Warfarin: Perioperative Management

Thrombosis Canada
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Objective:

- To provide an approach to the perioperative management of warfarin-treated patients who require an elective or urgent surgery/procedure.
- To provide an approach for bridging anticoagulation, if needed, during warfarin interruption.

For guidance on management of patients who require an urgent or emergency surgery/procedure, please refer to the Perioperative Anticoagulant Management Algorithm found on the Thrombosis Canada website under the "Clinical Tools" tab, then choose "Algorithms"

Background:

Bridging anticoagulation refers to giving a short-acting anticoagulant, typically a low molecular weight heparin (LWMH), before and after surgery or invasive procedure to minimize the time that warfarin-treated patients are not anticoagulated. This is different from providing routine thromboprophylaxis in the post-operative setting.

Indications for Bridging Anticoagulation:

There are no strong evidence-based indications for bridging anticoagulation; bridging is suggested in patients at high risk for thromboembolism (**Table 2**), not suggested in low-risk patients and optional in intermediate-risk patients based on individual patient characteristics.

Bridging Anticoagulation Options:

Pre- and post-operative dosing:

- Subcutaneous (SC) therapeutic-dose LMWH: enoxaparin 1 mg/kg twice daily or 1.5 mg/kg once daily, dalteparin 100 IU/kg twice daily or 200 IU/kg once daily, or tinzaparin 175 IU/kg once daily.
- Intravenous (IV) unfractionated heparin (UFH) to achieve a therapeutic activated partial thromboplastin time (aPTT) defined according to local laboratory parameters is not commonly used.

Alternative post-operative dosing:

- In patients having a high-bleed-risk surgery/procedure, an alternate post-operative management option should be considered with a prophylactic dose of SC LMWH: enoxaparin 40 mg once daily, dalteparin 5000 IU once daily or tinzaparin 4500 IU once daily. All agents should be given at half dose on the day prior to operative intervention.
- In patients having a high-bleed-risk surgery/procedure that is cardiac, spinal or intracranial, post-operative therapeutic-dose LMWH bridging should be avoided; alternate options are low-dose prophylactic LMWH, delaying anticoagulation until the bleed risk decreases *or* resuming warfarin alone.

Monitoring:

There is no need for laboratory monitoring with SC LMWH bridging. Monitoring of the aPTT is required for bridging with IV UFH.

Adverse Effects:

Bridging is associated with a 2% increase in risk for major bleeding and a 10-15% risk for minor bleeding. Bridging should be used carefully to minimize this bleeding risk.

Peri-Procedure Management Questions and Answers:

Is peri-procedure warfarin interruption always needed?

Deciding if warfarin interruption is needed is based on the bleeding risk of the surgery/procedure (see **Table 1**). Most surgeries/procedures require warfarin interruption but, in general, minimal-bleed-risk procedures (e.g. dental, cataract surgery, minor skin procedures) do not need warfarin interruption, unless there are specific patient circumstances associated with an increased bleeding risk (e.g., prior bleeding with warfarin continuation).

Table 1. Patient Stratification for Bleeding Risk

High-bleed-risk

- Any surgery or procedure with neuraxial (spinal or epidural) anesthesia
- Neurosurgery (intracranial or spinal)
- Cardiac surgery (e.g. CABG, heart valve replacement)
- Major vascular surgery (e.g. aortic aneurysm repair, aortofemoral bypass)
- Major thoracic surgery (e.g. lung resection)
- Major orthopedic surgery (e.g. hip/knee/shoulder joint replacement surgery)
- Urological surgery (e.g. prostatectomy, bladder tumour resection, transurethral prostate resection, tumour ablation)
- Extensive cancer surgery (e.g. pancreas, liver, lung, gastic, colon, esophagus)
- Gastrointestinal surgery (e.g. colonic polyp resection, bowel resection, endoscopic retrograde cholangiopancreatography, percutaneous endoscopic gastroscopy placement)

- Intestinal anastomosis surgery
- Reconstructive plastic surgery
- Selected procedures involving vascular organs (e.g. nephrectomy, kidney biopsy, prostate biopsy, liver, spleen)
- High bleed risk intervention (e.g. pericardiocentesis, spinal injection, polypectomy)

