Management of Anticoagulation in the Peri-Procedural Period (MAPPP) App:

Overview, Instructions and Case Studies

May 12, 2017
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Origin of the MAPPP app

- Evidence based clinician’s guide developed by the multidisciplinary members of the Peri-Procedural Task Force of the NYS Anticoagulation Coalition and IPRO, the CMS designated Quality Improvement Organization for NYS

- Task Force Lead: Dr. Alex Spyropoulos

- Members: Darren Triller, Jason Gilleylen, Peter Kouides, Carol Patrick, Katherine Cabral, MaryAnne Cronin, Patrick Meek, Anne Myrka, Susan Wymer
Why is Perioperative Anticoagulant Management Relevant?

- Perioperative management of patients on chronic warfarin is common…
  - 400,000-500,000 patients per year in North America alone
  - ~1 in 6 to 10 patients receiving long-term warfarin are assessed for periprocedural management annually
  - Every NYS Medicare beneficiary undergoes approximately 2 procedures annually requiring anticoagulant interruption

IPRO analysis of Medicare Fee for Service Claims 8/2014 –7/2015
The Perioperative Management of Antithrombotic Therapy*

American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition)

James D. Douketis, MD, FRCP(C); Peter B. Berger, MD, FACP; Andrew S. Dunn, MD, FACP; Amir K. Jaffer, MD; Alex C. Spyropoulos, MD, FACP, FCCP; Richard C. Becker, MD, FACP, FCCP; and Jack Ansell, MD, FACP, FCCP

Chest 2008;133;299-339

Periprocedural management of patients receiving a vitamin K antagonist or a direct oral anticoagulant requiring an elective procedure or surgery

A. C. Spyropoulos, A. Al-Badri, M. W. Sherwood and J. D. Douketis

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EXPERT CONSENSUS DECISION PATHWAY

2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients With Nonvalvular Atrial Fibrillation


Periprocedural Management of Anticoagulation

John U. Doherty, MD, FACC, Chair

Ty J. Gluckman, MD, FACC

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Thomas L. Ortel, MD, PhD

Sherry J. Saxonhouse, MD, FACC

Sarah A. Spinler, PharmD, AACC
Anticoagulant Overview

- **Warfarin**
- **Direct Oral Anticoagulants (DOACs)**
  - Pradaxa® (dabigatran)
  - Xarelto® (rivaroxaban)
  - Eliquis® (apixaban)
  - Savaysa® (edoxaban)
- **Common DOAC characteristics**
  - More consistent effects at fixed doses
  - Lack of routine laboratory testing
  - Rapid onset of effects (anticoagulation achieved ~2 hrs)
  - Rapid loss of activity (e.g. when doses missed)
Significance of the MAPPP App

Clinical Decision Support that guides:

- Whether to interrupt anticoagulation for a procedure by balancing:
  - Risk of bleeding from procedure
  - Risk of thrombosis from underlying indication
- Timing for interruption of anticoagulation
- Peri-procedural “bridging” when appropriate
- Clinical monitoring
- Timing and dosing for resumption of anticoagulants
Overview
Perioperative Management of Anticoagulation

Patient Risk Factors (congenital and acquired)
Bleeding ↔ Thrombosis
Risk Stratification

Surgical Risk Factors
Bleeding ↔ Thrombosis
Risk Stratification
Suggested Thromboembolic Risk Stratification when Discontinuing VKAs

**High**
Atrial Fibrillation
- recent (<3 months) stroke/TIA
- CHADS score 5-6
- rheumatic heart disease

Mechanical Heart Valves
- any caged-ball or tilting disc valve in mitral/aortic position
- any mitral valve prosthesis
- Recent (within 6 mos) stroke/TIA

Venous Thromboembolism (VTE)
- VTE within past 3 months
- severe thrombophilia
- deficiency of protein C, protein S or antithrombin
- antiphospholipid antibodies
- multiple thrombophilias

**Moderate**
Atrial Fibrillation
- CHADS score 3-4

Mechanical Heart Valves
- bileaflet AVR *with* major risk factors

VTE
- VTE within past 3-12 months
- Nonsevere thrombophilia
- Active cancer
- Recurrent VTE

