

# Guideline: Pediatric Pulmonary Embolism

Updated: 3/28/2023

## Clinical guideline summary

**CLINICAL PATHWAY/GUIDELINE NAME:** Pediatric Pulmonary Embolism

**PATIENT POPULATION AND DIAGNOSIS:** Patients less than 18 years of age who are being evaluated for suspected acute pulmonary embolism (PE). Patients can be presenting to the Emergency Department (ED), transferring from outside hospital, or while hospitalized for other reasons.

**APPLICABLE TO:** All Spectrum Health Sites

**BRIEF DESCRIPTION:** The algorithm outlines the initial management, diagnosis, and treatment of pediatric patients who have suspected pulmonary embolism. Although adult risk stratification models have not been validated in pediatric patients, they may serve as a basis for consideration of treatment options in a certain pediatric age range i.e., adolescents and young adults. The patient's hemodynamic status determines the initial steps which are particularly critical for those presenting with a massive pulmonary embolism. For patients who are hemodynamically stable, the algorithm outlines criteria for urgent advanced diagnostic imaging and factors that contribute to risk stratification. Patients with suspected acute pulmonary embolism benefit from a multidisciplinary team approach to determine treatment. The algorithm includes information on which service lines should be contacted to facilitate treatment discussions.

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**OWNING EXPERT IMPROVEMENT TEAM (EIT):** N/A

**MANAGING CLINICAL PRACTICE COUNCIL (CPC):** Children's Health

**CPC APPROVAL DATE:** February 28, 2023

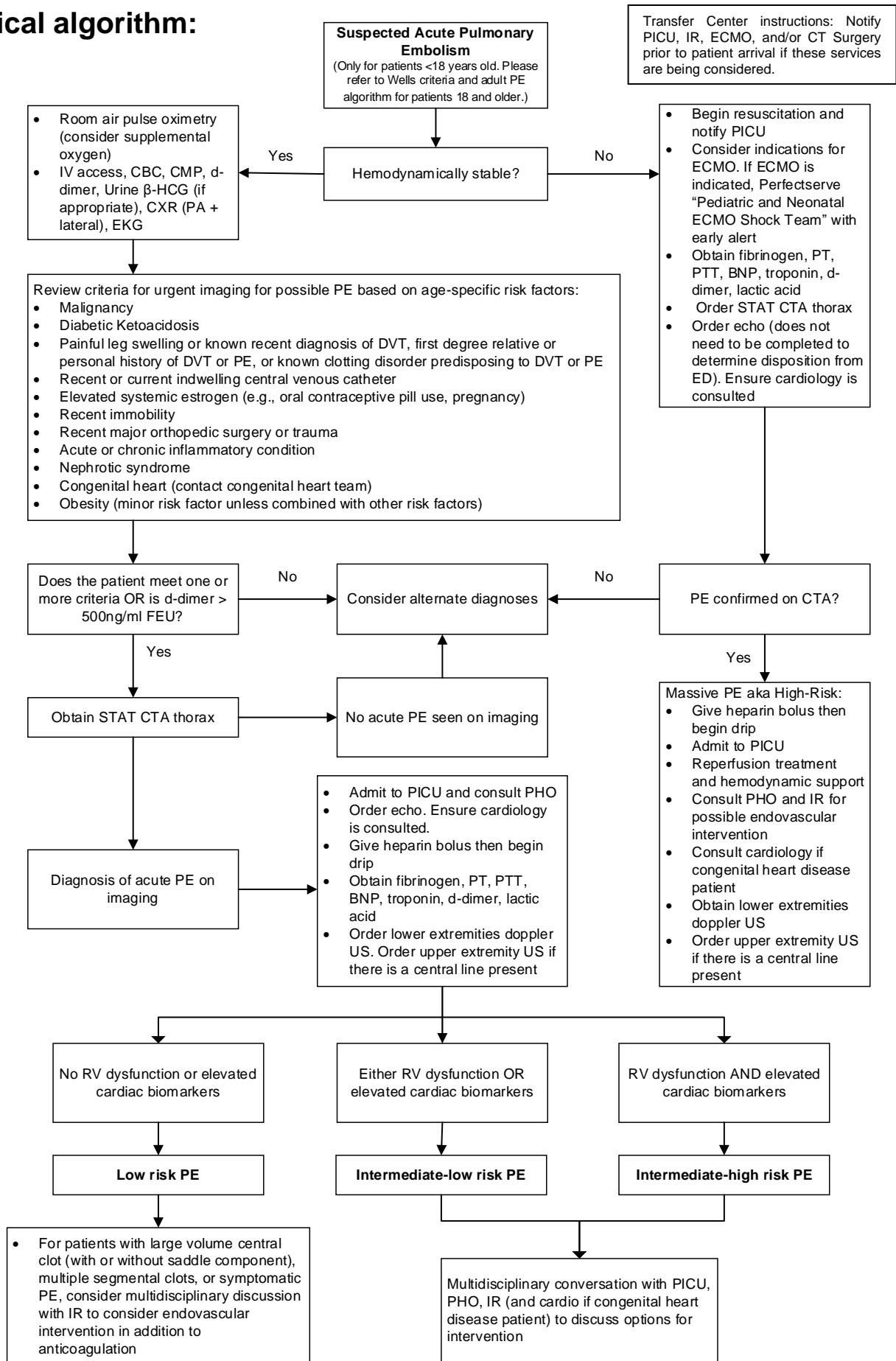
**OTHER TEAM(S) IMPACTED:** This guideline was reviewed with representatives from Interventional Radiology, Pediatric Critical Care Medicine, Emergency Medicine, and Pediatric Hematology and Oncology. Other teams that might be affected are ECMO and Cardiothoracic Surgery.

