PROTOCOL FOR PERIPROCEDURAL 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. This protocol is intended as guidance only and should not supercede clinical judgment. While protocols are intended to apply to the majority of patients, we acknowledge there will be patients who require management approaches other than those suggested in this document. In those instances, a multidisciplinary discussion between the patient's PCP, anesthesiologist, surgeon and anticoagulation clinic provider is strongly encouraged to ensure selection and implementation of the most appropriate approach.

Inpatient anticoagulation service 505-264-6970 Outpatient Coumadin Clinic 505-272-6202

Table of Contents:

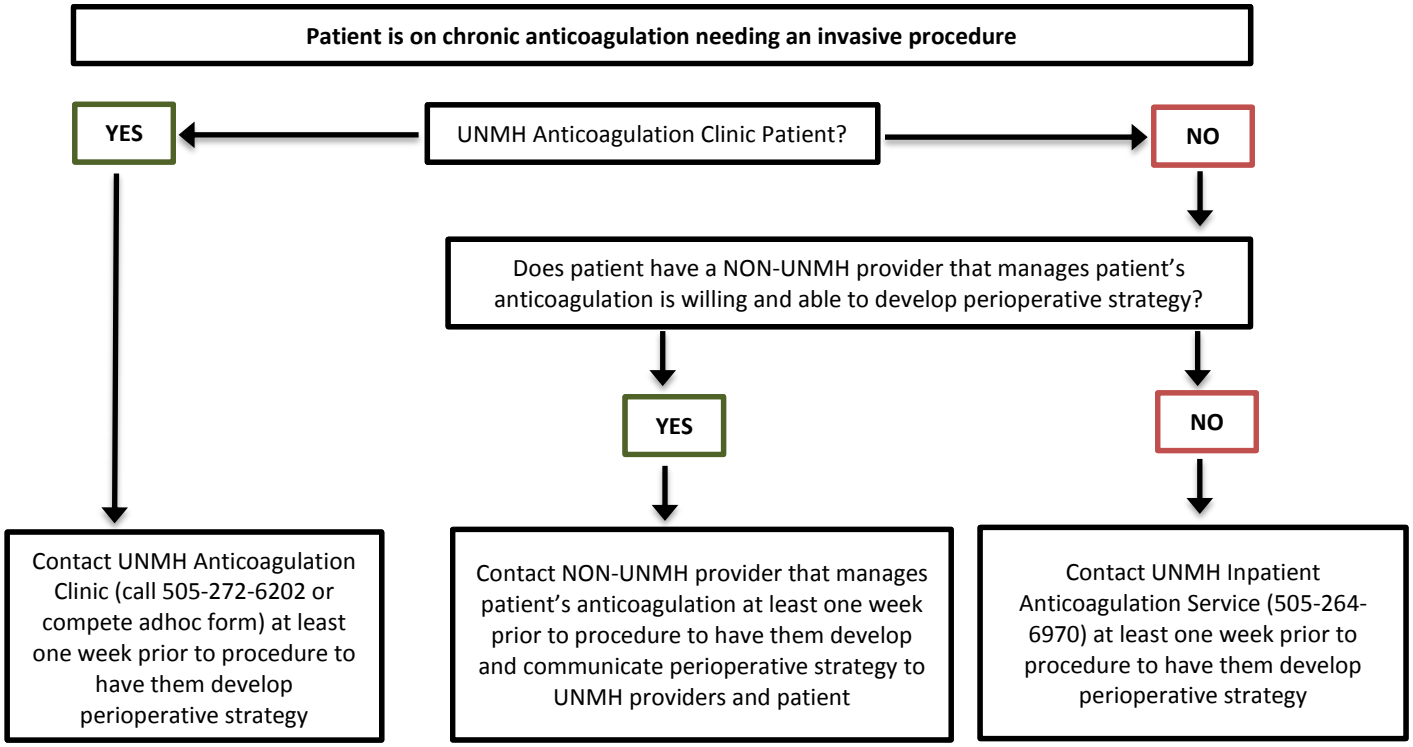
What is peri-operative bridging?

