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Venous Thromboembolism (VTE) Prophylaxis in Hospitalized Patients

General Background

- VTE, comprised of pulmonary embolism (PE) and/or deep vein thrombosis (DVT), is the result of the following underlying pathologic processes: vascular endothelial damage, venous stasis and/or hypercoagulability of blood
- BMCs formal, active strategy to prevent VTE events includes daily screening to evaluate patients' risk of VTE
    - Mandatory risk assessment for all patients on admission with reassessment at 48-72 hours if still hospitalized OR worsening clinical status, like transfer to ICU, acute respiratory distress, central line placement or evolving sepsis.
- ***Specific considerations vary by patient population, refer to patient-specific sections starting on page 3 for more information.***

General Risk Factor Assessment

- Risk factors are not equal but are cumulative

Surgery	Paroxysmal nocturnal hemoglobinuria
Trauma (major, or lower extremity injury)	SERMs
Central venous catheterization	Erythropoiesis-stimulating agents
Acute medical illness (acute MI, stroke, HF, respiratory failure, infection)	Estrogen containing OC or HRT
	Smoking
Previous VTE	Nephrotic syndrome
IBD	Obesity
Cancer (active or occult)	Inherited or acquired thrombophilia
Cancer treatment (chemotherapy, hormonal, angiogenesis inhibitors, radiotherapy)	Venous compression (tumor, hematoma, arterial abnormality)
Pregnancy and postpartum period	Prolonged immobility (≥3 days), lower extremity paresis
Myeloproliferative disorders	Varicose veins

Mechanical Thromboprophylaxis

- Methods include sequential compression devices (SCDs), venodynes, elastic stockings, IVC filters
- SCDs are preferred over compression stockings due to demonstrated superiority in preventing VTEs.
- **Contraindications** to use of SCDs:
    - Known DVT, acute fracture, or peripheral IV in extremity to be used
    - Local skin condition including active cellulitis
    - Poor fit due to patient habitus
- Never used as monotherapy except in:
    - Patients with contraindications to pharmacological prophylaxis (i.e. high bleeding risk)
    - Neurology or neurosurgery patients at increased risk for bleed
- There is little evidence regarding the efficacy of these modalities. Ensure proper use and optimal adherence.
- Moderate-high risk patients whose pharmacologic prophylaxis are withheld due to bleeding concerns, require re-evaluation of bleeding risk on a daily basis.
- When evaluating bleeding risk, consider:

Spinal tap within 12 hours	Severe head trauma	Stroke within 6 months
Epidural within 12 hours	Hx of HIT in last 100 days	Coagulopathy
Recent intraocular or intracranial surgery	Prior hemorrhagic CVA	Thrombocytopenia

Pharmacologic Agents for VTE Prophylaxis

- Pharmacologic agents are not recommended in active bleeding. If patient is at high bleeding risk, use mechanical methods instead.
- Caution with timing of chemoprophylaxis with neuraxial anesthesia. See Table 4.

