WHealth

Periprocedural Management of Antithrombotic Therapy - Adult - Inpatient/Ambulatory Consensus Care Guideline

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Population/Problem:

Patients receiving long term antithrombotic therapy who require surgery or an invasive procedure present a difficult therapeutic dilemma for clinicians. Efforts are made to minimize the patient's risk of both thromboembolism and bleeding in the periprocedural setting. When a long-acting antithrombotic (e.g., warfarin) is interrupted, some patients may temporarily receive a short-acting antithrombotic (e.g., enoxaparin) before and after the procedure. This practice is referred to as bridging therapy and is intended to reduce a patient's risk of periprocedural thromboembolism.¹ Emerging evidence suggests bridging therapy may significantly increase a patient's periprocedural bleeding risk and has not been shown to reduce the risk of thromboembolism.^{2,3} As such, bridging therapy is not recommended for most patients, but may be considered in select high-risk patients, as outlined in this guideline. Despite recent evidence, uncertainly remains regarding best practices for the majority of periprocedural antithrombotic management questions.⁴

This guideline is intended to serve as a framework for helping clinicians arrive at evidencebased decisions regarding periprocedural management of antithrombotics. It is understood that plans may need to be individualized to address unique patient- and procedure-specific risks and should involve shared decision making between various health care providers and the patient (or patient's representative).

Definitions:

- Antithrombotic includes any anticoagulant or antiplatelet medication
- ASA acetylsalicylic acid or aspirin
- ASRA American Society of Regional Anesthesia and Pain Medicine
- ATE arterial thromboembolism
- Bridging therapy use of a short-acting antithrombotic during the periprocedural interruption of a long-acting antithrombotic, often administered for a 10 to 12-day period
- CABG coronary artery bypass graft
- CHA₂DS₂-VASc congestive heart failure, hypertension, age 75 years or older, diabetes mellitus, prior stroke or transient ischemic attack, vascular disease history, age 65 to 74 years, female sex
- CHEST American College of Chest Physicians
- CrCl creatinine clearance
- DAPT dual antiplatelet therapy
- DOAC direct oral anticoagulant (i.e., apixaban, dabigatran, edoxaban, rivaroxaban)
- ICD internal cardiac defibrillator
- INR international normalized ratio
- ISTH International Society on Thrombosis and Haemostasis
- IV intravenous
- LMWH low molecular weight heparin
- Periprocedural the period of time prior to, during, and following an invasive procedure
- PLT platelet count
- TE thromboembolic
- TXA tranexamic acid
- UFH unfractionated heparin
- VTE venous thromboembolism

Recommendations:

Step 1. Identify the bleeding risk category of the procedure

Table 1. Surgical Procedure Bleeding Risk Categories^{4,5}

MINIMAL BLEED RISK	LOW/MODERATE BLEED RISK	HIGH BLEED RISK	PROCEDURES INVOLVING
30 day risk of major bleeding:	30 day risk of major bleeding:	30 day risk of major bleeding:	NEURAXIAL ANESTHESIA
~0%	0-2%	> 2%	
 Minor dental procedures Dental extractions Restorations Prosthetics Endodontics (root canals) Dental cleanings Dental fillings Minor dermatologic procedures Excision of basal or squamous cell skin cancer Excision of premalignant or cancerous skin nevi Ophthalmologic procedures Cataract surgery Pacemaker or cardioverter-defibrillator device implantation 	 Abdominal hernia repair Abdominal hysterectomy Arthroscopy Bronchoscopy +/- biopsy Colonoscopy +/- biopsy Coronary angiography* Cutaneous/lymph node biopsy Epidural injections Foot/hand surgery Gastrointestinal endoscopy +/- biopsy Hemorrhoidal surgery Laparoscopic cholecystectomy 	 Any major operation (procedure duration > 45 min) Bowel resection Cancer surgery, especially solid tumor resection Cardiac, intracranial, or spinal surgery Colonic polyp resection Endoscopic retrograde cholangiopancreatography (ERCP) Major orthopedic surgery, including shoulder replacement surgery Major surgery with extensive tissue injury Nephrectomy, kidney biopsy Percutaneous endoscopic gastrotomy (PEG) placement Reconstructive plastic surgery Surgery in highly vascularized organs (kidneys, liver, spleen) Transurethral prostate resection, bladder resection, or tumor ablation Urologic or gastrointestinal surgery, especially anastomosis surgery 	 Neuraxial anesthesia Spinal anesthesia Epidural anesthesia, including epidural pain procedures

For procedures with minimal bleed risk, may continue antithrombotic therapy uninterrupted; See Step #2 for more details

- 1. Procedures not listed in Table 1 should be categorized based on estimated 30-day rates of major bleeding defined as:
 - 1.1. Minimal bleed risk if the 30-day risk of major bleeding approximates 0%^{4,5} (UW Health GRADE very low quality of evidence, conditional recommendation)
 - 1.2. Low/moderate bleed risk if the 30-day risk of major bleeding is 0-2%^{4,5} (UW Health GRADE very low quality of evidence, conditional recommendation)
 - 1.3. High bleed risk if the 30-day risk of major bleeding exceeds 2%^{4,5} (UW Health GRADE very low quality of evidence, conditional recommendation)
 - 1.4. Procedures involving neuraxial anesthesia
 - 1.4.1. For procedures involving neuraxial anesthesia, including both spinal and epidural anesthesia or any neuraxial intervention (e.g., epidural pain management), consider both the bleed risk of the procedure itself and the potential catastrophic consequences of

bleeding in the neuraxial space (e.g., lower extremity paralysis resulting from epidural bleeding)⁴

