MedStar Health

Guideline: Perioperative Management of Antithrombotic Agents			Version Number: 2.0 10/24/17
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Purpose: To provide guidance on determining the appropriate management of anticoagulant and antiplatelet therapy in surgical and procedural patients. *Deviation from these guidelines may be warranted based on individual patient condition and provider discretion.*

Background:

The perioperative period is complicated by competing factors of bleeding risk associated with the operation and risk of thrombombosis secondary to the patient's underlying pathology and postoperative immobilization. The risk of thrombosis (e.g. VTE) depends on patient-specific risk factors, whereas the bleeding risk of a procedure is determined based on the estimated blood loss associated with a procedure. The intent of this document is to provide guidance on determining the bleeding risk of a procedure and recommendations on the management of anticoagulant therapy.

Guidelines:

A. Bleeding Risk

Table 1 classifies procedures as either high-risk or low-risk bleeding procedures. Based on the bleeding risk of the procedure, the timing of perioperative antithrombotic cessation and the need for bridging therapy and are determined (**Table 4**). The risk stratification recommendations in **Table 1** are to be used as a guidance tool and are not intended to supersede clinical judgment. For further details regarding specific procedure risk and stratification, please refer to respective specialty guidelines.

There is a significantly increased risk of serious bleeding complications associated with procedures involving neuraxial anesthesia or spinal involvement. In comparison to the recommendations for low- and high-risk procedures, the timing of perioperative antithrombotic cessation for these procedures is more conservative.[11,13]

Table 1: Bleeding Risk Stratification[1,2,3,4]

Procedure Class	Risk of Bleeding	
	Low Risk of Bleeding	High Risk of Bleeding
Breast	Breast biopsy (FNA or core needle)	All breast surgery or axillary dissection I&D of abscess
Cardiac Surgery	None	All cardiac surgery
Cardiovascular	Electrophysiology testing or ablation* (most) Intra-aortic balloon pump Diagnostic coronary angiography: radial access TAVR/TAVI (femoral/iliac)*	Ablation for VT structural or epicardial Coronary intervention Diagnostic coronary angiography: femoral or brachial access* TAVR/TAVI (transapical or axillary/direct access) Cardiac implantable electronic devices (pacemaker, ICD, lead management, pocket revision)
Dental	Endodontic procedures (root canal)	Tooth Extraction* Reconstructive procedures
Dermatology	All major or minor procedures	None
Gastroenterology	Passage of endoscope for diagnostic purposes (with or without biopsy) Endoscopic retrograde cholangiopancreatography (ERCP) w/o sphincterotomy Lumenal self-expanding metal stent placement* Enteroscopy (including balloon-assisted)	Large polypectomy (>1cm), ERCP or EUS with biopsy Biliary or pancreatic sphincterotomy Percutaneous endoscopic gastrostomy (PEG) placement Variceal band ligation* Coagulation or ablation of tumors, vascular lesions
General Surgery	Esophageal dilation or stent Tube Thoracostomy (chest tube)	Any Major Tissue injury Laproscopy, tracheostomy, thoracotomy or VATS

Hematology	Bone marrow biopsy	None
Interventional Radiology	Vascular access: Dialysis access, tunneled central line, PICC IVC filter Aspiration of abdominal or pelvic abscess Non-vascular: drainage exchange Placement of small-caliber drains: paracentesis, thoracentesis	Any arterial access (femoral or brachial): Angiography and/or arterial stenting Any embolization or tumor ablation (RFA, cryoablation) Biopsy of organs (liver, lung, kidney) Transjugular intrahepatic protosystemic shunt (TIPS) Gastrostomy tube initial placement, nephrostomy tube placement Large abscess drainage Biliary intervention (new intervention)
Nephrology	Arteriogram or venogram	Arteriovenous fistula management Kidney Biopsy
Neurology	None	Lumbar puncture Myelography or needle electromyography*
Neurosurgery	None	Intracranial, spinal surgery
Obstetrics & Gynecology	Colposcopy, Hysteroscopy Cervical LEEP, Vulvar biopsy/excision Dilation & curettage (D&C), Endometrial Biopsy Amniocentesis, CVS	Cesarean delivery or operative vaginal delivery Hysterectomy, Oopherectomy Laparotomy, Operative laprascopy
Ophthalmology	Cataract, blepharoplasty, pars plana vitrectomy Skin only eyelid procedures	Orbital Surgery Ptosis repair Corneal transplation Vitreoretinal procedures and submacular surgery
Orthopedic procedures	Arthrocentesis Minor hand surgery: carpal tunnel release, trigger finger, benign tumor	Arthroscopy or Joint replacement Moderate hand surgery: cubital tunnel release, ORIF distal radius, thumb arthroplasty Extremity fracture (trauma) All spine surgeries & Lumbar facet joint injections
Otolaryngologic surgery	Diagnostic fiberoptic laryngoscopy, nasopharyngoscopy or sinus endoscopy	Any sinus surgery Biopsy or removal of nasal polyps, turbinate cautery Thyroidectomy, parotidectomy, septoplasty Tracheostomy Head and neck tumor resection Neck dissection Head and neck reconstruction
Plastic Surgery	Injection treatment (Botox, fillers) Laser treatment	Reconstructive Surgery or Aesthetic Surgery Aesthetic (Cosmetic) surgery Hand surgery Breast Implant surgery
Pulmonary	Airway stent placement Endobronchial FNA Diagnostic bronchoscopy (w/ or w/o bronchioalveolar lavage)	Endobronchial tumor removal (laser, rigid bronchoscopy) Transbronchoscopic biopsy, cryobiopsy Stricture dilation
Rheumatology	Arthrocentesis	None
Urology	Cystoscopy w/o biopsy Ureteroscopy w/ or w/o lithotripsy Ureteral stent/exchange	Circumcision Extracorporeal shock-wave lithotripsy (ESWL) Transurethral prostatectomy Prostate outlet procedures, Bladder resection^ (TURBT) Penile Prosthesis Tumor ablation or lymph node dissection
Vascular Surgery	Venous ablation	Carotid endarterectomy Open or endovascular aneurysm repair Vascular bypass grafting, arterial stenting Venous phlebectomy

