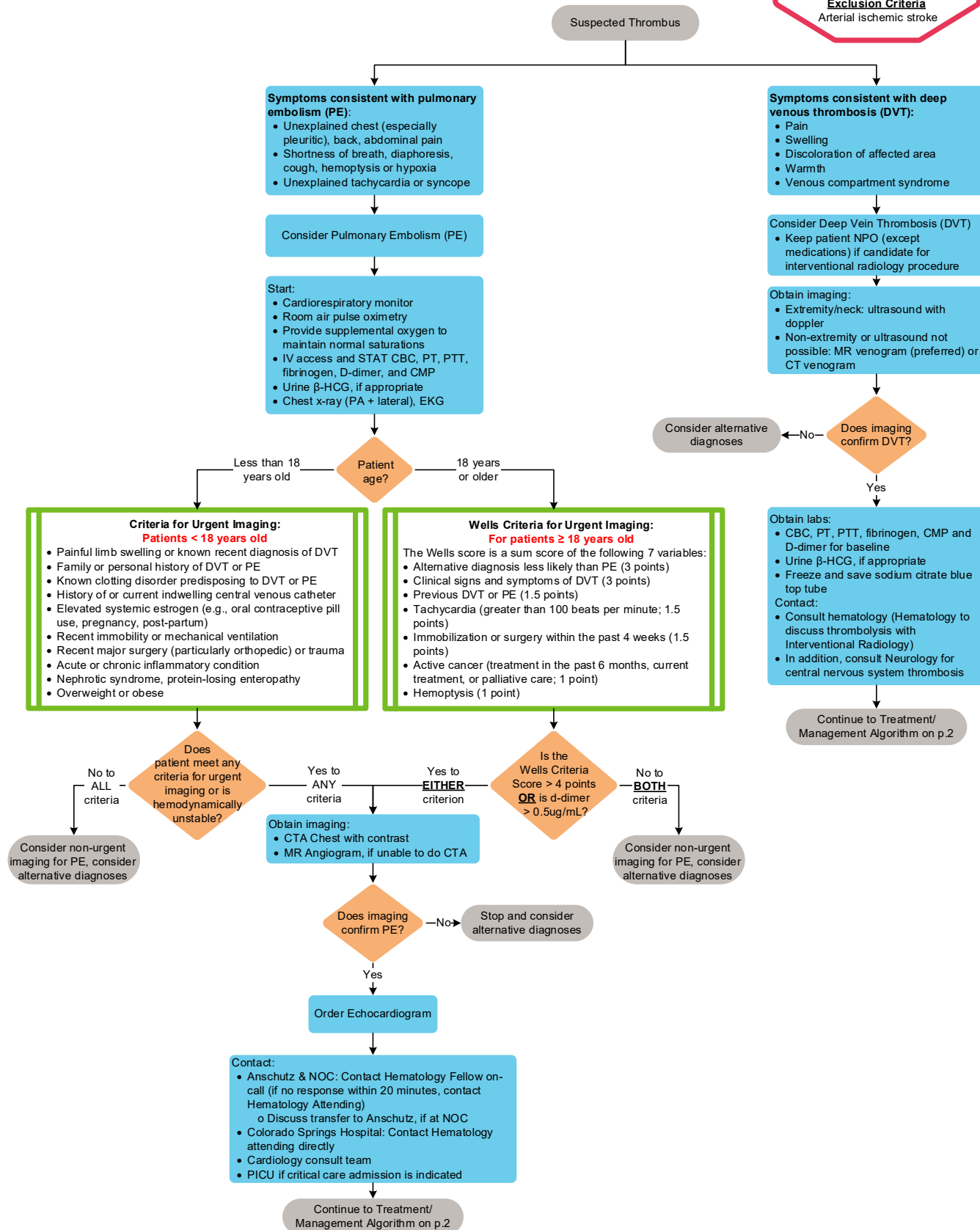


VENOUS THROMBOEMBOLISM DIAGNOSIS & MANAGEMENT

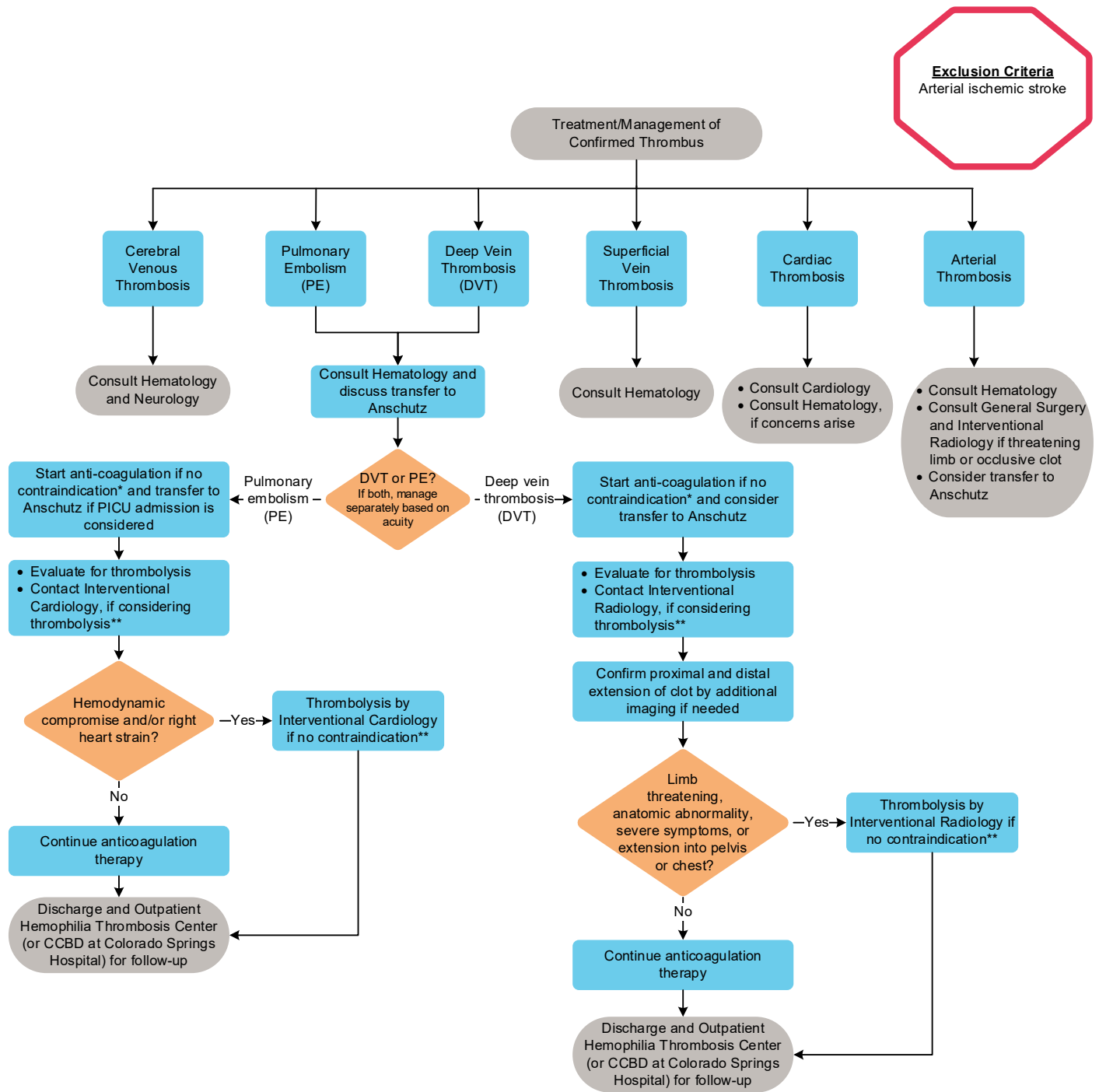
ALGORITHM 1. Diagnosis of Suspected Venous Thromboembolism

Inclusion Criteria
Patient presents with suspected Pulmonary Embolism (PE) or Deep Venous Thrombosis (DVT)

Exclusion Criteria
Arterial ischemic stroke



ALGORITHM 2. Treatment/Management of Confirmed Venous Thromboembolism



Quick Links

- [Anticoagulation Treatment](#)
- [*Anticoagulation Contraindications](#)
- [Thrombolysis Treatment](#)
- [**Thrombolysis Contraindications](#)

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TARGET POPULATION

Inclusion Criteria

Suspected Pulmonary Embolism (PE) or Deep Vein Thrombosis (DVT)

- PE: Recent onset/worsening of chest pain (especially pleuritic), back pain, abdominal pain, shortness of breath, diaphoresis, cough, hemoptysis, hypoxia, unexplained tachycardia or syncope
- DVT: Recent onset/worsening of unexplained pain, swelling, discoloration of affected area, or warmth

