CATHETER DIRECTED THERAPY FOR ACUTE PULMONARY EMBOLISM

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LSUHSC SHREVEPORT
OBJECTIVES

- Classification
- Pathophysiology
- Rationale for Lysis
- Catheter directed therapy
- Recent literature
PULONARY EMBOLISM

- 300k-600k per year
  - 1-2 per 1000 people, or as high as 1 in 100 if > 80

- 10-30% overall 30 day mortality
  - Sudden death is presenting symptom in ~ 25%

- 2012: 166,665 primary admissions for PE
  - In-hospital mortality ~ 3%

- Most commonly from lower extremity DVT
  - Evidence of DVT in > 50%

cdc.gov; Agency for Healthcare Research and Quality
### BACKGROUND AND DEFINITIONS

#### Patient risk stratification (per AHA Scientific Statement 2011)

<table>
<thead>
<tr>
<th>Massive PE</th>
<th>Submassive PE</th>
<th>Minor/Nonmassive PE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High risk</strong></td>
<td><strong>Moderate/intermediate 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>– Pulselessness</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>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### 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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ACUTE PE: PATIENT PROFILE

ICOPER. Lancet1999;353:1386

- Massive PE
  - < 5% of the PE population
  - 58% mortality at 3 months

- Submassive PE
  - 40% of the PE population
  - 21% mortality at 3 months

- Minor PE
  - 55% of the PE population
  - Good prognosis
  - No mortality
How to Determine Risk

- Registry of 1,416 patients
- Mortality rate:
  - 1.9% if RV/LV ratio < 0.9
  - 6.6% if RV/LV ratio ≥ 0.9
How to Determine Risk

- Retrospective analysis of 120 patients with hemodynamically stable PE based on chest CT

- PE-related mortality at 3 months:
  - 17% if $RV/LV \geq 1.5$
  - 8% if $1.0 \leq RV/LV < 1.5$
  - 0% if $RV/LV < 1.0$

How to Determine Risk

- Retrospective analysis of 63 patients with chest CT

- Adverse event rate at 30 days:
  - 80.3% if RV/LV ratio > 0.9
  - 51.3% if RV/LV ratio ≤ 0.9
Table 6. Mortality Rates for Acute PE From Published Results of Registries and a Publicly Available Database (HCUP-NIS)

<table>
<thead>
<tr>
<th>Source</th>
<th>Year</th>
<th>N</th>
<th>Follow-Up</th>
<th>Massive PE</th>
<th>Submassive PE</th>
<th>Massive PE Given Lytic</th>
<th>Submassive PE Given Lytic</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAPPET</td>
<td>1997</td>
<td>719</td>
<td>30</td>
<td>NA</td>
<td>9.6</td>
<td>NA</td>
<td>4.7</td>
</tr>
<tr>
<td>ICOPER</td>
<td>1999</td>
<td>2284</td>
<td>90</td>
<td>52.4</td>
<td>14.7</td>
<td>46.3</td>
<td>21</td>
</tr>
<tr>
<td>RIETE</td>
<td>2007</td>
<td>6264</td>
<td>90</td>
<td>9.3</td>
<td>3.0</td>
<td>1.3</td>
<td>7.7</td>
</tr>
<tr>
<td>EMPEROR</td>
<td>2008</td>
<td>1840</td>
<td>In-hospital</td>
<td>14.6</td>
<td>3.0</td>
<td>0</td>
<td>9.5</td>
</tr>
<tr>
<td>HCUP-2007 NIS</td>
<td>2007</td>
<td>146,323</td>
<td>In-hospital</td>
<td>3.5</td>
<td></td>
<td></td>
<td>NA</td>
</tr>
</tbody>
</table>

*ACC/AHA Guidelines 2011  Circulation 2006;113:577-82*
Why treat submassive PE patients aggressively?

