Non-cardiac Procedures and Surgery after Drug-Eluting Stent Implantation

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춘계순환기학회 **2008,**부산

Case; Timing of Surgery After PCI with DES

Q. A 48-yr old patient who underwent elective PCI with DES, Bor Type II AGC was found during routine check up 2wks after the PCI.

What would be your recommendation?

1. Surgery should be scheduled as soon as possible because the malignancy can be spread quickly.
2. At least one-month will be needed to do the early surgery.
3. At least 3-month will be needed due to the safety concern (DES ST)

Questions in Everyday Clinical Practice in the DES era

1. Routine check up for malignancy will be needed before elective PCI?
   (safety of work up?, cost-effective?)
2. First generation DES vs. Other DESs?
3. DES vs. BMS vs. New DES. vs.POBA vs. A variety of atheroablation?
4. Antiplatelets and antithrombotics regimen?
5. Optimal timing of Non-Cardiac Surgery (NCS) after the DES implantation?
6. Complex vs. Simple Surgery or procedure?
   (General vs. Local anesthesia, Dental…)

Balloon Angioplasty, BMS-Surgery Data?

Timing of Surgery After PCI : ACC/AHA Guidelines

1. Delaying surgery for at least a week after balloon angioplasty to allow for healing of the vessel injury at the balloon site.
2. Delaying non-cardiac surgery for more than 6-8 weeks increases the chance that restenosis at the angioplasty site will have occurred,and thus theoretically increases the chances of perioperative ischemia of MI.
3. If a stent is placed (bare metal), it appears reasonable to delay elective non-cardiac surgery for 2 weeks and ideally 4 weeks to allow for at least partial endothelialization of the stent, but not for more than 6-8 weeks, when restenosis begins to occur.

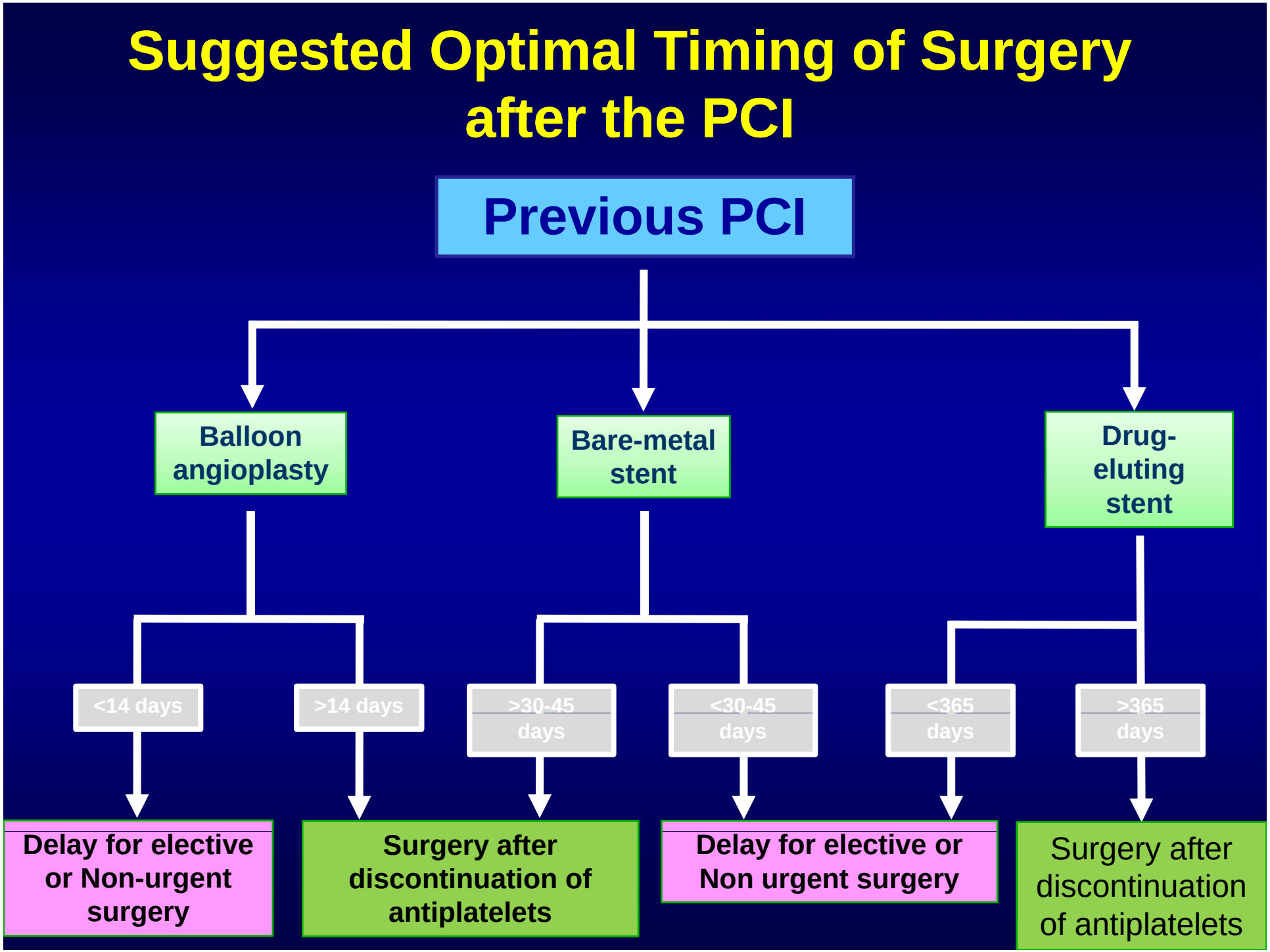
2002 ACC/AHA Practice Guideline

Possible Recommendations

** If PCI is needed before elective surgery:

1. POBA only; surgery between *1-2 wks*
2. Use a bare metal stent followed by *4-6 weeks* of clopidogrel and aspirin
3. If DESs are implanted, avoid elective surgery for *1 year* so as not to interrupt anti-platelet therapy
4. Atheroablation?; similar to POBA (no data)

