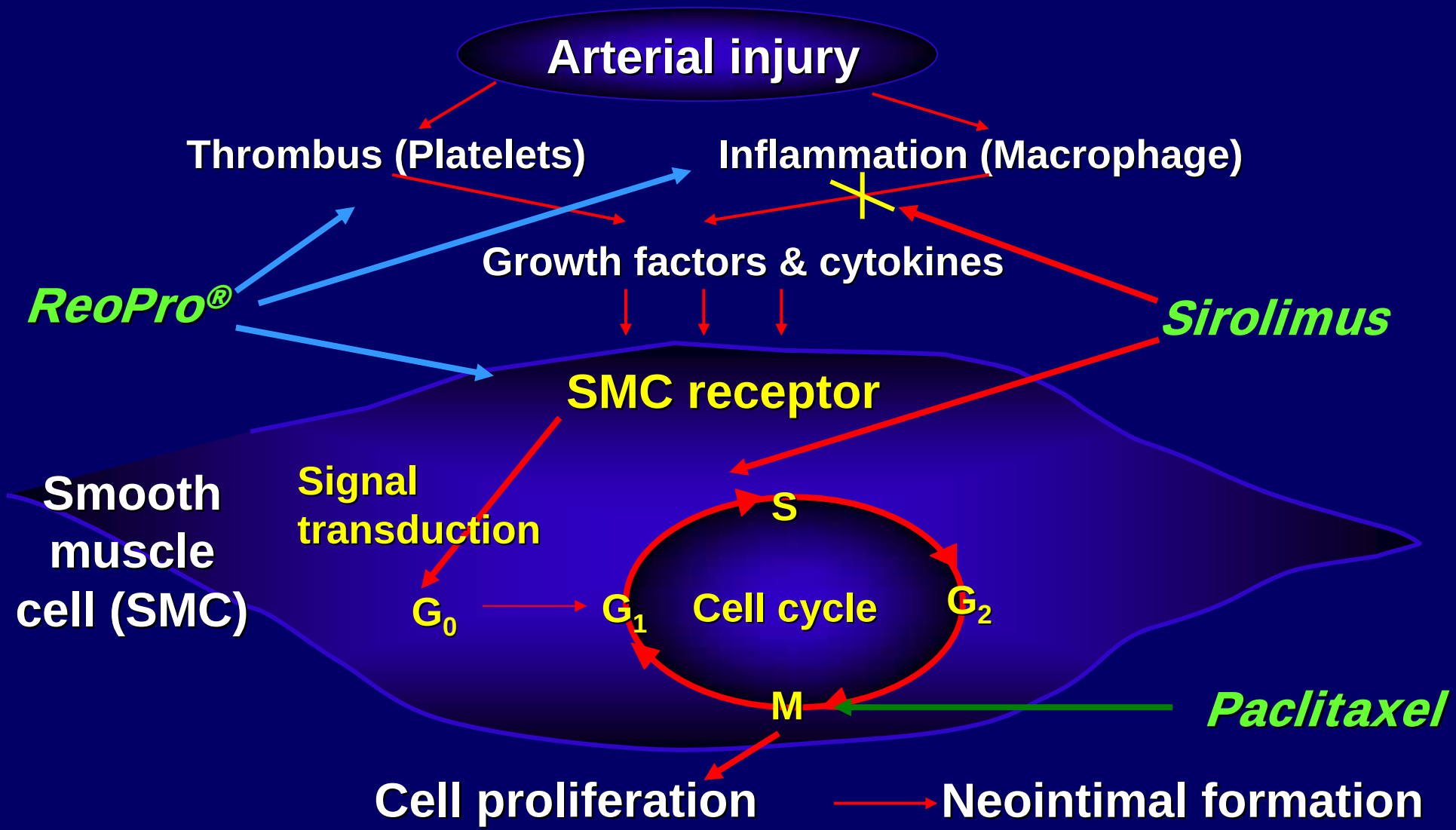
Platelet GP IIb/IIIa Inhibitor
Abciximab (ReoPro®)

- **Platelet activation and aggregation**
  - induces arterial thrombosis
  - play a pivotal role in the pathophysiology of ACS
- **Inhibitors of platelet glycoprotein IIb/IIIa receptor**
  - has expanded the therapeutic options for treating thrombotic disorders
- **Abciximab**
  - a potent inhibitor that block final pathway of platelet aggregation
  - decreases short- and long-term event rates after percutaneous coronary intervention

Platelet GP IIb/IIIa Inhibitor
Abciximab (ReoPro®)

- **Abciximab**
  - similar receptor binding affinity for the vitronectin receptor present on smooth muscle cells, endothelial cells, platelets
- **Vitronectin receptor blockade**
  - may inhibit smooth muscle cell migration and proliferation after acute arterial vessel injury.
- **CD11b/18 or macrophage-1 receptor** present on neutrophils and monocyte
  - modulates white-cell adhesion, white-cell-platelet interactions, and the inflammatory response to vessel injury
  - MAC-1 receptor is upregulated after PCI and is inhibited by abciximab

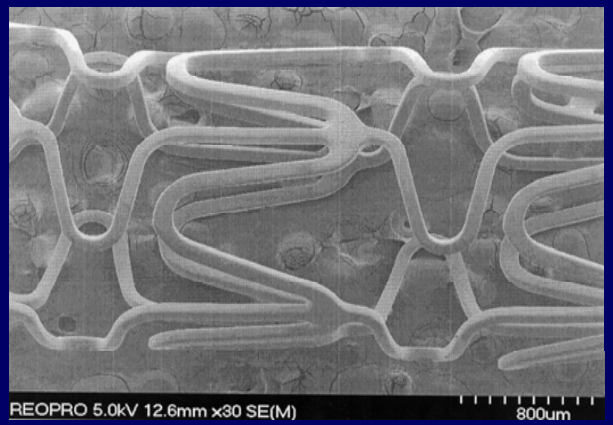
Therapeutic Mechanisms



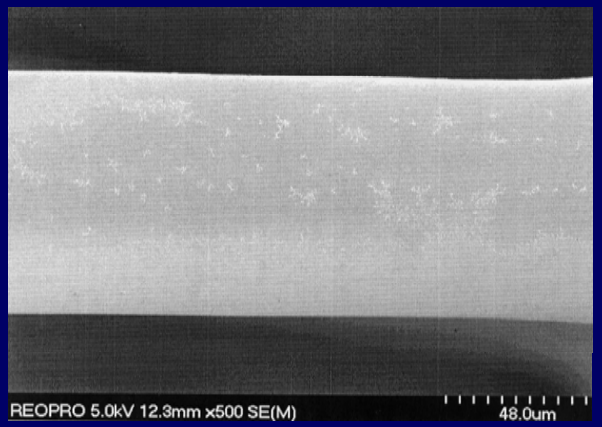
Expected Clinical Implications of Abciximab (ReoPro®)-coated Stent

- Effective in Thrombus Burden Lesion
- Possible short course of anti-platelets
- Reduce restenosis rate in diabetes
- Cost effective and safer than Cypher or TAXUS

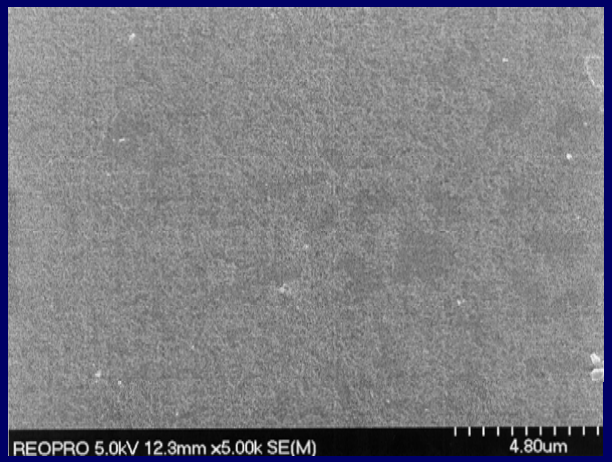
Scanning Electron Microscopy of ReoPro® Stent



