Guidelines for the Management of Patients on Oral Anticoagulation and Antiplatelet Therapy Undergoing Percutaneous Image-Guided Needle Procedures

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Introduction

This revision of the CDI Quality Institute Anticoagulation guidelines represents a summary and distillation of the 2015 American Society of Regional Anesthesia anticoagulation guidelines (Interventional Spine and Pain Procedures in Patients on Antiplatelet and Anticoagulant Medications by Narouze et al.). It is supplemented by relevant SIR guidelines which focus more on body and vascular interventions. (Patel, Jaffe) This merger necessitated the creation of separate risk stratifications for low-risk musculoskeletal/spine procedures and low-risk body/breast procedures as management of these two groups differs.

This is a guideline, not a policy. It is a summary and distillation of relevant subspecialty guidelines. The purpose of the CDI Quality Institute guidelines is to facilitate and accelerate the integration of medical evidence and best practices into daily clinical practices. Guidelines provide relevant medical evidence to support the development of policies within each individual practice. Guidelines should be adjusted for local standards of care, associated hospital or network policies, hospital versus outpatient settings, different patient populations, availability of resources, different experience levels, individual patient circumstances and different risk-tolerance profiles. Local practice policies should also be modified to account for new information or publications that become available between guideline revisions.
**Patient management**

The risk of bleeding in patients undergoing image-guided needle procedures is increased in patients with bleeding disorders and in patients on anticoagulant or antiplatelet medications. Depending on the procedure being performed, anticoagulation and antiplatelet drugs may need to be withheld prior to the procedure. Withholding medications may decrease the risk of bleeding; however, it may also increase the risk of recurrent thromboembolism. These risks need to be balanced on a patient-by-patient basis.

**Patient assessment:** Patients undergoing image-guided needle procedures need to be screened for a possible bleeding disorder and for anticoagulation and antiplatelet medication use. In general, outpatient needle procedures should be avoided in any patient with known bleeding disorders. If a needle procedure is absolutely needed, it should only be performed with hematology-directed management of their coagulation status (generally with assessment of the relevant clotting parameters and the administration of fresh frozen plasma or platelets depending on their particular condition). The management of these disorders is not addressed in this review.

The management of patients taking anticoagulation and antiplatelet medication is summarized in Table 1. Patients need to be screened for additional factors that may further increase the risk of bleeding. The risk of bleeding associated with the ordered needle procedure needs to be determined prior to the procedure. If the patient’s anticoagulant or antiplatelet medication needs to be withheld, the patient needs to contact their treating physician to get permission to withhold their medications or to obtain bridge therapy for the procedure. Laboratory data, if needed, should be obtained and checked prior to the procedure and compliance with instructions needs to be confirmed with the patient prior to the procedure.

**Risk stratification of injection procedures (Table 2):** Procedures are ranked relative to vascularity of the anatomic site, compressibility of the procedure site, needle size and procedural difficulty, risk of neurologic injury and risk of tumor dissemination.

**Anticoagulant and antiplatelet drug management (Table 3 and addendum):** If the treating provider approves, drug-specific instructions are given to the patient. The management of individual anticoagulation and antiplatelet drugs depends on the class of drug, any confounding medications, the procedure being ordered, and in some cases the liver and renal function.

**Bridge therapy (Table 4):** If the risk of thromboembolism is too high, the patient may be prescribed a bridge anticoagulation regimen for the procedure. In general, Coumadin is stopped and the patient is started on a subcutaneous regimen of Lovenox. Lovenox has a short half-life and can be discontinued just prior to the procedure minimizing the risk of thromboembolism to the patient.
Table 1: Procedural Anticoagulant Management Checklist:

1. Evaluate baseline patient risk factors:
   a. Screen for antiplatelet, antithrombotic or thrombolytic drug use;
   b. Screen for ASA or NSAID use;
   c. Screen for SSRI or herbal medication use;
   d. History of severe renal or liver disease;
   e. History or clinical evidence (excessive epistaxis or menorrhagia) of a bleeding disorder*;
   f. Family history of a bleeding disorder*;
   g. Order coagulation tests if a bleeding disorder is suspected based on this history.