Table 1. VTE Prophylaxis Agents and Dosing for all Patient Populations

Medication	Prophylaxis Dose	Monitor	Duration
Unfractionated Heparin (UFH)	Preferred for <u>all</u> patients with unstable renal function or CrCl < 10 mL/min, including HD, PD, CVVH • Standard dose: **5000 units SQ q8h** • Obese patients(BMI > 40 or > 160kg): **7500 units SQ q8h** • Obstetric patients (peri- and post-partum): o 1st trimester: **5000-7500 units q12h** o 2nd trimester: **7500-10,000 units q12h** o 3rd trimester: **10,000 units q12h**	PLTs, Hgb/Hct	Until fully ambulatory
Low Molecular Weight Heparin (LMWH): Enoxaparin	Indication-dependent dosing: • Standard dose: **40mg SQ q24h** • Trauma patients: **30mg SQ BID** • Unstable renal dysfunction and CrCl < 30 mL/min: **30mg SQ q24h** • Obese patients (BMI > 40 or > 160kg): o CrCl > 30 mL/min: **40 mg SQ q12h** o CrCl < 30 mL/min excluding HD, PD, CVVH: **30mg SQ q24h** • Pediatric patients: o ≥ 50kg: **40mg SQ q24h** o < 50kg: **0.5mg/kg SQ q12h**, max 25mg q12h (round to nearest 5) • Obstetric patients: o < 50kg: **20mg q24h** o 50-90kg: **40 mg q24h** o 91-130kg: **60 mg q24h** o 131-170kg: **40mg q12h** (80mg q24h if patient refuses q12h) o > 170kg: **0.6 mg/kg/day divided q12h** Contraindications • Severe renal disease (CrCl <10mL/min including HD, PD, CVVH) • Severe liver disease (prolonged PT) • Hemophilia or known bleeding disorder • Active or threatened antenatal bleeding • Thrombocytopenia (PLT < 75 x 10^9) • Recent stroke (hemorrhagic or ischemic) • Uncontrolled hypertension (SBP > 200, DBP > 120) • Active or threatened antenatal bleeding (i.e. placenta previa, placental abruption) based on clinical judgment of risks vs benefits (consider holding 12-24h after bleeding cessation) • Admission for delivery	PLTs, Hgb/Hct SCr	Indication-dependent duration; see patient populations below: **Surgical Specialties†:** Caprini scores 2 hrs prior to surgery • High Risk: <u>≥</u> 7-10 days post-op • Highest Risk: <u>≥</u> 30 days post-op **Major Trauma / Acute Spinal Cord Injury (SCI):** If prophylaxis with LMWH is delayed, mechanical modalities should be employed and continued during the rehabilitation phase of acute SCI
Fondaparinux	Indicated for patients with history of HIT • Standard dose: **2.5mg SC daily** • Start 6-8 hrs post-op Contraindicated in patients with CrCl < 30mL/min	Hgb/Hct SCr	Until fully ambulatory
Aspirin	Total Joint Patients: **325 mg po BID** Contraindications: Aspirin allergy or NSAIDs hypersensitivity • Avoid in patients with CrCl < 10mLmin • Caution in patients with history of GI bleeding	Hgb/Hct Scr	See Table 5

† Surgical specialties: General, thoracic, otolaryngology, urology, plastics, vascular, orthopedics, neurology, and gynecology

General Medicine Patients

Risk Assessment

Table 2. Modified PADUA Score		
+1 point/factor	**+2 points/factor**	**+3 points/factor**
☐ Ongoing hormonal treatment ☐ Obesity (BMI ≥ 30) ☐ Acute infection ☐ Rheumatologic disorder ☐ Inflammatory bowel disease ☐ Acute MI or Ischemic stroke ☐ Heart or respiratory failure ☐ Age ≥ 70 ☐ ICU patient	☐ Recent trauma or surgery (≤ 1 month)	☐ Previously diagnosed thrombophilic conditions ☐ Reduced mobility* ☐ Previous VTE (excluding superficial VTE) ☐ Active cancer

PADUA Risk Stratification		*See Table 1 for full prophylaxis dosing recommendations*
Low Risk	**Score < 4**	No prophylaxis indicated
High Risk	**Score ≥ 4**	Prophylaxis indicated with UFH, enoxaparin or fondaparinux

**Study defined as anticipated bedrest with bathroom privileges either because of patient limitations or provider orders for at least 3 days.*

Risk Assessment

Table 3. Caprini Score

+1 point/factor	+2 points/factor
☐ Age 41-60 ☐ Minor surgery planned ☐ Hx of prior major surgery (<1 mo) ☐ Varicose veins ☐ History of IBD ☐ Swollen legs ☐ Obesity (BMI > 25) ☐ Acute MI ☐ CHF ☐ Sepsis (< 1 mo) ☐ Serious lung disease (including PNA, < 1 mo) ☐ Abnormal pulmonary function (COPD) ☐ Medical patient currently at bed rest ☐ Oral contraceptive or HRT ☐ Pregnancy or postpartum (< 1 mo) ☐ Hx of unexplained stillbirth, recurrent spontaneous abortion (>3), premature birth	☐ Age 60-74 ☐ Arthroscopic surgery ☐ Malignancy (present or previous) ☐ Major surgery (>45 min) ☐ Laparoscopic surgery (>45 min) ☐ Patient confined to bed (>72 hr) ☐ Immobilizing plaster cast (<1 mo) ☐ Central venous access
+3 points/factor	**+5 points/factor**
☐ Age > 75 ☐ Hx of DVT/PE ☐ Family history of thrombosis ☐ Factor V Leiden ☐ Positive prothrombin 20210A ☐ Elevated homocysteine ☐ Positive lupus anticoagulant ☐ Elevated anticardiolipin antibodies ☐ HIT	☐ Elective major lower extremity arthroplasty ☐ Hip, pelvis, or leg fracture (<1 mo) ☐ Stroke (<1 mo) ☐ Multiple trauma (<1 mo) ☐ Acute spinal cord injury (<1 mo)

