DVT and PE
Interventional Pharmacomechanical Therapy

Indications, Drugs and Devices

Thrombosis and Thromboembolism
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No Disclosures

Objectives

- Understanding the rationale for catheter directed thrombolysis of iliofemoral deep vein thrombosis.
- Understanding the indications for endovascular treatment of pulmonary embolism.
Goals of DVT Therapy

- Diminish the severity and duration of limb symptoms
- Prevent PE
- Lower the risk of recurrent VTE
- Prevent the Post Thrombotic Syndrome (PTS)

Annual incidence of DVT in US: 250,000
Anticoagulation does not restore vein patency, but it prevents clot progression and embolism.
Not all DVTs are the same...

Iliofemoral DVT
- Present in 25% of LE DVT
- Obstruction at this level prevents drainage of primary anatomical and collateral routes
- Thus, more severe initial symptoms and later clinical sequela.

Proximal DVT

Distal DVT
Etiology of Iliofemoral Vein Obstruction

- Venous thrombosis
- May-Thurner Syndrome
- Uterine compression
- Pelvic mass compression
- IVC filter thrombosis
Sequela of iliofemoral venous obstruction

- **Phlegmasia Cerulea Dolens**
  - Acute limb ischemia due to complete thrombosis of venous outflow
  - Massive translocation of fluid into the interstitial space
  - Impediment to arterial inflow
  - Small artery compression, venous gangrene occurs in 40-60% of cases
  - Risk factors include malignancy, CHF, HIT, APL.
  - Bluish, mottled discoloration on exam
Sequela of iliofemoral venous obstruction

- Post-thrombotic syndrome (PTS)

- Iliofemoral DVT has significantly higher rate of PTS compared to proximal DVT.¹

¹Kahn SR Ann Intern Med 2008;149:698-707
Post-thrombotic syndrome

Affects 20-50% of all DVT patients

- Chronic pain
- Swelling
- Cramps
- Itching
- Heaviness
- Symptoms aggravated by standing/walking, improve with recumbency

- edema,
- hyperpigmentation,
- teleangiectasias,
- eczema,
- varicose collateral veins,
- lipodermatosclerosis,
- ulceration
Post-thrombotic syndrome in iliofemoral DVT

- 95% of patients treated with anticoagulation have evidence of venous hypertension 5 years after iliofemoral DVT
- 90% have signs and symptoms of chronic venous insufficiency
- 15% develop venous ulcers
- 15-40% develop venous claudication
- 81% develop loss of financial productivity

Delis KT. Ann Surg 2004;239:118
The Open Vein Hypothesis

Does immediate thrombus removal accelerate DVT-related symptom relief, protect venous valves and prevent PTS?
Acute thrombus removal strategies

- Systemic thrombolysis
- Endovascular therapies
  - Catheter-directed thrombolysis (CDT)
  - Ultrasound assisted thrombolysis
  - Percutaneous mechanical thrombectomy (PMT)
- Surgical embolectomy
Systemic Thrombolysis

Systemic streptokinase: disappointing results in RCT of proximal DVT

- Complete (50-100%) lysis occurred in 58% of partially obstructed veins compared to 0% with UFH (p=0.002) but only in 10% of fully obstructed veins. ¹
- Non significant improvement in PTS incidence (25% vs. 56% p=0.07). ¹
- Another trial of 35 pts showed reduction in PTS compared with UFH: 24% vs 67% (p=0.01). ²
- Inefficient diffusion under low flow.
- High bleeding risk

Catheter-directed Thrombolysis

- A multi-hole infusion catheter is placed across the thrombus filled segment
- Thrombolytic agent delivered directly to the thrombus
- Gradual infusion of lower dose of thrombolytic
Percutaneous Mechanical Thrombectomy

Angiojet Rheolytic Thrombectomy
Percutaneous Mechanical Thrombectomy

Trellis Catheter
Percutaneous Mechanical Thrombectomy

- Small randomized trials of PMT and CDT vs CDT alone:
  - Comparable rates of thrombus removal
  - 40-50% reduction in hospital resources, infusion times, thrombolytic dose, number of procedures.