**Low**
Atrial Fibrillation
- CHADS score 0-2

Mechanical Heart Valves
- bileaflet AVR *without* major risk factors

VTE
- VTE more than 12 months ago

Douketis J et al Chest 2008; 133:299 339S
# Suggested Procedural Bleed Risk

<table>
<thead>
<tr>
<th>HIGH BLEEDING RISK PROCEDURES (2 day risk of major bleed ≥ 2%)</th>
<th>LOW BLEEDING RISK PROCEDURES (2 day risk of major bleed &lt;2%)</th>
<th>MINIMAL BLEEDING RISK PROCEDURES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major surgery with extensive tissue injury</td>
<td>Arthroscopy</td>
<td>Minor dermatologic procedures (excision of basal and squamous cell skin cancers, actinic keratoses, and premalignant or cancerous skin nevi)</td>
</tr>
<tr>
<td>Cancer surgery</td>
<td>Cutaneous/lymph node biopsies</td>
<td>Cataract procedures</td>
</tr>
<tr>
<td>Major orthopedic surgery</td>
<td>Shoulder/foot/hand surgery</td>
<td>Minor dental procedures (dental extractions, restorations, prosthetics, endodontics), dental cleanings, fillings</td>
</tr>
<tr>
<td>Reconstructive plastic surgery</td>
<td>Coronary angiography</td>
<td>Pacemaker or cardioverter-defibrillator device implantation*</td>
</tr>
<tr>
<td>Urologic or Gastrointestinal surgery</td>
<td>Gastrointestinal endoscopy +/- biopsy</td>
<td></td>
</tr>
<tr>
<td>Transurethral prostate resection, bladder resection or tumor ablation</td>
<td>Colonoscopy +/- biopsy</td>
<td></td>
</tr>
<tr>
<td>Nephrectomy, kidney biopsy</td>
<td>Abdominal hysterectomy</td>
<td></td>
</tr>
<tr>
<td>Colonic polyp resection</td>
<td>Laparoscopic cholecystectomy</td>
<td></td>
</tr>
<tr>
<td>Bowel resection</td>
<td>Abdominal hernia repair</td>
<td></td>
</tr>
<tr>
<td>Percutaneous endoscopic gastrostomy (PEG) placement, endoscopic retrograde cholangiopancreatography (ERCP)</td>
<td>Hemorrhoidal surgery</td>
<td></td>
</tr>
<tr>
<td>Surgery in highly vascular organs (kidneys, liver, spleen)</td>
<td>Bronchoscopy +/- biopsy</td>
<td></td>
</tr>
<tr>
<td>Cardiac, intracranial, or spinal surgery</td>
<td>Epidural injections with INR &lt;1.2</td>
<td></td>
</tr>
<tr>
<td>Any major operation (procedure duration &gt;45 minutes)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Minimal Bleed Risk:**
Continue OAC

**Low Bleed Risk**
Allow residual AC effect pre-op
(i.e. 2-3 half lives)
Restart within 24 hrs

**High Bleed Risk**
No residual AC effect
(i.e. 4-5 half lives)
Restart within 48-72 hrs

Consequences of Thromboembolism and Major Bleeding

- **Arterial thromboembolism**
  - 15% case-fatality for heart valve thrombosis
  - 70% rate of death or disability in stroke

- **Venous thromboembolism**
  - 6% rate of death or permanent disability for DVT; 25% rate for PE

- **Major bleeding**
  - 8-9% case-fatality

Martinelli J et al. Circulation 1991; 84(3)
Longstreth JR et al. Neurology 2001; 56:368 75
Douketis JD et al JAMA 1998; 279: 458-62
Linkins L et al Ann Intern Med 2003; 893-900
Hypercoagulability Associated with Surgery: Newer Concepts

- Surgery increases risk of arterial thromboembolism
  [Wahl 1998]

- Perioperative arterial thromboembolic and stroke rates (1.6% and 0.6%) 10-fold higher than modeling suggests (~0.1-0.2% for 8d)
  [Dunn A et al Arch Intern Med 2003; White RH, JTH, 2007]
Three Key Questions Regarding Perioperative Management of Patients on Chronic OACs?

- Should oral anticoagulant therapy be discontinued?

- When VKA is discontinued, should the patient have perioperative “bridging” therapy with heparin (UFH or LMWH)?

- What is the optimal periprocedural management of patients on DOACs needing interruption?
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Minimal Bleed Risk Procedures

Minor dermatologic, cutaneous, dental, ophthalmologic procedures (cataract surgery), pacemaker/cardioverter-defibrillator device implantation

*Do not interrupt OAC* (Grade 2C)

*M*ay consider interrupting DOAC day of procedure

BRUISE Control Study for Pacemaker or Defibrillator Surgery (N = 681)

<table>
<thead>
<tr>
<th>Table 3. Primary and Secondary Outcomes.*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome</strong></td>
</tr>
<tr>
<td>------------------------------------------</td>
</tr>
<tr>
<td><strong>Primary outcome</strong></td>
</tr>
<tr>
<td>Clinically significant hematoma — no. (%)</td>
</tr>
<tr>
<td><strong>Components of primary outcome</strong></td>
</tr>
<tr>
<td>Hematoma prolonging hospitalization — no. (%)</td>
</tr>
<tr>
<td>Hematoma requiring interruption of anticoagulation — no. (%)</td>
</tr>
<tr>
<td>Hematoma requiring evacuation — no. (%)</td>
</tr>
</tbody>
</table>

COMPARE Trial for Catheter Ablation in AF (N = 1584)
Warfarin discontinuation/Heparin Bridging emerged as a strong predictor of periprocedural TE (OR 13; 95% CI, 3.1–55.6; P<0.001).

