2011 년 대한심장학회
개원의 강좌 - 증례중심으로 배우는 심장질환
2011. 12. 3.

관동맥 그물망 삽입술을 시행 받은 환자의 관리

전남대학교병원 심장센터
보건복지부 지정 심장질환 특성화 센터
한국심혈관계 스텐트 연구소

정 명 호

증례 1. 52-Year-Old Male

CC Chest pain (onset: 3 months ago, D: 2 min)

- related to exercise, squeezing nature

- NTG response (+)

PH HT (+), DM (+)

SH Smoker, Social alcohol drinker

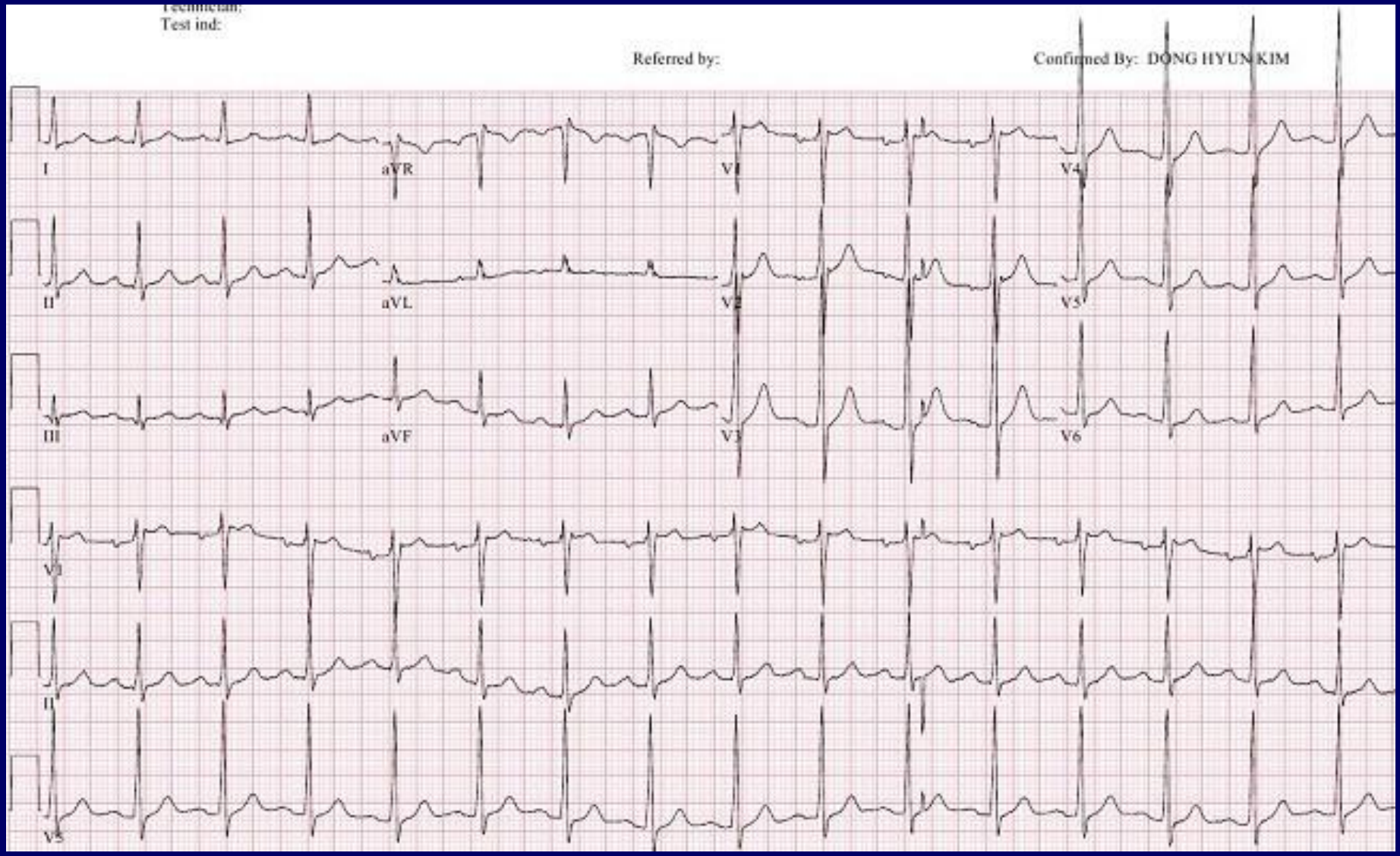
VS BP 140/80 mmHg, PR 72 /min

PE no S3

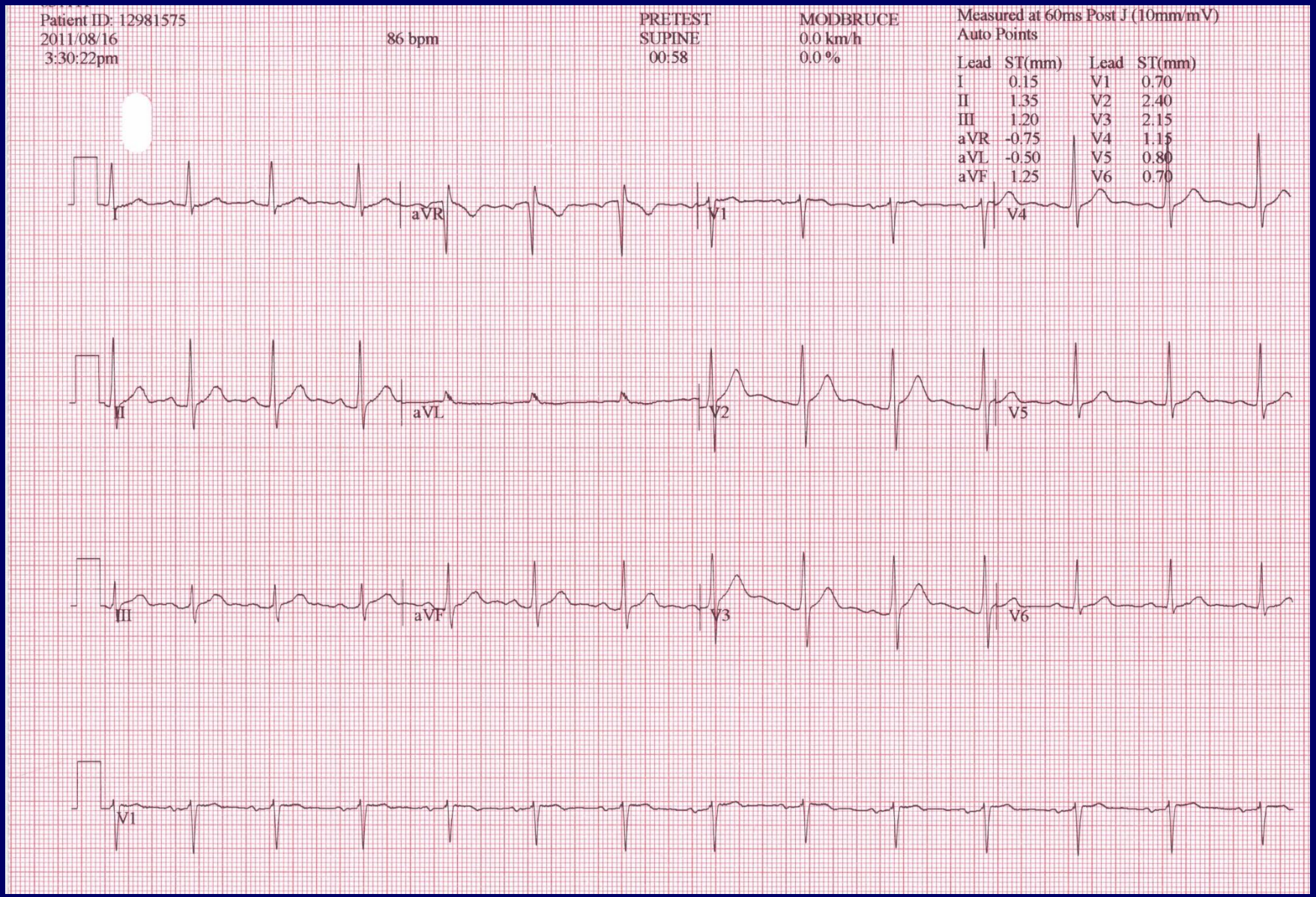
Lab CK / CK-MB 73 / 6.1 U/L, Tn-I 0.01 ng/mL

Total cholesterol: 188 mg/dL, LDL-C: 153 mg/dL

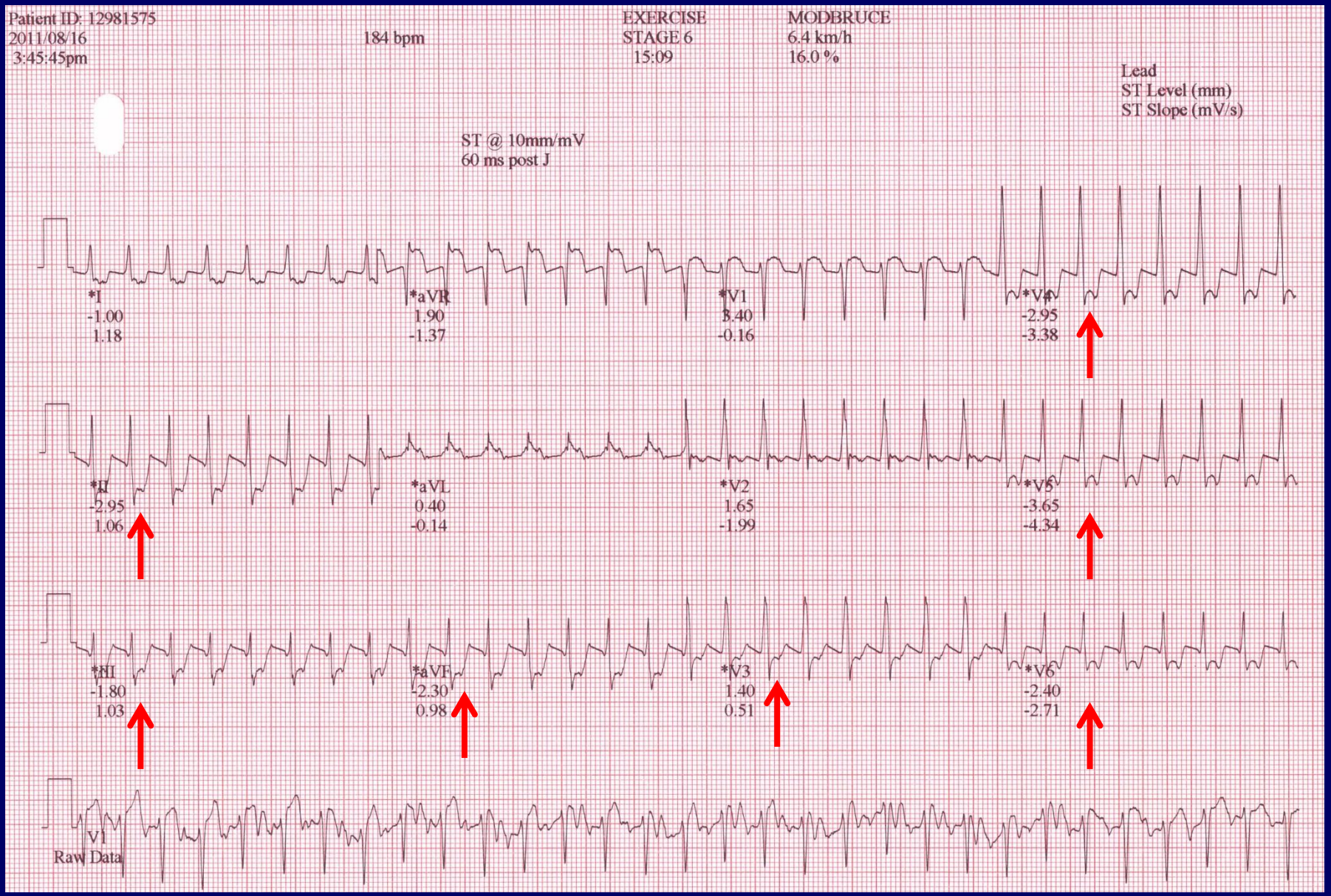
EKG at OPD


Technician:
Test ind:
Referred by:
Confirmed By: DONG HYUN KIM
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
V5
II
V5

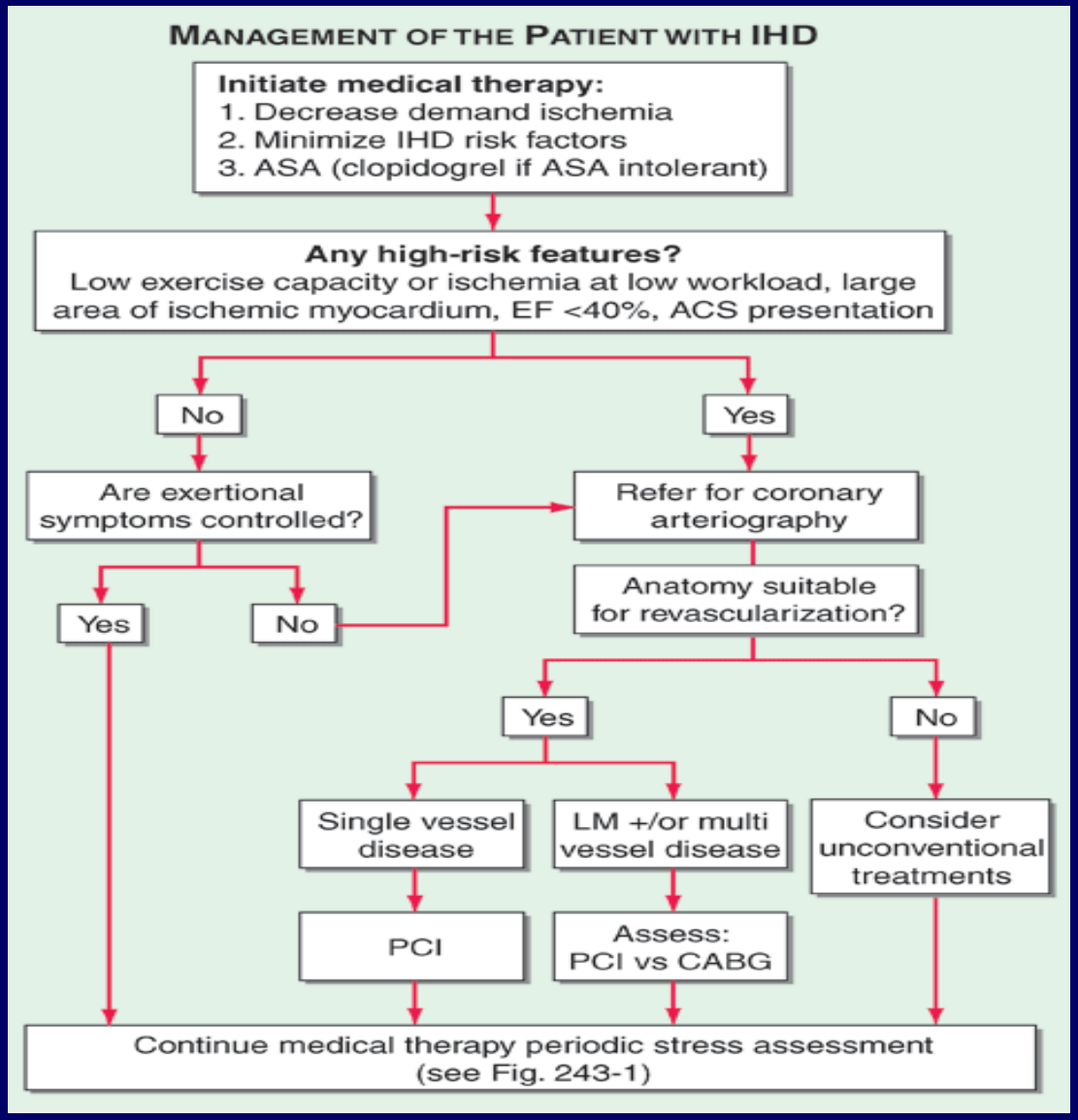
TMT at baseline



TMT at Stage 6

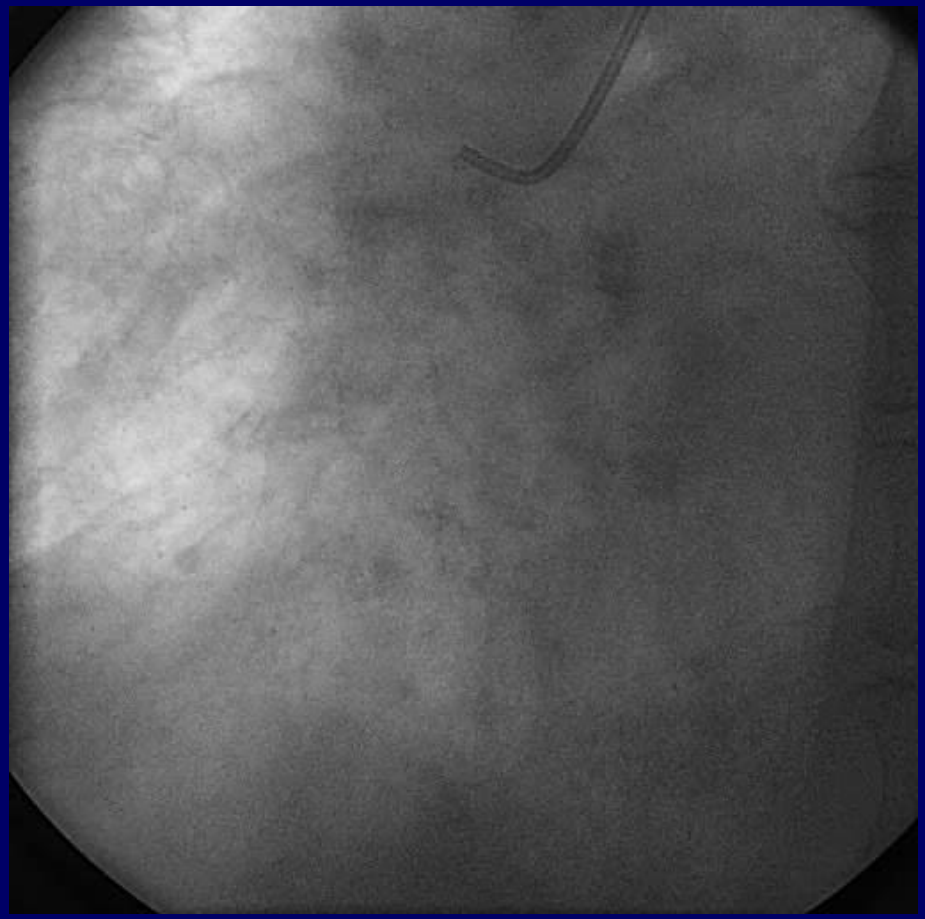


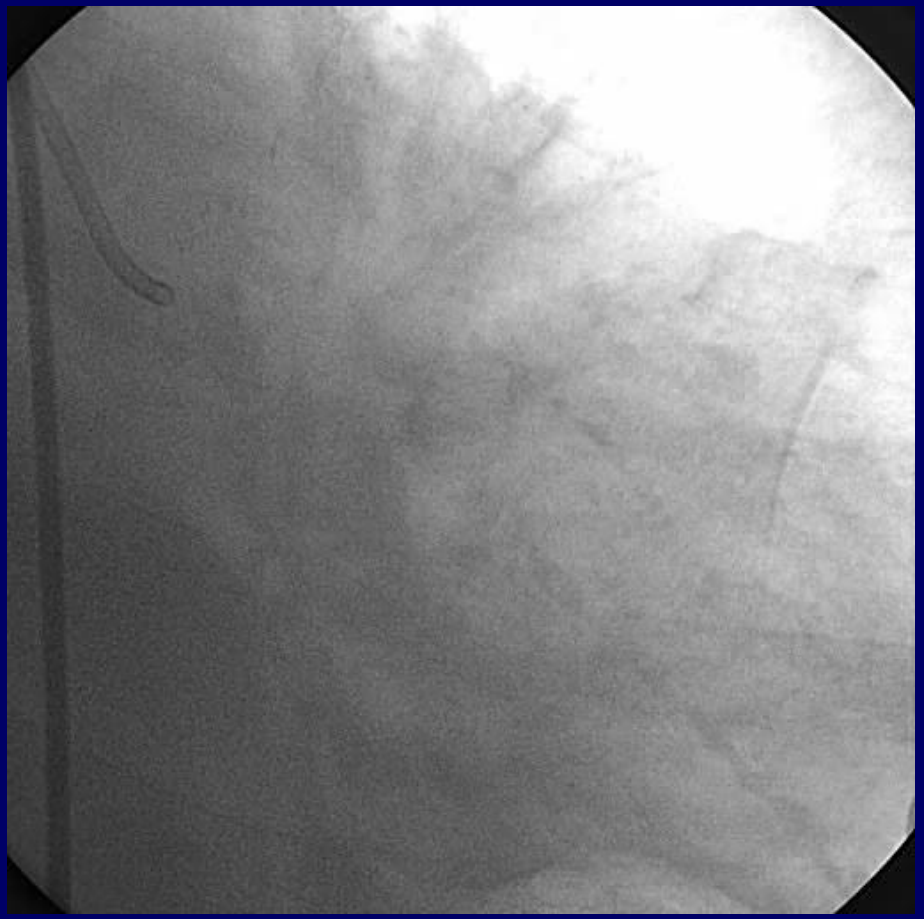
Algorithm for management of IHD



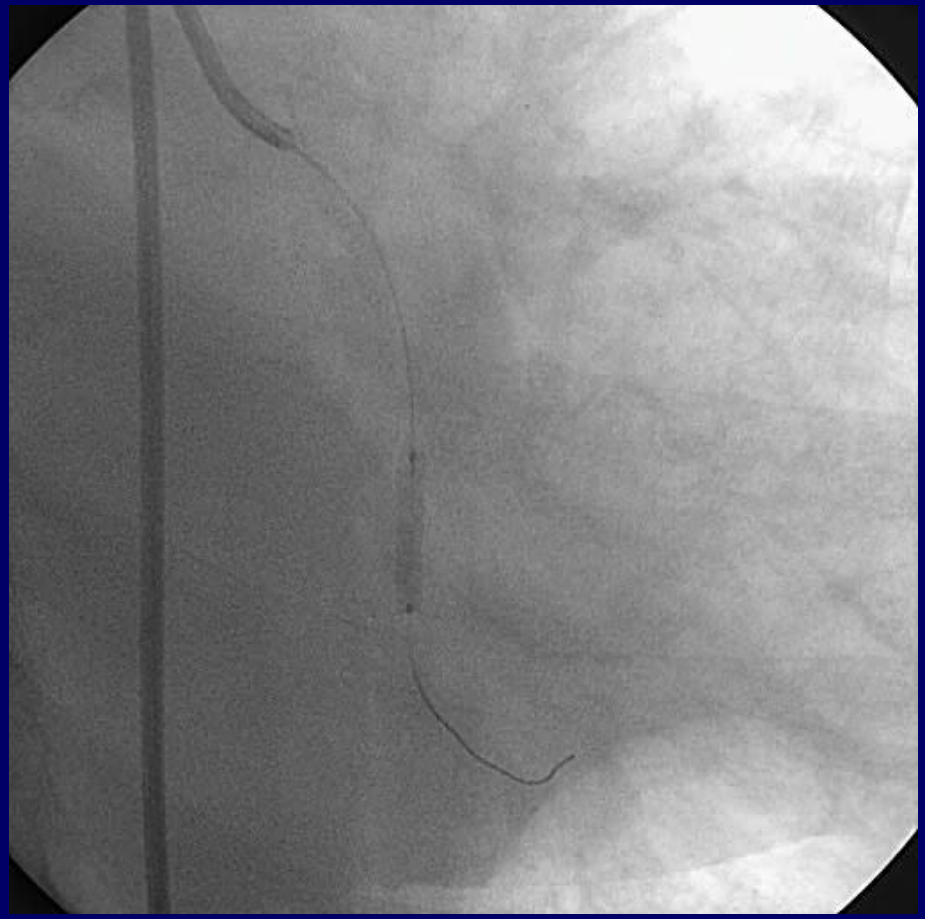
Harrison 18th 2012
Fig. 243-2

Coronary angiography





Percutaneous coronary intervention



3.5*18mm Bare-metal stent

증례 1 : 문제 1

이 환자의 치료에 도움이 되는 것은 ?

가. **Aspirin**

나. **β-blocker**

다. **Statin**

라. **Quit smoking**

1. 가, 나, 다 **2.** 가, 다 **3.** 나, 라

4. 라 **5. all of above**

증례 1 : 문제 2

이 환자에서 혈압, 혈당, **HbA1C, LDL-C Treatment Goal** 로 적절한 조합은?

	혈압(mmHg)	혈당 (mg/dL)	HbA1C (%)	LDL-C (md/dL)
1.	130/80	110	7.0	<70
2.	120/80	126	6.5	<100
3.	140/90	96	6.5	<130
4.	120/80	110	7.0	<160

JNC 7/ ESH 2007/ BHS IV

Goals of Therapy

	JNC 7	ESH 2007	BHS-IV
Non-DM	<140/90 mmHg	<140/90 mmHg	<140/85 mmHg
DM	<130/80 mmHg	<130/80 mmHg	<130/80 mmHg
CKD	<130/80 mmHg†	<130/80 mmHg*	<130/80 mmHg (<125/75 mmHg*)

* Proteinuria of ≥1g /24 h

† CKD in diabetic pts:
- Overt albuminuria (>300 mg/D or >200 mg/g Cr on spot urine)
- Renal insufficiency (estimated GFR <60 mL/min, serum Cr > 1.3~1.5 mg/dL)

2011 Draft Recommendations

Diabetes and Hypertension

Persons with diabetes mellitus should be treated to attain systolic blood pressure of <130 mmHg (Grade C) and diastolic blood pressures <80 mmHg (Grade A).

These target blood pressure levels are the same as the blood pressure treatment thresholds.

The targets for patients with diabetes and hypertension have remained unchanged post- ACCORD-BP!

문제 2 : 65-Year-Old Male

CC Chest pain (D: 12 hours)

PH HT (+), DM(+)

SH non-smoker

VS BP 120/80 mmHg, PR 60/min

Lab TnI 9.90 ng/ml

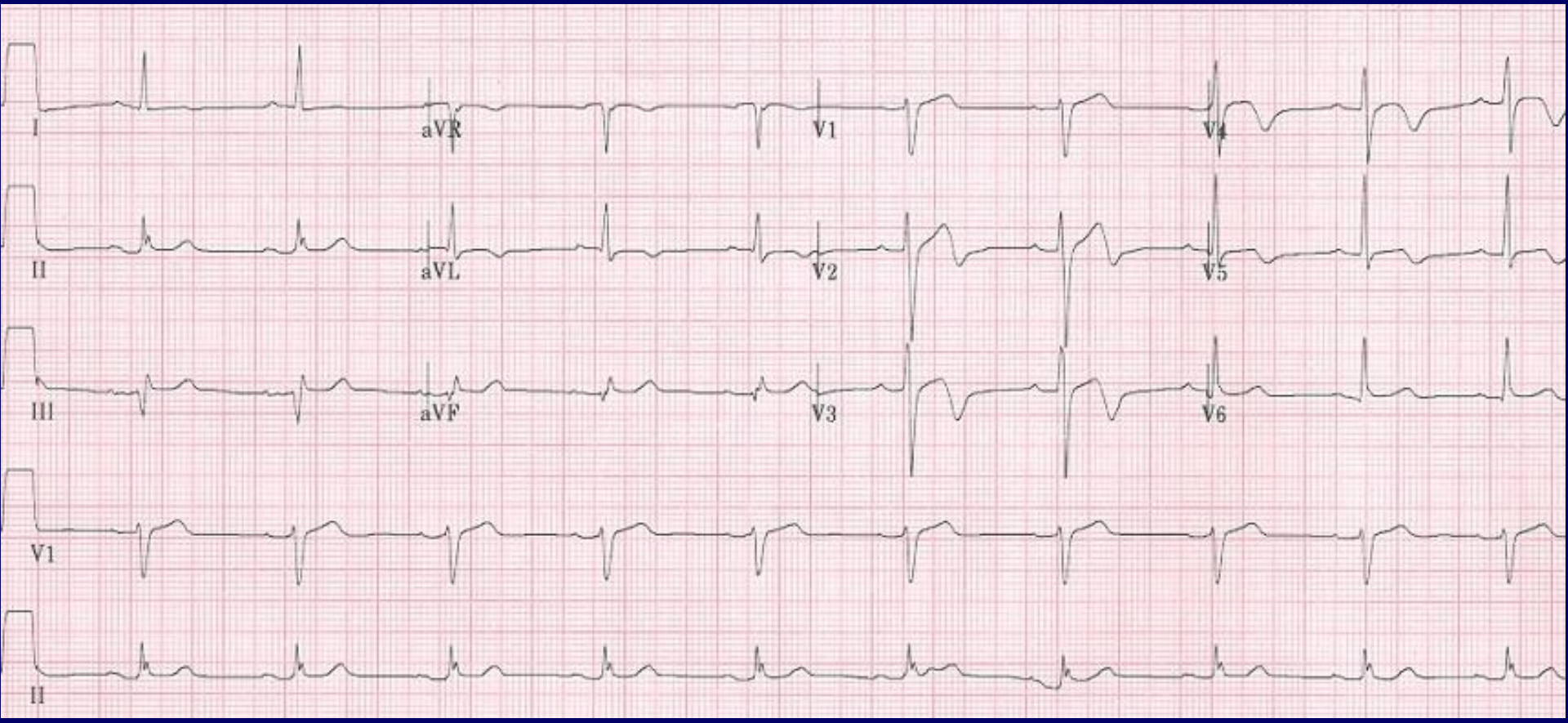
CK 389 U/L

CK-MB 14.8 U/L

hsCRP 3.4 mg/dL

LDL-C 117 mg/dL

Baseline ECG



증례 2 : 문제 1

이 환자의 초기 치료에 적절한 약제는?

