Warfarin Therapy – Management During Invasive Procedures and Surgery

Effective Date: April 1, 2015

Scope

This guideline provides recommendations for the management of warfarin therapy in adults aged ≥ 19 years requiring invasive procedures and surgery.

Perioperative management of non-vitamin K antagonist oral anticoagulants can be found in BCGuidelines.ca – Use of NOACs in Non-Valvular Atrial Fibrillation. Non-perioperative management of warfarin is covered in BCGuidelines.ca – Warfarin Therapy Management.

Key Recommendations

• Warfarin discontinuation prior to invasive procedures is necessary for all interventional procedures except for minor skin procedures, routine dental work, cataract surgery, endoscopies without biopsy, and percutaneous venous access.
• For elective procedures, warfarin should be stopped for 5 to 6 days prior to the procedure to allow gradual normalization of the international normalized ratio (INR).
• For urgent procedures, use of prothrombin complex concentrate is highly effective in rapidly reversing warfarin anticoagulant activity and has a duration of action of ~ 6 hours.
• The use of bridging heparin therapy is dependent on the risk of thrombosis.
• Discuss the risk of bleeding with the surgeon and anesthesiologist to determine optimal timing for resuming warfarin and bridging heparin therapy after surgery.

Risks

The management of warfarin therapy in patients undergoing surgery or other invasive procedures involves a fine balance between the risk of hemorrhage if the procedure was performed while on warfarin, and the risk of thrombosis if warfarin was discontinued. The thrombotic risk in the perioperative period depends on pre-existing conditions, the time since the last episode of thrombosis, and the thrombotic effect of surgery.1-8

The risk of hemorrhage in the perioperative period depends on the patient’s age, associated medical conditions, type of procedure, approach, site, type of incision and closure, and the method of administration of anesthesia and analgesia. It is recommended that the anesthesiologist and the surgeon be consulted in determining the hemorrhagic risk.

Preoperative management of warfarin therapy consists of timely discontinuation of warfarin and replacement (known as “bridging”) with therapeutic low molecular weight heparin (LMWH) or unfractionated heparin if the risk of thrombosis is considered to be sufficiently high. Almost all patients will achieve an international normalized ration (INR) of < 1.5 within 4 – 5 days of stopping warfarin,9 although patients with a higher (2.5 – 3.5) target INR and the elderly (> 70 years) will require a longer period of warfarin withdrawal before surgery. Patients with a high risk of thromboembolism or stroke may benefit from bridging with heparin during the preoperative period, either as outpatients (LMWH subcutaneously) or inpatients (unfractionated heparin intravenously) by shortening the duration of subtherapeutic anticoagulation.
Postoperative management of warfarin therapy consists of re-initiation of anticoagulation. Postoperative anticoagulation increases the rate of major bleeding. Typically, warfarin can resume the evening of or next day after the procedure because the anticoagulant activity is not established for several days. Restarting warfarin may be delayed in neurosurgical patients, those receiving epidural analgesia and in patients who are bleeding. For patients at high risk of thrombosis, LMWH by injection is given concurrently with warfarin and the overlap is maintained until a therapeutic INR has been reached. LMWH used postoperatively may allow earlier discharge of the patient compared with using unfractionated heparin.

If urgent or emergent procedures are to be undertaken in < 4-5 days and warfarin reversal is required, it may be satisfactory to give 1-2 mg of vitamin K orally in order to expedite the reversal process. When reversal of anticoagulation is required within 6 hours, intravenous vitamin K and prothrombin complex concentrate (PCC) (e.g., Octaplex®, Beriplex®) is highly effective and is recommended over frozen plasma infusion.

**Management**

**Therapeutic Measures for Reversal of Warfarin Therapy**

**Vitamin K**
- Intravenous (IV) delivery is the fastest and most reliable way to obtain the effect of vitamin K.
- Intramuscular (IM) or subcutaneous delivery should be avoided.
- If the procedure is in more than 24 hours, there is no difference between using IV and oral (PO).
- Useful for postoperative periods as well.
- Excessive dose of vitamin K can lead to difficulty with re-anticoagulation.
- Effect on INR is observed after 8 – 12 hours, depending on route of administration.
- Recommended doses:
  - Oral 1 – 2 mg, or
  - IV 5 mg in 50cc normal saline infused over 30 minutes.

