

Our Lady of the Lake Regional Medical Center

Pharmacy Anticoagulation Stewardship

Clinical Practice Guideline: Pre and Post- procedural management of Antithrombotic therapy

1.1 Introduction

These clinical practice guideline recommendations are for patients on antithrombotic therapy with a plan for surgery or other invasive procedures.

Its purpose is to help with appropriate management of antithrombotic agents during perioperative period with a desired outcome of minimizing bleeding risks for patients undergoing surgical procedure. It will also provide a standardize recommendation and approach for the management of antithrombotic agents during perioperative period and timing of resuming antithrombotic therapy post procedure when hemostasis is achieved.

Target population

The target population of this guideline are all inpatient adult patient who are currently taking any antithrombotic agent (i.e. antiplatelet or anticoagulant) and will undergo surgical procedure.

Definitions

Anti-thrombotic – agents that are used to prevent blood clots. These agents include both anti-platelet and anticoagulant agents

Anti-platelet – agents that work on different receptors (i.e. P2Y₁₂, ADP, GPIIb/IIIa) on platelets to prevent platelet aggregation including aspirin, clopidogrel, prasugrel, and ticagrelor

Anticoagulant – agents that inhibit the coagulation cascade and prevent clot formation. The following are different pharmacological classes of anticoagulants and the drugs in each pharmacologic class:

- **Vitamin K antagonist** – agents that inhibit VCOR complex and decrease clotting factors (i.e. warfarin)
- **DOAC** – Direct oral anticoagulants are a newer class of anticoagulant that includes Dabigatran, Rivaroxaban, Apixaban, Edoxaban, and Betrixaban
- **Direct Thrombin Inhibitor** – oral anticoagulants that inhibit thrombin or factor II (i.e. dabigatran)
- **Factor Xa Inhibitors** – oral anticoagulants that only inhibit factor Xa (i.e. rivaroxaban, edoxaban, apixaban, and betrixaban)

1.2 Patient risk factors for bleeding¹

The following risk factors increase risk for bleeding:

Active or metastatic cancer	ICU admission
Age > 65 years	Hepatic or renal dysfunction
Anemia	History of bleeding complications
Thrombocytopenia	Concomitant medications (i.e. antiplatelet, anticoagulants, NSAIDs)
Past or active gastroduodenal ulcer	

Table 1. Bleeding risk per surgical procedure^{1,2}

Bleeding risk	Surgical procedure^{1,2}
High	Knee replacement Coronary artery bypass surgery Nephrectomy Thoracic surgery Spinal and epidural anesthesia Bilateral knee replacement Chest tube placement Heart valve replacement Any procedure >45 minutes
Moderate	Abdominal hernia repair Cholecystectomy
Low	Colonoscopy; Gastroscopy; Sigmoidoscopy Bronchoscopy Tooth extraction Endoscopic ultrasound without fine needle aspiration Permanent pacemaker implantation or battery change

1.3 Patients risk factors for VTE after surgery ^{2,3}

Moderate	High	Very High
<ul style="list-style-type: none"> • Bileaflet aortic valve prosthesis CHADs-2-VASc score of 2-3 • VTE within 12 months 	<ul style="list-style-type: none"> • CHADs 2-Vasc 4-5 • Bileaflet aortic valve prosthesis with any of the following: <ul style="list-style-type: none"> • Active malignancy • Age >75 years • Heart failure • Prior stroke or TIA • Hypertension • Diabetes • Atrial fibrillation 	<ul style="list-style-type: none"> • Mitral valve replacement CHADs 2-Vasc \geq 6 • Recent stroke • Recent VTE within the past 3 months • Severe thrombophilia

2.0: Pre-procedural management of direct oral anticoagulants ^{2,4,7,8,9,10,14, 15,16}

