Disclosure

Chad Triplett reports no actual or potential conflicts of interest associated with this presentation.

Objectives

- Review Chest Guidelines recommendation for VTE treatment
- Review role of warfarin and direct oral anticoagulants (DOACs)
- Identify appropriate candidates eligible to receive warfarin vs DOACs
- Review conversion from warfarin to DOACs and vice-versa
- Discuss DOAC reversibility and management of bleeding
- Briefly review topics with less established evidence
CHEST Recommendations

- Non-cancer related thrombois, DOACs are recommended over vitamin K antagonist (VKA) therapy (Grade 2B)
  - No direct comparison between agents so efficacy seems similar between agents
  - Bleeding risk with DOACs is less than VKA therapy
- In patients who receive extended therapy, there is no need to change the choice of anticoagulant after the first 3 months (Grade 2C)

CHEST Recommendations

- In patients where VTE is provoked by surgery or a nonsurgical transient risk factor, 3 months of treatment is recommended (Grade 1B)
- In patients with a first unprovoked VTE, treat at least 3 months (Grade 1B).
  - In patients with a low or moderate bleed risk, extended treatment is recommended (Grade 2B).
  - In those with a high bleed risk, 3 months is recommended over extended therapy (Grade 1B)
Ideal Anticoagulant
- No need for routine monitoring ✓
- Oral administration ✓
- Use in acute and chronic conditions ✓
- Use in both hospital and home settings ✓
- Minimal or no adverse effects
- Proven efficacy in treating and/or preventing thrombosis ✓
- No drug or diet interactions
- Easily reversible

Appropriate DOAC Patient
- Appropriate indication (atrial fibrillation (AF), venous thromboembolism (VTE), VTE prophylaxis post joint replacement, or risk reduction of CV events (rivaroxaban)
- Adequate kidney function
- Excellent medication compliance
- Insurance coverage
- Not on strong p-glycoprotein (p-gp) or cytochrome (CYP) P450 inhibitors or inducers

Current DOACs
- Dabigatran (Pradaxa®)
- Rivaroxaban (Xarelto®)
- Apixaban (Eliquis®)
- Edoxaban (Savaysa®)
- Betrixaban (Bevyxxa®)
Mechanism of Action

Figure adapted from Dipiro et al. Pharmacotherapy: A Pathophysiologic Approach, 3rd Ed. 1997.

Warfarin
- 1st new anticoagulant in U.S. in >50 years
  - FDA approved October 2010
  - Oral direct thrombin (Factor IIa) inhibitor
  - Inhibits both clot-bound and circulating thrombin
  - Prodrug: dabigatran etexilate → dabigatran
  - Conversion by plasma esterase
  - Indications:
    - Reduction in risk of stroke and systemic embolism in non-valvular atrial fibrillation
    - Treatment of DVT and PE
    - Risk reduction of recurrence of DVT and PE following initial treatment
    - Prevention of VTE in total hip replacement
- Capsules: 75 mg, 110 mg and 150 mg

Dabigatran

- 1st new anticoagulant in U.S. in >50 years
- FDA approved October 2010
- Oral direct thrombin (Factor IIa) inhibitor
- Inhibits both clot-bound and circulating thrombin
- Prodrug: dabigatran etexilate → dabigatran
- Conversion by plasma esterase
- Indications:
  - Reduction in risk of stroke and systemic embolism in non-valvular atrial fibrillation
  - Treatment of DVT and PE
  - Risk reduction of recurrence of DVT and PE following initial treatment
  - Prevention of VTE in total hip replacement
- Capsules: 75 mg, 110 mg and 150 mg

Rivaroxaban

- First approved (July 2011) oral, direct, selective Factor Xa inhibitor
- Indications:
  - Prevention of DVT and PE in total hip and knee replacement surgery
  - Prevention of stroke and systemic embolism in atrial fibrillation
  - Treatment of DVT and PE
  - Risk reduction of recurrent DVT and/or PE after at least 6 months of initial treatment. CV risk reduction in combination with aspirin
- Tablets: 10 mg, 15 mg and 20 mg
**Apixaban**

