

GUIDELINES & PROTOCOLS

ADVISORY COMMITTEE

Warfarin Therapy - Management During Invasive Procedures and Surgery

Effective Date: October 1, 2010

Scope

This guideline is directed towards those physicians involved in the management of warfarin therapy when the patient (19 years of age and over) requires invasive procedures and surgery. For patients younger than 19, refer to the BC Children's Hospital anticoagulation protocol. A summary (Appendix A) of this document in flowchart format is included.

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 post-operative 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 administrationRecommended doses:
 - oral 1 to 2 mg
 - IV 5 mg in 50 cc normal saline infused over 30 minutes
- Virally Inactivated Plasma-Derived Concentrate (Octaplex®)
 - 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
 - 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 (~4hours) of action
 - Indicated for rapid reversal when Octaplex® is not available
 - Slight risk of infectious agent transmission
 - Available in large centres; rural centres can have FP shipped quickly from nearby larger centres as needed

Considerations for Perioperative Anticoagulation:

Note: Always consult with the surgeon and anesthesiologist about:
- Risk of bleeding
- Goal INR

1) Acceptable INR for surgery

- a) Baseline INR is recommended in every case and this will guide further therapy.
- b) Always discuss with surgeon and anesthesiologist what the INR should be before surgery (goal INR).
- c) 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

- a) In general, the type of procedure determines the risk of bleeding and how long anticoagulation must be withheld post-operatively.
- b) Discontinuation of warfarin is essential for these procedures associated with a high risk of bleeding:
 - i) procedures that the body cavity is entered, e.g., open thoracic, abdominal or pelvic surgery
 - ii) percutaneous needle procedures in non-compressible sites, including organ biopsies
 - iii) any type of prostatic surgery
 - iv) surgery sites where minor bleeding can cause significant morbidity (e.g., central nervous system (CNS) and intraocular procedures)
 - v) major arthroplasty surgery, e.g., hip or knee replacement
- c) Discontinuation of warfarin is usually not necessary for these procedures associated with a low risk of bleeding:
 - i) percutaneous needle procedures in readily compressible sites (e.g., peripheral venous access)
 - ii) many skin procedures
 - iii) routine dental procedures (e.g., hygiene, simple extractions, restorations, endodontics, prosthetics)⁶
 - iv) endoscopy without biopsy
- d) Assess the risk of bleeding from the procedure with the assistance of the surgeon and anaesthesiologist.

3) Risk of thrombosis and need for peri-procedural bridging therapy

- a) Determine risk of thrombosis
 - i) Assess the risk of thrombosis from pre-existing conditions:

LOWER RISK CONDITIONS

 - Newer model mechanical aortic valve prostheses and any tissue valves
 - Atrial fibrillation without additional risk factors for stroke
 - Deep vein thrombosis (DVT)/pulmonary embolism (PE) occurring more than three months ago
 - Hypercoagulable state without recent thrombotic episode, recurrent thrombosis or history of life-threatening thrombosis

HIGHER RISK CONDITIONS

 - Mechanical mitral valve & old model aortic prosthesis (e.g., ball, Bjork-Shiley, Lillehei-Kaster)
 - Atrial fibrillation plus, either history of stroke/TIA, or ≥ 2 additional risk factors for cardioembolic events (recent cardiac failure, hypertension, age > 75 years, diabetes – see stroke guideline www.bcguidelines.ca/gpac/pdf/stroke.pdf)
 - DVT/PE occurring within past three months
 - DVT/PE in patients with active cancer
 - Hypercoagulable state with recent thrombotic episode, recurrent thrombosis or history of life-threatening thrombosis
 - ii) Assess the risk of thrombosis from the procedure with the assistance of the anesthesiologist and surgeon.

4) Management based on risk of thrombosis

- a) See Appendix A – Management Tool for Physicians
- b) Low risk of thrombosis (including risk associated with procedure)
 - i) Discontinue warfarin 5 days prior to surgery (i.e. give last dose on day -6; to achieve 5 warfarin free days; 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 pre-op 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, for example, medication changes or change in nutrition.
- c) High risk of thrombosis (including risk associated with procedure)
 - i) Discontinue warfarin at least 5 days prior to surgery (i.e. give last dose day -6 to achieve 5 warfarin free days; day of surgery = day 0). Stop 6 days prior if the target INR is 3.0 (range 2.5 to 3.5) (i.e. give last dose day -7 to achieve 6 warfarin free days; day of surgery = day 0).
 - ii) If indicated, start therapeutic dose of low molecular weight heparin (LMWH) on day -3 in consultation with local expert (see Resources).
 - 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 therapeutic or prophylactic dose LMWH 12 – 24 hours after surgery/procedure provided hemostasis is assured. Discuss dose and timing of post-operative LMWH with surgeon.
 - vi) Restart warfarin at pre-op 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 for two consecutive days.
 - viii) See Patient Guide: Schedule for Anticoagulation Medications.

