

PULMONARY EMBOLISM (PE), SUSPECTED ACUTE ALGORITHM

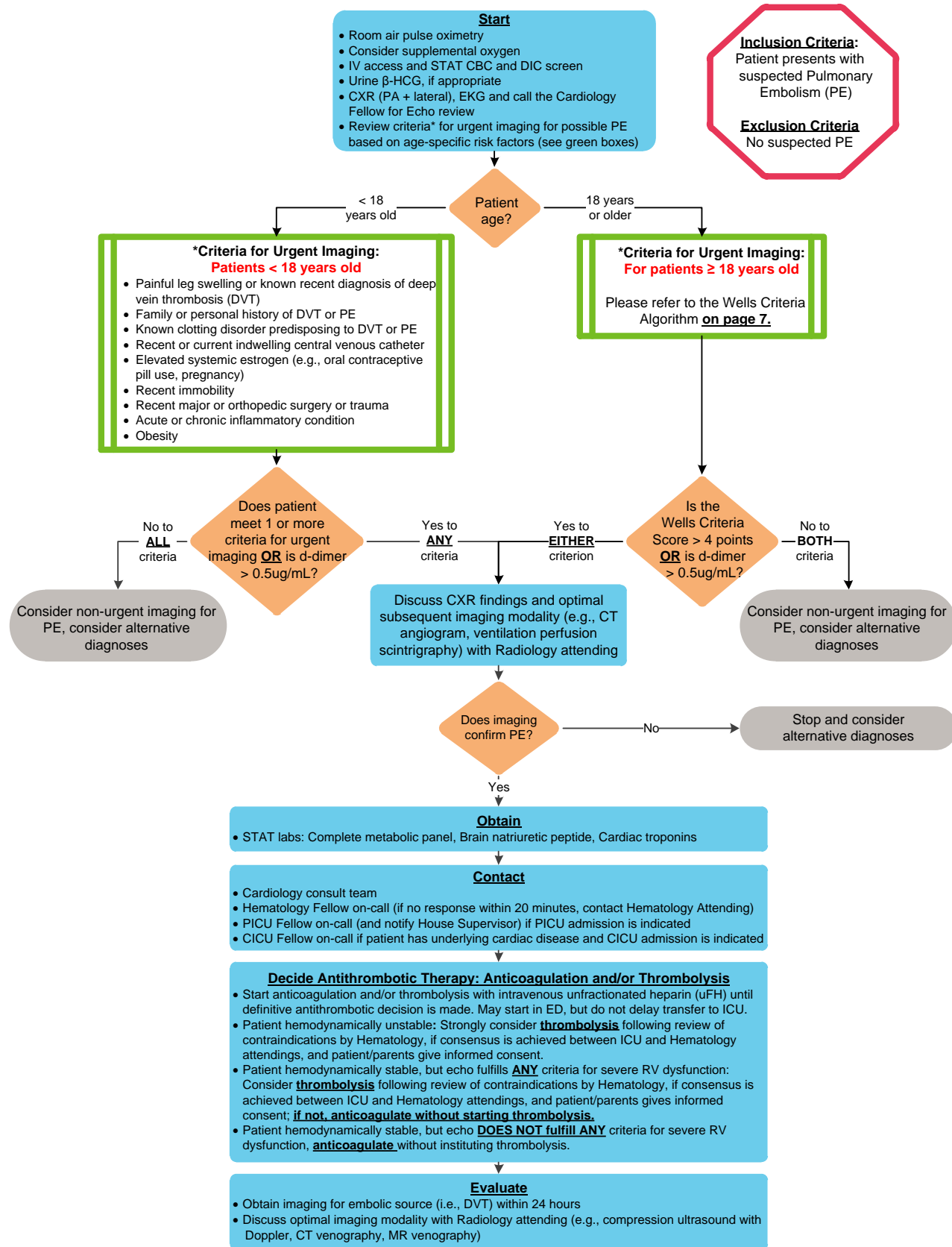


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TARGET POPULATION

Inclusion Criteria: PE Risk Factors

- Recent onset/worsening of unexplained shortness of breath or pleuritic chest pain (absence of known underlying cardiac disease, lung disease, or suspected acute pneumonia)
- Recent onset/worsening of shortness of breath or pleuritic chest pain, in the presence of known underlying cardiac disease, lung disease, or suspected acute pneumonia, but with one of the following PE risk factors present:
 - Painful leg swelling or known recent diagnosis of deep vein thrombosis (DVT)
 - Family or personal history of DVT or PE
 - Known clotting disorder predisposing to DVT or PE
 - Recent or current indwelling central venous catheter
 - Elevated systemic estrogen (e.g., oral contraceptive pill use, pregnancy)
 - Recent immobility
 - Recent major or orthopedic surgery
 - Acute or chronic inflammatory condition
 - Obesity

Exclusion Criteria

- No suspected PE

BACKGROUND | DEFINITIONS

- PE - Pulmonary Embolism
- DVT - Deep Vein Thrombosis
- LMWH - Low Molecular Weight Heparin
- UFH - Unfractionated Heparin

CLINICAL MANAGEMENT

Goal: Complete steps 1 and 2 within one hour of presentation of suspected PE

Step 1. Start

- Room air pulse ox
- Consider supplemental oxygen
- IV access and STAT CBC and DIC screen
- Urine β -HCG, if appropriate
- Chest x-ray (CXR) (PA + lateral), EKG and call the Cardiology Fellow for Echo review

Step 2. Evaluate for Urgent Imaging

Does patient meet one or more of the following criteria for urgent imaging for possible PE?

- Painful leg swelling or known recent diagnosis of DVT
- Family or personal history of DVT or PE, especially before age 55 yrs.
- Known clotting disorder predisposing to DVT or PE (“thrombophilia”)
- Recent or current indwelling central venous catheter
- Elevated systemic estrogen (e.g., oral contraceptive pill use, pregnancy)
- Recent immobility
- Recent major or orthopedic surgery
- Recent major or orthopedic trauma
- Acute or chronic inflammatory condition (e.g., severe infection, systemic lupus erythematosus or other autoimmunity)