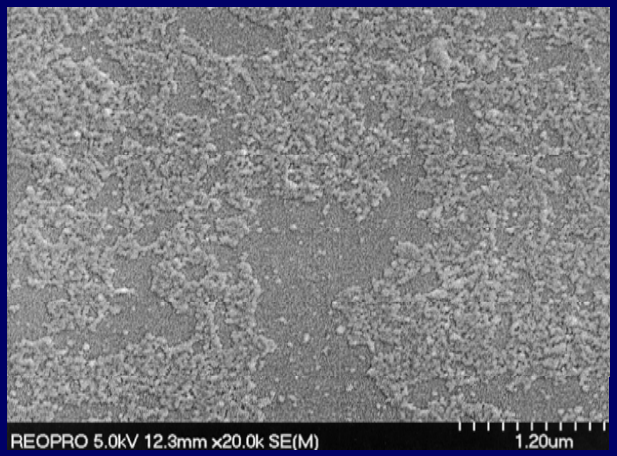
1 X 30



1 X 500



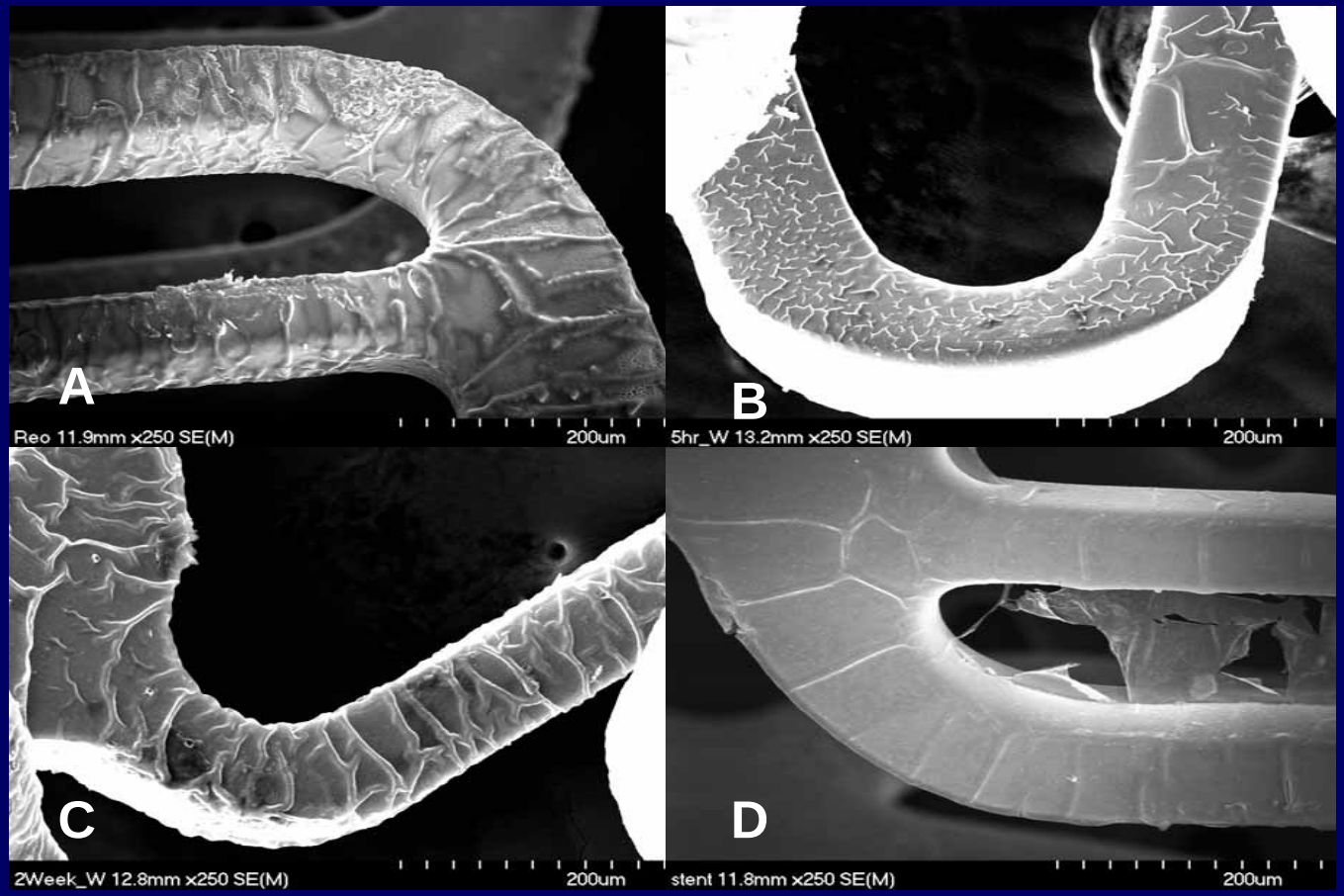
1 X 5,000



1 X20,000

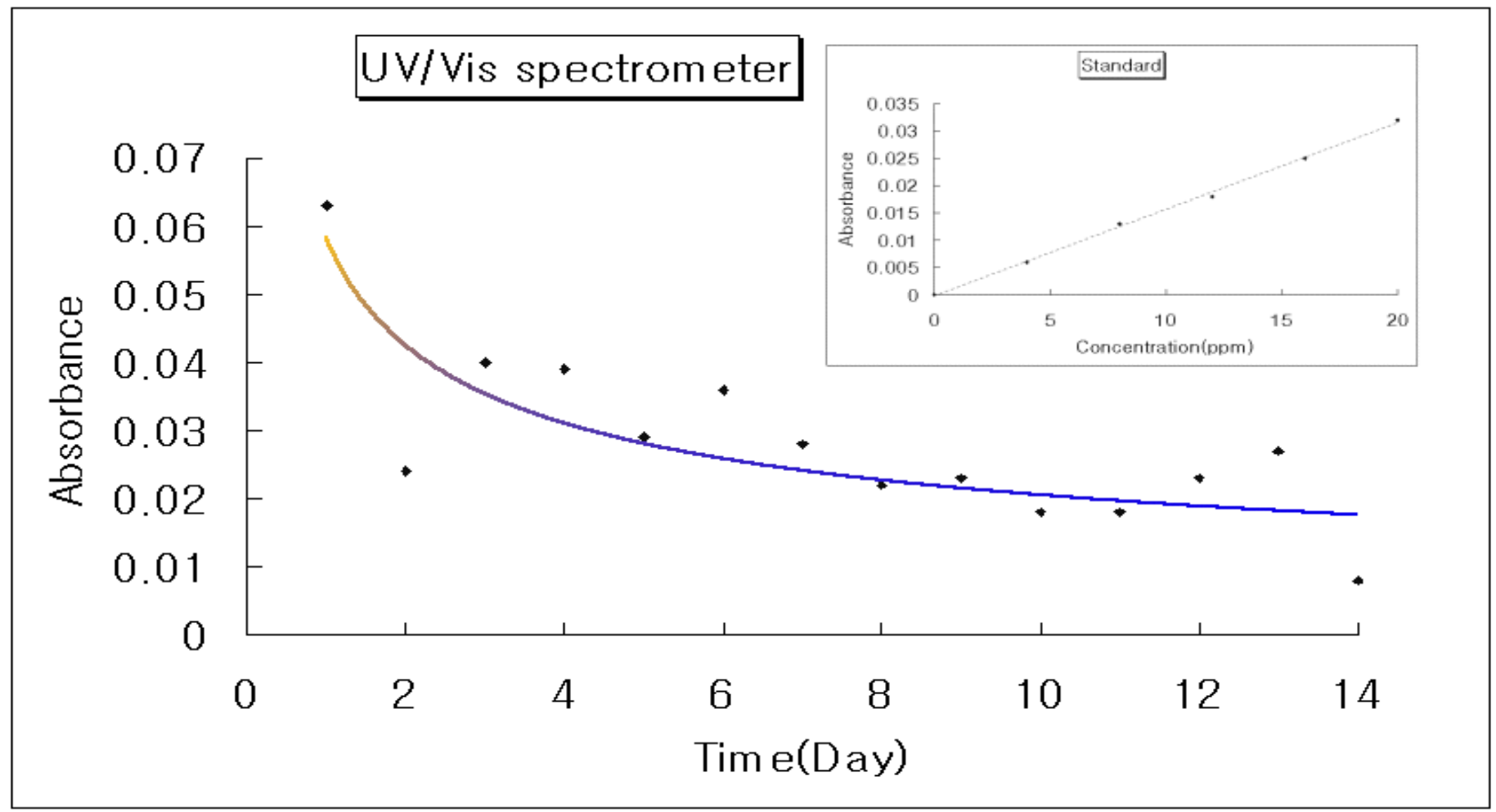
Stent surface coated
Plasma polymerization
Amine coating
(Diaminocyclohexane)
Stent ReoPro® Grafting
Amine and COOH
The weight of ReoPro®
about 90 μg
The thickness of coating
about 0.5 - 2 μm