5) Timing of procedure

- a) Whenever possible, surgery in a chronically anticoagulated patient should be undertaken on an elective basis to allow for planned anticoagulant reversal.
- b) In patients receiving a fixed duration of anticoagulation (e.g., 3 months), consider delaying invasive procedures until after the completion of anticoagulation.
- c) **Urgent or emergent surgery/procedure** - when an urgent or emergent surgery/procedure is required and warfarin reversal is indicated, perform a baseline INR and proceed as follows:
 - i) **Surgery/procedure to be done in < 24 hours**
 - Discontinue warfarin and administer IV vitamin K
 - If surgery will be performed within 6 hours Octaplex® is recommended (if not available then give FP)
 - Check INR immediately after product infusion and prior to surgery to document correction. If INR not corrected, consider repeat administration of Octaplex® or FP in consultation with specialist
 - ii) **Surgery/procedure to be done in 24 - 96 hours**
 - Discontinue warfarin and administer IV or PO vitamin K
 - Check INR in 24 hours
 - If INR is not corrected after a dose of vitamin K, give another dose of IV vitamin K and recheck INR in 12 hours
 - If INR is not corrected after 2 doses of vitamin K, consider other conditions that may elevate INR (e.g., DIC, liver disease)
 - Check INR immediately prior to surgery to document correction
 - iii) **Elective surgery with planned anticoagulant reversal**
 - Patient should be 5 or 6 days warfarin-free prior to surgery depending on therapeutic INR range
 - Consider need for LMWH bridging therapy (see *Management based on risk of thrombosis* above and Patient Guide)
 - Check INR one day prior to surgery or on day of surgery if possible, especially with high risk bleeding procedures

- 6) Type of anesthesia:** elective, urgent, or emergent surgery/procedure
- 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.
 - If central venous access is needed, a compressible site is preferred.
 - In patients with epidural catheters: i) prophylactic dosing of LMWH are 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, v) do not give LMWH until after 2 hours of catheter removal.

Rationale

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 were performed while on warfarin, and the risk of thrombosis if warfarin were discontinued. The thrombotic risk in perioperative patients depends on pre-existing conditions, the time since the last episode of thrombosis, and the thrombotic effect of surgery.¹⁻⁷

The risk of hemorrhage in the perioperative period depends on the patient's age, associated medical conditions, type of procedure, approach, site, expected amount of bleeding, 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 with LMWH as necessary. Patients with a higher (2.5 – 3.5) target INR and the elderly (> 70 years) will require a longer period of anticoagulation withdrawal before surgery. Almost all patients will achieve an INR of < 1.5 within 4-5 days of stopping warfarin.⁸ Patients with a high risk of thromboembolism require heparin during this period, either as outpatients (LMWH subcutaneously) or inpatients (unfractionated heparin intravenously).

Postoperative management of warfarin therapy consists of re-initiation of anticoagulation. Postoperative anticoagulation increases the rate of major bleeding by approximately 3%.³ Restarting the anticoagulant therapy may be delayed in neurosurgical patients or 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 for two days after 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 reverse the effect of warfarin. When reversal of anticoagulation is required within 6 hours, intravenous Vitamin K and Octaplex® is required.

References

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- Ansell J, Hirsh J, Hylek E, et al. Pharmacology and management of the Vitamin K antagonist: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008;133:123S-131S.
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- White RH, McKittrick T, Hutchinson R, et al. Temporary discontinuation of warfarin therapy: changes in the international normalized ratio. *Ann Intern Med.* 1995;122(1):40-42.

Resources

For local information contact a hematologist at your closest referral centre/ major hospital, or call the following anticoagulation/thrombosis clinics:

- Vancouver Coastal Health – Vancouver General Thrombosis Clinic, Vancouver (604) 875-4111 ext. 69275
- Vancouver Island Health – Royal Jubilee Hospital, Victoria (250) 370-8776
- Fraser Health - Outpatient Anticoagulation Program, Burnaby Hospital, Burnaby (604) 412-6288

List of Abbreviations

FP - frozen plasma	DVT - deep vein thrombosis
INR - international normalized ratio	PE - pulmonary embolism
IV - intravenous	LMWH - low molecular weight heparin
IM - intramuscular	CNS - central nervous system
PO - orally	

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

The 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 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