*unclear consensus in literature, communication with proceduralist

B. Cessation of Anticoagulant Therapy

Based on the bleeding risk of the procedure, the timing of perioperative antithrombotic cessation and the need for bridging therapy and are determined (**Table 4**). Due to limited randomized, controlled studies, the timing of perioperative antithrombotic cessation is based primarily on pharmacokinetic data. For high-risk bleeding procedures, a calculated "minimal" remaining anticoagulant effect (3-6%) is desired and therefore, the timing of perioperative antithrombotic cessation is calculated to be 4-5 half-lives. For low-risk bleeding procedures, a calculated "mild" anticoagulant effect (12-25%) is desired and antithrombotics should be discontinued 2-3 half-lives prior to the procedure.

For each indication for anticoagulant and/or antiplatelet therapy (e.g. non-valvular atrial fibrillation, VTE, etc.), there is a window of time during which cessation of anticoagulant therapy is **not** recommended due to increased risk of a thromboembolic event (**Table 2**). In these cases, which are considered contraindications to anticoagulant cessation, surgery should be delayed if possible. If the procedure cannot be delayed, anti-platelet/anti-thrombotic therapy may be continued/discontinued based on the patient's risk of thrombosis, the risk of bleeding associated with the procedure, and clinical judgment.

Table 2. Contraindications to Cessation of Antithrombotic Therapy

Indication	Cessation of Therapy Contraindicated
Anticoagulant Therapy	
Non-Valvular Atrial Fibrillation	<3 months status post Transient Ischemic Attack (TIA), Ischemic Stroke, or Systemic Embolism
Venous Thromboembolism	<3 months status post venous thromboembolism or pulmonary embolism
Prosthetic Heart Valve	<3 months status post prosthetic heart valve replacement
Antiplatelet Therapy	
Stable Ischemic Heart Disease (no recent ACS) PCI Angioplasty Bare Metal Stent (BMS) Drug Eluting Stent (DES) Coronary Artery Bypass Graft (CABG)	 <2 weeks <4 weeks <6 months <12 months
Acute Coronary Syndrome (NSTEMI or STEMI, regardless of s/p specific PCI)	<12 months

There are a select group of procedures for which perioperative cessation of antiplatelet therapy is NOT recommended. Antiplatelet therapy should NOT be discontinued prior to surgery in the following cases:

- Carotid Endarterectomy (CEA)
- Lower Extremity Bypass
- Endovascular Abdominal Aortic Aneurysm Repair (EVAR)
- Open Abdominal Aortic Aneurysm Repair (oAAA): *P2Y12 inhibitors (e.g. clopidogrel) must be stopped prior to this procedure, but aspirin may be continued.*

C. Bridging Antithrombotic Therapy

Bridging antithrombotic therapy with heparin or enoxaparin is recommended only for vitamin K antagonists (i.e. warfarin) interruption in the case of the **high thromboembolic risk** and **low bleeding risk procedure.** Criteria for high thromboembolic risk, and therefore, for bridging is outlined in Table 4 below.