Suggested Optimal Timing of Surgery after the PCI



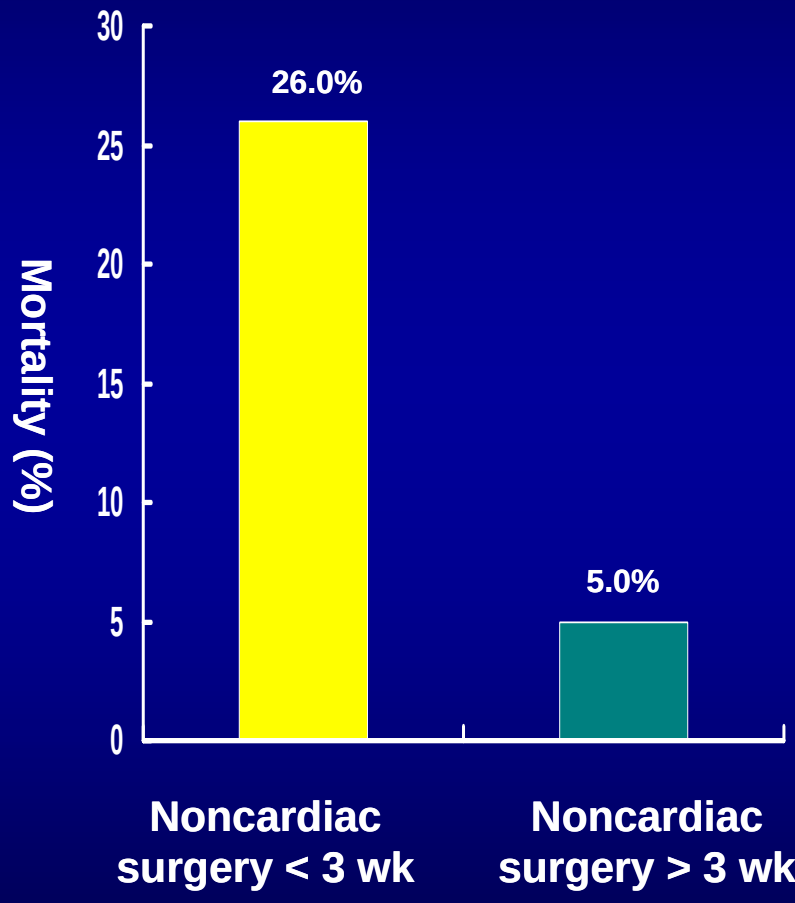
Especially for the DES…

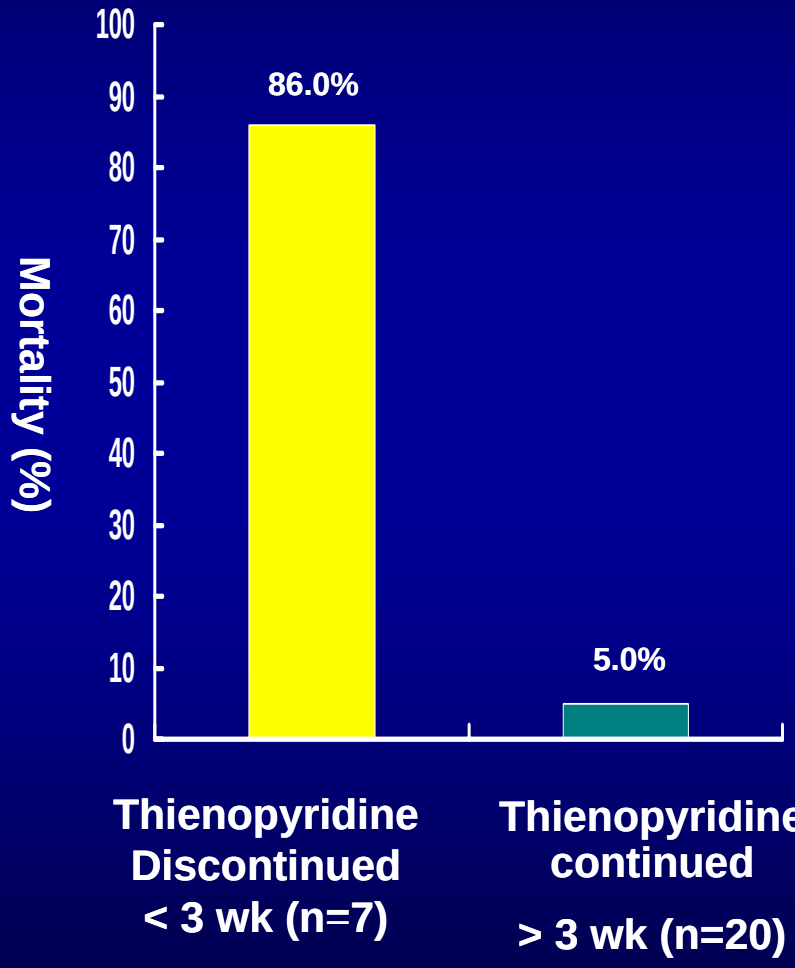
** Balance between the disadvantage and advantage, potentially harmful outcomes and benefits..

- Safety (DES thrombosis) vs.

