PERI-OPERATIVE MANAGEMENT OF ANTITHROMBOTICS

A. PERI-OPERATIVE MANAGEMENT OF ANTITHROMBOTICS

1. Management of antithrombotics before and after invasive procedures requires careful, patient-specific evaluation of the risk of bleeding associated with the surgical procedure as well as the risk of thromboembolism associated with the underlying disease state for which anticoagulation is indicated. Management plans should be made in consultation with the physician performing the surgery/procedure.
2. In general, hold antithrombotics 2-3 half-lives if low risk of bleeding, hold 4-5 half-lives if high risk of bleeding
3. This tool is intended to guide the clinician in deciding *if* bridging is necessary based on the risk profile, and if indicated, how to construct a plan that is consistent with expert guidelines.
   - Bridging during the 24-48 hours of interruption and prior to intervention is usually not necessary with drugs that have short half-lives, quick onset of action
   - Bridging is usually necessary with long half –life medication such as warfarin

TABLE 1: PERI-OPERATIVE MANAGEMENT OF ANTITHROMBOTICS

DRUGS	HALF-LIVES	HOLD PRIOR TO PROCEDURE (Assess renal function for renally cleared drugs*)	RESUME POST PROCEDURE (*After hemostasis is achieved*)
ANTIPLATELETS - ORAL (weigh cardiac risk versus bleeding risk when holding antiplatelets - may have to check with cardiologist)			
ASA	20 min (inhibits for the life of platelets 7-10 days)	• Continue ASA if high cardiac risks (acute coronary syndrome, coronary stents, recent CVA), low bleeding risk • Hold 5-7 days if low cardiac risk, high bleeding risk	Within 24 hrs ❖ ASAP if coronary stents
Clopidrogrel (Plavix®)	6 hrs (inhibits for the life of platelets 7-10 days)	• Patients with stent insertion usually require a minimum of 1 years DAPT (Dual antiplatelet therapy) • Bare metal stent (BMS): may interrupt DAPT after a minimum of 6 weeks of therapy • Drug eluting stent (DES): may interrupt DAPT after a minimum of 6-12 months of therapy, ***must check with cardiologist first*** • If urgent surgery within 6 weeks of BMS or 6 months of DES, continue DAPT around the time of surgery (do not hold DAPT) • Elective surgeries (patients not with coronary stents or stents > 1 year): hold for at least 5-7 days pre-procedure	Within 24 hrs ❖ ASAP if coronary stents
Prasugrel (Effient®)	7 hrs (2-15 hrs) (inhibits for the life of platelets 7-10 days)		
Ticagrelor (Brellinta®)	7 hrs (ticagrelor) 9 hrs (active metabolite) (inhibits for the life of platelets 7-10 days)		
ANTICOAGULANTS - ORAL (bridging is usually not necessary during the 24-48 hrs interruption)			
Apixaban* (Eliquis®)	8-15 hrs (renal ~ 27%) (longer in renal insufficiency)	Any CrCl (apixaban is only 27% renally eliminated): • Lower risk bleeding*: hold 1 day pre-procedure • Higher risk bleeding*: hold 2 days pre-procedure	• Low risk bleeding*: resume 24hrs post-procedure • High risk bleeding*: resume 48-72hrs post-procedure ❖ If NPO post-op, consider using parenteral anticoagulant until no longer NPO
Dabigatran* (Pradaxa®)	12 - 17 hrs (renal 80%) (longer in renal insufficiency)	CrCl ≥50 mL/min: • Lower risk bleeding*: hold 1 day pre-procedure • Higher risk bleeding*: hold 2 days pre-procedure CrCl 30-50 mL/min: • Lower risk bleeding*: hold 2-3 days pre-procedure • Higher risk bleeding*: hold 4-5 days pre-procedure CrCl < 30 mL/min: • Lower risk bleeding*: hold 3-5 days pre-procedure • Higher risk bleeding*: hold > 5 days pre-procedure	
Rivaroxaban* (Xarelto®)	5 - 9 hrs (renal 66%); 11-13 hrs (elderly (longer in renal insufficiency)	CrCl ≥ 50mL/min: • Lower risk bleeding*: hold 1 day pre-procedure • Higher risk bleeding*: hold 2 days pre-procedure CrCl < 50mL/min: • Lower risk bleeding*: hold 2 days pre-procedure • Higher risk bleeding*: hold 3-4 days pre-procedure	
Warfarin	40 hrs	See section **B. *Bridging anticoagulation during warfarin interruption***	
ANTICOAGULANTS - PARENTERAL			
Argatroban	40-50 min Hepatic impairment: ≤181 min	Hold 2-3 hours until PTT < 40 Hold longer in hepatic impairment, until PTT <40	Treatment: • Low risk bleeding*: resume 24hrs post-procedure • High risk bleeding*: resume 48-72hrs post-procedure Prophylaxis: • Resume ≥ 12 hrs post-procedure
Enoxaparin* (Lovenox®)	3-5 hrs (longer in renal insufficiency)	Treatment: • Cl > 30 mL/min: hold 24 hrs pre-procedure • CL ≤ 30 mL/min: hold at least 48-72 hrs pre-procedure Prophylaxis: • 30mg bid: hold 12 hrs pre-procedure • 40mg daily: hold 24 hrs pre-procedure ➢ Hold longer if renal insufficiency	
Fondaparinux* (Arixtra®)	17-21 hrs (longer in renal insufficiency)	Treatment: hold at least 4-5 days pre-procedure Prophylaxis: hold at least 24 hrs pre-procedure ➢ Hold longer if renal insufficiency	
Heparin IV	30-90 min (dose dependent)	Treatment : hold 4-6 hrs pre-procedure until PTT < 40 Prophylaxis: hold 4-8 hrs pre-procedure	

