Regional anaesthesia & Anticoagulant

DR ANSUL GOYAL

INTRODUCTION

- Improvement in patient outcomes, including mortality and major morbidity has been demonstrated with neuraxial techniques, particularly with epidural anesthesia and analgesia.

- It is due to the attenuation of the hypercoagulable response and the associated reduction in the frequency of thromboembolism.

Cont’d

- Although this beneficial effect of neuraxial techniques is recognized but the effect is insufficient as the sole method of thromboprophylaxis.

- Consequently, anticoagulant, antiplatelet, and thrombolytic medications have been increasingly used in the prevention and treatment of thromboembolism.

Cont’d

- Long-term anticoagulation with warfarin is often indicated for patients with a history of VTE, mechanical heart valves, and atrial fibrillation.

- In addition, patients with bare metal or drug-eluting coronary stents require antiplatelet therapy with aspirin and thienopyridine derivatives (e.g, clopidogrel) for varying durations.

Cont’d

- Coagulation defects are the principal risk factors for regional anesthesia.
- Spinal hematoma is a rare but potentially devastating complication of regional anesthesia.
- Trauma to epidural veins in the presence of coagulopathies may result in large hematoma.

Cont’d

- Neuraxial blockade should be performed cautiously in the presence of prophylactic anticoagulation
- Clinician should have familiarity with pharmacology of hemostasis altering drugs, clinical studies as well as the case reports of spinal hematoma.

Table 2 Relative risk related to neuraxial and peripheral nerve blocks in patients with abnormalities of coagulation.

	Block category	Examples of blocks in category
Higher risk	Epidural with catheter	
	Single-shot epidural	
	Spinal	
	Paravertebral blocks	Paravertebral block
		Lumbar plexus block
		Lumbar sympathectomy
		Deep cervical plexus block
	Deep blocks	Coeliac plexus block
		Stellate ganglion block
		Proximal sciatic block (Labat, Raj, sub-gluteal)
		Obturator block
		Infraclavicular brachial plexus block
		Vertical infraclavicular block
		Supraclavicular brachial plexus block
	Superficial perivascular blocks	Popliteal sciatic block
		Femoral nerve block
		Intercostal nerve blocks
		Interscalene brachial plexus block
		Axillary brachial plexus block
	Fascial blocks	Ilio-inguinal block
		Ilio-hypogastric block
		Transversus abdominis plane block
		Fascia lata block
	Superficial blocks	Forearm nerve blocks
		Saphenous nerve block at the knee
		Nerve blocks at the ankle
		Superficial cervical plexus block
		Wrist block
		Digital nerve block
		Bier's block
Normal risk	Local infiltration	

Epidural Space vs Intrathecal Space

- Epidural space is richly supplied with a venous plexus
- Area around the spinal cord is fixed. Bleeding results in compression, ischemia, nerve trauma, and paralysis.
- Bleeding into the intrathecal space is diluted by the Cerebral Spinal Fluid (usually less devastating)

Incidence of Epidural Hematoma Formation

- Epidural anesthesia: 1:150,000 to 1:190,000
- Spinal anesthesia: 1:220,000
- Epidural anesthesia and anticoagulants administered during surgery: 33:100,000
- Spinal anesthesia and anticoagulants administered during surgery: 1:100,000

- The incidence of neuraxial bleeding increases with age, female sex, underlying coagulopathy, difficult placement, and indwelling catheter

Risk Factors for the Development of Epidural Hematoma

- Anatomic abnormalities of the spinal cord or vertebral column
- Vascular abnormalities
- Pathologic/medication induced alterations in homeostasis
- Alcohol abuse
- Chronic renal insufficiency
- Difficult and traumatic needle placement
- Epidural catheter removal

Signs and Symptoms of an Epidural Hematoma

- Low back pain (sharp and irradiating)
- Sensory and motor loss (numbness and tingling/motor weakness long after block should have abated)
- Bowel and/or bladder dysfunction
- Paraplegia

Diagnostic Testing

- MRI (preferred)
- CT scan (may miss small hematomas)
- Myelogram

Treatment and Outcome

- Must be treated within 8-12 hours of onset of symptoms
- Emergency decompressive laminectomy with hematoma evacuation
- Outcome is generally poor

Factors Affecting Recovery

- Size and location of the hematoma
- Speed of hematoma development
- Severity and nature of pre-existing neurological problems

The need for formalized guidance for anticoagulated patient:

- Advances in pharmacology
- Desire to prevent thromboembolism
- Formulation of thromboembolism prophylaxis
- Use of regional anesthesia

ASRA Guidelines

- 1998 the first Consensus Conference on Neuraxial Anesthesia and Analgesia was held.
- 2002 the second Consensus Conference was held.
- In 2010 third edition of guidelines
- In 2015 fourth edition.
- The result: formalized guidelines to assist the anesthesia provider in decision making.

