Iliofemoral DVT should be treated with thrombolysis/mechanical thrombectomy

Em. prof. dr. Cees H.A. Wittens
## Previous trials

<table>
<thead>
<tr>
<th>CaVenT(^1)</th>
<th>ATTRACT(^2)</th>
<th>CAVA(^3)</th>
</tr>
</thead>
</table>
| • 209 patients  
  ○ All iliofemoral DVTs | • 692 patients  
  ○ 391 iliofemoral DVTs | • 184 patients  
  ○ All iliofemoral DVTs |
| Catheter-Directed Thrombolysis (rtPA + stenting)  
  vs. Conventional Therapy | Pharmaco-mechanical Thrombolysis (rtPA + stenting)  
  vs. Conventional Therapy | Ultrasound-Accelerated Catheter-Directed Thrombolysis (uPA + stenting)  
  vs. Conventional Therapy |
| • PTS at 24 months | • PTS at 6-24 months | • PTS at 12 months |
| ✓ 41.1% vs. 55.6%  
  \(P = 0.047\) | ✓ 47% vs. 48%  
  \(P = 0.56\) | ✓ 29.3% vs. 35.1%  
  \(P = 0.45\) |

Conclusion could be as defended by Peter Verhamme that:

Aggressive endovascular treatment for iliofemoral DVT does not prevent PTS

BUT
CAVA¹ – Subanalysis

Does successful thrombolysis have a preventative effect on the development of PTS²?

Successful thrombolysis:  Restored patency of ≥90%

CAVA¹ – Subanalysis

Flow Chart

- Acute IFDVT, N = 152
  - Additional UACDT, N = 77
    - Successful, N = 41
    - Unsuccessful, N = 36
  - Conventional treatment, N = 75

1. Thrombolysis was successful in 53.2%

## CAVA<sup>1</sup> – Subanalysis Thrombolysis

**Thrombus characteristics**

<table>
<thead>
<tr>
<th>Vein Segments Affected, LET classification&lt;sup&gt;2&lt;/sup&gt; – no. (%)</th>
<th>Additional Successful UACDT N = 41</th>
<th>Additional Unsuccessful UACDT N = 36</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LET IV</td>
<td>9 / 41 (22.0)</td>
<td>6 / 36 (16.7)</td>
<td>0.559</td>
</tr>
<tr>
<td>LET III</td>
<td>29 / 41 (70.7)</td>
<td>27 / 36 (75.0)</td>
<td>0.675</td>
</tr>
<tr>
<td>LET II</td>
<td>3 / 41 (7.3)</td>
<td>1 / 36 (2.8)</td>
<td>0.618</td>
</tr>
</tbody>
</table>

CAVA\textsuperscript{1} – Subanalysis Thrombolysis
Thrombolytic Success - Differences

<table>
<thead>
<tr>
<th>no. (%)</th>
<th>Successful Additional UACDT</th>
<th>Unsuccessful Additional UACDT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of symptoms at inclusion</td>
<td>2 / 41 (4.9)</td>
<td>8 / 36 (22.2)</td>
<td>0.039</td>
</tr>
</tbody>
</table>

# CAVA\textsuperscript{1} – Subanalysis Thrombolysis

## Complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>Successful Additional UACDT N = 41</th>
<th>Unsuccessful Additional UACDT N = 36</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major bleeding</td>
<td>1 (2.4)</td>
<td>3 (8.4)</td>
<td>0.335</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>3 (7.3)</td>
<td>4 (11.1)</td>
<td>0.699</td>
</tr>
<tr>
<td>Low Fibrinogen</td>
<td>13 (31.7)</td>
<td>10 (27.8)</td>
<td>0.707</td>
</tr>
<tr>
<td>Procedural failure</td>
<td>4 (9.8)</td>
<td>1 (2.8)</td>
<td>0.364</td>
</tr>
<tr>
<td>Recurrent DVT</td>
<td>2 (4.9)</td>
<td>3 (8.3)</td>
<td>0.660</td>
</tr>
<tr>
<td>In-stent-thrombosis</td>
<td>6 (14.6)</td>
<td>4 (11.1)</td>
<td>0.742</td>
</tr>
<tr>
<td>Death</td>
<td>1 (2.4)</td>
<td>0</td>
<td>0.559</td>
</tr>
</tbody>
</table>