가. **Aspirin + Clopidogrel**

나. **ACE inhibitor**

다. **Heparin or LMWH**

라. **Statin**

1 가, 나, 다　　**2.** 가, 다　　**3.** 나, 라

4. 라　　**5. all of above**

증례 2 : 문제 2

응급실에서 약물치료를 시행하였음에도 불구하고
흉통이 지속되었고, **Tn-I** 증가소견을 보였다.

이 환자에서 관상동맥 조영술을 언제 시행하는 것이 좋은가?

1. **< 2 hours**
2. **< 24 hours**
3. **< 72 hours**
4. **Conservative strategy**

ESC 2011 guideline for NSTEMI

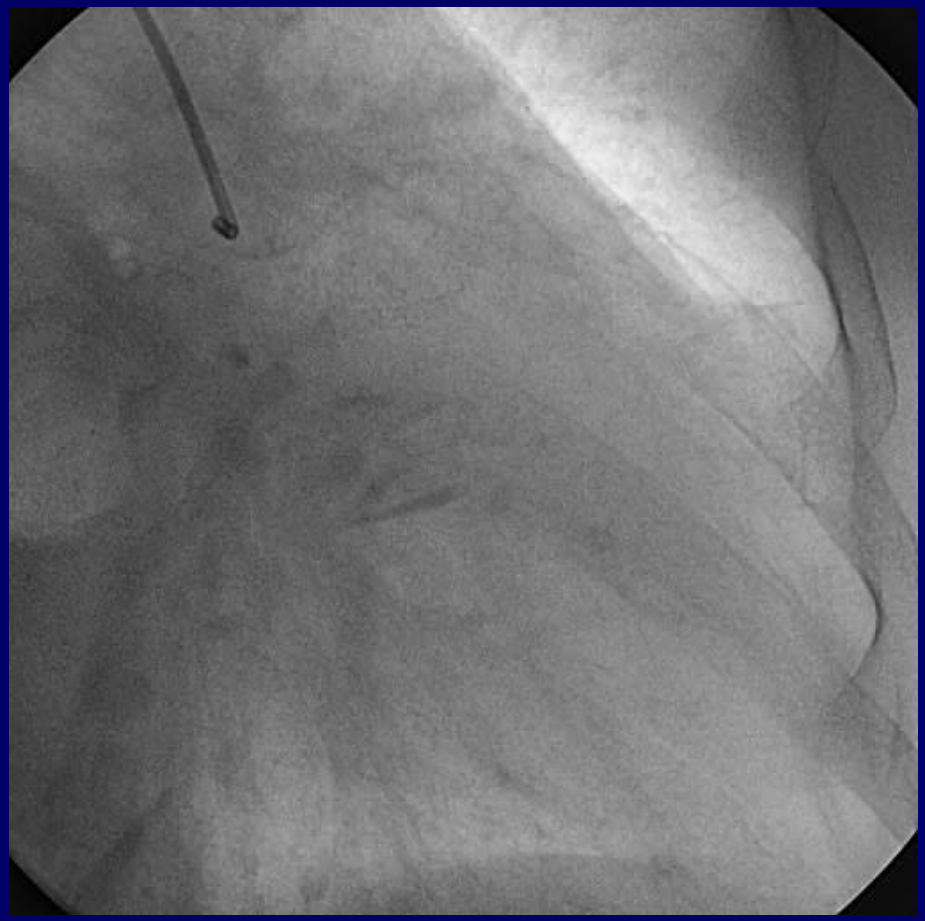
Emergent (<2 h, IIaC): very high ischemic risk
persistent angina, heart failure,
hemodynamic instability or arrhythmia

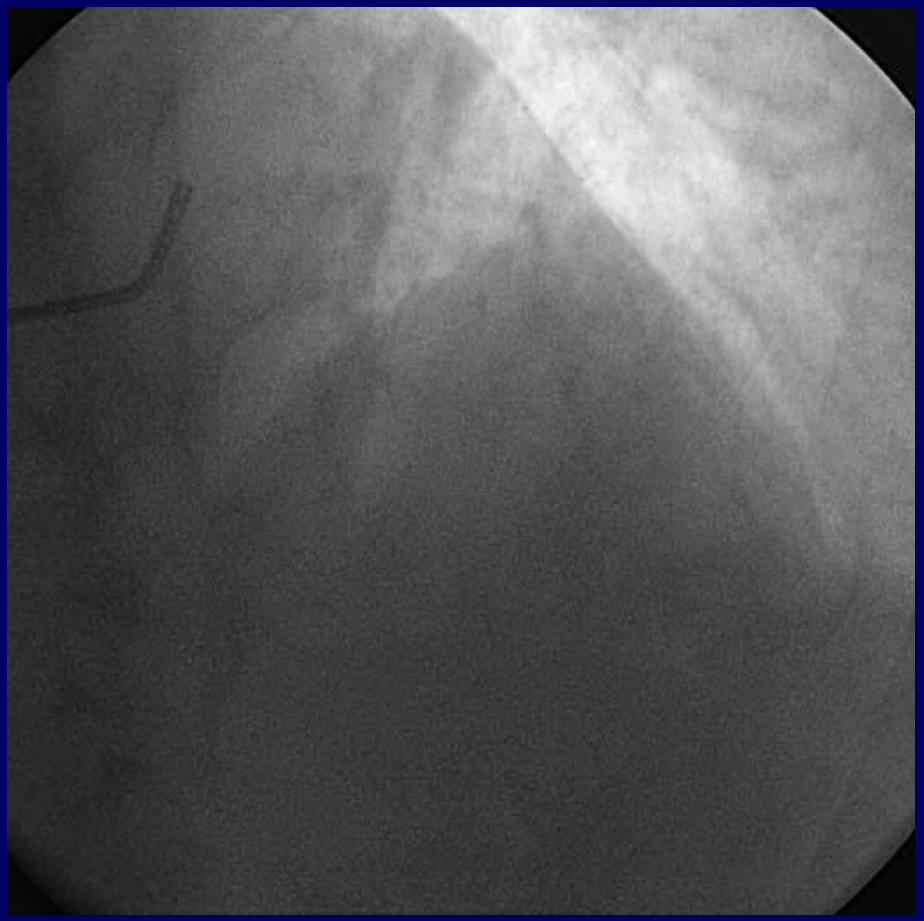
Early invasive (<24 h, IA): medium-to-high ischemic risk
GRACE score >140, multiple other high-risk criteria
(troponin +, dynamic ST changes, recurrent angina)

Late invasive (<72 h, IA)
GRACE score<140 or absence of multiple other risk criteria,
but recurrent symptoms or stress inducible ischemia

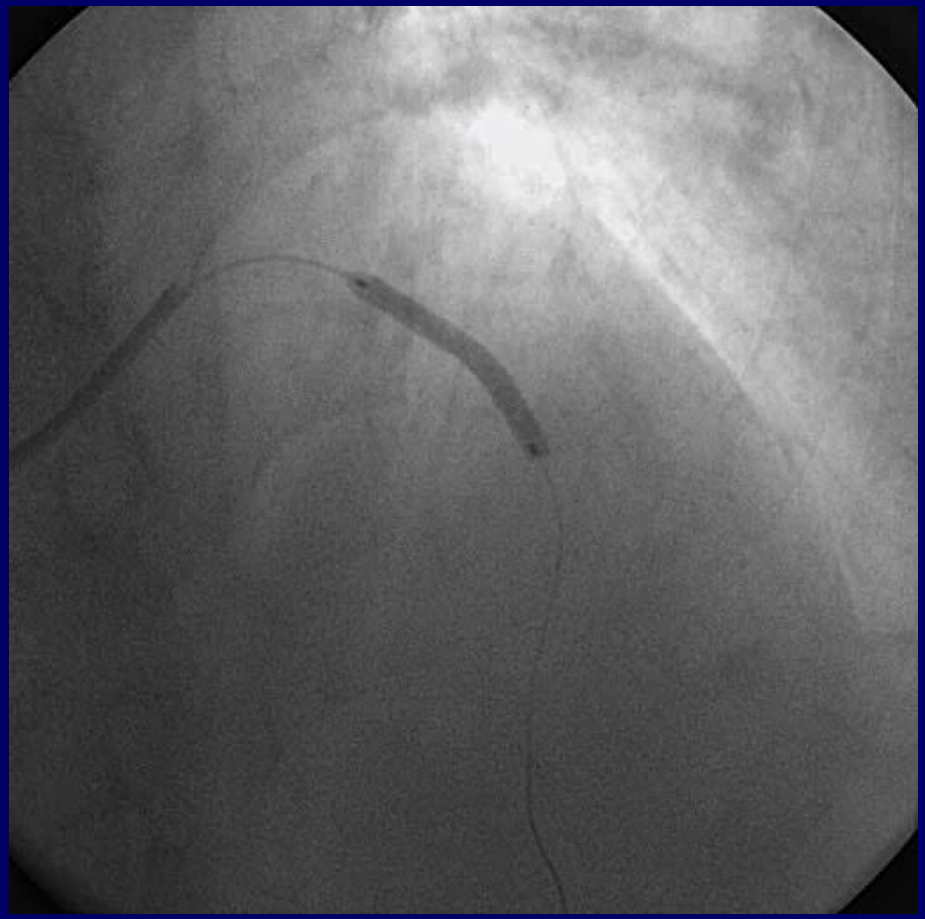
Conservative strategy (Invasive, IIIA): low ischemic risk
troponin -, no ST changes (noninvasive test recommended)

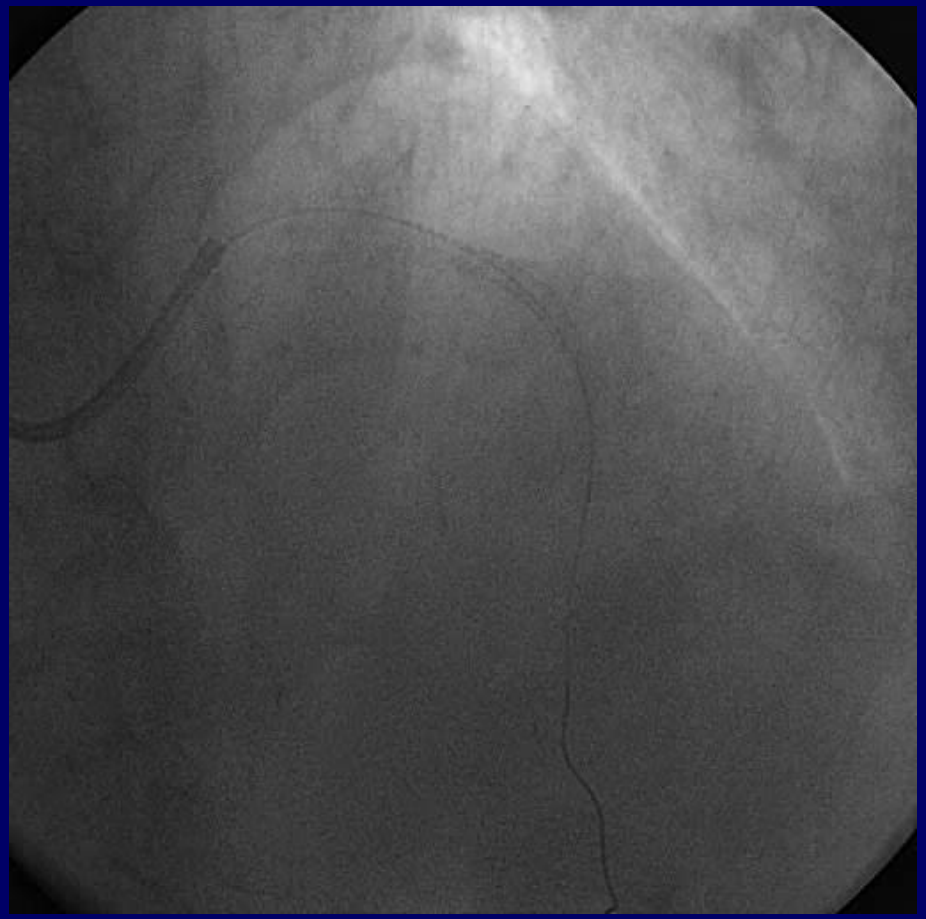
Coronary angiography





Percutaneous coronary intervention





3.5*25 mm Everolimus eluting stent (drug-eluting stent)

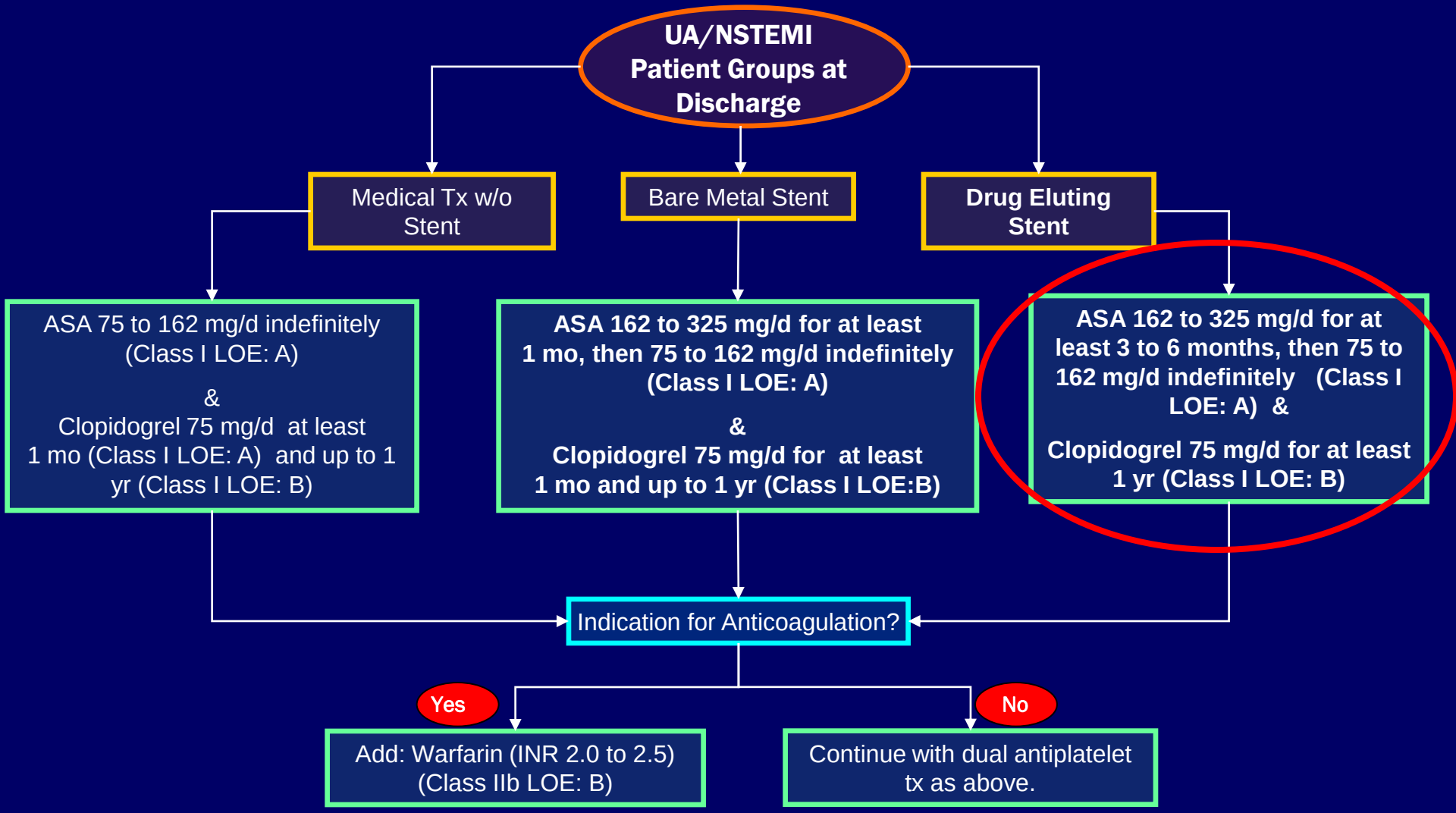
증례 2 : 문제 3

환자는 시술 후 상태가 양호하여 **6**개월 후 집 근처의 개인의원으로 전원 되었고 이 환자에게 투여해야 할 약제는**?**

가. **Aspirin**
나. **Clopidogrel**
다. **β1 selective blocker**
라. **Statin**

1 가, 나, 다 **2.** 가, 다 **3.** 나, 라
4. 라 **5. all of above**

Long-term Antithrombotic therapy for NSTEMI-ACS



J Am Coll Cardiol 2007;50:e1-157.

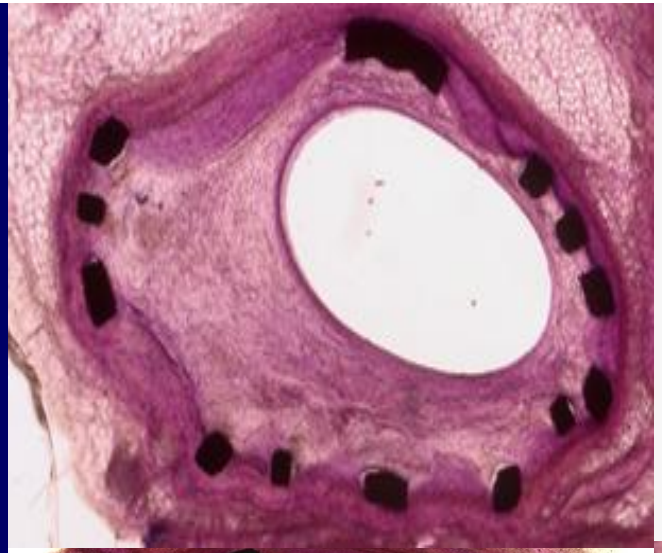
Drug-Eluting Stent

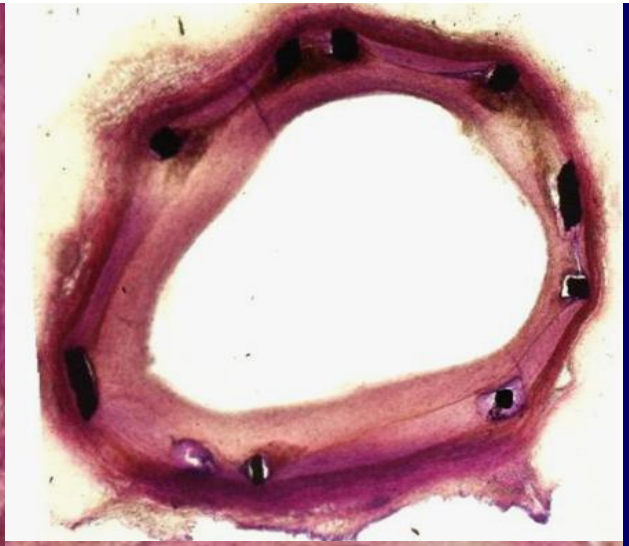
	Balloon (1977)	*BMS (1987)*	*DES (2003)*
RS	**30~50%**	**10~30%**	**0~9%**

DES: Very promising, NOT perfect !

Pathologic Findings of Overlapped DES in Porcine Model

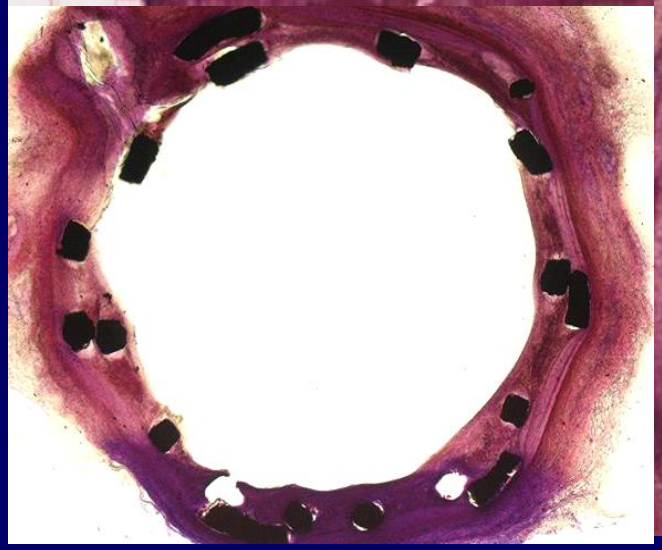
BMS + BMS

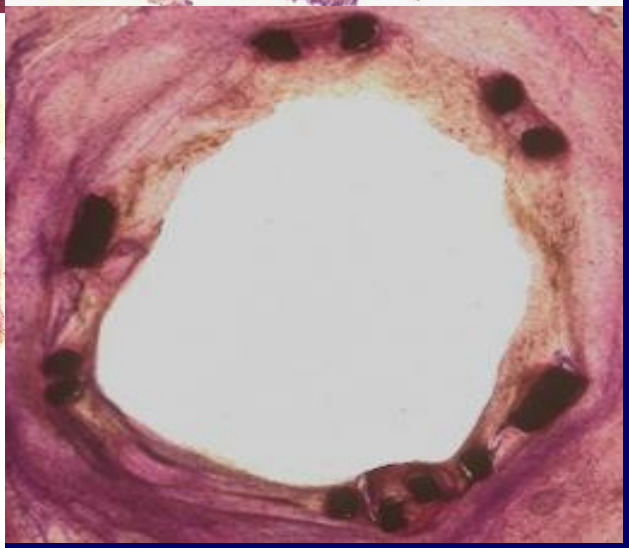




SES + SES

PES + PES

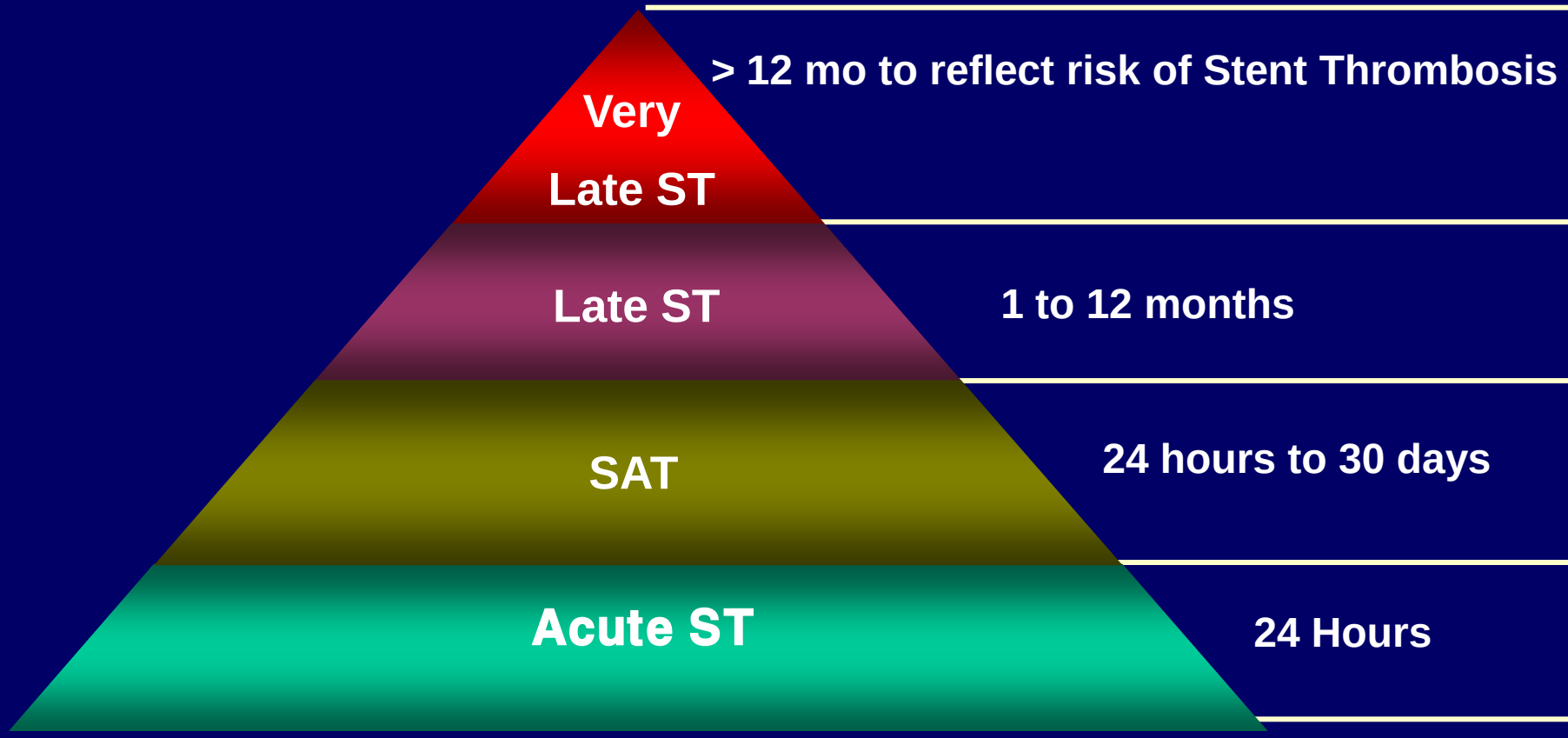




SES + PES

CNUH data. Circ J 2008;72:463-8.

Stent thrombosis

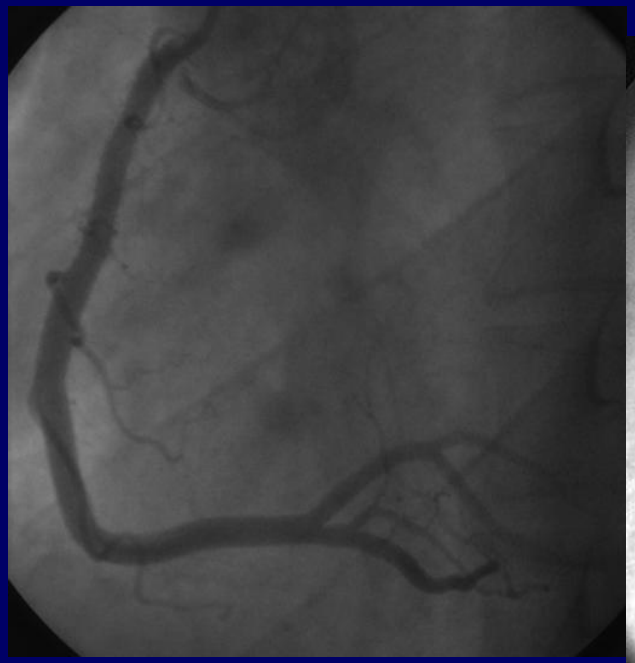


ST = stent thrombosis; SAT = subacute stent thrombosis;

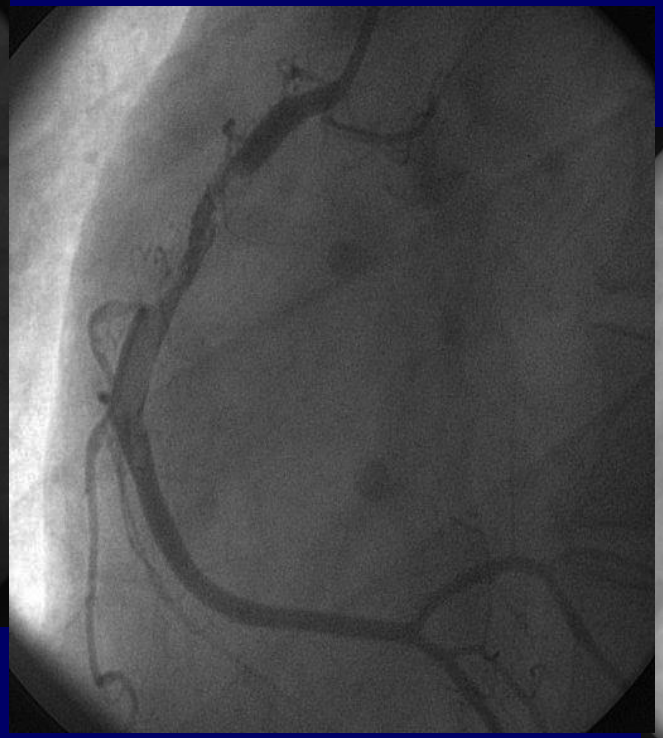
LST = late stent thrombosis; VLST = very late stent thrombosis.

