Perioperative Management of Antithrombotic Therapy 2022:
An American College of Chest Physicians Clinical Practice Guideline Executive Summary

Friday | September 9, 2022 | 12:00 – 1:00pm ET

Presenters:
James D. Douketis, MD, FRCP(C), FCAHS
Alex C. Spyropoulos, MD, FACP, FCCP, FRCPC

Webinar Co-Chair:
Geoffrey Barnes, MD, MSc (Moderator)

Panelist:
William E. Dager, PharmD, BCPS, MCCM
Presenters

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**Alex C. Spyropoulos, MD, FACP, FCCP, FRCPC**
Professor of Medicine, Zucker School of Medicine at Hofstra/Northwell
System Director, Anticoagulation and Clinical Thrombosis Services
*Northwell Health*
Objectives

1. Identify compelling questions relating to the periprocedural management of antithrombotic agents

2. Describe major changes to guideline recommendations since the prior release in 2012

3. Discuss the implications of the recommendations of the new treatment guidelines

4. Explore approaches to accelerate the spread and adoption of the guideline’s recommendations through anticoagulation stewardship programs
Perioperative Management of Antithrombotic Therapy: An American College of Chest Physicians Clinical Practice Guideline

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Journal pre-proof: DOI: https://doi.org/10.1016/j.chest.2022.08.004
### Lifetime Disclosures for: J. Douketis

<table>
<thead>
<tr>
<th>Research Support*</th>
<th>CIHR, HSFC, Boehringer-Ingelheim</th>
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<td>Up-to-Date, Merck Manual</td>
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<td>Consultant or Advisory Board Fees*</td>
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<td>Stockholder, Speaker’s Bureau</td>
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<tr>
<td>Unlabeled/Unapproved Use Disclosure</td>
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<tr>
<td>Speaker’s Fees*</td>
<td>Bayer, Boehringer-Ingelheim, Pfizer, Leo Pharma, Sanofi</td>
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*Funds deposited into university-based research accounts or St. Joseph’s Healthcare Foundation.

Last 3 years
Guideline Overview

• Evidence: **43 PICOs, 44 Guideline Statements**
  - Patients receiving a VKA, focused on warfarin.
  - Among patients receiving a VKA, the use of perioperative heparin bridging.
  - Patients receiving a DOAC.
  - Patients receiving an antiplatelet drug.

• Practical Guidance: “**how to**…”
  - ...assess perioperative thromboembolism and bleed risk?
  - ...interrupt and resume VKA, DOACs and AP drugs?
  - ...bridge with LMWH?
Guideline Development Process

1) **Oversight**: ACCP/CHEST and Mayo Clinic Evidence-Based Practice Center, Rochester, MN

2) **Selection**: Panel members and COI disclosure

3) **Selection**: PICO questions

4) **Data sources**: direct and indirect evidence

5) **Guideline framework**: GRADE approach

6) **Evidence synthesis**: outcomes expressed as RR (95% CI)

7) **Development of recommendations**: modified Delphi technique; to achieve consensus for final guideline, each statement required at least 80% agreement among at least 75% of eligible (non-conflicted) panel members.
Clinical Case

- 75-yr old female with AF on apixaban, 5 mg BID or rivaroxaban, 15 mg daily
- Comorbidities: hypertension, diabetes, CHF, TIA 2 years ago ($CHADS_2=6$), CrCl = 45 mL/min

- For hip replacement Friday, September 16$^{th}$ at 8AM with spinal anesthesia
Questions you are asked (when referred):

1) When do I interrupt apixaban/rivaroxaban?
   2 days, 3 days or 5 days before surgery?

2) If I interrupt apixaban/rivaroxaban for 3 or 5 days, do I need to bridge with LMWH?

1) Do I need to check DOAC levels before surgery (on Thursday)?
When do I interrupt apixaban?

