Does Ilio-Femoral Venous Lysis and Stenting Prevent Post-Thrombotic Syndrome

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UCSF Vascular Surgery Symposium 2016

Iliofemoral DVT (IFDVT)

- VTE is the 3rd most frequent CV disease
- 1 case per 1000 person-years
- Most powerful predictor of post-thrombotic syndrome is presence of IFDVT (HR: 2.23)
- IFDVT over 5 years treated with anticoagulation:
  - 70% persistent obstruction
  - 90% venous insufficiency
  - 40% venous claudication
  - 15% venous ulceration

Systemic Thrombolitics:
Phlebographic Outcomes (Lysis)
12 Randomized trials

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No lysis (%)</th>
<th>Partial lysis (%)</th>
<th>Significant/complete lysis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin (n=212)</td>
<td>81</td>
<td>14</td>
<td>5</td>
</tr>
<tr>
<td>Lytic (n=253)</td>
<td>40</td>
<td>15</td>
<td>45</td>
</tr>
</tbody>
</table>

Lytics:
- 10x fold increase in significant/complete lysis
- 3x fold increase risk of bleeding

I have no disclosures

Goals of “Clot Removal” - Catheter-directed thrombolysis (CDT)

1. Diminish the inflammatory response
2. Preserve vein wall integrity
3. Restore patency
4. Preserve valve function

1) DECREASE PTS
2) DECREASE RECURRENT DVT

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Egypt Trial

- Randomized trial
- Iliofemoral DVT within 10 days
- N=35
- Tx= anticoagulation + streptokinase, initially infused into the clot using a pulse-spray technique followed by low-dose infusion vs anticoagulation alone

- Results at 6 months:
  - Iliofemoral patency in 72% of lysis patients versus 12% of those anticoagulated (p=0.001)
  - Valvular function normal in 89% of lysis patients versus 59% of those randomized to anticoagulation alone (p=0.04).
  - Complications minimal


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Trials on the use of CDT for IFDVT

- Liew and Douketis, Exp Rev Card Ther 2016
- Trials on the use of CDT for IFDVT

- Torpedo Trial (Arizona)
  - Thrombus Obliteration by Rapid Percutaneous Endovenous Intervention in Deep Venous Occlusion
  - -randomized study
  - -183 patients
  - -PEVI vs anticoag alone
  - -Primary outcome: Recurrent VTE at 6 months

- At 6 months
  - Recurrent VTE
    - 2.3% (PEVI)
    - 14.8% (anticoagulation)
    - p = 0.003
  - PTS
    - 3.4% (PEVI)
    - 27.2% (anticoagulation)
    - p<0.001

Sharifi et al, J Endovasc Ther 2012
In patients with proximal DVT, PEVI is superior to anticoagulation alone in the reduction of VTE and PTS. This benefit, which appears early in the course of treatment, extends to 2.5 years.

Sharifi et al, J Endovasc ther 2012

**CaVenT Trial**

(Catheter-directed venous thrombolysis)

- Randomized, open-label, multicenter trial, Norway
- Ilio-femoral DVT < 21 days
  - Upper half of thigh, common iliac vein or combined iliofemoral segment
  - With no anticoag prior to the trial entry for > 7 days
- N=200
- CDT with Alteplase, 0.01mg/kg/hr (max dose 20mg in 24 hours and maximal duration of 96 hours) or standard treatment alone
- Adjunctive BA/stent for >50% stenosis

**Primary endpoints:**
- Patency at 6 months (compressibility, flow, obstruction)
- Nonsurviving assessment of veins:
  - Doppler ultrasonography
  - AIR plethysmography
- Postthrombotic syndrome at 24 months
- Quality of life questionnaires:
  - EQ-5D
  - VEINES

**Investigations at 6, 24, 60 months:**

- **Objective:**
  - Lower limb edema
  - Venous anatomy

- **Clinical status:**
  - CEAP classification
  - Villarla score

- **Interventions:**
  - Catheter-directed venous thrombolysis

**Primary and points for investigations.**


**Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliо-femoral deep vein thrombosis (the CaVenT study): a randomised controlled trial**

Tone Inder, Husteg, Inge Lie, Kjell-Egil Sigvardsen, Lea Sandvik, Wided Ghernaie, Carola Pedersen, Pål Andres Holme, Leif Steil Holme, Anne Marie Sparrsco, Gunnar Sandvik, Per Morten Sandvik, on behalf of the CaVenT Study Group

**CaVenT Trial 6 months analysis**

- **Iliofemoral patency**
  - 64% in the CDT group
  - 36% in the controls (p < 0.004)
  - Risk reduction: 28%

- **Functional venous obstruction**
  - 20% of the CDT group
  - 49% of the controls (P < 0.004)
  - Risk reduction: 59%

- **Venous insufficiency:**
  - No different

- 1 patient had major bleeding and 2 patients had clinically relevant bleeding in the CTD group