General ASRA recommendations related to perioperative use of anticoagulants

- Concurrent use of coagulation altering medications may increase risk of bleeding without altering coagulation studies.
- When providing postoperative analgesia with an epidural use opioids or dilute local anesthetic to allow for neurological evaluation.
- Remove catheters at the end of anticoagulant activity and do not give additional anticoagulants immediately after removal.

General ASRA recommendations related to perioperative use of anticoagulants

- Frequent evaluation of neurological status for early detection of an epidural hematoma.
- In high risk cases continue monitoring neurological status for 24 hours post catheter removal.

Common anticoagulants encountered in the surgical setting.

- Antiplatelet medications
- Oral anticoagulants
- Standard Heparin
- Herbal preparations
- New anticoagulants

Thromboembolism prophylaxis when we need it?

TABLE 1. Risk Factors for VTE

Surgery
Trauma (major trauma or lower extremity injury)
Immobility, lower extremity paresis
Cancer (active or occult)
Cancer therapy (hormonal, chemotherapy, angiogenesis inhibitors, radiotherapy)
Venous compression (tumor, hematoma, arterial abnormality)
Previous VTE
Increasing age
Pregnancy and the postpartum period
Estrogen-containing oral contraceptives or hormone replacement therapy
Selective estrogen receptor modulators
Erythropoiesis-stimulating agents
Acute medical illness
Inflammatory bowel disease
Nephrotic syndrome
Myeloproliferative disorders
Paroxysmal nocturnal hemoglobinuria
Obesity
Central venous catheterization
Inherited or acquired thrombophilia

Table 1 Levels of thromboembolism risk and recommended thromboprophylaxis in hospital patients (Section 1.3). *Rates based on objective diagnostic screening for asymptomatic DVT in patients not receiving thromboprophylaxis. †Mechanical thromboprophylaxis includes intermittent pneumatic compression, venous foot pump, and/or graduated compression stockings: consider switch to anticoagulant thromboprophylaxis when high bleeding risk decreases. LMWH, low molecular weight heparin; LDUH, low dose unfractionated heparin; INR, international normalized ratio. From Geerts and colleagues[9]

Levels of risk	Approximate DVT risk without thromboprophylaxis (%)*	Suggested thromboprophylaxis options
Low risk	<10	
Minor surgery in mobile patients		No specific thromboprophylaxis
Medical patients who are fully mobile		Early and 'aggressive' ambulation
Moderate risk	10–40	
Most general, open gynaecological or urological surgery patients		LMWH (at recommended doses), LDUH bid or tid, fondaparinux
Medical patients, bed rest, or sick		
Moderate VTE risk plus high bleeding risk		Mechanical thromboprophylaxis†
High risk	40–80	
Hip or knee arthroplasty, hip fracture surgery		LMWH (at recommended doses), fondaparinux, oral vitamin K antagonist (INR 2–3)
Major trauma, spinal cord injury		
High VTE risk plus high bleeding risk		Mechanical thromboprophylaxis†

TABLE 5. Perioperative Management of Patients on Antiplatelet Therapy

Patients with coronary stents

- Elective surgery postponed for the following durations if aspirin and thienopyridine (eg, clopidogrel) therapy must be discontinued
  - Bare metal stents: 4–6 wk
  - Drug-eluting stents: 12 mo
- If surgery cannot be postponed, continue aspirin throughout perioperative period

Patients at high risk for cardiac events (exclusive of coronary stents)

- Continue aspirin throughout the perioperative period
- Discontinue clopidogrel at least 5 d (and preferably 10 d) before surgery
- Resume clopidogrel 24 hrs postoperatively

Patients at low risk of cardiac events

- Discontinue antiplatelet therapy 7–10 d before surgery
- Resume antiplatelet therapy 24 hrs postoperatively

Antiplatelet

- NSAIDs
- Thienopyridine (ticlopidine and clopidogrel)
- GP IIb/IIIa receptor antagonists (abciximab, eptifibatide, and tirofiban)
- Phosphodiesterase Inhibitors(dipyridamole and cilostazole)

NSAIDS

- Inhibit COX and prevent the synthesis of thromboxane A2
- Dose dependent effects on the hemostatic mechanism.

