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Catastrophic Outcomes of Noncardiac Surgery Soon After Coronary Stenting

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OBJECTIVES To assess the clinical course of patients who have undergone coronary stent placement less than six weeks before noncardiac surgery.

BACKGROUND Surgical and percutaneous transluminal coronary angioplasty revascularization performed before high-risk noncardiac surgery is expected to reduce perioperative cardiac morbidity and mortality. Perioperative and postoperative complications in patients who have undergone coronary stenting before a noncardiac surgery have not been studied.

METHODS Forty patients who underwent coronary stent placement less than six weeks before noncardiac surgery requiring a general anesthesia were included in the study (1–39 days, average: 13 days). The records were screened for the occurrence of adverse clinical events, including myocardial infarction, stent thrombosis, peri- and postoperative bleeding and death.

RESULTS In 40 consecutive patients meeting the study criteria, there were seven myocardial infarctions (MIs), 11 major bleeding episodes and eight deaths. All deaths and MIs, as well as 8/11 bleeding episodes, occurred in patients subjected to surgery fewer than 14 days from stenting. Four patients expired after undergoing surgery one day after stenting. Based on electrocardiogram, enzymatic and angiographic evidence, stent thrombosis accounted for most of the fatal events. The time between stenting and surgery appeared to be the main determinant of outcome.

CONCLUSIONS Postponing elective noncardiac surgery for two to four weeks after coronary stenting should permit completion of the mandatory antiplatelet regimen, thereby reducing the risk of stent thrombosis and bleeding complications. (J Am Coll Cardiol 2000;35:1288–94) © 2000 by the American College of Cardiology

Preoperative identification and treatment of coronary artery disease (CAD) is a commonly accepted practice when referring patients for noncardiac surgery requiring general anesthesia. This practice is felt to reduce perioperative morbidity and mortality (1). Studies indicate that patients with CAD who are revascularized by coronary artery bypass grafting (CABG) before undergoing noncardiac surgery have a reduced incidence of myocardial infarction (MI) and postoperative death (2). The impact of percutaneous transluminal coronary angioplasty (PTCA) procedures on the complications after noncardiac surgery is less explored. Several clinical studies have examined perioperative complications in patients who underwent PTCA before noncardiac surgery and found a low perioperative morbidity (3–6). However, no studies to date have reviewed postoperative outcomes in patients who undergo PTCA and implantation of a coronary stent before a noncardiac surgery.

Therefore, this study attempted to estimate whether similar perioperative benefit exists for patients who undergo PTCA with stent placement before noncardiac surgery.

METHODS

Between 1996 and the end of 1998 at the Methodist Hospital, Houston, Texas, 40 consecutive patients who underwent coronary stent placement less than six weeks before a noncardiac surgical procedure requiring general anesthesia were identified. The records were reviewed and surgical outcomes were carefully scrutinized for evidence of adverse clinical events such as: stent thrombosis, MI, bleeding complications and death in the perioperative period. Special attention was given to initiation, withdrawal and continuation of each patient's antiplatelet therapy during the perioperative and postoperative period.

Bleeding complications were more difficult to grade as many of the surgical procedures performed are considered inherently associated with high blood loss. Excessive bleed-

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CAD = coronary artery disease
CX = circumflex coronary artery
ECG = electrocardiogram
LAD = left anterior descending coronary artery
MI = myocardial infarction
OM = obtuse marginal branch
PTCA = percutaneous transluminal coronary angioplasty
RCA = right coronary artery

ing was, therefore, defined as the postoperative need for transfusion or bleeding that necessitated reoperation. Unusual blood loss or drainage in the perioperative period was also assessed. Myocardial infarction was diagnosed by characteristic electrocardiogram (ECG) changes or an increase in creatinine kinase levels.

Statistical analysis. Continuous variables are presented as mean value ± SD. Discrete variables are described as frequencies and percentages and were compared by chi-square and Fisher exact test. $P < 0.05$ was considered statistically significant.