- Patients who are chronically anticoagulated with warfarin and require an invasive procedure may need to have their warfarin temporarily interrupted to minimize bleeding risk around the procedure.
- Peri-operative bridging refers to the use of a rapid-acting parenteral anticoagulant (unfractionated heparin, low molecular weight heparin) in the pre- and/or post-operative period(s) while the patient's INR is subtherapeutic to prevent thromboembolic events. This practice is largely based on biological plausibility and expert opinion.
- Emerging evidence suggests that, in many patient populations, bridging does not reduce thromboembolic events but does increase bleeding.[1]
- As such, bridging therapy should be reserved for those patients at highest risk of a thrombotic event as they are most likely, though not guaranteed, to derive benefit.
- Additionally, evidence suggests that prophylactic dose bridging may be equally effective, but much safer than therapeutic dose bridging, in some patient populations.
- **It is important to note that bridging therapy only pertains to warfarin patients. Patients on direct oral anticoagulants (DOACs) such as apixaban, dabigatran, edoxaban and rivaroxaban do not require bridging therapy, and this practice should be avoided in those patients.[2]**

I. Outpatient to inpatient management

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

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



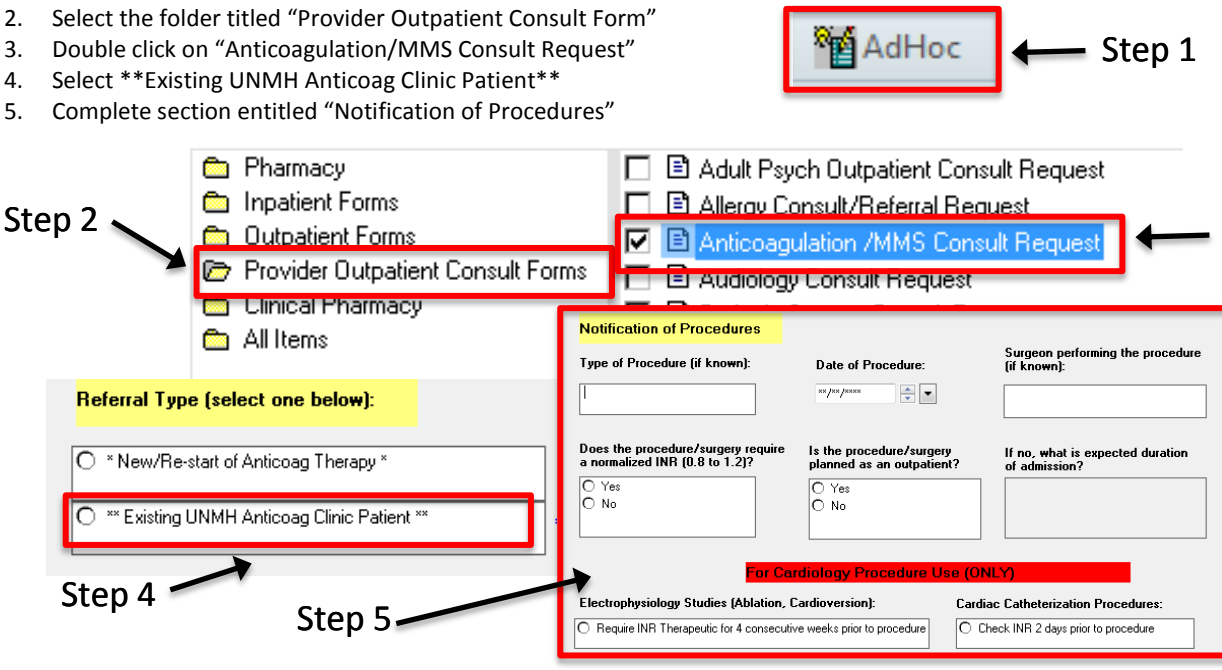
c. See Table 4 above for a general template for a warfarin patient who warrants bridging
   i. It is strongly recommended that a dosing template with specific instructions be filled out and given to patient at pre-operative clinic visit, along with any needed prescriptions, such as LMWH, etc.

d. For the DOACs, see Table 1 above, refer to package insert or, preferably, consult with a more experienced provider.

