Why EKOS?
A future of an effective and smart treatment of thrombosis

More effective than normal CDT, easier than mechanical thrombectomy: my experience with EKOS™ in DVT and PAO patients

Marcus Treitl, MD, EBIR
Institute for Clinical Radiology
University Hospitals of Munich
Disclosure

Speaker name: Marcus Treitl

I have the following potential conflicts of interest to report:

- Consulting: Abbott, ab medica, Biotronik, BTG, Endoscout, Medtronic, Straub
The target for invasive treatment of DVT

- **Iliofemoral DVT**
  - includes iliac and femoral veins
  - Descending; originates in iliac veins
  - Often caused by iliac compression

- **Impact and course of iliofemoral DVT**
  - 20 – 25% of symptomatic DVTs
  - *With anticoagulation therapy (Heparin):*
    - 10% complete lysis within 10 days
  - *Follow-up studies 5 – 10 yrs. after sufficient anticoagulation*
    - 50% develop venous claudication
    - 86% develop venous ulcer
    - 95% develop valve insufficiency
    - Almost all suffer from chronic leg oedema
Available Treatment options for iliofemoral DVT

• Conservative: LMWH, followed by long term anticoagulation
  – Avoids PE, death, (recurrence)
  – High rate of PTS

• Catheter-directed thrombolysis (CDT)
  – Simple CDT: multi-hole catheter in thrombus

• Pharmaco-mechanical thrombolysis (PMT):
  – E.g. ultrasound assisted (EKOS™)
  – E.g. rheolytic: AngioJet™, etc.

• Isolated mechanical thrombectomy (MT)
  – Aspirex™, etc.
Role of residual thrombus

- Comerota AJ, et al.: effect of mechanical component on residual thrombus
  - 71 pat. with DVT: PMT (Trellis™ or EKOS™)

Postthrombotic morbidity correlates with degree of thrombus reduction

Postthrombotic morbidity correlates with residual thrombus following catheter-directed thrombolysis for iliofemoral deep vein thrombosis
Working hypothesis for acute treatment of iliofemoral dvt

Important reason for post thrombotic syndrome (PTS), therefore

1. Fast removal of thrombus can safe valve function and reduce the risk for PTS

2. Reduction of residual thrombus reduces risk for recurrence of DVT
   – 11 different trials demonstrated higher risk for DVT recurrence in case of residual thrombus
Male, 16yrs

- Acute abdominal pain and swelling of left leg for 10 days
- No thrombophilia known

Mechanical Thrombectomy (Aspirex™ 10F)

- Good result in fem-pop vein
- Large residual thrombus in common iliac vein

EKOS™ lysis for 24hrs

- 30mg / 24hrs
- Good thrombus reduction
- Restoration of flow after additional stenting
Female, 70yrs
- Breast-Ca. + Radiatio
- Upper venous congestion
- Bilateral thrombosis of subclavian vein

Bilat. EKOS™ lysis
- 30cm EKOS™ right
- 18cm EKOS™ left
- 30mg rtPA / 24 hrs

Control phlebo 24hrs
- Good recanalization right
- Partial recanalization left
- Ctd.- EKOS™ rs

Control phlebo 48hrs
- Good recanalization left
- PTA SCV (10 x 40mm) and Stent 14 x 40mm

Aftercare:
- Rivaroxaban 20mg/die for 6 months
- 1yr control: no recurrence

Control after 1 year
**EKOS™ in DVT: Available Data**

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients (n) / Lesions (n)</th>
<th>Duration of symptoms</th>
<th>Treatment length</th>
<th>Dosage rtPA (mg)</th>
<th>Technical success</th>
<th>Primary patency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tichelaar VY et al. CVIR (2016)</td>
<td>33 EKOS 62 sCDT</td>
<td>Acute &lt; 10d</td>
<td>24 – 120h</td>
<td>0.01mg/kg/h</td>
<td>100%</td>
<td>12M: 76 – 79%</td>
</tr>
<tr>
<td>Engelberger et al. Circ Cardiovasc Interv (2015)</td>
<td>24 EKOS™ 24 sCDT</td>
<td>acute</td>
<td>15h</td>
<td>20mg</td>
<td>100%</td>
<td>3M: 100% vs. 96%</td>
</tr>
<tr>
<td>Engelberger et al. Thromb Haemost (2013)</td>
<td>87</td>
<td>66% acute</td>
<td>15h ± 0.8 h</td>
<td>20mg</td>
<td>85%</td>
<td>12M: 87%</td>
</tr>
<tr>
<td>Dumantepe et al. Diag Interv Rad (2013)</td>
<td>26 / 80% unt. Ext.</td>
<td>6 – 183d</td>
<td>25.3 ± 5.3 h</td>
<td>37 ± 9 (0.02mg/kg/h)</td>
<td>53.8%</td>
<td>12M: 91.6%</td>
</tr>
<tr>
<td>Grommes et al. Eur J Vasc Endo S (2011)</td>
<td>12 / 13</td>
<td>0 – 21d</td>
<td>24 – 48h</td>
<td>Bolus 5mg 1mg/h</td>
<td>85%</td>
<td>7M: 100%</td>
</tr>
</tbody>
</table>