Aspirin

- Greater affinity for COX 1
- Peak effect in 30 min and platelet inhibition in 1 hr
- irreversibly effect on platelet
- Effect last for lifespan of a platelet(7-10 day)
- Long term use ↑ PT.
- Large dose cause prothrombotic effect

ASRA Recommendation

- Alone does not increase risk.
- Adjust dose with concomitant medications
- No wholly accepted laboratory tests.
- A normal bleeding time does not indicate normal homeostasis.
- An abnormal bleeding time does not necessarily indicate abnormal homeostasis.

In addition to assessment of concomitant medications look for the following:

- History of bruising easily
- History of excessive bleeding
- Female gender
- Increased age

Thienopyridine

- Block the ADP receptor, P2Y12 subtype
- With aspirin – dual antiplatelet therapy(ACS and post PCI)
- Ticlopidine – cause hypercholesterolemia, thrombocytopenia, aplastic anemia, and thrombotic thrombocytopenic purpura and delayed onset

Clopidogrel

- Prodrug ,requiring 2 metabolic steps to form the active drug.
- Drug drug interactions and genetic polymorphisms.
- Time to peak 24 hours, loading dose of 300 to 600 mg peaks in 4 to 6 hours.
- The maximum percentage of platelet inhibition 50% to 60%, which normalizes 7 days after discontinuation

Prasugrel

- Prodrug causes irreversible inhibition of the P2Y12 receptor
- 1 metabolic step to form its active drug
- No drug-drug interactions and genetic polymorphisms
- Rapid onset of effect, Peak plasma concentration occurs in 30minutes
- Causes 90% inhibition of platelet function
- 7- to 10-day interval before a neuraxial injection has been recommended by the ASRA

Ticagrelor(Brilinta)

- Direct acting P2Y12 receptor inhibitor.
- Both the parent compound and the active metabolite have antiplatelet activities
- Metabolism via liver with minor clearance via kidney
- No drug interactions and genetic polymorphism
- Rapid onset, peak effect 2 to 4 hours
- 90% platelet inhibited by ticagrelor
- Platelet recovery is more rapid

ASRA Recommendation

- For clopidogrel
  - ASRA and the European guidelines --- 7-day interval
  - Scandinavian guidelines --- 5 days is probably adequate.
  - Low dose clopidogrel started after 12 hr of procedure
  - Loading dose(300-600mg) can be given after 24 hr of procedure
- For prasugrel, 7 to 10 days is advisable, can be started after 24 hr of procedure
- For ticagrelor, 5 days is adequate ,same as prasugrel

GP IIb/IIIa inhibitors

- Potent platelet inhibitors.
- Abciximab(ReoPro)
- Eptifibatide (Integrilin)
- Tirofiban (Aggrastat)

GP IIb/IIIa inhibitors

- MECHANISM OF ACTION:
  - Reversibly inhibits platelet aggregation

- DURATION OF ACTION:
  - Abciximab -- 24-48 hours
  - Eptifibatide and tirofiban it takes 4-8 hours

ASRA Recommendation

- No neuraxial blockade should be undertaken until platelet function is normal.
- Contraindicated within 4 weeks of surgery. But now regional can be given after 2 days in abciximab and 8-12 hr in other.
- If one is received postoperatively, after a neuraxial block, there should be careful monitoring of the neurological status.

Warfarin

- Inhibiting the γ-carboxylation of the vitamin K–dependent coagulation factors (II, VII, IX, and X) and proteins C and S
- Initial anticoagulation due to decrease in factor VII. Half life of factors are
  - Factor VII (6–8 hours) is shorter
  - Factor IX (20–24 hours)
  - Factor X (20–42 hours)
  - Factor II (48–120 hours)

- Full anticoagulant effect not occur until 4 days, when the levels of factor II are significantly decreased.
- Clotting factors ≥ 40% adequate for hemostasis
- Below 20% are associated with bleeding.
- Narrow therapeutic index
- Measured by INR

Table 3 Summary of patient characteristics associated with enhanced PT response to warfarin

