

Perioperative management of patients with coronary stents for non-cardiac surgery

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Summary

This article describes the differences between bare metal and drug eluting stents with the implications for duration of antiplatelet therapy. Up to 5% of patients with coronary stents require non-cardiac surgery within one year of placement and so it is important for anaesthetists to have a full understanding of the balance between stopping and continuing antiplatelet drugs.

INTRODUCTION

Percutaneous coronary intervention (PCI) is a common method for management of patients with coronary artery disease. PCI has evolved from balloon angioplasty to insertion of coronary stents. Currently, 90% of all PCIs involve the placement of at least one coronary stent. The popularity of cardiac stent insertion for a patient with coronary artery disease (CAD) implies that an increasing number of patients of CAD with coronary stents in place may present to the anaesthesiologist for non-cardiac surgery. It is estimated that 5% of patients who have undergone PCI require non-cardiac surgery within the first year after stenting.¹

TYPES OF CORONARY STENTS

Coronary stents may be:

1. Bare metal stent (BMS)
2. Drug eluting stent (DES)
3. Bioabsorbable stent.

Bare metal stents (BMS) were introduced in 1986 as a development of balloon angioplasty, however 10-30% of patients with BMS develop in-stent restenosis, due to neointimal hyperplasia and increased thrombogenicity, thus requiring repeat coronary intervention.²

The problem of re-stenosis with BMS led to the introduction of drug eluting stents (DES) in 2003. Their design includes a coating of thin polymer containing an antiproliferative substance that inhibits neointimal hyperplasia and so are associated with a lower incidence of in-stent re-stenosis. DES have reduced the need for repeat coronary intervention to about 2-4%.³

Over a period of time endothelialization of the stent causes the device to become incorporated into the artery, like a part of the vessel. While near complete endothelialization of BMS occurs within 4-6 weeks of implantation, this process takes several months for DES. Until adequately covered by a layer of endothelial cells, the exposed metal struts of a newly implanted stent are a potent focus for the formation of platelet rich microthrombi, resulting

in stent thrombosis. The drug coating in the DES delays re-endothelialization, thus the precautions against thrombosis (i.e. antiplatelet drugs) have to be observed for a longer period than with the BMS.⁴

Bioabsorbable stents are a new generation of stents which, like metal stents, allow vessel healing and restore blood flow. Their main advantage is that the stent gets gradually reabsorbed within the body and does not require surgical removal.⁵

ANTIPLATELET THERAPY FOR PATIENTS WITH CORONARY STENTS

Activation of platelets is the primary source of stent thrombosis, hence dual antiplatelet therapy combining **aspirin** (acetylsalicylic acid) and **clopidogrel** (thienopyridine) is the most commonly used regime for coronary stents. A third-generation thienopyridine, **prasugrel** has been recently introduced into clinical practice, it is more potent than others, while clopidogrel has a more predictable patient response.^{2,6}

For BMS insertion, a loading dose of 300-600mg clopidogrel is given followed by continued use of both aspirin 150mg and clopidogrel 75mg for 4-6 weeks after the procedure. For DES, the dual antiplatelet therapy is continued for at least a year until the stent is fully endothelialized. For a bioabsorbable stent the duration of dual antiplatelet therapy is 6 months. For all types of stents low dose aspirin must be continued for life.⁷

PERIOPERATIVE CONCERNS IN PATIENTS WITH CORONARY STENTS

The chief concern is to weigh the risk of perioperative stent thrombosis and myocardial infarction (MI) due to abrupt discontinuation of antiplatelet drugs against the risk of excessive surgical bleeding due to continuation of aspirin and clopidogrel.

Since endothelialization may not be complete at the time of surgery, abrupt discontinuation of antiplatelet drugs along with the prothrombotic state of patient during surgery increases the risk of acute perioperative stent thrombosis (Table 1). Premature cessation of dual antiplatelet therapy during the first six weeks

