Endovascular Therapy for Acute Deep Vein Thrombosis and Pulmonary Embolism
Disclosures

• Consultant: Medtronic, Boston Scientific
• Research Support: Medtronic, Boston Scientific, Venite, Bard, BTG
• Clinical Events Committee: Disrupt PAD (Shockwave), TOBA and TOBA 2 (Intact Vascular)
“I’m telling you…….we should really start thinking about how to get rid of blood clots…………”
Deep Vein Thrombosis
Why do we treat?

• Obvious: To prevent P.E.
• Less obvious: To prevent late and devastating consequences of lower extremity venous HTN
• Prolonged swelling, debilitation, pain, leg ulcers
• Loss of work of a healthy individual
Post Thrombotic Syndrome (PTS)

- Chronic leg heaviness
- Leg aching
- Venous claudication
- Edema
- Venous varicosities
- Chronic skin changes
Catheter Directed Lysis

• Why did the CDT studies not change the treatment paradigm?
• Need for randomized trials?
• Concern for Morbidity? Bleeding?
• Concern for:
  • Cost?
  • ICU stays?
  • Large doses of Lytics?
Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis (the CaVenT study): a randomised controlled trial

Tone Ender, Ylva Haig, Nils-Einar Kløw, Carl-Erik Slagsvold, Leiv Sandvik, Waleed Ghanima, Geir Hafsaahl, Pål Andre Holme, Lars Olaf Holmen, Anne Mette Njaastad, Gunnar Sandbæk, Per Morten Sandset, on behalf of the CaVenT Study Group

<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.

Table 2: Short-term and long-term outcomes
Post-thrombotic syndrome after catheter-directed thrombolysis for deep vein thrombosis (CaVenT): 5-year follow-up results of an open-label, randomised controlled trial

Ylva Haig, Tone Enden, Ole Grøtta, Nils-Einar Kløw, Carl-Erik Slagsvold, Waleed Ghanima, Leiv Sandvik, Geir Hafsaht, Pål Andre Holme, Lars Olaf Holmen, Anne Mette Njaaastad, Gunnar Sandbæk, Per Morten Sandset, on behalf of the CaVenT Study Group*

<table>
<thead>
<tr>
<th>Adjunctive catheter-directed thrombolysis (n=87)</th>
<th>Standard treatment (n=89)</th>
<th>p value*</th>
<th>Risk difference (absolute risk reduction)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-thrombotic syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>63</td>
<td>&lt;0.0001</td>
<td>28% (14-42)</td>
</tr>
<tr>
<td>Villalta severity category</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (score 5-9)</td>
<td>31/37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>83.8% (68.5-92.7)</td>
<td>49/63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate (score 10-14)</td>
<td>2/37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.4% (0.57-18.6)</td>
<td>13/63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe (score &gt;14)</td>
<td>4/37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10.8% (3.7-25.3)</td>
<td>1/63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iliofemoral patency†</td>
<td>68/86</td>
<td></td>
<td></td>
</tr>
<tr>
<td>79.1% (69.2-86.4)</td>
<td>61/86</td>
<td>0.218</td>
<td>-8% (-21 to 5)</td>
</tr>
<tr>
<td>Femoropopliteal reflux</td>
<td>54/87</td>
<td></td>
<td></td>
</tr>
<tr>
<td>62.1% (51.6-71.6)</td>
<td>75/89</td>
<td></td>
<td></td>
</tr>
<tr>
<td>84.3% (75.2-90.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are n, n/N, or % (95% CI), unless otherwise stated.*χ² test. †Four patients had inconclusive iliofemoral patency assessments at 5 years.

Table 2: Post-thrombotic syndrome 5 years after acute deep vein thrombosis
### Single Center Trials for CDT for DVT

100% for complete and partial lysis with pharmacomechanical thrombectomy (PMT)