2. Assess the risk of bleeding for the ordered injection procedure. The risk of bleeding for various image-guided needle procedures are categorized in Table 2 with respect to the following factors:
   a. Needle size;
   b. Compressibility;
   c. Procedural difficulty;
   d. Risk of neurologic injury; and the
   e. Risk of tumor dissemination.

3. If indicated, manage anticoagulation drug use as follows:
   a. Ask the patient to contact their treating physician to make sure it is safe to discontinue anticoagulation therapy, and if not, to secure bridge therapy if indicated;
   b. If the treating provider has given permission, instruct the patient to withhold their medication according to the instructions in Table 3;
   c. Immediately prior to the procedure, confirm with the patient that the anticoagulation medication was withheld as instructed; and
   d. Check the INR, PTT and platelet levels if indicated prior to the procedure.

* In general, spinal procedures should be avoided in any patient with a known bleeding disorder. If a needle procedure is absolutely needed, it should only be performed with directed management of their coagulation status (generally with the administration of fresh frozen plasma or platelets depending on their particular condition).
Table 2: Risk stratification of injection procedures†:

**MSK/Peripheral nerve low risk of bleeding** (ASRA 2015): MSK and ultrasound-guided injections with low risk of bleeding. No need to withhold anticoagulant or antiplatelet therapy. Check INR (<3.0)

- **MSK injections**
  - Peripheral joint injections and aspirations
  - Sacroiliac joint injections and aspiration
  - Tendon injections
  - Bursal injections
  - Trigger point injections including piriformis injections
- **Ultrasound-guided neural injections***
  - Peripheral nerve blocks

**Body/Breast low risk of bleeding** (SIR 2015, 2013, 2012): Body and vascular procedures with a low risk of bleeding and/or bleeding easy to detect and control. Hold Warfarin for 5 days. Check INR prior to the procedure, should be <1.5. Hold remaining fibrinolytic, antiplatelet and anticoagulant drugs per guideline.

- **Body procedures**
  - Venography, IVC filter placement, PICC line placement
  - Superficial aspiration and biopsy (LN, mass or breast)
  - Superficial abscess drainage
  - Drainage catheter exchange
  - Thoracentesis and paracentesis
  - Thyroid FNA (Hold anticoagulants per radiologist)
  - Breast procedures
  - Breast and axillary biopsies
  - Cyst aspirations (Hold anticoagulation per radiologist as some may convert to biopsies.)

**Moderate risk of bleeding:** Bleeding more difficult to control or detect, or has risk of catastrophic neurologic compromise. Hold warfarin for 5 days. Check INR prior to the procedure, should be <1.5. Do not need to withhold ASA, NSAIDs or phosphodiesterase inhibitors. aPTT and Platelet count may be checked prior to body and vascular procedures.

- **Neural/spine injections and procedures***
  - Interlaminar ESI (C, T, L, S)
  - Transforaminal ESI (C, T, L, S) (Hold ASA per radiologist.)
  - Facet Injections, MBNB, RFA and cyst aspiration/rupture (C, T, L)
  - Intradiscal injections (C, T, L)
  - Sympathetic blocks (stellate, thoracic splanchnic, celiac, lumbar and hypogastric)
- **Body procedures**
  - Intra-abdominal and retroperitoneal biopsies excluding renal, hepatic and splenic
  - Lung biopsies
• Thoracic and abdominal abscess drainage
• Gastrostomy tube: initial placement and exchanges
• Biliary tube exchanges
• Straightforward radiofrequency ablation procedures

**Vascular procedures**
• Angiography arterial intervention with access size up to 7 F
• Venous interventions

**High risk of bleeding:** This group includes procedures that have a high risk of uncontrolled or excessive bleeding. This group also includes biopsies of suspected sarcomas as hemorrhage can result in tumor dissemination and can have an adverse effect on patient prognosis. Hold anticoagulation drugs, antiplatelet drugs, ASA, NSAIDs and phosphodiesterase inhibitors per guidelines. Check INR (<1.5), aPTT, platelet count (>50,000) and hematocrit prior to the procedure.

