Iliofemoral DVT: An update on TORPEDO, CaVent, ATTRACT Trials and more....

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University of California San Francisco
UCSF Vascular Surgery Symposium 2015

Should we thrombolyse patients with iliofemoral DVT (IFDVT)?

Aims

- Reviewing risk factors for post-thrombotic syndrome (PTS)
- Examine current evidence for iliofemoral DVT (IFDVT)
- Review evidence for adjunctive treatment in IFDVT

I have no disclosures
Aims

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- Review evidence for adjunctive treatment in IFDVT

Post-thrombotic syndrome (PTS)

- First episode of DVT ~50/100,000 person-years
- DVT increases the risk of chronic venous disease by 26 fold
- Incidence PTS is 25-46% of patients DVT
- 6 x increase in PTS with recurrent DVT
- Anticoagulation safe, 2% risk of major hemorrhage and 3 months recurrence rate ~5.5%

Incidence and risk factors for PTS

<table>
<thead>
<tr>
<th>DVT location</th>
<th>PTS incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pop/BK</td>
<td>43%</td>
</tr>
<tr>
<td>Fempop</td>
<td>57%</td>
</tr>
<tr>
<td>Iliofem</td>
<td>74%</td>
</tr>
</tbody>
</table>

- Predictors of more severe postthrombotic syndrome
  - involvement of the common femoral or iliac veins
  - previous ipsilateral thrombosis
  - higher body mass index
  - older age
  - female sex

- MOST POWERFUL PREDICTOR OF SEVERE PTS IS IFDVT (HR: 2.23)

PTS Pathophysiology

- If treated with anticoagulation alone, IFDVT patients:
  - 90% have ambulatory venous hypertension
  - 40% have venous claudication
  - 15% will develop ulceration within 5 years

- Pathophysiology
  - Valvular incompetence
  - Luminal venous obstruction
  - Combination of the above

References:

Kahn et al., Ann Intern Med. 2008
Goals of “Clot Removal”

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

Aims

• Reviewing risk factors for post-thrombotic syndrome (PTS)
• Examine current evidence for iliofemoral DVT (IFDVT)
• Review evidence for adjunctive treatment in IFDVT

Early studies support removal of thrombus is beneficial

Table 1: Results of a Multicenter Randomized Trial of Operative Venous Thrombectomy with Anterograde Fibrin Plugs Anticoagulation versus Anticoagulation Alone in Patients with Iliofemoral Deep Veins Thrombosis

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Anticoagulation (n = 230)</th>
<th>Thrombectomy (n = 240)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient's iliac veins</td>
<td>8/27</td>
<td>8/23</td>
<td>.375</td>
</tr>
<tr>
<td>Patient femoral/iliofemoral veins with functional valves</td>
<td>7/26</td>
<td>7/23</td>
<td>.652</td>
</tr>
</tbody>
</table>

Early studies support removal of thrombus is beneficial


Treatment of acute iliofemoral deep vein thrombosis

Edward T. Casey, DO, MD, Hassan Murad, MD, MPH, Maya Zamaacta Garcia, MD,*
Mohamed B. Elamin, MBBCh, Qian Shi, PhD,†† Peter Gloviczki, MD, and Maruis Molinero, MD,*
Victoria M. Moonen, MD, MSc,‡ Peter Glavicki, MD,* and Mark Molinero, MD,* Rochester, Minn, and Seattle, Wash.

(J Vasc Surg 2012;55:1463-73.)

Surgical Thrombectomy vs systemic anticoagulation
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>

**SVS Guidelines** recommend against the use of non-catheter-directed, systemically administered thrombolytic agents for the treatment of iliofemoral thrombosis - Meissner JVS 2012

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

3 large series - CDT

<table>
<thead>
<tr>
<th>Efficacy (%)</th>
<th>Bjarnason et al.</th>
<th>Mewissen et al. (NVR)</th>
<th>Comerota et al.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Success</td>
<td>79</td>
<td>83</td>
<td>84</td>
</tr>
<tr>
<td>Primary Patency at 1 year</td>
<td>63</td>
<td>64</td>
<td>78</td>
</tr>
<tr>
<td>Iliac stent patency at 1 year</td>
<td>54</td>
<td>74</td>
<td>89</td>
</tr>
</tbody>
</table>

Complications (%)
- Major bleed: 5%
- Intra-cranial bleed: 0%
- PE: 1%
- Fatal PE: 0%
- Death 2yr to lysis: 0%

