

Discontinuation of Antiplatelet Therapy prior to Low-Risk Noncardiac Surgery in Patients with Drug-Eluting Stents: A Retrospective Cohort Study

Daniel J. Brotman¹
Mihir Bakhru²
Wael Saber⁴
Ashish Aneja²
Deepak L. Bhatt³
Katherina Tillan-Martinez²
Amir K. Jaffer²

¹Hospitalist Program, Department of Medicine, Johns Hopkins Hospital, Baltimore, Maryland (DJB)

²Departments of General Internal Medicine, Section of Hospital Medicine, Cleveland Clinic, Cleveland, Ohio

³Department of Cardiology, Cleveland Clinic, Cleveland, Ohio

⁴Department of Hematology, University of Wisconsin, Madison, Wisconsin

BACKGROUND: Drug-eluting coronary stents (DESs) pose a challenge in the perioperative period. Sirolimus and paclitaxel may inhibit reendothelialization of the traumatized vessel, making it vulnerable to platelet-mediated thrombosis. Given the anecdotal evidence and case series suggesting that DESs may be more vulnerable to thrombosis on discontinuation of antiplatelet agents than are bare-metal stents, we sought to quantify this risk.

METHODS: We linked the Cleveland Clinic Heart Center database with the Cleveland Clinic Internal Medicine Preoperative Assessment Consultation and Treatment (IMPACT) Center database to identify all patients who had undergone DES placement at the Cleveland Clinic and subsequently were evaluated for noncardiac surgery between July 2003 and July 2005. Outcome measures included 30-day rate of postoperative myocardial infarction (MI), DES thrombosis, major bleeding, and all-cause mortality.

RESULTS: We identified 114 patients who underwent noncardiac surgery a median of 236 days (IQR 125-354) after stent placement. Forty-five patients (40%) underwent surgery within 180 days of stenting, 15 of whom (13%) underwent surgery within 90 days of stenting. Eighty-eight patients (77%) discontinued all antiplatelet agents a median of 10 days before surgery. No patients died. Two patients (1.8%, 95% CI 0.5%-6.2%) suffered postoperative MIs, but postoperative catheterization showed neither had DES thrombosis (0%, 95% CI 0%-3.3%). One patient developed major bleeding (0.9%, CI 0.2%-4.8%).

CONCLUSIONS: These data suggest that the overall risk of stent thrombosis is low in low-risk noncardiac surgery patients with DESs, particularly those who have undergone at least 180 days of antiplatelet therapy, even after complete discontinuation of antiplatelet agents. *Journal of Hospital Medicine* 2007;2:378-384.

© 2007 Society of Hospital Medicine.

KEYWORDS: drug-eluting stents, perioperative, antiplatelet therapy, noncardiac surgery, myocardial infarction.

There are currently limited data to guide perioperative management of antiplatelet therapy after drug-eluting stent (DES) implantation. The clinician must balance the risk of excessive bleeding if antiplatelet agents are continued perioperatively with the risk of stent thrombosis if antiplatelet agents are discontinued for surgery—a risk that may be amplified in the perioperative period because of the prothrombotic state that accompanies the stress of surgery.

Paclitaxel- and sirolimus-eluting stents have supplanted bare-metal stents as first-line treatment for coronary stenosis because of their efficacy in preventing in-stent restenosis by inhibiting

neointimal proliferation. However, the antiproliferative effects of DESs may also delay endothelialization, rendering them vulnerable to stent thrombosis when antiplatelet therapy is prematurely discontinued.¹⁻⁵ Some patients with DESs may be vulnerable to stent thrombosis when antiplatelet therapy is discontinued even after a year or more of treatment.⁶ Although stent thrombosis is uncommon, it is deadly, with a mortality rate approaching 50%.¹ Generally, antiplatelet therapy is discontinued prior to surgery. This presents a clinical dilemma for patients with DES because guidelines recommend lifelong aspirin therapy and at least 3-6 months of clopidogrel for patients who have undergone DES placement.⁷⁻⁹