- Obesity

Consider [Wells' Criteria](#)⁸ for patients 18 years and older. Refer to [Wells Scoring algorithm](#)⁸.

YES: (Step 2a.)

- Consider chest spiral CT angiogram for all patients as first line. If chest spiral CT angiogram is contraindicated discuss lung perfusion scintigraphy with radiology attending to determine availability.
- Proceed to [Step 3](#).

NO: (Step 2b.)

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

Step 3. Evaluate for Imaging**Does appropriate imaging confirm the diagnosis of PE?****YES: PE Confirmed (Step 3a.)**

- Proceed to [Step 4.](#)

NO: PE is not confirmed (Step 3b.)

- If clinical suspicion for PE is high, consider further imaging for DVT.
- If not, STOP and evaluate for alternative diagnoses.

Step 4. Obtain

- STAT Labs: Complete metabolic panel, brain natriuretic peptide (BNP), cardiac troponins.

Step 5. Contact

1. Contact Cardiology Consult team to discuss indications (any ONE of the following) for urgent echocardiogram:
 - Hemodynamic instability
 - RV strain on EKG
 - Room air oxygen saturation less than/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 none of the above is present, discuss the need for non-urgent Echo with Cardiology.**

2. Contact Hematology Fellow on-call (if no response within 20 minutes, contact Hematology Attending)
 - Discuss initial antithrombotic management using decision tree below.
 - If urgent echocardiogram is indicated or thrombolysis will otherwise be considered, then Hematology to evaluate patient at bedside within 1 hour of consultation.
 - If urgent echocardiogram is indicated, start anticoagulation with intravenous uFH until definitive antithrombotic decision is made.
3. Contact the appropriate ICU (PICU or CICU) Fellow on-call (and notify House Supervisor) if admission is indicated.

Step 6. 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.
- Patient is hemodynamically unstable: Strongly consider thrombolysis ([Step 6b](#)), following review of [indications and contraindications for thrombolytic therapy](#), if consensus achieved between ICU and Hematology attendings, and informed consent given by patient/parents.