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

How to notify the UNM Anticoagulation Clinic that your patient is undergoing an invasive procedure:

1. Click on the AdHoc button from the task bar
2. Select the folder titled "Provider Outpatient Consult Form"
3. Double click on "Anticoagulation/MMS Consult Request"
4. Select **Existing UNMH Anticoag Clinic Patient**
5. Complete section entitled "Notification of Procedures"



II.

III. Assessment of patient and surgical risk factors for thromboembolism/bleeding

a. Risk stratification with consideration for patient and procedure-related bleed and thromboembolic event risk as well as consequences of these events is essential for the creation of an appropriate perioperative antithrombotic management plan.

TABLE 1. PERIOPERATIVE ANTICOAGULANT MANAGEMENT RECOMMENDATIONS BASED ON RISK ASSESSMENT[1,3,4,5,7,14,18,23,24]

INSTRUCTIONS

1. Perform patient anticoagulation assessment 7+ days prior to procedures.
2. Categorize underlying thromboembolic risk using the columns to the right and procedure-related bleeding risk using the rows below.
3. View suggestions for anticoagulant interruption and bridging in cell where rows and column interact.
4. View specific guidance for warfarin users in Table 1 and DOACs in Table 2.

Disclaimer: Anticoagulation prescribing is highly complex and should be conducted with the greatest care on a case-by-case basis, considering the complete patient medical profile. The information presented is for general guidance only and is not all-inclusive. Prescribers are encouraged to consult the current medical evidence and organizational policies and procedures.

Decisions to interrupt, bridge, and resume anticoagulants MUST be clearly communicated among providers and to patient.

