ADULT VENOUS THROMBOEMBOLISM (VTE) PROPHYLAXIS GUIDELINE

This document is intended as a guideline only and should not replace sound clinical judgment.

I. VTE risk assessment and selection of prophylaxis:
   A. All inpatients at risk of VTE should receive either mechanical prophylaxis (sequential compression devices (SCDs)) OR pharmacologic prophylaxis, unless contraindications exist, in accordance with The Joint Commission (TJC) Core Measures and Centers for Medicare and Medicaid (CMS) initiatives.
   B. Risk of thromboembolism and risk for bleeding should be assessed in all patients at admission and as changes in clinical status occur.
   C. Historically, pharmacologic prophylaxis has been the default mode of prophylaxis for the majority of inpatients who do not have contraindications. However, emerging research is showing that the benefits of VTE prophylaxis may not outweigh the risks for some patients, in particular, medical patients not undergoing surgery.2,3
   D. Providers should activate either the “DVT / VTE Prophylaxis Protocol Adult” Powerplan or SCIP post-op Powerplan in Cerner to facilitate VTE risk assessment for ALL patients, even if use of prophylaxis is not anticipated.
      i. The Powerplan(s) will prompt providers to document reason if prophylaxis is withheld, maintaining hospital compliance with TJC and CMS requirements.
   E. Providers, pharmacists, and nurses are encouraged to utilize the “VTE Dashboard” function in Cerner to assess VTE prophylaxis status of their patients.
      i. In Cerner, go to Custom Views -> Dashboard -> select by Med Service, Location or Patient List
   F. The following sections are divided into medical patients and surgical/trauma patients to better highlight the differences in risk stratification between the two groups:

Table 1. Risk assessment in medical patients*
(examples of patients that may fall in this category include, but are not limited to, those admitted to internal medicine, family medicine, neurology, cardiology, hematology-oncology, & maternal-fetal medicine teams. Numerous factors influence an individual patient’s risk for developing VTE. These categories are intended to serve as a guideline, not to replace sound clinical judgment.

<table>
<thead>
<tr>
<th>DEFINITION</th>
<th>PROPHYLAXIS:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Risk</td>
<td>Non-surgical medicine patients without any of the risk factors listed below</td>
</tr>
<tr>
<td>High Risk</td>
<td>Patients with ANY one of following: Active cancer (+ mets or tx w/in last 6 mos.) Any prior VTE/PE Known thrombophilia (e.g. Factor V Leiden, antiphospholipid antibody syndrome) Critically ill (ICU patients) OR- Bedrest/immobility PLUS any one of the following: systemic infection, age ≥ 70, CHF, Acute MI, acute ischemic CVA, BMI ≥ 30, use of hormones.</td>
</tr>
</tbody>
</table>

*Based on Padua Prediction Score4. Above chart intended to serve as a guide only and does not encompass all scenarios.
Table 2. Risk assessment in surgical/trauma patients