Various studies report presence of right ventricular dysfunction (RVD) as a predictor of poor clinical outcomes:

1. Mortality
2. Adverse events
3. VTE recurrence
PATHOPHYSIOLOGY OF VTE

EPINEPHRINE

HISTAMINE

THROMBOXANE A2

SEROTONIN
PATHOPHYSIOLOGY OF VTE

LYSIS

IMPROVES RV HEMODYNAMICS
DECREASED PVR
DECREASED RV PRESSURE
RESTORES VENTRICULAR SEPTAL POSITION

IMPROVES LV HEMODYNAMICS
INCREASED PBF
INCREASED PRELOAD TO THE LA AND LV
IMPROVED LV OUTPUT
IMPROVED BP
PATHOPHYSIOLOGY OF PULMONARY EMBOLISM

- Hypotension
- RV Dysfunction
- RV Dilatation
- Decreased RV Cardiac Output
- Decreased distensibility of the LV due to interventricular dependency
- Decreased preload to the LV
- Decreased LV cardiac output
- Tricuspid regurgitation
- Decreased RV cardiac output
- Myocardial ischemia
- Decreased left heart cardiac output

Diagram:

- MYOCARDIAL ISCHEMIA
- RV DYSFUNCTION
- RV DILATATION
- TRICUSPID REGURGITATION
- DECREASED LEFT HEART CARDIAC OUTPUT
- DECREASED DISTENSIBILITY OF THE LV DUE TO INTERVENTRICULAR DEPENDENCY
- DECREASED PRELOAD TO THE LV
- DECREASED RV CARDIAC OUTPUT
Figure 3  Proposed diagnostic algorithm for patients with suspected high-risk PE, i.e. presenting with shock or hypotension.
Suspected PE without shock or hypotension

Assess clinical probability of PE
Clinical judgment or prediction rule

Low/intermediate clinical probability or PE unlikely
D-dimer

negative
CT angiography
no PE
No treatment

positive
PE confirmed
Treatment

High clinical probability or PE likely
CT angiography
no PE
No treatment

PE confirmed
Treatment or investigate further

CT = computed tomographic; PE = pulmonary embolism.

*Two alternative classification schemes may be used for clinical probability assessment, i.e. a three-level scheme (clinical probability defined as low, intermediate, or high) or a two-level scheme (PE unlikely or PE likely). When using a moderately sensitive assay, D-dimer measurement should be restricted to patients with low clinical probability or a PE-unlikely classification, while highly sensitive assays may also be used in patients with intermediate clinical probability of PE. Note that plasma D-dimer measurement is of limited use in suspected PE occurring in hospitalized patients.

*Treatment refers to anticoagulation treatment for PE.

*CT angiogram is considered to be diagnostic of PE if it shows PE at the segmental or more proximal level.

*In case of a negative CT angiogram in patients with high clinical probability, further investigation may be considered before withholding PE-specific treatment.
Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis

Christophe Marti¹*, Gregor John¹, Stavros Konstantinides², Christophe Combescure³, Olivier Sanchez⁴, Mareike Lankeit², Guy Meyer⁴, and Arnaud Perrier¹

RCT’S COMPARING SYSTEMIC THROMBOLYSIS PLUS ANTICOAGULATION WITH ANTICOAGULATION ALONE IN PATIENTS WITH ACUTE PE.

RISCKS AND BENEFITS COMPARED

15 RCT’S
N= 2057 PATIENTS
Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis


![Figure 2](image)

**Figure 2** Early mortality by pulmonary embolism severity, Forest plot.
CRITERIA FOR THROMBOLYSIS IN PULMONARY EMBOLISM: PRINCIPAL INCLUSION CRITERIA

MASSIVE PULMONARY EMBOLISM
ANATOMICALLY SMALL OR MODERATE PE WITH HEMODYNAMIC INSTABILITY

HEMODYNAMICALLY STABLE, BUT RV DYSFUNCTION DETECTED ON BASELINE ECHOCARDIOGRAM

NORMAL ECHOCARDIOGRAM AND MODERATE-SIZED PE ASSOCIATED WITH MASSIVE PELVIC OR LEG THROMBOSIS
RESULTS OF SYSTEMIC THROMBOLYTIC THERAPY OF PULMONARY EMBOLISM