*See TABLE 2 for bleeding risks

B. BRIDGING ANTICOAGULATION DURING WARFARIN INTERRUPTION

This tool will help:

- Estimate bleeding risk of procedure – if warfarin were continued
- Estimate the risk of thrombosis – if warfarin were interrupted
- Formulate a patient-specific plan based on the recommendations of ACCP Guidelines (*Chest*, February 2012)

TABLE 2: BLEEDING RISKS (does warfarin require interruption?)

LOW	MODERATE	HIGH / VERY HIGH
Skin biopsy Simple excision; MOHS Cataract Extraction Simple dental extraction; Restorations Endodontics; Prosthetics Dental hygiene; Periodontal therapy Colonoscopy ± biopsy* Small bowel push enteroscopy EGD ± biopsy; Flex sigmoidoscopy ± biopsy ERCP without sphincterotomy Biliary/pancreatic stent w/o sphincterotomy Endosonography w/o fine needle aspiration Joint/soft-tissue aspiration or injection Minor podiatric procedures *For patients w/ **high thrombosis risk**, colonoscopy without polypectomy may be done under full anticoagulation.	Complicated dental extractions Gingival and alveolar surgery Hair transplantation Blepharoplasty Facelifts Other intra-abdominal surgery Other intra-thoracic surgery Other orthopedic surgery **Procedures not in HIGH or LOW list**	**VERY HIGH:** Intracranial or Spinal surgery, epidural/spinal anesthesia CABG, Mechanical Valve surgery **HIGH:** Polypectomy Prostate surgery or biopsy Renal or Hepatic biopsy Cervical cone biopsy Cardiac defibrillator/ pacemaker insertion Esophageal dilation PEG tube placement Treatment of varices Intestinal anastomosis surgery Laser ablation & coagulation Endoscopic sphincterotomy Endosonography w/ fine needle aspiration **Major Surgery**: Hip/knee replacement, vascular, urologic, cancer, or reconstructive plastic surgery

