

STATE-OF-THE-ART PAPER

Perioperative Management of Patients With Coronary Stents

Emmanouil S. Brilakis, MD, PhD, FACC,* Subhash Banerjee, MD, FACC,*
Peter B. Berger, MD, FACC†

Dallas, Texas; and Danville, Pennsylvania

Perioperative coronary stent thrombosis is a catastrophic complication that can occur in patients receiving both bare-metal and drug-eluting stents. Noncardiac surgery appears to increase the risk that recently-placed stents thrombose, especially when surgery is performed early after stenting, and particularly if dual antiplatelet therapy is discontinued. We reviewed the existing data about the frequency of stent thrombosis after noncardiac surgery and explored the impact of delay from surgery and discontinuation of antiplatelet therapy. We also reviewed the data about the impact of preoperative revascularization in patients known to require noncardiac surgery. Based on these published data, we offer recommendations that can be used to guide the treatment of patients who require noncardiac surgery after having received a stent. (J Am Coll Cardiol 2007;49:2145–50) © 2007 by the American College of Cardiology Foundation

Coronary revascularization before noncardiac surgery may decrease the perioperative and postoperative risk in selected patients (1). The number of percutaneous coronary interventions (PCIs) now exceeds the number of coronary artery bypass surgeries performed each year, and the difference continues to grow. Stents currently are used in the majority of PCIs because they increase procedural success and decrease restenosis (2). A rare but severe complication after coronary stent implantation is stent thrombosis (3). Stent thrombosis is associated with a suboptimal angiographic result (4–6), specific high-risk lesion characteristics (such as small vessels [7–9] and bifurcation lesions [3]), high-risk patients such as those with diabetes and renal failure (3), and, importantly, early cessation of dual antiplatelet therapy with aspirin and a thienopyridine (3,10). Obtaining a good angiographic result and administering dual antiplatelet therapy (11) (currently aspirin and clopidogrel) are the cornerstones of stent thrombosis prevention.

Noncardiac surgery and most invasive procedures increase the risk of stent thrombosis, especially when the procedure is performed early after stent implantation, likely because stents are not yet endothelialized early after placement, because antiplatelet therapy is often discontinued in the

periprocedural period, and because surgery creates a prothrombotic state (12); this may be particularly true when done under general anesthesia compared with regional anesthesia (13). Perioperative stent thrombosis has been studied primarily in patients who received bare-metal stents (BMS). There are limited data about the risk of perioperative thrombosis of drug-eluting stents (DES), even though DES currently are used in 70% to 80% of PCI procedures in the U.S. Clinicians caring for patients with coronary stents who need surgery often have difficulty choosing a treatment strategy that allows the surgery to be as safe as possible while minimizing the risk of perioperative stent thrombosis. The goal of this review is to offer guidance to clinicians by summarizing the available data on the incidence, risk factors, prevention, and treatment of perioperative coronary stent thrombosis.

Risk of Surgery After Stent Implantation

BMS. The high risk of surgery early after coronary stenting was first described in 2000 (14): 8 of the 25 patients undergoing noncardiac surgery within 2 weeks of BMS placement died (32%, 95% confidence interval (CI) 15 to 54). In contrast, none of the 15 patients who underwent surgery 15 to 39 days after stenting died. Six of the 8 deaths were caused by acute myocardial infarction (AMI) and 2 were caused by bleeding (14). A total of 7 patients had AMI that was probably or definitely caused by stent thrombosis, and 6 of them died. Three of the 5 patients who underwent operations while taking ticlopidine died, 1 from bleeding and 2 from AMI and bleeding.

In a much larger population of patients undergoing surgery within 2 months after receiving a BMS at the Mayo Clinic, only 8 of the 207 patients (3.9%, 95% CI 1.7 to 7.5)

From the *Division of Cardiovascular Diseases, University of Texas Southwestern Medical Center, and Dallas VA Medical Center, Dallas, Texas; and †Geisinger Clinic, Danville, Pennsylvania. Dr. Brilakis received support from the Clark R. Gregg Fund, the Harris Methodist Health Foundation, and a Veterans Affairs VISN 17 startup award. Dr. Berger has received research support from Conor Medsystems; honoraria for speaking at continuing medical education-approved scientific symposia supported by Bristol-Myers Squibb, Sanofi-Aventis, and Lilly/Daiichi-Sankyo; honoraria from Biogen and Schering-Plough; and has served as a consultant to Cordis/Johnson & Johnson and Boston Scientific.

