

A Fatal Case of Simultaneous, Very Late Thrombosis Involving Three Drug-Eluting Stents in Three Coronary Arteries

Yong Soo Ahn, MD¹, Jang Hyun Cho, MD¹, Dong Han Kim, MD¹, Young June Hwang, MD¹, Hong Myong Jung, MD¹, Min Seok Choi, MD¹, Joon Young Kim, MD¹ and Myung Ho Jeong, MD²

¹Division of Cardiology, Department of Internal Medicine, St. Carollo Hospital, Suncheon,

²The Heart Center of Chonnam National University Hospital, Gwangju, Korea

ABSTRACT

Late stent thrombosis is one of the most serious complications associated with morbidity and mortality after coronary drug-eluting stent implantation, and is mainly caused by the withdrawal of antiplatelet agents. We report our experience of late stent thrombosis simultaneously involving three different coronary arteries in a young male patient who was treated with three drug-eluting stents two years ago. The patient stopped taking antiplatelet agents for several days. The patient did not recover from cardiogenic shock, even after repeated ballooning with thrombus aspiration, intra-aortic balloon pumping, and temporary pacing during cardiopulmonary resuscitation. (Korean Circ J 2008;38:564-569)

KEY WORDS: Stents; Thrombosis; Platelets.

Introduction

Since the initial introduction of drug-eluting stents (DES), their use has increased rapidly because the clinical and angiographic outcomes have been favorable.¹⁻³⁾ However, random trials with strict inclusion criteria have revealed that the incidence of thrombosis associated with DES is not different from bare-metal stents (BMS).⁴⁾⁵⁾ In the clinical setting, this finding may be relevant because complex lesions, the length or extent of the occluded lesion, the underlying disease, and the compliance of patients has more influence on stent thrombosis than the material from which stents are made.⁶⁻⁸⁾ Late stent thrombosis is an especially remarkable severe complication of DES, which has caused myocardial infarctions or deaths, and these events have been mainly associated with the withdrawal of antiplatelet agents.⁹⁾¹⁰⁾

We will report our experience with late stent thrombosis simultaneously involving three different coronary arteries after cessation of an antiplatelet agent for several days in a young patient treated with DES implantation.

Received: June 17, 2008

Revision Received: August 18, 2008

Accepted: August 21, 2008

Correspondence: Jang Hyun Cho, MD, Division of Cardiology, Department of Internal Medicine, St. Carollo Hospital, 1742 Jorye-dong, Suncheon 540-719, Korea

Tel: 82-61-720-2113, Fax: 82-61-720-6160

E-mail: goodnew8@naver.com

Case

A 35 year-old man with a history of heavy smoking presented to the emergency room with the sudden onset of chest pain of 2 hours duration. The electrocardiogram (ECG) obtained in the emergency room showed ST-segment elevation in the anterior and inferior leads. Two years previously, he was admitted with similar symptoms at another hospital. The ECG at that time showed T wave inversion in the inferior leads (Fig. 1). Coronary angiography (CAG) revealed the presence of three vessel disease with total occlusion of the middle right coronary artery (RCA) and critical stenosis in the proximal left ascending coronary artery (LAD) and intermediate branch. Immediately after the CAG, percutaneous coronary intervention (PCI) for mid - RCA was performed with a 3.0 × 28 mm Taxus stent (Boston Scientific, Boston, MA, USA). One week later, the follow-up angiography for the RCA lesion revealed a patent stent and a second stage PCI for the proximal LAD and intermediate branch lesions was performed with 3.5 × 24 mm and 3.0 × 24 mm Taxus stents, respectively. The final CAG showed no residual stenosis with good distal flow (Fig. 2).