- Hemodynamic instability is defined as the requirement for any pressor support in a patient without underlying primary cardiac disease, or as the requirement for any new/increase in pressor support in a patient with underlying primary cardiac disease.
- Patient is hemodynamically stable, but Echo fulfills **ANY** of the RV dysfunction criteria:
 - RV dysfunction is defined as: Severe RV dilation, (or) D-shaped LV (significant intraventricular septal flattening), (or) right ventricular hypertension (TR velocity greater than >3 m/s or estimated RV pressure greater than 50% of systemic pressure).
 - Consider thrombolysis following review of [indications and contraindications for thrombolytic therapy](#), if consensus achieved between ICU and Hematology attendings, and informed consent given by patient/parents ([Appendix 1](#)); If not, anticoagulate without starting thrombolysis ([Step 6b](#)).
 - 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 [Step 6a](#).
- Patient hemodynamically stable and Echo **DOES NOT fulfill ANY criteria** for thrombolysis, anticoagulate without instituting thrombolysis ([Step 6a](#)).

Step 6a. Anticoagulant Treatment

1. Give unfractionated heparin IV bolus and continuous IV infusion per CHCO formulary.
2. Obtain anti-Xa level, specify “unfractionated heparin”, by peripheral venipuncture 4 hours after the initiation of heparin infusion (8 hours if bolus is withheld because of clinical judgement).
 - Anti-Xa goal is 0.3-0.7 unit/mL
 - Adjust per Anticoagulation Dosing and Monitoring Protocols
3. Maintain platelet count greater than/equal to 50K/ μ L, 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 FFP transfusion, if required).
4. Monitor clinically for signs/symptoms of bleeding (premature neonates: add serial head U/S). Recheck anti-Xa level when necessary for bleeding concerns.
5. CBC with platelet count every 24 to 48 hrs. in the absence of interim bleeding concerns. Notify Hematology 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 100K/ μ L.

If no major bleeding concerns or unstable renal function:

1. May give low molecular weight heparin (LMWH) as a subcutaneous injection: for current LMWH on-formulary, view enoxaparin in LexiComp.
2. Anti-Xa goal range: 0.5-1.0 units/mL
3. Adjust per CHCO's Anticoagulation Dosing and Monitoring Protocols. Maintain platelet count greater than/equal to 50,000 (units?), 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 FFP transfusion, if required).
4. Monitor clinically for signs/symptoms of bleeding. Recheck 4 hours post-dose anti-Xa LMWH assay prn bleeding concerns or changes in renal function.
5. Proceed to [Step 7](#).

Step 6b. Thrombolytic Treatment ([see contraindications](#))

Hematology bedside patient evaluation within 2 hours of consult request (if performed by fellow, includes review with attending)

If no contraindications to systemic tPA:

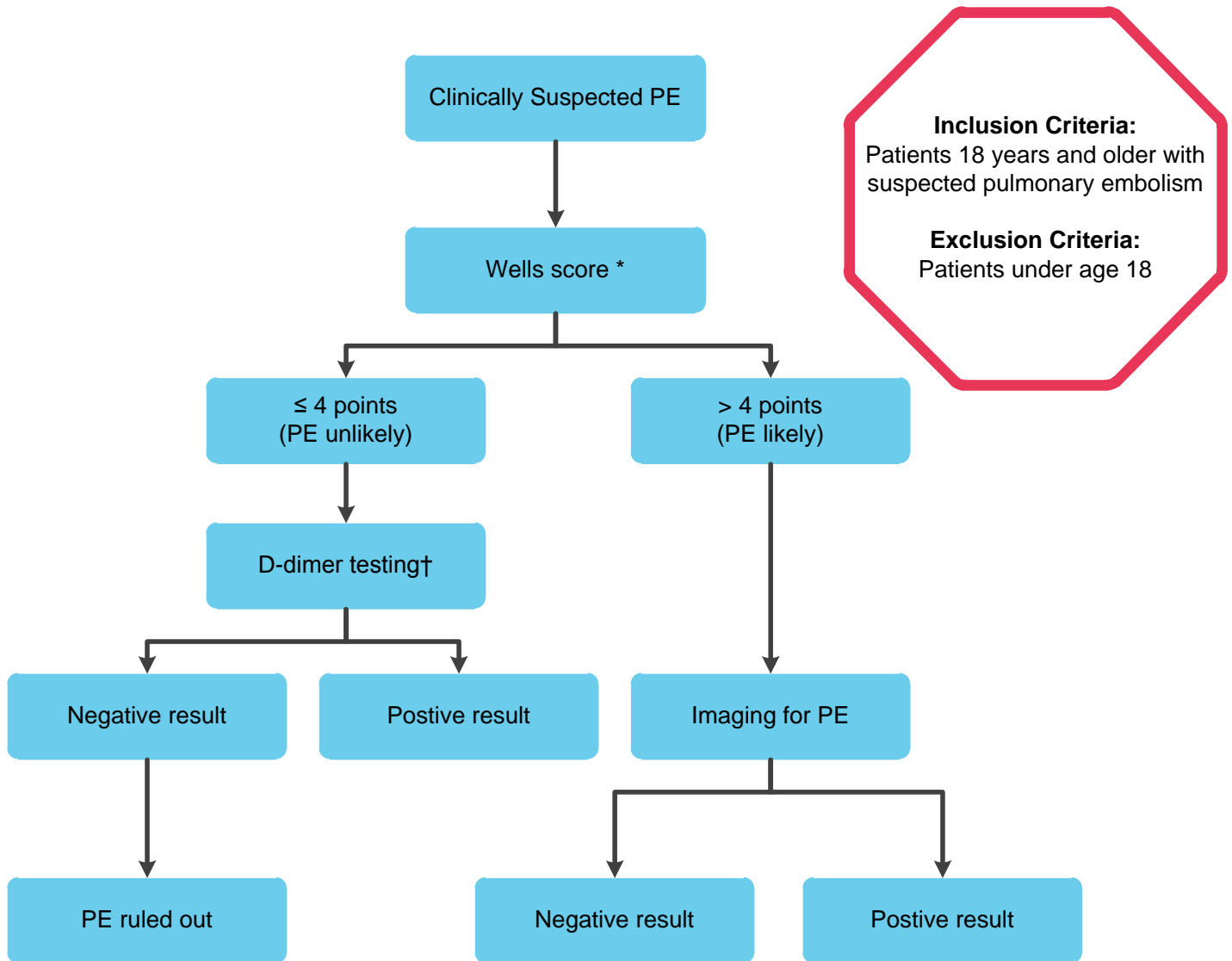
1. Hematology to assist in discussion of risk and benefits of systemic thrombolysis with patient/family.
2. Document patient/family agreement with systemic thrombolysis.
3. Begin continuous IV infusion of systemic tPA at 0.03 mg/kg/hour to 0.1 mg/kg/hour (max: 2.5 mg/hr). For adults or teens weighing at least 50kg, may consider tPA 100mg IV infused over 15 minutes to 2 hours depending upon clinical severity.
4. Give concomitant IV infusion of low-dose unfractionated heparin at 10 units/kg/hr while receiving tPA, when tPA is complete patient should be immediately changed to therapeutic doses of heparin.
5. Check plasminogen level and CBC daily, and DIC screen every 6 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 echocardiogram daily for up to four days or stop sooner if severe RV dysfunction resolves.
8. When RV dysfunction by echocardiography resolves OR after 96 hours post-initiation of tPA infusion, consider discontinue tPA infusion and switch low-dose unfractionated heparin infusion to therapeutic anticoagulation (see part 6a above). If longer infusion is being considered this needs to be a deliberate decision by all treating providers and parents/patient.

Step 7. Evaluate for Source

Obtain imaging for embolic source (i.e. DVT) within 24 hours

- Discuss optimal imaging modality with Radiology attending (e.g., compression ultrasound with Doppler, CT venography, MR venography)
- *Patient with unilateral chest/arm swelling or central venous catheter at chest/arm:* image ipsilateral arm
- *Patient with unilateral leg swelling or central venous catheter at leg:* image ipsilateral leg and pelvis
- *Patient without signs/symptoms of DVT:* image bilateral legs and pelvis.
- If evidence of proximal DVT, see also [Acute Proximal DVT Clinical Pathway](#).

ALGORITHM. Wells Scoring⁸



* 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 deep venous thrombosis (3 points), previous deep venous thrombosis or PE (1.5 points), tachycardia (1.5 points), immobilization or surgery within the past 4 wk (1.5 points), active cancer (treatment in the past 6 mo, current treatment, or palliative care; 1 point), and hemoptysis (1 point).

