The Newcastle upon Tyne Hospitals NHS Foundation Trust

Pulmonary Embolism in children and adolescents

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1 Introduction

Pulmonary embolism (PE), the most severe manifestation of venous thromboembolism (VTE), is increasingly recognised in paediatric practice, with reported diagnoses rising by approximately 200%, particularly among adolescents. VTE affects around 1 in 200 hospitalised children, highlighting its clinical relevance in this population (1,2). Despite this, the overall incidence in the general paediatric population remains low, estimated at approximately 0.1–1 per 100,000 children, with some cohorts reporting rates closer to 0.5 per 10,000. Population-based studies suggest a PE-related mortality of approximately 8.3%, underscoring the importance of early recognition and management guidelines (3).

A bimodal age distribution is recognised, with increased incidence in infants and toddlers, and a second peak in adolescents. Ethnic variation in PE incidence has been clearly documented in adult population, whilst limited data is available for paediatric populations some studies have reported a higher incidence in black children compared to white (4). However, the true incidence is likely underestimated due to the often nonspecific or asymptomatic presentation of PE in children. Underdiagnosis remains a key challenge (5). Autopsy data demonstrate a significant discrepancy between clinically suspected and confirmed cases, with PE considered in only a minority of affected patients prior to death(5).

PE in children is typically associated with identifiable risk factors, including malignancy, congenital heart disease, inherited and acquired thrombophilia's, and the presence of central venous catheters (6). The observed increase in incidence is likely multifactorial, reflecting improved survival of critically ill children with complex comorbidities, as well as the increased use of invasive vascular devices. Risk assessment is essential in the management of paediatric pulmonary embolism and should be undertaken at the time of diagnosis. Patients should be stratified into low-, intermediate-, or high-risk categories based on clinical status, haemodynamic stability, imaging findings, and underlying risk factors. This stratification guides management, including the choice of anticoagulation, need for thrombolysis, and consideration of advanced supportive measures such as ECMO (7). Early and accurate risk assessment is critical to optimise outcomes and reduce morbidity and mortality (8,9).

2 Guideline scope

This guideline aims to support clinicians in the timely recognition, investigation, and management of suspected paediatric PE, promoting a systematic and evidence-informed approach to improve patient outcomes.

3 Main Body of the guideline

3.1 Clinical features (6,7)

Pulmonary embolism (PE) should be considered in any child who is acutely unwell where the clinical presentation is not fully explained by an alternative diagnosis.

Clinicians should assess for key signs and symptoms, including:

- Shortness of breath (dyspnoea)
- Tachypnoea
- Sinus tachycardia or persistent unexplained tachycardia
- Pleuritic chest pain
- Hypoxia
- Cough ± haemoptysis

Additional features that may indicate PE include:

- Unexplained hypotension or features of shock
- Syncope or presyncope (the sensation that one is about to pass out, without actually losing consciousness)
- Cyanosis
- Signs of right heart strain (ECG: ST-segment depressions, T-wave inversions and Echo: right ventricle becoming enlarged and abnormally rounded)
- Low-grade pyrexia
- Anxiety or unexplained agitation

Please note children may present subtly or atypically, thus a high index of suspicion should be maintained, particularly in the context of unexplained clinical deterioration or the presence of known risk factors.

3.2 Risk Factors

Assess for predisposing risk factors for pulmonary embolism in accordance with the major pathogenic mechanisms. These include **endothelial injury** (e.g. indwelling central venous catheters, systemic infection, inflammatory conditions, antiphospholipid antibodies), **altered blood flow or stasis** (e.g. congenital or acquired heart disease, post-surgical anatomical changes such as Fontan circulation, immobility, abnormal vascular malformations (AVMs), recent surgery and **thrombophilia**. Thrombophilia may be **acquired** (e.g. malignancy, nephrotic syndrome, medications such as L-asparaginase, pregnancy or hormonal therapy,

antiphospholipid syndrome) or **inherited** (e.g. protein C or S deficiency, antithrombin deficiency, Factor V Leiden, prothrombin gene mutation) and family history of venous thromboembolism. The presence of one or more of these risk factors should increase clinical suspicion and prompt further evaluation for PE (10).