- High technical success rate, less residual thrombus
- Shorter treatment, shorter hospital stay (Tichelaar et al.)
- Treatment of underlying venous stenosis essential for long term clinical success
EKOS™ in DVT: own experience

- Since 2012: 73 patients with iliofemoral or upper extremity DVT
  - In 7 patients after unsuccessful MT
  - With involvement of caval vein: 8 (3 filtered)
  - PE during treatment: none
- Treatment time: $32.5 \pm 14h$ (min 24hrs, max. 48hrs)
- rtPA dosage: $45mg \pm 17mg$
  - Minor bleedings: 7 (puncture site)
  - Major bleedings: none

Primary patency: $n = 71$
- $> 90\%$ reduction of thrombus: 65
- $50 – 90\%$ reduction of thrombus: 4
- $< 50\%$ reduction of thrombus: 2
- No success: 2
- Success: 96.8\% ($71/73$)
Possible treatment algorithm DVT

Iliofemoral DVT

Yes
Mechanical thrombectomy

No success / not available
Open thrombectomy + AV fistula / bypass

Success?
Oral anticoagulation

Success?

No

Contraindications for thrombolysis

Age unclear / long lesions:
Pharmacomechanical thrombolysis (EKOS™)

Short lesions / short onset:
Mechanical thrombectomy (Aspirex™)

No

Success?

Plus stenting of underlying obstruction!

Adapted from Grommes / Wittens
Treatment options for arterial thrombembolic / bypass occlusions

- Emergency: fast restoration of flow mandatory
- Endovascular treatment for Rutherford I / IIa
- Aspiration thrombectomy
  - Short occlusions
  - Straight vessel anatomy
  - Blood loss, risk of dissection and distal embolization
- Mechanical thrombectomy
  - Longer occlusions
  - Blood loss, expert tool, risk of perforation and distal embolization
  - Not all vascular beds
- Standard Catheter directed thrombolysis
  - Any occlusion length
  - Any vascular bed
  - ICU-stay, risk of bleeding, contraindications
- Ultrasound-assisted thrombolysis
  - Any occlusion length
  - Any vascular bed
  - ICU-stay, risk of bleeding, contraindications
  - Thought to: reduce dose / length of ICU stay / be more effective than sCDT
Our rationale for use of EKOS™

• Venous or composite bypass
  – No risk of rupture of venous component
• Recently implanted bypass (> 14 days < 8 weeks)
  – No risk to capture intraluminal sutures / destroy anastomosis
• Chronic recurrent bypass occlusions with high burden of older thrombus
  – Insufficient removal of wall adherent thrombus
• Single vessel run off
  – No / lower risk of distal embolization with EKOS
• Experience of user
  – Not all staff trained with use of mechanical thrombectomy
• In our experience more effective than sCDT
  – Shorter treatment length
  – Lower total dose of rt-PA
Female, 85yrs
Femoro-crural ePTFE bypass

8/2012: Rotarex™ thrombectomy of acute occlusion

1/2014: Re-Occlusion

EKOS™-Lysis:
50cm working length
rt-PA:
2mg/h for 5hrs
1mg/h for 13hrs
Total dose: 23mg
Duration: 18hrs
No bleeding

1/2017: Re-Occlusion

After EKOS™-thrombolysis 2-fold increased patency in comparison to mechanical thrombectomy

1/2017: sCDT for 3 days (!) with insufficient result +
- Severe bleeding complications
- Re-occlusion
- Amputation
- Death
Male, 76yrs
Iliaco-visceral triple bypass after peri-renal aortic aneurysm

11/2013: acute occlusion after myocardial infarction untreated for 6 weeks
Patient under dialysis

First attempt: Rotarex™ 8F
EKOS™ Lysis: 20hrs 25mg rt-PA

Renal function recovered
Dialysis could be stopped

Mechanical thrombectomy:
- deficient thrombus clearance
- Risk of rupture in anastomotic region (single kidney)

EKOS™:
- complete thrombus clearance
- Atraumatic clearance of the anastomotic region
## EKOS™ in PAO: Available Data

