Anticoagulants and the National Patient Safety Goals

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  – Pfizer/Bristol-Myers Squibb

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  – Janssen
  – Portola
  – AMAG Pharmaceuticals

• Board of Directors
  – Anticoagulation Forum
  – National Certification Board of Anticoagulation Providers
Outline

• Oral Anticoagulants - Review
• Recent Updates in Anticoagulation
• Joint Commission Anticoagulation Safety Goals
• Tips for Implementation
Outline

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  • Recent Updates in Anticoagulation
  • Joint Commission Anticoagulation Safety Goals
• Tips for Implementation
Anticoagulation Timeline

- 1936: First IV Heparin Approved
- 1954: Warfarin Approved
- 1980s: LMWHs Introduced
- 2010: First DOAC FDA Approved
- 1986: First ACCP Anticoag Forum Established
- 1991: Anticoagulation Guidelines
- 2010’s: Expanded DOAC Indications

LMWH – Low-molecular-weight heparin
DOAC – direct oral anticoagulant
ACCP – American College of Chest Physicians
# Available Oral Therapies

<table>
<thead>
<tr>
<th>Available Oral Therapies</th>
<th>Warfarin (Coumadin)</th>
<th>Dabigatran (Pradaxa)</th>
<th>Apixaban (Eliquis)</th>
<th>Edoxaban (Savaysa)</th>
<th>Rivaroxaban (Xarelto)</th>
<th>Betrixaban (BevyXa)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target</strong></td>
<td>Factors II, VII, IX, X</td>
<td>Factor II (Thrombin)</td>
<td>Factor Xa</td>
<td>Factor Xa</td>
<td>Factor Xa</td>
<td>Factor Xa</td>
</tr>
<tr>
<td><strong>Half-Life (effective)</strong></td>
<td>40 hours</td>
<td>8-15 hours</td>
<td>12 hours</td>
<td>10-14 hours</td>
<td>7-11 hours</td>
<td>19 hours</td>
</tr>
<tr>
<td><strong>Time to Peak Effect</strong></td>
<td>4-5 days</td>
<td>1-3 hours</td>
<td>1-2 hours</td>
<td>1-2 hours</td>
<td>2-4 hours</td>
<td>3-4 hours</td>
</tr>
<tr>
<td><strong>Renal Clearance</strong></td>
<td>None</td>
<td>80%</td>
<td>25%</td>
<td>50%</td>
<td>33%</td>
<td>&lt;10%</td>
</tr>
<tr>
<td><strong>FDA Approved Indication</strong></td>
<td>• AF</td>
<td>• AF (non-valvular)</td>
<td>• AF (non-valvular)</td>
<td>• AF</td>
<td>• AF</td>
<td>• VTE</td>
</tr>
<tr>
<td></td>
<td>• VTE</td>
<td>• VTE</td>
<td>• VTE</td>
<td>• VTE</td>
<td>• VTE</td>
<td>• Prophylaxis</td>
</tr>
<tr>
<td></td>
<td>• Treatment</td>
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<td>• Treatment</td>
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<tr>
<td></td>
<td>• 2º Prevention</td>
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<tr>
<td></td>
<td>• Valve Replacement</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Reversal Available?</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>+/-</td>
<td>Yes</td>
<td>+/-</td>
</tr>
</tbody>
</table>

www.anticoagulationtoolkit.org
Changing Use of Anticoagulants

Pharmacotherapy 2018;38:907-920
Risk of Anticoagulant Medications

#1 Cause of “Adverse Drug Events”

<table>
<thead>
<tr>
<th>Drug Product</th>
<th>ED Visits for ADEs</th>
<th>National Estimate, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients (N = 42 585)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>6179</td>
<td>15.1 (12.3-17.9)</td>
</tr>
<tr>
<td>Insulin</td>
<td>4859</td>
<td>10.7 (8.6-12.7)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>1778</td>
<td>4.4 (2.9-5.9)</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>1780</td>
<td>3.8 (3.3-4.3)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>1518</td>
<td>3.5 (2.2-4.9)</td>
</tr>
<tr>
<td>Sulfamethoxazole-trimethoprim</td>
<td>1152</td>
<td>3.2 (2.7-3.7)</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>1096</td>
<td>2.4 (1.8-3.0)</td>
</tr>
<tr>
<td>Metformin</td>
<td>766</td>
<td>1.7 (1.4-2.1)</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>722</td>
<td>1.6 (1.3-2.0)</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>526</td>
<td>1.3 (0.8-1.8)</td>
</tr>
<tr>
<td>Acetaminophen-hydrocodone</td>
<td>492</td>
<td>1.3 (1.0-1.6)</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>431</td>
<td>1.2 (0.9-1.5)</td>
</tr>
<tr>
<td>Acetaminophen-oxycodone</td>
<td>459</td>
<td>1.1 (0.8-1.4)</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>479</td>
<td>1.0 (0.8-1.2)</td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>422</td>
<td>1.0 (0.9-1.2)</td>
</tr>
</tbody>
</table>
Anticoagulation Management

