Periprocedural and Regional Anesthesia Management with Antithrombotic Therapy – Adult – Inpatient and Ambulatory– Clinical Practice Guideline

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Committee Approvals/Dates:
Anticoagulation Committees: November 2012; August 2015
Pharmacy and Therapeutics: February 2013

Release Date:
Original: October 2011
Revised: February 2013; August 2015

Next Review Date:
October 2017

Executive Summary

Guideline Overview
The following guideline provides recommendations for patients receiving antithrombotic therapy and who require surgery, other invasive procedures, neuraxial or peripheral nerve procedures. Evaluating thromboembolic and bleeding risks are outlined, as well as considerations for administering antithrombotic therapy in the periprocedural setting and prior to regional anesthesia placement and removal.

Target Population
Inpatient and ambulatory adult patients who have indication(s) for antithrombotic medications and require either a surgical procedure and/or the need for neuraxial analgesia.

Key Practice Recommendations
1. The use of periprocedural bridging with antithrombotic agents should be reserved for high thrombotic risk patients.
2. Each antithrombotic agent has individual recommendations for how long it should be held pre-procedure, so advanced planning (in a non-emergent situation) is recommended.
3. Antithrombotic therapy should be resumed post procedure when hemostasis is achieved and the risk for bleeding has minimized.
4. Most antithrombotic agents should not be given during neuraxial anesthesia.
5. Each antithrombotic agent has individual recommendations for how long it should be held pre and post spinal epidural catheter placement and removal, so a medication review of both active and inactive antithrombotic medications is recommended.

Companion Documents
UW Health Procoagulant Clinical Practice Guideline

Pertinent UWHC Policies & Procedures
UW Health Administrative Policy 8.92: Epidural and Intrathecal (Neuraxial) Analgesia

Patient Resources:
Health Facts For You #4322: Epidural Analgesia
Health Facts For You #5915: Spinal Analgesia for Chronic Pain
Health Facts For You #6115: Stopping Anticoagulation and Antiplatelet Therapy
Health Facts For You #6404: Medicines, Herbs, and Vitamins Which Affect Bleeding
Health Facts For You #6915: Heparin (Unfractionated and Low Molecular Weight)

Scope

Disease/Condition(s):

Any disease or condition that would necessitate the need for anticoagulant, antiplatelet, or thrombolytic therapy. (ex. atrial fibrillation, cardiac disease, stroke)

Clinical Specialty:

Surgical services
Proceduralists
Anesthesia Pain Service
Primary care providers
Anticoagulation clinic

Intended Users:

Physicians
Advanced Practice Providers
Pharmacists
Nurses

CPG objective(s):

To assist clinicians by providing recommendations for holding, bridging and resuming antithrombotic therapy for procedures and holding, administering and resuming antithrombotic therapy for neuraxial analgesia.

Target Population:

Inpatient and ambulatory adult patients who have indication(s) for antithrombotic medications and require either a surgical procedure and/or the need for neuraxial analgesia.

Interventions and Practices Considered:

This guideline contains strategies and recommendations designed to assist clinicians in developing periprocedural antithrombotic management plans. It begins with providing recommendations on how to identify patients who are in need of periprocedural bridging based on thrombosis and bleeding risks. It focuses on antithrombotic medications by drug class (ex. anticoagulant, antiplatelet and thrombolytic) and provides recommendations for holding prior to surgery/procedure and when to resume therapy (if indicated). The second half of the guideline provides recommendations for holding antithrombotic agents prior to spinal/epidural catheter placement. It also provides recommendations for when to resume therapy (if indicated) after catheter removal.

Major Outcomes Considered:

Thromboembolic events in the absence of antithrombotic therapy in the periprocedural setting
Hemorrhagic events with antithrombotic therapy in the periprocedural setting
Hemorrhagic events with antithrombotic therapy with epidural or spinal catheter placement and removal

Guideline Metrics:

Metrics will include appropriate patient selection for “bridge” therapy, thromboembolic event up to 30 days after procedure, bleeding event up to 30 days after procedure, appropriate hold time of antithrombotic in relation to procedure or neuraxial catheter placement or removal and inappropriate administration of antithrombotic medications during neuraxial catheter placement.

Methodology

Methods Used to Collect/Select the Evidence:

(1) completing a comprehensive literature search of electronic databases; (2) conducting an in-depth review of relevant abstracts and articles; (3) conducting thoughtful discussion and interpretation of findings; (4) ranking strength of evidence underlying the current recommendations that are made.

