Überbrückungstherapie beim antikoagulierten Patienten

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Disclosures

Consultancies, member of advisory boards, speaker fees

Boehringer-Ingelheim
Bayer Healthcare
Daiichi-Sankyo
Bristol Myers Squibb
Pfizer
Anticoagulants

• Vitamin K antagonists (VKA)
  – Phenprocoumon (Marcoumar)
  – Acenocoumarol (Sintrom)

• Direct oral anticoagulants (DOAC)
  – Dabigatran (Pradaxa)
  – Rivaroxaban (Xarelto)
  – Apixaban (Eliquis)
  – Edoxaban (Lixiana)
## Bridging: meta-analysis

<table>
<thead>
<tr>
<th>Group</th>
<th>TE Events</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>Bridged cohort</td>
<td>0.9% (0.0-3.4)</td>
</tr>
<tr>
<td>LMWH dose</td>
<td></td>
</tr>
<tr>
<td>therapeutic</td>
<td>0.4% (0.0-0.9)</td>
</tr>
<tr>
<td>prophylactic/intermediate</td>
<td>0.2% (0.0-0.6)</td>
</tr>
<tr>
<td>Nonbridged cohort</td>
<td>0.6% (0.0-1.2)</td>
</tr>
</tbody>
</table>
Bridging – bleeding risk: meta-analysis

<table>
<thead>
<tr>
<th>Group</th>
<th>TE Events % (95% CI)</th>
<th>Major Bleeding % (95% CI)</th>
<th>Overall Bleeding % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bridged cohort</td>
<td>0.9% (0.0-3.4)</td>
<td>4.2% (0.0-11.3)</td>
<td>13.1% (0.0-45.2)</td>
</tr>
<tr>
<td>LMWH dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>therapeutic prophylactic/intermediate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bridging</td>
<td>3.2% (1.3-5.2)</td>
<td>3.4% (0.0-8.7)</td>
<td>13.6% (2.9-24.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>8.5% (2.9-14.2)</td>
</tr>
<tr>
<td>Non-bridged cohort</td>
<td>0.6% (0.0-1.2)</td>
<td>0.9% (0.2-1.6)</td>
<td>3.4% (1.1-5.8)</td>
</tr>
</tbody>
</table>
Periprocedural Management

Bleeding risk

Thrombotic risk
Periprocedural Management (Scenario 1)

Bleeding risk
→
low
→
Do not stop anticoagulants

Thrombotic risk
Low bleeding risk → do not stop anticoagulation

- Tooth extraction
- Root canal procedures
- Small skin excisions
- Endoscopic procedures for diagnosis
- Cataract surgery
- Pacemaker, loop recorder, defibrillator
Low bleeding risk → do not stop anticoagulation

- **VKA**: INR < 3
- **DOAC**: at trough level (skip morning dose)
Periprocedural Management

Bleeding risk

\[
\text{high} \quad \downarrow \quad \downarrow \quad \downarrow
\]

stop anticoagulants

Thrombotic risk
High bleeding risk → stop anticoagulation

- Intracranial or intraspinal surgery
- Major vascular surgery
- Major orthopedic surgery
- Major cancer surgery
- Urogenital surgery
- Colon polypectomy
- Organ biopsy

Consult interventionist
Periprocedural Management (Scenario 2)

- **Bleeding risk**: high → stop anticoagulants
- **Thrombotic risk**: low → Do not bridge
Low thrombosis risk → do not bridge

- Non-valvular atrial fibrillation (CHA$_2$DS$_2$-Vasc ≤ 3, no prior stroke)
- Mechanical aortic valve prosthesis (no additional risk factor)
- VTE > 3 months
Periprocedural Management (Scenario 3)

**Bleeding risk**
- high
- stop anticoagulants

**Thrombotic risk**
- high
- bridge
High thrombosis risk → bridge

- Non-valvular atrial fibrillation (CHA\textsubscript{2}DS\textsubscript{2}-Vasc ≥ 4, prior stroke)
- Mechanical mitral valve prosthesis
- Mechanical aortic valve prosthesis + additional risk factor(s)
- VTE < 3 months
Bridging – 3 steps

1. Stop oral anticoagulant
2. Choose alternative anticoagulant
3. Switch from alternative anticoagulant to oral anticoagulant
When to stop oral anticoagulants before surgery??

- NOT TOO EARLY!

