Hypercoaguable States

Review risks for VTE
Thrombophilas testing
Duration of anticoagulation therapy
provoked VTE
unprovoked VTE

Risk Factors for VTE

<table>
<thead>
<tr>
<th>Transient/Provoked</th>
<th>Persistent</th>
<th>Idiopathic/Unprovoked</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery</td>
<td>Obesity</td>
<td>????</td>
</tr>
<tr>
<td>Trauma</td>
<td>Chronic Medical Illnesses</td>
<td>High FVIII</td>
</tr>
<tr>
<td>Acute medical illness</td>
<td>Cancer and its therapy</td>
<td>Acquired APCR</td>
</tr>
<tr>
<td>Immobilization</td>
<td>Inflammatory bowel disease</td>
<td>High FIX, XI</td>
</tr>
<tr>
<td>Estrogen-containing contraceptives or hormone replacement therapy</td>
<td>Nephrotic syndrome</td>
<td></td>
</tr>
<tr>
<td>Pregnancy/puerperium</td>
<td>Myeloproliferative neoplasms/PNH</td>
<td></td>
</tr>
<tr>
<td>HIT</td>
<td>Paralysis</td>
<td></td>
</tr>
</tbody>
</table>

VTE

- VTE annual incidence 2-3 cases per 1000 people in general population

- Risks
  - Acquired
  - Inherited
  - Mixed/unknown

- “Provoked” vs “Unprovoked”
  - Transient risk
  - Persistent risk
  - Unidentified, unknown, “idiopathic”

VTE Risk Factor Model

- Genes
  - Anticoagulant deficiencies
    - Anti-thrombin
    - Protein S
    - Protein C
    - Prothrombin
    - Factor V Leiden
- Acquired Risk Factors
  - Age
  - Previous VTE
  - Cancer
  - Obesity
  - LAC

- Triggering Factors
  - Estrogens
  - Pregnancy
  - Surgery
  - Immobilization
  - Inflammation

- Prophylaxis

- Threshold

No conflicts of interest
### Clinical Clues for Thrombophilias

- Age of onset <50
- Recurrent thrombosis
- Positive family history in 1st degree relative
- Unusual location/site

### Thrombophilia Testing

- **When does it change care?**
  - Explain etiology
  - Prophylaxis
  - Pregnancy
  - OCP/hormone therapy
  - Family members
- **When does it not change care?**
  - Duration of anticoagulation therapy in most provoked VTE cases
  - Antiphospholipid syndrome
  - Known malignancy
  - Other fixed requirements for anticoagulation

### Who to Test?

**Yes**
- VTE at age <50 with positive family history (1st degree relatives)
- Cerebral venous thrombosis
- Portal/mesenteric vein thrombosis (r/o MPD, PNH)
- Pregnancy loss (2nd and 3rd trimester)

**Reasonable**
- VTE in association with OCPs/HRT or pregnancy

**No**
- Patients > 50 with first spontaneous VTE
- VTE in patients with active cancer
- Elderly patients with postoperative VTE
- Retinal vein thrombosis
- Arterial thrombosis (except paradoxical emboli)
- Asymptomatic patients with no personal or familial hx of VTE
- Women going on OCPs with no familial hx of VTE

### The “Hypercoagulable Workup”

**Genetic test for Factor V Leiden mutation**

**Genetic test for Prothrombin G20210A mutation**

**Functional assay of Antithrombin**

**Functional assay of Protein C**

**Functional assay of Protein S**

**Free Protein S Antigen**

**Total Protein S Antigen**

**Tests for Antiphospholipid Antibody Syndrome**

- Lupus anticoagulant: screen and confirmatory
  - screen: PPT-LA, DRVVT. Confirm: PNP, hexagonal phospholipids
  - Anti-Cardiolipin/β2-glycoprotein I antibodies

### Inherited Thrombophilias

- **Increased procoagulant activity**
  - Factor V Leiden mutation
  - Prothrombin gene G20210A mutation
- **Decreased anticoagulant activity**
  - Protein C
  - Protein S
  - antithrombin

