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Periprocedural Management of Antithrombotics

Warfarin: New Recommendations

Surgery and medical procedures can be challenging in warfarin-managed patients. Warfarin increases bleeding risk; therefore, it must be discontinued approximately 5 days before some procedures to allow clotting factors to be reestablished. Likewise, when warfarin is restarted after the procedure, it takes 4 to 5 days to establish maximum effect. The patient is thought to be at risk for thromboembolism during this warfarin-free period. Low molecular weight heparins (LMWH) have often been used in place of warfarin to "bridge" this gap.

A 2015 study, BRIDGE, looked at perioperative bridging with LMWH in warfarin-treated patients with atrial fibrillation undergoing an elective surgery or invasive procedure.[1] It found that bridging was not associated with a reduction in stroke, systemic embolism, or transient ischemic attack in this population; in fact, the risk of bleeding was significantly increased. These findings support changes to bridging recommendations for patients with low/moderate thromboembolic risk.[2-4] Bridging is still recommended for patients at high risk of thromboembolism undergoing procedures or surgeries that carry a high bleeding risk.[2-4]

The options for management include:

1. continuing warfarin therapy through the procedure ensuring the INR remains therapeutic;
2. stopping warfarin with no bridging; and
3. stopping warfarin with bridging.[1-4]

For options 2 and 3, warfarin is stopped 5 days before the procedure (Day – 5) and restarted the day of (Day 0) or the day after (Day + 1) the procedure depending on its bleed risk .[1-4] For option 3 (bridging), LMWH or unfractionated heparin (UFH) is started 2 days after discontinuing warfarin (Day – 3), stopped prior to the procedure according to the protocol for the type of heparin product being used[1-4], and resumed post-procedure after an interval determined by the patient's hemostasis status and the bleed risk of the procedure.[1,2] The heparin product is discontinued once therapeutic INR is achieved.[1-4] See Table 4 and Figure 1 for details. The remainder of this article provides a detailed guide for optimal perioperative anticoagulation management.

The decision to bridge must be based on each individual's bleeding versus thromboembolic risks. Steps to determine if bridging is necessary are as follows:

1. **Determine bleeding risk of procedure:**

Table 1 can be used to help guide the bleeding risk of a procedure; however, **final determination of bleeding risk rests with the surgeon/physician.**

Table 1: Bleeding Risk of Surgery/Procedure

Standard	Moderate to High
• Abdominal surgery, minor (abdominal hernia repair, abdominal hysterectomy)[2] • Arthrocentesis[3] • Bone marrow aspirate[3] • Bronchoscopy ± biopsy[2] • Cardiac catheterization (with or without coronary intervention)[1] • Carpal tunnel repair[2] • Cataract surgery[1,3,4] • Catheter ablation[4] • Central venous catheter removal[2] • Cholecystectomy[2] • Coronary angiography[3,4] • Dental extractions (simple)[1-4] • Dermatologic procedures (most)[1,3,4] • Endodontic procedures (simple)[3] • Gastrointestinal endoscopy without polyp removal[1-3] • Hemorrhoidal surgery[2] • Hydrocele repair[2] • Node biopsies[2]: e.g. cutaneous,[3] bladder, thyroid, breast, lymph[3] • Paracentesis[3] • Thoracentesis[3] • Any surgery or procedure <1 hr[1]	• Abdominal surgery, major[1-4] • Biliary sphincterectomy[2] • Biopsies: e.g. cervical cone,[3] liver,[3] prostate,[1,3] renal[1-3] • Cardiac surgery[2-4] • Dental – more invasive (e.g. multiple tooth extractions)[2] • Endodontic – more invasive • Fine-needle aspiration, endoscopically guided[2] • Intestinal anastomosis surgery[3] • Laminectomy[2] • Neurosurgery[2-4] • Ophthalmic surgery – more invasive • Orthopedic surgery[1-4] • Pacemaker or implantable device placement[1,3,4] • PEG placement[4] • Pericardiocentesis[3] • Pneumatic dilation[2,4] • Polypectomy during colonoscopy[2-4] • Thoracic surgery[1,3,4] • Transurethral prostate resection[2] • Urologic surgery[1-4] • Vascular surgery[1-4] • Any other procedures >1hr[1,2]
CABG: coronary artery bypass graft; PEG=percutaneous endoscopic gastrostomy	

Patient factors also contribute to bleeding risk. The HAS-BLED calculator assigns a number out of 9 based on risk factors for bleeding. A score of ≥3 indicates an increased bleeding risk would be associated with any surgery or procedure for that particular individual.

2. Determine individual thromboembolic risk

Table 2 can be used to determine a thromboembolic risk category for the three most common indications for warfarin therapy. The $CHADS_2$ calculator and CHA_2DS_2-VASc calculator score stroke risk factors (e.g. hypertension, diabetes mellitus) in individuals with atrial fibrillation and assign a number value; the higher the score, the greater the risk of stroke.