2. Durability (Reduced restenosis and revascularization) ?

Mortality and Timing of Surgery After PCI

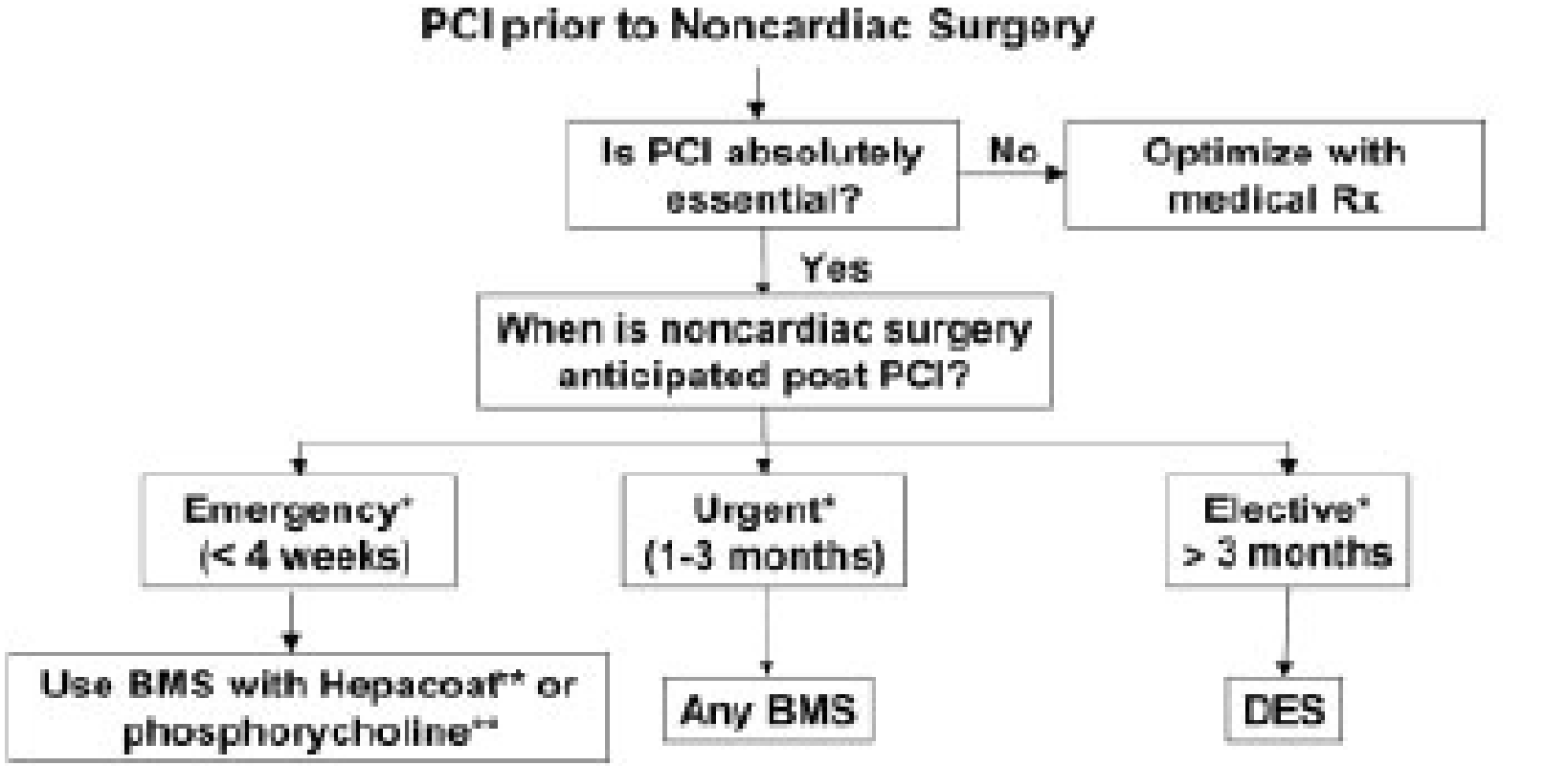




WHC data, 47 pts

Salter LF. Catheter Cardiovasc Interv 63;246-247 2004

Recommendation of Stent Selection for PCI followed by NCS



Salter LF. Catheter Cardiovasc Interv 63;246-247 2004

Washington Hospital Center/ Georgetown University

1. Ron Waksman et al
   1) Clinical Study; Washington DES Registry (REWARD)
   2) April 2003-June 2004
2. Neil J Weissman et al; IVUS study

At 16th JSIC meeting

Waksman R & Rha SW, June 21, 2007 at Koriyama, Japan

Is Early Surgery Possible?

Q. When can I receive the operation after DES implantation?

1. Newly diagnosed cancer patient
2. Unexpected trauma
3. So many Type A personality patients….

Is One-Month Clopidogrel Treatment Only before Major Surgery Safe and Feasible in Patients Undergoing Percutaneous Coronary Intervention with Drug-Eluting Stents?

Seung-Woon Rha, Soon Yong Suh, Jin Won Kim, Chang Gyu Park, Hong Seog Seo, Dong Joo Oh.

Cardiovascular Center,
Korea University Guro Hospital, Seoul, Korea

TCT 2005 Oral Presentation

Background & Purpose

1. Clopidogrel (Plavix), a thienopyridine, is a potent inhibitor of platelet aggregation used concomitantly with percutaneous coronary intervention (PCI) and is known to reduce early stent thrombosis.
2. However, possible deleterious effects of 1-month clopidogrel treatment on hemostasis and stent thrombosis before major surgery in the setting of contemporary PCI with drug-eluting stents (DES) have not been fully investigated.

Methods (I)

1. **Study population**

   Patients were randomly assigned to treat angiographically significant lesions with

   1) Sirolimus-eluting stent (SES, Cypher™)
   2) Paclitaxel-eluting stent (PES, Taxus™)

   or

   3) Hybrid Stent (Both SES & PES)

Methods (II)

2. Antiplatelet therapy

1) All pts received Aspirin; 100 mg orally, indefinitely

2) All pts received Clopidogrel (Plavix)
preloaded 300-600 mg before PCI, followed by daily administration of 75 mg.