Lin PH. Am J Surg 2006;192:782
Kim HS. J Vasc Interv Radiol 2006;17:1099
Ultrasound-assisted thrombolysis

- Shown in vitro to increase thrombus permeability to thrombolytic agents
- Shown clinically to reduce duration of thrombolysis and amount of thrombolytic used
- Approved in Europe and US for PE treatment
- Approved in US for peripheral arterial and venous therapy
- Potential clinical benefits: less bleeding, shorter ICU stay, safety for wider spectrum of patients
Ultrasound–assisted thrombolysis

- EKOS assisted DVT thrombolysis in 47 patients with DVT.
- Complete lysis achieved in 70% of patients, overall lysis (complete or partial) in 91%, median infusion time 22 hrs, no systemic bleeding, hematoma in 3.8% of patients.
- Compared to historical controls duration of tPA infusion reduced by 41% and dose of tPA by 35%.

Venous Thrombolysis: *Where is the Data?*

- Different lytic agents
- Different doses
- Local infusion vs. adjunctive thrombectomy devices
- Different outcome measures
- Different definitions of success
- Short follow up
Catheter Directed Thrombolysis

National Venous Thrombolysis Registry

- 287 pts (71% with iliofemoral DVT) treated with CDT (urokinase) or UFH and followed for 1 yr
- > 50% clot dissolution noted in 83% of patients
- Primary patency at 1 year was 60%, better in iliofemoral DVT than in femoro-popliteal DVT.
- Valvular competence preserved in 72% of patients with complete thrombolysis.
- PTS reduced in CDT arm compared to UFH (p=0.006)
- Quality of life was better in CDT than in AC alone

Mewissen MW, Radiology 1999; 211:39
CDT for iliofemoral DVT

The Egypt Trial

35 patients with iliofemoral DVT randomized to thrombolysis plus AC vs AC alone:

- Thrombolysis was associated with better 6-month patency rates (72% vs 12% \( p<0.001 \))
- Thrombolysis preserved valvular competence (89% vs 59% \( p=0.04 \)) at 6 months
- No major bleeding complications

Elsharawy M, Eur J Vasc Endovasc Surg 2002;24:209
Catheter-directed Thrombolysis vs. Anticoagulation

*Meta-analysis*

**Outcome**

<table>
<thead>
<tr>
<th></th>
<th>RR</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Events / Total</th>
<th>Relative risk and 95% CI</th>
</tr>
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<tbody>
<tr>
<td>Postthrombotic syndrome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AbuRahma, 2001</td>
<td>0.32</td>
<td>0.13</td>
<td>0.78</td>
<td>4 / 18</td>
<td>23 / 33</td>
</tr>
<tr>
<td>Markevicus, 2004</td>
<td>0.10</td>
<td>0.03</td>
<td>0.29</td>
<td>3 / 43</td>
<td>47 / 64</td>
</tr>
<tr>
<td>Pooled RR</td>
<td>0.18</td>
<td>0.05</td>
<td>0.62</td>
<td>7 / 61</td>
<td>70 / 97</td>
</tr>
<tr>
<td>Markevicus, 2004</td>
<td>0.20</td>
<td>0.11</td>
<td>0.34</td>
<td>11 / 60</td>
<td>84 / 90</td>
</tr>
<tr>
<td>Elsharawy, 2002</td>
<td>0.27</td>
<td>0.06</td>
<td>1.12</td>
<td>2 / 18</td>
<td>7 / 17</td>
</tr>
<tr>
<td>Enden, 2009</td>
<td>0.91</td>
<td>0.67</td>
<td>1.22</td>
<td>30 / 50</td>
<td>35 / 53</td>
</tr>
<tr>
<td>Pooled RR</td>
<td>0.39</td>
<td>0.16</td>
<td>1.00</td>
<td>43 / 128</td>
<td>126 / 160</td>
</tr>
<tr>
<td>Venous reflux</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AbuRahma, 2001</td>
<td>0.56</td>
<td>0.33</td>
<td>0.97</td>
<td>8 / 18</td>
<td>26 / 33</td>
</tr>
<tr>
<td>Markevicus, 2004</td>
<td>0.07</td>
<td>0.01</td>
<td>0.52</td>
<td>1 / 60</td>
<td>21 / 90</td>
</tr>
<tr>
<td>Elsharawy, 2002</td>
<td>0.31</td>
<td>0.15</td>
<td>0.68</td>
<td>5 / 18</td>
<td>15 / 17</td>
</tr>
<tr>
<td>Enden, 2009</td>
<td>0.56</td>
<td>0.37</td>
<td>0.85</td>
<td>18 / 50</td>
<td>34 / 53</td>
</tr>
<tr>
<td>Pooled RR</td>
<td>0.38</td>
<td>0.17</td>
<td>0.87</td>
<td>32 / 146</td>
<td>96 / 193</td>
</tr>
<tr>
<td>Venous obstruction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Casey ET, J Vasc Surg 2012
CaVenT Trial