- 1.4.2. There is a lack of consensus regarding how to manage antithrombotic therapy for procedures involving neuraxial anesthesia. Some organizations (e.g., CHEST, ISTH) categorize these procedures the same as other "high bleed risk" procedures, whereas the American Society of Regional Anesthesia and Pain Medicine (ASRA) have separate recommendations that may be more conservative (i.e., longer interruptions in therapy prior to procedure), based on data from pharmacokinetic studies⁴⁻⁶
- 1.4.3. ASRA recommendations are presented in Table 2 and Table 3, alongside recommendations for high bleed risk procedures, so that it is apparent to clinicians when recommendations differ, and to prompt discussion and shared decision-making amongst various members of the healthcare team⁶

Step 2. Identify the usual recommendation for stopping the antithrombotic prior to the procedure

Table 2. Stopping Antithrombotics Prior to Surgical Procedures⁴⁻⁶

1 day = all doses on the calendar day prior to the procedure 24 hours = any dose within 24 hours from the time of the procedure

Oral Anticoagulant	Patient-Specific	Low/ Moderate Bleed	High Bleed Risk	Neuraxial Anesthesia ⁶
Warfarin⁴	INR 2.0-3.5	Stop 5 days prior		Stop 5 or more days prior; check INR 1-2 days
	INR > 3.5	Stop 6 or mo	ore days prior	consider 1 to 2 mg oral vitamin K
Apixaban (Eliquis) ⁴		Stop 1 day prior	Stop 2 days prior	Stop 72 hours prior
Dabigatran (Pradaxa) ⁴	CrCl ≥ 80 ml/min CrCl 50-79 ml/min	Stop 1 day prior	Stop 2 days prior	Stop 72 hours prior* Stop 96 hours prior*
	CrCl < 50 ml/min	Stop 2 days prior	Stop 4 days prior	Stop 120 hours prior
Edoxaban (Savaysa) ⁴		Stop 1 day prior	Stop 2 days prior	Stop 72 hours prior
Rivaroxaban (Xarelto) ⁴		Stop 1 day prior	Stop 2 days prior	Stop 72 hours prior
Parenteral Anticoagulant	Patient-Specific Criteria	Low/Moderate Bleed Risk Procedure	High Bleed Risk Procedure	Neuraxial Anesthesia ⁶
Argatroban [¥]	Normal liver function	Stop 3 hours prior	Stop 5 hours prior	Neuraxial anesthesia is not recommended
	Child-Pugh > 6	Stop 9 hours prior	Stop 15 hours prior	
Bivalirudin [¥]	CrCl ≥ 30 ml/min	Stop 1.5 hours prior	Stop 2.5 hours prior	_
	CrCl < 30 ml/min	Stop 3 hours prior	Stop 5 hours prior	
Enoxaparin (Lovenox) ⁴	Prophylactic Dose	Stop 12 h	ours prior [¥]	Stop ≥ 12 hours prior
	Therapeutic Dose	Stop 24 h	ours prior	Stop \geq 24 hours prior
Fondaparinux	CrCl ≥ 50 ml/min	Stop 3 days prior	Stop 4 days prior	See ASRA Guidelines for
(Arixtra) [¥]	CrCl < 50 ml/min	Stop 5 days prior	Stop 6 days prior	details
Unfractionated	5000 units BID/TID	Stop at least	4 hours prior [¥]	Stop 4 to 6 hours prior
heparin (UFH) ⁴	UFH infusion	Stop at least	4 hours prior	Stop 4 to 6 hours prior
Antiplatelet Agent	Patient-Specific Criteria	Low/Moderate Bleed Risk Procedure	High Bleed Risk Procedure	Neuraxial Anesthesia [®]
Aspirin (ASA) ⁴		Continue ASA	uninterrupted	ASA may be continued
		(If ASA interruption is re prio	equired, stop ASA 7 days pr**)	
Cangrelor [¥]		Stop 1 to 3 hours prior		Stop 3 hours prior
Cilostazol (Pletal) [¥]		Stop 1 to 2 days prior		Stop 2 days prior
Clopidogrel (Plavix) ⁴		Stop 5 da	ys prior**	Stop 5 to 7 days prior
Prasugrel ⁴		Stop 7 da	ys prior**	Stop 7 to 10 days prior
Ticagrelor ⁴		Stop 3 to 5	days prior**	Stop 5 to 7 days prior

- * For patients with additional risk factors for bleeding (e.g., age > 65 years, hypertension, concurrent antiplatelet medication), consider holding dabigatran 120 hours prior to procedure
- **For patients taking dual antiplatelet therapy (DAPT) with stents in place, ANY interruption in antiplatelets should be coordinated with surgeon, anesthesiologist, the prescribing provider (e.g., cardiologist, neurosurgeon, vascular surgeon); elective noncardiac surgery should be delayed at least 30 days after bare metal stent and at least 6 months after drug-eluting stent
- ¥ UW Health-specific recommendation based on institutional standards and/or opinion of guideline workgroup members

