Inclusion of Pulmonary Embolism Response In a Level I Vascular Emergency Program

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Georgia Vascular Society
2016 Annual Meeting
Lake Oconee, Georgia
## Disclosures

**Financial Conflicts:** None

**Competition of Interest:** Clinical Trial Participation (Venous)

<table>
<thead>
<tr>
<th>Device 1</th>
<th>Device 2</th>
<th>Institution/Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPTALYSE – PE</td>
<td>EKOS – BTG</td>
<td>Site Principal Investigator, Piedmont Heart Institute</td>
</tr>
<tr>
<td>ACCESS – PTS</td>
<td>EKOS – BTG</td>
<td>Site Principal Investigator, Piedmont Heart Institute</td>
</tr>
<tr>
<td>VIVO</td>
<td>Cook</td>
<td>Site Principal Investigator, Piedmont Heart Institute</td>
</tr>
</tbody>
</table>

**Mention of Devices Not In Possession of Specific PE Indication/Off-label Use**
- Inari Flowtriever
- 8F Penumbra Indigo System
- AngioVac
Objectives

1. What is a Level I Cardiovascular Emergency Program?
   How does PE fit in?
   Understand risk stratification
   Identify candidates for intervention
3. PE experience in the Piedmont Level I Program
Piedmont Healthcare

Piedmont Heart Institute
Piedmont Atlanta Hospital
Piedmont Healthcare

2015 Volume Indicators

455 beds
50,211 ED visits
1,157 CV pump cases
1,543 PCI cath cases
116 TAVR
43 VAD implants
77 ECMO cases
160 kidney transplants
90 liver transplants
12 heart transplants
24/7/365 MD critical care

Emory Gen Surg Residents
Mercer Transplant Surg Fellows
Mercer PA Students
PA and Nursing Residents
Level I Vascular Emergency Program

A natural evolution in emergency cardiovascular care
Do we need another emergency system?

Just a few issues
Can you image 24/7/365?
Call team skillset?
Can you offer REVAR?
Inventory?
Blood bank?
Data Collection?
Etc., etc., etc.
Should Vascular Emergency Care Aspire To Emulate Established Emergency Care Models?

Process Driven

Time Critical
Level I Vascular Emergency Programs

- Acute Aortic Syndromes
- Acute Limb Ischemia
- Catastrophic VTE

- same logistics
- similar processes of care
- similar advanced imaging requirement
- same physicians and teams
- same care venues and resources
- same coordinator
- same outreach program

Vascular Emergency Program
# Level I Vascular Emergency Programs

Who’s out there? Who’s taking this on?

<table>
<thead>
<tr>
<th>Institution</th>
<th>Region</th>
<th>Leadership</th>
<th>Setting</th>
<th>STEMI/ Shock</th>
<th>AAS</th>
<th>ALS</th>
<th>VTE</th>
<th>PERT</th>
<th>stroke</th>
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</thead>
<tbody>
<tr>
<td>Minneapolis Heart / ANH</td>
<td>MN</td>
<td>Integrated</td>
<td>Institute</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>IU- Methodist</td>
<td>IN statewide</td>
<td>VS + CT</td>
<td>Academic Med Ctr.</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>OSU - Wexner</td>
<td>OH central</td>
<td>Integrated</td>
<td>Academic Med Ctr.</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Cooper-Rowan</td>
<td>Metro/South Jersey</td>
<td>VS + CT</td>
<td>Academic Med Ctr.</td>
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<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Piedmont Heart/PHC*</td>
<td>MetroATL NW GA</td>
<td>VS + CT .....</td>
<td>Institute</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

* Limited scope of marketing to date

STEMI: acute ST elevation myocardial infarction
AAS: acute aortic syndrome
ALS: acute limb ischemia
VTE: catastrophic venous thromboembolism
PERT: pulmonary embolism rapid response

Who does what, where, and when is “locally” decided. VS + CT co-leadership is most common.
Level I Vascular Emergency Programs

