Pulmonary Embolism (PE): Evaluation and Initial Management

Goal
Improve patient outcomes through the use of a standardized, collaborative, multidisciplinary, team-based urgent consult to treat massive and submassive PE.

Key Points
- For suspected massive PE (hemodynamically unstable patient) or cardiac arrest due to PE, proceed to page 3.
- Massive or submassive PE: Activate Pulmonary Embolism Response Team (PERT). Call 6-8111.
- For suspected PE in pregnancy, see Algorithm 4.

Algorithm 1. Use of PE Criteria Based on Patient Location at Time of Event

Any Suspicion for PE

Inpatient or ED/Outpatient (OP)?

Inpatient

Calculate Wells Criteria and see Algorithm 2 for additional treatment recommendations

ED/OP

Do any PERC Criteria apply?

Yes

Exclude other clinical etiologies based on clinical judgment and individual signs/symptoms

No

PE Excluded

Pulmonary Embolism Rule-out Criteria (PERC)

| Age ≥ 50 |
| HR ≥ 100 bpm (In pregnant women, HR ≥ 105 bpm) |
| Room air SaO2 < 95% |
| Prior History of DVT/PE |
| Recent trauma or surgery (<4 weeks) |
| Hemoptysis |
| Exogenous estrogen* |
| Unilateral leg swelling |

*Etonogestrel/Ethinyl estradiol (NuvaRing) must be included as a source of estrogen when doing the PERC

Patient meets ANY of the above PERC criteria: PE is not ruled out

Patient DOES NOT meet any of the above PERC criteria: There is < 2% risk of PE and therefore, the patient will not benefit from an evaluation for PE
Algorithm 2. Patient PE Risk Stratification Based on Wells Criteria Score

**Calculated Wells Criteria Score**

- Score>4?
  - Yes → PE Likely
  - No → PE less likely

**PE Likely**

- Suggested Empiric Treatment - Options:
  - Enoxaparin
  - Heparin
- See Appendix A for preferred option and dosing

**PE less likely**

- Perform High sensitivity d-dimer* test to rule out PE

**d-dimer Result**

- Positive → CTPE Study or V/Q scan (if contraindication to CTPE)
- Negative → PE excluded. Evaluate for another diagnosis

**CTPE Study Result**

- Positive → PE confirmed; proceed to Algorithm 3
- Negative
  - Possible repeat CTPE study
  - Consult with radiology prior to ordering any additional imaging

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**Algorithm 2. Patient PE Risk Stratification Based on Wells Criteria Score**

**Criteria Points**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical signs and symptoms of DVT</td>
<td>3.0</td>
</tr>
<tr>
<td>PE is more likely than an alternative diagnosis**</td>
<td>3.0</td>
</tr>
<tr>
<td>HR &gt; 100 bpm</td>
<td>1.5</td>
</tr>
<tr>
<td>Immobilization (&gt;3 days) or surgery in past 4 weeks</td>
<td>1.5</td>
</tr>
<tr>
<td>Previous DVT/PE</td>
<td>1.5</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1.0</td>
</tr>
<tr>
<td>Malignancy (On treatment, treated in the past 6 months, or palliative)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

**Wells Criteria: Pretest Probability for PE**

- **Notes**
  - Adjust high-sensitivity d-dimer for age among patients ≥ 50 years:
    - (Age x 0.01)
  - See Algorithm 4 for d-dimer references.

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Algorithm 3. Patient Pulmonary Embolism Severity Stratification

Hemodynamically Stable?

- Yes
  - Simplified PESI Score 0?
    - Yes
      - Normal Troponin (<0.11ng/mL) AND BNP* AND No RV Strain on TTE or CT?
        - Yes
          - Anticoagulant treatment (Appendix A or C)
        - No
          - Admit to med/surg monitored unit
    - No
      - Later hemodynamic deterioration?
        - Yes
          - Anticoagulant treatment (Appendix A or C)
        - No
          - Stat consult to PERT; call transfer center at 6-8111
      - PERT to determine need for and facilitate:
        - Placement in PCU or ICU
        - Follow-up monitoring / testing
        - Consideration of escalation of therapy
      - Usual care as indicated (Appendix C)

- No
  - Massive PE Risk
    - Consider full-dose systemic lytics if no absolute contraindications (Appendix B Lytics Checklist)
    - See OSUWMC Pharmacy for recommendations on the use of alteplase
    - Anticoagulant treatment (Appendix A)
    - Stat consult to PERT; call transfer center at 6-8111
    - Other treatment options may include:
      - Catheter directed lytics
      - Surgical embolectomy
      - ECLS
    - Admit to ICU
  - Low PE Risk
    - Anticoagulant treatment (Appendix A or C)
    - Outpatient treatment is appropriate. If warranted, admit to ED, MedEx OBS or monitored unit for observation.