Category	Subcategory	Risk Factors
1. Endothelial Injury Damage to the endothelium promotes thrombosis.		• Central venous catheters • Inflammation (e.g. lupus, inflammatory bowel disease) • Systemic infection • Antiphospholipid antibodies
2. Altered Blood Flow (Stasis / Flow Disturbance) Changes in laminar flow can predispose to clot formation.		• Congenital or acquired heart disease • Local anatomical causes (e.g. pulmonary artery anomalies, post-cardiac surgery such as Fontan) • Total parenteral nutrition • Obesity • Abnormal vascular malformations (AVM)
3. Thrombophilia A prothrombotic tendency increases the risk of thrombosis.	Acquired	• Nephrotic syndrome • Malignancy • Medications (e.g. L-asparaginase) • Pregnancy or hormonal therapy • Antiphospholipid antibodies
	Inherited	• Deficiency of natural anticoagulants (Protein C, Protein S, Antithrombin III) • Factor V Leiden, prothrombin gene mutation • Hyperhomocysteinaemia

3.3 Clinical probability of PE

Risk of pulmonary embolism (PE) should be stratified by combining clinical presentation with identified risk factors. Risk stratification in children (6,7):

Low probability if no risk factors are present and an alternative diagnosis is more likely.

Intermediate probability includes those with one or more risk factors in combination with compatible clinical features, such as unexplained tachycardia, shortness of breath, or pleuritic chest pain, or additional features including syncope or a family history of PE or deep vein thrombosis.

High probability is defined by the presence of multiple risk factors and/or features of haemodynamic compromise, ie. hypotension, or a history of previous PE or thromboembolism.

3.4 Basic investigation

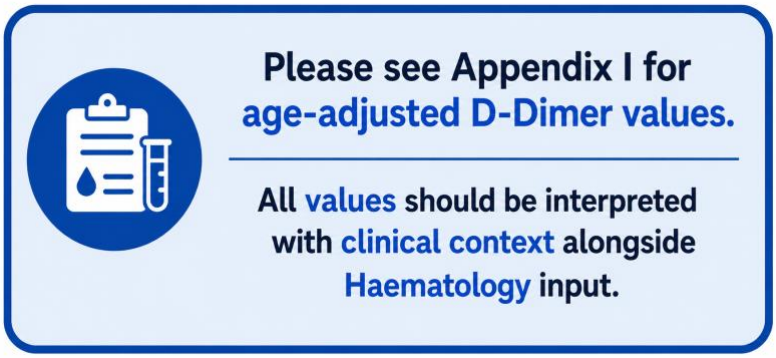
In children who are clinically stable, investigations should be guided by pre-test probability:

Low or intermediate probability, a D-dimer test should be performed; a positive result should prompt progression to CT pulmonary angiography (CTPA), a negative result does not exclude PE especially in younger children with existing comorbidities. If no likely alternative diagnosis, consider CTPA.

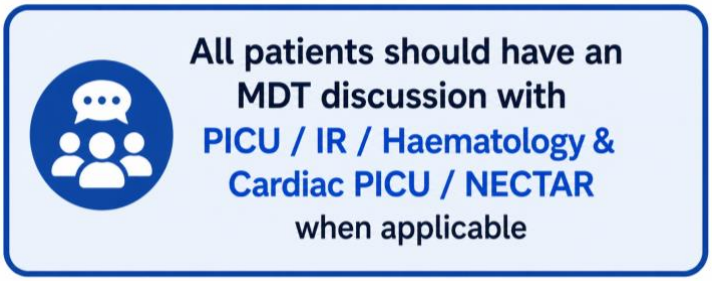
High probability, CTPA should be performed directly without prior D-dimer testing. If CTPA is negative, PE is excluded and alternative diagnoses should be considered or further investigations undertaken as clinically indicated.