RESULTS

The 40 patients included in this study underwent surgery 1 to 39 days after coronary stent placement (average 13 days). The surgical procedures included: carotid endarterectomy (n = 12), thoracic or abdominal aortic aneurysm resection (n = 9), aortoiliac bypass grafting (n = 2), aortobifemoral of femoral-popliteal bypass grafting (n = 3), arteriovenous shunt placement or revision (n = 2), mitral valve replacement (n = 1), lung transplantation (n = 1), cholecystectomy (n = 2), sigmoid colectomy (n = 1), femoral embolectomy (n = 1), nephrectomy (n = 1), prostatectomy (n = 1), left upper lobectomy of the lung (n = 1), foot amputation (n = 1), parathyroidectomy (n = 1) and cystectomy (n = 1).

All 40 patients received at least one dose of ticlopidine (250–500 mg) immediately after the stenting procedure. All patients were receiving aspirin before stenting. Both antiplatelet drugs were continued after stenting for a variable period of time. Nine patients received abciximab during coronary intervention.

The CAD history, risk profile and procedural details of the studied group are summarized in Table 1.

Eight out of 40 patients expired. Relevant clinical details of the patients who expired are summarized in Table 2. In six patients (A.S., G.W., H.L., W.A., V.G., J.C.), death was related to MI. In two other patients (R.C., J.H.), death was associated with a bleeding complication. Four patients (G.W., H.L., W.A., J.C.) had both MI and bleeding complications ultimately leading to death. Seven patients suffered MIs, of which six were fatal and one (F.D.) was minimized due to successful emergent PTCA. Of these seven patients, two had single vessel disease, three had double vessel disease and two had triple vessel disease. All critically stenosed vessels were successfully stented. In three patients (A.S., G.W., V.G.) the residual diseased vessels had lesions of borderline severity (50%) and were not associated with demonstrable ischemia. In two patients (F.D., W.A.), the untreated vessels were right coronary arteries (RCAs), which were chronically occluded and well-collateralized.

Stent thrombosis was presumed to be the cause of all of the MIs; in two patients (F.D., J.C.), stent thrombosis was confirmed angiographically. In four others, ECG changes of infarction or ischemia were in the areas subtended by the stented artery. One patient (G.W.) who experienced chest pain and sudden death at home had triple vessel disease with two severe stenoses (left anterior descending coronary artery [LAD] and RCA), which were treated with multiple stents.

All deaths and MIs as well as 8 of 11 bleeding episodes occurred in patients who underwent surgery in less than two weeks after coronary stent placement. The incidence of death and MI was significantly higher in this subset than it was in patients subjected to surgery more than 14 days after stenting ($p = 0.015$ by Fisher exact test). As such, the mortality rate among 25 patients operated within this two-week timeframe was 32%. Of five patients who underwent surgery one day after stenting, four expired (bleeding was involved in three patients). The fifth patient underwent surgery the day after stent placement, had no discontinua-

Table 1. History, Risk Factors and Procedural Details of the Study Group

Age (yrs)	66.7 ± 7.2 (mean ± SD)		
Female gender	13/40 (32.5%)		
Risk Factors			
Tobacco smoking	22/40 (55%)		
Hypercholesterolemia	11/40 (28%)		
Arterial hypertension	25/40 (63%)		
Diabetes mellitus	9/40 (23%)		
Family history	6/40 (15%)		
CAD Status at the Time of Stenting		**Target Vessel (n = 44)**	
Asymptomatic	9 (22%)	LAD	14 (32%)
Stable angina	18 (45%)	CX and OM	14 (32%)
Unstable angina	13 (33%)	RCA	14 (32%)
		OM graft	2 (4%)
Stent Type (n = 47)		**Stent Size (n = 47)**	
Palmaz-Schatz	28 (59%)	3.0	37 (79%)
Gianturco-Roubin II	4 (9%)	3.5	6 (13%)
Multilink	6 (13%)	4.0	3 (6%)
AVE	6 (13%)	4.5	1 (2%)
Crown	3 (6%)		

CX = circumflex; LAD = left anterior descending; OM = obtuse marginal; RCA = right coronary artery.