Manuscript received December 12, 2006; revised manuscript received February 21, 2007, accepted February 27, 2007.

Abbreviations and Acronyms

AMI	= acute myocardial infarction
BMS	= bare-metal stent(s)
CI	= confidence interval
DES	= drug-eluting stent(s)
PCI	= percutaneous coronary intervention
PES	= paclitaxel-eluting stent(s)
SES	= sirolimus-eluting stent(s)

died or suffered an AMI or stent thrombosis (15). In contrast to the study by Kaluza et al. (14), the risk of death, MI, or stent thrombosis was elevated for 6 weeks, not for just 2 weeks, and to a much lesser degree, with the risk during each of the first 6 weeks ranging from 3.8% to 7.1%; no events occurred among the 39 patients who underwent surgery in the 6th through 8th weeks after stent placement.

Another study analyzed the outcome of 27 patients who underwent noncardiac surgery

within 3 weeks after BMS implantation (16). Six of 7 patients (86%), in whom the thienopyridine was stopped for >5 days died (only 1 patient had angiographically documented stent thrombosis) compared with only 1 of the 20 patients (5%) who underwent noncardiac surgery within 3 weeks from stent implantation and continued to take a thienopyridine ($p < 0.001$). Among 20 patients undergoing surgery 3 weeks to 3 months after stenting (70% of whom continued taking a thienopyridine), only 1 patient died (5%), and 2 suffered a non-ST-segment elevation AMI.

In another series, thrombotic events or major bleeding occurred in 8 of 16 patients (50%) undergoing noncardiac surgery within 42 days after receiving a BMS, and in none of 40 patients who underwent surgery >42 days after receiving a BMS (17). Vicenzi et al. (18) reported a 43% frequency of adverse cardiac events in 103 patients undergoing surgery after stent deployment, but those events were poorly characterized.

These studies have appropriately increased attention to the potential risks of surgery early after stent implantation, and highlighted the importance of delaying surgery when possible and continuing dual antiplatelet therapy in the perioperative period when surgery is not delayed.

DES. There are limited data about the risk of noncardiac surgery after DES placement. McFadden et al. (19) reported DES thrombosis in 3 patients undergoing surgery (bladder polyp resection, colon cancer resection, and colonoscopy with polypectomy) late (343 to 442 days) after implantation. Nasser et al. (20) reported sirolimus-eluting stent (SES) thrombosis in 2 patients after surgery performed 4 and 21 months after SES implantation.

Compton et al. (21) reported a single-center series of 38 patients who underwent 41 major and 18 minor noncardiac surgeries a median of 9 months from successful DES implantation: no major adverse cardiac events or deaths occurred during or after the 41 major (0%, 95% CI 0 to 9%), and 18 minor noncardiac surgical procedures (0%, 95% CI 0 to 19%). Schouten et al. (22) reported that stent thrombosis occurred in 3 of 99 (3%) patients undergoing surgery within 2 years after DES implantation. Bakhru et al. (23) reported no stent thrombosis among 114 patients undergo-

ing noncardiac surgery after a median of 236 days from stent placement.

Although stent thrombosis can occur before surgery (caused by cessation of antiplatelet therapy), most (24) stent thromboses occur during or after the surgical procedure.

Prevention of Perioperative Stent Thrombosis

Perioperative stent thrombosis could be prevented by: 1) avoiding preoperative revascularization; 2) revascularizing patients without using stents; 3) appropriate selection of the type of stent to be implanted; 4) delaying surgery after stent implantation; 5) continuing antiplatelet therapy throughout the perioperative period or only discontinuing it briefly; and 6) improving awareness of this catastrophic complication among all physicians involved in the care of these patients (Fig. 1).