- Randomized, controlled trial of CDT and anticoagulation vs. anticoagulation alone for patients with iliofemoral DVT.
- Primary end-point: post-thrombotic syndrome at 24 months
- Secondary endpoint: patency at 6 months

Enden T. J Thromb Haemost 2009:7;1268
CaVenT Trial

209 pts randomized to AC vs. AC+CDT

- ARR 14.4%, NNT 7
- 15% stent use
- No clinically evident PE in AC+CDT arm
- No death, ICH or life threatening bleeding

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**Table 2: Short-term and long-term outcomes**

<table>
<thead>
<tr>
<th></th>
<th>Additional catheter-directed thrombolysis (n=90)</th>
<th>Standard treatment only (n=99)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>% (95% CI)</td>
<td>n</td>
</tr>
<tr>
<td>Post-thrombotic syndrome at 24 months†</td>
<td>37</td>
<td>41.1% (31.5-51.4)</td>
<td>55</td>
</tr>
<tr>
<td>Iliofemoral patency at 6 months‡‡</td>
<td>58</td>
<td>65.9% (55.5-75.0)</td>
<td>45</td>
</tr>
<tr>
<td>Post-thrombotic syndrome at 6 months§</td>
<td>27</td>
<td>30.3% (21.8-40.5)</td>
<td>32</td>
</tr>
</tbody>
</table>

Post-thrombotic syndrome defined as Villalta score of 5 points or higher. *χ² test. †Co-primary outcomes. ‡Five patients had inconclusive patency assessments and one was lost to follow-up at 6 months. §Secondary outcome.

Enden T, Lancet 2012;379:31
CaVenT Trial
Surprisingly high PTS Rates?
CaVenT Trial: Surprisingly high PTS rates?
Catheter-directed Thrombolysis: 18 hrs. later

- Residual obstruction
- Low rate of stent use
Hypothesis:
Initial use of adjunctive Catheter-Directed Thrombolysis (CDT) in symptomatic, acute proximal DVT patients will result in a lower incidence and severity of Post-Thrombotic Syndrome (PTS).

Design:
• Multicenter, open-label, assessor-blinded, randomized controlled trial
• Adjunctive CDT + standard DVT therapy vs. standard DVT RX
• 550 patients, 4.5 year follow up
ATTRACT TRIAL

Primary Endpoint:
Cumulative incidence/severity of PTS at 12 months (Villalta scale)

Secondary Endpoints:
1. Incidence/severity of PTS at 6 months (Villalta scale)
2. QOL at 6 months and 1 year (VEINES-QOL, SF-36).
3. % patients with early symptom relief (1 week & 1 mo)
4. % patients with death, major bleed, intracranial bleed, transfusion, clinical PE, symptomatic recurrent VTE
5. Venous patency and valve reflux (Duplex US - 12 mo)
Lower Extremity DVT

Infrapopliteal only
- Medical mgt:
  - Anticoagulation
  - Compression stockings

Isolated popliteal
- Young Patient
  - First/recent clot
  - Occupation
  - Symptoms

Isolated femoral
- Anticoagulation Contraindicated?
  - Yes
  - IVC Filter
    - Compression stockings
    - Yes
    - No
  - No
    - Consider Catheter Directed Thrombolysis

Iliofememoral
- Medical Rx
  - Yes
  - Lysis Contraindicated?
    - Yes
    - No
    - No
  - No
    - Yes
    - No
    - No
    - Consider Catheter Directed Thrombolysis
Pulmonary Embolism

Wide spectrum of clinical manifestations and risk

Low Clinical Risk
- Subsegmental, hemodynamically tolerated PE.
- Favorable prognosis with AC alone

Intermediate Clinical Risk
- 30-50% are sub-massive PE
- RV strain w/o hemodynamic compromise.
- Increased mortality,
  - ?10% progress to massive PE

