Single Center 4 year series of 114 consecutive patients treated for massive and submassive PE

Mark Goodwin, MD
Disclosure

Speaker name:

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

- I do not have any potential conflict of interest
Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td>Consultant/Proctor</td>
<td>Boston Scientific, Abbott Vascular, Medtronic, Asahi, Vascular Solutions, Cook Medical, Philips, Edward Lifesciences</td>
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Risk stratification

- **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 hemoptyysis

- **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

1. CTA
2. Venous Duplex
3. 2D Doppler
4. EKG
5. CXR
6. ABG Not Useful
7. BNP
8. Troponin
9. Clinical Judgment
Heparin Rx

- 75% clot persist 1-4 week
- 50% 4 months - NEJM 1976
Thrombolytic

- Relieves obstruction
- Improves PFT’s
- Prevent pulmonary HTN (Sasahara et. al.)
- Prevent recurrent PE
Risks

- Clinical scores
- Echo RV dysfunction
- CT RV dilatation increase 30 day & 3 month modification
- Clot burden not always predictive
- Increased Troponin, mortality odds ratio 5.9
- Increased BNP, increased mortality, odds ratio 5.9
- EKG — Sinus Tach, RBBB, Qr V1, ST-T changes
- V1-4, S1 Q3 T3 all worse outcomes
Pulmonary Embolism is Misnomer

- Do Not Die of Hypoxemia
- Nothing Wrong with Lungs
- Clinical Signs Misleading
- All Markers of Mortality are Cardiac Related
- Acute Right Ventricular Afterload Syndrome - ARVAS
Why Do We Treat

- **Mortality** — 15% at 3 Months
- **Massive PE** — IN Hospital Mortality >50%
- **Submassive PE** — Mortality 6-8%
- **Pulmonary Hypertension**
- **PEITHO**
- **ULTIMA**
- **Seattle II**
Right ventricular systolic pressures at diagnosis and 6 months after acute submassive pulmonary embolism.
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
Seattle II Trial

- 150 patients massive & submassive PE
- Massive 31 patients
- 17 bleeds — 1 severe & 16 moderate
- No deaths at 30 days in massive PE
- 1 death during study period attributed to PE
- RV/LV decreased 1.55 to 1.13 (p<.0001)
The Ekosonic Endovascular System with Mach4e rapid pulse modulation ... 3rd Generation

Ekosonic Control Unit

Ekosonic Mach4e

Endovascular Device

5.4 fr Intelligent side-hole drug delivery catheter

Ultrasound MicroSonic™ Core
Case Presentation

47 y/o female presents with near syncope, saddle pulmonary embolus and is treated with heparin and warfarin. 4 months later severe fatigue and exertional dyspnea. Husband thinks she is malingering. Multiple physicians have told her to exercise more.
Stress Echo
Pulmonary Embolism Response Team

- Protocols for MI, hypothermia, chest pain, stroke, pneumonia, DM etc.
- DVT prophylaxis
- Everyone treats PE — Hospitalist, Intensivist, ER, Pulmonary, IR, Cardiology, Internal Medicine, Family Practice, CV Surgery
- Rarely are there pathways for treating DVT/PE
- TEAM APPROACH
4 Year Experience

- 116 consecutive patients age 20-88 mean 55
- Catheter directed lytics 90 patients with 100% survival and no significant bleeds. 78 EKOS
- Surgical embolectomy 26 patients – 100% survival
- Average TPA dose 25.6 mg. Heparin 200 units/hr
- Surgical vulnerable periods are at induction and opening of chest. Start EPI at induction
4 Year Experience
Massive and Submassive PE

• Surgery Embolectomy - 26 Patients
• Age 20-88, Avg 57.1 yr.
• Pump Time 18-90, Avg 28 min
• Vulnerable period at induction with loss of catecholamines and vasodilatation. Also when sternum opened as RV dilates. Start EPI !!
4 Year Experience
Massive and Submassive PE
(Continued)

• Lytics 90 patients
• Age 19-88, Ave 53.6yrs
• Avg Infusion Time 15.8Hours
• TPA Total average dose 25.6 mg
  (Last 51 patients average 23mg)
• 1 Patient Transfused
• Heparin 200 units/hour
Suggested treatment algorithm for use to treat acute pulmonary embolism

1. EVIDENCE OF SHOCK OR RESPIRATORY FAILURE:
   - Any hypotension (SBP < 90 mm Hg)
   - Shock index > 1.0
   - Respiratory distress (SaO2 < 95% with Borg score > 8, or altered mental status, or appearance of suffering)

2. EVIDENCE OF MODERATE TO SEVERE RV STRAIN:
   - RV dysfunction (RV hypokinesis or estimated RVSP > 40 mm Hg)
   - Clearly elevated biomarker values (e.g., troponin above borderline value, BNP > 100 pg/mL or pro-BNP > 900 pg/mL)

