RECOMMENDATIONS FOR THE MANAGEMENT OF MASSIVE AND SUBMASSIVE PULMONARY EMBOLISM IN ADULT PATIENTS.

Target Audience:
Physicians managing adult patients with massive and submassive pulmonary emboli in the inpatient setting.

Scope/Patient Population:
This guideline applies to adult patients who are diagnosed with either massive or submassive pulmonary emboli. Patients may present to a MultiCare Emergency Department with this condition, may be transferred from another facility for management of this condition or may develop this condition while hospitalized for a different medical problem.

Rationale:
Pulmonary embolism (PE) is a common medical problem, with several hundred cases treated annually in the MultiCare system. There are subgroups within the population of PE patients that carry higher risks of mortality. These are categorized as massive pulmonary embolism (MPE), estimated at 5% of PE cases, and submassive PE (SPE), estimated at 20-25% of PE cases. The management of MPE is relatively straightforward but there is not agreement in the medical literature on the best management approach for SPE. There are advantages and disadvantages to each therapeutic approach and not all therapies are available at all MC hospitals. The goal of this guideline is to summarize current knowledge on the treatment of MPE and SPE and to propose algorithms for use in the MC system. The algorithms may vary between hospitals due to the availability of different therapies at the different hospitals.

Objective
To provide information to providers to support decision making regarding the management of MPE and SPE patients. The goal is to provide the optimal therapy for each PE patient, balancing anticipated benefits (reduced PE related morbidity and mortality) against the risks of therapy (primarily bleeding).

As this guideline is being developed, efforts have begun to create a Pulmonary Embolism Response Team (PERT) to be available for consultation for cases of MPE and SPE. This will allow a treating physician to consult a small group of
experts on short notice to determine the best therapeutic approach for a given patient and to facilitate such therapy. The first PERT will serve West Pierce and may serve as a model for the creation of an East Pierce PERT.

Background:

Definitions:
- **Submassive PE**: evidence of new RV dysfunction by echo or CT but hemodynamically stable. Commonly used criteria for RV dysfunction include: RV/LV ratio > 0.9 (echo or CT) or RV hypo contractility. The use of biomarkers suggesting cardiac injury (elevated cTnI) or acutely elevated right pressures (BNP level) can help to stratify severity of pulmonary emboli. Consideration must be given to the possibility of preexisting right heart dysfunction when evaluating chamber sizes and BNP levels. A newly elevated BNP level is more significant in this context than a chronically elevated level. Expected mortality of SPE: 4-30% based upon severity of RV dysfunction.

- **Massive PE**: any PE causing hemodynamic instability. Expected mortality with MPE: 70% when associated with cardiac arrest, 30% with ‘cardiogenic shock’, 15% with hypotension.

- **Hemodynamic instability**: systolic BP < 90 for greater than 15 mins or requiring pressor support of BP.

- **Clot in transit**: thrombus visualized in the RA or RV.

Notes:

1. The size and location of clots do not enter into the definition of submassive and massive PE.

2. Clot burden and preexisting cardiopulmonary disease will influence the hemodynamic impact of pulmonary embolism and thus indirectly influence whether a PE will result in the clinical picture of SPE or MPE.

Therapeutic ‘quiver’ - the therapies available in the MC System:

1. **Heparin anticoagulation** (AC): prevents formation of more clot, does not speed resolution of clots. Low molecular weight heparin products (LMWH) are favored over unfractionated heparin (UFH) due to the more predictable pharmacokinetics, greater ease of administration and lower incidence of heparin induced thrombocytopenia with LMWH. Bleeding risk: hemorrhagic stroke risk <0.5%. **Availability: all hospitals.**

2. **Systemic thrombolysis**: speeds clot resolution. Tenecteplase is favored over tPA for it’s faster administration and effect. Bleeding risk: 2-3% risk of hemorrhagic stroke, 6% risk of extracranial bleeding. **Availability: all hospitals.**
3. Catheter directed thrombolysis (CDT): delivers thrombolytic agent to the pulmonary arteries, accelerates clot resolution. Probably of comparable or superior efficacy compared to systemic lysis. Utilizes a smaller dose of thrombolytic agent (eg 24 mg of tPA vs 100 mg for systemic therapy). Can be safely performed in patients with contraindications to systemic thrombolysis. Probably no increase in bleeding risk compared to AC alone. Therapy is provided via a simple catheter or via an ultrasound enhanced catheter (EKOS) inserted via a femoral approach. RBBB is a contraindication to CDT. Availability: TG, GSH, AMC (soon)