Low/moderate-bleed-risk

- Abdominal surgery (e.g. cholecystectomy, hernia repair, colon resection)
- Other general surgery (e.g. breast, abdominla hysterectomy)
- Other intrathoracic surgery (e.g. bronchoscopy)
- Other orthopedic surgery (e.g., hand/foot, arthroscopy)
- Other vascular surgery
- Non-cataract ophthalmologic surgery
- Gastroscopy or colonoscopy *with* biopsies
- Coronary angiography (using femoral artery approach)
- Selected procedures with large-bore needles (e.g. bone marrow biopsy, lymph node biopsy)
- Complex dental procedure (e.g. multiple tooth extractions)
- Hemorrhoidal surgery

Minimal-bleed-risk*

- Cataract surgery
- Dermatologic procedures (e.g. biopsy)
- Gastroscopy or colonoscopy *without biopsies*
- Coronary angiography (using radial arterial approach)
- Permanent pacemaker insertion or internal defibrillator placement (if bridging anticoagulation is not used)
- Selected procedures with small-bore needles (e.g. thoracentesis, paracentesis, arthrocentesis)
- Dental extractions (1 or 2 teeth)
- Endodontic (root canal) procedure
- Subgingival scaling or other cleaning

***There may be circumstances when a patient is considered at low/moderate bleeding risk that necessitates periprocedural warfarin interruption.**

Is bridging anticoagulation needed during warfarin interruption?

The need for bridging is driven by patients' estimated risk for thromboembolism (see **Table 2**).

Table 2. Patient Stratification for Thromboembolism Risk*

High thromboembolic risk *(bridging anticoagulation suggested)*:

- Mechanical prosthetic mitral valve with ≥1 risk factors**

- Rheumatic valvular heart disease
- Older generation (cage-ball, tilting disc) mechanical aortic valve
- Chronic atrial fibrillation (valvular or non-valvular) with a $CHADS_2$ score*** of 5-6
- Recent (within 3 months) arterial thromboembolism (stroke, systemic embolism, transient ischemic attack [TIA])
- Recent (within 3 months) venous thromboembolism (deep vein thrombosis, pulmonary embolism)†
- Prior arterial or venous thromboembolism during appropriate interruption of warfarin
- Severe thrombophilia (deficiency of protein C, protein S or antithrombin; homozygous factor V Leiden or prothrombin gene G20210A mutation or double heterozygous for each mutation; multiple thrombophilias; antiphospholipid antibodies), active cancer associated with high VTE risk (pancreatic, primary brain, gastric, esophageal, myeloproliferative)

Intermediate thromboembolic risk *(bridging anticoagulation optional and based on individual patient characteristics)*:

- Chronic atrial fibrillation with a $CHADS_2$ score*** of 3-4
- Mechanical prosthetic mitral valve without additional risk factors**
- Newer generation (bileaflet) mechanical aortic valve with major risk factors for stroke (e.g. multiple prior strokes, prior perioperative stroke, prior valve thrombosis)
- Prior venous thromboembolism within last 3-12 months
- Non severe thrombophilia (heterozygous factor V Leiden or prothrombin gene mutation)
- Active cancer or history of cancer

Low-risk *(bridging anticoagulation is not recommended)*:

- Chronic atrial fibrillation (valvular or non-valvular) with a $CHADS_2$ score*** of 0-2
- Prior venous thromboembolism over 12 months ago
- Bileaflet aortic replacement without any risk factors for stroke

*Empiric risk stratification used as a starting point for assessing perioperative thromboembolic risk; should be combined with clinical judgment that incorporates patient- and surgery-related factors.

**Risk factors include: AF, prior stroke/TIA during anticoagulant interruption or other prior stroke/TIA, prior valve thrombosis, rheumatic heart disease, hypertension, diabetes, congestive heart failure, age ≥75 years.