Drs. Mark Davies and Alan Lumsden – Methodist DeBakey, Houston, Texas
- Advanced Aortic Treatment Center
- “Door to intervention time of 90 minutes”

Dr. Michael Dalsing at Indiana University - Methodist Hospital in Indianapolis 2009
- model statewide referral system for vascular emergencies
- Tera Recon system for transfer of imaging data prior to patient arrival
- extended the AATC concept to all vascular emergencies

Piedmont Atlanta Hospital
- program build-out: August 2012-June 2014
- program “live” July 2014
- multidisciplinary
- program incorporates PE rapid response
Level I Vascular Emergency Program

PE
- Contributes 38% of Level I volume

*Downstream intangibles* .......
- Maintains vascular surgical leadership in major venous interventions
- iliofemoral venous thrombosis
- vena cava thrombosis
- vena cava tumors
- right atrial thrombus
- Maintains high-profile vascular visibility in the critical care units
- Platform for collaboration

Level I Activity: July 2014 – August 2016
## Venous Thromboembolism – Scope of the problem

<table>
<thead>
<tr>
<th>900,000 cases annually</th>
<th>7.9 – 39 billion dollars U.S. Healthcare Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>117/100,000 person-years increases with age</td>
</tr>
<tr>
<td>PE - Leading cause of preventable in-hospital death in the United States</td>
<td></td>
</tr>
<tr>
<td>PE - 3rd leading cause of cardiovascular mortality</td>
<td></td>
</tr>
<tr>
<td>100,000 to 180,000 deaths/year</td>
<td>25-33% present as sudden death</td>
</tr>
<tr>
<td></td>
<td>4% incidence of CTPH</td>
</tr>
<tr>
<td>DVT – at least 350,000 cases annually</td>
<td>29 – 79% Post-thrombotic Syndrome</td>
</tr>
<tr>
<td></td>
<td>- develops slowly</td>
</tr>
<tr>
<td></td>
<td>- progressively debilitating</td>
</tr>
<tr>
<td></td>
<td>- 6 to 7 million patients today</td>
</tr>
<tr>
<td></td>
<td>- 400,000 – 500,000 venous ulcers</td>
</tr>
</tbody>
</table>

*All practicing physicians interface with patients with or at risk for VTE*
Venous Thromboembolism – Scope of the problem

VTE – PE
- different population compared to straight VS
- unmet need for interventional care
- incredibly rewarding
Pulmonary Embolism – Pathophysiology

- Thrombus travels from legs to the right heart and lungs
- Acutely obstructs pulmonary arteries
- Increases PVR
- Right ventricular strain and failure
- Hypotension, Hypoxemia
- Decreased coronary artery perfusion
- Cardiac output
- DEATH
PE 2016 and Beyond: *In a nutshell*

1. Stratify Risk for Adverse Outcome
   - *identify RV strain*
2. Relieve PA Obstruction
   - *facilitate rapid RV recovery*
   - *Possibly prevent late CTePH*
PE in 2016 (and beyond) : Focus on the Right Ventricle

Poor Outcome Associated with Right Ventricular Dysfunction

1. ICOPER Registry + RV hypokinesis 18% in-hospital mortality
   57% higher mortality at 3 months (compared to normal RV function)

2. RV:LV ratio > 0.9 by CTA → independent risk factor for mortality

3. Risk of mortality  → increases stepwise with increasing RV:LV ratio

4. RV dysfunction  → increased risk of recurrent PE and death

5. Elevated biomarkers  → risk factor for mortality
Methods to Unload the Right Ventricle

<table>
<thead>
<tr>
<th>Technique</th>
<th>Variations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic Thrombolysis (TPA)</td>
<td>Half-dose; Full Dose 50 mg + 50 mg; Full Dose 10 mg bolus + 90 mg infusion next 2 hrs</td>
</tr>
</tbody>
</table>
| Catheter-based Intervention      | Standard infusion catheter  
Pharmacomechanical – EKOS Acoustic Pulse Therapy system  
Mechanical – Cat 8 Indigo, Penumbra  
- Flowtriever, Inari  
- AngioVac on venovenous bypass, Angiodynamics |
| Surgical                         | Pulmonary (and right heart) Embolectomy on CPB                                                                                           |
| Rescue                           | VA ECMO ; RV Impella (used only after mechanical obstruction has been relieved)                                                           |
PE in 2016 (and beyond) : Focus on the Right Ventricle