In the bare-metal stent era, studies demonstrated an alarming risk of stent thrombosis in the setting of noncardiac surgery within 2-6 weeks of stent placement.^{10,11} However, the appropriate interval before elective noncardiac surgery following DES placement has not been defined and may be longer. Case reports and case series have highlighted this risk¹² and have even suggested that a DES may be susceptible to stent thrombosis as long as a year after its placement.⁶ More recently, pooled data from controlled trials have suggested that although the overall rate of DES thrombosis may not be consistently higher than that of bare-metal stents, the risk appears to persist far longer (probably from delayed endothelialization of the target vessel) and may be more pronounced following discontinuation of antiplatelet agents.^{9,13-16} This has led to recent recommendations to continue dual antiplatelet therapy (with aspirin and clopidogrel) for at least a year following DES placement and possibly indefinitely, provided that the therapy is tolerated.⁹ Whether this risk is accentuated in the perioperative setting independent of discontinuation of antiplatelet therapy remains unknown. In 1 registry, the strongest predictor of DES thrombosis was premature discontinuation of antiplatelet therapy (hazard ratio 90, 95% confidence interval 30-270, $P < .001$), and noncardiac surgery was the most frequent reason for discontinuation of antiplatelet therapy.¹ However, the actual incidence of stent thrombosis in patients undergoing surgery was unavailable because the denominator was unknown (ie, number of patients with stents who underwent surgery). Although it is certainly plausible that the prothrombotic and proinflammatory postoperative state augments the risk of stent thrombo-

sis independent of discontinuation of antiplatelet therapy alone, this remains unproven.

At the time of the present study, protocol-based clinical practice at the Cleveland Clinic Foundation's Internal Medicine Preoperative Assessment Consultation and Treatment (IMPACT) Center included routine discontinuation of all antiplatelet agents (including aspirin and clopidogrel) at least 7 days prior to noncardiac surgery, including in patients with coronary stents. Exceptions to this policy were generally made only for very minor procedures. The purpose of this study was to systematically quantify the risk of adverse cardiovascular events in patients who had DES placement and subsequently underwent elective or semielective noncardiac surgery, most of whom had discontinued all antiplatelet agents at least 7 days before surgery.

Methods

We identified all patients who had DES placement at the Cleveland Clinic who subsequently underwent preoperative evaluation for noncardiac surgery at the IMPACT Center between July 2003 and July 2005. About half the patients undergoing surgery at the Cleveland Clinic were seen in the IMPACT Center prior to surgery during the study period. Preoperative evaluation at the IMPACT Center included a standardized assessment by a hospitalist with expertise in preoperative medicine. Clinical data for each patient were contemporaneously entered into an electronic medical record. Written preoperative medication instructions were provided to each patient and documented in the electronic record, indicating specific instructions to discontinue any antiplatelet agents 7-10 days preoperatively.

The IMPACT Center database was crosslinked to the Cleveland Clinic Foundation Heart Center Database, which contains records of all patients who have undergone coronary stenting at the Cleveland Clinic. Computerized and written medical records of all patients in both databases were reviewed using a standardized data collection instrument. All medical data generated up to 30 days postoperatively at the Cleveland Clinic were reviewed. Social Security numbers were linked with the Social Security Death Index to verify that no patients died within 30 days of surgery.

Predefined outcomes included catheterization-confirmed DES thrombosis, any myocardial infarction, and major bleeding within 30 days of the sur-

gical procedure. Myocardial infarction was defined as elevation of troponin T to more than twice the upper limit of normal (0.2 mg/mL) with or without associated electrocardiographic changes or symptoms. This biochemically based definition was used with the understanding that cardiac enzyme tests are consistently ordered for patients at the Cleveland Clinic with suspected coronary events and that postoperative myocardial infarction may be atypical in presentation (eg, delirium or hypotension without chest pain). Stent thrombosis was considered present if confirmed by catheterization or autopsy and considered possible if a patient suffered from a myocardial infarction but did not have a definitive diagnostic procedure performed. DES thrombosis was considered absent if a patient underwent postoperative catheterization and the DES appeared patent. Major bleeding was defined as any bleeding requiring unplanned reoperation or bleeding in a critical location (intracranial or retroperitoneal). Invasiveness of surgery was defined prospectively according to a Cleveland Clinic bleeding classification scheme based on that of Pasternak^{17,18}:

- *Category 1.* Minimal risk to patient; little or no anticipated blood loss (eg, breast biopsy, cystoscopy).
- *Category 2.* Mild risk to patient; minimal to moderately invasive procedure; estimated blood loss < 500 cc (eg, laparoscopy, arthroscopy, hernia repair).
- *Category 3.* Moderate risk to patient and moderate to significantly invasive; blood loss potential 500-1000 cc (eg, laminectomy, total hip or knee replacement).
- *Category 4.* Major risk to patient; highly invasive procedure; anticipated blood loss > 1500 cc (eg, major spinal reconstruction, major reconstruction of GI tract, major vascular repair without intensive care unit stay).
- *Category 5.* Critical risk to patient; highly invasive procedure; anticipated blood loss > 1500 cc with anticipated postoperative intensive care unit stay (eg, cardiac procedure, major vascular repair with anticipated intensive care unit stay).

Statistical analyses were descriptive. We determined the rate of adverse outcomes with 95% confidence intervals (CIs) in the entire patient cohort and among prespecified patient subsets, based on timing of discontinuation of antiplatelet therapy. Predefined subsets included those who had clopidogrel and aspirin discontinued less than 3 months and less than 6 months following DES implantation. The χ^2 test was used to test the hypothesis that

discontinuation of antiplatelet therapy was a function of the type of surgery or timing of stent placement.

The study was approved by the Cleveland Clinic Foundation's institutional review board. The requirement for informed consent was waived.

RESULTS

In total, 114 patients were evaluated in the IMPACT Center following DES placement. Baseline patient characteristics are shown in Table 1. The median age was 71 years (interquartile range 64-76 years), and 66% were male. Patients had a moderate degree of comorbidity: 41% had diabetes, 12% had an ejection fraction < 45%, 34% had undergone coronary bypass, 17% had atrial fibrillation or flutter, and 20% had chronic renal insufficiency (creatinine \geq 2.0 or end-stage renal disease). Most patients received β -adrenergic blockers (97%), statins (95%), and either angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (77%) preoperatively. Patients underwent a variety of surgeries (Table 1).

Patients had received both paclitaxel and sirolimus stents (28% and 73% of patients, respectively); 33% of patients had had more than 1 DES (Table 2). Most patients underwent surgery within 1 year of stent placement (77%), but only 40% had surgery within 180 days of stenting and only 13% within 90 days of stenting. Most patients (77%) had antiplatelet therapy completely discontinued a median of 10 days before surgery and remained off antiplatelet therapy for a median of 14 days total. Ten of the 15 patients (67%) who underwent surgery within 90 days of stenting had all antiplatelet agents discontinued preoperatively, 24 of the 30 patients (80%) who had surgery between 91 and 180 days after stenting had antiplatelet therapy completely discontinued, and 54 of the 69 patients (78%) who had surgery more than 180 days after stenting had antiplatelet therapy completely discontinued. There was no significant relationship between timing of stent placement relative to surgery (<90, 91-180, or >180 days) and decision about whether to discontinue antiplatelet therapy ($P = .59$). However, invasiveness of the surgery was associated with antiplatelet management: 85% of those who continued antiplatelet therapy (aspirin or aspirin and clopidogrel) during the perioperative period were patients who underwent minimally invasive surgery ($P < .0001$).

The outcome events are presented in Table 3.

TABLE 1
Characteristics of Patients (n = 114)

