Aflac Clinical Practice Guideline for Work Up and Treatment of Venous Thromboembolism (VTE)

**RISK FACTORS**
- Central venous access device (CVAD) *
- Infection *
- Decreased mobility from baseline
- Surgery, trauma *
- Personal history of or first degree relative with DVT/VTE *
- Active cancer *
- Congenital heart disease
- Inflammatory/Rheumatologic diseases *
- Renal disorders (nephrotic syndrome)
- Sickle cell disease *
- Pregnancy
- Estrogen use
- Obesity
- Aberrant venous anatomy
- Post pubertal age or age <1

* Indicates risk factors for Cerebral Sinus (CSVT)

**INCLUSION CRITERIA**
- Patient with venous thromboembolism on imaging or line-associated atrial clots in children with structurally normal hearts

**EXCLUSIONS**
- Thrombi in intracardiac connections and devices or patients with significant renal disease or superficial thrombi

**WORK UP**

**Suspected Acute VTE**

- **Imaging**
  - Extremity or Internal Jugular
    - Doppler Ultrasound
    - MRV if:
      - Left sided iliofemoral VTE (May-Thurner Syndrome)
      - Unprovoked upper extremity VTE (Thoracic Outlet Syndrome)
      - Proximal end of lower extremity clot is not seen on ultrasound
      - Replace MRV with CT with contrast if morbidly obese
  - Pulmonary Embolism (PE)
    - CT Angiogram
    - ECHO
    - Bilateral upper and lower extremity Doppler Ultrasound
  - Renal or Portal
    - Abdominal Doppler Ultrasound
  - Cerebral Sinus (CSVT)
    - MRI/MRV

- **Labs**
  - CBC
  - DIC Panel
  - CMP
  - Antiphospholipid antibody testing (Lupus anticoagulant profile) in age ≥12 yo and/or post pubertal and/or personal or FHx of autoimmune conditions
  - If PE, send troponin and BNP

- **Provoked clot? See risk factors**
  - Yes
    - Send: Protein C activity, Protein S activity, Antithrombin activity, Factor V Leiden Mutation, Prothrombin G20210A Gene Mutation
  - No

- **Do NOT send thrombophilia testing**
  - No
  - Yes
    - Consult Hematology

- **Consult interventionalist for**
  - Central venous system thrombosis
  - Axillary vein to heart
  - Iliac vein to heart
  - Massive PE with right heart strain or shock
  - May Thurner or Padget-Schrotter syndromes
  - Bilateral renal vein thrombi
  - SVC syndrome
  - See also catheter directed thrombolysis guideline

Interventional cardiology should be consulted for children with structurally abnormal hearts or history of cardiac surgery. Consult IR for all other children.

* Indicates risk factors for Cerebral Sinus (CSVT)

**Consider Treatment Options (see page 2)**

Developed through the efforts of the Aflac Cancer and Blood Disorders Center at Children’s Healthcare of Atlanta and physicians on Children’s medical staff in the interest of advancing pediatric healthcare. This is a general guideline and does not represent a professional care standard governing providers’ obligation to patients. Ultimately, the patient’s physician must determine the most appropriate care. © 2021 Children’s Healthcare of Atlanta, Inc.
TREATMENT

1. Anticoagulation Contraindications
   - Recent/active bleeding
   - Invasive procedure in past 24 hrs
   - History of heparin-induced thrombocytopenia
   - Uncorrected coagulopathy/severe thrombocytopenia (<30K)
   - Epidural catheter
   - Religious objection to pork/pork allergy (heparin and enoxaparin only)

   Are there contraindications for anticoagulation?
   - Yes
   - No

   Supportive care
   - Order bleeding precautions:
     - Avoid use of aspirin or NSAIDs for fever/pain
     - No rectal temperatures
     - Use soft toothbrush or water irrigating device
     - Apply direct pressure to cuts for 10-15 minutes
     - Avoid arterial punctures if possible

2. Unfractionated Heparin Indications
   - Significant renal impairment
   - Increased bleeding risk
   - Planned invasive procedure(s) OTHER than thrombolysis in next 24-48 hrs

   Is unfractionated heparin indicated?
   - Yes
   - No

   Going for thrombolysis?
   - Yes
     - Update ECMO team and ICU for support
     - See CDT Guideline
   - No

3. Direct Oral Anticoagulant (DOAC) Contraindications
   - **ABSOLUTE**
     - "Triple +" APLA
     - Left ventricular thrombosis
     - CHILD PUGH grade ≥ 8
   - **RELATIVE**
     - Nephrotic syndrome
     - End stage renal disease
     - Risk of GI bleeding

   Are there contraindications for DOAC?
   - Yes
   - No

4. Length of MINIMUM initial treatment
   - 6 Weeks if: <2 months old and VTE resolves OR central line associated clot and VTE resolves
   - 3 Months if: Provoked VTE (DVT or PE) OR Cerebral Sinus Venous Thrombosis
   - 6 Months if: Idiopathic/Unprovoked VTE (DVT or PE), May-Thurner Syndrome, OR Antiphospholipid antibody syndrome (may need indefinite treatment)

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*Must be ordered by hematology or cardiology

**DOAC as 1st line**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Weight</th>
<th>Absorption site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>≥35 kg</td>
<td>Colon</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>≥50 kg</td>
<td>Stomach</td>
</tr>
</tbody>
</table>

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Therapeutic Unfractionated Heparin Dosing
**GOAL: 0.35-0.70 units/mL**