Exclusion Criteria

- Arterial ischemic stroke (see the [arterial ischemic stroke clinical pathway](#))

BACKGROUND | DEFINITIONS

- PE: pulmonary embolism
- DVT: deep vein thrombosis
- CTA: computed tomography angiogram
- LMWH: low molecular weight heparin
- UFH: unfractionated heparin

INITIAL EVALUATION: SUSPECTED PULMONARY EMBOLISM (PE)

Start

- Cardiorespiratory monitor
- Room air pulse oximetry
- Provide supplemental oxygen to maintain normal saturations
- IV access and STAT CBC, PT, PTT, fibrinogen, D-dimer, and CMP
- Urine β -HCG, if appropriate
- Chest x-ray (PA + lateral), EKG

Evaluate for Urgent Imaging

For patients less than 18 years old, evaluate the following criteria for urgent imaging for possible PE

- Painful limb swelling or known recent diagnosis of DVT
- Family or personal history of DVT or PE
- Known clotting disorder predisposing to DVT or PE (“thrombophilia” or “hypercoagulability”)
- History of or current indwelling central venous catheter
- Elevated systemic estrogen (e.g., oral contraceptive pill use, pregnancy, post-partum)
- Recent immobility or mechanical ventilation
- Recent major surgery (particularly orthopedic) or trauma
- Acute or chronic inflammatory condition (e.g., severe infection/sepsis, systemic lupus erythematosus or other autoimmunity)
- Nephrotic syndrome, protein-losing enteropathy
- Overweight or obese

If patient meets one or more criteria for urgent imaging or is hemodynamically unstable, proceed to [Patient Meets Criteria for Urgent Imaging](#). If no to all criteria, proceed to [Patient does NOT meet criteria for urgent imaging](#).

For patients 18 years and older, evaluate the following [Wells Criteria](#)⁸ for urgent imaging for possible PE, as Wells Score is only validated for adults.

The Wells Score is a sum score of the following 7 variables:

- Alternative diagnosis less likely than PE (3 points)
- Clinical signs and symptoms of DVT (3 points)
- Previous DVT or PE (1.5 points)
- Tachycardia greater than 100 beats per minute (1.5 points)
- Immobilization or surgery within the past 4 weeks (1.5 points)
- Active cancer (treatment in the past 6 months, current treatment, or palliative care; 1 point)
- Hemoptysis (1 point)

If Wells Score is greater than 4 points or d-dimer is greater than 0.5ug/mL, proceed to [Patient Meets Criteria for Urgent Imaging](#). If no to both criteria, proceed to [Patient does NOT meet criteria for urgent imaging](#).

Patient meets criteria for urgent imaging

- Consider STAT CTA Chest with contrast (specify “PE protocol” in comments) for all patients as first line. If CTA Chest is contraindicated or unavailable, obtain MR angiogram.

Patient does NOT meet criteria for urgent imaging

- Consider alternative diagnoses, especially if d-dimer is negative. Consider non-urgent imaging for possible PE.

Evaluate Imaging Results

Imaging confirms diagnosis of PE

- Proceed to [Order Echocardiogram](#).

Imaging does NOT confirm PE

- If risk factors for thrombosis are present, consider further imaging for DVT and evaluate for alternative diagnoses.

Order Echocardiogram

Contact

- If at Anschutz or NOC, contact Hematology Fellow on-call (if no response from fellow within 20 minutes, contact Hematology Attending directly). If at Colorado Springs Hospital, contact Hematology Attending.
 - Discuss transfer to Anschutz, if at NOC
 - Discuss initial antithrombotic management.
 - If imaging confirms PE or thrombolysis will otherwise be considered, then Hematology will evaluate patient at bedside within 1 hour of consultation.
 - Start anticoagulation with intravenous UFH until definitive antithrombotic decision is made. See [CHCO Formulary: Heparin](#).
- Contact Cardiology Consult team to discuss the need for STAT echocardiogram
 - Indications for STAT echocardiogram include (any ONE of the following):
 - Hemodynamic instability
 - Right heart strain on EKG (look for right heart strain S1Q3T3 pattern)

