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

**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.

### Pulmonary Embolism Rule-out Criteria (PERC)

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 50</td>
</tr>
<tr>
<td>HR ≥ 100 bmp (In pregnant women, HR ≥ 105 bpm)</td>
</tr>
<tr>
<td>Room air SaO₂ &lt; 95%</td>
</tr>
<tr>
<td>Prior History of DVT/PE</td>
</tr>
<tr>
<td>Recent trauma or surgery (≤4 weeks)</td>
</tr>
<tr>
<td>Hemoptysis</td>
</tr>
<tr>
<td>Exogenous estrogen*</td>
</tr>
<tr>
<td>Unilateral leg swelling</td>
</tr>
</tbody>
</table>

*Etonogestrel/Ethynyl 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

Suggested Empiric Treatment - Options:
- Enoxaparin
- Heparin

See Appendix A for preferred option and dosing

No

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)

Confirmed

PE confirmed; proceed to Algorithm 3

Not Confirmed

- Possible repeat CTPE study
- Consult with radiology prior to ordering any additional imaging

Negative

PE excluded. Evaluate for another diagnosis

Notes*

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

Wells Criteria: Pretest Probability for PE

<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 (≥ 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>

***Chest X-ray reviewed, with no reasonable evidence found for alternative diagnosis.
Algorithm 3. Patient Pulmonary Embolism Severity Stratification

Hemodynamically Stable?

Yes

Simplified PESI Score 0?

No

Submassive PE Risk

Yes

Normal Troponin (<0.11ng/mL) AND BNP* AND No RV Strain on TTE or CT?

No

Anticoagulant treatment (Appendix A or C)

Yes

Admit to med/surg monitored unit

Anticoagulant treatment (Appendix A or C)

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.

Massive PE Risk

Consider full-dose systemic lysics 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 lysics
- Surgical embolectomy
- ECLS

Admit to ICU

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

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.

Submassive PE Risk

Normal Troponin (<0.11ng/mL) AND BNP* AND No RV Strain on TTE or CT?

No

Anticoagulant treatment (Appendix A or C)

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

Later hemodynamic deterioration?

Yes

Usual care as indicated (Appendix C)

No

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

Other treatment options may include:

- Catheter directed lysics
- Surgical embolectomy
- ECLS

Admit to ICU

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

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
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

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)

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

High Pre-test Probability?

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

Yes

CTPE Study

Confirmed

Begin LMWH (Appendix A)

Not Confirmed

Positive

d-dimer Result

Negative

No PE

Yes

No PE

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.

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
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:
- EBPVTEPERC
- EBPVTIFESI
- EBPVTEWELLSCRITERIA

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></td>
<td></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*:  
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> | LMWH<sup>a, c, e, f</sup>  
Preferred if no procedure / intervention planned | LMWH<sup>a, d, e, f</sup> |
|------------------|---------------------------------|------------------|
| Enoxaparin 1 mg/kg SQ q12h  
**Goal Anti-Xa**: 0.6 – 1 IU/mL  
(Consider monitoring Anti-Xa levels) | | |

**Ongoing Therapy**

<table>
<thead>
<tr>
<th>Warfarin</th>
<th>DOAC</th>
<th>LMWH&lt;sup&gt;a, d, e, f, g&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>DOAC</td>
<td>LMWH&lt;sup&gt;a, d, e, f, g&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>May continue with above therapies&lt;sup&gt;g&lt;/sup&gt;</th>
</tr>
</thead>
</table>

**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.

---

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

Patient/family members understood potential risks and benefits from treatment.
Information Source: ☐ Patient  ☐ Family _________  ☐ Outside Medical Record _________

<table>
<thead>
<tr>
<th>Yes/No</th>
<th>General Eligibility for IV treatment with ALTEPLASE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Clinical diagnosis of pulmonary embolism</td>
</tr>
<tr>
<td>Yes</td>
<td>Hemodynamic instability secondary to PE</td>
</tr>
<tr>
<td></td>
<td>SBP &lt; 100 mmHg for at least 15 minutes OR requiring vasopressors OR decrease in SBP &gt; 40 mmHg from baseline</td>
</tr>
<tr>
<td>Yes</td>
<td>Cardiac arrest with confirmed or high clinical suspicion for PE</td>
</tr>
</tbody>
</table>

Contraindications (Answer NO to questions 4-7 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 |
| 6 | Active internal bleeding |
| 7 | Recent major trauma / major surgery / any neurosurgery / head injury /major bleeding within 3 weeks |

Warning/Precaution Considerations
Check all that apply:

*Use careful consideration and risk vs. benefit analysis. Patient may receive thrombolytic therapy despite ≥ 1 of the below.*

| 8 | SBP > 180 mmHg or DBP > 110 mmHg |
| 9 | Known bleeding diathesis or acquired coagulopathies |
| 10| Platelet count < 100,000/mm³ |
| 11| Therapeutic anticoagulation |
| 12| Current or recent use of: Ticagrelor (Brilinta®) within last 5 days or Prasugrel (Effient®) within last 7 days |
| 13| Arterial puncture at non-compressible site, organ biopsy or lumbar puncture within last 7 days |
| 14| Any history of ischemic stroke |
| 15| Any neurosurgical procedure within 3 months, consider contacting surgeon to balance risk and benefit |
| 16| Pregnancy, or within one week postpartum |
| 17| Low body weight (< 60 kg), consider reduced dose (0.6 mg/kg) |
| 18| Suspected or known infective endocarditis |
| 19| Suspected or known pericardial effusion |
| 20| 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.
## Appendix C: Long-term Oral Anticoagulation

<table>
<thead>
<tr>
<th>MOA</th>
<th>Apixaban (Eliquis®)*</th>
<th>Rivaroxaban (Xarelto®)*</th>
<th>Dabigatran (Pradaxa®)*</th>
<th>Warfarin (Coumadin®)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing for DVT/PE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl &gt; 30mL/min</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>CrCl &gt; 30mL/min</td>
<td>For prevention of DVT/PE recurrence after initial treatment of 6 months a dose reduction may be considered: 2.5 mg BID</td>
<td>For prevention of DVT/PE recurrence after initial treatment of 6 months a dose reduction may be considered: 10 mg daily</td>
<td>Consider 2.5 mg for high bleeding risk patients (elderly, malnourished, congestive heart failure, hepatic dysfunction, interacting drugs)</td>
<td></td>
</tr>
<tr>
<td><strong>Starter Pack</strong></td>
<td>30 day starter pack includes: 5 mg tablets (#74 tablets) *Check pharmacy availability</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><strong>Requires initial parenteral anticoagulation</strong></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><strong>Percentage of renal clearance</strong></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><strong>Renal Dysfunction</strong></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</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>No specific adjustment necessary</td>
<td></td>
</tr>
<tr>
<td><strong>Liver Dysfunction</strong></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>
<tr>
<td>Dyspepsia or history of GI Bleeding</td>
<td>Apixaban (Eliquis®)*</td>
<td>Rivaroxaban (Xarelto®)*</td>
<td>Dabigatran (Pradaxa®)*</td>
<td>Warfarin (Coumadin®)</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>---------------------</td>
<td>------------------------</td>
<td>------------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>PREFERRED DOAC</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>
<td></td>
</tr>
<tr>
<td>No increased risk of GI bleeding compared to warfarin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>History of intracranial hemorrhage (ICH)/hemorrhagic stroke</th>
<th>PREFERRED</th>
<th>PREFERRED</th>
<th>PREFERRED</th>
<th>Similar or lower incidence of ICH compared to DOACs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less ICH than warfaran</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight</th>
<th>Reduced efficacy if &gt; 120 kg</th>
<th>PREFERRED if must use DOAC and BMI ≥ 40 kg/m²</th>
<th>Close clinical monitoring if &lt; 50kg</th>
<th>PREFERRED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased exposure if &lt; 50 kg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>Avoid</th>
<th>Avoid</th>
<th>Avoid</th>
<th>Contraindicated</th>
<th>Parenteral Therapy Preferred in Pregnant Patients (see Appendix A).</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Drug interactions</th>
<th>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)</th>
<th>Avoid in presence of combined P-gp and strong CYP3A4 inhibitors (e.g. ketoconazole, ritonavir)</th>
<th>Avoid in presence of combined P-gp and moderate CYP3A4 inhibitors with CrCl &lt; 80 mL/min (e.g. erythromycin)</th>
<th>Avoid in presence of inducers of CYP3A4 (e.g. carbamazepine, phenytoin, rifampin, St. John’s Wort)</th>
<th>PREFERRED if must use DOAC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<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 combined P-gp inhibitors with CrCl &lt; 50 mL/min (e.g. dronedarone, ketoconazole)</td>
<td>Avoid in presence of P-gp inhibitors with CrCl &lt; 50 mL/min (e.g. dronedarone, ketoconazole)</td>
<td>Avoid in presence of 2C9 inhibitors or drugs that interfere with Vitamin K production and metabolism (e.g. metronidazole, fluconazole, clarithromycin, ciprofloxacin, levofloxacin, sulfamethoxazole-trimethoprim, ketoconazole, certain chemotherapeutic agents)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient assistance program</th>
<th>Yes</th>
<th>Yes</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>


*Click on Medication for link to Medication Fact Sheet

**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.