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients (n) / Lesions (n)</th>
<th>Duration of treatment</th>
<th>Mean treatment length</th>
<th>Dosage lysis</th>
<th>Technical success</th>
<th>Primary patency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wissgott et al.</td>
<td>25 arterial occlusions</td>
<td>16.9h</td>
<td>25.1cm</td>
<td>rt-PA 1mg/h</td>
<td>100%</td>
<td>1M: 80%</td>
</tr>
<tr>
<td>JEV (2007)</td>
<td></td>
<td></td>
<td></td>
<td>Mean: 17mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wissgott et al.</td>
<td>20 fem-pop Bypasses</td>
<td>904min vs 64.5 min</td>
<td>33.1 / 33.7cm</td>
<td>rt-PA 1mg/h</td>
<td>90% vs. 100%</td>
<td>N/A</td>
</tr>
<tr>
<td>RöFo (2008)</td>
<td>EKOS™ vs. Rotarex 1:1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schrijver et al.</td>
<td>57 / 62 arterial occlusions</td>
<td>21h</td>
<td>N/A</td>
<td>Urokinase 100,000IU/h</td>
<td>97%</td>
<td>6M: 82.3%</td>
</tr>
<tr>
<td>J Cardiovasc Surg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2011)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schrijver et al.</td>
<td>60 arterial occlusions</td>
<td>17.7h vs. 29.5h</td>
<td>32 vs. 29cm</td>
<td>Urokinase 1.8Mil vs. 2.8Mil IU</td>
<td>75% vs. 84%</td>
<td>1M: 71% vs. 82%</td>
</tr>
<tr>
<td>J EVT (2015)</td>
<td>EKOS™ vs. sCDT 28:32</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
EKOS™ in PAO: own experience

• Since 2012: 27 patients with
  – Bypass occlusion: ePTFE / composite = 16; vein = 11
  – EKOS after failure of mechanical thrombectomy: n = 9
• Treatment time: 29.3 ± 16.6h (median 24hrs, min 16hrs, max. 29hrs)
  – Compared to historic sCDT: 48 ± 24h
• rtPA dosage: 31mg ± 14.5mg (median 25mg)
  – Compared to historic sCDT: 58 ± 39mg
  – Minor bleedings: 6 (puncture site)
  – Major bleedings: 1 (2 re-do thrombolysis within 14 days; unknown disease)
• Technical success:
  – n = 26; 96.3%
• Follow-Up: 18 ± 11 mths
  – Primary patency: 93.7%
    • Compared to historic own sCDT results: PP = 78.2%
Possible decision pathway arterial thrombembolic occlusions

Acute arterial / bypass occlusion

Rutherford IIb or higher

Yes

Surgical thrombectomy

Catheter aspiration

≤ 10cm in length

No

≤ 10cm in length

No

ePTFE Bypass
First occlusion
Straight Anastomosis
> 8 weeks implanted
> 1 vessel run off

No

Vein or composite Bypass
Recurrent occlusion
Angled anastomosis
< 8 weeks
Single vessel run off

Mech. thrombectomy
Rotarex™

Success?

No

Ultrasound-assisted thrombolysis with EKOS™

Plus PTA of stenosis of anastomosis
Comparison of PMT with EKOS™ vs. MT in DVT and PAO

<table>
<thead>
<tr>
<th>Mechanical thrombectomy</th>
<th>Thrombolysis with EKOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefits</td>
<td>Benefits</td>
</tr>
<tr>
<td>Often single session</td>
<td>Easy, no expert tool</td>
</tr>
<tr>
<td>Immediate restoration of flow</td>
<td>Short session times</td>
</tr>
<tr>
<td>No complications by systemic action of lysis</td>
<td>Better thrombus clearance (even wall adherent thrombus)</td>
</tr>
<tr>
<td>Better reimbursement</td>
<td>Lower risk of distal embolization</td>
</tr>
</tbody>
</table>
EKOS™: Tips, tricks, pitfalls

• Instruct ICU staff!
• In case of longer transit times to ICU:
  – Start thrombolysis in cath lab or block catheter with rtPA
• In case of frequent temperature alarms:
  – Increase coolant flow up to 70ml / hr
• In case of multiple vascular beds involved:
  – Several EKOS™ catheters usable (depends on main units available)
  – Keep total dose of drug in mind!
Summary and conclusions

• EKOS™ for treatment of DVT and PAO:
  • PMT is important supplement to interventional arsenal
  • Especially in complex situations or with less experienced staff: less risky than MT
  • In our experience
    • Shorter treatments / lower dosages than sCDT
    • Especially beneficial in arterial / venous occlusions of unclear age
Thank you very much for your attention!

- CORRESPONDING AUTHOR:
  Prof. Dr. med. Marcus Treitl, EBIR, MBA
  Hospitals of the Ludwig-Maximilians-University of Munich
  Institute for Clinical Radiology

- Fon: +49-89-44005-9240
- E-Mail: mtreitl@med.uni-muenchen.de
- Internet: www.klinikum.uni-muenchen.de
  www.radiologie-lmu.de
Why EKOS?
A future of an effective and smart treatment of thrombosis

More effective than normal CDT, easier than mechanical thrombectomy: my experience with EKOS™ in DVT and PAO patients

Marcus Treitl, MD, EBIR
Institute for Clinical Radiology
University Hospitals of Munich