| Characteristic | n (%) unless otherwise noted |
|--|---------------------------------|
| Demographics | |
| —Age (years), median (IQR) | 71 (64-76) |
| —Male | 75 (65.7%) |
| —White | 88 (77.2%) |
| Comorbid illnesses | |
| —Diabetes mellitus | 47 (41.2%) |
| —History of prior myocardial infarction | 48 (42.1%) |
| —Hypertension | 108 (94.7%) |
| —History of stroke or transient cerebral ischemia | 15 (13.2%) |
| —Dyslipidemia or treatment with lipid-lowering drugs | 106 (93.0%) |
| —Ejection fraction < 45% | 14 (12.3%) |
| —History of coronary artery bypass | 39 (34.2%) |
| —Atrial fibrillation or flutter | 19 (16.7%) |
| —End-stage renal disease on dialysis | 13 (11.4%) |
| —Chronic renal impairment (creatinine ≥ 2.0) without dialysis | 10 (8.8%) |
| Other medical treatments | |
| —Angiotensin converting enzyme inhibitor or angiotensin receptor blocker | 88 (77.2%) |
| —β-blocker | 111 (97.3%) |
| —Statin | 108 (94.7%) |
| Invasiveness of surgery* | |
| —Category 1 (lowest risk) | 37 (32.5%) |
| —Category 2 | 22 (19.3%) |
| —Category 3 | 48 (42.1%) |
| —Category 4 | 7 (6.1%) |
| —Category 5 (highest risk) | 0 (0%) |
| Outpatient or short-stay surgery† | 50 (47.2%) |
| Type of surgery | |
| —Major orthopedic | 39 (34.2%) |
| —Minor orthopedic | 5 (4.4%) |
| —Ophthalmologic | 30 (26.3%) |
| —General abdominal | 8 (7.0%) |
| —Gynecological | 5 (4.4%) |
| —Urological | 11 (9.6%) |
| —Head and neck | 5 (4.4%) |
| —Vascular | 1 (0.9%) |
| —Other | 10 (8.8%) |

IQR, interquartile range; DES, drug-eluting stent.

*Refer to Methods section for details on classification scheme.

†Defined as admission and discharge on the same calendar day.

Two patients (1.8%, 95% CI 0.5%-6.2%) suffered a non-ST-elevation myocardial infarction (NSTEMI) postoperatively, and another patient (0.9%, 95% CI 0.2%-4.8%) developed major bleeding, a retroperitoneal hemorrhage following kidney transplantation. This patient had been taking both aspirin and clopidogrel until 7 days prior to surgery and began to hemorrhage the day after surgery; antiplatelet agents were resumed 12 days postoperatively. No patients died (0%, 95% CI 0%-3.3%). One of the 2

TABLE 2
Stenting History, Antiplatelet Therapy, and Perioperative Management (n = 114 Patients)

| Characteristic | n (%) unless otherwise noted |
|--|------------------------------|
| Timing of surgery and antiplatelet agent discontinuation relative to Percutaneous coronary intervention | |
| —Duration of most recent intervention relative to surgery (days), median (IQR) | 236 (125-354) |
| —Surgery within 90 days of DES placement | 15 (13.2%) |
| —Surgery within 180 days of DES placement | 45 (39.5%) |
| —Surgery within 1 year of DES placement | 88 (77.2%) |
| Percutaneous Coronary Intervention History | |
| Number of drug-eluting stents | |
| 1 | 76 (66.7%) |
| 2 | 26 (22.8%) |
| 3+ | 12 (10.5%) |
| Paclitaxel stent ≥1 | 32 (28.1%) |
| Sirolimus stent ≥1 | 83 (72.8%) |
| Bare-metal stent ≥1 | 10 (8.8%) |
| Perioperative antiplatelet treatment | |
| —Clopidogrel and aspirin continued through surgery | 24 (21.1%) |
| —Aspirin alone continued through surgery | 2 (1.8%) |
| —Clopidogrel alone continued through surgery | 0 (0%) |
| —No antiplatelet treatment at time of surgery | 88 (77.2%) |
| —Among the 15 patients who had surgery within 90 days of stenting | 10 (66.7%) |
| —Among the 45 patients who had surgery within 180 days of stenting | 34 (75.6%) |
| Duration of discontinuance of aspirin | |
| —Median number of days discontinued preoperatively (IQR) | 10 (8-12) |
| —Median total duration of discontinuance [days, IQR] | 14 (10-19) |
| Duration of discontinuance of clopidogrel | |
| —Median number of days discontinued preoperatively [days, IQR] | 10 (8-13) |
| —Median number of days discontinued in total (IQR) | 14 (10-20) |

IQR, interquartile range; DES, drug-eluting stent.

