

GUIDELINES FOR THE MANAGEMENT OF PULMONARY EMBOLISM IN CHILDREN

A. Background

Pulmonary embolism is an uncommon but potentially fatal disease in children. The overall average age- and sex-adjusted annual incidence of pulmonary embolism in the United States was estimated to be 69 per 100,000 in a large retrospective review. In selected pediatric patient populations, the incidences of pulmonary embolism varied between less than 1% and 40%, reflecting different suspicion index, diagnostic tests and underlying clinical conditions. Anticoagulation is the mainstay of therapy. More than 50% of patients with PE still have defects on imaging 6 months after diagnosis.

B. Imaging

Clinical pulmonary embolism prediction rules have not been validated in children

1. Imaging spiral computed tomography pulmonary angiography is recommended, although is not as sensitive for subsegmental emboli.
2. If available, multi-detector CTPA and V/Q scans are more sensitive at picking up subsegmental emboli; a normal multi-detector CTPA or V/Q scan confidently rules out a PE. While pulmonary angiography is the gold standard for diagnosis, it is invasive and may be technically difficult in children.
3. V/Q scans are available at CCHMC base 7 days a week from 7a-11p, with radiopharmaceuticals arriving to bedside within 1-2 hours
4. Obtain 12 lead ECG.** Obtain a cardiac ECHO.
5. Obtain Doppler ultrasound of IVC, lower and upper extremities unless patient has a known DVT

*** Electro- cardiogram findings useful in the diagnostic evaluation for acute pulmonary embolism in adults include right bundle branch block and S wave in lead I, a Q wave in lead III, and inverted T wave in lead III; these comprise the classic S1Q3T3 pattern*

C. Laboratory Testing

1. Draw CBC, PT, PTT, fibrinogen, d-dimer, and factor VIII
2. For symptomatic PE, also draw troponin I, troponin T, and BNP at diagnosis. Troponin I >1ng/ml portends a more adverse clinical outcome.
3. All pubertal females should get a pregnancy test
4. Renal/hepatic profiles
5. Recommend thrombophilia work up (thrombotic profile, thrombophilic polymorphism panel, antiphospholipid syndrome). Consider also sending homocysteine risk assay and lipoprotein (a).

D. Acute management of ASYMPTOMATIC Pulmonary Embolism (ie, incidentally found)

1. Treat with therapeutic LMWH with or without transition to warfarin. See *CCHMC LMWH and warfarin guidelines*.
2. May consider treating for 3 months if uncomplicated and provoked, treatment for 6 months or more if unprovoked.

E. Acute management of SYMPTOMATIC Pulmonary embolism (including massive and submassive PE)*

1. Bolus with unfractionated heparin (see UFH guidelines), begin continuous infusion. Initial LMWH therapy can be considered for those patients with minimally symptomatic patients.
2. For patients with evidence of severe right heart strain, myocardial necrosis or hemodynamic instability requiring inotropic support, consider administration of systemic recombinant tissue plasminogen activator (t-PA). See *CCHMC systemic thrombolysis guidelines*.
3. For patients who have (i) contraindications to thrombolysis, (ii) failed thrombolysis, or (iii) shock that is likely to cause death before systemic thrombolysis can take effect (eg, within hours), if appropriate expertise and resources are available, recommend catheter-assisted thrombus removal with IR and interventional cardiology.
4. Continue heparin (UFH or LMWH) for a minimum of 5 days before switching to warfarin

DEFINITIONS OF MASSIVE AND SUBMASSIVE PE

MASSIVE PE*

Defined by persistent (>15min) hypotension or requiring inotropic support, bradycardia with signs or symptoms of shock.

SUBMASSIVE PE*

Defined as normal blood pressure, but evidence of RV dysfunction means the presence of at least 1 of the following:

- RV dilation (apical 4-chamber RV diameter divided by LV diameter >0.9) or RV systolic dysfunction on echocardiography
- RV dilation (4-chamber RV diameter divided by LV diameter >0.9) on CT
- Elevation of BNP (>90 pg/mL)
- Elevation of N-terminal pro-BNP (>500 pg/mL); or
- Electrocardiographic changes (new complete or incomplete right bundle-branch block, anteroseptal ST elevation or depression, or anteroseptal T-wave inversion)
- Myocardial necrosis is defined as either of the following:
 - Elevation of troponin I (>0.4 ng/mL) or
 - Elevation of troponin T (>0.1 ng/mL)

Systemic Thrombolysis for PE

Please see CCHMC systemic thrombolysis guidelines for complete protocol, contraindications, etc.

1. Recommend a two-hour infusion of alteplase 0.6mg/kg/hr, max of 50mg/hour. (*Common adult dose is alteplase 50mg/hr for 2 hours*)
2. Lower dose alteplase at 0.03-0.06mg/kg/hr for 6-12 hours can also be considered
3. Recommend decreasing unfractionated heparin to half the therapeutic dose during alteplase infusion for full dose tPA. For low dose tPA, continue therapeutic unfractionated heparin infusion.
4. Follow platelet count, aPTT, PT, FDPs, and fibrinogen prior to and after thrombolysis, or every 4-6 hours during longer duration alteplase infusion
5. Infants receiving alteplase may require FFP prior to thrombolysis to increase their plasminogen level
6. Use clinical evaluation and possible repeat imaging/ECHO after thrombolysis to assess need for further treatment
7. After alteplase infusion, increase unfractionated heparin to therapeutic doses, goal UFH anti-Xa 0.35-0.7.
8. Goal of systemic thrombolysis is to alleviate circulatory compromise or right heart strain.

F. IVC Filters in PE

1. In general, IVC filters are not recommended unless there are contraindications to anticoagulation
2. A long-term IVC filter can be considered in a patient who has had recurrent PE despite adequate anticoagulation or those with high risk of PE with poor adherence to anticoagulation
3. IVC filters without anticoagulation can predispose to lower extremity thrombosis

G. Outpatient management of PE

1. Anticoagulation
 - a) LMWH, warfarin or other anticoagulant should be continued for a minimum of 6 months for large or unprovoked PE. Three months may be sufficient for asymptomatic, provoked PE
 - b) Patients do not require supra-therapeutic dosing of anticoagulants for PE
2. All patients need a referral to pulmonary hypertension/cardiomyopathy clinic within 3 months of presentation
3. Follow up imaging with V/Q scan WITHOUT ventilation portion (reduces radiation exposure by 50%) can be considered at 6 months or end of therapy for patients with symptomatic PE, large clot burden on initial imaging, or recurrent PE. This sets a new baseline for the patient.

4. Recommend checking a D-dimer and factor VIII at the end of therapy and after 2-4 weeks off anticoagulation. Restarting anticoagulation should be considered if there is an increase in d-dimer after coming off anticoagulation.
5. Anticipatory guidance should be given to patients and families about chest pain after pulmonary embolism, which can last for several weeks after an acute event. A D-dimer should be drawn prior to imaging in patients with recent PE on anticoagulation.

References

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