- **Guideline 22**: *In patients receiving apixaban who require an elective surgery/procedure, we suggest stopping apixaban for 1-2 days, before the surgery/procedure over apixaban continuation.* *(Conditional recommendation, very low certainty of evidence.)*

**Guideline implementation considerations:**

- The total duration of perioperative apixaban interruption will depend on surgery/procedure bleed risk:
  - 1 day off before low/moderate-bleed-risk;
  - 2 days off before high-bleed-risk.

- This management may be applied irrespective of whether patients are receiving apixaban for AF or VTE.
When do I interrupt rivaroxaban?

• **Guideline 25**: In patients receiving rivaroxaban who require an elective surgery/procedure, we suggest stopping rivaroxaban for 1-2 days, before the surgery/procedure over its continuation. (Conditional recommendation, very low certainty of evidence.)

Guideline implementation considerations:

• The total duration of perioperative rivaroxaban interruption will depend on surgery/procedure bleed risk:
  - 1 day off before low/moderate-bleed-risk;
  - 2 days off before high-bleed-risk.

• This management may be applied irrespective of whether patients are receiving rivaroxaban for AF or VTE.
If I interrupt apixaban/rivaroxaban for 3 or 5 days, do I need to bridge with LMWH?

• **Guideline 26:** *In patients who require DOAC interruption for an elective surgery/procedure, we suggest against perioperative heparin bridging. (Conditional recommendation, very low certainty of evidence)*

Guideline implementation considerations:

• *The rapid offset and rapid onset of action of DOACs obviates the need for heparin bridging with short-acting anticoagulants such as UFH or LMWH in a perioperative setting.*
Do I need to check apixaban/rivaroxaban levels?

- **Guideline 28:** In patients who had DOAC interruption for an elective surgery/procedure, we suggest against routine DOAC coagulation function testing to guide perioperative DOAC management. (Conditional recommendation, very low certainty of evidence.)

**Guideline implementation considerations:**

- DOAC level testing may be considered, on a case-by-case basis, in non-elective perioperative clinical situations, for example, in patients who require an urgent/emergency surgery/procedure in whom DOAC level testing may inform the need for active DOAC reversal with administration of blood products or DOAC-specific reversal agents.
**Figure 2. Perioperative Management of Direct Oral Anticoagulants**

<table>
<thead>
<tr>
<th>Direct Oral Anticoagulant</th>
<th>Procedure Bleeding Risk</th>
<th>Pre-Procedural DOAC Interruption</th>
<th>Post-Procedural Resumption*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day -6</td>
<td>Day -5</td>
<td>Day -4</td>
</tr>
<tr>
<td><strong>Apixaban</strong></td>
<td>High</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Low/Mod</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dabigatran (CrCl ≥ 50 ml/min)</strong></td>
<td>High</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low/Mod</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dabigatran (CrCl &lt; 50 ml/min)</strong></td>
<td>High</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Low/Mod</td>
<td></td>
<td></td>
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<tr>
<td><strong>Edoxaban</strong></td>
<td>High</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Low/Mod</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Rivaroxaban</strong></td>
<td>High</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low/Mod</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- No DOAC administered that day

*DOAC can be resumed ~24 hours after low/moderate-bleed-risk procedures, and 48-72 hours after high-bleed-risk procedures. In selected patients at high risk for VTE, low-dose anticoagulants (i.e., enoxaparin, 40 mg daily or dalteparin, 5000 IU daily) can be given for the first 48-72 hours post-procedure.*
Clinical Case

• 65-year old man with ischemic stroke 3 years ago and likely TIA 9 months ago
• PMHx: hypertension, obesity, type 2 diabetes
• Meds include: ASA, 81 mg daily
• Needs bilateral inguinal hernia repair

Question during pre-op assessment:
What to do with ASA perioperatively?
Should I interrupt ASA perioperatively?