**MOST HOSPITALIZED SURGERY PATIENTS WILL BE AT LEAST MODERATE RISK**

<table>
<thead>
<tr>
<th>DEFINITION</th>
<th>PROPHYLAXIS</th>
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<tbody>
<tr>
<td>Low Risk</td>
<td>Mechanical prophylaxis</td>
</tr>
<tr>
<td>Minor surgery (anesthesia time &lt;45 minutes) if otherwise at low risk for VTE, age &lt; 75 and no history of VTE/thrombophilia</td>
<td></td>
</tr>
<tr>
<td>Moderate &amp; High Risk</td>
<td>Pharmacologic prophylaxis with enoxaparin 40 mg SQ daily or heparin 5000 units SQ TID recommended, unless patient at high risk of bleeding, then mechanical prophylaxis until bleeding risk subsides. If heparin or enoxaparin contraindicated (e.g. pork allergy), may use fondaparinux (less evidence in surgery / trauma populations)</td>
</tr>
<tr>
<td>Most major general surgery (anesthesia time &gt;45 minutes) bariatric, vascular, thoracic, and cardiac surgery</td>
<td></td>
</tr>
<tr>
<td>Highest Risk</td>
<td>Pharmacologic prophylaxis: High-dose enoxaparin 30mg SQ q12h unless special population (see section V.), or rivaroxaban 10mg daily for THA, TKA, hip fracture. If enoxaparin contraindicated (e.g. pork allergy), may use fondaparinux (less evidence in surgery / trauma populations)</td>
</tr>
<tr>
<td>Hip or knee orthopedic surgery</td>
<td></td>
</tr>
<tr>
<td>Pelvic, hip, or leg fracture (&lt;1 month)</td>
<td></td>
</tr>
<tr>
<td>Multiple trauma (&lt;1 month)</td>
<td></td>
</tr>
<tr>
<td>Acute spinal cord injury (&lt;1 month)</td>
<td></td>
</tr>
<tr>
<td>Abdominal/pelvic surgery + active cancer</td>
<td></td>
</tr>
<tr>
<td>Stroke (&lt;1 month)</td>
<td></td>
</tr>
</tbody>
</table>

* See Caprini scoring system for more detailed risk stratification system that has been validated in several types of surgery patients. Above chart intended to serve as a guide only and does not encompass all scenarios.

II. Bleeding risk assessment

A. Risk of bleeding should be considered when deciding whether to use pharmacologic prophylaxis. The risk of developing a VTE must be weighed against the risk of bleeding in each individual patient.

B. Table 3. Risk factors for bleeding in medical and surgical patients

**RISK FACTOR AT ADMISSION (including but not limited to)**

- Active bleeding
- Active gastroduodenal ulcer
- Platelets <50 x 10^9/L
- Age ≥ 85 years
- Previous major bleeding
- Severe renal or hepatic failure
- Known, untreated bleeding disorder
- Concomitant use of anticoagulants, anti-platelets or thrombolytics
- Acute stroke
- Uncontrolled systemic hypertension
- Lumbar puncture, epidural, or spinal anesthesia within prev. 4 h or next 12h
- Other lesser risk factors:
  - ICU or CCU admission
  - Central venous catheter
  - Rheumatic disease
  - Current cancer
  - Male
PROCEDURE-SPECIFIC RISK FACTORS FOR BLEEDING:

Abdominal surgery:
- Male sex, preoperative hemoglobin level <13 g/dL, malignancy and complex surgery defined as two or more procedures, difficult dissection, or more than one anastamosis
- Pancreaticoduodenectomy:
- Sepsis, pancreatic leak, sentinel bleed
- Hepatic resection: Number of segments, concomitant extrahepatic organ resection, liver malignancy, lower preoperative hemoglobin

Cardiac surgery:
- BMI ≥25 kg/m², nonelective surgery, placement of five or more grafts, older age, renal insufficiency, operation other than CABG, longer bypass time

Thoracic surgery:
- Pneumonectomy or extended resection
- Craniotomy, spinal surgery or spinal Trauma:
- Risk of pharmacologic prophylaxis may outweigh benefit unless operation is for malignancy, or combined anterior-posterior approach for spinal surgery, then utilize pharmacologic prophylaxis (Grade 2C)

III. Contraindications to prophylaxis (medical OR surgical/trauma patients):

A. Absolute contraindications
   i. Active bleeding
   ii. At risk for intracranial or intraspinal hemorrhage (recent acute trauma, high-risk spine/intracranial surgery, or stroke within 72 hours)
   iii. Thrombolytics within last 24 hours

B. Relative contraindications
   i. Recent arteriotomy
   ii. Platelets <50 x 10⁹ L or coagulopathy (INR >1.5)
   iii. Post-operative bleeding concern