- Oral, direct, selective Factor Xa inhibitor. Approved December 2012

- **Indications:**
  - Prevention of stroke and systemic embolism in patients with atrial fibrillation
  - Treatment of DVT and PE
  - Risk reduction of recurrent DVT and PE following at least 6 months of initial therapy
  - Prevention of DVT and PE in total hip and knee replacement surgery

- **Tablets:** 2.5 mg and 5 mg

**Edoxaban**

- Oral, direct, selective Factor Xa inhibitor. Approved January 2015

- **Indications:**
  - Prevention of stroke and systemic embolism in patients with atrial fibrillation
  - Treatment of DVT and PE

- **Tablets:** 15 mg, 30 mg and 60 mg

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**DOAC Comparison**

<table>
<thead>
<tr>
<th>Property</th>
<th>Warfarin (coumadin®)</th>
<th>Delegent (Pexelos®)</th>
<th>Apixaban (Eliquis®)</th>
<th>Edoxaban (Savaysa®)</th>
<th>Revlimid (Rekastra®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor Inhibition</td>
<td>X, PII, III, IV, and V</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>FDA-Labelled Indications</td>
<td>APE - VTE treatment - VTE recurrence - PLX prophylaxis</td>
<td>APE - VTE treatment - VTE recurrence - PLX prophylaxis</td>
<td>APE - VTE treatment - VTE recurrence - PLX prophylaxis</td>
<td>APE - VTE treatment - VTE recurrence - PLX prophylaxis</td>
<td>APE - VTE treatment - VTE recurrence - PLX prophylaxis</td>
</tr>
<tr>
<td>Therapeutic Level</td>
<td>3:0-4:0</td>
<td>2.0-3.0</td>
<td>2.0-3.0</td>
<td>2.0-3.0</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Normal Oiling</td>
<td>Daily</td>
<td>BD</td>
<td>BD</td>
<td>BD</td>
<td>Daily</td>
</tr>
<tr>
<td>VTE 2 mg 40+1 units</td>
<td>BD</td>
<td>BD</td>
<td>BD</td>
<td>BD</td>
<td>BD</td>
</tr>
<tr>
<td>Reversibility</td>
<td>Vitamin K, Factora®</td>
<td>Pentadon®</td>
<td>Andexan®</td>
<td>None</td>
<td>Andexan®</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>X</td>
<td>C</td>
<td>B</td>
<td>C</td>
<td>C</td>
</tr>
</tbody>
</table>

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*Source: adapted from www.medicine.com (Pharmacy, 2015, 2016)*
### DOAC Comparison

**Table created by Deanna McDanel, PharmD, BCPS, BCACP**

<table>
<thead>
<tr>
<th>Labeling</th>
<th>Dabigatran (Pradaxa®)</th>
<th>Apixaban (Eliquis)</th>
<th>Edoxaban (Lixiana)</th>
<th>Rivaroxaban (Xarelto®)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Labeling</strong></td>
<td>No oral administration</td>
<td>No oral administration</td>
<td>No oral administration</td>
<td>No oral administration</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>Twice daily</td>
<td>Twice daily</td>
<td>Twice daily</td>
<td>Twice daily</td>
</tr>
<tr>
<td><strong>Administration</strong></td>
<td>Doses: 150 mg or 220 mg</td>
<td>Doses: 100 mg or 150 mg</td>
<td>Doses: 60 mg, 120 mg</td>
<td>Doses: 20 mg, 20 mg, 40 mg</td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td>Renal function, laboratory monitoring of D-dimer, and INR</td>
<td>Renal function, laboratory monitoring of D-dimer, and INR</td>
<td>Renal function, laboratory monitoring of D-dimer, and INR</td>
<td>Renal function, laboratory monitoring of D-dimer, and INR</td>
</tr>
<tr>
<td><strong>Advantages</strong></td>
<td>Blending, gastrointestinal side effects, no food restrictions</td>
<td>Blending, gastrointestinal side effects, no food restrictions</td>
<td>Blending, gastrointestinal side effects, no food restrictions</td>
<td>Blending, gastrointestinal side effects, no food restrictions</td>
</tr>
</tbody>
</table>