- **Guideline 29a:** In patients receiving ASA who are having elective non-cardiac surgery, we suggest ASA continuation over interruption. (Conditional recommendation, moderate certainty of evidence.)

  **Guideline implementation considerations:**
  
  - This guidance may be modified on a case-by-case basis. For example, in select patients undergoing a non-cardiac surgery associated with a high bleeding risk we suggest ASA interruption.

- **Guideline 29b:** In patients receiving ASA who are having elective surgery and require ASA interruption, we suggest stopping ASA ≤7 days instead of 7-10 days before the surgery. (Conditional recommendation, very low certainty of evidence.)
**Based on surgery/procedure bleed risk assessment.**

**Routine use not suggested; if used, initiate within 72 hrs from P2Y\(_{12}\) inhibitor discontinuation at 0.75 mcg/kg/min; resume <6 hrs post-procedure for minimum of 48 hrs and maximum of 7 days.

***P2Y\(_{12}\) inhibitors resumed within 24 hrs post-procedure (maintenance dose).

†For ticagrelor, 3-5 day interruption

††For clopidogrel, 5 day interruption

§ For prasugrel, 7-10 day interruption.
The Perioperative Management of Warfarin and Heparin Bridging

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Professor of Medicine
The Donald and Barbara Zucker School of Medicine at Hofstra/Northwell
Professor – The Institute of Health Systems Science
The Feinstein Institutes for Medical Research
System Director – Anticoagulation and Clinical Thrombosis Service
Northwell Health System at Lenox Hill Hospital
New York, NY
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** (Annual ATE >10%; 1 month VTE > 10%)

- **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** (Annual ATE 5 - 10%; 1 month VTE 2 - 10%)

- **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** (Annual ATE <5%; 1 month VTE < 2%)

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

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

- **VTE**
  - VTE more than 12 months ago

<table>
<thead>
<tr>
<th>HIGH BLEEDING RISK PROCEDURES (2 day risk of MB 2 - 4%)</th>
<th>LOW BLEEDING RISK PROCEDURES (2 day risk of MB &lt;2%)</th>
<th>MINIMAL BLEEDING RISK PROCEDURES (essentially no MB risk)</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>
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<tr>
<td>Bowel resection</td>
<td>Abdominal hernia repair</td>
<td></td>
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<tr>
<td>Percutaneous endoscopic gastrostomy (PEG) placement, endoscopic retrograde cholangiopancreatography (ERCP)</td>
<td>Hemorrhoidal surgery</td>
<td></td>
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<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>
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<tr>
<td>Any major operation (procedure duration &gt;45 minutes)</td>
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</tr>
</tbody>
</table>

Spyropoulos et al J of Thromb Haemost 2016; 14(5):875-85
### Periprocedural Management of Patients on Chronic VKA

**Based on Patient TE and Procedural Bleed Risk Classifications**

<table>
<thead>
<tr>
<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></td>
<td>C</td>
</tr>
<tr>
<td>Annual ATE &gt;10%</td>
<td></td>
<td></td>
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<tr>
<td>1 month VTE &gt; 10%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intermediate Thromboembolic Risk</strong></td>
<td></td>
<td>F</td>
</tr>
<tr>
<td>Annual ATE 5 - 10%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month VTE 2 - 10%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Low Thromboembolic Risk</strong></td>
<td></td>
<td>H</td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annual ATE &lt;5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month VTE &lt; 2%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **WAIT 48-72 HRS, THEN RX DOSE LMWH**
- **STEPWISE PX-THEN RX-DOSE LMWH**
- **NO BRIDGING**
- ? HEPARIN BRIDGING
Two Key Questions Regarding Perioperative Management of Patients on Chronic VKA?

• Should oral anticoagulant therapy be discontinued?

• When VKA is discontinued, should the patient have perioperative “bridging” therapy with heparin (UFH or LMWH)?
  • How to bridge with heparin?
Two Key Questions Regarding Perioperative Management of Patients on Chronic VKA?