**Neural/spine injections and procedures***
• **SCS trial and implant**
• **Vertebral augmentation (vertebroplasty and kyphoplasty)**
• **Intrathecal catheter and pump placement**

**Body procedures**
• Renal, hepatic and splenic biopsies
• Primary bone and soft tissue biopsies with possible diagnosis of sarcoma
• Nephrostomy
• Biliary interventions, new tract
• Complex radiofrequency ablation procedures

**Vascular procedures**
• TIPS


* Patients at high risk for bleeding undergoing low or intermediate risk procedures should be treated as intermediate or high risk respectively. Factors placing patients at increased risk of bleeding include old age, history of bleeding tendency, concurrent use of other anticoagulants/antiplatelets, liver cirrhosis, advanced liver disease and advanced renal disease.
### Table 3: Summary of Peri-procedural Management recommendation for Anticoagulant and Antiplatelet Medications †:

<table>
<thead>
<tr>
<th>DRUG</th>
<th>When to stop Spine/MSK low risk procedures</th>
<th>When to stop Body/breast low risk procedures</th>
<th>When to stop Moderate risk procedures</th>
<th>When to stop High risk procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA</td>
<td>No</td>
<td>No</td>
<td>No*</td>
<td>6 days</td>
</tr>
<tr>
<td>NSAIDs:</td>
<td>No</td>
<td>No</td>
<td>No*</td>
<td>5 half lives</td>
</tr>
<tr>
<td>Diclofenac (Cambia®, Cataflam®, Voltaren®, Voltaren-XR®, Zipsor®, Zorvolex®)</td>
<td>1 day</td>
<td></td>
<td></td>
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<tr>
<td>Ketorolac (Toradol ®)</td>
<td>1 day</td>
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<td></td>
<td></td>
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<tr>
<td>Mefenamic acid (Ponstel®)</td>
<td>1 day</td>
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<tr>
<td>Ketoprofen</td>
<td>1 day</td>
<td></td>
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<td></td>
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<tr>
<td>Ibuprofen (Motrin®, Advil®, Vicoprofen®, Combuon®)</td>
<td>1 day</td>
<td></td>
<td></td>
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<tr>
<td>Etodolac (Lodine®, Lodine XL®)</td>
<td>2 days</td>
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<tr>
<td>Indomethacin (Indocin®)</td>
<td>2 days</td>
<td></td>
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<tr>
<td>Naproxen (Aleve®, Naprosyn®, Anaprox®, Naprelan®, Naprapac®)</td>
<td>4 days</td>
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<tr>
<td>Meloxicam (Mobic®, Vivlodex®)</td>
<td>4 days</td>
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<td></td>
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<tr>
<td>Nabumetone (Relafen®)</td>
<td>6 days</td>
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<tr>
<td>Oxaprozin (Daypro®)</td>
<td>10 days</td>
<td></td>
<td></td>
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<tr>
<td>Piroxicam (Brexidol®, Candyl®, Feldene ®)</td>
<td>10 days</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Phosphodiesterase inhibitors:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Dipyridamole (Persantine)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>2 days</td>
</tr>
<tr>
<td>Dipyridamole/ASA (Aggrenox ®)</td>
<td>No</td>
<td>2 days</td>
<td>5 days (body procedures)</td>
<td>6 days</td>
</tr>
<tr>
<td>Cilostazol (Pletal ®)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>2 days</td>
</tr>
<tr>
<td>Pentoxifylline (Trental ®, Pentoxil ®)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>2 days</td>
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<tr>
<td><strong>Cox-2 inhibitors:</strong></td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Celecoxib (Celebrex)</td>
<td></td>
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<tr>
<td><strong>Anticoagulants</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Warfarin (Jantoven®, Coumadin®, Marevan®, Uniwarfin®)</td>
<td>No, therapeutic INR</td>
<td>5 days, normal INR</td>
<td>5 days, normal INR</td>
<td>5 days, normal INR</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>DRUG</th>
<th>When to stop</th>
<th>When to restart</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acenocoumarol</td>
<td>No, therapeutic INR</td>
<td>3 days, normal INR</td>
</tr>
<tr>
<td><strong>P2Y12 inhibitors:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel (Plavix®)</td>
<td>No</td>
<td>5 days</td>
</tr>
<tr>
<td>Prasugrel (Effient ®)</td>
<td>No</td>
<td>5 days</td>
</tr>
<tr>
<td>Ticagrelor (Brilinta ®)</td>
<td>No</td>
<td>5 days</td>
</tr>
<tr>
<td><strong>Direct factor Xa inhibitors</strong></td>
<td></td>
<td>5 half lives</td>
</tr>
<tr>
<td>Rivaroxaban (Xarelto®)</td>
<td>No</td>
<td>24 hours</td>
</tr>
<tr>
<td>Apixaban (Eliquis)</td>
<td>No</td>
<td>24 hours</td>
</tr>
<tr>
<td>Fondaparinux (Arixtra®)</td>
<td>No</td>
<td>24 hours</td>
</tr>
<tr>
<td><strong>Direct thrombin inhibitors:</strong></td>
<td></td>
<td>5 half lives</td>
</tr>
<tr>
<td>Dabigatran (Pradaxa®)</td>
<td>No</td>
<td>24 hours</td>
</tr>
</tbody>
</table>

