Provincial Clinical Guideline

Treatment and Referral Guidelines for High-Risk and Intermediate-Risk Pulmonary Embolism in Adult Patients
Service Area: Emergency Departments, Urgent Care Centres, Intensive Care Units, Inpatient Medical Settings
Guideline Number: XX-XXX-XXX V1.0
Approved By: Provincial Clinical Leadership Team (PCLT)
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1. CLINICAL GUIDELINE STATEMENT:

1.1. To provide guidance, information and a standardized process for health care professionals in emergency departments (ED), urgent care (UC), intensive care units (ICU) and inpatient units to identify and manage patients with Intermediate Risk (submassive) or High Risk (massive) Pulmonary Embolism (PE) and consulting of Pulmonary Embolism Response Team (PERT).

1.2. To provide a rapid response to manage confirmed or highly suspected **acute PE** in adult patients by utilizing the PERT pathway (refer to Appendix A).

2. INCLUSION/EXCLUSION CRITERIA:

2.1. **Inclusion Criteria:** patients with High-Risk PE and Intermediate Risk PE with and without high-risk features.

2.2. **Exclusion Criteria:** patients with Low-Risk PE that are hemodynamically stable and show no clinical evidence of cardiac dysfunction.

3. GUIDELINE:

3.1. **PULMONARY EMBOLISM RESPONSE TEAM (PERT) CONSULT**

3.1.1. PERT is established to assist with the complex care of patients with PE.

3.1.1.1. PERT activation starts with calling the appropriate critical care attending physician on call (see 3.1.2) and may include shared decision-making with interventional radiology (IR), cardiac surgery and other specialties as needed.

3.1.2. Consult PERT for **all** High Risk (massive) PE, see 3.2, and Intermediate Risk PE (submassive) PE **with** high-risk features, see 3.4.

3.1.2.1. **For HSC, St. Boniface, Grace and Brandon Hospitals**: activate PERT by contacting the site ICU on-call attending physician.

3.1.2.2. **For Urgent Care Centres and all other sites (i.e. outside Winnipeg)**: activate PERT by contacting the ICU Provincial On-Call Attending Physician (POAP) via Shared Health - HSC paging (204) 787-2071.

3.2. **HIGH RISK (MASSIVE) PULMONARY EMBOLISM CRITERIA, includes at least one of the following:**

3.2.1. CARDIAC ARREST;
3.2.2. systolic blood pressure (SBP) LESS than 90 mmHg for GREATER than 15 minutes;
3.2.3. SBP drop GREATER than 40mmHg from known baseline;
3.2.4. Vasopressors and/or inotropes required;
3.2.5. cardiogenic shock;
3.2.6. persistent bradycardia heart rate (HR) LESS than 40 beats per minute (BPM).

DO NOT DELAY alteplase (tissue plasminogen activator (tPA)) administration in patients without contraindications while awaiting PERT consult.

3.3. **INTERMEDIATE RISK (SUBMASSIVE) PULMONARY EMBOLISM CRITERIA:**

3.3.1. right ventricular (RV) dysfunction determined by echocardiogram (ECHO) or computed tomography (CT) **WITHOUT** hypotension (i.e. SBP GREATER than 90 mmHg); defined as any of the following:

3.3.1.1. RV dilation (GREATER than 35mm mid-cavitary diameter);
3.3.1.2. right ventricular (RV): left ventricular (LV) ratio GREATER than 0.9;
3.3.1.3. McConnell's Sign (hypokinesis of RV free wall with apical sparing);
3.3.1.4. contrast reflux into inferior vena cava (IVC)/liver on CT.