Avoiding preoperative revascularization. Many patients with coronary disease who require noncardiac surgery do not benefit from preoperative revascularization. The CARP (Coronary Artery Revascularization Prophylaxis) trial enrolled 510 stable patients with angiographic coronary artery disease (one-third had 3-vessel disease) undergoing major vascular surgery (33% abdominal aortic aneurysm repair and 67% lower extremity revascularization) (25). Patients with significant left main disease, unstable coronary syndromes, and severe cardiomyopathy were excluded. Patients were randomized to revascularization versus no revascularization before surgery. Revascularization was accomplished with coronary bypass surgery in 41% and with PCI in 59%. Patients who did or did not undergo revascularization had a similar incidence of postoperative AMI (8.4% vs. 8.4%, $p = 0.99$) and survival after a median of 27 months from randomization (78% vs. 77%, $p = 0.98$).

Therefore, if a patient with coronary disease is known to require surgery, the first question to ask is whether the patient really needs revascularization. The CARP study results suggest that revascularization may not be necessary for a large number of patients without an unstable coronary syndrome or other very high-risk features. This is further supported by the findings of a recent pilot study of 103 patients with extensive ischemia undergoing vascular surgery, in whom preoperative revascularization did not improve postoperative outcomes (26).

Revascularization without stents (balloon only). Despite the CARP study, many patients are believed to require revascularization before noncardiac surgery, such as patients with acute coronary syndromes or with profound ischemia on noninvasive testing at a heart rate and blood pressure likely to be exceeded in the perioperative period. Although stents are currently used in the vast majority of PCIs, coronary revascularization may be more safely performed in such patients without stents, either with coronary artery bypass grafting or percutaneously with balloon angioplasty.

In an early study of 50 patients undergoing noncardiac surgery after a median of 9 days from balloon angioplasty,

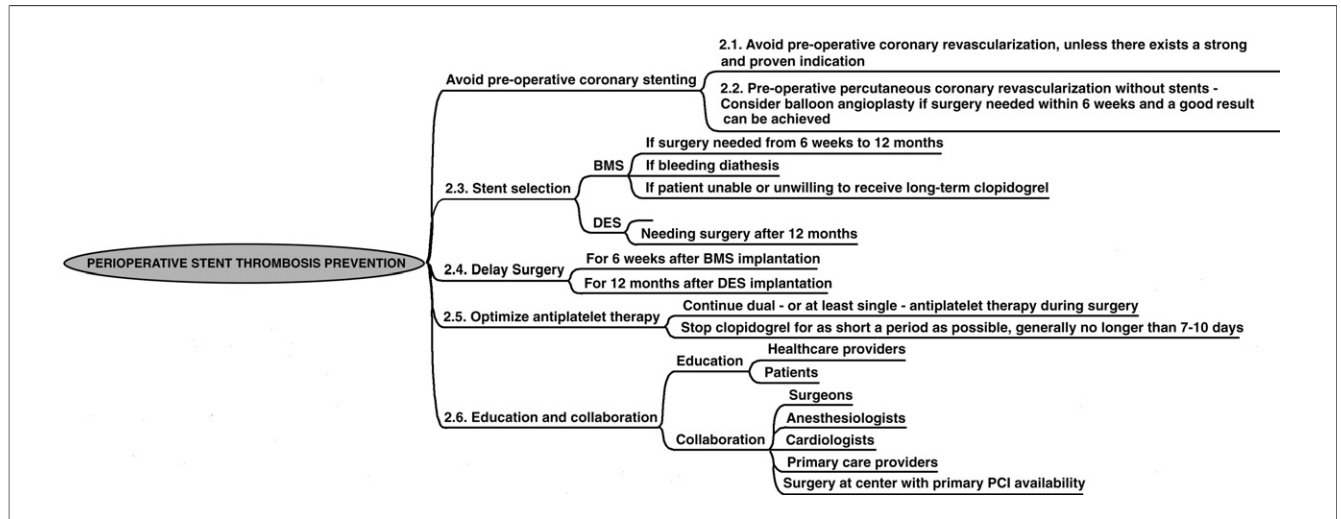


Figure 1 Perioperative Stent Thrombosis Prevention Strategies

Outline of different strategies to prevent perioperative stent thrombosis. BMS = bare-metal stents; DES = drug-eluting stents; PCI = percutaneous coronary intervention.