Adapted from Bhatt. *J Invasive Cardiol*. 2003;15(suppl B):3B.

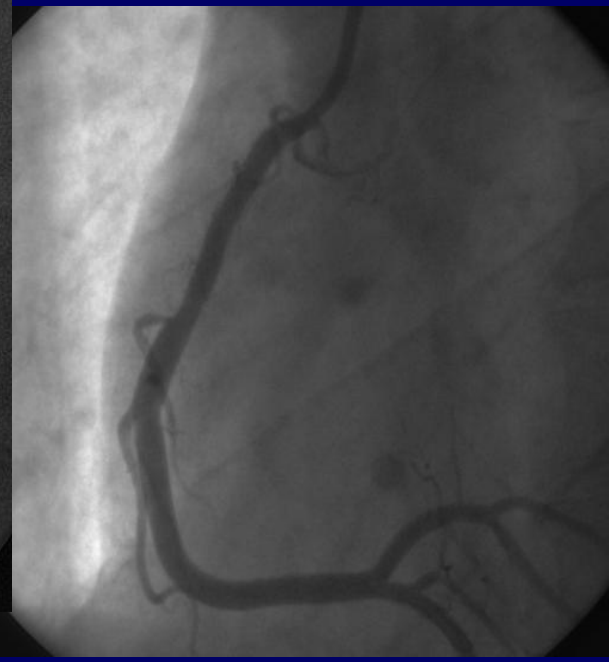
43 Year-Old Man
Late Stent Thrombosis at 12 Months After PES
(A Case #5 of 2005 Gwangju Interventional Cardiology Live Demonstration, Jun 10th 2005)



9 M F/U CAG after PES
2005. 3. 24.

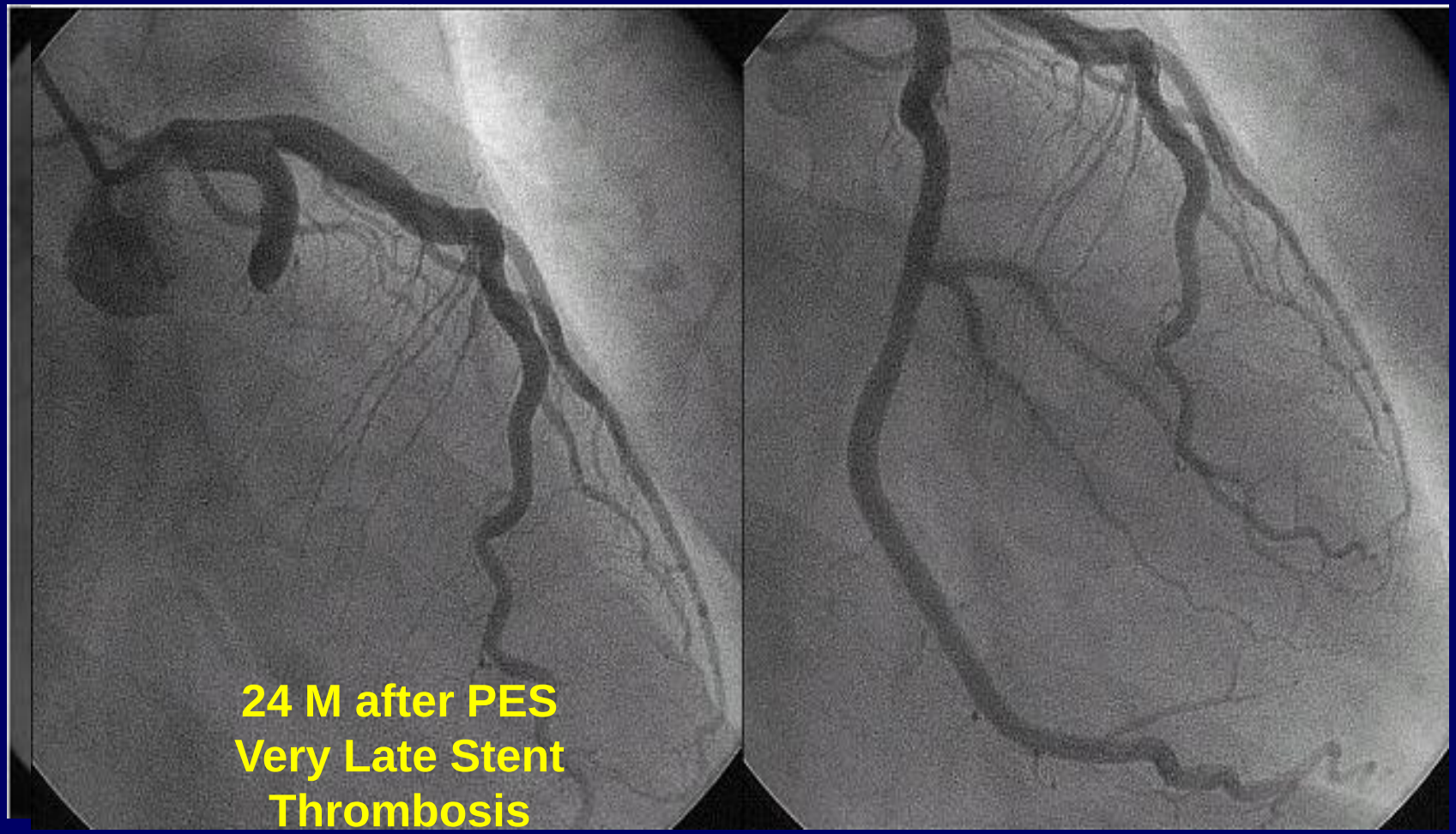


ASTEMI 2005.6.1.



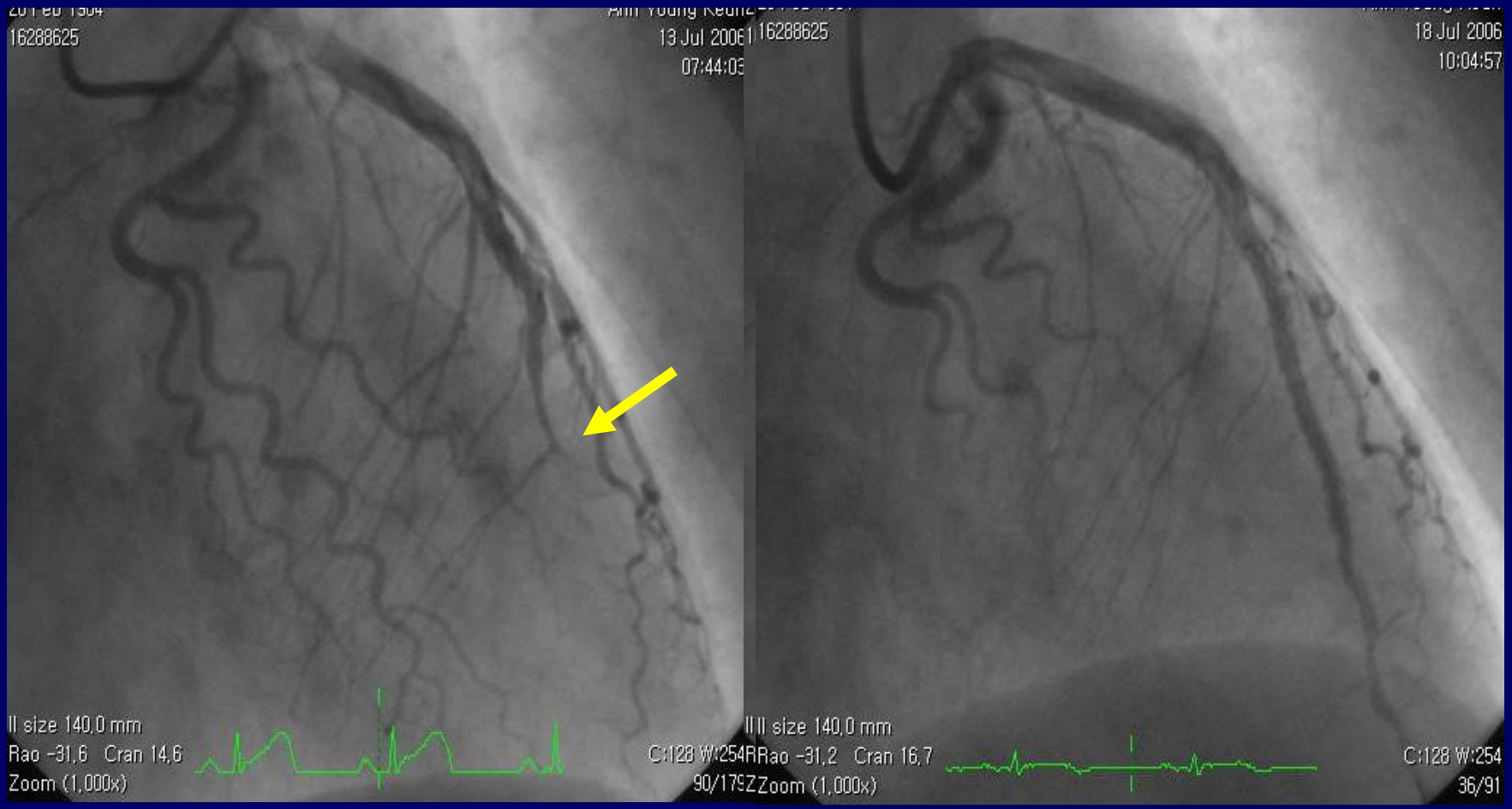
PCI with ReoPro 2005.6.10.
Case #5 2005 Live Course

48 Year-Old Man
Very Late Stent Thrombosis at 24 Months After PES due to Aneurysm



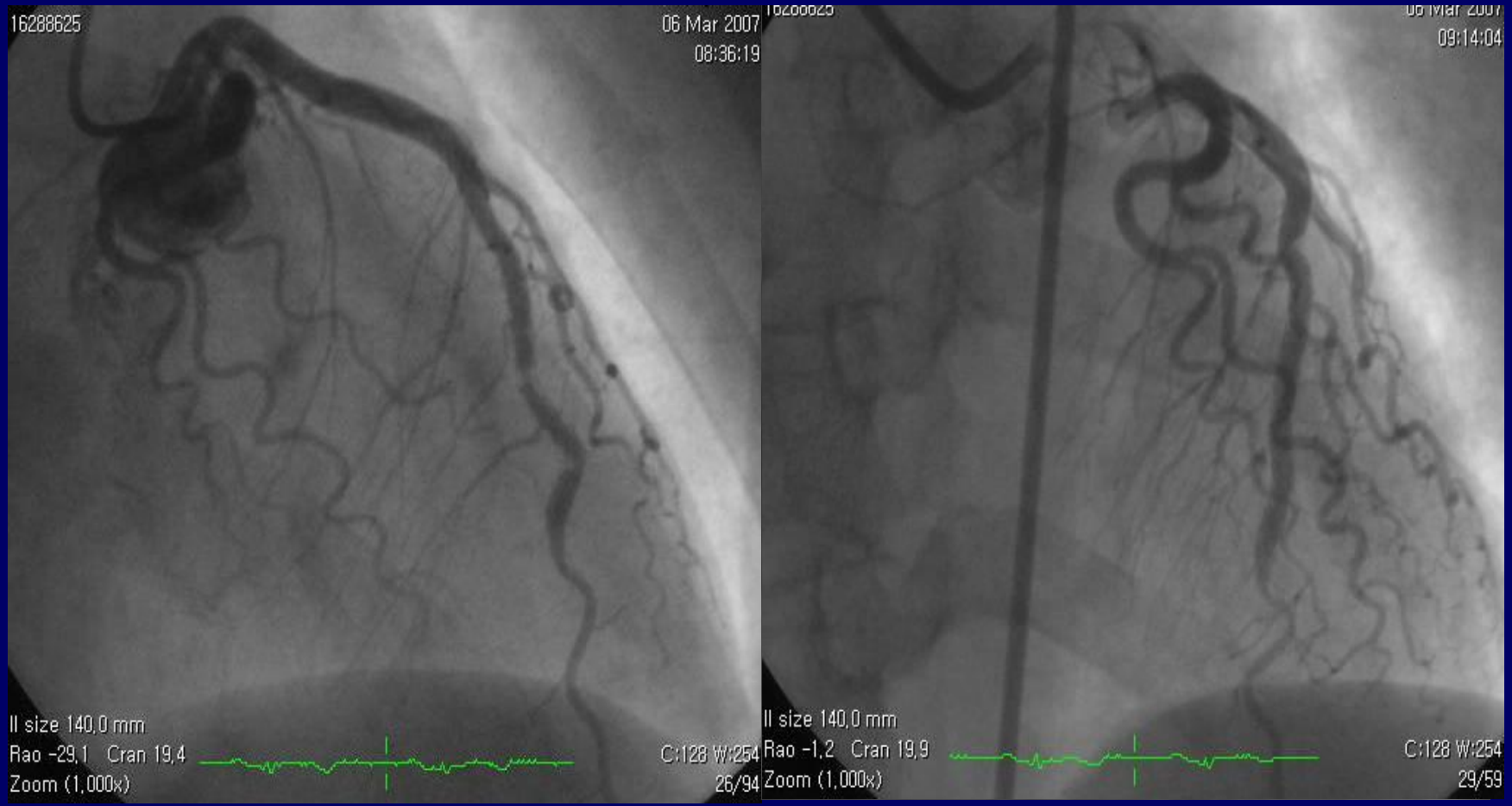
CNUH case (Aug 2006) www.circulation.or.kr

42 Year-Old Female
Cypher Stent for AMI due to Long Angulated Lesion in LAD



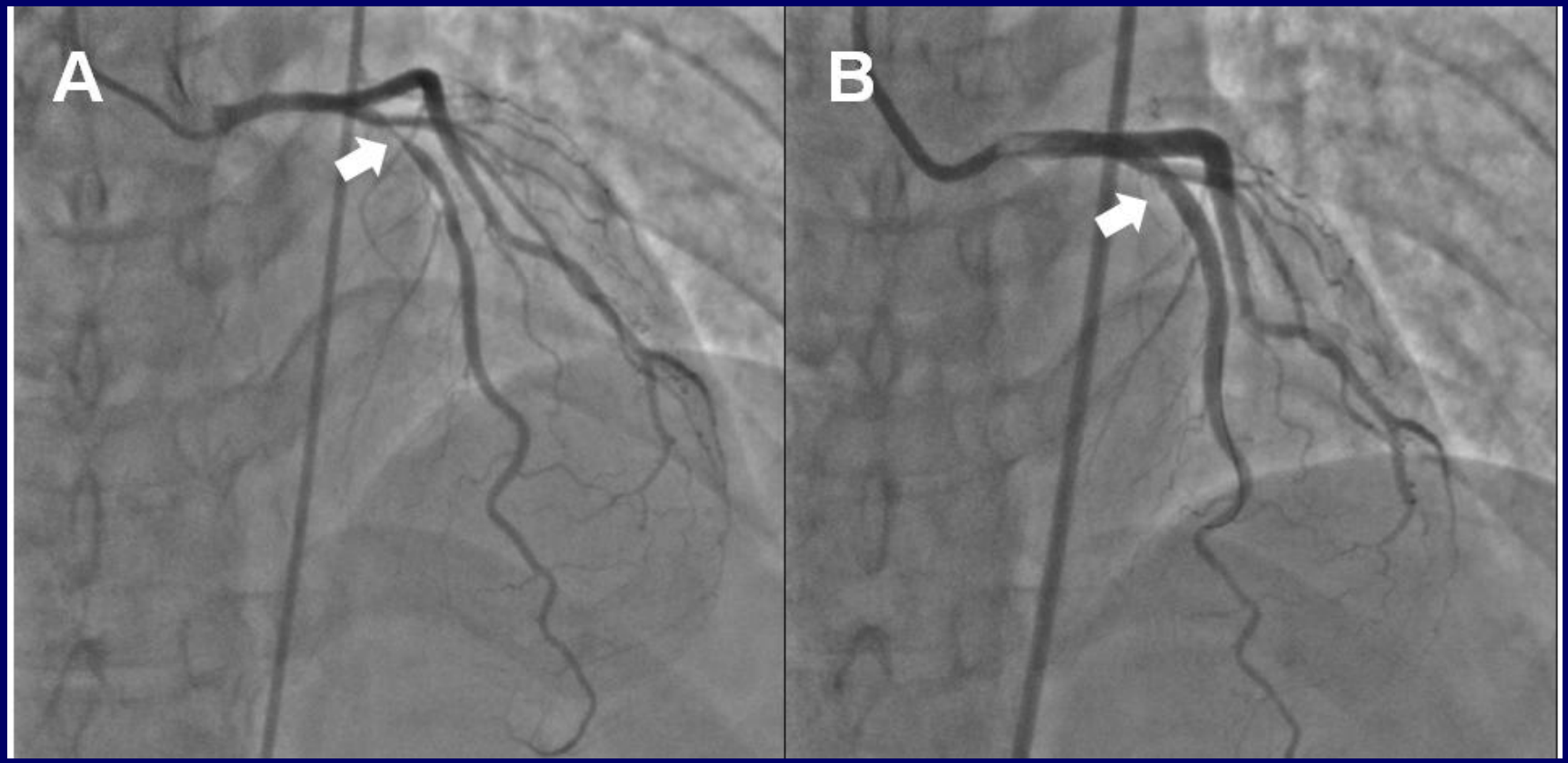
CNUH case (Mar 2007) www.circulation.or.kr

42 Year-Old Female
Two Site Stent Fracture Associated with Restenosis on 8-Month FU CAG



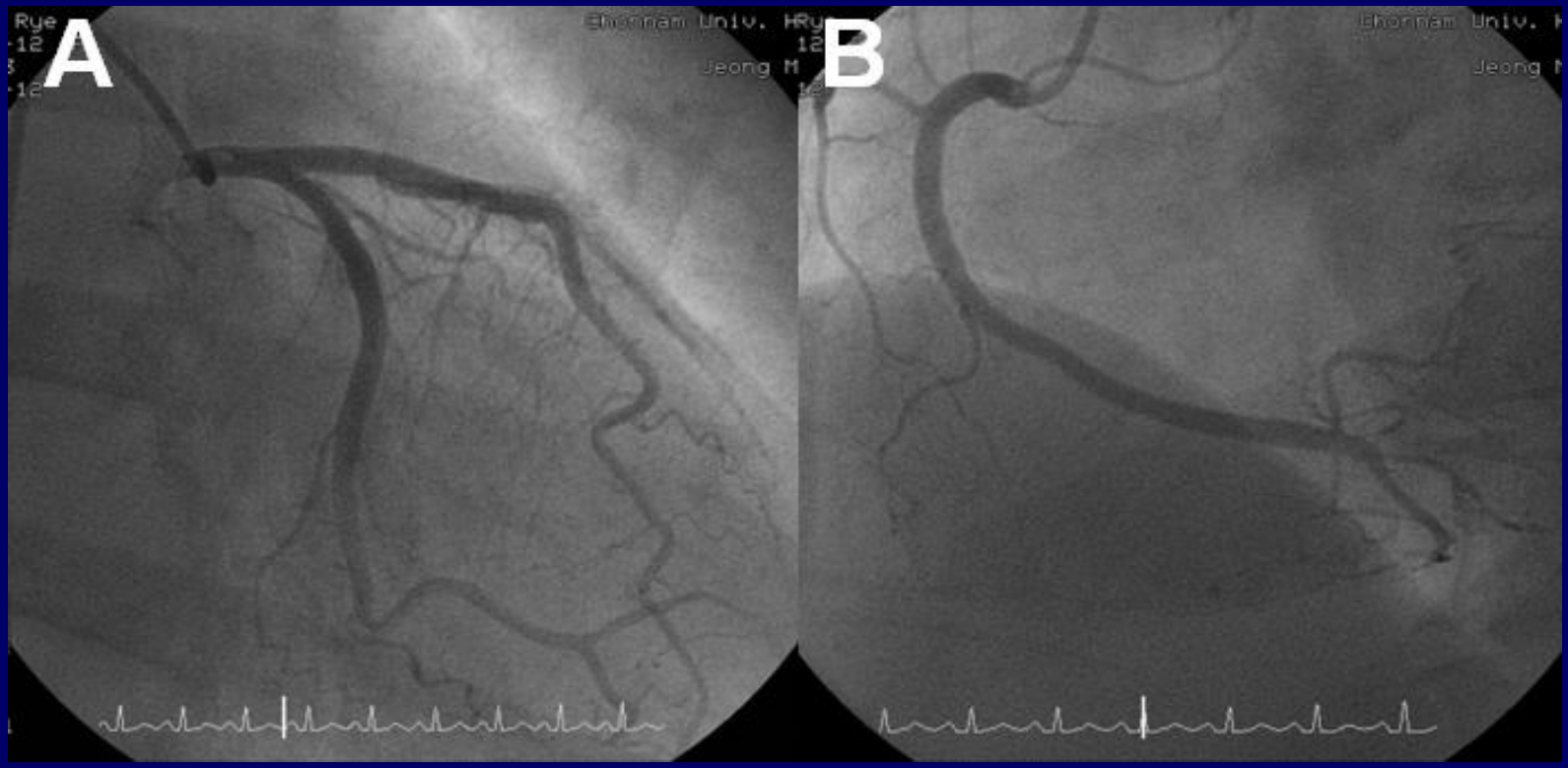
CNUH case (Mar 2007) www.circulation.or.kr

58 Year-Old Female
Very Late Stent Thrombosis 5 Years after DES Implantation



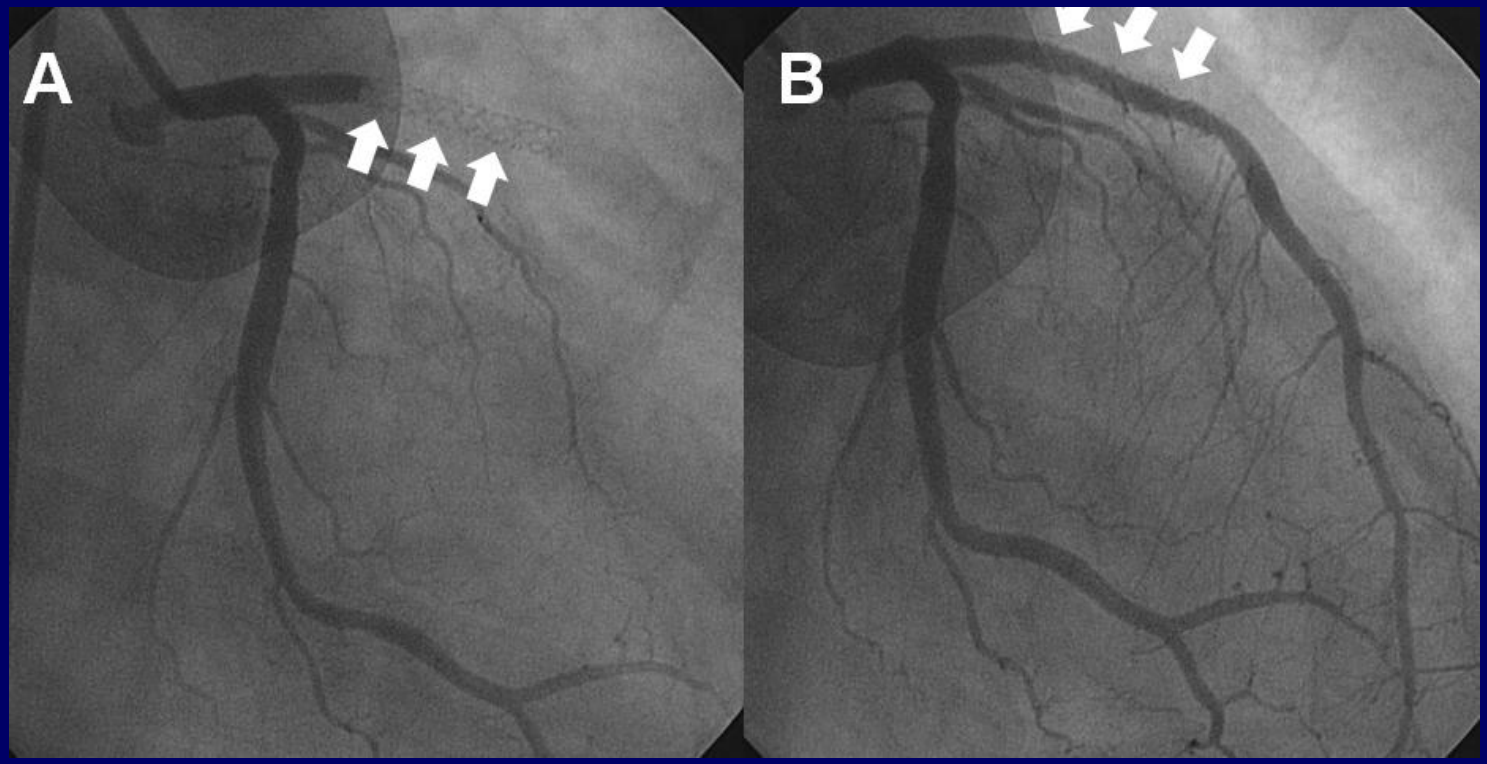
SES Implantation in LAD
2005. 11. 8.

58 Year-Old Female
Very Late Stent Thrombosis 5 Years after DES Implantation



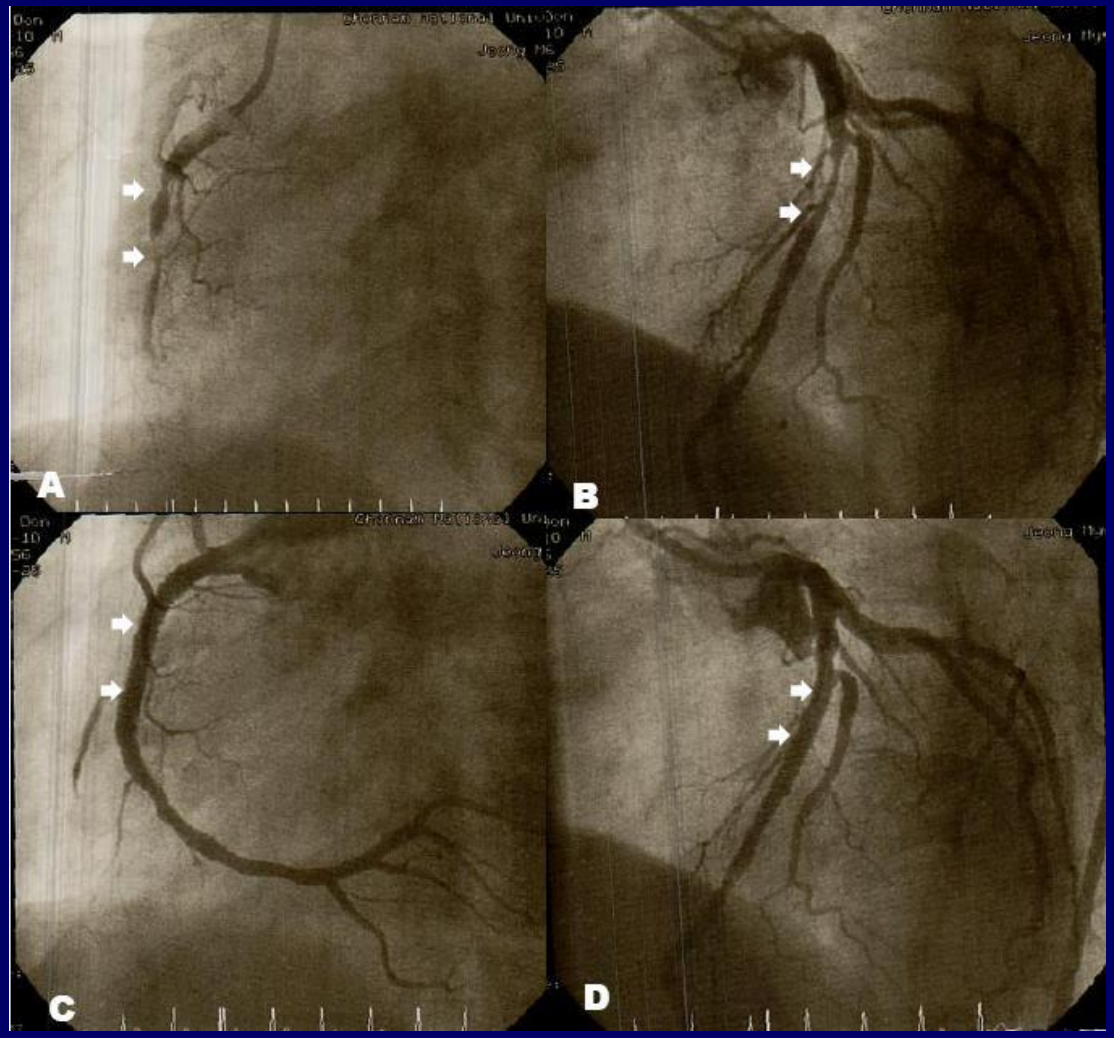
No ISR in LAD on FU CAG
2006. 5. 12.