RV:LV Ratio > 0.9
- marks RV dysfunction
Intermediate Risk - 25%

Paradigm Shift favoring Intervention

Low Risk 70%

Standard VTE management
PE 2016: Risk Stratification and Management Implications

**Paradigm Shift** favoring Intervention

- **Low Risk** 70%
- **Intermediate Risk** 25%
- **High Risk** 5%

Standard VTE management
- Normal BP
- Normal Biomarkers
- CTA RV:LV ratio < 0.9
- 30-day risk of death < 3%
Intermediate risk or “Submassive”
- normal BP but + RV:LV ratio > 0.9

Intermediate high-risk
- biomarkers are +
  - *consider intervention*

Intermediate low-risk
- biomarkers are –

30 day risk of death: 3 to 21%

**Paradigm Shift** favoring intervention

Standard VTE management

**PE 2016: Risk Stratification and Management Implications**
Intermediate Risk - 25%

High-risk or Massive
Hypotension
Hemodynamic instability or collapse
Consider Intervention
30-day risk of death = 50%

Low Risk - 70%

Paradigm Shift favoring Intervention

Standard VTE management
# Acute PE Risk Stratification/Management 2016

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Anticoagulation</td>
</tr>
<tr>
<td>Intermediate low-risk</td>
<td>Anticoagulation</td>
</tr>
<tr>
<td>Intermediate high-risk</td>
<td>Intervention in appropriately selected patients</td>
</tr>
<tr>
<td>Massive</td>
<td>Intervention</td>
</tr>
</tbody>
</table>
PE Risk Stratification

Risk Stratification – Quick guide

Vital Signs

Standard ED chest pain work up battery
- ECG
- troponin
- BNP

CTA
- RV/LV ratio > than 0.9

ECHO
- multiple components

MD Calc.com (Use your smart phone)
- simplified PESI
Summary of Paradigm Shifts In Management of Acute PE

Acknowledgement that PE with RV dysfunction is associated with poor outcome

Risk stratify all patients presenting with Acute PE

Consider intervention to unload the right ventricle in patients stratifying to.....
  Intermediate, high-risk
  and
  Massive

Chose treatment modality to minimize risk and maximize benefit for each patient
(Precision Medicine 2016)
Piedmont Healthcare Clinical Pathway
Acute Venous Thromboembolism: Large Thrombus Burden PE Treatment Pathway

CTA-PE Protocol
CTA Large Thrombus Burden PE
Emergency Physician and GLA Pulmonary Critical Care Consult

Hemodynamically Unstable Massive PE
Institute hemodynamic and respiratory support
Immediate consultation through Carelink:
- Cardiothoracic Surgery
- PE Interventional Team
- ECMO Team

COLLABORATIVE DECISION

Hemodynamically Stable Submassive PE
Check BNP and troponin
Evaluate echocardiogram
LE Venous Duplex to identify source

(+): Right heart dysfunction
(-): Right heart dysfunction

Consult PE Intervention Team

No contraindications to lytic therapy
- Catheter-directed Thrombolysis (APT)
- Consider IVC Filter

Contraindications to lytic therapy
- Anticoagulation
- Catheter Thrombectomy
- Consider IVC Filter