SEM of ReoPro® Grafting after Washing Test



Stent surface of ReoPro® grafting; immediately(A), 5 hours(B), 2 weeks(C), 4 weeks(D) after washing test. Magnification 250×

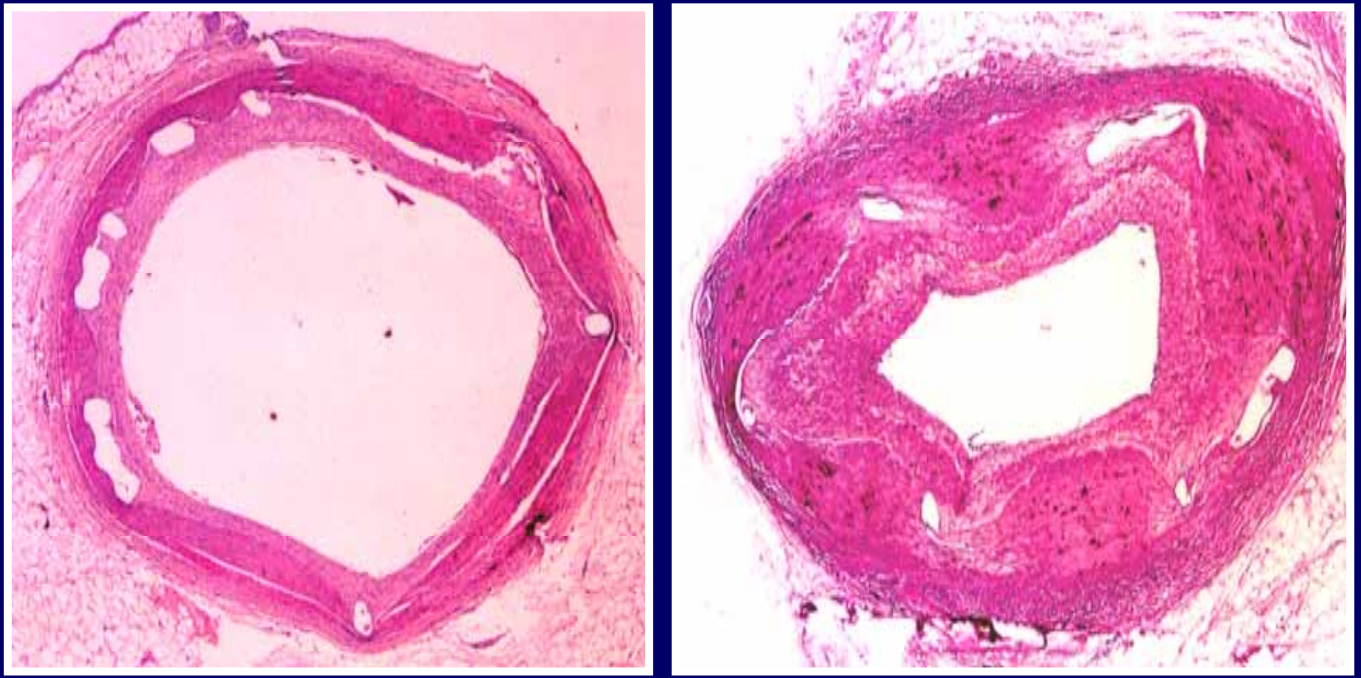
In vitro Screening of ReoPro® Release from Stent



Upper panel revealed absorbance in concentration of control drug

ReoPro®-coated Stent in A Porcine Stent Restenosis Model

ReoPro® Stent



Bare Stent

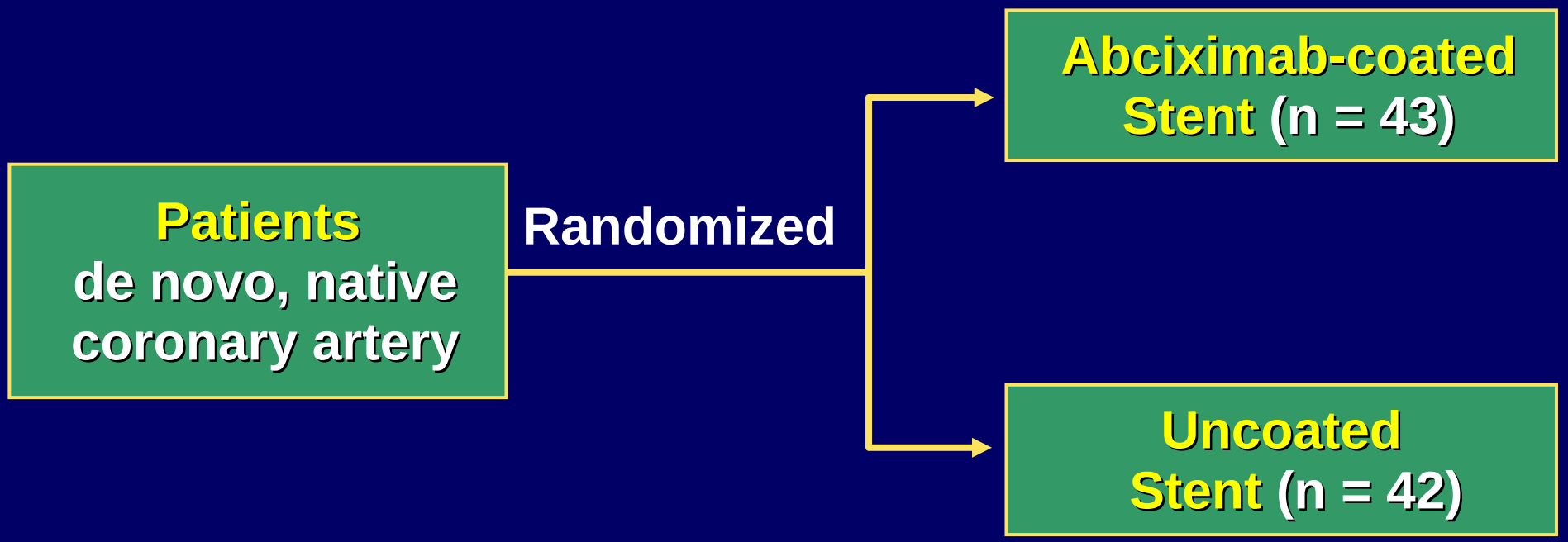
No thrombus and small area of neointima in the ReoPro®-coated stent