Methods Used to Assess the Quality and Strength of the Evidence:

The same grading system for recommendations from the American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines was utilized.

Rating Scheme for the Strength of the Evidence and Recommendations:

For all other recommendations a modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology (Figure 1.) has been used to assess the Quality and Strength of the Evidence in this Clinical Practice Guideline.[1] See Appendix A.

Definitions

1. Periprocedural or Bridging Anticoagulation – administration of a short acting anticoagulant during the interruption of long-term antithrombotic therapy for major/minor surgery or procedures. Usually administered for a 10-12 day period.[2]

2. Regional anesthesia – includes techniques and administration of analgesics through the epidural or intrathecal routes. Also referred to as neuraxial analgesia or spinal/epidural analgesia.

3. Antithrombotic therapy – includes any anticoagulant or antiplatelet medication

Introduction

Patients receiving long term antithrombotic therapy who require surgery or an invasive procedure present a difficult therapeutic dilemma for clinicians. In this periprocedural interval when antithrombotic therapy is halted, periprocedural anticoagulation (bridging therapy) with a heparin product may be recommended for some patients.[2,3] There is new evidence to support the use of bridging therapy in a small group of high risk patients which has been outlined in this guideline. Studies have shown an increase in bleeding events when bridging therapy with a heparin agent was used both before and after procedures, with no difference in the incidence of thromboembolic events, compared to patients who did not receive bridging therapy around the time of procedures.[4-5]

The use of antithrombotics for venous thromboembolism (VTE) prevention, VTE treatment, cardiac and vascular disease, and the use of thrombolytics can increase the risk of spinal hematoma if these medications are not appropriately held prior to, during and after removal of an epidural catheter. Spinal hematoma, while rare, is a serious complication that is closely associated with antithrombotic administration during spinal and epidural analgesia.[6]

This guideline will be separated into 2 sections for antithrombotic management: Periprocedural and Neuraxial Anesthesia.

Recommendations

Periprocedural Antithrombotic Management

1. Weigh the consequences of short-term risk for thromboembolism and bleeding for the individual patient.[2]
   1.1. **Very few patients will need periprocedural anticoagulation or bridging therapy[4-5] *(Class IIa, Level B).***
   1.2. Overall risk stratification should focus on the patient's risk of thromboembolism since the consequences of a thromboembolic event are more likely to have serious, lasting effects than compared to consequences of major bleeding[2-3]. ***(Class IIa, Level C)***
   1.3. Use Table 1 to evaluate the bleeding risk of procedure or surgery[2] ***(Class IIa, Level C)***
   1.4. Use Table 2 to identify patients at risk for systemic embolism if antithrombotic agent is discontinued[2-5] ***(Class IIa, Level C)***
      1.4.1. It is recommended to use periprocedural (bridge) therapy for patients identified in Table 2.[2-5] ***(Class IIa, Level B)***
   1.5. Endoscopic procedures
      1.5.1. For low thromboembolic risk patients: for warfarin hold and proceed with endoscopic procedure when the INR < 1.5 and for other anticoagulants see specific recommendations in Tables 4-8.[2,7,8]***(Class IIa, Level C)***
      1.5.2. For high thromboembolic risk patients: see Table 3. Hold anticoagulation based on specific recommendations for each drug listed in Tables 4-8. [2,7,8]***(Class IIa, Level B)***

Table 1. Bleeding Risk for Surgery/Procedure[2,8,9]

Bleed Risk	Surgery/Procedure Type
High	• Aortic aneurysm repair • Bladder surgery • Bowel polypectomy • Coronary artery bypass grafting (CABG) • Heart valve replacement • Intracranial surgery • Major cancer surgery • Major orthopedic surgery (hip or knee replacement) • Peripheral artery bypass and other major vascular surgery • Prostate surgery • Reconstructive plastic surgery • Spinal surgery/Epidural procedure
Moderate	• Renal biopsy • Resection of colon polyps • Prostate biopsy • Pacemaker or defibrillator implantation • Major intraabdominal surgery • Major intrathoracic surgery • More invasive dental or ophthalmic procedures
Low	• Cataract surgery • Dental procedures Dental hygiene Simple extractions Restorations Endodontics Prosthetics • Cutaneous surgeries (most)