Twenty months after the initial procedure, the patient was transferred to our hospital with an acute inferior wall ST elevation myocardial infarction (STEMI) after emergency treatment with a thrombolytic agent {Tenec-

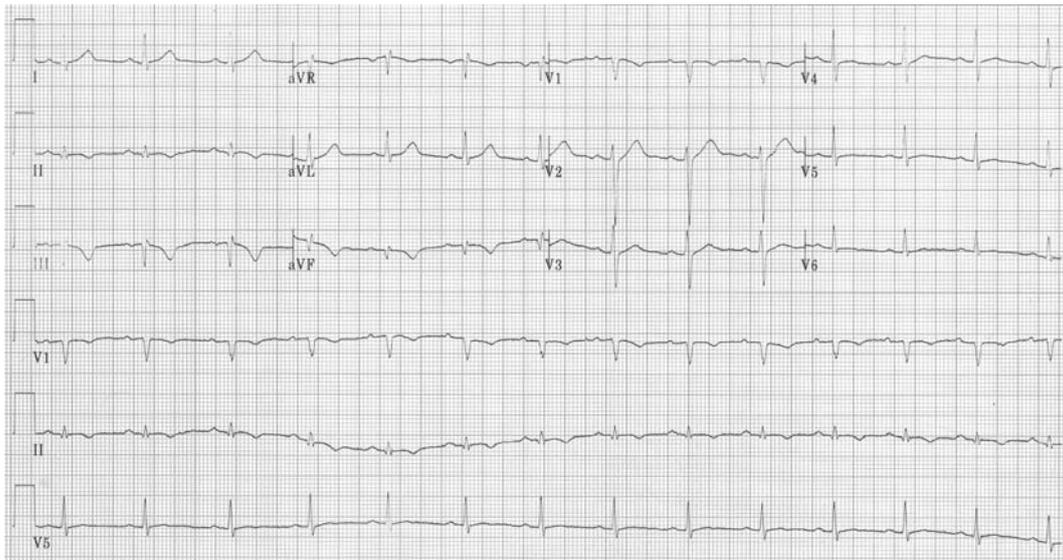


Fig. 1. The first cardiac event, ECG obtained in the emergency room of another hospital showed Q and T wave inversions in the inferior leads. ECG: electrocardiogram.