1. THROMBOLYTIC TX RESULTS IN FASTER THROMBUS RESOLUTION THAN TX W/ HEPARIN ALONE.
2. THROMBOLYTIC TX RESULTS IN A SIGNIFICANT REDUCTION OF PE INDUCED PULMONARY HYPERTENSION W/IN 24 HRS. OF TX
3. THROMBOLYTIC TREATMENT RESULTS IN A SIGNIFICANT IMP. OF PULMONARY PERFUSION SCANS AT 24 HRS.
4. THROMBOLYTIC TX APPEARS TO REDUCE MORTALITY IN PXS WITH SHOCK DUE TO MASSIVE PE (RCT, Jerjes-Sanchez et. al J ThrombThrombolysis 1995;2: 227-229).
5. THROMBOLYTIC TX IN PXS W/ ACUTE PE, NORMAL BP AND 2D ECHO SIGN OF RV DYSFUNCTION HAS BEEN SHOWN TO REDUCE MORTALITY AND RECURRENT PE (CONTROVERSIAL) (RCT Goldhaber et. al. Lancet 1993; 341:507-511)
RESULTS OF THROMBOLYTIC THERAPY OF PULMONARY EMBOLISM

6. THROMBOLYTIC TX DOES NOT REDUCE MORTALITY OR INCIDENCE OF RECURRENT PE IN HEMODYNAMICALLY STABLE PXS.

7. THROMBOLYTIC TX POSSIBLY IMPROVES HEMODYNAMIC RESPONSE TO EXERCISE.
   (REVIEW ARTICLE Arcasoy, Chest 1999; 115:1695-1707)
Contraindications to Systemic Lysis

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any prior intracranial hemorrhage</td>
<td>Age &gt;75</td>
</tr>
<tr>
<td>Brain AVM or tumor</td>
<td>Current anticoagulation</td>
</tr>
<tr>
<td>CVA in last 3 months</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>Active bleeding or bleeding diathesis</td>
<td>Noncompressible vascular puncture</td>
</tr>
<tr>
<td>Recent surgery encroaching on spinal canal or brain</td>
<td>Traumatic/prolonged CPR</td>
</tr>
<tr>
<td>Recent significant head trauma</td>
<td>Internal bleeding in last month</td>
</tr>
<tr>
<td></td>
<td>Uncontrolled HTN (SBP &gt;180 or DBP &gt;110)</td>
</tr>
<tr>
<td></td>
<td>Remote stroke</td>
</tr>
<tr>
<td></td>
<td>Major surgery in last 3 weeks</td>
</tr>
</tbody>
</table>
Recent RCT examined benefit of IV thrombolysis in submassive or intermediate risk PE

**PEITHO Trial**

**Primary Objective:**
To investigate the clinical benefits (efficacy) of thrombolysis with tenecteplase over placebo in normotensive patients with acute intermediate-risk PE (both treatment arms receive standard heparin anticoagulation)

**Secondary Objective:**
To assess the safety of tenecteplase in patients with intermediate-risk PE

http://clinicaltrialresults.org/Slides/ACC%202013/Konstantinides_PEITHO_ACC%202013.pdf
IV thrombolysis reduces the risk of hemodynamic collapse

<table>
<thead>
<tr>
<th></th>
<th>Tenecteplase (n=506)</th>
<th>Placebo (n=499)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause mortality within 7 days</td>
<td>6 (1.2%)</td>
<td>9 (1.8%)</td>
<td>0.43</td>
</tr>
<tr>
<td>Hemodynamic collapse within 7 days</td>
<td>8 (1.6%)</td>
<td>25 (5.0%)</td>
<td>0.002</td>
</tr>
<tr>
<td>• Need for CPR</td>
<td>1</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>• Hypotension / BP drop</td>
<td>8</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>• Catecholamines</td>
<td>3</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>• Resulted in death</td>
<td>1</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

http://clinicaltrialresults.org/Slides/ACC%202013/Konstantinides_PEITHO_ACC%202013.pdf
But the benefit of lysis came at the cost of major bleeds (including ICH)

