Managing New Anticoagulants in the Perioperative Period

Susan Elczyna CRNA, PhD
Conflict of Interest

The presenter certifies that she has NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers’ bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this presentation.
Anticoagulants

Common uses:

- DVT prophylaxis

- Atrial fibrillation - stroke prevention
What about the Valves?

- phase 2 dose-finding RE-ALIGN trial of dabigatran in prosthetic heart valves
- halted post-interim review
- patients taking dabigatran were more likely to experience strokes, myocardial infarction, and valve thromboses vs patients taking warfarin
- More bleeding post-op
- The FDA has now taken the stance that dabigatran is contraindicated in patients with mechanical heart valves, further noting that its use in bioprosthetic recipients “has not been evaluated and cannot be recommended.”
Past treatments

- Low molecular weight heparin
- Unfractionated heparin
- Vitamin K antagonists - Warfarin

1. PROS - Reversible
2. CONS - Require monitoring
New Oral Anticoagulants

- NOAC - Novel Oral Anticoagulants
- DAOC - Direct Acting Oral Anticoagulants
- Why?
  1. Rapid onset
  2. Short half-life
  3. Fewer drug interactions
  4. No food interactions
  5. No monitoring
  6. Equivalent to Warfarin in prevention of stroke and VTE
Direct oral anticoagulants (DOAC)

- Work directly on:
  1. Factor IIa = direct thrombin inhibitors
  2. Factor Xa = Xabans
- Without using antithrombin as a mediator
The Effect of Antithrombin III

**Intrinsic**
- XII → XIII
- XI → X
- IX
- IXa
- Phospholipid, Ca²⁺, VIII
- X
- Xa
- Phospholipid, Ca²⁺, V
- II
- IIa
- I
- Ia (fibrin)

**Extrinsic**
- Tissue factor
- VIlia
- TF Ca²⁺

**Heparin**
- Activates
- Antithrombin III
- Neutralizes
- Thrombin

**Inhibits acid phosphatase**

**No fibrin clot formation**

**Fibrinogen** → **Fibrin**
4 steps of hemostasis:

1. **Vessel injury**: Ruptured epithelium
2. **Vessel spasm**: Spasm
3. **Platelets adhere to injury site and aggregate to form plug**: Platelets
4. **Formation of insoluble fibrin strands and coagulation**: Fibrin

**Tissue injury:**

- **Liquid** → **clot** → **liquid**
- **1. vascular spasm**
- **2. platelet plug**
- **3. Fibrin cross linked**
- **4. fibrinolysis** → **break down clot**
The Precarious Balance

**Anticoagulants**
- Bleeding
- Bleeding Diathesis

**Procoagulants**
- Clotting
- Hemostasis
- Coagulation
- Thrombophilia

*the anticoagulants vs. the procoagulants*
New oral anticoagulants

Direct Thrombin inhibitors

PRADAXA
New oral anticoagulants

Direct Thrombin inhibitors

- **Bivalent**
  1. Hirudin
  2. Desirudin
    - Peptides in salivary glands of blood sucking leeches
  3. Lepirudin - reflidan - HIT
  4. Bivalirudin - angiomax
    - STEMI, NSTEMI, PCI
    - HIT
New Oral anticoagulants

Direct Thrombin Inhibitors

Univalent

1. Ximelagatran - Exanta, pulled from the market in 2006, liver failure

2. Argatroban - Acova

3. Dabigatran - Pradaxa
Bivalent block active site and exosite 1, univalent only block active site
Thrombin

- Thrombin activated from prothrombin
- Converts soluble fibrinogen to fibrin
- Activates factors V, VIII, XI
- Generates more thrombin and activates platelets
Dabigatran - Pradaxa

- Reversible direct thrombin inhibitor
- Rapid onset of action
- No food interactions
- Few drug interactions
- No coagulation monitoring
- Peak - 1-3 hr, ½ life 12-14 hrs
- 35% plasma bound, 80% renal excretion
Dabigatran

• Safe with liver impairment
Dabigatran

- FDA Approved 2010
  1. Non-valvular A-fib
- FDA approved 2014
  1. VTE and PE prophylaxis after hip surgery
  2. Treat DVT/PE after 5-10 days of parenteral anticoagulant
  3. Reduce recurrence of DVT/PE
Pradaxa Lawsuits

Timeline of Pradaxa Warnings and Label Updates

- **2010:** Researchers discover additional bleeding events in RE-LY trial data, resulting in an update to Pradaxa’s drug label.

