Pulmonary Embolism Response Team

Scott J. Cameron, PhD, MD, RPVI, FACC, FSVM
Assistant Professor of Medicine and Surgery
University of Rochester Medical Center

scott_cameron@urmc.rochester.edu
@2scottish

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Learning Objectives

1. Assess true risk in a patient with PE
2. Introduce the Pulmonary Embolism Response Team (PERT) Concept
3. Present some challenging high risk PE cases
4. Show real world data from UR Medical Center
PE: A true thrombotic emergency: 3rd leading cause of death (#1 MI, #2 CVA).
1. **Low Risk PE**: segmental, sub-segmental, no hemodynamic changes/RV strain.

2. **Intermediate Risk PE (“submassive”)**: Evidence of RV strain (CT, Echo, MRI etc.) or positive plasma cardiac biomarkers (troponin, BNP, NT-proBNP).

3. **High Risk PE (“massive”)**: SBP < 90 mmHg for at least 15 minutes and/or pressor/inotrope-dependence to keep SBP > 90 mm Hg.
Pre-test probability of PE and Risk Assessment
Is this really a PE?

Modified Well’s Score

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>Score</th>
</tr>
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<tbody>
<tr>
<td>Previous pulmonary embolism or deep vein thrombosis</td>
<td>+1.5</td>
</tr>
<tr>
<td>Heart rate &gt;100 bpm</td>
<td>+1.5</td>
</tr>
<tr>
<td>Recent surgery or immobilization (within last 30 days)</td>
<td>+1.5</td>
</tr>
<tr>
<td>Clinical signs of deep vein thrombosis</td>
<td>+3</td>
</tr>
<tr>
<td>Alternative diagnosis less likely than PE</td>
<td>+3</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>+1</td>
</tr>
<tr>
<td>Cancer (treated within last six months)</td>
<td>+1</td>
</tr>
</tbody>
</table>

Clinical probability of pulmonary embolism: 0–1, low; 2–6, intermediate; 7 or more, high.

Practical considerations at the bedside:
1. Respiratory distress but clear lung fields by auscultation.
2. (1) + unexplained hypotension + Jugular venous distention.
3. Unexplained A-a $O_2$ gradient: ABG can be your friend.
ECG Findings in Acute PE (Helpful Only)

- Sinus Tachycardia or Atrial Arrhythmias
- Complete/Incomplete RBBB
- Precordial and inferior T wave inversions
- S1Q3T3
- Isolated aVR Elevation
Determine the PE Severity

- Pulmonary Embolism Severity Index (PESI) Score:
  https://www.mdcalc.com/pulmonary-embolism-severity-index-pesi

- Assumes patient is NOT extremely hypotensive
- Assumes no right heart strain (RV/LV ratio <0.9)
- If right heart strain (hypokinesis, or RV/LV > 0.9), 90 day mortality is already ~ 25%

PESI is generally only useful for low RISK PE

Chen and Cameron, Submitted for Publication
Approximately 25% obstruction of the pulmonary vascular bed is required for the echocardiographic findings to be noticeable.
RV Dysfunction in PE

RV dysfunction means the presence of at least 1 of the following:

1. RV dilation (apical 4-chamber RV diameter divided by LV diameter 0.9) or RV systolic dysfunction on echocardiography

2. RV dilation (4-chamber RV diameter divided by LV diameter 0.9) on CT

3. BNP > 90 pg/mL or N-terminal pro-BNP >500 pg/mL.

4. ECG changes (new complete or incomplete RBBB, anteroseptal STEMI or depression, or anteroseptal T-wave inversion).

5. Evidence for myocardial necrosis (+ plasma troponin).

(Circulation. 2011;123:1788-1830.)
A Good Treatment Paradigm

**Treatment Options**

1. Systemic Thrombolysis + Anticoagulation
2. Surgical Embolectomy
3. VA-ECMO

1. Anticoagulation
2. Catheter-Directed Thrombolysis (CDT)
3. Systemic thrombolysis

**Anticoagulation Alone**

**90 Day Mortality**

- Massive PE: 60%
- Submassive PE: 20%
- Low Risk PE: 1%

- All patients with PE *should* receive anticoagulation immediately at diagnosis:
  - Recommend LMWH (Enoxaparin): 1mg/Kg.
Does Treatment Beyond Heparin Impact Morbidity and Mortality in PE?

