DEEP VENOUS THROMBOSIS (DVT), SUSPECTED ACUTE, INVOLVING A PROXIMAL LIMB

Step 1. Evaluate
- Signs of limb ischemia (reduced pulses or perfusion)?
- If YES, then Consult Surgeon STAT. (Consult Hematologist if presentation compatible with arterial thrombosis.)
- Clinical presentation compatible with extremity DVT (may include limb pain, swelling, and/or discoloration)?

Step 2. Start
- Full vital signs, including pulse ox
- IV access
- Labs: STAT CBC, CMP, PT/PTT, fibrinogen, factor VIII, D-dimer, Urine β-HCG if post-menarchal female
- Diagnostic imaging: Compression Ultrasound with Doppler: r/o DVT
- If study is non-diagnostic and DVT is suspected clinically, further imaging with MR venogram (or CT venogram)

Step 3. Confirm and Proceed or Consider Alternate Diagnosis

Step 4. Evaluate
- Radiologic imaging concerns
- Clinical concerns

Step 5. Obtain
- Consider obtaining Hypercoagulable panel
- Hematology consult

Step 6. Evaluate

Step 7a. Anticoagulation Treatment for Thrombolysis

Step 7b. Systemic tissue Plasminogen Activator (tPA)
- Goal: Hematologist bedside patient evaluation within 2 hours of consult request (if performed by Fellow, includes review with Attending).
- NOTE: SYSTEMIC tPA TO BE ADMINSTERED ONLY IN CRITICAL CARE UNITS OR IN CCBD

Step 7c. Local Pharmacomechanical Thrombolysis
- Hematologist to assist Interventional Radiologist in discussion of risk and benefits of thrombolytic procedure with patient/family.
- Interventional Radiologist (+/- Hematologist) to document patient/family agreement with thrombolysis.

Step 8. Evaluate
- Extent or occlusiveness of DVT has worsened while receiving anticoagulation at documented therapeutic levels: 
  Consider possible diagnosis of thrombotic storm or catastrophic antiphospholipid antibody syndrome.

Further Management: CCBD/Critical Care Units

Appendix 1. Sample Post-Procedural Orders for Local Pharmacomechanical Thrombolysis
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Algorithm - N/A
Target Population - N/A
Background | Definitions - N/A

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Step 2. Start

Step 3. Confirm and Proceed or Consider Alternate Diagnosis

Step 4. Evaluate

Step 5. Obtain

Step 6. Evaluate

Step 7a. Anticoagulant Treatment

Step 7b. Systemic tPA

Step 7c. Local Pharmacomechanical Thrombolysis

Step 8. Evaluate

Further Management, CCBD/Critical Care Units

Laboratory Studies | Imaging - N/A

Therapeutics - N/A

Parent | Caregiver Education - N/A

Appendix 1. Sample Post-Procedural Orders for Local Pharmacomechanical Thrombolysis

References

Clinical Improvement Team

PURPOSE

To provide a framework for rapid diagnostic evaluation and management of suspected acute deep vein thrombosis (DVT) involving the proximal limb in children.

INITIAL EVALUATION AND MANAGEMENT

Setting: ED/Floor/PICU. (Goal: complete within 2 hrs of diagnostic suspicion)

Step 1. Evaluate

1. Signs of limb ischemia (reduced pulses or perfusion)?

   If YES, then Consult Surgeon STAT. (Consult Hematologist if presentation compatible with arterial thrombosis.)

2. Clinical presentation compatible with extremity DVT (may include limb pain, swelling, and/or discoloration)?

   If YES, then proceed to Step 2
Step 2. Start

- Full vital signs (including pulse ox)
- IV access
- Labs:
  STAT CBC, CMP, PT/PTT, fibrinogen, factor VIII, D-dimer, Urine β-HCG if post-menarchal female
- Diagnostic imaging:
  
  **Compression Ultrasound with Doppler: r/o DVT**
  
  If study is non-diagnostic and DVT is suspected clinically, further imaging with MR venogram (or CT venogram)*

Step 3.