Table 2: Thromboembolic Risk (modified[2,3])

Thromboembolic Risk Category	Clinical Indication for Warfarin Therapy		
	Atrial Fibrillation	Mechanical Heart Valve	Venous Thromboembolism
Very High	CHA_2DS_2-VASc ≥6 (or $CHADS_2$ 5-6)	Any mechanical mitral valve	Recent DVT or PE (within 3 months)
	Recent stroke/TIA (within 3 months)	Older aortic mechanical aortic valve (caged-ball, tilting disk)	Severe thrombophilia (deficiency of: protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
	Rheumatic valvular heart disease	Recent stroke/TIA (within 6 months)	Prior ATE or VTE during warfarin interruption
High	CHA_2DS_2-VASc 4-5 or $CHADS_2$ 3-4	Bileaflet aortic valve prosthesis with ≥1 risk factor†	VTE within 3-12 months
			Non-severe thrombophilia (heterozygous factor V Leiden; prothrombin gene mutation)
			Recurrent VTE
			Active cancer
Moderate	CHA_2DS_2-VASc 2-3 or $CHADS_2$ 0-2 (no prior stroke or TIA)	Bileaflet aortic valve prosthesis without other risk factors† for stroke	VTE >12 months ago and no other risk factors†
Low	CHA_2DS_2-VASc <2		

†Risk factors: atrial fibrillation, prior stroke or TIA, hypertension, diabetes, congestive heart failure, age > 75 years

ATE = arterial thrombotic event; DVT= deep vein thrombosis; PE = pulmonary embolism; TIA = transient ischemic attack; VTE = venous thrombotic event;

3. **Using bleeding and thromboembolic risks, determine warfarin management and bridging requirements**

Table 3: Perioperative management of warfarin[2-4]		
Bleed Risk	**Thromboembolic Risk**	**Management**
Standard	Any	No interruption required
	Very high and transient	Delay procedure until risk returns to baseline if possible; otherwise, no interruption.
High	Low-moderate	Stop warfarin, no bridge
	High	Bridge, see exceptions*
	Very high and transient	Delay procedure until risk returns to baseline if possible; otherwise, bridge
* **Implantation of cardiac devices** (e.g. pacemakers, cardioverter-defibrillator): continuing warfarin was associated with lower bleeding than bridging based on one trial.[5] A position document by the European Heart Rhythm Association,[6] recommends continuing warfarin over bridging. **Angioplasty, catheter ablation, atherectomy**: continuing warfarin associated with the same or fewer complications compared to bridging according to a meta-analysis involving > 20 000 patients.[7]		

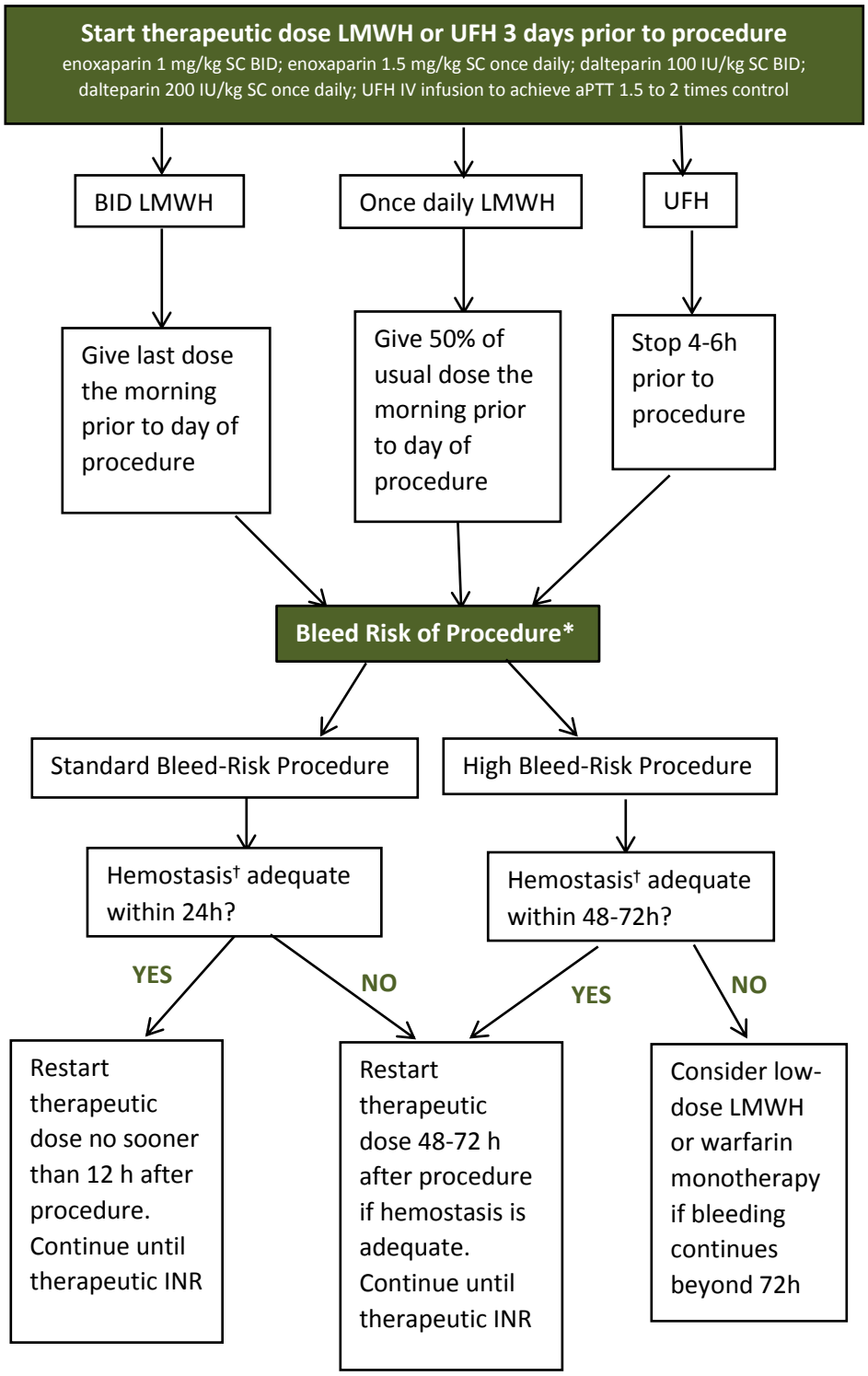
This table is a guide ONLY. Each patient must be individually assessed and managed.

