Antiplatelet drugs, anticoagulants and elective surgery

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Summary

There is an increased risk of bleeding when patients taking anticoagulant or antiplatelet drugs require surgery. This risk must be balanced against the risk of harm if treatment is stopped. For many minor procedures aspirin or warfarin can be continued. Patients having non-cardiac surgery may be able to continue aspirin, but clopidogrel should be stopped unless there is a high risk of thrombosis. Patients taking warfarin may require bridging anticoagulation around the time of major surgery. This involves replacing the warfarin with unfractionated or low molecular weight heparin. Consultation with a cardiologist is particularly recommended if a patient with a coronary stent requires surgery.

Key words: aspirin, clopidogrel, heparin, warfarin.

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Introduction

A growing number of patients are taking oral anticoagulant or antiplatelet drugs for primary or secondary prevention of arterial or venous thrombosis. The perioperative management of anticoagulation in these patients at the time of elective surgery is contentious yet important. It involves balancing the risks of arterial or venous thromboembolism (such as ischaemic stroke, myocardial infarction, pulmonary embolism or deep vein thrombosis) if the drug is stopped, against the risk of bleeding if the anticoagulant or antiplatelet drug is continued.

Antiplatelet therapy

Aspirin irreversibly inhibits platelet function via the acetylation of cyclo-oxygenase-1. Clopidogrel, a thienopyridine, selectively inhibits adenosine diphosphate-induced platelet aggregation.1 The effect of both drugs lasts for the lifespan of the platelet (approximately 7–10 days). Although it seems logical to stop either drug 7–10 days before an elective procedure, platelet function is only one of the many important mechanisms of coagulation necessary for adequate haemostasis. Aspirin can be continued for most procedures but whether or not clopidogrel can be safely continued depends on the risk of recurrent thrombosis versus bleeding.

Risk of perioperative bleeding

Clinical studies have shown that patients who have taken aspirin preoperatively have an increased risk of postoperative bleeding after cardiac and non-cardiac surgery. Use of aspirin within seven days of coronary artery bypass grafting has been associated with increased blood loss and the need for re-operation, but this does not increase mortality.1 However, another study showed that aspirin use in the five days before coronary artery bypass grafting was associated with a lower risk of postoperative mortality, without a concomitant increase in re-operation for bleeding or the need for blood transfusion.2 This applied to a range of aspirin doses, 100 mg to 975 mg daily. It is generally considered safe to continue aspirin throughout the perioperative period, for both cardiac and non-cardiac surgery, unless there is a significant bleeding risk (Fig. 1).

The use of clopidogrel throughout the perioperative period is more controversial. Some studies have shown an increased risk of major bleeding with the use of clopidogrel within five days of coronary artery bypass grafting.3 While recognising the increased risk of bleeding complications after coronary artery bypass grafting, some experts recommend a more tailored approach depending on individual risk with respect to ischaemic complications and bleeding.4 For percutaneous coronary intervention, pretreatment with clopidogrel is recommended before and throughout the perioperative period.

Patients with coronary stents in situ have a high thrombotic risk if antiplatelet drug therapy is interrupted. Elective non-cardiac surgery should therefore be avoided after stent placement when patients are most prone to thrombosis. This is during the first six weeks for bare metal stents, and during the first 12 months for drug-eluting stents.5 For patients without coronary stents who are not at high risk of cardiac events, clopidogrel can be ceased 5–7 days before surgery.5 It is often routine clinical practice to consult the patient’s cardiologist before stopping the drug. Clopidogrel should be resumed following the procedure as soon as there is adequate haemostasis, usually the morning after surgery. Fig. 1 shows a suggested perioperative management strategy.
Warfarin

The most common indications for oral anticoagulant therapy are atrial fibrillation, the presence of a mechanical heart valve, and venous thromboembolism. Warfarin is the most common oral anticoagulant prescribed for the treatment and prophylaxis of venous or arterial thromboembolism in Australia. The mean half-life of warfarin activity is approximately 40 hours and the anticoagulant effect lasts 2–5 days. For most patients, the therapeutic target for the international normalised ratio (INR) range is 2.0–3.0. For patients with a mechanical heart valve, the recommended INR range is 2.5–3.5.