PROCEDURE BLEEDING RISK	THROMBOEMBOLIC RISK: HIGH	THROMBOEMBOLIC RISK: LOW
	Mechanical heart valve patients: • Any mechanical mitral valve • Older caged ball or tilting disk valve in mitral/aortic position • Aortic mechanical valve in patients with additional stroke risk factors, such as Afib, MI, LA enlargement, hypercoagulable condition, EF<40% • Stroke or TIA in the past 6 months **Atrial fibrillation patients:** • Valvular atrial fibrillation (rheumatic heart disease, severe mitral stenosis) • With mechanical heart valve • Any cardioembolic event, including stroke or TIA, in the past 3 months **Venous thromboembolism patients:** • VTE (DVT *or* PE) in the past 3 months • History of VTE associated with a confirmed **severe** thrombophilia (antiphospholipid syndrome, Protein C or S deficiency, or AT deficiency) **Other:** • Mural thrombus or left atrial appendage clot within the past 1 month • History of venous or arterial thromboembolism while on therapeutic anticoagulation or during temporary interruptions of anticoagulation	Most other patients not listed in the high-risk category including, but not limited to, all atrial fibrillation patients without any of the concomitant thrombotic risk factors listed to the left. *Bridging in atrial fibrillation patients with a higher risk for stroke (e.g. CHADS2 >4) may be considered on a case-by-case basis.*
HIGH ***Major surgery with extensive tissue injury*** • Head/neck/abdominal/breast cancer surgery • General/vascular/thoracic/lung surgery • Reconstructive plastic surgery • Cardiac, intracranial, or spinal surgery • Bilateral hip or knee arthroplasty ***Urologic or Gastrointestinal surgery*** • Transurethral prostate resection, bladder resection, or tumor ablation • Abdominal hysterectomy • Nephrectomy, kidney biopsy • Colonic polyp resection • Bowel resection • PEG placement, ERCP ***Other*** • Surgery in highly vascular organs • Multiple tooth extractions • Any procedure duration >45 minutes • Epidural injections with INR >1.2	1. **INTERRUPTION: Recommend interruption of anticoagulation for warfarin and DOAC patients.** 2. **BRIDGING: <u>Suggest bridging</u> with warfarin patients only. Bridging is not necessary in DOAC patients due to the rapid onset and offset.** *Consider a "step-up" approach in which prophylactic dosing of an injectable anticoagulants is initiated ≥6-24 hours post-procedure then, if well-tolerated, transition to treatment dose anticoagulation at 48 – 72 hours post-procedure.* ***It should be noted that this only applies to the inpatient setting.*** MEDICATION CESSATION GUIDANCE: See Table 2 (for warfarin) and Table 3 (for DOACs) for guidance regarding cessation.	1. **INTERRUPTION: Recommend interruption of anticoagulation in warfarin and DOAC patients.** 2. **BRIDGING: <u>Suggest NO bridging.</u>** *Consider use of appropriate post-op VTE prophylaxis based on patient risk factors (see VTE prophylaxis guidelines for determination).* MEDICATION CESSATION GUIDANCE: See Table 2 (for warfarin) and Table 3 (for DOACs) for guidance regarding cessation.
LOW • Cutaneous/lymph node biopsies • Shoulder/foot/hand/knee surgery • Joint arthroplasty with use of tranexamic acid • Coronary angiography or catheterization via femoral access • Heart biopsy • Gastrointestinal endoscopy +/- biopsy • Colonoscopy +/- biopsy • Laparoscopic cholecystectomy • Abdominal hernia repair • Hemorrhoidal surgery • Bronchoscopy +/- biopsy • Pacemaker battery change • Arthroscopy • Chest tube insertion • Pacemaker or ICD implantation • Catheter ablation	1. **INTERRUPTION: <u>Recommend</u> interruption of anticoagulation for DOAC patients and <u>consider</u> interruption of anticoagulation for warfarin patients.** 2. **BRIDGING: <u>Suggest bridging</u> with warfarin patients only. Bridging is not necessary in DOAC patients due to the rapid onset and offset.** *Consider a "step-up" approach in which prophylactic dosing of an injectable anticoagulants is initiated ≥6-24 hours post-procedure then, if well-tolerated, transition to treatment dose anticoagulation at 48 – 72 hours post-procedure.* ***It should be noted that this only applies to the inpatient setting.*** MEDICATION CESSATION GUIDANCE: See Table 2 (for warfarin) and Table 3 (for DOACs) for guidance regarding cessation.	1. **INTERRUPTION: Recommend interruption of anticoagulation in warfarin and DOAC patients.** 3. **BRIDGING: <u>Suggest NO bridging.</u>** *Consider use of appropriate post-op VTE prophylaxis based on patient risk factors (see VTE prophylaxis guidelines for determination).* MEDICATION CESSATION GUIDANCE: See Table 2 (for warfarin) and Table 3 (for DOACs) for guidance regarding cessation.
MINIMAL • IVC filter or CVC removal • Cataract or glaucoma surgery • Minor dental procedures • Minor dermatologic procedures • Cardiac catheterization via radial access • Chest tube removal • Fistulogram by IR	**Do <u>not</u> interrupt anticoagulation.** Consider use of oral pro-hemostatic agent with simple dental procedures. **Cardiac catheterization via radial access:** ▪ **Elective procedure*** – no warfarin interruption; hold DOAC per Table 3 recommendations for low-bleed risk procedure ▪ **NSTEMI** – no warfarin interruption; hold DOAC 24 hours in advance regardless of DOAC ▪ **STEMI** – no warfarin or DOAC interruption	

***May consider holding warfarin in cardiac catheterization in procedures at higher risk of perforation (e.g. recanalization of chronic total occlusion or rotation atherectomy) or when percutaneous coronary intervention with stent placement via the femoral approach is scheduled.**

Abbreviations: VTE = venous thromboembolism; PEG = percutaneous endoscopic gastrostomy; ERCP = endoscopic retrograde cholangiopancreatography; ICD = implantable cardioverter defibrillator; Afib = atrial fibrillation; MI = myocardial infarction; LA = left atrial; EF = ejection fraction; AT = antithrombin

IV. Timing of antithrombotic therapy cessation and re-initiation perioperatively

a. These guidelines pertain to elective procedures or those in which there is adequate time to implement recommended cessation periods. For all other situations (e.g. urgent or emergent surgery), providers are encouraged to collaborate with the inpatient anticoagulation service and refer to the "Antithrombotic Reversal Guideline" on the pharmacy webpage to develop a safe, effective perioperative plan.