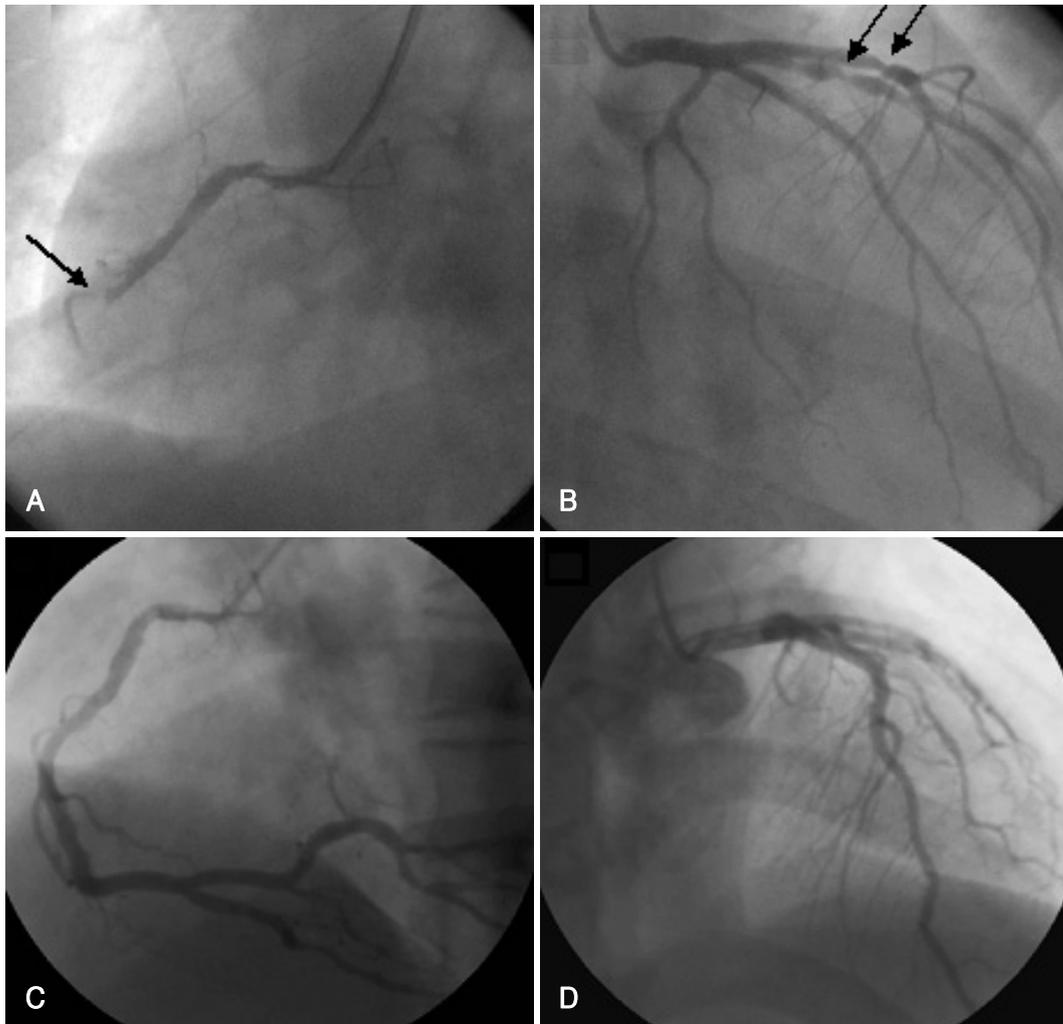


Fig. 2. During the first cardiac event. A and B: an emergency coronary angiography revealed total occlusion of the middle RCA, and critical stenosis in the proximal LAD and intermediate branch (A: LAO view, B: RAO cranial view). C and D: after coronary stenting, distal flow was restored to TIMI III in three coronary arteries (C: LAO view, D: AP cranial view). RCA: right coronary artery, LAD: left anterior descending artery, LAO: left anterior oblique, RAO: right anterior oblique, AP: anteroposterior, TIMI: thrombolysis in myocardial infarction.

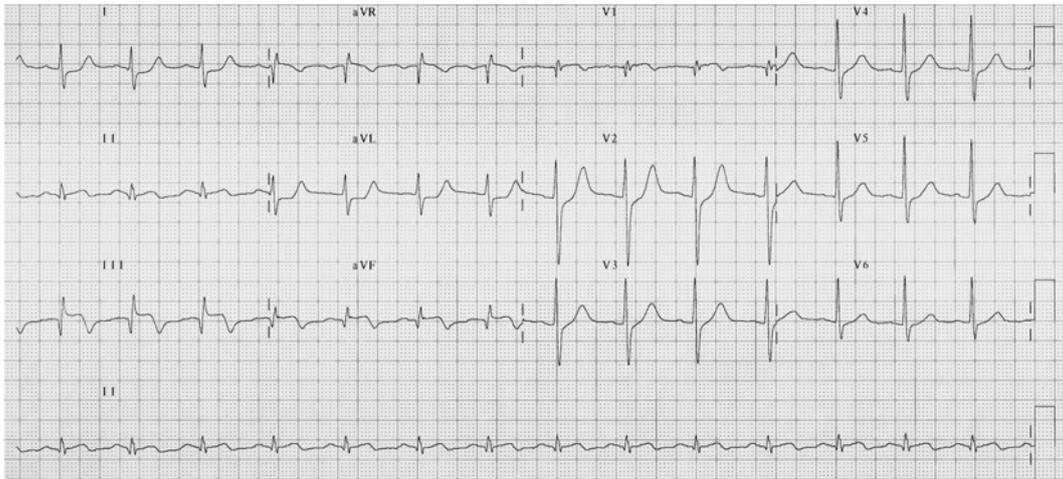


Fig. 3. The ECG taken in the emergency room during the second cardiac event showed ST elevation in the inferior leads. ECG: electrocardiogram.