Simplified PESI

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 80</td>
<td>1</td>
</tr>
<tr>
<td>History of cancer</td>
<td>1</td>
</tr>
<tr>
<td>History of chronic cardiopulmonary disease</td>
<td>1</td>
</tr>
<tr>
<td>HR ≥ 110 bpm</td>
<td>1</td>
</tr>
<tr>
<td>SBP &lt; 100 mmHg</td>
<td>1</td>
</tr>
<tr>
<td>O₂ saturation &lt; 90%</td>
<td>1</td>
</tr>
</tbody>
</table>

*BNP - Brain Natriuretic Peptide: 0-100 pg/mL

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Algorithm 4: PE in Pregnancy

Pregnant with suspected PE

Hemodynamically Stable?

Yes → Low Risk PE

Leg Symptoms? Yes → Positive Bilateral LE Ultrasound? Yes → Begin LMWH (Appendix A)

No → No PE

Hemodynamic instability defined as:
- SBP < 100 mmHg for >15 minutes (secondary to PE) or requiring pressors
- Decrease in SBP > 40 mmHg from baseline
- Cardiac Arrest

No → Massive or Submassive PE

Stat consult to PERT; call transfer center at 6-8111.

Proceed to CTPE
Initiate heparin standard sliding scale infusion (Appendix A)

High Pre-test Probability?

Yes → Wells > 4 (see page 2)
Simplified Revised Geneva Score >4
Third trimester
Unexplained hypoxemia

No → No PE

d-dimer Result

Positive → CTPE Study
Confirmed → Begin LMWH (Appendix A)
Not Confirmed → No PE

The following tests should be considered for risk stratification after confirmed PE diagnosis:

- Troponin
- Consider BNP

Adapted from: J Emerg Med 2015;49:104-117

*D-dimer Thresholds
Non-preg: <0.5 mcg/mL
1st trimester: <0.75 mcg/mL
2nd trimester: <1 mcg/mL
3rd trimester: <1.25 mcg/mL

*Although supported by current literature, this algorithm utilizing d-dimers has not yet been adopted by the American College of Obstetrics and Gynecology, the American College of Emergency Physicians or the American Thoracic Society.
Additional Considerations

- PE most often missed in obese, young, healthy, hemodynamically stable women on estrogen AND older patients with a good alternative diagnosis
- Sudden onset of chest pain occurs in 39% of PE (+) and 51% of PE (-) patients
- Reproducible chest pain occurs in 20% of PE (+) patients

Inferior Vena Cava (IVC) Filters:
- In patients with acute DVT or PE who are treated with anticoagulants, we recommend against the routine use of an IVC filter.

Follow-Up Recommendations

- 7–14 days post discharge: Anticoagulation follow-up
- 3 months post discharge: follow-up to determine hypercoagulation testing, direction of anticoagulation, need for repeat ECHO, further follow-up

OSUWMC Tools

Smart Phrases:
- EBPVTTEPERC
- EBPVTTEPSI
- EBPYTEWELLSCRITERIA

Order Sets:
- OSUWMC PVS: EKOS Device Orders [1775]
- OSUWMC RAD: Post-Procedure Intravascular Lysis [2626]
- OSU IP GEN: Pulmonary Embolism [6222]

References


Quality Measures

- Number of PERT activations

Guideline Authors

- Pulmonary Embolism Response Team

Guideline reviewed by: Critical Care Quality Committee

Date Approved

September 26, 2018. Fourth Edition

Disclaimer: Clinical practice guidelines and algorithms at The Ohio State University Wexner Medical Center (OSUWMC) are standards that are intended to provide general guidance to clinicians. Patient choice and clinician judgment must remain central to the selection of diagnostic tests and therapy. OSUWMC’s guidelines and algorithms are reviewed periodically for consistency with new evidence; however, new developments may not be represented.
## Appendix A: Initial Injectable Anticoagulation