3. Antithrombotic therapy

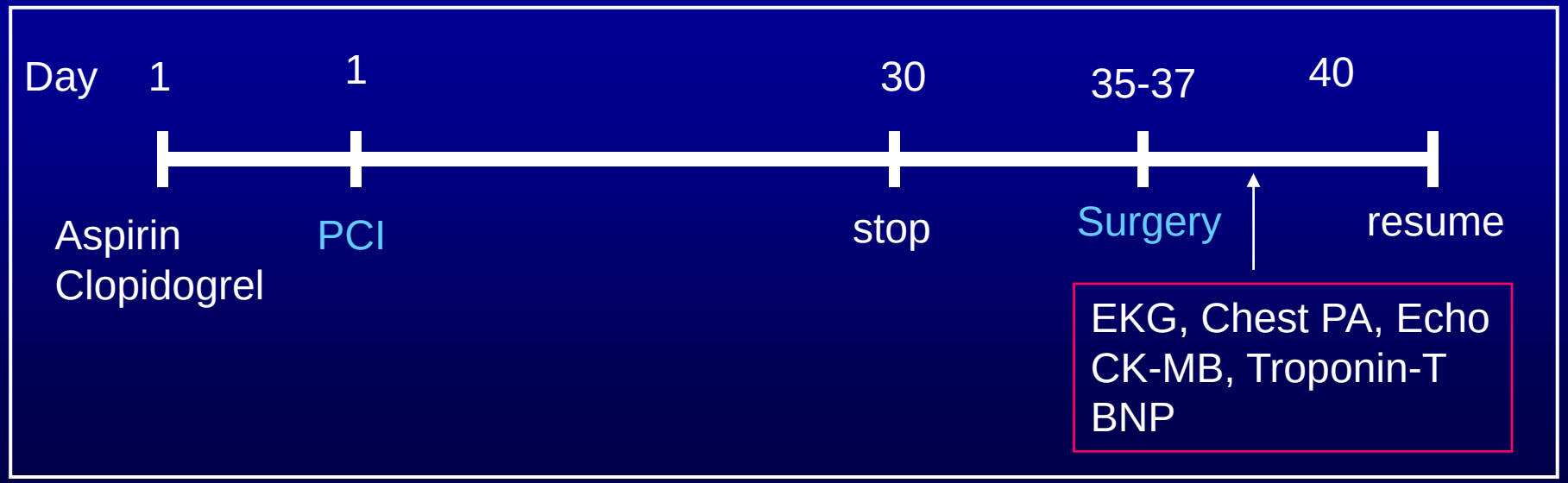
1) Enoxaparin (Clexane); 60mg bid before PCI and after PCI during the hospital stay (within 7 days).

2) Unfractionated Heparin; a bolus of 50 U/kg prior to PCI

Methods (III)

4. Perioperative Antiplatelet Schedule

1) All pts were encouraged to have aspirin and clopidogrel for at least 30 days
2) Discontinue aspirin and clopidogrel 5 to 7 days before surgery.
3) Resume aspirin and clopidogrel postop 3 days unless there is significant risk of postop bleeding complications.



Methods (IV)

5. Study End Points

1) In-hospital complications, bleeding and vascular complications were assessed.

2) Biochemical indices such as cardiac enzymes (CKMB and Troponin-T) and B-type natriuretic peptide (BNP) were assessed after surgery.

Results (I)

1. Study Population

; A total 15 pts (Male 10, mean age, 62.8 ± 11 years) who underwent standard PCI with DES before major surgery were enrolled.

2. DES & Procedural Information

1) A total 28 DESs (8-Cypher, 20-Taxus) were utilized to treat 28 lesions.
2) Mean DES diameter; 2.98 mm
3) Mean DES length; 27.5 mm.
4) Multivessel disease; 26.7% (4/15)-3 or more DESs
5) All lesions; type B/C lesions

Results (II)

3. Perioperative Antiplatelets Information

1) Mean duration of discontinuation of aspirin and clopidogrel before surgery

; 5.8 ± 1.1 days

2) Mean duration of discontinuation of aspirin and clopidogrel after surgery; 4.4 ± 2.7 days

3) Total duration of discontinuation of aspirin and clopidogrel; 8.3 ± 4.8 days.

4) Mean duration from PCI to surgery

; 44.6 ± 11.0 days (range; 29 - 56 days)

Results (III)

4. Surgery and Clinical & Biochemical Outcomes (I)

1) Forty seven percent of pts (7/15) underwent cancer surgery.
   (Possible adverse prognosis due to op delay)
2) One pt suffered from post op wound oozing and received 2 units of Pack RBC transfusion (1/15, 6.7%).
3) No major vascular & bleeding complications.
4) One pt showed CK-MB>2 X normal (1/15, 6.7%) and 2 pts mildly elevated B-type natriuretic peptide (BNP, 2/15, 13.3%) without clinically manifested heart failure.

Results (IV)

5. Surgery and Clinical & Biochemical Outcomes (II, continued)

5) There were no in-hospital target lesion and vessel revascularization, Q-wave myocardial infarction, major adverse cardiac events and deaths.

6) No reported acute and subacute stent thrombosis

7) Mean duration of intensive care unit (ICU) stay was 0.6 ± 1.3 days

8) Mean duration of hospital stay was 16 ± 9.9 days.

Conclusion at TCT 2005

One month (possibly up to two months) administration of aspirin and clopidogrel after PCI with DES before major surgery, discontinuation 5 days before surgery and resume 3 days after surgery appears to be safe and feasible without significant postop bleeding complications, acute / subacute stent thrombosis or major adverse cardiac events.