Table 2. A Summary of Time Frames of PTCA, Surgery, Antiplatelet Therapy and Complications in Patients Who Experienced Major Complications After Noncardiac Surgery Preceded by Intracoronary Stent Placement

Patient's Initials	Age	Gender	Time from Angioplasty	Ticlid Withheld	Aspirin Withheld	Type of Surgery	MI (Time After Surgery)	Major Bleeding	Death (Days After Surgery)
A.S.	82	M	1 day	Yes	Yes	Left femoral embolectomy	Yes (11 days)	No	Yes (11 days)
G.W.	62	M	1 day	No	No	Left carotid endatherectomy	Yes (7 days)	Yes	Yes (7 days)
R.C.	72	M	1 day	No	Yes	Mitral valve replacement	No	Yes	Yes (3 days)
H.L.	68	F	1 day	Yes	Yes	Right carotid endatherectomy	Yes (12 h)	Yes	Yes (8 days)
F.D. (case 1)	67	M	2 days	Yes	Yes	Thoracoabdominal aortic aneurysmectomy	Yes (6 days)	No	No
W.A.	67	M	3 days	No	Yes	Thoracoabdominal aortic aneurysmectomy	Yes (8 h)	Yes	Yes (8 days)
V.G. (case 3)	72	F	5 days	Yes	Yes	Sigmoid colectomy	Yes (2 h)	No	Yes (2 days)
J.C. (case 2)	62	F	6 days	Yes	Yes	Single lung transplantation	Yes (24 h)	Yes	Yes (11 days)
J.H.	74	M	11 days	Yes	Yes	Thoracoabdominal aortic aneurysmectomy	No	Yes	Yes (9 days)

F = female; M = male; MI = myocardial infarction.

tion of either antiplatelet drug and experienced no adverse event. One patient (F.D.), who was subjected to surgery two days after stenting, experienced stent thrombosis with cardiac arrest. He was successfully treated with an emergency PTCA but required hospitalization for more than seven weeks.

Five patients had no discontinuation of ticlopidine before surgery. Three of these patients (G.W., R.C., W.A.) underwent surgery less than three days from stenting, and each expired. One (G.W.) required reoperation twice for hematoma. Ticlopidine was then stopped. He died suddenly four days later at home while experiencing severe chest pain and was presumed to have an MI. Another patient (R.C.) required reoperation for hemothorax and needed 11 units of blood transfused. He died of deteriorating heart failure on postoperative day 3. A third patient, (W.A.) required reoperation 4 h after surgery for bleeding. Four hours later he developed an acute inferior MI with recurrent ventricular tachycardia and died seven days later. Two other patients underwent surgery one day and five days after stenting, respectively, and both made uneventful recoveries.

Of eight deceased patients, one had no discontinuation of either antiplatelet drug, two patients had ticlopidine withdrawn and aspirin continued, and six patients had both drugs stopped 0 to 2 days before going to surgery (zero denoting the day of surgery).

In the remaining 32 patients, most had both antiplatelet drugs discontinued 0 to 1 day before and restarted 0 to 1 day after surgery.

Patients who underwent surgery less than two weeks after coronary stenting (n = 25) were subjected to similar types of surgical procedures as those undergoing surgery between two and six weeks (n = 15). The percent of patients receiving abciximab during the stent placement was also similar in both subgroups (5/25 vs. 4/15). The following case histories provide insight into the dynamics of these events.

CASE REPORTS

Case 1 (1996). A 67-year-old man with a history of CAD treated with PTCA and COPD was evaluated before resection of an infrarenal aortic aneurysm. A 90% restenosis lesion in the midportion of the circumflex artery was successfully treated with PTCA and a 3.0-mm Palmaz-Schatz stent (Fig. 1, A and B). Ticlopidine was started the day of PTCA and was stopped one day later. Aspirin, continued from before the procedure, was stopped two days after stenting, i.e., the day the patient underwent aneurysmectomy.

Six days after surgery, the patient became hypotensive. His ECG at that time revealed 2 to 3 mm ST segment depression in leads V3 to V6. An episode of ventricular fibrillation followed the hypotension, and the patient was successfully defibrillated. The patient underwent emergent cardiac catheterization that revealed 100% occlusion of the