Patient History or data lending increased bleeding risk

Recent GI Bleed (< 6mo)	Thrombocytopenia (<100K)
Chronic renal or hepatic dz	Anemia (HCT <30%)
Bleed assoc w/ surgery/bridging	Age > 75
Active or prior peptic ulcer dz	**Spinal anesthesia or epidural**

Bridging Exclusion Criteria

- Allergy to unfractionated heparin or LMWH
- H/o HIT or severe thrombocytopenia
- H/o bleeding disorder or intracranial hemorrhage
- Gastrointestinal bleeding within the last 10 days
- Major trauma or stroke within the past 2 weeks
- Unsuitable home environment to support therapy

TABLE 3: THROMBOSIS RISKS (is bridging needed?)

Indication	LOW	MODERATE	HIGH
	1-year risk of arterial embolism less than 5%, or 1-month of VTE < 2%.	1-year risk of arterial embolism 5% - 10% or 1-month risk of VTE 2% to 10%.	1-year risk of arterial embolism greater than 10%, or 1-month risk of VTE greater than
AFib	AFib + CHA_2DS_2-VASc score < 2 without previous stroke	AFib + CHA_2DS_2-VASc = 2 or 3	AFib + CHA_2DS_2-VASc ≥ 4 AFib with Rheumatic heart disease
Heart valve	Mechanical Aortic Valve (bileaflet*) **without** AFib or CHA_2DS_2-VASc risk factors	Mechanical Aortic Valve (bileaflet*) **plus** AFib or CHA_2DS_2 VASc risk	Any Mitral Valve prosthesis Older Mech. Aortic Valve (caged-ball or tilting disc) Recent (within 3 mo) stroke or TIA
VTE	Single VTE > 12 months ago; No other risk factors	3-12 months since VTE Recurrent idiopathic VTE Active Cancer **Heterozygous for**: Factor V Leiden Prothrombin mutation	**Deficiency of** Protein C, Protein S, or Antithrombin III Antiphospholipid antibody syndrome Multiple hypercoagulable abnormalities Homozygous for Factor V Leiden Less than 3 months since VTE Prior thrombosis during warfarin interruption

CHA_2DS_2-VASc Score	Stroke risk (%)
0	0%
1	1.3%
2	2.2%
3	3.2%
4	4.0%
5	6.7%
6	9.8%
7	9.6%
8	6.7%
9	15.2%

CHA_2DS_2-VASc scores (A. FIB.)

CONDITIONS	PTS
Congestive heart failure (systolic)	1
HTN (consistently >140/90 mmHg or on BP meds)	1
Age 75 years and older	2
Diabetes Mellitus	1
h/o Stroke/TIA or thromboembolism	2
Vascular disease (h/o MI, CAD, peripheral arterial disease or aortic plaque)	1
Age 65-74 years	1
Sex category (female)	1

Past history or data lending increased VTE risk

- History of VTE associated with surgery
- History of malignancy
- VTE rick associated with the procedure to be done
- Strong family history of VTE
- Age > 60
- Obesity
- Smoker
- Peripheral vascular occlusive disease

TABLE 4: BLEEDING and THROMBOSIS RISKS

Thrombosis \ Bleeding Risks	LOW	MODERATE	HIGH / VERY HIGH
LOW	Stopping warfarin is not necessary; alternatively, consider omitting 2 doses	Last warfarin dose 6 days pre-procedure No bridging	Last warfarin dose 6 days pre-procedure No bridging
MODERATE	Continue warfarin	BRIDGING; Therapeutic dosing preferred; Alternatively, use prophylactic dosing. **See TABLE 5 -** Bridging Plan	BRIDGING; Therapeutic dosing preferred; Alternatively, use prophylactic dosing. **See TABLE 5 -** Bridging Plan
HIGH	Continue warfarin	BRIDGING; Therapeutic dosing. **See TABLE 5 -** Bridging Plan	BRIDGING; Therapeutic dosing. **See TABLE 5 -** Bridging Plan

