Anticoagulation with Neuraxial/Peripheral Nerve Injections and Catheters

Anesthesia and Pain Management Guidelines
University of Washington Medical Center
Department of Anesthesiology and Pain Medicine

Overview

All discussions on altering or holding anticoagulation therapy should include the admitting service and/or the attending physician primarily responsible for anticoagulation.

Oral Anticoagulants (Warfarin)

1. Chronic warfarin: Stop 5 days prior. Measure PT/INR prior to confirm INR<1.5
2. Low intensity warfarin (goal INR < 1.5 for maintaining line patency), administered for > 36 hours during neuraxial/peripheral nerve analgesia or prior to catheter removal: daily PT + INR. Do not remove catheter if INR > 1.5.
3. INR > 3 with catheter: hold or reverse warfarin.
4. Warfarin initiated or received within 24 hours prior to surgery: check PT + INR prior to regional anesthesia procedure to ensure INR < 1.5
5. Monitor extremity motor function: correct if abnormal. Continue checks for 24 hours post catheter removal

Perioperative Management of Patients on Warfarin

1. Preoperative:
   a. Discontinue warfarin at least 5 days before elective procedure**
   b. Assess INR 1-2 days before surgery, if >1.5, consider 2.5 mg of oral vitamin K (onset 24-48 hours)
   c. Reversal for urgent surgery/procedure, consider 1-2 mg of intravenous vitamin K (onset ≈24 hours); for immediate reversal, consider fresh-frozen plasma
   d. No bridging necessary for patients at low risk for thromboembolism
   e. Patients at moderate to high risk for thromboembolism:
      i. Bridge with therapeutic subcutaneous low molecular weight heparin (LMWH) (preferred) or intravenous unfractionated heparin (UFH)
ii. Last dose of preoperative LMWH administered 24 hours before surgery; administer half of the daily dose

iii. Intravenous heparin discontinued 4 hours before surgery

2. Postoperative:
   a. Patients at low risk for thromboembolism:
      i. Resume warfarin 12-24 hours after surgery if adequate hemostasis has occurred (do not “load” warfarin)
   b. Patients at moderate to high risk for thromboembolism (who received preoperative bridging therapy):
      i. Resume warfarin 12-24 hours after surgery if adequate hemostasis has occurred (do not “load” warfarin)
      ii. Minor surgical procedure: resume therapeutic LMWH 24 hours postoperatively (if adequate hemostasis has occurred)
      iii. Major surgical procedure: resume therapeutic LMWH 48-72 hours postoperatively if adequate hemostasis, or administer low-dose LMWH
   c. Assess bleeding risk and adequacy of hemostasis when considering timing of the resumption of LMWH or UFH therapy

Antiplatelet Drugs

1. Antiplatelet medications, including NSAIDs, thienopyridine derivatives (ticlopidine Ticlid, clopidogrel Plavix and prasugrel Effient) and platelet glycoprotein GP IIb/IIIa antagonists (abciximab ReoPro, eptifibatide Integrilin and tirofiban Aggrastat) exert diverse effects on platelet function.

2. NSAIDs (including aspirin) alone: no risk

3. Other oral antiplatelet agents are contraindicated while neuraxial/nerve catheters are in place:
   a. For clopidrogel (Plavix) and prasugrel (Effient), discontinue drug 7 days prior to neuraxial/nerve catheter placement or spinal injection.
   b. For ticlopidine (Ticlid), d/c drug 10-14 days prior to these procedures

4. Platelet GP IIb/IIIa inhibitors are also contraindicated while neuraxial/nerve catheters are in place:
   a. Eptifibatide and tirofiban must be stopped at least 8 hours* prior to neuraxial/nerve catheter placement or spinal injection
   b. Abciximab must be stopped at least 48 hours prior to procedure.

