

Management of Periprocedural Anticoagulation (Neuraxial Access or Peripheral Nerve Procedures)

Anticoagulation Guidelines for Neuraxial Access or Peripheral Nerve Procedures

Below are guidelines to prevent spinal hematoma following Epidural/Intrathecal/Spinal procedures and perineural hematoma following peripheral nerve procedures. Procedures include epidural injections/infusions, intrathecal injections/infusions/pumps, spinal injections, peripheral nerve catheters, and plexus infusions. Decisions to deviate from guideline recommendations given the specific clinical situation are the decision of the provider. See 'Additional Comments' section for more details.

	PRIOR to Neuraxial/Nerve Procedure	WHILE Neuraxial/Nerve Catheter in Place	AFTER Neuraxial/Nerve Procedure	Comments
Anticoagulant	How long should I hold prior to neuraxial procedure? (i.e., minimum time between the last dose of anticoagulant and spinal injection OR neuraxial/nerve placement)	Can I give anticoagulants concurrently with neuraxial, peripheral nerve catheter, or plexus placement?	When can I restart anticoagulants after neuraxial procedures? (i.e., minimum time between catheter removal or spinal/nerve injection and next anticoagulation dose)	What additional information do I need to consider?
Low-Molecular Weight Heparins, Unfractionated Heparin, and Fondaparinux				
Unfractionated Heparin SQ Prophylaxis Dosing	5000 units Q 12 hrs – no time restrictions	Yes	2 hrs	Maximum total heparin dose of 10,000 units per day (5000 SQ Q12 hrs) Heparin 5000 units SQ 8 hrs is NOT recommended with concurrent neuraxial catheter in place For IV prophylactic dosing, use 'treatment' IV dosing recommendations.
Unfractionated Heparin SQ/IV Treatment Dosing	SQ: 8-10 hrs IV: 4 hrs	No	2 hrs	See 'Additional Comments'
Enoxaparin (Lovenox), Dalteparin (Fragmin) Prophylaxis Dosing	12 hrs	No Note: May be used for Enhanced Treatment Protocol	4 hrs	Caution in combination with other hemostasis-altering medications See 'Additional Comments' for Enhanced Treatment protocol specifics
Enoxaparin (Lovenox), Dalteparin (Fragmin) Treatment Dosing	24 hrs	No	4 hrs	Recommendations for treatment remain same regardless of dosing (1mg/kg twice daily vs. 1.5mg/kg daily for enoxaparin)
Fondaparinux (Arixtra)	4 days	No	24 hrs	See 'Additional Comments'
Vitamin K Antagonist				
Warfarin (Coumadin)	INR <1.4 See comments*	No Yes for peripheral nerve catheters	2 hrs	*Typically takes holding warfarin 4-5 days prior to insertion *See reference specific to warfarin
Factor Xa Inhibitor				
Rivaroxaban (Xarelto)	3 days	No Yes for peripheral nerve catheters	6 hrs	
Apixaban (Eliquis)	3 days	No Yes for peripheral nerve catheters	6 hrs	