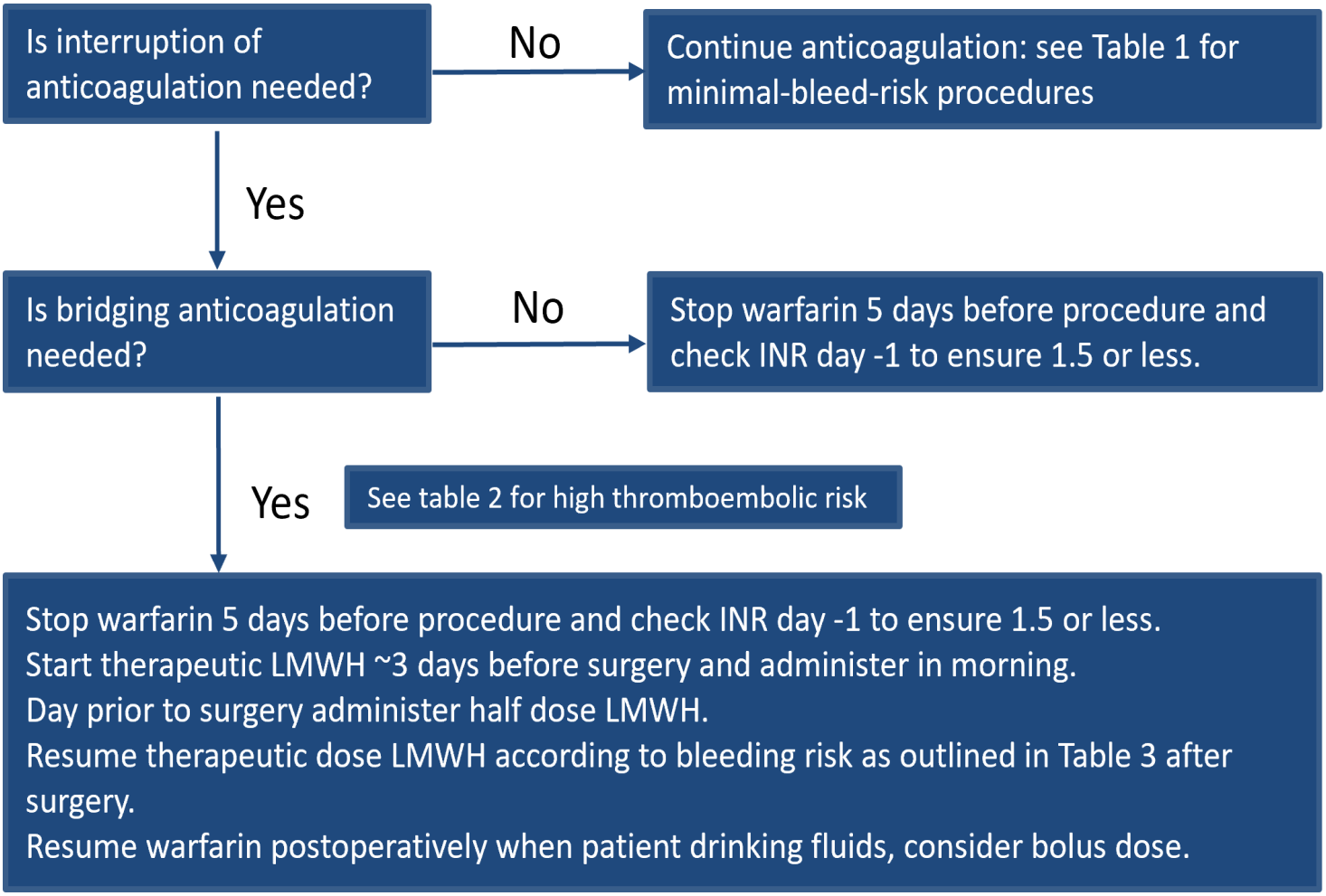
***$CHADS_2$ score estimates the risk of stroke in patients with non-valvular atrial fibrillation. The score is the total points for the presence of congestive heart failure (1), hypertension (1), age $\geq$ 75 yrs (1), diabetes (1), stroke, transient ischemic attack or systemic embolism (2).