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**LAST REVISED:** March 2023

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# Clinical algorithm:



# Clinical pathways clinical approach

## DEFINITIONS

1. Although not specifically validated in pediatric populations, right ventricular (RV) dysfunction in adults is typically defined as RV: Left Ventricular (LV) luminal ratio of  $> 0.9$ . Ancillary signs may include bowing of the intraventricular septum or reflux of IV contrast on CT angiogram (CTA) into the inferior vena cava (IVC) or hepatic veins. There is not one specific finding that defines the presence of RV function. A discussion with cardiology after obtaining a transthoracic echo (TTE), radiologist, and/or ED or critical care attendings (assessment of vital signs) are critical in determining if RV dysfunction is present.

2. Massive PE (also referred as “high-risk PE”) is defined by the presence of hemodynamic instability in *adults*, which may be applicable in pediatric patients. Hemodynamic instability in pediatric patients, especially in infants and young children, can manifest as tachycardia with or without hypotension.

- PALS uses the following guidelines to define a normal heart rate in pediatric patients. Sustained heart rates above the values below are concerning.

Age	Awake rate	Sleeping rate
Neonate (28 days or younger)	100-205	90-160
Infant (29 days to 1 year)	100-180	90-160
Toddler (1 to <3 years)	98-140	80-120
Preschool (3 to 5 years)	80-120	65-100
School-aged child (6 to 12 years)	75-118	58-90
Adolescent (>12 years)	60-100	50-90

Data from Pediatric Advanced Life Support Provider Manual, American Heart Association, 2016, p. 48.

- Of note, hypotension in children is defined as SBP  $< 5^{\text{th}}$  percentile for age despite adequate volume or requiring pressors to maintain normal BP. Based on that definition, PALS uses the following:
  - Neonate:  $< 60$  mm Hg
  - Infant:  $< 70$  mm Hg
  - Age 1-10:  $< 70 + (\text{age in years} \times 2)$  mm Hg
  - Age above 10:  $< 90$  mm Hg

<b>Massive Pulmonary Embolism (also referred to as “high-risk PE”) is defined, in adults, by the presence of <i>hemodynamic instability</i> and includes having one of the following clinical manifestations at presentation</b>		
<b>(1) Cardiac Arrest</b>	<b>(2) Obstructive Shock</b>	<b>(3) Persistent Hypotension</b>
Need for cardiopulmonary resuscitation	SBP < 90 mmHg or vasopressors required to achieve a BP ≥ 90 mmHg despite adequate filling status	SBP < 90 mmHg or SB drop ≥ 40 mmHg, lasting longer than 15 min and not caused by new-onset arrhythmia, hypovolemia, or sepsis
	AND	
	End-organ hypoperfusion (altered mental status, cold clammy skin, oliguria/anuria, increase serum lactate)	

Table taken from ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Konstantinides SV, et al. Eur Heart J. 2020 Jan 21;41(4):543-603

3. Intermediate Risk PE (also referred to as “submassive PE” to describe patients who are hemodynamically stable) can be divided, according to the European Respiratory Society 2019 Guideline, into intermediate-high and intermediate-low risk PE groups in *adults*, which may be applicable in pediatric patients.