† Fixed D-dimer testing (≤500 µg/L) or age-adjusted D-dimer testing (age x 10 µg/L in patients aged >50 years), according to study protocol.

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 – refer to the [proximal VTE clinical pathway](#)
4. Completely veno-occlusive limb DVT with factor VIII greater than/equal to 150 units/dL and D-dimer greater than/equal to 0.5 µg/mL

***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 tPA)

1. Evidence of active hemorrhage
2. Prior history of intracranial hemorrhage
3. Neurosurgery, serious head trauma, or arterial ischemic stroke during preceding 4 weeks
4. Gastrointestinal or urinary tract hemorrhage during preceding 3 weeks
5. Major surgery (other than neurosurgery) or other serious trauma (other than head trauma) during preceding 2 weeks
6. Lumbar puncture or other invasive procedure during preceding 72 hours
7. Uncontrolled hypertension
8. Clinical presentation suggesting endocarditis, pericarditis or large myocardial infarction
9. Platelet count less than 100,000/mm³ at time of planned thrombolysis (if clinically appropriate, may transfuse platelets to increase platelet count, in order to avert contraindication)
10. 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)
11. 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)
12. Known AVM, aneurysm, CNS mass, or moyamoya
13. Status epilepticus
14. History of anaphylaxis to tPA

Additional RELATIVE Contraindications*

15. Pregnant female
16. Recent unfractionated heparin use with anti-factor Xa activity (on a blood sample drawn by clean peripheral venipuncture) 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 tPA)
17. Recent low molecular weight heparin (LMWH) use with LMWH anti-factor Xa activity (on a blood sample drawn by clean peripheral venipuncture) 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 tPA)
18. INR (specimen drawn by clean peripheral venipuncture) 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)
19. Arterial puncture at non-compressible site during preceding 5 days
20. Lumbar puncture during preceding 5 days
21. Stroke or serious head trauma during preceding 3 months
22. CPR with chest compressions within past 10 days
23. Recent dabigatran administration within the preceding 24 hours (consider the use of idaracizumab to reverse the anticoagulant effect of dabigatran prior to tPA administration)
24. Invasive procedure (other than major surgery or lumbar puncture) within past 5 days
25. Known bleeding disorder/tendency (includes significant renal and hepatic insufficiency)
26. Aspirin or other irreversible platelet inhibitor use within preceding 7 days
27. Life expectancy less than 6 months from other causes

CARDIOLOGY CHECKLIST FOR RIGHT VENTRICULAR (RV) DYSFUNCTION EVALUATION IN ACUTE PE

(Patient meets any ONE of the following criteria)

- | | | |
|-----------|----------|---|
| Yes _____ | No _____ | 1. Severe RV dilation |
| Yes _____ | No _____ | 2. D-shaped LV (significant intraventricular septal flattening) |
| Yes _____ | No _____ | 3. Right ventricular hypertension (TR velocity greater than >3 m/s or estimated RV pressure greater than 50% of systemic RV pressure) |

FURTHER MANAGEMENT SETTING: FLOOR/ICU

- Continue anticoagulant and/or thrombolytic treatment
- Consider institution of peptic ulcer prophylaxis
- For systemic tPA: No central lines, Foley catheters, NG tube placement, arterial punctures, or other similar invasive procedures until at least 1 hour after completion of tPA infusion. If any of those are needed, stop tPA for 1 hour and do not restart unless there is clinical consensus that the benefits outweigh the risks.
- For systemic tPA: Compression of arterial and venous puncture sites x 4 hours after completion of tPA infusion
- Hematology bedside patient evaluation within 24 hours of consult request (within 2 hours of consult request if thrombolysis is being considered)
- If recurrent PE (new, radiologically-documented event) occurs on therapeutic anticoagulation or during systemic thrombolysis: consult IR for temporary IVC filter placement
- If patient's cardiorespiratory signs/symptoms worsen, obtain urgent repeat spiral CT angiogram of the chest
- If extension of PE has occurred on therapeutic anticoagulation, strongly consider systemic tPA
- If extension of PE has occurred on systemic tPA, strongly consider urgent UCH IR consultation for possible interventional thrombectomy/thrombolysis, therapeutic or at minimum prophylactic levels of anticoagulation (typically with unfractionated heparin) should be maintained during interventional thrombectomy/thrombolysis.
- If patient is hemodynamically unstable and not responding to systemic tPA, strongly consider urgent UCH IR consultation for possible interventional thrombectomy/thrombolysis. Therapeutic or at minimum prophylactic levels of anticoagulation (typically with unfractionated heparin) should be maintained during interventional thrombectomy/thrombolysis.