†Consider a temporary inferior vena cava filter to be inserted after warfarin interruption and prior to surgery for patients in whom surgery is necessary within 1 month of a proximal DVT; filter can be left *in situ* for 1-2 weeks until therapeutic anticoagulation is re-established. Elective surgery within 3 months after a diagnosis of deep vein thrombosis or pulmonary embolism should generally be avoided.

What is the perioperative anticoagulant management after warfarin interruption for elective procedures?

A suggested management algorithm is shown in the **Figure below.**

Figure 1. Peri-Operative Management of Warfarin-Treated Patients Before and After Surgery/Procedure



When is it safe to resume bridging anticoagulation after surgery/procedure?

The timing of post-procedure resumption of bridging depends on:

1. the bleeding risk of the procedure (see **Table 1**),
2. whether there has been adequate post-operative hemostasis (based on wound inspection and drainage tubes to detect bleeding), and
3. the class of anticoagulant used.

Minimizing bleeding is important because of associated morbidity; a delay in warfarin resumption because of bleeding also exposes patients to an increased thromboembolic risk.

Table 3. Post-operative resumption of bridging anticoagulation

Resumption of therapeutic doses of any anticoagulant should not occur earlier than the time periods suggested below.

Low/moderate-bleed-risk procedure:

- Therapeutic-dose LMWH/UFH, starting approximately 24 hours after surgery (i.e. day after surgery)
- Oral VKA resun=me 12-24 hours postoperatively, assuming no further operative intervention expected

High-bleed-risk procedure:

- Therapeutic-dose LMWH/UFH, starting 48-72 hours after surgery
- *Alternate management*: prophylactic LMWH, starting 12-24 hours after surgery (i.e. day after surgery) or resume warfarin alone with no post-operative LMWH/UFH

Special considerations:

Dental procedures: In patients having 1-2 dental extractions or endodontic (root canal) procedures, warfarin can be safely continued. To reduce the incidence of gingival bleeding, patients can take oral tranexamic acid mouthwash (5 mL just before the procedure, and 2-3 times daily after the procedure until bleeding subsides).

Eye procedures: In patients having a cataract extraction, especially if done with topical and not retrobulbar anesthesia, warfarin can be safely continued. For other eye procedures, warfarin is generally interrupted but consultation with an ophthalmologist is advised.

Colonoscopy & gastroscopy: Warfarin interruption will be needed for most patients who undergo colonoscopy because the potential for polyp removal cannot always be determined beforehand. Caution is warranted after removal of large (>1 cm) polyps since bleeding can occur 2-7 days after polypectomy due to dislodgement of eschar. Polyp-related bleeding may be reduced with endoscopic application of clips to the polyp stalk.

Diagnostic or other procedures: Caution is warranted with anticoagulation after selected diagnostic tests (e.g. biopsy of kidney, liver or prostate; endoscopic retrograde cholangiopancreatography [ERCP] with sphincterotomy) or minor surgeries (e.g. pacemaker placement) when excessive bleeding can lead to serious complications.

Perioperative management of patients receiving antiplatelet therapy:

Please see the **Clinical Guides** on **Acetylsalicylic Acid (ASA), Clopidogrel (Plavix®), Ticagrelor (Brilinta®), Prasugrel (Effient®),** Additional information can be found as well in the 2018 Canadian Cardiovascular Society/Canadian Association of Intervention Cardiology focused update of the Guidelines for the Use of Antiplatelet Therapy [https://www.ccs.ca/en/guidelines].

Pediatrics: Pediatricians with expertise in thromboembolism should manage, where possible, pediatric patients on warfarin. Adult guidelines are appropriate in children although holding warfarin 3 days instead of 5 days is usually sufficient. Consultation with an experienced pediatric hematologist and cardiologist (as appropriate) is recommended to determine the need for bridging anticoagulation.

Other Relevant Thrombosis Canada Clinical Guides

- Acetylsalicylic acid (ASA)
- Clopidogrel (Plavix®)
- Perioperative Management of Antiplatelet Therapy
- Prasugrel (Effient®)
- Ticagrelor (Brilinta®)
- Unfractionated Heparin, Low Molecular Weight Heparin and Fondaparinux
- Warfarin

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Date of version: 05September2023

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