High Clinical Risk
- 4.5% of PE are “massive”:
  - RV failure
  - Hemodynamic instability
  - SBP < 90 mmHg,
  - ↓ BP by 40 mmHg > 15 min
  - Syncope, cardiac arrest.
  - 90-day mortality of 50%.
Massive PE: Therapy

- Reversal of RV failure, restoration of hemodynamic stability
- Despite paucity of data, thrombolysis is the accepted standard of care
- 50% of these patients have contraindication to thrombolysis
- Delayed onset of action, prolonged infusion
# Modern Systemic Thrombolysis for PE

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alteplase</td>
<td>100mg over 2 hrs</td>
</tr>
<tr>
<td>Alteplase¹,²</td>
<td>0.6 mg/kg over 15 min</td>
</tr>
<tr>
<td>Retaplace³</td>
<td>Two bolus injections 10 U 30 min apart</td>
</tr>
<tr>
<td>Tenectaplace⁴</td>
<td>30-50 mg weight-adjusted bolus (5-10 min)</td>
</tr>
</tbody>
</table>

2. Goldhaber SZ. Chest 1994;106:718
3. Tebbe U. Am Heart J 1999;138:39
In vitro model of obstruction in the right main PA.

High-speed photo of systemically injected glass beads demonstrates how a vortex forms proximal to the obstruction and alters systemic drug delivery away from target embolus. This concept emphasizes the importance of intra-thrombus drug delivery

Massive PE
Surgical embolectomy

- Surgical embolectomy proposed by Trandelenburg 1908
- First performed by Kirschner 1924 and soon abandoned
- Revisited in 1960s and associated with 30% mortality
- Technical advances lead to renewed interest, systemic reviews over last 10-20 years still describe 20% mortality
- Limited to centers with expertise and ability to rapidly mobilize the resources
- Complete or near complete thrombus removal and reduction in RV afterload
Endovascular Therapy

- Less invasive, rapidly available
- Lack of devices designed to deal with large volume of organized thrombus
- Adaptation of techniques designed for acute thrombus in small vessels
- Incomplete relief of obstruction – maybe enough to reverse RV failure in massive PE
Catheter-Directed Therapy for Massive PE

Systematic Review

- 594 pts in 35 studies between 1990-2008
- Modern therapy: catheters ≤ 10F, modern devices
- Massive PE defined by source series
- Clinical success: stabilization of hemodynamics, resolution of hypoxia, survival.
- 96% of patients did not receive systemic thrombolysis
- 77% of patients received local lytic delivery
- Fragmentation therapy most common (70%)

Kuo WT, JVIR 2009;20:1431
Pooled clinical success rate: 86.5% (p=0.004)

Clinical success much higher with local lytic delivery during procedure and higher still with extended delivery

Minor complication rate was 8%

Major complication rate was 2.4%

Kuo WT, JVIR 2009;20:1431
Fragmentation Strategies

- First described by Brady in 1991 using standard coronary catheters.
- Schmitz-Rode introduced the rotating pigtail.
- Cumulative experience (<100 pts) suggests improved hemodynamics when technique combined with tPA infusion.
- In some series, ~30% patients developed distal embolisation with elevation of PA pressures.
Fragmentation Strategies

- Fragment large proximal thrombus, redistribute obstruction into multiple smaller branches
- Larger volume of peripheral branches will increase pulmonary flow
- Increased surface area for intrinsic/extrinsic lysis
- Fragmenting a 10mm$^3$ sphere into 1000 1mm$^3$ spheres could increase area of obstruction from 1cm$^2$ to 10 cm$^2$
Aspiration Strategies

- Greenfield embolectomy catheter designed in 1960
- The only FDA approved device
- Initial series of 46 pts with massive PE: 30-day survival 70%, CO ↑ 2.59 to 4.47 l/min, mean PA↓ by 8 mmHg
- Cumbersome to use despite modifications, outcomes difficult to reproduce