### DOAC Drug Interactions

**Table created by Deanna McDanel, PharmD, BCPS, BCACP**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Drugs that increase levels</th>
<th>Drugs that decrease levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>Dabigatran</td>
<td>Warfarin (Coumadin)</td>
</tr>
<tr>
<td>Apixaban</td>
<td>Apixaban</td>
<td>Warfarin (Coumadin)</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>Edoxaban</td>
<td>Warfarin (Coumadin)</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Rivaroxaban</td>
<td>Warfarin (Coumadin)</td>
</tr>
</tbody>
</table>

**A3: Increased risk of bleeding with other anticoagulants, antithrombotic agents, and non-steroidal anti-inflammatory drugs (NSAIDs).**
Major VTE Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Study Arms</th>
<th>Primary Efficacy (VTE Incidence)</th>
<th>Major Bleeding</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran 150 mg BID (n=6,544)</td>
<td>2/4/6/8</td>
<td>Dabigatran 150 mg vs. Placebo (n=6,544)</td>
<td>Non-significant, 2.3 vs. 2.4% (p=0.481)</td>
<td>Non-significant, 1.6 vs. 1.9 (p=0.18)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Apixaban 5/10 mg BID (n=5,335)</td>
<td>2/4/6/8</td>
<td>Apixaban 5 or 10 mg BID vs. Placebo (n=5,335)</td>
<td>Not applicable, 2.1 vs. 2.7% (p=0.150)</td>
<td>Not applicable, 1.3 vs. 1.7 (p=0.173)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Rivaroxaban 20 or 15 mg BID (n=6,092)</td>
<td>2/4/6/8</td>
<td>Rivaroxaban 15 mg BID vs. Placebo (n=6,092)</td>
<td>Not applicable, 2.1 vs. 2.4% (p=0.170)</td>
<td>Not applicable, 1.4 vs. 1.9 (p=0.175)</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

VTE Dosing

<table>
<thead>
<tr>
<th>VTE Treatment</th>
<th>Dabigatran</th>
<th>Apixaban</th>
<th>Edoxaban</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Treatment Dose</td>
<td>150 mg BID AFTER 5-30 days of parenteral anticoagulation (i.e., heparin or LMWH)</td>
<td>15 mg BID for 7 days</td>
<td>5 mg BID</td>
<td>15 mg BID for 10 days with fondaparinux</td>
</tr>
<tr>
<td>Risk of Recurrence Reduction</td>
<td>150 mg BID + UFH 3-4 (x/m, min)</td>
<td>2.5 mg BID</td>
<td>Not in labeling</td>
<td>10 mg daily (weight-adjusted)</td>
</tr>
<tr>
<td>Other Dosing</td>
<td>15 mg BID</td>
<td>10 mg BID</td>
<td>5 mg BID</td>
<td>10 mg BID</td>
</tr>
<tr>
<td>Renal Dosing (mg/min)</td>
<td>Dabigatran: 0.23 mg/min</td>
<td>Apixaban: 0.21 mg/min</td>
<td>Edoxaban: 0.21 mg/min</td>
<td>Rivaroxaban: 0.23 mg/min</td>
</tr>
</tbody>
</table>

VTE Treatment Course

- Rivaroxaban 15 mg BID
  - 8 days
  - 8 Months/Ongoing
- Apixaban 10 mg BID
  - 8 days
  - 8 Months/Ongoing
- Parenteral/Anticoagulant 5-10 days FIAST
  - Dabigatran 150 mg BID
- Parenteral/Anticoagulant 5-10 days FIAST
  - Rivaroxaban 60 mg daily
Duration

- Risk of recurrence
  - Nonsurgical transient risk factor – 15% at 5 years
  - Unprovoked – 30% at 5 years
  - Men have a 75% higher risk of recurrence than women