3.4. **INTERMEDIATE RISK (SUBMASSIVE) PE WITH HIGH-RISK FEATURES CRITERIA:**

3.4.1. RV dysfunction as above, see 3.3; PLUS any of the following:

3.4.1.1. SBP LESS than 100 mmHg (but GREATER than 90 mmHg);
3.4.1.2. HR GREATER than 110 bpm;
3.4.1.3. shock index (HR/SBP) GREATER than 1;
3.4.1.4. pulse pressure LESS than 30 mmHg;
3.4.1.5. syncope/near-syncope;
3.4.1.6. elevated troponin;
3.4.1.7. abnormal ECG - new complete or incomplete right bundle branch block (RBBB), S1Q3T3, STsegment elevation (STE) in lead aVR, ST depression, or T-wave inversion in anteroseptal leads (V1-V3);
3.4.1.8. elevated lactate (GREATER than 2.0 mmol/L);
3.4.1.9. hypoxia - SpO2% LESS than 92% on room air, PaO2 LESS than 70 mmHg, increasing supplemental oxygen requirements (in the absence of baseline pulmonary disease);
3.4.1.10. clot burden and location on CT – main pulmonary artery (saddle), bilateral pulmonary arteries (right and left).

Note: Patients with Intermediate Risk PE with high-risk features should be assessed on an ongoing basis for lack of clinical response, hemodynamic instability, and progression to High Risk (massive) PE criteria.
The majority of submassive PE patients will respond favourably to anticoagulation alone.

3.5. **CONTRAINDICATIONS TO THROMBOLYTICS**

3.5.1. **ABSOLUTE** CONTRAINDICATIONS TO THROMBOLYTICS:

3.5.1.1. previous intracranial hemorrhage;
3.5.1.2. ischemic cerebrovascular accident (CVA) within 3 months;
3.5.1.3. brain/spine surgery within 3 months;
3.5.1.4. head trauma with fracture or intracranial injury within 3 months;
3.5.1.5. Serious, active bleeding.

3.5.2. **RELATIVE** CONTRAINDICATIONS TO THROMBOLYTICS:

3.5.2.1. major surgery LESS than 3 weeks (non-central nervous system);
3.5.2.2. coagulopathy (international normalized ratio (INR) GREATER than 1.6, Platelets LESS than 50);
3.5.2.3. anticoagulation or antiplatelet medication; acetylsalicylic acid (ASA) monotherapy is not considered a contraindication, but does increase bleeding risk;
3.5.2.4. SBP GREATER than 180 mmHg or diastolic blood pressure (DBP) GREATER than 110 mmHg;
3.5.2.5. age GREATER than 75 years of age;
3.5.2.6. structural abnormality (tumour, arteriovenous malformation (AVM)) –intracranial, gastrointestinal (GI), and liver lesions are the highest risk;
3.5.2.7. pregnancy - 3rd trimester and post-partum (consult obstetrician (OB)/ maternal-fetal medicine (MFM) recommended);
3.5.2.8. puncture of a non-compressible vessel;

3.5.2.9. traumatic cardiopulmonary resuscitation (CPR) (i.e. hematoma, multiple rib fractures).

Absolute and relative contraindications are guidelines only and all cases should be discussed and decided on an individual basis. Discussions may require consultation with the specific subspecialty service.

3.6. **ALTEPLASE (tPA) DOSING**

3.6.1. If a patient is receiving unfractionated heparin (UFH) infusion, **stop heparin infusion** prior to the administration of systemic thrombolysis. A prior dose of low molecular weight heparin (LMWH) is not a contraindication to tPA.

3.6.2. **High Risk (massive) PE Without Cardiac Arrest:**

3.6.2.1. tPA 10 mg IV bolus then 90 mg IV infusion over 2 hours.

3.6.3. **PE with Cardiac Arrest:**

3.6.3.1. tPA 50 mg IV bolus over 1 to 2 min, consider repeating in 10 to 15 min if return of spontaneous circulation (ROSC) not achieved; maximum total dose 100 mg;

3.6.3.2. If ROSC is achieved after one tPA dose, administer tPA 50 mg over 1 hour to complete a 100 mg IV dose.

3.6.4. **Post tPA:**

3.6.4.1. check activated partial thromboplastin time (aPTT) 2 hours post-tPA and every 3 hours;

3.6.4.2. if aPTT is LESS than 90 seconds resume heparin infusion at the previous rate (**no bolus**); if starting heparin de novo, see 3.7.1;

3.6.4.3. target aPTT 59.9 to 99.9, adjust as per venous thromboembolism (VTE) (non-acute coronary syndrome (ACS)) high-intensity UFH nomogram.