Suction cup attached to a syringe
Aspiration Strategies

Aspirex Catheter

Amplatz Thrombectomy Catheter

Hydrolyser Catheter
Rheolytic Thrombectomy

Angiojet Device

- Fragmentation/aspiration via Venturi effect
- Designed for coronary anatomy
- Reversing suction to spraying mode allows lacing thrombus with lytic agents
- High rates of bradycardia, hypotension
<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Clinical characteristics</th>
<th>Adjunctive RX</th>
<th>Definition of success</th>
<th>Outcomes</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Koning 1997</td>
<td>2</td>
<td>SPAP 45 mmHg, SPAP 51 mmHg, Stable BP</td>
<td>none</td>
<td>30-day survival</td>
<td>100%</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Angiographic result</td>
<td>Good</td>
<td></td>
</tr>
<tr>
<td>Voigtlander 1999</td>
<td>5</td>
<td>Massive in 3 pts</td>
<td>none</td>
<td>Modest improvement in Miller Index (MI) and PA pressures</td>
<td>Mortality 20%, surgical thrombectomy in 2 pts</td>
<td></td>
</tr>
<tr>
<td>Zeni 2003</td>
<td>17</td>
<td>Massive</td>
<td>Local tPA in 10 pts</td>
<td>Miller Index (MI) improved in 16/17</td>
<td>Mortality 12%</td>
<td>Bradycardia in 2 pts,</td>
</tr>
<tr>
<td>Chauhan 2007</td>
<td>14</td>
<td>Massive and submassive, 6 with hypotension, mean pre-procedural BP 119 mmHg</td>
<td>Local tPA in 5 pts</td>
<td>Post procedure BP&gt;90 mmHg in 85%, Mean PA from 32 to 28 mmHg</td>
<td>Mortality 22%.</td>
<td>Bradycardia 7 pts, asystole in 2 Hemoptysis 7% Hematuria 36%</td>
</tr>
<tr>
<td>Vecchio 2008</td>
<td>30</td>
<td>Massive and submassive</td>
<td>Local tPA in 11 pts</td>
<td>MI improved in all</td>
<td>Mortality 16.7%</td>
<td>NA</td>
</tr>
<tr>
<td>Margheri 2008</td>
<td>25</td>
<td>Massive 8, submassive 12 well tolerated 5</td>
<td>Local tPA in 8 pts</td>
<td>MI improved in all patients</td>
<td>25% mortality rate (half in massive PE)</td>
<td>Bradycardia 12%</td>
</tr>
<tr>
<td>Chechi 2009</td>
<td>51</td>
<td>Massive and submassive,</td>
<td>Local tPA in 22%</td>
<td>reduction in MI</td>
<td>Mean MI ↓ 51% Mortality 15%</td>
<td>Pacing 8% Major bleed 8%</td>
</tr>
</tbody>
</table>
Aspiration Thrombectomy

**Angiovac Device**

- Large bore “funneled” catheter
- Suction applied via cardiopulmonary bypass pump
- Blood filtered and returned to the venous circulation via a femoral cannula
Submassive PE

More of a dilemma....

- Many of these patients do well with AC and support
- Some do not.....
- Chronic PHT rare, RV remodels.....
- Escalation of therapy may be harmful in many
- Systemic thrombolysis not shown to be effective
- But want is the long-term fate of the RV??
PE-related mortality in submasive PE  
*Retrospective Analysis*

![Bar chart showing PE death percentages](image)

**Figure 1.** In-hospital death from PE in stable patients with PE who had an enlarged right ventricle (RV) and those without an enlarged right ventricle in relation to levels of cTnI.

Stein PD, Am J Cardiol 2010;106:558
IV Thrombolytic Therapy for Submassive PE

Meta-Analysis

Recurrence of PE or death
Lysis 6.7% vs UFH 9.6%
p=NS

TABLE 3. Major and Nonmajor Bleeding and Intracranial Hemorrhage in Patients Randomized to Thrombolysis Compared With Heparin

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Thrombolysis, n/N (%)</th>
<th>Heparin, n/N (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major bleeding</td>
<td>34/374 (9.1)</td>
<td>23/374 (6.1)</td>
<td>1.42 (0.81–2.46)*</td>
</tr>
<tr>
<td>Nonmajor bleeding</td>
<td>53/233 (22.7)</td>
<td>22/221 (10.0)</td>
<td>2.63 (1.53–4.54)†</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>2/374 (0.5)</td>
<td>1/374 (0.3)</td>
<td>1.04 (0.36–3.04)‡</td>
</tr>
</tbody>
</table>

*Heterogeneity: P=0.92.
†Heterogeneity: P=0.53.
‡Heterogeneity: P=1.00.