**SSRI and SNRI** - Routine discontinuation not recommended. If the patient is at high risk of bleeding, these drugs may be slowly tapered in patients with stable depression under the supervision of the patient's treating psychiatrist.

**Herbal medications:**

- **Garlic** - Test platelet function if excessive doses are taken (>1000mg/day) or if taken with ASA, NSAIDs, SRIs or other antiplatelet drugs. Hold 7 days if needed.
- **Ginkgo biloba** - Test platelet function if taken with ASA, NSAIDs, SRIs or other antiplatelet drugs. Hold 3 days if needed.
- **dong quai** - Check INR in patients on Warfarin or Acenocoumarol.
- **Danshen** - Check INR in patients on Warfarin or Acenocoumarol.

*Consider holding ASA and NSAIDs for certain intermediate-risk procedures such as cervical interlaminar epidural steroid injections and stellate ganglion blocks.*

**Sources:**


Therapeutic INR <3.0, Normal INR<1.5.
Table 4: Example bridge therapy regimen:

The following is a low-dose bridging regimen currently utilized by Dr. Michael Cumming in the Vascular Center at St. Louis Park, MN.

1. Hold Coumadin starting 5 days prior to procedure.

2. Pre-procedure (three days of bridging)
   a. Initiate Lovenox Injections 3 days prior to procedure with one AM dose of 40mg Lovenox SQ each day.
   b. Do not take Lovenox on the morning of your procedure.

3. Post-Procedure (5 days of bridging post-procedure)
   a. Lovenox 40mg SQ AND Coumadin (double patient's lowest dose) PM for two days beginning the day of the procedure.
   b. Continue Lovenox 40mg PM SQ WITH Coumadin (return to normal scheduled dose) for 3 more days.
   c. Check INR (6 days post procedure) and call us with your result at 952-738-4498.
   d. Based on your INR, may prescribe additional doses of Lovenox.

Low Molecular Weight Heparins (LMWH): Heparin is an injectable anticoagulant that activates antithrombin III, preventing fibrin formation and platelet activation. Low-dose heparin inhibits clot formation, while higher doses prevent clot extension. LMWH is often used as a bridge for patients on warfarin therapy. A black-box warning has been issued concerning the risk of epidural or spinal hematoma in patients undergoing neuraxial procedures.

Recommendations:

- **Enoxaparin (Lovenox®, Xaparin®, Clexane®); Dalteparin (Fragmin®, Eisai®); Tinzaparin (Innohep®)**
  - SQ
  - Elimination is impaired in patients with severe renal disease (Stage IV and V).
  - Withhold one dose or 12 hours prior to the procedure (ARSA 2015).
  - Withhold 24 hours with higher doses, such as enoxaparin 1.0 mg/kg daily, dalteparin 200 IU/kg daily, or tinzaparin 175 U/kg daily (NEJM 24 hours, ARSA 2015).
  - May restart 6-8 hours after the procedure.
Addendum A: Anticoagulation and antiplatelet drug management.

