Venous Thromboembolism Clinical Algorithm

Suspected DVT/PE

Positive pretest probability for DVT/PE
- Send off: CBC, INR, aPTT, D-Dimer, BNP, Cardiac ECHO, Vital Signs, Wells Score, Chem7, pregnancy test
- assess bleeding risk

Decision to treat
Initiate Anticoagulation

Inpatient Treatment

Suspected PE
PESI Score

Risk Stratify

RV Strain
(High or Intermediate)
Massive/Sub-massive PE

Low Risk
(No RV Strain – sPESI)

Initiate PERT

Outpatient Treatment

Considerations*:
- Pt willing to inject?
- Outpatient prescription coverage for LMWH or DOAC
- Arrange and communicate anticoagulation f/u
  - Clinic: Warfarin, NOAC: PCP f/u
  - Patient education on therapy
  - Lab/INR draw 2-3 days post-discharge

Transition to outpatient with bridge therapy

Mortality/Morbidity Risk**

- Lytic Therapy
- Heparin
- +/- IVC Filter

Transition to outpatient with bridge therapy

Continue therapy in hospital until able to transition to outpatient therapy

Suspected PE
Initiate Anticoagulation

Outpatient Treatment

Considerations*:
- Pt willing to inject?
- Outpatient prescription coverage for LMWH or DOAC
- Arrange and communicate anticoagulation f/u
  - Clinic: Warfarin, NOAC: PCP f/u
  - Patient education on therapy
  - Lab/INR draw 2-3 days post-discharge

*See appendix 1-2 for considerations in monitoring/management

**See appendix 3-6 for additional PERT information

Approved by UCDH Pharmacy & Therapeutics Committee 3/2017.
Considerations for monitoring:
- CBC
- D-dimer (no repeat necessary)
- INR
- Chem 7 (renal function for newer oral agents and LMWH)
- Antiplatelet therapy/Interacting medications
- Upcoming procedures
- Follow up issues (adherence/compliance)
- Symptoms of clot extension or PE
  - Consider repeat imaging if concerning
- Symptoms of bleeding
### Drug therapies:

- **Warfarin** to target INR 2.0-3.0
- **Dalteparin** 200 units/kg ABW* SQ if VTE within 30 days
- **Dalteparin** 150 units/kg ABW SQ if VTE greater than 30 days
  - CrCl < 20 ml/min contraindicated
- **Enoxaparin** 1 mg/kg ABW SQ BID
  - Contact Pharmacy if CrCl < 30 ml/min
  - Alternative dosing: 1.5 mg/kg daily
    - Not recommended if high risk, obese, cancer patient
- **Fondaparinux** 7.5mg SQ Q24
  - 5 mg if less than 50 kg
  - 10 mg if greater than 100 kg
  - Contact Pharmacy if patient has a estimated CrCl 30 ml/min
- **Heparin** 2500 or 5000 unit bolus
  - VTE treatment order set (Protocol ID # 180)
- **Rivaroxaban** 15mg twice daily x21 days, then 20mg daily
  - Contact pharmacy if patient has a estimated CrCl < 30 ml/min
- **Dabigatran** 150mg twice daily after 5-10 days parenteral therapy
  - Contact pharmacy if patient has a estimated CrCl < 30 ml/min
- **Apixaban** (not approved) 10 mg twice daily x 7 days, then 5 mg twice daily
  - Contact pharmacy if patient has a estimated CrCl < 25 ml/min, or Scr > 2.5
- **Edoxaban**: Contact Pharmacy for dosing recommendations

*Patients >150 kg, please contact pharmacy
Round to closest syringe size
** Contact Pharmacy if weight is over 120kg

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PERT Guidelines based on risk for mortality/morbidity: Appendix 3

<table>
<thead>
<tr>
<th>Bleed Risk</th>
<th>Low</th>
<th>Moderate</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE Risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>Heparin +/- Lytic</td>
<td>Heparin +/- Catheter Lytic</td>
<td>+/- IVC Filter, watch</td>
</tr>
<tr>
<td>High</td>
<td>Systemic Thrombolysis</td>
<td>Catheter Directed Lytic</td>
<td></td>
</tr>
<tr>
<td>911</td>
<td>Contraindication or failed anticoagulation/thrombolytic: CT Surgery, ECLS team, Vascular Surgery</td>
<td></td>
<td></td>
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</tbody>
</table>