When considering how to manage patients on warfarin who require surgery, it is helpful to weigh up the risk of bleeding versus the risk of thromboembolism (Table 1). This requires consideration of:

- indication for anticoagulation
- history of any thrombotic events
- type of surgery and its associated risks of bleeding and thromboembolism, particularly with respect to postoperative venous thromboembolism.

The patient’s management is guided by the risk of thromboembolism (Fig. 2). The options include:

- if low risk, stop warfarin five days before surgery (that is, missing four doses before the day of surgery) to allow the INR to drop to less than 1.5, then resume it on the evening of the procedure if there is no evidence of bleeding

- if high risk, stop warfarin and start heparin (unfractionated heparin infusion or low molecular weight heparin) before and after the surgery, during the period when the INR is below the therapeutic range. This option is referred to as ‘bridging’ anticoagulation. Heparin is usually started on the third morning after the last dose of warfarin when the INR becomes subtherapeutic.

Stopping heparin preoperatively

For patients who receive bridging anticoagulation with therapeutic doses of low molecular weight heparin, the last dose should be administered at least 24 hours before the procedure. There is evidence suggesting that there will be a residual anticoagulant effect if low molecular weight heparin is given too close to the time of the procedure. It is recommended...
**Table 1**

Patient risk stratification for perioperative arterial or venous thromboembolism

<table>
<thead>
<tr>
<th>High risk</th>
<th>Low risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any mechanical heart valve</td>
<td>Atrial fibrillation with CHADS2* score of ≤2 and no history of stroke or transient ischaemic attack</td>
</tr>
<tr>
<td>Atrial fibrillation with CHADS2* score &gt;2 or history of stroke or transient ischaemic attack or rheumatic valvular heart disease</td>
<td>Single venous thromboembolism occurring &gt;3 months ago and with no other risk factors</td>
</tr>
<tr>
<td>Recent venous thromboembolism (within 3 months)</td>
<td>Recurrent venous thromboembolism receiving long-term anticoagulation</td>
</tr>
</tbody>
</table>

* CHADS2 score for non-valvular atrial fibrillation

- Congestive heart failure, past or current (1 point)
- Hypertension (1 point)
- Age ≥ 75 years (1 point)
- Diabetes (1 point)
- Stroke (ischaemic), transient ischaemic attack or thromboembolism (2 points)

**Fig. 2**

Perioperative management of patients receiving warfarin for atrial fibrillation, venous thromboembolism or mechanical heart valves

- Assess risk of thromboembolism
- High
  - Bridge with therapeutic doses of LMWH or UFH.
  - Last LMWH dose to be administered 24 hours before surgery, stop UFH infusion 4–6 hours prior.
- Low
  - Prophylactic dose LMWH or no bridging

- Pre-surgery or procedure
- Post-surgery or procedure

Warfarin can be resumed on the evening of the procedure. LMWH or UFH can be resumed 12–72 hours following the procedure, depending on the type of surgery. The initial dose will vary from prophylactic dose (for example enoxaparin 40 mg daily) to therapeutic dose (for example enoxaparin 1 mg/kg twice daily) depending on the risk of thrombosis.

LMWH Low molecular weight heparin
UFH Unfractionated heparin
that the last preoperative dose be half the usual total daily dose. For unfractionated heparin, it is recommended that the infusion be stopped 4–6 hours before the procedure.

**Resuming heparin postoperatively**

The factors that affect the risk of postoperative bleeding include the timing of the anticoagulant dose after surgery, the dose of anticoagulant and the type of surgery along with its associated bleeding risk. The following recommendations take all of these factors into consideration:

- Warfarin can be resumed on the evening of the procedure (regardless of whether the procedure is performed in the morning or afternoon), at the usual maintenance dose (no loading dose)
- Low molecular weight heparin or unfractionated heparin can be resumed 12–24 hours following the procedure for minor surgery. For major surgery, the first dose should be 24–72 hours post surgery. The initial dose will vary from the prophylactic dose (for example, enoxaparin 40 mg daily) to the therapeutic dose (for example, enoxaparin 1 mg/kg twice daily) depending on the risk of thrombosis, and the risk of bleeding. This needs to be individualised for each patient.