Oral antiplatelet agents - aspirin and NSAIDs: Nonsteroidal anti-inflammatory drugs inhibit platelet cyclooxygenase and prevent the synthesis of thromboxane A2. Platelets from patients being treated with NSAIDS have normal subendothelial plug formation and normal primary plug formation.

With aspirin, platelet function is compromised for the life of the platelet. Restoration of clotting depends on the restoration of functioning platelets. Approximately 10% of the platelet pool is replaced daily. At 5-6 days, approximately 50% of platelets will function normally.

NSAIDs produce a short-term reversible effect and restoration of platelet function parallels the plasma half-life of the individual NSAID drug. For high-risk procedures, an NSAID should be held for five times the plasma half-life of the drug.

Recommendations:

- Low-dose Aspirin (ASA)
  - Not been shown to increase the risk of bleeding with low-risk procedures.
  - Consider holding ASA for certain intermediate-risk procedures, including interlaminar cervical ESIs and stellate ganglion blocks, where anatomical configurations may increase the risk and consequences of procedural bleeding (ARSA 2015).
  - For patients taking ASA for primary prophylaxis, hold 6 days for patients undergoing high-risk procedures (ARSA 2015 6 days, JVIR, NEJM 7-10 days, ACCP 7-10 days).
  - For patients taking ASA for secondary prophylaxis, after shared decision making and risk stratification, consider holding for 4 days for patients undergoing high risk procedures (ARSA 2015).
  - Consider withholding ASA in patients taking ASA in combination with anticoagulation drugs, other antiplatelet drugs, dipyridamole, Vitamin E, feverfew, Ginkgo, garlic, fish oil or SSRI drugs (Celexa, Lexapro, Prozac, Paxil, Pexeva, Zoloft, Viibryd) (ARSA 2015).
  - May restart 24 hours after a high-risk procedure (ARSA 2015, ACCP, NEJM). The anticoagulant effect of ASA can be seen as soon as 1 hour after an oral dose.

- NSAIDs
  - Do not need to be withheld for low and most intermediate-risk injection procedures.
  - Consider holding NSAIDs for certain intermediate-risk procedures, including interlaminar cervical ESIs and stellate ganglion blocks, where certain anatomical configurations may increase the risk and consequences of procedural bleeding (ARSA 2015).
  - Hold for 5 half-lives prior to high-risk procedures.
• Diclofenac (Cambia®, Cataflam®, Voltaren®, Voltaren-XR®, Zipsor®, Zorvolex®) - Hold 1 day;
• Ketorolac (Toradol ®) - Hold 1 day;
• Mefenamic acid (Ponstel®) - Hold 1 day;
• Ketoprofen - Hold 1 day
• Ibuprofen (Motrin ®, Advil®, Vicoprofen®, Combunox®) – Hold 1 day;
• Etodolac (Lodine®, Lodine XL®) - Hold 2 days.
• Indomethacin (Indocin®) - Hold 2 days.
• Naproxen (Aleve®, Naprosyn®, Anaprox®, Naprelan®, Naprapac®) - Hold 4 days.
• Meloxicam (Mobic®, Vivlodex®) - Hold 4 days.
• Nabumetone (Relafene®) - Hold 6 days.
• Oxaprozin (Daypro®) - Hold 10 days.
• Piroxicam (Brexidol®, Candyl®, Feldene®) - Hold 10 days.

  Consider holding longer in patients with severe renal or hepatic dysfunction, or with hypoalbuminemia.
  Consider holding longer in patients with renal dysfunction, hepatic dysfunction, alcohol abuse or a history of serious post-procedural bleeding.
  May restart 24 hours after a high-risk procedure (ARSA 2015, NEJM).

Oral antiplatelet agents – Phosphodiesterase inhibitors: These drugs selectively inhibit phosphodiesterase, thereby increasing the intracellular level of CAMP. Phosphodiesterase inhibitors have vasodilatory and weak reversible platelet aggregation inhibitory actions.