New Cath Lab (Oct 2007)

Cath Lab Nurses 2008

고대구로 순환기내과 (심장내과) 2008.3

1. 오 동 주 **Dong Joo Oh;** 의무부총장
2. 서 홍 석 **Hong Seog Seo;** 심혈관센터 소장
3. 박 창 규 **Chang Gyu Park;** 순환기내과 분과장
4. 나 승 운 **Seung-Woon Rha;** 전임 심도자실장
5. 김 응 주 **Eung Ju Kim;** 현 의국장, 학생지도교수
6. 김 진 원 **Jin Won Kim;** 학술부장
7. 임 홍 의 **Hong Euy Lim;** 부정맥 분과 책임교수
8. 최 철 웅 **Cheol Ung Choi;** 임상교수
9. 나 진 오 **Jin Oh Na;** 임상교수
10. 박 재 형 **Jae Hyoung Park;** 임상교수
11. 용 환 석 **Hwan Seok Yong (**방사선과**); 임상교수**
12. **Kang-Yin Chen (China); Research Fellow (2007.6-)**
13. **Yong-Jian Li (China); Research Fellow (2008.4-)**
14. **Kanhaiya Lal Poddar (India); Research Fellow (2008-4)**

International Research Fellow 2006

Dr. Wani from India

International Research Fellow 2007

*** KUMC Guro Hospital Research Fellows 2007**

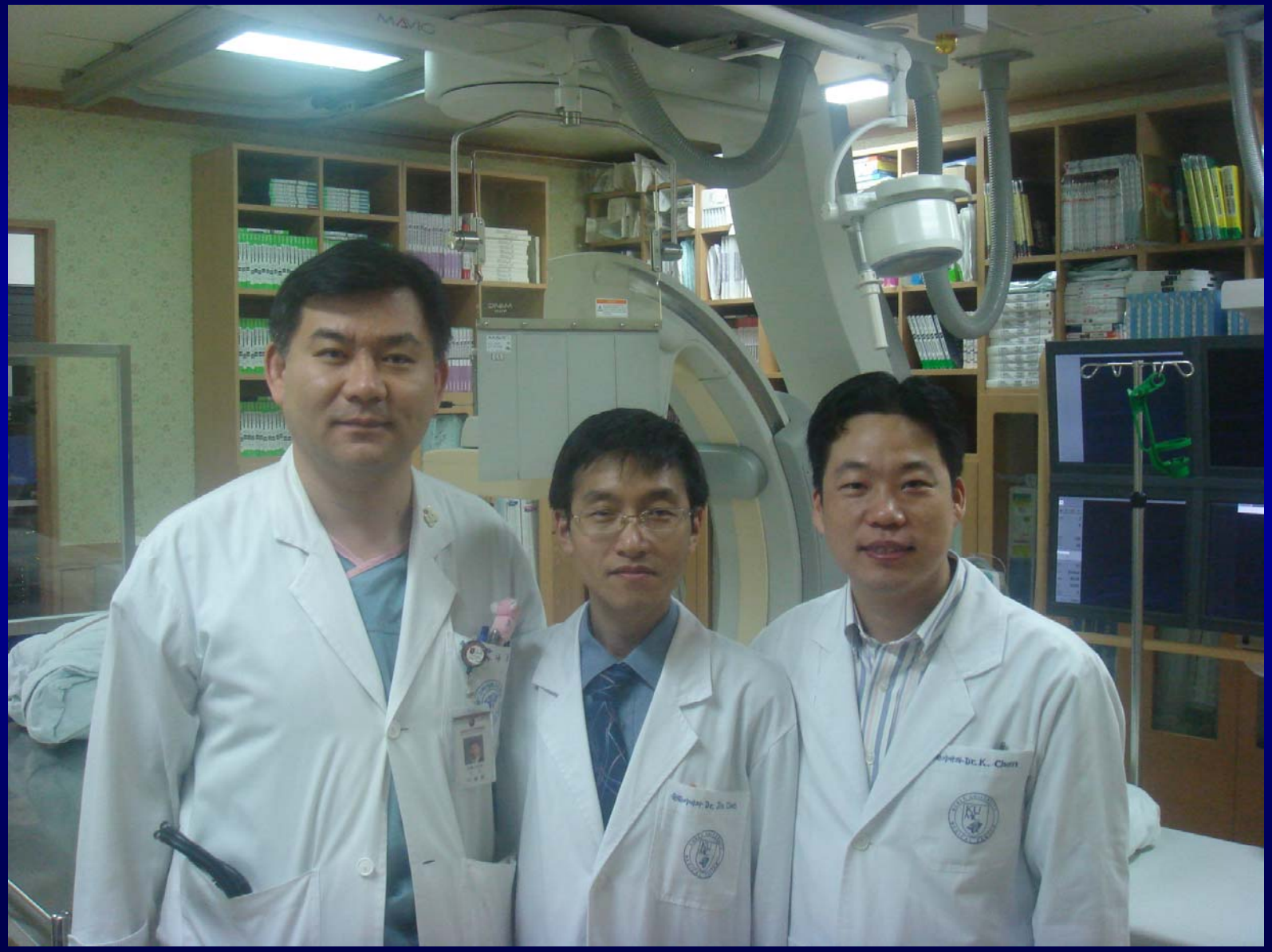
Zhe Jin, Tianjin Medical University Nankai Hospital

Kang-yin Chen, Tianjin Medical University Second Hospital

Yoshiyasu Minami, Kamakura General Hospital

Research Fellows 2007

Research Fellow 2008



The Optimal Timing for Non-cardiac Surgery after Percutaneous Coronary Intervention with Drug-Eluting Stents

Cheol Ung Choi, Seung-Woon Rha*,
Zhe Jin, Kang-yin Chen, Yoshiyasu Minami, Jin Oh Na,
Soon Yong Suh, Jin Won Kim, Eung Ju Kim,
Chang Gyu Park,Hong Seog Seo, Dong Joo Oh

Cardiovascular Center,
Korea University Guro Hospital, Seoul, Korea

KUMC Guro data, IJC 2008 Submitted

Background

1. Delayed endothelialization has been suggested with both sirolimus- (SES, CypherTM) and paclitaxel-(PES, TaxusTM) eluting stents.
2. Elution of antiproliferative agents delays endothelialization, which, consequently, may increase the risk of stent thrombosis.
3. Therefore, a prolonged course of antiplatelet therapy has been recommended with the use of DES.

