Preoperative Management of Patients Receiving Antithrombotics

Bleeding complications remain an important concern for most surgical procedures. Attempts to minimize the risk of these complications by removing risk factors such as the use of anticoagulants are therefore legitimate. However in many instances withholding anticoagulants in the perioperative period may place the patients at risk of thrombotic complications which outweigh the benefits of normal hemostasis.

The approach to this dilemma has been inconsistent from physician to physician and so we sought to provide working guidelines for the management of perioperative anticoagulation based on our limited available evidence and opinion from major stakeholders.

These are by no means strict protocols because we can not account for all possible scenarios and inter-patient variability.
Management of patients on ASA
(Includes Aggrenox)

***** The following is only a guide. Please review the 2014 ACC/AHA guidelines. This document does not at this time incorporate all the recommendations from those guidelines

A. Patients taking ASA for Primary prevention

- Hold 7 or more days preoperatively
- If patient at high risk of CAD with low risk of bleeding complications – consider continuing ASA 81mg

B. Patients taking ASA for Secondary prevention
(History of Coronary Artery Disease (CAD), suspected CAD, Cerebrovascular disease (CVD) – including post carotid endarterectomy, Peripheral Vascular Disease)

- Patients should remain on their ASA 81mg perioperatively if low bleeding risk
- Consider holding ASA for 7 days preoperatively for procedures considered to be at high risk of bleeding complication. (The list is at the end of this document)
- Weigh risk and benefit
- The most recent study by Deveraux et al published in NEJM in 2014, suggests less benefit of continuing ASA than previously suggested in patients without stents.

C. Patients with a cardiac stent should not stop their ASA

D. Patients with a carotid stent should not stop their ASA in most cases

** Primary prevention: The use of ASA to prevent acute coronary syndromes or ischemic cerebrovascular accidents in patients with no prior history of these events whether they have risk factors or not.
References:


**Antithrombotic Therapy for Peripheral Artery Occlusive Disease** Michael Sobel, *Chest June 2008 133:815S-843S; doi:10.1378/chest.08-0686*

**The Primary and Secondary Prevention of Coronary Artery Disease** Richard C. Becker et al., *Chest June 2008 133:776S-814S; doi:10.1378/chest.08-0685*

**Increased risk of stroke after discontinuation of acetylsalicylic acid. A UK primary care study.** Luis A. García Rodríguez, MD, Lucía Cea Soriano, BPharm, Catherine Hill, PhD, Saga Johansson, MD, PhD, Neurology 2011;76:740–746

**To continue or discontinue ASA in the perioperative period: a randomized controlled clinical trial**- Oscarsson et al, Br J Anaesth. 2010 Mar;104(3):305-12.


Management of patients on Coumadin

Effective withdrawal of Coumadin is expected for the majority of surgical patients. Documentation of a return to normal coagulation (INR ≤ 1.5) is expected before surgery can safely proceed. Exceptions to this approach include cataracts, minor dental surgery, examinations under anaesthesia.

Withdrawal of Coumadin exposes a number of high risk individuals to a risk of recurrent thrombosis and potential pulmonary embolus or cerebrovascular accident. In such cases “bridging anticoagulation” with low molecular weight heparin may be indicated to maintain anticoagulation during Coumadin withdrawal.

We will recommend that the patient be assessed in the Thrombosis Unit, to determine the need for “bridging anticoagulation” therapy with low molecular weight heparin as well as post-op anticoagulation therapy. (The Thrombosis Unit is not the appropriate service for assessing Plavix requirements for patients with CAD or CVD). Patients should hold their Coumadin for a minimum period of 5 days in order to return to a normal coagulation state, therefore the thrombosis unit assessment needs to be arranged with sufficient lead time. (Ideally a minimum of 2 weeks is needed to book a visit in this clinic)