1. Birnie DH et al NEJM 2013; 368(22):2084 93
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Do We Need To Bridge?
The goal of bridging therapy with parenteral heparin (either UFH or LMWH), usually in therapeutic doses, is to allow for continued anticoagulation during temporary discontinuation of vitamin K antagonist (VKA) therapy, usually for an elective procedure or surgery.

“This makes intuitive sense”
Bridging vs No-Bridging: Thromboembolic Events

No risk reduction for TE with heparin bridging; no difference in ATE or VTE risks.
No difference in TE risk between full and intermediate/prophylactic dose LMWH.
**Meta-Analyses and Systematic Review of Bridging vs No-Bridging: Major Bleeding**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Bridging Events</th>
<th>Bridging Total</th>
<th>No bridging Events</th>
<th>No bridging Total</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daniels et al., 2009</td>
<td>15</td>
<td>342</td>
<td>5</td>
<td>213</td>
<td>1.91 [0.68, 5.33]</td>
</tr>
<tr>
<td>Garcia et al., 2008</td>
<td>4</td>
<td>108</td>
<td>2</td>
<td>1185</td>
<td>22.75 [4.12, 125.68]</td>
</tr>
<tr>
<td>Jaffer et al., 2010</td>
<td>13</td>
<td>229</td>
<td>3</td>
<td>263</td>
<td>5.22 [1.47, 18.54]</td>
</tr>
<tr>
<td>McBane et al., 2010</td>
<td>14</td>
<td>514</td>
<td>2</td>
<td>261</td>
<td>3.63 [0.82, 16.08]</td>
</tr>
<tr>
<td>Wysokinski et al., 2008</td>
<td>6</td>
<td>204</td>
<td>4</td>
<td>182</td>
<td>1.35 [0.37, 4.86]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1397</td>
<td>2104</td>
<td></td>
<td></td>
<td>3.60 [1.52, 8.50]</td>
</tr>
</tbody>
</table>

Heterogeneity: $I^2 = 52\%$

Bridging associated with an increase in major bleeding. Significant heterogeneity noted across studies.

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Siegel D et al Circulation 2012;126:1630-39
## Periprocedural Bridging vs No-Bridging Studies

<table>
<thead>
<tr>
<th>Study (N)</th>
<th>Year</th>
<th>Population</th>
<th>Comparators</th>
<th>30-day event (post-procedure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RELY (N = 1,415)</td>
<td>2014</td>
<td>AF</td>
<td>Bridging vs No Bridging</td>
<td>ATE or VTE OR</td>
</tr>
<tr>
<td>MVR Study (N = 1,777)</td>
<td>2014</td>
<td>MHV</td>
<td>Rx-dose vs Px-dose Bridging</td>
<td>(0.90, 2.18)</td>
</tr>
<tr>
<td>Kaiser VTE (N = 1,178)</td>
<td>2015</td>
<td>VTE</td>
<td>Bridging vs No Bridging</td>
<td>0 vs 3</td>
</tr>
</tbody>
</table>

### Background 30d Event Rates in No Bridging Arms:
- **ATE** = ~ 0.5 – 1.0%
- **MB** = ~ 1.0 – 1.5%

- ATE or VTE: ~ (0.58, 1.78) (2.07, 7.14)
- MB +/- CRNMB: ~ (0.37, 2.18) (1.58, 6.62)
In patients having a surgery/procedure associated with a low risk for bleeding, dalteparin/placebo was resumed within 24 hours afterward.

In patients having a surgery/procedure associated with a high risk for bleeding, dalteparin/placebo was resumed 48–72 hours afterward.

Douketis JD, Spyropoulos AC et al NEJM 2015; 373(9):823-33
## BRIDGE Trial - Primary Outcomes

<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><strong>ATE</strong></td>
<td>4 (0.4)</td>
<td>3 (0.3)</td>
<td>0.01 (non-inf)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.73 (sup)</td>
</tr>
<tr>
<td>Stroke</td>
<td>2 (0.2)</td>
<td>3 (0.3)</td>
<td></td>
</tr>
<tr>
<td>TIA</td>
<td>2 (0.2)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Systemic embolism</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td><strong>Major bleeding</strong></td>
<td>12 (1.3)</td>
<td>29 (3.2)</td>
<td>0.005 (sup)</td>
</tr>
</tbody>
</table>

The mean CHADS₂ score in patients who sustained a thromboembolic event was 2.6 (range, 1-4)
The median time to an arterial thromboembolic event was 19.0 days (IQR, 6.0-23.0 days)
The median time to a major bleeding event after a procedure was 7.0 days (IQR, 4.0-18.0 days)
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### Periprocedural DOAC Outcomes in SPAF Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>DOAC</th>
<th>30-day rate (post-procedure)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>stroke/systemic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.50)</td>
</tr>
<tr>
<td>Vast majority of patients underwent minor (non-high bleed risk) procedures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Majority of patients (~80%) held DOAC 2 – 3 days prior to procedure and restarted within 2 days post-procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Only minority underwent bridging (except RELY)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARISTOTLE (N = 5439)</td>
<td>apixaban</td>
<td>0.60% (0.32-1.12)</td>
</tr>
</tbody>
</table>