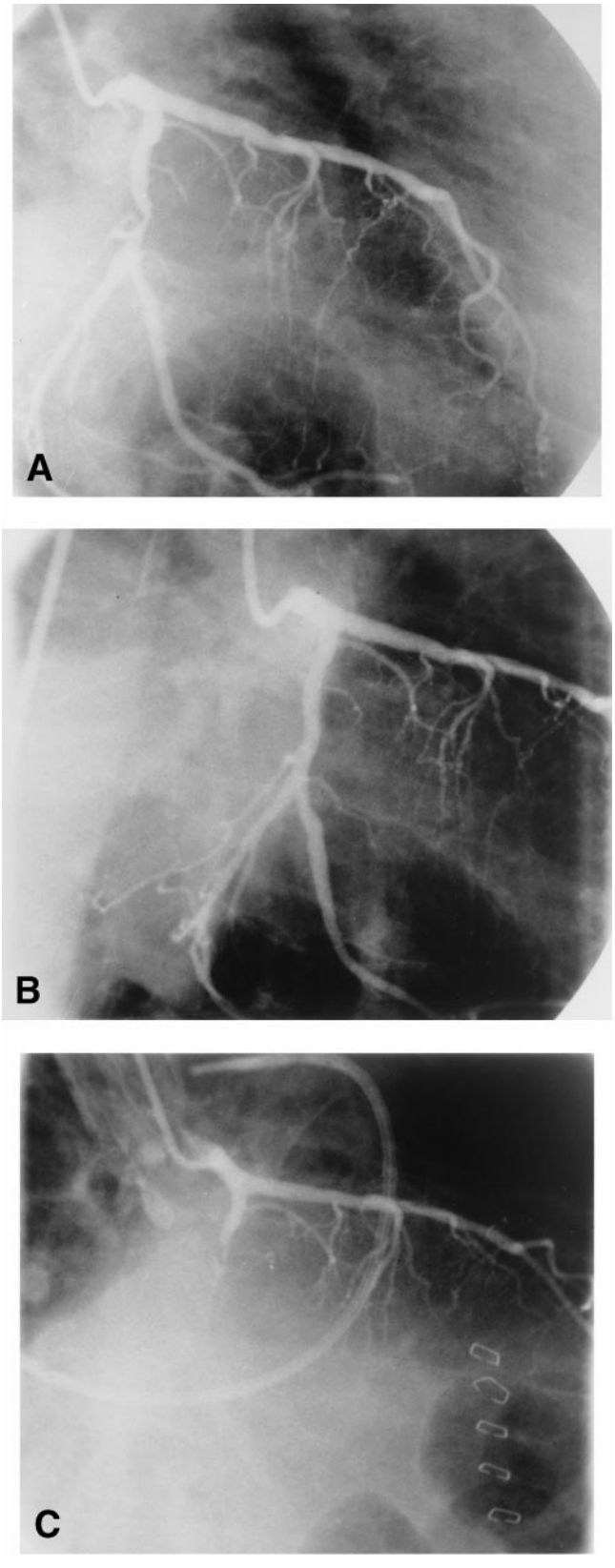

Figure 1. Patient F.D., case history #1. **(A)** 70% eccentric stenosis of the circumflex coronary artery. **(B)** After successful placement of 3.0 Palmaz-Schatz coronary stent. **(C)** Total occlusion due to stent thrombosis on the sixth day after surgery.