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Edoxaban (Savaysa)	3 days	No Yes for peripheral nerve catheters	6 hrs	
Betrixaban (Bevyxxa)	5 days	No Yes for peripheral nerve catheters	6 hrs	
Direct Thrombin Inhibitors				
Dabigatran (Pradaxa)	4 days 6 days (renal disease)	No – See additional comments Yes for peripheral nerve catheters	6 hrs	
Argatroban (Argatra)	4-6 hrs or aPTT <40 sec	No	2 hrs	t _{1/2} = 39-51 minutes – see ‘Additional comments’
Bivalirudin (Angiomax)	4-6 hrs or aPTT <40 sec 18 hrs if HD dependent	No	2 hrs	T _{1/2} 22-40 minutes Up to 3.5 hours in HD
NSAIDs & Antiplatelet				
NSAIDs	No time restrictions	Yes	May resume immediately after catheter removal/procedure	For planned procedure may consider holding NSAID based on half-life. See ‘Additional Comments’
COX-2 Inhibitors	No time restrictions	Yes	May resume immediately after catheter removal/procedure	See ‘Additional Comments’
Aspirin	No time restrictions – see comments	Yes – if no concurrent drugs affecting coagulation	May resume immediately after catheter removal/procedure	For planned procedure, consider holding ASA for 3 days in primary prophylaxis and 12 hrs in secondary prophylaxis. Recommendations are the same regardless of dose (81 mg versus 325 mg)
Clopidogrel (Plavix)	7 days	No	12 h 75 mg dose 24 h ≥300 mg dose	
Prasugrel (Effient)	7 days	No	24 hrs	Per ASRA recommendations
Ticagrelor (Brillinta)	5 days	No	24 hrs	Per ASRA recommendations
Cangrelor (Kengreal)	1 hour	No	24 hrs	No data, recommendations based on pharmacokinetics and recs from the same drug class
Dipyridamole/Aspirin (Aggrenox)	7 days	No	24 hrs	Per ASRA recommendations
Cilostazol (Pletal)	2 days	No	2 hrs	Per ASRA recommendations, limited information available.
Pentoxifylline (Trental)	7 days	No	2 hrs	Limited information available to guide use
Vorapaxar (Zontivity)	28 days	No	24 hrs	No data, recommendations based on pharmacokinetics and recs from P2Y ₁₂ antagonist drug class

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Glycoprotein IIb/IIIa Inhibitors				
Abciximab (Reopro)	5 days	No	8 hrs	
Eptifibatide (Integrelin)	24 hrs	No	8 hrs	
Tirofiban (Aggrastat)	24 hrs	No	8 hrs	

Additional Comments

Low-Molecular Weight Heparin

- Concurrent antiplatelet medications are contraindicated. Case reports since 2003 have demonstrated an increase in spinal hematoma incidence when LMWH is administered with other antiplatelet agents.^{1,5,6}
- The guidelines have recommended against twice-daily dosing, but have accepted that once-daily dosing is safe.¹
- **Enhanced Treatment Protocol NOTE approved for enoxaparin 40mg SQ daily, NOT 30mg SQ every 12 hours:**
 - Must wait 8 hrs after catheter PLACEMENT before giving dose
 - Must wait 12 hrs after last dose before REMOVING catheter

Fondaparinux (Arixtra)

- Studies have looked at the use of fondaparinux with indwelling catheters. The practice is currently not recommended in the United States, however, the interval as described in the EXPERT study showed no increased incidence of spinal epidural hematoma.⁷

Warfarin (Coumadin)

- The guidelines have consistently recommended an INR of <1.5 before removal of epidural catheter, although it has been questioned. A series of 11,235 patients received epidural analgesia for total knee replacement in which they were given 5-10 mg of warfarin the night before surgery. Epidural catheters were removed within 48 hours, and the mean INR of 1,030 patients at the time of removal was 1.5 (nearly 40% of this subset). No spinal hematomas were reported in this series.⁸
- **Peripheral nerve catheters:** in a review of 3588 patients receiving a variety of prophylactic dosed anticoagulants (LMWH, fondaparinux, warfarin, and ASA), no recorded perineural hematomas were documented after receiving single or continuous peripheral nerve blocks.¹⁰

Unfractionated Heparin

- Assessment of sensory and motor function should be monitored for at least 12 hours after catheter removal.
- is this needed? Noted above

Thrombin Inhibitors (Desirudin, Lepirudin, Bivalirudin, and Argatroban)

- Lack of information available and looking at the population these agents are often used for (HIT patients who need therapeutic anticoagulation), no recommendations can be made.^{1,2}
- Recommendations are based on half-life elimination of the medication and waiting approximately five half-lives for the medication to clear.

NSAIDs and Antiplatelet Agents

- Nonsteroidal anti-inflammatory drugs alone do not increase the risk of bleeding, however in combination with UFH, LMWH, oral anticoagulants, and thrombolytics, there is an increased frequency of bleeding and spinal hematoma.¹
- Nabumetone is part of the Enhanced Recovery order set
- For selective COX-2 inhibitors, there is no evidence of any effects on platelet aggregation or increased bleeding tendency.⁴
- Recommended discontinuation times of NSAIDs for planned procedures vary by the half-life of the drug. Discontinuation for 5 half-lives is sufficient to allow the drug's effects on platelets to be inactive (see table below).