1-year results: National Venous Registry

<table>
<thead>
<tr>
<th>Initial Lytic Response</th>
<th>&lt;50%</th>
<th>50-99%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residual thrombus (%)</td>
<td>73</td>
<td>45</td>
<td>16</td>
</tr>
<tr>
<td>Reflux (%)</td>
<td>89</td>
<td>48</td>
<td>39</td>
</tr>
<tr>
<td>Asymptomatic (%)</td>
<td>36</td>
<td>68</td>
<td>84</td>
</tr>
</tbody>
</table>

Adverse events
- Bleeding (11%)
  - 4% venous insertion site
  - 1% retroperitoneal
  - 6% other
- Neurological complications (0.4%)
- PE (1%)
- Death (0.4%)

**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


**Torpedo Trial (Arizona)**

- 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

“Torpedo” 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, 0.03mg/kg/hr (max dose 20mg in 24 hours and maximal duration of 96 hours) or standard treatment alone
- Adjunctive BA/stent for >50% stenosis

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: 29%

- Venous insufficiency:
  - No different
  - 1 patient had major bleeding and 2 patients had clinically relevant bleeding in the CTD group


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

Enden et al, Lancet 2012

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 syndrome at 24 months</td>
<td>37 (41.3%) (31.5–51.4)</td>
<td>55 (35.5%) (24.7–45.0)</td>
<td>0.047</td>
</tr>
<tr>
<td>Iliofemoral patency at 6 months</td>
<td>58 (65.9%) (55.5–75.0)</td>
<td>45 (40.4%) (32.7–52.3)</td>
<td>0.012</td>
</tr>
<tr>
<td>Post-thrombotic syndrome at 6 months</td>
<td>27 (30.3%) (21.8–40.5)</td>
<td>32 (33.2%) (23.5–42.4)</td>
<td>0.77</td>
</tr>
</tbody>
</table>

Post-thrombotic syndrome defined as Villalta score of 5 points or higher. *p test. 120–primary outcomes. 75 patients had in-clinic post-treatment assessments and one was lost to follow-up after 6 months. Secondary outcomes.

-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 vegetal osteomyelitis)

Enden et al, BMJ Open 2013

CaVenT Trial- QOL

Secondary analysis- QOL

<table>
<thead>
<tr>
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<th>Mean difference</th>
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</tr>
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<tr>
<td>24 months</td>
<td>Genetically GQOL</td>
<td>88.8 (82.4–95.2)</td>
<td>93.7 (88.0–99.5)</td>
<td>0.04</td>
</tr>
<tr>
<td>Disease-specific GQOL</td>
<td>VEINES-QOL (46.4–58.9)</td>
<td>73.1 (68.6–77.6)</td>
<td>58.6 (56.0–61.2)</td>
<td>0.012</td>
</tr>
<tr>
<td>6 months</td>
<td>Genetically GQOL</td>
<td>88.2 (82.6–95.5)</td>
<td>92.1 (86.4–97.8)</td>
<td>0.02</td>
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Enden et al, BMJ Open 2013

Enden et al, Lancet 2012

Table 2: Non-invasive assessment of veins 6 months after iliofemoral deep vein thrombosis (n = 104)

<table>
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<tr>
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<th>CDT group</th>
<th>Standard treatment</th>
<th>N (%)</th>
<th>P value</th>
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Table 3: Genetically and disease-specific quality of life and symptom severity according to treatment allocation

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Enden et al, BMJ Open 2013
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 just completed)
- Phase 3, open-label, multicenter randomized controlled trial

Comerota AJ. Perspect Vasc Surg Endovasc Ther. 2009 Dec;21(4):221-4; Am Heart J 2013

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

Comerota AJ. Perspect Vasc Surg Endovasc Ther. 2009 Dec;21(4):221-4; Am Heart J 2013

ATTRACT Study: Schedule of Assessments

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Baseline</th>
<th>Initial Ts</th>
<th>10 d</th>
<th>20 d</th>
<th>30 d</th>
<th>9 m</th>
<th>12 m</th>
<th>18 m</th>
<th>24 m</th>
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</thead>
<tbody>
<tr>
<td>Leg pain (1-8)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Leg circumference</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Venous GCS (1-4)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>General GCS (CT scan and 3)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Duplex ultrasonography</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Vascular (CT) only</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>X</td>
<td>X</td>
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<tr>
<td>Vascular (MRI) only</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Venous PTS (Villalta)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>VQ/CT</td>
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<td>X</td>
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<td>X</td>
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<tr>
<td>CE classification</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