<table>
<thead>
<tr>
<th>Study</th>
<th>Subject(s)</th>
<th>Treatment Groups</th>
<th>Complete Results</th>
<th>Partial Results</th>
<th>Bleeding Numbers</th>
<th>PE/DEATH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laiho 2004</td>
<td>32</td>
<td>CDT 16 Systemic 16</td>
<td>8(50%) 5(31%)</td>
<td>5(31%) 8(50%)</td>
<td>NA NA</td>
<td>4(25%) 6(38%) 2(13%) 5(31%)</td>
</tr>
<tr>
<td>Silleson 2005</td>
<td>45</td>
<td>CDT with PTA/STENT</td>
<td>42(93%) NA</td>
<td>NA</td>
<td>NA</td>
<td>4(8%) 0 1(2%)</td>
</tr>
<tr>
<td>Jackson 2005</td>
<td>28</td>
<td>CDT with PTA/STENT</td>
<td>5(18%) 20(72%)</td>
<td>NA</td>
<td>NA</td>
<td>2(7%) 0 0</td>
</tr>
<tr>
<td>Kim 2006</td>
<td>37</td>
<td>CDT 23 CDT + PMT 14</td>
<td>21(81%) 16(84%)</td>
<td>3(11%) 3(16%)</td>
<td>2(8%) 0</td>
<td>1(4%) 2(7%) 1(5%) 1(4%)</td>
</tr>
<tr>
<td>Lin 2006</td>
<td>98</td>
<td>CDT with Stent PMT with Stent</td>
<td>32(70%) 39(75%)</td>
<td>14(30%) 13(25%)</td>
<td>5(11%) 4(8%)</td>
<td>2(4%) 2(4%) 1(2%) 0</td>
</tr>
</tbody>
</table>
Why Pharmacomechanical Thrombectomy?
Why Single Session?

• Thrombolysis alone has drawbacks
  – Long infusion times (mean infusion time during the Venous Registry was 48 hours (30-80 hours))
  – Bleeding risks
  – ICU costs (> $10,000/day)
Modern Thrombectomy Systems for Pharmacomechanical Thrombectomy

- Angiojet (Boston Scientific)
- Trellis (Covidien; Bacchus Medical)
  - Combined pharmacological thrombolysis & mechanical thrombectomy

**PHARMACOMECHANICAL THROMBECTOMY**

- Advantages
  - Enhance the delivery of thrombolytic agent
  - Reduce duration of thrombolytic agent
  - Enhance efficacy of thrombus removal with mechanical thrombectomy
  - Reduce/ Eliminate ICU stay
Benefits and Risks

• Advantages
  • No ICU stay
  • Lower cost to health system
  • Less dose of thrombolytic
  • Greater patient satisfaction

• Disadvantages
  • Need for thrombectomy device
  • Need for balloons and stents
  • Larger sheath
  • Rapid protocol may leave clot behind
  • Poor outcomes
  • More trauma to valvular system
Catheter-Directed Thrombolysis with Percutaneous Rheolytic Thrombectomy Versus Thrombolysis Alone in Upper and Lower Extremity Deep Vein Thrombosis

Hyun S. Kim,¹ Ajanta Patra,¹ Ben E. Paxton,¹ Jawad Khan,¹ Michael B. Streiff²

<table>
<thead>
<tr>
<th>Table 2. Clinical efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>(n = 40)</td>
</tr>
<tr>
<td>Treatment duration (hr)</td>
</tr>
<tr>
<td>Urokinase doses (million units)</td>
</tr>
<tr>
<td>Clot reduction</td>
</tr>
<tr>
<td>Grade III</td>
</tr>
<tr>
<td>Grade II</td>
</tr>
<tr>
<td>Grade I</td>
</tr>
<tr>
<td>Stent placements</td>
</tr>
<tr>
<td>Major bleeding</td>
</tr>
<tr>
<td>Minor bleeding</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
</tr>
</tbody>
</table>
CDT vs Pharmacomechanical Thrombectomy

- **Results:**
  - Duration mean 48 hours vs. 26.3 hours
  - Mean dose 5.6 mill U vs. 2.7 mill U
  - Success 73% had >90% lysis vs. 82%
  - Cost was $10,127 vs $5,128
  - No difference in bleeding rates

Catheter-direct thrombolysis versus pharmacomechanical thrombectomy for treatment of symptomatic lower extremity deep venous thrombosis