# CAVA¹ – Subanalysis Thrombolysis

Outcomes at 12 months

<table>
<thead>
<tr>
<th>Villalta score: Total score, mean ± SD</th>
<th>Successful Additional UACDT (N = 41)</th>
<th>Unsuccessful Additional UACDT (N = 36)</th>
<th>P = 0.045</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective score, mean ± SD</td>
<td>3.35 ± 3.10</td>
<td>4.72 ± 3.19</td>
<td></td>
</tr>
<tr>
<td>Subjective score, mean ± SD</td>
<td>1.32 ± 1.77</td>
<td>1.97 ± 1.93</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.03 ± 2.17</td>
<td>2.75 ± 2.41</td>
<td></td>
</tr>
<tr>
<td>Post-Thrombotic Syndrome, Definition by Villalta²</td>
<td>9 (22.0)</td>
<td>13 (36.1)</td>
<td>P = 0.020</td>
</tr>
<tr>
<td>None (0-4)</td>
<td>32 (78.1)</td>
<td>23 (63.9)</td>
<td></td>
</tr>
<tr>
<td>Mild (5-9)</td>
<td>6 (14.6)</td>
<td>4 (11.1)</td>
<td></td>
</tr>
<tr>
<td>Moderate (10-14)</td>
<td>2 (4.9)</td>
<td>9 (25.0)</td>
<td></td>
</tr>
<tr>
<td>Severe (≥ 15)</td>
<td>1 (2.4)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Moderate/Severe (≥ 10)</td>
<td>3 (7.3)</td>
<td>9 (25.0)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>VCSS at 12 months, mean ± SD</th>
<th>Successful Additional UACDT (N = 41)</th>
<th>Unsuccessful Additional UACDT (N = 36)</th>
<th>P = 0.025</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.50 ± 2.57</td>
<td>4.88 ± 2.25</td>
<td></td>
</tr>
</tbody>
</table>

CAVA¹ – Subanalysis Thrombolysis

Quality of Life

Successful UACDT

Unsuccessful UACDT

P = 0.011
CAVA\textsuperscript{1} – Subanalysis Thrombolysis

Quality of Life

Successful UACDT

- SF-36 Physical Health
- SF-36 Role Physical Limitations
- SF-36 Mental Health
- SF-36 Role Mental Limitations
- SF-36 Vitality
- SF-36 Pain
- SF-36 General Health
- SF-36 Health Change
- EQ5D
- Pain Disability Index
- VEINES-total
- VEINES-intrinsic

Unsuccessful UACDT

- SF-36 Physical Health
- SF-36 Role Physical Limitations
- SF-36 Mental Health
- SF-36 Role Mental Limitations
- SF-36 Vitality
- SF-36 Pain
- SF-36 General Health
- SF-36 Health Change
- EQ5D
- Pain Disability Index
- VEINES-total
- VEINES-intrinsic

\( P = 0.015 \)
CAVA\textsuperscript{1} – Subanalysis Thrombolysis

Quality of Life

**Successful UACDT**

- SF-36 Physical Health
- SF-36 Social Health
- SF-36 Role Physical Limitations
- SF-36 Role Mental Limitations
- SF-36 Mental Health
- SF-36 Vitality
- SF-36 General Health
- SF-36 Health Change
- EQ5D
- VEINES-total
- VEINES-intrinsic