Primary outcome

PTS (score of >5 on Villalta PTS Scale) or ulcer in that leg, 6-24 months

Treatment of acute iliofemoral deep vein thrombosis

Edward T. Casey, DO,** M. Hassan Murad, MD, MPH,** Magaly Zumaeta Garcia, MD,* Mohamed R. Elshorbagy, MBBS,* Qin Shi, PhD,** Pritish J. Irwin, MSL*; Victor M. Monteser, MD, MSc,* Peter Tschiesicht, MD,* and Mark Mooney, MD,* Rochester, Minn, and Seattle, Wash

(J Vasc Surg 2012;55:1463-73.)
Cochrane Review - 2014

Thrombolysis for acute deep vein thrombosis (Review)

Waters L, Broderick C, Aronson MP

CDT on Venous Patency

Analysis 4.1. Comparison 4 Catheter-directed thrombolysis versus control, Outcome 1 Any improvement in venous patency (early).

Review: Thrombolysis for acute deep vein thrombosis
Comparison: 4 Catheter-directed thrombolysis versus control
Outcome: 1 Any improvement in venous patency (early)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Thrombolysis</th>
<th>Standard anticoagulation</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elshaoury 2002</td>
<td>18/18</td>
<td>0/17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Odds ratio: 35.05 [2.28, 539.63]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p value: 0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CDT on PTS

Analysis 4.8. Comparison 4 Catheter-directed thrombolysis versus control, Outcome 8 Post-thrombotic syndrome (intermediate - 24 months).

Review: Thrombolysis for acute deep vein thrombosis
Comparison: 4 Catheter-directed thrombolysis versus control
Outcome: 8 Post-thrombotic syndrome (intermediate - 24 months)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Thrombolysis</th>
<th>Standard anticoagulation</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elshaoury 2002</td>
<td>0/18</td>
<td>0/17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enden 2011</td>
<td>55/99</td>
<td>3/90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Odds ratio: 0.74 [0.55, 1.00]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p value: 0.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CDT on Bleeding

Analysis 4.3. Comparison 4 Catheter-directed thrombolysis versus control, Outcome 3 Bleeding (early).

Review: Thrombolysis for acute deep vein thrombosis
Comparison: 4 Catheter-directed thrombolysis versus control
Outcome: 3 Bleeding (early)

<table>
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<tr>
<td>Elshaoury 2002</td>
<td>0</td>
<td>0/17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Odds ratio: Not estimable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test for overall effect: Z = 1.36 (P = 0.18)
Test for subgroup differences: Not applicable

Total events: 3 (Thrombolysis), 0 (Standard anticoagulation)

Heterogeneity: not applicable

Test for overall effect: Z = 1.36 (P = 0.18)
Test for subgroup differences: Not applicable
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 who attach 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

Phlegmasia Cerulea Dolens

- Characterized by massive swelling, cyanosis and pain
- Pulses palpable in ~50%
- Complicated by venous gangrene (~60%)
  - Venous HTN leads to small arterial collapse
- Often underlying hypercoagulable state
  - Malignancy, HIT
SVS 2012 Guidelines: phlegmasia cerulea dolens

- We recommend early thrombus removal strategies as the treatment of choice in patients with limb-threatening venous ischemia due to IFDVT with or without associated femoropopliteal venous thrombosis (phlegmasia cerulea dolens) (Grade 1A).

RISKS & BENEFITS

Meissner et al, JVS 2012

SVS 2012 Guidelines: femoropopliteal DVT

We recommend that patients with isolated femoropopliteal DVT be managed with conventional anticoagulation therapy because there is currently insufficient evidence to support early thrombus removal strategies in this patient population (Grade 1C).

Meissner et al, JVS 2012

Evidence...

