Bridging Anticoagulation with Oral Anticoagulants

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Indication for Anticoagulation Therapy

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Mechanical Heart Valve</th>
<th>Atrial Fibrillation</th>
<th>VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Risk</td>
<td>Any mechanical MVR</td>
<td>CHADS2 score 5-6</td>
<td>VTE + 3 mo</td>
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<tr>
<td></td>
<td>Old atrial fibrillation</td>
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<tr>
<td></td>
<td>Recent CVA or TIA &lt;6 mo</td>
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<tr>
<td></td>
<td>Severe thrombophilia</td>
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<tr>
<td></td>
<td>Antiphospholipid Ab</td>
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<td></td>
</tr>
<tr>
<td>Moderate Risk</td>
<td>Any mechanical MVR</td>
<td>CHADS2 score 3-4</td>
<td>VTE + 6 mo</td>
</tr>
<tr>
<td></td>
<td>Old atrial fibrillation</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Recent CVA or TIA &lt;6 mo</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Non-severe thrombophilia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low Risk</td>
<td>Any mechanical MVR</td>
<td>CHADS2 score 0-2</td>
<td>VTE + 12 mo</td>
</tr>
<tr>
<td></td>
<td>Old atrial fibrillation</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Recent CVA or TIA &lt;6 mo</td>
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</tbody>
</table>

Perioperative Management of Anticoagulation: To Bridge or Not to Bridge

- Additional Risk Stratification
  - Procedure-related thromboembolism risk (ATE and VTE)
  - Procedure-related bleeding risk
  - Pharmacokinetics of OAC medications (renal function)
  - Ability to administer and absorb

Surgical and Invasive Procedures: Suggested Stratification by Bleeding Risk

Meta-analysis of peri-procedural OAC management in 12,278 patients

No difference in perioperative thromboembolism

3x to 5x increased risk of perioperative bleeding with bridging

Disclosures

Timothy K. Liem, MD discloses the following:
* None
1884 pts with atrial fibrillation who had perioperative interruption of warfarin 5 days prior to surgery. Randomized to:

- LMWH (preop days 3-1)
- Placebo (preop days 3-1)

Surgery

- Warfarin restarted POD 0-1

Placebo Low bleed risk - 12-24 hrs postop
High bleed risk - 48-72 hrs postop

LMWH Low bleed risk - 12-24 hrs postop
High bleed risk - 48-72 hrs postop

continued until INR >2.0


In patients with a-fib who had warfarin interrupted for elective procedures:

- Forgoing bridging anticoagulation was non-inferior to LMWH bridging for prevention of arterial thromboembolism, and decreased the risk of major bleeding.

Limitations:
- Only 3% had CHADS2 score 5-6
- Only 11% had major surgery


A Double Blind Randomized Control Trial of Postoperative Low Molecular Weight Heparin Bridging Therapy Versus Placebo Bridging Therapy for Patients Who Are at High Risk for Arterial Thromboembolism (PERIOP 2)

1773 pts with prosthetic heart valves or high risk a-fib/a-flutter who require elective non-cardiac surgery or invasive procedure requiring VKA reversal

- VKA stopped 5 d preop
- LMWH Tx dosing (preop days 3-1)
- Surgery
- Warfarin restarted POD 0-1
- LMWH High bleed risk - Px dose (postop day 1) Low bleed risk - Tx dose
- Placebo (postop day 1)
- continued until INR >2.0

www.clinicaltrials.gov

541 pts underwent 324 (60%) standard-risk and 217 (40%) high-risk procedures.

- Dabigatran stopped 1-6 days preop
- Minor procedures: Resumed at ½ dose (75mg) POD #0
- Major procedures: Resumed at full dose at 48-72 hrs (unless NPO/ epidural)
- Major bleeding 1.8%
- Minor bleeding 5.2%
- Periop thromboembolism 0.2%

Adapted from Spyropoulos, JTH 2016

High Bleeding Risk
- DOAC: Interrupt DOAC therapy
- Bridging NOT suggested
- Warfarin: Interrupt VKA with LMWH bridging suggested

Moderate Risk
- DOAC: Interrupt DOAC therapy
- Bridging NOT suggested
- Warfarin: Consider interrupting VKA without bridging

Low Risk
- DOAC: Interrupt DOAC therapy
- Bridging NOT suggested
- Warfarin: Interrupt VKA

** May administer LMWH VTE prophylaxis

November 14-16, 2017, Veith Symposium, New York, NY

Perioperative Management of Dabigatran: A Perspective Cohort Study

S. S. Schulman, MD, PhD, Marc Gurwitz, MD, Eric Agnis VN-Lee, MD, MS, N. Shapshay, MD, PhD, Shahnaz R. Khan, MFSc, I. A. Agnis VN, MD, MMSc, Nancy Holbrook, MSc, James D. Douketis, MD, on behalf of the Dabigatran Study Group

Periprocedure (30-d)
Thromboembolism
Risk vs VKA
HR (95% CI)
1.01 (0.35-2.87)
P=0.99
0.74 (0.36-1.50)
P=0.40
0.60 (0.32-1.12)
P=NS

Periprocedure (30-d)
Bleeding Risk vs VKA
HR (95% CI)
1.09 (0.80-1.49)
P=0.58
1.26 (0.80-2.00)
P=0.34
0.85 (0.61-1.21)
P=NS

Shulman, Circulation 2015

Perioperative bridging anticoagulation in patients with atrial fibrillation

11/18/2017
### Periprocedural management of patients receiving a vitamin K antagonist or a direct oral anticoagulant requiring an elective procedure or surgery

<table>
<thead>
<tr>
<th></th>
<th>Low Bleed Risk Surgery</th>
<th>High Bleed Risk Surgery</th>
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<tbody>
<tr>
<td><strong>Dabigatran</strong></td>
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<tr>
<td>CrCl &gt; 50</td>
<td>LAST DOSE: 2d preop</td>
<td>LAST DOSE: 2d preop</td>
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<tr>
<td>CrCl 30-50</td>
<td>3d preop</td>
<td>4d-5d preop</td>
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<tr>
<td></td>
<td>RESUME</td>
<td>RESUME</td>
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<tr>
<td></td>
<td>~24h postop</td>
<td>48h-72h postop*</td>
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<tr>
<td><strong>Rivaroxaban</strong></td>
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<tr>
<td>CrCl &gt; 30</td>
<td>2d preop</td>
<td>3d preop</td>
</tr>
<tr>
<td>CrCl 15-30</td>
<td>Individualize</td>
<td>Individualize</td>
</tr>
<tr>
<td></td>
<td>~24h postop</td>
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<tr>
<td><strong>Apixaban</strong></td>
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<tr>
<td>CrCl &gt; 30</td>
<td>2d preop</td>
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<tr>
<td>CrCl 15-30</td>
<td>Individualize</td>
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<tr>
<td><strong>Edoxaban</strong></td>
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<tr>
<td>CrCl &gt; 50</td>
<td>2d preop</td>
<td>3d preop</td>
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</table>

* Assumes adequate GI absorptive capacity and no neuraxial anesthetic

Adapted from Spyropoulos, JTH 2016

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### Summary

- The perioperative management of OAC is complex and is dependent on numerous factors:
  - Risk for periop thromboembolism
  - Type of surgery/procedure (minimal/ moderate/ high risk)
  - Clinical characteristic of the anticoagulant (half-life, renal excretion, drug interactions)
  - Absorptive function of the GI tract
  - Neuraxial anesthetic adjuncts

- Avoidance of perioperative bridging may be a safer strategy, especially in patients at moderate- and low-risk for thromboembolism.