- Room air oxygen saturation less than or equal to 92% and not known to be patient's baseline
- Sudden change in oxygen requirement
- PE involves the main or proximal branch of a pulmonary artery (PA)
- PE involves multiple lobar/segmental PA branches bilaterally
- If patient is hemodynamically stable and none of the above criteria are met (and there are no plans for thrombolysis), then discuss with Cardiology the plans and timing for non-emergent echocardiogram.
- If PE (cardiopulmonary circulation) is associated with right ventricular dysfunction/strain and/or hemodynamic instability, Cardiology Consult Team will request emergent Interventional Cardiology consultation for catheter-directed thrombolysis. Cardiology consult team will alert the following, as indicated: Cardiac Intensive Care Unit, ECMO, and Cardiothoracic Surgery.
- For co-existent DVT (outside cardiopulmonary circulation), see [evaluation of DVT section](#).
- **Contact the PICU if critical care admission is indicated.**
- **At Colorado Springs Hospital, discuss with PICU and transfer to Anschutz if critical care admission is indicated.**

Decide Antithrombotic Therapy and/or Thrombolysis

- Start anticoagulation with intravenous unfractionated heparin (UFH) until definitive antithrombotic decision is made. May start in ED, but do not delay transfer to the ICU for UFH initiation. See [CHCO Formulary: Heparin](#) for bolus and maintenance dosing recommendations ([Anticoagulant Treatment](#)).
- 1. Patient is **hemodynamically unstable**: Consider thrombolysis ([Thrombolytic Treatment](#)), following review of [indications and contraindications for thrombolytic therapy](#), if consensus achieved between Cardiology, PICU, and Hematology attending physicians and informed consent given by patient/parents.
- 2. Patient is **hemodynamically stable**, but echocardiogram demonstrates RV dysfunction:
 - Consider thrombolysis, following review of [indications and contraindications for thrombolytic therapy](#), if consensus achieved between Cardiology, PICU, and Hematology attendings and informed consent given by patient/parents. If not, start UFH anticoagulation without starting thrombolysis ([Anticoagulant Treatment](#)).
 - If renal insufficiency or concern for increased bleeding risk (e.g., recent surgery, impending non-elective surgery, clinical instability, disseminated intravascular coagulation (DIC), liver disease), thrombolysis is not recommended. Proceed to [Anticoagulant Treatment](#).
- 3. Patient **hemodynamically stable** and echocardiogram **DOES NOT demonstrate RV dysfunction**: Start UFH anticoagulation without instituting thrombolysis ([Anticoagulant Treatment](#)).
- **For management of antithrombotic therapy and/or thrombolysis, see [Clinical Management of Anticoagulation and Thrombolysis section](#).**

INITIAL EVALUATION I SUSPECTED DEEP VEIN THROMBOSIS (DVT)

If signs of venous compartment syndrome, then consult Hematology and General Surgery for consideration of vascular surgery.

Evaluate

- Vital signs and physical exam
- Keep patient NPO (except medications) if considering interventional radiology procedure

Obtain Imaging and Labs

- Extremity/neck: ultrasound with Doppler
- Non-extremity or ultrasound not possible: MR venogram (preferred) or CT venogram
- Consider IV access and CBC, PT, PTT, fibrinogen, and D-dimer
- Urine β -HCG, if appropriate

Evaluate Imaging Results

If DVT confirmed:

- Proceed to [Contact section below](#)

If NO DVT diagnosed:

- Consider alternative diagnoses

Contact

- Contact Hematology
 - Page Hematology Fellow on-call (if at Colorado Springs Hospital, page Hematology Attending directly)
 - Discuss initial antithrombotic management
 - Consider obtaining ESR, CRP, and hypercoagulability evaluation (or parts of the panel that will guide acute clinical care)
 - Hematology will contact Interventional Radiology for considerations of thrombolysis ([Thrombolytic Treatment](#))
- If central nervous system thrombosis, consult Neurology in addition to Hematology

Evaluate for Thrombolysis

- Primary team, hematology, and interventional radiology to discuss need for thrombolysis
- For management of antithrombotic therapy and/or thrombolysis, see [Clinical Management of Anticoagulation and Thrombolysis](#)

Other Considerations

- Adequacy of imaging to evaluate the full extent and occlusiveness of thrombus (consider CT or MR)
- Vascular anatomic variants (e.g. May-Thurner Syndrome, atretic inferior vena cava, Paget-Schroetter, cervical rib)

CLINICAL MANAGEMENT OF ANTICOAGULATION AND THROMBOLYSIS IN CONFIRMED PE AND/OR DVT

Anticoagulant Treatment

- Give UFH IV bolus (unless contraindicated per [Anticoagulation Dosing and Monitoring Guideline](#)) and continuous IV infusion per [CHCO Formulary: Heparin](#).
- Obtain heparin assay – unfractionated (code L1220) by peripheral draw (venipuncture/fingerstick/heelstick) 4 hours after the initiation of heparin infusion.
 - Heparin assay- unfractionated goal is 0.3-0.7 unit/mL with UFH.
 - Adjust per [CHCO Formulary: Heparin](#).