58 Year-Old Female
Very Late Stent Thrombosis 5 Years after DES Implantation



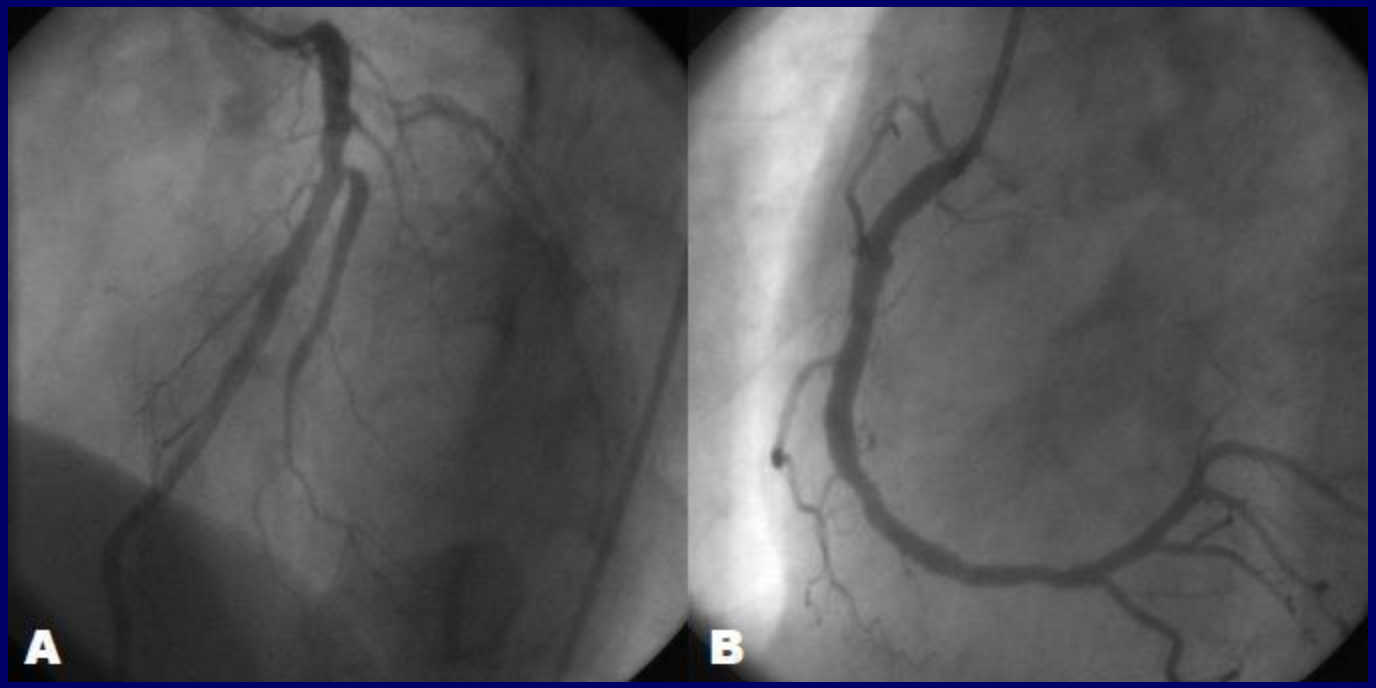
No ISR in LAD on FU CAG
2010. 7. 31.

39 Year-Old Male
Very Late Stent Thrombosis d/t Neointima Rupture 6 Years after PES Implantation



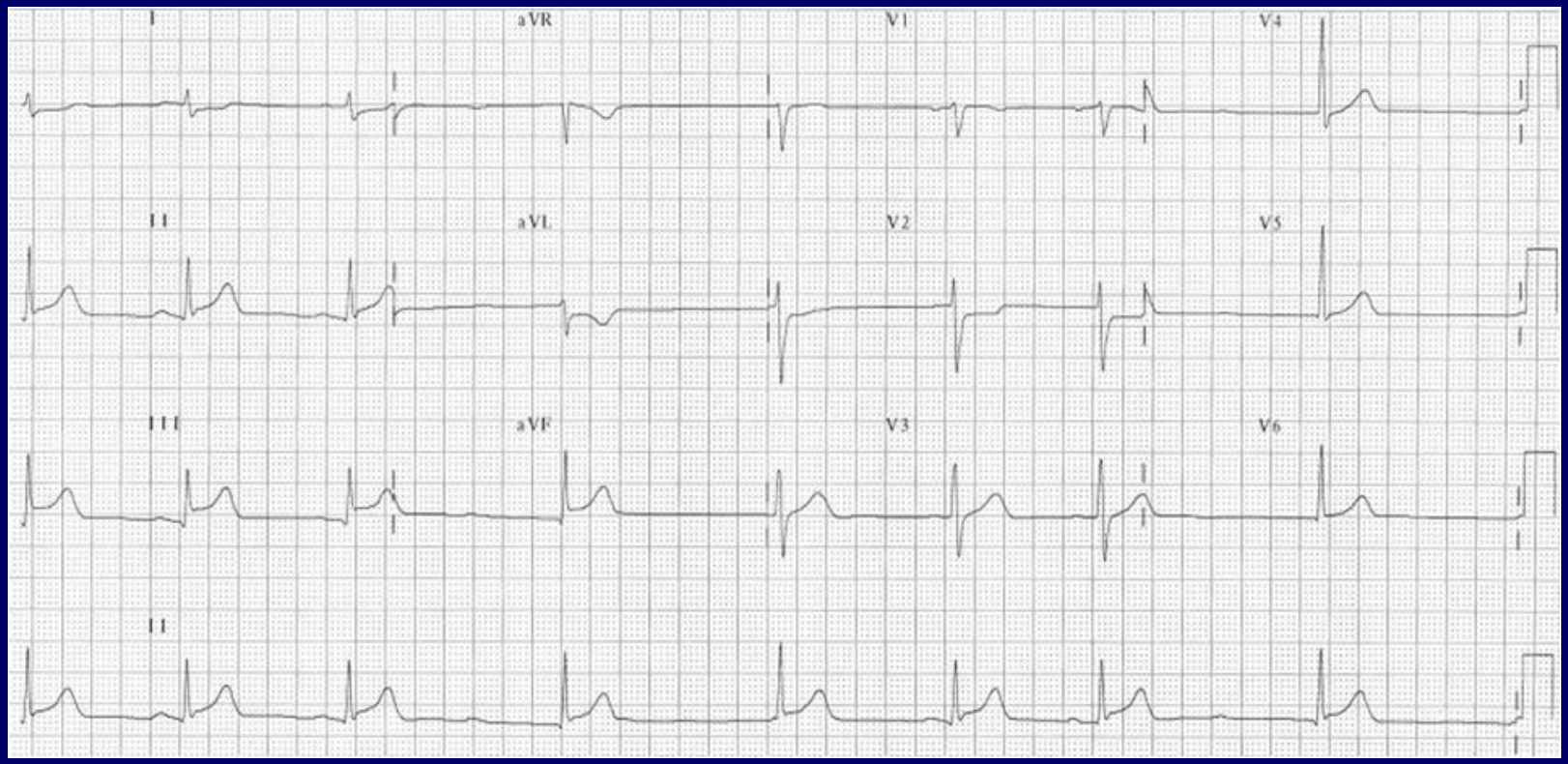
PES in RCA and LAD
Sep 2004

39 Year-Old Male
Very Late Stent Thrombosis d/t Neointima Rupture 6 Years after PES Implantation



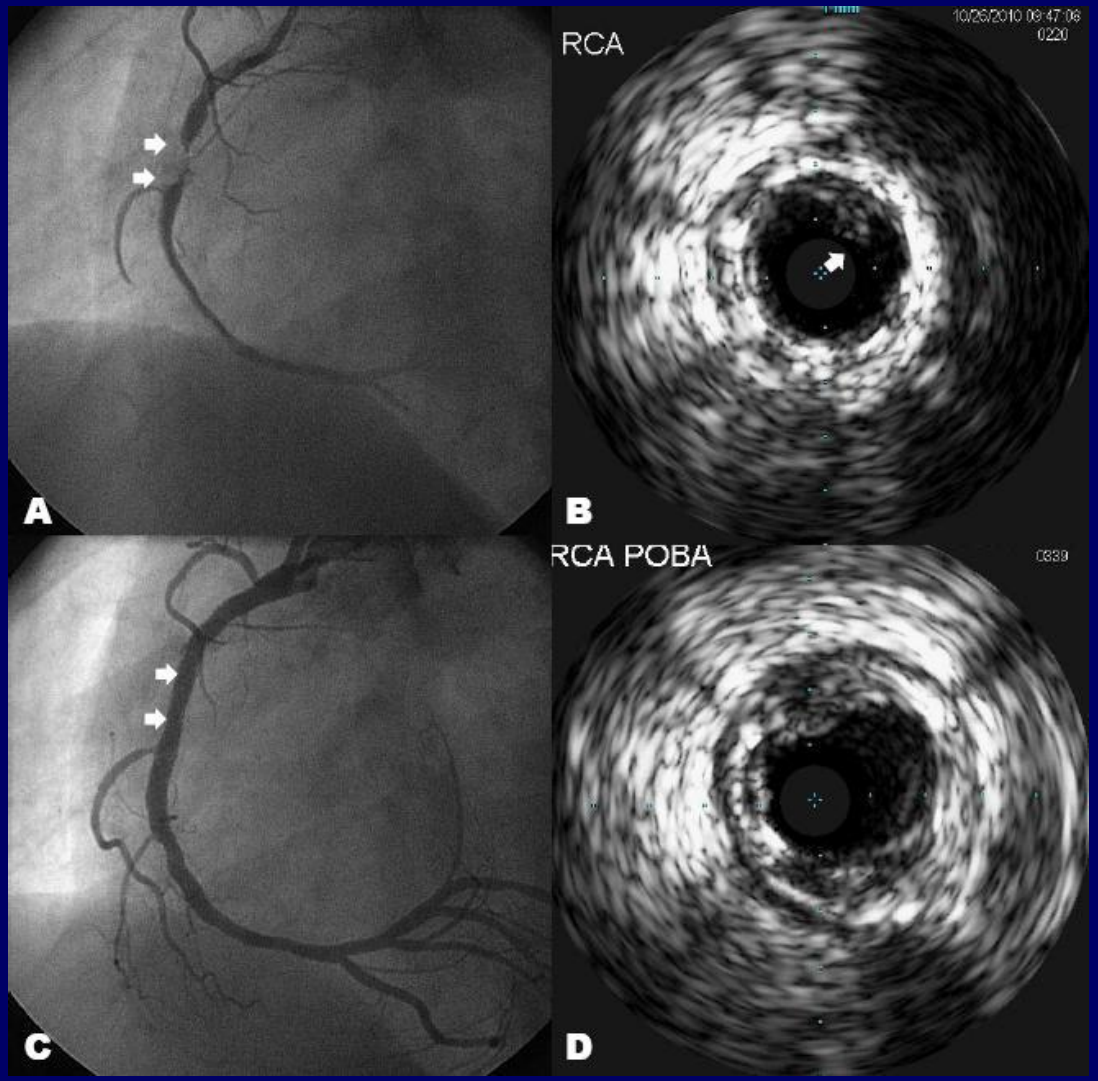
No ISR in LAD and RCA on FU CAG Mar 2005

39 Year-Old Male
Very Late Stent Thrombosis d/t Neointima Rupture 6 Years after PES Implantation



Acute Inf STEMI
Mar 2011

39 Year-Old Male
Very Late Stent Thrombosis d/t Neointima Rupture 6 Years after PES Implantation



VLST d/t NI
Rupture in RCA
Treated by POBA
Mar 2011

DES: *Things We Should Overcome…*

- Stent thrombosis – late or very late
- Polymer-mediated inflammation
- Local hypersensitivity of drug
- Aneurysm
- Stent fracture
- Availability of coating methods
- In specific lesion
  such as **AMI, DM, CKD,** ISR, bifurcated lesion, CTO, SVG, diffuse long lesion ….

증례 3 : 46 Year-Old Male

CC Chest pain (1 hour)

PH HT (-) DM (-)

SH 25 PYS current smoker

VS BP 120/80 mmHg, PR 70/min

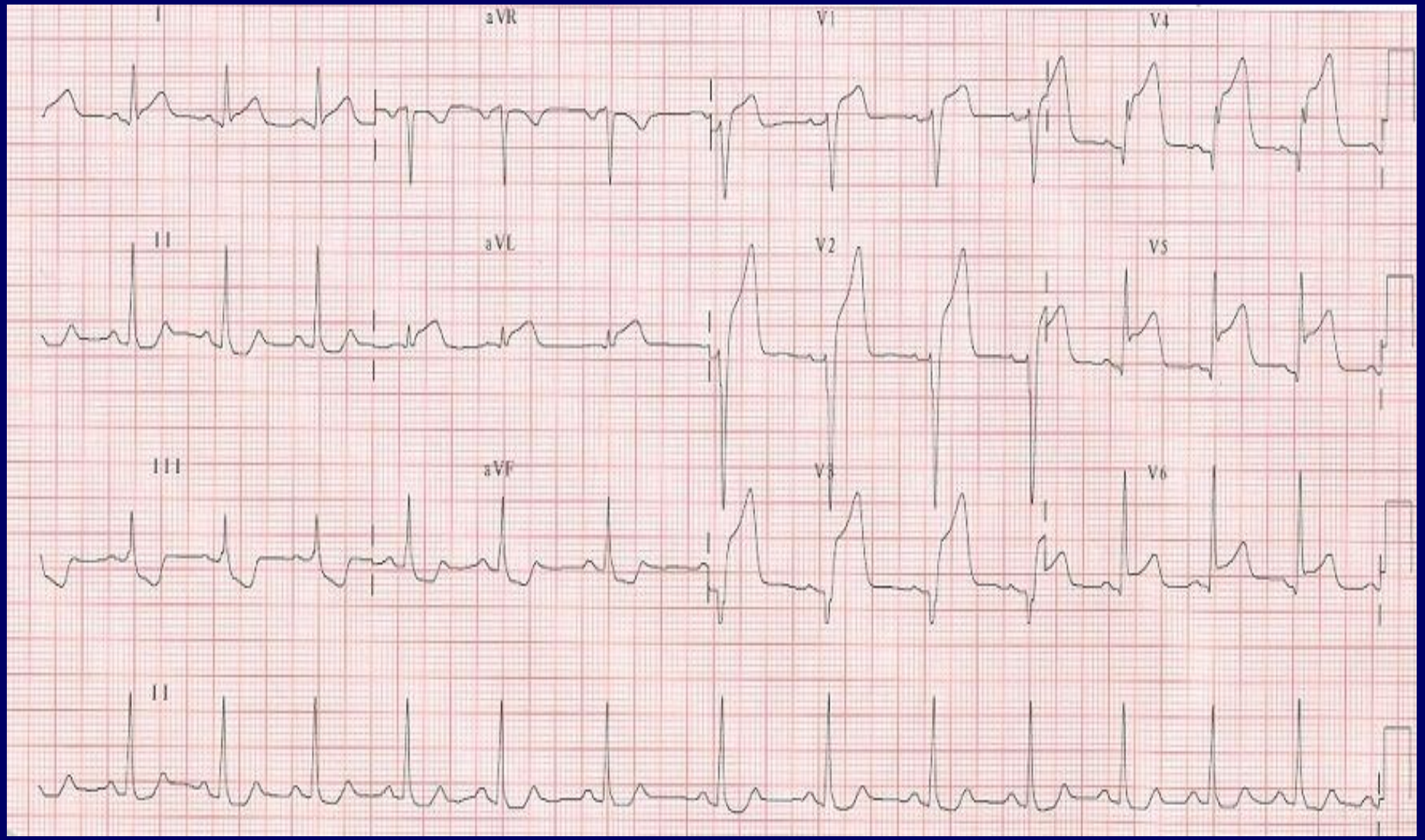
Lab Tn-I 2.16 ng/ml (0.06)

Tn-T 0.381 ng/ml (<0.010)

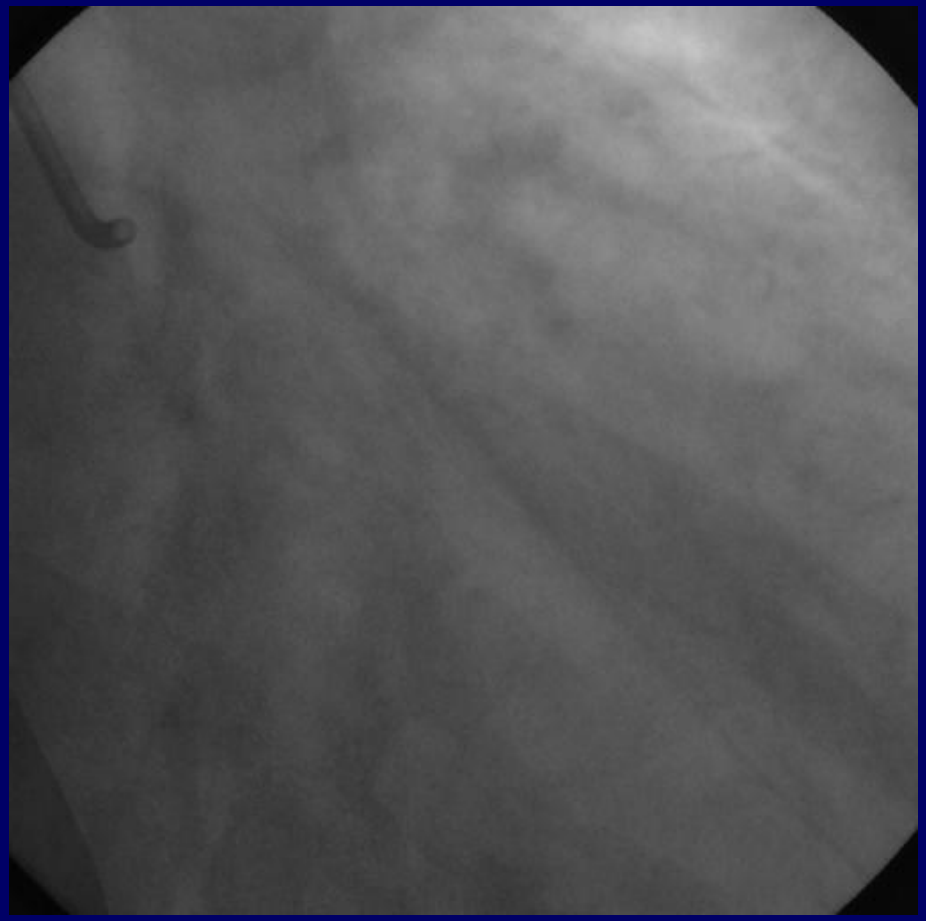
CK 325 U/L (67)

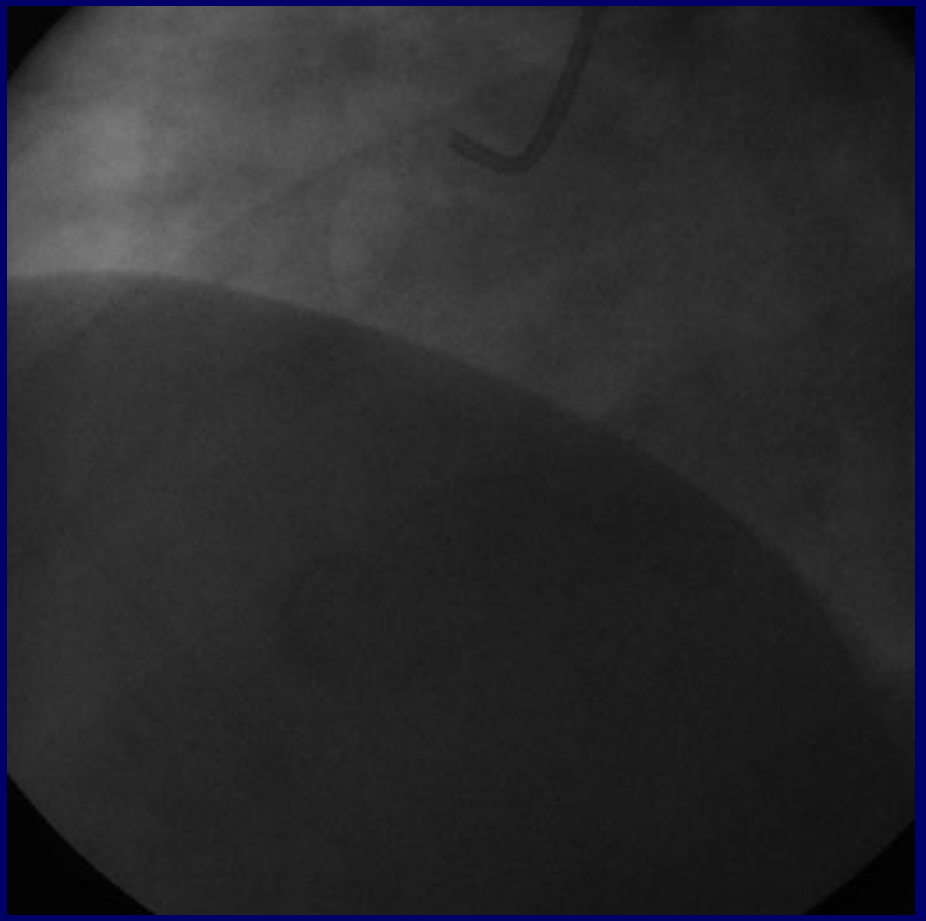
CK-MB 16.9 U/L (3.8)

EKG

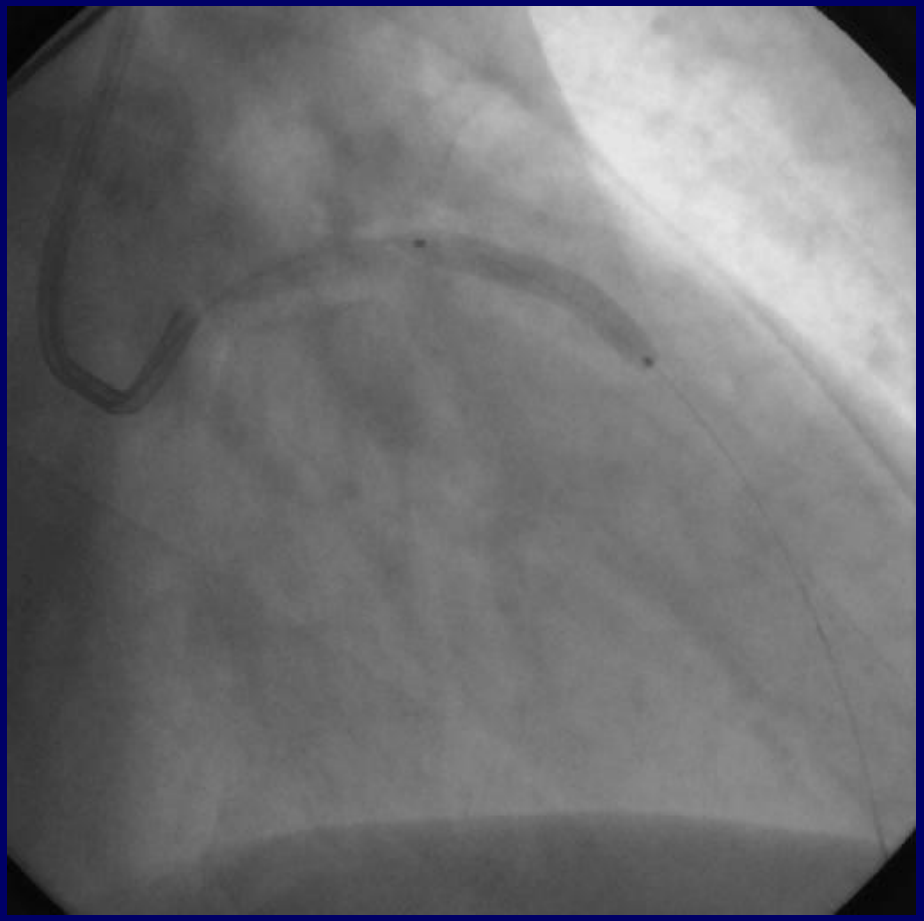


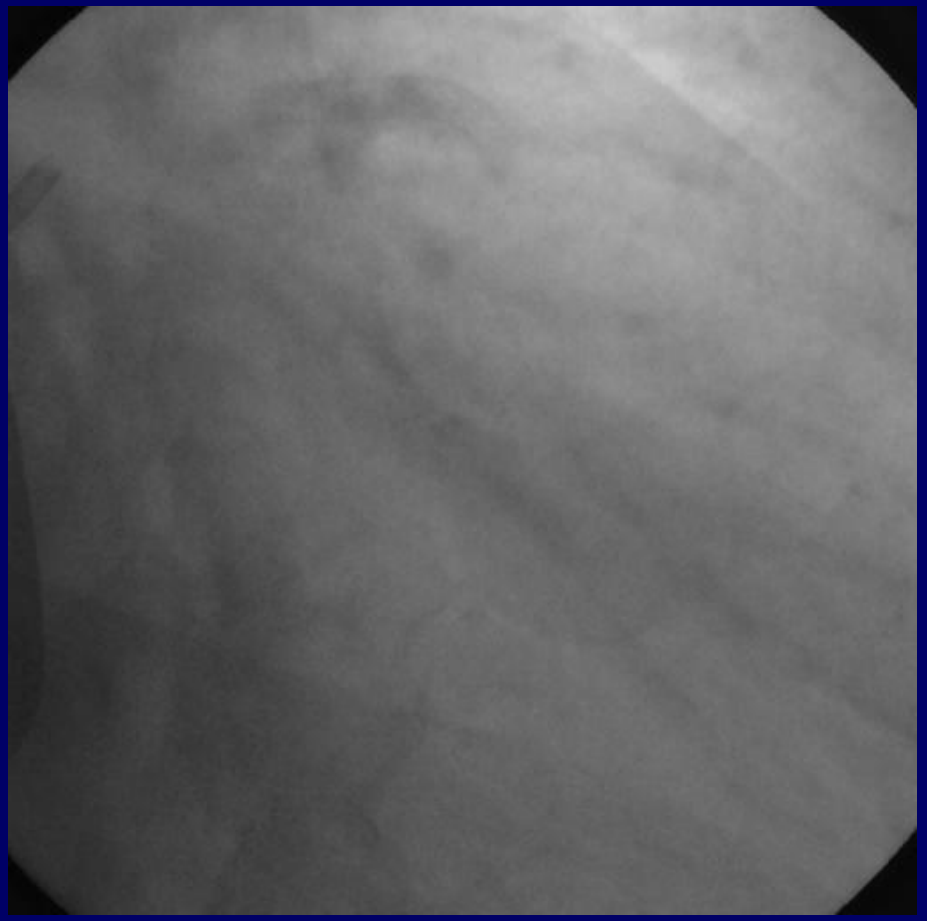
Coronary angiography





Percutaneous coronary intervention



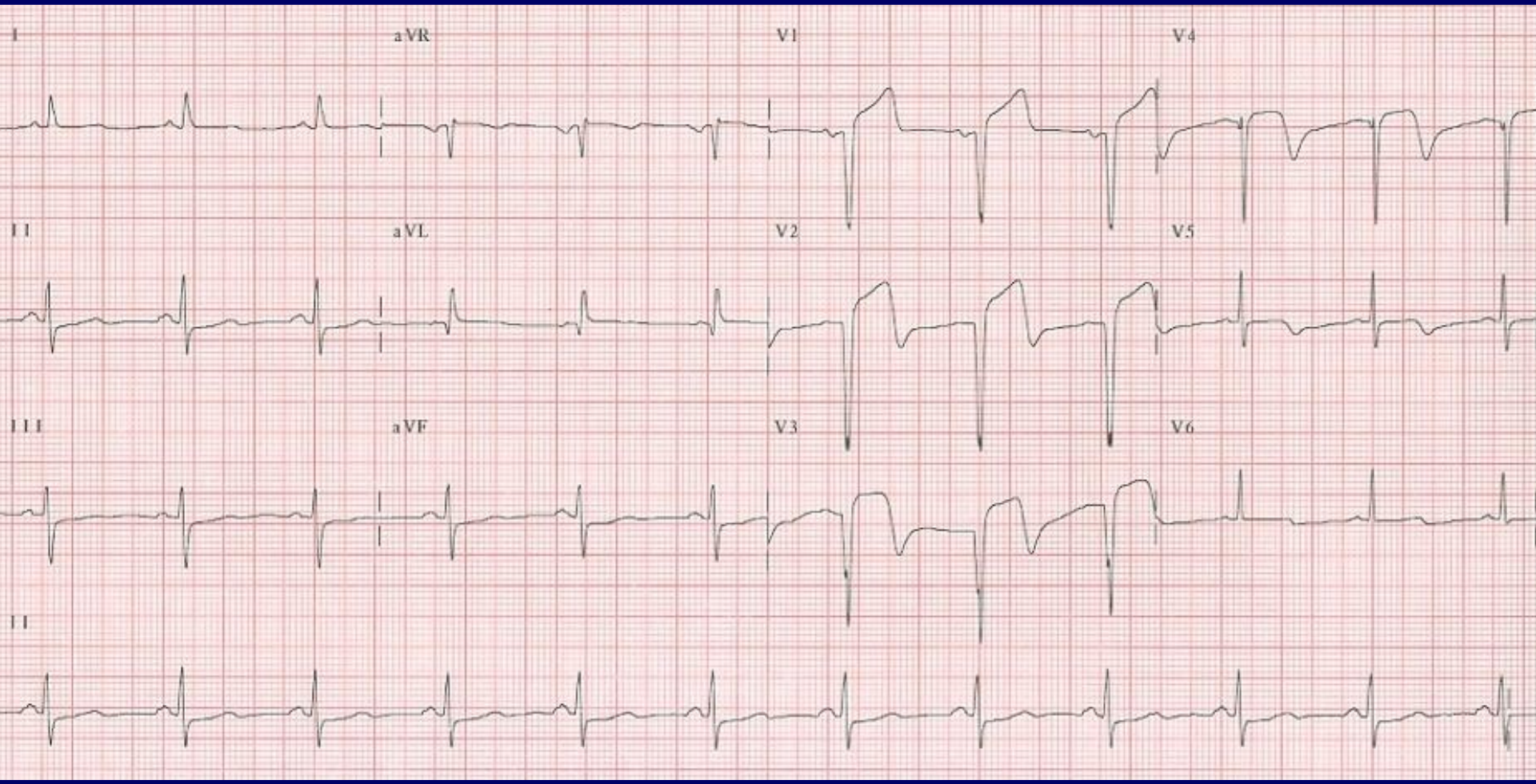


4.0*25 mm Zotarimus eluting stent
(drug-eluting stent)