PRIOR TO DISCHARGE

- Schedule follow-up in Thrombosis Clinic at 2-4 weeks post-diagnosis
- Arrange Hematology oversight of any anticoagulation (LMWH/warfarin) and its monitoring, as warranted

APPENDIX 1. ADDITIONAL DIAGNOSTIC CONSIDERATIONS FOR PE

Indications for radiologic imaging for possible PE rely upon clinical judgment; however, a few issues discussed below are worthy of consideration.

Who should (and should not) be imaged for diagnosis of possible PE?

Data in adults suggests that patients in whom there is high clinical suspicion for PE and in whom D-dimer is elevated are highly likely to have PE, while patients with low clinical suspicion who have a negative D-dimer have a low likelihood for PE. This has not been systematically evaluated in children. Therefore, diagnostic radiologic evaluation for PE should be strongly considered in any pediatric patient for whom the diagnosis of PE is suspected clinically.

What imaging modality should be used to diagnose PE?

There are no published studies documenting the sensitivity and specificity of diagnostic imaging tests for pulmonary embolism in children. Protocols are usually extrapolated from adult studies with little justification for their applicability to children. The following imaging modalities have been used to evaluate children with clinical concern for PE: chest radiograph, chest CT angiography (CTA), pulmonary magnetic resonance angiography (MRA) and conventional pulmonary angiography. If indicated, may use ventilation/perfusion scintigraphy in lieu of CTA (refer to [Radiology Diagnostic Imaging algorithm](#)).

Evaluation should begin with **chest radiograph** (frontal and lateral views). Radiographic findings in a patient with PE include airspace disease, atelectasis, pleural effusion, hypovascularity in a lung zone (Westermark sign) and a pyramid-shape opacity with peak directed to the hila (Hampton hump). Unexpected findings (pneumothorax, mass) may alter the diagnostic algorithm away from evaluation for PE.

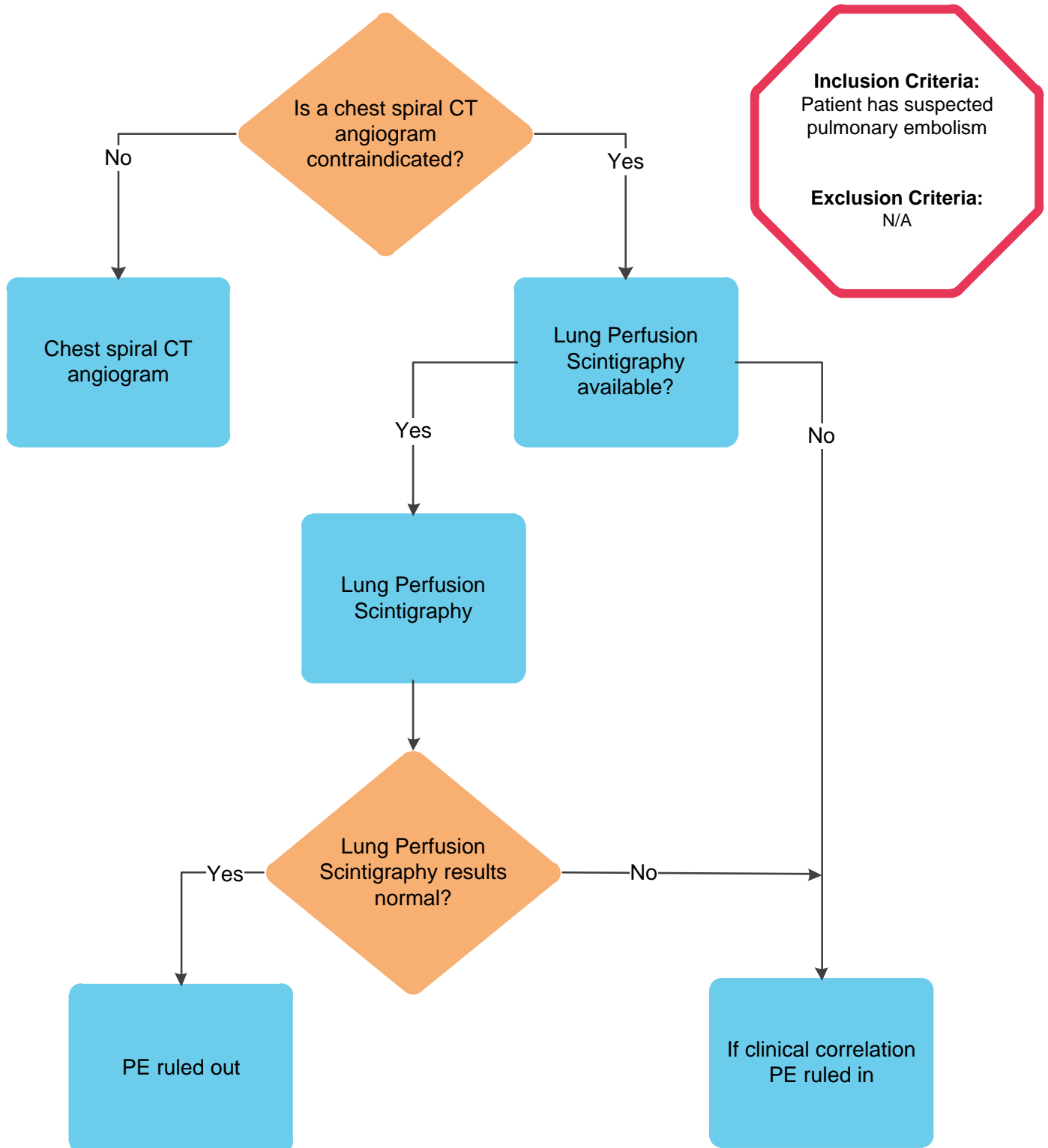
CTA should be considered the preferred imaging modality, given the lower radiation dose and increased yield regarding pulmonary parenchymal disease and other differential diagnoses. Perfusion Scintigraphy should be reserved for those with renal impairment or other contraindications to CT/MR.

There are several proven advantages of CTA over V/Q scan in adults: ability to visualize the thrombus directly, identify other diagnoses if PE is not present, more cost-effective (with fewer indeterminate and non-diagnostic results) and higher inter-observer agreement. Central non-obstructive emboli can be clearly visible on CTA but may have normal pulmonary perfusion on scintigraphy. CTA has demonstrated high sensitivity and specificity in detection of main, lobar and segmental pulmonary arteries but less with sub-segmental emboli, although this may be improved with use of dual energy CT technology which enables a map of the distribution of iodine within the lung parenchyma, providing functional and quantitative information comparable to scintigraphy.

Pulmonary MRA is a noninvasive imaging technique in diagnosis of PE without the need for ionizing radiation or iodinated contrast media. Disadvantages include long imaging time, need for sedation in young children, and insensitivity to peripheral emboli. MRA is currently contraindicated in patients with pacemakers and some other implants. Sedation should be undertaken with caution in the setting of PE. MRA may be useful in children with suspected PE in whom iodinated contrast allergy poses a contraindication to CTA, particularly when lung perfusion scintigraphy is non-diagnostic. At present PIOPED III investigators suggest that pulmonary MRA should be considered only for patients with contraindications to standard tests and in centers that routinely perform it, however many studies have been recently performed showing MRA to have a similar diagnostic efficacy to CT.

Conventional pulmonary angiography is considered the gold standard for diagnosing PE but has largely been replaced by CTA. Its use is limited because of invasiveness, expense and potential risk (arrhythmia, bleeding, infection, death). The risk of pulmonary angiography in children suspected of PE is not known.

ALGORITHM. Radiology Diagnostic Imaging Schema for Possible PE in a Hemodynamically Stable Patient



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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.