Massive Pulmonary Embolism

Next frontier

Leipzig Interventional Course 2015

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Disclosures

• None
Objectives

Pulmonary embolism

- Definition
- Epidemiology
- Data Review
- Treatment
- Case Presentation
Venous Thromboembolism: A National Public Health Crisis

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th># of Annual Deaths¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE</td>
<td>Up to 200,000</td>
</tr>
<tr>
<td>AIDS</td>
<td>18,017</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>40,870</td>
</tr>
</tbody>
</table>

- After acute coronary syndrome and stroke, VTE is the third most common cardiovascular illness, affecting 1 in 1,000 in the United States annually⁶
- 600,000 new cases of DVT are diagnosed each year²
  - 1/3 of these patients will have a PE
  - estimated that more than 250,000 patients are hospitalized annually w DVT³
- up to 200,000 of those with PE,
- —killing more people than MRSA, AIDS, traffic accidents, and breast cancer combined⁴,⁵

¹. American Heart Association Fact Sheet - 2008
². SIR 2008
⁵. Rep of IWG 2005
Pathophysiology

- Most common source are deep veins of the lower extremities
- Thrombus dislodges and embolizes in the pulmonary arterial tree
- Obstruction triggers physiologic changes
- Pressure overloads the pulmonary artery and right ventricle

www.benlovejoy.com/pulmonary_embolism_main.html
55% of PE patients: 15% 90-day mortality rate
Presenting with small clots in the distal pulmonary vessels, pleuritic chest pain, mild tachycardia and possibly hemoptysis

40% of PE patients: 22% 90-day mortality rate
Presenting with thrombosis usually in one or both of the left and right pulmonary arteries, hemodynamic compensation and maintenance of adequate systolic arterial blood pressure albeit with right heart strain consistent with imminent right heart failure

5% of PE patients: 58% 90-day mortality rate
Patients present in hemodynamic collapse with cardiogenic shock; high early mortality rate due in part to right ventricular failure
Diagnosis: history and physical

History
• Dyspnea (SOB)
• Hemoptysis (Coughing out blood)
• Pleuritic chest pain
• Cough
• Syncope

Physical
• Tachypnea (rapid breathing)
• Anxious appearance
• Tachycardia (accelerate heartbeat)
• Fever
• Elevated jugular venous pressure
• Loud P2 (pulmonic valve closure sound)
Diagnostic tools

- **Plasma D-dimer**
  - 99.5% negative predictive value
  - < 500 mcg/L in low risk
  - < 275 mcg/L in mod-high risk

- **Electrocardiography**
  - S₁, Q₃, T₃ (30% of cases)
  - RBBB (25%)
  - Sinus tachycardia

- **Cardiospecific biomarkers**
  - BNP
  - Tropinin

- **LE ultrasound**
- **Echocardiography**

- **V/Q lung scanning**
  - Correlates well with pulmonary angio in high and low pretest prob
  - V/Q low prob- PE in 40% HPTP, 15% IPTP, 4% low PTP
  - V/Q High Prob – PE in 95% high PTP, 86% IPTP, 50% LPTP

- **Chest X-ray**
- **Chest CT**
- **Magnetic resonance (MR) angiography**
- **Contrast pulmonary angiography**
- **Spiral CT**
\[ \sum (n \cdot d) / 40 \times 100 = \% \text{ vasc. obstruction} \]

- **CPTE index**: \( \sum (n \cdot d) / 40 \times 100 \)
  - \( n \) = number of segments dependent from the obstructed pulmonary artery involved [min 1, max 20];
  - \( d \) = obstruction severity [complete = 2; >50% <100% = 1; <50% = 0]

- **Ghanima score**:
  - 4 = main pulmonary artery and its branches
  - 3 = lobar arteries
  - 2 = segmental arteries
  - 1 = sub-segmental arteries

- **RV/LV diameter ratio > 1**
Echocardiographic findings of acute PE

- Right ventricular dilatation
- Right ventricular hypokinesis (McConnell’s sign)
- Septal deviation

Am J Respir Crit Care Med 2002;166:1310-1319
Right ventricular dilatation

Apical 4-chamber

Normal

Dilated RV

Lakshmanadoss et al. Cardiology Research. Volume 2, Number 1, February 2011, Pages 48-49
Septal deviation

- RV pressure overload leads to deviation of the interventricular septum towards the LV in diastole.
- Intraventricular septal flattening is seen during systole creating a so-called D-shaped LV.

