Status of anticoagulation therapy in 2016: Is there a need for venous revascularization?

Rupert M. Bauersachs

Dept. of Vascular Medicine, Darmstadt
Center of Thrombosis Hemostasis, Mainz
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Disclosures

Research support / Principal Investigator:
Bayer, BMS, Boehringer, Daiichi-Sankyo, Leo, Pfizer, Portola

Consultant & Speakers Bureau:
Bayer, BMS, Boehringer, Daiichi-Sankyo, Pfizer

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Status of anticoagulation in 2016: Need for venous revascularization?

- Guidelines, State of the Art
- Current Evidence for Anticoagulation
- Need for Revascularization?
- Current Evidence
In proximal DVT we recommend long-term anticoagulant therapy over no such therapy (1B)…. we suggest dabigatran, rivaroxaban, apixaban or edoxaban over VKA therapy (all 2B).

NOAC Meta-analyses: significant reduction in major bleeding ≈40%
Significantly reduced intracranial and fatal bleedings and CR-NMB.
Results consistent for several sub-groups, e.g.
• Body weight > 100 kg; GFR <60 ml/min; age > 75 y; cancer
Evidence: Which concepts have been studied?

**Standard-Therapy**

- **LMWH /VKA**

**Rivaroxaban (Xarelto®)**
- Single-drug
  - Day 5–11
  - 2x15 mg
  - 3 wks
  - 1x20 Rivaroxaban

**Apixaban (Eliquis®)**
- Single-drug
  - 2x10mg
  - 1wk
  - 2x5 mg Apixaban

**Dabigatran (Pradaxa®)**
- LMWH Acute treatment
  - Paren-teral AC ≥ 5d
  - Dabigatran 2x 150 mg

**Edoxaban (Lixiana®)**
- LMWH Acute treatment
  - Paren-teral AC ≥ 5d
  - Edoxaban 1x60 mg

**Switching**

**Heparin**
- **VKA**
- **VTE**
- **MB**
- **CRB**

**Evidence:** Which concepts have been studied?

- **VTE**
- **MB**
- **CRB**
Evidence: Which concepts have been studied?

Standard-Therapy
LMWH /VKA

Rivaroxaban (Xarelto®)
Single-drug

Apixaban (Eliquis®)
Single-drug

Dabigatran (Pradaxa®)
LMWH Acute treatment

Edoxaban (Lixiana®)
LMWH Acute treatment

Single-drug approach

Rivaroxaban (Xarelto®)

Apixaban (Eliquis®)

Dabigatran (Pradaxa®)

Edoxaban (Lixiana®)

Switching

Heparin

VKA

Single-drug approach

Day 5–11
Week 3

Paren-teral AC ≥ 5d

Paren-teral AC ≥ 5d

Day 5–11
Week 3

Evidence:
Which concepts have been studied?
Evidence: Which concepts have been studied?

Recurrent VTE

Combined (random) 271/13430 (2.0%) 301/13442 (2.2%)

Major Bleeding

Evidence: Which concepts have been studied?

- **Standard-Therapy**
  - LMWH / VKA
  
- **Heparin**
  - VKA

**RCT NOACs**

**RCT**

with PTS as an endpoint

**Graphs**

- **PE**
  - DVT

- **CDT**
  - DVT
Revascularization Treatment

Inclusion
Iliofemoral vein thrombosis:
- common iliac vein
- combined iliofemoral segment
- upper half of the thigh

PTA | Stents | Aspiration | Caval Filter
---|---|---|---
23 | 15 | 1 | 1

Score >5 (6Mo) severe PTS Ulcer
<5 = No PTS
5-9 = mild PTS
10-14 = moderate PTS
≥15 = severe PTS

Revascularization Treatment

N=90 CDT + Standard

24 mts FU

N=99 Standard

Revascularization Treatment

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<th>CDT N=90</th>
<th>Standard n=99</th>
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*abdominal wall haematoma req. transfusion, compartment syndrome req. surgery puncture site haematoma

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*abdominal wall haematoma req. transfusion, compartment syndrome req. surgery puncture site haematoma

CDT
- Phlebography
- Puncture popliteal vein
- Flouroscopy
- Several days of bed-rest during Infusion
- 2nd Phlebography
- UFH-Infusion
- APTT monitoring

Revascularization Treatment

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*abdominal wall haematoma req. transfusion, compartment syndrome reg. surgery puncture site haematoma

**Benefit with CDT (24 Months FU):**
moderate PTS reduced by 14.4% (55 % => 41 %)
Quality of life identical

Revascularization Treatment

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**Subtherapeutic anticoagulation is associated with increased PTS**

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<td>INR &lt;2 for &gt;20% of the time</td>
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<td>INR &lt;2 for &gt;50% of the time</td>
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OR (95%CI) for PTS

INR <2 for >20% of the time 1.9 (1.2–3.1)

INR <2 for >50% of the time 2.7 (1.4–5.1)

⇒ Benefit with CDT (24 Months FU):
moderate PTS reduced by 14.4% (55 % => 41 %)

Quality of life identical

Rivaroxaban dose - finding studies

≥4-point improvement in thrombus burden by CCUS without recurrent VTE

Without recurrent VTE
Per-protocol population (n=528)

Rivaroxaban Phase III studies

N=335

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<th>Enox / VKA</th>
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<tr>
<td>Age (yrs)</td>
<td>58±16</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>59 %</td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td>57 mts (48-64)</td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban/VKA</td>
<td>48 / 52 %</td>
<td></td>
</tr>
<tr>
<td>Good Compliance</td>
<td>94% (R) vs 75% (E)</td>
<td></td>
</tr>
<tr>
<td>ECS</td>
<td>69% (R) vs 80% (E)</td>
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RR 0.74; (0.54–1.01).

Middeldorp S et al JTH 2015, 13 (Suppl. 2) 219-220
# Institutional Volume on Outcome in CDT

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<tr>
<th></th>
<th>Hi-Vol Centers ≥6/y</th>
<th>Low-Vol Centers &lt;6/y</th>
<th>NOACs</th>
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<tbody>
<tr>
<td>n</td>
<td>1.310</td>
<td>1.310</td>
<td>13.512</td>
</tr>
<tr>
<td>Complication - Period</td>
<td>6 days</td>
<td>6 days</td>
<td>6 months</td>
</tr>
<tr>
<td>Age</td>
<td>53.3</td>
<td>53.2</td>
<td>55 (18–97)</td>
</tr>
<tr>
<td>Intracranial hemorrhage, (%)</td>
<td>0.4</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Blood transfusion, (%)</td>
<td>10.4</td>
<td>10.8</td>
<td>All major: 1.0</td>
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<td>GI bleed, (%)</td>
<td>1.4</td>
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<td>Pulmonary embolism, (%)</td>
<td>18.4</td>
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<td>Hematoma, (%)</td>
<td>2.8</td>
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<tr>
<td>IVC filters, (%)</td>
<td>37.0</td>
<td>32.8</td>
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<tr>
<td>Not hospitalized</td>
<td>0</td>
<td>0</td>
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<td>Charges, median, $</td>
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Anticoagulation 2016 - Need for revascularization?

Conclusion

- Abundance of evidence
- High efficacy (2.0% rec.VTE) and high safety (1.1% Major Bleed)
- High QoL Scores

Any proposed additional treatment has to provide evidence that it surpasses the current standard

DVT treatment – ACTS Burdens*1

Thank you very much for your attention!
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7. FRANKFURTER GERINNUNGSSYMPOSIUM

2. – 3. SEPTEMBER 2016