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Review Individuals/Bodies:
Inpatient Anticoagulation Committee – November 14, 2016
Ambulatory Anticoagulation Committee – November 28, 2016

Committee Approvals/Dates:
Pharmacy & Therapeutics Committee (Last Periodic Review: August 2015)
•  Interim revisions (December 15, 2016)

Release Date: December 2016  |  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 and spine pain 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 pain interventions.

Key Revisions (Interim Update November 2016)
1. Addition of recommendations for spinal pain procedures
2. Update to recommendations for antiplatelet agents when used for cardiac stents

Key Practice Recommendations
1. Recommendations for periprocedural antithrombotic management on the following:
   - Table 1 Procedural bleeding risk
   - Table 2 Evaluating individual thrombotic risk
   - Table 3 Endoscopic procedures
   - Table 4 Warfarin
   - Table 5 Creating a bridge plan for warfarin
   - Table 6 Direct oral anticoagulants
   - Table 8 Parenteral anticoagulants
   - Table 10 Antiplatelet agents
2. Recommendations for antithrombotic agents in neuraxial anesthesia and interventional spine pain procedures:
   - Table 11 Antithrombotics and neuraxial anesthesia
   - Table 12 Antithrombotics and spine pain procedures

Companion Documents
1. UW Health Procoagulant Therapy for Bleeding Associated with Acquired Bleeding Disorders - Adult - Guideline
2. Peri-operative Medication Management – Adult – Guideline

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
- Procedurals
- Anesthesia Pain Service
- Primary care providers
- Hospitalists
- Anticoagulation clinic

Intended Users:
- Physicians, Advanced Practice Providers, Pharmacists, Nurses
Objective(s): To assist clinicians with providing recommendations for holding, bridging and resuming antithrombotic therapy for procedures and holding, administering and resuming antithrombotic therapy for neuraxial analgesia and spine pain procedures.

Target Population: Adult patients who have indication(s) for antithrombotic medications that require either a surgical procedure and/or the need for neuraxial analgesia or spine pain procedure.

Interventions and Practices Considered:
- Identification of high risk patients in need of periprocedural bridging
- Consideration of bleeding risks for procedures
- Recommendations for antithrombotic medications by drug class
- Recommendations for antithrombotic medications prior, during and after spinal/epidural catheter placement
- Recommendations for antithrombotic medication prior and after spine pain procedures.

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
- Hemorrhagic events with antithrombotic therapy with spine pain procedures

Methodology
Methods Used to Collect/Select the Evidence:
Electronic database searches (e.g., PUBMED) were conducted by the guideline author(s) and workgroup members to collect evidence for review. Expert opinion and clinical experience were also considered during discussions of the evidence.

Methods Used to Formulate the Recommendations:
The workgroup members agreed to adopt recommendations developed by external organizations and/or arrived at a consensus through discussion of the literature and expert experience. All recommendations endorsed or developed by the guideline workgroup were reviewed and approved by other stakeholders or committees (as appropriate).

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 1 in Appendix A).

Rating Scheme for the Strength of the Evidence/Recommendations:
See Appendix A for the rating scheme(s) used within this document.
Recognition of Potential Health Care Disparities:
Under or uninsured patients may have difficulty acquiring low molecular weight heparin or other agents commonly used for bridging in the periprocedural period due to cost. In some situations direct oral anticoagulants may be considered. Thromboembolic risks while off anticoagulant therapy should be discussed with the patient. The medication assistance program may be able to assist with acquiring medications.

Definitions
1. 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.\(^1\)

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.