- **2011:** The FDA reviews post-market reports of serious bleeding events to determine whether such incidents were occurring more than expected.

- **2013:** Boehringer Ingelheim adds a black box warning about risks of prematurely discontinuing the drug, and an increased risk of spinal hematomas in some patients.

- **2014:** The FDA issues a safety communication stating that the blood thinner caused a higher risk of gastrointestinal bleeding than warfarin (although, it had a similar risk for myocardial infarction and a lower risk for ischemic stroke, intracranial hemorrhage and death).
Injuries
Sudden uncontrollable gastrointestinal, rectal and brain bleeding

Manufacturer/Defendant
Boehringer Ingelheim Pharmaceuticals

Top Settlement
The company announced in 2014 that it would settle thousands of cases for $650 million.
Idarucizumab - Praxbind

- Presently available in 3,100 sites in US
- 5 gm dose in 2 separate 2.5 gm vials - bolus or gtt
- Immediately neutralizes anticoagulant effect
- Binds to dabigatran and its acylglucuronide metabolites with higher affinity than the binding affinity of dabigatran to thrombin
- May have rebound effect, (especially in renal failure)
New oral anticoagulants

Oral Direct factor Xa inhibitors
Factor Xa Inhibitors

Xa – rate limiting factor in thrombin generation
And amplification (converts prothrombin to thrombin)
Direct factor Xa inhibitors

- Inhibit:
  1. free Factor Xa
  2. Factor Xa in thrombinase complex
  3. Factor Xa found in clots

- (unfractionated and LMW heparins are dependent on antithrombin III to inhibit thrombin)
Factor Xa inhibitors

- Rivaroxaban - Xarelto
- Apixaban - Eliquis
- Endoxaban - Savaysa
- Betrixaban - Bevyyxa

- Arixtra - fondaparinux - parenteral Factor Xa inhibitor, released in 2010
Rivoroxaban - Xarelto

- 80% bioavailability
- Highly protein bound (non dializable)
- Few drug interactions
- Peak - 2-4 hrs
- Half life 5-9 hrs, elderly 11-13 hrs
- Primary clearance is non-renal (67% eliminated by kidney, 33% is inactive)
Rivaroxiban - Xarelto

- Assess effectiveness:
  1. Prolongs INR in dose dependent manner - not reliable d/t interassay variability (reagent and lab equipment)
  2. aPTT - less sensitive. (Prolonged in supra- therapeutic levels)
  3. Chromogenic anti-factor Xa assays - best method, developed for Xa inhibitors with specific calibrators for both rivaroxaban and apixaban
Apixaban - Eliquis

- Bioavailability 80%
- Highly protein bound (non dialyzable)
- Peak 2-3 hrs
- Limited drug interactions
- Half life 8-15 hrs
- Primary clearance is non renal - hepatic, biliary, intestinal and renal
Reversal for Xa inhibitor

- Prothrombin complex concentrates (PCCs) - activated PCC or factor VIII inhibitor
- 2 types, may contain 3 (II, IX, X) or 4 factors (II, VII, IX, X)
- Cotting factors are 25 times more concentrated than FFP
- Reversal in 15-20 mins
- CONS = Pro-thrombotic risk, availability and cost
- PCCa - Recombinant factor VIIa, require extremely high doses to reverse DOACs - not recommended
What about FFP??

DOACs **do not inhibit production of inactive factors**, bind to specific sites

Concentration of factors in FFP would require > 2 liter replacement to have an affect
Reversal for Factor Xa inhibitor

- **COST**
  - FFP = $200 - $400
  - Kcentra (4 factor PCC) + $1.27/unit, single dose for 80 kg patient is approximately $5,080
  - NovoSeven (recombinant factor VIIa) = $1.58 / mcg, full 80 mcg/kg dose for 70 kg patient = $9,840
Reversal for Factor Xa inhibitor

- COST
- FFP = $200 - $400
- Kcentra (4 factor PCC) + $1.27/unit, single dose for 80 kg patient is approximately $5,080
- NovoSeven (recombinant factor VIIa) = $1.58 / mcg, full 80 mcg/kg dose for 70 kg patient = $9,840
Reversal for Xa Inhibitors

- **Tranxenamic Acid**
  - Inhibits binding of plasma to fibrin (fibrinolysis)

- **Desmopressin**
  - Stimulates release of vWF, increases Factor VIII production