TABLE 2. CONVENTIONAL ANTICOAGULANT CESSATION/RE-INITIATION GUIDANCE[3,4]

Conventional Anticoagulant	TREATMENT DOSING			PROPHYLACTIC DOSING	
	CESSATION	RE-INITIATION POST-OP*		CESSATION	RE-INITIATION POST-OP*
		Low Bleed Risk[#]	High Bleed Risk[#]		
WARFARIN ($t_{1/2}$ ≈ 40 hrs)	5 – 6 days	12 – 24 hours		Not applicable	
UFH ($t_{1/2}$ = 1 – 2 hrs)	4 – 6 hours	12 – 24 hours[Δ]	48 – 72 hours	4 – 6 hours	≥ 6-12 hours
LMWH[□] ($t_{1/2}$ = 4 – 7 hrs)	24 hours**	24 hours	48 – 72 hours	30 mg BID: 12 hours 40 mg daily: 12-24 hours	
FONDAPARINUX ($t_{1/2}$ = 17 – 21 hrs)	3 – 4 days	Consider a shorter acting agent until patient is tolerant to anticoagulation		≥ 48 hours	

*Depending on surgical hemostasis. For all injectable anticoagulants, a "step-up" approach may be considered where prophylactic dosing is initiated ≥6-24 hours post-procedure then, if well-tolerated, transition to treatment dose anticoagulation at 48 – 72 hours post-procedure.
**If using 1.5 mg/kg LMWH once daily, consider hold for 36 hours prior to procedure or giving ½ of dose at 24 hours prior to procedure.
[Δ]For cardiac catheterizations, may start IV UFH low intensity protocol without a bolus 6 hours after sheath or TR band removal
[#]Refer to Table 1 for procedure bleeding risk
[□] BID (1 mg/kg BID) dosing may be preferred over once daily treatment dosing (1.5 mg/kg daily) to mitigate bleed risk

TABLE 3. DIRECT ORAL ANTICOAGULANT (DOAC) CESSATION/RE-INITIATION GUIDANCE[2,8,9,10,11,16]

Direct Oral Anticoagulant	NUMBER OF DOSES TO HOLD PRIOR TO PROCEDURE		RE-INITIATION TIME POST-OP*	
	Low Bleed Risk Procedure[#]	High Bleed Risk Procedure[#]	Low Bleeding Risk	High Bleeding Risk
DABIGATRAN (Pradaxa) – Twice daily dosing			~24 hours	~48 – 72 hours
CrCl > 80 mL/min ($t_{1/2}$ ~ 14 hrs)	2 doses	5 – 6 doses		
CrCl 50 – 80 mL/min ($t_{1/2}$ ~ 17 hrs)	3 – 4 doses	6 – 7 doses		
CrCl 30 – 49 mL/min ($t_{1/2}$ ~ 19 hrs)	4 – 5 doses	7 – 8 doses		
CrCl 15 – 29 mL/min ($t_{1/2}$ ~ 28 hrs)	5 – 7 doses	9 – 12 doses		
CrCl < 15 mL/min ($t_{1/2}$ unknown)	Hold until resolved or consider transition to warfarin or UFH			
RIVAROXABAN (Xarelto) – Once daily dosing				
CrCl ≥ 30 mL/min ($t_{1/2}$ ~ 8 – 9 hrs)	1 dose	2 doses		
CrCl 15 – 29 mL/min ($t_{1/2}$ ~ 10 hrs)	1 – 2 doses	2 – 3 doses		
CrCl < 15 mL/min ($t_{1/2}$ unknown)	Hold until resolved or consider transition to warfarin or UFH			
APIXABAN (Eliquis®) – Twice daily dosing				
CrCl > 50 mL/min ($t_{1/2}$ ~ 7 – 8 hrs)	2 doses	4 doses		
CrCl 15 – 49 mL/min ($t_{1/2}$ ~ 17 – 18 hrs)	3 – 4 doses	6 – 7 doses		
CrCl < 15 mL/min ($t_{1/2}$ unknown)	Hold until resolved or consider transition to warfarin or UFH			
EDOXABAN (Savaysa®) – Once daily dosing				
CrCl > 30 mL/min ($t_{1/2}$ ~ 8 – 10 hrs)	1 dose	2 doses		
CrCl 15 – 29 mL/min ($t_{1/2}$ ~17 hrs)	2 doses	3 – 4 doses		
CrCl < 15 mL/min ($t_{1/2}$ unknown)	Hold until resolved or consider transition to warfarin or UFH			