4. **Implement peri-procedural warfarin management**

Use Table 4 to guide when to stop and restart warfarin; if bridging is warranted, use Figure 1 to guide starting and stopping LMWH or UFA.

Table 4: Peri-procedural discontinuation and resumption of warfarin[2-4]					
Bleed risk of procedure*	**Day -5**	**Day -1**	**Day 0 (Day of Surgery)**	**Day +1**	**Day +2**
Standard	Stop warfarin (no dose this day)	Check INR If >1.5, give Vit K_1 1-2 mg PO	Start evening of Day 0 if drinking fluids	Continue with usual dose	Continue with usual dose
High				Start AM if drinking fluids	Continue with usual dose
*See Table 1					

Figure 1: Implementing peri-procedural bridging[2-4]



aPTT=activated partial thromboplastin time; LMWH=low molecular weight heparin; UFH=unfractionated heparin *See Table 1

†Based on assessment of wound site, drainage fluid, and expected post-procedural bleeding.

Bridging NOACs (Novel Oral Anticoagulants) and Antiplatelets:

In general, the short half-lives of the NOACs eliminate the need for bridging. Renal function affects NOAC's elimination, so must be taken into account when discontinuing the medications before a surgery/procedure.[8]

Table 5: General Recommendations for Periprocedural Management of Other Antithrombotics – Time to Stop Prior to Procedure

Novel Oral Anticoagulants			
		Standard Bleeding Risk	High Bleeding Risk†
Dabigatran (Pradaxa®)[9]			
Renal Function (CrCl)	≥80 ml/min	≥24 h	≥48 hr
	50-79 m//min	≥36 hr	≥ 72 hr
	30 -49 ml/min	≥48 hr	≥96 hr
	<30 ml/min	CONTRAINDICATED (≥ 5 days)	CONTRAINDICATED (≥ 5 days)
Rivaroxaban (Xarelto®)[10]			
Renal Function (CrCl)	≥30 ml/min	≥24 hr	≥ 48 hr
	<30 ml/min	CONTRAINDICATED (≥36 hr)	CONTRAINDICATED (≥48 hr)
Apixaban (Eliquis®)[11]			
Renal Function (CrCl)	>30 ml/min	≥24 hr	≥48 hr
	15-29 ml/min	≥36 hr	≥48 hr
	<15 ml/min	CONTRAINDICATED (Likely >36 hr required)	CONTRAINDICATED (Likely >48 hr required)
Parenteral Anticoagulant			
Fondaparinux (Arixtra®)[12]	2 to 4 days prior (If low bleeding risk, 24 hr may be sufficient) Extend if CrCl 30-50 ml/min		
Antiplatelets[13]*			
ASA ASA/Dipyridamole (Aggrenox®)	Low CV Risk	7-10 days before	
	Moderate to High CV Risk	Do not stop	
Clopidogrel (Plavix®)	5 days before		
Prasugrel (Effient®)	5 to 7 days before		
Ticagrelor (Brilinta®)	5 days before		

CrCl= creatinine clearance; CV= cardiovascular

†Hold longer if major surgery, spinal puncture, or other reginal anesthesia where complete hemostasis required; consult specialist. *If patient has stent, defer procedure x 6 weeks after bare metal stent, defer x 6 months after drug-eluting stent. If cannot be deferred, do not stop antiplatelet.

Conclusion

Patients on antithrombotics requiring surgery or invasive procedures present a challenge. Striking a balance between adequate, but not overanticoagulation, is made difficult by the sheer number of factors affecting hemostasis and thromboembolism both in the individual and as a result of the procedure. Data demonstrating an increased risk of bleeding with no change in VTE risk supports abandonment of bridging in some lower-risk patients.

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