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  • How to bridge with heparin?
BRUISE Control Study for Pacemaker or Defibrillator Surgery

*N = 681*

1. Birnie DH et al NEJM 2013; 368(22):2084-93

### Table 3. Primary and Secondary Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Heparin Bridging (N=338)</th>
<th>Continued Warfarin (N=343)</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinically significant hematoma — no. (%)</td>
<td>54 (16.0)</td>
<td>12 (3.5)</td>
<td>0.19 (0.10–0.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Components of primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematoma prolonging hospitalization — no. (%)</td>
<td>16 (4.7)</td>
<td>4 (1.2)</td>
<td>0.24 (0.08–0.72)</td>
<td>0.006</td>
</tr>
<tr>
<td>Hematoma requiring interruption of anticoagulation — no. (%)</td>
<td>48 (14.2)</td>
<td>11 (3.2)</td>
<td>0.20 (0.10–0.39)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hematoma requiring evacuation — no. (%)</td>
<td>9 (2.7)</td>
<td>2 (0.6)</td>
<td>0.21 (0.05–1.00)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

COMPARE Trial for Catheter Ablation in AF (N = 1584)²
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
Guideline Statement 14: In patients receiving VKA therapy who require a pacemaker or ICD implantation, we recommend continuation of VKA over VKA interruption and heparin bridging. (Strong recommendation, moderate certainty of evidence.)

Guideline implementation considerations:
Continuation of VKAs around cardiac device procedures is based on the premise that the patient’s INR at the time of the procedure is <3.0.
Patients Who Require Dental, Dermatologic, Ophthalmologic, or Colonoscopic Procedures (Minimal Bleed Risk)
10th Edition ACCP Guidelines 2022

Guideline Statement 10: In patients receiving VKA therapy who need a dental procedure, we suggest continuation of VKA over VKA interruption (Conditional recommendation, low certainty of evidence.)

Guideline Statement 11: In patients receiving VKA therapy who need a dental procedure, we suggest using a pro-hemostatic agent with continuation of VKA over alternative management options (e.g., discontinuation of VKA with or without heparin bridging). (Conditional recommendation, low certainty of evidence.)

Guideline Statement 12: In patients receiving VKA therapy who require a minor dermatologic procedure, we suggest continuation of VKA over VKA interruption. (Conditional recommendation, very low certainty of evidence.)

Guideline Statement 13: In patients receiving VKA therapy who require a minor ophthalmologic procedure, we suggest continuation of VKA over VKA interruption. (Conditional recommendation, very low certainty of evidence)

Guideline Statement 15: In patients receiving VKA therapy who require VKA interruption for a colonoscopy with anticipated polypectomy, we suggest against heparin bridging during the period of VKA interruption. (Conditional recommendation, very low certainty of evidence.)

Douketis JD, Spyropoulos AC et al Chest 2022
Two Key Questions Regarding Perioperative Management of Patients on Chronic VKA?

• Should oral anticoagulant therapy be discontinued?

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  • How to bridge with heparin?
Two Key Questions Regarding Perioperative Management of Patients on Chronic VKA?

- Should oral anticoagulant therapy be discontinued?

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

• The perceived need for bridging therapy is driven by TE risk
  • In high TE risk patients, the need to prevent TE will dominate management irrespective of bleed risk and thus an aggressive strategy (such as bridging) is justified
  • In moderate TE patients, a single strategy is not dominant and management will depend on individual RFs for bleeding/thrombosis
  • In low TE risk patients, the need to prevent TE is less dominant thus strategies to avoid bleeding are justified
Do We Need To Bridge?
## 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></td>
<td></td>
<td></td>
<td></td>
<td>ATE or VTE OR (95% CI)</td>
</tr>
<tr>
<td>Meta-analysis</td>
<td>2012</td>
<td>MHV, AF, VTE</td>
<td>Bridging vs No Bridging</td>
<td>0.80 (0.42, 1.54)</td>
</tr>
<tr>
<td>ORBIT</td>
<td>2014</td>
<td>AF</td>
<td>Bridging vs No Bridging</td>
<td>1.62 (0.95, 2.78)</td>
</tr>
<tr>
<td>RELY</td>
<td>2014</td>
<td>AF</td>
<td>Rx-dose vs Px-dose Bridging</td>
<td>2.70 (0.38, 19.3)</td>
</tr>
<tr>
<td>MVR Study</td>
<td>2014</td>
<td>MHV</td>
<td>Rx-dose vs Px-dose Bridging</td>
<td>0.90 (0.37, 2.18)</td>
</tr>
</tbody>
</table>