TABLE 5: IMPLEMENTATION OF BRIDGING PLAN

DAY	ACTION	LABS/NOTES
7-10 days Pre-procedure	Obtain **INR** for patients on warfarin	**INR** to r/o extremely elevated INR
Day (-6)	**Last Dose of warfarin**	Patients w/ low doses of warfarin (≤ 2.5mgdaily) will reverse more slowly than patients w/ high doses (> 7.5mg daily)
Day (-5)	Begin therapeutic enoxaparin in evening In moderate thrombosis risk and/or high bleed risk, prophylactic enoxaparin dosing is an alternative to full dose.	See **TABLE 6** for Enoxaparin dosing
Day (-4)	Enoxaparin **Last enoxaparin dose in renal impairment*** ***(CrCl < 30ml/min)**	**INR** – 1 to 2 days prior to high bleeding risk procedures If INR is ≥ 1.5 , consider low dose vitamin K 2.5mg PO on Day (-1)
Day (-1)	**Last enoxaparin at least 24hrs pre-procedure**	Give vitamin K if needed as above
Procedure Day 0	Restart warfarin this evening *(150% of usual dose)*	Moderately increased warfarin doses for 1-2 days may avoid prolonged low INRs Recheck INR if gave vitamin K on Day (-1) Proceed with surgery if INR ≤ 1.4
Day 1	Restart enoxaparin – no closer than **24hrs** post-procedure Establish hemostasis before starting LMWH. Resume antiplatelet agents – 24hrs post procedure Warfarin *(100%-150% of usual dose)*	Same dose of enoxaparin as given pre-procedure See **TABLE 6** for Enoxaparin dosing ***If high bleeding risk**, omit LMWH or do not resume until 48 to 72hrs post procedure.*
Day 2	Warfarin usual dose	
Day 3	Continue enoxaparin until INR approaches target range. Warfarin doses based on INR Results	**INR**
Day 5		**INR** – and every 2-3 days until in target range.

TABLE 6: ENOXAPARIN DOSING TABLE

ENOXAPARIN	THERAPEUTIC DOSING	PROPHYLACTIC DOSING	Enoxaparin syringes availabilities
CrCl ≥ 30mL/min	1 mg/kg SC q12h	40mg SC q24h 30mg SC q12h	30mg, 40mg, 60mg, 80mg, 100mg, 120mg, 150mg (no partial doses)
CrCl 10-30mL/min	1 mg/kg SC q24h	30mg SC q24h	
CrCl < 10mL/min or dialysis	Do NOT use enoxaparin (suggest heparin instead)	Do NOT use enoxaparin (suggest heparin instead)	

REFERENCES:

1. Darvish-Kazem S et al. Perioperative management of antiplatelet therapy in patients with coronary stent who need noncardiac surgery. A systemic review of clinical practice guidelines. Chest 2013;144(6)1848-56
2. Douketis JD et al. Perioperative management of antithrombotics. Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-based practice guidelines. Chest 2012;141(2)(suppl):e326S-e350S
3. Ferraris VA et al. 2012 Update to the society of thoracic surgeons guideline on use of antiplatelet drugs in patients having cardiac and noncardiac operations. Ann Thorac Surg 2012;94:1761-81
4. Spahn DR. Perioperative antiplatelet therapy. Am Fam Physician 2010;82(12):1484-89
5. Douketis JD, Woods K, Crowther MA. Anticoagulant Management of Patients Undergoing Elective Surgery who Require Temporary Interruption of Warfarin Therapy; Second Edition, June, 2005. Jaffer AK, Brotman DJ, Chukwumerije N. When Patients on Warfrin Need Surgery. Clev Clin J Med; Vol 70(11) Nov 2003.
6. Eisen GM, B aron TH, Dominitz JA, Faigel DO, Goldstein JL, Johanson JF, et al. Guidelines on the management of anticoagulation and antiplatelet therapy for endoscopic procedures. Gastrointest Endosc 2002;55:775-9.