



## Q: How soon can a patient undergo noncardiac surgery after receiving a drug-eluting stent?

### HOWARD H. WEITZ, MD

Vice Chairman, Department of Medicine, Jefferson Medical College of Thomas Jefferson University; Co-Director, Jefferson Heart Institute, Philadelphia, PA

**A:** Because patients who receive a stent require antiplatelet therapy after stent implantation, the timing of noncardiac surgery presents a difficult problem, complicated by the advent of drug-eluting stents. These stents often require a longer period of antiplatelet therapy than bare-metal stents.

Unfortunately, at present we have no direct data to guide us in the care of patients with drug-eluting stents who need noncardiac surgery. Our approach to the timing of noncardiac surgery and to perioperative care for these patients is based on data from patients with bare-metal stents who underwent noncardiac surgery and from patients receiving antiplatelet therapy for acute coronary syndromes who subsequently underwent coronary surgery.

#### ■ SOON, MOST STENTS WILL BE DRUG-ELUTING

Drug-eluting stents have dramatically decreased the incidence of coronary artery restenosis after coronary angioplasty. The restenosis rate—30% to 40% with angioplasty without stenting—has declined to 20% to 30% with bare-metal stents, and to less than 10% with drug-eluting stents. We foresee that soon nearly all patients who undergo coronary angioplasty in the United States will have a stent implanted as part of the procedure, and most of these stents will be drug-eluting.

#### ■ WHEN IS NONCARDIAC SURGERY SAFE AFTER BARE-METAL STENTING?

Kaluza et al<sup>1</sup> observed an extraordinarily high incidence of adverse events among 40

patients who underwent noncardiac surgery less than 6 weeks after they received bare-metal coronary stents: 7 myocardial infarctions, 11 major bleeding episodes, and 8 deaths. All of the deaths and myocardial infarctions and 8 of the 11 bleeding episodes were in patients who underwent surgery less than 14 days after stenting. The authors postulated that the high rates of myocardial infarction and death were due to stent thrombosis as a result of stopping antiplatelet therapy (aspirin plus ticlopidine) in anticipation of surgery. Perioperative hemorrhage was most common in patients whose noncardiac surgery took place while they were receiving combination antiplatelet therapy.

The authors concluded that noncardiac surgery should be delayed for 2 to 4 weeks after bare-metal stent implantation to allow patients to complete their combination antiplatelet therapy.


In a subsequent retrospective study,<sup>2</sup> Wilson et al reported lower rates of major adverse cardiac events than those reported by Kaluza et al<sup>1</sup>: only eight deaths, myocardial infarctions, or cases of stent thrombosis among 207 patients who underwent noncardiac surgery within 2 months of stent placement. All of the events were in patients whose surgery was within 6 weeks after stenting. The authors recommended that surgery be delayed for 6 weeks to allow a full course of antiplatelet therapy to be completed and for platelet function to return to normal.

#### ■ DURATION OF ANTIPLATELET THERAPY AFTER DRUG-ELUTING STENTING

Four randomized trials have shown that drug-eluting stents are effective and pose a low risk of thrombosis.<sup>3-6</sup>

Because of the potential risk of delayed

Drug-eluting stents often require longer antiplatelet therapy than bare-metal stents



endothelialization with stent thrombosis, patients in these studies received a prolonged course of combination antiplatelet therapy after the stent was placed (aspirin and a thienopyridine derivative, most often clopidogrel). Two European trials of sirolimus-eluting (Cypher) stents used antiplatelet combination therapy for 2 months; a US trial used it for 3 months. The trial of the paclitaxel-eluting (Taxus) stent used a 6-month course of combination antiplatelet therapy.

The US Food and Drug Administration therefore approved the sirolimus-eluting stent for use with a 3-month course of post-deployment combination antiplatelet therapy, and the paclitaxel-eluting stent with a 6-month course. In Europe, implantation of a sirolimus-coated stent is typically followed by a 2-month course of combination antiplatelet therapy.