Peter H. Lin, M.D.\textsuperscript{a,*}, Wei Zhou, M.D.\textsuperscript{a}, Alan Dardik, M.D.\textsuperscript{b}, Firas Mussa, M.D.\textsuperscript{a}, Panos Kougias, M.D.\textsuperscript{a}, Nasim Hedayati, M.D.\textsuperscript{a}, Joseph J. Naoum, M.D.\textsuperscript{a}, Hosam El Sayed, M.D.\textsuperscript{a}, Eric K. Peden, M.D.\textsuperscript{a}, Tam T. Huynh, M.D.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Variable</th>
<th>PMT therapy</th>
<th>CDT therapy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>49</td>
<td>44</td>
<td>n/a</td>
</tr>
<tr>
<td>No. of treated limbs</td>
<td>52</td>
<td>46</td>
<td>n/a</td>
</tr>
<tr>
<td>Mean age (y)</td>
<td>45 ± 12</td>
<td>49 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>Male (%)</td>
<td>22 (45%)</td>
<td>19 (43%)</td>
<td>NS</td>
</tr>
<tr>
<td>Complete treatment success</td>
<td>39 (75%)</td>
<td>32 (70%)</td>
<td>NS</td>
</tr>
<tr>
<td>Partial treatment success</td>
<td>13 (25%)</td>
<td>14 (30%)</td>
<td>NS</td>
</tr>
<tr>
<td>Immediate clinical improvement</td>
<td>42 (81%)</td>
<td>33 (72%)</td>
<td>NS</td>
</tr>
<tr>
<td>No clinical improvement</td>
<td>4 (8%)</td>
<td>5 (11%)</td>
<td>NS</td>
</tr>
<tr>
<td>Adjuvant balloon angioplasty/iliac venous stenting</td>
<td>43 (82%)</td>
<td>36 (78%)</td>
<td>NS</td>
</tr>
<tr>
<td>No of venograms (mean)</td>
<td>.4 ± .2</td>
<td>2.5 ± .7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mean ICU stay (d)</td>
<td>.6 ± .3</td>
<td>2.4 ± 1.2</td>
<td>&lt;.04</td>
</tr>
<tr>
<td>Overall hospital length of stay (d)</td>
<td>4.6 ± 1.3</td>
<td>8.4 ± 2.3</td>
<td>&lt;.02</td>
</tr>
<tr>
<td>Hemorrhagic complication</td>
<td>2 (4%)</td>
<td>3 (6%)</td>
<td>NS</td>
</tr>
<tr>
<td>PRBC transfusion (U)</td>
<td>.2 ± .3</td>
<td>1.2 ± .7</td>
<td>&lt;.05</td>
</tr>
</tbody>
</table>
Comparison of the hospital cost between the PMT and CDT treatment groups

<table>
<thead>
<tr>
<th></th>
<th>Mean hospital cost per patient</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PMT group</td>
<td>CDT group</td>
</tr>
<tr>
<td>Operating room cost</td>
<td>$16,252 ± $4,621</td>
<td>None</td>
</tr>
<tr>
<td>Radiology cost</td>
<td>None</td>
<td>$8,972 ± $1,952</td>
</tr>
<tr>
<td>Hospital room cost</td>
<td>$18,392 ± $8,321</td>
<td>$53,632 ± $1,743</td>
</tr>
<tr>
<td>Other costs</td>
<td>$13,865 ± $7,336</td>
<td>$17,197 ± $9,133</td>
</tr>
<tr>
<td>Total hospital cost</td>
<td>$47,742 ± $19,247</td>
<td>$85,301 ± $24,832</td>
</tr>
</tbody>
</table>

Mark J. Garcia, MD, MS, Robert Lookstein, MD, Rahul Malhotra, MD, Ali Amin, MD, RVT, Lawrence R. Blitz, MD, Daniel A. Leung, MD, Eugene J. Simoni, MD, and Peter A. Soukas, MD
# PEARL Comparison

## Treatment of LE DVT

<table>
<thead>
<tr>
<th>Onset of DVT Symptoms</th>
<th>PEARL</th>
<th>Venous Registry*</th>
<th>CaVenT**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>CDT</td>
</tr>
<tr>
<td>Acute</td>
<td>67% (≤14 days)</td>
<td>66% (≤10 Days)</td>
<td>100% ≤21 days</td>
</tr>
<tr>
<td>Chronic</td>
<td>33% (&gt;14 days)</td>
<td>16% (&gt;10 Days)</td>
<td>NA</td>
</tr>
<tr>
<td>Acute &amp; Chronic</td>
<td>NA</td>
<td>19%</td>
<td>NA</td>
</tr>
<tr>
<td>Primary Lytic</td>
<td>TPA</td>
<td>Urokinase</td>
<td>TPA</td>
</tr>
<tr>
<td><strong>CDT Drip Times (mean)</strong></td>
<td>17 hrs</td>
<td>48 hrs</td>
<td>57.6 hrs (2.4 days)</td>
</tr>
<tr>
<td>Procedure Times</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDT (N=29)</td>
<td>40.9 hrs</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>CDT+PPS/RL (N=172)</td>
<td>22.0 hrs</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>PPS/RL (N=115)</td>
<td>2.0 hrs</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Bleeding Complications</td>
<td>5% (major &amp; minor combined)</td>
<td>11% (major); 16% (minor)</td>
<td>22% (major &amp; minor combined)</td>
</tr>
</tbody>
</table>


Initial Venogram
Completion Venogram at 8 hours
Conclusions

• Single day PCDT is a technically feasible and reasonably safe method of endovascular treatment of DVT.