Caprini Risk Stratification		*See Table 1 for full prophylaxis dosing recommendations*
Low Risk	**Score 0-1**	No specific thromboprophylaxis recommended, early and aggressive ambulation • < 10% risk of DVT without prophylaxis • Minor surgery in mobile patients
Medium Risk	**Score 2-4**	Thromboprophylaxis with LMWH or UFH • 10-40% risk of DVT without prophylaxis • Most general, gynecologic, or urologic surgery patients
High Risk	**Score 5-8**	Thromboprophylaxis with LMWH or UFH, fondaparinux, or warfarin • 40-80% risk of DVT without prophylaxis • Hip or knee arthroplasty, major trauma, spinal cord injury • Recommended duration in subspecialty patients is **7-10 days** post-operatively
Highest Risk	**Score ≥ 9**	Thromboprophylaxis with LMWH or UFH, fondaparinux, or warfarin • Recommended duration in surgical subspecialty patients is a **30 days** post-operatively at minimum.

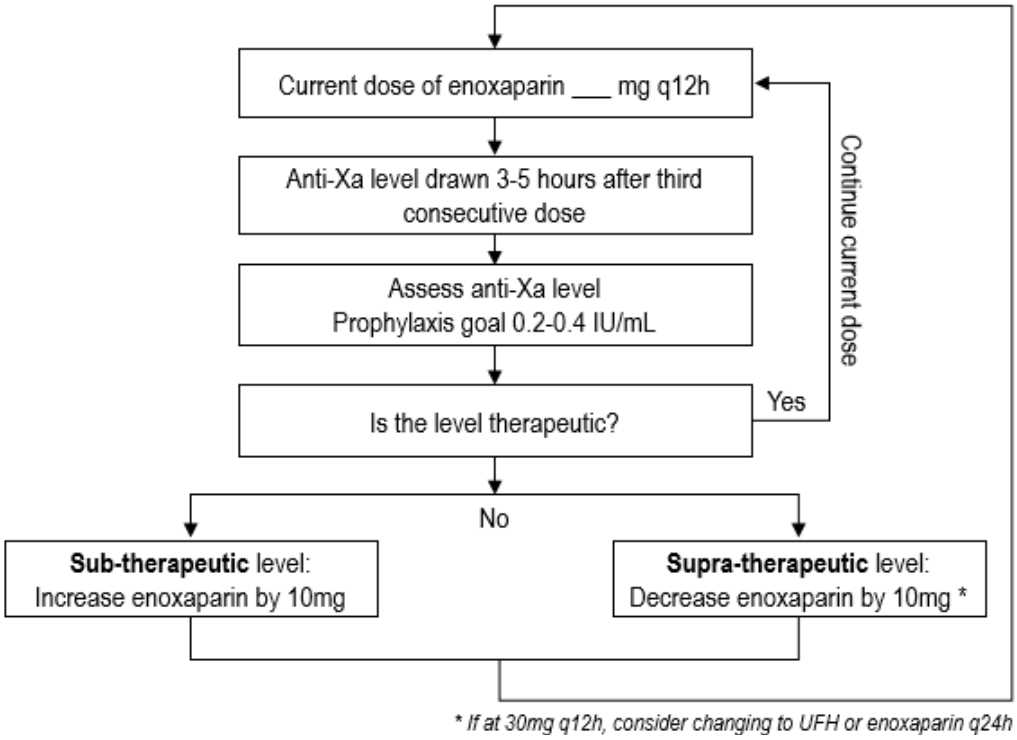
Enhanced Caprini Protocol

- Identifies patients at high risk for VTE despite standard enoxaparin prophylaxis. Eligible patients are identified by the HER, which alerts providers to order anti-Xa levels to monitor for adequate response and appropriate adjustments.
- Eligible patients include general surgery patients (excluding orthopedics) with two or more of the following:
  - Emergency operation
  - > 1 Surgery
  - Perioperative sepsis