Drug	Current renal function	Low bleeding risk procedure	Moderate/High bleed risk procedure
Rivaroxaban	CrCl > 50 mL/min	Stop 1 day before procedure	Stop 2 days prior to procedure
	CrCl 15 - 50 mL/min	Stop 1 - 2 days prior to procedure	Stop 2 - 3 days prior to procedure
Edoxaban	CrCl \geq 50 mL/min	Stop 1 day prior to procedure	Stop 2 days prior to procedure
	CrCl 15 - 49 mL/min	Stop 1 - 2 days prior to procedure	Stop 2 - 3 days prior to procedure
Dabigatran	CrCl \geq 50 mL/min	Stop 1 day prior to procedure	Stop 2 - 3 days prior to procedure
	CrCl 30 - 49 mL/min	Stop 2 - 3 days prior to procedure	Stop 4 - 5 days prior to procedure
Apixaban	CrCl > 50 mL/min	Stop 1 day prior to procedure	Stop 2 days prior to procedure
	CrCl 30 - 50 mL/min	Stop 1 - 2 days prior to procedure	Stop 2 - 3 days prior to procedure

2.1: Post-procedure management of direct oral anticoagulants ^{4, 7,8,9,10,14, 15}

Drug	Low bleeding risk/minor surgical procedure	High bleed risk/major surgical procedure
Rivaroxaban	Resume 24 hours if approved by surgeon	Resume 48 - 72 hours if approved by surgeon
Edoxaban	Resume 24 hours if approved by surgeon	Resume 48 - 72 hours if approved by surgeon
Dabigatran	Resume 24 hours if approved by surgeon	Resume 48 - 72 hours if approved by surgeon
Apixaban	Resume 24 hours if approved by surgeon	Resume 48 - 72 hours if approved by surgeon

2.3: Pre and Post management of vitamin K antagonist ^{2, 6, 11, 12, 13,16}

Drug	Pre-procedure management	Post-procedure management
Warfarin	Stop ≥ 5 days before procedure with <ol style="list-style-type: none"> 1. Low to moderate bleed risk 2. High-bleed risk <p style="text-align: center;">OR</p> until INR ≤ 1.5 for high-risk procedures*	Within 24 hours after surgical procedure if hemostasis is achieved and approved by surgeon Resume patient pre-procedure usual dose ¹⁶ *High risk for VTE patients should receive bridge anticoagulant therapy

*If INR is greater than 1.5, within 48hrs prior to procedure; the use of pre-operative vitamin K is not recommended due to concern for potential resistance to post-operative re-anticoagulation¹⁶

In patients with high risk for thromboembolism; bridge with unfractionated heparin or Low molecular weight heparin ^{3, 6, 16}

Consider continuation of warfarin therapy for procedures with minimal bleeding risk or if undergoing minor procedure (Dental, dermatologic and ophthalmic, Pacemaker/ICD)¹⁶.

3.0 Parental Anticoagulant ^{3,6,16}

3.1: Pre-procedure interruption management of parental anticoagulant

Drug	Pre-procedure status	Time to hold prior to procedure
Unfractionated heparin	Prophylactic dosing	May give the morning
	Treatment dosing	Stop 4-6 hours prior to procedure
Enoxaparin	Prophylactic dosing	Stop 12 hours prior to procedure
	Treatment dosing	Stop 24 hours prior to procedure
Fondaparinux	CrCl > 50 mL/minute	Stop 72 hours prior to procedure
	CrCl 30 – 50 mL/minute	Stop 5 – 6 days prior to procedure
Argatroban	Normal hepatic function	Stop 3 hours prior to procedure
	Child-Pugh score > 6	Stop 9 hours prior to procedure

3.2 Post-procedure management of parental anticoagulant ^{2,3,6}

Drug Class	Drug	Low bleeding risk/minor surgical procedure	High bleed risk/major surgical procedure
Unfractionated heparin	Unfractionated heparin	At least 24 hours if approved by surgeon	48 - 72 hours if approved by surgeon
Low molecular weight heparin	Enoxaparin	At least 24 hours if approved by surgeon	48 - 72 hours if approved by surgeon
Factor Xa Inhibitor	Fondaparinux	At least 24 hours if approved by surgeon	72 hours if approved by surgeon
Direct thrombin inhibitors	Argatroban	At least 12 hours if approved by surgeon	24 hours if approved by surgeon