Stopping Warfarin Prior to Procedures

- 2. For procedures with **minimal bleed risk**, warfarin may be continued uninterrupted^{4,5} (CHEST GRADE low certainty of evidence, conditional recommendation)
 - 2.1. For dental procedures, recommend using a pro-hemostatic agent (e.g., tranexamic acid (TXA) mouthwash 2 to 3 times daily, extra sutures, gauze soaked in TXA)⁴ (CHEST GRADE low certainty of evidence, conditional recommendation)
 - 2.2. For patients having pacemaker or ICD placement procedures, the recommendation to continue warfarin therapy is based on the premise that the INR is < 3.0⁴ (CHEST GRADE moderate certainty of evidence, strong recommendation)
- 3. For procedures with **low/moderate bleed risk**, recommend stopping warfarin 5 days prior to the procedure to achieve normal or near-normal INR results⁴ (CHEST GRADE low certainty of evidence, conditional recommendation)
 - 3.1. Consider holding warfarin for less than 5 days if the procedure can be performed with some residual anticoagulation or if the patient's INR is below 2.0 prior to stopping warfarin⁵
- 4. For procedures with **high bleed risk**, recommend stopping warfarin 5 days prior to the procedure to achieve normal or near-normal INR results⁴ (CHEST GRADE low certainty of evidence, conditional recommendation)
 - 4.1. Warfarin may need to be stopped 6 or more days prior to the procedure in select patients in which normalization of INR results is expected to be delayed (e.g., patients with INR > 3.5, elderly patients, patients with genetic polymorphisms expected to delay warfarin metabolism)⁴
- 5. For procedures involving **neuraxial anesthesia**, recommend stopping warfarin 5 or more days prior to the procedure and allowing INR results to normalize⁶ (ASRA grade 1B)

Stopping DOACs Prior to Surgical Procedures

- 6. For procedures with **minimal bleed risk**, DOACs may be continued uninterrupted
 - 6.1. May consider withholding DOAC on the day of the procedure to avoid peak anticoagulation effects^{4,5}
- 7. For procedures with **low/moderate bleed risk**, recommend stopping DOAC therapy 1 day prior to the procedure⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
 - 7.1. For patients taking dabigatran who have CrCl < 50 mL/min, recommend stopping dabigatran 2 days prior to high bleed risk procedures⁴
- 8. For procedures with **high bleed risk**, recommend stopping DOAC therapy 2 days prior to the procedure⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
 - 8.1. For patients taking dabigatran who have CrCl < 50 mL/min, recommend stopping dabigatran 4 days prior to high bleed risk procedures⁴
- 9. For procedures involving **neuraxial anesthesia**, consider stopping (non-dabigatran) DOAC therapy 72 hours prior to the procedure⁶ (ASRA grade 2C)
 - 9.1. For patients taking dabigatran who have CrCl 80 mL/min or greater and no additional risk factors for bleeding (e.g., age > 65 years, hypertension, concomitant antiplatelet medications), consider stopping dabigatran 72 hours prior to procedures involving neuraxial anesthesia (ASRA grade 2C)
 - 9.2. For patients taking dabigatran who have CrCl 50 to 79 mL/min. and no additional risk factors for bleeding, consider stopping dabigatran 96 hours prior to procedures involving neuraxial anesthesia⁶ (ASRA grade 2C)
 - 9.3. For patients taking dabigatran who have CrCl < 50 mL/min and/or have additional risk factors for bleeding, consider stopping dabigatran 120 hours prior to procedures involving neuraxial anesthesia⁶ (ASRA grade 2C)

Stopping Parenteral Anticoagulants Prior to Surgical Procedures

- 10. For patients receiving therapeutic dose low molecular weight heparin (LMWH), recommend administering the last pre-procedure LMWH dose no less than 24 hours prior to the procedure *(CHEST GRADE very low certainty of evidence, conditional recommendation)*
 - 10.1. Recommend that the final pre-procedure LMWH dose is half the total daily dose of LMWH, particularly for patients having high bleed risk procedures or procedures involving neuraxial anesthesia⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
- 11. For patients receiving therapeutic dose IV unfractionated heparin (UFH), recommend stopping UFH at least 4 hours before the procedure⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
- 12. For all other parenteral anticoagulants listed in Table 2 (argatroban, bivalirudin, fondaparinux), recommendations for stopping therapy prior to procedure are approximations of 2 to 3 drug half-lives (for low/moderate bleed risk procedures) or 4 to 5 drug half-lives (for high bleed risk procedures), based on 2019 ISTH recommendations by Spyropoulous et al.⁵
- 13. Recommendations listed in Table 2 for stopping parenteral anticoagulants prior to procedures involving **neuraxial anesthesia** are derived from ASRA 2018 guidelines⁶

Stopping Antiplatelet Medications Prior to Surgical Procedures

Patients taking single antiplatelet therapy

- 14. For elective non-cardiac procedures with **minimal bleed risk**, *single* antiplatelet therapy may be continued uninterrupted⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
- 15. For elective non-cardiac procedures with low/moderate or high bleed risk
 - 15.1. Recommend continuing ASA therapy uninterrupted⁴ (CHEST GRADE moderate certainty of evidence, conditional recommendation)
 - 15.1.1. If ASA interruption is required for an elective non-cardiac surgery, recommend stopping ASA 7 days prior to the procedure⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
 - 15.2. Recommend stopping clopidogrel 5 days prior to the procedure⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
 - 15.3. Recommend stopping ticagrelor 3 to 5 days prior to the procedure⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
 - 15.4. Recommend stopping prasugrel 7 days prior to the procedure⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)

Patients with coronary stents taking dual antiplatelet therapy (DAPT)

- 16. Elective non-cardiac surgical procedures should be delayed 30 days after bare metal stent (BMS) implantation and optimally 6 months after drug-eluting stent (DES) implantation⁷ (ACC/AHA Class I, Level B-NR Recommendation)
- 17. If surgical procedure cannot be delayed or if elective non-cardiac procedure is being considered within first 12 months following DES implantation, recommend communication with Cardiology or Interventional Cardiology for interdisciplinary shared decision making. (UW Health GRADE very low quality of evidence, conditional recommendation)
- 18. For elective non-cardiac surgical procedures occurring more than 30 days after BMS implantation and more than 6 months after DES implantation, recommend continuing ASA therapy uninterrupted and stopping the P2Y₁₂ inhibitor^{4,7} (*UW Health GRADE very low quality of evidence, conditional recommendation*)