*Depending on surgical hemostasis.
[#]Refer to Table 1 for procedure bleeding risk. For low bleeding risk procedures, aiming for mild-moderate residual anticoagulant effect (<12-25%) at surgery. For high bleeding risk procedures, aiming for no or minimal residual anticoagulant effect (<3-6%) at surgery. In the patient with decreased renal clearance, allowance should be made for lower dosing and/or increased hold time prior to procedure to minimize bleeding risk. For patients at high risk for both thromboembolism and bleeding after surgery, consider a step-up approach of administering prophylactic dose dabigatran (75 mg twice daily), rivaroxaban (10 mg once daily), or apixaban (2.5 mg twice daily) at around 24 hours post-op, then increasing back to therapeutic dosing at 48-72 hours if tolerated.

V. Perioperative Management of Warfarin in Dialysis Patients

a. In patients with end-stage renal disease on hemodialysis, outpatient bridging with low molecular weight heparin (i.e., enoxaparin) is contraindicated. While therapeutic-dose unfractionated heparin may be employed, challenges associated with retail availability and insurance coverage essentially preclude its use. Thus, perioperative bridging in dialysis patients is discouraged except in clinical situations that pose the highest thromboembolic risk (see Table 1 above).
    i. In instances in which perioperative bridging is indicated, providers have two options:
        1. Hold warfarin for a shorter duration of just 2-3 days (rather than a full 5 days) in order to provide a low level of residual anticoagulant effect.
        2. Admit the patient to the hospital for bridging therapy with IV unfractionated heparin.
b. A multidisciplinary discussion between the patient's PCP, surgeon, and anticoagulation clinic provider is strongly encouraged to ensure selection and successful implementation of the most appropriate approach.

VI. Example Warfarin Bridging Template

TABLE 4. WARFARIN BRIDGING TEMPLATE EXAMPLE[4]

Day	Warfarin Dose	Bridging with LMWH	INR Monitoring
-7 to -10	Maintenance dose (MD)	Assess for perioperative bridging anticoagulation; classify patients as undergoing high or low bleeding risk procedures	Check baseline labs (hemoglobin, platelet count, serum creatinine, INR)
-6- or -5	Begin to hold warfarin day -5 or day -6	No LMWH	None
-4	No Warfarin	No LMWH	None
-3	No Warfarin	Start LMWH at therapeutic dose**	None
-2	No Warfarin	LMWH at therapeutic dose**	None
-1	No Warfarin	Last preoperative dose of LMWH administered ≥ 24 hours before start of surgery**	Assess INR before the procedure; proceed with surgery if INR <1.5; If INR > 1.5 and <1.8, consider FFP or oral vit K (1-2.5mg)
0	Resume MD (or slightly higher booster dose) of warfarin on evening of procedure	None	INR if FFP or oral vit K administration was necessary
+1	MD (or slightly higher booster dose)	Low-bleeding risk: restart LMWH at previous treatment dose; High-bleeding risk: no LMWH administration or prophylactic LMWH administration	Per clinician judgment
+2 or +3	MD	Low-bleeding risk: LMWH administration continued High-bleeding risk: restart LMWH at previous dose	Per clinician judgment
+4	MD	Continue LMWH administration until INR is >2	INR
+7 to +10	MD		INR

NOTE: This template addresses patients with a target INR of 2 – 3 and who are in the therapeutic range at the initial check prior to starting the bridging plan. If the patient has a higher target INR or has a supratherapeutic INR, longer warfarin hold times may be necessary. If the patient has a subtherapeutic INR, the duration of enoxaparin bridging may need to be altered. In these instances, consultation with a clinician more experienced with perioperative antithrombotic management is strongly recommended.
**Therapeutic LMWH regimens include enoxaparin 1.5 mg/kg once daily or 1 mg/kg twice daily subcutaneously. If using 1.5 mg/kg LMWH once daily, consider hold for 36 hours prior to procedure or giving ½ of dose at 24 hours prior to procedure.