- Advanced therapies beyond heparin alone was an independent predictor of improved mortality.

Am J Med. 2018 Dec;131(12):1506-1514.e
Case #1: Two Kinds of Shock

66 year old M with gastric bypass p/w uncontrollable bleeding in hemorrhagic shock from a GI ulcer. On HD#3, profoundly hypotensive after bleeding had stopped.

VS  BP 88/67, HR 148, RR 26, SaO₂ 80s.

Found to have a large PE (massive PE)
Case #1: Two Kinds of Shock

- PERT Activation: MICU, CCU, CT surgery, IR all involved in rapid decision-making.
- Lines placed for presumed VA-ECMO need (10 minutes!).
- CDT initiated by IR (trerotola device). Patient coded in IR suite, CPR administered, intubated, ECMO, and CDT successful.
- Heparin gtt started two days later.
- Decannulated from ECMO on HD#6. Non-invasive imaging suggested RV recovery.
- Discharged on HD #17 and is still alive.

Peripheral VA-ECMO

Echo before  Angiogram before  Angiogram After  Echo After
VA-ECMO Use for PE and Cardiogenic Shock

US National Inpatient Sample, n=77,479

Elbadawi and Cameron, Vascular Medicine. 2019 March
Case # 2: Massive PE following Intracranial Surgery

60 year old male on the neurosurgery service POD #30 with a cerebellar drain for an abscess.

VS  BP 80/60, HR 125, RR 24, SaO$_2$ 90% on 4L O$_2$ n/c.

Found to have a large right PA thrombus.
Case #2: Massive PE following Intracranial Surgery

Has both absolute and relative contraindications to systemic thrombolysis.

PERT recommended Catheter-directed mechanical thrombolysis (1/5 dose Alteplase)

Heparin > Coumadin

Good hemodynamic result. Patient was discharged in a stable condition
Clinical predictors of doing well on VA-ECMO for cardiogenic shock can probably be applied also to a patient with massive PE (with the addition of female sex and as independent predictor of mortality).
Inpatient PERT activation for peri-operative code

- 57 yo F with traumatic right ankle fracture brought to the OR for stabilization.
- Prior to induction with anesthesia, SaO₂ abruptly fell to 70s, and SBP to 50s.
- PEA arrest > CPR > PERT activation.
- CCU cardiologist performed a TEE - IVC and PA thrombosis with giant hypoknetic RV.
- Emergent surgical embolectomy by (< 60 mins).
- Discharged on HD #11 on rivaroxaban.
• 65 yo M with a prior hx CVA without residual defects p/w AMS, R-sided weakness and L MCA infarct with hemorrhagic transformation.
• New atrial flutter and chronic RLE DVT.
• Fever, hypotension, and placed on pressors.
• CTA chest showed PE and TTE showed right-sided thrombus in transit. SBP 124/73, HR 105, RR 28, SaO₂ 98%, Temp 38.1 degrees C.

Underwent suction thrombectomy (AngioVac with b/l ICA protection filters, PFO closure with Amplatzer occluder device, and IVC filter placement).
7,205 people guessed the weight of a cow

Here's how they did...

- Team consensus is probably better for the patient
The Team Approach

• Based on the success of the “Heart Team Approach”.

• PE is an ‘orphan disease’: benefits from physicians experienced in critical care, pulmonary and cardiac mechanics, and interventional procedures (ECMO, CDT).

• MGH started the first PERT in 2012 – massive PE mortality has decreased by 50%.

• Two options:
  1. PERT has a ‘point person’ > virtual online conference with 5-10 specialists.
  2. PERT has a ‘point specialty’ (vascular medicine or cardiology or MICU) > involves other PERT members as expertise is required.