- Risk of bleed (annual rate)
  - 0 risk factors – 0.8%
  - 1 risk factor – 1.6%
  - 2 or more factors - ≥6.5%
**D Dimer**

- Increased rate of recurrence with + D-Dimer; 9-16% vs 4-7%
- Most studies drawn 1 month after anticoagulation stopped
- May be a tool to help guide further treatment

**D-Dimer Issues**

- Not specific
- Variation across labs
- Age and sex variations
- No standard on timeframe to draw

**DOACs in Obesity**

- International Society on Thrombosis and Haemostasis (ISTH) guidance recommendations
  - We suggest that DOACs should NOT be used in patients with a BMI >40 kg/m² or weight >120 kg due to limited clinical data and kinetic data showing decreased drug levels and shorter half lives
  - If a DOAC is used in these patients, we suggest checking a peak and trough drug level:
    - Anti-factor Xa for apixaban, edoxaban and rivaroxaban
    - Ecarin time or dilute thrombin time for dabigatran
  - If level falls within expected range, continue DOAC
  - If the level is below expected range, change to warfarin rather than adjusting the DOAC dose
Prosthetic Heart Valves??

- **RE-ALIGN trial** (open-label, N=252)
  - Dabigatran 150 mg, 220 mg or 300 mg BID (dosed on CrCl) vs warfarin (2-3 or 2.5-3.5 INR) in bileaflet mechanical heart valves
  - **TERMINATED EARLY**
    - Significantly more thromboembolic events (valve thrombosis, stroke, transient ischemic attack, and myocardial infarction)
    - Excess of any and major bleeding (predominantly post-operative pericardial effusions requiring intervention for hemodynamic compromise)
  - **IN APX 60X ERA version**: dabigatran is contraindicated in patients with mechanical prosthetic valves
  - **Terminated early** on the basis of these findings
  - Not studied in bioprosthetic valves or other valvular heart disease
- Safety and efficacy of apixaban, edoxaban and rivaroxaban have not been studied in patients with prosthetic heart valves → NOT RECOMMENDED

DOAC’s and Malignancy?

<table>
<thead>
<tr>
<th></th>
<th>Edoxaban (Daxid)</th>
<th>Apixaban (AstraZeneca)</th>
<th>Rivaroxaban (Janssen)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran (Genentech)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>852</td>
<td>456</td>
<td>350</td>
</tr>
<tr>
<td>Follow-up time</td>
<td>12 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VTE recurrence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>


www.google.com/images_superman
Converting from Warfarin to DOAC

<table>
<thead>
<tr>
<th>DOAC</th>
<th>Conversion FROM Warfarin TO a DOAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivaroxaban</td>
<td>STOP warfarin and START rivaroxaban when INR &lt;3.0</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>STOP warfarin and START edoxaban when INR &lt;2.5</td>
</tr>
<tr>
<td>Apixaban</td>
<td>STOP warfarin and START apixaban when INR &lt;2.0</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>STOP warfarin and START dabigatran when INR &lt;2.0</td>
</tr>
</tbody>
</table>

Converting from Dabigatran to Warfarin

<table>
<thead>
<tr>
<th>Renal Function (mL/min)</th>
<th>Dabigatran Conversion TO Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl &gt;50</td>
<td>START warfarin 3 days before STOPPING dabigatran</td>
</tr>
<tr>
<td>CrCl 30-50</td>
<td>START warfarin 2 days before STOPPING dabigatran</td>
</tr>
<tr>
<td>CrCl 15-30</td>
<td>START warfarin 1 day before STOPPING dabigatran</td>
</tr>
<tr>
<td>CrCl &lt;15</td>
<td>No recommendations</td>
</tr>
</tbody>
</table>