- Age >65 yr
- Female gender
- Weight <100 lb
- Excessive surgical blood loss
- Liver, cardiac, renal disease
- Oriental race
- CYP2C9, VKORC1 genetic variation, or both

TABLE 4. Perioperative Management of Patients on Warfarin

Preoperative

- Discontinue warfarin at least 5 d before elective procedure*
- Assess INR 1 to 2 d before surgery, if >1.5, consider 1–2 mg of oral vitamin K
- Reversal for urgent surgery/procedure, consider 2.5–5 mg of oral or intravenous vitamin K; for immediate reversal, consider fresh-frozen plasma
- Patients at high risk for thromboembolism
  - Bridge with therapeutic subcutaneous LMWH (preferred) or intravenous UFH
  - Last dose of preoperative LMWH administered 24 hrs before surgery, administer half of the daily dose
  - Intravenous heparin discontinued 4 hrs before surgery
- No bridging necessary for patients at low risk for thromboembolism

Postoperative

- Patients at low risk for thromboembolism
  - Resume warfarin on postoperative day
- Patients at high risk for thromboembolism (who received preoperative bridging therapy)
  - Minor surgical procedure—resume therapeutic LMWH 24 hrs postoperatively
  - Major surgical procedure—resume therapeutic LMWH 48–72 hrs postoperatively or administer low-dose LMWH
- Assess bleeding risk and adequacy of hemostasis when considering timing of the resumption of LMWH or UFH therapy

Recommendations from Douketis et al.[29]

ASRA Recommendations:

- Caution should be made in performing neuraxial block in patients recently discontinued warfarin therapy.
- Ideally stopped 4 – 5 days before performing the block
- Monitor PT/INR prior to initiation of the block.
- No Regional Anesthesia if in combination of other drugs affecting the clotting like aspirin and clopilet

Recommendations cont'd

- If the first dose given >24 hrs- check PT/INR
- Patients receiving warfarin during epidural analgesia do PT/INR on daily basis.
- Check PT/INR before catheter removal if initial doses of warfarin are given more than 36 hours preoperatively.
- Epidural catheters can be removed if INR is < 1.5.

Recommendations cont'd

- Neurological testing of motor and sensory functions should be done.
- Minimize the degree of motor block.
- If INR > 3, Hold warfarin
- Reduced doses of warfarin in patients with enhanced drug response.

Heparin

- Inactivates thrombin (factor IIa), factor Xa, and Ixa
- Effect of IV heparin is immediate, whereas SC heparin takes 1 hour
- Heparin has a half-life of 1.5 to 2 hours and its therapeutic effect ceases 4 to 6 hours after its administration
- Monitoring is via the activated partial thromboplastin time (aPTT)
- Therapeutic anticoagulation --- aPTT is 1.5 to 2.5 times
- Reversal is achieved with protamine

ASRA Recommendation

- Mini-dose SC BD dose heparin does not contraindicate a neuraxial block.
- IV stopped before 4 hrs and SC stopped before 8-10hrs
- Patients should be screened for concurrent medications that may impact clotting.
- Heparin > 4 days, check platelet count.

Recommendations cont'd

- Heparin administration should be delayed for 2 hour after neuraxial blockade.
- Catheters should be removed 2-4 hours after the last dose.
- If a "bloody tap" has occurred it should be communicated to the surgeon. No data suggests the mandatory cancellation of the surgical case.

LMWH

- Dalteparin (Fragmin)
- Enoxaparin (Lovenox)
- Tinzaprain (Innohep)
- Dose
  - Prophylactic dose – enoxaparin 30 mg OD and dalteparin 70U/kg OD
  - Therapeutic dose --- enoxaparin 1mg/kg BD or 1.5 mg/kg daily and dalteparin 120U/kg BD or 200U/kg OD

- Dose-dependent antithrombotic effect
- Assessed by the anti-Xa activity level
- Half-life 2 to 4 hours after an IV injection and 3 to 6 hours after a subcutaneous injection.
- Higher and more predictable bioavailability

LMWH administration and risk of hematoma formation

- Continuous epidural administration and LMWH increases the risk of hematoma formation to 1:3,000.
- 1:40,000 for patients receiving spinal anesthesia.