<table>
<thead>
<tr>
<th>Less deranged hemodynamics</th>
<th>Less PTS</th>
<th>Less DVT recurrence</th>
<th>Less favorable outcomes with thrombolytic therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1 years patency: 47% fempopDVT vs 64% IFDVT)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ATTRACT TRIAL

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 <strong>percutaneous catheter-based techniques</strong> (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 <strong>pharmacomechanical thrombolysis</strong> 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 <strong>open surgical venous thrombectomy</strong> 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 <strong>self-expanding metallic stents</strong> for treatment of chronic ilio caval 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 <strong>stents not be used in the femoral and popliteal veins</strong>.</td>
<td>2</td>
<td>C</td>
</tr>
</tbody>
</table>

Meissner, JVS 2012

IVC filters

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>We recommend <strong>against routine use</strong> of inferior vena cava filters (permanent or temporary) in conjunction with catheter-directed pharmacologic thrombolysis of the iliofemoral venous segments.</td>
<td>1</td>
<td>C</td>
</tr>
<tr>
<td>We suggest that the relative risks vs benefits of peri/procedural retrievable inferior vena cava filter placement be considered in patients undergoing pharmacomechanical thrombolysis and those with thrombus extending into the inferior vena cava or having markedly limited cardiopulmonary reserve.</td>
<td>2</td>
<td>C</td>
</tr>
</tbody>
</table>

Meissner, JVS 2012

An IVC filter should not be used routinely in the treatment of IFDVT (Class III; Level of Evidence B). Jaff et al. Circulation 2011.
Aims

• Reviewing risk factors for post-thrombotic syndrome (PTS)
• Examine current evidence for iliofemoral DVT (IFDVT)
• Review evidence for adjunctive treatment in IFDVT

Recommendations for Initial Anticoagulation for Patients with IFDVT

• AHA Guidelines 2011
  – IV UFH, s/c UFH, LMWH, fondaparinux
  – Direct thrombin inhibitor if HIT +

• Duration of treatment
  – if reversible RF: 3 months
  – If unprovoked or recurrent: 6 months – indefinite

• Cancer patients:
  – LMWH for 3-6 months or duration of cancer

• Chest Guidelines 2012
  – LMWH or fondaparinux over IV UFH (Grade 2C) and over SC UFH (Grade 2B for LMWH, Grade 2C for fondaparinux)

• Duration of treatment
  – If provoked: 3 months
  – Unprovoked and low/mod bleeding risk: extended over 3 months
  – Unprovoked and high bleeding risk: 3 months over extended duration

Recommendations for the Use of Compression Therapy

• Compression therapy (30-40mm Hg) knee-high graduated stockings recommended
  – AHA: Class I, level of evidence B
  – Chest: Grade 1A
  – SVS: Grade 1C

• Should be worn for 2 years after initial DVT

• Also consider intermittent sequential pneumatic compression if patients have severe edema

Venous Compression for Prevention of Postthrombotic Syndrome: A Meta-analysis

SOX Trial
Compression Stockings to Prevent the Post-Thrombotic Syndrome

- Multicenter randomized, placebo-controlled trial
- Compression (30-40 mm Hg) or placebo (5 mm Hg) used for 2 years
- Symptomatic proximal DVT
- ** also thrombolysed
- Primary endpoint:
  - PTS at 6 months

Kahn et al., Lancet 2014

Should we thrombolys patients with iliofemoral DVT (IFDVT)?

**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

Kahn et al., Lancet 2014
Summary

• Evidence continues to grow in support of CDT for patients with IFDVT
  – Reducing post-thrombotic syndrome
  – Maintaining venous patency after DVT
• Some doubt shed on role of compression therapy with the SOX Trial
  – Still recommended (Grade 1)
Diagnosis

If iliofemoral venous thrombosis is suspected but not confirmed using standard diagnostic modalities such as venous ultrasound imaging, we recommend the use of **adjunctive imaging modalities**, such as **computed tomography venography** or **magnetic resonance venography** to characterize the most proximal thrombus extent.

Extent of adequate evaluation of the common iliac vein with U/S: 47%

Meissner et al, JVS 2012

Nomenclature

"We recommend use of precise anatomic terminology to characterize the most proximal extent of venous thrombosis."

<table>
<thead>
<tr>
<th>OLD</th>
<th>NEW</th>
</tr>
</thead>
<tbody>
<tr>
<td>proximal</td>
<td>iliofemoral +/- extension into IVC</td>
</tr>
<tr>
<td>distal</td>
<td>isolated calf veins</td>
</tr>
</tbody>
</table>

Iliofemoral DVT +/- IVC extension

Percutaneous Mechanical Thrombectomy

*A Systematic Review of Percutaneous Mechanical Thrombectomy in the Treatment of Deep Venous Thrombosis*