5. All agents can be re-started 2 hours after catheter removal/spinal injection
Perioperative Management of Patients on Antiplatelet Therapy

1. All patients with coronary stents:
   a. Consult Cardiology
   b. Elective surgery postponed for the following durations if aspirin and thienopyridine (e.g. clopidogrel) therapy must be discontinued
      i. Bare metal stents: minimum 6 weeks (preferred: 3 months)
      ii. Drug-eluting stents: 12 months
   c. If surgery cannot be postponed, strong consideration should be given to continuing aspirin and clopidogrel throughout perioperative period

2. Patients at high risk for cardiac events (exclusive of coronary stents):
   a. Continue aspirin throughout the perioperative period
   b. Discontinue clopidogrel at least 5 days (and preferably 7 days) before surgery
   c. Resume clopidogrel 24 hours postoperatively. Loading doses of clopidogrel achieve therapeutic effects within 12 hours; maintenance doses achieve maximal inhibition of platelet function 5-10 days after resumption.

3. Patients at low risk of cardiac events:
   a. Discontinue antiplatelet therapy 7-10 days before surgery
   b. Resume antiplatelet therapy 24 hours postoperatively

Heparin-Induced Thrombocytopenia (HIT)

1. Suspect if platelet count decreased by >50% of pre-heparin baseline and heparin exposure within previous 14 days.
2. Discontinue all heparin products and warfarin
3. If acute thrombosis, treat with direct thrombin inhibitor and check heparin antibody ELISA assay for confirmation. (see UWMC Guidelines for Diagnosis and Management of HIT at www.uwmcacc.org)
4. If HIT confirmed, assume hypercoagulable status even in presence of low (<80,000/mL) platelet count. Patient should not receive platelet transfusion for neuraxial/nerve catheter removal.
5. If warfarin and/or direct thrombin inhibitor therapy planned, remove catheter even in setting of low platelet count.

Fibrinolytic/Thrombolytic Drugs (alteplase, streptokinase, urokinase)

1. Avoid neuraxial procedures except in highly unusual circumstances.
2. Avoid neuraxial procedures within 10 days of puncture of noncompressible vessels.
3. Low-dose alteplase (TPA), 2 mg, may be given for IV catheter clearance. TPA may be administered for catheter clearance during neuraxial analgesia to a maximum dose of 4 mg/24 hours.

**Unfractionated Heparin**

1. Mini-dose VTE prophylaxis with UFH:
   a. No contraindication.
   b. Check platelet count if duration > 4 days (to assess for heparin-induced thrombocytopenia)
   c. Doses must not exceed 5000 units TID subcutaneously
   d. Consider dose reduction to 5000 units BID subcutaneously if aPTT elevated on TID dosing

2. Full intraoperative systemic anticoagulation with UFH after neuraxial/pain catheter placement or injection:
   a. Delay heparin administration for 2 hours after needle placement.
   b. Monitor patient postoperatively to enhance early detection of spinal hematoma.
   c. Bloody or difficult neuraxial needle placement - no data to support case cancellation.

3. Full postoperative systemic anticoagulation with UFH:
   a. Spinal injections:
      i. Wait 2 hours after injection to resume heparin
   b. Neuraxial/nerve catheters:
      i. May be used ONLY if neuraxial/nerve catheter deemed essential for pain management.
      ii. Do not use neuraxial/nerve catheter if anticoagulation cannot be stopped to allow catheter removal
      iii. If anticoagulation planned or started, cap neuraxial/nerve catheter and trial alternative methods for pain control.
      iv. If pain inadequately controlled, neuraxial infusion may be restarted after patient informed of unknown risk of hematoma. This discussion with the patient should be documented in the clinical record.
      v. aPTT should be maintained within normal therapeutic range (minimal monitoring is daily aPTT) while neuraxial/nerve catheter in situ
      vi. Use concentrations of local anesthetic that allow ability to check for normal motor function
      vii. Prior to catheter removal, discontinue heparin for 4-6 hours to attain aPTT< 40. After catheter removal, wait 2 hours before resuming heparin. Check aPTT (< 40 sec for catheter removal). Check platelet count if > 4 days to assess for heparin induced thrombocytopenia
Low Molecular Weight Heparin

1. Concomitant administration of medications affecting hemostasis, such as antiplatelet drugs, standard heparin, or dextran may represent an additional risk of spinal hematoma.