Patients with non-coronary peripheral stents on DAPT

For patients with non-coronary peripheral stents who require continued DAPT (both ASA and a P2Y₁₂ inhibitor), recommend communication with provider managing the stents to determine if safe to interrupt one antiplatelet agent (decision dependent on timing and nature of stents) (UW Health GRADE very low quality of evidence, conditional recommendation)

If unable to reach the provider managing the stents, see recommendations above pertaining to coronary stents; similar considerations should apply to most peripheral stents

Step 3. Identify the usual recommendation for restarting the antithrombotic after the procedure

	Antitin oniboti	es Alter Ourgiear i h	occurres	
Oral Anticoagulant	Patient-Specific Criteria	Low or Moderate Bleed Risk Procedure	High Bleed Risk Procedure	Neuraxial Anesthesia°
Warfarin⁴		Restart within 2	24 hours post-op	Remove neuraxial catheter when INR < 1.5
Apixaban (Eliquis) ⁴		Destant at least 24 hours	Destart 40 to 72 hours	Destart at least Chause
Dabigatran (Pradaxa) ⁴		Restart at least 24 hours	Restart 48 to 72 nours	Restart at least 6 hours
Edoxaban (Savaysa) ⁴		post-op	μοςι-ομ	allel catheter removal
Rivaroxaban (Xarelto) ⁴				
Parenteral	Patient-Specific	Low or Moderate Bleed	High Bleed Risk	Neuraxial Anesthesia ⁶
Anticoagulant	Criteria	Risk Procedure	Procedure	
Argatroban [*]		Restart at least 24 hours post-op	Restart 48 to 72 hours post-op	Neuraxial anesthesia not recommended
Bivalirudin [¥]		Restart at least 24 hours	Restart 48 to 72 hours	
		post-op	post-op	
Enoxaparin (Lovenox) ⁴	Prophylactic Dose (once daily)	Restart at least 12 hours post-op [¥]	Restart at least 24 hours post-op [¥]	Restart once-daily prophylactic LMWH at least 12 hours after neuraxial catheter placement and at least 4 hours after catheter removal [¥]
	Prophylactic Dose (twice daily)	Restart at least 12 hours post-op [¥]	Restart at least 24 hours post-op [¥]	Restart twice-daily prophylactic LMWH no sooner than the day after the procedure, at least 4 hours after catheter was removed
	Therapeutic Dose	Restart at least 24 hours post-op	Restart 48 to 72 hours post-op	Restart at least 4 hours after neuraxial catheter was removed, and at least 24 hours after catheter was placed
Fondaparinux (Arixtra) [¥]		Restart at least 24 hours	Restart 48 to 72 hours	Restart at least 6 hours
Unfractionated heparin (UFH) ⁴	5000 units BID/TID	Post-op Restart at least 12 hours post-op [¥]	Post-op Restart at least 24 hours post-op [¥]	OK to use with indwelling neuraxial catheter; remove indwelling neuraxial catheters 4 to 6 hours after last heparin dose; restart at least 1 hour after catheter removal
	UFH infusion	Restart at least 24 hours po dose UFH is used for bridgi and start with a lower inter	ost-op; when therapeutic ng therapy, omit bolus dose nsity infusion⁴	Delay restarting UFH at least 1 hour after needle placement; remove indwelling neuraxial catheters 4 to 6 hours after last UFH dose; restart at least 1 hour after catheter removal

Table 3. Restarting Antithrombotics After Surgical Procedures^{4,6}

Antiplatelet	Patient-Specific	Low or Moderate Bleed	High Bleed Risk	Neuraxial Anesthesia ⁶
Aspirin ⁴		Restart within 24 hours po	ist-op	Restart 24 hours post-op; neuraxial catheter may be maintained and removed without regard to ASA
Cangrelor ⁴		Restart within 4 to 6 hours minimum of 48 hours and	post-op, continue for a maximum of 7 days total	Restart at least 8 hours after catheter removal
Cilostazol (Pletal) [¥]		Restart within 24 hours po	st-op	Restart at least 6 hours after catheter removal
Clopidogrel (Plavix) ⁴		Restart within 24 hours po	st-op	Restart 24 hours post-op, neuraxial catheter may be maintained for 1 to 2 days provided no loading dose is given; if loading dose is planned, wait at least 6 hours after catheter removal
Prasugrel ⁴		Restart within 24 hours po	st-op	Restart 24 hours post-op, after neuraxial catheter has been removed (if a loading dose is planned, wait at least 6 hours after catheter removal)
Ticagrelor ⁴		Restart within 24 hours po	st-op	Restart 24 hours post-op, after neuraxial catheter has been removed (if a loading dose is planned, wait at least 6 hours after catheter removal)

¥ UW Health-specific recommendation, based on institutional standards and/or expert opinion of guideline workgroup members

Restarting Warfarin After Surgical Procedures

- 20. When warfarin is interrupted for a surgical procedure, recommend resuming warfarin within 24 hours after the procedure⁴ (CHEST GRADE low certainty of evidence, conditional recommendation)
 - 20.1. Warfarin resumption may need to be delayed in select clinical scenarios (e.g., inadequate procedure-site hemostasis, anticipated need for additional intervention, patient unable to take oral medications)⁴
 - 20.2. Following a procedure involving **neuraxial anesthesia**, the neuraxial catheter should be removed when the patient's INR is $< 1.5^{6}$
- 21. When warfarin is interrupted for a surgical procedure, recommend resuming warfarin at the patient's usual dose⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)

Restarting DOACs After Surgical Procedures

- 22. Following a procedure with **low/moderate bleed risk**, recommend resuming DOAC therapy at least 24 hours after the procedure⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
- 23. Following a procedure with **high bleed risk**, recommend resuming DOAC therapy 48 to 72 hours after the procedure⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
- 24. Following a procedure involving **neuraxial anesthesia**, restart DOAC therapy at least 6 hours after the neuraxial catheter has been removed⁶ (ASRA grade 2C)