**Unsuccessful UACDT**

- SF-36 Physical Health
- SF-36 Social Health
- SF-36 Role Physical Limitations
- SF-36 Role Mental Limitations
- SF-36 Mental Health
- SF-36 Vitality
- SF-36 General Health
- SF-36 Health Change
- EQ5D
- VEINES-total
- VEINES-intrinsic

\[ P = 0.012 \]
CAVA\textsuperscript{1} – Subanalysis Thrombolysis

Quality of Life

**Successful UACDT**

*SF-36 Physical Health*
*SF-36 Social Health*
*SF-36 Role Physical Limitations*
*SF-36 Role Mental Limitations*
*SF-36 Mental Health*
*SF-36 Vitality*
*SF-36 Pain*
*SF-36 General Health*
*SF-36 Health Change*
*EQ5D*
*VEINES-total*
*VEINES-intrinsic*

**Unsuccessful UACDT**

*SF-36 Physical Health*
*SF-36 Social Health*
*SF-36 Role Physical Limitations*
*SF-36 Role Mental Limitations*
*SF-36 Mental Health*
*SF-36 Vitality*
*SF-36 Pain*
*SF-36 General Health*
*SF-36 Health Change*
*EQ5D*
*VEINES-total*
*VEINES-intrinsic*

\[ P = 0.001 \]
CAVA\textsuperscript{1} – Subanalysis Thrombolysis

Quality of Life

\begin{align*}
P &= 0.045
\end{align*}
CAVA¹ – Subanalysis Thrombolysis

Quality of Life

**Successful UACDT**

- SF-36 Physical Health
- SF-36 Social Health
- SF-36 Role Physical Limitations
- SF-36 Role Mental Limitations
- SF-36 Mental Health
- SF-36 Vitality
- SF-36 General Health
- SF-36 Health Change
- Pain Disability Index
- EQ5D
- VEINES-total
- VEINES-intrinsic

**Unsuccessful UACDT**

- SF-36 Physical Health
- SF-36 Social Health
- SF-36 Role Physical Limitations
- SF-36 Role Mental Limitations
- SF-36 Mental Health
- SF-36 Vitality
- SF-36 General Health
- SF-36 Health Change
- Pain Disability Index
- EQ5D
- VEINES-total
- VEINES-intrinsic

**P = 0.002**
Longterm follow-up CAVA trial:

<table>
<thead>
<tr>
<th></th>
<th>Additional Thrombolysis (n=62)</th>
<th>Standard Treatment (n=58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTS at final follow-up visit assessed by Villalta criteria</td>
<td>19 (30.6)</td>
<td>26 (44.8)</td>
</tr>
<tr>
<td>PTS diagnosed at final follow-up visit</td>
<td>3 (4.8)</td>
<td>5 (8.6)</td>
</tr>
<tr>
<td>None (&lt;5)</td>
<td>43 (69.4)</td>
<td>32 (55.2)</td>
</tr>
<tr>
<td>Mild (5–9)</td>
<td>5 (8.1)</td>
<td>12 (20.7)</td>
</tr>
<tr>
<td>Moderate (10–14)</td>
<td>13 (21.0)</td>
<td>10 (17.2)</td>
</tr>
<tr>
<td>Severe (≥15)</td>
<td>1 (1.6)</td>
<td>4 (6.9)</td>
</tr>
<tr>
<td>PTS at final follow-up visit according to the ISTH score</td>
<td>29 (46.8)</td>
<td>40 (69.0)</td>
</tr>
<tr>
<td>PTS diagnosed at final follow-up visit</td>
<td>5 (8.1)†</td>
<td>13 (22.4)†</td>
</tr>
<tr>
<td>None (&lt;5)</td>
<td>33 (53.2)†</td>
<td>18 (31.0)</td>
</tr>
<tr>
<td>Mild (5–9)</td>
<td>12 (19.4)†</td>
<td>24 (41.4)</td>
</tr>
<tr>
<td>Moderate (10–14)</td>
<td>15 (24.2)</td>
<td>12 (20.7)</td>
</tr>
<tr>
<td>Severe (≥15)</td>
<td>2 (3.2)</td>
<td>4 (6.9)</td>
</tr>
<tr>
<td>Mean venous clinical severity score at final follow-up visit</td>
<td>2.82±2.36</td>
<td>3.48±2.34</td>
</tr>
</tbody>
</table>