3a. **DVT confirmed**

Proceed to Step 4

3b. **No DVT disclosed:**

Consider alternative diagnoses.

* MR venogram spares the patient of radiation exposure engendered by CT venogram; discuss optimal modality with attending Radiologist as needed.

Step 4. Evaluate

1. Radiologic imaging concerns:

   a. Was full extent of thrombus identified (i.e., proximal and distal termini)? - If not, then obtain MR venogram or CT venogram of abdo/pelvis (lower limb DVT) or of chest (upper limb DVT) [discuss with attending Radiologist]. Indication: “Define proximal extent and occlusiveness of DVT”

   b. Is thrombus completely occlusive or instead partially/non-occlusive? - Discuss with Radiologist if not conclusively reported

2. Clinical concerns:

   a. Does the patient have tense edema of the limb with bluish discoloration, and cannot walk or move the limb due to pain (despite standard doses of analgesia)? - If so, strongly consider thrombolysis (7b or 7c)

   b. Is there suspicion for anatomic obstruction (e.g. May-Thurner, Paget-Schroetter, cervical rib*) - If so, strongly consider local pharmacomechanical thrombolysis (7c)

   c. Is there concern for pulmonary embolism (chest pain, shortness of breath, or hypoxemia)? - If so, provide supplemental oxygen and obtain STAT spiral CT chest.

   If PE is diagnosed, refer to Acute PE Care Pathway and admit to PICU.
Step 5. Obtain

1. Consider Obtaining Hypercoagulable panel** (or parts of the panel that will guide acute clinical care), ESR and CRP
2. Hematology consult
   - Page Hematology Fellow on-call.
   - Discuss initial antithrombotic management using decision tree below.

* Occlusive L iliac or R/L subclavian DVT that is extensive and/or occurs in the absence of strong clinical risk factors (e.g., prolonged immobility, indwelling central line).


Step 6. Evaluate

1. Complete veno-occlusive proximal thrombus with factor VIII greater than/equal to 150 units/dL and D-dimer greater than/equal to 1.0: Consider thrombolytic therapy (7b or 7c—Hematologist to discuss with Interventional Radiologist).
   - If thrombolysis contraindicated (see p. 4), if consensus to offer thrombolysis not achieved among Primary Service Attending, Hematology Attending, +/- Interventional Radiology Attending (as appropriate), or if patient/parent declines thrombolysis, then start anticoagulant therapy (7a).

2. Complete veno-occlusive thrombus with factor VIII less than 150 units/dL or D-dimer less than 0.5: Anticoagulant therapy (7a) if clinical concerns 2a and 2b are absent in Step 4.

3. Non-occlusive thrombus: Anticoagulant therapy (7a) if clinical concerns 2a and 2b are absent in Step 4 above.

Step 7a. Anticoagulant Treatment for use following, or in lieu of, thrombolysis

If renal insufficiency or concern for increased bleeding risk (e.g., recent surgery, impending non-elective surgery, clinical instability, DIC, liver disease):

1. Give unfractionated heparin IV bolus 50 units/kg followed by a continuous IV infusion at 15 units/kg/hour (pre-term neonates: 20 units/kg/hour; term neonates: 25 units/kg/hour).

2. Obtain heptest (anti-Xa level) by peripheral venipuncture 6 hours following start of infusion (8 hours if bolus is withheld).
   - If anti-Xa level less than 0.3 units/mL, increase infusion dose; if level greater than 0.7 units/mL, decrease infusion dose (discuss with Hematology) and recheck anti-Xa level 6 hours following change in dose (8 hours if bolus is withheld).
   - If anti-Xa level greater than/equal to 0.3 units/mL and less than/equal to 0.7 units/mL, maintain same dose and recheck heptest every 24-48 hours in the absence of interim bleeding concerns.