VII. **Antiplatelet Management**

a. Assess use of anti-platelets at least 7 days prior to procedure to allow for adequate hold time, if necessary. Collaboration with additional specialty services, such cardiology, cardiothoracic surgery, neurology, or anesthesia, is encouraged when deciding cessation options for antiplatelet therapy.

TABLE 5. PERIOPERATIVE MANAGEMENT OF ANTI-PLATELET MEDICATIONS[4,12,16,17]

ANTIPLATELET		CESSATION		RE-INITIATION POST-OP[Δ]
Aspirin		Low CV risk	7 – 10 days	24 hours
		High CV risk*	May continue	
Cilostazol		1 – 2 days		
Dipyridamole		1 – 2 days		
P2Y12 Inhibitors	**Clopidogrel**	5 days		24 – 48 hours
	Prasugrel	5 – 7 days		
	Ticagrelor	5 days		

[Δ]Depending on surgical hemostasis.
Abbreviations: CV = cardiovascular

* **Primary prevention:** most men and women ≥50 y with diabetes and with ≥1 other ASCVD risk factors; adults with diabetes, <50 y; multiple ASCVD risk factors (10-y ASCVD risk 5%-10%)
Secondary prevention: known coronary artery disease (CAD), cerebrovascular disease (CVD), significant peripheral vascular disease (PVD)

TABLE 6. PERIOPERATIVE ANTI-PLATELET MANAGEMENT BASED ON RISK ASSESSMENT[4,12,13,15,16,18-22]

PROCEDURE TYPE	CARDIOVASCULAR RISK	
	HIGH	LOW
Minor (dental/dermatologic/ophthalmologic)	Continue antiplatelet therapy	Continue antiplatelet therapy
Non-cardiac	Continue antiplatelet therapy*	Hold antiplatelet therapy
Carotid endarterectomy	Continue aspirin	Not applicable as these procedures imply high CV risk patient
Coronary Artery Bypass Graft (CABG)	Continue aspirin Hold P2Y12 inhibitors	
Any procedure that cannot be delayed in patients in the 4-6 weeks post-BMS or minimum 6 months post-DES placement**	Consult cardiology[□] Continue dual anti-platelet therapy	
Any procedure that cannot be delayed in patients following 4-6 weeks post-BMS or minimum 6 months post-DES placement, but prior to 1 year of dual anti-platelet therapy	Consult cardiology[□] Continue aspirin and hold P2Y12 inhibitor for shortest time possible	

*Except for intracranial, middle ear, posterior chamber of eye, intramedullary spin, and possibly transurethral prostatectomy (TURP) procedures as these confer a very high risk of hemorrhagic complications.
**Strongly recommend deferring surgery for at least 6 weeks after placement of a bare-metal stent (BMS) and for at least 6 months after placement of a drug-eluting stent (DES), if possible. Ideally, a minimum of 1 year of uninterrupted dual anti-platelet therapy in both BMS and DES is preferred.
[□]Risk for stent thrombosis is extremely high in the 4-6 weeks post-BMS and 6 months post-DES placement. Strongly recommend consultation with a cardiologist to discuss appropriateness of antiplatelet therapy as well as cessation time as some providers may be more comfortable with shorter holding periods.