Risk factor of spinal haematoma

TABLE 8. Patient, Anesthetic, and LMWH Dosing Variables Associated With Spinal Hematoma

Patient factors
Female sex
Increased age
Ankylosing spondylitis or spinal stenosis
Renal insufficiency
Anesthetic factors
Traumatic needle/catheter placement
Epidural (compared with spinal) technique
Indwelling epidural catheter during LMWH administration
LMWH dosing factors
Immediate preoperative (or intraoperative) LMWH administration
Early postoperative LMWH administration
Concomitant antiplatelet or anticoagulant medications
Twice-daily LMWH administration

ASRA Recommendations

- Monitoring of anti – Xa level is not recommended.
- No RA in patients taking other clotting inhibitors in addition.
- In the presence of blood during needle and catheter placement.
  - Delay LMWH therapy for 24 hours
  - Should be discussed with the surgeon.

Recommendations cont'd

- Preoperative LMWH:

1. Thromboprophylaxis: Needle placement should be delayed up to 10 – 12 hours.
2. Treatment dose: A delay of at least 24 hours is recommended.
3. No RA if the dose is given in morning preoperatively.

Recommendations cont'd

- Postoperative LMWH: may undergo RA technique, but removal of the catheter depends upon total daily dose and timing.

a. Twice daily dose:
   - increased risk of spinal hematoma.
   - First dose of LMWH should not be administered 24 hours postoperatively.
   - Catheters should be removed prior to initiation of thrombo-prophylaxis.
   - LMWH dose should be started after 2 hours removing the catheter.

Recommendations cont'd

b. Single daily dose:

- First dose should be administered 6 – 8 hours postoperatively.
- Second dose after 24 hours and catheters may be safely maintained.
- Catheters should be removed after 12 hours of last LMWH dose.
- LMWH dose can be started after two hours.

Fondaparinux (Arixta®)

- Used for DVT prophylaxis
- Binds with antithrombin III which neutralizes factor Xa.
- Peak effect in 3 hours with half life of 17-21 hours
- Irreversible effect
- At least stop for 5 days before procedures.

- Bivalirudin- thrombin inhibitor used in interventional cardiology.
- Lepirudin used to treat heparin-induced thrombocytopenia.
- Caution advised. No recommendations related to limited clinical experience.

NEWER ORAL ANTICOAGULANT

- DABIGATRAN
- RIAROXABAN
- APIXABAN
  - Not require regular monitoring
  - More expensive,shorter acting
  - No specific antidote