	• Laparoscopic cholecystectomy or hernia repair • Coronary angiography • Endoscopy with or without biopsy • Colonoscopy with or without biopsy

Table 2. Periprocedural Risk for Thromboembolism[2,4,5,10]

Risk	High: Periprocedural Anticoagulation advised
Mechanical Heart Valve	• Any mechanical mitral valve • Older mechanical valve model (caged ball or tilting disc) in mitral or aortic position • Recently placed mechanical valve (< 3 months) in mitral or aortic position • Recent stroke or TIA (within 6 months) with mitral or aortic valve
Atrial Fibrillation	• With mechanical heart valve in mitral or aortic position • With recent stroke or TIA (within 3 months)
Venous Thromboembolism	• VTE within previous 3 months

Table 3. Anticoagulation Considerations for Endoscopic Procedures[2,8,9]

Endoscopic Procedure	High Thromboembolic Risk
Diagnostic or Screening	Hold anticoagulation* Determine if peri-procedural bridging is needed
Low biopsy risk Removal of < 10 mm polyps with cold snare or forceps	Hold anticoagulation* Determine if peri-procedural bridging is needed
Large polyp removal (> 10 mm)	Hold anticoagulation* Determine if peri-procedural bridging is needed
Sphincterotomy Esophageal Dilation Fine Needle Aspiration	Hold anticoagulation* Determine if peri-procedural bridging is needed

*See individual anticoagulant recommendations for holding prior to procedure

2. Warfarin[2,9-11]
   - 2.1. Assess INR at least 7 days before surgery or procedure to allow for planning of perioperative management. ***(Class IIa, Level C)***
   - 2.2. Warfarin may be continued during procedures where bleed risk is low.[2,9,]
     - 2.2.1. Simple dental procedures (including extractions) if there is coadministration of an oral prohemostatic agent. (If no oral prohemostatic agent is coadministered, then warfarin should be held for 2-3 days before the procedure) ***(Class IIa, Level B)***
     - 2.2.2. Cataract surgery ***(Class IIa, Level C)***
     - 2.2.3. Diagnostic or screening colonoscopies ***(Class IIa, Level C)***
     - 2.2.4. Some cutaneous surgeries ***(Class IIa, Level C)***
     - 2.2.5. For endoscopic procedures – see Table 3 ***(Class IIa, Level B)***
   - 2.3. Check INR within 24 hours of surgical procedure to ensure that INR goal has been attained.[2] ***(Class IIa, Level C)***

2.4. If timing does not allow for gradual reduction of INR from withholding warfarin alone, administration of phytonadione (vitamin K), fresh frozen plasma, or prothrombin complex concentrates may be necessary. ***(Class IIb, Level C)***

Table 4 Periprocedural planning for warfarin[2,9-11] ***(Class I, Level C)***

Drug	Pre-procedure INR	Pre-Procedure Plan	Post Procedure Plan
Warfarin	2.0 – 3.0	Stop 5 days before procedure	Within 24 hours after surgical procedure or on postoperative day 1 if hemostasis is achieved and if approved by surgeon
	3.0 – 4.5	Stop 6 days before procedure	
	> 4.5	Stop 6-7 days before procedure Consider rechecking INR after 2-3 days of held doses If indicated consider phytonadione	

3. Direct Oral Anticoagulants[2,3,12-15] – *Listed Alphabetically*
   3.1 Assess renal function at least 7 days before surgery to allow for planning of perioperative management. Pre-operative parenteral anticoagulation (bridging) is not needed. ***(Class IIb, Level C)***
   3.2 If timing does not allow for reversal of anticoagulant effect from withholding doses alone, administration of procoagulant agents may be necessary.***(Class IIb, Level C)***
   3.3 Tables 5 and 6 provide recommendations for periprocedural management

Table 5 Pre-procedural planning for the direct oral anticoagulants[12-15] ***(Class IIb, Level C)***