4. Catheter aspiration: used primarily for clots in the heart. Availability: TG only

5. Open surgical embolectomy: salvage procedure, very rarely performed. Availability: TG only

6. ECMO: circulatory support to be considered for patients deteriorating despite other therapies. Availability: TG only

SPE management, knowns and unknowns:
Patients with SPE are at increased risk for cardiovascular collapse and death as compared to PE patients without RV dysfunction. This is the impetus behind more aggressive therapy for SPE. The risks associated with these therapies must be weighed against the anticipated benefits. “Patients with the highest risk of dying from PE and the lowest risk of bleeding obtain the greatest net benefit from thrombolytic therapy. Patients with the lowest risk of dying from PE and the highest risk of bleeding obtain the least net benefit from thrombolytic therapy and are likely to be harmed”\(^1\). Thus, it is important to assess PE severity and bleeding risk in each patient when selecting therapy. It is recommended that a discussion of the risks and benefits of different management strategies be held with patients and families whenever possible. Informational material useful for these discussions is appended to this guideline.

Systemic thrombolysis of SPE has been shown to reduce the incidence of cardiovascular collapse but also increases the chance of major bleeding\(^2\). “These benefits and harms are finely balanced, with no convincing net benefit from thrombolytic therapy. ‘Rescue thrombolytic therapy' appears to be of benefit in patients who develop cardiovascular collapse after initially being treated with AC alone”\(^1\). Systemic thrombolysis has not been shown to reduce mortality in SPE.

The optimal intensity of and agent for systemic thrombolysis is not certain. The 100 mg dose of tPA that is typically used was derived from studies in non-PE patients. Wang et al compared a 50 mg and 100 mg dose of tPA in the
treatment of SPE and found similar efficacy and less bleeding using the lower dose of tPA\(^3\). Lower dose systemic thrombolysis was also studied in the MOPETT trial, showing improvement in pulmonary pressures without an increase in bleeding events compared to AC alone.\(^4\)

Catheter directed thrombolysis has shown a high success rate in speeding the resolution of clots in the pulmonary vasculature and improving RV function at 24 hours.\(^1,5\) Nonetheless, CDT has not yet been demonstrated to reduce mortality in PE.

**Suggested management for SPE:**

1. Risks stratify PE as well as the risk of bleeding from therapy (see appendices \(1\) & \(2\)).
2. Discuss with patient and family (see appendix \(3\)).
3. Choose one of the following:
   a) Provide AC and observe for hemodynamic deterioration -> escalate therapy if there is deterioration (CDT or systemic lysis) or
   b) Provide half dose systemic thrombolysis or
   c) Proceed directly to CDT. (once available, consultation with the PERT will be recommended).
4. Admit to ICU.

**Suggested algorithm for MPE:**

1. Assess bleeding risk (see appendices \(1\) & \(2\)), proceed to systemic lysis or CDT.
2. If there is an absolute contraindication to lytic therapy, consider mechanical extraction (catheter or surgical) and/or circulatory support. (once available, consultation with the PERT will be recommended)
3. Admit to ICU.

**Algorithm:** [Link to algorithm.](#)

**Evidence:**


(half dose lytic therapy for “moderate PE”)


**List of Implementation Items and Patient Education:**

1. Tools for risk stratification of PE.

2. Contraindications to thrombolysis.

3. Patient and family informational material.

**Metrics Plan:**

N/A

**PDCA Plan:**

Guideline to be reviewed by the Critical Care Collaborative every two year cycle, unless more frequent review is mandated.

**Point of Contact:** Medical Lead of the Critical Care Collaborative

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<tbody>
<tr>
<td>Collaborative (Critical Care)</td>
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Distribution: MultiCare Connected Care + MultiCare Health System
Appendix 1

Tools for PE Risk Stratification

The stratification of risk for complication or mortality with pulmonary embolism is an inexact science with poorly defined criteria. Essentially one is trying to identify evidence of developing circulatory or respiratory insufficiency, or evidence of moderate to severe RV injury. Criteria include: patient distress, reduced blood pressure, tachycardia, reduced oxygenation, echocardiographic or CT evidence of RV dysfunction, elevated biomarkers (BNP, troponin) and more. These are not dichotomous criteria and there are not universally agreed upon thresholds that define minor or major abnormalities, thus judgement of the bedside physician is required. Below are two validated indices to help identify low risk and high risk PE patients.