Converting Xa Inhibitors to Warfarin

<table>
<thead>
<tr>
<th>Factor Xa inhibitor</th>
<th>Conversion TO Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>STOP, begin BOTH warfarin PLUS a parenteral anticoagulant when next dose of factor Xa inhibitor due</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>STOP, begin BOTH warfarin PLUS a parenteral anticoagulant when next dose of edoxaban is due OR Decrease dose in HALF and start warfarin concomitantly. INR at least weekly before edoxaban dose; STOP when INR ≥2.0</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>STOP, begin BOTH warfarin PLUS a parenteral anticoagulant when next dose of edoxaban is due OR Decrease dose in HALF and start warfarin concomitantly. INR at least weekly before edoxaban dose; STOP when INR ≥2.0</td>
</tr>
</tbody>
</table>
### Peri-Procedural Management

<table>
<thead>
<tr>
<th>Drug</th>
<th>Surgery/Procedure with Low/Normal Risk</th>
<th>Surgery/Procedure with High/Very High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>Last Dose</td>
<td>Reverse Dose</td>
</tr>
<tr>
<td>Admin Taken</td>
<td>24h prior to surgery</td>
<td>4h prior to surgery</td>
</tr>
<tr>
<td></td>
<td>4h after surgery</td>
<td>4h after surgery</td>
</tr>
<tr>
<td></td>
<td>40h after surgery</td>
<td>48h after surgery</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>Last Dose</td>
<td>Reverse Dose</td>
</tr>
<tr>
<td>Admin Taken</td>
<td>24h prior to surgery</td>
<td>4h prior to surgery</td>
</tr>
<tr>
<td></td>
<td>4h after surgery</td>
<td>4h after surgery</td>
</tr>
<tr>
<td></td>
<td>40h after surgery</td>
<td>48h after surgery</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>CIV 150 or 220 mg/kg</td>
<td>CIV 180 or 210 mg/kg</td>
</tr>
<tr>
<td></td>
<td>24h prior to surgery</td>
<td>1h prior to surgery</td>
</tr>
<tr>
<td></td>
<td>3h after surgery</td>
<td>4h prior to surgery</td>
</tr>
<tr>
<td></td>
<td>4h after surgery</td>
<td>4h after surgery</td>
</tr>
<tr>
<td></td>
<td>40h after surgery</td>
<td>48h after surgery</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>CIV 10 mg/kg</td>
<td>CIV 15 mg/kg</td>
</tr>
<tr>
<td></td>
<td>24h prior to surgery</td>
<td>1h prior to surgery</td>
</tr>
<tr>
<td></td>
<td>3h after surgery</td>
<td>4h prior to surgery</td>
</tr>
<tr>
<td></td>
<td>4h after surgery</td>
<td>4h after surgery</td>
</tr>
<tr>
<td></td>
<td>40h after surgery</td>
<td>48h after surgery</td>
</tr>
</tbody>
</table>
Dabigatran Reversal

Idarucizumab (Praxbind®)

- Humanized monoclonal antibody fragment to bind dabigatran
- Approved October 2015
- Indication is reversal of dabigatran if needed for:
  - Emergency surgery/urgent procedures
  - Life-threatening or uncontrolled bleeding
- Accelerated approval based healthy volunteers study
- Continued approval contingent upon the results of an ongoing cohort case series study
- Dosing:
  5 g (2 vials of 2.5 g/50 mL) idarucizumab – Cost $3482
  Limited data to support administration of an additional 5 g
- Resulted in rapid, complete reversal of anticoagulation in patients experiencing life-threatening bleed or requiring urgent surgery

Idarucizumab (cont.)

- Warnings/Precautions:
  - Thromboembolic risk: Reversing dabigatran exposes patients to the thrombotic risk of their underlying disease so resume anticoagulant as soon as medically appropriate
  - Re-elevation of coagulation parameters: If this happens and there is reappearance of clinically relevant bleeding or requiring a second emergency surgery/urgent procedure, an additional 5 g dose may be used
  - Hypersensitivity reactions: Discontinue administration and evaluate
  - Hereditary fructose intolerance: Patients with hereditary fructose intolerance may be at risk of adverse reactions due to sorbitol excipient
- Adverse Effects (>5%):
  - Headache, hypokalemia, delirium, constipation, pyrexia, and pneumonia