Overall goal: rapid treatment decision within 60 minutes (like STEMI or stroke).
Adult Pulmonary Embolism Response Team (PERT) Members at SMH

- **ED**: Justin Mazzillo

- **Cardiology**: Joe Delehanty, Vijay Krishnamoorthy, Scott Cameron

- **Cardiothoracic Surgery**: Sunil Prasad, Igor Gosev, Brian Barrus, Neil Kumar

- **Pulmonary Medicine**: David Trawick, Jim White, Anthony Pietropaoli

- **IR**: David Lee

- **Pharmacy**: Nicole Acquisto, Jennifer Falvey
Simplified Adult PERT Activation Criteria at URMC

Call: x52222 and ask for the “Pulmonary Embolism Response team”.

Massive PE
1. DVT or PE by imaging.
2. SBP < 90 mmHg for >10 minutes, or pressor/inotrope-dependence.
3. Hypotension due to another medical issue excluded.

Submassive PE
1. DVT or PE by imaging.
2. Right heart strain (CT imaging or echocardiography) OR cardiac hs-TnT > 14 ng/L and/or NT-proBNP > 500 pg/mL.

* If the above criteria are met, the PERT pager should be activated.
** PERT pager should not be activated for low risk PE.
PERT Activation at URMC for Consulting Clinicians

Criteria for Submassive or Massive PE are Met

- Patient presented to ED
- Patient is already admitted to URMC
- Transfer center alerted that patient is in another hospital

** Call 275-2222
** “Pulmonary Embolism Response Team Activation”**

CCU and MICU will evaluate and involve other PERT services only if needed within 60 minutes for a treatment plan

- Patient does not have a massive or submassive PE
- Patient has a massive or submassive PE

Patient disposition per consulting clinician

Patient treatment plan and disposition per PERT if patient is in the ED

** PERT Page Goes To (no overhead):
1. CCU and MICU Fellow
2. CCU and MICU Residents
3. CCU and MICU Attending
4. Emergency Pharmacist
5. QA Statisticians
URMC Diagnosis of PE: Locations

- Around 2 PERT Activations per Week
- False Activations over 2 years: 17%
  - Low risk PE
  - Undifferentiated PEA arrest
  - Sepsis + sub-segmental PE
  - RV Dysfunction secondary to a non-PE issue (OSA, PAH etc) + subsegmental PE

![URMC PERT (first 24 months): n=258](chart1)
- ED Activations 72.5%
- Inpatient Activations 27.5%

![URMC PERT (first 24 months): n=213](chart2)
- Massive (22%)
- Submassive (78%)
URMC Treatment of PE: Before and after PERT

Pre-PERT, n=258
- Heparin (85%)
- Systemic Lysis (7%)
- IVC Filter (7%)
- VA-ECMO (1%)

Post-PERT, n=213
- Heparin Alone (68%)
- Systemic Lysis (10%)
- Catheter Lysis (6%)
- VA-ECMO (1.3%)
- Thromboendarterectomy (0.7%)
- IVC Filter (7%)
- Surgical Embolectomy (7%)
PE Mimetics

Respect the undifferentiated patient!

1. RV Myocardial Infarction: Hypotension, clear lungs fields, JVD.
2. Pure Right Heart Failure: secondary to severe pulmonary hypertension.
3. Cardiac tamponade: Hypotension, clear lungs fields, JVD.
4. Aortic dissection: Hypotension, clear lung fields, can have "RV Strain".

** Always remember: Rx for massive PE (systemic thrombolysis) will take away any chance of survival if the patient has an aortic dissection
The Masqueraders...
Case #5: one of several causes of RV dilation

55 year old female with “sudden onset of back and chest pain”, SOB, tachypnea, hypotensive, with syncope at home.

VS: BP 84/62, HR 130

Asystole > CPR. Persistently bradycardic.

BP documented to be 238/163 in the chart at 11:12 AM after ROSC.

Echo in ED stated to have “RV strain”.
Case #5: one of several causes of RV dilation

TNKase given by the ED presumptively for massive PE.

Patient’s hemoglobin dropped 13 > 7 > 3 over hrs.

Patient Ultimately died. Heparin given (3000 U) at 12:45 PM.
Case #6: The Myocardial Infarction that was Not…

- 69 yo M p/w PEA arrest > CPR > inferior STEMI > clean cors and incidental anomalous left main CA from noncoronary cusp.
- Remained hypotensive with gigantic RV (SBP >90, though) > CTA with very large PE. RV/LV ratio 2.1. Patient elected extraction.
- Patient underwent surgical embolectomy.
- Discharged on HD #14 on apixaban.