Increased bleeding risk, p=NS

Wan Circulation 2004
Systemic thrombolysis in submassive PE: ongoing randomized trials

- **PEITHO: Pulmonary Embolism Thrombolysis Study (tenectaplast):**
  - 1000 pts in Europe with RV dysfunction on echo and elevated troponin
  - Primary outcome: development of circulatory shock or respiratory failure
- **TOPCOAT: Tenectaplastase or Placebo: Cardiopulmonary Outcomes at Three Months**
  - 200 patients in US with RV HK on echo, elevated troponin, elevated BNP or RA sat<95%
  - Primary outcome: RV dysfunction and NYHA association worse than II and 6 minute walk <330m
Rapid thrombus removal in sub-massive PE

Long-term clinical benefit or impatient clinician?
Hemodynamic evolution of PE treated with Heparin

- Earliest complete resolution of hemodynamic and angiographic abnormalities occurred at 14 days
- Hemodynamic abnormalities in follow up studies correlate with degree of vascular obstruction
- Hypoxemia persisted in all patient irrespective of angiographic and hemodynamic resolution

Altaplaste vs. Heparin in PE with RV strain

Echocardiographic assessment of RV function

Konstantinides S. Am J Cardiol 1998;82:966
Perfusion scintigraphy showed significant baseline differences between the two groups in total lung score (p<0.05)

Within group analysis showed a significant decrease from baseline values in both groups

There was no difference between the two groups in the two follow up scans

Dalla-Volta S. J Am Coll Cardiol 1992;20:520
Does early reduction of RV afterload and vascular obstruction translate into better functional outcomes?
RV Function and Functional Status 6 Months After Submassive PE

200 pts treated with UFH, 21 with subsequent IV tPA for worsening cardiopulmonary status

Figure 2. Doppler-estimated RVSPs at diagnosis and the 6-month follow-up in (A) patients initially treated with heparin alone and (B) patients receiving heparin and alteplase. B: shows only 16 lines because two patients had an RVSP of 0 at diagnosis and the 6-month follow-up.

Kline JA, Chest 2009;136:1202
Table 3—Patient Outcomes by Treatment Group

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Heparin-Only Group</th>
<th>Heparin-Plus-Alteplase Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive</td>
<td>159 (89)</td>
<td>19 (95)</td>
</tr>
<tr>
<td>Recurrent PE</td>
<td>2 (1)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Returned for follow-up</td>
<td>144 (91*)</td>
<td>18 (95*)</td>
</tr>
<tr>
<td>6MWD, m</td>
<td>334 (120)</td>
<td>364 (116)</td>
</tr>
<tr>
<td>NYHA score†</td>
<td>144</td>
<td>18</td>
</tr>
<tr>
<td>1</td>
<td>64 (44)</td>
<td>11 (61)</td>
</tr>
<tr>
<td>2</td>
<td>55 (38)</td>
<td>4 (22)</td>
</tr>
<tr>
<td>3</td>
<td>14 (10)</td>
<td>2 (11)</td>
</tr>
<tr>
<td>4</td>
<td>8 (6)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>6MWD &lt; 330 m or NYHA score &gt; 2</td>
<td>60 (42)</td>
<td>5 (28)</td>
</tr>
<tr>
<td>6MWD &lt; 330 m and NYHA score &gt; 2</td>
<td>13 (9)</td>
<td>2 (11)</td>
</tr>
</tbody>
</table>

Values are given as No. (%), unless otherwise indicated.
*Value is given as % of survivors.
†Values are given as the mean (SD).
Long-term Effects of PE Thrombolysis
23 Patients Randomized to UFH vs. systemic thrombolysis: 7 year follow up.

Long-term Effects of PE Thrombolysis

23 patients randomized to UFH vs. systemic thrombolysis: 7 year follow up.

Figure 3  Functional class of patients at follow-up.