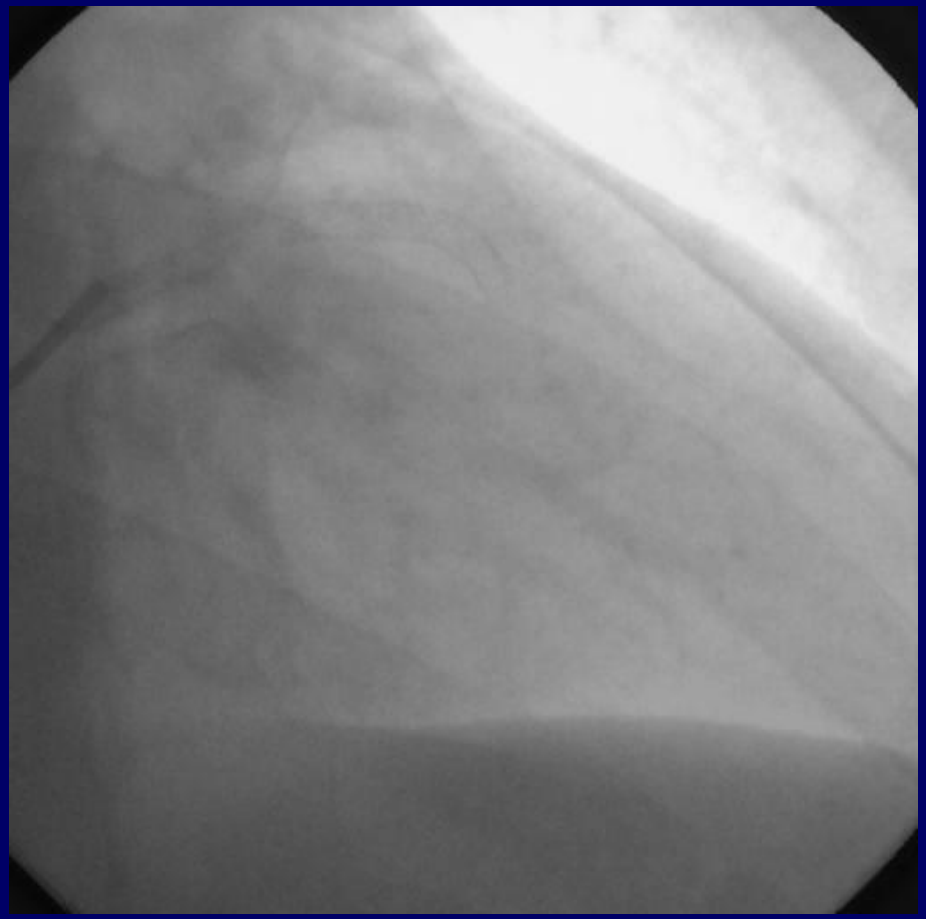
이 환자는 스텐트 시술 1개월 후 일주일 동안 해외 출장에 다녀오면서 약을 복용하지 않았다고 한다.

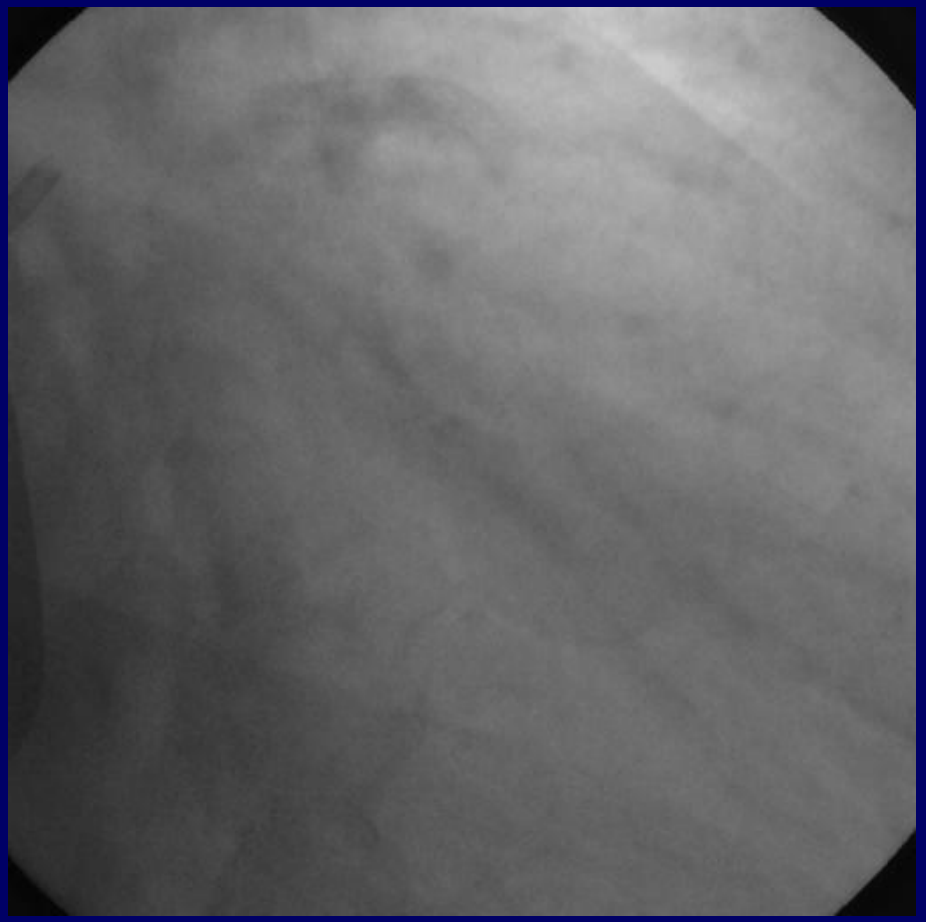
귀국 후 심한 흉통이 있어 응급실에 재내원하였다.

EKG at admission



Percutaneous coronary intervention





Thrombosuction
Balloon angioplasty

증례 3 : 문제 1

이 질환에 대한 옳은 설명은?

가. 약물용출 스텐트 사용으로 이 질환의 빈도가 감소하였다.
나. 고혈압이 중요한 위험인자로 작용한다.
다. 신생내막 과증식이 주로 관여한다.
라. **P2Y12 receptor resistance**를 검사해야 한다.

1. 가, 나, 다 **2.** 가, 다 **3.** 나,라
4. 라 **5. all of above**

이 환자에서 **platelet resistance test**를 시행하였다.

Asprin : 538 ARU (<550 ARU)

P2Y12 : 306 PRU (<235 PRU)

증례 3 : 문제 2

이 환자의 향후 치료로 올바른 조합은?

가. **Aspirin, clopidogrel**을 유지하면서 **cilostazol**을 추가한다.
나. **Clopidogrel**을 **prasugrel**로 변경하여 투약한다.
다. **Clopidogrel**을 **ticagrelor**로 변경하여 투약한다.
라. **Clopidogrel 75 mg**을 **150 mg**으로 증량하여 투약한다.

1. 가, 나, 다　　**2.** 가, 다　　**3.** 나,라
4. 라　　**5. all of above**

Prevention of Stent thrombosis

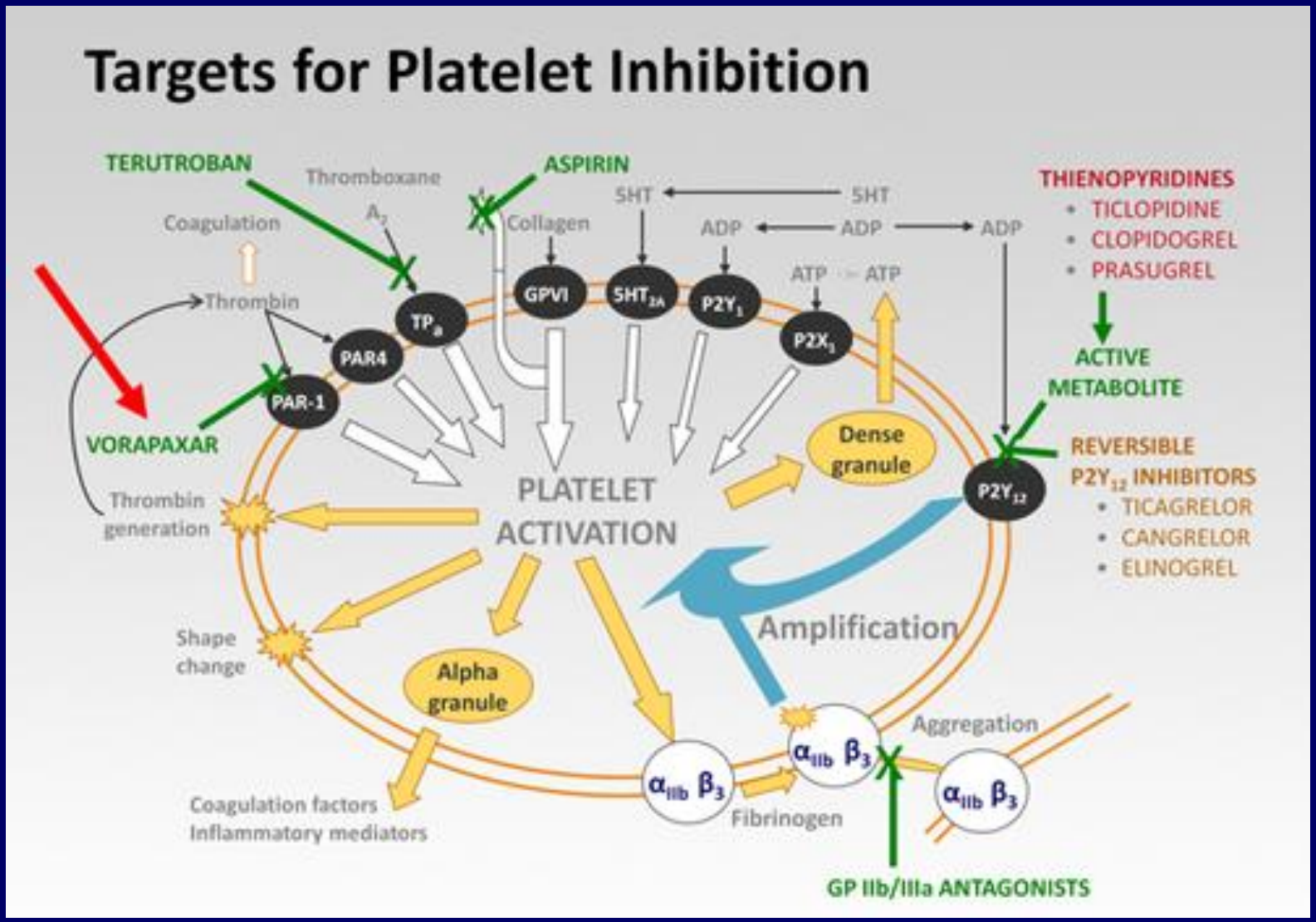
I. Optimal anti-platelet therapy

1. Longer duration of dual anti-platelet therapy
2. Clopidogrel resistance
    1. Dose elevation of clopidogrel from 75mg to 150mg
    2. Switch to triple anti-platelet therapy
    3. Switch to new drugs

    => prasgurel

    => ticagrelor

Targets for platelet inhibition



Triple Versus Dual Antiplatelet Therapy in Patients With Acute ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

Kang-Yin Chen, MD; Seung-Woon Rha, MD; Yong-Jian Li, MD; Kanhaiya L. Poddar, MBBS; Zhe Jin, MD; Yoshiyasu Minami, MD; Lin Wang, MD; Eung Ju Kim, MD; Chang Gyu Park, MD; Hong Seog Seo, MD; Dong Joo Oh, MD; Myung Ho Jeong, MD; Young Keun Ahn, MD; Taek Jong Hong, MD; Young Jo Kim, MD; Seung Ho Hur, MD; In Whan Seong, MD; Jei Keon Chae, MD; Myeong Chan Cho, MD; Jang Ho Bae, MD; Dong Hoon Choi, MD; Yang Soo Jang, MD; In Ho Chae, MD; Chong Jin Kim, MD; Jung Han Yoon, MD; Wook Sung Chung, MD; Ki Bae Seung, MD; Seung Jung Park, MD; for the Korea Acute Myocardial Infarction Registry Investigators

Background—Whether triple antiplatelet therapy is superior or similar to dual antiplatelet therapy in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention in the era of drug-eluting stents remains unclear.

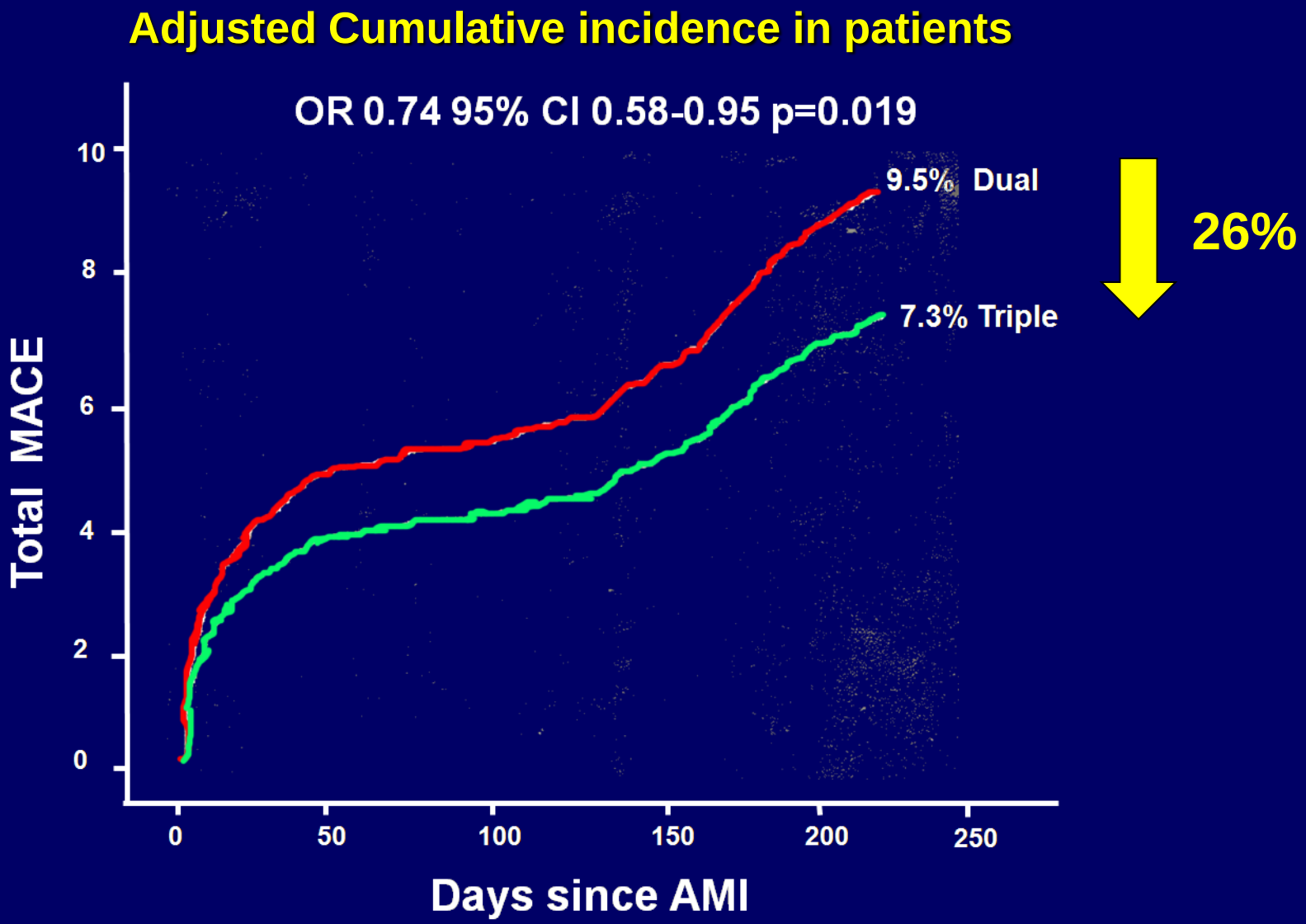
Methods and Results—A total of 4203 ST-segment elevation myocardial infarction patients who underwent primary percutaneous coronary intervention with drug-eluting stents were analyzed retrospectively in the Korean Acute Myocardial Infarction Registry (KAMIR). They received either dual (aspirin plus clopidogrel; dual group; n=2569) or triple (aspirin plus clopidogrel plus cilostazol; triple group; n=1634) antiplatelet therapy. The triple group received additional cilostazol at least for 1 month. Various major adverse cardiac events at 8 months were compared between these 2 groups. Compared with the dual group, the triple group had a similar incidence of major bleeding events but a significantly lower incidence of in-hospital mortality. Clinical outcomes at 8 months showed that the triple group had significantly lower incidences of cardiac death (adjusted odds ratio, 0.52; 95% confidence interval, 0.32 to 0.84; P=0.007), total death (adjusted odds ratio, 0.60; 95% confidence interval, 0.41 to 0.89; P=0.010), and total major adverse cardiac events (adjusted odds ratio, 0.74; 95% confidence interval, 0.58 to 0.95; P=0.019) than the dual group. Subgroup analysis showed that older (>65 years old), female, and diabetic patients got more benefits from triple antiplatelet therapy than their counterparts who received dual antiplatelet therapy.

Conclusions—Triple antiplatelet therapy seems to be superior to dual antiplatelet therapy in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention with drug-eluting stents. These results may provide the rationale for the use of triple antiplatelet therapy in these patients. (***Circulation***. **2009;119:3207-3214.**)

Key Words: cilostazol ■ myocardial infarction ■ thrombosis ■ platelets

Rha SW et al. Circulation 2009;119:3207-14

Triple vs. dual anti-platelet therapy in STEMI



Rha SW et al. Circulation 2009;119:3207-14

Prasugrel

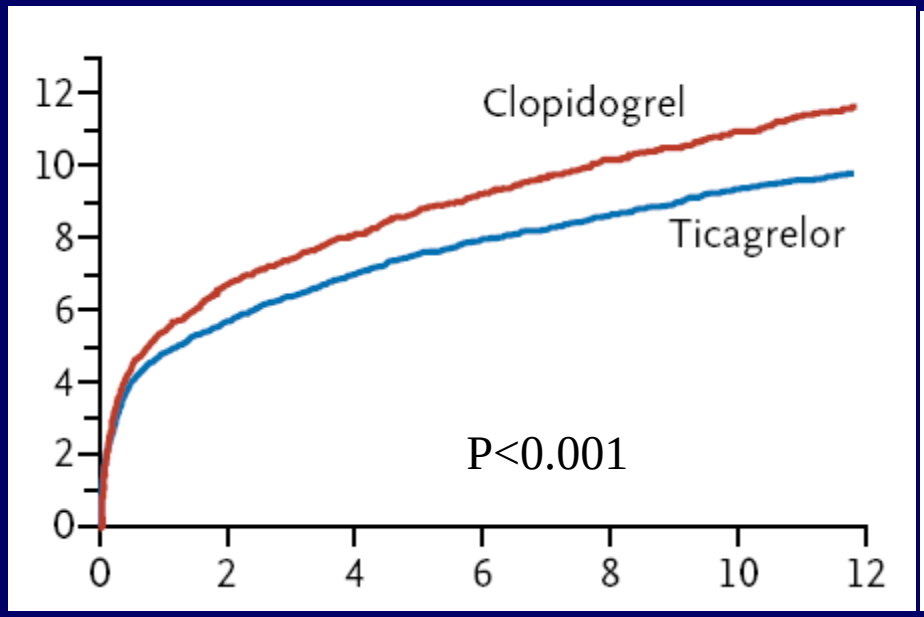
TRITON-TIMI 38 TRIAL

End Point	Prasugrel (N=6813)	Clopidogrel (N=6795)	Hazard Ratio for Prasugrel (95% CI)	P Value†
	no. of patients (%)			
Death from cardiovascular causes, nonfatal MI, or nonfatal stroke (primary end point)	643 (9.9)	781 (12.1)	0.81 (0.73–0.90)	<0.001
Death from cardiovascular causes	133 (2.1)	150 (2.4)	0.89 (0.70–1.12)	0.31
Nonfatal MI	475 (7.3)	620 (9.5)	0.76 (0.67–0.85)	<0.001
Nonfatal stroke	61 (1.0)	60 (1.0)	1.02 (0.71–1.45)	0.93
Death from any cause	188 (3.0)	197 (3.2)	0.95 (0.78–1.16)	0.64
Death from cardiovascular causes, nonfatal MI, or urgent target-vessel revascularization	652 (10.0)	798 (12.3)	0.81 (0.73–0.89)	<0.001
Death from any cause, nonfatal MI, or nonfatal stroke	692 (10.7)	822 (12.7)	0.83 (0.75–0.92)	<0.001
Urgent target-vessel revascularization	156 (2.5)	233 (3.7)	0.66 (0.54–0.81)	<0.001
Death from cardiovascular causes, nonfatal MI, nonfatal stroke, or rehospitalization for ischemia	797 (12.3)	938 (14.6)	0.84 (0.76–0.92)	<0.001
Stent thrombosis‡	68 (1.1)	142 (2.4)	0.48 (0.36–0.64)	<0.001

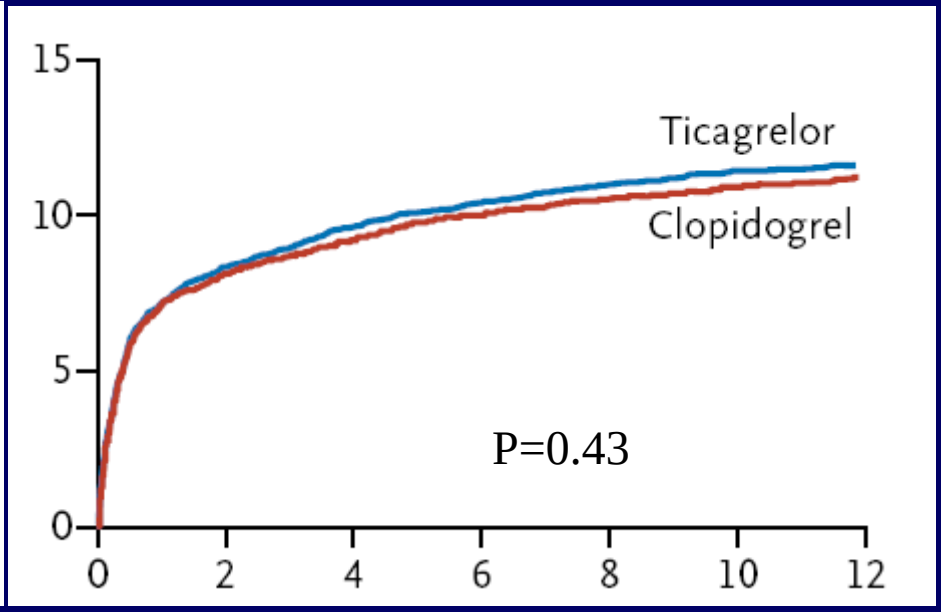
Wiviott SD et al. *NEJM* 2007;357:2001

Ticagrelor

PLATO TRIAL



K-M curve for the primary end point



K-M curve for the first major bleeding

Primary end point: the composite of death from cardiovascular causes, MI, stroke

Wallentin L et al. *NEJM* 2009;361:1045

증례 4 : 60 Year-Old Male

CC For dental implant

PH DES d/t AMI 2 YA

Present medications

Aspirin, Clopidgrel, ACEI, beta-blocker, statin

증례 4 : 문제 1

이 환자에게 적합한 조치는?

1. 현재 복용대로 약물치료하고 임플란트를 시행한다.
2. **Clopidogrel**만 중단하고 임플란트를 시행한다.
3. **Aspirin, Clopidogrel** 모두 중단하고 임플란트를 시행한다.
4. 임플란트 시술을 연기한다.

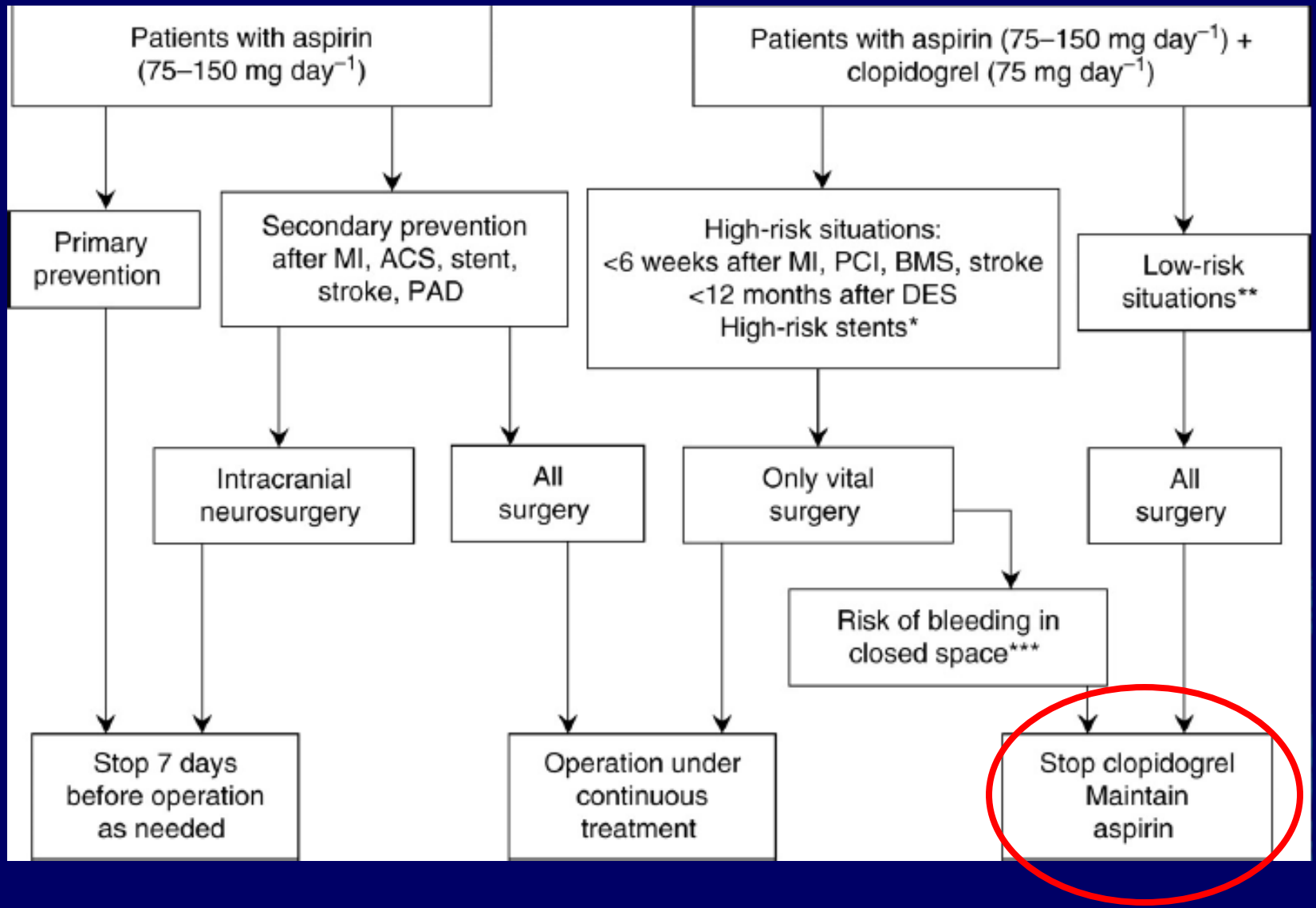
Bleeding Risk (Aspirin Alone)

Aspirin alone: 1.5 times without an increased surgical mortality or morbidity.