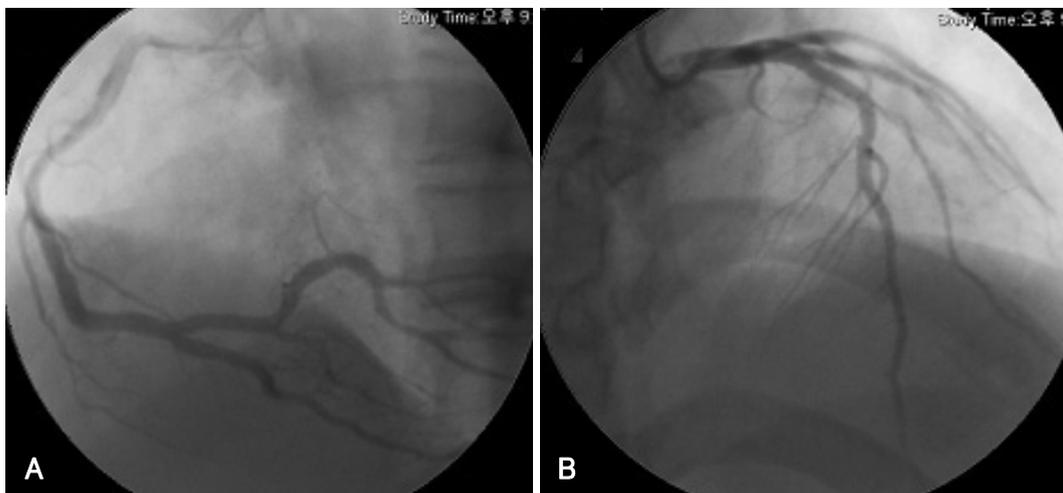


Fig. 4. During the second cardiac event (A and B) an emergency coronary angiography revealed patency in the previous stented sites of the middle right coronary artery, the proximal left anterior descending artery, and the intermediate branch with good distal flow (A: LAO view, B: AP cranial view). LAO: left anterior oblique, AP: anteroposterior.

teplase (40 mg)) at a local hospital.

He complained of chest pain continuously during the 3 hours prior to thrombolytic therapy. The follow-up ECG obtained in our hospital showed persistent ST elevation in the inferior leads (Fig. 3), the cardiac enzymes as (CK, CK-MB, and troponin-I) were elevated, and echocardiography also showed hypokinetic movement of the inferoposterior wall. After loading with 300 mg of aspirin and 300 mg of clopidogrel, he was taken directly to the catheterization room for rescue PCI. The CAG showed patency in the previously stented sites of the middle RCA, proximal LAD, and intermediate branch, with good distal flow (Fig. 4). Gradually, the chest pain and ST elevation on the ECG resolved. The post-treatment clinical course was uneventful and the patient was discharged 2 weeks later on dual antiplatelet agents (aspirin (100 mg) and clopidogrel (75 mg)).

Four months after the second diagnostic CAG, the patient presented to the emergency room with an in-

ferior and anteroseptal wall STEMI. He complained of severe chest pain and dyspnea, and dull mental status, and became stuporous in the emergency room. He had not taken his medication over several days because of a disregard for his health, including the heavy consumption of alcohol. The ECG showed complete AV block, a right bundle branch block, and ST-segment elevation in both the anterior and inferior leads (Fig. 5). The systolic blood pressure decreased to 60 mmHg and the heart rate dropped to 25 beats/min. Several minutes later, the patient's mental state changed to coma and his blood pressure was not checked. Cardiopulmonary resuscitation (CPR) was started promptly and he was transferred to the catheterization room. His condition deteriorated further, so CPR was continued. An emergency CAG revealed simultaneous total occlusion of the middle RCA, proximal LAD, and intermediate branch, the previously paced sites of the deployed sites of the Taxus stents. After insertion of an intra-aortic balloon coun-

terpulsation and a temporary pacemaker, thrombus aspiration was performed with a Thrombuster catheter. Later, antegrade flow for the middle RCA was obtained

by thrombectomy and ballooning at the occluded lesion. However, coronary flow at the occluded lesions of the proximal LAD and intermediate branch and vital status