Table 3. Criteria for Heparin/Enoxaparin Bridging

Anticoagulation Indication	Criteria for Heparin/Enoxaparin Bridging
Atrial Fibrillation	CHA_2DS_2-VASc > 7
Venous thromboembolism risk	• VTE within <3 months • Prior VTE during interruption of VKA therapy during high-risk surgery • Severe thrombophilia (protein C/S deficiencies, antithrombin deficiency, antiphospholipid antibody • Caprini Score >8
Mechanical Heart Valve	• Any mitral valve or tricuspid prosthesis • Any "old" mechanical aortic valve prosthesis (caged-ball or tilting disc) • Recent thromboembolic event: <6months s/p stroke or TIA • Prior thromboembolism during interruption of anticoagulation • High-risk thromboembolism surgery: cardiac valve replacement, carotid endarectomy, major vascular surgery

*Additional consideration on case-by-case basis for patient's individual bleeding risk factors (apart from procedure risk), which may also exclude bridging therapy.

Table 4. Perioperative Management of Antithrombotic Agents

Drug		Labs	Onset of Action	Duration of action (normal renal function)	*Perioperative Cessation[1]			**Post-procedure restart timing[3, 4, 5] (NA = for neuraxial)[8]	Notes
					Low Risk Bleeding[1,3,4,7,9, 39]	High Risk Bleeding[1,3,4,7,9,39]	Neuraxial[6,8]		
Abciximab (Reopro)[11, 27]		ACT	IV: 2 hours	48 hours	12-24 hours	12-24 hours	5 days	Not specified (8-12 hours NA)	
Alteplase (tPA)[35]		plasma fibrinogen	immediate	<5mins	Not specified.	Not specified.	48 hours	48 hours	No restrictions for low-dose tPA.
Apixiban (Eliquis)[12]	CrCl > 30	Anti-Xa	3-4 hours	>24-48h (T½ = 12 hours)	24 hours	48 hours	5 days	24-72 hours (24 hours NA)	PPX dose (2.5 mg BID) can be restarted started 6-8 hours post-op.
	CrCl 15-29				36 hours	72 hours	5 days	24-72 hours (24 hours NA)	
	CrCl <15				48 hours	120 hours	5 days	12-72 hours (24 hours NA)	
Argatroban (Acova)[10, 13, 31]		ACT, aPTT	IV: 3 min subQ: 2-4 hours	1-2 hours	3 hours	3 hours	6 hours (aPTT<40 sec or DTI assay <40)	12-24 hours (2 hours NA)	Caution for Child Pugh >6 (cessation at 9 hours).
Aspirin[23]	1° stroke prevention (no history of stroke)	Platelet function assay	1-7.5mins	4-6 hours	7-10 days	7-10 days	6 days	Within 24 hours (24 hours NA)	
	2° stroke prevention (history of stroke or TIA)				Stop DOS	Stop DOS	No restrictions	<24 hours (24 hours NA)	
	3° stroke prevention (Cardiac/ Vascular Surgery)				Do not d/c	Do not d/c	No restrictions	Within 24 hours (24 hours NA)	
Bivalirudin (Angiomax)[14, 15, 24]	CrCl >30	ACT, aPTT, DTI	IV bolus: 2 min PCI: 15 mins	2-6 hours	1.5 hours	1.5 hours	6 hours (aPTT<40 sec or DTI assay <40)	12-24 hours (2 hours NA)	
	CrCl <30				3 hours	3 hours	6 hours	12-24 hours (2 hours NA)	
Cilostazol (Pletal)[36]		Platelet function assay	Not specified	11-13 hours	2 days	2 days	2 days	Within 24 hours (24 hours NA)	