Surgical embolectomy: best for central PE and contraindications to thrombolytics or those who are hemodynamically unstable with RV dysfunction after receiving thrombolytic therapy (Class IIa; LOE C)
Fluid Status in RV Obstructive Shock

PE + Severe RV Dysfunction: Reflexive bolus IVF is probably wrong!

- ↑ RV afterload: fluids can create a congested state → cardiogenic shock
- **Solution:**
  1) ↑ Preload: norepinephrine, vasopressin etc.
  2) ↓ RV afterload: epoprostenol
  3) Really ↓ RV afterload: VA-ECMO
Airway Management in RV Obstructive Shock

PE + Severe RV Dysfunction: Avoid Intubation or NIPPV, if possible.

(+ intrathoracic pressure from mechanical ventilation \(\rightarrow\) ↓ venous return \(\rightarrow\) ↑ RV failure with massive PE.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Survivors</th>
<th>Nonsurvivors</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of mechanical ventilation</td>
<td>71.7%</td>
<td>92.6%</td>
<td>0.01</td>
</tr>
<tr>
<td>Abnormal chest X ray</td>
<td>60.8%</td>
<td>85.3%</td>
<td>0.01</td>
</tr>
<tr>
<td>pH</td>
<td>7.41 ± 0.06</td>
<td>7.38 ± 0.08</td>
<td>0.04</td>
</tr>
<tr>
<td>Blood urea (mmol/l)</td>
<td>8.6 ± 14</td>
<td>12.8 ± 8.2</td>
<td>0.002</td>
</tr>
<tr>
<td>Blood creatinine (μmol/l)</td>
<td>85 ± 45.9</td>
<td>131.5 ± 126</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean Prothrombinaemia (%)</td>
<td>70.3 ± 11</td>
<td>60.6 ± 20</td>
<td>0.009</td>
</tr>
<tr>
<td>Mean number of organ failure</td>
<td>2</td>
<td>2.7</td>
<td>0.006</td>
</tr>
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Ongoing Controversies: Submassive PE Management

1. Who is appropriate for systemic thrombolysis?
2. Who is appropriate for surgical embolectomy?
3. Who is appropriate for Catheter-Directed Therapy (Optalyse study)?
4. Who is appropriate for IVC Filters (PREPIC study)?
Submassive PE – Systemic Thrombolysis (PEITHO)

• RCT systemic tenecteplase/heparin vs. placebo/heparin in normotensive patients with submassive PE.

**Results:** Hemodynamic decompensation prevented but incr. risk bleeding/ICH.
Submassive PE – Systemic Thrombolysis (PEITHOII)

**CENTRAL ILLUSTRATION:** Thrombolysis for Pulmonary Embolism: Kaplan-Meier Survival Curves of Patients Randomized to Tenecteplase Compared With Placebo

Log-rank p=0.4266

<table>
<thead>
<tr>
<th>Follow-Up (Days)</th>
<th>N at risk</th>
<th>Placebo</th>
<th>Tenecteplase</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>350</td>
<td>359</td>
<td></td>
</tr>
<tr>
<td>360</td>
<td>316</td>
<td>317</td>
<td></td>
</tr>
<tr>
<td>720</td>
<td>299</td>
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</tr>
<tr>
<td>1,080</td>
<td>188</td>
<td>198</td>
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<tr>
<td>1,440</td>
<td>120</td>
<td>129</td>
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<td>1,800</td>
<td>71</td>
<td>69</td>
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<tr>
<td>2,160</td>
<td>38</td>
<td>35</td>
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</tbody>
</table>


- RCT systemic tenecteplase/heparin vs. placebo/ heparin in normotensive patients with submassive PE → long-term follow up at 3 years.

**Results:** No long-term mortality benefit from *routine* systemic thrombolysis
Case #7: Systemic thrombolysis for an evolving submassive PE?