Anti-Xa Peak Level Monitoring

- Anti-Xa levels are ordered as peaks. A steady state peak level is drawn 3-5 hours after administration of the 3rd dose of enoxaparin.
- If drawn early, the level may be falsely low as the subcutaneous space has not finished absorbing the drug.
- If drawn late, the level may be falsely low as the drug has begun to be eliminated.
- **Goal anti-Xa level for q12h regimens:**
  - Prophylaxis: 0.2 – 0.4 IU/ml
  - Treatment: 0.5 – 1.0 IU/ml

Enoxaparin Dose Adjustment Based on Anti-Xa Level



- **Example Titration**
  - Enoxaparin 30mg q12h is started.
  - Anti-Xa level drawn 4 hrs after the third consecutive dose is 0.1 IU/ml.
  - Recommend increasing dose to 40mg q12h.
  - Repeat level after the third dose of 40mg.
  - For additional support, contact the patient's care team pharmacist via pager.

Timing of Neuraxial Anesthesia with Chemoprophylaxis in Surgery Patients

- In patients requiring spinal/epidural anesthesia or analgesia, consider the following to prevent occurrence of peri-spinal hematoma:
  - Avoid neuraxial blockade in patients with bleeding disorders
  - Delay needle insertion until anticoagulant effects of concomitant medications that may impair hemostasis is at a minimum
  - Delay anticoagulation if there is a "bloody tap" during the initial needle placement.
  - Remove catheters when anticoagulant effect are at a minimum (just before next dose of anticoagulant is due)

Table 4. Timing Neuraxial Anesthesia with Chemoprophylaxis	
LMWH	Delay placement or removal of catheter for: • **≥ 12 hours** after administration of low-dose enoxaparin (30-60mg/day) • **≥ 24 hours** after administration of high-dose enoxaparin (0.75-1mg/kg BID or 1/5mgkg daily) Upon catheter removal, consider withholding enoxaparin for **≥ 4 hours**
UFH	Prophylaxis UFH: No contraindications to timing Treatment UFH: Wait **≥ 6 hours** after last dose to initiate neuraxial anesthesia

Total Joint: Total Hip Arthroplasty (THA) and Total Knee Arthroplasty (TKA)

- Risk of VTE in THA/TKA are amongst the highest in all surgical subspecialties, with rates up to 30% when appropriate prophylaxis is not initiated. Current rates for risk of hospitalization for DVT or PE are reported to be <1% with appropriate prophylaxis.

Risk Assessment

Table 5. Total Joint Risk Score

+2 point/factor	+5 point/factor
☐ THA/TKA ☐ Total hip/knee revision ☐ High tibial osteotomy ☐ Femoral osteotomy ☐ Oral contraceptive/ hormone replacement therapy ☐ BMI > 35 and < 40	☐ Bilateral THA/TKA ☐ Staged Bilateral THA/TKA (within 14 days) ☐ Peri acetabular osteotomy ☐ Hip fracture ☐ Girdlestone / hip resection ☐ Knee resection ☐ Hx of pulmonary embolus ☐ Hx DVT (phlebitis requiring warfarin) ☐ Cancer within the past year/ Currently being treated ☐ BMI ≥ 40

Total Joint Risk Stratification		*See Table 1 for full prophylaxis dosing recommendations*
Low Risk	**Score ≤ 4**	• **If quick to clear PT:** ASA 325 BID x 6 weeks • **If slow to clear PT:** Enoxaparin 40mg SQ q24h^ x 2 weeks, followed by ASA 325mg BID x 4 weeks *
High Risk	**Score > 4**	• Enoxaparin 40mg SQ q24h^ x 2 weeks, followed by ASA 325mg BID x 4 weeks
All patients (Low-High Risk)		• All patients are discharged with **pantoprazole 40mg daily x 4 weeks.**
If ASA allergy		• Enoxaparin 40mg SQ q24hrs x 4 weeks
If history of HIT		• Fondapirunox in place of enoxaparin

**PT=Physical therapy; slow vs quick clearance to be determined in collaboration with orthopedic service and physical therapist.*