Additional investigations to support diagnosis and help identify alternative pathology (3):

- Chest X-ray to assess for other causes
- ECG for features of right heart strain
- Echocardiography for further assessment of RV function
- Blood tests: full blood count, coagulation profile, troponin & BNP



3.5 Management



3.5.1 Basic Management

Management should focus on early stabilisation, supportive care, and prompt initiation of treatment, in collaboration with haematology, cardiology, and PICU teams. The PE pathway is summarised in appendix III with NECTAR workflows highlighted in appendix IV.

Airway and breathing:

Oxygen should be administered to maintain SpO_2 > 90%, with escalation of respiratory support as required, including high-flow nasal cannula, CPAP, or intubation and ventilation in cases of severe instability.

Care should be taken during induction of anaesthesia and use of positive pressure ventilation, as these may reduce venous return and cardiac output. In patients with right heart strain, strategies to optimise intubation and rapid sequence induction (RSI) include maintaining adequate preload with cautious fluid administration, avoiding hypotension through early use of vasopressors, and selecting haemodynamically stable induction agents such as ketamine. Pre-oxygenation should be maximised, while avoiding excessive positive pressure. During laryngoscopy, minimise apnoea time and avoid prolonged attempts. Following intubation, use lung-protective ventilation with low airway pressures, avoiding high PEEP and hyperinflation, and aim to prevent hypoxia, hypercapnia, and acidosis, all of which can worsen pulmonary vascular resistance and right ventricular failure.

Circulation:

All patients should undergo fluid resuscitation to normovolemia. In the presence of right ventricular (RV) failure in the form of echocardiography &/or biomarkers, cautious fluid resuscitation is essential, avoiding fluid overload as this may worsen cardiac output; vasopressor support (e.g. vasopressin as first line or noradrenaline) should be considered.

Vasopressin is often preferred in right heart strain from pulmonary embolism because it increases systemic vascular resistance without significantly raising pulmonary vascular resistance, helping maintain coronary perfusion to the right ventricle. In

contrast, noradrenaline can increase pulmonary vascular resistance, potentially increasing right ventricular afterload and impairing right heart function.

Haematology:

Anticoagulation should be initiated in accordance with GNCH guideline and discussed early with haematology.

3.5.2 Management based on risk (3,8)

Management of confirmed paediatric pulmonary embolism should be guided by risk stratification into low, intermediate, and high-risk categories.

Low-risk PE

- Patients are typically haemodynamically stable without evidence of right ventricular strain.
- Consultation with haematology and consideration of cardiology review (particularly for echocardiography).
- Anticoagulation should be initiated, most commonly with low molecular weight heparin (LMWH).
- Patients are usually managed in an inpatient setting.
- An echocardiogram should be performed within 24 hours.

Intermediate-risk PE

- Patients remain normotensive but demonstrate evidence of right ventricular strain on imaging &/or biomarkers.
- Early consultation with haematology cardiology & interventional radiology (IR) teams.
- Anticoagulation should be initiated with either LMWH or unfractionated heparin.
- In selected cases, particularly those who are deteriorating despite adequate anticoagulation, escalation to systemic or catheter-directed thrombolysis (e.g. alteplase) may be considered on a case-by-case basis following multidisciplinary discussion.
- Close monitoring is required, and many patients will require high dependency (HDU) level of care, including consideration of PICU admission depending on clinical status. An echocardiogram should be performed within 6 hours.

High-risk PE

- Characterised by haemodynamic instability, shock, or cardiac arrest.
- Immediate involvement of PICU, cardiac ICU, IR, haematology, and cardiology teams.
- Management includes prompt discussion with haematology and initiation of reperfusion strategies such as systemic thrombolysis if no contraindications exist (Appendix II)
- Consultation with IR for consideration of thrombectomy particularly if there are major contraindications to systemic thrombolysis.