CaVenT Primary endpoints

<table>
<thead>
<tr>
<th></th>
<th>Additional catheter-directed thrombolysis (n=90)</th>
<th>Standard treatment only (n=95)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-thrombotic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>syndrome at 24 months</td>
<td>57</td>
<td>55</td>
<td>0.426</td>
</tr>
<tr>
<td></td>
<td>35%</td>
<td>55%</td>
<td></td>
</tr>
<tr>
<td>Femoral artery rupture</td>
<td>58</td>
<td>45</td>
<td>0.012</td>
</tr>
<tr>
<td></td>
<td>65.9%</td>
<td>47.4%</td>
<td></td>
</tr>
<tr>
<td>Post-thrombotic</td>
<td>56</td>
<td>33</td>
<td>0.77</td>
</tr>
<tr>
<td>syndrome at 6 months</td>
<td>30%</td>
<td>32%</td>
<td></td>
</tr>
<tr>
<td>Post-thrombotic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>syndrome defined as Vila score of ≥5 or higher *p test</td>
<td>16%</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>patients had inclusion patency assessments and one was lost to follow-up at 6 months. Secondary outcome.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Bleeding: 20 bleeding complications (3 major, 5 clinically relevant)
- No deaths, PE or cerebral hemorrhage in CDT
- 4 non-bleeding complications (2 transient peripheral neuro deficits of treated limb, 1 local infection puncture site, 1 vertebral osteomyelitis)

Table 2: Short- and long-term outcomes

Absolute RR: 14%, NNT: 7

Secondary analysis - QOL

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<tr>
<td>24 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genital QOL</td>
<td>0.80 (0.73–0.86)</td>
<td>0.84 (0.75–0.93)</td>
<td>0.04 (0.81 to 0.95)</td>
</tr>
<tr>
<td>Disease-specific QOL</td>
<td>VENUS-QOL: 0.81 (0.74–0.88)</td>
<td>0.84 (0.75–0.93)</td>
<td>0.01 (0.81 to 0.95)</td>
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<td>VENUS-Byn: 0.83 (0.76–0.90)</td>
<td>0.84 (0.75–0.93)</td>
<td>0.01 (0.81 to 0.95)</td>
</tr>
<tr>
<td>6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genital QOL</td>
<td>0.82 (0.75–0.89)</td>
<td>0.81 (0.72–0.90)</td>
<td>0.01 (0.81 to 0.95)</td>
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Ongoing Trials

- ATTRACT Trial
- DUTCH CAVA Trial
Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis (ATTRACT)

- Funded by NIH
- Largest randomized trial on CDT vs anticoagulation
- PI: Dr. Suresh Vedantham
- 692 patients (enrollment completed)
- Phase 3, open-label, multicenter randomized controlled trial


ATTRACTION Study: Schedule of Assessments

Enrollment completed

DUTCH CAVA-trial: CAtheter Versus Anticoagulation Alone for Acute Primary (Ilio)Femoral DVT

- Randomized trial
- 180 patients with IFDVT, < 14 days
- Device: Ekos endowave system thrombolysis
- Primary outcome: PTS
- Secondary outcomes: QOL, recurrent VTE, clot lysis, inflammatory markers

Antithrombotic Therapy and Prevention of Thrombosis: ACCP Evidence-Based Clinical Practice Guidelines, 10th ed (2016)…

...remain unchanged for CDT of acute proximal DVT

Catheter-Directed Thrombolysis for Patients With Acute DVT

“In patients with acute proximal DVT of the leg, we suggest anticoagulant therapy alone over catheter-directed thrombolysis (CDT) (Grade 2C).”

Remarks: Patients who are most likely to benefit from CDT (see text), who attach a high value to prevention of postthrombotic syndrome (PTS), and a lower value to the initial complexity, cost, and risk of bleeding with CDT, are likely to choose CDT over anticoagulation alone.
SVS 2012 Guidelines iliofemoral DVT

We suggest a strategy of early thrombus removal in selected patients meeting the following criteria (Grade 2C):

a) First episode of acute IFDVT
b) Symptoms < 14 days in duration
c) Low risk of bleeding
d) Ambulatory with good functional capacity and an acceptable life expectancy

Meissner et al, JVS 2012

A Word on the Technique

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>We suggest percutaneous catheter-based techniques (pharmacologic or pharmacomechanical) as first-line therapy for early thrombus removal in patients meeting the criteria.</td>
<td>2</td>
<td>C</td>
</tr>
<tr>
<td>We suggest a strategy of pharmacomechanical thrombolysis be considered over catheter-directed pharmacologic thrombolysis alone if expertise and resources are available.</td>
<td>2</td>
<td>C</td>
</tr>
<tr>
<td>We suggest open surgical venous thrombectomy in selected patients who are candidates for anticoagulation but in whom thrombolytic therapy is contraindicated.</td>
<td>2</td>
<td>C</td>
</tr>
<tr>
<td>We recommend the use of self-expanding metallic stents for treatment of chronic iliofemoral compressive or obstructive lesions that are uncovered by any of the thrombus removal strategies.</td>
<td>1</td>
<td>C</td>
</tr>
<tr>
<td>We suggest that stents not be used in the femoral and popliteal veins.</td>
<td>2</td>
<td>C</td>
</tr>
</tbody>
</table>

Meissner, JVS 2012

Summary

• Does Ilio-Femoral Venous Lysis and Stenting Prevent Post-Thrombotic Syndrome? **YES**

• Evidence continues to grow in support of CDT for patients with IFDVT
  – Reducing post-thrombotic syndrome
  – Maintaining venous patency after DVT

**Should be considered in patients:**

a) First episode of acute IFDVT
b) Symptoms < 14 days in duration
c) Low risk of bleeding
d) Ambulatory with good functional capacity and an acceptable life expectancy

Phlegmasia Cerulea Dolens: early thrombus removal indicated

Thank you!