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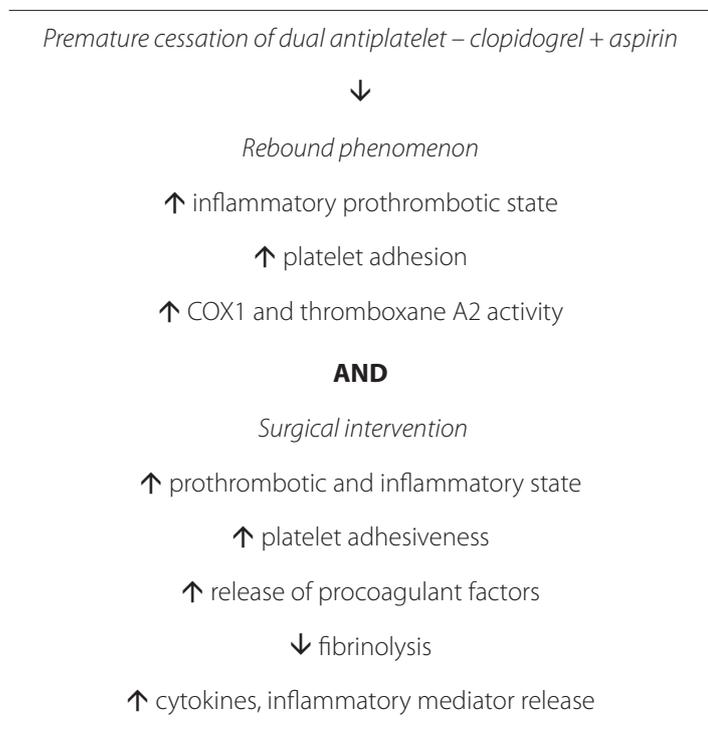
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after angioplasty and stenting, can cause a cardiovascular mortality of up to 71%.⁸ This risk is likely to be greatest in patients with recently implanted, poorly endothelialized stents.

Table 1. Pathogenesis of perioperative stent thrombosis



However, both aspirin and clopidogrel may result in ‘resistance’ which is another predisposing factor to stent thrombosis. The incidence of resistance to aspirin and clopidogrel treatment is 10-20%.⁹ Pharmacogenomics play a major role in resistance to clinical effect of these two drugs. Aspirin resistance occurs due to cyclooxygenase-1 polymorphism. Cytochrome P450 gene polymorphism and P2Y₁₂ receptor polymorphism are involved in clopidogrel resistance. Other factors involved in variability in response to aspirin and clopidogrel are patient non-compliance, inappropriate dosing and inter-drug interactions.¹⁰ Prasugrel, a new antiplatelet drug, like clopidogrel is an irreversible thienopyridine P2Y₁₂ receptor antagonist, having a faster onset of action and results in more effective inhibition of platelet aggregation.¹² Other antiplatelet drugs undergoing clinical trials are thromboxane A₂/prostaglandin H₂ receptor antagonist S-18886 (tetratoban) and protease-activated receptor (PAR1) antagonist SCH 530348.¹¹

Other risk factors for thrombosis are:

- multiple recently implanted DES stents
- renal failure
- diabetes
- low cardiac ejection fraction, and
- procedures involving bifurcation lesions.

Despite concerns regarding perioperative bleeding, the protective effect of clopidogrel against MI, stroke and death are proven.^{1,12,13,14}

PERIOPERATIVE MANAGEMENT OF PATIENTS WITH CORONARY STENTS

It is essential to know the indication for stenting, the date of implantation, the type of stent used, the patient’s current oral antiplatelet drug therapy and its duration. It is important that the decision regarding perioperative management is taken in consultation with the cardiologist. The patient’s haemorrhagic and thrombotic risk should be assessed (Table 2).

Table 2. Assessment of haemorrhagic and thrombotic risk in patients with coronary stents

A. Haemorrhagic risk

- What is the planned operation and anaesthetic technique?
- How necessary is the surgery?
- What is the perceived haemorrhagic risk for the surgical procedure?
- What is the urgency of the surgery?
- Can the surgery be delayed?
- Is there any alternative to surgery available?
- Are there any other haemorrhagic risk factors?
- What will be the consequences of excessive bleeding?

B. Thrombotic risk

- When was the stent placed?
- What type of stent has been inserted?
- Number of stents and their location
- Past history of stent thrombosis
- What antiplatelet regime is being followed?
- What is the duration of therapy that has been recommended?
- Are there any associated risk factors e.g. diabetes, renal impairment, low left ventricular ejection fraction?