- Advanced support measures, including veno-arterial extracorporeal membrane oxygenation (VA-ECMO) may be required in refractory cases.
- These patients should be managed in a critical care setting with continuous monitoring, multidisciplinary input and echocardiography.

3.5.3 PICU Admission

Escalation to PICU should be considered in children with pulmonary embolism (PE) who demonstrate clinical instability or require advanced monitoring and organ support (typically moderate- to high-risk PE). Indications include**:**

- **Airway and respiratory compromise**
  - Severe hypoxaemia despite supplemental oxygen
  - Requirement for invasive or non-invasive ventilation
- **Haemodynamic instability**
  - Shock requiring fluid resuscitation or inotropic/vasoactive support
  - Persistent hypotension
  - Evidence of right ventricular dysfunction or failure
- **Neurological compromise**
  - Altered mental status
  - Reduced level of consciousness
- **Clinical course**
  - Ongoing or rapid clinical deterioration
  - Severe or escalating symptoms requiring close monitoring
- **Treatment-related factors**
  - Requirement for advanced therapies (e.g. thrombolysis)
  - Complex anticoagulation management or high bleeding risk
- **Multi-organ involvement**
  - Evidence of multi-organ dysfunction

3.5.4 ECMO Referral

Some studies demonstrate a favourable survival in selected cases for children with PE who are supported by ECMO (9), therefore cardiac/ECMO team input is essential in MDT decision for high-risk PE category.

3.5.5 Surgical Embolectomy

SE may be considered in selected cases such as high suspicion for tumour embolism, high-risk PE & refractory cardiogenic shock or patients on ECMO (8).

3.6 Trigger assessment

In the paediatric population, the management of venous thromboembolism (VTE) is a highly targeted, context-dependent process. Over 90% of paediatric VTE events are "provoked" by identifiable triggers. Investigations are focused on the clinical context rather than broad, routine screening.

3.6.1 Diagnostic Imaging (8)

Imaging is essential to define the extent of the thrombus and identify the source, particularly within the lower limbs and the vena cava.

- Lower Limb Compression Ultrasound (USS): This is the first-line, non-invasive modality used to identify proximal deep vein thrombosis (DVT).
- CT Venography/Angiography: Reserved for cases where ultrasound is non-diagnostic or when there is high clinical suspicion of pelvic vein or inferior vena cava (IVC) thrombosis.
- Targeted Investigations: Broad systemic screening is not standard in paediatrics. Instead, further imaging—such as targeted abdominal ultrasound or MRI—is performed based on clinical suspicion to identify anatomical anomalies, venous obstruction, or underlying pathology.

3.6.2 Thrombophilia Screening

Routine screening is not recommended. Testing is reserved for specific clinical scenarios—such as adolescent unprovoked VTE, recurrent events, strong family history, or neonatal purpura fulminans and must be coordinated by a paediatric haematologist.

When testing is indicated, the panel typically includes:

- Antithrombin III, Protein C, and Protein S activity.
- Factor V Leiden and Prothrombin Gene G20210A mutation.
- Lupus anticoagulant and antiphospholipid antibodies.

Essential Timing and Interpretation with accuracy depends on strict adherence to the following protocols:

- Avoid the Acute Phase**:** Never test during the acute thrombotic event; markers like Protein C and Antithrombin are consumed by the active clot, which can yield misleading, false-positive results. Testing should be performed several weeks after an acute thrombosis or inflammatory condition to allow serum levels to return to baseline (11)
- Anticoagulant Washout: Testing must be deferred until at least 2–4 weeks after the cessation of all anticoagulants (e.g., LMWH or heparin) to ensure the coagulation system has normalized.
- Developmental Haemostasis: Clinicians must use age-adjusted reference ranges for interpretation, as neonates and infants naturally possess different coagulation factor levels compared to older children and adolescents.