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

We hypothesized that in patients with AF on chronic VKA with at least one stroke risk factor undergoing temporary interruption of VKA for an elective procedure:

1. Forgoing bridging anticoagulation would be non-inferior to bridging with low-molecular-weight heparin (LMWH) for the prevention of perioperative arterial thromboembolism (ATE)

- and –

2. Forgoing bridging anticoagulation would be superior to bridging with respect to major bleeding
BRIDGE - Trial Design
(N=1884, AF)

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 N Engl J Med 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></td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATE</td>
<td>4 (0.4)</td>
<td>3 (0.3)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>(non-inf)</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>Major bleeding</td>
<td>12 (1.3)</td>
<td>29 (3.2)</td>
<td>0.005 (sup)</td>
</tr>
</tbody>
</table>

Source: Douketis J, Spyropoulos AC et al NEJM 2015
### BRIDGE Trial - Secondary 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>Death</td>
<td>5 (0.5)</td>
<td>4 (0.4)</td>
<td>0.88 (sup)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>7 (0.8)</td>
<td>14 (1.6)</td>
<td>0.10 (sup)</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>0 (0)</td>
<td>1 (0.1)</td>
<td>0.25 (sup)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>0 (0)</td>
<td>1 (0.1)</td>
<td>0.25 (sup)</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>110 (12.0)</td>
<td>187 (20.9)</td>
<td>&lt;0.001 (sup)</td>
</tr>
</tbody>
</table>

The mean CHADS<sub>2</sub> 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)

Douketis J, Spyropoulos AC et al NEJM 2015
PERIOP 2 - Trial Design
(N=1471, AF=1166, MHV=305)

Kovacs M et al BMJ 2021
### Table 3 | Study outcomes for whole population and subgroups of patients with atrial fibrillation and mechanical valves at 90 days. Data are numbers (%) unless indicated otherwise

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Whole study population</th>
<th>Atrial fibrillation</th>
<th>Mechanical valve</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No bridging (n=650)</td>
<td>Bridging (n=820)</td>
<td>P value</td>
</tr>
<tr>
<td><strong>Primary</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major thromboembolism*</td>
<td>8 (1.2)</td>
<td>8 (1.0)</td>
<td>0.64</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischaemic stroke</td>
<td>3 (0.5)</td>
<td>1 (0.1)</td>
<td>0.33</td>
</tr>
<tr>
<td>Transient ischaemic attack</td>
<td>0</td>
<td>1 (0.1)</td>
<td>1</td>
</tr>
<tr>
<td>Symptomatic myocardial infarction</td>
<td>3 (0.4)</td>
<td>3 (0.5)</td>
<td>1</td>
</tr>
<tr>
<td>Peripheral embolism</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Valve thrombosis</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Venous thromboembolism</td>
<td>2 (0.3)</td>
<td>3 (0.4)</td>
<td>1</td>
</tr>
<tr>
<td>Vascular death</td>
<td>3 (0.5)</td>
<td>0</td>
<td>0.09</td>
</tr>
<tr>
<td>All deaths</td>
<td>8 (1.2)</td>
<td>6 (0.7)</td>
<td>0.33</td>
</tr>
<tr>
<td><strong>Major bleeding</strong></td>
<td>13 (2.0)</td>
<td>11 (1.3)</td>
<td>0.32</td>
</tr>
<tr>
<td>Clinically relevant non-major bleeding</td>
<td>25 (3.9)</td>
<td>50 (6.1)</td>
<td>0.05</td>
</tr>
<tr>
<td>Trivial bleeding</td>
<td>16 (2.5)</td>
<td>22 (2.7)</td>
<td>0.79</td>
</tr>
<tr>
<td>Major thromboembolism or major bleeding</td>
<td>21 (3.2)</td>
<td>19 (2.3)</td>
<td>0.28</td>
</tr>
<tr>
<td>Major thromboembolism or major bleeding, or death</td>
<td>25 (3.9)</td>
<td>24 (2.9)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