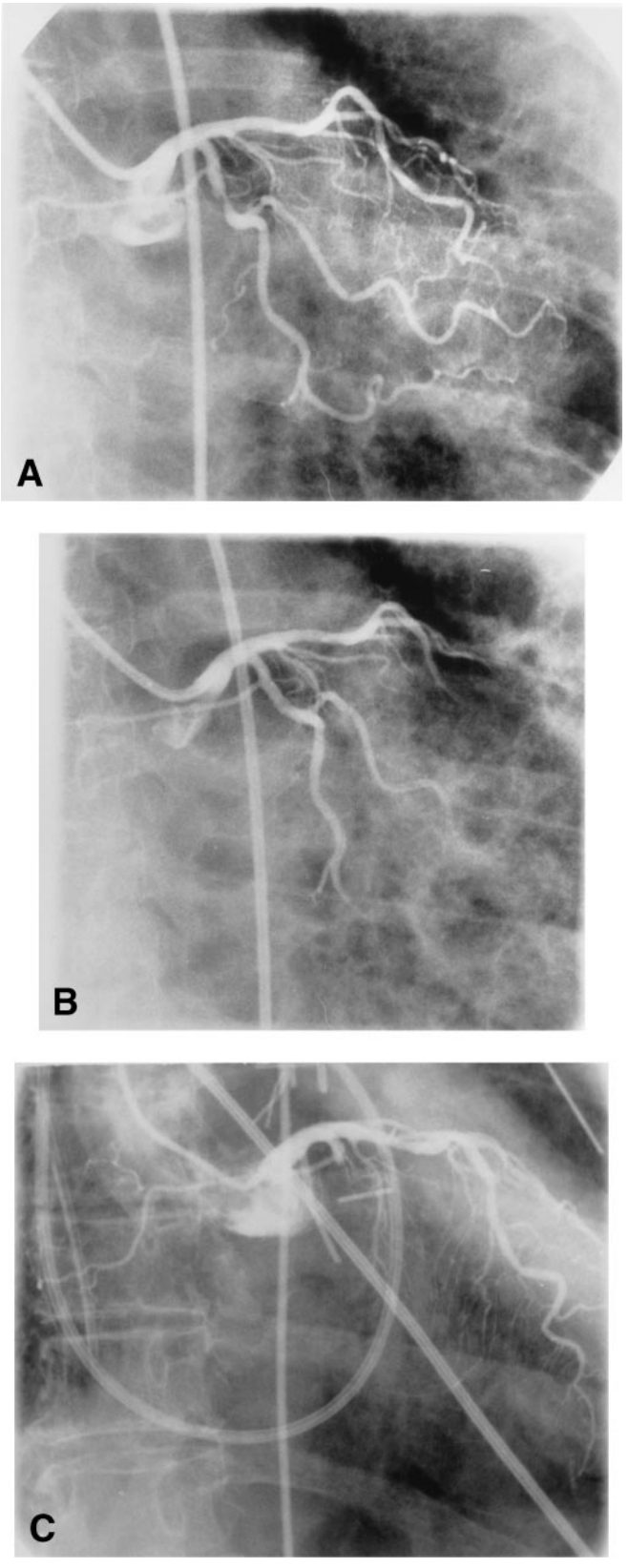

Figure 2. Patient J.C., case history #2. **(A)** Initial angiographic appearance of the lesion in the circumflex coronary artery. **(B)** Postprocedural result with 3.0 Palmaz-Schatz stent. **(C)** Total thrombotic occlusion of the previously stented site on the first postoperative day, not amenable to angioplasty.

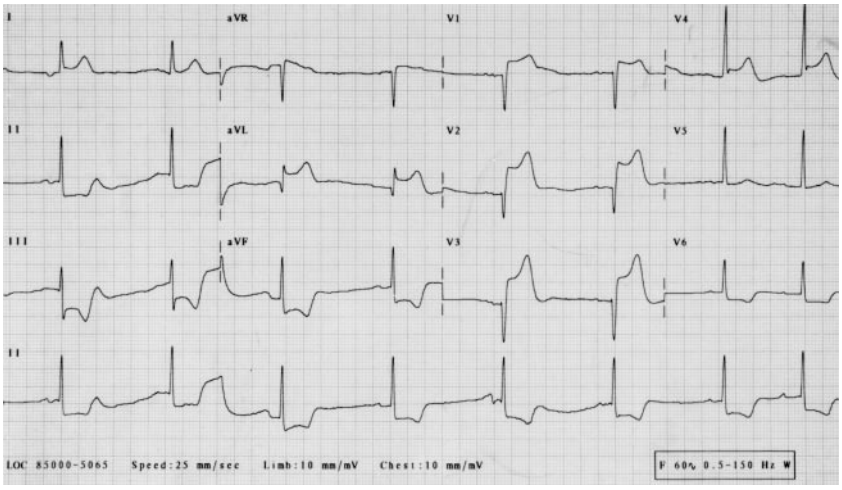

Figure 3. Patient V.G., case history #3. Electrocardiogram recorded during chest pain and symptoms of pulmonary edema. Bradycardia and ST segment changes consistent with myocardial infarction.

circumflex artery in the previously stented segment (Fig. 1C). The occluded artery was successfully opened by PTCA. The ECG changes resolved after PTCA, and there was no subsequent formation of Q waves. Creatine kinase MB levels were not obtained. Ticlopidine was restarted and continued for four weeks from stenting. The patient survived; however, his hospitalization was prolonged to over seven weeks because of slow weaning from the mechanical ventilator.