Clopidrogrel (Plavix) [16, 17]		Platelet function assay	oral, 2-7 days	5 days	5 days	5 days	7 days	Within 24-48 hours (12-24 hours NA)	Clopidogrel can safely be continued through CEA, LE bypass, EVAR, and open AAA repair.
Dabigatran (Pradaxa)[18]	CrCl ≥ 80	Dilute thrombin time	2 hours	T½ = 12-17 hours	24 hours	48 hours	5 days	24-72 hours (24 hours NA)	No data for CrCl <15 mL/min; consider withholding >4 days peri-operatively.
	CrCl 50-79				36 hours	72 hours	5 days	24-72 hours (24 hours NA)	
	CrCl 30-49				48 hours	96 hours	6 days	24-72 hours (24 hours NA)	
	CrCl 15-29				72 hours	120 hours	6 days	6-72 hours (24 hours NA)	
Dalteparin (Fragmin)[19] **Prophylactic Dose (<5000 Units)**	CrCl > 30	anti-Xa activity	1-2 hours	SubQ 10-24h (T½ = 2 hours)	12-24 hours	24 hours	15 hours	6-8 hours (4 hours NA)	
	CrCl < 30				12-24 hours	24 hours	30 hours	6-8 hours (8 hours NA)	
Dalteparin (Fragmin)[19] **Therapeutic Dose (≥5000 U)**	CrCl > 30	anti-Xa activity	1-2 hours	SubQ 10-24h (T½ = 2 hours)	12-24 hours	24 hours	30 hours	6-12 hours (6 hours NA)	
	CrCl < 30				12-24 hours	24 hours	60 hours	6-12 hours (8 hours NA)	
Dipyramidole (Aggrenox)[37]		Platelet function assay	45-150 min	10-12 hours	7-10 days	7-10 days	2 days	Within 24 hours (24 hours NA)	
Edoxaban (Savaysa)[20]	CrCl > 30	Anti-Xa activity	1-2 hours	T½ =10-14 hours	24 hours	48 hours	48 hours	6-72 hours (6 hours NA)	
	CrCL 15-29				36 hours	72 hours	72 hours	6-72 hours (6 hours NA)	
	CrCl <15				48 hours	120 hours	5 days	6-72 hours (6 hours NA)	
Enoxaparin (Lovenox) [21, 34]	**PPX dose**	anti-Xa activity	3-5 hours	<12 hours (T½ =4.5-7h)	12 hours	12 hours	12 hours	6-24 hours (6-24 hours NA)	
	Therapeutic dose				24 hours	24 hours	24 hours		
Eptifibatide (Integrilin)[22, 27]		aPTT, ACT	IV: 1 hour	IV: 2-4 hours	4-6 hours	4-6 hours	24 hours	Incomplete info (8-12 hours NA)	

Fondaparinux (Arixtra)[38] Prophylactic Dose (2.5 mg daily)		anti-Xa activity	2-3 hours	T½ = 17-21 hours	No restrictions	No restrictions	48 hours	6 hours (24 hours NA)	
Fondaparinux (Arixta)[38] 5-10mg	CrCl > 50	anti-Xa activity	2-3 hours	T½ = 17-21 hours	3 days	3 days	4 days	24-72 hours (8-24 hours NA)	
	CrCl < 50	anti-Xa activity			5 days	5 days	4 days	24-72 hours (8-24 hours NA)	
Heparin SubQ Prophylactic Dose (5000 units BID)[26, 29]		aPTT	20-30min (Tmax 2-4 hours)	up to 6 hours	No restrictions	No restrictions	No restrictions	No restrictions	
Heparin SubQ Therapeutic Dose (5000 units TID)[26, 29]		aPTT	20-30min (Tmax 2-4 hours)	up to 6 hours	4-6 hours	4-6 hours	10 hours	12-24 hours (2 hour NA)	
Heparin IV[25, 26, 29]		aPTT	immediate	up to 6 hours	2-4 hours	2-4 hours	4 hours	12-24 hours (2 hour NA)	
Prasugrel (Effient)[28]		Platelet function assay	Initial: 15-30min peak: 2 hours	5-9 days	7 days	7 days	7-10 days	Within 24-48 hours (12-24 hours NA)	Restart >6h after catheter removal.
Rivaroxaban (Xarelto)[30]	CrCl > 30	Anti-Xa activity	2-4 hours	T½ = 5-9h	24 hours	48 hours	72 hours	12-72 hours (24 hours NA)	
	CrCL 15-29		2-4 hours	T½ = 5-9h	36 hours	72 hours	96 hours	12-72 hours (24 hours NA)	
	CrCl <15		2-4 hours	T½ = 5-9h	48 hours	120 hours	5 days	12-72 hours (24 hours NA)	
Ticagrelor (Brilanta)[32]		Platelet function assay	2 hours	36-48 hours	5 days	5 days	5 days	Within 24-48 hours (12-24 hours NA)	Restart >6h after catheter removal.
Tirofiban (Aggrastat)[27]		aPTT, ACT	30 min	T½ = 2 hours	4-6 hours	4-6 hours	24 hours	Incomplete info (8-12 hours NA)	
Warfarin[33] (Coumadin)	INR 2.0-3.0	INR	24 hours (T_{max} 72-96 hours)	2-5 days (T½ = 21-89 hours)	5 days	5 days	5 days AND INR < 1.5	12-24 hours (12-24 hours NA)	
	INR 3.0-4.5				6 days	6 days	6 days AND INR < 1.5	12-24 hours (12-24 hours NA)	
	INR > 4.5				6-7 days	6-7 days	6-7 days AND INR < 1.5	12-24 hours (12-24 hours NA)	

*Peri-operative cessation time listed as negative from start of surgery or catheter placement.

**Post-Procedure restart time listed as hours post-procedure. Neuraxial (NA) restart times listed post-catheter removal; in the case of traumatic catheter placement, restart antithrombotic therapy >24 hours from catheter removal. Restarting any antithrombotic with catheter in place is not recommended with exception of aspirin/NSAID and prophylaxis dosing listed.

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