C. Special scenarios:
   i. Heparin-induced thrombocytopenia (may consider fondaparinux)
   ii. Length of stay anticipated ≤ 48 hours (e.g. observation status, EEG monitoring)
   iii. Epidural catheter or spinal block (see Section VI. Neuraxial anesthesia and VTE prophylaxis)

IV. Monitoring – pharmacists may order necessary labs under the authority of the P&T committee:

A. Platelets (for UFH or enoxaparin)
   i. Baseline platelet count and every 3 days to monitor for HIT

B. Serum creatinine
   i. Baseline serum creatinine needed prior to dispensing any doses of anticoagulants
      a. Pharmacist may dispense one dose of anticoagulant in emergent situations prior to knowing the current serum creatinine, but should order a serum creatinine and ensure follow-up
   ii. Routine creatinine at least every 3-5 days, depending on patient's clinical status

C. Anti-Factor XA monitoring of enoxaparin in special populations
   i. It is recommended to consider monitoring anticoagulation levels in the following adult patients that are ordered for enoxaparin:
      a. Morbid obesity (BMI ≥ 40)
      b. Underweight (<50 kg)
      c. Significantly changing renal function
      d. Pregnancy
   ii. Anti-Factor Xa levels have not been correlated with clinical outcomes such as bleeding or thrombosis, and should only be utilized as a tool to ensure the patient is neither grossly over- nor under-anticoagulated

<table>
<thead>
<tr>
<th>AGENT</th>
<th>TIMING OF LEVEL DRAW</th>
<th>TARGET (ANTI-XA IU/ML)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enoxaparin</td>
<td>4 hours after 2nd or 3rd dose</td>
<td>0.2-0.6</td>
</tr>
</tbody>
</table>

iii. Pharmacists should write a note in Powerchart in response to enoxaparin anti-Xa levels
### V. VTE PROPHYLAXIS DOSING GUIDE & SPECIAL POPULATIONS

<table>
<thead>
<tr>
<th>AGENT</th>
<th>USUAL DOSE</th>
<th>USE IN RENAL IMPAIRMENT (CRCL&lt;30 ML/MIN)</th>
<th>DOSE FOR MORBID OBESITY* (BMI &gt;40)</th>
<th>USE IN LOW WEIGHT PATIENT (&lt;50 KG)</th>
<th>USE WITH EPIDURAL OR SPINAL ANESTHESIA*</th>
</tr>
</thead>
<tbody>
<tr>
<td>enoxaparin</td>
<td>30 mg SQ q12h</td>
<td>Relatively contraindicated</td>
<td>0.5mg/kg SQ q12h</td>
<td>30 mg SQ once daily</td>
<td>NOT allowed</td>
</tr>
<tr>
<td></td>
<td>HIGHEST RISK PATIENTS ONLY (hip/knee surgery, trauma or spinal cord injury) ONLY</td>
<td>See table 2</td>
<td>(Consider monitoring anti-Factor Xa level)</td>
<td>(Consider monitoring anti-Factor Xa level)</td>
<td></td>
</tr>
<tr>
<td>enoxaparin</td>
<td>40 mg SQ once daily</td>
<td>Relatively contraindicated</td>
<td>0.5 mg/kg SQ once daily</td>
<td>30 mg SQ once daily</td>
<td>ALLOWED</td>
</tr>
<tr>
<td></td>
<td>May consider renally adjusted enoxaparin 30 mg SQ once daily (Consider monitoring anti-Factor Xa level)</td>
<td></td>
<td>(Consider monitoring anti-Factor Xa level)</td>
<td>(Consider monitoring anti-Factor Xa level) Or UFH 5000 units SQ q8h</td>
<td></td>
</tr>
<tr>
<td>UFH</td>
<td>5000 units SQ q8H</td>
<td>No adjustment</td>
<td>7500 units SQ q8h**</td>
<td>No adjustment</td>
<td>ALLOWED (but must be dosed BID until epidural removed)</td>
</tr>
<tr>
<td></td>
<td>IF BMI &gt;60, see note below</td>
<td></td>
<td></td>
<td>May consider 5000 units SQ q12h in very low weight patients &lt;35kg</td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban***</td>
<td>10 mg po daily</td>
<td>Use with caution in CrCl 30-50ml/min</td>
<td>No adjustment</td>
<td>No adjustment</td>
<td>NOT Allowed</td>
</tr>
</tbody>
</table>