4.0 Procedural management of Antiplatelet Therapy^{2, 3,6,16}

Drug	Time to hold before surgery	Time to resume therapy after surgery
Aspirin (high cardiovascular risk)	May continue throughout perioperative period	≤ 24 hours after procedure
Aspirin (low cardiovascular risk)	Stop ≤ 7 days	≤ 24 hours after procedure
Clopidogrel	Stop 5 days before surgery	≤ 24 hours after procedure
Prasugrel	Stop 7 days before surgery	≤ 24 hours after procedure
Ticagrelor	Stop 3 - 5 days before surgery	≤ 24 hours after procedure
Dipyridamole	Stop 7-10 days	≤ 24 hours after procedure
Cilostazol	Stop 2 days	≤ 24 hours after procedure

Consider continuation of antiplatelet therapy for minor procedure (Dental, dermatologic, and ophthalmic, Pacemaker/ICD)¹⁶.

5.0 Antithrombotic management during regional/spinal anesthesia

- Risk factors for development of spinal hematoma:
 - o Elderly
 - o Female gender
 - o Congenital or acquired coagulopathies
 - o Spinal abnormalities
 - o Traumatic procedure
 - o Epidural catheter insertion > Simple epidural puncture > Simple spinal puncture
 - o Use of anticoagulant or antiplatelet therapy

5.1: Antiplatelet management in spinal/epidural anesthesia ^{2, 6}

Drug	Discontinuation prior to catheter placement	Time to resume therapy after catheter removal
Aspirin	No time restriction	No time restriction
Clopidogrel	Stop 7 days before catheter placement	After catheter removal
Prasugrel	Stop 7 - 10 days before catheter placement	6 hours after catheter removal
Ticagrelor	Stop 5 days before catheter placement	6 hours after catheter removal
Dipyridamole	Stop 1 day before catheter placement	6 hours after catheter removal
Cilostazol	Stop 2 days before catheter placement	6 hours after catheter removal

5.2: Oral Anticoagulant management in regional/spinal anesthesia ^{2, 6,7,8,9,10}

Drug	Discontinuation prior to catheter placement	Time to resume therapy after catheter removal
Apixaban	Stop 48 -76 hours before catheter placement	6 hours after catheter removal
Betrixaban	Stop 72 hours before catheter placement	6 hours after catheter removal
Dabigatran	Stop 72 - 96 hours before catheter placement	6 hours after catheter removal
Edoxaban	Stop 48 -72 hours before catheter placement	6 hours after catheter removal
Rivaroxaban	Stop 48 -72 hours before catheter placement	6 hours after catheter removal 24 hours after catheter removal if traumatic puncture occurred
Warfarin	INR of ≤ 1.4 before catheter placement	After catheter removal

5.3: Parental Anticoagulant management in regional/spinal anesthesia ^{2,6}

Drug	Discontinuation prior to catheter placement	Time to resume therapy after catheter removal
Heparin (prophylaxis)	Stop 4-6 hours before catheter placement	4 hour after catheter removal
Heparin (Treatment)	Stop 6 -12 hours before catheter placement	4 hour after catheter removal
Enoxaparin (prophylaxis)	Stop 12 hours before catheter placement	4 - 6 hours after catheter removal
Enoxaparin (Treatment)	Stop 24 hours before catheter placement	Within 12 hours after catheter removal
Fondaparinux (Prophylaxis)	Stop 36 – 42 hours before catheter placement	6 – 12 hours after catheter removal
Argatroban	Stop 4 hours before catheter placement	2 hours after catheter removal

6.0 Procedures in which continuation of anticoagulant may be considered^{3, 6, 11,12,13,16}

1. Minor dental procedure with low bleeding risk
2. Cutaneous procedure such as skin biopsy with low bleeding risk
3. Cardiac procedures such as implantable device and catheter ablation procedures

7.0 Disclaimer

This clinical practice guideline provides recommendations and strategies for pre and post procedural antithrombotic management. It is not intended to replace clinical judgment while addressing patient variability, bleeding and thrombosis risk prior and post procedure.

This Guideline Review and Revision information

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