3.6.5. May consider a transition to LMWH after 24 hours if the patient has clinically stabilized.

3.7. **ANTICOAGULATION DOSING**

3.7.1. **Massive PE:**

3.7.1.1. Unfractionated heparin 18 units/kg/hr IV (**no bolus**);

3.7.1.2. target aPTT 59.9 to 99.9, adjust as per VTE (non-ACS) high-intensity UFH nomogram

3.7.2. **Submassive PE with high-risk features:**

3.7.2.1. dalteparin 100 units/kg subcut every 12 hours;

3.7.2.2. enoxaparin 1 mg/kg subcut every 12 hours.

Note: Twice a day (BID) dosing may provide a lower bleeding risk in the event of clinical deterioration and tPA is required (i.e. progression to massive PE).

3.7.3. **Submassive PE without high-risk features:**

3.7.3.1. dalteparin 200 units/kg subcut daily;

3.7.3.2. enoxaparin 1.5 mg/kg subcut daily.

Caution in patients with renal insufficiency (i.e. glomerular filtration rate (GFR) LESS than 30 mL/min/1.73m^2) OR elevated body mass index (BMI) (i.e. GREATER than 30 kg/m^2). Do not exceed 18,000 units dalteparin or 100 mg enoxaparin per injection (consider twice a day (BID) dosing).

Note: Direct oral anticoagulants (DOAC) should be avoided for massive and submassive PE patients until they are stable for an extended period of time (at least 72 hours after diagnosis).

3.8. **ADDITIONAL DIAGNOSTIC TESTS**

3.8.1. **Echocardiogram (Echo)**

3.8.1.1. Dynamic cardiac assessment aids with risk stratification of PE and provides functional information about the right ventricle (RV) that is distinct from CT pulmonary angiogram.

3.8.1.2. Echocardiogram is not mandatory for hemodynamically stable PE patients. Interfacility transfer for the sole purpose of obtaining an echocardiogram is not recommended.

3.8.1.3. Echocardiogram or point-of-care ultrasound (POCUS) by a skilled practitioner is recommended at the time of diagnosis, when available, for patients with high-risk PE and patients with suspected PE and significant hemodynamic instability.

3.8.1.4. Echocardiogram or POCUS by a skilled practitioner should be considered early in admission (within 24 hours) for selected patients with intermediate risk PE and high-risk features to inform decisions regarding advanced therapies (see section 3.9).

3.8.1.5. Echocardiogram should be considered before discharge or shortly thereafter in patients with significant clot burden to screen for the presence of pulmonary hypertension.

3.8.2. **Lower extremity ultrasound (U/S)**

3.8.2.1. Presence of deep vein thrombosis (DVT) is common in PE patients.

3.8.2.2. For most PE patients, the co-occurrence of DVT does not change overall management, as the treatment for both is systemic anticoagulation.

3.8.2.3. Routine screening for DVT is not required at the time of PE diagnosis.

3.8.2.4. In patients with bleeding complications that preclude ongoing anticoagulation, the presence of DVT and PE often requires consideration for the insertion of an IVC filter. This should be discussed with the PERT team during the initial phase of consultation and treatment.

3.8.2.5. In patients with significant hemodynamic instability and/or cardiac arrest, consideration for insertion of IVC filter will be made in discussion with the PERT team.

3.9. **ADVANCED THERAPY - REQUIRES PERT CONSULTATION**

3.9.1. Decision for advanced therapies is based on applied clinical judgement within individual circumstances.

3.9.1.1. **Interventional Radiology** (IR) for catheter-directed therapies (CDT) for High-Risk PE with contraindications to systemic thrombolysis, and select cases of Intermediate Risk PE with high-risk features.