Coagulation Factor Xa (Andexxa®)

- Recombinant modified human factor Xa protein
- Approved May 2018
- Indication is reversal of apixaban and rivaroxaban if needed for life-threatening or uncontrolled bleeding
- Accelerated approval based healthy volunteers study
- Continued approval contingent upon the results of an ongoing cohort case series study
- Not shown effective and not indicated for other Xa inhibitors
- Warnings/Precautions:
  - Thromboembolic risk: arterial/venous thromboembolism, ischemic and cardiac events (including sudden death) have occurred
  - Resume anticoagulation as soon as medically appropriate
  - Re-elevation of coagulation parameters
- Adverse Effects:
  - Urinary tract infections and pneumonia (>5%), infusion-related reactions (>5%)
Andexxa®

**Dosing:** Based on specific Xa inhibitor, dose of Xa inhibitor and time since the patient’s last dose of the Xa inhibitor

<table>
<thead>
<tr>
<th>Xa Inhibitor</th>
<th>FXa Inhibitor Last Dose</th>
<th>Timing of FXa Inhibitor Last Dose Before ANDEXXA Initiation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥ 90 mg</td>
<td>Low Dose</td>
</tr>
<tr>
<td></td>
<td>≤ 15 mg or Unknown</td>
<td>High Dose</td>
</tr>
<tr>
<td></td>
<td>≤ 5 mg or Unknown</td>
<td>Low Dose</td>
</tr>
<tr>
<td></td>
<td>&gt; 5 mg or Unknown</td>
<td>High Dose</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dose*</th>
<th>Initial IV Rate</th>
<th>Follow On IV Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Dose</td>
<td>40 mg at a target rate of 10 mg/min</td>
<td>4 mg/min for up to 120 minutes</td>
</tr>
<tr>
<td>High Dose</td>
<td>80 mg at a target rate of 10 mg/min</td>
<td>8 mg/min for up to 120 minutes</td>
</tr>
</tbody>
</table>

*The safety and effectiveness of more than one dose have not been evaluated.
Triple Therapy

- Dual therapy added to an oral anticoagulant increases bleeding risk 2-3 fold
- Limited high quality data to clarify therapy, especially with VTE treatment
- Patient thrombosis and bleed risk must be evaluated
- Duration will be patient specific and should be made in conjunction with cardiology

Factors to consider:
- Use aspirin 81 mg
- Use a proton pump inhibitor (PPI) if previous GI bleed and consider in other patients (pantoprazole preferred with clopidogrel)
- Use clopidogrel over prasugrel or ticagrelor
- More data with warfarin in triple therapy regimens but DOAC studies are ongoing
- If using warfarin, target lower end of goal range
Distal DVT

- Serial imaging (no evidence based protocol)
  - If thrombus remains stable, no anticoagulation
  - Begin anticoagulation if thrombus extends in distal veins or extends into proximal veins

Distal DVT

- Anticoagulation favored
  - + D Dimer
  - Extensive thrombosis (>5 cm long, multiple veins, >7 mm in diameter)
  - Close proximity to proximal veins
  - No reversible cause
  - Cancer
  - History of previous VTE
  - Inpatient

Subsegmental PE

- No randomized trials
- Risk of false positives
  1) High quality pulmonary angiography
  2) Multiple intraluminal defects
  3) More proximal subsegmental arteries
  4) Seen on more than one image
  5) Seen on more than one projection
  6) Symptomatic patient
  7) High clinical pretest probability
  8) D-Dimer is elevated

Subsegmental PE

- Hemodynamically stable patient obtain bilateral US to rule out proximal DVT
- Consider treatment if unstable or increased risk of recurrent or progressive PE

Summary

- DOAC’s are now preferred by the CHEST guidelines in appropriate patients
- DOAC’s should not be used with heart valves or in most obese patients
- Duration of therapy a very individualized decision
- Evaluation of need of long term therapy should be re-evaluated as patient factors change
- Limited data on conclusive treatment of more distal VTE’s