- 52-year-old female p/w SOB and dyspnea on exertion for the past 3 weeks. Had right calf pain; negative DVT study.
- VS on admission 104/90, 108, 14, 90% on room air.
- given LMWH, but increased WOB on the day of admission and SaO₂ fell to 75% with BP 88/60 so Alteplase 1mg/Kg given.
- Patient did well, and was discharged on rivaroxaban.
Importance of Follow up after High Risk PE (Post PE Syndrome and CTEPH)
Case #8: Consequences of conservative management

- 46 year old M 1 wk out from orthopaedic knee surgery p/w syncope.
- VS BP 93/66, HR 91, RR 20, SaO₂ 96% on R.A.
- + Troponin T at 0.3 ng/mL, RV/LV ratio 1.8 on CT chest
- TTE with severely hypokinetic, dilated RV, moderately elevated PA pressure
- LE venous Duplex shows significant DVT in both lower extremities

Evolved from sick submassive to massive PE.
Case #9: The clot you Cannot Swot...

- 51 year old male with exertional SOB for weeks presented to cardiology for a stress test.
- Referred to SMH for CCU admission based on echo findings.
- VS: BP 92/62, HR 86, RR 18, SaO2 95% room air.
- Relevant Labs: Platelet count 46K, aPTT 61.
- Echo and CT findings noted below. PA Systolic Pressure 109!
Case #9: The clot you Cannot Swot...

PERT activation: CCU, Pulmonary, IR, hematology
Admitted to CCU. Diagnosed with anti-phospholipid syndrome and factor XII deficiency. IR catheter directed lysis attempted.

Diagnosis: CTEPH
Rx:
1. Pulmonary endarterectomy.
2. Heparin > Coumadin (INR 2.5-3.5)
Case #10: One Large Thrombus...

- 49 year old with history of unprovoked PE who completed Coumadin x 6 months, then stopped
- Started back Coumadin by himself. A day later with severe DOE at home
- VS 145/101, 110, 26, SaO₂ 95 % on high flow O₂ > 70s > 40s. NT-proBNP 756, hs-Trop T 43.

CTA at OSH with large thrombus burden.

PERT recommended he underdo surgical embolectomy.
Does a Multi-disciplinary PERT affect Mortality?
URMC High Risk PE Overall Mortality Post-PERT

Submassive PE + Massive PE Together (ED Only)

<table>
<thead>
<tr>
<th>Mortality (months)</th>
<th>RRR</th>
<th>ARR</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15%</td>
<td>2%</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>30%</td>
<td>7%</td>
<td>14</td>
</tr>
<tr>
<td>6</td>
<td>26%</td>
<td>7%</td>
<td>14</td>
</tr>
</tbody>
</table>
URMC High Risk PE Overall Mortality Post-PERT

Submassive PE + Massive PE Together

Submassive PE + Massive PE Separately

*Unadjusted Data
The Impact of PERT on Workflow in the ED

Wright and Cameron, Submitted for Publication
The Impact of PERT on Education of Housestaff

- Patient care has improved for high risk PE: 89%
- There is a positive impact on my education: 83%
- My knowledge base has increased: 77%
- Every hospital should have a high risk PE team: 71%
- I am more aware of high risk PE: 60%
- I have more autonomy: 51%
- I have less autonomy: 37%

Likert Rating

- Identifying High Risk PE: P < 0.001
- Managing High Risk PE: P = 0.003
- Indications for Systemic Thrombolysis (Submassive PE): P = 0.012
- Indications for Systemic Thrombolysis (Massive PE): P = 0.043
- Indications for Surgical Embolectomy: P < 0.001
- Contraindications to Systemic Thrombolysis: P = 0.156
- Selecting an Anticoagulant: P = 0.137
When Setting up a PERT

• Need ‘buy-in’ from several specialties

• A ‘point person’ who demonstrates availability

• Ideally a healthy PERT should have 3 components:
  1. A streamlined clinical algorithm
  2. An educational component
  3. QA (3-4 times each year) – refinement, discuss difficult cases
Intermediate/High Risk PE management: Take home points

1. Avoid reflexive IVF for hypotension in a patient with a large PE
2. Avoid intubation if possible
3. Patient placement matters (Step down/ICU for at least 1 day)
4. Know PE mimetics: RV infarction, tamponade, aortic dissection
5. RV dilation is **NOT** specific for PE: usually seen peri-arrest
October 4 - 5, 2019 / Renaissance Boston Waterfront Hotel

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“Bringing it home to Boston”