Right ventricular hypokinesis

- Frequently diagnosed quantitatively
- Often described as **McConnell’s sign**
  - Free wall hypokinesis
  - Normal apex motion

Am J Respir Crit Care Med 2002;166:1310-1319
Am J Cardiol 1996;78:469-473
Cardiac biomarkers

- Brain natriuretic peptides (BNP)
- Cardiac troponins

↑ Troponins = ↑ short-term and long-term mortality

↑ BNP = ↑ mortality and severe adverse events

↑ Troponins + ↑ BNP = ↑ mortality and severe adverse events
PE Management

Minor PE [Low risk]
- 55% PE population
- Good prognosis
- Low mortality rate

Massive PE [High risk]
- 5% PE population
- 58% mortality @ 3 months

Submassive PE [Moderate risk]
- 40% PE population
- 21% mortality @ 3 months

Nonmassive 55%
Submassive 40%
Massive 5%

Treatment
- 55% of PE patients: Conservative therapy
- 40% of PE patients: Remains a topic of debate
- 5% of PE patients: Aggressive therapy

Why treat Submassive PE patients aggressively?

- Patients with persistent RV dysfunction at discharge
  - 8 times more likely to have recurrent PE
  - 4 times the mortality rate of pts. in whom RV dysfunction had regressed

- At 1 year post PE, 44% of sub-massive PE patients with right heart dysfunction at hospital discharge will have chronic PHT

- RV hypokinesis on baseline echocardiography was associated with a 57% higher mortality rate at 3 months, even though 89% of the patients were hemodynamically stable

- Anticoagulation interrupts the clotting cascade preventing thrombus propagation but does not resolve existing clot

- Compared to anticoagulation alone, systemic thrombolysis can reverse right ventricular dilatation within 24 hours of treatment

2. Ribeiro, Circ 1999;99:1352-1330
4. Becattini, Thromb Res 2010; 125:e82-86
5. Konstantinides, Am J Cardiol 1998;82:966-970
## Pulmonary Embolism

### Patient risk stratification (per AHA 2011 guidelines)

<table>
<thead>
<tr>
<th>Massive PE</th>
<th>Submassive PE</th>
<th>Minor/Nonmassive PE</th>
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</thead>
<tbody>
<tr>
<td><strong>High risk</strong></td>
<td><strong>Moderate risk</strong></td>
<td><strong>Low risk</strong></td>
</tr>
<tr>
<td>• Sustained hypotension (systolic BP &lt;90 mmHg for ≥15 min)</td>
<td>• Systemically normotensive (systolic BP ≥90 mmHg)</td>
<td>• Systemically normotensive (systolic BP ≥90 mmHg)</td>
</tr>
<tr>
<td>• Inotropic support</td>
<td>• RV dysfunction</td>
<td>• No RV dysfunction</td>
</tr>
<tr>
<td>• <strong>Pulselessness</strong></td>
<td>• Myocardial necrosis</td>
<td>• No myocardial necrosis</td>
</tr>
<tr>
<td>• Persistent profound bradycardia (HR &lt;40 bpm with signs or symptoms of shock)</td>
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**RV dysfunction**
- RV/LV ratio > 0.9 or RV systolic dysfunction on echo
- RV/LV ratio > 0.9 on CT
- Elevation of BNP (>90 pg/mL)
- Elevation of NTpro-BNP (>500 pg/mL)
- ECG changes
  - new complete or incomplete RBBB
  - anteroseptal ST elevation or depression
  - anteroseptal T-wave inversion