patients who suffered an MI was a 72-year-old man who had had placement of a single sirolimus-eluting stent in the posterior descending artery 284 days prior to elective hip arthroplasty. He had no history of myocardial infarction but had undergone coronary bypass surgery 4 years earlier. Echocardiography showed he had aortic stenosis, with a calculated valve area of 0.9 cm². He had a baseline left ventricular ejection fraction of 45%. His preoperative cardiac medications included lovastatin, lisinopril, and atenolol; he discontinued both aspirin and clopidogrel 7 days before the surgery. His NSTEMI occurred on the day of his operation, presenting with hypotension and anterolateral ST de-

TABLE 3
Thirty-Day Outcomes in Predefined Patient Subsets

| Outcome | Entire cohort (n = 114) [all antiplatelet therapy stopped in 88 patients (77%)] | Surgery < 90 days after DES (n = 15) [all antiplatelet therapy stopped in 10 patients (67%)] | Surgery < 180 days after DES (n = 45) [all antiplatelet therapy stopped in 34 patients (76%)] |
|---------------------------|---|--|---|
| Death | 0 (0%, 0%-3.3%) | 0 (0%, 0%-20.4%) | 0 (0%, 0%-7.9%) |
| Any myocardial infarction | 2 (1.8%, 0.5%-6.2%) | 1 (6.7%, 1.2%-29.8%) | 1 (2.2%, 0.4%-11.6%) |
| DES thrombosis | 0 (0%, 0%-3.3%) | 0 (0%, 0%-20.4%) | 0 (0%, 0%-7.9%) |
| Major bleeding | 1 (0.9%, 0.2%-4.8%) | 0 (0%, 0%-20.4%) | 0 (0%, 0%-7.9%) |

Outcomes expressed as n (%; 95% confidence interval).

DES, drug-eluting stent.

pressions. His troponin T peaked at 0.48 mg/mL, with a peak creatinine kinase of 795 U/L (MB fraction 6%). His left ventricular ejection fraction was 45% on postoperative day 2 (unchanged from baseline). He was discharged on postoperative day 8 and returned for catheterization 3 weeks later, at which time he was found to have a 70% ostial lesion in a saphenous vein graft to an obtuse marginal, which was stented. The previously placed DES was widely patent. The other patient who suffered a postoperative NSTEMI was a 68-year-old man with a history of carotid artery stenting and renal artery stenosis who had undergone placement of 3 sirolimus-eluting stents in the right coronary artery 50 days prior to cervical laminectomy. He had had elective placement of the stents following a positive pharmacologic stress test. He was taking 50 mg of atenolol daily and had been taking aspirin and clopidogrel until 17 days before surgery. On postoperative day 3 he developed dyspnea, and leads V4 and V5 showed ST depressions. His troponin T peaked at 1.24 mg/mL, with a peak creatinine kinase of 879 U/L (MB fraction 6%). The patient underwent left-heart catheterization on hospital day 10. All 3 DESs were widely patent. His left ventricular ejection fraction was estimated at 65%. He was discharged on postoperative day 15. Because neither of the patients who had a postoperative NSTEMI showed evidence of stent thrombosis on catheterization, the overall rate of stent thrombosis was 0% (95% CI 0%-3.3%).

DISCUSSION

Although 2 patients in our study cohort suffered a postoperative myocardial infarction and underwent postoperative catheterization, neither was found to have stent thrombosis, and the MIs of both patients were NSTEMIs with modest cardiac enzyme elevations only. No patients died. A rate of myocardial

infarction of less than 2% is well within that expected for patients with established coronary disease undergoing noncardiac surgery.¹⁹ That most of our patients discontinued both aspirin and clopidogrel and did not receive antiplatelet agents for a median of 14 days suggests that transient termination of antiplatelet agents in the perioperative setting is not associated with high morbidity or mortality in patients with DES, even when patients have had their stents implanted in the preceding 3-6 months.