<table>
<thead>
<tr>
<th>Massive PE</th>
<th>Submassive PE</th>
<th>Low-Risk PE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial Anticoagulation</strong></td>
<td><strong>Initial Anticoagulation</strong></td>
<td><strong>Initial Anticoagulation</strong></td>
</tr>
</tbody>
</table>
| UFH<sup>a, c</sup>  
Stop UFH if it has been started prior to the alteplase infusion. Re-initiate UFH at the completion of the alteplase infusion WITHOUT a bolus.  
*After systemic lytics<sup>b</sup>: Standard Sliding Scale: NO BOLUS, start 18 units/kg/hr (if less than 125 kg) or 12 units/kg/hr (if greater than or equal to 125 kg)  
*Without systemic lytics: Standard Sliding Scale: 80 units/kg bolus followed by 18 units/kg/hr (if less than 125 kg) or 12 units/kg/hr (if greater than or equal to 125 kg) | UFH<sup>a, c</sup>  
Standard Sliding Scale: 80 units/kg bolus followed by 18 units/kg/hr (if less than 125 kg) or 12 units/kg/hr (if greater than or equal to 125 kg) | DOAC  
See Appendix C  
UFH/LMWH Bridge to Warfarin<sup>a, g</sup>  
See Appendix C |

**Goal PTT:** [Per OSUWMC Established Heparin Therapeutic Range for Standard Sliding Scale](#)  
LMWH<sup>a, d, e, f</sup>  
Preferred if no procedure / intervention planned  
Enoxaparin 1 mg/kg SQ q12h  
**Goal Anti-Xa:** 0.6 – 1 IU/mL  
(Consider monitoring Anti-Xa levels)  
LMWH<sup>a, d, e, f</sup> |

**Ongoing Therapy**  
Warfarin  
DOAC  
LMWH<sup>a, d, e, f, g</sup>  
Warfarin  
DOAC  
LMWH<sup>a, d, e, f, g</sup>  
May continue with above therapies<sup>i</sup> |

**Special Considerations**  
<sup>a</sup>HIT: UFH and LMWH contraindicated; options include bivalirudin and argatroban – consult pharmacy for dosing  
(See Heparin-Induced Thrombocytopenia Guideline)  
<sup>b</sup>Systemic thrombolytics administered or likely to be administered: UFH preferred  
<sup>c</sup>May require procedure/ECMO: UFH preferred  
<sup>d</sup>Cancer: Consider hematology/oncology consult; LMWH may be preferred for ongoing therapy  
<sup>e</sup>Pregnancy: LMWH recommended for ongoing therapy  
<sup>f</sup>CrCl < 30 mL/min: Avoid LMWH; DOACs not preferred for ongoing therapy  
<sup>g</sup>Enoxaparin is not FDA approved for the outpatient treatment of pulmonary embolism.

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DOAC = Direct Oral Anticoagulant; ECMO = Extracorporeal Membrane Oxygenation; HIT = Heparin-Induced Thrombocytopenia; LMWH = Low Molecular Weight Heparin; UFH = Unfractionated Heparin


Appendix B: SYSTEMIC THROMBOLYTIC CHECKLIST FOR PULMONARY EMBOLISM COMPLETED PRIOR TO/IN CONJUNCTION WITH PERT CONSULT

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

**Contraindications (Answer NO to questions 4-8 to be eligible)**

**Absolute contraindications to thrombolysis become relative in patient with cardiac arrest or immediately life-threatening high-risk PE.**

| 4   |    | Known intracranial neoplasm, arteriovenous malformation or aneurysm |
| 5   |    | History of hemorrhagic stroke or stroke of unknown origin at any time |
| 7   |    | Active internal bleeding |
| 8   |    | Recent major trauma / major surgery / any neurosurgery / head injury /major bleeding within 3 weeks |

**Warning/Precaution Considerations**

*Check all that apply:*

| 9   |    | SBP > 180 mmHg or DBP > 110 mmHg |
| 10  |    | Known bleeding diathesis or acquired coagulopathies |
| 11  |    | Platelet count < 100,000/mm³ |
| 12  |    | Therapeutic anticoagulation |
| 13  |    | Current or recent use of: Ticagrelor (Brilinta®) within last 5 days or Prasugrel (Effient®) within last 7 days |
| 14  |    | Arterial puncture at non-compressible site, organ biopsy or lumbar puncture within last 7 days |
| 15  |    | Any history of ischemic stroke |
| 16  |    | Any neurosurgical procedure within 3 months, consider contacting surgeon to balance risk and benefit |
| 17  |    | Pregnancy, or within one week postpartum |
| 18  |    | Low body weight (< 60 kg), consider reduced dose (0.6 mg/kg) |
| 19  |    | Suspected or known infective endocarditis |
| 20  |    | Suspected or known pericardial effusion |
| 21  |    | Age < 18 years old |

**Futility Considerations**

- Thrombolytic therapy should not be used without a high clinical suspicion for PE as cause of arrest.
- If pursued, thrombolytic therapy should be given as soon as possible after arrest while following routine Advanced Cardiac Life Support (ACLS) resuscitative measures.
- In scenarios where resuscitation may be considered futile, such as patients with unknown down time or prolonged resuscitation, use of thrombolytic therapy may not offer clinical benefit.