Restarting Parenteral Anticoagulants After Surgical Procedures

25. Following a procedure with **low/moderate bleed risk**, when therapeutic dose LMWH is being used, recommend administering the first post-procedure LMWH dose at least 24 hours after the procedure⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)

- 26. Following a procedure with **high bleed risk**, when therapeutic dose LMWH is being used, recommend administering the first post-procedure LMWH dose 48 to 72 hours after the procedure⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
 - 26.1. Patients considered high risk for postoperative VTE may receive low-dose LMWH until therapeutic dose LMWH is resumed⁴
- 27. When therapeutic dose IV UFH is used for bridging therapy, recommend resuming IV UFH at least 24 hours after the procedure, omitting bolus dosing, and starting with a lower intensity infusion⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
- 28. For all other parenteral anticoagulants listed in Table 3 (argatroban, bivalirudin, fondaparinux), recommendations for restarting therapy after a procedure are extrapolated from CHEST 2022 guidelines for restarting therapeutic enoxaparin and UFH (waiting at least 24 hours after low/moderate bleed risk procedures and 48 to 72 hours after high bleed risk procedures)
- 29. Recommendations listed in Table 3 for restarting parenteral anticoagulants following procedures involving **neuraxial anesthesia** are derived from ASRA 2018 guidelines⁶, except where noted to be UW Health-specific recommendations based on institutional standards and/or expert opinion of guideline workgroup members

Restarting Antiplatelet Medications After Surgical Procedures

- 30. When antiplatelet therapy is interrupted for an elective surgical procedure, recommend resuming antiplatelet medications within 24 hours after the procedure⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
- 31. When ASA or P2Y₁₂ inhibitor therapy is interrupted for CABG surgery, recommend resuming the ASA or P2Y₁₂ inhibitor within 24 hours after the procedure⁴ (CHEST GRADE low certainty of evidence, conditional recommendation)
 - 31.1. Antiplatelet therapy resumption may need to be delayed in patients who develop post-CABG thrombocytopenia (PLT < 50,000 x 10⁹/L)⁴
- 32. Recommendations listed in Table 3 for restarting antiplatelet medications following procedures involving **neuraxial anesthesia** are derived from ASRA 2018 guidelines⁶

Step 4. Determine if bridging therapy is usually recommended





^a Empiric risk stratification that is a starting point for assessing periprocedural thromboembolic risk and should be combined with clinical judgement that incorporates individual patient- and surgical procedure-related risk factors

^b Atrial fibrillation; prior stroke or TIA during anticoagulant interruption or other prior stroke or TIA; prior valve <u>thrombosis;</u> rheumatic heart disease; hypertension; diabetes; congestive heart failure; age > 75 years

^C Deficiency of protein C, protein S, or antithrombin; *homozygous* factor V Leiden or prothrombin gene mutation or *double heterozygous* for each mutation; multiple thrombophilias

Bridging Therapy for Patients Taking Warfarin

- 33. For patients taking warfarin for atrial fibrillation, recommend against bridging therapy, except in select individuals at high risk for TE included in Figure 1⁴ (CHEST GRADE moderate certainty of evidence, strong recommendation)
- 34. For patients taking warfarin for venous thromboembolism (VTE), recommend against bridging therapy, except in select individuals at high risk for TE included in Figure 1⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
- 35. For patients taking warfarin for a mechanical heart valve, recommend against bridging therapy, except in select individuals at high risk for TE included in Figure 1⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)
- 36. For patients identified in Figure 1 as high risk for TE who require warfarin interruption for an elective procedure, recommend bridging therapy⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)

How to bridge a warfarin patient

- 37. If bridging therapy is indicated, select the bridging therapy medication and identify the appropriate dose
 - 37.1. Enoxaparin is frequently the drug of choice for bridging warfarin patients, because it has similar efficacy to unfractionated heparin and subcutaneous (SQ) injections may be self-administered in the ambulatory setting *(UW Health GRADE very low quality of evidence, conditional recommendation)*
 - 37.1.1. The preferred dose of enoxaparin when used as bridging therapy is 1 mg/kg SQ every 12 hours, dose rounded to the nearest prefilled syringe strength
 - 37.1.2. Patients with a CrCl < 30 mL/min should receive enoxaparin 1 mg/kg SQ every 24 hours, or may be admitted for unfractionated heparin (UFH) bridging
 - 37.1.2.1. For patients on dialysis who require bridging anticoagulation, consider hospital admission for UFH bridging
 - 37.1.3. Once daily enoxaparin (1.5 mg/kg SQ every 24 hours) is not preferred due to less desirable pharmacokinetics (i.e., higher peaks, lower troughs) and less clinical data, but may be considered in patients who are unable to receive twice daily SQ injections
 - 37.1.4. Prophylactic dose enoxaparin (e.g., 40 mg SQ once daily, etc.) is not dosed to prevent ATE complications, but may be used to help prevent VTE following high VTE risk procedures⁴
 - 37.2. UFH may be used for patients with severe renal impairment/dialysis or those requiring more rapid onset/offset of anticoagulant activity. Therapeutic dose UFH requires continuous infusion and is not suitable for most non-hospitalized patients. See UW Health Guidelines for Therapeutic Dosing of Unfractionated Heparin. *(UW Health GRADE very low quality of evidence, conditional recommendation)*
 - 37.3. Fondaparinux may be an option for patients with an allergy/intolerance to heparin products but has not been well studied as bridging therapy. Its long half-life requires that it be stopped 3 or more days prior to procedure (see Table 2), making its use as a pre-procedure bridging therapy impractical but might be considered for post-procedure bridging therapy. *(UW Health GRADE very low quality of evidence, conditional recommendation)*
 - 37.4. DOACs may affect INR results and have not been studied as bridging therapy for patients taking warfarin; recommend against using DOACs as bridging therapy (UW Health GRADE very low quality of evidence, conditional recommendation)
- 38. Start the bridging therapy medication when the INR is either known or expected to be subtherapeutic, typically following two held doses of warfarin (UW Health GRADE very low quality of evidence, conditional recommendation)
- 39. Stop the bridging therapy medication prior to the procedure based on information in Table 2
- 40. Restart the bridging therapy medication <u>after</u> the procedure when adequate hemostasis is achieved and based on information in Table 3
- 41. Continue_the bridging therapy medication concomitantly with warfarin until the patient's INR is known or expected to be 2.0 or higher, then stop the bridging therapy medication (UW Health GRADE very low quality of evidence, conditional recommendation)