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Standard PE therapy

ANTICOAGULATION (AC) – HEPARIN

- AC therapy prevents further clot growth
- Studies\(^1\)\(^-\)\(^3\) found:
  - LMWH as effective as UFH in reducing recurrent PE
  - LMWH carries reduced bleeding risk compared to UFH

STANDARD OF CARE: usually UFH or LMWH, followed by oral warfarin or DTI

- However, AC therapy relies on endogenous t-PA to dissolve occluding clot
  - Endogenous fibrinolysis may often be incomplete
  - Up to 33% patients have ongoing RV dysfunction

2. Buller et al. NEJM 2003;349:1695-1702
Literature review

Focus on outcomes of acute PE patients with signs of RV dysfunction
An echocardiographic RV/LV ratio > 0.9 was shown to be an independent predictive factor for hospital mortality.

Fremont B, Pacouret G, Jacobi D. CHEST 2008;133:358-362

Mortality rate:

1.9% if RV/LV ratio < 0.9
6.6% if RV/LV ratio ≥ 0.9
Mortality risk increases **11-fold** for PE patients with an **obstructive index > 40%** who are treated solely with anticoagulant therapy.


At 3 months:

- **11.2-fold increased risk** with an obstruction index of 40% or greater
- **PE-related mortality:**
  - **17%** if RV/LV ≥ 1.5
  - **8%** if 1.0 ≤ RV/LV < 1.5
  - **0%** if RV/LV < 1.0
RV hypokinesis on baseline echo was associated with ~40% higher mortality rate at 3 months.

Goldhaber S, Visani L, DeRosa M. The Lancet; Apr 24, 1999; 353, 9162; Health Module pg. 1386
PE patients with **Right Ventricle Dysfunction (RVD)** unresolved prior to discharge were **8-times** more likely to have a **recurrent PE** than pts whose RVD was resolved.


**Figure.** Cumulative incidence of recurrent venous thromboembolism. RVD indicates right ventricular dysfunction.

*Incidence of VTE at 4 years:*

- 0.4 if RVD unresolved
- <0.1 if RVD resolved
44% of PE patients with RV dysfunction at time of diagnosis had chronic pulmonary hypertension at 1-year follow-up.


If PAP (systolic) > 50mmHg at diagnosis:

- 44% of PE patients with RVD had pulmonary hypertension at 1-year follow-up
- Risk for persistent pulmonary hypertension increases 3X
These studies demonstrate...

Poor outcomes (short & long term) in PE patients with signs of **RV dysfunction** when treated conservatively or inadequately.

**Aggressive treatment** to resolve clot burden and reverse **RV dysfunction** and prevent progression to long-term sequelae and mortality.
ACCP (2012) guidelines suggest administration of **thrombolytic therapy** in **selected high-risk patients** with and **without hypotension**

Kearon et al. CHEST 2012; 141(2)(Suppl):e419S–e494S
AHA (2011) scientific statement now recommends fibrinolysis and catheter-based interventions for submassive PE patients

• **Anticoagulation (UFH, LMWH, Fondaparinux)**
  – Relies on endogenous tPA to resolve clot

• **Systemic thrombolysis**
  – Associated with high bleeding rates

• **Catheter-directed thrombolysis**
  – Lack of clinical evidence of efficacy; yet proven to be more superior than systemic thrombolysis

• **Mechanical & pharmacomechanical interventions**
  – Associated with high rates of complication; no level I data

• **Surgical embolectomy**
  – High rate of patient morbidity
Surgical embolectomy

• Operation mandates a median sternotomy, incision of the main PA, and circulatory arrest with cardiopulmonary bypass

• Performed in only 1% of PE patients with massive PE and cardiogenic shock (based on the two largest PE registries)\(^1,2\)