3. Maintain platelet count greater than/equal to 50,000-100,000/μL, with higher level required for intubation, insertion of central vascular access devices, and invasive procedures (via platelet transfusion, if required) and fibrinogen greater than/equal to 100 g/dL (via infusion of cryoprecipitate [preferred] or fresh frozen plasma [alternative], if required)

5. CBC with platelet count every 24-48 hours in the absence of interim bleeding concerns. Notify Hematologist for decline in platelet count (concern for heparin-induced thrombocytopenia).

If recent bleeding or evidence of ongoing bleeding:

Management as above, with the exception that unfractionated heparin continuous infusion should be given with no bolus, and platelet count should be maintained at greater than/equal to 100,000/μL.

If no major bleeding concerns:

1. May give low molecular weight heparin (LMWH) as a subcutaneous injection* every 12 hours: for current LMWH on-formulary (enoxaparin [Lovenox]): starting dose for children greater than 6 years is 1.25 mg/kg.

2. Obtain heptest (anti-Xa level) by peripheral venipuncture 4 hours following first or second injection.
   - If LMWH anti-Xa level less than 0.5 units/mL, increase dose; if level greater than 1.0 unit/mL, decrease dose and recheck anti-Xa level 4 hours following the first or second dose.
   - If LMWH anti-Xa level greater than/equal to 0.5 units/mL and less than/equal to 1.0 units/mL, maintain same dose.

3. Maintain platelet count greater than/equal to 50,000-100,000/μL, with higher level required for intubation, insertion of central vascular access devices, and invasive procedures (via platelet transfusion, if required) and fibrinogen greater than/equal to 100 g/dL (via infusion of cryoprecipitate [preferred] or fresh frozen plasma [alternative], if required)

4. Monitor clinically for signs/symptoms of bleeding. Recheck 4 hour post-dose anti-Xa level as needed for bleeding concerns, change in renal function, or weight change greater than/equal to 10% from time of prior establishment of therapeutic dose.

* If insufficient subcutaneous tissue, LMWH may be given by IV route at same dose in select circumstances, with additional anti-Xa trough monitoring (e.g., 12 hours post-dose; discuss with Hematologist).

If anticoagulation is absolutely contraindicated and patient is at high risk for pulmonary embolism, consider temporary inferior vena cava filter placement (consult Interventional Radiologist). Filter should be removed as soon as anticoagulation can be instituted.

Step 7b. Systemic tPA (see contraindications)

Goal: Hematologist bedside patient evaluation within 2 hours of consult request  (if performed by Fellow, includes review with Attending).

NOTE: SYSTEMIC tPA TO BE ADMINISTERED ONLY IN CRITICAL CARE UNITS OR IN CCBD

If no contraindications to systemic tPA:

1. Hematologist to assist in discussion of risk and benefits of systemic thrombolysis with patient/family.

2. Document patient/family agreement with systemic thrombolysis.

3. Begin continuous IV infusion of tPA at 0.03 mg/kg/hr (max: 2.5 mg/hr).

4. Give concomitant IV infusion of low-dose unfractionated heparin at 10 units/kg/hr.

5. Check plasminogen level, CBC and DIC screen every 24 hours during systemic tPA infusion. Give FFP as needed to achieve plasminogen greater than/equal to lower limit of normal values for age (e.g., 70 units/dL or 70% in non-neonatal children) and platelet transfusion as needed to maintain platelet count greater than/equal to 100K

6. Monitor clinically for signs/symptoms of bleeding. Stop tPA for any major bleeding concerns (i.e., other than bruising, transient epistaxis, or oozing from puncture sites, which are expected minor bleeding side-effects). Stop tPA
for any severe headache or any neurologic changes (until intracranial hemorrhage is excluded by STAT CT of the head).

7. Repeat radiologic imaging (Doppler compression ultrasound and/or MR venography) at 48 hrs following the start of tPA infusion.