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Agent	Recommended Discontinuation Time, days
diclofenac	1
etodolac	2
ibuprofen	1
indomethacin	2
ketorolac	1

Agent	Recommended Discontinuation Time, days
meloxicam	4
nabumetone	6
naproxen	4
oxaprozin	10
piroxicam	10

Aspirin

- 81 mg versus 325 mg: Recommendations remain the same regardless of dose
- It is known that low-dose aspirin (60-325 mg) creates the largest effect on platelet function, however a study in high-risk obstetric patients who were given aspirin 60 mg daily with epidural anesthesia produced no neurologic deficits.⁹

Glycoprotein IIb/IIIa Inhibitors

- Used only in acute coronary syndromes in combination with anticoagulants and aspirin, and generally cardiac procedures are usually conducted as emergencies, so neuraxial blockade is contraindicated
- Platelet counts should always be obtained due to thrombocytopenia effects if neuraxial blockade is required.²

Conclusion

An assortment of guidelines can be found on neuraxial access in the anticoagulated patients with slight variations between each. The United States (American Society of Regional Anesthesia and Pain Medicine) guidelines tend to be more conservative versus those in Europe (European Society of Anaesthesiology). Much of what is known is based on case reports and limited trial reviews. New anticoagulants (rivaroxaban and dabigatran) and antiplatelet agents (ticagrelor and prasugrel) have information regarding use perioperatively and postoperatively listed in the product insert, however this information does not specifically address neuraxial access. Close patient monitoring for sensory and motor dysfunction should be reviewed frequently postoperatively. Performing neuraxial procedures before, during, and after anticoagulation is a controversial topic, and providers should be aware of the risks of such procedures in the anticoagulated patient.

1. Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). *Reg Anes and Pain Med.* 2010. 35: 64 – 101.
2. Gogarten W, Vandermeulen E, Van Aken H, et al. Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. *Eur J Anaesthesiol.* 2010. 26: 999 – 1015.
3. Green L, Machin SJ. Managing anticoagulated patients during neuraxial anaesthesia. *Brit J of Haem.* 2010. 149: 195 – 208.
4. Catella-Lawson F, Reilly MP, Kapoor SC, et al. Cyclooxygenase inhibitors and the antiplatelet effects of aspirin. *N Engl J Med* 2001 ; 345: 1809 – 1817. FOR COX 2 INHIBITORS
5. Ain RJ, Vance MB. Epidural hematoma after epidural steroid injection in a patient withholding enoxaparin per guidelines. *Anesthesiology.* 2005; 102:701 – 703.
6. Litz RJ, Gottschlich B, Stehr SN. Spinal epidural hematoma after spinal anesthesia in a patient treated with clopidogrel and enoxaparin. *Anesthesiology.* 2004; 101:1467 – 1470.
7. Singelyn FJ, Verheyen CC, Piovello F, et al. The safety and efficacy of extended thromboprophylaxis with fondaparinux after major orthopedic surgery of the lower limb with or without a neuraxial or deep peripheral nerve catheter: the EXPERT Study. *Anesthesia & Analgesia.* 105: 1540 – 1547.
8. Parvizi J, Viscusi ER, Frank HG, et al. Can epidural anesthesia and warfarin be coadministered? *Clin Orthop Relat Res.* 2007; 456: 133 – 137.
9. CLASP: a randomized trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. CLASP (Collaborative Low-dose Aspirin Study in Pregnancy). Collaborative Group. *Lancet.* 1994. 343: 619-629.
10. Chelly, J, Schilling D. Thromboprophylaxis and Peripheral Nerve Blocks in Patients Undergoing Joint Arthroplasty. *The Journal of Arthroplasty* Vol. 23 No. 3 2008; 350-354.
11. Buckenmaier CC, Shields CH, Auton AA, Evans SL, Croll SM, Bleckner LL, Brown DS, Stojadinovic A. Continuous Peripheral Nerve Block in Combat Casualties Receiving Low Molecular Weight Heparin. *British Journal of Anaesthesia.* 2006; 97(6):874-877.