### AT, Proteins S and C

<table>
<thead>
<tr>
<th>ANTITHROMBIN</th>
<th>PROTEIN C</th>
<th>PROTEIN S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>Liver Disease</td>
<td>Liver Disease</td>
</tr>
<tr>
<td>DIC</td>
<td>DIC</td>
<td>DIC</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>Inflammation</td>
<td>Acute thrombosis</td>
</tr>
<tr>
<td>Major surgery</td>
<td>Acute thrombosis</td>
<td>Acute thrombosis</td>
</tr>
<tr>
<td>Acute thrombosis</td>
<td>Acute thrombosis</td>
<td>Acute thrombosis</td>
</tr>
</tbody>
</table>

**Treatment with:**

- Heparin
- Warfarin
- Estrogens
  - Warfarin
  - Estrogens

- Levels decrease in the setting of above factors.
- Results drawn at initial presentation of VTE or while on anticoagulants often not valid.
- Abnormal results must be confirmed after discontinuation of anticoagulation.
Prevalence of Defects in Caucasian Patients with VTE

<table>
<thead>
<tr>
<th>Factor V Leiden</th>
<th>12-40%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prothrombin Gene Mutation</td>
<td>6-18%</td>
</tr>
<tr>
<td>Deficiencies of AT, Protein C, Protein S</td>
<td>5-15%</td>
</tr>
<tr>
<td>Antiphospholipid Antibody Syndrome</td>
<td>-5%</td>
</tr>
<tr>
<td>Unknown</td>
<td>20-70%</td>
</tr>
</tbody>
</table>

Several new variants have been found by candidate and genome-wide screens – all common and weak (OR < 1.5)

Risk vs. Incidence of First Episode of Venous Thrombosis

<table>
<thead>
<tr>
<th></th>
<th>Risk</th>
<th>Incidence/year (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1</td>
<td>.008</td>
</tr>
<tr>
<td>OCP</td>
<td>4x</td>
<td>.03</td>
</tr>
<tr>
<td>Factor V Leiden</td>
<td>7x</td>
<td>.06</td>
</tr>
<tr>
<td>(heterozygote)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OCP + Factor V L</td>
<td>35x</td>
<td>.3</td>
</tr>
<tr>
<td>(homozygote)</td>
<td>80x</td>
<td>.5-1.0</td>
</tr>
</tbody>
</table>

Initial VTE Therapy

Parenteral Agent
- LMWH
- fondaparinux
- IV UFH or sc UFH

Warfarin
- Start on day 1 with parenteral agent
- Overlap for at least 5 days, INR >2.0
- INR target range 2.0-3.0
- Role of pharmacogenomic testing not defined
  - VKORCI and CYP2C9

Duration of Anticoagulation

Provoked
- 3 months sufficient if risk gone
- 1% risk per year of recurrence, not changed by 3 vs 6 months

Idiopathic
- Recurrence rate highest in first 2 years
  - 10% per year in 1st 2 years
  - 40% at 5 years

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</tr>
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<td>(homozygote)</td>
<td>80x</td>
<td>.5-1.0</td>
</tr>
</tbody>
</table>

APS

- True antiphospholipid syndrome has high risk of recurrence.
  - Updated Sapporo criteria 2006
  - Blood 2009

- Long term anticoagulation in the setting of 1st unprovoked VTE event and persistently positive LA test results is required.
- Warfarin target range 2.0-3.0 sufficient
**Risk of Recurrent VTE in Inherited Thrombophilia**

<table>
<thead>
<tr>
<th>Thrombophilic Defect</th>
<th>Rel. Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>AT, protein S or C deficiency</td>
<td>2.5</td>
</tr>
<tr>
<td>Factor V Leiden mutation</td>
<td>1.4</td>
</tr>
<tr>
<td>Prothrombin 20210A mutation</td>
<td>1.4</td>
</tr>
<tr>
<td>Antiphospholipid antibodies</td>
<td>2 – 9</td>
</tr>
</tbody>
</table>

**Unprovoked VTE**

**Is longer better?**

>90% risk reduction if continue anticoagulation but need to consider

- **Bleeding risk:** case fatality rates similar for recurrent VTE vs bleeding
  - Recurrent VTE case fatality rate 0.3-1%
  - Major bleeds 1-3%/yr, fatal bleeds 0.4-0.6%
- **Patient preference and lifestyle**
- **Reurrence risk**
- **Alternatives?** ASA, risk modification

At 5 years, 60% will have had unnecessary treatment

**Duration of Anticoagulation**

**Unprovoked or idiopathic**

- 3 mo vs 12 mo OAC
- risk of recurrence 8.3% vs 0.7% in 1st year
- At 2 yrs both groups: 5% per year
  - Benefit is lost after stopping anticoagulation

**DASH STUDY**

“Predicting disease recurrence in patients with previous unprovoked venous thromboembolism: a proposed prediction score (DASH).”