Drug	Pre-procedure renal function	Minor surgery or Standard bleed risk surgery	Major surgery or high bleed risk surgery
Apixaban	Scr < 1.5 mg/dL	Stop 24 hours before procedure	Stop 48 hours before procedure
	Scr ≥ 1.5 mg/dL	Stop 48 hours before procedure	Stop 72 hours before procedure
Dabigatran	CrCl ≥ 50 mL/min	Stop 1 to 2 days before procedure	Stop 2 to 4 days before procedure
	CrCl < 50 mL/min	Stop 3 to 5 days before procedure	Stop ≥ 5 days before procedure
Edoxaban	CrCl ≥ 50 mL/min	Stop 24 hours before procedure	Stop 48 hours before procedure
	CrCl < 50 mL/min	Stop 48 hours before procedure	Stop 72 hours before procedure
Rivaroxaban	CrCl > 30 mL/min	Stop 24 hours before procedure	Stop 48 hours before procedure
	CrCl ≤ 30 mL/min	Stop 48 hours before procedure	Stop 72 hours before procedure

Table 6 Post-procedural planning for the direct oral anticoagulants[12-15] ***(Class IIb, Level C)***

Drug	Minor surgery or Standard bleed risk surgery	Major surgery or high bleed risk surgery	Onset of anticoagulation
Apixaban	Within 24 hours if approved by surgeon	Within 72 hours if approved by surgeon	3 – 5 hours
Dabigatran	Within 24 hours if approved by surgeon	Within 72 hours if approved by surgeon	2 hours
Edoxaban	Within 24 hours if approved by surgeon	Within 72 hours if approved by surgeon	2 hours
Rivaroxaban	Within 24 hours if approved by surgeon	Within 72 hours if approved by surgeon	2 – 4 hours

4. Parenteral Anticoagulants[2,9,11,16-20] – *Listed Alphabetically*
   - 4.1 Parenteral anticoagulation may be used for periprocedural anticoagulation management (bridging) in certain high risk patients.
   - 4.2 If timing does not allow for reversal of anticoagulant effect from withholding doses alone, administration of reversal agents or procoagulant agents may be necessary.***(Class IIb, Level C)***
   - 4.3 Tables 7 and 8 provide recommendations for periprocedural management
   - 4.4 Appendix B provides dosing recommendations for parenteral anticoagulants

Table 7 Pre-procedural planning for parenteral anticoagulants[16-20] ***(Class IIb, Level C)***

Drug	Pre-procedure	Any bleed risk surgery
Argatroban	Normal hepatic function Child-Pugh Score > 6	Stop 3 hours before procedure Stop 9 hours before procedure
Bivalirudin	CrCl ≥ 30 mL/min CrCl < 30 mL/min	Stop 1.5 hours before procedure Stop 3 hours before procedure
Enoxaparin	Prophylactic Dosing Therapeutic Dosing	Stop 12 hours before procedure Stop 24 hours before procedure
Fondaparinux	CrCl ≥ 50 mL/min CrCl < 50 mL/min	Stop 3 days before procedure Stop 5 days before procedure
Unfractionated Heparin	Prophylactic Dosing Therapeutic Dosing	May give the morning before procedure Stop 4-6 hours before procedure

Table 8 Post-procedural planning for parenteral anticoagulants[16-20] ***(Class IIb, Level C)***

Drug	Minor surgery or Standard bleed risk surgery	Major surgery or high bleed risk surgery	Onset of anticoagulation
Argatroban	Within 12 hours if approved by surgeon	Within 24 hours if approved by surgeon	30 minutes
Bivalirudin	Within 12 hours if approved by surgeon	Within 24 hours if approved by surgeon	15 minutes
Enoxaparin	Within 24 hours if approved by surgeon	Within 72 hours if approved by surgeon	3 – 5 hours
Fondaparinux	Within 24 hours if approved by surgeon	Within 72 hours if approved by surgeon	3 hours
Unfractionated Heparin	Within 12 hours is approved by surgeon	Within 24 hours if approved by surgeon	Immediate

5. Antiplatelet Therapy[2,21-23] – *Listed Alphabetically*
   5.1 For periprocedural management of antiplatelet therapy, assess use at least 7 days before surgery or procedure to allow for adequate hold time. ***(Class IIb, Level C)***
   5.2 If timing does not allow for reversal of antiplatelet effect from withholding doses alone, the surgeon may still elect to proceed with surgical procedure. ***(Class IIb, Level C)***
      5.2.1 Patients with coronary artery stent requiring surgery it is recommended to defer surgery for at least 6 weeks after stent placement.[2] ***(Class I, Level C)***
   5.3 Table 9 provide recommendations for periprocedural management

Table 9 Periprocedural management for antiplatelet drugs[2,21-23] ***(Class IIb, Level B)***