Timing of elective surgery after stent placement

Elective non-cardiac surgery should be deferred for at least 6 weeks and ideally 3 months after placement of BMS; and for at least 1 year after DES placement (Table 3). The longer surgery is delayed after stent placement, the lower the risk of **major adverse cardiac events** (MACEs).^{14,15}

Management of antiplatelet therapy

Dual antiplatelet therapy should be continued in all patients with coronary stents presenting for surgery. However, if there is a high risk of surgical bleeding then clopidogrel should be stopped 5-7 days before surgery and monotherapy with aspirin should be continued. Clopidogrel should be restarted as soon as possible post surgery.^{14,16,17} Cessation of aspirin therapy may be considered during intracranial surgery and transurethral resection of prostate as these procedures

Table 3. Timing of elective surgery after PCI (PCI- percutaneous coronary intervention; BMS- bare metal stents; DES- drug eluting stents)

Procedure	Timing of elective surgery after intervention
Angioplasty without stenting	2-4 weeks after placement
PCI and BMS	6 weeks after placement
PCI and DES	12 months after placement

are associated with an increased risk of bleeding, but only after contemplating the risk-benefit ratio.¹⁸

In patients presenting for emergency surgery, if the length of dual antiplatelet medication is less than 6 months, then both medications (aspirin and clopidogrel) should be continued. If more than 6 months, discontinue clopidogrel but continue aspirin therapy.

Bridging therapy with short-acting platelet-GPIIb/IIIa receptor inhibitors (tirofiban or eptifibatid) may be considered in patients considered at high risk of stent thrombosis, in whom either clopidogrel, or both clopidogrel and aspirin, have been stopped. GPIIb/IIIa inhibitors prevent platelet aggregation and displace fibrinogen from GPIIb/IIIa receptors. Antiplatelet therapy should be restarted as soon as possible after surgery.

Heparin has minimal antiplatelet action and so may not be suitable as a drug for bridging therapy.^{2,12,15}

Anaesthesia technique

Both general and regional anaesthesia technique can be used for surgery in patients with coronary stents. It is desirable to crossmatch blood if excessive surgical bleeding is anticipated.

Central neuraxial blocks are contraindicated in patients on dual antiplatelet therapy. Aspirin monotherapy in a dose up to 300mg per day is not a contraindication to neuraxial block. Clopidogrel therapy is an absolute contraindication for neuraxial blockade and should be stopped 5-7 days preoperatively.^{19,20} If a patient on dual antiplatelet therapy is undergoing emergency surgery, which involves a high risk of bleeding or if neuraxial block is essential then it may be necessary to give a platelet transfusion before surgery. A platelet count of 50,000mcL⁻¹ is sufficient for subarachnoid block and a count of 80,000mcL⁻¹ is sufficient for epidural block.^{1,21} However it is worth remembering that an adequate platelet count does not guarantee good platelet function.

For patients requiring emergency postoperative PCI for perioperative MI or coronary stent thrombosis, presence of an indwelling epidural catheter may increase the risk of neuraxial haematoma, as these patients must receive antiplatelet and thrombolytic drugs during the PCI. For this reason continuous neuraxial anaesthesia via an indwelling catheter is generally avoided in patients with coronary stents.^{1,8,12}

Perioperative monitoring

Besides standard monitoring, it is important to diagnose any myocardial insult as quickly as possible. New onset irregular cardiac rhythm, or pulmonary oedema suggests myocardial ischaemia.

Postoperatively, where available, patients should be monitored in a high dependency area. Serial 12-lead electrocardiogram (ECG) is the most cost effective means of detecting ischaemia. Although most perioperative myocardial infarctions are 'silent', onset of angina and other objective signs of ischaemia in patients with coronary stents warrants an urgent cardiology opinion. Stent thrombosis most often presents as an ST elevation MI (STEMI), for which early reperfusion with PCI is recommended. Systemic thrombolytic therapy is not possible since it increases the risk of excessive bleeding and also is less effective than primary PCI.¹

CONCLUSION

The number of patients with coronary stents presenting for noncardiac surgery is increasing in many parts of the world. It is essential that the anaesthesiologists are aware of balance of risks and benefits to be considered in patients on antiplatelet therapy, particularly as our surgical colleagues are understandably swayed in favour of avoiding surgical bleeding. These management decisions should involve the patient, surgeon, cardiologist, anaesthesiologist and the haematologist. Surgery for patients with coronary stents should ideally be performed at centers where interventional cardiology and cardiac surgery facilities are available.

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