*Major thromboembolism—any one of first seven secondary outcomes: ischaemic stroke, transient ischaemic attack, symptomatic myocardial infarction, peripheral embolism, valve thrombosis, venous thromboembolism (pulmonary embolism or deep vein thrombosis), or vascular death.

†With or without atrial fibrillation.

### Table 4 | Study outcomes for whole study population at 30 days. Data are numbers (%)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No bridging (n=650)</th>
<th>Bridging (n=820)</th>
<th>P value</th>
<th>Risk difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major thromboembolism</td>
<td>8 (1.2)</td>
<td>3 (0.4)</td>
<td>0.06</td>
<td>-0.9 (-1.8 to 0.1)</td>
</tr>
<tr>
<td>Major thromboembolism or major bleeding</td>
<td>16 (2.5)</td>
<td>12 (1.5)</td>
<td>0.16</td>
<td>-1.0 (-2.5 to 0.5)</td>
</tr>
<tr>
<td>Major thromboembolism or major bleeding, or death</td>
<td>16 (2.5)</td>
<td>13 (1.6)</td>
<td>0.23</td>
<td>-0.9 (-2.3 to 0.6)</td>
</tr>
</tbody>
</table>
Guideline Statement 6: In patients receiving VKA therapy for atrial fibrillation who require VKA interruption for an elective surgery/procedure, we recommend against heparin bridging. (Strong recommendation, moderate certainty of evidence.)

Guideline implementation considerations:
In selected patients considered at high risk for thromboembolism, for example those with a recent (< 3 month) history of stroke or transient ischemic attack or with a CHA$_2$DS$_2$VASc score $\geq$7 or CHADS$_2$ score of 5 or 6, pre- and post-operative heparin bridging is suggested (see Guideline Statement 8).
Guideline Statement 5: In patients receiving VKA therapy for a mechanical heart valve who require VKA interruption for an elective surgery/procedure, we suggest against heparin bridging. (Conditional recommendation, very low certainty of evidence.)

Guideline implementation considerations:
In selected patients considered at high risk for thromboembolism, for example those with (i) an older-generation mechanical heart valve (i.e., tilting-disc valve), (ii) a mechanical mitral valve with one or more risk factors for thromboembolism, (iii) a recent (within last 3 months) thromboembolic event, or (iv) with prior perioperative thromboembolism, pre- and post-operative heparin bridging is suggested (see Guideline Statement 8).

Guideline Statement 7: In patients receiving VKA therapy for VTE as the sole clinical indication who require VKA interruption for an elective surgery/procedure, we suggest against heparin bridging. (Conditional recommendation, very low certainty of evidence.)

Guideline implementation considerations:
Suggesting against bridging with a therapeutic-dose heparin regimen does not preclude the empiric use of a low-dose heparin regimen, typically started within 24 hours after surgery and continued for up to 5 days while VKA therapy is resumed, to decrease the risk for postoperative VTE.