- **If thrombus is resolved at 48 hrs**, discontinue tPA infusion and switch low-dose unfractionated heparin infusion to therapeutic anticoagulation (see part 5a above).

- **If thrombus persists at 48 hrs and is still completely veno-occlusive**, increase tPA infusion dose to 0.06 mg/kg/hr (max: 2.5 mg/hr), and continue clinical and lab monitoring as above. At 96 hrs post-start of infusion, discontinue tPA, switch low-dose unfractionated heparin infusion to therapeutic anticoagulation (see part 5a above), and repeat radiologic imaging (same modality as at 48 hrs). If thrombus is still completely veno-occlusive, consider salvage local pharmacomechanical thrombolysis via Interventional Radiology (discuss with Hematologist; contact Interventional Radiologist if warranted). Therapeutic anticoagulation should be resumed following completion of any local pharmacomechanical thrombolysis.

- **If thrombus persists at 48 hrs but is no longer completely veno-occlusive**, continue same tPA infusion dose, and continue clinical and lab monitoring as above. At 96 hrs post-start of infusion, discontinue tPA, switch low-dose unfractionated heparin infusion to therapeutic anticoagulation (see part 5a above), and repeat radiologic imaging (same modality as at 48 hrs).

**If patient is recently post-op from a major surgery, local pharmacomechanical thrombolysis is preferred over systemic tPA, due to risk of bleeding.**

**Step 7c. Local Pharmacomechanical Thrombolysis**


2. Interventional Radiologist (+/- Hematologist) to document patient/family agreement with thrombolysis.

3. Peri-procedural anticoagulant of choice is unfractionated heparin
   a) If patient does not have severe thrombophilia*, then run unfractionated heparin gtt at 10 Units/kg/hr throughout procedure.
   b) If patient has severe thrombophilia*, document adequate D-dimer response (i.e., trend to normalization) on anticoagulant regimen prior to scheduling procedure, and maintain therapeutic anticoagulation with unfractionated heparin throughout procedure (see 7a for dosing and monitoring).

4. Procedure will typically be performed in interventional radiology suite.

5. Procedure will typically consist of the following steps:
   a) Diagnostic venography;
   b) Insertion of infusion catheter into the thrombus, with possible mechanical thrombus disruption;
   c) Catheter-directed infusion of tPA for approximately 24 hours;
   d) Repeat venography:
      o If residual thrombus, then mechanical thrombus disruption, with possible stent placement, followed by catheter-directed infusion of tPA for approximately 24 hours, then repeat venography;
   e) Removal of infusion catheter.
6. See also Appendix 1: Sample Post-procedural Orders for Local Pharmacomechanical Thrombolysis for Occlusive DVT Involving a Proximal Limb.

* Severe thrombophilia may be defined by antiphospholipid antibody syndrome, severe deficiency of protein C, protein S, or antithrombin, or multi-trait thrombophilia (Hematologist to discuss with Interventional Radiologist).

HEMATOLOGY CHECKLIST FOR SYSTEMIC TPA FOR ACUTE VTE

**Step 8. Evaluate**

Extent or occlusiveness of DVT has worsened while receiving anticoagulation at documented therapeutic levels: *Consider possible diagnosis of thrombotic storm or catastrophic antiphospholipid antibody syndrome.*

*If consensus achieved among primary service Attending, Hematology Attending, +/- Rheumatology Attending, +/- Interventional Radiology Attending (as appropriate):*

1. Switching from standard anticoagulation to IV direct thrombin inhibitor (e.g., argatroban or bivalirudin) may be warranted.
2. Immunosuppressive therapies may be warranted (consult Rheumatologist to participate in diagnostic and therapeutic discussion and decision-making).
3. Thrombolytic therapy may be warranted (7b or 7c—discuss with IR).