* Includes only 150mg non-bridging groups

Healey JS et al. Circulation 2012;126:343
Sherwood MW et al. Circulation 2014; 129(18):1850
General principles of pre-procedure DOAC discontinuation

Stratify by procedural bleed risk (type, urgency) and renal function

‘Low’ bleed risk:
2–3 half-lives
i.e. 1 – 2 days pre-op

‘High’ bleed risk:
4–5 half-lives
i.e. 2 or more days pre-op

For moderate renal insufficiency: add 1–2 days pre-op

Consider coagulation tests in specific situations
aPTT, PT, TT, dTT (e.g. Hemoclot®), ECT

Pay special attention in patients on antiplatelet therapy
and those requiring neuraxial anaesthesia

No heparin bridging!

Spyropoulos AC et al Blood. 2012;120(15):2954-62
General principles of post-procedure DOAC resumption

Only after good control of hemostasis

Dependent on bleeding risk and type of operation

Wait at least 24 hours after operation to restart NOAC for minor or “low-bleed” risk procedures

Wait 48–72 hrs after operation to restart NOAC for major or “high-bleed” risk procedures
Consider initial prophylactic doses of NOAC

No full-dose heparin bridging!
In patients who cannot tolerate orals consider prophylactic doses of heparin for VTE prevention

Spyropoulos AC et al Blood. 2012;120(15):2954-62
Validated Periprocedural VKA, Bridging, and DOAC Protocols
# Suggested Periprocedural Strategies of VKA and DOACs Based on Procedural Bleed Risk

<table>
<thead>
<tr>
<th></th>
<th>HIGH BLEEDING RISK PROCEDURES</th>
<th>LOW BLEEDING RISK PROCEDURES</th>
<th>MINIMAL BLEEDING RISK PROCEDURES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIGH THROMBOEMBOLIC RISK</strong></td>
<td>DOAC users: Interrupt DOAC. Bridging with LMWH not suggested for DOACs</td>
<td>DOAC users: Interrupt DOAC. Bridging with LMWH not suggested for DOACs</td>
<td>Do not interrupt anticoagulants**</td>
</tr>
<tr>
<td></td>
<td>Warfarin users: Interrupt warfarin with LMWH bridging suggested based on clinician judgment and most current evidence* †</td>
<td>Warfarin users: Interrupt warfarin with LMWH bridging suggested based on clinician judgment and most current evidence*</td>
<td></td>
</tr>
<tr>
<td><strong>INTERMEDIATE THROMBOEMBOLIC RISK</strong></td>
<td>DOAC users: Interrupt DOAC. Bridging with LMWH not suggested for DOACs</td>
<td>DOAC users: Interrupt DOAC. Bridging with LMWH not suggested for DOACs</td>
<td>Do not interrupt anticoagulants**</td>
</tr>
<tr>
<td></td>
<td>Warfarin users: Consider interrupting warfarin without LMWH bridging based on clinician judgment and most current evidence* †</td>
<td>Warfarin users: Consider interrupting warfarin without LMWH bridging based on clinician judgment and most current evidence*</td>
<td></td>
</tr>
<tr>
<td><strong>LOW THROMBOEMBOLIC RISK</strong></td>
<td>DOAC users: Interrupt DOAC. Bridging with LMWH not suggested for DOACs</td>
<td>DOAC users: Interrupt DOAC, Bridging with LMWH not suggested for DOACs</td>
<td>Do not interrupt anticoagulants**</td>
</tr>
<tr>
<td></td>
<td>Warfarin users: Interrupt warfarin. Bridging with LMWH not necessary †</td>
<td>Warfarin users: Interrupt warfarin. Bridging with LMWH not necessary</td>
<td></td>
</tr>
</tbody>
</table>

*† Suggested bridging based on clinician judgment and most current evidence.*

---

*Spyropoulos AC et al J of Thromb Haemost 2016;14(5):875 85*
Validated Periprocedural and Bridging Protocol