Cancer Res. 2002;62:6938-43.
Circulation. 2003;107:1340-1.

Background

1. The AHA/ACC has recently released scientific advisory recommending *delaying all elective surgery within 12 months of DES placement.*

Circulation 2007;115:813-8.
Circulation 2007;116:e418-99.

2. However, there was no definite guideline about the optimal timing for NCS after PCI with DES.

3. Currently, high-level evidence is lacking in the literature to support strong recommendations on the perioperative antiplatelet schedules in patients who received DES undergoing surgery.

Purpose

1. Major thrombotic complications such as stent thrombosis and bleeding complications should be taken into consideration to propose a good strategy.

2. The aim of our study was to assess the safety and durability of DES in patients waiting NCS, especially cancer patients requiring early surgery and to determine the optimal time for elective NCS.

Methods (I)

1. Study population

A total 27 Patients were assigned to treat angiographically significant lesions with

1) Sirolimus-eluting stent (SES, Cypher™)
2) Paclitaxel-eluting stent (PES, Taxus™) or
3) Zotarolimus-eluting stent (ZES. Endeavor™)

Methods (II)

2. Antiplatelet therapy

1) All pts received Aspirin; 100 mg orally, indefinitely

2) All pts received Clopidogrel (Plavix)
preloaded 300-600 mg before PCI, followed by daily administration of 75 mg.

3. Antithrombotic therapy

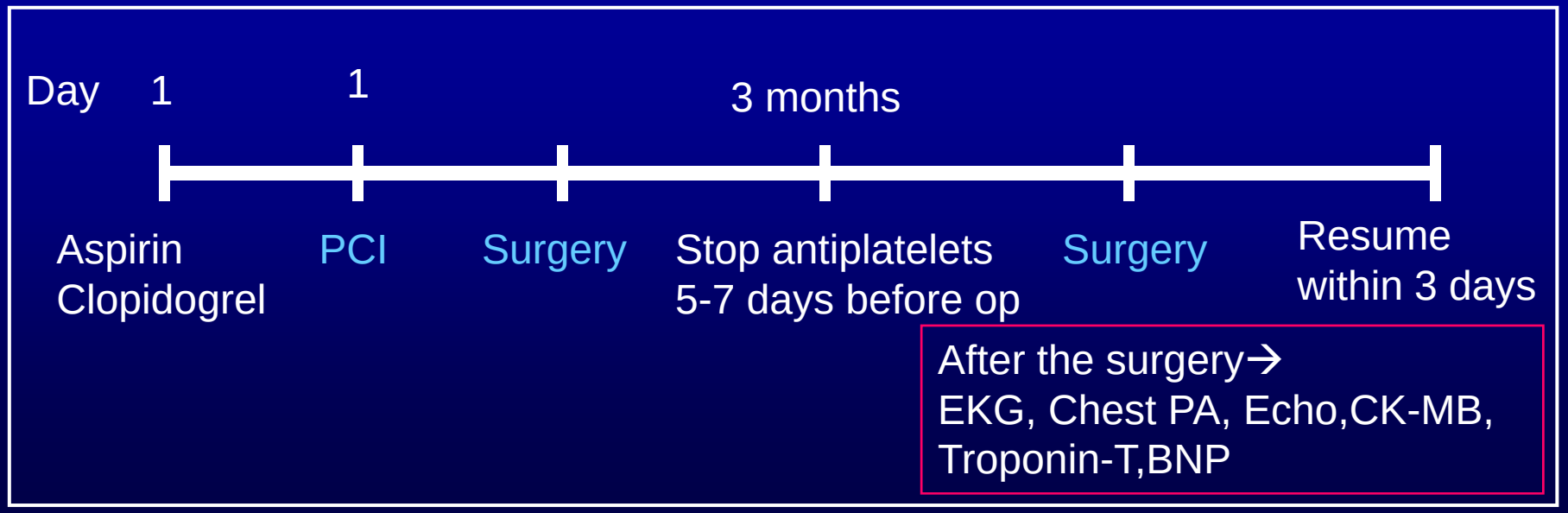
1) Enoxaparin (Clexane); 60mg bid before PCI and after PCI during the hospital stay (within 7 days).

2) Unfractionated Heparin; a bolus of 50 U/kg prior to PCI

Methods (III)

4. Perioperative Antiplatelet Schedule

1) All pts were encouraged to have aspirin and clopidogrel for at least 1 month
2) Discontinue aspirin and clopidogrel 5 to 7 days before surgery.
3) Resume aspirin and clopidogrel postop 3 days unless there is significant risk of postop bleeding complications.



Methods (IV)

5. Study End Points

1) In-hospital complications, bleeding and vascular complications were assessed.

2) Biochemical indices such as cardiac enzymes (CKMB and Troponin-T) and B-type natriuretic peptide (BNP) were assessed after surgery.

Statistics

1. All statistical analyses were performed using SPSS 13.0.
2. Continuous variables were expressed as means ± standard deviation and were compared using Student's t-test.
3. Categorical data were expressed as percentages and were compared using chi-square statistics or Fisher's exact test.
4. A p-value of 0.05 was considered statistically significant.