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.\(^1,2\) 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.\(^3,4\)

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 or spinal pain procedure. Spinal hematoma, while rare, is a serious complication that is closely associated with antithrombotic administration during spinal and epidural analgesia.\(^5\)

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

Recommendations
Periprocedural Antithrombotic Management
1. Weigh the consequences of short-term risk for thromboembolism and bleeding for the individual patient.\(^1\)
   1.1. Only high risk patients should be considered for periprocedural anticoagulation or bridging therapy\(^3,4\) (UW Health moderate quality of evidence, weak/conditional recommendation)
   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\(^1\). \textit{(UW Health low quality of evidence, weak/conditional recommendation)}

1.3. Use Table 1 to evaluate the bleeding risk of procedure or surgery\(^1\) \textit{(UW Health low quality of evidence, weak/conditional recommendation)} Use Table 2 to identify patients at risk for systemic embolism if antithrombotic agent is discontinued\(^1\).\(^4\) \textit{(UW Health moderate quality of evidence, weak/conditional recommendation)}

1.3.1. It is recommended to use periprocedural (bridge) therapy for patients identified in Table 2.\(^1\).\(^4\) \textit{(UW Health moderate quality of evidence, weak/conditional recommendation)}

1.3.2. There are specific recommendations provided for endoscopic and breast biopsy procedures in section 2 and 3 of this guideline.

### Table 1. Bleeding Risk for Surgery/Procedure\(^1\),\(^7\),\(^8\)

<table>
<thead>
<tr>
<th>Bleed Risk</th>
<th>Surgery/Procedure Type</th>
</tr>
</thead>
</table>
| 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\(^1\),\(^3\),\(^4\),\(^9\)

<table>
<thead>
<tr>
<th>Risk</th>
<th>High: Periprocedural Anticoagulation advised</th>
</tr>
</thead>
</table>
| Mechanical Heart Valve | • Any mechanical mitral valve  
                                      • Older mechanical valve model (caged ball or tilting disc) in mitral or |
2. Endoscopic procedures

2.1. For low thromboembolic risk patients\(^1,6,7\) (UW Health moderate quality of evidence, weak/conditional recommendation)

2.1.1. Hold warfarin and proceed with endoscopic procedure when the INR < 1.5

2.1.2. Other anticoagulants see specific recommendations in Tables 5-8.

2.2. For high thromboembolic risk patients: see Table 3. Hold anticoagulation based on specific recommendations for each drug listed in Tables 5-8.\(^16,7\) (UW Health moderate quality of evidence, weak/conditional recommendation)

<table>
<thead>
<tr>
<th>Endoscopic Procedure</th>
<th>High Thromboembolic Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic or Screening</td>
<td>Hold anticoagulation*</td>
</tr>
<tr>
<td></td>
<td>Create bridge plan (see Table 5)</td>
</tr>
<tr>
<td>Low biopsy risk</td>
<td>Hold anticoagulation*</td>
</tr>
<tr>
<td>Removal of &lt; 10 mm polyps with cold snare or forceps</td>
<td>Create bridge plan (see Table 5)</td>
</tr>
<tr>
<td>Large polyp removal (&gt; 10 mm)</td>
<td>Hold anticoagulation*</td>
</tr>
<tr>
<td></td>
<td>Create bridge plan (see Table 5)</td>
</tr>
<tr>
<td>Sphincterotomy</td>
<td>Hold anticoagulation*</td>
</tr>
<tr>
<td>Esophageal Dilation</td>
<td>Create bridge plan (see Table 5)</td>
</tr>
<tr>
<td>Fine Needle Aspiration</td>
<td>Create bridge plan (see Table 5)</td>
</tr>
</tbody>
</table>

*See individual anticoagulant recommendations for holding prior to procedure

3. Warfarin\(^1,8-10\)

3.1. Assess INR at least 7 days before surgery or procedure to allow for planning of perioperative management. (UW Health moderate quality of evidence, strong recommendation)

3.2. Warfarin may be continued during procedures where bleed risk is low.\(^1,8\) (UW Health moderate quality of evidence, weak/conditional recommendation)

3.2.1. 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)