**Virally Inactivated Plasma-Derived Prothrombin Complex Concentrate**
- Use only in consultation with specialist.
- Preferred product for rapid reversal of warfarin when available.
- Duration of action is ~6 hours, typically only one dose is needed.
- Virally inactivated plasma-derived concentrate containing factors II, VII, IX, X and Protein C and Protein S.
- Must be used in conjunction with IV vitamin K.
- Indicated for immediate INR reversal in patients:
  - with active, serious bleeding, and/or
  - who require surgery within next 6 hours.
- Contains heparin and is contraindicated in patients with heparin induced thrombocytopenia and liver insufficiency (see product monograph).
- May be associated with clinically important thrombosis.

**Frozen Plasma (FP)**
- Short duration of action at ~4 hours.
- Indicated for rapid reversal when PCC not available.
- Risk of infectious agent transmission.
- Available in large centres; rural centres can have FP shipped quickly from nearby larger centres as needed.
Management of Perioperative Anticoagulation

1) Acceptable INR for surgery
   - Discuss with surgeon and anesthesiologist what the goal INR should be before surgery.
   - Baseline INR is recommended in every case and this will guide further therapy.
   - An INR < 1.5 is generally acceptable except for neurosurgery, ocular surgery and procedures requiring spinal anesthesia or epidural analgesia.\(^1\)

2) Risk of bleeding
   - In general, the type of procedure determines the risk of bleeding and how long anticoagulation must be withheld post-operatively.
   - Discontinuation of warfarin is essential for procedures (refer to Table 1) associated with a high risk of bleeding.
   - Discontinuation of warfarin is usually not necessary for procedures (refer to Table 1) associated with a low risk of bleeding.
   - Assess with surgeon and anesthesiologist what the risk of bleeding from the procedure.

<table>
<thead>
<tr>
<th>Higher Risk Procedures for Bleeding</th>
<th>Lower Risk Procedures for Bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedures that the body cavity is entered (e.g., open thoracic, abdominal or pelvic surgery)</td>
<td>Percutaneous needle procedures in readily compressible sites (e.g., peripheral venous access)</td>
</tr>
<tr>
<td>Percutaneous needle procedures in non-compressible sites, including organ biopsies</td>
<td>Many skin procedures</td>
</tr>
<tr>
<td>Any type of prostatic surgery</td>
<td>Routine dental procedures (e.g., hygiene, simple extractions, restorations, endodontics, prosthetics)(^6)</td>
</tr>
<tr>
<td>Surgery sites where minor bleeding can cause significant morbidity (e.g., central nervous system and intraocular procedures)</td>
<td>Endoscopy without biopsy</td>
</tr>
<tr>
<td>Major arthroplasty surgery (e.g., hip or knee replacement)</td>
<td>Cataract surgery</td>
</tr>
</tbody>
</table>

3) Risk of thrombosis and need for peri-procedural bridging therapy
   - Assess the preoperative risk of thrombosis from pre-existing conditions (refer to Table 2) before the procedure.
   - Assess the postoperative risk of thrombosis from the procedure with the anesthesiologist and surgeon.

<table>
<thead>
<tr>
<th>Higher Risk Conditions</th>
<th>Lower Risk Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical mitral valve and old model aortic prosthesis (i.e., ball, Bjork-Shiley, Lillehei-Kaster)</td>
<td>Newer model mechanical aortic valve prostheses and any tissue valves</td>
</tr>
<tr>
<td>Atrial fibrillation plus either history of stroke/TIA, or ≥ 3 additional risk factors(^<em>) for cardioembolic events</em></td>
<td>Atrial fibrillation without additional risk factors* for stroke/TIA</td>
</tr>
<tr>
<td>DVT/PE occurring within past 3 months</td>
<td>DVT/PE occurring more than 3 months ago</td>
</tr>
<tr>
<td>DVT/PE in patients with active cancer</td>
<td>Hypercoagulable state without recent thrombotic episode, recurrent thrombosis or history of life-threatening thrombosis</td>
</tr>
<tr>
<td>Hypercoagulable state with recent thrombotic episode, recurrent thrombosis or history of life-threatening thrombosis</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: DVT = deep vein thrombosis; PE = pulmonary embolism; TIA = transient ischemic attack.
Footnote: *Risk Factors include recent cardiac failure, hypertension, age > 75 years, and diabetes. For more information, refer to BCGuidelines.ca – Atrial Fibrillation – Diagnosis and Management.
4) Management based on risk of thrombosis

For low risk of thrombosis (including risk associated with preoperative and postoperative):

i) Discontinue warfarin 5 days prior to surgery. Therefore, give last dose on day 6, to achieve 5 warfarin-free days if day of surgery = day 0.

ii) Check INR the day before procedure to ensure it is lower than the goal INR (< 1.5 for most procedures). If INR is higher than goal INR, discuss with physician performing procedure.

iii) Restart warfarin at preoperative dose as soon as hemostasis is assured and only after epidural catheters are removed post-surgery.

iv) Recheck INR within one week after starting warfarin at the last stable dose and resume regular monitoring and dose adjustment. Warfarin doses may change postoperatively if there were significant changes in medication (especially use of antibiotics) or nutrition.

v) Patients can receive prophylactic doses of unfractionated heparin or LMWH for thromboprophylaxis until the INR is therapeutic.