<table>
<thead>
<tr>
<th>Day</th>
<th>Warfarin dose</th>
<th>Bridging with LMWH</th>
<th>INR monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>-7 to -10</td>
<td>Maintenance dose</td>
<td>Assess for perioperative bridging anticoagulation; classify patients as undergoing high or low bleeding risk procedures</td>
<td>Check baseline laboratory findings (hemoglobin, platelet count, serum creatinine, INR)</td>
</tr>
<tr>
<td>-6 to -5</td>
<td>Begin to hold warfarin on day -5 or day -6</td>
<td>No LMWH</td>
<td>None</td>
</tr>
<tr>
<td>-4</td>
<td>No warfarin</td>
<td>No LMWH</td>
<td>None</td>
</tr>
<tr>
<td>-3</td>
<td>No warfarin</td>
<td>Start LMWH at a therapeutic or intermediate dose*</td>
<td>None</td>
</tr>
<tr>
<td>-2</td>
<td>No warfarin</td>
<td>LMWH at a therapeutic or intermediate dose*</td>
<td>None</td>
</tr>
<tr>
<td>-1</td>
<td>No warfarin</td>
<td>Last preprocedural dose of LMWH administered no less than 24 h before the start of surgery as half the total daily dose</td>
<td>None</td>
</tr>
<tr>
<td>0 or +1</td>
<td>Resume the maintenance dose of warfarin on the evening of or morning after the procedure</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>+1</td>
<td>Maintenance dose</td>
<td>Low bleeding risk: restart LMWH at the previous dose; High bleeding risk: no LMWH administration</td>
<td>According to clinician judgement</td>
</tr>
<tr>
<td>+2 or +3</td>
<td>Maintenance dose</td>
<td>Low bleeding risk: LMWH administration continued; High bleeding risk: restart LMWH at the previous dose</td>
<td>According to clinician judgement</td>
</tr>
<tr>
<td>+4</td>
<td>Maintenance dose</td>
<td>Low bleeding risk: INR testing (discontinue LMWH if the INR is &lt; 1.9); High bleeding risk: INR testing (discontinue LMWH if the INR is &gt; 1.9)</td>
<td>INR</td>
</tr>
<tr>
<td>+7 to +10</td>
<td>Maintenance dose</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Table 6 Suggested periprocedural direct oral anticoagulant therapy interruptions (adapted from [4])**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Renal function</th>
<th>Low bleeding risk surgery</th>
<th>High bleeding risk surgery*</th>
<th>High bleeding risk surgery</th>
<th>Resumption of therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CrCl &gt; 50 mL min⁻¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dabigatran</td>
<td>CrCl 30–50 mL min⁻¹</td>
<td>Last dose: 2 days before procedure</td>
<td>Last dose: 3 days before procedure</td>
<td>Resume ~ 24 h after procedure</td>
<td>Resume 2–3 days after procedure (48–72 h postoperatively)†</td>
</tr>
<tr>
<td></td>
<td>CrCl 15–29.9 mL min⁻¹‡</td>
<td>Last dose: indvidualized on the basis of patient and procedural factors for bleeding and thrombosis</td>
<td>Last dose: indvidualized on the basis of patient and procedural factors for bleeding and thrombosis</td>
<td>Resume ~ 24 h after procedure</td>
<td>Resume 2–3 days after procedure (48–72 h postoperatively)†</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>CrCl &gt; 50 mL min⁻¹</td>
<td>Last dose: 2 days before procedure</td>
<td>Last dose: 3 days before procedure</td>
<td>Resume ~ 24 h after procedure</td>
<td>Resume 2–3 days after procedure (48–72 h postoperatively)†</td>
</tr>
<tr>
<td></td>
<td>CrCl 30–50 mL min⁻¹</td>
<td>Last dose: 2 days before procedure</td>
<td>Last dose: 3 days before procedure</td>
<td>Resume ~ 24 h after procedure</td>
<td>Resume 2–3 days after procedure (48–72 h postoperatively)†</td>
</tr>
<tr>
<td></td>
<td>CrCl 15–29.9 mL min⁻¹‡</td>
<td>Last dose: indvidualized on the basis of patient and procedural factors for bleeding and thrombosis</td>
<td>Last dose: indvidualized on the basis of patient and procedural factors for bleeding and thrombosis</td>
<td>Resume ~ 24 h after procedure</td>
<td>Resume 2–3 days after procedure (48–72 h postoperatively)†</td>
</tr>
<tr>
<td>Apixaban</td>
<td>CrCl &gt; 50 mL min⁻¹</td>
<td>Last dose: 2 days before procedure</td>
<td>Last dose: 3 days before procedure</td>
<td>Resume ~ 24 h after procedure</td>
<td>Resume 2–3 days after procedure (48–72 h postoperatively)†</td>
</tr>
<tr>
<td></td>
<td>CrCl 30–50 mL min⁻¹</td>
<td>Last dose: 2 days before procedure</td>
<td>Last dose: 3 days before procedure</td>
<td>Resume ~ 24 h after procedure</td>
<td>Resume 2–3 days after procedure (48–72 h postoperatively)†</td>
</tr>
<tr>
<td></td>
<td>CrCl 15–29.9 mL min⁻¹‡</td>
<td>Last dose: indvidualized on the basis of patient and procedural factors for bleeding and thrombosis</td>
<td>Last dose: indvidualized on the basis of patient and procedural factors for bleeding and thrombosis</td>
<td>Resume ~ 24 h after procedure</td>
<td>Resume 2–3 days after procedure (48–72 h postoperatively)†</td>
</tr>
</tbody>
</table>

CrCl, creatinine clearance. *Includes any procedure/surgery requiring neuraxial anesthesia. †For patients at high risk for thromboembolism and with a high bleeding risk after surgery, consider administering a reduced dose of dabigatran (75 mg twice daily), rivaroxaban (10 mg once daily) or apixaban (2.5 mg twice daily) on the evening after surgery and on the following day (first postoperative day) after surgery. ‡Value for patients receiving rivaroxaban 15 mg once daily.

