GUIDELINE for PERIOPERATIVE MANAGEMENT OF ANTITHROMBOTIC THERAPY

This document is intended as a guideline only and should not replace sound clinical judgment

Bridging therapy is a complex process that usually requires expert level review. Consultation with a provider with significant experience in this area such as a benign hematologist, outpatient anticoagulation clinic or inpatient anticoagulation service is strongly recommended.

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Most of these CHEST 2012 recommendations are WEAK (i.e. 2C) because they are based on little or no high-quality evidence. Therefore, while we hope they will serve as a useful starting point, it is anticipated that clinical practice will deviate from these suggestions in many instances and these suggestions should never supercede the judgment of an experienced clinician who is best positioned to evaluate the risks and benefits of different strategies for an individual patient.

Note: Peri-operative bridging is different from induction of anticoagulation for an acute thrombotic event. When bridging, it is not necessary to complete 5 full days of overlap therapy with warfarin and parenteral anticoagulant, as it is for an acute thrombotic event. The bridge may be discontinued once the INR is >2 even if that occurs before day 5.

I. Assessment of need for bridging versus no bridging in MAJOR procedures

A. Perioperative management is assessed based on the risk of bleeding and risk of thromboembolism

B. Recommendations for perioperative bridging are outlined below based on the most common indications for warfarin therapy and risk stratification for perioperative thrombosis

RISK STRATUM	MECHANICAL HEART VALVE	ATRIAL FIBRILLATION	VTE	RECOMMEND
High* (>10% annual risk of thrombo-embolism (TE))	– Any mitral valve prosthesis – Any caged-ball or tilting disc aortic valve prosthesis – Recent stroke or TIA (within 6 mo)	– $CHADS_2$ of 5 or 6 – Recent stroke or TIA (within 3 mo) – Rheumatic valvular heart disease	– Recent VTE (within 3 mo) – Severe thrombophilia: ▪ Protein C, protein S, or antithrombin deficiency ▪ Antiphospholipid antibodies ▪ Multiple abnormalities	***Suggest bridging*** (Grade 2C)
Moderate (5-10% annual risk of TE)	Bileaflet aortic valve prosthesis and one or more risk factors: – Atrial fibrillation – Prior stroke or TIA – Hypertension – Diabetes – Congestive heart failure – Age> 75 years	$CHADS_2$ of 3 or 4	– VTE within the past 3-12 mo – Non-severe thrombophilia: ▪ Heterozygous factor V Leiden ▪ Prothrombin gene mutation – Recurrent VTE – Active cancer (treated within 6 mo or palliative)	Assess need for bridging based on patient-specific and surgery related factors (see section D. below)
Low (<5% risk of TE)	Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke	$CHADS_2$ of 0 to 2 (assuming no prior stroke or TIA)	VTE >12 mo previous and no other risk factors	***Suggest no bridging*** (Grade 2C)

$CHADS_2$= congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and stroke or TIA

C. Patients may be also considered high thromboembolic risk* in the following scenarios and bridging should be considered

- Prior stroke or TIA occurring >3 months before the planned surgery and a $CHADS_2$ score <5
- Prior thromboembolism during temporary interruption warfarin
- Patient with remote (> 1 year ago), severe VTE with resultant pulmonary hypertension
- Surgery associated with an increased risk for stroke or other thromboembolism (i.e. cardiac valve replacement, carotid endarterectomy, major vascular surgery)

  ** In the above patients at high risk for thromboembolism AND undergoing high-bleeding risk procedures (major cardiac surgery, carotid endarterectomy surgery), it is not unreasonable to consider no bridging

D. Assessing need for bridging in moderate risk patients

i. Consider *bridging* with surgeries/procedures associated with a low risk for bleeding (Appendix I)

ii. Consider *no bridging* with surgeries /procedures associated with a high bleeding risk (Appendix II)

II. Inpatient Management

A. Major procedures

i. Recommendations for interruption and re-initiation of ***anticoagulants*** in admitted patients

a. Assessment of bleeding risk and adequate post-operative hemostasis should be considered prior to anticoagulation re-initiation