- 41.1. It may take 5 to 10 days after resuming warfarin for most patients to achieve an INR result of 2.0 or higher
- 42. See Appendix A for examples of typical bridge therapy plans for warfarin patients

Bridging Therapy for Patients Taking DOACs

43. The rapid onset and offset of DOAC activity negate the need for bridging therapy in a periprocedural setting⁴ (CHEST GRADE very low certainty of evidence, conditional recommendation)

Bridging Therapy for Patients Taking Antiplatelet Medications

- 44. When antiplatelet therapy is interrupted for a surgical procedure in patients with coronary stents, recommend against routine bridging therapy with a glycoprotein IIb-IIIa inhibitor, cangrelor, or LMWH (CHEST GRADE low certainty of evidence, conditional recommendation)
 - 44.1. Bridging therapy may be considered in select high-risk patients (e.g., patients with a coronary stent in a critical location placed within the past 3 months)⁴
- 45. See Appendix B for additional considerations regarding use of cangrelor as bridging therapy

Step 5. Individualize Recommendations

- 46. Consider the patient's unique bleeding risk factors and the patient's history of bleeding and thromboembolic (TE) complications with previous invasive procedures; individualize recommendations as appropriate⁴ (UW Health GRADE very low quality of evidence, conditional recommendation)
- 47. Consider the unique bleeding and TE risks of the procedure; revise recommendations as appropriate⁴ (UW Health GRADE very low quality of evidence, conditional recommendation)

Step 6. Communicate and Document Plan

- 48. Review recommendations with other members of the patient's healthcare team and the patient (or patient's representative)⁴ (UW Health GRADE very low quality of evidence, conditional recommendation)
 - 48.1. Other members of the healthcare team include, but are not limited to the proceduralist and the provider or anticoagulation clinic managing the patient's antithrombotic therapy
- 49. Utilize shared decision-making, including the patient's values and preferences, cost, and feasibility to arrive at a final recommendation (UW Health GRADE very low quality of evidence, conditional recommendation)
- 50. Provide clear written (paper or electronic) instructions to the patient (or patient's representative)⁴ (UW Health GRADE very low quality of evidence, conditional recommendation)
- 51. Document the plan in the patient's electronic medical record (UW Health GRADE very low quality of evidence, strong recommendation)

Step 7. Revisit the plan after the procedure and revise as necessary

- 52. After the procedure, assess for the occurrence of bleeding or TE complications and revise the postprocedure antithrombotic therapy plan if necessary (UW Health GRADE very low quality of evidence, conditional recommendation)
- 53. Contact the patient (or patient's representative) to clarify whether/how to modify the post-procedure antithrombotic therapy plan and confirm understanding of instructions (UW Health GRADE very low quality of evidence, conditional recommendation)

Disclaimer

Consensus care models assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

Content Expert(s):

Name: Anne Rose, PharmD – Pharmacy Email Address: arose@uwhealth.org

Contact for Changes:

Drug Policy Program Email Address: <u>DrugPolicyProgram@uwhealth.org</u>

Guideline Author(s):

Name: Anne Rose, PharmD – Pharmacy Email Address: arose@uwhealth.org

Name: Erin Robinson, PharmD – Drug Policy Program Email Address: <u>erobinson@uwhealth.org</u>

Reviewer(s):

Deepak Gopal, MD – Department of Medicine, Gastroenterology Vanessa Grapsas, PharmD – Pharmacy Lisa Klesius, MD – Anesthesiology Jennifer Lai, PharmD - Pharmacy Anne O'Connor, MD – Department of Medicine, Cardiology Kevin Patel, MD – Department of Medicine, Gastroenterology Gregory Tester, MD – Department of Medicine, Cardiology Philip Trapskin, PharmD – Drug Policy Program

Committee Approval(s):

Ambulatory Anticoagulation Committee: Jan 2023 Inpatient Anticoagulation Committee: Jan 2023 Pharmacy & Therapeutics Committee:

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- Revisions: 2013, 2015, 2019, 2023

Methodology

Methods Used to Assess the Quality of the Evidence/Strength of the Recommendations: Recommendations developed by external organizations maintained the evidence grade assigned within the original source document and were adopted for use at UW Health.

Internally developed recommendations, or those adopted from external sources without an assigned evidence grade, were evaluated by the guideline workgroup using an algorithm adapted from the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology (see Figure 2).

Figure 2. GRADE Methodology Adapted by UW Health



GRADE Ranking of Evidence (used by UW Health and CHEST)

High	We are confident that the effect in the study reflects the actual effect.
Moderate	We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.
Low	The true effect may differ significantly from the estimate.
Very Low	The true effect is likely to be substantially different from the estimated effect.