Case 2 (1997). A 62-year-old woman with interstitial pulmonary fibrosis was evaluated for lung transplantation. Cardiac catheterization revealed an 80% stenosis of the proximal circumflex artery. The patient underwent PTCA resulting in a nonocclusive dissection, which was successfully treated with a 3.0-mm Palmaz-Schatz stent (Fig. 2, A and B). Ticlopidine was started on the day of the PTCA. Aspirin, continued from before the procedure, was stopped together with ticlopidine five days after stenting, i.e., the day the patient underwent single lung transplant.

Twenty-four hours after transplantation, the patient developed respiratory distress, hypotension and 2 to 3 mm ST segment elevation in ECG leads V3 to V6. Emergency coronary angiography revealed 100% occlusion of the stent (Fig. 2C). All attempts to cross this occlusion with a guidewire were unsuccessful. An intraaortic balloon pump was placed. New Q waves were subsequently noted on the ECG. Ticlopidine and aspirin were restarted one day later. On the sixth postoperative day, the patient suffered a hemorrhagic cerebrovascular accident. She was declared brain dead and expired on postoperative day 11. An autopsy revealed a recent lateral wall MI. The stent site was patent.

Case 3 (1998). A 72-year-old woman with known CAD was admitted for work-up of chronic iron deficiency anemia. On cardiac catheterization, a 95% lesion in mid-LAD was revealed and treated with a 3.5-mm Crown stent. Three days later the colonoscopy disclosed an infiltrating, partially obstructing sigmoid adenocarcinoma. Thus, she was subjected to sigmoid colectomy five days after coronary stenting. Ticlopidine and aspirin were discontinued on the day of surgery. Two hours after surgery, she developed bradycardia and severe ECG changes consistent with an acute anterior MI (Fig. 3) and pulmonary edema requiring reintubation. Two days later, in the intensive care unit, she extubated herself, went into respiratory arrest and could not be resuscitated.

DISCUSSION

This study reveals an extraordinarily high incidence of catastrophic perioperative complications in patients who undergo elective or semielective noncardiac surgery soon after implantation of a coronary stent. These complications include acute MI and death, which appear to be directly or indirectly related to the preceding coronary intervention because all the ischemic manifestations occurred in the distribution of the stented arteries.

Through their use in interventional cardiology, intracoronary stents have dramatically improved the outcome of percutaneous coronary intervention by reducing the need for emergent bypass surgery, improving immediate angiographic results and reducing the rate of subsequent restenosis. Consequently, they are now used in more than 50% of all PTCA procedures (7) and up to 90% in some hospitals. Some of these procedures are performed for the purpose of treating critical coronary lesions in patients who will subsequently undergo elective or semielective surgery. Treating these lesions before surgery is expected to reduce the incidence of perioperative and postoperative complications.

When first introduced, stents were plagued by a high rate of acute or subacute thrombosis, which was generally attended by acute MI (8). However, current technical

advances, such as high pressure balloon deployment (9) and more effective antiplatelet regimens, have reduced the rate of thrombosis to less than 1%. This low rate of thrombotic closure is supported by recent clinical trial data (10–13).

The Fifth American College of Chest Physicians Consensus on Antithrombotic Therapy has recently formulated recommendations for antiplatelet therapy after coronary stent placement. Patients who are at high risk for stent thrombosis should be given ticlopidine for 30 days, and all other patients should receive ticlopidine for at least 14 days (14). It is also known that the use of aspirin without ticlopidine results in a five times greater incidence of stent thrombosis (12). Ticlopidine reaches peak antiplatelet effect in approximately three to five days from initiation (15), and patients who are treated with ticlopidine for several days before stent placement have a significantly lower incidence of procedural non-Q wave MI than those who begin ticlopidine the day of the procedure (16).

In the group of patients reported herein, the most catastrophic adverse event appeared to be stent thrombosis, which usually leads to MI and death. In two patients, stent thrombosis was documented angiographically. In five others, stent thrombosis was presumed to be responsible since the MI occurred in the territory supplied by the stented artery. In this group of patients, one or both antiplatelet drugs were typically interrupted one to two days before surgery, which would be the general practice in patients about to undergo surgery. The impact of abrupt withdrawal or interruption from this antithrombotic regimen seems to account for the unacceptable rate of acute coronary thrombosis.