**References**

- Standard OSUWMC clinical practice.

Individual completing form: _________________________________
# Appendix C: Long-term Oral Anticoagulation

<table>
<thead>
<tr>
<th>MOA</th>
<th>Apixaban (Eliquis&lt;sup&gt;®&lt;/sup&gt;)*</th>
<th>Rivaroxaban (Xarelto&lt;sup&gt;®&lt;/sup&gt;)*</th>
<th>Dabigatran (Pradaxa&lt;sup&gt;®&lt;/sup&gt;)*</th>
<th>Warfarin (Coumadin&lt;sup&gt;®&lt;/sup&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosing for DVT/PE</td>
<td>10 mg BID for 7 days followed by 5 mg BID</td>
<td>CrCl &gt; 30mL/min: 15 mg BID with food for first 21 days then 20 mg daily with food</td>
<td>CrCl &gt; 30 mL/min: 150 mg BID after 5-10 days of parenteral anticoagulation</td>
<td>Initial dose recommendation 2.5-5mg titrated for to goal INR</td>
</tr>
<tr>
<td>For prevention of DVT/PE recurrence after initial treatment of 6 months a dose reduction may be considered:</td>
<td>2.5 mg BID</td>
<td>For prevention of DVT/PE recurrence after initial treatment of 6 months a dose reduction may be considered:</td>
<td></td>
<td>Consider 2.5 mg for high bleeding risk patients (elderly, malnourished, congestive heart failure, hepatic dysfunction, interacting drugs)</td>
</tr>
<tr>
<td>Starter Pack</td>
<td>30 day starter pack includes: 5 mg tablets (#74 tablets)</td>
<td>30 day starter pack includes: 15 mg (#42 tablets) &amp; 20 mg (9 tablets) *Check pharmacy availability</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Requires initial parenteral anticoagulation</td>
<td>No</td>
<td>No</td>
<td>Yes (5-10 days of parenteral anticoagulation)</td>
<td>Yes (minimum of 5 days of parenteral anticoagulation and to goal INR)</td>
</tr>
<tr>
<td>Percentage of renal clearance</td>
<td>27%</td>
<td>36%</td>
<td>80% active dabigatran</td>
<td>92% (primarily inactive metabolites – does not require dose adjustment)</td>
</tr>
<tr>
<td>Renal Dysfunction</td>
<td>PREFERRED if must use DOAC</td>
<td>Patients with CrCl &lt; 30 mL/min not included in trials leading to FDA approval</td>
<td>Patients with CrCl &lt; 30 mL/min not included in trials leading to FDA approval</td>
<td>PREFERRED No specific adjustment necessary</td>
</tr>
<tr>
<td>Patients with CrCl &lt; 25 mL/min or Scr &gt; 2.5 not included in trials leading to FDA approval, but approved for use in patients with CrCl &lt; 15 mL/min and ESRD</td>
<td>Avoid in presence of combined P-gp and moderate CYP3A4 inhibitors with CrCl &lt; 80 mL/min</td>
<td>Avoid in the presence of P-gp inhibitors with CrCl &lt; 50 mL/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver Dysfunction</td>
<td>Child-Pugh C: not recommended</td>
<td>Child-Pugh B &amp; C: not recommended</td>
<td>Child-Pugh B: large inter-subject variability, but no evidence of a consistent change in exposure or pharmacodynamics</td>
<td>Liver impairment or genetic variations in CYP2C9 or VK0RC1 may lead to supratherapeutic INR levels requiring dose adjustment</td>
</tr>
<tr>
<td>Not recommended in setting of coagulopathy with increased INR</td>
<td>Not recommended in setting of coagulopathy with increased INR</td>
<td>Not recommended in setting of coagulopathy with increased INR</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Check pharmacy availability

PREFERRED

No specific adjustment necessary

Initial dose recommendation 2.5-5mg titrated for to goal INR

Consider 2.5 mg for high bleeding risk patients (elderly, malnourished, congestive heart failure, hepatic dysfunction, interacting drugs)

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**Edoxaban (Savaysa®)** is a Factor Xa inhibitor that is approved for VTE/PE, but is not on formulary at OSUWMC. This medication requires a minimum of 5 days of parenteral therapy prior to initiation. Notably, edoxaban is not recommended in those with CrCl > 95 mL/min in the atrial fibrillation population due to reduced efficacy. While this same labeling is not present for the indication of VTE/PE, careful consideration should be given as the drug exhibits the same kinetics regardless of indication. Please refer to the edoxaban fact sheet available on the intranet if considering for outpatient prescribing.