	TREATMENT DOSING		PROPHYLACTIC DOSING	
MEDICATION	**Cessation**	**Re-initiation Post-Op***	**Cessation**	**Re-initiation Post-Op***
Warfarin**	5 days (Grade 1C)	12 to 24 hours after surgery (evening of or next morning) (Grade 2C)	5 days	12 to 24 hours after surgery
UFH	4 to 6 hours (Grade 2C)	Low bleed risk surgery: 12-24 hours High bleed risk surgery: 48-72 hours	4 to 6 hours	≥ 12 hours
LMWH	24 hours*** (Grade 2C)	Low bleed risk surgery: 24 hours (Grade 2C) High bleed risk surgery: 48-72 hours (Grade 2C)	30mg BID: 12 hours 40mg daily: 24 hours	≥ 12 hours
Fondaparinux	72-96 hours	Consider a shorter acting agent until the pt is tolerant to anticoagulation	≥ 24 hours	≥ 12 hours
Dabigatran♦	1-2 days (CrCl≥ 50 ml/min) 3-5 days (CrCl < 50 ml/min) Consider longer period for more invasive procedures	▪ No specific information available ▪ Peak plasma concentrations reached in 1-2 hours ▪ Recommend re-initiate ≥ 24 hours and only if hemostasis achieved ▪ If oral anticoagulant cannot be used post-procedure, consider initiation of parenteral agent ▪ Recommend consultation with anticoagulation service	N/A	N/A
Rivaroxaban♦	≥ 24 hours	▪ No specific information available ▪ Peak plasma concentrations reached in 2-4 hours ▪ Recommend re-initiate ≥ 24 hours and only if hemostasis achieved ▪ If oral anticoagulant cannot be used post-procedure, consider initiation of parenteral agent ▪ Recommend consultation with anticoagulation service	≥ 24 hours	▪ No specific information available ▪ Peak plasma concentrations reached in 2-4 hours ▪ Recommend re-initiate ≥ 24 hours and only if hemostasis achieved. ▪ If oral anticoagulant cannot be used post-procedure, consider initiation of parenteral agent ▪ Recommend consultation with anticoagulation service

*Depending on surgical hemostasis

**If warfarin cannot be held for a full 5 days prior to surgery, refer to "Anticoagulant Reversal Guidelines" on UNMH RX webpage

***If using 1.5 mg/kg once daily, give ½ of dose 24 hours prior to procedure

♦Should not be used concomitantly with warfarin at either prophylactic or treatment doses, as this has not been studied. If overlap therapy is needed, use UFH or enoxaparin

ii. Recommendations for interruption and re-initiation of ***antiplatelet therapies***

SURGERY	RECOMMENDATION
Non-cardiac surgery	– Moderate to high risk for cardiovascular events*: suggest continuing ASA (Grade 2C) – Low risk for cardiovascular events: suggest stopping ASA 7 to 10 days before surgery (Grade 2C)
CABG	– With ASA monotherapy: Suggest continuing ASA (Grade 2C) – With dual antiplatelet therapy: (Grade 2C) ▪ Suggest continuing ASA around the time of surgery ▪ Suggest stopping clopidogrel/prasugrel 5 days before surgery
Patient with coronary stents having surgery	– Recommend deferring surgery for at least 6 weeks after placement of a bare-metal stent and for at least 6 months after placement of a drug-eluting stent (Grade 1C) – In patients who require surgery within 6 weeks of placement of a bare-metal stent or within 6 months of placement of a drug-eluting stent: ▪ Suggest continuing dual antiplatelet therapy around the time of surgery instead of stopping dual antiplatelet therapy (Grade 2C)

iii. Moderate to high-risk for CV events*: ischemic heart disease, compensated or prior CHF, diabetes, renal insufficiency or cerebrovascular disease
   a. Non-cardiac surgeries associated with increased risk of perioperative cardiovascular events (carotid endarterectomy/peripheral artery disease bypass surgery) may also benefit from aspirin continuation

iv. **Re-initiation**: Consider resuming ASA at the same time of warfarin within 24 hours after surgery
   a. Maximal antiplatelet effect occurs within minutes of administration of ASA

B. MINOR procedures (dental/dermatologic/ophthalmologic)

i. Anticoagulant therapy**

PROCEDURE	RECOMMENDATION
Minor dental procedures (Tooth extraction, endodontic procedures)	Suggest continuing warfarin with co-administration of an oral prohemostatic agent* OR stopping warfarin 2 to 3 days before the procedure (Grade 2C)
Minor dermatologic procedures (Excision of basal and squamous cell skin cancers, actinic keratosis, premalignant or cancerous skin nevi)	Suggest continuing warfarin around the time of the procedure and optimizing local hemostasis (Grade 2C)
Minor ophthalmologic procedures (Cataract surgery)	Suggest continuing warfarin around the time of the surgery (Grade 2C)