CNUH Data. Circulation 2000;102:II-666

Histopathologic Assessment of Porcine Stent Restenosis Model

	Control	Reopro	P value
Injury score	2.07 ± 0.6	2.14 ± 0.8	NS
EEL area (mm^2)	9.66 ± 1.5	9.44 ± 1.0	NS
IEL area (mm^2)	6.88 ± 0.9	6.83 ± 0.7	NS
Lumen area (mm^2)	3.59 ± 1.4	4.77 ± 1.4	0.04
Media area (mm^2)	2.77 ± 1.2	2.62 ± 0.9	NS
Neointima area (mm^2)	3.29 ± 1.2	2.02 ± 1.0	0.01
Neointima/Media ratio (%)	1.35 ± 0.7	0.82 ± 0.4	0.02
Percent stenosis area(mm^2)	48.1 ± 17	30.5 ± 16	0.01
PCNA index (%)	4.22 ± 2.1	2.48 ± 1.8	0.04

Abciximab-Coated Stent
IVUS Study



Primary Endpoint

- Late loss and area stenosis measured by QCA
- Lumen and NIH CSA by IVUS at 6 months
- MACE at 1 year

Baseline Clinical Characteristics

Variable	Abciximab stent (n=43)	Control stent (n=42)	p value
Age (years)	56±10	57±11	0.584
Men	36 (84%)	33 (79%)	0.544
Diabetes mellitus	10 (23%)	7 (17%)	0.256
Hypertension	22 (51%)	22 (52%)	0.895
Dyslipidemia	16 (37%)	14 (33%)	0.628
Smoking	25 (58%)	23 (55%)	0.613
Prior bypass surgery	0 (0%)	0 (0%)	1.000
LV EF (%)	63±10	63±12	0.994

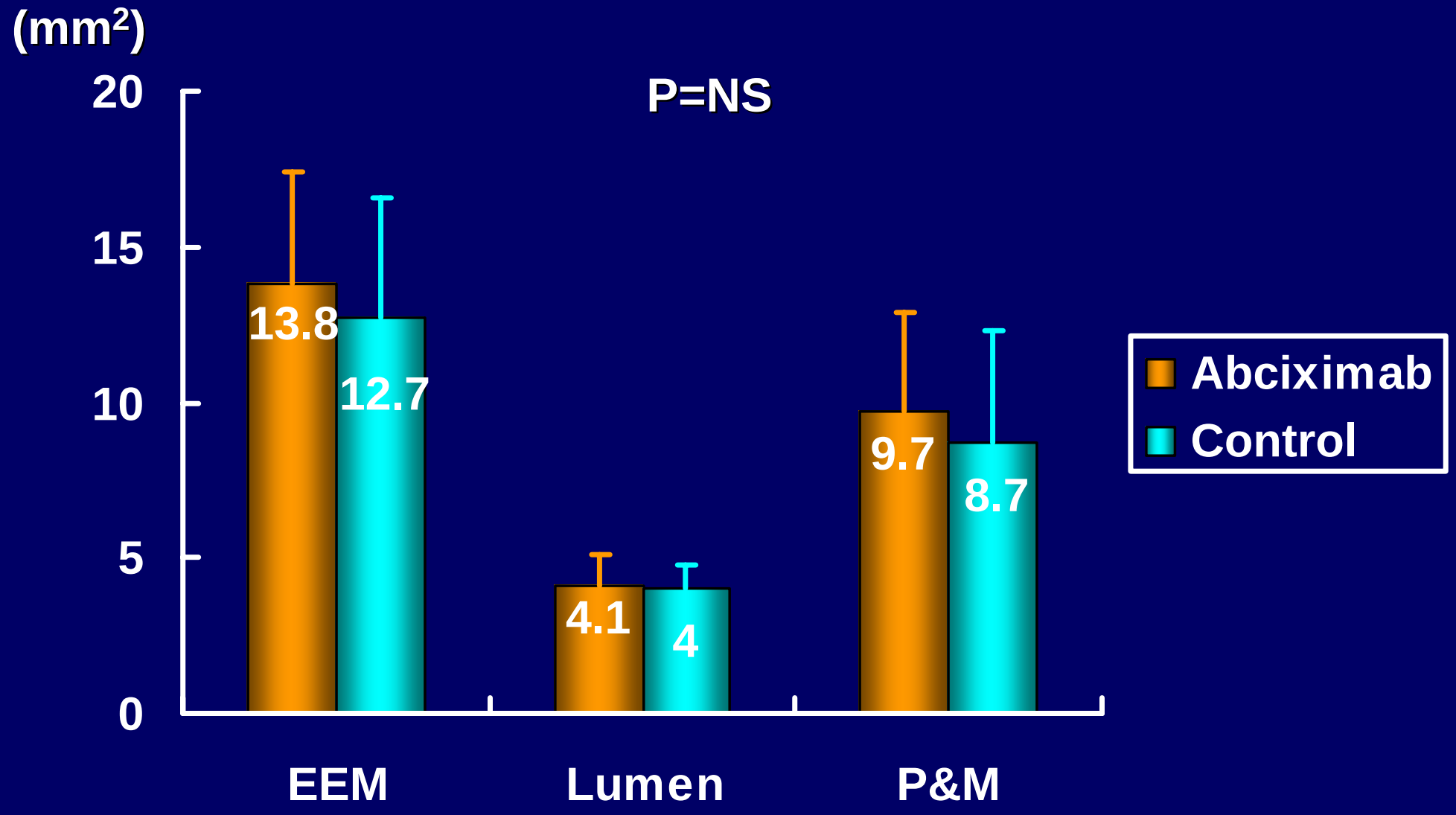
Coronary Angiographic Findings

Variable	Abciximab stent (n=43)	Control stent (n=42)	p value
Narrowed coronary arteries			0.274
1	40 (93%)	36 (86%)	
2	3 (7%)	6 (14%)	
3	0 (0%)	0 (0%)	
Target coronary arteries			0.704
Left anterior descending artery	25 (58%)	27 (64%)	
Left circumflex artery	7 (16%)	6 (14%)	
Right coronary artery	11 (26%)	9 (21%)	
ACC/AHA type			0.117
B_1	38 (88%)	32 (76%)	
B_2	4 (9%)	9 (21%)	
C	1 (2%)	1 (2%)	