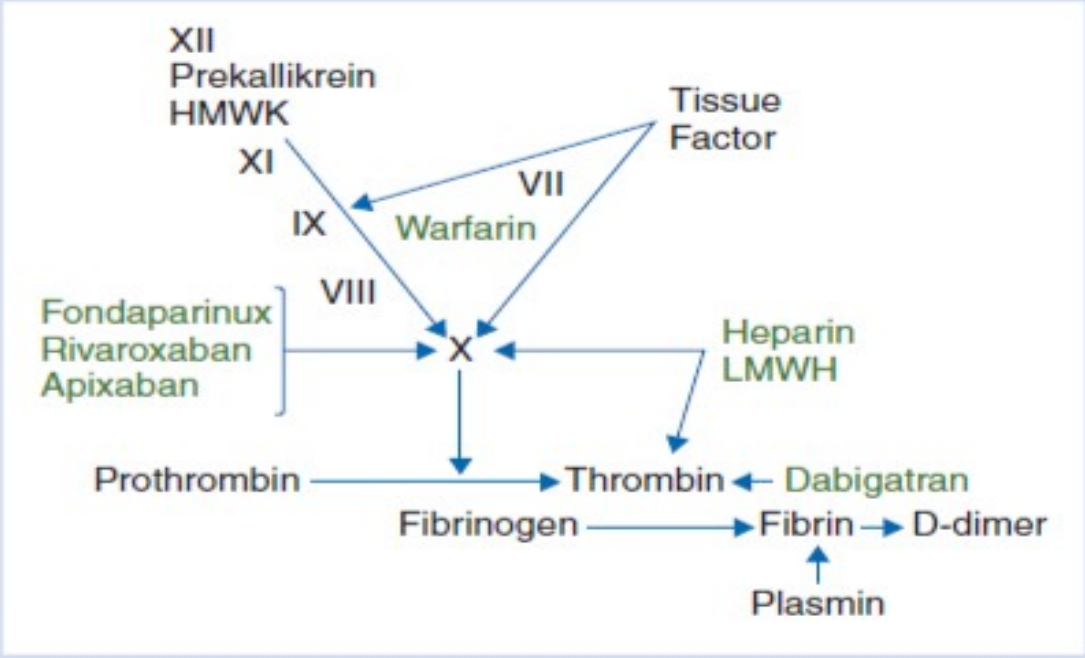


Fig 1 Sites of action of anticoagulant drugs. Clotting factors are indicated by Roman numerals. Warfarin reduces production of factors VII, IX, X, and prothrombin. Heparin and LMWH inhibit factor Xa and thrombin. Fondaparinux, rivaroxaban, and apixaban are direct factor Xa inhibitors. Dabigatran is a DTI. HMWK, high molecular weight kininogen; LMWH, low molecular weight heparin.

Table 1 New anticoagulant drugs approved by the US FDA. AF, atrial fibrillation; VTE, venous thromboembolism; DVT, deep venous thrombosis. *Approved indication, references: Garcia and colleagues,[16] Siegal and Cuker,[17] and Siegal and Crowther.[18] †Efficacy of dabigatran in studies not uniform (see text). ‡Efficacy when added to antiplatelet therapy. ¶Apixaban is non-inferior to conventional therapy (subcutaneous enoxaparin followed by warfarin) in the treatment of acute VTE (from Agnelli and colleagues)[107]

Drug	Mechanism of action	Efficacy in clinical syndromes	Approved indications*
Dabigatran (Pradaxa®)	DTI	Prevention of postoperative VTE after total joint surgery† Prevention of stroke in AF Treatment of acute VTE	Prevention of stroke in patients with non-valvular AF (USA, Canada, and Europe) Prevention of VTE after knee or hip arthroplasty (Europe and Canada)
Rivaroxaban (Xarelto®)	Factor Xa inhibitor	Prevention of postoperative VTE after total joint surgery Prevention of stroke in AF Treatment of acute VTE Acute coronary syndromes‡	VTE prophylaxis and stroke prevention in non-valvular AF (USA, Canada, and Europe) Treatment of VTE (USA, Europe, and Canada) Prevention of VTE after orthopaedic surgery (USA, Europe, and Canada)
Apixaban (Eliquis®)	Factor Xa inhibitor	Prevention of postoperative VTE after total joint surgery Prevention of stroke in AF Treatment of acute VTE¶	Stroke prevention in patients with non-valvular AF (USA, Europe, and Canada) VTE prophylaxis after hip and knee arthroplasty (Europe and Canada)

Elective procedures requiring neuraxial anaesthesia taking newer anticoagulant should be delayed if

1. A thrombotic event (VTE, MI,TIA, or stroke)has occurred within the previous 3 months;
2. A major haemorrhage (↓Hb by 2g/dl), transfusion of 2 units of packed red blood cells, or bleeding into an organ, has occurred within the previous 3 months
3. Patient is pregnant or ,6 weeks post-partum

DABIGATRAN

- Prodrug that inhibits both free and clot-bound thrombin.
- The drug is absorbed from GI tract with a bioavailability of 5%.
- Half-life is 8-17 hrs. renal disease pt get prolonged
- Prolongs the aPTT

Rivaroxaban and Apixaban

- Direct factor Xa inhibitor
- Rapid onset and peak plasma concentrations are observed within 2.5–4hr.
- Half life
  - Rivaroxaban -- 9-13hr
  - Apixaban --- 15 hr

Drug	Metabolism, renal, and faecal/biliary elimination*	Elimination half-life	Five half-lives
Dabigatran	Renal 80%, faecal 20%	12–17 h 28 h (end-stage renal disease)	85 h (4 days) 140 (6 days) (end-stage renal disease)
Rivaroxaban	Metabolism 33%, renal 33% (33% inactive metabolites)	9–13 h	65 h (3 days)
Apixaban	Renal 25%, metabolism and faecal elimination 75%	15.2 (8.5)	75 h (3–4 days)

ASRA Recommendations

- Stop Dabigatran 3 to 4 days before. Can be given after 6 hr.
- Stop Rivaroxaban and Apixaban 48 hrs before. Can be given after 6 hr.

Fibrinolytics and Thrombolytics

Exogenous plasminogen activators.

.Streptokinase

.Urokinase

Endogenous tissue plasminogen activator formulation

.Alteplase

.Tenecteplase

.Reteplase

more fibrin selective,less effect on circulating plasminogen.