A. Karthikesalingam, E.L. Young, R.J. Hinchcliffe, I.M. Loftus, M.M. Thompson, P.J.E. Holt

Results: 16 retrospective case series have reported the use of rheolytic, rotational, or ultrasound-assisted PMT in a total of 481 patients. No randomised trials were available. Technical success of 82–100% was reported with Grade II or III lysis in 83–100% of patients. The different devices all appeared to be safe, with no reported procedure-related deaths or strokes and <1% incidence of symptomatic PE. Bleeding complications were reported in 6/16 studies, in which 4–14% of patients required transfusion (global incidence 11/146 patients, 7%).
SVS 2012 Guidelines: phlegmasia cerulea dolens

We recommend early thrombus removal strategies as the treatment of choice in patients with limb-threatening venous ischemia due to IFDVT with or without associated femoropopliteal venous thrombosis (phlegmasia dolens). (Grade 1A).

We suggest that fasciotomy ONLY be considered if compartment pressures in the thigh or calf remain elevated (>30mm Hg) despite efforts to restore iliofemoral venous outflow using procedures outlined above (Grade 2C).

Meissner et al, JVS 2012

Successful thrombolysis

1. Maximal clearance of thrombus
2. Correction of underlying occlusive lesion in the iliac veins with angioplasty and adequately size stents
3. Therapeutic anticoagulation of appropriate duration


Evidence

Table: Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach to treatment recommendations

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Benefit/ harm</th>
<th>Quality of evidence</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>Clear</td>
<td>Strong recommendation, generalizable</td>
<td></td>
</tr>
<tr>
<td>1B</td>
<td>Clear</td>
<td>Moderate: RCTs with limited number of patients, very strong observational studies</td>
<td></td>
</tr>
<tr>
<td>1C</td>
<td>Clear</td>
<td>Low: Observational studies</td>
<td></td>
</tr>
<tr>
<td>2A</td>
<td>Balanced or moderate</td>
<td>Low: Observational studies with large effect size</td>
<td></td>
</tr>
<tr>
<td>2B</td>
<td>Balanced or moderate</td>
<td>Low: Observational studies with very strong observational evidence</td>
<td></td>
</tr>
<tr>
<td>2C</td>
<td>Balanced or moderate</td>
<td>Low: Observational studies</td>
<td></td>
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Meissner et al, JVS 2012

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**ATTRACT Study**

**Hypothesis:** “Because the persistence of thrombus within the venous system has been linked to the development of PTS, it is hypothesized that early, active elimination of venous thrombus in DVT patients may prevent PTS.”


**National Venous Registry**

- 1 year patency better with stents vs no stents
  - 74% vs 53% (p<0.001)

Mewissen et al, Radiology 1999

**Grade of Lysis:**
- I=<50%
- II=50-90%
- III= complete

**ATTRACT Questions of Interest**

1. Is CDT better than anticoagulation alone for IFDVT and femoropopliteal DVT?
2. Are pharmacomechanical techniques better than drip infusion of plasminogen activators?
3. Is treatment cost-effective?
4. Is postthrombotic morbidity related to vein patency and/or venous valve function?


**Antithrombotic Therapy and Prevention of Thrombosis: ACCP Evidence-Based Clinical Practice Guidelines, 9th ed (2012)**

In patients with acute DVT of the leg who undergo thrombosis removal, we recommend the same intensity and duration of anticoagulant therapy as in comparable patients who do not undergo thrombosis removal (Grade 1B).

In patients with acute proximal DVT of the leg, we suggest anticoagulant therapy alone over operative venous thrombectomy (Grade 2C).

In patients with acute proximal DVT of the leg, we suggest anticoagulant therapy alone over operative venous thrombectomy (Grade 2C).
CaVenT Trial 6 months analysis

- **Puncture**
  - Popliteal vein under U/S guidance

- **Catheter**
  - Unifuse 5Fr

- **Thrombolysis**
  - TNK 5mg bolus
  - TNK 0.5mg/hr x 5 hours, then 0.25 mg/hr for 12-24 hours

- **Repeat venogram next day**
  - In incomplete lysis, Angiojet

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<table>
<thead>
<tr>
<th>Complication</th>
<th>n</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Total</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>12.5%</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>4.17%</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>7.5%</td>
</tr>
</tbody>
</table>

*Grade I: AE; grade II: AE > 95% plus grade III; complete.*

The sample size included only patients with grade I-III complications. The follow-up period was 6 months. The data presented includes the patients who did not receive thrombolysis. Source: Enden et al., J. Thromb. Hemost., 2009.