No contraindications to fibrinolysis

Alteplase
100 mg over 2 h IV

PERT
Embolectomy

CDT
Summary

1. PE is Acute Right Ventricular Afterload Syndrome
2. All Mortality Markers are Cardiac
3. Massive and submassive PE should be treated with cdt lytics or surgery
4. CDT with low dose heparin is safe and effective
5. PERT improves communication
Massive PE
Thank you
Summary

7. Think of PE as RV Afterload Syndrome

8. RV Dysfunction, ↑ Troponin, ↑ BNP & EKG Changes all increase mortality

9. For massive and submassive PE, strongly consider catheter based Lysis or surgery

10. IVC Filter should be considered when
    CONTRAINDICATION TO ANTICOAGULATION OR POOR CARDIO/PULM RESERVE
Clinical Symptoms

- DySpneA 84%
- PleuritIC C.P. 74%
- Cough 53%
- Hemoptysis 30%
- SyncoPe 13%
Clinical Signs

- Tachypnea 92%
- Rales 58%
- Tachycardia 44%
- Fever 43%
- Cyanosis 19%
## MHS Experience - 39 pt (1991)

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<th>POST</th>
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<tr>
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<td>42/18</td>
<td>35/12</td>
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<tr>
<td>CO</td>
<td>2.7</td>
<td>4.1</td>
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<tr>
<td>PVR</td>
<td>410</td>
<td>190</td>
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<tr>
<td>Mortality</td>
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<td>0%</td>
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MHS (1991)

- 5cm gastric ulcer
- Platelet 25,000
- Ongoing bleeding hematoma
- 3 day post ACBP Shock
Low Risk PE

- Acute PE with absence of clinical markers of massive or submassive PE
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

44% of PE patients with RV dysfunction at time of diagnosis had **chronic pulmonary hypertension** at 1-year follow-up.


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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
AHA Lytic Recommendations

1. Depending on local expertise catheter or surgery for massive PE & contraindication to lytic reasonable

2. Catheter or surgery embolectomy if unstable after lytics

3. If cannot receive lytics or unstable after lytic transfer to experienced institution

4. Catheter or surgery for submassive PE to be considered if clinical evidence of adverse prognosis

5. Not indicated for low risk PE
PULMONARY EMBOLISM

• Massive PE

Acute PE with sustained hypotension for >15 minutes or requiring pressure support or HR 40
PULMONARY EMBOLISM

• Submassive PE
  — RV Dysfunction defined as
    • RV Dilatation or RV Systolic Dysfunction on Echo
    • RV Dilatation on CT
    • Elevated BNP
    • Elevated Nterminal Pro-BNP
    • EKG change — new complete or incomplete RBBB,
      anteroseptal ST Elevation or Depression or antero Septal T-wave change
  — Elevated Troponin
Representative pulmonary endarterectomy specimens
Surgical embolectomy

47 patients survival 97% (Sarkiya)
Minimal pump time
No fibrillatory arrest
Milk the lung
Vulnerable periods are induction and opening the chest
Venous Clots are a Big Problem
Significantly Under Treated

- Deep Vein Thrombosis (DVT)
  - 600,000 cases per year
- Pulmonary Embolism (PE)
  - >600,000 cases per year

- About 6% death occurs within 1 month of diagnosis
- Up to 75% treated with blood thinners alone
- The blood clot or part of it can break free and become lodged in the blood vessels of the lung, causing PE
- If PE can be appropriately diagnosed and appropriate therapy started, mortality can be reduced from 30% to 10%
Catheter Intervention Techniques

- Thrombus Fragmentation
- Rheolytic Thrombectomy
- Suction Thrombectomy
- Ultrasound Therapy
- Catheter Directed Thrombolysis
Percutaneous Catheter Based Intervention

1. Aspiration
2. Thrombus Fragmentation
3. Rheolytic Thrombectomy

348 patients massive PE success 80% & with Lytics over 95%
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.
RV hypokinesis on baseline echo was associated with \textbf{\~40\% higher mortality rate} at 3 months.

\textit{Goldhaber S, Visani L, DeRosa M. The Lancet; Apr 24,1999; 353,9162; Health Module pg. 1386}

\textbf{THE LANCET}

Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER)

\textit{Samuel Z Goldhaber, Luigi Visani, Marisa De Rosa, for ICOPER*}

\begin{itemize}
  \item \textbf{Mortality rate:}
  \begin{itemize}
    \item 21\% with RV hypokinesis
    \item 15\% no RV hypokinesis
  \end{itemize}
\end{itemize}
Primary endpoint:
Reduction in RV/LV ratio (echo)

- Baseline to 24 hrs: EKOS + Heparin = 0.30
- Baseline to 90 days: EKOS + Heparin = 0.38
  - P < 0.0001
- Baseline to 24 hrs: Heparin = 0.03
- Baseline to 90 days: Heparin = 0.22
  - P = 0.03
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