Mechanism of action

- Activates plasminogen to form plasmin, which digest fibrin and dissolve clot
- Although the plasma half life of thrombolytic drugs is mainly hours, it may take days for the thrombolytic effect to resolve.

ASRA Recommendations

- No RA in the presence of these drugs.
- In patients with catheters already in and with sudden initiation of these drugs,
  - Neuraxial monitoring is necessary which should not be more than 2 hour interval.
  - Infusion should be limited to drugs minimizing sensory and motor blockade.
  - Fibrinogen level measurement.
  - No definite recommendation regarding the removal of catheters.

Herbal Preparations

- Garlic, ginger - inhibit platelet aggregation.
- Ginseng- antiplatelet components
- Alfalfa, chamomile, horse chestnut, ginseng- contain a coumadin component
- Vitamin E- reduces platelet thromboxane production
- Ginko- inhibits platelet activating factor

ASRA Recommendations

- Unknown risk
- Most patients advised to stop for 5-7 days prior to surgery
- Screen for concomitant use of medications that alter coagulation
- Assess the patient for bleeding tendencies

Table 2 Pharmacological activities of anticoagulants, antiplatelet agents, and thrombolytics. PT, prothrombin time; aPTT, activated partial thromboplastin time; ↑, clinically insignificant increase; ↑↑, possibly clinically significant increase; ↑↑↑, clinically significant increase; NSAID, non-steroidal anti-inflammatory drug. Adapted from Horlocker and Wedel.[10] With permission

Agent	Effect on coagulation variables		Time to peak effect	Time to normal haemostasis after discontinuation
	PT	APTT		
I.V. heparin	↑	↑↑↑	Minutes	4–6 h
Subcutaneous heparin	—	↑	40–50 min	4–6 h
Low molecular weight heparin	—	—	3–5 h	12–24 h
Warfarin	↑↑↑	↑	4–6 days (Less with loading dose)	4–6 days
Dabigatran	↑	↑↑	2 h	4–7 days
Antiplatelet agents				
Aspirin	—	—	Hours	5–8 days
Other NSAIDs			Hours	1–3 days
Ticlopidine, clopidogrel, prasugrel			Hours	5–14 days
Platelet glycoprotein IIb/IIIa receptor inhibitors			Minutes	8–48 h
Fibrinolytics	↑	↑↑	Minutes	24–36 h

Antithrombotic Therapy and Pregnancy

- 5 to 50 times increased VTE in pregnancy
- Risk factors
  - Increasing age
  - Prolonged immobilization
  - obesity
  - Thrombophilia
  - Previous thromboembolism
  - Cesarean delivery
- In pregnancy LMWH or UFH can be given

MEDICATION	PRIOR TO NEURAXIAL/NERVE PROCEDURE Minimum time between last dose of antithrombotic agent AND neuraxial injection or neuraxial/nerve catheter placement	WHILE NEURAXIAL/NERVE CATHETER IN PLACE Restrictions on use of antithrombotic agents while neuraxial/nerve catheters are in place and prior to their removal	AFTER NEURAXIAL/NERVE PROCEDURE Minimum time between neuraxial injection or neuraxial/nerve catheter removal AND next dose of antithrombotic agent
ANTICOAGULANTS FOR VTE PROPHYLAXIS			
heparin unfractionated 5000 units Q8H or Q12H	May be given; no time restrictions for neuraxial injection or neuraxial/nerve catheter placement **Does not require Pain Service approval**		
heparin unfractionated 7500 units SQ Q8H	8 hrs	**CONTRAINDICATED while catheter in place. May NOT be given unless approved by Pain Service Attending**	4 hrs
dalteparin (Fragmin) 5000 units SQ QDay	12 hrs (longer in renal impairment)	**May be given BUT:** **•Must wait 8 hrs after catheter PLACEMENT before giving dose** **•Must wait 12 hrs after last dose before REMOVING catheter**	4 hrs
enoxaparin (Lovenox) 40mg SQ QDay			
enoxaparin (Lovenox) 30mg SQ Q12H or 40mg SQ Q12H	12 hrs (longer in renal impairment)	**CONTRAINDICATED while catheter in place. May NOT be given unless approved by Pain Service Attending**	4 hrs
fondaparinux (Arixtra) 2.5mg SQ QDay	48 hrs (longer in renal impairment)		
apixaban (Eliquis) 2.5mg bid	48 hrs[2] (longer in renal impairment)	**May be given BUT:** **•Must wait 8 hrs after catheter PLACEMENT before giving dose** **•Must wait 12 hrs after last dose before REMOVING catheter**	6 hrs
rivaroxaban (Xarelto) 10mg po QDay	48 hrs[2] (longer in renal impairment)		