Results

Baseline Clinical Characteristics

Variables, n (%)	NCS < 3 months (n =17)	NCS > 3 months (n = 10)	Total (n = 27)	P-value
Age, years	67.12 ± 7.89	68.5 ± 14.22	67.63 ± 10.43	0.359
Interval between PCI and OP, days	44.59 ± 9.43	186.10 ± 88.45	97.00 ± 87.25	<0.001
Male	12 (70.6)	7 (70.0)	19 (70.4)	0.974
Diabetes mellitus	4 (23.5)	4 (40.0)	8 (29.6)	0.415
Hypertension	8 (47.1)	7 (70.0)	15 (55.6)	0.424
Hyperlipidemia	13 (76.5)	7 (70.00)	20 (74.2)	1.000
Smoking	4 (23.5)	4 (40.0)	8 (29.6)	0.415
Previous MI	3 (17.6)	1 (10.0)	4 (14.8)	1.000
Previous PCI or CABG	1 (5.9)	1 (10.0)	2 (7.4)	1.000
CVA History	0 (0)	1 (10)	1 (3.7)	0.37
Ejection Fraction	55.88 ± 8.68	54.50 ± 15.29	55.37 ± 11.30	0.786

Duration of Peri-operative Discontinuation of Antiplatelet Agents

Interval, days	NCS < 3 months (n =17)	NCS > 3 months (n = 10)	Total (n = 27)	p-value
Before surgery	4.94 ± 0.89	5.00 ± 0.00	4.96 ± 0.71	1.000
After surgery	7.35 ± 6.41	4.78 ± 3.19	6.46 ± 5.58	0.287
Total duration	12.29 ± 6.96	9.78 ± 43.19	11.42 ± 5.98	0.339

Lesion Data

Variables, n (%)	NCS < 3 months **(n =17)**	NCS > 3 months **(n = 10)**	Total **(n = 27)**	p-value
Target vessel				
LAD	11 (64.7)	5 (50.0)	16 (3859.3)	0.687
LCX	6 (35.3)	1 (10.0)	7 (25.9)	0.204
RCA	8 (47.1)	3 (30.0)	11 (40.7)	0.448
Multivessel	6 (35.3)	2 (20.0)	8 (29.6)	0.666
Saphenous vein	0 (0)	1 (10)	1 (3.7)	0.370
Lesion type				
B2	4 (23.5)	2 (20.0)	6 (22.2)	1.000
C	13 (76.5)	8 (80.0)	21 (77.8)	1.000

Stent Data

Variables, n (%)	NCS < 3 months **(n =17)**	NCS > 3 months **(n = 10)**	Total **(n = 27)**	p-value
Stent type				
Cypher	6 (35.3)	5 (50.0)	11 (40.7)	0.687
Taxus	12 (70.6)	5 (50.0)	17 (63.0)	0.415
Endeavor	1 (5.9)	0 (0)	1 (3.7)	1.000
Cypher + Taxus	2 (11.8)	0 (0)	2 (7.4)	0.516
Number of Stent	2.24 ± 1.52	1.20 ± 0.42	1.85 ± 1.32	0.059
Number of target vessel	1.53 ± 0.72	1.20 ± 0.42	1.41 ± 0.64	0.334
Stent Diameter	2.72 ± 0.45	2.97 ± 0.38	2.81 ± 0.44	0.264
Stent Length	24.74 ± 4.04	28.00 ± 6.18	25.94 ± 5.08	0.155

Surgical Procedure Type and Anesthesia

Variables, n (%)	NCS < 3 months (n =17)	NCS > 3 months (n = 10)	Total (n = 27)	p-value
Chest surgery	1 (5.9)	0 (0)	1 (3.7)	1.000
GI/Abdominal	6 (35.3)	3 (30.0)	9 (33.3)	0.778
Head and Neck	1 (5.9)	0 (0)	1 (3.7)	1.000
Orthopedic	1 (5.9)	0 (0)	1 (3.7)	1.000
Genitourinary	3 (17.6)	1 (10.0)	4 (14.8)	1.000
Ophthalmologic	2 (11.8)	3 (30.0)	5 (18.5)	0.326
Others	3 (17.6)	3 (30.0)	6 (22.2)	0.638
General Anesthesia	14 (82.4)	5 (50.0)	19 (70.4)	0.146
Malignancy	8 (47.1)	3 (30.0)	11(40.7)	0.384

Post-operative Bleeding and Clinical Events of the Study Population

Variables, n (%)	NCS < 3 months (n =17)	NCS > 3 months (n = 10)	Total (n = 27)	p-value
Bleeding Cx	4 (23.5)	0 (0)	4 (14.8)	0.264
Chest pain	2 (11.8)	0 (0)	2 (7.4)	0.516
ECG change	0 (0)	0 (0)	0 (0)	1.000
CK-MB > 2 X normal	3 (27.3)	0 (0)	3 (21.4)	1.000
BNP elevation	2 (11.8)	0 (0)	2 (7.4)	1.000
Repeat CAG	1 (5.9)	0 (0)	1 (3.7)	1.000
ICU stays	0.53 ± 1.18	0 ± 0	0.33 ± 0.96	0.473
Hospital days	12.65 ± 9.16	12.80 ± 11.20	12.70 ± 9.75	0.902

Six Patients with Postop Events

Pt	Interval between Surgery and PCI, days	DES Type	Target Vessels	DES No	Total Duration of Antiplatelet Discontinuation, days	NCS	Clinical Events
1	40	SES	LAD	2	20	Colon CA	transfusion 2 pints,chest pain
2	34	PES	LAD, LCX	2	13	Uterine CA	transfusion 2 pints,chest pain,repeat CAG
3	55	PES	LAD	1	5	Lung CA	transfusion 2 pints
4	50	PES	RCA	1	8	Cataract	CK-MB > 2 times normal
5	36	PES	LAD, RCA	6	8	Colon CA	transfusion 2 pints,CK-MB > 2 times normal
6	48	SES	LAD, RCA	2	12	Stomach CA	CK-MB > 2 times normal

Summary

1. The most important finding of this study is that elective NCS at least 3 months after DES implantation appears to be safe and feasible without obvious adverse events.