Sharma GVRK, Vascular Medicine 2000;5:91
New Devices

- EKOS catheter: US accelerated lysis
  - Renders thrombus more susceptible to lysis
  - Shortens duration and amount of lytic Rx.
- Angiovac thrombectomy system
  - Large volume suction thrombectomy
  - 24F+ access
Engelhardt’s retrospective registry of 24 patients: 19 with submassive PE (RV dysfxn, nl BP) and 5 with massive PE (transient or prolonged hypotension)

EKOS catheter placed in each affected lung, bolus of 6-10 mg tPA, infusion of 0.8mg/hr (+/- 0.3 mg). Last 7 pts treated with 12 hr infusion and total 20 mg tPA.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV/LV on CT 38+/−14 hrs after Rx</td>
<td>1.33 +/- 0.24</td>
<td>1.00 +/-0.13 (p&lt;0.001)</td>
</tr>
<tr>
<td>Miller Score</td>
<td>17.8 +/-5.3</td>
<td>8.7 +/- 5.1 (p&gt;0.001)</td>
</tr>
</tbody>
</table>

No in-hospital deaths, no systemic bleeding. Access site hematoma limited to initial higher dose group, none noted once limit of 24 mg tPA established.

Ultrasound-assisted, Catheter-directed Thrombolysis

RV/LV ratio before and after the procedure

Mean RV/LV 1.33±0.24
Mean RV/LV 1.00±0.13
P<0.001

CTA 38±14 hrs after intervention

Comparison of US-assisted thrombolysis vs. catheter-directed thrombolysis in patients with massive PE

- Fifteen patients treated with EKOS catheter retrospectively compared to 18 patients treated with CDT over a 10-year period.

<table>
<thead>
<tr>
<th>Variable</th>
<th>EKOS</th>
<th>CDT</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete thrombus removal</td>
<td>100% cases</td>
<td>50% cases</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>Mean infusion time</td>
<td>17.4 hrs</td>
<td>25.5 hrs</td>
<td>0.3</td>
</tr>
<tr>
<td>Mortality rate</td>
<td>9.1%</td>
<td>14.2%</td>
<td>NS</td>
</tr>
<tr>
<td>Bleeding complications</td>
<td>0%</td>
<td>21.4%</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Lin PH et al. Vascular 2009, 17:S137-47
**Hypothesis:** Treatment of selected pulmonary embolism (PE) patients with intra-clot delivery of ultrasound-accelerated, low-dose thrombolysis will significantly improve their right heart function at 48 hours compared to anticoagulan-treated historical controls.

**Safety objectives:** Major bleeding within 72 hours, periprocedural complications, death and recurrent PE at 30 d

**Study population:** 100 pts with acute, symptomatic PE and RV/LV end-diastolic ratio >0.9 on CT

**Treatment:** EKOS catheter delivered tPA 1mg/hr per lung for 12 hrs. if bilateral PE or 1mg/hr for 24 hrs if unilateral PE

**Primary Efficacy Outcome:** Change in RV/LV ratio from baseline to 48hrs.

**Secondary Efficacy Outcome:** Change in PA pressure from baseline to end of tPA infusion. PA pressure on echo 48 hrs. after start of procedure.
Right PA Angiogram

RA 12 mmHg
RV 64/11 mmHg
PA 60/26/40 mmHg
Ultrasound-assisted CDT

PA 40/17 mmHg
48 hrs after intervention....

RV:LV Pre CDT

RV:LV Post CDT

HR 121 bpm

HR 80 bpm
4 weeks later....

**Cardiopulmonary Exercise Testing**

- **Resting**
  - HR 57 bpm
  - Blood pressure 112/62 mmHg
  - Oxygen saturation 98%

- **Peak exercise**
  - HR 155 bpm
  - Blood pressure 190/70 mmHg
  - Oxygen Saturation 93%

- **Echocardiogram**
  - Normal RV size
  - Normal RV function
US-assisted CDT for submassive PE

• BWH Experience
  • Safe
  • Convincing and rapid reduction in PA pressures, improved RV function and symptom relief
  • Increased resource utilization

▪ Need for a RCT to define functional outcomes
  • Passive CDT vs. US-assisted CDT vs. Anticoagulation

▪ Rapid triage system similar to ACS care:
  ▪ Clinical evaluation, RV size and function assessment
  ▪ Anticoagulation, Endovascular Rx or Surgical embolectomy
Pulmonary Embolism
Suggested Indications for Endovascular Therapy

Massive PE

Lowering mortality
- Contraindication to systemic lysis
  - Bleeding risk
  - Failure of systemic lysis
- Contraindication to surgical embolectomy
  - Patient comorbidities
  - Local expertise
- Increasingly an alternative therapy

Submassive PE

Improving functional capacity
- RV strain
- Reasonable baseline functional status
- Favorable long-term prognosis