3.2.2. Cataract surgery

3.2.3. Diagnostic or screening colonoscopies

3.2.4. Some cutaneous surgeries

3.2.5. For endoscopic procedures – see Table 3

3.3. Check INR within 24 hours of surgical procedure to ensure that INR goal has been attained.\(^1\) (UW Health low quality of evidence, weak/conditional recommendation)

3.4. If a bridge plan is needed see Table 6 for assistance

3.4.1. The most common bridge plan incorporates a 5 day warfarin hold

3.4.2. A 3 day warfarin hold or bridging in the post-procedural phase can also be considered
3.5. 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 if the procedure or surgery cannot be delayed. *(UW Health moderate quality of evidence, weak/conditional recommendation)*

Table 4: Periprocedural planning for warfarin<sup>1,8-10</sup>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pre-procedure INR</th>
<th>Last Dose Prior to Procedure</th>
<th>Post Procedure Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>2.0 – 3.0</td>
<td>5 days</td>
<td>Within 24 hours after surgical procedure or on postoperative day 1 if hemostasis is achieved and if approved by surgeon</td>
</tr>
<tr>
<td></td>
<td>3.0 – 4.5</td>
<td>6 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt; 4.5</td>
<td>6-7 days</td>
<td>Recheck INR after 2-3 days of held doses If indicated consider phytonadione</td>
</tr>
</tbody>
</table>

Table 5. Example of a warfarin 5 day hold with low molecular weight heparin (LMWH) periprocedural bridge plan

<table>
<thead>
<tr>
<th>Date</th>
<th>LMWH AM</th>
<th>LMWH PM</th>
<th>Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 5</td>
<td>Hold</td>
<td>Hold</td>
<td>Hold</td>
</tr>
<tr>
<td>Day 4</td>
<td>Hold</td>
<td>Hold</td>
<td>Hold</td>
</tr>
<tr>
<td>Day 3</td>
<td>Bridging Dose</td>
<td>Bridging Dose</td>
<td>Hold</td>
</tr>
<tr>
<td>Day 2</td>
<td>Bridging Dose</td>
<td>Bridging Dose</td>
<td>Hold</td>
</tr>
<tr>
<td>Day 1</td>
<td>Bridging Dose</td>
<td>Hold</td>
<td>Hold</td>
</tr>
<tr>
<td>Procedure Day</td>
<td>Hold</td>
<td>Hold</td>
<td>Warfarin Dose</td>
</tr>
<tr>
<td>Post Day 1</td>
<td>Bridging Dose</td>
<td>Bridging Dose</td>
<td>Warfarin Dose</td>
</tr>
<tr>
<td>Post Day 2</td>
<td>Bridging Dose</td>
<td>Bridging Dose</td>
<td>Warfarin Dose</td>
</tr>
<tr>
<td>Post Day 3</td>
<td>Bridging Dose</td>
<td>Bridging Dose</td>
<td>Warfarin Dose</td>
</tr>
<tr>
<td>Post Day 4</td>
<td>Bridging Dose</td>
<td>Bridging Dose</td>
<td>Warfarin Dose</td>
</tr>
<tr>
<td>Post Day 5</td>
<td>Bridging Dose</td>
<td>Bridging Dose</td>
<td>Warfarin Dose Recheck INR</td>
</tr>
</tbody>
</table>
4. **Direct Oral Anticoagulants**\(^{1,2,11-14}\) – Listed Alphabetically

4.1 Assess renal function at least 7 days before surgery to allow for planning of perioperative management. Pre-operative parenteral anticoagulation (bridging) is not needed. (*UW Health low quality of evidence, weak/conditional recommendation*)

4.2 If timing does not allow for reversal of anticoagulant effect from withholding doses alone, administration of procoagulant agents may be necessary if the procedure or surgery cannot be delayed. (*UW Health low quality of evidence, weak/conditional recommendation*)