Recommendations:

• Dipyridamole (Persantine®)
  • Oral, T½ = 12 hours
  • Not been shown to increase the risk of clinically significant post-procedural bleeding.
  • Does not need to be withheld for low or moderate-risk procedures (ASIPP 2013, ACCP, AAPM&R 7 days).
  • Hold for 2 days prior to high-risk procedures (ARSA 2015).
  • May restart as soon as possible after the procedure.

• Dipyridamole/ASA (Aggrenox®)
  • Oral
  • Does not need to be withheld for low or moderate-risk Neuro/MSK procedures (ASRA 2015, ASIPP 2013, ISIS 3 days, UWMC 7 days, ACCP).
  • Hold 2 days for low-risk body/breast procedures and 5 days for Intermediate body/breast procedures (SIR 2015).
- Hold for 6 days in patients for high-risk procedures (ARSA 2015, NEJM 7-10).
- May restart 24 hours after the procedure (ARSA 2015).

**Cilostazol (Pletal ®)**
- Oral, T½ = 10 hours
- Does not need to be withheld prior to low or moderate-risk injection procedures (ASIPP 2013).
- Hold for 2 days prior to high-risk procedures (ARSA 2015, NEJM).
- May restart after hemostasis is achieved.

**Pentoxifylline (Trental ®, Pentoxil ®)**
- Oral
- Biologic T½ = 1-1.6 hours.
- Does not need to be withheld prior to low or moderate-risk injection procedures.
- Hold for 2 days prior to high-risk procedures (AAPM).
- Restart as soon as possible after the procedure.

**COX-2 inhibitors:** Celecoxib inhibits COX-2, an enzyme that is not expressed in platelets. Platelet dysfunction has not been reported in patients undergoing therapy with COX-2 inhibitors.

Recommendations:

- **Celecoxib (Celebrex ®)**
  - COX-2 inhibitors do not need to be withheld in anticipation of a neural axis procedure (ARSA 2015).
  - These drugs can be used for pain management in patients who might require injection therapy.
**Warfarin:** Warfarin and Acenocoumarol are oral anticoagulants that inhibit Vitamin K oxide reductase, an enzyme that recycles oxidized vitamin K, thereby affecting the production of coagulating factors II, VII, IX and X.

The biologic response to warfarin therapy can vary significantly between patients. It can vary with age, sex, and preexisting medical conditions. It can also be affected by certain foods, dietary supplements and commonly used medicines. As a result, regular blood monitoring (international normalized ratio-INR) is done to check for effectiveness and safety, and is recommended prior to injection therapy and invasive procedures. Please note that concomitant administration of antiplatelet medications and heparin can potentiate the anticoagulant effect of warfarin.

Management of Warfarin and acenocoumarol is based on the time for vitamin K components to regenerate. When long-term warfarin therapy is discontinued, the activity of factors II, VII, IX and X recover at different rates. Factor VII activity rapidly increases. An INR of 1.5 is associated with a factor VII activity of 40% and should be associated with normal hemostasis. However, factors II, IX and X activities recover much more slowly. Theoretically, there may be a time when the INR is normal and factors II and X have not recovered to the 40% level impairing hemostasis. As a result, infusion of Vitamin K or fresh frozen plasma may be needed in urgent or emergent cases. An FDA boxed warning has been issued concerning the risk of epidural or spinal hematoma with spinal procedures.

Recommendations:

- **Warfarin (Jantoven®, Coumadin®, Marevan®, Uniwarfin®)**
  - Does not need to be held for low risk MSK/neuro procedures providing the INR is within therapeutic ranges (<3.0), the patient is not a high risk for bleeding, and the patient does not have a history of serious post-procedural bleeding (ARSA 2015).
  - Hold 5 days for low risk body/breast procedures with the INR normalized (<1.5) (SIR/Jaffee, Patel).
  - Hold 5 days with INR normalized (<1.5) for moderate-risk (including spine) and high-risk procedures (NEJM, ARSA 2015, ACCP).
  - In patients receiving concomitant therapy with ASA, NSAIDs, ticlopidine, clopidogrel, UFH and LMWH, further delay may be considered depending on the specific medication used. These medications might increase the risk of bleeding complications without influencing the INR.
  - Restart the next day after the procedure (ARSA 2015, NEJM).
• **Acenocoumarol**
  - Does not need to be held for low-risk MSK/neuro procedures providing the INR is within therapeutic ranges (<3.0), the patient is not a high risk for bleeding, and the patient the patient does not have a history of serious post-procedural bleeding (ARSA 2015).
  - Hold 3 days with INR normalized (<1.5) for low-risk body/breast procedures.
  - Hold 3 days with INR normalized (<1.5) for moderate-risk (including spine) and high-risk procedures (NEJM, ARSA 2015, ACCP).
  - In patients receiving concomitant therapy with ASA, NSAIDs, ticlopidine, clopidogrel, UFH and LMWH, further delay may be considered depending on the specific medication used. These medications might increase the risk of bleeding complications without influencing the INR.
  - Restart the next day after the procedure (ARSA 2015, NEJM).

**Antiplatelet agents – P2Y12/Platelet aggregation inhibitors:** These drugs are thienopyridine derivatives whose pharmacologic effect derives from the inhibition of adenosine diphosphate-induced platelet aggregation. These drugs affect both primary and secondary platelet aggregation and interfere with platelet-fibrinogen binding and subsequent platelet-platelet interactions.

The effects of clopidogrel and prasugrel are irreversible and management is based on the time for new platelets to regenerate. 10-15% of platelets are turned over each day. At 5-6 days, approximately 50% of platelets will function normally. A black-box warning has been issued for epidural and spinal hematoma with neuraxial procedures.

**Recommendations:**

• **Clopidogrel (Plavix®)**
  - Do not need to hold for low risk MSK/Neuro procedures. (ASRA 2015).
  - Hold for 5 days for low-risk body/breast procedures. (SIR 2015).
  - Stop 7 days prior to intermediate (spine) and high-risk procedures (NEJM 5 days, ISIS 2013 7 days, ACCP 7 days, ARSA 2010/2015 7 days, AAPM&R 10 days, ACCP 7-10 days, SIR 5days).
  - In patients at high risk for thromboembolism, may withhold for 5 days if platelet function tests show adequate platelet function prior to the procedure.
  - May restart the usual daily dose (75mg) 12 hours after the procedure, or 24 hours after the procedure if a loading dose is used (ASRA 2015).

• **Prasugrel (Effient ®)**
  - Do not need to hold for low-risk MSK/Neuro procedures (ASRA 2015).
  - Hold for 5 days for low-risk body/breast procedures (SIR 2015).
- Stop **7-10 days** prior to intermediate (spine) and high-risk procedures (**NEJM 7 days**, ISIS, **ASRA 2015 7-10 days**).
- May restart 24 hours after the procedure (**ARSA 2015**).

- **Ticagrelor (Brilinta ®)**
  - Oral, $T_{1/2} = 7-9$ hours
  - Do not need to hold for low-risk MSK/Neuro procedures. (**ASRA 2015**).
  - Hold for 5 days for low-risk body/breast procedures (**SIR 2015**).
  - Discontinue 5 days before intermediate (spine) and high-risk procedures (**NEJM, ASRA 2015, SIR 7 days**).
  - May restart 24 hours after the procedure (**ARSA 2015**).

**Direct factor Xa inhibitors:** Factor Xa inhibitors are synthetic compounds composed of the essential pentasaccharide sequence that selectively inhibits factor Xa. Factor Xa is generated by both the extrinsic and intrinsic coagulation pathways. It activates prothrombin to thrombin, which activates the final components of the coagulation pathway to form clots.

Anticoagulant management is based on 5 half-lives for moderate or high-risk procedures and 2 half-lives for low-risk procedures. A black-box warning has been issued concerning the risk of epidural or spinal hematomas with neuraxial procedures.