- **Hemodialysis**

- **Activated Charcoal**
  - Reduce absorption, time of last dose
<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Reversal treatment options</th>
</tr>
</thead>
</table>
| Dalteparin   | **Idarucizumab (Praxbind)**  
50mg total dose (given as divided doses of 25mg, 15 minutes apart)  
Alternatives if idarucizumab is unavailable:  
Hemodialysis  
Activated charcoal  
100g po/NG if ingestion time <2 hours  
4F-APCC (FEIBA)  
50 units/kg IV; not to exceed 5000 units (single dose only)  
Tranexamic acid  
25mg/kg IV  
Desmopressin  
0.3mcg/kg SQ or IV; limit to 2 IV doses given  
Increased risk of tachyphylaxis  
FFP: Not recommended  
rFVIIa: Not recommended |
| Apixaban     | **Activated charcoal**  
100g po/NG if ingestion time <6 hours  
4F-PCC (Kcentria / Octaplex)**  
50 units/kg IV; not to exceed 5000 units (single dose only)  
Tranexamic acid  
25mg/kg IV  
Desmopressin  
0.3mcg/kg SQ or IV; limit to 2 IV doses given  
Increased risk of tachyphylaxis  
Andexanet alfa*  
400mg IV bolus at 30mg/min followed by continuous infusion at 4mcg/min for 120 minutes  
FFP: Not recommended  
rFVIIa: Not recommended |
| Rivaroxaban  | **Activated charcoal**  
100g po/NG, if ingestion time <8 hours  
4F-PCC (Kcentria / Octaplex)**  
50 units/kg IV; not to exceed 5000 units (single dose only)  
Tranexamic acid  
25mg/kg IV  
Desmopressin  
0.3mcg/kg SQ or IV; limit to 2 IV doses given  
Increased risk of tachyphylaxis  
Andexanet alfa*  
800mg IV bolus at 30mg/min followed by continuous infusion at 8mcg/min for 120 minutes  
FFP: Not recommended  
rFVIIa: Not recommended |
Factor Xa Inhibitors

2016:
- More ER visits than any other class of drug
- 22,000 hospital admits for bleeding due to Xa inhibitors
- >3000 bleeding deaths
- Up 40% from previous years
- 1800 U.S lawsuits pending
- Push for specific reversal agent
Reversal for Xa Inhibitors

- Adexanet (ANDEXXA)- recombinant factor Xa protein
- FDA Approved in May 2018 for Limited release (to patients that need it) until 2019
- Portola pharmaceuticals
- Factor Xa decoy
- https://www.andexxa.com/find-andexxa/
Reversal for Xa Inhibitors

- 400 - 800 mg IV bolus followed by a continuous infusion of 2-4 mg/min for 2 hours
- $3300 per 100 mg vial = $49,500 for high dose
WARNING: THROMBOEMBOLIC RISKS, ISCHEMIC RISKS, CARDIAC ARREST, AND SUDDEN DEATHS

See full prescribing information for complete boxed warning

Treatment with ANDEXXA has been associated with serious and life-threatening adverse events, including:

- Arterial and venous thromboembolic events
- Ischemic events, including myocardial infarction and ischemic stroke
- Cardiac arrest
- Sudden deaths

Monitor for thromboembolic events and initiate anticoagulation when medically appropriate. Monitor for symptoms and signs that precede cardiac arrest and provide treatment as needed.
Andexxa

- \( \frac{1}{2} \) life = 1 hr
- Factor Xa inhibitors are not cleared by Andexxa
- Dependant on pts ability to eliminate them
- May begin to inhibit Xa after Adnexxa dose is completed due to short half life
Universal reversal agent

- Cirpanantag - binds and neutralizes all heparins, dabigatran and other factor Xa inhibitors
- Currently in phase II clinical trials
- Reverse Xa inhibitors, thrombin inhibitors and heparin
Perioperative Management

- Check list for direct oral anticoagulants (DOAC)
  1. Thromboembolic risk of the patient
  2. The bleeding risk of the patient
  3. Timing of stopping DOAC before an invasive procedure
     - Bleeding risk of procedure
     - Elimination half-life of DOAC - renal function, liver function, co-medications
  4. Specific concerns of certain invasive procedures
     - Neuraxial anesthesia
     - A-fib ablation
  5. When should bridging therapy begin?
  6. Resuming DOAC after procedure
Monitoring

- Creatinine clearance - Renal function
- Coagulation function tests in cases of acute bleed, suspected overdose or emergency surgery
- Dabigatran and thrombin inhibitors
  1. Thrombin time (Hemaclot assay)
  2. aPTT - alternative if Thrombin time is unavailable
- Rivaroxiban and factor Xa inhibitors
  1. Anti-factor Xa assay
  2. Prothrombin Time - inter-assay variability
Thromboembolic risk to patient

Surgery in Patients Requiring Long-term Anticoagulants

1. Thrombosis risk versus
2. Bleeding risk

Need to individualize the approach
# Stroke assessment - CHADS

<table>
<thead>
<tr>
<th>CHADS&lt;sub&gt;2&lt;/sub&gt; score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>Congestive heart failure (1 point)</td>
</tr>
<tr>
<td>H</td>
<td>Hypertension (1 point)</td>
</tr>
<tr>
<td>A</td>
<td>Age 75 years or older (1 point)</td>
</tr>
<tr>
<td>D</td>
<td>Diabetes mellitus (1 point)</td>
</tr>
<tr>
<td>S&lt;sub&gt;2&lt;/sub&gt;</td>
<td>Previous stroke or transient ischaemic attack (2 points).</td>
</tr>
</tbody>
</table>

The CHADS<sub>2</sub> system scores 1 point, up to a maximum of 6, for each of the following risk factors (except previous stroke or transient ischaemic attack, which scores double, hence the ‘2’). A score of 0 is classified as low risk, 1–2 moderate risk, and ≥ 3 = high risk.

## CHADS<sub>2</sub> vs. CHA<sub>2</sub>DS<sub>2</sub>-VASc

<table>
<thead>
<tr>
<th>CHADS&lt;sub&gt;2&lt;/sub&gt;</th>
<th>Points</th>
<th>CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt;-VASc</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factors</td>
<td>Points</td>
<td>Risk factors</td>
<td>Points</td>
</tr>
<tr>
<td>CHF</td>
<td>1</td>
<td>CHF/LVEF ≤ 40%</td>
<td>1</td>
</tr>
<tr>
<td>HTN</td>
<td>1</td>
<td>HTN</td>
<td>1</td>
</tr>
<tr>
<td>Age≥ 75</td>
<td>1</td>
<td>Age≥ 75</td>
<td>2</td>
</tr>
<tr>
<td>DM</td>
<td>1</td>
<td>DM</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/embolism</td>
<td>2</td>
<td>Stroke/TIA/embolism</td>
<td>2</td>
</tr>
</tbody>
</table>

Max 6

Vascular disease (prior MI, PAD, or aortic plaque) | 1
Age 65-74 years                                   | 1
Sex category (Female)                            | 1
Max 9
<table>
<thead>
<tr>
<th>Risk stratification</th>
<th>High</th>
<th>Intermediate</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Any mechanical mitral valve</td>
<td>• Bileaflet AVR plus major risk factors for stroke</td>
<td>• Bileaflet AVR without major risk factors for stroke</td>
</tr>
<tr>
<td></td>
<td>• Mitral/aortic caged ball or tilting disc valve</td>
<td>• CHADS₂ score of 3 or 4</td>
<td>• CHADS₂ score of 0–2</td>
</tr>
<tr>
<td></td>
<td>• MHV with history of stroke or TIA in previous 6 months</td>
<td>• VTE within 3–12 months</td>
<td>• No prior stroke or TIA</td>
</tr>
<tr>
<td></td>
<td>• CHADS₂ &gt;5</td>
<td>• Heterozygous factor V Leiden, prothrombin gene mutation</td>
<td>• No VTE in previous 12 months</td>
</tr>
<tr>
<td></td>
<td>• Atrial fibrillation with history of stroke or TIA in previous 3 months</td>
<td>• Active cancer (treatment within 6 months or palliative)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Recent (within 3 months) VTE</td>
<td>• Recurrent VTE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Deficiency of protein C, protein S, or antithrombin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Presence of antiphospholipid antibodies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>Bridging anticoagulation recommended</td>
<td>Bridging anticoagulation if low bleeding risk</td>
<td>Bridging anticoagulation not required</td>
</tr>
<tr>
<td>recommendations</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** VTE, venous thromboembolism; ATE, arterial thromboembolism; AVR, aortic valve replacement; MHV, mechanical heart valve; CHADS₂, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke history; TIA, transient ischemic attack.
TABLE 2. Risk of bleeding depending on the procedure.

- **Procedures associated to low risk of bleeding.**
  - Skin surgery or biopsy.
  - Endoscopies without biopsy.
  - Minor peripheral, plastic surgery.
  - Anterior chamber eye surgery (cataracts).
  - Dental extractions.
  - Central catheterization.
  - Intubation.