• Consult Thrombosis (613-737-5888 ext. 17622)
  o Individual assessment needed for bridging therapy with LMWH
  o Exceptions
    ▪ Patients with a single episode of secondary DVT who have been on Coumadin for >3 months do not require bridging but should be advised to see the physician responsible for the Coumadin order to determine if this therapy is still required
    ▪ Patients with atrial fibrillation with a CHADS score of 0 (See below)

• Hold Coumadin minimum 5 days preoperatively

• INR Stat am of surgery
**Secondary DVT**: DVT arising secondary to a now resolved high risk state (trauma, pregnancy, post-surgical) and not associated with a thrombophilia (Factor V Leiden, Hyperhomocysteinemia, Protein C deficiency, Protein S deficiency, Antiphospholipid Antibody Syndrome, Antithrombin III Deficiency, prothrombin gene mutation)

**CHADS score**: Score 1 point for each of the following –
- History of CHF
- Hypertension
- Age >75
- Diabetes Mellitus
- History of Stroke or TIA (2 points)

**CHADS score** does not apply to patients with **mitral stenosis**; they need to be seen be the thrombosis clinic for possible bridging.

Management of patients on dabigatran (Pradax™)  
(Indicated for treatment of atrial fibrillation)

Effective withdrawal of dabigatran is expected for the majority of surgical patients. Exceptions to this include cataracts, minor dental surgery, examinations under anaesthesia. There is no test available to document a return to normal coagulation before surgery can safely proceed, other than a normal TT which is actually too sensitive and will likely be abnormal with any residual dabigatran in the blood, despite acceptable coagulation capacity.

An appropriate period of time without taking the medication should provide adequate coagulation. Renal dysfunction can prolong the effect of Dabigatran and so the period of time will depend on the surgical bleeding risk and the renal function.

Here are the currently (as of Nov 2014) used wash-out periods for dabigatran. These are slightly different than before and reflect the timelines followed in a current study looking at bleeding and thrombosis in patients taking NOACs.  *Neuraxial techniques are considered high risk procedures. The decision to perform these techniques will rest with the attending anaesthesiologist.

<table>
<thead>
<tr>
<th>Dabigatran:</th>
<th>Drug Half-life, hrs (range)</th>
<th>Interval between Last NOAC Dose and Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl (mL/min)†</td>
<td>Low-bleed Risk</td>
<td>High-bleed Risk</td>
</tr>
<tr>
<td>&gt;50</td>
<td>14 (12-18)</td>
<td>1 days (skip 2 doses)</td>
</tr>
<tr>
<td>≥30 to ≤50</td>
<td>18 (13-23)‡</td>
<td>at least 48 hrs (skip 4 doses)</td>
</tr>
</tbody>
</table>

The dose on the day of surgery counts as 1 dose. You will notice that the Tables no longer includes patients with creatinine clearance < 30 cc/min. The decision about length of discontinuation before procedure (especially before neuroaxial anesthesia) for these patients should be done on a case by case (risk benefit) basis with the anesthesiologist. This will occur very infrequently. We haven’t had a patient with a GFR < 30 on a DOAC requiring elective surgery that I am aware of.
We will recommend that the patient be assessed in the Thrombosis Unit, to determine the need for “bridging anticoagulation” therapy with low molecular weight heparin and more importantly well post-op anticoagulation therapy planning.

The same approach as described above in the management of the patient on Coumadin should be applied to arrange a consult with the thrombosis unit. All patients taking Dabigatran will have a Creatinine drawn at the PAU visit.

**Reversal:**

Although there is no proven method to reverse the effects of dabigatran, The Ottawa Hospital Thrombosis unit should be contacted to approve the possible use of Factor Eight Inhibitor Bypassing Activity (FEIBA). This could be considered for actively bleeding patients treated with dabigatran and potentially for patients about to undergo urgent surgery with a high risk of bleeding complications.
Management of patients on rivaroxaban (Xarelto™) and Apixaban (ELIQUIS®)

Effective withdrawal of rivaroxaban and apixaban is expected for the majority of surgical patients. Exceptions to this include cataracts, minor dental surgery, examinations under anaesthesia. There is no test available to document a return to normal coagulation before surgery can safely proceed.