• Mortality rate across institutions ranges widely; recent (2013) nationwide large-sample analysis reported 27.2% inpatient mortality\(^3\)

Endovascular Technology
Placement of 22F AnioVac catheter in LCFV

16F return catheter in RCFV
Has specialized funnel tip, tracks over 0.035” guidewire
Maintains local bloodflow
AngioJet

Rheolytic thrombectomy system designed to remove thrombus with Venturi-Bernoulli effect

Multiple high-velocity, high-pressure saline jets are introduced to create a localized low pressure zone, resulting in a vacuum effect with Reholytic thrombectomy
Benefits of Ultrasound Accelerated Thrombolysis

• UAT Advantages over CDT
  ◇ Shortens time to re-canalization
  ◇ Significantly lowers the risk of bleeding
  ◇ Shortens patient hospitalization time (time to complete lysis)

• UAT Advantages over PMT
  ◇ Single device solution (no follow up required)
  ◇ No hemolysis
  ◇ Low risk of distal emboli
  ◇ No vessel wall damage
  ◇ Completely removes thrombus (no other follow up with second type procedure)
  ◇ Cath lab utilization can be significantly less

![Ultrasound + Thrombolysis](https://example.com)
Forces TPA into thrombus-> rapid resolution at low drug dose

Ultrasound accelerated thrombolysis rapidly reverses RV dysfunction

- Single-center retrospective analysis of both massive and sub-massive PE patients with ultrasound-accelerated thrombolysis (EKOS)

- From February 2009 to April 2012, 42 PE patients were treated with ultrasound accelerated thrombolysis
  - Retrospective data analysis on 37 consecutive patients with pre- and post-treatment contrast-enhanced CT imaging
    - Clinical history
    - RV/LV ratio reduction
    - Clot burden reduction
Case 1

Pre-treatment
(RV/LV = 1.64)

Post-treatment
(RV/LV = 1.10)
Ultrasound accelerated thrombolysis achieves greater clearance with lower lytic dose compared to CDT.

Baylor College of Medicine retrospective PE series

- EKOS (n=11) vs. CDT (n=14)
- All enrolled patients are considered massive PE, defined as having a Miller score ≥ 17
- Thrombus clearance graded as:
  - Complete lysis (>90%)
  - Near-complete lysis (70-90%)
  - Partial lysis (<50%)
Inclusion criteria

- Acute symptomatic PE confirmed by contrast-enhanced chest CT with embolus located in at least one main or proximal lower lobe pulmonary artery

- RV/LV ratio > 1 on echocardiography
Primary endpoint:
Reduction in RV/LV ratio (echo)

- EKOS + Heparin
  - Baseline to 24 hrs: 0.30
  - Baseline to 90 days: 0.38
  - P < 0.00001

- Heparin
  - Baseline to 24 hrs: 0.03
  - Baseline to 90 days: 0.22
  - P = 0.03
Assessment of Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE)

- Venous thromboembolism (VTE), which encompasses DVT and PE, is one of the three major cardiovascular causes of death.
- Up to 900,000 cases of VTE are diagnosed per year in the United States, with approximately 550,000 Americans hospitalized and 100,000 deaths from PE.
- There are clinical tools available to help estimate the clinical probability of VTE and severity of disease.

<table>
<thead>
<tr>
<th>Estimating pretest probability of DVT</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active cancer</td>
<td>1</td>
</tr>
<tr>
<td>Paralysis, paresis, or recent casting of leg(s)</td>
<td>1</td>
</tr>
<tr>
<td>Recently bedridden 3 or more days or major surgery within 12 weeks</td>
<td>1</td>
</tr>
<tr>
<td>Localized tenderness along the distribution of the deep venous system</td>
<td>1</td>
</tr>
<tr>
<td>Entire leg swollen</td>
<td>1</td>
</tr>
<tr>
<td>Calf swelling &gt;3 cm comparatively</td>
<td>1</td>
</tr>
<tr>
<td>Pitting edema of leg</td>
<td>1</td>
</tr>
<tr>
<td>Collateral superficial veins</td>
<td>1</td>
</tr>
<tr>
<td>Previously diagnosed DVT</td>
<td>1</td>
</tr>
<tr>
<td>Alternate diagnosis more likely</td>
<td>-2</td>
</tr>
</tbody>
</table>