3.7 Discharge & Follow Up

Children with pulmonary embolism can be considered for discharge when all clinical criteria are met and a safe management plan is in place. The patient should be haemodynamically stable, with no hypotension, stable heart rate, and no requirement for escalating support. Oxygenation should be adequate on room air or with a stable minimal oxygen requirement. Anticoagulation must be established and well tolerated, for example with low molecular weight heparin or an oral agent, and there should be no evidence of ongoing clinical deterioration. Pain and symptoms should be well

controlled, and right ventricular function should be stable or improving if previously abnormal.

In addition, safe discharge requires a clear anticoagulation plan with drug, dose, and duration documented, along with an appropriate monitoring strategy where required (e.g. anti-Xa levels).

Follow-up should be arranged with relevant specialties such as haematology, cardiology and respiratory teams, with imaging follow-up if indicated. A full risk factor assessment should be completed, including consideration of thrombophilia testing where appropriate, and any provoking factors reviewed and addressed. Refer to paediatric thrombosis clinic at GNCH. nuth.rvihaematologyreferral@nhs.net

Families and patients should receive education regarding anticoagulation safety, bleeding risk, and when to seek urgent medical attention. Finally, discharge should only occur where there is reliable safeguarding and adequate support at home.

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Appendix I – Age adjusted d-dimer results

	D-Dimer (ng/mL FEU)
Adult (>16 years)	<500
Paediatric (11-16 years)	160-390
Paediatric (6-10 years)	100-560
Paediatric (1-5 years)	90-530
Paediatric (Day 4 – 1 year)	110-420
Paediatric (Day 2 – Day 3)	580-2740
Paediatric (Day 0-Day 1)	410-2470

Adapted from North West London pathology services data sourced from a selection of sources (12–14).

Appendix II – Thrombolysis for paediatric PE

Indications for Systemic Thrombolysis

- High risk PE leading to cardiopulmonary arrest
- High risk PE with hemodynamic instability
- Intermediate risk PE with high risk of decompensation (with ECHO/CT findings of both RV strain and elevated biomarkers)
- PE with associated proximal limb deep vein thrombosis (DVT) with concern for acute limb ischemia

Contraindications for Thrombolysis

- Haemorrhagic stroke or stroke of unknown origin at any time
- Ischemic stroke in the preceding 6 months
- Central Nervous System (CNS) neoplasms
- Recent major trauma/surgery/head injury in the preceding 3 weeks
- Bleeding diathesis
- Active bleeding

