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


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Presenter: Michael Streiff, MD
Moderators: Tracy Minichiello, MD; Sara Vazquez, PharmD; and Diane Wirth, ANP, CACP
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Background

- Post-thrombotic syndrome (PTS) affects 20-50% of patients after deep venous thrombosis
- PTS characterized by pain, swelling and ulceration of the affected leg
- PTS has a significant impact on QOL and productivity
- PTS is caused by chronic venous hypertension and inflammation
  - “Open vein hypothesis”

Rabinovich A and Kahn SR. J Thromb Haemost 2017
How Does Catheter-Directed Thrombolysis (CDT) Work?

**Thrombectomy**
- **Catheter aspiration thrombectomy**: Blood clot is removed using suction
- **Mechanical thrombectomy**: Blood clot is broken up into small pieces and removed

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Figures from Healthwise incorporated; Suresh Vedantham MD and cirse.org
The CaVenT Trial

• Open RCT of AC v. CDT for 1st acute proximal DVT
• CDT with TPA up 96 hrs. with angioplasty and stent
• Outcome: Patency at 6 mos., PTS at 24 mos.
• CDT improves patency and reduces PTS

Enden T et al Lancet 2011
The ATTRACT Trial Study Design

• Prospective, multicenter, open-label, blinded outcome-assessor, RCT comparing catheter-directed pharmacomechanical thrombolysis with anticoagulation for acute proximal DVT
• Sponsor: NHLBI, Boston Scientific, Medtronic, Genentech, BSN Medical

- Primary efficacy outcome: Post Thrombotic syndrome as defined by Villalta scale (score ≥ 5 or leg ulcer) evaluated at 6, 12, 18 and 24 months
- Secondary outcomes: Severity of PTS (Villalta and Venous Clinical severity score), Moderate-severe PTS (Villalta ≥ 10), major non-PTS treatment failure- unplanned endovascular procedure or venous gangrene within 6 months or amputation within 24 months, patient-reported QOL at baseline and 24 months with SF-36 and VEINES-QOL
- Primary safety outcome: Major bleeding, recurrent VTE, death

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Study Population

28,507 patients met inclusion criteria
- 26,715 excluded
- 1,100 declined participation
692 patients randomized
- 1 excluded post-randomization

355 AC only patients
- 5 underwent CDT
- 12 underwent LEP during 24 mo.
- 243 completed 24 mo follow up
- 112 did not (8 died, 18 withdrew consent, 86 lost to FU)
- 194 completed 4 PTS assessments
- 109 completed 1-3 PTS assessments
- 52 missed all PTS assessments
- 355 patients in modified ITT analysis
- 350 in pre-protocol analysis

336 CDT patients
- 11 did not received CDT
- 20 underwent LEP during 24 mo.
- 257 completed 24 mo follow up
- 79 did not (7 died, 10 withdrew consent, 62 lost to FU)
- 215 completed 4 PTS assessments
- 93 completed 1-3 PTS assessments
- 52 missed all PTS assessments
- 336 patients in modified ITT analysis
- 325 in pre-protocol analysis

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### Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CDT+AC (N=336)</th>
<th>AC alone (N=355)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (IQR)</td>
<td>52 (41-62)</td>
<td>53 (43-62)</td>
</tr>
<tr>
<td>Male sex</td>
<td>205 (61%)</td>
<td>221 (62%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>265 (79%)</td>
<td>276 (78%)</td>
</tr>
<tr>
<td>Black</td>
<td>61 (18%)</td>
<td>62 (17%)</td>
</tr>
<tr>
<td>Other</td>
<td>10 (3%)</td>
<td>17 (5%)</td>
</tr>
<tr>
<td>Median weight-kg (IQR)</td>
<td>95 (81-111)</td>
<td>92 (79-110)</td>
</tr>
<tr>
<td>Index DVT in common femoral vein</td>
<td>195 (58%)</td>
<td>196 (55%)</td>
</tr>
<tr>
<td>Previous ipsilateral DVT</td>
<td>5 (1%)</td>
<td>14 (4%)</td>
</tr>
<tr>
<td>Median time, symptoms to randomization-days</td>
<td>6 (4-10)</td>
<td>6 (4-9)</td>
</tr>
</tbody>
</table>

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## Treatment after Randomization