Spyropoulos AC et al J of Thromb Haemost 2016; 14:875-85
TABLE 4. Recommended Intervals Between Discontinuation of the New Anticoagulants and Interventional Pain Procedure and Between the Procedure and Resumption of the New Anticoagulants

<table>
<thead>
<tr>
<th>Drug</th>
<th>Half-life</th>
<th>Recommended Interval Between Discontinuation of Drug and Interventional Pain Procedure* (5 Half-lives)†‡</th>
<th>Recommended Interval Between Procedure and Resumption of Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>12–17 h</td>
<td>4–5 d</td>
<td>24 h</td>
</tr>
<tr>
<td></td>
<td>28 h (renal disease)</td>
<td>6 d (renal disease)</td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>9–13 h</td>
<td>3 d</td>
<td>24 h</td>
</tr>
<tr>
<td>Apixaban</td>
<td>15.2 ± 8.5 h</td>
<td>3–5 d‡</td>
<td>24 h</td>
</tr>
</tbody>
</table>

*The procedures include medium- and high-risk interventional pain procedures. For low-risk procedures, a shared decision making should be followed, a 2 half-life interval may be considered.

†Because of the lack of published studies and in view of the added risks involved in patients with spine abnormalities, we took the upper limit of the half-life of each drug in calculating the 5 half-lives.

‡The potency and the wide variability in the pharmacokinetics of these drugs make us recommend a longer interval.
How to Apply the MAPPP App
Applicability of the MAPPP App

- Performs patient anticoagulation assessment 7+ days prior to procedures
- Categorizes procedure-related bleeding risk and underlying thrombosis risk for each patient
- Provides final recommendation for anticoagulant interruption and bridging related to bleeding and thromboembolic risk
- Each recommendation is coupled to specific guidance for DOAC users, warfarin users and/or antiplatelet users
MAPPP Instructions

- To download the app or view the web-based version, please visit: http://mappp.ipro.org/

MAPPP!
Welcome to IPRO’s Management of Anticoagulation in the Peri-Procedural Period app.

Try out the app yourself!

Download on the App Store
Get it on Google Play
MAPPP Instructions

- Once clicking on accept and continue (disclaimer screens), you’ll be presented with a screen displaying various antithrombotic options
- Select the antithrombotic agent relevant to your patient
MAPPP Instructions

- The next screen then prompts you to categorize the specific procedure bleeding risk as High, Low or Minimal.
- If the procedure bleeding risk is known simply click on the appropriate choice.
- If the procedure bleeding risk is unknown, click on the “Click here for more information on the above choices” which will allow you to view definitions of each level of bleeding risk.

(44)
MAPPP Instructions

- The “Click here for more information on the above choices” selection reveals the full definition guidance for High, Low and Minimal Bleeding Risk Procedures.

- Procedure bleeding risk can also be selected from this page by clicking on the appropriate choice.
MAPPP Instructions

- This screenshot depicts the Low Bleeding Risk and Minimal Bleeding Risk Procedure categories.
MAPPP Instructions

- The next screen then prompts you to categorize the specific thromboembolic risk as High, Moderate/Medium or Low.
- If the thromboembolic risk is known simply click on the appropriate choice.
- If the thromboembolic risk is unknown, click on the “Click here for more information on the above choices” which will allow you to view definitions of each level of thromboembolic risk.
MAPPP Instructions

- The “Click here for more information on the above choices” selection reveals the full definition guidance for High, Moderate/Medium and Low Thromboembolic Risk

- Thromboembolic risk can also be selected from this page by clicking on the appropriate choice
MAPPP Instructions

- Once a Bleeding Risk and Thromboembolic Risk is selected for each patient, the MAPPP app will automatically select the appropriate recommendation.

- The final “Results” section will provide a Recommendation with References (upper right corner) and option to select another patient (upper left corner).

- At any point in time, you can double check your input data for Antithrombotic agent selection, Bleeding Risk and Thromboembolic Risk by viewing the information bar at bottom of the screen. Backward navigation can occur by clicking this bar or swiping the screen.

Interrupt warfarin with LMWH bridging suggested based on clinician judgment and most current evidence:

- Atrial fibrillation: Bridging NOT recommended based on Level 1 evidence, but evidence in few high risk CHADS2 patients (score 5 and 6); MHV and VTE: Retrospective studies suggest bridging increases bleeding risk without reducing thrombosis.
Case 1

A 58-year-old female with a bileaflet AVR without major risk factors for stroke is scheduled for a laparoscopic cholecystectomy. She is on warfarin 4mg daily with stable INR within therapeutic range.