4.3 Tables 6 and 7 provide recommendations for periprocedural management (*UW Health moderate quality of evidence, weak/conditional recommendation*)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pre-procedure renal function</th>
<th>Minor or standard bleed risk surgery last dose prior to procedure</th>
<th>Major or high bleed risk surgery last dose prior to procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>Scr &lt; 1.5 mg/dL</td>
<td>24 hours</td>
<td>48 hours</td>
</tr>
<tr>
<td></td>
<td>Scr ≥ 1.5 mg/dL</td>
<td>48 hours</td>
<td>72 hours</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>CrCl ≥ 50 mL/min</td>
<td>1 - 2 days</td>
<td>2 – 4 days</td>
</tr>
<tr>
<td></td>
<td>CrCl &lt; 50 mL/min</td>
<td>3 – 5 days</td>
<td>≥ 5 days</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>CrCl ≥ 50 mL/min</td>
<td>24 hours</td>
<td>48 hours</td>
</tr>
<tr>
<td></td>
<td>CrCl &lt; 50 mL/min</td>
<td>48 hours</td>
<td>72 hours</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>CrCl &gt; 30 mL/min</td>
<td>24 hours</td>
<td>48 hours</td>
</tr>
<tr>
<td></td>
<td>CrCl ≤ 30 mL/min</td>
<td>48 hours</td>
<td>72 hours</td>
</tr>
</tbody>
</table>

Table 7 Post-procedural planning for the direct oral anticoagulants\(^{11-14}\)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Minor surgery or Standard bleed risk surgery resume</th>
<th>Major surgery or high bleed risk surgery resume</th>
<th>Onset of anticoagulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>Within 24 hours if approved by surgeon</td>
<td>Within 72 hours if approved by surgeon</td>
<td>3 – 5 hours</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>Within 24 hours if approved by surgeon</td>
<td>Within 72 hours if approved by surgeon</td>
<td>2 hours</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>Within 24 hours if approved by surgeon</td>
<td>Within 72 hours if approved by surgeon</td>
<td>2 hours</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Within 24 hours if approved by surgeon</td>
<td>Within 72 hours if approved by surgeon</td>
<td>2 – 4 hours</td>
</tr>
</tbody>
</table>

5. **Parenteral Anticoagulants**\(^{1,8,10,15-19}\) – Listed Alphabetically

5.1 Parenteral anticoagulation may be used for periprocedural anticoagulation management or bridging therapy in certain high risk patients.

5.2 If timing does not allow for reversal of anticoagulant effect from withholding doses alone, administration of reversal agents or procoagulant agents may be necessary
if the procedure or surgery cannot be delayed. *(UW Health low quality of evidence, weak/conditional recommendation)*

5.3 Tables 8 and 9 provide recommendations for periprocedural management *(UW Health moderate quality of evidence, weak/conditional recommendation)*

Table 8 Pre-procedural planning for parenteral anticoagulants

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pre-procedure</th>
<th>Last dose prior to procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argatroban</td>
<td>Normal hepatic function</td>
<td>3 hours</td>
</tr>
<tr>
<td></td>
<td>Child-Pugh Score &gt; 6</td>
<td>9 hours</td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>CrCl ≥ 30 mL/min</td>
<td>1.5 hours</td>
</tr>
<tr>
<td></td>
<td>CrCl &lt; 30 mL/min</td>
<td>3 hours</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>Prophylactic Dosing</td>
<td>12 hours</td>
</tr>
<tr>
<td></td>
<td>Therapeutic Dosing</td>
<td>24 hours</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>CrCl ≥ 50 mL/min</td>
<td>3 days</td>
</tr>
<tr>
<td></td>
<td>CrCl &lt; 50 mL/min</td>
<td>5 days</td>
</tr>
<tr>
<td>Unfractionated Heparin</td>
<td>Prophylactic Dosing</td>
<td>12 hours</td>
</tr>
<tr>
<td></td>
<td>Therapeutic Dosing</td>
<td>4-6 hours</td>
</tr>
</tbody>
</table>