Post-Operative Transition to Therapeutic Anticoagulation

Table 6. Risk of Embolization Requiring Therapeutic Anticoagulation** *See Table 1 for full prophylaxis dosing recommendations*

	Warfarin	DOACs
High Risk*	**POD #1:** Resume warfarin + enoxaparin 40mg SQ q24h^ **POD #2-3:** Therapeutic enoxaparin+ + bridge until INR within goal	**POD #1:** Enoxaparin 40mg SQ q24hr^ **POD #2-3:** Resume home oral agent
Low-Moderate Risk	**POD #1**: Resume warfarin + enoxaparin 40mg SQ q24h^ Continue enoxaparin at prophylactic dose until INR within goal	**POD #1:** Enoxaparin 40mg SQ q24h^ x 2 weeks then resume home oral agent

** High embolic risk = CHADS2-VaSc 7-9, recent CVA/TIA, mechanical MVR, or systemic embolization/DVT within 3 months.*

+Therapeutic enoxaparin typically 1mg/kg q12h. See Anticoagulation in Adults-Parenteral Agents for more information.

***Consult appropriate specialist to optimize therapy based on embolic vs hemorrhagic risk. See Perioperative Management of Antiplatelet and Anticoagulation for more information.*

Pediatric Patients

- Patients age 10-17 should be assessed for VTE risk factors and assigned to a risk category (low, moderate, or high) with determination of appropriate prophylaxis.

Risk Assessment

Table 7. Pediatric VTE Risk Assessment		
	NO	**YES**
Personal history of DVT or PE?	0	3
Reduced mobility from baseline for this patient	0	1
Known acquired or inherited thrombophilia?	0	1
History of DVT or PE in a first degree relative?	0	1
Active inflammatory bowel disease (IBD)	0	3
Other active inflammatory process (nephrotic syndrome, SLE, vasculitis, etc.)	0	1
Acute, severe infectious process	0	1
Active cancer	0	3
Sickle cell disease	0	1
Current smoker or intravenous substance use	0	1
Currently pregnant or < 6 weeks from pregnancy or termination	0	1
Surgery or trauma in the past 30 days	0	1
Travel >8 hours in the past 30 days	0	1
Ongoing hormonal treatment (estrogens or corticosteroids)	0	1
Is the patient obese (BMI > 95th percentile for age or ≥ 30)?	0	1
Does the patient have a Central Venous Catheter (CVC) or Peripherally Inserted Central Catheter (PICC)?	0	1
ICU admission?	0	1
	Total Risk Score:	

Pediatric VTE Risk Stratification		*See Table 1 for full prophylaxis dosing recommendations*
Low Risk	**Score = 0**	• Activity order: out of bed as clinically appropriate
Medium Risk	**Score 1-2**	• Activity order: out of bed as clinically appropriate • Mechanical prophylaxis order: sequential compression devices (SCD)

High Risk	**Score ≥ 3**	• Activity order: out of bed as clinically appropriate
		• Pharmacologic prophylaxis order: **enoxaparin**
		  ○ Check CBC, PT/PTT, SCr with next lab draw (if not already checked)
		  ○ Consider daytime Pediatric Hematology consult

Special Considerations in Pediatrics

- Enoxaparin is preferred for pediatric patients at BMC, assuming normal renal function and no other contraindications to use. In the setting of renal dysfunction, please contact the pediatric pharmacist at x45605.
- Order prophylactic enoxaparin using "Pediatric Enoxaparin Order Set" in Epic, which determines correct dosing based on the patient's age and weight. This dosing recommendation is only for patients ages 10-17 with a medical admission.
- Enoxaparin is a high-risk agent so patient-specific doses are made in the IV room unless an exact prefilled syringe is available
- The following dispensing table is applicable to both prophylactic and treatment doses:

Table 8. Enoxaparin Syringe Dispensing Table		
Dose	**Rounding Increment**	**Dispense Method**
0 - <5 mg	0.1 mg	Dispense in TB syringes from neonatal 20mg/mL dilution
5 - <10mg	1 mg	Dispense in TB syringes from 100mg/mL vials
10 - <30mg	5 mg	Dispense in TB syringes from 100mg/mL vials or prefilled syringe if available

**patients > 50kg will be dosed as adults and dispensed pre-filled syringes*

Obstetric Patients

- VTE is a leading cause of maternal mortality and morbidity. The American Congress of Obstetrics and Gynecologists (ACOG) developed the Safe Motherhood Initiative, which put forth recommendations for risk assessments and prophylaxis of maternal patients based on recommendations from the Royal College of Obstetricians and Gynecologists. Using these recommendations, BMC has developed a risk stratification and prophylaxis protocol.