*P* < 0.05
MRV value:

- Normal
- Acute
- Subacute
- Old
- PTS
- Acute on chronic
## MRV value:

<table>
<thead>
<tr>
<th></th>
<th>Acute N = 27</th>
<th>Subacute N = 17</th>
<th>Old N = 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypointense signal intensity vein lumen</td>
<td>27 (100.0%)</td>
<td>17 (100.0%)</td>
<td>12 (100.0%)</td>
</tr>
<tr>
<td>Dilated vein *</td>
<td>27 (100.0%)</td>
<td>16 (94.1%)</td>
<td>3 (25.0%)</td>
</tr>
<tr>
<td>Signs of recanalization *</td>
<td>2 (7.4%)</td>
<td>17 (100.0%)</td>
<td>9 (75.0%)</td>
</tr>
<tr>
<td>Thickened vein wall with halo sign around vein *</td>
<td>0</td>
<td>17 (100.0%)</td>
<td>4 (33.3%)</td>
</tr>
<tr>
<td>Partial very hypointense vein lumen *</td>
<td>0</td>
<td>0</td>
<td>10 (83.3%)</td>
</tr>
<tr>
<td>Post-thrombotic scarring †</td>
<td>0</td>
<td>1 (5.9%)</td>
<td>4 (33.3%)</td>
</tr>
</tbody>
</table>

C. Arnoldussen et al under review
## MRV value:

<table>
<thead>
<tr>
<th>Duration of complaints at start</th>
<th>Acute (N=27)</th>
<th>Subacute (N=17)</th>
<th>Old (N=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- 0-7 days</td>
<td>9 (33.3%)</td>
<td>2 (11.8%)</td>
<td>0</td>
</tr>
<tr>
<td>- 7-14 days</td>
<td>12 (44.4%)</td>
<td>9 (52.9%)</td>
<td>4 (33.3%)</td>
</tr>
<tr>
<td>- 14-21 days §</td>
<td>4 (14.8%)</td>
<td>6 (35.3%)</td>
<td>7 (58.3%)</td>
</tr>
<tr>
<td>- &gt;21 days</td>
<td>1 (3.7%)</td>
<td>0</td>
<td>1 (8.3%)</td>
</tr>
<tr>
<td>- Unknown</td>
<td>1 (3.7%)</td>
<td>0</td>
<td>1 (1.8%)</td>
</tr>
</tbody>
</table>

| Successful thrombolysis §       | 19 (70.4%)  | 11 (64.7%)     | 2 (16.7%) |
| Total time of thrombolysis, hours – | 23.3 ± 7.4 | 47.9 ± 19.3    | 85.3 ± 16.3 |
Conclusions:

- **Low percentage of successful treatment with all available techniques**
  - CaVenT ?
  - CAVA 53,2 %
  - ATTRACT 50 % (subgroup analyses)

- **If thrombus removal is successful (patency restored to ≥90%),**
  - It **does** lower the incidence moderate and severe PTS;
  - It **does** have a positive effect on:
    - Generic QoL
    - Disease specific QoL
    - Villalta
    - VCSS

- **The success is mainly determined by**
  - Thrombus age detected with MRV (duration of symptoms)
  - technical issues
    - Material
    - Experience
Conclusions:

- Faster referral
  - Awareness
- Better preop workup
  - MRV (do not treat when the thrombus is old on the MRV!!)
- Better tools
  - Mechanical thrombectomy devices (Improve success rate!!)
  - Costs ↓
  - Bleeding complications ↓
  - Indications
    - Postop cancer
- Better scoring system
  - No Villalta
  - Adjusted VCSS
  - Venous claudication
  - QoL
Conclusion for the Debate:

YES:

Successful aggressive endovascular treatment for iliofemoral DVT does prevent PTS?