Table 9 Post-procedural planning for parenteral anticoagulants

<table>
<thead>
<tr>
<th>Drug</th>
<th>Minor or standard bleed risk surgery resume</th>
<th>Major surgery or high bleed risk surgery resume</th>
<th>Onset of anticoagulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argatroban</td>
<td>Within 12 hours if approved by surgeon</td>
<td>Within 24 hours if approved by surgeon</td>
<td>30 minutes</td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>Within 12 hours if approved by surgeon</td>
<td>Within 24 hours if approved by surgeon</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>Within 12-24 hours if approved by surgeon</td>
<td>Within 72 hours if approved by surgeon</td>
<td>3 – 5 hours</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>Within 24 hours if approved by surgeon</td>
<td>Within 72 hours if approved by surgeon</td>
<td>3 hours</td>
</tr>
<tr>
<td>Unfractionated Heparin</td>
<td>Within 12 hours is approved by surgeon</td>
<td>Within 24 hours if approved by surgeon</td>
<td>Immediate</td>
</tr>
</tbody>
</table>

6. Antiplatelet Therapy – *Listed Alphabetically*

6.1 For periprocedural management of antiplatelet therapy, assess use at least 7 days before surgery or procedure to allow for adequate hold time. *(UW Health moderate quality of evidence, strong recommendation)*

6.1.1 If timing does not allow for reversal of antiplatelet effect from withholding doses alone, the surgeon may still elect to proceed with surgical procedure. *(UW Health low quality of evidence, strong recommendation)*

6.2 For patients with cardiac stents any interruption in antiplatelet therapy should be coordinated with the surgeon, anesthesiologist and the prescribing provider. *(UW Health strong recommendation, low quality evidence)*

6.2.1 If the prescribing provider is a non-UW provider, every effort should be made to engage this provider in the coordination of care. If unable to connect with the non-UW provider, it is reasonable to contact UW Cardiology for recommendations. *(UW Health conditional recommendation, low quality evidence)*

6.3 Antiplatelet use with cardiac stents for elective (non-cardiac) surgery:
6.3.1 Bare metal stent (BMS): surgery should not be performed within 30 days after placement *(UW Health moderate quality of evidence, strong recommendation)*

6.3.2 Drug eluting stent (DES): surgery should not be performed within 3 months after placement and should ideally be delayed 6 months after placement *(UW Health moderate quality of evidence, strong recommendation)*

6.3.3 If surgical procedure requires discontinuation of antiplatelet therapy, it is recommended to continue aspirin (if possible). *(UW Health low quality of evidence, strong recommendation)*

6.4 Table 10 provide recommendations for periprocedural management *(UW Health moderate quality of evidence, weak/conditional recommendation)*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Last Dose Prior to Procedure</th>
<th>Post-Procedural Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin (low cardiovascular event risk)</td>
<td>7 – 10 days</td>
<td>Within 24 hours if approved by surgeon</td>
</tr>
<tr>
<td>Aspirin (high cardiovascular event risk)</td>
<td>May continue aspirin</td>
<td>Within 24 hours if approved by surgeon</td>
</tr>
<tr>
<td>Clopidogrel*</td>
<td>5 days</td>
<td>Within 24-48 hours if approved by surgeon</td>
</tr>
<tr>
<td>Cilostazol</td>
<td>1 -2 days</td>
<td>Within 24 hours if approved by surgeon</td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>1 -2 days</td>
<td>Within 24 hours if approved by surgeon</td>
</tr>
<tr>
<td>Prasugrel*</td>
<td>5 – 7 days</td>
<td>Within 24-48 hours if approved by surgeon</td>
</tr>
<tr>
<td>Ticagrelor*</td>
<td>5 days</td>
<td>Within 24-48 hours if approved by surgeon</td>
</tr>
</tbody>
</table>

*If used for cardiac stent notify the patient’s cardiologist prior to stopping therapy

Neuraxial Anesthesia, Interventional Spine and Pain Procedures and Antithrombotic Management