Using the MAPPP app, what recommendations would you make regarding the patient’s peri-procedural anticoagulation?
Case 1- Antithrombotic Agent Selection

Step 1:
- Since the patient is currently taking warfarin, select warfarin (Coumadin) as the proper Antithrombotic.
Case 1- Bleeding Risk Evaluation

Step 2

- You now have access to the Bleeding Risk screen and will be prompted to select a procedure-specific Bleeding Risk

- Click on the “Click here for more information on the above choices”

- Note that the drug selection confirmation appears in the bottom information navigation bar
Case 1- Bleeding Risk Evaluation

- Since patient is scheduled for a laparoscopic cholecystectomy, the Low Bleeding Risk category should be selected.
Case 1- Thromboembolic Risk Evaluation

Step 3

- You now have access to the Thromboembolic Risk screen and will be prompted to select the Thromboembolic Risk
- Click on the “Click here for more information on the above choices”
- Note that the drug selection and the Bleeding Risk confirmation appears in the bottom information navigation bar
Case 1- Thromboembolic Risk Evaluation

- Since patient presents with a bileaflet AVR without major risk factors for stroke, the Low Thromboembolic Risk category should be selected.
**Case 1 - Recommendation**

- Based on patient’s anticoagulant, procedure bleeding risk and thromboembolic risk, the MAPPP-generated result is shown.

- The Warfarin Interruption guidance appears below the recommendation.

**Recommendation**

Interrupt warfarin. Bridging with LMWH not necessary.

**Warfarin Interruption (show/hide)**

<table>
<thead>
<tr>
<th>Day</th>
<th>Warfarin Dose</th>
<th>Bridging with Low Molecular Weight Heparin (LMWH)</th>
<th>International Normalized Ratio (INR) Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>-7 to -10</td>
<td>Maintenance dose</td>
<td>Assess for perioperative bridging anticoagulation; classify patients as undergoing high or low bleeding risk procedures</td>
<td>Check baseline labs (hemoglobin, platelet count, serum creatinine, INR)</td>
</tr>
<tr>
<td>-6 or -5</td>
<td>Begin to hold warfarin day 5 or day 6</td>
<td>No LMWH</td>
<td>None</td>
</tr>
</tbody>
</table>
Case 1- Recommendation

- The Warfarin Interruption guide provides a detailed chart guiding anticoagulation bridging or interruption protocols on days leading up to procedures:

<table>
<thead>
<tr>
<th>Day</th>
<th>Warfarin Dose</th>
<th>Bridging with Low Molecular Weight Heparin (LMWH)</th>
<th>International Normalized Ratio (INR) Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>-7 to -10</td>
<td>Maintenance dose</td>
<td>Assess for perioperative bridging anticoagulation; classify patients as undergoing high or low bleeding risk procedures</td>
<td>Check baseline labs (hemoglobin, platelet count, serum creatinine, INR)</td>
</tr>
<tr>
<td>-6 or -5</td>
<td>Begin to hold warfarin day -5 or day -6</td>
<td>No LMWH</td>
<td>None</td>
</tr>
<tr>
<td>-4</td>
<td>No Warfarin</td>
<td>No LMWH</td>
<td>None</td>
</tr>
<tr>
<td>-3</td>
<td>No Warfarin</td>
<td>Start LMWH at therapeutic or intermediate dose†</td>
<td>None</td>
</tr>
<tr>
<td>-2</td>
<td>No Warfarin</td>
<td>LMWH at therapeutic or intermediate dose†</td>
<td>None</td>
</tr>
<tr>
<td>-1</td>
<td>No Warfarin</td>
<td>Last preprocedural dose of LMWH administered no less than 24h before start of surgery at half the total daily dose</td>
<td>Assess INR before the procedure; proceed with surgery if INR &lt;1.5; If INR &gt; 1.5 and &lt;1.8, consider low-dose oral vitamin K reversal (1-2.5 mg)</td>
</tr>
</tbody>
</table>
Case 1 - Recommendation

The recommendation will additionally extend guidance to include anticoagulation regimens for days following a patient’s procedure:

| 0 or +1 | Resume maintenance dose of warfarin on evening of or morning after procedure | None | None |
| +1 | Maintenance dose | Restart LMWH at previous dose | Per clinician judgment |
| +2 or +3 | Maintenance dose | LMWH administration continued | Per clinician judgment |
| +4 | Maintenance dose | INR testing (discontinue LMWH if INR > 1.9) | INR |
| +7 to +10 | Maintenance dose | | INR |

† Either twice daily LMWH regimens (i.e. enoxaparin 1mg/kg subcutaneous, dalteparin 100 IU/kg subcutaneous) or once-daily LMWH regimens have been used (i.e. enoxaparin 1.5 mg/kg subcutaneous, dalteparin 200 IU/kg subcutaneous). Intermediate-dose LMWH has been less studied in this setting.

Decisions to interrupt, bridge, and resume anticoagulants MUST be clearly communicated among providers and to patient.
Case 2

A 76-year-old female with a history of HF, Atrial Fibrillation and HTN is scheduled to undergo a total hip replacement. She is currently on warfarin therapy for a recent DVT (2 months ago).