Dental, opthalmological, visceral and minor general surgery, endoscopies, biosies and dialysis catheter insertion

Increase in bleeding rate in specific procedure : Hip arthroplasty, cardiac surgery with cardiopulmonary bypass, tonsillectomy, transurethral prostatectomy

Algorithm for preoperative management of patients under antiplatelet therapy



Chassot, P.-G. et al. Br. J. Anaesth. 2007 99:316-328

Surgery-Related Risk

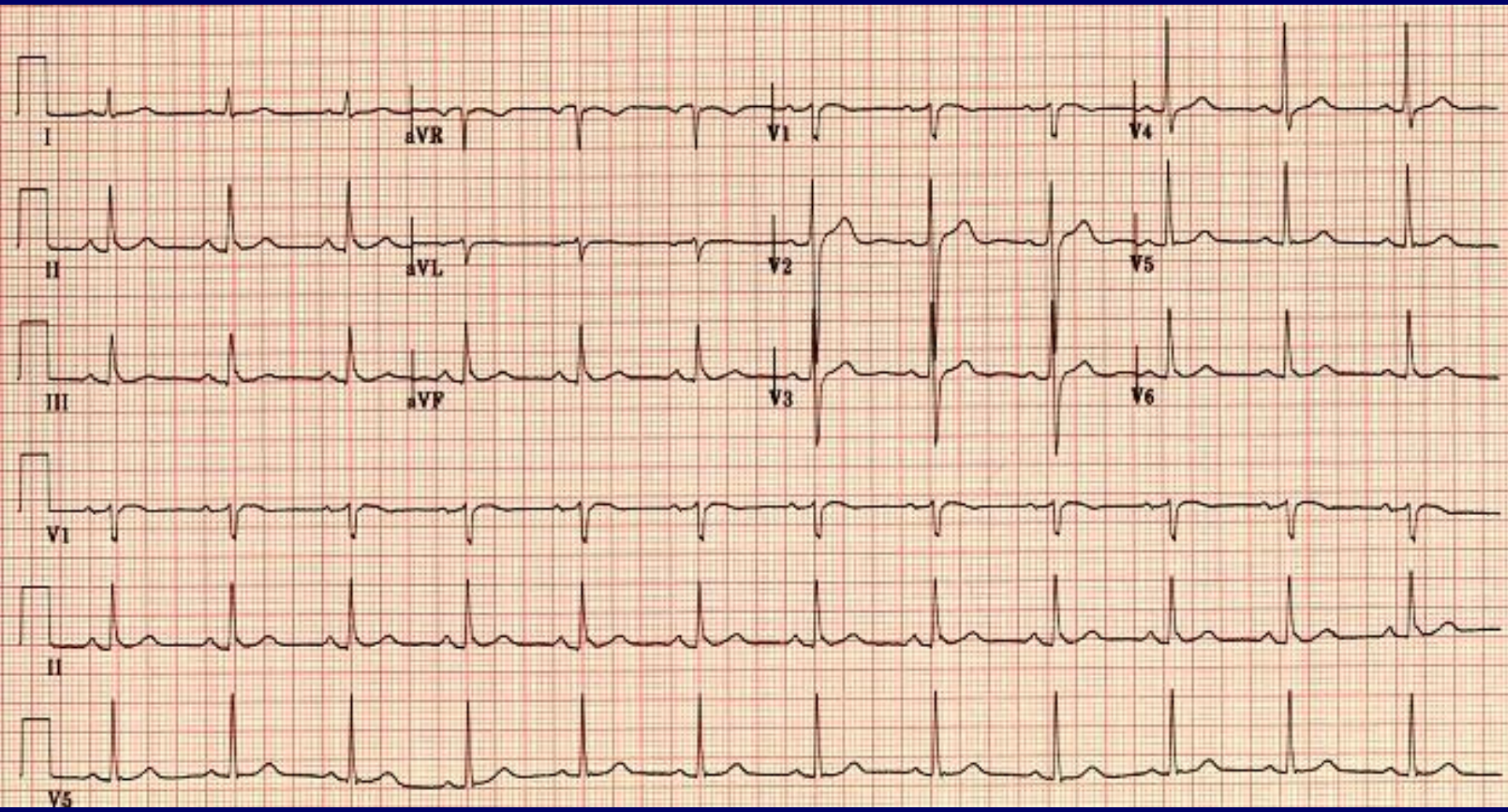
High (>5%)	Aortic and other major vascular surgery Peripheral vascular surgery
Intermediate (1 – 5%)	Carotid endarterectomy Head and neck surgery Intraperitoneal and intrathoracic surgery Orthopedic surgery Prostate surgery
Low (<1%)	Endoscopic procedures Superficial procedures Cataract surgery Breast surgery Ambulatory surgery

2009 ACC/AHA Practice Guidelines

증례 5 : 65 Year-Old Male

CC	RUQ pain, fever (onset: 4 DA)
PH	HT (+)
	UAP (+): PCI with DES 5 MA
	Med: aspirin, clopidogrel, BB, ACEI, statin
FC	Able to walk up a hill
PI	Urgent surgery: acute cholecystitis
	No chest pain or DOE
VS	140/90 mmHg, 91/min

ECG on admission



LAB

CBC

WBC	17600 /mm^3
Hb	13.3g /dL
PLT	133x10^3 /mm^3

LFT

AST	84 U/L
ALT	84 U/L
T-bil	1.1 mg/dL

RFS and electrolytes

BUN/Cr	25.3/0.8 mg/dL
Na/K/Cl	139/4.5/107 mEq/L

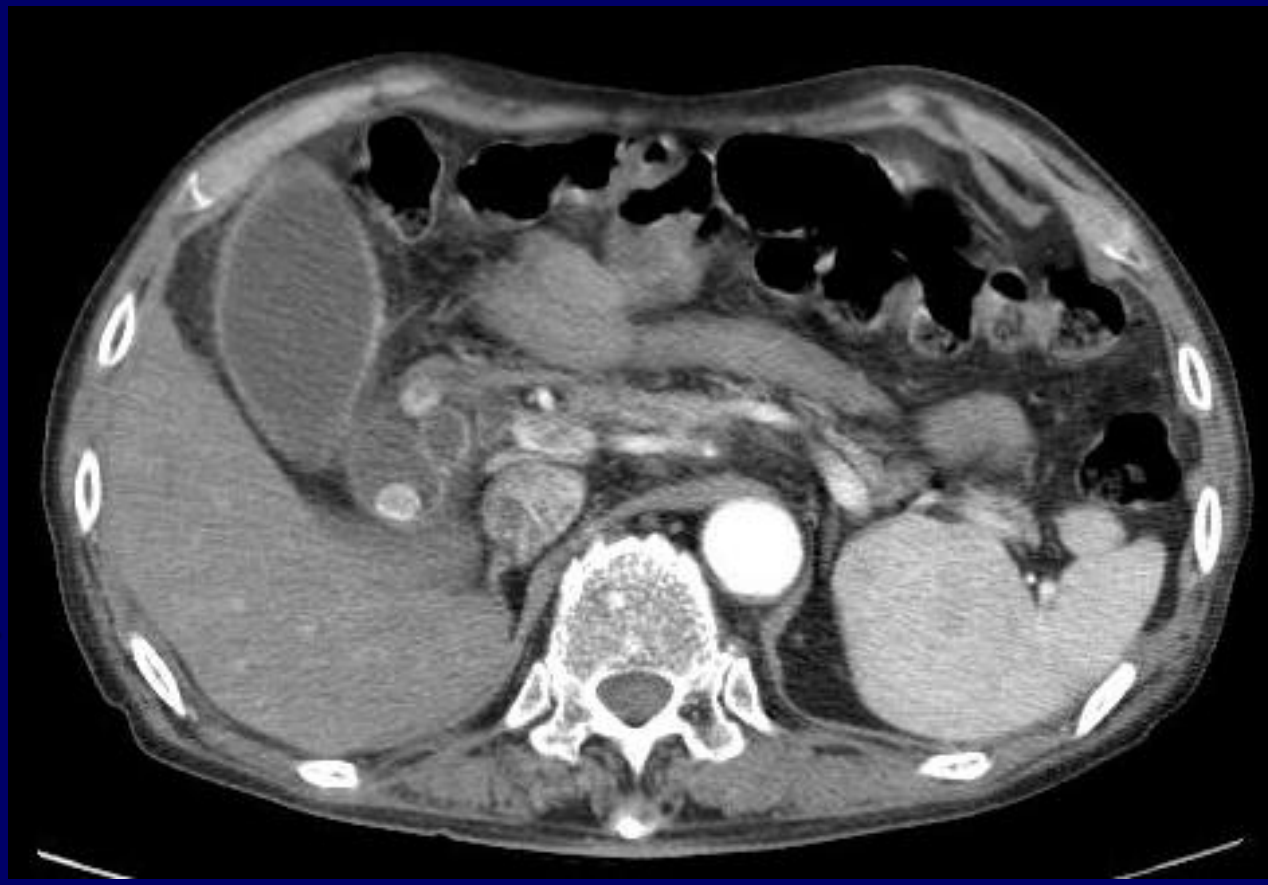
Acute phase reactant

CRP	12.1 mg/dL

Cardiac enzymes

Tn-I	0.01	ng/mL
CK	47	U/L
CK-MB	5.9	U/L
proBNP	229	pg/mL

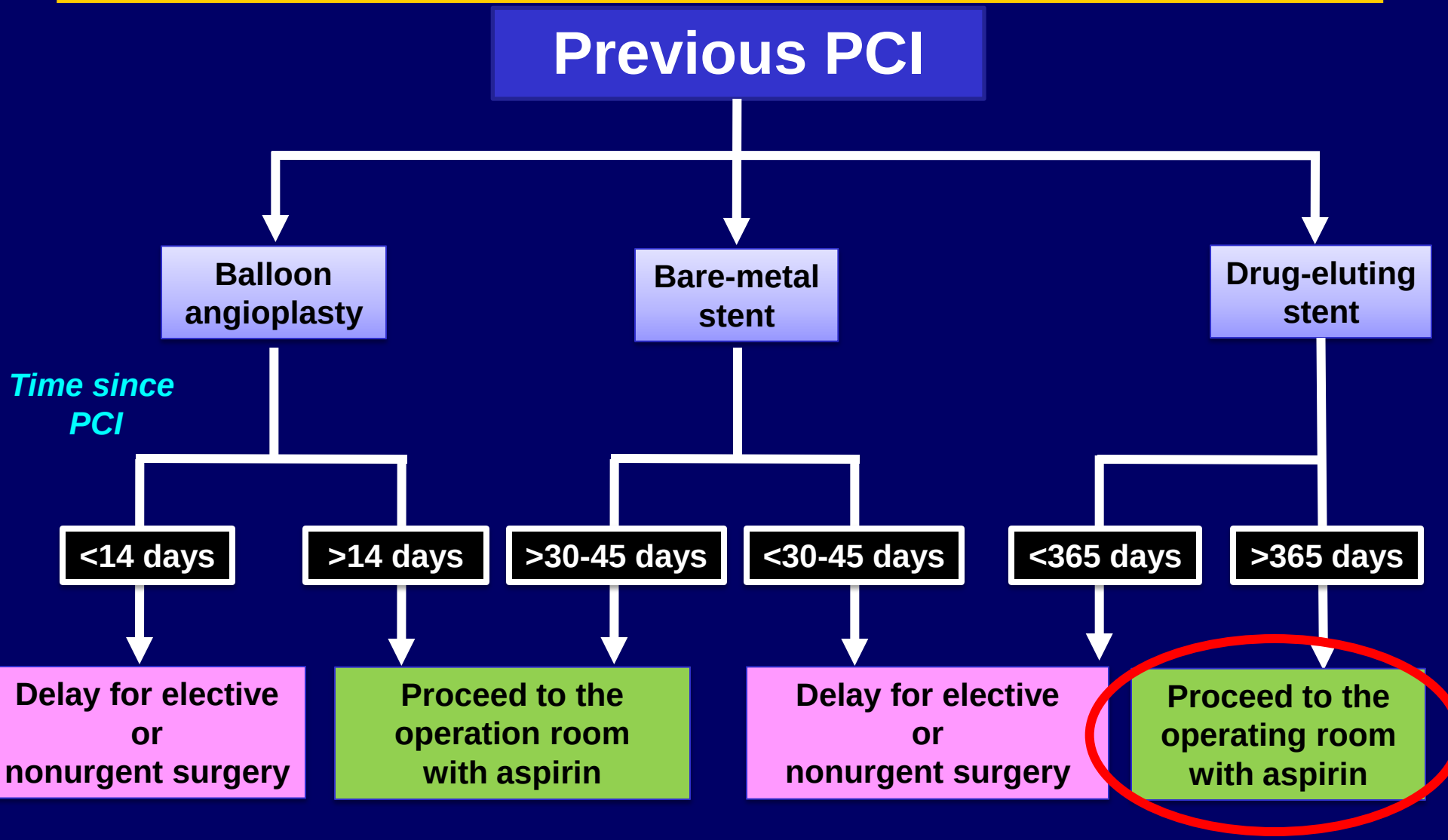
Abdominal CT



수술 전 항혈전요법으로 가장 적절한 권고는?

	Aspirin PO	Clopidogrel PO	Heparin IV
1.	Quit	Quit	No
2.	Quit	Quit	Yes
3.	Maintain	Quit	No
4.	Maintain	Quit	Yes

Timing of Surgery after PCI



2009 ACC/AHA Practice Guidelines

Prevention of Stent thrombosis

I. Optimal anti-platelet therapy
   1. Longer duration of dual anti-platelet therapy
   2. Clopidogrel resistance
      1. Dose elevation of clopidogrel from 75mg to 150mg
      2. Switch to triple anti-platelet therapy
      3. Switch to new drugs

      => prasgurel

      => ticagrelor

II. New stent design
   1. DES with biodegradable polymers
   2. non-polymeric drug delivery

Animal And Clinical Experiences of New Coronary Stents at CNUH

1. Bare Metal Stent

   Carbon coated stent, Co-Cr stent

2. Radioactive (Ho-166) stent

3. Drug-coated stent

   Heparin stent, Paclitaxel Carbon stent, Hepamin (Heparin+Dopamine) Stent

   Abciximab (ReoPro®) stent, ACEI coated stent

   Anti-oxidants (carvedilol, probucol, alpha-lipoic acid) stent,

   Echinomycin-heparin double coating on Co-Cr stent

   Phospholipid-coating biocompatible stent

   Biodegradable PLGA (polylactic glycolic acid, Fucoidan) stent

   Nanotech stent (TiO2, NO-doped TiO2 coated stent)

   Dual coating stent (ReoPro and ALA)

4. Gene-coated stent: Natural polymer (LMWSC)-mediated gene coating stent

   TiO2-drug-plasmid stent

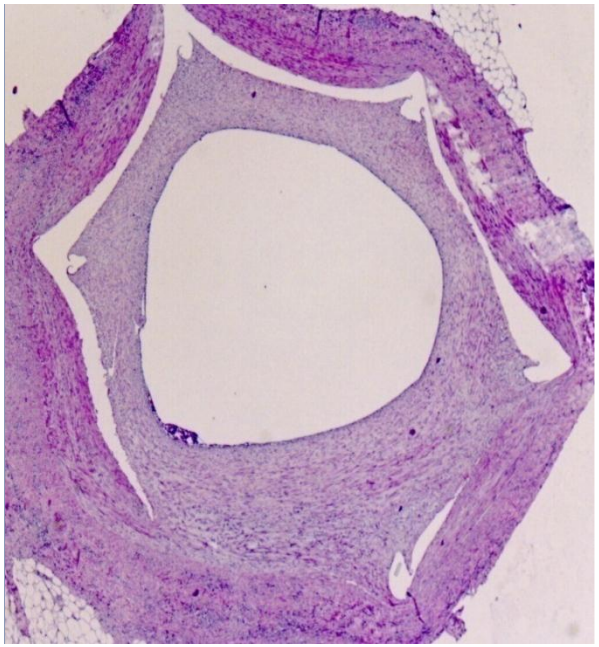
5. Endothelial progenitor cell capture stent – Aptamer stent

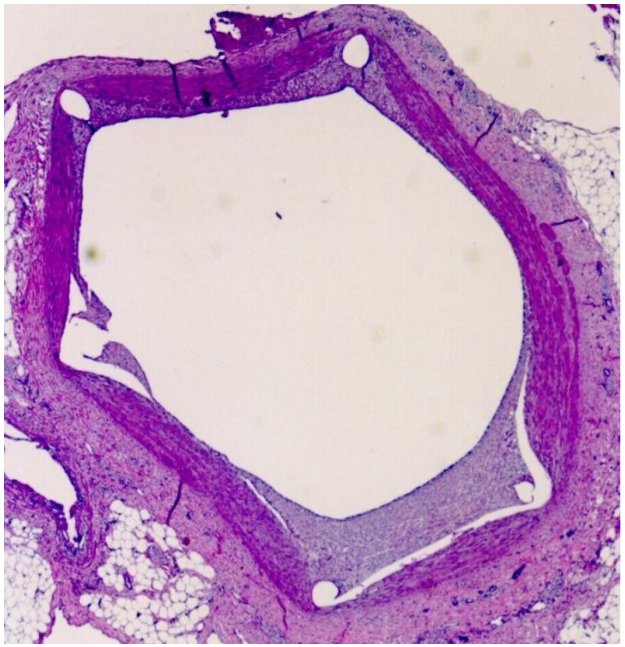
Heparin-Coated Stent

Conclusions in animal study:

Heparin-coated stent Inhibits neointimal cell proliferation within stent compared with non-coated stent

Bare Stent

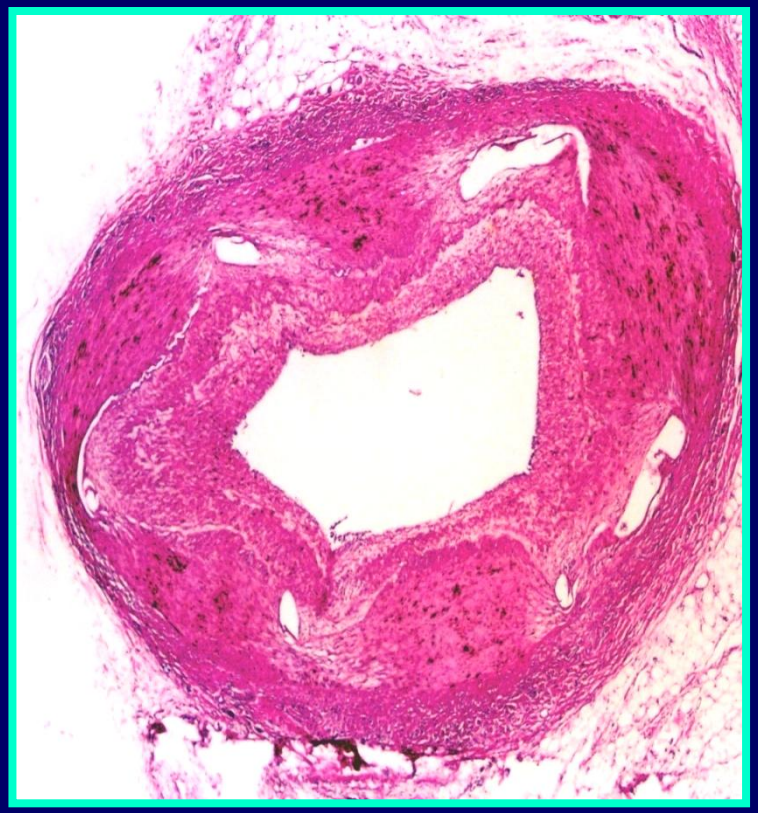


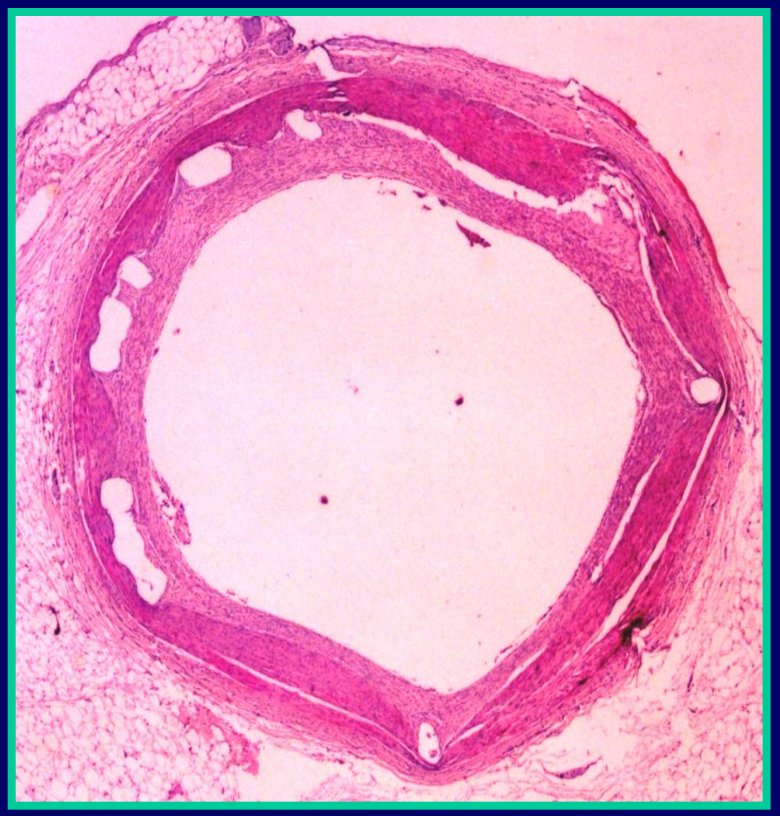


Heparin -Coated Stent

Catheter Cardiovasc Interv 1999;48:324-30, Korea Patent: 0336508

Platelet GP IIb/IIIa Receptor Blocker (ReoPro®)-Coated Stent in A Porcine Model





Control stent **ReoPro-coated stent**

CNUH data. Circulation 2000;102:II-666, JACC 2001;37:1A
Korea Patent : 0371008, 10-0778656, US Patent: 11/744,010

Effect of *Abciximab*-Coated Stent on In-Stent Intimal Hyperplasia in Human Coronary Arteries

Young Joon Hong, MD, Myung Ho Jeong, MD, PhD, Weon Kim, MD, Sang Yup Lim, MD, Sang Hyun Lee, MD, Seo Na Hong, MD, Ju Han Kim, MD, Young Keun Ahn, MD, Jeong Gwan Cho, MD, PhD, Jong Chun Park, MD, PhD, Dong Lyun Cho, PhD, Hoon Kim, MS, and Jung Chaee Kang, MD, PhD

The investigators tested whether abciximab-coated stents prevent neointimal hyperplasia (NIH) formation in coronary de novo lesions. Abciximab-coated stents were compared with control stents. All patients underwent follow-up coronary angiography and intravascular ultrasound (IVUS). All stents were successfully deployed, and patients were discharged home without clinical events. At follow-up coronary angiography, the restenosis rate and late loss were 14% and 0.33 ± 0.28 mm in the abciximab-coated stent group and 28.6% and 0.64 ± 0.32 mm in the control stent group (p = 0.099 and p = 0.014, respectively). At follow-up IVUS, the intrastent luminal area and intrastent NIH area were 5.7 ± 1.6 and 2.0 ± 1.6 mm^2, respectively, in the abciximab-coated stent group and 4.2 ± 0.8 and 3.4 ± 1.7 mm^2, respectively, in the control stent group (p = 0.001 and p = 0.001, respectively). Abciximab-coated stents are feasible and significantly inhibit NIH, with potential therapeutic benefit in preventing stent restenosis.

(Am J Cardiol 2004;94:1050–1054)

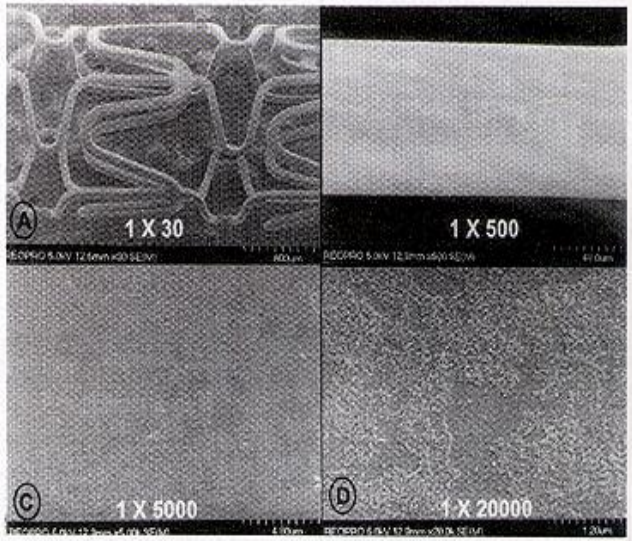


FIGURE 1. Scanning electron microscopic findings after abciximab coating on the surface of the stent.

Platelet activation and aggregation induce arterial thrombosis and play a pivotal role in the pathophysiology of acute coronary syndromes.[1,2] The development of inhibitors of fibrinogen binding to the platelet glycoprotein IIb/IIIa receptor has expanded the therapeutic options for treating patients with thrombotic disorders.[3,4] Abciximab (ReoPro, Eli Lilly

The Clinical Results of a Platelet Glycoprotein IIb/IIIa Receptor Blocker (Abciximab: ReoPro)-Coated Stent in Acute Myocardial Infarction

Weon Kim, MD,* Myung Ho Jeong, MD, FACC, FAHA, FESC,* Kye Hun Kim, MD,* Il Suk Sohn, MD,* Young Joon Hong, MD,* Hyung Wook Park, MD,* Ju Han Kim, MD,* Young Keun Ahn, MD, FACC,* Jeong Gwan Cho, MD, FACC,* Jong Chun Park, MD,* Dong Lyun Cho, PHD,† Jung Chae Kang, MD*

Gwangju, Korea

OBJECTIVES This study is a prospective randomized trial investigating clinical outcomes of patients with acute myocardial infarction (AMI) treated with abciximab (ReoPro)-coated stents.

BACKGROUND Recently we have demonstrated that abciximab-coated stents have inhibitory effects in the prevention of coronary restenosis.

METHODS Ninety-six patients with AMI were randomly allocated into two groups; group I received abciximab-coated stents (n = 48, 57.1 ± 12.0 years), and group II received bare metal control stents (n = 48, 58.4 ± 11.6 years).

RESULTS At baseline, clinical characteristics, percent diameter stenosis, and minimal luminal diameter were no different between the two groups. One patient in group II had reinfarction and target lesion reintervention during hospital stay. Follow-up coronary angiography was obtained in 77.1% (37 of 48) in group I and 75.0% (36 of 48) in group II. Percent diameter stenosis and late loss were significantly lower in group I than group II (18.9 ± 5.54% vs. 37.9 ± 6.25%, p = 0.008; and 0.39 ± 0.29 mm vs. 0.88 ± 0.45 mm; p = 0.008, respectively). At follow-up intravascular ultrasound, intrastent lumen area and intrastent neointimal hyperplasia (NIH) area were 5.4 ± 1.8 mm^2 and 2.2 ± 1.5 mm^2, respectively, in group I and 4.3 ± 1.6 mm^2 and 3.4 ± 1.8 mm^2, respectively, in group II (p = 0.045). And, in-stent restenosis rate was lower in group I than group II (p = 0.011 and p = 0.008, respectively). During 1-year follow-up, two patients in group II (4.1%) had AMI, whereas no patient in group I suffered AMI. Target lesion revascularization and total major adverse cardiac events rates were relatively lower in group I compared with those in group II (10.4% [5 of 48] vs. 20.8% [10 of 48], p = 0.261, and 10.4% vs. 25.0%, p = 0.107, respectively).