An appropriate period of time without taking the medication should provide adequate coagulation. Renal dysfunction can prolong the effect of rivaroxaban and apixaban and so the period of time will depend on the surgical bleeding risk and the renal function.

Here are the currently (Nov 2014) used wash out periods for rivaroxaban and apixaban. These are slightly different than previously used timelines and reflect those used in the current study looking at bleeding and thrombosis in surgical patients taking NOACs. *Neuraxial techniques are considered high risk procedures. The decision to perform these techniques will rest with the attending anaesthesiologist.

Rivaroxaban and apixaban patients (rivaroxaban is given daily and apixaban is BID):

<table>
<thead>
<tr>
<th>Rivaroxaban:</th>
<th>Drug Half-life, hrs (range)</th>
<th>Interval between Last NOAC Dose and Procedure</th>
<th>Low-bleed Risk</th>
<th>High-bleed Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl (mL/min)†</td>
<td>8 (7-10)</td>
<td>at least 24 hrs (skip 1 dose)</td>
<td>at least 48 hrs (skip 2 doses)</td>
<td></td>
</tr>
<tr>
<td>&gt;50</td>
<td>11 (9-13)‡</td>
<td>at least 24 hrs (skip 1 dose)</td>
<td>at least 48 hrs (skip 2 doses)</td>
<td></td>
</tr>
<tr>
<td>≥30 to ≤50 (≥25 for apixaban)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Apixaban:</th>
<th>Drug Half-life, hrs (range)</th>
<th>Interval between Last NOAC Dose and Procedure</th>
<th>Low-bleed Risk</th>
<th>High-bleed Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl (mL/min)†</td>
<td>8 (7-10)</td>
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<td></td>
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The dose on the morning of surgery counts as one dose. You will notice that the Tables no longer includes patients with creatinine clearance < 30 cc/min. The decision about length of discontinuation before procedure (especially before neuroaxial anesthesia) for these patients should be done on a case by case (risk benefit) basis with the anesthesiologist. This will occur very infrequently. We haven’t had a patient with a GFR < 30 on a DOAC requiring elective surgery that I am aware of.

We will recommend that the patient be assessed in the Thrombosis Unit, to determine the need for “bridging anticoagulation” therapy with low molecular weight heparin as well as post-op anticoagulation therapy.

The same approach as described above in the management of the patient on Coumadin should be applied to arrange a consult with the thrombosis unit. All patients taking rivaroxaban and apixaban will have a Creatinine drawn at the PAU visit.

**Reversal:**

Although there is no proven method to reverse the effects of rivaroxaban and apixaban, high doses of prothrombin complex concentrates (PCC – Beriplex, Octaplex) may be effective. More recently the use of FEIBA (Factor Eight Inhibitor Bypassing Activity) has been suggested to reverse the anticoagulant effect. The Thrombosis service should be consulted to consider this option. This could be considered for actively bleeding patients treated with rivaroxaban and Apixaban and for those patients about to undergo urgent surgery with a high risk of bleeding complications.
Management of patients on Low molecular Weight Heparin (LMWH)

• **Prophylactic Dose**
  - Daltaparin (Fragmin) 5000 units once per day
  - Enoxaparin (Lovenox) 40 mg once per day
  - Tinzaparin (Inohep) 4500 IU

Most outpatients treated with prophylactic LMWH do not require a preoperative visit to the Thrombosis unit.

Patients receiving a prophylactic dose of LMWH should hold their dose on the day of surgery only.