<table>
<thead>
<tr>
<th></th>
<th>Tenecteplase (n=506)</th>
<th>Placebo (n=499)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All strokes by day 7</td>
<td>12 (2.4%)</td>
<td>1 (0.2%)</td>
<td>0.003</td>
</tr>
<tr>
<td>• Hemorrhagic</td>
<td>10</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>• Ischemic</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Serious adverse events (SAE)</td>
<td>29 (5.7%)</td>
<td>39 (7.8%)</td>
<td>0.19</td>
</tr>
</tbody>
</table>

http://clinicaltrialresults.org/Slides/ACC%202013/Konstantinides_PEITHO_ACC%202013.pdf
Catheter Directed Therapies

catheter-directed therapy (CDT)

- Alternative or additive treatment for massive PE

- Wide variety of devices and techniques, with the goal of rapidly reducing clot burden
  - Thrombus fragmentation
  - Thrombus aspiration
  - Intra-thrombus lytic administration
## Table 1. Catheter Intervention Techniques and Devices

<table>
<thead>
<tr>
<th>Catheter Interventions Without Thrombolysis</th>
<th>Catheter Interventions With Thrombolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technique</td>
<td>Device examples</td>
</tr>
<tr>
<td>Thrombus fragmentation</td>
<td>Pigtail catheter (5–6F)</td>
</tr>
<tr>
<td></td>
<td>Peripheral balloon catheters (6–7F, balloon diameter 5–10 mm)</td>
</tr>
<tr>
<td></td>
<td>Amplatz thrombectomy device 7 F</td>
</tr>
<tr>
<td></td>
<td>(Bard-Microvena, White Bear Lake, MN)</td>
</tr>
<tr>
<td>Rheolytic thrombectomy</td>
<td>AngioJet 6F PE catheter (MEDRAD, Minneapolis, MN)</td>
</tr>
<tr>
<td></td>
<td>Oasis catheter (Boston Scientific, Galway, Ireland)</td>
</tr>
<tr>
<td></td>
<td>Hydrolyzer (6–7F, Cordis, Miami, FL)</td>
</tr>
<tr>
<td>Suction embolectomy</td>
<td>Sheath with detachable hemostatic valve 8–9F (Argon Medical Devices, Athens, TX) plus multipurpose guide catheter (8–9F) plus aspiration syringe (60 mL)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotational thrombectomy</td>
<td>Aspirex* 8F, 10F catheter (Straub Medical, Switzerland)</td>
</tr>
<tr>
<td>Combined techniques</td>
<td>eg, Pigtail fragmentation (5F) plus Aspirex* 8F, 10F thrombectomy</td>
</tr>
</tbody>
</table>

*Not available in the United States.
†Requires placement of a tip-occluding guide wire.
‡Hemostatic valve at the end of the catheter provides endhole occlusion without the need for placing a tip-occluding guide wire.

(Circulation. 2011;124:2139-2144.)
Techniques – pigtail rotation
Technique – Balloon Angioplasty
Technique – Aspiration Thrombectomy
Technique – Rheolytic Aspiration
Technique – Suction Thrombectomy
Technique – Ultrasound Enhanced Lysis
Figure 7. Coronal CT images demonstrate emboli in the right (A) and left (B) pulmonary arteries. Catheters were placed in the right (C) and left (D) pulmonary arteries. Initial DSA pulmonary angiograms demonstrate filling defects corresponding to the emboli noted on CT. Following Ekos infusion thrombolysis, right (E) and left (F) angiograms demonstrate clearance of the filling defects and improved blood flow, although perfusion defects remain.
Figure 1A-1B. Chest CT images pre and post Ekos therapy. (A) Substantial dilatation of the right ventricle (RV) at pre-treatment; (B) 48-hours post treatment, showing resolution of the RV dilatation.
5 cm infusion length
McNamara lysis catheter