*UNMH formulary agent is aminocaproic acid oral solution (Amicar); dose = 10mL by mouth q 6 hours x 2 days post-procedure

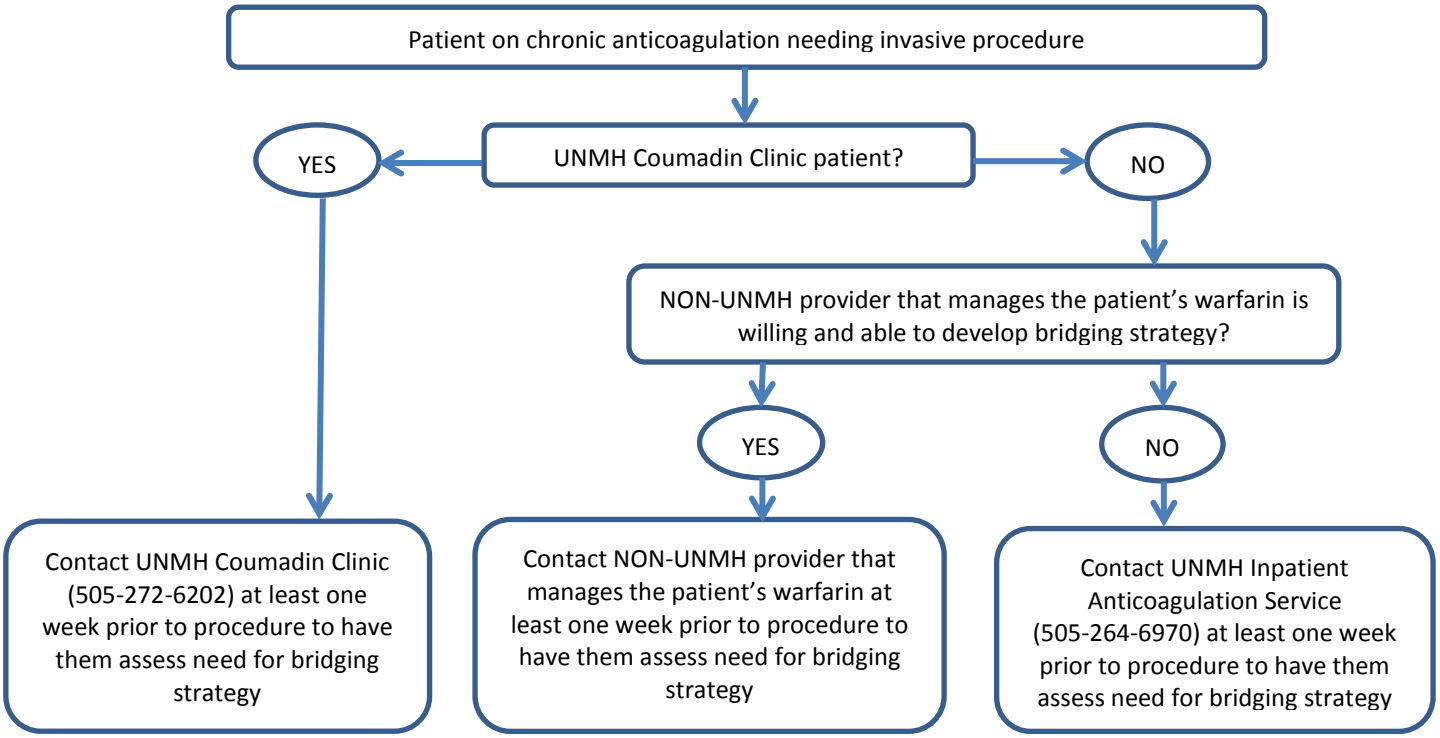
** Recommendations are for warfarin only. There is currently no available evidence as to how to manage patients on new oral anticoagulants undergoing minor procedures. Recommend consultation with anticoagulation service

ii. Antiplatelet therapy
   a. Low incidence of major bleeding when continuing aspirin therapy
   b. Recommendation: In patients receiving ASA for the secondary prevention of cardiovascular disease, suggest continuing ASA around the time of the procedure (Grade 2C).