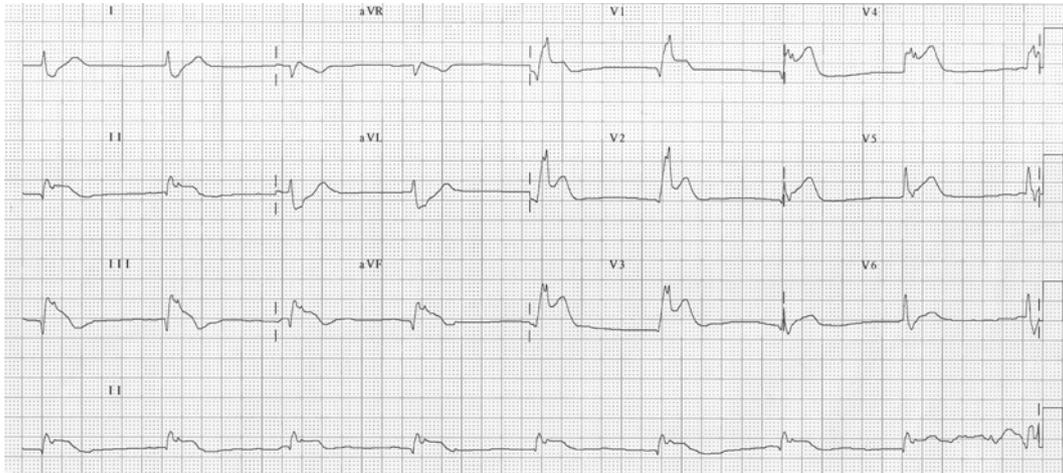


Fig. 5. The ECG obtained in the emergency room during the third cardiac event revealed complete AV block, a right bundle branch block, and ST elevation over the precordial and inferior leads. ECG: electrocardiogram, AV: atrioventricular.