2. Traumatic placement/blood in catheter:
   a. Do not postpone surgery.
   b. Delay initiation of LMWH therapy for 24 hours postoperatively.

3. Full systemic anticoagulation with LMWH:
   a. Contraindicated while neuraxial/nerve catheter is in place
   b. Therapeutic doses of LMWH such as enoxaparin (Lovenox) 1 mg/kg q 12 hours or 1.5 mg/kg daily, dalteparin (Fragmin) 100-120 U/kg q 12 hours or 200 U/kg daily, or tinzaparin (Innohep) 175 U/kg daily must be discontinued at least 24 hours* prior to spinal injection or neuraxial/nerve catheter placement.
   c. Fondaparinux 5-10 mg q day must be stopped at least 72 hours* prior to such procedures.
   d. Full systemic anticoagulation with LMWH or fondaparinux may be resumed 2 hours after catheter removal.

4. Preoperative VTE thromboprophylaxis with LMWH:
   a. Assume altered coagulation.
   b. Consider single-dose spinal anesthetic as safest neuraxial technique.
   c. Prophylactic doses of LMWH include enoxaparin 40 mg once or twice daily, enoxaparin 30mg q 12 hr, or dalteparin 5000 units once daily:
      i. Must be stopped at least 12 hours* prior to spinal injection or neuraxial/nerve catheter placement.
      d. Once daily prophylactic dose fondaparinux (2.5mg) must be stopped at least 48 hours* prior to such procedures.
      e. As discussed above, higher doses of LMWH or fondaparinux require a longer delay between the last dose and time to procedure (24 hours* for enoxaparin/ dalteparin and 72 hours* for fondaparinux).

5. Postoperative initiation of VTE thromboprophylaxis with LMWH:
   a. Management is based on total daily dose, timing of 1st postoperative dose and dosing schedule.
   b. **Single** daily dosing (enoxaparin 40 mg daily/dalteparin 5000 units daily):
      i. Indwelling neuraxial catheters may be safely maintained.
      ii. 1st dose may be administered no sooner than 6-8 hours* after neuraxial procedure.
      iii. Frequency of dosing should be no more than every 24 hours.
iv. These agents must be stopped for a minimum of 18-24 hours before catheter removal. Resumption may occur a minimum of 2 hours after catheter removal.

c. **Twice** daily dosing (enoxaparin 30 or 40 mg q 12hour):
   
   i. Contraindicated while neuraxial/nerve catheter is in place as twice daily dosing may be associated with an increased risk of spinal hematoma.

   ii. If a catheter is in situ and twice daily dosing is to commence, the catheter must be removed. Twice daily enoxaparin dosing may be initiated 2 hours after catheter removal.

Monitoring of enoxaparin/dalteparin activity:

1. Trough Anti Xa activity level (measured at end of dosing interval immediately prior to next dose) may in certain circumstances be useful to rule out residual effects from enoxaparin/dalteparin. A laboratory result should be available 8 hours after being drawn. Normal coagulation status may be assumed if the residual activity level is < 0.1 u/ml.

**Herbal Therapy**

1. No added risk for the development of spinal hematoma in patients having neuraxial anesthesia.

2. Concurrent use of other meds affecting clotting mechanisms, (oral anticoagulants or heparin), may increase risk of bleeding complications in these patients.