- Maintain platelet count greater than/equal to 30 K/ μ L, and fibrinogen greater than/equal to 75 g/dL. If patient requires invasive procedure, discuss coagulation and platelet parameters with proceduralist.
- Monitor clinically for signs/symptoms of bleeding (premature neonates: add serial head U/S). Recheck heparin assay – unfractionated (code L1220) as necessary per [CHCO Formulary: Heparin](#).
- CBC at least every 5 days during heparin therapy in the absence of interim bleeding concerns. Notify Hematology for decline in platelet count (concern for heparin-induced thrombocytopenia).

If no major bleeding concerns and renal function stable:

- May give LMWH ([CHCO Formulary: Enoxaparin](#)) as a subcutaneous injection.
- Obtain Heparin – Low Molecular Weight assay (code L1221) after at least 2 doses of LMWH (enoxaparin), by peripheral draw (venipuncture/fingerstick/heelstick) 4 hours after LMWH (enoxaparin) dose given.
- Heparin – Low Molecular Weight assay goal range: 0.5-1.0 units/mL.
- Adjust per [CHCO Formulary: Enoxaparin](#).
- Maintain platelet count greater than/equal to 30 K/ μ L. If patient requires invasive procedure, discuss coagulation and platelet parameters with proceduralist.
- Monitor clinically for signs/symptoms of bleeding. Recheck Heparin- Low Molecular Weight assay (code L1221) 4 hours post-dose change or as needed for bleeding concerns, changes in renal function, or change in weight by greater than 10%.

Thrombolytic Treatment

Cardiology Consult team to request catheter-directed thrombolysis by Interventional Cardiology for pulmonary embolism (cardiopulmonary circulation) with hemodynamic compromise.

Hematology Consult team to request catheter-directed thrombolysis by Interventional Radiology for deep vein thrombosis outside of cardiopulmonary circulation.

In consultation with Hematology, consider systemic thrombolysis if emergent hemodynamic compromise not amenable for catheter-directed thrombolysis.

[See contraindications to alteplase in Appendix 1 on page 11](#)

If no contraindications to alteplase:

1. Hematology to assist in discussion of risk and benefits of thrombolysis with patient/family.
2. Document patient/family agreement with thrombolysis.
3. Catheter-directed thrombolysis with alteplase:
 - Initial rate:
 - Infants and children less than 12 years: administer alteplase through catheter per [CHCO Formulary: Alteplase](#) up to 1mg/hour.
 - Adolescents and adults: administered alteplase through 1 or 2 lysis catheters per [CHCO Formulary: Alteplase](#) up to a total max of 1 mg/hour.
 - If insufficient clot dissolution following initial rate:
 - Consider increasing alteplase rate to a total max of 2.5mg/hour.
 - Higher alteplase doses should be discussed with applicable consulting teams.
 - While infusing catheter-directed alteplase, infuse concomitant low-dose UFH through vascular sheath (side-port).
 - Infants and children less than 12 years: infuse starting at 20 units/kg/hr (consider titrate to target Anti-Xa level of 0.1-0.3 u/ml).