- VKA
  - Phenprocoumon: 7 days before procedure
  - Acenocoumarol: 2 days before procedure

- DOAC
  - according to kidney function and type of surgery

Bridging usually not required for patients treated with acenocoumarol or a DOAC
Which anticoagulant? At what dose?

- **LMWH**
  - at therapeutic dose, once or twice daily
- **Unfractionated heparin**
  - at therapeutic dose (~ 1.5-fold PTT prolongation)
- (Bivalirudin)
- (Fondaparinux)
From when on?

- INR < 2.0 (2.5)
When to stop heparin before surgery?

- LMWH: (at least) 1 day
- Unfractionated heparin: 1 hour
After surgery: when to resume and at what dose?

- Prophylactic LMWH: day of surgery
- Therapeutic LMWH: $\geq$ 48 hours after surgery
- VKA: day after surgery (at maintenance dose)
- DOAC: $\geq$ 48 hours after surgery
- **Stop warfarin**
- **Stop acenocoumarol**

### THROMBOPROPHYLAXIS

- **Days**
  - -6
  - -5
  - -4
  - -3
  - -2
  - -1
  - 0P

#### Check INR
- **if > 2.0 (>2.5): check daily**
- **if < 2.0 (<2.5): LMWH (except low thrombotic risk)**
- **if < 1.5: surgery possible**

- **Check INR**
  - **if > 2.0: 6-10 mg vit. K p.o.**
High THROMBOTIC RISK

RESUME VKA

STOP LMWH IF INR >2.0

LMWH DOSE

PROPHYLACTIC

THERAPEUTIC

Low THROMBOTIC RISK

RESUME VKA

STOP LMWH IF INR >2.0

USUAL THROMBOPROPHYLAXIS

DAYS

OP +1 +2 +3 +4 +5 +6
Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation

BRIDGE Study

- Mean age 74 yrs, 74% males
- Mean body weight 96 kgs
- Mean CHADS\(_2\) score 2.3
- 12% had a CHADS\(_2\) score \(\geq 4\)
- Patients with mechanical heart valves excluded
- 42% received a platelet inhibitor
- 89% underwent a procedure classified as „minor“
## BRIDGE Study

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No Bridging (N=918)</th>
<th>Bridging (N=895)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>number of patients (percent)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Primary</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial thromboembolism</td>
<td>4 (0.4)</td>
<td>3 (0.3)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>2 (0.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>2 (0.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic embolism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td></td>
<td>29 (3.2)</td>
<td>0.005†</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>5 (0.5)</td>
<td>4 (0.4)</td>
<td>0.88†</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>7 (0.8)</td>
<td>14 (1.6)</td>
<td>0.10†</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>0</td>
<td>1 (0.1)</td>
<td>0.25†</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>0</td>
<td>1 (0.1)</td>
<td>0.25†</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>110 (12.0)</td>
<td>187 (20.9)</td>
<td>&lt;0.001†</td>
</tr>
</tbody>
</table>
Perioprocedural Management

Direct oral anticoagulants

Stop

Start
DOAC - Perioperative management

- Do not bridge
- Do not monitor with coagulation tests
## Elective surgery/interventions - dabigatran

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<th>Renal function (CrCl in ml/min)</th>
<th>Half life</th>
<th>Last intake before surgery</th>
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<tr>
<td></td>
<td></td>
<td><strong>High bleeding risk or major surgery</strong></td>
</tr>
<tr>
<td>≥ 80</td>
<td>~ 13 h</td>
<td>≥48 h</td>
</tr>
<tr>
<td>≥ 50 to &lt; 80</td>
<td>~ 15 h</td>
<td>≥72 h</td>
</tr>
<tr>
<td>≥ 30 to &lt; 50</td>
<td>~ 18 h</td>
<td>≥96 h</td>
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EHRA guidelines, Heidbuchel, Eur Heart J 2013
## Elective surgery/interventions - apixaban, rivaroxaban

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Postoperative management

- Not licensed for postoperative thromboprophylaxis except for elective hip/knee replacement
- Maximum concentration within 2-3 hours
- Therapeutic dose not before 48-72 h postop.
- Prophylactic LMWH dose until it is safe to use therapeutic dose
Bridging - Conclusion

• confers a considerable risk of bleeding
• only for patients with (very) high thrombosis risk
• only for patients on a long-acting VKA
• not for patients on a DOAC