*If patients are receiving anesthesia/analgesia via the perineural route (aka continues peripheral nerve block, CPNB), this is NOT within the spinal or epidural space and anticoagulation is NOT contraindicated

** For patients with a BMI >60, calculate dose according to the following equation and administer in the subcutaneous fat of the upper arm every 12 hours:

Unfractionated heparin dose = (71.34 x weight in kg) + (83.75 x height in inches) – 3467.59

Routine monitoring of anti-factor Xa is not necessary with this regimen, but if desired, the study protocol used a target level of 0.11-0.25 units/mL measured 4 hours post administration

*** rivaroxaban should not be used concomitantly with warfarin, as this has not been studied. See bridging guideline for more information

A. Pharmacists should verify the weight of the patient before any doses of anticoagulant are dispensed. The weight should be entered by the pharmacist into the patient’s electronic medication profile.

VI. Neuraxial anesthesia and VTE prophylaxis

A. Epidural anesthesia and analgesia have many proven benefits and are often used in surgical patients.

Bleeding into the epidural space can cause spinal cord compression, ischemia and subsequent paralysis.

Due to the gravity of this potential complication, the American Society of Regional Anesthesiologists (ASRA) and the American College of Chest Physicians (ACCP) have stated specific recommendations for concomitant neuraxial blockade and anticoagulant therapy. The specific recommendations from the most recent ASRA and ACCP reports follow:

i. neuraxial anesthesia/analgesia should generally be avoided in patients with a known bleeding disorder
ii. neuraxial anesthesia/analgesia should generally be avoided in patients who are on antithrombotic drugs pre-operatively.

iii. aspirin and NSAIDS do not appear to increase the risk of perispinal hematoma and therefore do not pose a risk

iv. patients on clopidogrel (Plavix®), prasugrel (Effient®) or ticagrelor (Brilinta®) should discontinue these drugs 7 days prior to the procedure if possible

v. if a patient is receiving pre-operative VTE prophylaxis:
   a. UFH:
      i. Wait 4 hours after a prophylactic dose of unfractionated heparin before placing or removing an epidural catheter or administering spinal block
      ii. Initiate or resume unfractionated heparin thromboprophylaxis 1-2 hours after placing or removing an epidural catheter
      iii. Initiate unfractionated heparin thromboprophylaxis no sooner than 6 hours postop when spinal block has been administered
   b. Enoxaparin:
      i. Wait 12 hours after a prophylactic dose of enoxaparin before placing or removing an epidural catheter or administering spinal block
      ii. Initiate or resume enoxaparin thromboprophylaxis 4 hours after placing or removing an epidural catheter
      iii. Initiate enoxaparin thromboprophylaxis no sooner than 6 hours postop when spinal block has been administered
   vi. prophylaxis with an anticoagulant should be delayed for 24 hours if there is a bloody tap during the initial needle placement

B. The only VTE prophylaxis regimens permitted with concomitant epidural/spinal anesthesia at UNMH are:
   - UFH 5000 units SQ BID
   - Enoxaparin 40 mg SQ daily

C. Concomitant use of spinal/epidural anesthesia/analgesia and warfarin is not recommended due to the unpredictable anticoagulation profile of warfarin.