Risk Assessment during Initial Pregnancy

Table 9. Initial Assessment During Pregnancy	*See Table 1 for full prophylaxis dosing recommendations*
Clinical History	**Recommendation**
☐ Multiple VTE episodes ☐ VTE with high risk thrombophilia ☐ VTE with acquired thrombophilia	Treatment doses of LMWH or UFH
☐ Idiopathic VTE ☐ VTE with pregnancy or OC ☐ VTE with low risk thrombophilia ☐ Family history of VTE	Prophylactic doses of LMWH or UFH (table X)
☐ 1st provoked VTE* ☐ Family history of VTE with low risk thrombophilia ☐ Low risk thrombophilia	No treatment

**Provoked VTE: occurring in the setting of a temporary risk factor (orthopedic surgery, indwelling catheter, immobilization, etc.)*

**Unprovoked VTE: VTE occurring in the absence of a temporary risk factor*

Risk Assessment during Delivery or Antepartum Hospitalization

- All patients should ambulate as early as patient is able (regular ambulation, not on prescribed bedrest > 3 days)
- All surgical OB patients should receive mechanical prophylaxis if they are not ambulatory

Table 10. Assessment During Delivery or Antepartum Hospitalization	
+1 point/factor	**+2 points/factor**
☐ Hemorrhage (if stable after 12-24h) ☐ Hysterectomy ☐ General anesthesia ☐ Postpartum infection ☐ Age >40 or <15 ☐ Pre-pregnancy obesity (BMI30-39) ☐ Low risk thrombophilia ☐ Heart disease ☐ Lupus ☐ Renal disease ☐ Sickle cell ☐ Major infection: SIRS, sepsis, chorioamnionitis ☐ Other medical condition ☐ IUGR (intrauterine growth restriction) ☐ Preeclampsia ☐ Multiple Gestation ☐ Assisted reproductive technology (ART)	☐ Already receiving prophylactic LMWH or UFH as outpatient ☐ Pre-pregnancy morbid obesity (BMI ≥ 40) ☐ Any history of VTE ☐ High risk thrombophilia ☐ Thrombophilia and family history VTE ☐ Any surgery (including cesarean delivery) ☐ Bed rest ≥3 days
Risk Stratification during Delivery or Antepartum Hospitalization	*See Table 1 for full prophylaxis dosing recommendations*
Score ≥ 2	• Prophylactic doses of LMWH or UFH
	• Consult MFM team for patients requiring treatment doses with LMWH or UFH

Risk Assessment during Post-Partum Discharge

Table 11. Risk Stratification during Post-Partum Discharge	*See Table 1 for full prophylaxis dosing recommendations*	
Score ≥ 2	Prophylactic doses of LMWH or UFH	x 10 days
Score ≥ 2 plus any of the following: • Prior VTE: idiopathic or provoked, VTE with pregnancy or OC, VTE with low risk thrombophilia • Family history of VTE with low or high risk thrombophilia • HR thrombophilia		x 6 weeks

Consideration for Post-Cesarean Prophylaxis

Table 12. Post-Cesarean Prophylaxis		
	LMWH	**UFH**
1st Dose	No sooner than **6 hours** post-op regardless of anesthesia technique	Upon meeting criteria for PACU discharge. Standard order is 5000 units SQ q12h
Epidural catheter remains in-situ	Should not remove until **12 hours** after last dose	Should not be removed until **4 hours** (ideally **6 hours**) after last dose of UFH
Other scenarios	If epidural catheter is to be removed prior to a dose of LMWH, then LMWH should not be given until **4 hours** after removal	Intra-operative UFH may be given immediately after neuraxial blockade or catheter removal

Timing of Neuraxial Anesthesia with Chemoprophylaxis in Obstetrics

Table 13. Timing of Neuraxial Anesthesia with Chemoprophylaxis *		
	Antepartum/Intrapartum (Wait before regional anesthesia)	**Postpartum (Restart after epidural catheter removal)**
UFH SQ Prophylaxis, Low Dose (5000 units BID or TID)	Wait **4-6 hours** after last dose or check PTT	May restart immediately after epidural catheter removal
UFH SQ Prophylaxis, High Dose (7500-10,000 units BID)	Wait **12 hours** and check PTT	May restart immediately after epidural catheter removal
UFH SQ Therapeutic (>20,000 units/day)	Wait **24 hours** and check PTT	May restart immediately after epidural catheter removal
UFH IV Therapeutic	Wait **4-6 hours** and check PTT	Restart **1 hour** after epidural catheter removal
Enoxaparin SQ Prophylaxis	Wait **12 hours** and check PTT	Restart **4 hours** after epidural catheter removal and wait at least **12 hours** after neuraxial procedure
Enoxaparin SQ Therapeutic (1 mg/kg q12h or 1.5 mg/kg q24h)	Wait **24 hours** and check PTT**	Restart **4 hours** after epidural catheter removal and wait at least **24 hours** after neuraxial procedure

** Based on the American Society of Regional Anesthesia Practice Advisory on Regional Anesthesia 2018. In situations where high-risk patients receiving VTE prophylaxis require urgent interventions for maternal or fetal indications, the risk of general anesthesia may be greater than neuraxial anesthesia, and exceptions/modifications of guidelines may be appropriate.*

*** Consider checking anti-Xa level in patients with renal insufficiency*

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Responsibility:

Nurses
Physicians
Pharmacists

Forms: N/A

Other Related Guidelines or Policies:

Anticoagulation in Adults - Oral Therapy
Anticoagulation in Adults – Parenteral Therapy
Perioperative Antiplatelet and Anticoagulation Management

Section:

Pharmacy

Title:

Venous Thromboembolism (VTE) Prophylaxis

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Appendix A

Rationale for TID UFH for VTE Prophylaxis Instead of BID UFH

There are no direct comparisons of BID vs. TID dosing of subcutaneous unfractionated heparin for VTE prophylaxis. However, a review of the literature shows that bid dosing may be ineffective and that TID dosing should be used instead.

The original study looking at heparin for DVT/PE prophylaxis in medically ill patients in 1973 compared heparin 5000 units TID to placebo, with heparin being superior.[1]

In 1988, a meta-analysis of 49 trials in general surgery patients revealed that DVT occurred more frequently with BID dosing (11.8%) than with TID dosing (7.5%).[2]

In 1996 Gardlund et al. conducted a randomized controlled trial 11,693 patients admitted to the hospital with acute infections to prophylaxis with either UFH 5000 units SQ BID or placebo. Overall mortality, incidence of VTE and PE were no different between the groups.[3]

In 1996, the Enoxaparin in Medicine Study Group (EMSG) compared UFH 5000 units BID to enoxaparin 20 mg/day, and found no difference in the frequency of VTE between the two groups.[4] Additionally, there was no difference in bleeding between the groups. Because the efficacy of UFH BID had already been questioned due to data from previous trials, and because it was unknown whether either of the treatment arms in the EMSG trial were superior to placebo, another study was conducted.

The MEDENOX study was conducted in 1102 medically ill patients and compared enoxaparin 20 mg/day or enoxaparin 40 mg/day to placebo.[5] The data revealed that enoxaparin 20 mg/d is equal to placebo. Thus, if enoxaparin 20 mg/d = placebo, and enoxaparin 20mg/d = UFH 5000 units BID (from EMSG trial), then **UFH 5000 units BID is also likely no better than placebo.**

More recently, the PRIME study compared UFH 5000 units TID to enoxaparin 40 mg/d to prevent VTE in medically ill patients.[6] There was no difference in frequency of VTE or bleeding between the two treatment arms.

Finally, the PRINCE study compared UFH 5000 units TID to enoxaparin 40 mg/d to prevent VTE in 665 medically ill patients.[7] There was no difference in efficacy between the groups. Additionally, there was no difference in bleeding between the enoxaparin and heparin groups.

Thus, the total available body of literature, along with the pharmacokinetic profile UFH (short t ½ of 1.5 hours), clearly suggest that if UFH is to be used for VTE prophylaxis that the dose should be at least 5000 units SQ TID.

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