Individual
Doctor or Nurse

- Frequent dose changes
- Frequent INR lab draws

Dedicated Anticoagulation Clinic

- Driven by need to manage warfarin:
- Frequent dose changes
- Frequent INR lab draws

Dedicated Hospital Staff

- Protocol

- Driven by need to manage heparin:
- Frequent dose changes
- Improve quality
Outline

• Oral Anticoagulants - Review

• Recent Updates in Anticoagulation

• Joint Commission Anticoagulation Safety Goals

• Tips for Implementation
Cancer-associated VTE: LMWH vs. Warfarin

LMWH > Warfarin for VTE Recurrence

CLOT Trial

CATCH Trial

NEJM 2003; 349:146-53

JAMA 2015; 314:677-686
Treat Cancer-VTE: Hokusai VTE Study

Primary Outcome: Recurrent VTE or Major Bleed

Modest increase in Major Bleed with edoxaban:
6.9% vs. 4.0%
(Upper GI Cancer)

NEJM 2018;378:615-624
Preventing Cancer-associated VTE: The AVERT Trial

**Prevent VTE**

HR 0.41 (0.26-0.65)

**Avoid Bleeding**

HR 2.00 (1.01-3.95)

NEJM 2019;380:711-719
Anticoagulation for CAD/PAD?

Stable CAD or PAD

Low-dose rivaroxaban + aspirin vs aspirin alone
Rivaroxaban alone vs aspirin alone

ASA only
Riva only
ASA + Riva

New dose & indication
• Riva 2.5mg BID

Lancet 2018;391:205-218
# DOAC Reversal Agents

<table>
<thead>
<tr>
<th>Drug Reversed</th>
<th>Idarucizumab</th>
<th>Andexanet Alpha</th>
<th>Ciraparantag</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td></td>
<td>Rivaroxaban,</td>
<td>Dabigatran,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Apixaban,</td>
<td>Xa Inhibitors</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Edoxaban (non-FDA),</td>
<td>LMWH,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LMWH (non-FDA)</td>
<td>UFH</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Monoclonal Ab</th>
<th>Recombinant Factor Xa</th>
<th>Covalent bonds to drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Binds Dabigatran</td>
<td>• High affinity for Xa Inhibitors</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Frees Thrombin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Published Clinical Studies</th>
<th>Bleeding Patients &amp; Emergent Reversal</th>
<th>Healthy Volunteers &amp; Bleeding Patients</th>
<th>Healthy Volunteers</th>
</tr>
</thead>
</table>

| FDA Approval | Approved! | Approved! | TBA |

[Anticoagulationtoolkit.org](Anticoagulationtoolkit.org)
Recent Advances in Anticoag

- New indications
  - Cancer-VTE treatment
  - Cancer-VTE prevention
  - Stable CAD & PAD

- New doses
  - Rivaroxaban 2.5mg BID (similar to apixaban)

- Specific DOAC Reversal agents
  - $$
  - Potential thrombotic risk?
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• Tips for Implementation
National Patient Safety Goals

• “To reduce the likelihood of patient harm associated with the use of anticoagulant therapy”

• Effective July 1, 2019

• 8 new elements of performance

• All Joint Commission-accredited hospitals, nursing care centers, and medical centers (ambulatory health care program)

https://www.jointcommission.org/assets/1/18/R3_19_Anticoagulant_therapy_FINAL2.PDF
Resources

Comprehensive Resources

Now for the first time the best and most recent clinical tools available have been carefully researched and collected in one place. Our selection process ensures that we provide only proven and genuinely useful resources.

Welcome to Anticoagulation Centers of Excellence

The Anticoagulation Centers of Excellence program was created in 2012 to help healthcare professionals provide the highest level of care and achieve the best possible outcomes for their patients on antithrombotic medications. Through access to evidence-based guidelines and constantly researched and updated best practices, tools and information, healthcare professionals will be able to improve outcomes through active participation in their patients’ care. The Anticoagulation Centers of Excellence program offers a roadmap to achieving consistent, sustainable excellence in patient care.

Why Become a Center of Excellence?

The landscape of anticoagulation is advancing, evolving and changing. Until now, there has not been a comprehensive standard to define ideal practices for an anticoagulation service.

excellence.acforum.org
Anticoagulation Toolkit
(Version 1.9)

A Consortium-Developed Quick Reference for Anticoagulation

anticoagulationtoolkit.org
Element of Performance 1: Protocols for Anticoag Therapy

Address the following issues:

• Medication selection
• Dosing
  – Adjustment for age and renal/liver function
• Drug-drug interactions
• Drug-food interactions
• Other applicable risk factors
Element of Performance 1: Protocols for Anticoag Therapy

- **Areas to cover**
  - Acute care
  - Transitions of care
  - Ambulatory care

- **Who is responsible?**
  - MD
  - RN
  - Pharmacist

- **Multidisciplinary Oversight Group**
  - P&T committee?
  - Physician & Pharmacists