3.9.1.2. **Cardiac Surgery** for ECMO in cases of refractory shock, and/or surgical embolectomy (RV clot in transit, patent foramen ovale (PFO)).

3.9.1.3. **Anesthesia on call** will support procedures in the IR suite. They will be contacted through the PERT team (either by ICU or IR).

3.9.1.4. **Half-dose thrombolytics (50 mg tPA over 2 hours)** may be considered for cases of Intermediate Risk PE with high-risk features where access to IR/ICU/Surgery is delayed (e.g. rural centres) and/or rapid deterioration may be anticipated.

3.10. **MANAGEMENT OF LIFE-THREATENING HEMORRHAGE POST THROMBOLYTICS**

3.10.1. Discontinue tPA infusion.

3.10.2. Discontinue unfractionated heparin infusion or LMWH.

3.10.3. Labs:

3.10.3.1. STAT complete blood count (CBC,) aPTT, INR, fibrinogen and Type and Screen; recheck fibrinogen every 4 hours until bleeding resolves;

3.10.3.2. CBC, aPTT, INR every 12 hours until bleeding resolves.

3.10.4. Imaging: if suspected intracerebral hemorrhage (ICH) – STAT CT brain (uninfused).

3.10.5. Medications:
- 3.10.5.1. fibrinogen concentrate, to keep fibrinogen GREATER than 1.5 g/L (the usual initial dose is 4 grams). If fibrinogen concentrate is unavailable, use cryoprecipitate (usual dose 10 units IV);
- 3.10.5.2. tranexamic acid 1 gram IV over 10 min, then 1 gram IV or PO every 8 hours until bleeding controlled (caution with gross hematuria);
- 3.10.5.3. consider platelets transfusion 1 to 2 units to keep platelets GREATER than 100;
- 3.10.5.4. if IV unfractionated heparin was given within the last 6 hours use protamine sulfate 1mg/100 units of heparin (maximum of 50 mg IV) over 10 minutes for heparin reversal. If aPTT remains elevated after 4 hours, may repeat 0.5 mg/100 units of heparin.

3.10.6. Consultations to consider: Neurosurgery (for ICH), General surgery or Trauma (hemorrhage), hematology (for any anticoagulation concerns or bleeding complications).

4. DEFINITIONS:

4.1. **Acute Pulmonary Embolism**: acute thrombus causing obstruction of one or both pulmonary arteries or their branches. It can affect oxygenation and can also cause obstructive cardiac shock (due to right ventricular failure).

4.2. **High Risk (massive) Pulmonary Embolism**: patients with hemodynamic decompensation with hypotension, cardiogenic shock or cardiac arrest.

4.3. **Intermediate Risk (submassive) Pulmonary Embolism**: normotensive patients with evidence of right ventricular compromise.

4.4. **Low-Risk Pulmonary Embolism**: normotensive patients with no evidence of right ventricular compromise.

4.5. **McConnell's Sign**: is an echocardiographic finding of segmental right ventricular wall-motion abnormality (hypokinesis) with apical sparing, is highly specific in acute Pulmonary Embolism and may guide rapid intervention when other testing is not feasible.

4.6. **Pulmonary Embolism Response Team (PERT)**: a multidisciplinary approach to facilitate the management of high risk and intermediate risk pulmonary embolism which includes ICU, IR, cardiac surgery and other specialties as needed.

4.7. **Right Ventricular Dysfunction**: impairment of cardiac function caused by acute pulmonary embolism. This results from pressure overload of the right ventricle, and leads to RV dilation, impaired contractility, and ischemia. Bowing to the interventricular septum into the left ventricle causes impaired LV filling and reduced cardiac output (ventricular interdependence).

5. CONTACT:

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Document Review History

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APPENDIX A: Acute Pulmonary Embolism Algorithm