**Recommendations:**

- **Rivaroxaban (Xarelto®)**
  - Oral, $T_{1/2} = 9-13$ hours
  - After shared assessment, risk stratification, and management decision making in conjunction with the treating physician, may consider holding 1 day for low-risk procedure (**ASRA 2015**).
  - Hold 24 hours for low-risk body/breast procedures (**SIR 2015**).
  - Hold 3 days for moderate or high-risk procedures (**ASIPP 2013, ASRA 2015 3 days**).
  - May restart 24 hours after the procedure. If the risk of VTE is high, $\frac{1}{2}$ the usual dose can be given at 12 hours (**ASRA 2015**).
• **Apixaban (Eliquis)**
  - Oral, $T_{1/2} = 15.2 +/− 8.5$ hours
  - After shared assessment, risk stratification and management decision in conjunction with the treating physician, may consider holding 1 day for low-risk procedure (ASRA 2015).
  - Hold 24 hours for low-risk body/breast procedures (SIR 2015).
  - Hold 3-5 days for moderate or high-risk procedure (ASRA 2015).
  - May restart 24 hours after the procedure. If the risk of VTE is high, $\frac{1}{2}$ the usual dose can be given at 12 hours (EMA, ASRA 2015).

• **Fondaparinux (Arixtra®)**
  - SQ, $T_{1/2} = 17-21$ hours
  - After shared assessment, risk stratification and management decision in conjunction with the treating physician, may consider holding two half-lives (2 days) for low-risk procedure (ASRA 2015 2 days, SIR 1 day).
  - Hold 24 hours for low-risk body/breast procedures (SIR 2015).
  - Hold 4 days before the moderate or high-risk procedure (ASRA 2015, NEJM 36-48 hours).
  - May restart 24 hours after the procedure (ASRA 2015).

**Direct Thrombin Inhibitors:** Thrombin inhibitors are anticoagulants that bind to and inhibit the activity of both free and fibrin-bound thrombin.

Anticoagulant management is based on 5 half-lives for moderate or high-risk procedures and 2 half-lives for low-risk procedures. There is an FDA black-box warning concerning the risk of epidural or spinal hematoma and paralysis with neuraxial anesthesia. Risk increases with concomitant treatment with NSAIDs, platelet inhibitors, and other anticoagulants.

Recommendations:

• **Dabigatran (Pradaxa®)**
  - Oral, $T_{1/2} = 12-17$ hours
  - After shared assessment, risk stratification and management decision in conjunction with the treating physician, consider holding 1-2 days for low-risk MSK/neuro procedures (ASRA 2015 2days).
  - Withhold 24 hours for low-risk body/breast procedures (SIR 2015).
  - Withhold 4-5 days for moderate or high-risk procedures, 6 days if renal disease (ASIPP 2013 2-4 days, ASRA 2015 4-5 days).
  - May restart 24 hours after the procedure, 12 hours if the risk of VTE is high (ASRA 2015).
**SRIs:** Both SSRI and SRNI have been associated with increased risk of bleeding.

- **Paroxetine, Escitalopram, Citalopram, Fluvoxamine, Fluoxetine, Setraline, Valfaxine, Duloxetine**
  - Routine discontinuation of SRIs before pain procedures is not recommended.
  - Consider stopping in patients with stable depression who are at high risk for bleeding (old age, advanced liver disease, concomitant ASA, NSAIDs, antiplatelets or anticoagulants use).
  - If SRI therapy is to be discontinued, the dose should be gradually tapered and discontinued 1-2 weeks prior to the procedure, and should be coordinated with the treating psychiatrist.

**Herbal Medications:**

- **Garlic**
  - Consider stopping in patients undergoing high-risk procedures.
  - Consider stopping in patients at high risk for bleeding, such as patients with advanced age, renal and/or hepatic disease, or a history of major bleeding following previous injection procedures.
  - Consider stopping or checking the bleeding time when patients with comorbidities take doses greater than 1000mg/d, or when there is concomitant intake with ASA, NSAIDs or SSRIs.
  - Discontinue for 7 days if indicated.

- **Dong quai**
  - Check INR in patients on warfarin.

- **Danshen**
  - Check INR in patients on warfarin.

- **Ginkgo biloba**
  - If indicated hold for 36 hours.
  - Check platelet function in patients taking other antiplatelet drugs.
References:


