Suspected Acute Pulmonary Embolism (PE) Emergency Department

Center for Clinical Excellence

Inclusion criteria:
Patient of any age with suspected pulmonary embolism

[1]Signs and Symptoms of PE:
(absence of alternate diagnosis or explanation)

- *Shortness of breath
- *Pleuritic and non-reproducible chest pain
- *Cough
- Hemoptysis
- +/-Limb swelling (atraumatic)
- Tachycardia
- Tachypnea
- Oxygen saturations <95%
- +/-Fever

* *This triad is most common*

Patient with Congenital Heart Disease

[3]Work-up

- CBC
- CMP
- D Dimer
- PT
- PTT
- Fibrinogen
- Thrombin Time
- Serum β HCG (female ≥ 10)
- Lactate
- BNP
- Troponin
- EKG
- Hypercoagulable panel

Concern for Pulmonary Embolism (PE)

- Oxygen for O2 sats < 90%
- Make NPO
- Place IV
- Continuous Monitors

Consider Risk Factors[2]

Evaluate for Signs and Symptoms[1]

Signs of shock?

Yes → **Proceed to Management**

No → **Decision support for D Dimer versus CTPA**

- CT Pulmonary Angiogram *(if indicated)*
- Complete work-up[3]

Imaging confirms PE?

Yes →

Start Unfractionated Heparin (UFH)
(see order set)

- Ensure labs[3] drawn prior to starting UFH
- Order associated monitoring labs

UFH relative contraindications

- **Consult Hematology**
- **Consult Cardiology**
- **Order STAT echocardiogram**
- **Place 2nd IV**
- **If at Lewis Center ED, initiate rapid transfer to Main Campus ED**
- **Proceed to PE Classification and Management**

No → **Off Pathway**

[2]Risk Factors for PE:

- Recent (< 1 month) or current indwelling venous catheter
- Significant family history of thrombosis (DVT, PE, early MI or stroke prior to age of 50, recurrent first trimester miscarriages)
- Exogenous estrogen or pregnancy within the past 6 months
- Impaired mobility due to pelvic or long bone fractures (past 3 months)
- Major surgeries, immobility, or illness (past 1 month)
- Acute or chronic inflammatory condition (cancer, nephrotic syndrome, lupus, IBD)
- Inherited thrombophilia (protein S, protein C and antithrombin deficiency, Factor V Leiden, prothrombin gene mutation)
- Antiphospholipid antibodies
- Obesity (weight > 95% for age)
- Current DVT

Consider **PERC-Peds**

Do Not Use **PERC and Wells criteria**

Clinical status can change quickly
Escalate care and for worsening tachycardia, hypotension, or signs of inadequate perfusion

D Dimer Versus CTPA

- If pre-test probability is high based on risk factors and/or symptoms, proceed with CTPA

- If pre-test probability is low (based on assessment of risk factors and/or symptoms), clinical context and expertise should guide further diagnostic decisions regarding d-dimer and/or CTPA.

- In regards to d-dimer screening, the available pediatric literature is limited and consists of mostly small single center retrospective studies. There are studies that show sensitivity of a positive d-dimer in diagnosing PE of 89-90%. With a low pre-test probability, a negative d-dimer may be helpful in ruling out PE without a CTPA.

Initial Evaluation

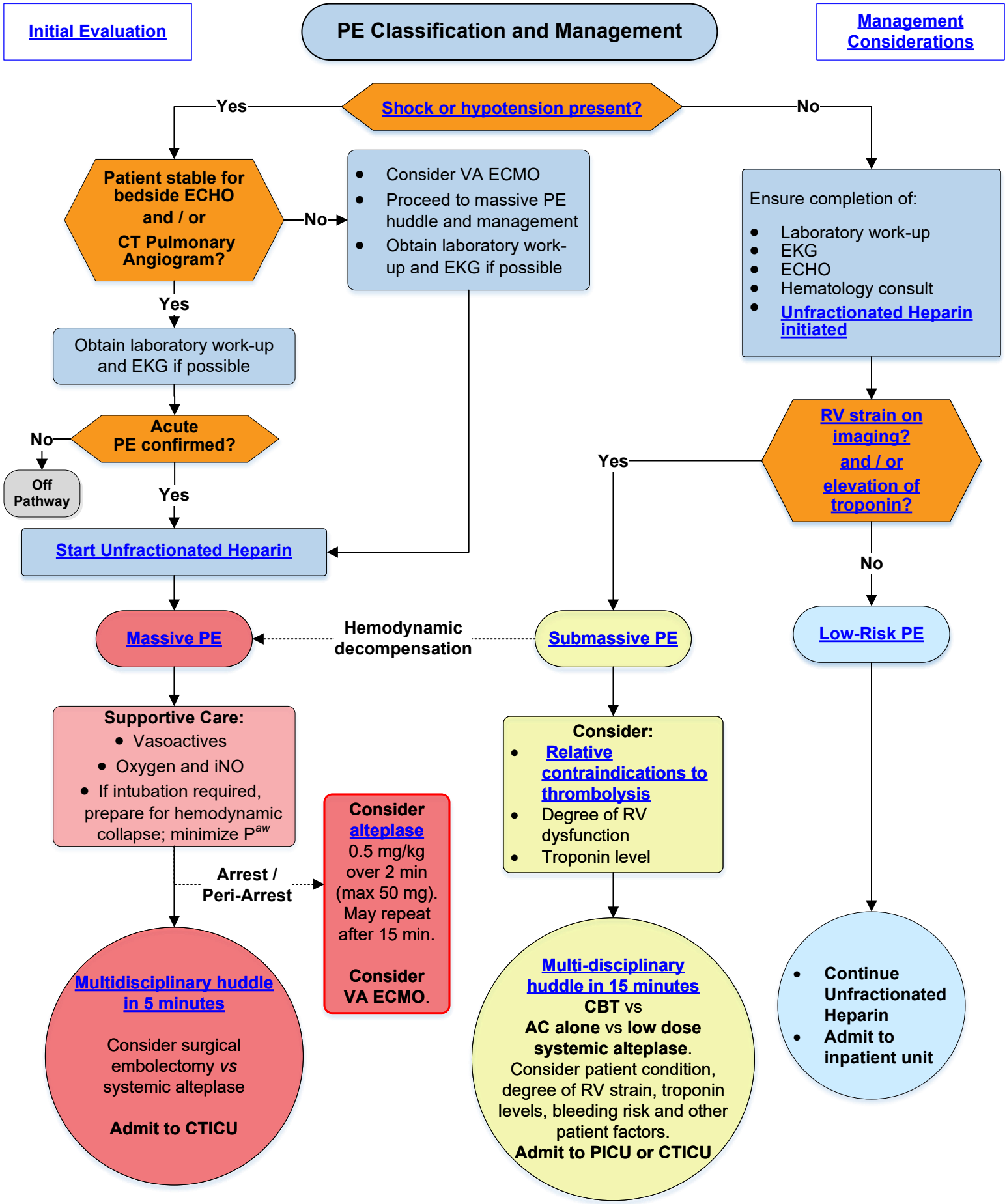
Initial Work-up

- CBC
- CMP
- D Dimer
- PT
- PTT
- Fibrinogen
- Thrombin Time
- Serum β HCG (female > 10)
- Lactate
- BNP
- Troponin
- EKG
- STAT echocardiogram
- Hypercoagulable panel including: Factor 5 Leiden, Prothrombin gene mutation, Antithrombin 3 deficiency, Protein C deficiency, Protein S deficiency, Antiphospholipid, Homocysteine, Lupus anticoagulant, Antinuclear antibody (ANA), Anti-cardiolipin antibodies, Plasminogen. Ideally these labs would be obtained prior to starting anticoagulation – however treatment and anticoagulation should **NOT** be delayed with obtaining these labs.

For patients transferring from an outside hospital, please request completion prior to transport (if time allows) or complete immediately upon arrival to NCH

Initial Evaluation

Management



AC = anticoagulation; CBT = catheter-based therapy; iNO = inhaled nitric oxide; RV = right ventricle; VA ECMO = venoarterial extracorporeal membrane oxygenation

Ross C, Kumar R, et al. Acute management of high-risk and intermediate risk pulmonary embolism in children. CHEST 2022; 161 (3):791-802

PE Huddle

PE Huddle for Submassive or Massive PE
Initiated by ED Attending/Fellow

Call the Emergency Communication Center (ECC): 614-722-6899 and provide the following information:

- Age and gender of patient
- Patient location
- Specific meeting time (within 15 minutes)

The Emergency Medicine Physician initiating the huddle will join the Teams Meeting at the designated time of the huddle via any of the following:

Meeting Link: https://www.NationwideChildrens.org/PEHuddle

Use cell phone or landline for audio

Call-in:
Conference number:
614-653-7909
Access code:
565726249#

QR Code:

Huddle participants will be automatically contacted as part of the huddle process:

Emergency Medicine
Hematology
Cardiology
Interventional Cardiology
Cardiothoracic surgery
Interventional radiology
CTICU
PICU

Medical Record Number to be provided via Teams chat and/ or verbally during huddle

If ED Attending must leave the call to provide patient care, the Pediatric Intensivist on the call will update the ED Attending with management plans.

Please use .PEHUDDLENOTE to document.

Initial Evaluation | Management

Management Considerations for Submassive & Massive PE

Diagnostic Guidance in Critically Ill Patients:

Definitive imaging may be immediately available and performed safely and more rapidly than echo in a patient with shock (in the ED, IR or cardiac cath lab). **If acute PE is confirmed and the patient remains in shock, obtaining an echo should not delay life saving therapy.**

Echo cannot rule out all PE, especially small distal PE that are not hemodynamically significant. However, in a patient with ongoing undifferentiated shock, lack of RV strain by echo should prompt consideration and treatment of other causes of shock.

Considerations for Submassive PE:

Catheter-directed alteplase in Interventional Radiology is preferred for most patients with intermediate-risk PE *who require primary reperfusion.*

If catheter-directed alteplase is unavailable or patient is a poor candidate, anticoagulation **ALONE is often preferred over systemic alteplase** given associated risks and lack of evidence supporting benefits in adult patients with submassive PE.

If systemic thrombolysis is used, low-dose alteplase may be used to mitigate bleeding risks.

Considerations for Massive PE:

Favor surgical embolectomy for:
- Suspected tumor embolus (patients with Wilms Tumor, Ewings Sarcoma, osteosarcoma) or other non-thrombotic sources
- Patients with relative contraindications to alteplase
- Patients with concomitant intracardiac thrombus
- Patients with intracardiac communications on echo
- Patients on ECMO

Potential Alteplase relative contraindications

Alteplase Infusion Guidelines

Favor alteplase for:
- Thrombi extending distally which are not amenable to surgical embolectomy
- Patients with comorbidities that confer additional surgical or anesthetic risk
- Patients in whom surgical embolectomy is not readily available (within 2 hours from diagnosis of PE)

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Management

Congenital Heart Disease

- Patients with Congenital Heart Disease (CHD) with pulmonary embolism may present atypically secondary to complex cardiac anatomy and prior surgical interventions.
- If a patient with CHD has concerns for pulmonary embolism WITHOUT evidence of shock, please discuss with the cardiology fellow/attending before initiation of PE pathway.
- If there are signs of shock escalate care while concurrently notifying the Cardiology team.

Initial Evaluation

Management

Presentation, Differential Diagnosis & Definition

Clinical presentation:

Classic PE symptom triad [2-4]:

- Pleuritic chest pain
- Shortness of breath
- Hemoptysis (can be a late finding).

Most common:

- Shortness of breath
- Pleuritic and non-reproducible chest pain
- Cough

Additional signs and symptoms [2-5]:

- Fever
- Tachycardia
- Hypoxemia
- Hypotension
- Dyspnea
- Syncope
- Signs of right-sided ventricular dysfunction/ failure
- Pulseless electrical activity
- Sudden death

Differential Diagnosis:

- Pneumonia:
  - Cough
  - Fever
  - Shortness of breath
- Costochondritis:
  - Chest pain
  - Focal tenderness with palpation of sternum/ribs
- Trauma:
  - Rib fracture
- Pneumothorax
- Asthma exacerbation
- Pulmonary neoplasm and / or metastases
- Heart Disease

Pulmonary embolism (PE) occurs when a clot breaks loose and travels through the bloodstream to the lungs [1]. Most blood clots originally form in one of the deep veins of the legs, thighs, or pelvis; this condition is known as deep vein thrombosis (DVT). Rarely, material other than blood clots can block blood flow, including fatty emboli, tumor emboli, amniotic fluid, or air bubbles “non thrombotic PE”.

Symptoms of PE are nonspecific and can mimic other common childhood conditions.

In the absence of alternative diagnosis or explanations for symptoms, PE must be considered in children with or without risk factors.

The diagnosis of PE in children thus requires a high index of suspicion. [2-4]

Initial Evaluation

Management

Risk Factors

PE Risk Factors:

- Painful leg swelling or known/recent diagnosis of DVT
- Family or personal history of DVT or PE
- Known thrombophilia
- Congenital: Protein C, S or antithrombin deficiency, Factor V Leiden mutation, Prothrombin G20210A mutation, hyperhomocysteinemia
- Acquired: Antiphospholipid antibody syndrome, HIT/T, High fVIII (factor 8).
- Anatomic: May-Thurner, Thoracic Outlet Syndrome, IVC agenesis/atresia (congenital or acquired)
- Recent (< 1 month) or current indwelling CVC
- Exogenous estrogen or pregnancy in the past 6 months
- Within three months of long bone fracture, orthopedic surgery, or major trauma
- Within one month of any major surgery, prolonged period of immobility, or major medical illness
- Acute or chronic inflammatory conditions
- Obesity (weight > 95% for age)

Risk Factors to be Considered in Pulmonary Embolism Adapted from Zaidi et al, Front Pediatr. 2017	
Damage to the endothelium	• Central venous catheters • Inflammation (lupus, inflammatory bowel disease, etc.) • Infection, mostly bacterial • Antiphospholipid antibodies • Ventriculoatrial shunts
Change in laminar flow	• Congenital or acquired heart disease • Local anatomical causes (e.g., congenital anomalies of pulmonary arteries or after corrective heart surgery, e.g., Fontan surgery, congenital disorders leading to vascular compression (e.g. May-Thurner or Paget-Schroetter syndrome) • Total parenteral nutrition • Impaired mobility due to pelvic or long bone fractures/major surgeries or paralysis
Thrombophilia • Acquired	• Active nephrotic syndrome • Cancer • Medications e.g., L-asparaginase therapy • Pregnancy or hormonal supplementation • Antiphospholipid antibodies
• Inherited	• Deficiency of anticoagulants, e.g. protein S, C, and antithrombin • Factor V Leiden, prothrombin gene variant, etc. • Elevated homocysteine
Other risk factors	• Significant family history of thrombosis (DVT, PE, early MI or stroke prior to age of 50, recurrent first trimester miscarriages)

Initial Evaluation

Management

Assessment & Monitoring

Initial evaluation and management:

- Frequency of vital signs after initial evaluation and management will depend on the clinical presentation
- Consider increased frequency of blood pressure, heart rate, and respiratory rate assessment if any vital sign is abnormal
- Consider critical care room if frequent vital sign assessments are indicated

Clinical status can change quickly
Escalate care and for worsening tachycardia, hypotension, or signs of inadequate perfusion

Low risk PE:

- Blood pressure, heart rate, and respiratory rate per ED protocol unless any vital sign is abnormal, then consider more frequent assessment

Submassive PE:

- Consider transfer to critical care room
- Blood pressure, heart rate, and respiratory should be obtained every 5-15 minutes until transfer from the ED

Massive PE:

- Transfer to critical care room if not already in that location
- Patients with either respiratory distress or hemodynamic instability (e.g. poor perfusion, sustained tachycardia, tachypnea, hypotension) should have continuous cardiac monitoring with blood pressure obtained every 5 minutes until transfer from the ED

Initial Evaluation

Management

Testing

Prompt diagnosis and clinical/radiological risk stratification of pulmonary embolism is essential to expedite immediate care to prevent acute and long-term complications.

While validated clinical prediction scores and risk stratification guidelines exist for PE in adult patients, [13-16] validated prediction tools do not yet exist for use in pediatrics.[17] In fact, the available tools commonly used for adults have been shown to perform poorly in children [3]. Thus, we have to rely on a high index of clinical suspicion, physical signs, and symptoms to guide further diagnostic evaluation of young children. Even in adolescents and young adults, the commonly used tools in the internal medicine setting have poor sensitivity and specificity, making them clinically less reliable and possibly misleading. For these reasons, **we do not recommend the routine use of Wells or PERC criteria** in the Nationwide Children's clinical setting.

Initial laboratory evaluation of patient presenting with symptoms of SUSPECTED PE:

- CMP
- CBC
- BNP
- D Dimer
- Lactate
- PT, PTT
- Fibrinogen
- Troponin
- Thrombin time
- Urine β-HCG (females >10)
- EKG
- Hypercoagulable panel including: Factor 5 Leiden, Prothrombin gene mutation, Antithrombin 3 deficiency, Protein C deficiency, Protein S deficiency, Antiphospholipid, Homocysteine, Lupus anticoagulant, Antinuclear antibody (ANA), Anti-cardiolipin antibodies, Plasminogen. Ideally these labs would be obtained prior to starting anticoagulation – however treatment and anticoagulation should **NOT** be delayed with obtaining these labs.

If risk factors, D-dimer > 0.5, or no reasonable alternative diagnosis:

- Obtain CT Pulmonary Angiogram

Initial Evaluation

Management

Not Recommended

Use of the PERC or Wells criteria is not recommended

While validated clinical prediction scores and risk stratification guidelines exist for PE in adult patients, [13-16] the available tools commonly used for adults have been shown to perform poorly in children [3]. Even in adolescents and young adults, the commonly used tools in the internal medicine setting have poor sensitivity and specificity, making their clinical less reliable and possibly misleading.

Ventilation perfusion scans have suboptimal diagnostic utility compared to CTPA

Consider the **PERC-Peds** rule.

Initial Evaluation

Management

PERC-Peds

Pulmonary Embolism Rule-Out Criteria in Children (PERC-Peds)

A child is considered PERC-Peds *negative* only if **ALL** the following are true:

- Clinician gestalt pretest probability <15%
- No prior PE or proximal DVT
- No surgery requiring intubation within 30 days
- No current estrogen use
- No hemoptysis
- Heart rate always:
  - <100 beats/min if older than 12 years
  - <120 beats/min if 12 years or younger
- Oxygen saturation consistently >94%
- No suspected DVT

Test Sensitivity: 99.6%
Test Specificity: 19.6%

Note: This rule should only be used as a support tool and not the ultimate decision-making tool; use clinical judgment and individualized care until further consensus and evidence is available.

Ellison AM, Kuppermann N, Shihabuddin BS, et al. PERC-Peds rule for bedside exclusion of pulmonary embolism without radiation in children in the USA (BEEPER): a multicentre, prospective, observational, diagnostic accuracy study. Lancet Respir Med. 2026;14(8):694-703. doi:10.1016/S2213-2600(26)00086-X

Initial Evaluation

Management

Severity Assessment & Escalation of Care

Signs of shock can include any of the following:
- Tachycardia
- Tachypnea
- Abnormal peripheral perfusion / delayed capillary refill
- Altered mental status (including agitation / anxiety)
- Pallor
- Metabolic acidosis or elevated lactate

Severity Assessment [6-12]
PE is stratified into massive, submassive and low risk based on hemodynamic status at presentation, EKG findings, finding on echocardiogram and cardiac enzymes.

Massive PE is an acute PE causing cardiopulmonary arrest, sustained hypotension (systolic BP < 5th percentile for age for at least 15 minutes or requiring vasoactive support), or normotension with signs or symptoms of shock.

Submassive PE is an acute PE without hypotension or compensated shock, but with evidence of RV strain by imaging, myocardial necrosis by elevated cardiac troponin levels, or both.

Right ventricular "strain," injury, and/or dysfunction can manifest in multiple ways:
Moderate or severe RV qualitative dysfunction by echocardiogram
Moderate or severe RV dilation by echocardiogram or CT
Greater than half-systemic RV pressure by tricuspid regurgitation or septal position
Significantly elevated BNP/troponin

Low-risk PE is an acute PE not meeting criteria for submassive or massive PE.

EKG findings of right heart strain:
- S1Q3T3
  Lead I: prominent S-wave
  Lead III: Q-wave & inverted T-wave
- Sinus tachycardia

In the setting of mild RV dysfunction, mild RV dilatation or mild BNP/ Troponin elevations

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Consider escalation of care for any of the following:
- Worsening
  - Respiratory distress
  - Hypoxia and / or oxygen requirement
  - Troponin/BNP
  - Chest pain
- Hypotension
- New onset hemoptysis

Urgent evaluation to reassign risk category

Initial Evaluation | Management | Management Considerations

Initiating Unfractionated Heparin (UFH) Therapy

1.Patient dosing weight should be used for heparin orders and programming of pump.

2. A brain ultrasound is suggested for patients less than 1 year old. A brain ultrasound is STRONGLY recommended for neonates less than 44 weeks corrected gestational age.

3. When possible, patients should have a dedicated IV line for heparin administration. The heparin infusion must not be stopped or interrupted for other medications except in cases of emergency.

4. Use caution if prescribing aspirin, non-steroidal anti-inflammatory drugs and other antiplatelet agents for patients on therapeutic heparin infusion.

5. Prior to starting any anticoagulation, please obtain CBC, APTT, PT/INR, fibrinogen activity, and d-dimer. Please ensure baseline labs and indicated radiology studies are reviewed by a provider prior to starting anticoagulation.

6. Initial dose: heparin 75 units/kg/dose IV once infused over 10 minutes. Do not give a loading dose of heparin in neonates less than 44 weeks corrected gestational age and children with stroke or when the risk of bleeding is perceived to be high.

7. Initial maintenance infusion:

- Less than 1 year: heparin 28 units/kg/hour IV
- 1 year to 17 years: heparin 20 units/kg/hour IV
- 18 years and older: heparin 18 units/kg/hour IV

Monitoring UFH

Reversing UFH

UFH CPG References

Management

Relative Contraindications to Starting UFH

Decision to pursue heparinization should be individualized and based on balancing the risk for bleeding versus progression/death due to pulmonary embolism. Please discuss with hematology.

- Active bleeding
- Recent surgery (< 1 week)
- Head trauma (current and within the past month)
- Thrombocytopenia (platelets < 50 K)
- Coagulopathy (e.g. liver failure)
- Lumbar puncture within past 24 hours
- Spinal anesthesia within past 24 hours
- Congenital bleeding disorder
- History of heparin induced thrombocytopenia

Initial Evaluation

Management

Potential Relative Contraindications to Thrombolytic (tPA) Therapy

Condition/Symptom	Strong Contraindication	Relative Contraindication
Bleeding	Evidence of active hemorrhage (intracranial bleed, internal bleeding)	
	History of intracranial hemorrhage during preceding 3 months	
	Gastrointestinal or urinary tract hemorrhage during preceding 3 weeks	
Trauma	Serious head trauma during preceding 4 weeks	
	Other serious trauma (other than head trauma) during preceding 10 – 14 days	
	Severe asphyxial event (including neonatal hypoxic ischemic encephalopathy) during preceding 7 days	
Surgery/ Invasive Procedures	Intracranial or intraspinal surgery during preceding 4 weeks	Recent arterial puncture at a noncompressible site
	Major surgery (other than neurosurgery) during preceding 10 – 14 days	
	Lumbar puncture during preceding 7 days	
	Other invasive procedure during preceding 72 hours	
Medical Conditions	Known arteriovenous malformation, aneurysm, CNS mass, or moyamoya	Life expectancy <1 year from other causes
	Uncontrolled seizure or seizures during preceding 48 hours	Pregnancy or first postpartum week
	Known bleeding disorder/ tendency (includes significant renal and hepatic insufficiency)	Transient ischemic attack in previous 6 months
	Extreme prematurity <32 weeks corrected gestational age	Uncontrolled hypertension at the time of alteplase therapy
	Hypersensitivity to alteplase or any component of the product	Advanced liver disease
	Cerebrovascular accident within 6 months	
	Systemic septicemia or endocarditis	
Laboratory Studies/ Medications*	Platelet count <100,000/microliter despite platelet transfusion support	Oral anticoagulation
	UFH anti-Xa activity ≥0.7 units/mL or LMWH anti-Xa activity ≥1 units/mL with recent/current unfractionated or low molecular weight heparin administration (consult hematology to discuss reversal)	Recent warfarin use with INR ≥1.6 at time of planned thrombolysis (specimen drawn by clean peripheral venipuncture) (consult hematology to discuss reversal)
	Fibrinogen <100 mg/dL despite cryoprecipitate support	
	*Note: aspirin is not considered a contraindication to thrombolytic therapy	

Alteplase Infusion CPG

PE Management

HEM-12 Alteplase Infusion for Thrombolysis CPG

PE Management

Alteplase appropriate use confirmed

Place 2 large-bore IVs and obtain baseline labs/imaging if not already available

Patient currently on therapeutic unfractionated heparin (UFH)?

No → Start therapeutic UFH or contact Hematology for urgent reversal of alternate anticoagulant

Yes

- Order blood products as "Hold for Procedure"
- Transfuse FFP 20 mL/kg for patients ≤ 12 months of age

Patient to receive catheter-directed or systemic alteplase?

Catheter-directed Alteplase →

- Notify pharmacy, charge RN and IR
- Determine who will order procedural alteplase dose

30 min prior to alteplase, change heparin to fixed-rate 10 units/kg/hr to run concurrently with alteplase

Catheter-directed alteplase: 0.03mg/kg/hr (max 2 mg/hr) intracatheter

Systemic Alteplase →

Notify pharmacy and charge RN of impending thrombolysis

30 min prior to alteplase, change heparin to fixed-rate 10 units/kg/hr to run concurrently with alteplase

Low-dose or high-dose systemic alteplase?

Low-dose →

Low-dose systemic alteplase:

- < 3 months: 0.06 mg/kg/hr IV
- ≥ 3months: 0.03 mg/kg/hr (max 2 mg/hr) IV

High-dose →

High-dose systemic alteplase:

- 0.5 mg/kg/hr IV for 6 hours (100 mg max dose)

OR

- 0.5 mg/kg/dose over 2 minutes (max 50 mg)*

**Recommended for arrest/peri-arrest secondary to massive PE. Not for undifferentiated cardiac arrest.*

Monitor labs, bedside evaluations and appropriate imaging throughout alteplase therapy and 4 hours after completion

Severe/life threatening bleed?

No → Resume therapeutic UFH (without initial bolus) 30 minutes after completion of alteplase

Yes →

- Discontinue alteplase/heparin
- Contact hematology/ICU attending
- Obtain STAT: CBC, fibrinogen, PT/aPTT

Monitoring Unfractionated Heparin (UFH) Therapy

1. APTT and anti-FXa (UFH) levels should ideally not be drawn from an extremity or line through which heparin is infusing. If not possible, ensure line is flushed adequately prior to drawing anticoagulation labs. Do NOT obtain heparinase APTT/anti-FXa (UFH).

2. Obtain blood for APTT and anti-FXa (UFH) 4 hours after the initial dose, or 6 hours after start of infusion (if no bolus is given).

3. Adjust heparin infusion to maintain an anti-FXa (UFH) level of 0.35 – 0.7 units/mL. Anti-FXa (UFH) levels will be used to titrate heparin infusions using the below nomogram. APTTs will be drawn simultaneously with all anti-FXa (UFH) levels to ensure APTTs are not greater than 150 seconds. If APTT is greater than 150 seconds, consider repeating the anti-FXa (UFH) and APTT by venipuncture STAT to rule out
sample contamination. Monitor closely for bleeding and ensure remaining coagulation parameters (platelet count, prothrombin time, fibrinogen) are optimized.

Anti-FXa (UFH) (units/mL)	Bolus (units/kg)	Hold (minutes)	Dose change	Reseat APTT and anti-FXa (UFH)
< 0.1	50*	0	Increase 10%	4 hours
0.1-0.34	0	0	Increase 10%	4 hours
0.35-0.7	0	0	0	24 hours**
0.71-0.89	0	0	Decrease 10%	4 hours
0.90-1.20	0	30	Decrease 10%	4 hours
<1.20	0	60	Decrease 15%	4 hours
*Do not give bolus doses in neonates less than 44 weeks corrected gestational age **When 2 consecutive anti-FXa (UFH) results obtained 4 hours apart are therapeutic, obtain anti-FXa (UFH) and APTT level every morning.				

4. Once two consecutive anti-FXa (UFH) results obtained 4 hours apart are therapeutic, it is recommended to obtain blood for anti-FXa (UFH) and APTT once daily. Do NOT obtain heparinase APTT/anti-FXa (UFH).

5. Obtain CBC and platelet counts daily for the first 10 days, thereafter monitor every 3 days.

6. Avoid any invasive procedures (intramuscular injections, arterial punctures and lumbar punctures) in patients receiving anticoagulation except in cases of emergency.

7. Consider hematology consult in the following situations:
• Abnormality of baseline labs and/or head imaging
• Platelet count drop by 50% or more from baseline platelet count
• Platelet count drops below 150 k/cu mm
• Abnormal or excessive bleeding
• Perioperative hemostatic management
• If APTT is greater than 150 seconds with therapeutic or subtherapeutic anti-FXa (UFH)

Initiating UFH | Reversing UFH | UFH CPG References

PE Management

Reversing Unfractionated Heparin (UFH) Therapy

1. In the event that reversal of heparin anticoagulation is required, recommend the use of protamine sulfate.

2. Protamine dose is determined by the most recent dose and time of heparin, up to a maximum protamine dose of 50 mg/dose. When heparin is given as a continuous infusion, only heparin given in the preceding 2 hours should be considered when administering protamine. Protamine doses are suggested as follows:

Time since last heparin dose (minutes)	Dose of protamine (mg) required to neutralize 100 units of heparin
< 30	1
30-60	0.5-0.75
61-120	0.375-0.5
>120	0.25-0.375

Example protamine calculation for a heparin infusion discontinued in previous 30 minutes: Multiply hourly rate (units/kg/hr) by patient weight (kg) to result in hourly heparin rate (units/hr). Multiply hourly heparin rate (units/hr) by 2 hours to result in heparin dose (units). Based on above table, 1 mg protamine is required to neutralize every 100 units of heparin if < 30 minutes since last heparin, therefore divide heparin dose (units) by 100 to result in protamine dose (mg). Do not exceed maximum 50 mg protamine per dose.

Initiating UFH

Monitoring UFH

UFH CPG References

PE Management

Helping Hands

- **Pulmonary Embolism Helping Hands**
- Enoxaparin Helping Hands

Initial Evaluation

Management

References

1. What is venous thromboembolism? National Heart Lung and Blood Institute. https://www.nhlbi.nih.gov/health/venous-thromboembolism. Published September 19, 2022.

2. Ramiz S, Rajpurkar M. Pulmonary Embolism in Children. *Pediatr Clin North Am*. 2018;65(3):495-507. doi:10.1016/j.pcl.2018.02.002

3. Zaidi AU, Hutchins KK, Rajpurkar M. Pulmonary Embolism in Children. *Front Pediatr*. 2017;5:170. Published 2017 Aug 10. doi:10.3389/fped.2017.00170

4. Sista AK, Kuo WT, Schiebler M, Madoff DC. Stratification, Imaging, and Management of Acute Massive and Submassive Pulmonary Embolism. *Radiology*. 2017;284(1):5-24. doi:10.1148/radiol.2017151978

5. Beckerman Z, Bolotin G. Surgical Treatment of Acute Massive Pulmonary Embolism. *Adv Exp Med Biol*. 2017;906:75-88. doi:10.1007/5584_2016_107

6. Bavare AC, Naik SX, Lin PH, et al. Catheter-directed thrombolysis for severe pulmonary embolism in pediatric patients. *Ann Vasc Surg*. 2014;28(7):1794.e1-1794.e17947. doi:10.1016/j.avsg.2014.03.016

7. Belsky J, Warren P, Stanek J, Kumar R. Catheter-directed thrombolysis for submassive pulmonary embolism in children: A case series. *Pediatr Blood Cancer*. 2020;67(4):e28144. doi:10.1002/pbc.28144

8. Barco S, Konstantinides SV. Risk-adapted management of pulmonary embolism. *Thromb Res*. 2017;151 Suppl 1:S92-S96. doi:10.1016/S0049-3848(17)30076-2

9. Ross CE, Shih JA, Kleinman ME, Donnino MW. Pediatric Massive and Submassive Pulmonary Embolism: A Single-Center Experience. *Hosp Pediatr*. 2020;10(3):272-276. doi:10.1542/hpeds.2019-0290

10. Becattini C, Agnelli G. Risk stratification and management of acute pulmonary embolism. *Hematology Am Soc Hematol Educ Program*. 2016;2016(1):404-412. doi:10.1182/asheducation-2016.1.404

11. Cohen AT, Dobromirski M, Gurwith MM. Managing pulmonary embolism from presentation to extended treatment. *Thromb Res*. 2014;133(2):139-148. doi:10.1016/j.thromres.2013.09.040

12. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). *Eur Heart J*. 2020;41(4):543-603. doi:10.1093/eurheartj/ehz405

13. Kline JA, Mitchell AM, Kabrhel C, Richman PB, Courtney DM. Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism. *J Thromb Haemost*. 2004;2(8):1247-1255. doi:10.1111/j.1538-7836.2004.00790.x

14. Penaloza A, Verschuren F, Meyer G, et al. Comparison of the unstructured clinician gestalt, the wells score, and the revised Geneva score to estimate pretest probability for suspected pulmonary embolism. *Ann Emerg Med*. 2013;62(2):117-124.e2. doi:10.1016/j.annemergmed.2012.11.002

15. Kilic T, Gunen H, Gulbas G, Hacievliyagil SS, Ozer A. Prognostic role of simplified Pulmonary Embolism Severity Index and the European Society of Cardiology Prognostic Model in short- and long-term risk stratification in pulmonary embolism. *Pak J Med Sci*. 2014;30(6):1259-1264. doi:10.12669/pjms.306.5737

16. Ortel, Thomas & Neumann, Ignacio & Ageno, Walter, et al. (2020). American Society of Hematology 2020 Guidelines for Management of Venous Thromboembolism: Treatment of Deep Vein Thrombosis and Pulmonary Embolism. *Blood Advances*. 4. 4693-4738. doi: 10.1182/bloodadvances.2020001830.

17. Hennelly KE, Baskin MN, Monuteuax MC, et al. Detection of Pulmonary Embolism in High-Risk Children. *J Pediatr*. 2016;178:214-218.e3. doi:10.1016/j.jpeds.2016.07.046

18. Tarango C, Manco-Johnson MJ. Pediatric Thrombolysis: A Practical Approach. *Front Pediatr*. 2017;5:260. Published 2017 Dec 6. doi:10.3389/fped.2017.00260

19. Male C, Lensing AWA, Palumbo JS, et al. Rivaroxaban compared with standard anticoagulants for the treatment of acute venous thromboembolism in children: a randomised, controlled, phase 3 trial. *Lancet Haematol*. 2020;7(1):e18-e27. doi:10.1016/S2352-3026(19)30219-4

20. O'Brien SH. Can paediatricians move directly to direct oral anticoagulants?. *Lancet Haematol*. 2020;7(1):e2-e3. doi:10.1016/S2352-3026(19)30204-2

21. Young G, Lensing AWA, Monagle P, et al. Rivaroxaban for treatment of pediatric venous thromboembolism. An Einstein-Jr phase 3 dose-exposure-response evaluation. *J Thromb Haemost*. 2020;18(7):1672-1685. doi:10.1111/jth.14813

22. Ross C, Kumar R, Pelland-Marcotte MC, et al. Acute Management of High-Risk and Intermediate-Risk Pulmonary Embolism in Children: A Review. *Chest*. 2022;161(3):791-802. doi:10.1016/j.chest.2021.09.019

23. Biss TT, Brandão LR, Kahr WH, Chan AK, Williams S. Clinical features and outcome of pulmonary embolism in children. *Br J Haematol*. 2008;142(5):808-818. doi:10.1111/j.1365-2141.2008.07243.x

24. Hennelly KE, Ellison AM, Neuman MI, Kline JA. Clinical variables that increase the probability of pulmonary embolism diagnosis in symptomatic children. *Res Pract Thromb Haemost*. 2019;4(1):124-130. Published 2019 Oct 26. doi:10.1002/rth2.12265

25. Kanis J, Hall CL, Pike J, Kline JA. Diagnostic accuracy of the D-dimer in children. *Arch Dis Child*. 2018;103(9):832-834. doi:10.1136/archdischild-2017-313315

26. Dijk FN, Curtin J, Lord D, Fitzgerald DA. Pulmonary embolism in children. *Paediatr Respir Rev*. 2012;13(2):112-122. doi:10.1016/j.prrv.2011.09.002

27. Zaidi AU, Hutchins KK, Rajpurkar M. Pulmonary Embolism in Children. *Front Pediatr*. 2017;5:170. Published 2017 Aug 10. doi:10.3389/fped.2017.00170

28. Agha BS, Sturm JJ, Simon HK, Hirsh DA. Pulmonary embolism in the pediatric emergency department. *Pediatrics*. 2013;132(4):663-667. doi:10.1542/peds.2013-0126

29. Ellison AM, Kuppermann N, Shihabuddin BS, et al. PERC-Peds rule for bedside exclusion of pulmonary embolism without radiation in children in the USA (BEEPER): a multicentre, prospective, observational, diagnostic accuracy study. Lancet Respir Med. 2026;14(8):694-703. doi:10.1016/S2213-2600(26)00086-X

Initial Evaluation **Management**

Initiation, Monitoring and Reversal of UFH Therapy CPG References

1. Monagle P, Chan AKC, Goldenberg NA, et al. Antithrombotic therapy in neonates and children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines [published correction appears in Chest. 2014 Dec;146(6):1694. Dosage error in article text] [published correction appears in Chest. 2014 Nov;146(5):1422]. *Chest*. 2012;141(2 Suppl):e737S-e801S. doi:10.1378/chest.11-2308

2. Liveris A, Bello RA, Friedmann P, et al. Anti-factor Xa assay is a superior correlate of heparin dose than activated partial thromboplastin time or activated clotting time in pediatric extracorporeal membrane oxygenation*. *Pediatr Crit Care Med*. 2014;15(2):e72-e79. doi:10.1097/PCC.0000000000000028

3. Chan AK, Black L, Ing C, Brandão LR, Williams S. Utility of aPTT in monitoring unfractionated heparin in children. *Thromb Res*. 2008;122(1):135-136. doi:10.1016/j.thromres.2007.09.007

4. Ignjatovic V, Summerhayes R, Than J, Gan A, Monagle P. Therapeutic range for unfractionated heparin therapy: age-related differences in response in children. *J Thromb Haemost*. 2006;4(10):2280-2282. doi:10.1111/j.1538-7836.2006.02136.x

5. Newall F, Ignjatovic V, Johnston L, et al. Clinical use of unfractionated heparin therapy in children: time for change?. *Br J Haematol*. 2010;150(6):674-678. doi:10.1111/j.1365-2141.2010.08302.x

6. Protamine. Lexi-Drugs AHFS Drug Information [Internet database]. Lexi-Comp, Inc.; Accessed September 26, 2019.

Initiating UFH

Monitoring UFH

Reversing UFH

PE Management

Quality Measures

Process Measures
- ED Order Set utilization
- Time from CT angiogram confirming pulmonary embolism to initiation of unfractionated heparin

Outcome Measures
- ED:
  - ED length of stay
  - Admission rate
  - ICU admission rate

Balancing measure
- New diagnosis of PE with NCH ED/UC visit within 7 days

Initial Evaluation

Management

Team & Process

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Advisory Committee Date: *December, 2022*

Origination Date: *October, 2021*

Last Revision Date: *February, 2025*

Next Revision Date: *February, 2030*

Clinical Pathway Development

This clinical pathway was developed using the process described in the NCH Clinical Pathway Development Manual Version 6, 2022. Clinical Pathways at Nationwide Children's Hospital (NCH) are standards which provide general guidance to clinicians. Patient choice, clinician judgment, and other relevant factors in diagnosing and treating patients remain central to the selection of diagnostic tests and therapy. The ordering provider assumes all risks associates with care decisions. NCH assumes no responsibility for any adverse consequences, errors, or omissions that may arise from the use or reliance on these guidelines. NCH's clinical pathways are reviewed periodically for consistency with new evidence; however, new developments may not be represented, and NCH makes no guarantees, representations, or warranties with respect to the information provided in this clinical pathway.

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Initial Evaluation | Management