#### ■ RISK OF BLEEDING WITH SURGERY WHILE ON ANTIPLATELET THERAPY

The combination of clopidogrel and aspirin increases the risk of postoperative bleeding and the need for transfusion in patients who undergo coronary artery bypass surgery.

The Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) trial assessed the effect of clopidogrel plus aspirin in patients with acute coronary syndrome without ST-segment elevation.<sup>7</sup> The rate of major bleeding was 9.6% in patients who underwent coronary artery bypass surgery within 5 days of stopping clopidogrel, vs 6.3% in those not receiving clopidogrel.

Observational studies also documented increased blood loss and need for reoperation when coronary artery bypass surgery was performed 6 days after stopping clopidogrel or sooner.<sup>8-10</sup>

In view of these findings, the American College of Cardiology and American Heart Association's 2004 Guideline Update for Coronary Artery Bypass Graft Surgery recommends that clopidogrel be withheld for 5 days before bypass surgery.<sup>11</sup>

No randomized prospective study has assessed the risk of hemorrhage related to clopidogrel or the combination of clopidogrel plus aspirin when used immediately before noncardiac surgery.

Regarding the use of aspirin alone, we have evidence that its use in patients undergoing coronary artery bypass surgery leads to an increase in mediastinal blood loss, but its benefit in maintaining the patency of saphenous vein grafts exceeds the risk. Aspirin has also been shown to increase blood loss in general, gynecologic, and urologic surgery.

#### ■ OUR APPROACH

On the basis of this information, we delay noncardiac surgery, if possible, until a patient with a sirolimus-eluting stent has completed 3 months of combination antiplatelet therapy, or 6 months for a patient with a paclitaxel-eluting stent. After antiplatelet therapy is completed, we allow another 5 days for withdrawal from clopidogrel.

If surgery cannot be delayed, the decision is more complex. For a patient with a sirolimus-eluting stent, we try to complete at least 2 months of clopidogrel plus aspirin, a duration that has been validated by controlled trials in Europe and is a recommended option of the Seventh American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy.<sup>12</sup>

If a patient requires urgent surgery and cannot complete the combination antiplatelet regimen, we consider the degree of urgency of the surgery, the risk of hemorrhage, and the potential consequences of major bleeding in that patient. In most cases we try to continue the antiplatelet therapy and advise the surgical team of the increased risk of bleeding. Platelet transfusions are considered in the event of major bleeding. However, we are especially reluctant to allow a patient to undergo surgery while he or she is receiving combination antiplatelet therapy if bleeding at the operative site could have particularly deleterious effects (eg, in neurosurgery). If the bleeding risk requires stopping antiplatelet therapy prematurely, we consult with the surgeon and try to resume antiplatelet therapy as soon as possible.

In some patients, coronary angioplasty may be indicated as a prelude to noncardiac surgery. If so, and if the noncardiac procedure cannot be delayed to allow the course of

**We try to wait 3 months with a sirolimus stent, 6 months with a paclitaxel stent**



antiplatelet therapy necessitated by a drug-eluting stent, we have used bare-metal stents followed by 14 days of clopidogrel plus aspirin.

### ■ A NOTE OF CAUTION

McFadden et al<sup>13</sup> have reported four cases of late thrombosis of both paclitaxel-eluting and sirolimus-eluting stents many months after placement (two cases 11 months after stent placement and two cases more than 1 year

after stent placement). In all cases, the patient's course of dual antiplatelet therapy exceeded the 3 to 6 months currently recommended. In three of the four cases, antiplatelet therapy was stopped before noncardiac surgery.

Although reports of late stent thrombosis are exceedingly rare, they suggest that physicians should be vigilant for stent thrombosis when a patient with a drug-eluting stent undergoes noncardiac surgery.

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ADDRESS: Howard H. Weitz, MD, Jefferson Heart Institute, 925 Chestnut Street, Philadelphia, PA 19107; e-mail Howard.Weitz@jefferson.edu.

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