D. All patients receiving concomitant spinal/epidural anesthesia/analgesia and anticoagulation should be monitored for signs and symptoms of perispinal hematoma. These include:
   i. bowel or bladder dysfunction
   ii. new onset of back pain
   iii. numbness or weakness of the lower extremities

E. If patients are receiving anesthesia/analgesia via the perineural route (aka continues peripheral nerve block, CPNB), this is not within the spinal or epidural space and anticoagulation is not contraindicated

PRIOR TO INITIATING ANTICOAGULATION IN ANY PATIENT RECEIVING AN EPIDURAL, ACUTE PAIN SERVICE (951-1324) SHOULD BE NOTIFIED BY THE PRIMARY TEAM.

VII. Timing of initiation of VTE prophylaxis
A. Per CMS and TJC initiatives, all patients should be risk assessed for VTE within 24 hour of admission
B. If a patient is found to be at risk, prophylactic modalities (pharmacologic preferred over mechanical) should be employed within 24 hours of admission unless there is a potential contraindication (e.g. surgical procedure)
C. If a provider opts to not employ VTE prophylaxis with good clinical rationale, the reason must be documented in the electronic medical record.
D. Surgical patients should have prophylaxis administered within 24 hours of skin closure unless there is a documented contraindication.

E. There is no clear evidence of superiority between starting VTE prophylaxis pre- or post-operatively
   i. In the United States, pre-operative prophylaxis has generally been administered no later than 12-24 hours prior to the procedure to minimize bleeding complications.
      a. Studies have shown that administering prophylaxis within 2 hours of surgery leads to significant increases in bleeding complications.
   ii. Pharmacologic prophylaxis should generally not be administered any sooner than 6 hours post-procedure based on evidence that shows a clinically and statistically significant increase in bleeding complications when prophylaxis is started within 6 hours post-procedure.

F. Exact initiation times are at the discretion of providers and the UNMH VTE prophylaxis protocol incorporates clinical decision support based on the above statements (Ei-ii)

VIII. Duration of prophylaxis
   A. The duration of inpatient stay should be the default duration of prophylaxis in medical patients
   B. Most surgical patients should be prophylaxed for 7-14 days unless they fall into one of the following categories:
      i. Hip orthopedic surgery: 35 days (Grade 2B), knee orthopedic surgery 10-14 days
      ii. High risk abdominal or pelvic surgery for cancer: consider 4 weeks of prophylaxis if not at high risk for bleeding (Grade 1B).

IX. Mechanical prophylaxis
   A. Mechanical modalities for VTE prophylaxis include the following:
      i. graduated compression stockings (GCS) or TED hose
      ii. intermittent pneumatic compression devices (IPC) (scds, venodynes, etc)
      iii. inferior vena caval (IVC) filter
   B. These modalities have all been shown to reduce the risk of VTE in a number of patient groups. However, they are often considered less efficacious than pharmacological means of prophylaxis for the following reasons:
      i. the evidence in the literature pertaining to risk reduction of VTE with mechanical prophylaxis is weak due to the inability to blind the trials
      ii. skewed statistical results in favor of mechanical modalities
      iii. poor compliance in actual clinical practice compared to that in clinical trials
   C. The benefit of mechanical modalities over pharmacologic agents is the lack of bleeding potential. Therefore, these modalities should be reserved for patients at high risk for bleeding. Additionally, they may be considered adjunctive therapy to pharmacologic prophylaxis in patients at very high risk for VTE. Finally, they may be considered in patients with a very low risk for VTE, as long as early, aggressive ambulation is also part of the plan of care. Otherwise, they should not be considered first-line therapy for VTE prophylaxis. If a decision is made to use a mechanical modality, it is imperative that the interdisciplinary team ensure proper sizing and implementation of the device.

IX. Resources
   A. Anticoagulation Pharmacist 264-6970, 7 days/week 0800-1600.
   B. Patient Care Area Pharmacists based on patient location. See AmIOn -> “Pharmacy” for contact information

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Reviewed by: Allison Burnett, PharmD; Sheila Modi, MD; David Garcia, MD
Approved at: UNMH Antithrombosis Subcommittee September 2012
References:
1. Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. February 2012; 141 (2 suppl)