*Withhold thrombolytic therapy if: thrombolyis contraindicated and contraindications not waived (see p. 4); consensus to offer thrombolysis not achieved among primary service Attending, Hematology Attending, +/- Interventional Radiology Attending (as appropriate); or if patient/parent declines thrombolysis.*
Indications (ONE of the following criteria must be met)
Yes ___ 1. Acute pulmonary embolism with evidence of right heart strain
Yes ___ 2. Life-threatening pulmonary embolism
Yes ___ 3. Proximal limb DVT with tense edema of the limb, bluish discoloration and inability to walk or move the limb due to pain (despite standard doses of analgesia)
Yes ___ 4. Clinical suspicion for May-Thurner syndrome, Paget-Schroetter syndrome, or cervical rib
Yes ___ 5. Completely veno-occlusive limb DVT with factor VIII greater than/equal to 150 units/dL and D-dimer greater than/equal to 0.5
Yes ___ 6. Extent or occlusiveness of DVT has worsened while receiving anticoagulation at documented therapeutic levels.

Contraindications (ABSOLUTE for Systemic tPA by Continuous IV Infusion, RELATIVE for Local Pharmacomechanical Thrombolysis)
No ___ 1. Evidence of active hemorrhage
No ___ 2. Prior history of intracranial hemorrhage
No ___ 3. Neurosurgery, serious head trauma, or arterial ischemic stroke during preceding 4 weeks
No ___ 4. Gastrointestinal or urinary tract hemorrhage during preceding 3 weeks
No ___ 5. Major surgery (other than neurosurgery) or other serious trauma (other than head trauma) during preceding 2 weeks
No ___ 6. Lumbar puncture during preceding 72 hours
No ___ 7. Other invasive procedure within 72 hours
No ___ 8. Uncontrolled hypertension
No ___ 9. Clinical presentation suggesting endocarditis, pericarditis or large myocardial infarction
No ___ 10. PTT prolonged by greater than/equal to 4 seconds at time of planned thrombolysis and normalizes following 1:1 mixing with pooled plasma standard (specimen drawn by clean peripheral venipuncture).
No ___ 12. Fibrinogen less than 100 g/dL at time of planned thrombolysis
No ___ 13. Pregnant female
No ___ 14. Known AVM, aneurysm, CNS mass, or moyamoya
No ___ 15. Uncontrolled seizure
No ___ 16. History of anaphylaxis to tPA.

Additional RELATIVE Contraindications (both for Systemic tPA by Continuous IV Infusion and for Local Pharmacomechanical Thrombolysis)
No ___ 17. Recent unfractionated heparin use AND anti-factor Xa activity greater than/equal to 0.4 at time of planned thrombolysis (specimen drawn by clean peripheral venipuncture)
No ___ 18. Recent low molecular weight heparin (LMWH) AND anti-factor Xa activity greater than/equal to 0.6 at time of planned thrombolysis (specimen drawn by clean peripheral venipuncture)
No ___ 19. INR greater than/equal to 1.6 at time of planned thrombolysis (specimen drawn by clean peripheral venipuncture)
No ___ 20. Arterial puncture at non-compressible site during preceding 5 days
No ___ 21. Lumbar puncture during preceding 5 days
No ___ 21. Stroke or serious head trauma during preceding 3 months.
No ___ 23. CPR with chest compressions within past 10 days
No ___ 24. Invasive procedure (other than major surgery or lumbar puncture) within past 5 days
No ___ 25. Known bleeding disorder/tendency (includes significant renal and hepatic insufficiency)
No ___ 26. Aspirin or other irreversible platelet inhibitor use within preceding 7 days
No ___ 27. Life expectancy less than 6 months from other causes
FURTHER MANAGEMENT

Setting: CCBD/Critical Care Units

1. Continue anticoagulant and/or thrombolytic treatment as in 5a and 5b above.

2. Primary hospital service to document bilateral (affected and unaffected) mid-proximal and mid-distal limb circumferences in initial admission/transfer note.