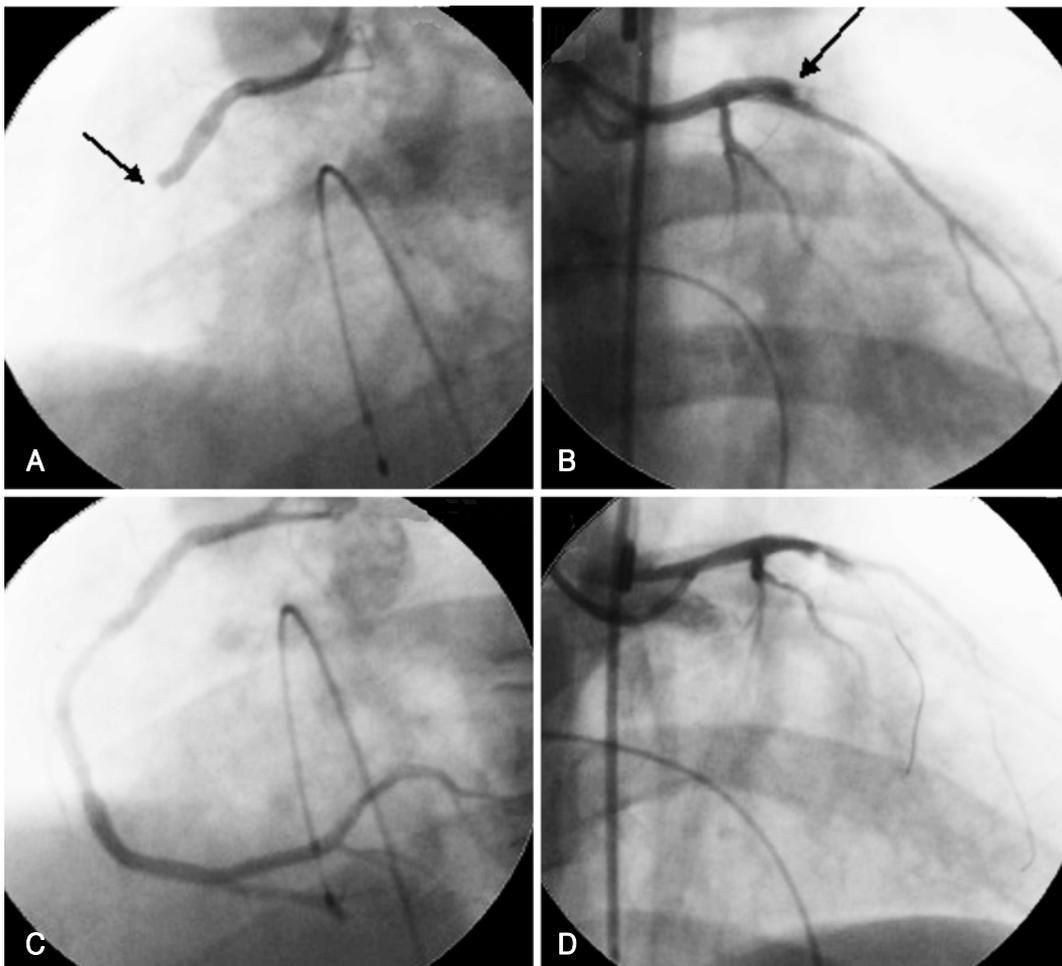


Fig. 6. During the third cardiac event. A and B: an emergent coronary angiography revealed simultaneous total occlusion of the middle RCA, proximal LAD, and intermediate branch, at the sites the three Taxus stents had been previously placed (A: LAO view, B: RAO cranial view). C and D: after placement of an intra-aortic balloon counterpulsation and temporary pacemaker, thrombus aspiration was performed by suction catheter. But, coronary flows at the occluded lesions of the proximal LAD and intermediate branch were not restored in spite of repeated ballooning and thrombus aspiration (C: LAO view, D: RAO cranial view). RCA: right coronary artery, LAD: left anterior descending artery, LAO: left anterior oblique, RAO: right anterior oblique.

was not recovered, despite continuous thrombus aspiration and repeated ballooning (Fig. 6). Unfortunately, the patient died in the catheterization room.

Discussion

Stent thrombosis is one of the most severe complications associated with morbidity and mortality after DES or BMS implantation.¹¹ By definition, early stent thrombosis occurs within 30 days after stent implantation, while late stent thrombosis occurs beyond 30 days.¹² Additionally, very late stent thrombosis is defined as a thrombus occurring beyond 1 year. Early stent thrombosis occurs in about 1.0-1.5% of patients with DES; the probability of occurrence with a BMS is similar. In the largest series of eight cases, late stent thrombosis unexpectedly occurred in 0.35-0.72% of patients with DES. In addition, most cases have been associated with discontinuation of antiplatelet therapy late after stent implantation.¹³⁾¹⁴

Delayed re-endothelialization of the stent, because of the antiproliferative nature of the agents, appears to be implicated in the pathophysiology of very late stent thrombosis. On the basis of this theory, DES causes delayed arterial healing and increased inflammatory reactions compared to BMS, so DES seems to be associated with higher rates of late stent thrombosis than BMS.¹⁵ Unlike DES, the overall rate of stent thrombosis which occurs in patients with BMS is the subject of but few reports. However, some recent studies have reported that there are no differences in the incidences of late stent thrombosis between patients treated with DES and BMS.¹¹

In the clinical setting, acute coronary syndrome, bifurcation treatment, diabetes, and premature discontinuation of antiplatelet therapy are considered strong predictors of stent thrombosis. Effective antiplatelet agents have a critical role in the prevention of stent thrombosis.⁶⁻⁸ Therefore, in most cardiac centers prolonged dual antiplatelet therapy with aspirin and clopidogrel is recommended for the prevention of stent thrombosis after PCI.

Previously, some studies have reported that aspirin withdrawal after PCI increases the occurrence of a coronary event, such as stent thrombosis.⁶⁾⁹⁾¹³ A study noted that aspirin withdrawal in patients with coronary artery disease increased morbidity within 1 month after cessation of aspirin, whether treated by BMS or DES,¹⁶ and another study reported that eight cases occurred during late stent thrombosis after the withdrawal of aspirin.¹⁴ Yet another study noted that the inadvertent interruption of clopidogrel therapy also can induce late stent thrombosis.¹⁷ Dual antiplatelet therapy can prevent stent thrombosis, but withdrawal of any one agent could result in the cardiovascular events at any time.

Even if a patient had a coronary stent deployed before elective non-cardiac surgery, aspirin should not be discontinued, except for intracranial neurosurgery and transurethral prostatectomy. A recent review proved that aspirin neither increased the perioperative severity nor the mortality associated with bleeding.¹⁸ In addition, whatever non-cardiac surgery is planned, it must be performed later than 6 weeks after stent implantation if possible, because stent thrombosis frequently develops within 3-6 weeks of a cardiac procedure.¹⁹ These events have been mainly related to insufficient stent re-endothelialization, heightened platelet reactivity, and withdrawal of the antiplatelet agent.

In this case, our patient did not take his prescribed medication continuously in spite of prescription of dual antiplatelet agents after the second attack, and he died due to very late stent thrombosis of three different coronary arteries at the same time, two years after DES implantation.