**Factor Xa Inhibitors (Fondaparinux *Arixtra*, Rivaroxaban *Xarelto*)**

1. Fondaparinux, a synthetic pentasaccharide, has a black box warning regarding risk of spinal/epidural hematoma similar to that of the LMWHs and heparinoids.
   
   a. Extreme caution is warranted given its sustained antithrombotic effect, early postoperative dosing, and "irreversibility".

   b. Until further clinical experience is available, performance of neuraxial techniques should occur under conditions utilized in clinical trials (single needle pass, a traumatic needle placement, avoidance of indwelling neuraxial catheters). If this is not possible, an alternate method of prophylaxis should be utilized.

   c. Close monitoring of the surgical literature for risk factors associated with surgical bleeding may be helpful in risk assessment and patient management.

   d. Prior to performing neuraxial/nerve procedures, prophylactic-dose fondaparinux (≤ 2.5mg daily) must be discontinued for at least 48 hours*. Full doses (5-10mg daily) require a longer delay of 72 hours between last dose and procedure.

2. Rivaroxaban is an oxazolidinone derivative and is the first orally active direct factor Xa inhibitor.
   
   a. Maximum inhibition of factor Xa occurs 4 hours after a dose.
b. Neuraxial/nerve procedures may be performed 18 hours* after the last dose (10mg PO daily).

c. Indwelling neuraxial catheters may be safely maintained while a patient is receiving rivaroxaban 10mg daily.

d. 1st dose may be administered no sooner than 6-8 hours* after neuraxial procedure.

e. Rivaroxaban must be stopped for a minimum of 18-24 hours before catheter removal. Resumption may occur a minimum of 6 hours after catheter removal.

Other New Antithrombotic agents*

1. New antithrombotic drugs target various steps in the hemostatic system, such as inhibiting platelet aggregation, blocking coagulation factors, or enhancing fibrinolysis.

2. Many of these antithrombotic agents have prolonged half-lives and are difficult to reverse without administration of blood components.

3. Administration of these medications in combination with neuraxial anesthesia must be carefully considered.

4. Dabigatran (Pradaxa):
   a. Offers an alternative to warfarin
   b. Does not require INR monitoring for efficacy
   c. Direct thrombin inhibitor
   d. At recommended therapeutic doses, dabigatran prolongs the aPTT, ECT, TT.
   e. Normal therapeutic dose is 150 mg PO bid
   f. Discontinue dabigatran 1 to 5 days before invasive or surgical procedures (longer times of up to 5 days needed for patients undergoing major surgery, neuraxial procedures, or patients with renal impairment).
   g. Dabigatran is not intended to be monitored using routine coagulation testing. However, to assess appropriate clearance prior to procedures, the direct thrombin inhibitor (DTI) assay might under certain circumstances be used to provide an approximation of dabigatran’s anticoagulant activity. The therapeutic range is 50-90 seconds.

* Indicates issues with renal impairment or deteriorating renal function. Recommended intervals may be considerably prolonged.

** Not all invasive procedures/surgeries require normalization of the INR
**ATTENTION!**
WHEN CAN YOU SAFELY DO NEURAXIAL/PERIPHERAL NERVE PROCEDURES OR GIVE ANTICOAGULANTS?
Neuraxial routes include epidural and intrathecal infusions, implanted intrathecal pumps, and spinal injections.
Peripheral routes include all peripheral nerve and plexus infusions.
NOTE: Bloody tap/procedure? Anesthesia to call Pain Service

### MEDICATION

<table>
<thead>
<tr>
<th>PRIOR TO NEURAXIAL/NERVE PROCEDURE</th>
<th>WHILE NEURAXIAL/NERVE CATHETER IN PLACE</th>
<th>AFTER NEURAXIAL/NERVE PROCEDURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum time between last dose of anticoagulant and spinal injection OR neuraxial/nerve catheter placement</td>
<td>Restrictions on use of anticoagulants in patients with neuraxial/nerve catheters in place</td>
<td>Minimum time between neuraxial/nerve catheter removal OR spinal/nerve injection and next anticoagulant dose</td>
</tr>
</tbody>
</table>