Our study builds on the limited data on this topic. One small case series examined outcomes in 38 patients who had had DES placement and subsequently underwent noncardiac surgery a median of 297 days after stenting.²⁰ None of the patients in this series suffered from stent thrombosis or myocardial infarction, but most underwent surgery without discontinuing aspirin, and 41% underwent surgery without discontinuing clopidogrel. Another recent study demonstrated a high rate of adverse cardiovascular events in patients with coronary stents who underwent noncardiac surgery up to a year after stenting, but the authors of this study did not differentiate between drug-eluting and bare-metal stents, and all patients were continued on antiplatelet agents and received parenteral antithrombotic treatment.²¹

The major strength of our study was its systematic approach. Using a computerized and comprehensive search strategy, we identified all patients who had undergone DES placement at the Cleveland Clinic who subsequently had a preoperative evaluation at the IMPACT Center. Therefore, we are confident that the number of patients in our cohort truly reflects a well-defined at-risk population, allowing for an accurate calculation of event rates. This approach contrasts sharply with prior case

reports and case series, in which the number of patients at risk was unknown. Nevertheless, these previous reports demonstrate that DES thromboses do occur and can be devastating, so even a small risk of DES thrombosis should be taken seriously. The upper bound of the 95% confidence interval of our estimate of the rate of DES thrombosis was 3.3%, so it is entirely plausible that sampling error contributed to the low rate of thrombosis that we observed.

One major limitation of our study is its sample size. Although our cohort was more than 3 times larger than the only other published cohort of DES patients undergoing noncardiac surgery,²⁰ we had only limited precision to quantify the risk of DES thrombosis. This limitation is particularly relevant for patients who have undergone stent implantation within 3-6 months of surgery, as they are the patients most likely to have incomplete reendothelialization of the stented artery. We believe that when possible it remains prudent to delay noncardiac surgery for at least 3-6 months and perhaps up to 12 months following DES implantation, in keeping with recent guidelines.^{7,8} However, for patients with conditions such as cancer whose surgery is semielective or patients with nonsurgical bleeding problems (such as gastrointestinal bleeding), our study provides at least some reassurance that short-term discontinuation of antiplatelet agents may not be as dangerous as some authors have suggested,¹ even within 3-6 months of DES placement. Another important limitation of our study is potential referral bias. At the Cleveland Clinic, most patients undergoing vascular and thoracic procedures are not evaluated at the IMPACT Center. Similarly, some of the patients with severe cardiovascular disease may also have bypassed the IMPACT Center and gone to a cardiologist for preoperative evaluation. As such, we believe our findings should not be generalized to high-risk cardiac patients or to those undergoing high-risk procedures.

A noteworthy distinction between our cohort and the cohort reported by Compton and colleagues is that in the perioperative period, most of our patients underwent complete discontinuation of antiplatelet therapy and remained off both aspirin and clopidogrel for an average of 2 weeks, whereas most patients in the other cohort were continued on antiplatelet therapy.²⁰ This highlights the continued controversy surrounding management of antiplatelet therapy in perioperative patients with established coronary disease, who are at

substantial risk for both bleeding and myocardial infarction because of the surgery.²² Our data offer little guidance on the optimal management of antiplatelet agents perioperatively because the incidence of both bleeding and thrombosis was low and whether or not patients were continued on antiplatelet agents was not random. We advocate individualized management strategies of perioperative patients with DES. Patients undergoing procedures that carry a high risk of outcome-affecting bleeding (such as brain surgery) should probably have their antiplatelet agents discontinued preoperatively, whereas those undergoing minor surgery may have their antiplatelet agents continued, provided the surgeon and the anesthesiologist are in agreement with this approach. The timing of DES placement should also be factored into this decision because recently placed stents carry a higher risk of thrombosis.

In summary, our findings clarify the risks of stent thrombosis and postoperative myocardial infarction in clinically stable patients with DES who undergo low- and intermediate-risk noncardiac surgery. Because it is unlikely to ever be ethically appropriate or logistically feasible to conduct a randomized study of patients with DES having early versus delayed noncardiac surgery, observational cohorts will have to suffice. Additional similar studies will help to validate (or refute) our findings and to more precisely quantify the risk of adverse cardiac events when patients with DES undergo surgery, which is real, feared, and potentially catastrophic but may be overestimated.