Regional anesthesia and interventional spine and pain procedures have a broad range of risk for spinal hematoma and therefore recommendations should consider both procedural and patient-specific risk factors for bleeding. Spinal hematoma, while rare, is a serious complication of spinal or epidural anesthesia and spine and pain procedures. 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, discontinuation of these agents should be timed appropriately when either neuraxial anesthesia is initiated, continued and/or removed or when a spine and pain procedure is planned.5,24

7. Anticoagulants—

7.1. Prior to neuraxial anesthesia or a spine and pain procedure, a review of the patient medication list, both current and prior to admission, should be reviewed for use of an antithrombotic.5,24 *(UW Health moderate quality of evidence, strong recommendation)*

7.2. Tables 11 and 12 provide recommendations on holding anticoagulants prior to spinal/epidural catheter placement or spine and pain procedures, use of anticoagulants during neuraxial therapy, and for resuming anticoagulation after
spina/epidural catheters have been removed or spine and pain procedures are complete in intermediate to high risk procedures.

7.2.1. For low risk procedures consider bleeding risks and individual patient risk factors to determine hold and resumption plan. (UW Health moderate quality of evidence, weak/conditional recommendation)

7.2.2. No anticoagulant may be administered unless approved by the Anesthesia Pain Service (APS). (UW Health low quality of evidence, strong recommendation)

7.2.3. Unfractionated heparin (subcutaneously) up to doses of 5,000 units every 8-12 hours have been approved for use by the APS with epidural catheters (UW Health low quality of evidence, weak/conditional recommendation)

8. Antiplatelets

8.1. Prior to neuraxial anesthesia or a spine and pain procedure a review of the patient medication list, both current and prior to admission, should be reviewed for use of an antiplatelet. (UW Health moderate quality of evidence, strong recommendation)

8.2. Antiplatelet use for coronary artery stents in elective (non-cardiac) procedure:

8.2.1. Bare metal stent (BMS): procedure should not be performed within 30 days after placement (UW Health moderate quality of evidence, strong recommendation)

8.2.2. Drug eluting stent (DES): procedure should not be performed within 3 months after placement and should ideally be delayed 6 months after placement (UW Health moderate quality of evidence, strong recommendation)

8.2.3. If procedure requires discontinuation of antiplatelet therapy, it is recommended to continue aspirin (if possible) and contact the patient’s cardiologist prior to stopping therapy. (UW Health low quality of evidence, strong recommendation)

8.3. Utilize Tables 11 and 12 for recommendations on holding antiplatelets prior to spinal/epidural catheter placement or spine and pain procedures, use of antiplatelets during neuraxial therapy, and for resuming antiplatelets after spinal/epidural catheters have been removed or spine and pain procedures are complete. (UW Health moderate quality of evidence, weak/conditional recommendation)

8.3.1. No antiplatelets may be administered unless approved by the APS (UW Health low quality of evidence, strong recommendation)

8.3.2. Aspirin up to doses of 325 mg twice daily and other non-steroidal anti-inflammatory medications have been approved for use by the APS with epidural catheters (UW Health low quality of evidence, weak/conditional recommendation)

9. Thrombolytics

9.1. Prior to neuraxial anesthesia or a spine and pain procedure a review of the patient medication list, both current and prior to admission, should be reviewed for use of a thrombolytic. (UW Health moderate quality of evidence, strong recommendation)

9.2. Utilize Tables 11 and 12 for recommendations on using thrombolytics prior to spinal/epidural catheter placement or spine and pain procedures, use of thrombolytics during neuraxial therapy, and for using thrombolytics after spinal/epidural catheters have been removed or spine and pain procedures are complete. (UW Health low quality of evidence, weak/conditional recommendation)