- Adolescents and adults: infuse starting at 10 units/kg/hr (consider titrate to target Anti-Xa level of 0.1-0.3 u/ml).
 - When alteplase therapy is complete, patient should be immediately converted to therapeutic anticoagulation with UFH, dosed per [CHCO Formulary: Heparin](#) to achieve Anti-Xa goal of 0.3-0.7 u/ml.
4. Systemic alteplase:
- Infants and children less than 12 years: Begin continuous IV infusion per [CHCO Formulary: Alteplase](#) up to a total max of 2.5 mg/hour.
 - Adolescents and adults with pulmonary embolism, may consider alteplase 100 mg IV bolus (infused over 15 minutes).
 - While infusing alteplase IV, infuse concomitant low-dose UFH:
 - Infants and children less than 12 years: infuse starting at 20 units/kg/hour to target Anti-Xa level of 0.1-0.3 u/ml.
 - Adolescents and adults: infuse starting at 10 units/kg/hour to target Anti-Xa level of 0.1-0.3 u/ml.
 - When alteplase therapy is complete, patient should be immediately converted to therapeutic anticoagulation with UFH, dosed per [CHCO Formulary: Heparin](#) to achieve Anti-Xa goal of 0.3-0.7 u/ml.
 - Efficacy monitoring of systemic alteplase administration:
 - Check d-dimer and plasminogen 6 hours after initiation of alteplase infusion
 - ❖ If d-dimer increases, there is evidence of fibrinolysis and infusion is likely adequate.
 - ❖ If d-dimer does not increase and plasminogen is below 70 units/dL or 70% in non-neonatal children, consider administering FFP 10ml/kg to enhance alteplase.
5. Safety Monitoring of alteplase: Check CMP daily, and CBC, PT/INR, PTT, anti-Xa (for heparin titration, consider goal range 0.1-0.3 u/mL) and fibrinogen every 6 hours during systemic alteplase infusion.
- If fibrinogen drops by 50%, decrease alteplase dose in half and recheck fibrinogen in 3 hours.
 - Run additional normal saline in catheter to maintain catheter patency.
 - If fibrinogen is less than 100 or platelets less than 100 K/ μ L, stop alteplase and evaluate for bleeding. Consult Hematology and Interventional Radiology.
 - Give cryoprecipitate as needed to achieve of 100 mg/dL and platelet transfusion as needed to maintain platelet count of 100 K/ μ L.
6. Strict bed rest (no bathroom privileges), elevate head of bed if appropriate, and clear liquid diet. May need to intubate and sedate patients who are unable to comply with bed rest. Hourly vital signs and access site checks. Neurologic checks every 2 hours.
7. Monitor clinically for signs/symptoms of bleeding. **Stop alteplase 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 alteplase for any severe headache or any neurologic changes** (until intracranial hemorrhage is excluded by STAT CT or ultrasound of the brain).
8. Notify Provider of any changes in patient's assessment:
- Fever or change in vital signs
 - Increase in pain
 - Irritability
 - Diaphoresis

FURTHER MANAGEMENT CONSIDERATIONS

- Continue anticoagulant and/or thrombolytic treatment
- Consider institution of peptic ulcer prophylaxis
- Consider risk of bleeding against benefits of any invasive or noninvasive procedure in the context of the bleeding risk of Alteplase (i.e. central or arterial lines, Foley catheter, feeding tube placement):
 - Consider waiting at least 1 hour after alteplase infusion is discontinued for procedures
 - Lumbar puncture is contraindicated until alteplase infusion has been discontinued
- Documentation of bilateral (affected and unaffected) limb circumferences:
 - Hematology to document bilateral (affected and unaffected) circumferences in initial consult note
 - Primary hospital service to document bilateral (affected and unaffected) circumferences in daily progress notes
- Flat time after systemic or catheter-directed Alteplase:
 - Hold pressure on any puncture sites until bleeding or hematoma development ceases.
 - For femoral vein access, bed rest with hips flat for 2 hours after removal of femoral venous sheath.
 - For femoral arterial access, bed rest with hips flat for 4 hours after removal of femoral arterial sheath.
- If patient's cardiorespiratory signs/symptoms worsen, obtain urgent repeat CTA Chest with contrast (specify "PE protocol" in comments)
- If extension of PE has occurred on therapeutic anticoagulation, strongly consider thrombolysis

APPENDIX 1. INDICATIONS AND CONTRAINDICATIONS FOR THROMBOLYTIC THERAPY FOR ACUTE VTE

Indications (ONE of the following criteria must be met)

1. Acute pulmonary embolism with evidence of severe right heart strain
2. Pulmonary embolism with hemodynamic instability
3. Proximal limb DVT with concern for acute limb ischemia
4. Completely veno-occlusive limb DVT with high risk for post thrombotic syndrome

***For all contraindications the risk versus benefit of treatment must be weighed in patients with life-threatening thrombosis where alteplase may be the only option.**

Contraindications* (ABSOLUTE for Systemic alteplase)