References:

1. Rose AJ, Allen AL, and Minichello T. A call to reduce the use of bridging anticoagulation. *Circ Cardiovasc Qual Outcomes.* 2016;9:00-00.
2. Burnett AE, Mahan CE, Vazquez SR, et al. Guidance for the practical management of the direct oral anticoagulants (DOACs) in VTE treatment. *J Thromb Thrombolysis*. 2016;41:206-232.
3. Douketis JD, Spyropoulos AC, and Kaatz S. Perioperative bridging anticoagulation in patients with atrial fibrillation. *N Engl J Med.* 2015;373(9):823-33.
4. Douketis JD, Spyropoulos AC, Spencer FA, et al. Perioperative management of antithrombotic therapy: antithrombic therapy and prevention of thrombosis, 9th edition: American college of chest physicians evidence-based clinical practice guidelines. *Chest*. 2012;141(2 Suppl):e326S-e350S.
5. Spyropoulos AC, Al-Badri A, Sherwood MW, and Douketis JD. Periprocedural management of patients receiving a vitamin K antagonist or a direct oral anticoagulant requiring an elective procedure or surgery. *J Throb Haemost*. 2016;14:875-85.
6. Steinberg BA, Peterson ED, Kim S, et al. Use and outcomes associated with bridging during anticoagulation interruptions in patients with atrial fibrillation: findings from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). *Circulation*. 2015;131(5):488-94.
7. Garcia DA, Regan S, Henault LE, et al. Risk of thromboembolism with short-term interruption of warfarin therapy. *Arch Intern Med*. 2008;168(1):63-9.
8. Pradaxa [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc; 2012.
9. Xarelto [package insert]. Gurabo, PR: Janssen Pharmaceuticals, Inc; 2012.
10. Eliquis [package insert]. Princeton, NJ. Bristol-Meyers Squibb, Inc. 2012.
11. Savaysa [package insert]. Parsippany, NJ: Daiichi Sankyo, Inc. 2015.
12. Hall R and Mazer CD. Antiplatelet drugs: a review of their pharmacology and management in the perioperative period. *Anesth Analg*. 2011;112(2):293-318.
13. Shahi V, Brinjikji W, Murad MH, et al. Safety of uninterrupted warfarin therapy in patients undergoing cardiovascular endovascular procedures: a systematic review and meta-analysis. *Radiology*. 2016;278(2):383-94.
14. Di Biase L, Burkhardt JD, Santangeli P, et al. Periprocedural stroke and bleeding complications in patients undergoing catheter ablation of atrial fibrillation with different anticoagulation management: results from the role of Coumadin in preventing thromboembolism in atrial fibrillation (AF) patients undergoing catheter ablation (COMPARE) randomized trial. *Circulcation*. 2014;129(25):2638-44.
15. Tun NM and Oo TH. Prevention and treatment of venous thromboembolism with new oral anticoagulants: a practical update for clinicians. *Thrombosis.* 2013;2013:183616.
16. Baron TH, Kamath PS, and McBane RD. Management of antithrombotic therapy in patients undergoing invasive procedures. *NEJM.* 2013;368:2113-24.
17. Eikelboom JW, Hirsh J, Spencer FA, et al. Antiplatelet drugs: American college of chest physicians evidence-based clinical practice guidelines. 9th edition. *Chest*. 2012; 141:e89s-119s.
18. Rubboli A, Faxon DP, Airaksinen KEJ, et al. The optimal management of patients on oral anticoagulation undergoing coronary artery stenting. *Thromb Haemost*. 2014; 112:1080-1087.
19. Dacey LJ, Munoz JJ, Johnson ER, et al. Effect of preoperative aspirin use on mortality in coronary artery bypass grafting patients. *Ann Thorac Surg*. 200;70(6):1986.
20. Chaturvedi S, Bruno A, Feasby T, et al. Carotid endarterectomy – an evidence-based review. *Neurology*. 2005;65:794-801.
21. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *J Am Coll Cardiol.* 2014;64(22):e77-137.
22. Singla S, Sachdeva R, and Uretsky BF. The risk of adverse cardiac and bleeding events following noncardiac surgery relative to antiplatelet therapy in patients with prior percutaneous coronary intervention. *J Am Coll Cardiol*. 2012;60(20):2005-16.
23. Nairooz R, Ayoub K, Sardar P, et al. Uninterrupted new oral anticoagulants compared with uninterrupted vitamin k antagonists in ablation of atrial fibrillation: a meta-analysis. *Can J Cardiol.* 2016;32(6):814-23.
24. Nishimura RA, Otto CM, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease. *J Am Coll Cardiol. 2014;*63(22):e57-185.