2. DES implantation in pts who were scheduled for early NCS (< 3 months after the PCI) such as cancer surgery might be associated with adverse clinical outcomes including post-operative bleeding and ischemic complications.

Dual Antiplatelet Discontinuation

1. Weber et al. found that after discontinuation of clopidogrel treatment, platelet function gradually recovers and that a complete restoration of ADP-induced platelet responses occurs 7 days after the last clopidogrel dose.

   Br J Clin Pharmacol. 2001;52:333-6.

2. Assays of platelet aggregation can be abnormal for up to 10 days after a single dose of aspirin, given the average platelet life span of 7-10 days.

   J Thromb Thrombolysis. 2004;17:21-7.

Rationale for the Temporary Discontinuation of Antiplatelets

1. We hypothesized that the antiplatelet effect will be remained before and after NCS despite of discontinuation aspirin and clopidogrel 7 to 10 days.

2. Therefore, in this study we strongly encouraged to discontinue aspirin and clopidogrel 5 to 7days before surgery and resume dual antiplatelets at post-operative 3 days unless there are significant post-operative bleeding complications.

Newer DES and Non-cardiac Surgery

1. Next generation DES such as Zotarolimus-eluting stent (ZES, EndeavorTM) which is better in terms of endothelialization within 3 months may have a different story and afford better outcomes compared with the previous first generation DESs such as SES & PES in patients undergoing NCS.

   (Challenging data from ***DATE registry*** in Korea)

2. However, further investigation with larger study population would be needed to clarify our suggestion.

Conclusion

We suggest that early NCS within 3 months after DES implantation may associate with adverse clinical outcomes and specifically, delaying the elective NCS at least 3 months after DES implantation appears to be safe and feasible without significant post operative adverse cardiac events.

Suggested Recommendations

When early non-cardiac surgery is needed (1)

1. Optimal timing for surgery

; at least more than 1 month after the DES implantation, however more than 3 months will be much safer.

2. Indication of early surgery

; Unexpected cancer or traumas which need early surgery after DES implantation

3. Perioperative dual antiplatelet regimen

; stop aspirin & clopidogrel 5-7days before the surgery and resume within 3 days after the surgery unless there are significant bleeding complications.

When early non-cardiac surgery is needed (2)

4. PCI strategy or Stent selection before the surgery

1) Scheduled elective major cancer surgery

; plain old balloon angioplasty (POBA only) or
cutting balloon angioplasty (CBA), or Safecut prior to surgery

→ No need of prolonged dual antiplatelet therapy

2) Stent selection

; BMS can be the primary option, but newer generation DES may be able to be a good option

Among the current commercially available DES, second generation Endeavor stents may be a best option before the surgery.

3) Medical therapy only before the surgery, and planned PCI after the surgery

; can be a good option in a series of selective patients

When elective non-cardiac surgery or procedure is needed

1. Optimal timing for surgery

; at least more than 1 year after the DES implantation should be the 1st option, however, at least more than 3 months will be safer.

2. Perioperative dual antiplatelet regimen

; stop aspirin & clopidogrel 5-7days before the surgery and resume within 3-5 days after the surgery unless there are significant bleeding complications.

KUMC Symposium 2008

1. 고대구로병원 순환기내과 제1회 Symposium
   (임상의사를 위한 최신 심장학 Core review,
   KOALA Symposium)
   ; 2008.5.10 (Sat), 심혈관센터 확장, 이전

2. 고대 구로병원 ***e-CTO Club meeting***
   with Dr S. Nakamura (New Tokyo Hospital)
   ; 2008.5.10 (Sat)

3. ***Arrhythmia Symposium (12th)***
   ; 2008.6.14 (고대 안암)

고려대학교구로병원
KOREA UNIVERSITY GURO HOSPITAL

제1회 임상의사를 위한 최신 심장학 Core Review

일시 2008. 5.10(토) 14:00~18:30

장소 고려대학교 구로병원 대강당

주관 | 고려대학교 구로병원 심장혈관센터

문의 | 심장내과 의국 (02)2626-1108

행사안내

연수평점

→ 대한의사협회 연수평점 3점

→ 순환기내과분과 연수평점 4점

등록비(등록비는 없습니다.)

사전등록안내

→ 심포지엄 준비에 차질이 없도록 사전등록을 해주시면 감사하겠습니다.
사전등록은 이메일, 팩스 또는 전화로 해 주십시오.

→ 사전등록 마감일은 5월 6일 (화) 까지 입니다.

→ 당일 현장에서의 등록은 오후 1시 30분부터 입니다.

고려대학교구로병원
KOREA UNIVERSITY GURO HOSPITAL

제1회 임상의사를 위한 최신 심장학 Core Review

일시 : 2008. 5.10(토) 14:00~18:30 장소 : 고려대학교 구로병원 대강당

주관 | 고려대학교 구로병원 심장혈관센터 문의 | 심장내과 의국 (02)2626-1108

사전등록안내

- 심포지엄 준비에 차질이 없도록 사전등록을 해주시면 감사하겠습니다. 사전등록은 이메일, 팩스 또는 전화로 해 주십시오.
- 사전등록 마감일은 5월 6일 (화) 까지 입니다.
- 당일 현장에서의 등록은 오후 1시 30분부터 입니다.

연수평점

- 대한의사협회 연수평점 3점
- 순환기내과분과 연수평점 4점

등록비(등록비는 없습니다.)

KOrea Guro CArdiovascuLAr Symposium
(KOALA Symposium)
in conjunction with e-CTO meeting

Session 1. 고혈압 (2pm-)

Session 2. 고지혈증/동맥경화증

Session 3. 관상동맥, 말초혈관질환

Session 4. 심부전(-6;30pm)

Thank You for Your Attention!!