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Element of Performance 1: Protocols for Anticoag Therapy

- Initiation (Hospital and Ambulatory)
  - Indications & Contraindications
  - Baseline renal & liver function assessment
  - Screen for drug-drug interactions
  - Protocol for dosing

- Follow up (Ambulatory)
  - Need for continued anticoagulation (VTE)?
  - Renal and Liver function (frequency?)
  - Drug-drug interactions
  - Bleeding risk
Element of Performance 2: Protocols for Bleeding Management

• Different reversal mechanisms
  – Heparin
  – Warfarin
  – Dabigatran
  – Apixaban, Rivaroxaban, Edoxaban, Betrixaban

• Assess severity of bleeding

• Select appropriate therapy
  – Stop anticoagulant
  – Use of clotting factors
  – Use of specific reversal agent
Element of Performance 2: Protocols for Bleeding Management

- Order sets & Decision-support tools
- Labs for DOAC-related bleeding management
- Guidance for managing high INR without bleeding (warfarin)
Element of Performance 2: Protocols for Bleeding Management

- Anticoagulation Reversal
  - Vitamin K protocol for high INR if no bleeding (outpatient)
  - Reversal strategy for warfarin, Factor Xa inhibitor, Direct Thrombin Inhibitor (hospital/ED)

- Management of Bleeding
  - Patient education on nuisance bleeding (outpatient)
    - Nose bleeding
    - Bruising

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Element of Performance 3: Protocols for Periop Management

Address the following issues:

• Should anticoagulant be stopped?
• Need for bridging anticoagulation (warfarin)
• When to stop
• When to restart
• What dose to restart
Element of Performance 3: Protocols for Periop Management

• Need for bridging anticoagulation
  – Very few warfarin patients (<10%?)

• Use visual tools
  – What day to take/not take medication

• Neuraxial anesthesia
  – When to stop anticoagulation pre-procedure?
Element of Performance 3: Protocols for Periop Management

- **Interruption – Yes/No?**
  - Dental, dermatologic, endoscopic → No

- **When to stop anticoag pre-procedure**
  - Warfarin → 5 days
  - DOAC → 2-3 days for most

- **When to restart**
  - Usually defer to procedural team

- **What dose to restart**
  - DOAC is effective within 1-3 hours
  - Warfarin takes 5-10 days

- **Is bridging necessary?**
  - DOAC → never
  - Warfarin → few patients
Element of Performance 4: Policy for Laboratory Testing

Address the following issues:

• Baseline and follow up labs
  – INR (warfarin)
  – Renal/Liver function (DOAC)

• When and how to adjust dose
Element of Performance 4: Policy for Laboratory Testing

• Clinical staff
  – When to check labs
  – Which labs to check
• Include laboratory staff on development team
• Baseline labs
  – Rule out coagulopathy
  – Select best anticoagulant & dose
  – CBC, PT/INR, PTT, Creatinine
Element of Performance 4: Policy for Laboratory Testing

- Hospital Protocol
  - Renal function at baseline (DOAC)
  - INR at baseline (warfarin)

- Ambulatory Protocol
  - Check INR goal (most 2-3 or 2.5-3.5)
  - INR-based dosing algorithm
  - Standardize INR documentation process

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Element of Performance 5: Adverse Drug Events

Address the following issues:

• Establish a process to identify, respond to, and report ADEs

• Evaluate & take action around safety practices in a timely manner
Element of Performance 5: Adverse Drug Events

• Identify responsible individual(s)/teams
  – Review ADE case
  – Assess for patterns and gaps in care
  – Facilitate change
Element of Performance 6: Patient/Family Education

Address the following issues:

• Importance of medication adherence
  – Dose and schedule

• Importance of follow up appointments/labs

• Potential drug-drug & drug-food interactions

• Potential adverse drug reactions
  – Bleeding (especially minor)
Element of Performance 6: Patient/Family Education

• Provide key information
  – Contact for anticoagulation clinic/provider
  – “Emergencies” vs. “non-emergencies”

• Use teach back with patient/family
  – Confirm understanding

• Consider group education
Element of Performance 6: Patient/Family Education

• Documentation
  – What was taught
  – How it was taught (handout, teachback, group session)
  – When it was given

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Element of Performance 7: Hospital Med Delivery

Use only the following (when available):

• Oral unit-dose products
• Prefilled syringes
• Premixed infusion bags

Note: Unchanged from prior version
Element of Performance 7: Hospital Med Delivery

- Develop a process for potential drug shortages
- Avoid multiple concentrations of medication

- Note: pediatric pre-filled syringe must be specifically designed for children
Element of Performance 8: Hospital Med Delivery IV Heparin

Intravenous Heparin Administration:

• Use programmable pumps

Note: Unchanged from prior version
Outline

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Advice from Joint Commission

• Process > Content
  – Be sure you can follow protocols

• Documentation is critical

• Staff/Provider knowledge is key
Thank You!