**Initial Loading**
- ≤1 year
  - 50-75 units/kg over 10 minutes (5,000 units max)
- ≥21 year
  - 50 units/kg IV over 10 minutes (5,000 units max)

**Maintenance**
- ≤1 year
  - 28 units/kg/hour
- ≥21 year
  - 20 units/kg/hour

*No loading dose in preterm, medically fragile, or child at high risk of bleeding*

**Therapeutic Unfractionated Heparin Dosage Titration**
**GOAL: 0.35-0.70 units/mL**

<table>
<thead>
<tr>
<th>Hep Assay (Units/mL)</th>
<th>Dosage Adjustment</th>
<th>Time to Repeat Heparin Assay (Anti-Xa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.2</td>
<td>Give 50 units/kg bolus (5,000 units max), and increase infusion rate by 15%</td>
<td>4 hours after rate change</td>
</tr>
<tr>
<td>0.21-0.34</td>
<td>Increase infusion rate by 10%</td>
<td>4 hours after rate change</td>
</tr>
<tr>
<td>0.35-0.7</td>
<td>Keep rate the same</td>
<td>Daily after 2 levels 4 hours apart are in goal range</td>
</tr>
<tr>
<td>0.71-0.79</td>
<td>Decrease infusion rate by 10%</td>
<td>4 hours after rate change</td>
</tr>
<tr>
<td>0.8-0.89</td>
<td>Hold infusion for 60 minutes, then decrease infusion rate by 10%</td>
<td>4 hours after infusion resumes</td>
</tr>
<tr>
<td>≥0.9</td>
<td>Hold infusion for 120 minutes, then decrease infusion rate by 15%</td>
<td>4 hours after infusion resumes</td>
</tr>
</tbody>
</table>

Therapeutic Enoxaparin Dosing
**GOAL: 0.5-1.0 units/mL; all levels should be drawn 4 hours after administration**

**Treatment**
- <2 mo
  - Goal: 0.5-1.0
  - 1.5-1.8 mg/kg q12 (80mg max)
- ≥2 mo
  - Goal: 0.5-1.0
  - 1-1.5 mg/kg q12 (80mg max)

- Enoxaparin is renally cleared; refer to formulary for dosage modifications based on creatinine clearance; needs peak and trough levels
- With changes in creatine, more frequent heparin assay may be needed.
- Round to the nearest whole number if possible

**Enoxaparin Dosage Titration while Inpatient**

<table>
<thead>
<tr>
<th>Heparin Assay (Units/mL)</th>
<th>Dose Titration</th>
<th>Time to Repeat Heparin Assay (Anti-Xa) Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.35</td>
<td>Increase dose by 25%</td>
<td>4 hours after 2nd dose</td>
</tr>
<tr>
<td>0.35-0.49</td>
<td>Increase dose by 10%</td>
<td>4 hours after 2nd dose</td>
</tr>
<tr>
<td>0.5-0.59</td>
<td>Keep same dosage</td>
<td>Next day, then weekly</td>
</tr>
<tr>
<td>0.6-0.89</td>
<td>Keep same dosage</td>
<td>Weekly</td>
</tr>
<tr>
<td>0.9-1</td>
<td>Keep same dosage</td>
<td>Next day, then weekly</td>
</tr>
<tr>
<td>1.1-1.5</td>
<td>Decrease dose by 20%</td>
<td>4 hours after 2nd dose</td>
</tr>
<tr>
<td>1.6-2</td>
<td>Hold next dose and decrease subsequent dose by 30%</td>
<td>12 hours (ensure level has dropped to &lt;0.5 units/mL then 4 hours after next dose given)</td>
</tr>
<tr>
<td>&gt;2</td>
<td>Hold all doses until HepAssay less than 0.5 units/mL then decrease dose by 40%</td>
<td>Every 12 hours until HepAssay is less than 0.5 units/mL then 4 hours after next dose given</td>
</tr>
</tbody>
</table>

Therapeutic DOAC Dosing

<table>
<thead>
<tr>
<th>DOAC</th>
<th>Loading Dose</th>
<th>Maintenance Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>10 mg PO BID for 7 days</td>
<td>5 mg PO BID</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>15 mg PO BID for 21 days</td>
<td>20 mg PO QD</td>
</tr>
</tbody>
</table>
Continue enoxaparin or unfractionated heparin until INR > 1.7

<table>
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<tr>
<th>Goal</th>
<th>Day</th>
<th>Level</th>
<th>Dosing Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-2</td>
<td>1.0-1.3</td>
<td>0.2 mg/kg (10 mg max dose)</td>
</tr>
<tr>
<td></td>
<td>3-5</td>
<td>50% of loading dose</td>
<td></td>
</tr>
<tr>
<td>INR of 2.0-3.0 for non-CICU patients</td>
<td>Maintenance</td>
<td>Check INR on day 4 or 5</td>
<td>Increase by 20% of dose</td>
</tr>
<tr>
<td></td>
<td>1.1-1.4</td>
<td>Increase by 10% of dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.5-1.9</td>
<td>No Change</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.0-3.0</td>
<td>Decrease by 10% of dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.1-3.5</td>
<td>Reduce dose to 20% of current dose x2 days then repeat INR, if INR &lt; 3.5, restart at 20% less than previous dose</td>
<td></td>
</tr>
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<td></td>
<td>&gt; 3.5</td>
<td>Reduce dose to 20% of current dose x2 days then repeat INR. If INR &lt; 3.5, restart at 20% less than previous dose</td>
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<td>Maintenance</td>
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REFERENCES


REVISION HISTORY

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<th>Change Description</th>
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