CONCLUSIONS Abciximab-coated stent implantation was safe and effective without stent thrombosis in AMI patients. (J Am Coll Cardiol 2006;47:933–8) © 2006 by the American College of Cardiology Foundation

Anti-Oxidant (Alpha-Lipoic Acid)

Journal of Cardiology (2009) 54, 375–385

ELSEVIER

JOURNAL of CARDIOLOGY
Official Journal of the Japanese College of Cardiology

www.elsevier.com/locate/jjcc

ORIGINAL ARTICLE

The effect of alpha lipoic acid in a porcine in-stent restenosis model

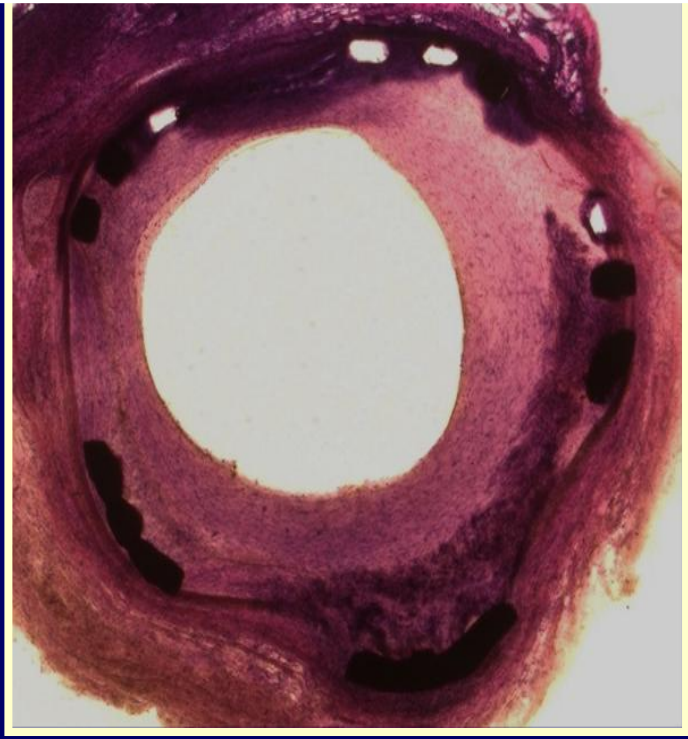
Sang Yup Lim (MD)[a], Eun Hui Bae (MD)[b], Myung Ho Jeong (MD)[b,*], Ju Han Kim (MD)[b], Young Joon Hong (MD)[b], Doo Sun Sim (MD)[b], Yong Sook Kim (PhD)[b], In Kyu Park (PhD)[b], Youngkeun Ahn (MD)[b], Sun-Jung Song (PhD)[c], Dong Lyun Cho (PhD)[c], Kyoung Seok Kim (MS)[c], Jung Chaee Kang (MD)[b]

[a] *The Cardiovascular Center of Korea University Ansan Hospital, Seoul, Republic of Korea*
[b] *The Heart Center of Chonnam National University Hospital, Gwang Ju, Republic of Korea*
[c] *Center for Functional Nano Fine Chemicals of Chonnam National University, Gwangju, Republic of Korea*

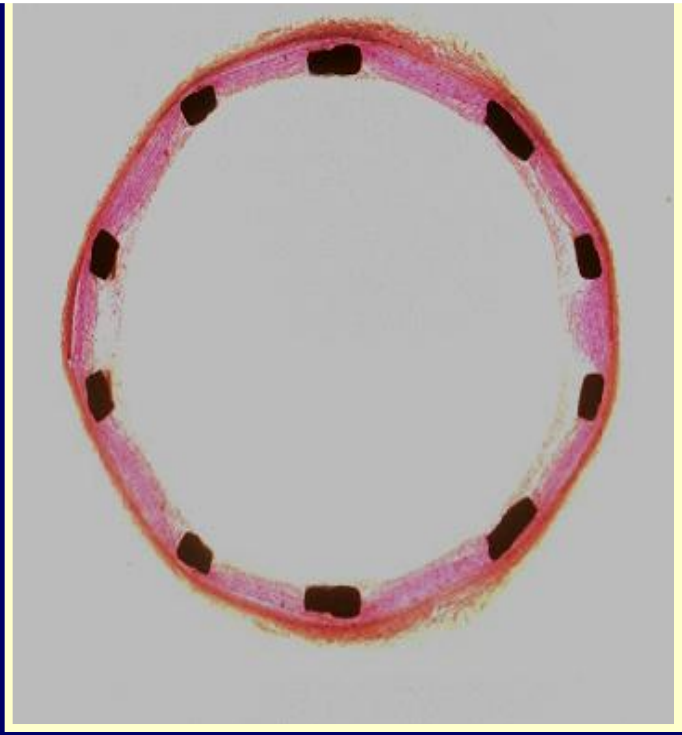
Received 10 April 2009; received in revised form 4 June 2009; accepted 12 June 2009
Available online 23 July 2009

J Cardiol 2009;54:375-85

A Novel Antioxidant, Alpha Lipoic Acid (ALA), Coated Stent for Diabetic AMI Patients



Control Stent



ALA Coated Stent

CNUH Data. J Mater Chem 2009;19:3248-52 . J Cardiol 2009;54:375-85, Korea Patent: 10-0778654

CREATED USING THE RSC ARTICLE TEMPLATE (VER. 3.1) - SEE WWW.RSC.ORG/ELECTRONICFILES FOR DETAILS

ARTICLE TYPE www.rsc.org/xxxxxx | XXXXXXXX

Preparation of a Drug-eluting Stent Using a TiO_2 Film Deposited by Plasma Enhanced Chemical Vapour Deposition as a Drug-combining Matrix

Sun-Jung Song [1], Yu Jeong Park [1], Jun Park [1], Myung Duck Cho [1], Jong-Ho Kim [2], Myung Ho Jeong[3], Yong Sook Kim[3], Dong Lyun Cho [*1,2]

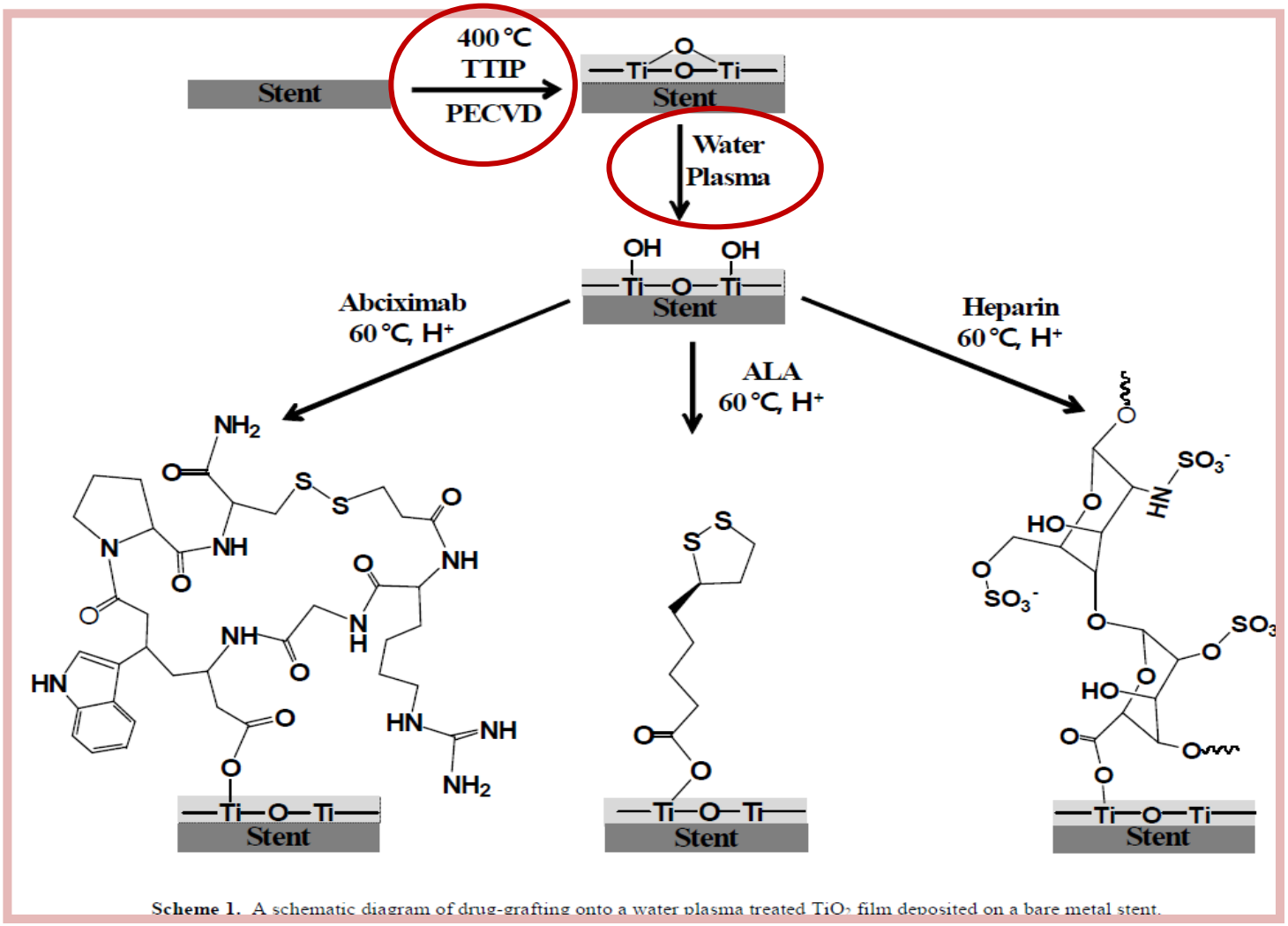
Received (in XXX, XXX) Xth XXXXXXXXX 200X, Accepted Xth XXXXXXXXX 200X
First published on the web Xth XXXXXXXXX 200X
DOI: 10.1039/b000000x

A TiO_2 thin film was deposited onto a bare metal stent by the plasma enhanced chemical vapour deposition (PECVD) process and its potential as a drug-combining matrix was investigated. When deposited at a discharge power of 5 W, the film showed a highly smooth surface with a surface roughness of 9.4 nm, mechanical stability with good adhesion, and good bloodcompatibility. The film was surface-modified with water plasma to introduce hydroxyl groups on the TiO_2 surface. Then, drugs could be chemically grafted to the modified surface through the formation of ester bonds between hydroxyl groups on the modified TiO_2 film and carboxyl groups in the drugs. When heparin, alpha-lipoic acid, and abciximab were grafted onto the TiO_2-deposited and surface-modified stents, the grafted amount was measured to be 106.1 μg for alpha-lipoic acid, 32.5 μg for abciximab, and 53.9 μg for heparin on average, respectively. In the in vitro drug-release test, heparin and abciximab were released continuously for 4 weeks but ALA showed a burst release within 6 days.

Keywords: Drug-eluting stent, TiO_2 film, PECVD, Surface-modification, Water plasma

CNUH Data. J Mater Chem 2010;20:4792-801

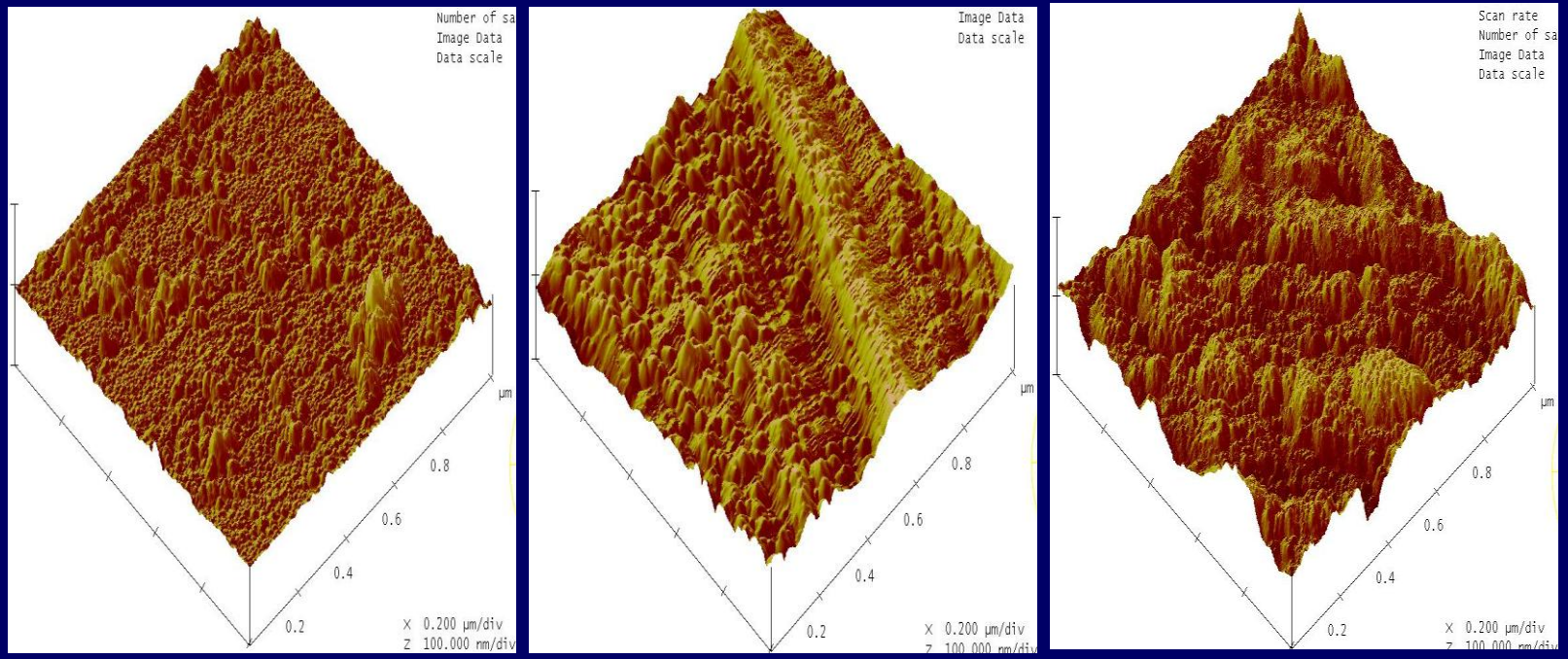
TiO2 Coating : Plasma Enhanced Vapor Deposition



Scheme 1. A schematic diagram of drug-grafting onto a water plasma treated TiO_2 film deposited on a bare metal stent.

CNUH Data. J Mater Chem 2010;20:4792-801

TiO2 Coating by Plasma Enhanced Vapor Deposition



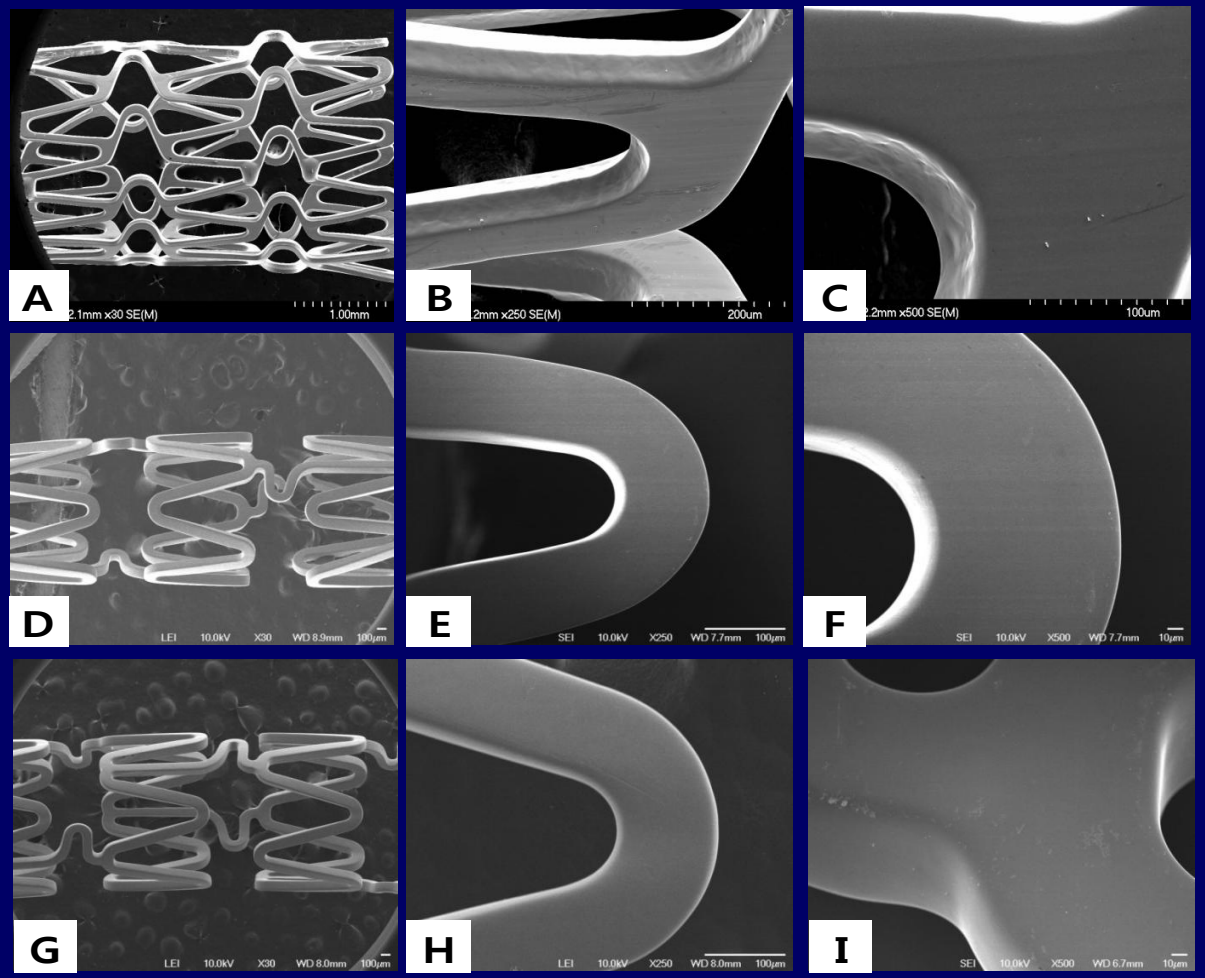
CNUH Data. J Mater Chem 2010;20:4792-801

One-Month Washing Test after Drug Coating using TiO2 Coating

ALA

Abciximab

Heparin



CNUH Data. J Mater Chem 2010;20:4792-801, Korea Patent:10-2009-0062571, US Patent:7466629

Biodegradable ALA Stent Coating with Electrospray

Metal Surface Coating using Electrospray of Biodegradable Polymers and Behavior of ALA Release for Drug-Eluting Stents

Dong Min Kim*,, Bong Soo Lee*, Cheol Ho Park*, Kwideok Park*, Tae-Il Son**, Myeong Ho Jeong***, and Dong Keun Han*,†**

**Biomaterials Center, Korea Institute of Science and Technology, P.O. Box 131, Cheongryang, Seoul 130-650, Korea*

***Department of Biotechnology and Bio-Environmental Technology (BET) Research Institute, Chung-Ang University, 72-1, Nae-Ri, Daedeok-Myeon, Anseong, Gyeonggi-Do 456-756, Korea*

****Department of Cardiovascular Medicine, Chonnam National University Medical School Jaebongro 671, Donggu, Gwangju, 501-757, Korea*

(Received January 16, 2010; Revised February 2, 2010; Accepted February 2, 2010)

Abstract: Medical metal stents inserted to patients with a cardiovascular disease associated with coronary artery system have relatively increased the survival rate. The development of new stents is, however, urgently required due to restenosis and late thrombosis generated in metal stents. To solve these problems, the biodegradable polymers such as poly(lactide-*co*-glycolide) (PLGA), poly(*L*-lactide) (PLLA), and poly(ε-caprolactone) (PCL) were mixed with alpha lipoic acid (ALA), which is well known to inhibit the proliferation of neointimal hyperplasia. Subsequently, the ALA-loaded polymers were coated on stainless steel by electrospray. The drug-eluting behaviors from the coated polymers were investigated according to kinds and concentrations of polymers, spray rates, and kinds of solvents. The drug-eluting rate from PCL with the lowest glass transition temperature was the fastest among three polymers and followed by PLGA and PLLA. The surface roughness increased as the spray rate increases and also the drug-eluting rate was affected by kinds of solvents with different boiling point. It is expected that drug-eluting stent (DES) coated with ALA-loaded polymers can be applied practically for clinical applications by controlling the behavior of drug release.

CNUH and KIST Data. Polymer 2010;34:1-6

Release Kinetics of PLLA, PLGA, PCL Coating ALA Stent

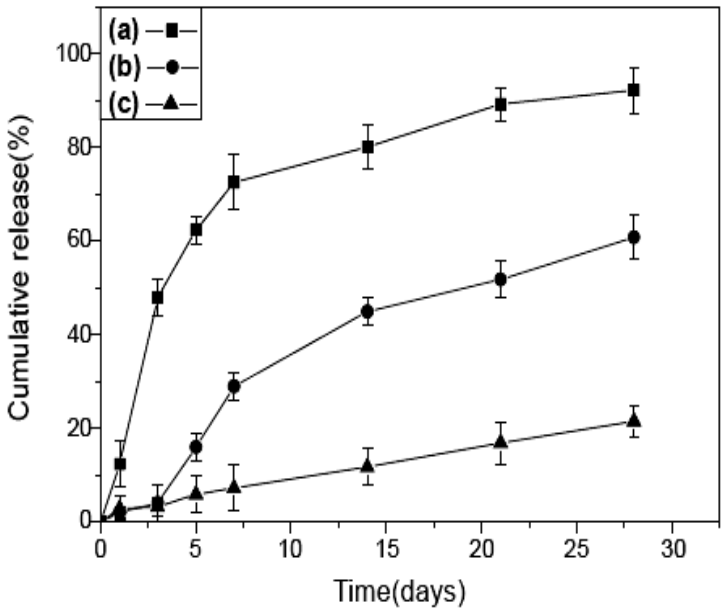


Figure 2. Cumulative ALA amount released from (a) PCL; (b) PLGA; (c) PLLA.

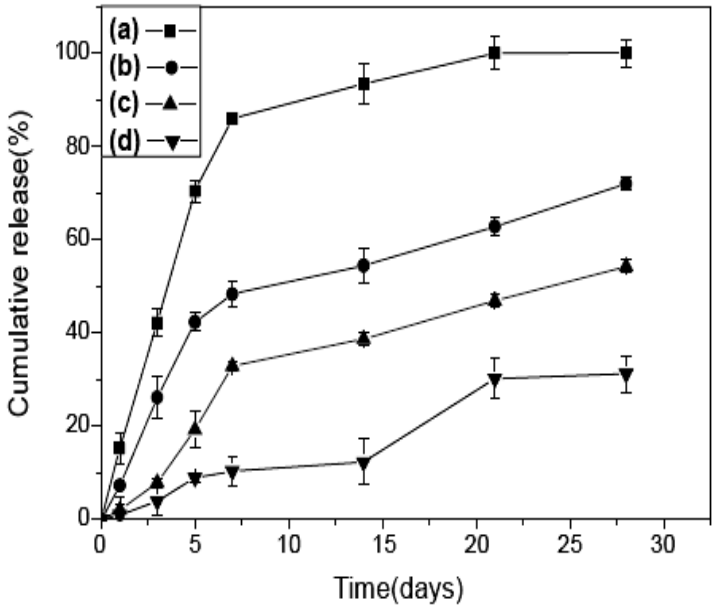


Figure 4. Cumulative ALA amount released from different concentration of PLGA: (a) 0.05 wt%; (b) 0.5 wt%; (c) 1.0 wt%; (d) 3.0 wt%.

CNUH and KIST Data. Polymer 2010;34:1-6

PAPER www.rsc.org/materials | Journal of Materials Chemistry

Preparation of a dual-drug-eluting stent by grafting of ALA with abciximab on a bare metal stent

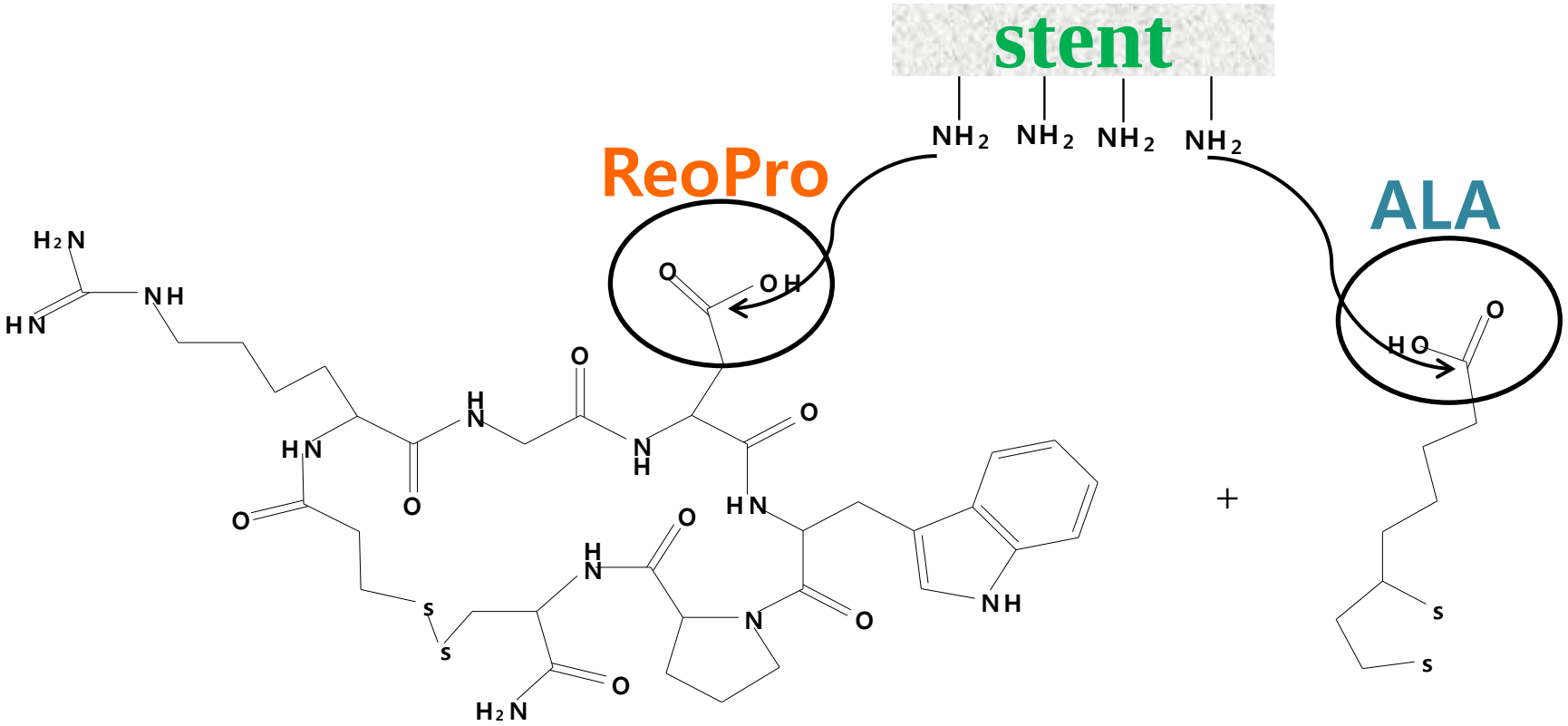
Sun-Jung Song,[a] Kyoung Seok Kim,[ab] Yu Jeong Park,[ab] Myung Ho Jeong,[c] Yeong-Mu Ko[d] and Dong Lyun Cho*[ab]

Received 27th May 2009, Accepted 24th August 2009
First published as an Advance Article on the web 22nd September 2009
DOI: 10.1039/b910351a

The preparation of a dual-drug-eluting stent was investigated by grafting α-lipoic acid (ALA) with abciximab on a bare metal stent coated with a polymer layer by plasma polymerization of 1,2-diaminocyclohexane (DACH). The plasma polymerization was carried out at 100 W for 5 min and then at 60 W for 15 min. ALA and abciximab were grafted to the polymer layer after activating in 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide methiodide. The amounts of grafted and released ALA and abciximab were affected by the grafting pattern. When the grafting reaction proceeded in a mixed solution of ALA and abciximab, the amount of grafted ALA was much larger than that of grafted abciximab, and the amount of not only abciximab, but also ALA, released was small. When the grafting reaction was started with the abciximab solution, and the ALA solution was added after a time interval, the amount of grafted abciximab increased and the released amount also increased not only for abciximab, but also for ALA. The released amount of abciximab increases with time while the released amount of ALA decreases with time. Approximately 150 μg of abciximab and 114 μg of ALA were grafted to a stent surface with a smooth and uniform surface morphology, and grafted with 10-min time interval: they were released continuously for 3 weeks in the *in vitro* drug-release test. The drug-eluting stent showed high blood compatibility in the *in vitro* platelet adhesion test.