Surgical Embolectomy
ECMO
Systemic Thrombolysis

Catheter-directed Thrombolysis (APT) or Catheter Thrombectomy with ECMO Backup

*Clinical pathways and guidelines are evidence-based tools that have been developed by a multidisciplinary team to assist clinicians in making appropriate health care decisions. They are not intended to replace individual clinician’s judgment.
## PE Interventionalists on call for Piedmont Level I

<table>
<thead>
<tr>
<th>Year</th>
<th>PE Interventionalists – Who is doing the cases at PAH?</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>Vascular/Endovascular Surgery</td>
</tr>
<tr>
<td>2013</td>
<td>Vascular/Endovascular Surgery</td>
</tr>
<tr>
<td>2014</td>
<td>Vascular/Endovascular Surgery</td>
</tr>
<tr>
<td>2015</td>
<td>Vascular/Endovascular Surgery</td>
</tr>
</tbody>
</table>
| 2016 | Vascular/Endovascular Surgery and Interventional Cardiology  
3 surgeons 2 cardiologists  
“PE Interventionalist of the Day” on Carelink Daily Schedule |
Piedmont PE Mortality

Level 1 PE Mortality July 2014-August 2016

<table>
<thead>
<tr>
<th>Category</th>
<th>Total Patients</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Submassive</td>
<td>68</td>
<td>0</td>
</tr>
<tr>
<td>Massive</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>Low Risk</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>
PAH PE Length of Stay

PE Length of Stay July 2014-August 2016

<table>
<thead>
<tr>
<th>Category</th>
<th>Level I Emergency</th>
<th>% Level I CM</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE</td>
<td></td>
<td>6 to 10%</td>
</tr>
<tr>
<td>All Others</td>
<td></td>
<td>90-94%</td>
</tr>
</tbody>
</table>

PE by Subcategory:
- Submassive
- Massive
- Low risk
PE Mortality by Quarter

Level 1 PE Mortality

GVS: PE 2016
Emergence of Level I Vascular Emergency Programs

Big Thank You Shout Out: PAH Level I Admin Team

Grant Reynolds, BS, RN

Mike Lunney MPH, NRP

Matt Robinson
Director of Clinical Integration
Level I Cardiovascular Emergency Programs and PE: Summary

1. Level I Cardiovascular Emergency Programs are emerging
2. Management of PE has shifted towards invasive intervention
3. PE Response (Teams) is a good fit in Level I Cardiovascular Emergency Programs
4. **Vascular surgeons who do not participate in PE Response Teams risk losing major venous case work**
## PE Risk Stratification

<table>
<thead>
<tr>
<th>Risk Assignment</th>
<th>Severity</th>
<th>% PE Population</th>
<th>% Mortality</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Massive (High)</td>
<td>Severe</td>
<td>5</td>
<td>&gt;50</td>
<td>Hypotension, circulatory collapse hemodynamic instability</td>
</tr>
<tr>
<td>Submassive Intermediate-High risk</td>
<td>High</td>
<td>10</td>
<td>21</td>
<td>RVD without hypotension; elevated troponin and elevated BNP</td>
</tr>
<tr>
<td>Submassive Intermediate-Low risk</td>
<td>Medium</td>
<td>15</td>
<td></td>
<td>RVD without hypotension and either elevated troponin or elevated BNP, but not both</td>
</tr>
<tr>
<td>Minor</td>
<td>Minor</td>
<td>45 to 70</td>
<td>15</td>
<td>Dyspnea; chest pain</td>
</tr>
</tbody>
</table>
Level I Vascular Emergency Programs

2015 PE Experience and Outcomes

42 large-burden PEs
- 4 low-risk, managed medically
- 28 submassive (No deaths)
  - 6 managed medically
  - 22 managed by UA-CDT (No ICH; 1 major bleeding complication)
- 10 massive
  - 2 ECMO + UA-CDT (1 death – hospice)
  - 2 surgical thromboembolectomy on cardiopulmonary bypass
  - 5 UA-CDT with ECMO standby (1 major bleeding comp)
  - 1 CPR in-progress treated by systemic thrombolysis (death)
Traditional Methods to Rapidly Relieve the RV