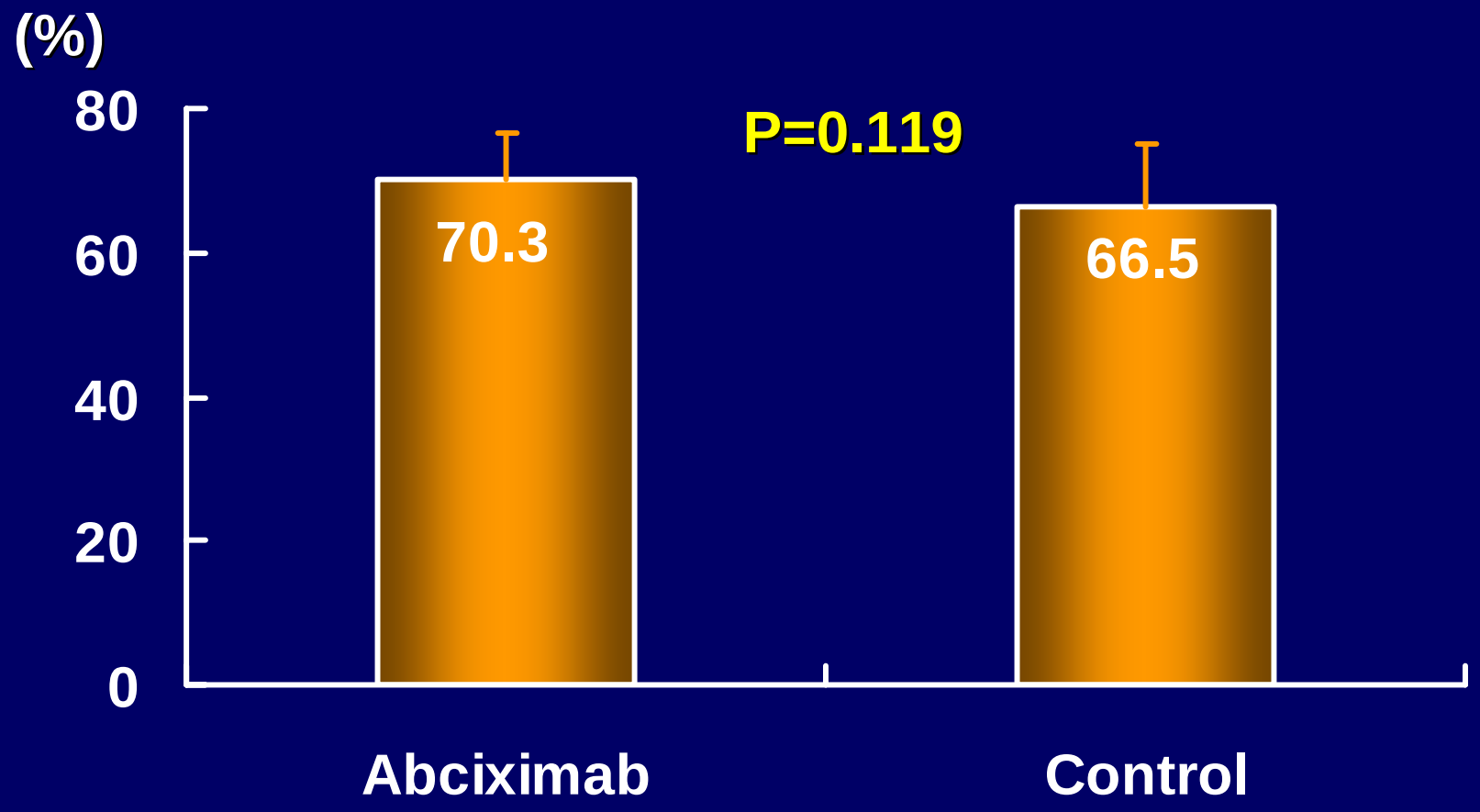
Coronary Stenting

Variable	Abciximab stent (n=43)	Control stent (n=42)	p value
Stent size (mm)	3.32±0.35	3.28±0.43	0.564
Stent length (mm)	17.1±1.1	17.5±4.4	0.432
Number of stents			0.320
1	42 (98%)	42 (100%)	
2	1 (2%)	0 (0%)	