Address for correspondence and reprint requests: Amir K. Jaffer, Associate Professor of Medicine, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Department of General Internal Medicine, Section of Hospital Medicine, Cleveland Clinic, Desk A13, Cleveland, OH 44195; Fax: (216) 445-1767; E-mail: jaffera@ccf.org

Received 26 January 2007; revision received 27 March 2007; accepted 1 April 2007

REFERENCES

1. Iakovou I, Schmidt T, Bonizzi E, et al. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. *JAMA*. 2005;293:2126-230.
2. 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.
3. Kuchulakanti PK, Chu WW, Torguson R, et al. Correlates and long-term outcomes of angiographically proven stent thrombosis with sirolimus- and paclitaxel-eluting stents. *Circulation*. 2006;113:1108-1113.

4. Spertus JA, Kettelkamp R, Vance C, et al. Prevalence, predictors, and outcomes of premature discontinuation of thienopyridine therapy after drug-eluting stent placement: results from the PREMIER registry. *Circulation*. 2006;113:2803-2809.
5. Shuchman M. Trading restenosis for thrombosis? New questions about drug-eluting stents. *N Engl J Med*. 2006;355:1949-1952.
6. McFadden EP, Stabile E, Regar E, et al. Late thrombosis in drug-eluting coronary stents after discontinuation of antiplatelet therapy. *Lancet* 2004;364:1519-1521.
7. Smith SC Jr, Feldman TE, Hirshfeld JW Jr, et al. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update 2001 Guidelines for Percutaneous Coronary Intervention). *Circulation*. 2006;113:e166–e286.
8. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1999 Guidelines for the Management of Patients With Acute Myocardial Infarction). *Circulation*. 2004;110:588-636.
9. Grines CL, Bonow RO, Casey DE Jr, et al. Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. *Circulation*. 2007;115:813-818.
10. Wilson SH, Fasseas P, Orford JL, et al. Clinical outcome of patients undergoing non-cardiac surgery in the two months following coronary stenting. *J Am Coll Cardiol*. 2003;42:234-240.
11. Kaluza GL, Joseph J, Lee JR, Raizner ME, Raizner AE. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. *J Am Coll Cardiol*. 2000;35:1288-1294.
12. Murphy JT, Fahy BG. Thrombosis of sirolimus-eluting coronary stent in the postanesthesia care unit. *Anesth Analg*. 2005;101:971-973.
13. Bavry AA, Kumbhani DJ, Helton TJ, Borek PP, Mood GR, Bhatt DL. Late thrombosis of drug-eluting stents: a meta-analysis of randomized clinical trials. *Am J Med*. 2006;119:1056-1061.
14. Lagerqvist B, James SK, Stenestrand U, Lindback J, Nilsson T, Wallentin L. Long-term outcomes with drug-eluting stents versus bare-metal stents in Sweden. *N Engl J Med*. 2007;356:1009-1019.
15. Stone GW, Moses JW, Ellis SG, et al. Safety and efficacy of sirolimus- and paclitaxel-eluting coronary stents. *N Engl J Med*. 2007;356:998-1008.
16. Spaulding C, Daemen J, Boersma E, Cutlip DE, Serruys PW. A pooled analysis of data comparing sirolimus-eluting stents with bare-metal stents. *N Engl J Med*. 2007;356:989-997.
17. Pasternak LR. Preoperative assessment: guidelines and challenges. *Acta Anaesthesiol Scand Suppl*. 1997;111:318-320.
18. Pasternak LR. Preoperative assessment of the ambulatory and same day admission patient. *Wellcome Trends Anesthesiol*. 1991;9:3-11.
19. Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation*. 1999;100:1043-1049.
20. Compton PA, Zankar AA, Adesanya AO, Banerjee S, Brilakis ES. Risk of noncardiac surgery after coronary drug-eluting stent implantation. *Am J Cardiol*. 2006;98:1212-1213.
21. Vicenzi MN, Meislitzer T, Heitzinger B, Halaj M, Fleisher LA, Metzler H. Coronary artery stenting and non-cardiac surgery—a prospective outcome study. *Br J Anaesth*. 2006;96:686-693.
22. Yan BP, Gurvitch R, Ajani AE. Double jeopardy: balance between bleeding and stent thrombosis with prolonged dual antiplatelet therapy after drug-eluting stent implantation. *Cardiovasc Revasc Med*. 2006;7:155-158.