Low clinical probability of DVT if score is 0 or less

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical signs/symptoms of DVT</td>
<td>1</td>
</tr>
<tr>
<td>Recent surgery (4 weeks) or immobilization</td>
<td>1</td>
</tr>
<tr>
<td>Heart rate &gt;100 beats/min</td>
<td>1</td>
</tr>
<tr>
<td>Previous VTE</td>
<td>1</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1</td>
</tr>
<tr>
<td>Malignancy</td>
<td>1</td>
</tr>
<tr>
<td>Alternative diagnosis less likely than PE</td>
<td>1</td>
</tr>
</tbody>
</table>

Clinical probability of PE is unlikely if score is 1 or less

| Clinical probability of PE is likely if score is 2 or more |

Testing for DVT and PE

- Pretest probability estimates help establish the appropriate diagnostic course.
- In DVT, a low/moderate estimate dictates D-dimer testing. If D-dimer is elevated, ultrasonography is indicated. In low estimate, if D-dimer is normal, DVT is ruled out. In moderate estimate, if a high-sensitivity D-dimer is normal, DVT can be ruled out.
- In DVT, a high estimate dictates ultrasonography. In PE, an unlikely estimate dictates D-dimer testing. If D-dimer is normal, a <1% rate of VTE during follow-up can be expected. If D-dimer is elevated, CT angiography is indicated.
- In PE, a likely estimate dictates D-dimer testing followed by CT angiography.

Risk stratification for VTE treatment

- VTE can cause death from PE. It can also cause chronic thromboembolic pulmonary hypertension or postthrombotic syndrome. Therefore, risk stratification is essential in determining optimal treatment strategy.
- High-risk patients include those with hemodynamic instability, right ventricle (RV) dysfunction, RV enlargement, or elevation of troponin levels due to RV microinfarction.
- Many patients with acute DVT can be treated on an outpatient basis.
- Initiation of treatment for patients with acute PE is typically preceded by a severity assessment.
- The simplified PE severity index, shown below, can help estimate 30-day mortality in patients with acute PE.

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;80 years</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>Heart rate &gt;110 beats/min</td>
<td>1</td>
</tr>
<tr>
<td>Systolic blood pressure &gt;100 mmHg</td>
<td>1</td>
</tr>
<tr>
<td>Oxygen saturation &lt;90%</td>
<td>1</td>
</tr>
</tbody>
</table>

Low risk if score is 0

| High risk if score is 1 or more |

References:
DMC
DETROIT MEDICAL CENTER

"Clot Buster"
PAGE "PE/DVT" (#73388)
DMC Massive Pulmonary Embolism (PE) Guidelines

Is there a strong suspicion or CT confirmation* of massive PE and:
- SBP < 90 mmHg
- ROSC from PEA arrest in young adult
- Signs of RV dysfunction* by echo

Is there strong clinical suspicion for PE and suspicion for RV dysfunction?

YES1
Obtain bedside or formal echocardiogram.

NO
Work up for PE per usual.

Does echo show RV dysfunction* and abnormal biomarkers (any 1):
- Lactate > 2
- Troponin > 0.2
- NT-proBNP > 900 pg/mL

Consult CTO for IA tPA or clot retrieval

Page "PE/DVT" (#73388)
If there is strong suspicion of a PE and is 1 of the following criteria, a massive PE may be present:
- SBP <90 mmHg or signs of shock
- ROSC from pulseless electrical activity (PEA)
- Severe refractory hypoxemia

ICU PE confirmed or high suspicion?

- Consult Cardio PE/DVT Team

Consult Catheter-mediated thrombolysis (CMT) vs. PA RV A.