Of note, all of the major adverse events occurred in patients who underwent surgery within 14 days of stent implantation. The interruption or withdrawal of the antiplatelet regimen in this two-week window coincidentally corresponds with the time frame during which stent thrombosis would likely occur and would appear to explain the high incidence of stent thrombosis. Of the total seven MIs, four occurred within 24 h of the surgical procedure, while the other three developed at 6, 7 and 11 days after procedure. Overall, 8 of the 25 patients who underwent surgery within 14 days of stent placement expired within 11 days of the surgical procedure after suffering an MI or significant bleeding episode.

Bleeding complications were unusually high and were often combined with stent thrombosis. Aspirin (17) and ticlopidine (18,19), used to prevent stent thrombosis, are known to increase the risk of bleeding when administered before a surgical procedure. Some of the patients had no discontinuation of either medication after stent placement, placing them at an even higher risk for bleeding. The pharmacodynamics of both drugs make stopping either drug 1 to 2 days before surgery ineffective in diminishing the risk of bleeding.

Thus, stent implantation before surgery appears to be a double-edge sword. If antiplatelet drugs are withheld, the likelihood of stent thrombosis is greatly enhanced. If antiplatelet therapy is continued, the risk of postoperative bleeding is increased. Since neither of these alternatives is acceptable, elective surgery should be delayed for at least two weeks after coronary stent implantation.

Some of the patients included in this study did undergo noncardiac surgery early after stenting but did not have a major cardiac complication. Five of these patients, however, did experience excessive, but not catastrophic, bleeding complications.

The relationship between performing elective noncardiac surgery shortly after coronary stenting and the serious adverse consequences of such action has been overlooked. From the perspective of individual physicians, these disastrous events may have been perceived as single-case complications. Yet, when data from a high volume angioplasty and surgery center is revealed, the results are alarming.

In contrast to the alarming results of this study, when PTCA was performed before, or in preparation for noncardiac surgery, earlier studies have demonstrated a reduction of perioperative cardiac complications (3–6). While patients who undergo PTCA without stent placement are benefited by antiplatelet therapy, they are less prone to thrombosis than patients who do have stents implanted since aspirin alone is protective (14). The discontinuation of antiplatelet therapy in the perioperative period does not appear to be attended by the same thrombotic catastrophe that we observed in stented patients. Hence, when a coronary intervention is performed in a patient who is being considered for surgery soon after coronary intervention, efforts should be made to avoid stent placement if possible.

This review provides guidelines for the care of a patient who undergoes stent implantation and proceeds to elective noncardiac surgery. Based on those observations, cardiologists and surgeons should refrain from performing noncardiac elective operations within 14 days of coronary stenting, when interruption of the poststent antiplatelet treatment appears to directly contribute to adverse and often fatal events after surgery. In patients whose surgery is semielective or emergent, the decision to proceed with or to delay surgery should be made with full weighing of the relative risks inherent in either choice.

Study limitations. It may be argued that this study represents a retrospective observational analysis performed in a cohort that is very heterogeneous in terms of the variety of stents used, the different complexities of the interventional and surgical procedures and the variety of operators. However, we believe that the uniformity of the outcome (unfavorable) despite the heterogeneity of the cohort bespeaks a strong message and obviates the need for a randomized trial.

Conclusions. We postulate that elective noncardiac surgery should be postponed for several weeks after coronary stenting, allowing the completion of currently recommended 2 to 4 weeks of antiplatelet therapy. This would be expected to keep the acute and subacute stent thrombosis

rates equal to the general population of patients undergoing coronary stenting. Additionally, for the limitation of perioperative bleeding, it would be ideal to wait several further days for aspirin and ticlopidine to stop exerting their effects.

It should be also borne in mind that optimal "stent-like" results can be obtained by conventional balloon PTCA with ultrasound guidance (20,21) and may be a substitute for elective coronary stenting. This alternative might be ideal for CAD patients awaiting later noncardiac surgery because such an approach would at least exclude the potential hazards of aggressive two-drug antiplatelet therapy obligatory after stenting. A recent study showed that optimal balloon angioplasty with provisional stenting (used for bail-out or early loss after 30 min only) is equivalent to primary stenting in event-free survival, target vessel revascularization and restenosis at six months (22). Although not universally accepted for patients undergoing percutaneous revascularization, such approaches are at least proven feasible and safe and, thus, may supersede stenting in the specific cohort of CAD patients undergoing PTCA as a result of cardiac work-up before elective noncardiac surgery.

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