Drug	Pre-Procedure Plan	Post-Procedure Plan
Aspirin (low cardiovascular event risk)	Stop 7-10 days before procedure	Within 24 hours if approved by surgeon
Aspirin (high cardiovascular event risk)	May continue aspirin	Within 24 hours if approved by surgeon
Clopidogrel	Stop 5 days before procedure	Within 24-48 hours if approved by surgeon
Cilostazol	Stop 1 -2 days before procedure	Within 24 hours if approved by surgeon
Dipyridamole	Stop 1 -2 days before procedure	Within 24 hours if approved by surgeon
Prasugrel	Stop 5-7 days before procedure	Within 24-48 hours if approved by surgeon
Ticagrelor	Stop 5 days before procedure	Within 24-48 hours if approved by surgeon

Neuraxial Anesthesia and Antithrombotic Management

Spinal hematoma, while rare, is a serious complication of spinal or epidural anesthesia. Risk factors for the development of spinal hematoma include: advanced age, underlying coagulopathy, difficult needle placement and administration of antithrombotic agents with an indwelling neuraxial catheter. To reduce the risk of spinal hematoma related to antithrombotics, administration of these agents should be timed appropriately when neuraxial anesthesia is initiated, continued and/or removed.[6]

6. Anticoagulants– *Listed alphabetically*
   6.1. Prior to initiating neuraxial anesthesia a review of the patient medication list, both current and prior to admission lists, should be reviewed for use of an anticoagulant. [6] ***(Class I, Level C)***
   6.2. Utilize Table 10 for recommendations on holding anticoagulants prior to spinal/epidural catheter placement, use of anticoagulants during neuraxial therapy, and for resuming anticoagulation after spina/epidural catheters have been removed.
      6.2.1. No anticoagulant may be administered unless approved by the Anesthesia Pain Service (APS). ***(Class I, Level C)***

6.2.2. Unfractionated heparin (subcutaneously) up to doses of 5,000 units every 8-12 hours have been approved for use by the APS ***(Class IIb, Level C)***

Table 10 Anticoagulant management for spinal/epidural analgesia[6,12-15] ***(Class IIb, Level C)***

Drug	Prior to placement	While in place	After removal*
Apixaban	Hold 3 days	Contraindicated	Restart after minimum of 6 hrs
Argatroban	Hold 3 hours or until aPTT < 35 seconds	Contraindicated	Restart after minimum of 6 hrs
Bivalirudin	Hold 3 hours or until aPTT < 35 seconds	Contraindicated	Restart after minimum of 6 hrs
Dabigatran	Hold 5 days	Contraindicated	Restart after minimum of 6 hrs
Edoxaban	Hold 3 days	Contraindicated	Restart after minimum of 6 hrs
Enoxaparin	Hold for 12 hours (CrCl > 30 mL/min) Hold for 24 hours (CrCl < 30 mL/min or after therapeutic dose)	Contraindicated	Restart after minimum of 6 hrs
Fondaparinux	Hold 48 hours (CrCl > 50 mL/min) Hold 72 hours (CrCl < 50 mL/min)	Contraindicated	Restart after minimum of 6 hrs
Rivaroxaban	Hold 3 days	Contraindicated	Restart after minimum of 6 hrs
Unfractionated Heparin for prophylaxis (subcutaneous)	May be given without time restrictions	May be given	May be given without time restrictions
Unfractionated Heparin (intravenous)	Hold 4-6 hours or until aPTT < 35 seconds	Contraindicated	Restart after minimum of 6 hrs
Warfarin	Hold or reverse INR until < 1.5	Contraindicated	Restart after minimum of 6 hrs

*If traumatic puncture occurs may delay administration of anticoagulant 24-48 hours after removal if appropriate based on indication for use.

7. Antiplatelets – *Listed Alphabetically*

7.1. Prior to initiating neuraxial anesthesia a review of the patient medication list, both current and prior to admission lists, should be reviewed for use of an antiplatelet.[6] ***(Class I, Level A)***

7.2. Utilize Table 11 for recommendations on holding antiplatelets prior to spinal/epidural catheter placement, use of antiplatelets during neuraxial therapy, and for resuming antiplatelets after spinal/epidural catheters have been removed.