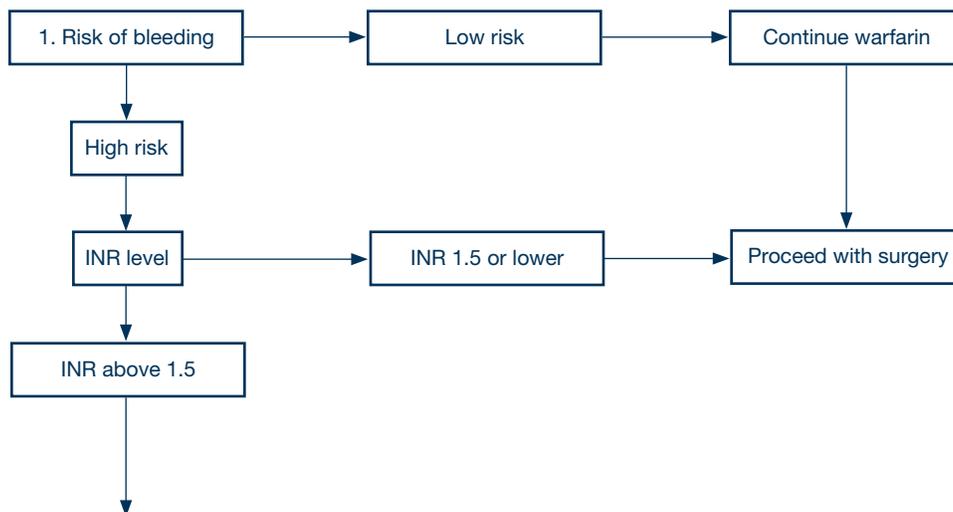
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DISCLAIMER

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 problems.

Appendix A: Management of Warfarin Therapy During Invasive Procedures and Surgery for a Desired Reversal INR of 1.5 or Lower (review sections 1, 2, 3 in text)



Intervention	2. Timing of Surgery			
	Elective	Urgent > 24hrs	Urgent 6-24hrs	Urgent < 6hrs
• Discontinue Warfarin	5 days before surgery. Last dose day -6	Immediately	Immediately	Immediately
• LMWH	+/- see below 3. Thrombosis risk	+/- see below 3. Thrombosis risk	NO	NO
• Vitamin K	NO	PO or IV	IV	IV
• Octaplex	NO	NO	NO	Preferred over FP
• Frozen Plasma (FP)	NO	NO	NO	If Octaplex not available or contraindicated
• Recheck INR	24hrs before surgery	In 12 hrs after vit K	In 12 hrs after Vitamin K	After FP or Octaplex
• INR above 1.5	Recheck in 24hrs. Postpone procedure if necessary	Repeat Vitamin K	Repeat Vitamin K. Consider Octaplex or FP if surgery now < 6 hrs	Repeat Vitamin K. Consider Octaplex or FP if surgery now < 6 hrs

	3. Risk of Thrombosis	
	Low Risk	High Risk
• Preoperative	Proceed to surgery when INR 1.5 or less	Elective – start therapeutic dose of LMWH on day -3 Discontinue at least 24 hrs before surgery
• Postoperative	Restart Warfarin at pre-operative dose as soon as hemostasis assured and after epidural catheter is removed post surgery.	
		Start LMWH 12-24hrs after surgery as soon as hemostasis assured and at least 2 hours after epidural catheter removal
		Stop LMWH when INR in therapeutic range for 2 consecutive days

PATIENT GUIDE

Schedule for Anticoagulation Medications Before and After Surgery/Procedure For patients with a target INR range of 2 to 3

Patient Name: _____

Patient Weight: _____ kg

Surgeon Name: _____

Warfarin dose: _____ mg

Type of Procedure: _____

LMWH Name: _____

Date dd/mm/yy	# Days before surgery	Please take your warfarin and LMWH injection as instructed below:	Blood Testing
	7	 aspirin, clopidogrel (Plavix®), ticlopidine (Ticlid®) if asked by your surgeon	
	6	LAST DOSE OF WARFARIN BEFORE SURGERY	
	5	 warfarin. Do not take any more warfarin before surgery.	INR
	4	No LMWH. No warfarin.	
	3	LMWH _____ units at 8 am. No warfarin.	
	2	LMWH _____ units at 8 am. No warfarin.	
	1	LMWH _____ units at 8 am. If you missed this dose, don't inject it later in the day. No warfarin.	INR
	Day of surgery	Warfarin ____ mg at bedtime if you have no bleeding	
	1 Day after surgery	LMWH _____ units at 8 am AND Warfarin ____ mg at supper	
	+2	LMWH _____ units at 8 am AND Warfarin ____ mg at supper	
	+3	LMWH _____ units at 8 am AND Warfarin ____ mg at supper	INR, CBC
	+4	LMWH _____ units at 8 am AND Warfarin ____ mg at supper	
	+5	LMWH _____ units at 8 am AND Warfarin ____ mg at supper	INR, CBC
	+6	Continue warfarin and LMWH (if needed) as instructed by your doctor.	

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

MD Signature: _____

Date: _____

Adapted from Sample Bridging Anticoagulation Patient Information Form, Thrombosis Interest Group of Canada, Overview of Perioperative Management of Warfarin Therapy, www.tigc.org/eguidelines/PerioperativeManagementTherapy.htm