• **Treatment Dose**
  - Daltaparin (Fragmin) 200 U/kg once per day
  - Enoxaparin (Lovenox) 1.5 mg/kg once per day
  - Tinzaparin (Inohep) 175 U/kg once per day

Those receiving a treatment dose of LMWH should be assessed by the Thrombosis unit.
Management of Patients on Clopidogrel (Plavix) and Ticlopidine (Ticlid) and patients with cardiovascular or cerebrovascular disease

The patient’s interventional cardiologist or his/her neurologist should be contacted for all patients taking Clopidogrel to assist decision making. At the Ottawa Heart Institute, cardiologists who are unavailable will be covered by one of their colleagues, and the same applies to neurologist at the Stroke Prevention Clinic.

Perioperative decisions to hold or continue Clopidogrel are complex. Continuing the drug may increase bleeding risk, but withholding the drug may increase the risk of in stent thrombosis, myocardial infarct, death and stroke. A discussion regarding risk and benefit should be had with the surgeon and the cardiologist or neurologist. The evidence supporting these decisions is constantly evolving.

***** The following is only a guide. Please review the 2014 ACC/AHA guidelines. This document does not at this time incorporate all the recommendations from those guidelines*****

**No patient should have surgery (unless life saving) within 2 weeks of any cardiac stent implantation.**

Refer to Table 1 for decision making tool.

1. **Recent MI (>7 days but < 1 month)**
   - Hold Clopidogrel if significant bleeding risk but continue ASA

2. **Stroke (ischemic)**
   - < 3 months ago
     - Delay non life saving surgery
     - If on ASA + Clopidogrel, proceed without discontinuing (unless risk of severe bleeding -hold Clopidogrel continue ASA)
If on Coumadin, bridge with LMWH

- > 3 months ago
  - Hold Clopidogrel and continue ASA (unless risk of severe bleed)
  - If on Coumadin, bridge with LMWH
  - If on Aggrenox or ASA continue (unless risk of severe bleed)
- In all cases preoperative therapy should be resumed ASAP

3. Carotid stents

- < 3 months
  - Delay non life-saving surgery OR
  - Proceed without discontinuing (unless risk of severe bleeding – Hold Clopidogrel but continue ASA)

- > 3 months
  - Proceed without discontinuing (unless risk of severe bleeding – Hold Clopidogrel but continue ASA)

- In all cases preoperative therapy should be resumed ASAP

4. Coronary Angioplasty without stent

- < 4 weeks ago
  - Delay non-life saving surgery or
  - Operate without discontinuing (unless risk of severe bleeding – Hold Clopidogrel but continue ASA)

- > 4 weeks ago
  - Hold Clopidogrel continue ASA, proceed with elective surgery

5. Patients with cardiac Bare Metal Stent (BMS)

Optimal time for surgery would be > 4 weeks but < 12 weeks after stent
• BMS < 4 weeks old
  - Delay non life-saving surgery or
  - Operate without discontinuing (unless very severe risk of bleeding - Hold Clopidogrel but continue ASA)

• BMS > 4 weeks old
  - Hold Clopidogrel, maintain ASA throughout
  - Proceed with elective surgery
  - Consider re-bolus of Clopidogrel 300mg as soon as safe, continue with Clopidogrel at 75mg per day (discuss with cardiology)

6. Patients with cardiac Drug Eluding Stent (DES)

• DES < 12 months old
  - Delay non-life saving surgery or
  - Operate without discontinuing (unless very severe risk of bleeding – In which case: hold Clopidogrel but continue ASA then Consider re-bolus of Clopidogrel 300mg as soon as safe (night of surgery) then continue with Clopidogrel 75mg per day) (Discuss with cardiology)

• DES > 12 months
  - Hold Plavix 7 days and continue with ASA throughout
  - Consider re-bolus of Clopidogrel 300mg as soon as safe (night of surgery) then continue with Clopidogrel 75mg per day
  (Discuss with cardiology)

NB

1. Guidelines for BM stents and DES are variable because some patients may be at even higher risk of in stent thrombosis (depending on the number and location of the stents placed and other factors) and may require a longer period of anticoagulation. **Some newer DESs require very short periods of dual antiplatelet therapy.
2. Contacting the patient’s cardiologist is preferable to asking for a cardiology consult, as they will have the required information to make the correct decision.