• Results in shorter thrombolytic infusion times compared to standard CDT
  – Decreased bleeding risks due to lower duration of thrombolysis
  – Decreased costs due to reduction/elimination of monitoring in an intensive care setting

• CDT performed in recovery room at Mount Sinai.
Rationale and design of the ATTRACT Study: A multicenter randomized trial to evaluate pharmacomechanical catheter-directed thrombolysis for the prevention of postthrombotic syndrome in patients with proximal deep vein thrombosis

Suresh Vedantham, MD, a Samuel Z. Goldhaber, MD, b Susan R. Kahn, MD, MSc, c Jim Julian, MMath, d Elizabeth Magnuson, ScD, e Michael R. Jaff, DO, f Timothy P. Murphy, MD, g David J. Cohen, MD, MSc, e Anthony J. Comerota, MD, h Heather L. Gornik, MD, i Mahmood K. Razavi, MD, j Lawrence Lewis, MD, k and Clive Kearon, MB, PhD d St Louis, and Kansas City, MO; Boston, MA; Quebec, and Ontario, Canada; Providence, RI; Toledo, and Cleveland, OH; and Orange, CA
STUDY ENROLLMENT
Patient with proximal DVT meets eligibility criteria and provides informed consent

PRE-RANDOMIZATION PROCEDURES
Initiation of AC (LMWH or UFH) and completion of baseline assessments

RANDOMIZATION (1:1)

CONTROL ARM SUBJECTS
Complete 5 days heparin therapy (LMWH or UFH) and immediately bridge to warfarin (INR 2.0 – 3.0)

QUAD ARM SUBJECTS
Complete 5 days heparin therapy (LMWH or UFH) concurrent with performance of PCDT procedure (within 3 days post-randomization), then bridge to warfarin (INR 2.0 – 3.0)

LONG-TERM TREATMENT - ALL SUBJECTS
Long-term (≥3 months) warfarin therapy and daily use of graduated elastic compression stockings (initiated 10 days post-randomization)

FOLLOW-UP VISITS – ALL SUBJECTS
Early (10 days & 30 days post-randomization)
Late (6, 12, 18, & 24 months post-randomization)
## Study Outcomes
### Long-Term Effects of PCDT

<table>
<thead>
<tr>
<th>Outcome (24 months)</th>
<th>PCDT n=336</th>
<th>No-PCDT n=355</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any PTS</td>
<td>46.7%</td>
<td>48.2%</td>
<td>0.56</td>
</tr>
<tr>
<td>Recurrent VTE</td>
<td>12.5%</td>
<td>8.5%</td>
<td>0.09</td>
</tr>
<tr>
<td>Generic QOL (SF-36 PCS)</td>
<td>11.8%</td>
<td>10.1%</td>
<td>0.37</td>
</tr>
<tr>
<td>Venous QOL (VEINES)</td>
<td>27.7%</td>
<td>23.5%</td>
<td>0.08</td>
</tr>
<tr>
<td>Moderate or Severe PTS</td>
<td>17.9%</td>
<td>23.7%</td>
<td>0.035</td>
</tr>
<tr>
<td>MS-PTS: IFDVT</td>
<td>18.4%</td>
<td>28.2%</td>
<td></td>
</tr>
<tr>
<td>MS-PTS: FPDVT</td>
<td>17.1%</td>
<td>18.1%</td>
<td></td>
</tr>
</tbody>
</table>

PCDT less effective in patients ≥ 65 years old (p = 0.038)
My own practice....

- I see a variety of patients with both symptomatic upper and lower extremity Deep Vein Thrombosis
  - the risks and benefits of PMT as I just presented the evidence
  - Different office visit for young, active vs elderly patients

Patients can choose to undergo treatment because we do not have conclusive level one evidence at present
Pulmonary Embolism: Epidemiology and Background
Treatment Options and Pulmonary Embolism Response Teams
Spectrum of Disease

**Massive PE (~5%)**
- High Risk
- Hypotension, syncope, cardiogenic shock, cardiac arrest
- Respiratory failure
- Often fatal if aggressive care not instituted

**Submassive PE (~40%)**
- Moderate Risk
- Normotensive
- Right ventricular (RV) dysfunction is present
- Increased risk of adverse outcomes