GRADE Ratings for Recommendations for or Against Practice (used by UW Health and CHEST)

Strong (S)	Generally, should be performed (i.e., the net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.)
Conditional (C)	May be reasonable to perform (i.e., may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.)

American Society of Regional Anesthesia and Pain Level of Evidence Grading:

Strength of Recommendation (used by ASRA)

Grade 1	General agreement on the efficacy
Grade 2	Conflicting evidence or opinion on the usefulness
Grade 3	May not be useful (and possibly harmful)

Quality of Evidence (used by ASRA)

A Level	Randomized clinical trials, meta-analyses, or observational/epidemiologic series yielding very large risk reduction
B Level	Observational or epidemiologic series
C Level	Case reports or expert opinion

American College of Cardiology (ACC)/American Heart Association (AHA) Level of Evidence Grading:

CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) Benefit >>> Risl

- Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
- Treatment/strategy A is recommended/indicated in preference to treatment B
- Treatment A should be chosen over treatment B

CLASS IIa (MODERATE)

- Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
- Treatment/strategy A is probably recommended/indicated in preference to treatment B
- It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK)

Benefit ≥ Risk

- Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE)

Benefit = Risk

Risk > Benefit

Suggested phrases for writing recommendations:

- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG)

Suggested phrases for writing recommendations:

- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A

- High-quality evidence[‡] from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R

- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR

- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LI

(Limited Data)

(Randomized)

(Nonrandomized)

- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO

(Expert Opinion)

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

- * The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).
- † For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.
- ‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Collateral Tools & Resources

Metrics

- % patients appropriately selected to receive bridge therapy
- Incidence of thromboembolic events up to 30 days after procedure
- Incidence of bleeding events up to 30 days after procedure
- % patients with appropriate hold time of antithrombotic in relation to procedure or neuraxial catheter placement or removal
- Incidence of inappropriate administration of antithrombotic medications during neuraxial catheter
 placement

Appendix A. Examples of Warfarin Bridging with Enoxaparin

Assumptions:

- Warfarin is being taken in the evening and is being held x 5 days prior to an outpatient procedure
- The patient has been deemed high risk for TE complications
- The patient's CrCl > 30 mL/min
- Enoxaparin dose = 1 mg/kg SQ every 12 hours, rounded to nearest commercially available strength

Low/Moderate Bleed Risk Procedure Example Bridge Plan

Date	Enoxaparin AM	Enoxaparin PM	Warfarin	Notes
Pre-Procedure Day -5	Hold	Hold	Hold	
Pre-Procedure Day -4	Hold	Hold	Hold	
Pre-Procedure Day -3	*** mg	*** mg	Hold	
Pre-Procedure Day - 2	*** mg	*** mg	Hold	
Pre-Procedure Day -1	*** mg	Hold	Hold	
Procedure Day	Hold	Hold	*** mg (*** tablets)	After your procedure, ask your proceduralist if it is safe to restart warfarin and enoxaparin at the times listed
Post Procedure Day 1	Hold	*** mg	*** mg (*** tablets)	
Post Procedure Day 2	*** mg	*** mg	*** mg (*** tablets)	
Post Procedure Day 3	*** mg	*** mg	*** mg (*** tablets)	
Post Procedure Day 4	*** mg	*** mg	*** mg (*** tablets)	
Post Procedure Day 5	*** mg	To Be Determined	To Be Determined	Check INR

KEY

Dark gray shaded cells: no doses administered

Unshaded cells: doses administered

Date	Enoxaparin AM	Enoxaparin PM	Warfarin	Notes
Pre-Procedure Day -5	Hold	Hold	Hold	
Pre-Procedure Day -4	Hold	Hold	Hold	
Pre-Procedure Day -3	*** mg	*** mg	Hold	
Pre-Procedure Day - 2	*** mg	*** mg	Hold	
Pre-Procedure Day -1	*** mg	Hold	Hold	
Procedure Day	Hold	Hold	*** mg (*** tablets)	After your procedure, ask your proceduralist if it is safe to restart warfarin and enoxaparin at the times listed
Post Procedure Day 1	Hold	Hold	*** mg (*** tablets)	
Post Procedure Day 2	Hold	Hold vs *** mg	*** mg (*** tablets)	
Post Procedure Day 3	Hold vs *** mg	*** mg	*** mg (*** tablets)	
Post Procedure Day 4	*** mg	*** mg	*** mg (*** tablets)	
Post Procedure Day 5	*** mg	To Be Determined	To Be Determined	Check INR

High Bleed Risk Procedure Example Bridge Plan

KEY

Dark gray shaded cells: no doses administered

Diagonal line shaded cells: determine whether to administer doses based on bleeding risk