CT scan confirms massive/submassive PE
- RV/LV ratio >1
- Cath Lab #58458

1. Does echo show severe RV dysfunction?
   a. RV hypokinesis/akinesis
   b. D shaped septum (septal flattening)
   c. McConnell's sign
   d. RV ratio to LV ≥ 1 (Dilatation)

Initial Evaluation
- IV (central line is preferred if administering TPA)
- Cardiac monitor and EKG
- Obtain CBC, BNP, troponin, PT/INR, aPTT and FIBT
- CT angiogram of chest or echo
- Empiric unfractionated heparin (Pharmacy dosing per protocol for VTE)

Obtain Echo
- Standard anticoagulation
- Monitor

Is there clinical suspicion for RV dysfunction?

- Yes
- No

CT Scan confirmed

1. Does echo show severe RV dysfunction?
   a. RV hypokinesis/akinesis
   b. D shaped septum (septal flattening)
   c. McConnell's sign
   d. RV ratio to LV ≥ 1 (Dilatation)

It is recommended that 15 minutes of CPR are to be performed prior to activation of this protocol.
DMC
(Harper, SG, and Receiving)

Average Length of Stay

DRG 175 - PE w/ MCC
DRG 176 - PE w/o MCC

www.ahd.com
2011
Case 1 - History

• 66 year old hx malignant mesothelioma presenting with sudden onset SOB while ambulating at home.

• He was suddenly unable to walk more than a few feet without becoming SOB.

• CT angiogram showed large saddle pulmonary arterial embolism.

• Due to severe hypoxia, hypotension and evidence of large embolism, patient was taken to the cath lab.
Baseline Echo

Echo on presentation
Case 1 – Pre-Treatment Images

Evidence of saddle embolism with large left pulmonary artery thrombus
Case 1 – EKOS catheter placement

0.035” Wholley wire placed in the left lower pulmonary artery, EKOS catheter then advanced over the wire distal to thrombus
After day 2 of ultrasound-Mediated thrombolysis, thrombus burden significantly improved. IVC filter was placed in the same setting.
Case 2 - History

- 67 year old with a history significant for hypertension, hyperlipidemia, diabetes, who presented respiratory distress.
- She noticed one week prior significant leg swelling.
- Given her symptoms and high suspicion for pulmonary embolism, she was brought directly to the catheterization laboratory.
Dilated right ventricle with RV/LV ratio > 0.9.

Septal deviation, “D-shaped” septum, and RV pressure overload.
Case 2: Pre-Treatment
12 cm EKOS catheter placed for 24 hours of tPA infusion at 2 mg/hr (12 hr) followed by 1 mg/hr. Heparin administered systemically at 500 U/hr.
EKOS catheter removed following day with resolution of symptoms
CASE -2
Take-Home Points

- Catheter directed thrombolytic for hemodynamically unstable patients is life saving and less major bleeding risk than systemic TPA
- Know the common VTE risk factors
  - Prevention
  - Prophylaxis
  - Assess VTE risk for each hospitalized patient individually
  - Utilize various VTE prophylaxis regimens for different at-risk patient groups
- Apply current ACCP guidelines to prevent and treat VTE in hospitalized pts
- Use hospital information systems to increase awareness of VTE and implement adequate prophylaxis in patients at risk
- Implement a patient pathway for DVT/PE diagnosed patients to be consulted with an Endovascular interventionalist for treatment Massive/sub PE
Summary

• Massive/submassive often untreated
• Gateway
  – Emergency department unstable pts presenting with PE
  – ICU, Cancer centers and post surgical
• Operators: IC, IR or Vascular surgery
  – Strong foundation for endovascular procedures
  – Experienced in treating hemodynamically compromised patients
• Last frontier: since actual surgical tx is < 2%
THANK YOU
Massive Pulmonary Embolism

Next frontier

Leipzig Interventional Course 2015

January 28, 2015

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