- Intermediate-high (the presence of RV dysfunction and elevated cardiac biomarkers)
- Intermediate-low (the presence of RV dysfunction OR elevated cardiac biomarkers)

d. Low Risk PE is the absence of RV dysfunction or elevated biomarkers that define high risk or intermediate risk, in *adults*, which may be applicable in pediatric patients.

## TREATMENT AND MANAGEMENT

### Anticoagulation for pulmonary embolism

#### 1. Unfractionated Heparin

<b>Table 1. Bolus and Initial Infusion Rates for Continuous Infusion UFH Treatment Dosing</b>			
<b>Age</b>	<b>Bolus Dose (units/kg)</b>	<b>Maximum Bolus (units)</b>	<b>Initial Infusion (units/kg/hr)</b>
Birth to 12 months	75	1,500	28
Children > 1 year	75	5,000	20
Children > 12 years	80	10,000	18

Table 2. Recommendations for Dose Adjustments Using Unfractionated Heparin Level Anti-Xa Assay <sup>3</sup>				
Unfractionated Heparin Level Anti-Xa Assay (units/mL)	Bolus Dose (Units/kg)*	Hold Infusion (minutes)	Infusion Rate Change (units/kg/hr)	Repeat Level (hours after dose adjustment)
< 0.1	50	0	Increase by 4	4
< 0.1-0.19	0	0	Increase by 3	4
0.2–0.29	0	0	Increase by 2	4
0.3–0.7	0	0	No change	In 4 h, then daily
0.71–0.8	0	0	Decrease by 1	4
0.81–0.9	0	30	Decrease by 2	4
0.91-1	0	60	Decrease by 3	4

## 2. Low Molecular Weight Heparin (e.g. Enoxaparin)

Table 4. Enoxaparin Dosing*				
Age	Prophylactic Dosing (mg/kg/dose)	Treatment Dosing (mg/kg/dose)	Route	Dosing Interval
< 2 months	0.75	1.5	Subcutaneous	every 12 hours
≥ 2 months	0.5	1	Subcutaneous	every 12 hours

\*There are no guidelines on LMWH dosing for morbidly obese patients. Physician discretion is advised and frequent monitoring of LMWH Blood Level should be considered.

Table 5. Guidelines for Treatment Dose Titration Using LMWH Blood Level		
LMWH Blood level (units/mL)	Dose Titration	Time to Repeat LMWH Blood Level
< 0.35	<b>Increase</b> dose by 25%	4 hours after next dose
0.35-0.49	<b>Increase</b> dose by 10%	4 hours after next dose
<b>0.5-1</b>	Keep <b>same</b> dose	Next day, then 1 week later, then monthly (4 hours after dose)
1.1-1.5	<b>Decrease</b> dose by 20%	Before next dose**
1.6-2	<b>Hold</b> dose for 3 hours and decrease dose by 30%	Before next dose and then 4 hours after next dose**
> 2	<b>Hold</b> all doses until level is ≤ 0.5 units/mL, then decrease dose by 40%	Before next dose and every 12 hours until LMWH blood level ≤0.5 units/mL**

\*\*Check serum creatinine if not recently checked

### 3. Direct Thrombin Inhibitors (Bivalirudin and Argatroban)

Bivalirudin and Argatroban, both administered intravenously, inhibit thrombin. They can be used in patients with heparin-induced thrombocytopenia, heparin-resistance, or progression of venous thromboembolism despite therapeutic heparin (“heparin failure”). A nomogram for *bivalirudin* use at HDVCH is being developed as of April 2022. Please consult Pharmacy and Pediatric Hematology and Oncology for the use of *bivalirudin* to treat PE or DVT.

### 4. Contraindications to anticoagulation with UFH or LMWH

Contraindications for UFH and LMWH should be carefully taken into consideration prior to initiation of UFH or LMWH which include weighing the risk of death and complications of the acute PE vs benefits of anticoagulation.

- Known allergy and history of heparin-induced thrombocytopenia
- Existence of coagulopathy and/or thrombocytopenia
- Recent/active bleeding
- Invasive procedures or trauma within the past 24 hours

### **Reperfusion Treatment Strategies Include:**

The decision to proceed with and the type of reperfusion treatment is determined after a multidisciplinary discussion between providers including ED, PCCU, IR, PHO, and/or CT surgery and/or ECMO team.