9.2.1. No therapeutic dose of thrombolytic may be administered unless approved by the APS (UW Health low quality of evidence, strong recommendation)
9.2.2. When administered via a chest tube into the intrapleural space, alteplase should have minimal systemic absorption. Use during spinal/epidural analgesia must be approved by APS prior to use. (UW Health low quality of evidence, weak/conditional recommendation)

Table 11 Antithrombotic Recommendations for Spinal/Epidural Analgesia

<table>
<thead>
<tr>
<th>Oral Anticoagulants</th>
<th>Drug Name</th>
<th>Last Dose Prior to Placement</th>
<th>Restart After Placement</th>
<th>Last Dose Prior to Removal</th>
<th>Time to Restart After Removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>3 days</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>Dabigatran</td>
<td>5 days</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>Edoxaban</td>
<td>3 days</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>3 days</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>Hold 4-5 days AND INR &lt; 1.2</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parenteral Anticoagulants</th>
<th>Drug Name</th>
<th>Last Dose Prior to Placement</th>
<th>Restart After Placement</th>
<th>Last Dose Prior to Removal</th>
<th>Time to Restart After Removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argatroban</td>
<td>3 hours or until aPTT &lt; 35 sec</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>3 hours or until aPTT &lt; 35 sec</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>Enoxaparin (CrCl &gt; 30 mL/min)</td>
<td>12 hours</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>Enoxaparin (CrCl &lt; 30 mL/min)</td>
<td>24 hours</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>Enoxaparin (Therapeutic dose)</td>
<td>24 hours</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>4 days</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>Unfractionated Heparin (IV)</td>
<td>6 hours or until Xa &lt; 0.1 IU/mL</td>
<td>1 hour</td>
<td>4 hours AND Xa &lt;0.1 IU/mL</td>
<td>1 hour</td>
<td></td>
</tr>
<tr>
<td>Unfractionated Heparin (SQ) 5000 units BID or TID</td>
<td>6 hours</td>
<td>Can restart immediately</td>
<td>6 hours</td>
<td>Can restart immediately</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antiplatelet Agents</th>
<th>Drug Name</th>
<th>Last Dose Prior to Placement</th>
<th>Restart After Placement</th>
<th>Last Dose Prior to Removal</th>
<th>Time to Restart After Removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>Doses up to 325 mg BID may be given prior, during and after removal without any time restrictions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cilostazol</td>
<td>2 days</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>7 days</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>2 days</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>NSAIDs may be given prior, during and after removal without any time restrictions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prasugrel</td>
<td>7-10 days</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>5-7 days</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>6 hours</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Thrombolytics</th>
<th>Drug Name</th>
<th>Last Dose Prior to Placement</th>
<th>Restart After Placement</th>
<th>Last Dose Prior to Removal</th>
<th>Time to Restart After Removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alteplase</td>
<td>10 days</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>10 days</td>
<td></td>
</tr>
<tr>
<td>Alteplase</td>
<td>(CVAD clearance)</td>
<td>May be given prior, during and after removal without any time restrictions</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*If traumatic puncture occurs may consider delaying administration of antithrombotic 24-48 hours after removal if appropriate

Table 12 Antithrombotic Recommendations for High Risk Spine Pain Procedures

<table>
<thead>
<tr>
<th>Oral Anticoagulants</th>
<th>Drug Name</th>
<th>Last Dose Prior to Procedure</th>
<th>Time to Restart After Procedure</th>
</tr>
</thead>
</table>

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Contact: CCKM@uwhealth.org
Last Revised: 12/2016
### Parenteral Anticoagulants