**Epidural or spinal anaesthesia**

In patients receiving bridging anticoagulation with heparin, the last dose of low molecular weight heparin should be given 24 hours before, and unfractionated heparin should be stopped four to six hours before the insertion or removal of the epidural or spinal needle. The procedure should be performed by an experienced anaesthetist. It is preferable to not give therapeutic doses of low molecular weight heparin with catheter in situ and to wait at least one hour after removing the catheter before recommencing intravenous unfractionated heparin.

**Dental, dermatological or ophthalmological procedures**

It is usually safe to continue aspirin around the time of the procedure. However, clopidogrel should be stopped 5–7 days before the procedure unless the patient has had a recent stent insertion.

Warfarin can usually be continued in patients having minor dental procedures (single or multiple tooth extraction and root canal procedures), minor dermatological procedures (including excisions of skin lesions) and minor ophthalmological procedures (including cataract extraction). Dentists can consider co-administration of an antifibrinolytic drug such as tranexamic mouth wash.

**Endoscopy**

For patients having elective gastroscopy or colonoscopy, the recommendations as for dental, dermatological and ophthalmological procedures can apply. However if the patient requires a biopsy, then follow the recommendations for patients undergoing general surgery.

**Other anticoagulant drugs**

There are an increasing number of patients participating in clinical trials that evaluate the efficacy and safety of other oral anticoagulants such as rivaroxaban and dabigatran for the treatment and prevention of venous and arterial thrombosis. Rivaroxaban, a direct factor Xa inhibitor, has a half-life of 4–9 hours. Dabigatran has a longer half-life of 14–17 hours. Bridging anticoagulation with a heparin can be used if indicated. This can be started 24 hours after the last dose of rivaroxaban or dabigatran.

**Conclusion**

The perioperative management of patients taking oral anticoagulant or antiplatelet drugs for primary or secondary prevention of arterial or venous thrombosis is a common and important problem. One must balance the risks of primary or recurrent thromboembolism if these drugs are stopped, against the risk of bleeding if these drugs are continued. For minor procedures, antiplatelet and oral anticoagulant drugs can usually be continued. For other elective cardiac and non-cardiac surgery, aspirin can be continued during the perioperative period. Clopidogrel should usually be withheld for non-cardiac surgery unless the patient is at high risk of cardiac events, and in this case the management should be individualised and discussed with a cardiologist. Warfarin and other oral anticoagulants should be stopped according to their half-lives and bridging anticoagulation with a heparin introduced as indicated.

**References**

Dental notes

Prepared by Michael McCullough, Chair, Therapeutics Committee, Australian Dental Association

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There can be a small increase in bleeding and bruising after tooth extraction, deep scaling, implant placement or minor soft tissue surgery in patients taking anticoagulants. However, the traditional approach of ‘ceasing all blood thinners’ before dental treatment has been challenged and overturned in the last decade. Practitioners should consider that ‘a stroke is a catastrophic event, whereas bleeding from the mouth, although messy and troublesome, can be easily managed by local means’.1 Current recommendations are that, provided anticoagulation is within the therapeutic range, anticoagulants should not be ceased and instead local measures are applied to stop bleeding.

The current guidelines were published in the Australian Dental Association’s News Bulletin in November 2007. These guidelines were reviewed by the National Heart Foundation and the Australasian Haemostasis and Thrombosis Society. These guidelines clearly outline a dental management plan for patients taking antiplatelet and anticoagulant drugs. Non-invasive treatment may be preferred over surgical options and in the first three months after a cardiovascular event or procedure, only emergency dental treatment should be provided. Routine dental extractions and minor soft tissue surgery may be performed using local measures such as resorbable haemostatic materials and resorbable sutures. Tranexamic mouthwash does not affect systemic clotting in patients taking clopidogrel. A patient needing extensive oral surgery, or who has unstable cardiovascular problems, is best referred to an oral and maxillofacial surgeon who will work in collaboration with the patient’s cardiologist.

Reference