1. Evidence of active hemorrhage
2. Major surgery or other serious trauma during preceding 2 weeks
3. Neurosurgery, serious traumatic brain injury, or arterial ischemic stroke during preceding 4 weeks
4. Recent history of intracranial hemorrhage
5. Lumbar puncture or other invasive procedure during preceding 72 hours
6. Gastrointestinal or urinary tract hemorrhage during preceding 3 weeks
7. Uncontrolled hypertension
8. Clinical presentation suggesting endocarditis, pericarditis or large myocardial infarction
9. Known AVM, aneurysm, CNS mass, or moyamoya
10. Status epilepticus
11. History of anaphylaxis to alteplase

Additional RELATIVE Contraindications*

1. Pregnant female
2. Recent unfractionated heparin use with anti-factor Xa activity greater than/equal to 0.4 at time of planned thrombolysis (therapeutic unfractionated heparin should be reduced to prophylactic dosing (10 units/kg/hr) at least 2 hours prior to initiation of systemic alteplase)
3. Recent low molecular weight heparin (LMWH, enoxaparin) use with LMWH anti-factor Xa activity greater than/equal to 0.6 at time of planned thrombolysis (therapeutic LMWH should be stopped or reduced to prophylactic dosing at least 12 hours prior to initiation of systemic alteplase)
4. PTT (specimen drawn by clean peripheral venipuncture) prolonged by greater than to 4 seconds at time of planned thrombolysis *that normalizes following 1:1 mixing* with pooled plasma standard (N.B.: a prolonged PTT that doesn't correct on 1:1 mix is NOT a contra-indication, as this likely represents a lupus anticoagulant rather than a factor deficiency)
5. INR greater than/equal to 1.6 at time of planned thrombolysis (if clinically appropriate, may consider FFP or low-dose vitamin K administration to reduce INR, in order to avert contraindication)
6. Fibrinogen less than 100 g/dL at time of planned thrombolysis (if clinically appropriate, may consider cryoprecipitate or FFP to increase fibrinogen, in order to avert contraindication)
7. Platelet count less than 100 K/ μ L at time of planned thrombolysis (if clinically appropriate, may transfuse platelets to increase platelet count, in order to avert contraindication)
8. Aspirin or other platelet inhibitor use within preceding 7 days (if clinically appropriate, may transfuse platelets to increase platelet count, in order to avert contraindication)
9. Direct oral anticoagulant (eg. dabigatran, rivaroxaban, apixaban, edoxaban) administered in the last 48 hours. If on these agents, discuss risks/benefits with hematology.
10. Arterial puncture at non-compressible site during preceding 5 days
11. Stroke or serious traumatic brain injury during preceding 3 months
12. Left heart thrombus (mechanical thrombolysis)
13. Left-to-right shunt (mechanical thrombolysis)
14. Infected thrombus (mechanical thrombolysis)
15. CPR with chest compressions within past 10 days
16. Invasive procedure (other than major surgery) or lumbar puncture within past 5 days
17. Known bleeding disorder/tendency (includes significant renal and hepatic insufficiency)
18. Hepatic or renal dysfunction
19. Life expectancy less than 6 months from other causes

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Pharmacy & Therapeutics Committee – December 5, 2019
 Clinical Pathways and Measures Committee – December 17, 2019
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REVIEW | REVISION SCHEDULE

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ማስታወሻ: የሚናገሩት ቋንቋ አማርኛ ከሆነ የትርጉም አገልግሎት ድርጅቶቹ በነጻ ሊያግዝዎት ተዘጋጅተዎልዎት ወይ ሚከተለው ቁጥር ይደውሉ 1-720-777-9800 (መስማት ስተሳናቸው)።

ملحوظة: إذا كنت تتحدث انكر اللغة، فإن خدمات المساعدة اللغوية تتوافر لك بالمجان. اتصل برقم 1-720-777-9800.

ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 1-720-777-9800.

ATTENTION : Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-720-777-9800.

ध्यान दनु होस्तपाइले नेपाल बोलनहनछ भन तपाइको निम्त भाषा सहायता सवाहूरू नःशुल्क रूपमा उपलब्ध छ । फोन गनु होस्तू 1-720-777-9800 ।

PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 1-720-777-9800.

注意事項: 日本語を話される場合、無料の言語支援をご利用いただけます。1-720-777-9800 まで、お電話にてご連絡ください。

Nti: O buri na asu lbo, asusu aka oasu n'efu, defu, aka. Call 1-720-777-9800.