In summary, this case emphasizes that late stent thrombosis should be considered in all patients treated with coronary DES implantation, and may be prevented by using an antiplatelet agent continuously.

REFERENCES

- 1) Grube E, Silber S, Hauptmann KE, et al. *Two year-plus follow up of paclitaxel-eluting stent in de novo coronary narrowing (TAXUS I)*. *Am J Cardiol* 2005;96:79-82.
- 2) Degertekin M, Serruys PW, Foley DP, et al. *Persistent inhibition of neointimal hyperplasia after sirolimus-eluting stent implantation: long-term (up to 2 years) clinical, angiographic, and intravascular ultrasound follow-up*. *Circulation* 2002;106:1610-3.
- 3) Fajadet J, Wijns W, Laarman GJ, et al. *Randomized, double-blind, multicenter study of the Endeavor zotarolimus-eluting phosphorylcholine-encapsulated stent for treatment of native coronary artery lesions: clinical and angiographic results of the ENDEAVOR II trial*. *Circulation* 2006;114:798-806.
- 4) Moreno R, Fernandez C, Hernandez R, et al. *Drug-eluting stent thrombosis: result from a pooled analysis including 10 randomized studies*. *J Am Coll Cardiol* 2005;45:954-9.
- 5) Schampaert E, Moses JW, Schofer J, et al. *Sirolimus-eluting stents at two years: a pooled analysis of SIRIUS, E-SIRIUS, and C-SIRIUS with emphasis on late revascularizations and stent thrombosis*. *Am J Cardiol* 2006;98:36-41.
- 6) Iakovou I, Schmodt T, Bonizzi E, et al. *Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stent*. *JAMA* 2005;293:2126-30.
- 7) Daemen J, Wenaweser P, Tsuchida K, et al. *Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institution cohort study*. *Lancet* 2007;369:667-78.
- 8) Park SH, Hong GR, Seo HS, Tahk SJ. *Stent thrombosis after successful drug-eluting stent implantation*. *Korean Circ J* 2005; 35:163-71.
- 9) McFadden EP, Stabile E, Regar E, et al. *Late thrombosis in drug-eluting coronary stents after discontinuation of antiplatelet therapy*. *Lancet* 2004;364:1519-21.
- 10) Moon JY, Jeong MH, Jun CH, et al. *The frequency, treatment and clinical outcomes of stent thrombosis after use of TAXUS*

- stent. *Korean Circ J* 2007;37:641-6.
- 11) Wernick MH, Jeremias A, Carrozza JP. Drug-eluting stents and stent thrombosis: a cause for concern? *Coron Artery Dis* 2006; 17:661-5.
 - 12) Park DW, Park SW. Stent thrombosis in the era of the drug-eluting stent. *Korean Circ J* 2005;35:791-4.
 - 13) Ong AT, Hoye A, Aoki J, et al. Thirty-day incidence and six-month clinical outcome of thrombotic stent occlusion after bare-metal, sirolimus, or paclitaxel stent implantation. *J Am Coll Cardiol* 2005;45:947-53.
 - 14) Ong AT, McFadden EP, Regar E, de Jaegere PP, van Domburg RT, Serruys PW. Late angiographic stent thrombosis (LAST) events with drug-eluting stents. *J Am Coll Cardiol* 2005;45:2088-92.
 - 15) Joner M, Finn AV, Farb A, et al. Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. *J Am Coll Cardiol* 2006;48:193-202.
 - 16) Collet JP, Montalescot G, Blanchet B, et al. Impact of prior use or recent withdrawal of oral antiplatelet agents on acute coronary syndromes. *Circulation* 2004;110:2361-7.
 - 17) Goel PK, Gill GS. Angioplasty for the late stent thrombosis, the new technical challenge: a single centre experience. *Int J Cardiol* 2008;123:335-7.
 - 18) Burger W, Chemnitz JM, Kneissl GD, Rucker G. Low-dose aspirin for secondary cardiovascular prevention-cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation: review and meta-analysis. *J Intern Med* 2005; 257:399-414.
 - 19) Leibowitz D, Cohen M, Planer D, et al. Comparison of cardiovascular risk of noncardiac surgery following coronary angioplasty with versus without stenting. *Am J Cardiol* 2006;97:1188-91.