Unshaded cells: doses administered

National Guidelines ⁴					
CHEST Guidelines 2022:	Guidance Statement 39:				
Perioperative	"In patients with coronary stents who require interruption of antiplatelet				
Management of	drugs for an elective surgery/procedure, we suggest against routine				
Antithrombotic Therapy	bridging therapy with a alvcoprotein IIb-IIIg inhibitor, canarelor, or LMWH				
	over routine use of bridaina therapy (Conditional recommendation. low				
	certainty of evidence)				
	Guideline implementation considerations:				
	• A bridging approach may be considered in selected high-risk natients				
	for example in those with a recent (within 3 months) coronary stent in				
	a critical location "				
Cangrelor Drug Information					
Machanism of Action	Cangrelor is a reversible ultra-shorting acting direct D2V inhibitor				
Time to Back	Within 2 minutes				
Time to Peak					
Half-Life of Elimination					
Bridging Therapy Dose (Off	-Label Use) ^{5,5,5}				
Routine use not sugges	sted				
Consult UW Health Inte	Consult UW Health Interventional Cardiology prior to initiating cangrelor as bridging therapy				
• UW Health restricts cangrelor use to high-risk patients with cardiac stents placed in the previous 6					
to 12 months who require surgical intervention with interruption in thienopyridine therapy					
Continue low dose ASA	Continue low dose ASA throughout				
• Prior to the procedure	:				
 Start cangrelor 48 to 72 hours after oral P2Y12 inhibitor discontinuation[¥] 					
o Dose = 0.75 mg	 Dose = 0.75 mg/kg/minute IV continuous infusion 				
 STOP cangrelo 	• STOP cangrelor 1 to 3 hours prior to the procedure ^{$*$}				
• 1 to 6 hours after the p	procedure, when adequate hemostasis is achieved:				
 Can the patien 	t take oral medications?				
If Yes	restart oral P2Y ₁₂ inhibitor including an oral loading dose				
•	Clopidogrel preferred over prasugrel or ticagrelor due to lower bleeding				
risk					
■ If No -	restart cangrelor infusion and continue for a minimum of 48 hours and				
maxim	um of 7 days total				
•	When able to tolerate oral medications, STOP cangrelor immediately prior				
	to restarting oral P2Y ₁₂ inhibitor including an oral loading dose				
	 Clopidogrel preferred over prasugrel or ticagrelor due to lower 				
	bleeding risk				
	5				

Appendix B. Considerations for Antiplatelet Bridging With Cangrelor

¥ UW Health-specific recommendation, based on institutional standards and/or expert opinion of guideline workgroup members

Appendix C. Holding Antithrombotics for Outpatient Endoscopy Procedures How to Use this Appendix

This appendix provides additional details regarding how UW Digestive Health Center (DHC) providers categorize the bleeding risk of specific outpatient endoscopic procedures, and their corresponding recommendations for stopping oral antithrombotics prior to the procedure. This appendix is meant to facilitate communication of recommendations between DHC providers and providers managing the patient's antithrombotic therapy.

Step 1. Identify the bleeding risk category of the patient's procedure
Step 2. Identify the recommendation for stopping the antithrombotic prior to the procedure
Step 3. The provider managing the antithrombotic therapy should determine whether they agree with the DHC recommendations for stopping antithrombotics prior to the procedure,

- based on their knowledge of the patient's thromboembolic risk and past medical history
 - If Yes \rightarrow please confirm instructions with the patient or their caregiver
 - If No (or if further discussion is needed) → please contact DHC at 608-890-5000 or (for UW Health providers) via Health Link In Basket: DHC ENDOSCOPY CLINICAL ALL

Step 4. Decisions about restarting antithrombotic therapy after the procedure should be made by the provider managing the antithrombotic therapy; DHC providers may provide updated post-procedure instructions, based on what occurred during the procedure

30 day bleed risk: ~0%	LOW/MODERATE BLEED RISK 30 day bleed risk: 0-2%	HIGH BLEED RISK 30 day bleed risk: > 2%
Video capsule endoscopy	 Argon plasma coagulation (APC) Balloon dilation of luminal stenoses Colonoscopy +/- biopsy Enteral stent deployment Esophagogastroduodenoscopy (EGD) +/- biopsy Flexible sigmoidoscopy +/- biopsy Marking (including clipping, electrocoagulation, tattooing) Push enteroscopy and diagnostic balloon-assisted enteroscopy 	 Ampullary resection Colonic polyp resection^a Cystogastrostomy Endoscopic hemostasis (excluding argon plasma coagulation) Endoscopic mucosal resection (EMR)/ endoscop submucosal dissection (ESD) Endoscopic retrograde cholangiopancreatograph (ERCP)^b Endoscopic ultrasound (EUS) with fine needle aspiration (FNA)^c Laser ablation and coagulation Percutaneous endoscopic gastrotomy (PEG) placement Percutaneous endoscopic jejunostomy (PEJ) placement Percutaneous endoscopic dilation for achalasia or esophageal strictures Radiofrequency ablation Therapeutic balloon-assisted enteroscopy Treatment of varices (including variceal band ligation) Tumor ablation

When to Stop Oral Antithrombotics Prior to Procedure^{4,5}

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- For minimal bleed risk procedures, antithrombotics may be continued uninterrupted
- For low/moderate bleed risk and high bleed risk procedures, see recommendations below
- This table is not all-inclusive; for more information, see Step 2 of the full guideline

Antithrombotic Medication	Patient-Specific Criteria	Low/Moderate Bleed Risk Procedure	High Bleed Risk Procedure
Warfarin (Coumadin)	INR 2.0-3.5	Stop 5 days prior	
	INR > 3.5	Stop 6 or more days prior	
Apixaban (Eliquis)		Stop 1 day prior	Stop 2 days prior
Dabigatran (Pradaxa)	CrCl ≥ 50 ml/min	Stop 1 day prior	Stop 2 days prior
	CrCl < 50 ml/min	Stop 2 days prior	Stop 4 days prior
Edoxaban (Savaysa)		Stop 1 day prior	Stop 2 days prior
Rivaroxaban (Xarelto)		Stop 1 day prior	Stop 2 days prior
Aspirin (ASA)		Continue ASA uninterrupted	
Cilostazol (Pletal)		Stop 1 to 2 days prior	
Clopidogrel (Plavix)		Stop 5 days prior ^d	
Prasugrel (Effient)		Stop 7 days prior ^d	
Ticagrelor (Brilinta)		Stop 5 days prior ^d	

coordinated between the proceduralist, anesthesiologist (if applicable), and the prescribing provider (e.g., cardiologist, neurosurgeon, vascular surgeon); elective procedures should be delayed at least 30 days after bare metal stent and at least 6 months after drug-eluting stent

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