For high risk of thrombosis (including risk associated with preoperative and postoperative):

i) Discontinue warfarin at least 5 days prior to surgery. Therefore, give last dose on day 6 to achieve 5 warfarin-free days if day of surgery = day 0. Unless target INR is 3.0 (range 2.5 to 3.5) stop 6 days prior. Therefore, give last dose on day 7 to achieve 6 warfarin-free days if day of surgery = day 0.

ii) If indicated, give therapeutic dose of LMWH on day 4, day 3, and day 2 in consultation with a haematologist at the closest referral centre/major hospital or thrombosis clinic.

iii) Last dose of LMWH is generally not given any later than 24 hours before the procedure. Exact timing of the last LMWH dose will depend on the type and dose of LMWH and risk of thrombosis.

iv) Check INR the day before procedure to ensure it is below the goal INR (< 1.5 for most procedures). If INR is higher than goal INR, discuss with physician performing the procedure.

v) In the absence of an indicated procedure-specific thromboprophylactic regimen, start prophylactic dose LMWH 12 – 24 hours after surgery/procedure provided hemostasis is assured. Consider escalation to therapeutic dose of LMWH starting postoperative day 3, if there are no bleeding concerns. Discuss dose and timing of postoperative LMWH with surgeon.

vi) Restart warfarin at preoperative dose as soon as hemostasis is assured and only after epidural catheters are removed post-surgery.

vii) Continue LMWH until the INR is in therapeutic range.

To help the patient with this process, provide them with an Associated Document: Anticoagulation Before & After Surgery – Patient Record Sheet.

5) Timing of surgery/procedure

• Whenever possible, surgery in a chronically anticoagulated patient should be undertaken on an elective basis to allow for planned anticoagulant reversal.

• In patients receiving a fixed duration of anticoagulation (e.g., 3 months), consider delaying invasive procedures until after the completion of anticoagulation.

• For when urgent or emergent surgery/procedure is required and warfarin reversal is indicated (See Appendix A: Flow Chart for Warfarin Reversal), perform a baseline INR and proceed as follows:

Surgery/procedure to be done in < 24 hours

i) Discontinue warfarin and administer IV vitamin K.

ii) If surgery will be performed within 6 hours PCC is recommended (if not available then give FP).

iii) Check INR immediately after product infusion and prior to surgery to document correction. If INR not corrected, consider repeat administration of PCC or FP in consultation with specialist.
Surgery/procedure to be done in 24 – 96 hours
i) Discontinue warfarin and administer IV or PO vitamin K.
ii) Check INR in 24 hours.
iii) If INR is not corrected after a dose of vitamin K, give another dose of IV vitamin K and recheck INR in 12 hours.
iv) If INR is not corrected after 2 doses of vitamin K, consider other conditions that may elevate INR (e.g., disseminated intravascular coagulopathy, liver disease).
v) Check INR immediately prior to surgery to document correction.

- For when an elective surgery is required and with planned anticoagulant reversal proceed as follows:
  i) Patient should be 5 or 6 days warfarin-free prior to surgery depending on therapeutic INR range.
  ii) Consider need for LMWH bridging therapy (see Management based on risk of thrombosis above).
  iii) Check INR one day prior to surgery or on day of surgery if possible, especially with high risk bleeding procedures.

6) Type of anesthesia

- Local and general anesthesia can be safely administered to a patient on warfarin.
- Neuraxial blocks (e.g., epidural analgesia, spinal anesthesia and retrobulbar blocks) should not be performed on patients on warfarin.
- In patients with epidural catheters:
  i) Prophylactic dosing of LMWH is okay with an epidural in place;
  ii) Do not give a therapeutic level dosing of LMWH with an epidural in place;
  iii) Catheter should not be removed within 12 hours after a dose of LMWH;
  iv) Do not start warfarin until epidural catheter is removed; and
  v) Do not give LMWH until after 2 hours of catheter removal.

Resources

References


Resources

- Thrombosis Canada, thrombosiscanada.ca

Appendices

- Appendix A: Flowchart for Warfarin Reversal
The following documents accompany this guideline:

- BCGuidelines.ca – Warfarin Therapy Management
- Anticoagulation Before & After Surgery – Patient Record Sheet

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association, and adopted by the Medical Services Commission.

THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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Disclaimer

The Clinical Practice Guidelines (the “Guidelines”) have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problem. We cannot respond to patients or patient advocates requesting advice on issues related to medical conditions. If you need medical advice, please contact a health care professional.
Appendix A: Flow Chart for Warfarin Reversal

INR > 1.5

URGENT reversal for:
• Major bleeding or
• Invasive procedure or Surgery within 6 hours

Vit K 5 mg IV if INR 1.6 – 5.0
10 mg IV if INR > 5.0

Order PCC according to INR and weight

STAT INR 15 minutes after PCC

INR > 1.5

INR ≤ 1.5

Call Transfusion Medicine for pathologist approval of 2nd dose of PCC

Non-URGENT reversal for:
• Non-major bleeding or
• Surgery in 6 hours or later

Vit K 5 mg IV if INR 1.6 – 5.0
10 mg IV if INR > 5.0

STAT INR 2 hours pre-surgery

INR > 1.5
INR ≤ 1.5

Surgery in > 24 hours

Vit K 5 mg IV if INR 1.6 – 5.0
10 mg IV if INR > 5.0

Repeat INR 24 hours after vit K

INR > 1.5
INR ≤ 1.5

Consult Hematology/GIM

Warfarin effect is reversed. Proceed to surgery if indicated.

Repeat INR 6 – 12 hours after surgery

Abbreviations: GIM = General Internal Medicine; INR = International Normalized Ratio; IV = Intravenous; LMWH = low molecular weight heparin; PCC = prothrombin complex concentrate; VTE = Venous thromboembolism; vit = vitamin.

Footnotes:
1) This algorithm is recommended for Warfarin reversal only and should not be used for reversal of other anticoagulants.
2) Do not give frozen plasma in addition to PCC. If indicated, transfuse red cells (for severe anemia) or platelets (e.g., platelet count < 50 x 10^9/L or patient on antiplatelet therapy).
3) If INR is greater than 1.5 after one dose of vitamin K or one dose of PCC, contact Transfusion Medicine and/or consult Hematology for further assistance.
4) Half-life of PCC is approximately 6 hours therefore, should reassess the need for repeat PCC infusion (e.g., if surgery is ongoing, INR > 1.5 and patient is still bleeding) at 6 – 12 hr after surgery or PCC infusion.
5) In patients with high or very high risk of stroke (e.g., atrial fibrillation with CHADS2 score ≥ 3, previous stroke, mechanical heart valve), thrombosis (e.g., VTE within past 3 months, cancer-associated thrombosis, antiphospholipid antibody syndrome), consider need for bridging therapy with LMWH if surgery is expected to occur later than 24 hours after INR reversal.
Anticoagulation Before & After Surgery – Patient Record Sheet

Patient Name: ___________________________________________  Patient Weight: ______________________ kg
Surgeon Name: ___________________________________________  Warfarin dose: _______________ mg
Type of Procedure: _________________________________________  LMWH: _______________________

<table>
<thead>
<tr>
<th>Date</th>
<th># Days before/after Surgery</th>
<th>Please take your warfarin and LMWH injection as instructed below:</th>
<th>Blood Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>7</td>
<td><strong>STOP</strong> aspirin, clopidogrel (Plavix®), ticlopidine (Ticlid®) if asked by your surgeon</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>LAST DOSE OF WARFARIN BEFORE SURGERY</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td><strong>STOP</strong> warfarin. Do not take any more warfarin before surgery.</td>
<td>INR</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>No LMWH. No warfarin.</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>LMWH __________ units at 8 am. No warfarin.</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>LMWH __________ units at 8 am. No warfarin.</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>No LMWH. No warfarin.</td>
<td>INR</td>
</tr>
<tr>
<td>Surgery</td>
<td>Warfarin ____ mg at bedtime if you have no bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+1</td>
<td>LMWH __________ units at 8 am AND Warfarin ____ mg at supper</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+2</td>
<td>LMWH __________ units at 8 am AND Warfarin ____ mg at supper</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+3</td>
<td>LMWH __________ units at 8 am AND Warfarin ____ mg at supper</td>
<td>INR,CBC</td>
<td></td>
</tr>
<tr>
<td>+4</td>
<td>LMWH __________ units at 8 am AND Warfarin ____ mg at supper</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+5</td>
<td>LMWH __________ units at 8 am AND Warfarin ____ mg at supper</td>
<td>INR,CBC</td>
<td></td>
</tr>
<tr>
<td>+6</td>
<td>Continue warfarin and LMWH (if needed) as instructed by your doctor.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If you have any questions or experience serious bleeding, call your doctor: ________________________________

MD Signature: ________________________________  Date: __________________________