- **Procedures associated with a medium risk of bleeding.**
  - Cardiovascular invasive procedures.
  - Minor abdominal and pelvic or limb surgery.
  - Minor orthopedic surgery.
  - Minor otolaryngology surgery.
  - Endoscopic urological procedure without biopsy.

- **Surgeries associated with high risk of bleeding.**
  - Myocardial revascularization surgery.
  - Valve replacement surgery.
  - Spine or spinal cord surgery or neurosurgery.
  - Surgery of the posterior chamber of the eye.
  - Aortic aneurysm repair.
  - Peripheral bypass and other major vascular surgeries.
  - Major orthopedic surgeries (total hip and knee replacement).
  - Reconstructive plastic surgery.
  - Major surgery due to cancer.
  - Prostate or bladder surgery
  - Colon polyps resection.
  - Prostate or renal biopsy.
  - Pacemaker or cardioverter defibrillator.
TABLE 2. Perioperative considerations in anticoagulant treatment of nonvalvular atrial fibrillation

<table>
<thead>
<tr>
<th>Creatinine clearance</th>
<th>Direct factor Xa inhibitors</th>
<th>Direct thrombin inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>STANDARD RISK OF BLEEDING</td>
<td>HIGH RISK OF BLEEDING</td>
</tr>
<tr>
<td>&gt; 50 mL/min</td>
<td>Discontinue 24 h prior to</td>
<td>Discontinue 48 h prior to</td>
</tr>
<tr>
<td></td>
<td>procedure</td>
<td>procedure</td>
</tr>
<tr>
<td>30–50 mL/min</td>
<td>Discontinue 24 h prior to</td>
<td>Discontinue 48 h prior to</td>
</tr>
<tr>
<td></td>
<td>procedure</td>
<td>procedure</td>
</tr>
<tr>
<td>&lt; 30 mL/min</td>
<td>Discontinue 48 h prior to</td>
<td>Discontinue 72 h prior to</td>
</tr>
<tr>
<td></td>
<td>procedure</td>
<td>procedure</td>
</tr>
</tbody>
</table>

*Warfarin is not included in this table but should be discontinued 5 to 6 days before a procedure. Consider bridge therapy in patients who are at high risk for developing blood clots.
Elective procedures requiring neuraxial anesthesia receiving NOC

- DELAY if:
  1. A thrombotic event (VTE, MI, TIA, or stroke) has occurred within the previous 3 months
  2. A major hemorrhage, (decrease in Hgb by 2GM/dl), transfusion of 2 units of PRBCs, or bleeding into an organ has occurred within previous 3 months
  3. Patient is pregnant or < 6 weeks post partum
Neuraxial Anesthesia

- A-fib, high risk for thrombosis, CHF, HTN, DM, vascular disease, previous thromboembolism
- Discontinuation based on half-life
- Recommendation = 2 to 3 half-lives (30 - 45 hrs)
- Leaves some residual coagulation for prevention of VTE
- Conservative approach = 5-6 half-lives (3-5 days), may bridge with LMW heparin

<table>
<thead>
<tr>
<th>Half-lives</th>
<th>% drug in circulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
</tr>
<tr>
<td>2</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>12.5</td>
</tr>
<tr>
<td>4</td>
<td>6.25</td>
</tr>
<tr>
<td>5</td>
<td>3.1</td>
</tr>
<tr>
<td>6</td>
<td>1.6</td>
</tr>
</tbody>
</table>
Prolonged half-lives
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target</td>
<td>Thrombin</td>
<td>FXa</td>
<td>FXa</td>
</tr>
<tr>
<td>Peak plasma levels</td>
<td>1 – 2 h*</td>
<td>2 – 4 h</td>
<td>3 – 4 h</td>
</tr>
<tr>
<td>Dosing in AF**</td>
<td>Twice daily</td>
<td>Once daily</td>
<td>Twice daily</td>
</tr>
<tr>
<td>Must take with food</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Renal clearance of active drug</td>
<td>80%</td>
<td>33%</td>
<td>25%</td>
</tr>
<tr>
<td>Half-life elimination with normal renal function</td>
<td>12 – 18 h</td>
<td>5 – 13 h</td>
<td>12 – 15 h</td>
</tr>
<tr>
<td>Dose adjustment in moderate liver impairment</td>
<td>No</td>
<td>Contraindicated</td>
<td>No</td>
</tr>
<tr>
<td>Significant drug interactions***</td>
<td>P-gp inhibitors or inducers</td>
<td>P-gp/CYP 3A4 inhibitors or inducers</td>
<td>P-gp/CYP 3A4 inhibitors or inducers</td>
</tr>
</tbody>
</table>

**Abbreviations:** AF = atrial fibrillation; CYP3A4 = cytochrome P450 3A4 isoenzymes; FXa = activated factor X; h = hours; P-gp = P-glycoprotein.