- CHADS$_2$ = 3
- CrCl = 42 ml/min

Using the MAPPP app, what recommendations would you make regarding the patient’s peri-procedural anticoagulation?
Case 2- Antithrombotic Agent Selection

Step 1:
- Since the patient is currently taking warfarin, select warfarin (Coumadin) as the proper Antithrombotic
Case 2- Bleeding Risk Evaluation

Step 2:

- Since patient is undergoing major orthopedic surgery, the High Bleeding Risk category should be selected
Case 2- Thromboembolic Risk Evaluation

Step 3:

- Due to patient’s recent DVT (2 months ago), the High Thromboembolic Risk category should be selected.
Case 2 - Recommendation

- Based on patient’s anticoagulant, procedure bleeding risk and thromboembolic risk, the MAPPP-generated result is shown.

- The Warfarin Interruption and Bridging Suggestions appear below the recommendation.

  Interrupt warfarin with LMWH bridging suggested based on clinician judgment and most current evidence.

  Atrial fibrillation: Bridging NOT recommended based on Level 1 evidence, but evidence in few high risk CHADS2 patients (score 5 and 6); MHV and VTE: Retrospective studies suggest bridging increases bleeding risk without reducing thrombosis.
Case 2- Recommendation

- The recommendation will provide a detailed chart guiding anticoagulation bridging or interruption protocols on days leading up to procedures:

<table>
<thead>
<tr>
<th>Day</th>
<th>Warfarin Dose</th>
<th>Bridging with Low Molecular Weight Heparin (LMWH)</th>
<th>International Normalized Ratio (INR) Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 to -10</td>
<td>Maintenance dose</td>
<td>Assess for perioperative bridging anticoagulation, classify patients as undergoing high or low bleeding risk procedures</td>
<td>Check baseline labs (hemoglobin, platelet count, serum creatinine, INR)</td>
</tr>
<tr>
<td>6 or -5</td>
<td>Begin to hold warfarin day -5 or day -6</td>
<td>No LMWH</td>
<td>None</td>
</tr>
<tr>
<td>-4</td>
<td>No Warfarin</td>
<td>No LMWH</td>
<td>None</td>
</tr>
<tr>
<td>-3</td>
<td>No Warfarin</td>
<td>Start LMWH at therapeutic or intermediate dose†</td>
<td>None</td>
</tr>
<tr>
<td>-2</td>
<td>No Warfarin</td>
<td>LMWH at therapeutic or intermediate dose†</td>
<td>None</td>
</tr>
<tr>
<td>-1</td>
<td>No Warfarin</td>
<td>Last preprocedure dose of LMWH administered no less than 24h before start of surgery at half the total daily dose</td>
<td>Assess INR before the procedure; proceed with surgery if INR &lt;1.5. If INR &gt; 1.5 and &lt;1.8, consider low-dose oral vitamin K reversal (1-2.5 mg)</td>
</tr>
</tbody>
</table>
Case 2- Recommendation

- The recommendation will additionally extend guidance to include anticoagulation regimens for days following a patient’s procedure:

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>Resume maintenance dose of warfarin on evening of or morning after procedure</th>
<th>None</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 or +1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+1</td>
<td>Maintenance dose</td>
<td>No LMWH administration</td>
<td>Per clinician judgment</td>
</tr>
<tr>
<td>+2 or +3</td>
<td>Maintenance dose</td>
<td>Restart LMWH at previous dose</td>
<td>Per clinician judgment</td>
</tr>
<tr>
<td>+4</td>
<td>Maintenance dose</td>
<td>INR testing (discontinue LMWH if INR &gt; 1.9)</td>
<td>INR</td>
</tr>
<tr>
<td>+7 to +10</td>
<td>Maintenance dose</td>
<td></td>
<td>INR</td>
</tr>
</tbody>
</table>
Case 3

A 64-year-old male with a history of Atrial Fibrillation, HTN, and Type 2 Diabetes is scheduled to undergo a coronary angiography in 2 weeks. He is on Eliquis (apixaban) 5mg BID.

- CHADS$_2$ = 2
- CrCl = 84 ml/min

Using the MAPPP app, what recommendations would you make regarding the patient’s peri-procedural anticoagulation?
Case 3 - Antithrombotic Agent Selection

Step 1:

- Since the patient is currently taking Eliquis, select Eliquis (apixaban) as the proper Antithrombotic
Case 3 - Bleeding Risk Evaluation

Step 2:
- Since patient is undergoing coronary angiography, the Low Bleeding Risk category should be selected.
Step 3:
- Due to patient’s CHADS₂ score of 2 and lack of significant past medical history (prior stroke/TIA), the Low Thromboembolic Risk category should be selected.
Case 3 - Recommendation

- Based on patient’s anticoagulant, procedure bleeding risk and thromboembolic risk, the MAPPP-generated result is shown.

- The Apixaban Interruption Suggestions appear below the recommendation.
Questions/Discussion

Please complete the program evaluation you will be directed to when you close the webinar.
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References


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