7.2.1. No antiplatelets may be administered unless approved by the APS ***(Class IIb, Level C)***

7.2.2. Aspirin up to doses of 325 mg twice daily and other non-steroidal anti-inflammatory medications have been approved for use by the APS ***(Class IIb, Level C)***

Table 11 Antiplatelet management for spinal/epidural analgesia[6] ***(Class IIb, Level C)***

Drug	Prior to placement	While in place	After removal
Aspirin	May be given without time restrictions	May be given	May be given without time restrictions
Clopidogrel	Hold 7-10 days	Contraindicated	Restart after a minimum of 4 hrs
Cilostazol	Hold 4 days	Contraindicated	Restart after a minimum of 4 hrs
Dipyridamole	Hold 7 days	Contraindicated	Restart after a minimum of 4 hrs
NSAIDs	May be given without time restrictions	May be given	May be given without time restrictions
Prasugrel	Hold 7-10 days	Contraindicated	Restart after a minimum of 4 hrs
Ticagrelor	Hold 5-7 days	Contraindicated	Restart after a minimum of 4 hrs

8. Thrombolytics
   8.1. Prior to initiating neuraxial anesthesia a review of the patient medication list, both current and prior to admission lists, should be reviewed for use of a thrombolytic. [6] ***(Class I, Level C)***
   8.2. Utilize Table 12 for recommendations on using thrombolytics prior to spinal/epidural catheter placement, use of thrombolytics during neuraxial therapy, and for using thrombolytics after spinal/epidural catheters have been removed.
      8.2.1. No therapeutic dose of thrombolytic may be administered unless approved by the APS ***(Class IIb, Level C)***
      8.2.2. When administered via a chest tube into the intrapleural space, alteplase should have minimal systemic absorption[24]. Use during spinal/epidural analgesia must be approved by APS prior to use. ***(Class IIb, Level C)***

Table 12 Thrombolytic management for spinal/epidural analgesia[6] ***(Class IIb, Level C)***

Drug	Prior to placement	While in place	After removal
Alteplase (tPA) – full therapeutic dose	Hold 10 days	Contraindicated	May be given after 10 days
Alteplase (tPA) – catheter clearance (1 mg/mL)	May be given without time restrictions	May be given	May be given without time restrictions

Companion/Collateral documents (as applies to CPG content)

UW Health Procoagulant Clinical Practice Guideline
UWHC Administrative Policy 8.92 – Epidural and Intrathecal (Neuraxial) Analgesia

UW Health Implementation

Potential Benefits:
This guideline will provide a standardized approach for the management of antithrombotic agents in the periprocedural and neuraxial analgesia settings. Through limited use of periprocedural bridging and appropriate timing of holding and administering antithrombotic agents it would be expected to see a decrease in the number of bleeding events related to antithrombotic agents in these settings.

Potential Harms:
There remain areas where there is limited literature and clear recommendations regarding periprocedural bridging with mechanical heart valves and significant heart valve disease, as well as, the use of alteplase for catheter clearance and intrapleural use during neuraxial anesthesia. In these situations clinical judgement, risk for thrombosis and bleeding risks will be weighed to determine the management strategy.

As with any antithrombotic agent, choosing therapy may result in an increased risk for bleeding, while withholding antithrombotic agents may result in an increased risk for thromboembolic event.

Implementation Plan
Recommendations provided by this guideline will be disseminated to clinic staff through a variety of venues including: primary care division meetings, newsletters, inservices and update of companion policies.

Implementation Tools
1. Guideline will be housed on UConnect in a dedicated folder for CPGs
2. UW Health Anticoagulation Newsletter
3. UW Health Anticoagulation Website: www.uwhealth.org/anticoagulation
4. Smart text for documenting periprocedural plans in the EMR
5. Electronic consults for Anticoagulation Clinic to assist with periprocedural plans

Disclaimer
CPGs are described to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice 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.