Alteplase Dosing

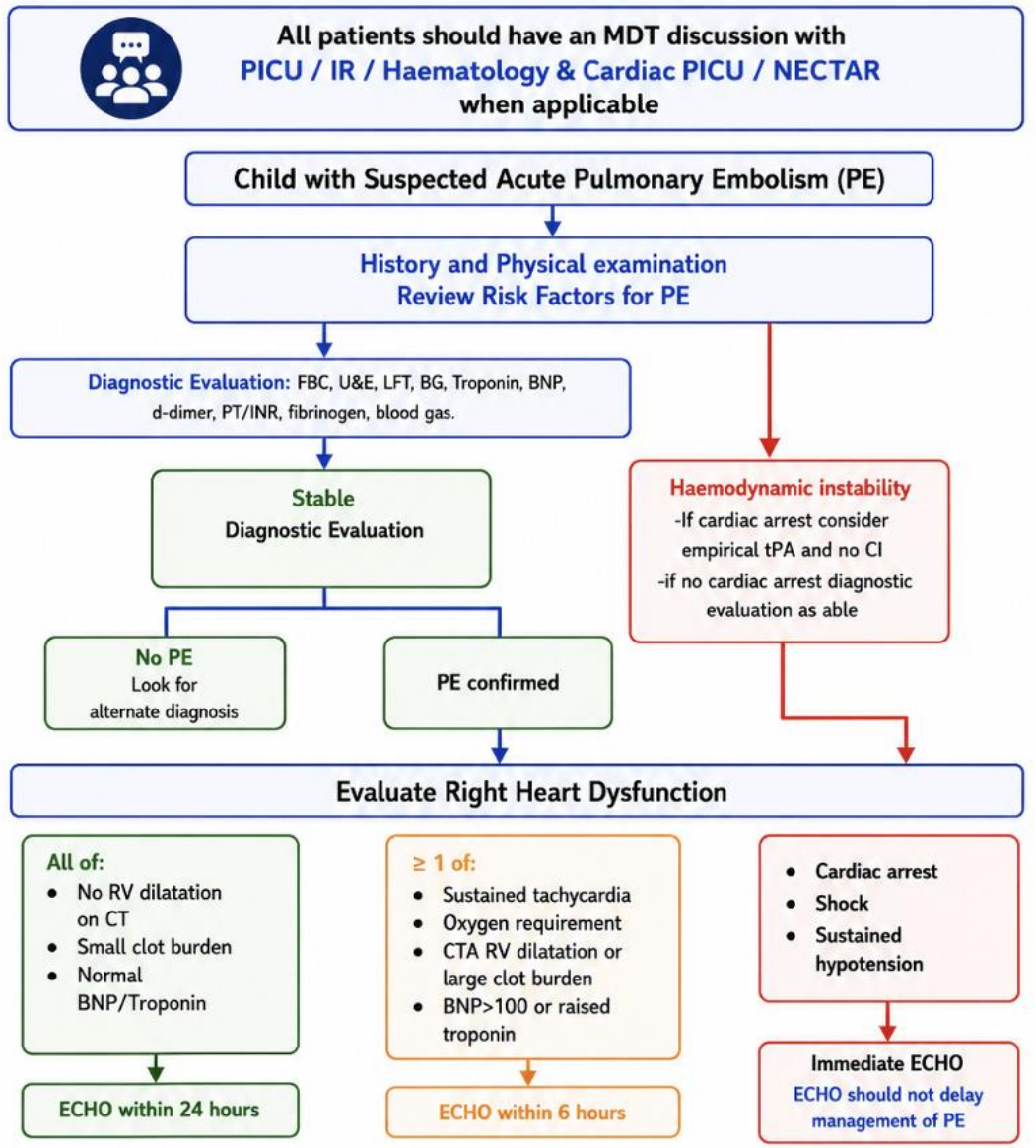
High dose alteplase

- < 60kg: 0.5mg/kg/hr run continuously for 6 hours (total 3 mg/kg, max 100 mg)
- 60 kg: 100 mg total dose run continuously over 2 hours (50mg/hr)

Rescue alteplase for cardiac arrest

- Dose
  - < 60 kg: 0.5 mg/kg over 2 minutes
  - > 60 kg: 50 mg over 2 minutes (max 50mg)
- Outcome
  - If ROSC not achieved within 15 minutes, then repeat dose
  - If ROSC is achieved, repeat dose, but infuse over 1 hour and initiate heparin infusion (no bolus)
- Consider 15mls/kg plasma prior to thrombolysis if <1 year of age (as a source of plasminogen to ensure efficacy)

Appendix III – PE Pathway Summary



RISK STRATIFICATION	Normal RV Normal BNP Normal Troponin	Abnormal RV Abnormal BNP &/or Troponin	Shock	Refractory Shock / cardiac arrest
STEP 1	Initiate PE MDT conference via NECTAR/PICU			
	Initiate heparin as per discussion with Haematology			
ACUTE MANAGEMENT OPTIONS DISCUSSED IN MDT CONFERENCE		Consider thrombolysis/catheter directed thrombolysis/thrombectomy/embolectomy		
			Vasoactive medications as required	
				Systemic thrombolysis/ECMO
ADMISSION AREA	Ward based care	Ward or HDU	PICU GNCH OR FRH agreed on MDT conference	
NEXT STEPS	Investigations to understand cause of PE – imaging and thrombophilia screen			

Appendix IV – NECTAR PE Pathway Summary