10 mg tPA given across each main PA

Still no improvement
6F Angiojet activated across clot

Hypotension and oxygenation improved
Treatment of High Risk patients

THE ULTIMA TRIAL

A PROSPECTIVE, RANDOMIZED, CONTROLLED STUDY OF ULTRASOUND ACCELERATED THROMBOLYSIS FOR THE TREATMENT OF ACUTE PULMONARY EMBOLISM

ULTrasound Accelerated Thrombolysis of PulMonAry Embolism

Annual Meeting of the American College of Cardiology, March 9, 2013
Treatment of High Risk patients

The ULTIMA Trial

Enrollment Criteria

- Symptoms < 14 days
- No hemodynamic collapse at presentation
- No active bleeding
- 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
Treatment of High Risk patients

The ULTIMA Trial

**RV/LV RATIO (ECHOCARDIOGRAPHY)**

- **EKOS + Heparin**
  - Baseline: 1.28
  - 24 hrs: 0.99
  - 90 days: 0.95
  - P < 0.0001

- **Heparin Alone**
  - Baseline: 1.20
  - 24 hrs: 1.17
  - 90 days: 0.98
  - P < 0.0001
  - P = 0.31
Right Ventricular Dysfunction

The ULTIMA Trial

Treatment of High Risk patients

Nils Kutcher, ACC.13
## Treatment of High Risk patients

The ULTIMA Trial

<table>
<thead>
<tr>
<th>Clinical outcomes at 90 days</th>
<th>EKOS + Heparin N = 30</th>
<th>Heparin N = 29</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0 0%</td>
<td>1* 3%</td>
<td>0.49</td>
</tr>
<tr>
<td>Recurrent venous thromboembolism</td>
<td>0 0%</td>
<td>0 0%</td>
<td>1.00</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>0 0%</td>
<td>0 0%</td>
<td>1.00</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>3** 10%</td>
<td>1§ 3%</td>
<td>0.61</td>
</tr>
</tbody>
</table>

- rehospitalization and death from advanced pancreatic cancer
- **two patients with transient mild hemoptysis without medical intervention, one patient with groin hematoma requiring manual compression**
- § one patient with transient anal bleeding following endoscopic removal of colon polyp
# Systemic Lytics vs EKOS

<table>
<thead>
<tr>
<th></th>
<th>Systemic Lytics vs Heparin</th>
<th>EKOS vs Heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Lytics Dose</td>
<td>100mg</td>
<td>20.7mg (12.2mg)</td>
</tr>
<tr>
<td>Mortality</td>
<td>5.9% -&gt; 4.3%</td>
<td>1/29 -&gt; 0/30</td>
</tr>
<tr>
<td>RV Size</td>
<td>Improved</td>
<td>Improved</td>
</tr>
<tr>
<td>RV Function</td>
<td>Improved</td>
<td>Improved</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>20%</td>
<td>0/30</td>
</tr>
<tr>
<td>ICH</td>
<td>3%</td>
<td>0/30</td>
</tr>
</tbody>
</table>
The SEATTLE II Trial

A PROSPECTIVE, SINGLE-ARM, MULTICENTER TRIAL OF ULTRASOUND-FACILITATED, LOW-DOSE FIBRINOLYSIS FOR ACUTE MASSIVE AND SUBMASSIVE PULMONARY EMBOLISM (SEATTLE II)
A prospective, single-arm, multicenter trial to:
Evaluate the efficacy of ultrasound-facilitated, catheter-directed low-dose fibrinolysis to reverse RV dysfunction as measured by CT-determined RV/LV diameter ratio in patients with acute massive and submassive PE.