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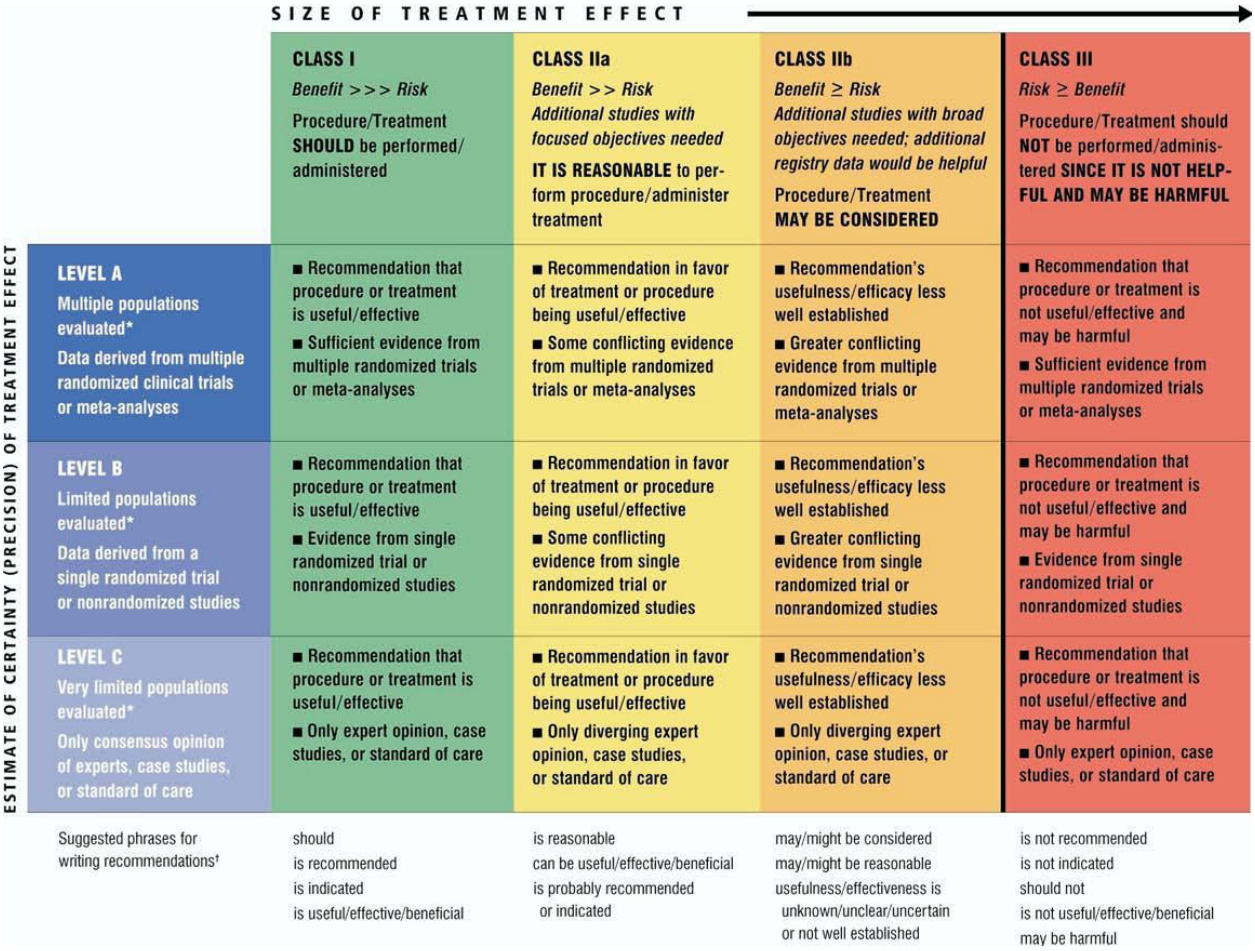
Appendix A. Modified Grading of Recommendations Assessment, Development, and Evaluation (GRADE)



ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	SIZE OF TREATMENT EFFECT →			
	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	**CLASS IIa** *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	**CLASS IIb** *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	**CLASS III** *Risk ≥ Benefit* Procedure/Treatment should **NOT** be performed/administered **SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL**
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations†	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	is not recommended is not indicated should not is not useful/effective/beneficial may be harmful

Appendix B. Periprocedural and Regional Anesthesia Management – Adult - CPG

Dosing of parenteral anticoagulants for periprocedural management

Drug	Therapeutic Dose	Prophylactic Dose
Enoxaparin (Lovenox®)	1 mg/kg SQ every 12 hours *(Round to nearest prefilled syringe size)*	40 mg SQ every 24 hours
Fondaparinux (Arixtra®)	Weight based < 50 kg: 5 mg SQ every 24 hours 50-100 kg: 7.5 mg SQ every 24 hours >100 kg: 10 mg SQ every 24 hours	2.5 mg SQ every 24 hours
UFH	Refer to UWHC Guidelines for therapeutic dosing of IV heparin	5000 units SQ every 12 hours **OR** 5000 units SQ every 8 hours