1. Systemic Thrombolysis
   - (generally) safe and effective
   - concern for increased risk of major bleeding, including ICH
   - PEITHO trial (6.3% major bleeding; 2% hemorrhagic stroke)

2. Transcatheter thrombus fragmentation/catheter-directed thrombolysis
   - PERFECT Trial

3. Surgical Pulmonary Thrombectomy (on cardiopulmonary bypass)
   - safe and effective with proper patient selection
   - lack of uniform availability
   - lack of agreement/decisiveness
     - often used only if systemic thrombolysis failed
     - or thrombolysis was contraindicated
   - late decisions with sicker patients yield less favorable results
     - 10% mortality if unstable; 3.6% if stable
Interventional Techniques for PE Management

Ideal Principles

*Immediate availability* in any cath lab environment

Delivery of thrombolytic agent *directly* into the pulmonary arterial bed and effective treatment with *far lower doses* than systemic thrombolysis

For mechanical devices, *safe and efficient* removal of pulmonary arterial thrombus

---

*Rescue availability*

- Immediate availability to convert to extracorporeal life support

- Patient selection and early transfer remains very important for sicker patients
ULTRASOUND-ACCELERATED (ASSISTED), CATHETER-DIRECTED THROMBOLYSIS
- 6F system with catheters (5.4 F) placed in one or both pulmonary arteries
- Dual sheath access in either the femoral or internal jugular veins
- 12 to 24 hour infusion of TPA with patient in ICU
- Well-tolerated; patient’s do not discern/feel treatment (stay in bed)
UA-CDT: Ultrasound-Accelerated, Catheter-Directed Thrombolysis

UA-CDT: The EKOS System
- Ultrasound-accelerated (assisted), catheter-directed thrombolysis
- Delivers low doses of TPA directly to the thrombus
- Employs ultrasound pressure waves to facilitate thrombolysis
  - Produces disaggregation of fibrin and increases binding sites for TPA
  - Produces acoustic streaming which increases penetration of TPA

Fibrin without Ultrasound
Fibrin With Ultrasound

Acoustic streaming drives lytic into clot
Level I Vascular Emergency Programs

- Natural evolution in cardiovascular emergency care
  - vascular emergency care is process driven and time dependent
  - vascular emergency care is resource dependent
    - logistical expertise (CARELINK Call Center)
    - professional expertise, capability, availability
    - advanced imaging (CTA, MRA, ECHO, Vasc Lab and Operating Hybrids)
    - rapid, precise diagnosis and management
    - extensive, redundant inventory requirement
    - critical care required 24/7/365
  - vascular emergency care may benefit from “economy of scale”
Evidence supporting UA-CDT for intermediate-risk and high-risk PE

1. Multiple single-center, case series 2008 – 2013
   - rapid reduction in pulmonary artery pressure and recovery of RV function
   - significant lysis with low-doses of TPA (12 to 40 mg total doses)
   - marked reduction in major bleeding complications and no ICH

2. ULTIMA Trial (European, multiple centers, 59 patients)
   - prospective, randomized trial comparing UA-CDT with standard anticoagulation
   - RV:LV ratio was significantly reduced with UA-CDT at 24 hours
   - RV systolic function was significantly better with UA-CDT at 24 hours and 90 days
   - no major bleeding complications or ICH

3. SEATTLE II Trial (22 US centers, 150 patients)
   - prospective single arm trial; primary endpoint RV:LV ratio at 48 hours
   - primary safety endpoint was absence of major bleeding complications
   - mean TPA dose was 23.4 +/- 2.9 mg
   - 25% reduction in RV:LV ratio at 24 hours
   - Significant reduction in PA pressures at end of treatment
   - no hemodynamic collapse, no intracranial hemorrhage, 10% bleeding comps

4. FDA Approval – EKOS approved for interventional management of PE – May 2014