the postoperative mortality and MI rates were 1.9% and 5.6%, respectively (27). In a study of 194 patients undergoing aortic abdominal surgery, carotid endarterectomy or peripheral vascular surgery after a median time of 11 days from balloon angioplasty, only 1 patient died (0.5%) and 1 patient suffered an AMI (0.5%) (28). In the largest study, in which 350 patients underwent noncardiac surgery in the 2 months after a successful balloon angioplasty procedure, only 3 of the 350 patients (0.9%, 95% CI 0.2% to 2.5%) died in the perioperative period (n = 1) or suffered a myocardial infarction (n = 2) (29).

Therefore, revascularization with balloon angioplasty may be safer than stent placement before planned noncardiac surgery, especially if a good angiographic result can be achieved, and particularly if the noncardiac surgery is planned early (within 4 to 6 weeks) after revascularization.

According to the 2002 American College of Cardiology/American Heart Association guidelines on perioperative cardiovascular care, “there is uncertainty regarding how much time should pass before noncardiac surgery is performed” for patients undergoing preoperative balloon angioplasty (1). Delaying noncardiac surgery for >6 to 8 weeks was discouraged because restenosis could have occurred, leading to perioperative ischemia or MI. However, performing noncardiac surgery too early after the PCI also may be risky because acute or subacute closure after balloon angioplasty usually occurs within hours to days after the procedure. Accordingly, the guidelines emphasize that delaying surgery “for at least a week after balloon angioplasty to allow for healing of the vessel injury at the balloon treatment site has theoretical benefits.”

Stent selection before surgery. Sometimes stenting cannot be avoided during PCI, either because of the complexity of the lesion or because of the inability to achieve an optimal

result with balloon angioplasty. The type of stent selected should be heavily influenced by the timing of surgery.

If surgery needs to be performed within 12 months from revascularization, then BMS implantation is likely preferable to DES, because BMS endothelialize more rapidly and may therefore carry a lower risk of stent thrombosis. This is particularly likely if dual antiplatelet therapy cannot be continued through the perioperative period. If restenosis, which is more likely to occur after BMS than DES, does develop, it almost always does so more than 2 to 3 months after stent placement, at which point the patient already will have undergone the surgical procedure. At that time, a DES could be used to treat the in-stent restenosis.

If surgery can be delayed for more than 12 months, then placement of a DES may not be inappropriate, although there are data suggesting that DES may have a greater risk of late stent thrombosis than BMS beyond 12 months after implantation, particularly in the perioperative period (19). If placement of a DES is planned, it may be preferable to use a sirolimus-eluting stent, which requires a minimum of 3 months of clopidogrel after placement (30), than a paclitaxel-eluting stent (PES), which requires at least 6 months of clopidogrel (31). However, little is known about the safety of surgery performed 6 to 12 months from DES implantation. An alternative approach would be placement of a heparin-coated stent (which is not considered a DES because the heparin does not elute off of the stent); such an approach is logical but unproven, because heparin-coated stents have not been shown to reduce the frequency of stent thrombosis in any situation with any medical regimen, let alone in the perioperative period. In the future, new stent types, such as bioresorbable stents or antibody-coated stents that can attract endothelial progenitor cells and re-

endothelialize more rapidly, may minimize the risk of stent thrombosis.

Regardless of the type of stent used, every effort should be made to optimally deploy the stent, which reduces the risk of stent thrombosis (4,6). Overlap of DES should be avoided because overlapping may delay their endothelialization significantly (32,33).

Delay of surgery. The earlier the surgery is performed after stenting, the higher the risk for stent thrombosis (14-17). According to the American College of Cardiology/American Heart Association guidelines, noncardiac surgery should be "delayed for at least 2 and ideally 4 weeks after BMS implantation to allow for at least partial endothelialization of the stent" (1). The best data suggest that delaying surgery for 6 weeks may be even better than 4 weeks (15). The optimal delay after implantation of a DES before surgery remains unknown but is likely to be more than 12 months (Fig. 1), particularly if antiplatelet therapy must be discontinued for the surgical procedure.