#### 1. Endovascular intervention

- Catheter-directed thrombolysis (Interventional Radiology Consultation)
- Mechanical embolectomy (Interventional Radiology Consultation)

#### 2. Systemic Thrombolysis

This is typically ordered and managed by Pediatric Hematology and Oncology (See Appendix 1)

#### 3. Surgical intervention

- Surgical pulmonary embolectomy
- Contact Peds Cardiothoracic Surgery to discuss

#### 4. Mechanical circulatory support

ECMO is a bridge to right ventricular recovery or definitive intervention

## APPENDIX

### 1. Pediatric and Neonatal Systemic Thrombolytic and Adjuvant Anticoagulation Regimen

(Greene, Goldenberg, & Goldenberg, 2012) (Wang, et al., 2003)

Thrombolytic Agent	Loading Dose	Maintenance Dose	Duration
rtPA (high dose) <sup>§</sup>	-	0.5 - 0.6mg/kg/hour	6 hours, may be repeated x 1
rtPA (low dose) <sup>#</sup>	-		
○ Pediatric	-	0.03mg/kg/hour, max 2.5mg/hr	24 - 96 hours
○ Neonatal (Wang 2003)	-	0.06 mg/kg/hour	24 - 96 hours
Adjuvant Anticoagulation <sup>*</sup>	Loading Dose	Maintenance Dose	Duration
Enoxaparin (LMWH)	-	0.5mg/kg/dose sq q12 hrs	
UFH	-	5 - 15 U/kg/hr	12 - 96 hours

rtPA: recombinant tissue plasminogen activator; LMWH: low molecular weight heparin; UFH:

Unfractionated heparin

\*Adjuvant anticoagulation is recommended if there are no concurrent bleeding risks (Manco-Johnson, et al., 2000)

§ High dose may be more beneficial in arterial thrombosis when rapid lysis is needed

#Low dose over a longer duration may be more beneficial in venous thrombosis

### 2. Precautions During Systemic Thrombolysis (Tarango & Manco-Johnson, 2017)

No arterial punctures or line placements

No intramuscular injections (LMWH is subcutaneous)

No urinary catheterization, rectal temperature, nasogastric tube placement

Avoid concurrent NSAIDs or anti-platelet therapy

### 3. Monitoring for bleeding during catheter-directed and systemic thrombolysis

Fibrinogen q 4-6 hours: administer cryoprecipitate to maintain fibrinogen > 150mg/dL

Platelet count q 6-12 hours: maintain > 75,000 to 100,000 x 10<sup>6</sup>/dL

CBC q 6-12 hours (to evaluate evidence of bleeding): notify provider with drop in hemoglobin ≥ 2gm/dL

Unfractionated Heparin for LMWH or aPTT q 6-12 hours

Ddimer q 24 hours

- If normal or low (lack of thrombolysis), may need to increase dose of rtPA
- Increased levels support activation of fibrinolysis

Neurologic check q 2-4 hours: hold rtPA for new neurologic symptoms or severe headaches

Consider Fresh Frozen Plasma (FFP) prior to rtPA to replete plasminogen concentrations, particularly for neonates (10ml/kg)

Head Ultrasound daily for neonates as long as they are receiving thrombolysis

### 4. Contraindications to thrombolytic regimens (systemic or catheter-directed) in adult patients

Absolute

- History of hemorrhagic stroke or stroke of unknown origin
- Ischemic stroke in the previous 6 months
- Central nervous system neoplasm currently receiving treatment
- Major trauma, surgery, or head injury in previous 3 weeks

- Bleeding diathesis
- Active bleeding

#### Relative

- Transient ischemic attack in previous 6 months
- Oral anticoagulation
- Pregnancy or first post-partum week
- Non-compressible puncture sites
- Traumatic resuscitation
- Refractory hypertension (systolic BP > 180 mmHg)
- Advanced liver disease
- Infective endocarditis
- Active peptic ulcer disease

2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Konstantinides SV, et al. Eur Heart J. 2020 Jan 21;41(4):543-603

#### 5. Labs not included in algorithm

Occasionally, Pediatric Hematology and Oncology will request for hypercoagulable panel or thrombophilia labs. These include:

- Factor V Leiden DNA analysis
- Prothrombin G20210A mutation
- Antithrombin III Activity
- Protein C Activity
- Protein S Activity
- Factor VIII Activity
- Lupus anticoagulant LA1
- Cardiolipin antibody reflex
- Beta-2 GP1 (glycoprotein) antibody panel
- "Peds Onc Plasma Hold"

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