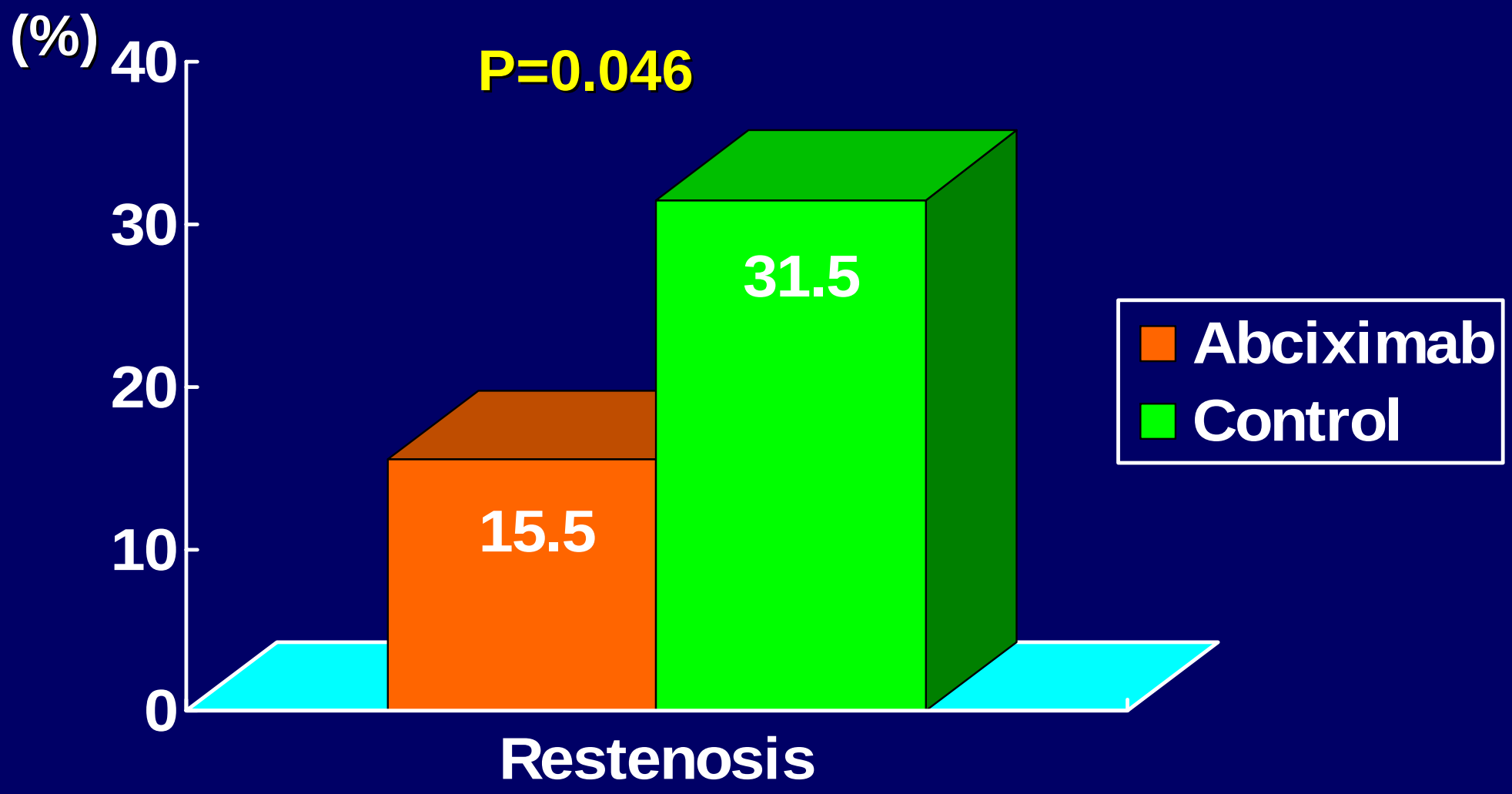
Preintervention Lesion Site



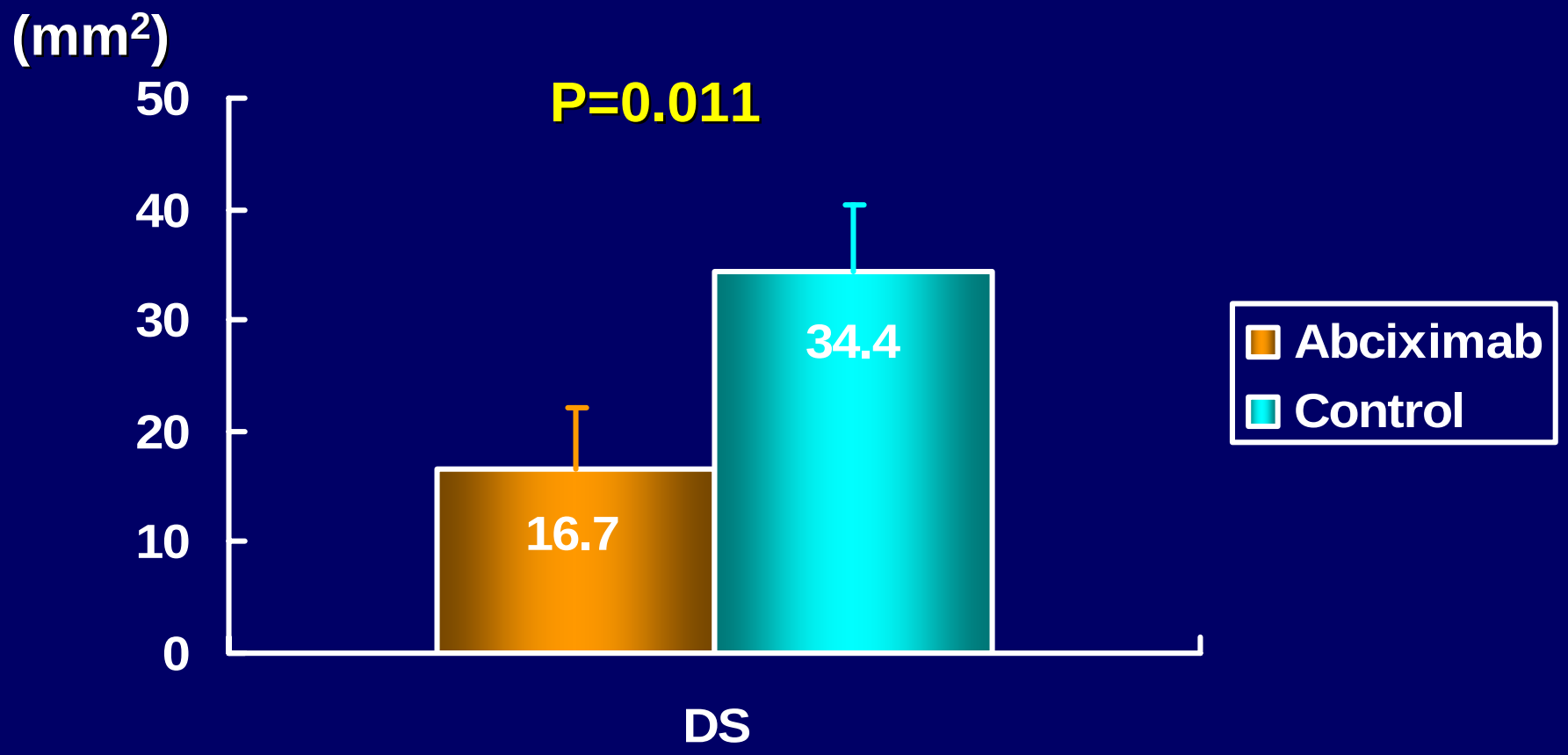
Preintervention Plaque Burden



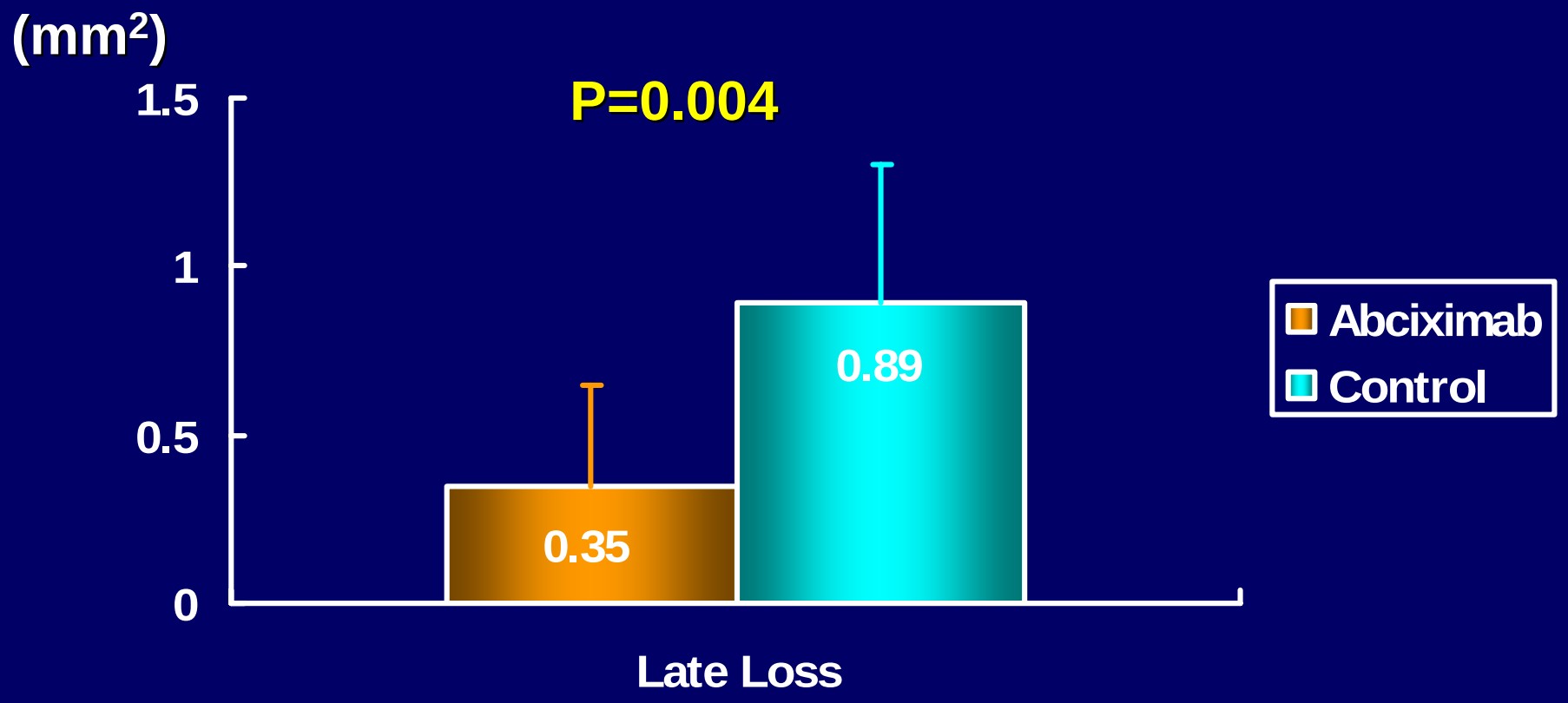
ISR At 6-Month F/U



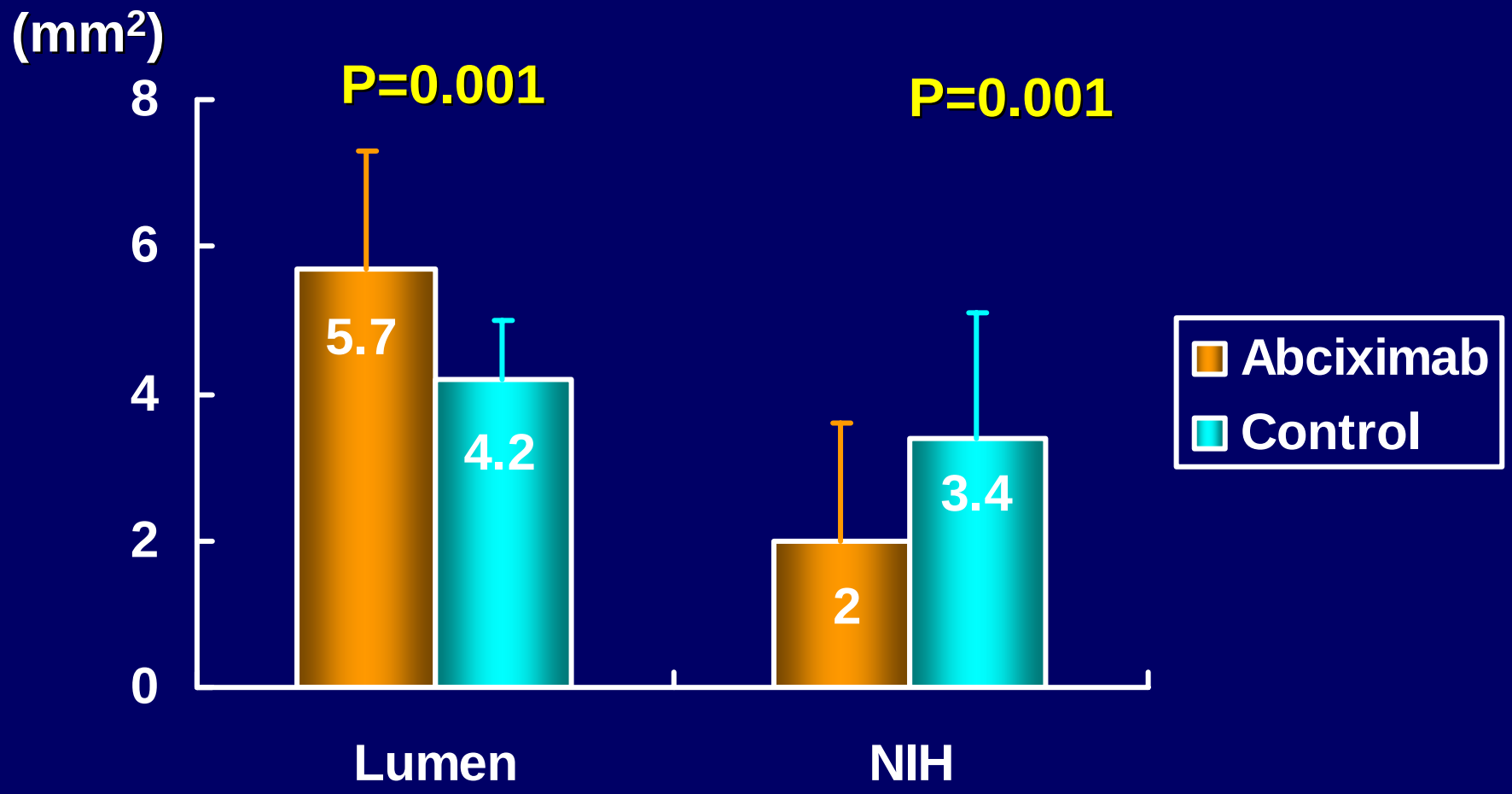
6-Month F/U Diameter Stenosis



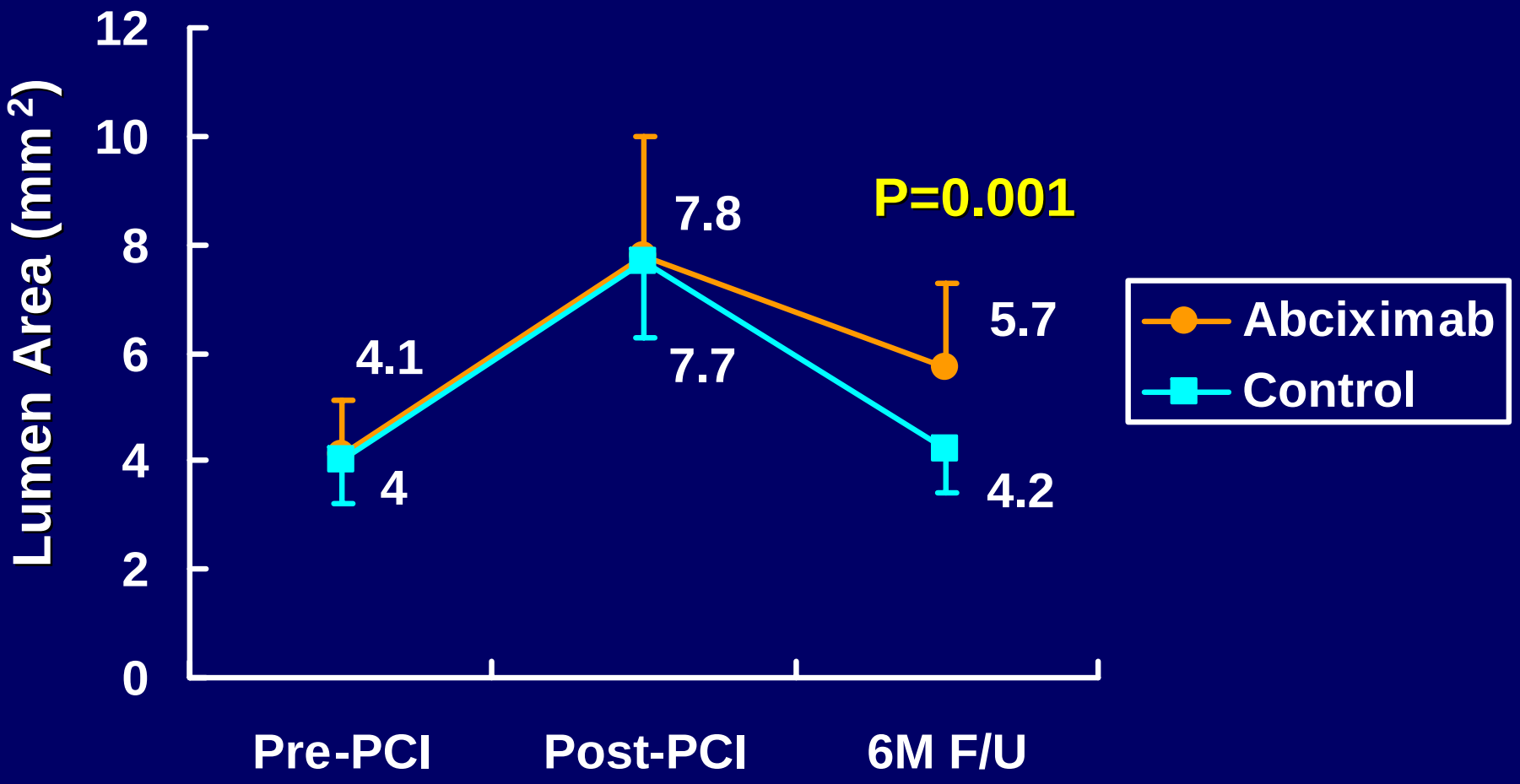