Assess the safety of ultrasound-facilitated, catheter-directed low-dose fibrinolysis in patients with acute massive and submassive PE.
Main Inclusion Criteria:

- Proximal PE on CT (filling defect in ≥ 1 main, lobar, or segmental pulmonary artery) **AND**
- Age ≥ 18 years **AND**
- PE symptom duration ≤ 14 days **AND**
- Massive PE (syncope, systemic arterial hypotension, cardiogenic shock, or resuscitated cardiac arrest) **OR**
- Submassive PE (RV/LV diameter ≥ 0.9 on contrast-enhanced chest CT)

Main Exclusion Criteria:

- Stroke/TIA, head trauma, or intracranial or intraspinal disease within 1 year
- Active or recent (within 1 month) bleeding from a major organ
- Major surgery within 7 days
- Hematocrit < 30%, platelets < 100k/μL, INR > 3, aPTT > 50 seconds on no anticoagulation
- Serum creatinine > 2 mg/dL
- Clinician-determined high-risk for catastrophic bleeding
- Hemodynamic instability despite medical therapy
- Pregnancy
Treatment of High Risk patients

The SEATTLE II Trial

- **Standard Anticoagulation for PE**
  - UFH goal PTT 40-60 sec during procedure

- **Catheter Placement and Treatment Based on Extent of Disease**
  - Unilateral: 1 catheter infusing t-PA 1 mg/hour for 24 hours
  - Bilateral: 2 catheters infusing t-PA 1 mg/hour/catheter for 12 hours

- **Baseline Right Heart Catheter Measurements**
  - Including pulmonary artery systolic pressure

- **Ultrasound-Facilitated, Low-Dose, Catheter-Directed Fibrinolysis**
  - t-PA Infusion
  - Activation of high frequency, low power ultrasound

- **Procedure Completion**
  - Post-Procedure Right Heart Catheter Measurements
  - Catheter Removal
## Treatment of High Risk patients

### The SEATTLE II Trial

<table>
<thead>
<tr>
<th>Procedural Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean dose of t-PA ± SD*, mg</td>
<td>23.7 ± 2.9</td>
</tr>
<tr>
<td>Successful device placement**, n (%)</td>
<td>278 (97.5)</td>
</tr>
<tr>
<td>Access sites***, n (%)</td>
<td></td>
</tr>
<tr>
<td>Right femoral vein</td>
<td>177 (63.7)</td>
</tr>
<tr>
<td>Left femoral vein</td>
<td>61 (21.9)</td>
</tr>
<tr>
<td>Right internal jugular vein</td>
<td>31 (11.2)</td>
</tr>
<tr>
<td>Other</td>
<td>9 (3.2)</td>
</tr>
<tr>
<td>Number of devices per patient*, n (%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>1</td>
<td>20 (13.3)</td>
</tr>
<tr>
<td>2</td>
<td>129 (86)</td>
</tr>
<tr>
<td>Completed infusion of t-PA***, n (%)</td>
<td>272 (97.8)</td>
</tr>
</tbody>
</table>

*N = 150 patients (1 patient died before devices could be placed)  
**N = 285 devices attempted  
***N = 278 devices placed
# Treatment of High Risk patients

## The SEATTLE II Trial

<table>
<thead>
<tr>
<th>Characteristics of PE, n (%)</th>
<th>N = 150</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>≤14 days</td>
<td>149 (99.3)</td>
</tr>
<tr>
<td>&gt;14 days</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td><strong>Any symptoms of PE</strong></td>
<td>150 (100)</td>
</tr>
<tr>
<td><strong>PE subtype</strong></td>
<td></td>
</tr>
<tr>
<td>Submassive</td>
<td>119 (79.3)</td>
</tr>
<tr>
<td>Massive</td>
<td>31 (20.7)</td>
</tr>
<tr>
<td><strong>Pre-procedure anticoagulation</strong>*</td>
<td></td>
</tr>
<tr>
<td>Intravenous unfractionated heparin</td>
<td>76 (50.7)</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>54 (36)</td>
</tr>
<tr>
<td>Warfarin</td>
<td>16 (10.7)</td>
</tr>
<tr>
<td>Other</td>
<td>7 (4.7)</td>
</tr>
<tr>
<td>None</td>
<td>24 (16)</td>
</tr>
</tbody>
</table>

*Patients could have received more than one anticoagulant.*
Treatment of High Risk patients