**PE with normal BP and RV function (~55%)**
- Low Risk
- Normotensive
- Normal RV function
- Excellent prognosis with anticoagulation alone

# Thrombolysis, a Meta-analysis

*JAMA 2014;311(23):2414-2421*

## Odds of Mortality in Patients with Intermediate-Risk PE

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of Events</th>
<th>No. of Patients</th>
<th>OR (95% CI)</th>
<th>Favors Thrombolitics</th>
<th>Favors Anticoagulants</th>
<th>Weight, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldhaber et al,² 1993</td>
<td>0</td>
<td>46</td>
<td>0.16 (0.01-2.57)</td>
<td></td>
<td></td>
<td>5.3</td>
</tr>
<tr>
<td>Konstantinides et al,³ 2002</td>
<td>4</td>
<td>118</td>
<td>1.58 (0.35-7.09)</td>
<td></td>
<td></td>
<td>18.4</td>
</tr>
<tr>
<td>TIPES,²⁹ 2010</td>
<td>0</td>
<td>28</td>
<td>0.14 (0.00-7.31)</td>
<td></td>
<td></td>
<td>2.7</td>
</tr>
<tr>
<td>Fasullo et al,¹¹ 2011</td>
<td>0</td>
<td>37</td>
<td>0.11 (0.02-0.58)</td>
<td></td>
<td></td>
<td>15.1</td>
</tr>
<tr>
<td>MOPETT,¹⁰ 2012</td>
<td>1</td>
<td>61</td>
<td>0.35 (0.05-2.57)</td>
<td></td>
<td></td>
<td>10.5</td>
</tr>
<tr>
<td>ULTIMA,³⁰ 2013</td>
<td>0</td>
<td>30</td>
<td>0.13 (0.00-6.59)</td>
<td></td>
<td></td>
<td>2.7</td>
</tr>
<tr>
<td>TOPCOAT,⁹ 2014</td>
<td>1</td>
<td>40</td>
<td>1.08 (0.07-17.53)</td>
<td></td>
<td></td>
<td>5.3</td>
</tr>
<tr>
<td>PEITHO,⁸ 2014</td>
<td>6</td>
<td>506</td>
<td>0.66 (0.24-1.82)</td>
<td></td>
<td></td>
<td>40.0</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>866</td>
<td>0.48 (0.25-0.92)</td>
<td></td>
<td></td>
<td>100.0</td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 7.63; P = .37; I^2 = 8\%$

Overall effect: $z = 2.22; P = .03$
Table 2. Absolute Risk Metrics of Outcomes of Major Interest

<table>
<thead>
<tr>
<th>Outcome of Interest (No. of Studies Reporting)</th>
<th>No. of Events/No. of Patients, Absolute Event Rate (%)</th>
<th>No. Needed to Treat or Harm</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Thrombolytic Group</td>
<td>Anticoagulant Group</td>
<td></td>
</tr>
<tr>
<td>All-cause mortality (16)</td>
<td>23/1061 (2.17)</td>
<td>41/1054 (3.89)</td>
<td>NNT = 59</td>
</tr>
<tr>
<td>Major bleeding (16)</td>
<td>98/1061 (9.24)</td>
<td>36/1054 (3.42)</td>
<td>NNH = 18</td>
</tr>
<tr>
<td>ICH (15)</td>
<td>15/1024 (1.46)</td>
<td>2/1019 (0.19)</td>
<td>NNH = 78</td>
</tr>
<tr>
<td>Recurrent PE (15)</td>
<td>12/1024 (1.17)</td>
<td>31/1019 (3.04)</td>
<td>NNT = 54</td>
</tr>
<tr>
<td>Age &gt;65 y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality (5)</td>
<td>14/673 (2.08)</td>
<td>24/658 (3.65)</td>
<td>NNT = 64</td>
</tr>
<tr>
<td>Major bleeding (5)</td>
<td>87/673 (12.93)</td>
<td>27/658 (4.10)</td>
<td>NNH = 11</td>
</tr>
<tr>
<td>Age ≤65 y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality (11)</td>
<td>9/388 (2.32)</td>
<td>17/396 (4.29)</td>
<td>NNT = 51</td>
</tr>
<tr>
<td>Major bleeding (11)</td>
<td>11/388 (2.84)</td>
<td>9/396 (2.27)</td>
<td>NNH = 176</td>
</tr>
<tr>
<td>Intermediate-risk PE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality (8)</td>
<td>12/866 (1.39)</td>
<td>26/889 (2.92)</td>
<td>NNT = 65</td>
</tr>
<tr>
<td>Major bleeding (8)</td>
<td>67/866 (7.74)</td>
<td>20/889 (2.25)</td>
<td>NNH = 18</td>
</tr>
</tbody>
</table>
Thrombolysis, a Meta-analysis