6-Month F/U Late Loss



6-Month F/U Lumen and NIH CSA

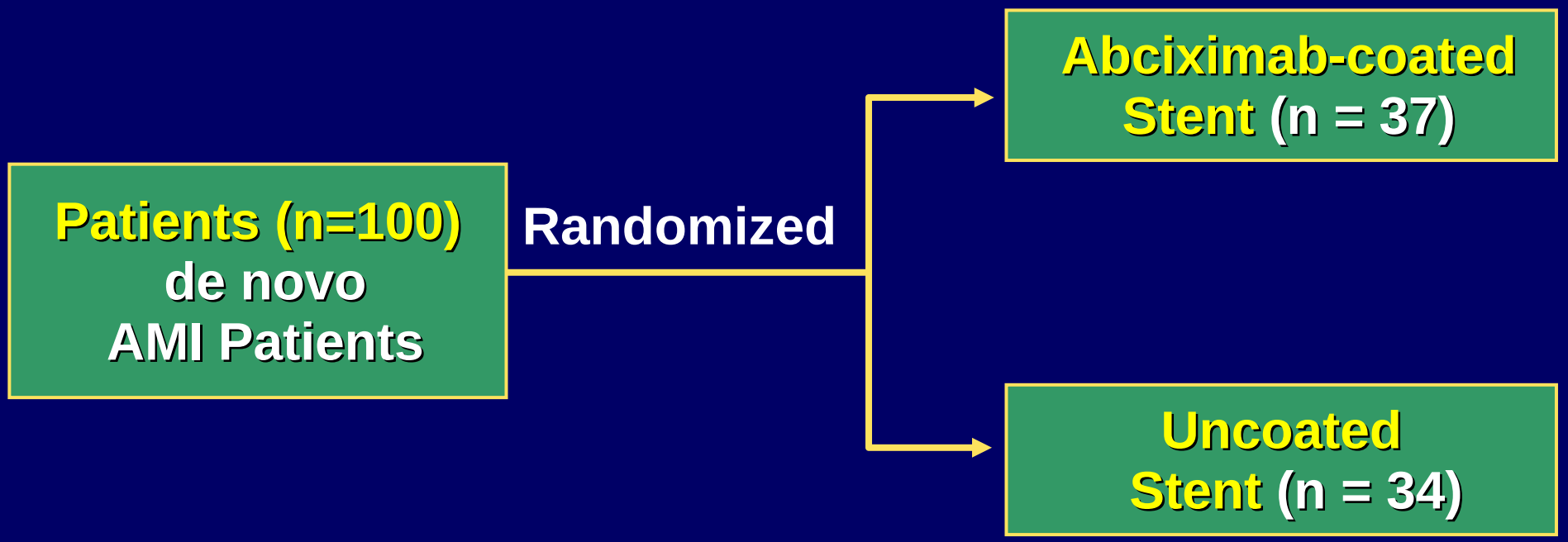


Change of Lumen Area



Am J Cardiol 2004;94:1050-4

Abciximab-Coated Stent
AMI Study : Ongoing



Primary Endpoint

- Late loss and area stenosis measured by QCA
- Lumen and NIH CSA by IVUS at 6 months
- MACE at 1 year