AGENTS USED FOR FULL SYSTEMIC ANTICOAGULATION			
apixaban (Eliquis) 2.5mg bid – 10mg bid	48 hrs[2] (longer in renal impairment)	**CONTRAINDICATED** **while catheter in place.** **May NOT be given unless approved by Pain Service Attending**	6 hrs
dabigatran (Pradaxa) 75mg bid – 150mg bid	72 hrs[3] (longer in renal impairment)		
edoxaban (Savaysa) 30-60mg qday	48 hrs (longer in renal impairment)		
rivaroxaban (Xarelto) 15-20mg po qday or 15mg bid	48 hrs[2] (longer in renal impairment)		
dalteparin (Fragmin) 200 Units/kg SQ QDay or 100 Units/kg SQ Q12H	24 hrs (longer in renal impairment)		4 hrs
enoxaparin (Lovenox) 1.0 - 1.5mg/kg SQ QDay or 1mg/kg SQ Q12H	24 hrs (longer in renal impairment)		
fondaparinux (Arixtra) 5-10mg SQ qday	72 hrs (longer in renal impairment)		
heparin unfractionated IV infusion or full dose SQ	when aPTT < 40 sec		
warfarin (Coumadin)	when INR < 1.5		4 hrs

DIRECT THROMBIN INHIBITORS, INJECTABLE			
argatroban IV continuous infusion **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**	4 hrs
ANTIPLATELET AGENTS			
Aspirin or NSAIDS	May be given; no time restrictions for neuraxial injection or neuraxial/nerve catheter placement **Does not require Pain Service approval**		
abciximab (Reopro)	48 hrs	**CONTRAINDICATED** **while catheter in place.** **May NOT be given unless approved by Pain Service Attending**	6 hrs
aspirin/dipyridamole (Aggrenox)	7 days		
clopidogrel (Plavix)	7 days		
eptifibatide (Integrelin)	8 hrs (longer in renal impairment)		
prasugrel (Effient)	7 days		
ticagrelor (Brilinta)	7 days		
tirofiban (Aggrastat)	8 hrs (longer in renal impairment)		
THROMBOLYTIC AGENTS			
alteplase (TPA) 1mg dose for catheter clearance	May be given; no time restrictions for neuraxial injection or neuraxial/nerve catheter placement **Does not require Pain Service approval** **(Maximum dose 4mg/24 hours)**		
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

Procedural Anticoagulation Management Checklist

Evaluate baseline patient specific risk factors for perioperative bleeding:

- History and physical examination signs suggestive of a bleeding disorder:
  - History of unexplained nosebleeds (epistaxis) or menorrhagia
  - Examination signs including petechiae, mucosal bleeding, purpura, or ecchymoses
- Family history of bleeding disorders.
- Screen for antiplatelet, antithrombotic, or thrombolytic therapy.
- Screen for SNRIs, SSRIs, and herbal therapies that may influence coagulation status.
- Order coagulation tests when needed based on history and physical examination and/or medication use.
- Identify aspirin and non-aspirin NSAIDs utilization.

For individuals on aspirin categorize reason for utilization:

- Primary prophylaxis → absence of established cardiovascular disease or risk factor.
- Secondary prophylaxis → presence of cardiovascular disease.

Process the anatomical location of procedural intervention into decision-making.

- Intracanal vs extracanal spinal procedures
- Cervicothoracic neuraxial area or lumbosacral neuraxial area.
- Surrounding vascular structures at risk for penetration.

Review appropriate radiographic imaging to identify and understand anatomic challenges

- Cervical, thoracic, and lumbar spinal stenosis that that alter spinal canal anatomy
- Epidural fibrosis and significant scar tissue from previous surgical intervention

Identify and manage pharmacologic coagulopathies

- Understand drug elimination and appropriate discontinuation time.
- Determine appropriate timing for reinitiation of anticoagulation and antiplatelet therapy.
- Practice Informed decision-making involving procedural physician, prescribing medical physician, and patient.

Employ post-procedure surveillance for the detection of bleeding complications

SNRIs = Selective serotonin norepinephrine reuptake inhibitors