3. For patients taking Clopidogrel for CVD, contacting the patient’s neurologist or neurosurgeon may be required.

4. Heparin and Low molecular Weight Heparin are not substitutes for Clopidogrel. If patients must stop Clopidogrel, then consideration should be to given to use ASA as a substitute.

5. If proceeding without stopping Clopidogrel, consider holding dose on day of surgery to allow washout of drug from the plasma. This would make a platelet transfusion more effective in the event of a major haemorrhage.

6. The Thrombosis Unit is not the appropriate service for decision making regarding Clopidogrel requirements preoperatively.

7. When held, the period of abstinence should be 7 days for Clopidogrel to keep us in agreement with the ASRA guidelines for neuraxial blockade. There is evidence that 5 or even 3 days would be sufficient to allow adequate platelet activity to proceed with surgery without increasing morbidity and mortality. For those patients at higher risk if Clopidogrel is stopped, consider a shorter abstinence period. The abstinence period should be 14 days for Ticlopidine, again in keeping with the ASRA guidelines and the product monograph (10-14 days before surgery).

Decisions regarding perioperative use of Clopidogrel are complex and continue to evolve. Monitoring information as it becomes available may alter these current recommendations.
Procedures that are felt to be high risk of bleeding complications according to our surgical colleagues:
(Obviously this can not cover all possibilities – judgement is required)

ENT
- Tonsillectomy, FESS, major neck dissection, free flaps

Plastics
- Free flaps

Orthopaedics
- Major oncologic surgery

General surgery
- Retroperitoneal sarcoma, large paraesophageal hernia, pelvic exentoration, liver resection

Ophthalmology
- Orbit, glaucoma and strabismus surgery, Penetrating Keratoplasty (full thickness corneal transplant), Iris reconstruction/Sutured secondary IOL and KPro (Keratoprosthesis)

Genecology
- Hysterectomy by Laparotomy
- Hysterectomy via vaginal route
- Myomectomy by Laparotomy
- Colposacropexy
- Retropubic urethropexy
- Cesarean Hysterectomy
- Staging laparotomy (gynecological malignancies)

Urology
- TURP, TURBT, Percutaneous nephrostomy tubes, cystectomy/neobladder

Neurology
- Intracranial intracerebral surgery (very high risk), Intraspinal surgery

Vascular surgery

Thoracic surgery
- Complex intrathoracic cases (i.e. decortication, redo-oesophageal surgery
- Dr Maziak – wants ASA held for all major lung and oesophagus cases and Clopidogrel held for all cases x 5 days
References


**Antithrombotic Therapy for Peripheral Artery Occlusive Disease** Michael Sobel, *Chest* June 2008 133:815S-843S; doi:10.1378/chest.08-0686


**The CURE trial: Using clopidogrel in acute coronary syndromes without ST-segment elevation**-GREGORY P. GERSCHUTZ, MD, DEEPAK L. BHATT, MD, *Cleveland Clinic Journal of Medicine* May 2002 vol. 69 5 377-378

**Peri-operative management of antiplatelet therapy in patients with coronary artery disease - Joint position paper by members of the working group on Perioperative Haemostasis of the Society on Thrombosis and Haemostasis Research (GTH), the working group on Perioperative Coagulation of the Austrian Society for Anesthesiology, Resuscitation and Intensive Care (ÖGARI) and the Working Group Thrombosis of the European Society for Cardiology (ESC)** Wolfgang Korte1 et al *Thrombosis and Haemostasis* 105.5/2011

**To continue or discontinue ASA in the perioperative period: a randomized controlled clinical trial**- Oscarsson et al, Br J Anaesth. 2010 Mar;104(3):305-12.


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