Antiplatelet therapy in the perioperative period. Dual antiplatelet therapy is the cornerstone of stent thrombosis prevention (11). The current recommendations that clopidogrel be administered for 3 months after placement of an SES and 6 months after placement of a PES are based on the duration of time that a thienopyridine was required in the pivotal trials of these stents that led to their approval; those durations were largely chosen empirically. Although an observational study showed reduced risk of death or MI when clopidogrel was continued up to 2 years after DES implantation (34), the optimal duration of clopidogrel required to prevent late DES thrombosis is unknown.

Antiplatelet treatment strategies to minimize perioperative stent thrombosis include:

- Continue dual antiplatelet therapy during and after surgery
- Discontinue clopidogrel but "bridge" the patient to surgery using a short-acting antiplatelet agent with a glycoprotein IIb/IIIa inhibitor or an antithrombin, and restart clopidogrel as soon as possible after surgery
- Discontinue clopidogrel before surgery and restart it as soon as possible after surgery

CONTINUE DUAL ANTIPLATELET THERAPY DURING SURGERY. This option would likely be associated with the lowest frequency of stent thrombosis, especially in patients undergoing surgery early after stent implantation. Surgeons who are concerned about the risk of perioperative bleeding may need help weighing the risk of bleeding with the particular operation planned against the benefits of continuing dual antiplatelet therapy throughout the perioperative period. In some procedures, such as dental extractions (35), cataract surgery (36), or routine dermatologic surgery (37), bleeding almost always can be controlled with local measures, and discontinuation of antiplatelet therapy is not necessary (38). Even in procedures with higher bleeding risk, when surgeons are informed that stent thrombosis

leads to death or a large MI in the majority of patients (39), and that the best available data suggest a greatly increased risk of stent thrombosis in patients undergoing surgery shortly after stent placement when dual antiplatelet therapy is discontinued, they often can be persuaded that the risk of thrombosis outweighs the risk of bleeding. This strategy would not be appropriate for patients in whom any excess bleeding could have catastrophic consequences, such as neurosurgery patients.

STOP CLOPIDOGREL AND "BRIDGE" THE PATIENT WITH A SHORT-ACTING ANTIPLATELET OR ANTITHROMBOTIC AGENT. Thienopyridines cause irreversible platelet inhibition, and need to be discontinued for 5 to 10 days to allow the production and release into the circulation of new platelets to replace the inhibited platelets and restore normal hemostasis. If surgery is needed early after stent placement and clopidogrel needs to be stopped, some clinicians "bridge" the patient to surgery using a short-acting antiplatelet agent or an anticoagulant. Because stent thrombosis is primarily a platelet-mediated phenomenon, platelet inhibitors might be a more logical choice if such a strategy is pursued. Furthermore, the cessation of heparin in a patient not on aspirin or other antiplatelet agents has been shown to cause platelet activation and a rebound phenomenon which may actually increase the likelihood of perioperative stent thrombosis compared to if no heparin bridging had been performed. However, it must be emphasized that admitting a patient to a hospital before surgery to bridge them to surgery does not offer complete protection because the greatest risk of stent thrombosis is actually during or after surgery. More data are needed that indicate that such a strategy improves outcome because this strategy is expensive, is logistically difficult, and exposes the patient to the risks associated with a prolonged hospitalization.

STOP CLOPIDOGREL AND RESTART IT AFTER SURGERY. This strategy may be sufficient when the stent is believed to be fully endothelialized and the risk of stent thrombosis is very low. It also should be used whenever clopidogrel cannot be continued throughout the perioperative period, such as in patients undergoing neurosurgery, in whom bleeding would likely be catastrophic. There is variability in the rate at which DES are re-endothelialized, and the risk of stent thrombosis may persist in some patients for many months or longer, especially in the prothrombotic state induced by surgery (19). Once the surgeon permits the re-initiation of clopidogrel, it might be wisest to administer a 600-mg loading, which not only reduces the time required to achieve maximal inhibition of platelet aggregation to 2 to 4 h, but also reduces the frequency of hyporesponsiveness to clopidogrel, particularly among patients with activated platelets as is uniformly the case among patients who have just undergone surgery.