CNUH Data. 2009 TCT, J Mater Chem 2009;19:8135-41

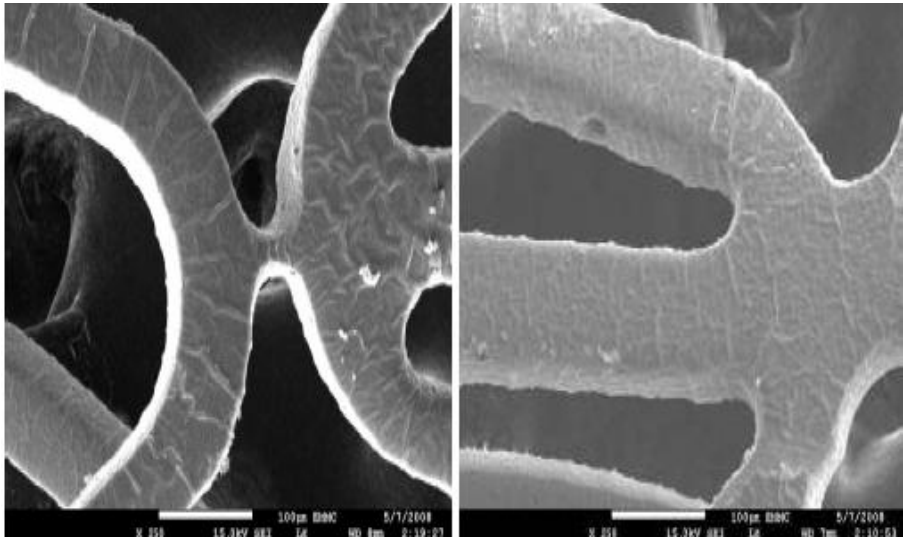
Dual Coating Stent : Plasma Polymerization



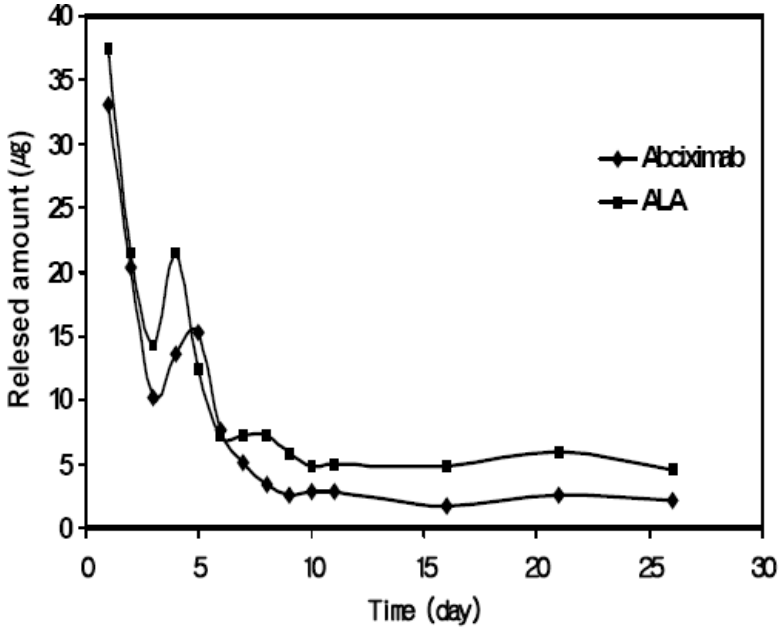
CNUH Data. 2009 TCT, J Mater Chem 2009;19:8135-41

Dual Coating Stents : ReoPro and ALA

SEM Findings of ReoPro/ALA Stent

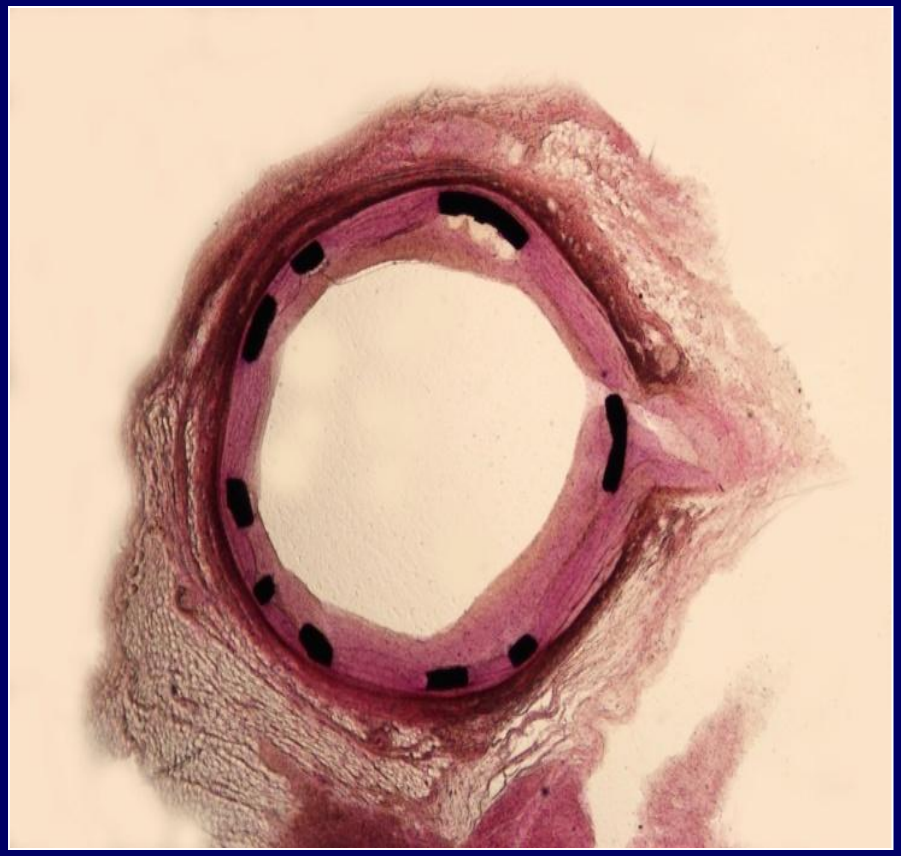


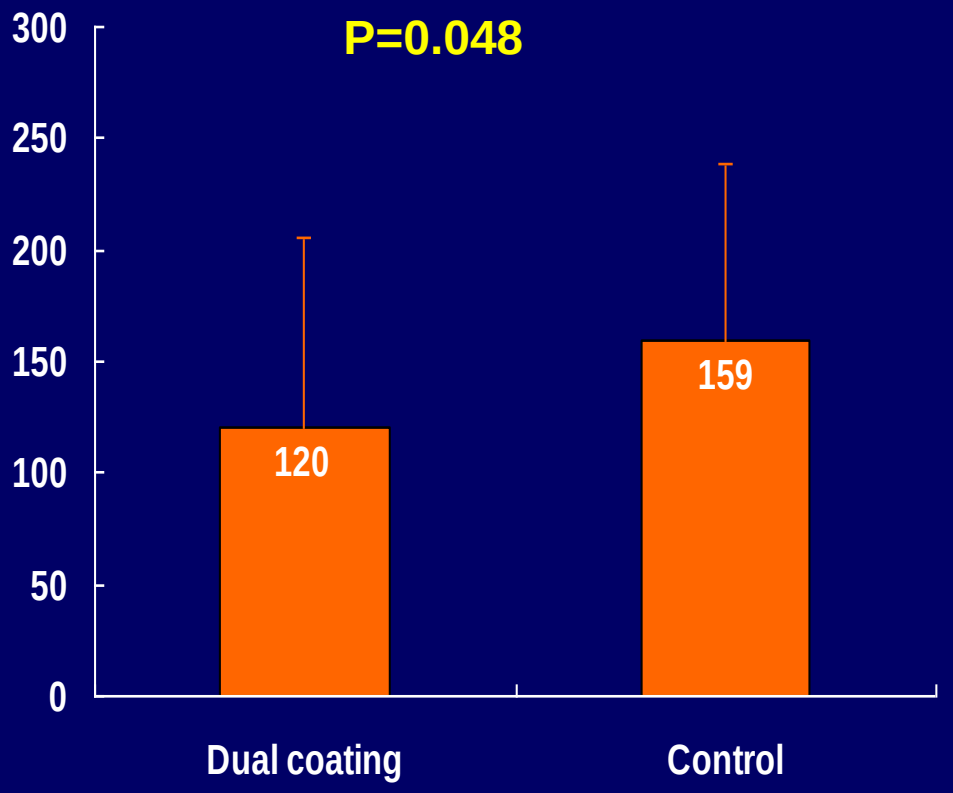
Release Kinetics of ReoPro/ALA Stent



CNUH Data. 2009 TCT, J Mater Chem 2009;19:8135-41

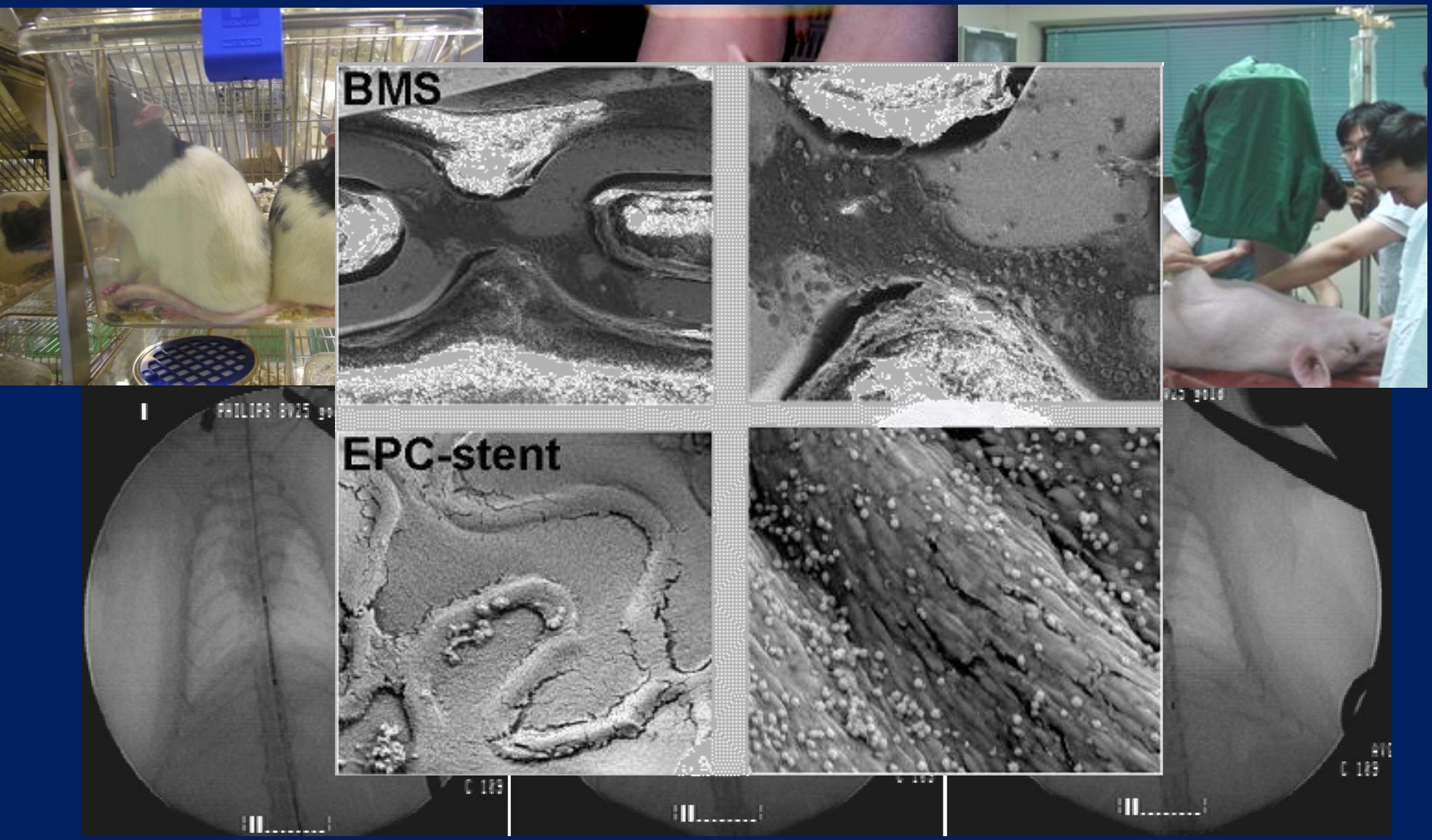
Dual Coating Stent (ReoPro and ALA) with Low Inflammation Cell Counts





CNUH Data. 2009 TCT, J Mater Chem 2009;19:8135-41

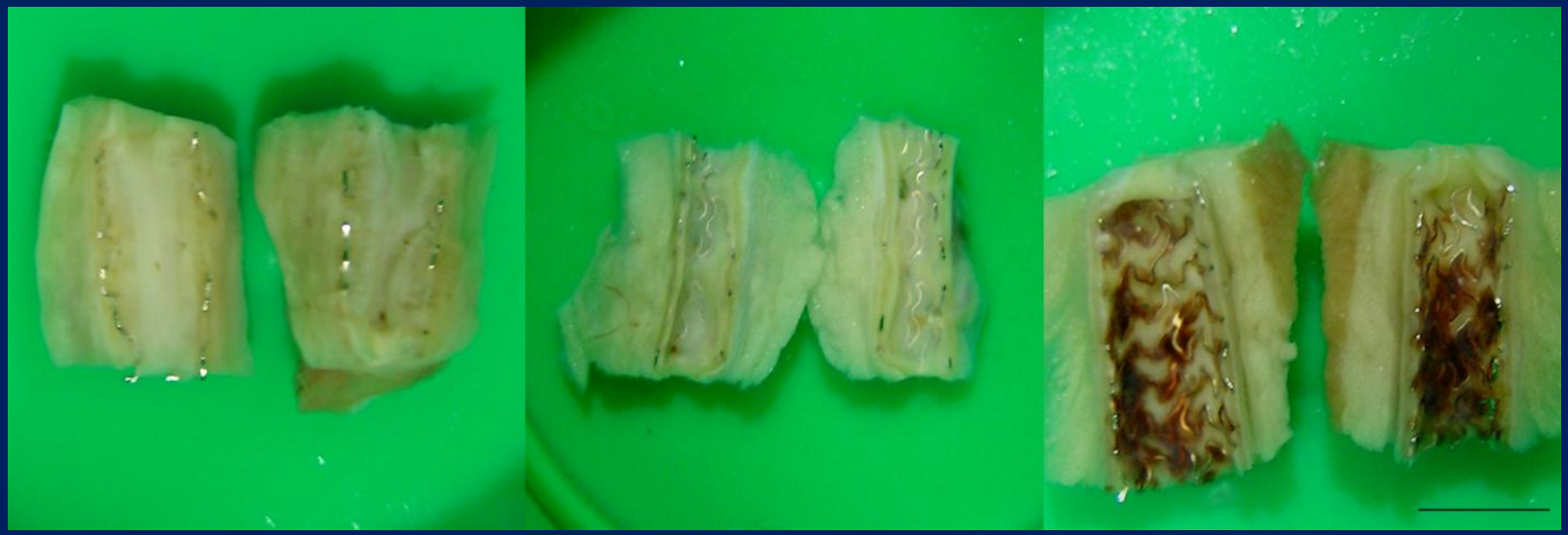
EPC-Capturing Aptamer Stent



CNUH data. 2009 ACC. Tissue Eng Regen Med 2009;6:555-61

EPC-Capturing Aptamer Stent

Aptamer | Cobalt-chromium | Taxus



Re-endothelialization score = 3.6; 3.4; 1.3
(complete: 4, ~75%: 3, ~50%: 2, ~25%: 1, ~0%)
Thrombus appearance rate = 16.7 %; 0%; 66.7%

CNUH data. 2009 ACC. Tissue Eng Regen Med 2009;6:555-61

Nitrogen-Doped TiO2 Film As A Drug Coating Matrix

Journal of
Materials Chemistry

Dynamic Article Links View Online

Cite this: *J. Mater. Chem.*, 2011, **21**, 8169

www.rsc.org/materials

PAPER

Nitrogen-doped TiO_2 films as drug-binding matrices for the preparation of drug-eluting stents†

Sun-Jung Song,[a] Kyoung Woon Jung,[a] Yu Jeong Park,[a] Jun Park,[a] Myung Duck Cho,[a] Myung Ho Jeong,[b] Yong Sook Kim[b] and Dong Lyun Cho*[a]

Received 19th November 2010, Accepted 25th March 2011
DOI: 10.1039/c0jm03994b

Nitrogen doped-TiO_2 thin film was deposited by plasma enhanced chemical vapour deposition (PECVD) process and its applicability as a drug-binding matrix was investigated in the preparation of drug eluting stents. N–TiO_2 film was deposited at 5 W and uniformly covered metallic stent surfaces. Films showed excellent mechanical stability and good adhesion. Alpha lipoic acid, heparin, and abciximab could then be grafted onto the N–TiO_2 film through ester bond formation after water plasma modification of the films' surfaces. Drug-grafted N–TiO_2 films showed smooth surfaces and good blood compatibility in *in vitro* platelet adhesion tests. The films maintained uniform coverings, without peeling, even after expansion by a balloon catheter. Grafted-heparin and abciximab could be released continuously for three weeks from drug-grafted N–TiO_2 stents in *in vitro* drug release test. Such immunosuppressive and antiproliferative drug-grafted N–TiO_2 film is expected to minimize potential problems related to organic polymers and the risk of direct contact of a bare metal surface with a blood vessel. Hence, the N–TiO_2 films prepared in this study are promising alternatives to organic polymers for the preparation of drug-eluting stents.

J Mater Chem 2011;21:8169-77

Nitrogen-Doped TiO2 Film As A Drug Coating Matrix

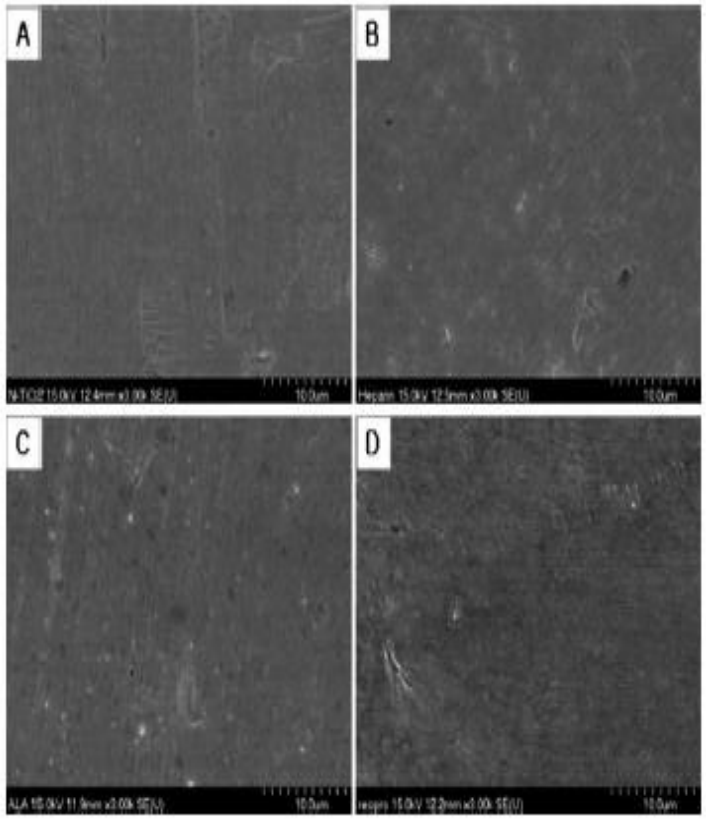
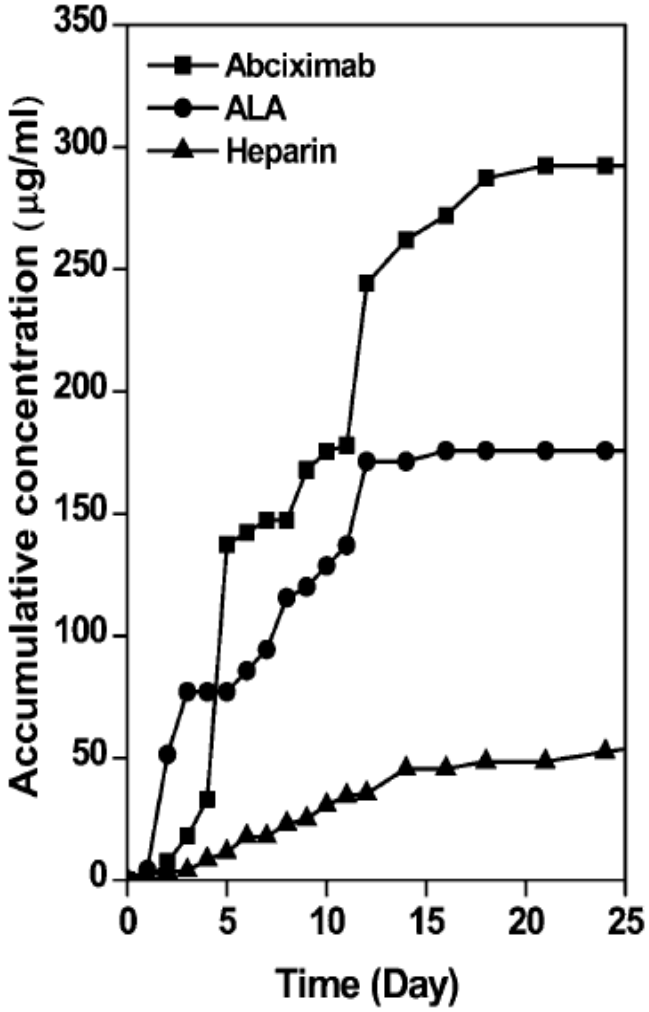
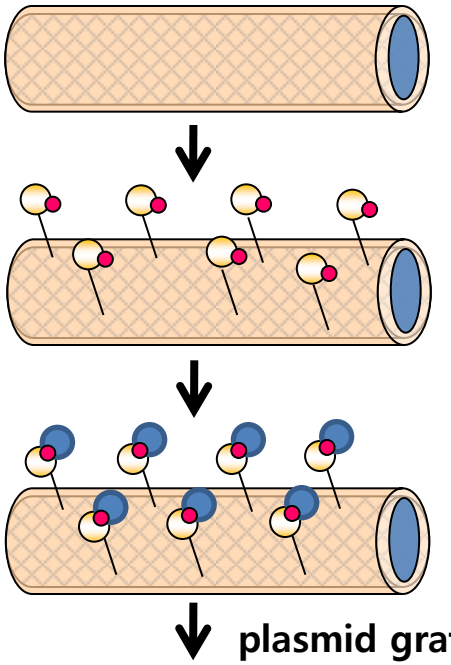


Fig. 7 SEM images of N-TiO_2 (A), heparin-grafted (B), ALA-grafted (C) and abciximab-grafted (D) surface after platelet adhesion test with 3 000× magnification.



J Mater Chem 2011;21:8169-77

Gene Delivery Stent using TiO2 and Drug Coating
Korea Patent 10-2010-0127251



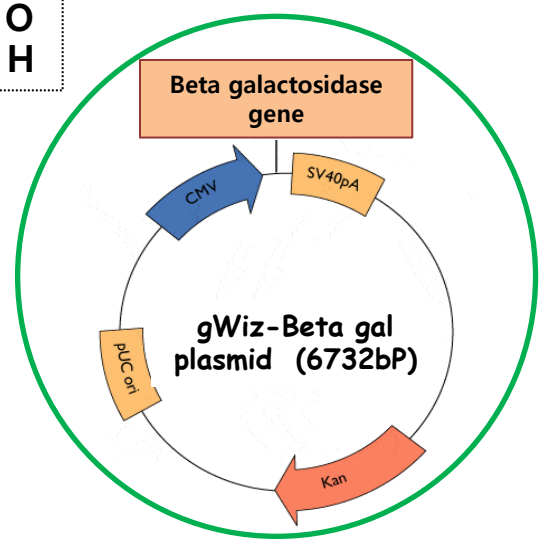
TiO_2 thin film coating

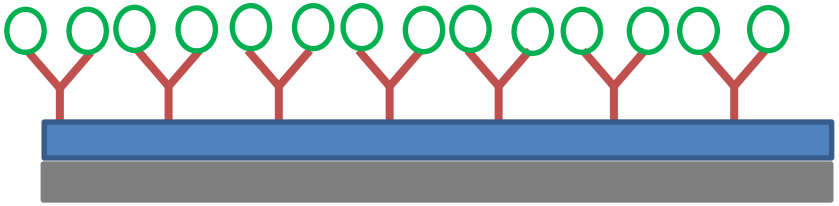
H_2O modification by H_2O plasma

: O
: H

drug grafting

plasmid grafting





Plasmid

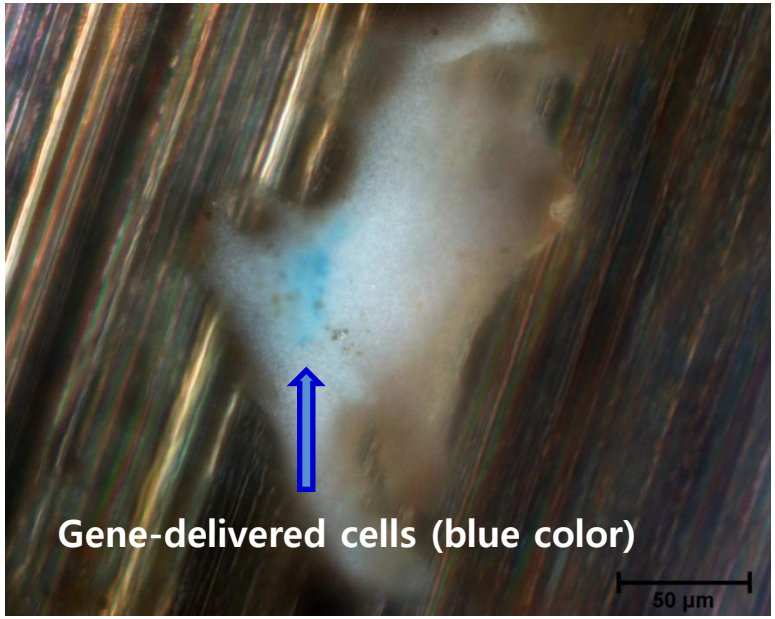
Drug (Abciximab or Heparin, ALA, sirolimus, paclitaxel)

TiO_2 thin film

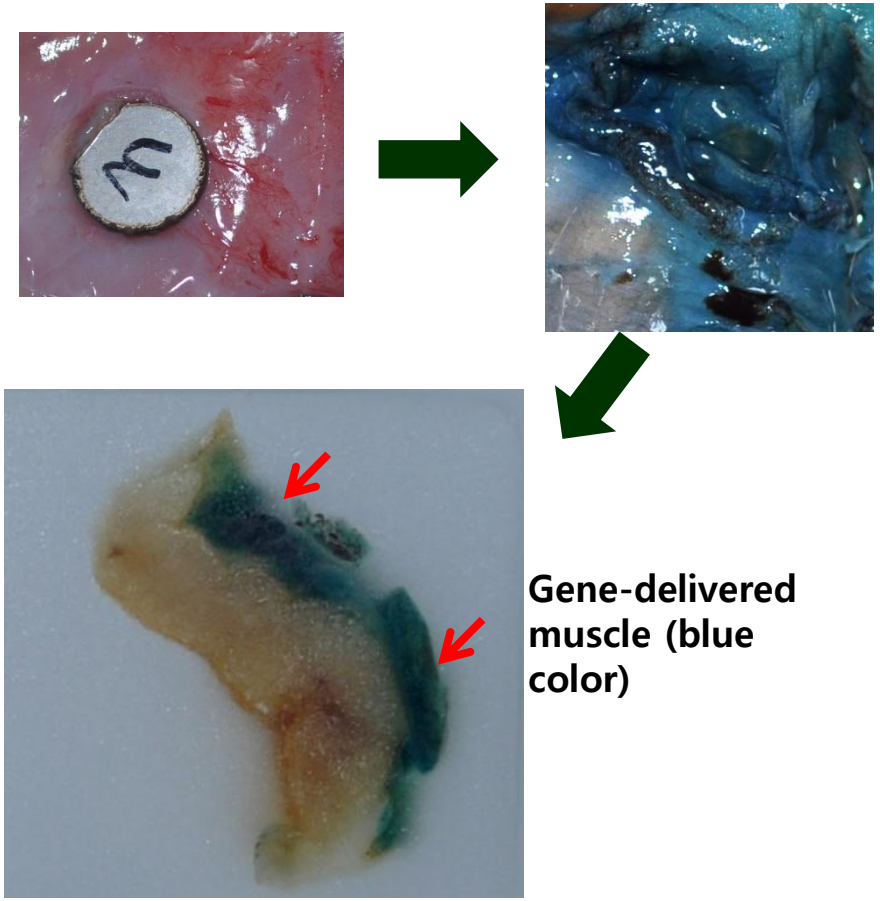
Metal

Gene Delivery Stent using TiO2 and Drug Coating
Korea Patent 10-2010-0127251

Porcine Coronary Artery Smooth Cells



Gene-delivery into Rat Abdominal wall using Gene-coated plate



Gene-delivered muscle (blue color)

Take Home Message for Coronary Artery Stent Thrombosis

1. DAT (aspirin & clopidogrel) recommended **for ≥1 Y after DES**
2. Premature (<6 M) cessation of antiplatelet therapy is the most important risk factor for late (30 D to 1Y) ST after DES
3. For patients with DES who are to undergo surgery that mandate discontinuation of clopidogrel, ***aspirin should be continued*** if at all possible and clopidogrel restarted as soon as possible after surgery
4. **New anti-platelet therapy and new DES** will be helpful to overcome stent thrombosis

국립심혈관센터 예정 부지

오늘 참석하신 모든 분들의 건강과
개원내과의사회의 무궁한 발전을 기원합니다