JAMA 2014;311(23):2414-2421

Table 2. Absolute Risk Metrics of Outcomes of Major Interest

<table>
<thead>
<tr>
<th>Outcome of Interest (No. of Studies Reporting)</th>
<th>No. of Events/No. of Patients, Absolute Event Rate (%)</th>
<th>No. Needed to Treat or Harm</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality (16)</td>
<td>23/1061 (2.17)</td>
<td>NNT = 59</td>
<td>.01</td>
</tr>
<tr>
<td>Major bleeding (16)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>98/1061 (9.24)</td>
<td>NNH = 18</td>
<td>&lt;.001</td>
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<tr>
<td>ICH (15)</td>
<td>15/1024 (1.46)</td>
<td>NNH = 78</td>
<td>.002</td>
</tr>
<tr>
<td>Recurrent PE (15)</td>
<td>12/1024 (1.17)</td>
<td>NNT = 54</td>
<td>.003</td>
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<tr>
<td>Age &gt;65 y</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality (5)</td>
<td>14/673 (2.08)</td>
<td>NNT = 64</td>
<td>.07</td>
</tr>
<tr>
<td>Major bleeding (5)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>87/673 (12.93)</td>
<td>NNH = 11</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age ≤65 y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality (11)</td>
<td>9/388 (2.32)</td>
<td>NNT = 51</td>
<td>.09</td>
</tr>
<tr>
<td>Major bleeding (11)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11/388 (2.84)</td>
<td>NNH = 176</td>
<td>.89</td>
</tr>
<tr>
<td>Intermediate-risk PE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality (8)</td>
<td>12/866 (1.39)</td>
<td>NNT = 65</td>
<td>.03</td>
</tr>
<tr>
<td>Major bleeding (8)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>67/866 (7.74)</td>
<td>NNH = 18</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
Acute Pulmonary Embolism: Before and After
Therapeutic Alternatives in Acute PE

• **Anticoagulation**
  – Unfractionated Heparin
    • Continuous Intravenous
    • Full-Dose Subcutaneous
  – Low-Molecular-Weight Heparin
  – Synthetic Pentasaccharide
  – Direct Thrombin Inhibitors
  – Xa Antagonist
  – Warfarin

• **Thrombolytic Therapy**
  – Systemic (full or half-dose)
  – Catheter Directed (CDT)
  – Pharmacomechanical Catheter-Directed Thrombolysis (P-CDT)

• **Mechanical**
  – Surgical Thrombectomy
  – Thrombo-aspiration
  – Clot maceration

• **Adjunct Rx**
  – Extracorporeal support (ECMO)
  – RVAD
  – IVC Filter
Pulmonary Embolectomy
Embolic Material

Right atrium

Left PA

Right PA
AngioVac “VORTEX” 22F

- 22F Suction Catheter
- 17 F Return
- Pump/Filter
AngioVac® Fundamentals

- Large bore cannula
- Circuit enabling visualization of removed material
- Cannula & Circuit to facilitate suction and simultaneous reinfusion of blood while maintaining hemodynamic stability
- Working superhighway enabling other devices to aid in debris removal
AngioVac® Basics
PERIPHERAL VASCULAR DISEASE

Original Studies

Thrombectomy Using Suction Filtration and Veno-venous Bypass: Single Center Experience with a Novel Device


<table>
<thead>
<tr>
<th>Indication</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep venous thrombosis involving vena cava</td>
<td>11 (73%)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>5 (33%)</td>
</tr>
<tr>
<td>Involving pulmonary trunk or main pulmonary artery</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>Right atrial mass</td>
<td>11 (73%)</td>
</tr>
<tr>
<td>Right ventricular mass</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>Catheter-associated thrombus</td>
<td>2 (13%)</td>
</tr>
</tbody>
</table>
Early Experience with AngioVac Aspiration in the Pulmonary Arteries

Ramsey Al-Hakim, MD, Jonathan Park, MD, Anshuman Bansal, MD, Scott Genshaft, MD, and John M. Moriarty, MD

ABSTRACT

Five consecutive cases in which the AngioVac aspiration cannula was used for the management of pulmonary embolism (PE) were retrospectively reviewed. Four cases (80%) presented with massive PE, and two (40%) were technically successful (reduction in Miller index ≥ 5). Four patients (80%) died at a mean of 7.3 days after the procedure, including one death related to right ventricular free wall perforation. Although the AngioVac aspiration cannula has shown clinical promise in a variety of clinical applications, early experience in the pulmonary arteries has shown limited success, and further study and careful patient selection are required.