The aforementioned recommendations are largely empiric and are based on indirect data, but they are mechanis-

tically sound and logical, and the consequences of perioperative stent thrombosis are severe.

Education and a team approach. Given the morbidity and mortality associated with stent thrombosis, there is a need for continuing education of physicians, particularly noncardiologists, about the perioperative risks of patients with coronary stents. The need to delay elective surgery whenever possible after stent implantation cannot be overemphasized. In a survey of anesthesiologists, 63% were not aware of recommendations about the appropriate length of time between stent placement and a subsequent surgical procedure, and one-third recommended no delay or a delay of only 1 to 2 weeks, which is insufficient for BMS, and even more so for DES (40).

Anesthesiologists and surgeons should be alerted to the high risk of stent thrombosis in patients who have received coronary stents (41). They should:

- Determine the type (BMS, SES, PES) and location in the coronary circulation of stents placed in their patient, and the date of implantation
- Consult with an interventional cardiologist and, whenever possible, with the patient's cardiologist
- Arrive at a joint decision with input from anesthesiologists, cardiologists, and surgeons about the timing of surgery and the most appropriate management of the patient's antiplatelet regimen
- Ideally, perform surgery in centers with 24-h interventional cardiology coverage so that stent thrombosis, if it occurs, could be treated with immediate PCI

Treatment of Perioperative Stent Thrombosis

Stent thrombosis is most often manifest as an ST-segment elevation acute myocardial infarction, and is best treated with early reperfusion. Thrombolytic therapy is less effective at restoring reperfusion than primary PCI among all patients and—although unproven—may be even less effective among patients with stent thrombosis, which is a platelet-mediated phenomenon. Moreover, thrombolytic therapy often carries a prohibitive risk of bleeding in the perioperative period. Primary PCI is, therefore, the treatment of choice for perioperative stent thrombosis, although it also carries increased risk of bleeding when performed early after surgery because antithrombin and antiplatelet agents need to be administered during the procedure. Yet, all that is required in patients with an acute coronary occlusion caused by stent thrombosis or any other cause who are at increased risk of bleeding is aspirin and 1 dose of an anticoagulant such as heparin or bivalirudin. In a retrospective analysis of 48 patients with acute myocardial infarction occurring within 1 week from surgery in whom aspirin and heparin were administered, survival with an early invasive strategy was 65%, which is encouraging given the high frequency of cardiogenic shock and cardiac arrest in the study population (42). Only 1 patient had significant bleeding at the operative site, a patient who had undergone knee replacement. Pa-

tients who had recently had brain and thoracic surgery were included in this series.

Conclusions

Perioperative coronary stent thrombosis is a catastrophic occurrence. The risk of stent thrombosis seems to be low when surgery is delayed for at least 4 to 6 weeks after implantation of a BMS. The risk of stent thrombosis after DES implantation remains poorly studied, but may occur even in patients who have completed the recommended duration of antiplatelet therapy (3 months for SES and 6 months for PES) and subsequently undergo surgery, in most cases after stopping aspirin and clopidogrel.

If major noncardiac surgery is planned within 1 month and certainly within 2 weeks, stent implantation generally should be avoided. If revascularization is required, then balloon angioplasty or coronary bypass surgery might well be preferred options. If surgery is planned between 1 and 12 months, particularly if complex anatomy is present, then BMS implantation may be preferable. If surgery is planned after 12 months, DES implantation may be an acceptable option. Awareness, prevention, and early treatment of perioperative stent thrombosis are best achieved by collaboration between surgeons, anesthesiologists, and cardiologists.

Acknowledgment

The authors acknowledge the contribution of Michele Roesle, RN, in this manuscript preparation.

Reprint requests and correspondence: Dr. Emmanouil S. Brilakis, Dallas VA Medical Center (111A), 4500 South Lancaster Road, Dallas, Texas 75216. E-mail: emmanouil.brilakis@utsouthwestern.edu.