**Simplified Pulmonary Embolism Severity Index (sPESI):**
The sPESI identifies patients at low risk for mortality and thus not in need of advanced therapies (patients potentially treatable at home). It does not necessarily identify patients at high risk for mortality.

- Age > 80 years 1 point
- History of cancer 1 point
- History of chronic cardiopulmonary disease 1 point
- Heart rate > 110 1 point
- Systolic BP < 100 1 point
- O2 saturation < 90% 1 point

\[
sPESI = 0: \text{30 day mortality} < 1\%
\]
\[
sPESI > 1: \text{30 day mortality} 10.9\%
\]

**BOVA Risk Score**
The BOVA risk score identifies patients at higher risk for complications, including mortality.

<table>
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<th>Predictor</th>
<th>Points</th>
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<tr>
<td>SBP 90–100 mmHg*</td>
<td>2</td>
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<tr>
<td>Elevated cardiac troponin</td>
<td>2</td>
</tr>
<tr>
<td>RV dysfunction (echocardiogram or CT scan)</td>
<td>2</td>
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<tr>
<td>Heart rate ≥110 beats per min</td>
<td>1</td>
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References:
Points are assigned for each variable of the scoring system to obtain a total point score (range 0–7). SBP: systolic blood pressure; RV: right ventricular; CT: computed tomography.

*Lower blood pressures imply hemodynamic instability and massive PE.*

<table>
<thead>
<tr>
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<td></td>
<td>I</td>
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<tr>
<td><strong>Points</strong></td>
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<td><strong>Patients %</strong></td>
<td>75.5</td>
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<td><strong>30-day PE-related complications %</strong></td>
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<td><strong>In-hospital PE-related complications %</strong></td>
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<tr>
<td><strong>30-day PE-related mortality %</strong></td>
<td>1.7</td>
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References:

Appendix 2

Contraindications to Systemic Thrombolysis

A relative contraindication may be acceptable in some situations, such as with a patient in extremis due to massive PE (as opposed to a stable patient with submassive PE).

CNS Pathology
- Any prior intracranial hemorrhage
- Ischemic CVA
  - within 3 months (absolute)
  - >3 mos. (relative)
- Structural cerebrovascular disease such as AVM (absolute)
- CNS neoplasm (absolute)
- Recent surgery involving the spinal canal or brain (absolute)

Trauma
- Recent head trauma with fracture or brain injury (absolute)
- “Minor head trauma due to syncope is not necessarily a barrier to fibrinolysis” (AHA/ACC guideline 2011)

Recent Surgery / Procedures
- Major non-CNS surgery within 3 weeks (relative)
- Recent puncture of non-compressible vessel (relative)

Bleeding History
- Bleeding
  - Active bleeding, excluding menses (absolute)
  - Recent internal bleeding within 2-4 weeks (relative)
- Known bleeding diathesis (absolute)
- Active bleeding (absolute)
- Internal bleeding within past month (relative)

Coagulation studies
- Platelets <100 (relative, depends on level however)
- Review INR & PTT (repeat PTT if on heparin drip)

Anticoagulants
- Current use of oral anticoagulation (relative)
- Multiple anticoagulating drugs (relative)

HTN
- Hx of chronic, severe, poorly controlled HTN (relative)
- BP on presentation >180 systolic or >110 diastolic (relative)
Age
- >75 YO (relative)
- Dementia (relative)

Specific situations
- Pregnancy or 1st postpartum week (relative)
- Traumatic or prolonged CPR (relative)
- Suspected aortic dissection (absolute)
Appendix 3

Pulmonary Embolism: Patient Education

You have been diagnosed with a pulmonary embolism. Here is some basic information pulmonary embolism and how it is treated.

What is a pulmonary embolism?