“...early experience in the pulmonary arteries has shown limited success, and further study and careful patient selection are required.”
AngioDynamics Announces First Patient Enrollment in RAPID Outcomes Database

ALBANY, N.Y., Aug. 6, 2015 (GLOBE NEWSWIRE) -- AngioDynamics (Nasdaq:ANGO), a leading provider of innovative, minimally invasive medical devices for vascular access, surgery, peripheral vascular disease and oncology, today announce the enrollment of the first patient into the Registry of AngioVac Procedures In Details (RAPID) Database at University of California-Los Angeles (UCLA) Health in Los Angeles, California.

The RAPID Database is designed to evaluate the patterns of use as well as safety and effectiveness data of the AngioVac® system in the en bloc removal of fresh, soft thrombi or emboli.

According to national principal investigator, Dr. John M. Moriarty, Assistant Professor of Radiology, Director of Cardiology-Interventional Radiology Innovation at UCLA, there has been significant interest in centers wanting to participate in the Registry.

"So far, we have centers in 31 states that want to take part in the Registry," said Dr. Moriarty. "Our goal is to include as many potential collaborators as possible, and start gathering much needed data regarding procedural and patient outcomes."

Dr. Moriarty added that the registry is also a way to become part of the community of physicians, nurses, and technologists who are working in this field, and connecting with researchers who may not be anywhere near you geographically, but by working with RAPID, "you can become part of a wider group of experts."

"AngioVac continues to impress clinically as the second-generation of the device, cleared for use earlier this year by the U.S. Food and Drug Administration (FDA) and released to the market in April, is driving broader interest among clinicians," said Chris Crisman, AngioDynamics’ Senior Vice President, Global Franchise Leader. "AngioDynamics is a pioneer when it comes to the minimally invasive en bloc removal of fresh, soft thrombi or emboli. We feel we have a responsibility to work with our physician partners to gather patient data and continue improving our procedures, products and patient outcomes. We are excited to launch this initiative and look forward to the collaboration which in the end will benefit patients."

The FlowTriever System is indicated for:

• The non-surgical removal of emboli and thrombi from blood vessels.
• Injection, infusion and/or aspiration of contrast media and other fluids into or from a blood vessel.

The FlowTriever System is intended for use in the peripheral vasculature system.
Inari FlowTriever™ Infusion Aspiration System

**Inari FlowTriever Device**
- Immediate flow restoration and relief of backpressure
- Thrombus disruption and retrieval
- Provides for direct infusion of tPA into the thrombus, if desired
- Enhanced thrombolysis by increasing flow and thrombus surface

**Inari Aspiration Guide Catheter**
- Designed to easily navigate through tortuous vascular anatomy
- Delivers FlowTriever system to the thrombus
- Wide bore catheter effective for aspiration of thrombus

**Retraction Aspirator Device**
- Retracts both the FlowTriever and thrombus into the AGC
- Synchronizes aspiration and FlowTriever retraction
- Aspirated thrombus is collected
FlowTriever Versatility and Compliance

Disk nominally compressed when deployed in an “in range” vessel

Disk uncompressed

Disk over-compressed when deployed in an undersized vessel
FlowTriever Early Clinical Experience, Thrombus Retrieval

Each photo taken from a separate case
FlowTriever Pulmonary Embolectomy Clinical Study

FLARE Study (NCT02692586)
Prospective, single-arm, controlled, multicenter study

Study Design
• Up to 168 patients / 20 sites
• Age ≥ 18 and ≤ 75 years
• Acute PE < 14 days
• No lytic therapy 30 days prior to treatment
  - Lytic during procedure not required but allowed
• RV/LV ratio ≥ 0.9
• Systolic blood pressure ≥ 80 mmHg
• Stable heart rate < 130 BPM

Study Endpoints
• Safety: Major Adverse Events
• Effectiveness: Reduction in RV/LV ratio from baseline to 48 hours

Enrollment Status
• Open clinical sites: 3
• Patients enrolled: 4
Clot Extraction With the FlowTriever Device in Acute Massive Pulmonary Embolism

Aaron Samuel Weinberg, MD¹, Suhail Dohad, MD², Danny Ramzy, MD, PhD³, Hooman Madyoon, MD², and Victor F. Tapson, MD⁴