The SEATTLE II Trial

RV to LV Ratio

Pre-Procedure

48 Hours
The SEATTLE II Trial

Treatment of High Risk patients

- Mean Decrease RV/LV Ratio
  - Submassive PE: 0.43
  - Massive PE: 0.51
  - $p = 0.31$

- Mean Decrease PA Systolic Pressure
  - Submassive PE: 14.3
  - Massive PE: 12.6
  - $p = 0.61$
## Treatment of High Risk patients

### The SEATTLE II Trial

<table>
<thead>
<tr>
<th>Clinical outcomes*</th>
<th>N = 150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean length of stay ± SD, days</td>
<td>8.8 ± 5</td>
</tr>
<tr>
<td>In-hospital death, n (%)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>30-day mortality**, n (%)</td>
<td>4 (2.7)</td>
</tr>
<tr>
<td>Serious adverse events due to device, n (%)</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Serious adverse events due to t-PA, n (%)</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>IVC filter placed, n (%)</td>
<td>24 (16)</td>
</tr>
<tr>
<td>Major bleeding within 30 days**, n (%)</td>
<td>17 (11.4)</td>
</tr>
<tr>
<td>GUSTO moderate**</td>
<td>16 (10.7)</td>
</tr>
<tr>
<td>GUSTO severe**</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Intracranial hemorrhage, n (%)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*All death, serious adverse, and bleeding events were adjudicated by an independent safety monitor.

**N = 149 (1 patient lost to follow-up)
# Treatment of High Risk patients

## The SEATTLE II Trial

<table>
<thead>
<tr>
<th>Study</th>
<th>Intracranial Hemorrhage (Fibrinolysis Group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICOPER</td>
<td>9/304 (3%)</td>
</tr>
<tr>
<td>(Goldhaber SZ, et al. 1999)</td>
<td></td>
</tr>
<tr>
<td>PEITHO</td>
<td>10/506 (2%)</td>
</tr>
<tr>
<td>(Meyer G, et al. 2014)</td>
<td></td>
</tr>
<tr>
<td>SEATTLE II</td>
<td>0/150 (0%)</td>
</tr>
</tbody>
</table>
Usefulness and Safety of Ultrasound-Assisted Catheter-Directed Thrombolysis for Submassive Pulmonary Emboli

James M. McCabe, MD\textsuperscript{a,}*; Pei-Hsiu Huang, MD\textsuperscript{b}; Lauren Riedl, PA\textsuperscript{c}; Andrew C. Eisenhauer, MD\textsuperscript{c}; and Piotr Sobieszczyk, MD\textsuperscript{c}

The optimal treatment for intermediate-risk pulmonary embolism (PE) remains unclear. Our goal was to describe the safety and efficacy of the EkoSonic ultrasound-assisted catheter-directed thrombolysis system (EKOS Corporation, Bothell, Washington) in a real-world registry of patients with intermediate-risk PE. Fifty-three consecutive patients with intermediate-risk PE treated with ultrasound-assisted catheter-directed thrombolysis at Brigham and Women's Hospital from 2010 to 2014 were analyzed. The primary outcome was a change in directly measured pulmonary artery pressures as assessed using logistic regression with generalized estimating equations to account for serial measurements. Patients received an average of 24.6 \pm 9 mg of alteplase using the EKOS catheter with an average treatment time of 15.9 \pm 3 hours. After treatment, there was a 7.2- and a 11.4-mm Hg reduction in mean and systolic pulmonary artery pressure (95\% confidence interval 4.7 to 9.7 mm Hg, p < 0.001, and 95\% confidence interval 7.8 to 15.0 mm Hg, p < 0.001), respectively. In this cohort, 9.4\% had any bleeding complication noted during their hospital stay. One patient's alteplase was prematurely discontinued for access site bleeding although no other interventions were required related to bleeding complications. \copyright 2015 Elsevier Inc. All rights reserved. (Am J Cardiol 2015;115:821–824)
THANK YOU