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CDT+AC (N=336)</th>
<th>AC only (N=355)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial AC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UFH</td>
<td>118 (35%)</td>
<td>69 (20%)</td>
</tr>
<tr>
<td>LMWH</td>
<td>181 (54%)</td>
<td>227 (64%)</td>
</tr>
<tr>
<td>Other</td>
<td>49 (15%)</td>
<td>71 (20%)</td>
</tr>
<tr>
<td><strong>Therapy at 30 days</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any AC</td>
<td>314 (98%)</td>
<td>316 (98%)</td>
</tr>
<tr>
<td>GCS used ≥ 3 days/week</td>
<td>252 (79%)</td>
<td>252 (79%)</td>
</tr>
<tr>
<td><strong>Therapy at 6 months</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any AC</td>
<td>227 (78%)</td>
<td>247 (86%)</td>
</tr>
<tr>
<td>GCS used ≥ 3 days/week</td>
<td>192 (66%)</td>
<td>197 (69%)</td>
</tr>
<tr>
<td><strong>Therapy at 24 months</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any AC</td>
<td>120 (48%)</td>
<td>117 (50%)</td>
</tr>
<tr>
<td>GCS used ≥ 3 days/week</td>
<td>138 (55%)</td>
<td>130 (55%)</td>
</tr>
<tr>
<td>Duration of AC-Days (IQR)</td>
<td>211 (179-360)</td>
<td>231 (189-371)</td>
</tr>
</tbody>
</table>

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CDT Treatment Details

- “Infusion first” TPA given to 194 patients (58%)
  - Median duration 22±6.5 hours
- Angiojet (Boston Scientific) used in 75 patients (22%)
  - Duration 20±5.3 hours
- Trellis (Covidien) used in 50 patients (15%)
  - Duration 19±5.7 hours
- Additional endovascular methods (≥1) used in 297 (88%)
  - Balloon venoplasty 184 (62%)
  - Balloon maceration 183 (62%)
  - Rheolytic thrombectomy with Angiojet 180 (61%)
  - Stent 82 (28%)
  - Catheter clot aspiration 63 (21%)
  - Trellis isolated thrombolysis 14 (5%)

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## Clinical Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>CDT (N=336)</th>
<th>AC (N=355)</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTS between 6-24 mos.</td>
<td>157 (47%)</td>
<td>171 (48%)</td>
<td>0.96 (0.82-1.11)</td>
</tr>
<tr>
<td>PTS at 6 mos.</td>
<td>78 (27%)</td>
<td>113 (40%)</td>
<td>0.68 (0.53-0.86)</td>
</tr>
<tr>
<td>PTS at 12 mos.</td>
<td>92 (34%)</td>
<td>88 (34%)</td>
<td>0.99 (0.78-1.26)</td>
</tr>
<tr>
<td>PTS at 18 mos.</td>
<td>85 (35%)</td>
<td>76 (34%)</td>
<td>1.01 (0.79-1.30)</td>
</tr>
<tr>
<td>PTS at 24 mos.</td>
<td>79 (31%)</td>
<td>86 (36%)</td>
<td>0.85 (0.66-1.09)</td>
</tr>
<tr>
<td>Moderate-severe PTS</td>
<td>60 (18%)</td>
<td>84 (24%)</td>
<td>0.73 (0.54-0.98)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>6 (1.7%)</td>
<td>1 (0.3)</td>
<td>6.18 (0.78-49.2)</td>
</tr>
<tr>
<td>Any bleeding</td>
<td>15 (4%)</td>
<td>6 (2%)</td>
<td>2.64 (1.04-6.68)</td>
</tr>
<tr>
<td>Recurrent VTE</td>
<td>6 (2%)</td>
<td>4 (1%)</td>
<td>1.53 (0.44-5.28)</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

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CDT Reduces Villalta PTS Score

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Additional Results

• No difference in SF-36 general QOL or VEINES disease-specific QOL between CDT and AC
• CDT resulted in greater reduction in early leg pain severity (-0.33±0.14; p=0.02) and leg circumference (-0.53±0.23; p=0.02) than AC
• Pre-specified subgroup analysis suggests patients age > 65 years are less likely to benefit from CDT

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Limitations

• Significant number of patients particularly in the AC group were followed for less than 24 months (CDT 79 [23.5%] v. AC 112 [31.5%])

• Significant number of missing data for PTS outcome
  • 215 CDT patients (64%) and 194 AC patients (54.6%) had all 4 PTS assessments
  • A sensitivity analysis using multiple imputation did not find a different result for the primary outcome

• Differences in CDT procedure between centers

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Conclusions

• Catheter-directed pharmacomechanical thrombolysis (CDT) did not result in a lower risk of PTS in patients with acute proximal DVT
  • CDT did reduce the incidence of moderate-severe PTS
  • CDT was associated with lower PTS scores between 6 and 24 months

• CDT did result in a greater risk of major bleeding within the first 10 days (1.7% v. 0.3%; p=0.049)

• CDT did not result in a significantly improved general or disease-specific quality of life
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