III. Outpatient to inpatient management

A. All surgical patients on chronic anticoagulant therapy being seen pre-operatively in clinic need to have a clearly delineated peri-operative anticoagulant management strategy.

B. Surgical provider should refer to algorithm below to identify appropriate resource for assistance:



C. See appendix III below for a general template for a warfarin patient who warrants bridging

D. For newer oral anticoagulants (dabigatran, rivaroxaban), see table above (inpatient management), refer to package insert or, preferably, consult with a more experienced provider.

E. It is strongly recommended that a dosing template with specific instructions be filled out and given to patient at pre-operative clinic visit, along with any needed prescriptions, such as LMWH, etc

F. An electronic copy of the bridging plan should also be placed in Powerchart well before the procedure to provide guidance to inpatient providers.

Appendix I: Surgeries and procedures associated with a low bleeding risk

- Abdominal hernia repair
- Abdominal hysterectomy
- Axillary node dissection
- Endoscopically- guided fine needle aspiration
- Bronchoscopy + biopsy
- Cataract and non-cataract eye surgery
- Cholecystectomy
- Dilatation and curettage
- GI endoscopy +biopsy, enteroscopy, biliary/pancreatic stent without sphinecterotomy, endonosonography, without fine needle aspiration
- Hydrocele repair
- Noncoronary angiography
- Simple dental extractions
- Sternotomy wire removal
- Bowel polypectomy
- Bowel resection
- Carpal tunnel repair
- Central venous catheter removal
- Cutaneous and bladder/prostate/thyroid/breast/lymph node biopsies
- Endarterectomy or carotid bypass surgery
- Hemorrhoidal surgery
- Knee/Hip replacement and shoulder/foot/hand surgery and arthroscopy
- Pacemaker and cardiac defibrillator insertion and electrophysiologic testing
- Skin cancer excision

Appendix II: Surgeries and procedures associated with a high bleeding risk

- **Urologic surgery** and procedures consisting of transurethral prostate resection, bladder resection, or tumor ablation; nephrectomy; or kidney biopsy in part due to untreated tissue damage (after prostatectomy) and endogenous urokinase release
- **Pacemaker or ICD implantation** in which separation of infraclavicular fascial layers and lack of suturing of unopposed tissues within the device pocket may predispose to hematoma development
- **Colonic polyp resection, typically of large (i.e. >1-2 cm long) sessile polyps**, in which bleeding may occur at the transected stalk following hemostatic plug release
- **Surgery and procedures in highly vascular organs**, such as the kidney, liver, and spleen
- **Bowel resection** in which bleeding may occur at the bowel anastomosis site
- **Major surgery with extensive tissue injury** (i.e. cancer surgery, joint arthroplasty, reconstructive plastic surgery)
- **Cardiac, intracranial, or spinal surgery**, especially as small pericardial, intracerebral, or epidural bleeds can have serious clinical consequences
- **Any major operation** (>45 minute duration)
- **Multiple tooth extractions**

Appendix III: General bridging template for warfarin patient

Days before procedure	Date	Warfarin	INR	LMWH* bridging agent
-5		none	none	none
-4		none	none	none
-3		none	none	LMWH
-2		none	none	LMWH
-1		none	Check INR- give 1-2.5 mg vit K po if INR >1.6	LMWH in AM only (hold for 24 hours prior to procedure)
procedure		Resume home dose	none	none
+1		Continue home dose and adjust based on INR	Check INR	LMWH (start at least 24 hours post-procedure)
+2		Continue home dose and adjust based on INR	Check INR	Continue LMWH until INR >2
+3		Continue home dose and adjust based on INR	Check INR daily until >2 then PRN	Continue LMWH until INR >2

* need for and dosing intensity (prophylactic versus therapeutic) of LMWH should be determined by experienced provider

References

1. Martin MT, Kuchta AM, Nutescu EA. A clinician's guide to perioperative bridging for patients on oral anticoagulation. J Pharm Pract. 2010 Aug;23(4):303-12.
2. Douketis JD, Spyropoulos AC, Spencer FA, Mayr M, Jaffer AK, Eckman MH, Dunn AS, Kunz R. Perioperative Management of Antithrombotic Therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):e326S-50S.
3. Dabigatran etexilate (Pradaxa®) package insert. Available at https://www.pradaxa.com/. Accessed 8/14/2012
4. Rivaroxaban (Xarelto®) package insert. Available at http://www.xareltohcp.com. Accessed 8/14/2012

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