Pulmonary embolism (or “PE”) is a blockage in one or more of the blood vessels that supply blood to the lungs. Most often these blockages are caused by blood clots that form elsewhere and then travel to the lungs.

Why are blood clots dangerous?

If a blood clot forms or gets stuck inside a blood vessel, it can clog the vessel and keep blood from getting where it needs to go. When that happens in the lungs, the lungs can get damaged and the heart can struggle to pump the blood through the lungs. Having blocked arteries in the lung can make it hard to breathe and can even lead to death. Most blood clots that end up in the lungs form in the legs or pelvic area (where the legs connect to the body) and then travel to the lungs.

How are blood clots in the lungs treated?

Most people being treated for a blood clot in the lung are treated first in the hospital. Blood clots in the lungs are treated with medicines that keep clots from getting bigger or dissolve clots. Some of these medicines are injected directly into a vein, while others come in shots or pills. Anti-clotting medicines do not dissolve existing blood clots, but they do keep them from getting bigger. They also help keep new blood clots from forming. The body is able to dissolve clots on its own over days to weeks.

Most cases of pulmonary embolism are considered "low risk", that is the chance of dying from them is low and the treatment is relatively simple. In some cases, a person has a clot that is severe enough to cause low blood pressure and even shock. (Shock is when blood pressure gets too low, and not enough blood can get to the body’s organs and tissues.) This condition is called "massive pulmonary embolism" and when this happens it is not safe to wait for the body to dissolve clots on its own. With massive pulmonary embolism doctors can give a medicine to dissolve the clot. The medical term for this is "thrombolysis", while a more common
term is "clot busting." This treatment is usually given through a vein. This treatment can help to break up clots and reduce the strain on the heart, but it can also cause bleeding elsewhere in the body. In some cases doctors may insert a catheter through the veins of the leg into the lungs and deliver the clot busting medicine directly into the lungs (this is called catheter directed therapy or CDT).

Some blood clots force the heart to work harder than normal but do not cause low pressure. This condition is called "submassive pulmonary embolism." Treatment for this condition must be determined on a case by case basis, weighing the benefits of various therapies against the risks of those therapies.

People who cannot take medicines to treat clots, or who fail to benefit from the medicines, can get a different treatment. This is called an "inferior vena cava filter" (also called an IVC filter). The inferior vena cava is the large vein that carries blood from your legs and the lower half of your body back up to your heart. IVC filters go inside the inferior vena cava. They filter and trap any large clots that form below the location of the filter. Your doctor might suggest one of these filters for you if:

- You cannot safely take warfarin or another anti-clotting medicine
- You form clots even while on warfarin or another anti-clotting medicine
- You have a dangerous bleeding problem while on warfarin or another anti-clotting medicine
- You are so sick that another pulmonary embolism could kill you

**Risk of dying from pulmonary embolism (ranges from different studies):**

- Low risk pulmonary embolism: 1%
- Submassive pulmonary embolism: 4-30%, depending on the severity or right heart impairment.
- Massive pulmonary embolism: 15% with hypotension, 30% with cardiogenic shock, 70% when associated with cardiac arrest.

**Risk of bleeding from blood thinning and clot dissolving therapies:**

- Heparin blood thinning: less than 1% chance of serious bleeding.
- Clot dissolving medication given into a vein: 2-3% chance of bleeding in the head, 6% chance of bleeding elsewhere.
- Clot dissolving medication given through a catheter into the lungs: less than 1% chance of serious bleeding (this therapy requires placement of a catheter through the groin veins into the lungs).
**Pulmonary Emboli Algorithm**

**Without RV dilation or hypotension**
- Anticoagulate admit to medical floor on consider outpatient or with sPESI=0

**Submassive PE (evidence of new RV dysfunction* but patient is hemodynamically stable)**
- Assess patient risk for fibrinolysis as well as PE severity (BOVA score)
  - CDT
  - Half dose fibrinolysis
  - Anticoagulate

**Massive PE (SBP <90 for >15m or requiring pressor support)**
- Assess patient for contraindications to fibrinolytic therapy?
  - Not ok
    - Teneclase plate AV
    - Consider CDT or mechanical extraction
  - ok
    - Admit to ICU

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* CT or echo RV/LV >1, moderate to severe RV dysfunction (not mild)
** escalate = consideration of CDT or systemic fibrinolysis