Douketis JD, Spyropoulos AC et al Chest 2022
Guideline Statement 8: In patients receiving VKA therapy who are classified as high-risk for thromboembolism and who require VKA interruption for an elective surgery/procedure, we suggest heparin bridging over no heparin bridging. (Conditional recommendation, very low certainty of evidence.)

Guideline implementation considerations:
Stratification of patients according to perioperative thromboembolic risk, as shown in Table 1, is empiric as there are no clinical prediction models that have been validated in this clinical setting. The type of surgery may also affect thromboembolic risk, for example an anticipated higher risk in patients having open cardiac or major vascular surgery.
**Figure 1. Perioperative Management of VKA and LMWH Bridging Therapy**

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**Legend**

*Warfarin can be resumed on the evening of procedure (D0) for most patients, or the day after procedure (i.e., D1) at the patient's usual maintenance dose.

**Bridging suggested for high thrombotic risk populations with full-dose, subcutaneous LMWH (e.g., enoxaparin, 1 mg/kg bid or 1.5 mg/kg daily or dalteparin, 100 IU/kg bid or 200 IU/kg daily), with the last dose given the AM of the day prior to the procedure (i.e., D-1) at half the total daily dose.

†Low-dose LMWH (e.g., enoxaparin, 40 mg daily or dalteparin 5000 IU daily) can be used for VTE prophylaxis for first 24-72 hours post-procedure, with full dose LMWH resumed 2-3 days post-procedure.

Guideline Statements 1-3 and 18-20 (all *conditional recommendations, very low to low certainty of evidence*)
Online Clinical Decision Support Tools

MAPPP – Management of Anticoagulation in the Peri-Procedural Period

MAPPP!
Welcome to IPRO Management of Anticoagulation in the Peri-procedural Period.

Patient Details
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mappp.ipro.org
The Management of Patients on Chronic VKA who Need Elective Surgery
10th Edition ACCP Guidelines 2022

• Is interruption of VKAs indicated?
  • COMPARE and BRUISE Control
    • No – RCT data for PM/defibrillator/catheter ablation.
    • Lower quality studies for strategy of VKA continuation in minimal/low bleed risk procedures (i.e. dental, dermatologic, ophthalmologic, or colonoscopic procedures)

• Is heparin bridging necessary with warfarin?
  • Large meta-analysis and large observational/sub-study data
    • Over 3-4 fold increased risk of major bleeding and no advantages in TE reduction
  • BRIDGE – landmark placebo controlled RCT in AF patients
    • Definitive study of no efficacy and harm of heparin bridging
    • Likely can be extended to high risk populations incl MHV (PERIOP-2)

• The “How To” of Managing Warfarin and Bridging in Elective Procedures Has Been Validated
Questions?
Thank you to our speakers!

Geoffrey Barnes, MD, MSc
Assistant Professor of Medicine
University of Michigan School of Medicine

James D. Douketis, MD, FRCP(C), FCAHS
Professor of Medicine, Vascular Medicine & Internal Medicine
David Braley – Nancy Gordon Chair in Thromboembolic Medicine
McMaster University, Hamilton Health Sciences, St. Joseph’s Healthcare

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Cardiovascular Pharmacist
University of California, Davis Medical Center

Alex C. Spyropoulos, MD, FACP, FCCP, FRCPC
System Director, Anticoagulation and Clinical Thrombosis Services
Northwell Health
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Hosted by the AC Forum IDEA Committee

Advancing Anticoagulation Stewardship: A Playbook

Tuesday | October 4, 2022 | 12pm ET

Presenters:
Allison Burnett, PharmD, PhC, CACP
Scott Kaatz, DO, MSc, FACP, SFHM
Chelsea Lynch, MPH, MSN, RN, CIC
Arthur Allen, PharmD, CACP

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- Improve patient safety in the use of anticoagulant medications

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- Anticoagulation Stewardship
- A “how to” on staying abreast of the literature

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“Boot Camp renewed my passion for what I do & definitely helped to increase my level of confidence in the subject matter”

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