### ANTICOAGULANTS FOR VTE PROPHYLAXIS

<table>
<thead>
<tr>
<th>HEPARIN</th>
<th>UNFRACTIONATED</th>
<th>5000 units q8 or q12 hr</th>
<th>May be given; no time restrictions for catheter placement/removal or spinal injections</th>
<th>Do NOT call Pain Service</th>
</tr>
</thead>
<tbody>
<tr>
<td>DALTIPARIN</td>
<td>7500 units SQ q8 hr</td>
<td>8 hrs</td>
<td>CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending</td>
<td>2 hrs</td>
</tr>
<tr>
<td>ENOXAPARIN</td>
<td>(LOVENOX) 40mg SQ qday</td>
<td>12 hrs (longer in renal impairment)</td>
<td>May be given BUT contact Pain Service regarding dose timing</td>
<td>2 hrs</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>(LOVENOX) 30mg SQ q12 hr or 40mg SQ q12 hr</td>
<td>12 hrs (longer in renal impairment)</td>
<td>CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending</td>
<td>2 hrs</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>(ARIXTRA) &lt; 2.5mg SQ qday</td>
<td>48 hrs (longer in renal impairment)</td>
<td>May be given BUT contact Pain Service regarding dose timing</td>
<td>6 hrs (per manufacturer recommendations)</td>
</tr>
<tr>
<td>RIVAROXABAN</td>
<td>(XARELTO) 10mg po qday</td>
<td>18 hrs (longer in renal impairment)</td>
<td>CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending</td>
<td>2 hrs</td>
</tr>
</tbody>
</table>

### AGENTS USED FOR FULL SYSTEMIC ANTICOAGULATION

| DABIGATRAN | (PRADAXA) | 72 hrs (longer in renal impairment) | CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending | 2 hrs |
| DALTIPARIN | (FRAGMIN) | 200 Units/kg SQ qday or 100 Units/kg SQ q12 hr | CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending | 2 hrs |
| DROTRECOGIN | (XIGRIS) | 24 hrs (longer in renal impairment) | CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending | 2 hrs |
| Enoxaparin | (LOVENOX) 1.5mg/kg SQ qday or 1mg/kg SQ q12h | 24 hrs (longer in renal impairment) | CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending | 2 hrs |
| Fondaparinux | (ARIXTRA) 5-10mg SQ qday | 72 hrs (longer in renal impairment) | CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending | 2 hrs |
| Heparin | Unfractionated | IV continuous infusion or >5000 Units SQ bid or tid | when aPTT<40 sec | CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending | 2 hrs |
| Warfarin | (COUMADIN) | when INR< 1.5 | CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending | 2 hrs |

### DIRECT THROMBIN INHIBITORS

| Argatroban | IV continuous infusion | 72 hrs (longer in renal impairment) | CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending | 2 hrs |
| Bivalirudin | (ANGIOMAX) IV continuous infusion | when DTI assay < 40 or aPTT < 40 sec | CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending | 2 hrs |
| Eptifibatide | (Integrelin) IV continuous infusion | 8 hrs (longer in renal impairment) | CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending | 2 hrs |

### ANTIPLATELET AGENTS

<table>
<thead>
<tr>
<th>Aspirin/NSAIDS</th>
<th>May be given; no time restrictions for catheter placement or removal</th>
<th>Do NOT call Pain Service</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abciximab</td>
<td>(Reopro)</td>
<td>48 hrs</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>(Plavix)</td>
<td>7 days</td>
</tr>
<tr>
<td>Eptifibatide</td>
<td>(Integrilin)</td>
<td>8 hrs (longer in renal impairment)</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>(Effient)</td>
<td>7 days</td>
</tr>
<tr>
<td>Tirofiban</td>
<td>(Aggrastat)</td>
<td>8 hrs (longer in renal impairment)</td>
</tr>
</tbody>
</table>

### THROMBOLYTIC AGENTS

| ALTEPLASE | (TPA) 2mg dose for catheter clearance | May be given; no time restrictions for catheter placement or removal (Maximum dose 4mg/24 hours) | CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending | 10 days |
| Alteplase | (TPA) full dose for stroke, MI, etc | 10 days | CONTRAINDICATED while catheter in place: may NOT be given unless approved by Pain Service Attending | 10 days |