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Last Dose Prior to Procedure</th>
<th>Time to Restart After Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argatroban</td>
<td>4 hours or until aPTT &lt; 35 sec</td>
<td>24 hours</td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>4 hours or until aPTT &lt; 35 sec</td>
<td>24 hours</td>
</tr>
<tr>
<td>Enoxaparin Prophylactic dose</td>
<td>12 hours</td>
<td>24 hours</td>
</tr>
<tr>
<td>Enoxaparin Therapeutic dose</td>
<td>24 hours</td>
<td>24 hours</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>4 days</td>
<td>24 hours</td>
</tr>
<tr>
<td>Unfractionated Heparin (IV)</td>
<td>6 hours or until Xa &lt; 0.1 IU/mL</td>
<td>24 hours</td>
</tr>
<tr>
<td>Unfractionated Heparin (SQ)</td>
<td>8-10 hours</td>
<td>24 hours</td>
</tr>
</tbody>
</table>

### Antiplatelet Agents

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Last Dose Prior to Procedure</th>
<th>Time to Restart After Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin Primary prevention: 6 days</td>
<td>24 hours</td>
<td>Secondary prevention: risk stratify</td>
</tr>
<tr>
<td>Cilostazol</td>
<td>2 days</td>
<td>24 hours</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>7 days</td>
<td>12 – 24 hours</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>1 day</td>
<td>24 hours</td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>2 days</td>
<td>24 hours</td>
</tr>
<tr>
<td>Etodolac</td>
<td>2 days</td>
<td>24 hours</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>1 day</td>
<td>24 hours</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>2 days</td>
<td>24 hours</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>1 day</td>
<td>24 hours</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>4 days</td>
<td>24 hours</td>
</tr>
<tr>
<td>Nabumetone</td>
<td>6 days</td>
<td>24 hours</td>
</tr>
<tr>
<td>Naproxen</td>
<td>4 days</td>
<td>24 hours</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>10 days</td>
<td>24 hours</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>7-10 days</td>
<td>12 - 24 hours</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>5 days</td>
<td>12 - 24 hours</td>
</tr>
</tbody>
</table>

### Thrombolytics

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Last Dose Prior to Procedure</th>
<th>Time to Restart After Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alteplase (Full dose)</td>
<td>48 hours</td>
<td>48 hours</td>
</tr>
<tr>
<td>Alteplase (CVAD clearance)</td>
<td>May be given prior to or after procedure without any time restrictions</td>
<td>24 hours</td>
</tr>
</tbody>
</table>
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.

Pertinent UW Health Policies & Procedures
1. 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)
Health Facts For You #6325: Going Home After Spinal or Epidural Anesthesia

Guideline Metrics
1. Metric #1: 30 day thromboembolic event following procedure
2. Metric #2: 30 day bleeding event following procedure
3. Metric #3: appropriate antithrombotic hold time in relation to individual patient risk, procedure, neuraxial catheter placement or removal, or prior to/after spine pain procedure and the inappropriate administration of antithrombotic medications during neuraxial catheter placement

Implementation Plan/Clinical Tools
1. Guideline will be posted on uConnect in a dedicated location for Clinical Practice Guidelines.
2. Content and hyperlinks within clinical tools, documents, or Health Link related to the guideline recommendations (such as the following) will be reviewed for consistency and modified as appropriate.
3. Guideline will be posted externally on UW Health Anticoagulation website: www.uwhealth.org/anticoagulation

Best Practice Alerts (BPA)
Name: Epidural catheter – no unapproved anticoagulants

Disclaimer
Clinical practice guidelines 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.
Appendix A. Evidence Grading Scheme(s)

Figure 1. GRADE Methodology adapted by UW Health

GRADE Ranking of Evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>We are confident that the effect in the study reflects the actual effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>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.</td>
</tr>
<tr>
<td>Low</td>
<td>The true effect may differ significantly from the estimate.</td>
</tr>
<tr>
<td>Very Low</td>
<td>The true effect is likely to be substantially different from the estimated effect.</td>
</tr>
</tbody>
</table>

GRADE Ratings for Recommendations For or Against Practice

<table>
<thead>
<tr>
<th>Rating</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong</td>
<td>The net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.</td>
</tr>
<tr>
<td>Weak/conditional</td>
<td>Recommendation may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.</td>
</tr>
</tbody>
</table>

References


