Coronary Artery Stents: Management of Perioperative Antithrombotic Therapy

William J. Mauermann, MD
Assistant Professor of Anesthesiology
Mayo Clinic College of Medicine
Rochester, Minnesota

Over the past two decades percutaneous coronary interventions (PCI) for the treatment of coronary artery disease have increased by more than 320% (1). Currently, most nonsurgical interventions for coronary artery disease involve placement of stents in the diseased coronary circulation (2) as stent placement improves the short and long-term patency rate of coronary vessels versus simple angioplasty (3,4). Currently, both bare metal stents (BMS) and drug eluting stents (DES) are available for use with DES being used in up to 80% of PCIs (5).

DEFINITION OF TERMS

- **Re-endothelialization** – gradual process of establishing native vascular endothelium over the denuded coronary endothelium and thrombogenic coronary struts
- **Instent re-stenosis** – neointimal hyperplasia resulting in re-narrowing or occlusion of the coronary vessel after coronary stenting. Occurs over a period of months in 30 – 40% of patients (6,7) and is asymptomatic in 50% of patients.
- **Stent thrombosis** – sudden partial or total occlusion of an intra-coronary stent. Usually associated with myocardial infarction and significant morbidity and/or mortality.

RATIONALE OF ANTIPLATELET THERAPY AFTER STENT PLACEMENT

Coronary angioplasty and stenting results in complete denudation of the coronary endothelium. In addition, the stent itself is thrombogenic until endothelialization of the stent struts occurs. Stent thrombosis is predominantly a platelet mediated event. Multiple regimens of anticoagulation have been used in an attempt to prevent acute stent thrombosis with the combination of aspirin and a thienopyridine (clopidogrel or ticlopidine) being superior to other agents. Aspirin inhibits the cyclooxygenase 1 enzyme to antagonize production of thromboxane while the thienopyridines irreversibly inhibit binding of adenosine diphosphate to its receptor. Without dual antiplatelet therapy rates of stent thrombosis within 30 days of placement approach 25% (8). This catastrophic complication of PCI is associated with myocardial infarction in 90% of cases and a mortality of 20 - 45% (9-11). With adequate antiplatelet therapy the rate of BMS thrombosis has decreased to 1.2% (8).

Without adequate antiplatelet therapy patients remain at high risk of stent thrombosis until complete endothelialization has occurred. For the BMS this usually occurs within 4
– 6 weeks of placement. More recently the DES have gained favor for their ability to decrease the incidence of instent re-stenosis. The two DES that are currently used secrete either sirolimus or paclitaxel. These slowly released molecules contain anti-inflammatory and anti-proliferative properties aimed at inhibiting neo-intimal hyperplasia and re-stenosis of the coronary vessel after PCI. While these stents are effective at decreasing the incidence of instent re-stenosis (12-15) they also inhibit normal re-endothelialization of the coronary vessel and stent. As such, patients with DES require longer courses of antiplatelet therapy than do patients with BMS.

CURRENT GUIDELINES FOR ANTIPLATELET THERAPY AFTER PCI

In 2007 the American Heart Association and American College of Cardiology published updated guidelines for antiplatelet therapy after PCI (11). All perioperative physicians are encouraged to review this publication. Important points are summarized below.

1. After PCI aspirin therapy should be continued indefinitely
2. Dual antiplatelet therapy with aspirin and a thienopyridine should be continued for at least one month after BMS placement
3. The risk for stent thrombosis with DES appears to be delayed as compared to BMS. Patients receiving DES should continue dual antiplatelet therapy for at least 12 months

These guidelines regarding DES differ from the original recommendations that suggested dual antiplatelet therapy for three months after a sirolimus stent and six months for paclitaxel stents. The impetus for prolonging dual antiplatelet therapy for DES was based on numerous reports of delayed thrombosis, particularly in patients receiving DES for high-risk, “off label” indications.

RISK AND TIMING OF SURGERY AFTER PCI AND STENT PLACEMENT

The current question facing clinical anesthesiologists is “When is a safe time after PCI for patients to undergo an operation?”. An estimated 5% of patients with coronary stents will present for non-cardiac surgery (NCS) within one year of PCI (16). While retrospective in nature, numerous series indicate that surgery within four weeks of BMS placement is associated with a significant increase in the risk of death or MI (17-21). One month after placement the perioperative risk decreases dramatically but may still be mildly elevated for up to 90 days after placement (21). Current recommendations state that elective procedures should be delayed for at least one month to allow for an adequate course of antiplatelet therapy in patients with a BMS (11).

DES in the perioperative period are less well studied. One series reported on 99 patients with DES undergoing NCS. In this study 80% of the adverse cardiac outcomes were found in patients undergoing NCS during the recommended period of antiplatelet therapy. A larger series of 520 patients with DES undergoing NCS within two years of PCI showed no statistically significant difference in the incidence of death or MI but the observed rates were lower in patients that waited > 1 year between PCI and NCS.
Current guidelines state that in patients with DES, elective procedures should be delayed one year in order to provide an adequate course of antiplatelet therapy (11). However, the choice of delaying surgery one year remains arbitrary and there are case reports of stent thrombosis in the perioperative period up to 29 months after DES placement (22).

In the case of a life threatening surgical emergency, operation is required regardless of the duration of time since PCI. If the risk of bleeding complications is high (i.e. intracranial surgery) platelet transfusions may be required to reverse the effects of aspirin and thienopyradines. Unfortunately, patients that require emergent operation within the recommended period of antiplatelet therapy seem to be at especially high risk of adverse cardiac outcomes (21).

Perhaps the most complicated patients are those which require surgery that is neither emergent nor elective (i.e. oncologic surgery) during the recommend period of dual antiplatelet therapy. In these patients a decision must be made regarding the risks of stent thrombosis versus the risk of disease progression. If possible the patient should be continued on dual antiplatelet therapy throughout the perioperative period. It is worth noting that in the majority of series evaluating patients with stents undergoing NCS, patients that continued dual antiplatelet therapy throughout the perioperative period had no, or only small increases in blood loss versus patients that stopped their thienopyradines preoperatively (18,19,21,23). If the risks of bleeding are felt to preclude continuation of theinopyradines, they should be stopped for the shortest time possible and reinstituted as soon as possible postoperatively (preferably in the recovery room). In addition, aspirin should be continued throughout this period if at all possible (11). The decisions regarding antiplatelet therapy should include not only the risk of bleeding but the magnitude of the operation. The stress response of major surgery likely confers an increased risk of thrombosis (21).

Some clinicians have advocated “bridging therapy” with heparin or glycoprotein (GP) IIB / IIIA inhibitors during thienopyradine withdrawal in patients who have not completed the recommended courses of antiplatelet therapy but require surgery. Both agents have relatively short half-lives. There is currently no evidence to support or refute this practice. However, it must be remembered that stent thrombosis is a platelet mediated event and heparin is likely the least helpful of these two agents.

If stent thrombosis occurs during the perioperative period morbidity and mortality are high. Thrombolytic therapy is contraindicated in the postoperative period and is significantly less effective than PCI in restoring coronary flow (24). Emergent PCI is the definitive therapy for stent thrombosis. At a minimum, consideration should be given to referring patients at high risk for stent thrombosis (premature discontinuation of antiplatelet therapy) to centers with 24 hour access to PCI therapy for their surgical procedures. Patients that prematurely discontinue antiplatelet therapy after PCI also warrant increased monitoring in the perioperative period.
References