**Footnotes:** * Dabigatran action onset may be delayed 2 hours by food.
** Potential variation exists in drug metabolism by different ethnic groups (i.e., lower dose may be indicated in Japanese). Further detailed dosing information found in Appendix A: Prescription Medication Table for Direct Oral Anticoagulants.
** See Appendix A: Potential NOAC Drug Interactions for more information about drug interactions.
Safety measures

- Avoid multiple attempts at catheter insertion
- Stop if excessive bleeding occurs
- Close follow-up with heightened awareness for bleeding complications
# Resuming NOACs

Recommendation is 24 - 48 hours after the procedure or catheter removal

The French Study Group recommended a 24 h interval before resumption of the oral anticoagulants.<sup>10</sup>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Time to peak effect of drug</th>
<th>Resumption of drug based on 8 h minus the time to peak anticoagulant effect&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Resumption of drug based on 24 h minus the time to peak anticoagulant effect&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Baron and colleagues: recommendations of high-risk procedures&lt;sup&gt;11&lt;/sup&gt;</th>
<th>Connolly and Spyropoulos: high bleeding risk&lt;sup&gt;12&lt;/sup&gt;</th>
<th>Liew and Douketis&lt;sup&gt;13&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>2 (1.5–3) h</td>
<td>6 h</td>
<td>22 h</td>
<td>48 h</td>
<td>24 h, half of the usual dose for first 2 days</td>
<td>24 h after operation for cases with low bleeding risk, 48–72 h for high bleeding risk</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>2.5–4 h</td>
<td>5.5 h</td>
<td>21.5 h</td>
<td>48 h</td>
<td>24 h, half of the usual dose for first 2 days</td>
<td>Same as dabigatran</td>
</tr>
<tr>
<td>Apixaban</td>
<td>1–2 h</td>
<td>7 h</td>
<td>23 h</td>
<td>48 h</td>
<td>24 h, half of the usual dose for first 2 days</td>
<td>Same as dabigatran</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>1 h</td>
<td>7 h</td>
<td>23 h</td>
<td>Caution (recommended within 24 h for aspirin and clopidogrel)</td>
<td>(Same as for prasugrel)</td>
<td>(Same as for prasugrel)</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>2–4 h</td>
<td>6 h</td>
<td>22 h</td>
<td>(Same as for prasugrel)</td>
<td>(Same as for prasugrel)</td>
<td>(Same as for prasugrel)</td>
</tr>
</tbody>
</table>
Interventional Spine and Pain procedures

- American Society of Regional and Pain Medicine
- Communicate with other providers - clear history of risk
- Chronic pain and stress = hypercoaguability
- High risk vs low risk procedures
- Fragility of epidural veins increases with age
<table>
<thead>
<tr>
<th>Risks</th>
<th>Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HI</strong></td>
<td>• SCS trial and implant</td>
</tr>
<tr>
<td></td>
<td>• Intrathecal implant with pump</td>
</tr>
<tr>
<td></td>
<td>• Vertebroplasty, kyphoplasty</td>
</tr>
<tr>
<td><strong>MOD</strong></td>
<td>• Interlaminar ESI</td>
</tr>
<tr>
<td></td>
<td>• Transforaminol ESI</td>
</tr>
<tr>
<td></td>
<td>• Paravertebral blocks</td>
</tr>
<tr>
<td></td>
<td>• Intradiscal procedures</td>
</tr>
<tr>
<td></td>
<td>• Sympathetic blocks</td>
</tr>
<tr>
<td><strong>LOW</strong></td>
<td>• Peripheral nerve blocks</td>
</tr>
<tr>
<td></td>
<td>• Joint injections</td>
</tr>
<tr>
<td></td>
<td>• Trigger point injections</td>
</tr>
<tr>
<td></td>
<td>• SI injections</td>
</tr>
</tbody>
</table>
Regional anesthesia

- American Society of Regional Anesthesia
  - Based on half-life
  - 5 half-lives between stopping DOAC and performing medium or high risk pain procedures
    1. Dabigatran - 4-5 days
    2. Rivaroxaban and apixaban - 3-5 days
  - Restart 24 hours
My crush!!
References


Thank you!!!