REFERENCES

1. Eagle KA, Berger PB, Calkins H, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). *Circulation* 2002;105:1257–67.
2. Al Suwaidi J, Berger PB, Holmes DR Jr. Coronary artery stents. *JAMA* 2000;284:1828–36.
3. Iakovou I, Schmidt T, Bonizzoni E, et al. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. *JAMA* 2005;293:2126–30.
4. Cheneau E, Leborgne L, Mintz GS, et al. Predictors of subacute stent thrombosis: results of a systematic intravascular ultrasound study. *Circulation* 2003;108:43–7.
5. Cutlip DE, Baim DS, Ho KK, et al. Stent thrombosis in the modern era: a pooled analysis of multicenter coronary stent clinical trials. *Circulation* 2001;103:1967–71.
6. Fujii K, Carlier SG, Mintz GS, et al. Stent underexpansion and residual reference segment stenosis are related to stent thrombosis after sirolimus-eluting stent implantation: an intravascular ultrasound study. *J Am Coll Cardiol* 2005;45:995–8.
7. Hausleiter J, Kastrati A, Mehilli J, et al. Predictive factors for early cardiac events and angiographic restenosis after coronary stent placement in small coronary arteries. *J Am Coll Cardiol* 2002;40:882–9.

8. Mehilli J, Dibra A, Kastrati A, Pache J, Dirschinger J, Schomig A. Randomized trial of paclitaxel- and sirolimus-eluting stents in small coronary vessels. *Eur Heart J* 2006;27:260-6.
9. Ardissino D, Cavallini C, Bramucci E, et al. Sirolimus-eluting vs. uncoated stents for prevention of restenosis in small coronary arteries: a randomized trial. *JAMA* 2004;292:2727-34.
10. Ong AT, McFadden EP, Regar E, deJaegere PP, vanDomburg RT, Serruys PW. Late angiographic stent thrombosis (LAST) events with drug-eluting stents. *J Am Coll Cardiol* 2005;45:2088-92.
11. Leon MB, Baim DS, Popma JJ, et al. A clinical trial comparing three antithrombotic-drug regimens after coronary-artery stenting. Stent Anticoagulation Restenosis Study Investigators. *N Engl J Med* 1998;339:1665-71.
12. Sautter RD, Myers WO, Ray JF 3rd, Wenzel FJ. Relationship of fibrinolytic system to postoperative thrombotic phenomena. *Arch Surg* 1973;107:292-6.
13. Rosenfeld BA, Beattie C, Christopherson R, et al. The effects of different anesthetic regimens on fibrinolysis and the development of postoperative arterial thrombosis. Perioperative Ischemia Randomized Anesthesia Trial Study Group. *Anesthesiology* 1993;79:435-43.
14. Kaluza GL, Joseph J, Lee JR, Raizner ME, Raizner AE. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. *J Am Coll Cardiol* 2000;35:1288-94.
15. Wilson SH, Fasseas P, Orford JL, et al. Clinical outcome of patients undergoing noncardiac surgery in the two months following coronary stenting. *J Am Coll Cardiol* 2003;42:234-40.
16. Sharma AK, Ajani AE, Hamwi SM, et al. Major noncardiac surgery following coronary stenting: when is it safe to operate? *Catheter Cardiovasc Interv* 2004;63:141-5.
17. Reddy PR, Vaitkus PT. Risks of noncardiac surgery after coronary stenting. *Am J Cardiol* 2005;95:755-7.
18. Vicenzi MN, Meislitz T, Heitzinger B, Halaj M, Fleisher LA, Metzler H. Coronary artery stenting and noncardiac surgery—a prospective outcome study. *Br J Anaesth* 2006;96:686-93.
19. 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.
20. Nasser M, Kapeliovich M, Markiewicz W. Late thrombosis of sirolimus-eluting stents following noncardiac surgery. *Catheter Cardiovasc Interv* 2005;65:516-9.
21. Compton PA, Zankar AA, Adesanya AO, Banerjee S, Brilakis ES. Risk of noncardiac surgery after coronary drug-eluting stent implantation. *Am J Cardiol* 2006;98:1212-3.
22. Schouten O, vanDomburg RT, Bax JJ, et al. Noncardiac surgery after coronary stenting: early surgery and interruption of antiplatelet therapy are associated with an increase in major adverse cardiac events. *J Am Coll Cardiol* 2007;49:122-4.