Baseline Clinical Characteristics

	ReoPro (n=37)	Control (n=34)	*P*
Age (yr)	54.4±11.3	56.1±11.9	0.558
Male (%)	33(89.2)	29(85.3)	0.622
Smoking (%)	22 (59.5)	20 (58.8)	0.919
HT (%)	18(48.6)	15(44.1)	0.702
Hypercholesterolemia (%)	10 (27.0)	11 (32.4)	0.623
Diabetes mellitus (%)	5 (13.5)	8 (23.5)	0.275
Family history (%)	4 (10.8)	2 (5.9)	0.451
Clinical Diagnosis(%)			0.836
Non-ST elevation MI	9 (24.3)	9 (26.5)	
ST elevation MI	28 (75.7)	25 (73.5)	
Previous PCI	1 (2.7)	1 (2.9)	0.952
LV EF after PCI (%)	58.9±9.6	57.1±11.9	0.489

Coronary Angiographic Characteristics (I)

	ReoPro (n=37)	Control (n=34)	*P*
Diseased vessels (%)			0.126
RCA	13(35.1)	5(14.7)	
LAD	19(51.4)	24(70.6)	
LCX	5(13.5)	5(14.7)	
ACC/AHA classification (%)			0.275
Type B1	32(86.5)	26(76.5)	
Type B2	5(13.5)	8(23.5)	
TIMI flow (%)			0.239
TIMI flow 0	3 (8.1)	4(11.8)	
TIMI flow 1	1(2.7)	0(0.0)	
TIMI flow 2	14(37.8)	10 (29.4)	
TIMI flow 3	19(51.4)	20 (58.8)	

Coronary Angiographic Characteristics (II)

	ReoPro (n=37)	Control (n=34)	*P*
Stent indication (%)			0.545
Elective and suboptimal	34(91.9)	31(91.2)	
Acute closure	3(8.1)	3(8.8)	
Stent size	3.40±0.38	3.30±0.38	0.299
Stent length(mm)	17.2±1.57	18.1±3.97	0.219

In-hospital Clinical Outcome

	ReoPro (n=37)	Control (n=34)	*P*
Success rate (%)	37 (100)	34 (100)	1.0
Major adverse cardiac event (%)			
Cardiac death	0(0.0)	0(0.0)	1.0
Acute myocardial infarction	0(0.0)	1(2.9)	0.479
Emergent revascularization	0(0.0)	0(0.0)	1.0
Emergent bypass surgery	0(0.0)	0(0.0)	1.0

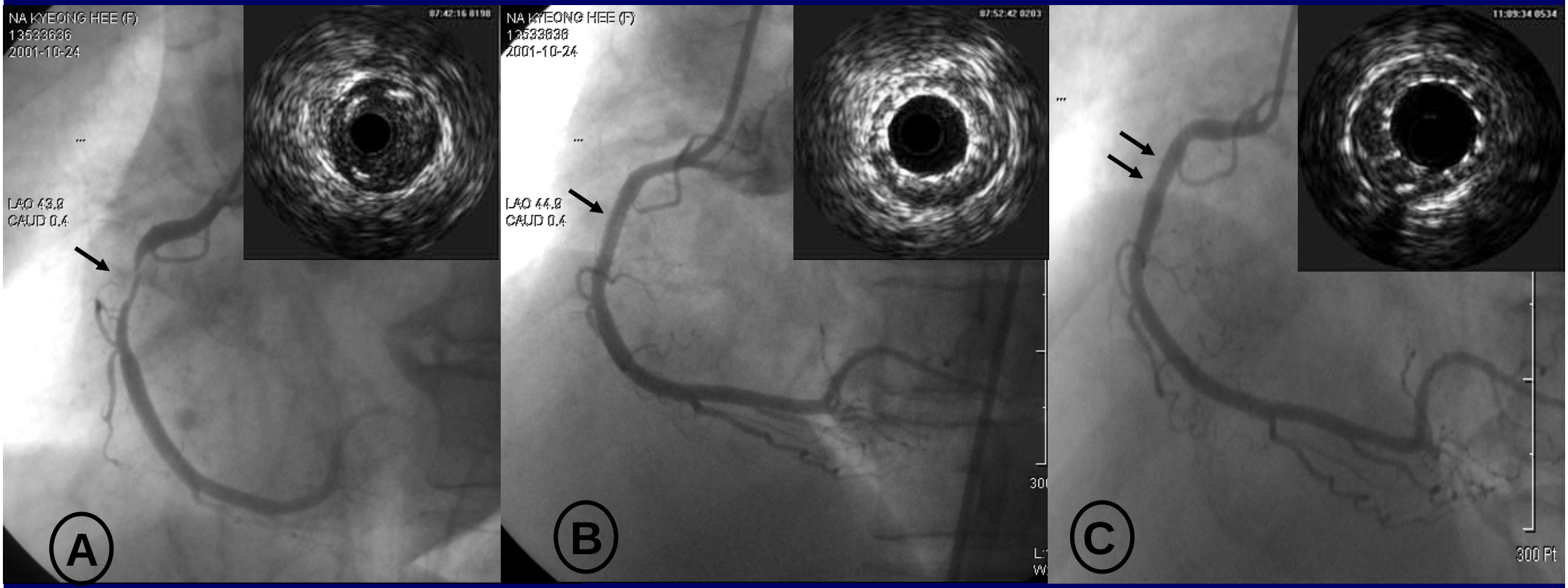
Quantitative Coronary Angiographic Results

	ReoPro(n=37)	Control (n=34)	*P*
Follow-up CAG number(%)	31(83.7)	25(73.5)	0.447
Restenosis rate (%)	5/31(16.1)	10/25(40.0)	0.044
Lesion length(mm)	15.5±1.7	14.4±1.8	0.731
Reference diameter(mm)	3.01±0.39	3.05±0.27	0.471
F/U Diameter stenosis (%)	18.7±5.4	35.4±6.0	0.011
Late loss (mm)	0.39±0.28	0.89±0.42	0.006

Long-term Clinical Results

	ReoPro (n=37)	Control (n=34)	*P*
Clinical follow-up number(%)	34(91.9)	33(97.1)	0.334
Total follow-up MACE	5(13.5)	11(32.3)	0.045
Cardiac death	0(0.0)	0(0.0)	1.00
AMI	0(0.0)	2(5.9)	0.226
TLR	5(13.5)	9(26.5)	0.169
CABG	0(0.0)	0(0.0)	1.00

CAG and IVUS Finding of ReoPro®-Coated Stent In A Patient with Acute Inferior STEMI



Before PCI

PCI with ReoPro® Stent

6 M F/U CAG and IVUS

Conclusion

A ReoPro®-coated coronary stent is safe and effective in the prevention of coronary stent restenosis without thrombus formation in AMI