3. Primary hospital service to document affected mid-proximal and mid-distal limb circumferences in daily progress notes.

4. For systemic tPA: No new central lines, Foley catheters, NG tube placement, arterial punctures, or other similar invasive procedures until at least 1 hour after completion of tPA infusion.

5. For systemic tPA: Compression of arterial and venous puncture sites x 24 hours after completion of tPA infusion.

6. Hematology bedside patient evaluation within 24 hours of consult request (unless systemic tPA is being considered; see 5b above)

7. Hematology to document bilateral (affected and unaffected) mid-proximal and mid-distal limb circumferences in initial consult note.

PRIOR TO DISCHARGE:

- Schedule for follow-up in Thrombosis Clinic at CHCO- Anschutz (contact clinic coordinator, via x 7-6578) or Hematology Clinic at CHCO – Briargate (719-305-9025) at 2 weeks post-diagnosis
- Arrange Hematological oversight of any anticoagulation (LMWH/warfarin) and its monitoring, as warranted.
APPENDIX 1
SAMPLE POST-PROCEDURAL ORDERS FOR LOCAL PHARMACOMECHANICAL THROMBOLYSIS FOR OCCLUSIVE DVT INVOLVING A PROXIMAL LIMB

IF INFUSION CATHETER IN PLACE (SERIAL PROCEDURES NOT YET COMPLETE):
1. Transfer to PICU
2. Bedrest
3. Vital signs every 15 minutes x 4, then every 30 minutes x 2, then per PICU routine
4. If popliteal sheath: [L,R] knee in immobilizer] [or: not applicable]
5. Clear liquids and advance as tolerated; NPO 8 hours prior to next procedure
6. Infuse continuous tPA (concentration: 1mg/mL) [0.5, 1.0] mL/hour x 24 hours through [BLUE, other color] infusion catheter at [L,R] [popliteal,jugular] sheath
7. Piggy-back NS 20 mL/hour x 24hours along with tPA through [BLUE, other color] infusion catheter at [L, R] [popliteal, jugular] sheath
8. Infuse continuous unfractionated heparin at XX units/kg/hour through [CLEAR, other color] tube at [L, R] [popliteal, jugular] sheath
9. No arterial or central venous punctures while on thrombolytic therapy
10. Labs:
   a. Hct, fibrinogen, D-dimer, and platelet count in p.m. post-procedure
   b. CBC, plasminogen, fibrinogen, PT/INR, PTT, and D-dimer in a.m.
11. Bilateral [mid-calf and mid-thigh, mid-forearm and mid-upper arm] circumferences every 12 hours, beginning upon return to PICU
12. Call H.O. for bleeding, new-onset chest pain or shortness of breath
13. Call H.O. for fibrinogen less than 150 mg/dL, plasminogen less than 70%, or platelet count less than 100/μL (to discuss plan with Hematology)
14. Other orders per routine PICU

IF INFUSION CATHETER REMOVED (SERIAL PROCEDURES COMPLETE):
1. Transfer to PICU.
2. Bedrest x 6 hours, then out of bed/ambulate as tolerated
3. Clear liquids and advance as tolerated
4. Unfractionated heparin IV at XX units/kg/hour
5. Labs:
   a. Hct, fibrinogen, D-dimer, and platelet count in p.m. post-procedure
   b. CBC, plasminogen, fibrinogen, PT/INR, PTT, and D-dimer in a.m.
6. Bilateral [mid-calf and mid-thigh, mid-forearm and mid-upper arm] circumferences every 12 hours x 2, beginning upon return to PICU, then daily

7. Call H.O. for bleeding, new-onset chest pain or shortness of breath

8. Call H.O. for fibrinogen less than 150 mg/dL or platelet count less than 100,000/μL (to discuss plan with Hematology)

9. Other orders per routine PICU orders
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<th>Reference</th>
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