**Betrixaban (Bevyxxa®)** is not recommended for this indication.

---

<table>
<thead>
<tr>
<th>Dyspepsia or history of GI Bleeding</th>
<th>Apixaban (Eliquis®)*</th>
<th>Rivaroxaban (Xarelto®)*</th>
<th>Dabigatran (Pradaxa®)*</th>
<th>Warfarin (Coumadin®)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PREFERRED DOAC</strong></td>
<td>Associated with more GI bleeding compared to warfarin</td>
<td>Associated with more GI bleeding than warfarin</td>
<td>Associated with more GI bleeding and dyspepsia than warfarin</td>
<td>Similar or lower incidence of dyspepsia compared to DOACs</td>
</tr>
<tr>
<td>History of intracranial hemorrhage (ICH)/hemorrhagic stroke</td>
<td><strong>PREFERRED</strong> Less ICH than warfarin</td>
<td><strong>PREFERRED</strong> Less ICH than warfarin</td>
<td><strong>PREFERRED</strong> Less ICH than warfarin</td>
<td>Increased risk of ICH compared to DOACs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight</th>
<th>Apixaban (Eliquis®)*</th>
<th>Rivaroxaban (Xarelto®)*</th>
<th>Dabigatran (Pradaxa®)*</th>
<th>Warfarin (Coumadin®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced efficacy if &gt; 120 kg</td>
<td><strong>PREFERRED</strong> if must use DOAC and BMI ≥ 40 kg/m²</td>
<td>Close clinical monitoring if &lt; 50kg</td>
<td><strong>PREFERRED</strong></td>
<td></td>
</tr>
<tr>
<td>Increased exposure if &lt; 50 kg</td>
<td><strong>AVOID IF BMI ≥ 40 kg/m²</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>Apixaban (Eliquis®)*</th>
<th>Rivaroxaban (Xarelto®)*</th>
<th>Dabigatran (Pradaxa®)*</th>
<th>Warfarin (Coumadin®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid</td>
<td><strong>Avoid</strong></td>
<td><strong>Avoid</strong></td>
<td><strong>Contraindicated</strong></td>
<td></td>
</tr>
<tr>
<td>Parenteral Therapy Preferred in Pregnant Patients (see Appendix A).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug interactions</th>
<th>Apixaban (Eliquis®)*</th>
<th>Rivaroxaban (Xarelto®)*</th>
<th>Dabigatran (Pradaxa®)*</th>
<th>Warfarin (Coumadin®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease dose by 50% (if on 5 mg or 10mg BID) or avoid (if on 2.5mg BID) when co-administered with drugs that are strong dual inhibitors of CYP3A4 and P-gp (e.g. ketoconazole, itraconazole, ritonavir, or clarithromycin)</td>
<td>Avoid in presence of combined P-gp and strong CYP3A4 inhibitors (e.g. ketoconazole, ritonavir)</td>
<td>Avoid in presence of combined P-gp and moderate CYP3A4 inhibitors with CrCl &lt; 80 mL/min (e.g. erythromycin)</td>
<td><strong>PREFERRED if must use DOAC</strong> Avoid in the presence of P-gp inhibitors with CrCl &lt; 50 mL/min (e.g. dronedarone, ketoconazole)</td>
<td></td>
</tr>
<tr>
<td>Avoid concomitant use with strong dual inducers of CYP3A4 and P-gp (e.g. rifampin, carbamazepine, phenytoin, St. John’s Wort)</td>
<td>Avoid in presence of inducers of CYP3A4 (e.g. carbamazepine, phenytoin, rifampin, St. John’s Wort)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient assistance program</th>
<th>Apixaban (Eliquis®)*</th>
<th>Rivaroxaban (Xarelto®)*</th>
<th>Dabigatran (Pradaxa®)*</th>
<th>Warfarin (Coumadin®)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Yes</strong></td>
<td><strong>Yes</strong></td>
<td><strong>Yes</strong></td>
<td><strong>No</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reversible</th>
<th>Apixaban (Eliquis®)*</th>
<th>Rivaroxaban (Xarelto®)*</th>
<th>Dabigatran (Pradaxa®)*</th>
<th>Warfarin (Coumadin®)</th>
</tr>
</thead>
</table>

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*Click on Medication for link to Medication Fact Sheet

**Betrixaban (Bevyxxa®)** is not recommended for this indication.