23. Bakhru M, Saber W, Brotman D, et al. Is discontinuation of antiplatelet therapy after 6 months safe in patients with drug-eluting stents undergoing noncardiac surgery? *Cleve Clin J Med* 2006;73:S23.
24. Fleron MH, Dupuis M, Mottet P, LeFeuvre C, Godet G. Non cardiac surgery in patient with coronary stenting: think sirolimus now! *Ann Fr Anesth Reanim* 2003;22:733-5.
25. McFalls EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery. *N Engl J Med* 2004;351:2795-804.
26. Poldermans D, Schouten O, Vidakovic R, et al., DECREASE Study Group. A clinical randomized trial to evaluate the safety of a noninvasive approach in high-risk patients undergoing major vascular surgery: the DECREASE-V pilot study. *J Am Coll Cardiol* 2007;49:1763-9.
27. Huber KC, Evans MA, Bresnahan JF, Gibbons RJ, Holmes DR Jr. Outcome of noncardiac operations in patients with severe coronary artery disease successfully treated preoperatively with coronary angioplasty. *Mayo Clin Proc* 1992;67:15-21.
28. Gottlieb A, Banoub M, Sprung J, Levy PJ, Beven M, Mascha EJ. Perioperative cardiovascular morbidity in patients with coronary artery disease undergoing vascular surgery after percutaneous transluminal coronary angioplasty. *J Cardiothorac Vasc Anesth* 1998;12:501-6.
29. Brilakis ES, Orford JL, Fasseas P, et al. Outcome of patients undergoing balloon angioplasty in the two months prior to noncardiac surgery. *Am J Cardiol* 2005;96:512-4.
30. Morice MC, Serruys PW, Sousa JE, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N Engl J Med* 2002;346:1773-80.
31. Stone GW, Ellis SG, Cox DA, et al. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med* 2004;350:221-31.
32. Finn AV, Kolodgie FD, Harnek J, et al. Differential response of delayed healing and persistent inflammation at sites of overlapping sirolimus- or paclitaxel-eluting stents. *Circulation* 2005;112:270-8.
33. Chu WW, Kuchulakanti PK, Torguson R, et al. Impact of overlapping drug-eluting stents in patients undergoing percutaneous coronary intervention. *Catheter Cardiovasc Interv* 2006;67:595-9.
34. Eisenstein EL, Anstrom KJ, Kong DF, et al. Clopidogrel use and long-term clinical outcomes after drug-eluting stent implantation. *JAMA* 2007;297:159-68.
35. Valerin M, Brennan M, Noll J, et al. Relationship between aspirin use and postoperative bleeding from dental extractions in a healthy population. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006;102:326.
36. Kumar N, Jivan S, Thomas P, McLure H. Sub-Tenon's anesthesia with aspirin, warfarin, and clopidogrel. *J Cataract Refract Surg* 2006;32:1022-5.
37. Alam M, Goldberg LH. Serious adverse vascular events associated with perioperative interruption of antiplatelet and anticoagulant therapy. *Dermatol Surg* 2002;28:992-8; discussion 998.
38. 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. *J Am Coll Cardiol* 2007;49:734-9.
39. Orford JL, Lennon R, Melby S, et al. Frequency and correlates of coronary stent thrombosis in the modern era: analysis of a single center registry. *J Am Coll Cardiol* 2002;40:1567-72.
40. Patterson L, Hunter D, Mann A. Appropriate waiting time for noncardiac surgery following coronary stent insertion: views of Canadian anesthesiologists. *Can J Anaesth* 2005;52:440-1.
41. Dupuis JY, Labinaz M. Noncardiac surgery in patients with coronary artery stent: what should the anesthesiologist know? *Can J Anaesth* 2005;52:356-61.
42. Berger PB, Bellot V, Bell MR, et al. An immediate invasive strategy for the treatment of acute myocardial infarction early after noncardiac surgery. *Am J Cardiol* 2001;87:1100-2.