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# Thrombolytic Management

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dosing</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TPA</strong></td>
<td><strong>Full dose:</strong> 100 mg over 2 hours (10 mg bolus with remaining 90 mg over 2 hours) &lt;br&gt; <strong>Half dose:</strong> 50 mg over 2 hours (10 mg bolus with remaining 40 mg over 2 hours) &lt;br&gt; - &lt;50 kg, the total dose is calculated as 0.5 mg/kg, which is given as a 10-mg initial bolus followed by the remainder over 2 hours. &lt;br&gt; <strong>Up front option in cardiac arrest:</strong> &lt;br&gt; - Up to 50 mg IVP over 1 minute in the setting of cardiac arrest with high suspicion for PE.  &lt;br&gt;  - Repeat dosing allowed at 15 mins based on bedside clinical decision. (Case report data)  &lt;br&gt;  - Infuse additional 50 mg over the next 2 hours at physician discretion) (Total dose 100mg)</td>
<td>Common approach if time available – preferred option in sub-massive PE, non-cardiac arrest setting.  &lt;br&gt; <strong>PEAPETT study (Am J Emerg Med 2016) n=23</strong> – dose just 50mg and heparin initiated immediately with a 2000-5000 bolus followed by a infusion 10 Unit/kg/hr for 24-30 hours then transitioned to long term therapy (rivaroxaban/apixaban)</td>
</tr>
<tr>
<td><strong>Tenecteplase (TNK)</strong></td>
<td><strong>Full dose:</strong> 30-50 mg (weight dependent) single intravenous bolus  &lt;br&gt; &lt;60 kg = 30 mg  &lt;br&gt; ≥60 to &lt; 70 = 35 mg  &lt;br&gt; ≥70 to &lt; 80 = 40 mg  &lt;br&gt; ≥80 to &lt; 90 = 45 mg  &lt;br&gt; &gt;90 kg = 50 mg</td>
<td><strong>PEITHO Trial - Fibrinolysis for patients with intermediate-risk pulmonary embolism. N Engl J Med. 2014;370:1402-11.</strong></td>
</tr>
<tr>
<td><strong>Heparin/ LMWH</strong></td>
<td><strong>Initiate a heparin infusion (with option of a small bolus) as soon as feasible after administration of the lytic therapy.</strong> If concurrently receiving a LWMH, initiate a heparin infusion 12 hours after the last LMWH dose.  &lt;br&gt; <strong>Initiate heparin infusion after administration of the lytic agent, or if already on heparin and a high aPTT, re-initiate heparin once the aPTT (or anti-Xa) value has fallen into the target range</strong></td>
<td></td>
</tr>
</tbody>
</table>

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Pulmonary Embolism Severity Index (PESI): Appendix 4

- Estimate of 30-day mortality and severity of complications from PE based on 11 clinical criteria: age, sex, history of cancer/CHF/chronic lung disease, tachycardia, hypotension, tachypnea, hypothermia, hypoxia, AMS
- Externally validated for newly diagnosed PE, in patients treated with enoxaparin then transitioned to vitamin K antagonists, excluded patients with renal failure or severe comorbidities
- Scored from 0 to >125; Risk classes I to V with corresponding range in mortality estimated 1% to 25%
- Very low risk (score <65) and low risk (score 66-85) PE patients had 30-day mortality <1% and may be candidates for outpatient care
- Sources: Derivation/Validation (Aujesky D, 2005), Prospective Validation (Donze J, 2008), Outpatient Management Trial (Aujesky D, 2011)
- Simplified PESI (sPESI)
### PESI Score

<table>
<thead>
<tr>
<th>PESI Score</th>
<th>Class</th>
<th>Risk 30 day Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-65</td>
<td>I</td>
<td>0.0-1.6%</td>
</tr>
<tr>
<td>76-85</td>
<td>II</td>
<td>1.7-3.5%</td>
</tr>
<tr>
<td>86-105</td>
<td>III</td>
<td>3.2-7.1%</td>
</tr>
<tr>
<td>106-125</td>
<td>IV</td>
<td>4.0-11.4%</td>
</tr>
<tr>
<td>≥125</td>
<td>V</td>
<td>10-24.5%</td>
</tr>
</tbody>
</table>

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Simplified PESI (sPESI): Appendix 5

• Abbreviated version of the PESI score; uses 6 clinical criteria instead of 11
• Best used to determine LOW risk PE patients that may be candidates for outpatient care
• As accurate as the original PESI for 30-day mortality from PE
• Compared to PESI the sPESI derivation categorized fewer patients as low risk; patients in the sPESI study had more comorbidities
• Low risk by sPESI = 0 points; associated mortality 1.1% and severe morbidity 1.5%
• High risk >/= to 1 point; however increasing points on the sPESI does not correlate to increasing mortality
• Calculator: http://www.mdcalc.com/simplified-pesi-pulmonary-embolism-severity-index/#how-to-use
• Sources: Derivation (Jimenez D, 2010), Meta-analysis (Zhou, 2012)
PE Rule-out Criteria (PERC): Appendix 6

• In low risk patients (pre-test probability <15%) helps rule out PE to <2% chance, and avoids unnecessary testing and treatment for PE
• Based on 8 clinical criteria; All criteria must be absent/negative to be able to apply PERC
• Any positive criteria makes PERC non-applicable; D-dimer may then be considered, however PERC does not mandate further testing
• Based on estimated test threshold of 1.8%, below which the risks of workup are considered to equivalent to risk of missing PE
• Calculator: http://www.mdcalc.com/perc-rule-pulmonary-embolism/
• Sources: Original PERC derivation and validation (Kline J, 2004), Second multi-center validation (Kline J, 2008)