Percutaneous Pulmonary Embolus Mechanical Thrombectomy

Deepali Nivas Tukaye, MBBS, PhD, Michael McDaniel, MD, Henry Liberman, MD, Yelena Burkin, MD, Wissam Jaber, MD
Penumbra CAT8 Thromboaspiration system
Pulmonary Artery Thrombus

Horacio D'Agostino and Chaitanya Ahuja, M.D.
LSU Shreveport, LA
Penumbra

Discussions are underway to develop Registry and possible pivotal trial
En bloc embolectomy

• Difficult to setup
• Requires intensive resources
• Usually reserved for Massive PE

• Can you keep it simple????????
Fixed low-dose ultrasound-assisted catheter-directed thrombolysis for intermediate and high-risk pulmonary embolism

Rolf P. Engelberger\textsuperscript{1,\dagger}, Aris Moschovitis\textsuperscript{\dagger}, Jennifer Fahrni\textsuperscript{1}, Torsten Willenberg\textsuperscript{1}, Frederic Baumann\textsuperscript{1}, Nicolas Diehm\textsuperscript{1}, Do-Dai Do\textsuperscript{1}, Iris Baumgartner\textsuperscript{1}, and Nils Kucher\textsuperscript{1,\dagger,*}

Randomized, Controlled Trial of Ultrasound-Assisted Catheter-Directed Thrombolysis for Acute Intermediate-Risk Pulmonary Embolism

Nils Kucher, MD; Peter Boekstegers, MD; Oliver J. Müller, MD; Christian Kupatt, MD; Jan Beyer-Westendorf, MD; Thomas Heitzer, MD; Ulrich Tebbe, MD; Jan Horstkotte, MD; Ralf Müller, MD; Erwin Blessing, MD; Martin Greif, MD; Philipp Lange, MD; Ralf-Thorsten Hoffmann, MD; Sebastian Werth, MD; Achim Barmeyer, MD; Dirk Härtel, MD; Henriette Grünwald, MD; Klaus Empen, MD; Iris Baumgartner, MD
ULTIMA – Catheter Directed Lysis

59 patients with acute main or lower lobe PE and RV/LV \( \geq 1.0 \) on TTE randomized and followed up at 24h and 90-days:

1. UFH and ultrasound-assisted catheter directed thrombolysis (USAT)
   - Ultrasound (2.2 MHz) increases permeability of the drug
   - Recombinant tPA 10mg per lung, (max dose 20mg/16 hrs)

2. UFH alone

Results:
- USAT+UFH resulted in resolution of PA pressures and improved CI.
- Mortality: 1 death in the UFH group; 3 episodes of major bleeding.
- Caveats: clinical outcomes were not evaluated (ie dyspnea), USAT not compared to other catheter-based therapies, and study NOT powered to draw conclusions regarding safety against anticoagulation alone.
Catheter Directed Thrombolysis

- Results in rapid improvements in main pulmonary artery pressures
Acute PE

Vital Signs
Functional Status
CT Angiogram
BNP, TTE, Troponin

Moderate Risk
(RV strain w/o hypotension)
Evaluate for Intervention

Low Risk
Anticoagulate
Or filter if contraindicated

High Risk
(Hypotension)
Evaluate for Intervention
Algorithm for Submassive PE

Submassive PE
(RV strain w/o hypotension)

- Abnormal Vitals
  - BNP>100
  - Troponin ++
  - Tachycardia/Hypoxia/Tachypnea

- Catheter Directed Therapy
  - Low dose lysis
    - Aspiration
    - Fragmentation
    - IVC filter

- Surgical Embolectomy if contraindication to lysis
  - IVC filter

- Stable Vitals
  - BNP<100
  - Troponin –
  - HD stable

- Anticoagulate or IVC Filter
  - If contraindication
“Treatment gap” in PE

- <5% of patients with PE receive “advanced therapy”, including those with clear indications (hypotension, RV dysfunction, biomarkers, etc.)
- Many more are eligible than receive
- Reasons
  - Failure to recognize potential benefit and integrate data in “real-time”
  - Fear of complications
  - Inability to respond rapidly (“systems” issues)
  - “Paralysis” in decision-making
Question:

- How can we share information in real time with other PERT centers?
- How do we disseminate innovations rapidly and seamlessly?
- How do we define best Practice? Value? Quality?
- How can we research these concepts as efficiently as possible?
Pulmonary Embolism Response Team

- 3rd Annual Scientific Meeting
- June 20-23th, Sonesta Hotel
- Boston, Massachusetts
THANK YOU