- Meta analysis of 7 prospective studies.
- 1818 patients
  - 1st unprovoked event
  - 3 months or more treatment with warfarin
- Main predictors of recurrence identified using stratified Cox regression analysis.
- Prognostic recurrence score identified and validated using these main predictors and multiple methods.

**DASH score**

<table>
<thead>
<tr>
<th>D</th>
<th>D-dimer</th>
<th>+ 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Age &lt; 50 years</td>
<td>+ 1</td>
</tr>
<tr>
<td>S</td>
<td>Male Sex</td>
<td>+ 1</td>
</tr>
<tr>
<td>H</td>
<td>Hormone use at time of VTE</td>
<td>- 2</td>
</tr>
</tbody>
</table>

In males, the score may range from 1 to 4
In females, the score may range from -2 to 3

**Unprovoked VTE**

Recent ISTH consensus considers an annual risk of VTE recurrence below 5% as acceptable to deny life-long anticoagulant therapy. (Kearon et al, JTH 2010)

**How to determine risk?**

- **D-dimer**
  - Elevated level associated with increased recurrence
  - Measure at end of initial duration and one month after d/c

**Residual vein thrombosis**

- Persistent clot associated with increased recurrence
- Continue anticoagulation until resolution

**Clinical prediction scores**

Vienna nomogram, DASH score, others
**Requirements proseductive validation in large population**

**WARFASA STUDY**

**Alternative to indefinite warfarin?**

Double-blind randomized placebo controlled study

1st idiopathic VTE
6-12 mo warfarin

N = 402

- ASA
  - 100 mg po QD
  - n = 205

- Placebo
  - n = 197

- Minimum duration of treatment 2 years
- Mean on study period 22 months
- Exclusions: need for aspirin or anticoagulation, bleeding risk
- Event driven:
  - Efficacy endpoint recurrent VTE
  - Safety endpoint: major and non-major bleeding

---

**WARFASA STUDY**

**Conclusions**

- Close to 40% reduction in recurrent VTE with ASA compared to placebo.
- Highly selected patient population may affect results
  - No other need for ASA or anticoagulation, no risks for bleeding
- Gold standard warfarin at target INR 2.0-3.0 confers > 90% risk reduction compared to placebo.
- Further validation required but may be an alternative to warfarin for some patients.

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**WARFASA STUDY**

**Conclusions**

- ACCP Evidence Based Clinical Practice Guidelines 9th Ed—Feb 2012 (Chest)
- Rigorous, systematic review of the quality of the data has led to changes in the grade of the recommendation but usually not duration or type of treatment.
- Increased emphasis on patient preference and individual risk/benefit analysis
**8th ACCP Evidenced-Based Clinical Practice Guidelines—AT9 revisions**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Duration of anticoagulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal DVT/PE secondary to a transient risk factor Grade 1A: 1B</td>
<td>3 months</td>
</tr>
<tr>
<td>1st isolated, unprovoked distal DVT Grade 2B: same</td>
<td>At least 3 months then assess risk/benefit, extended duration favored</td>
</tr>
<tr>
<td>1st Idiopathic proximal DVT/PE Grade 1A: 1B</td>
<td>&gt; 3 months</td>
</tr>
<tr>
<td>2nd Unprovoked DVT/PE Grade 1A:</td>
<td></td>
</tr>
<tr>
<td>1B low bleed risk</td>
<td></td>
</tr>
<tr>
<td>2B mod bleed risk</td>
<td></td>
</tr>
<tr>
<td>2B high bleed risk: only 3 mo</td>
<td></td>
</tr>
</tbody>
</table>

**CS**

27 yo woman on OCP undergoes L ACL repair. No prior history of VTE, no family history of VTE. Develops L popliteal vein DVT.

She should be treated with anticoagulation for:
1. 3 months
2. 9 months
3. Depends on d-dimer level
4. Depends on inherited thrombophilia work up results
5. Indefinitely

---

**CS**

Answer: 1.

3 months sufficient for provoked VTE.

D-dimer risk stratification does not apply in this setting.

Results of inherited thrombophilia testing do not significantly affect risk of recurrence.

**CS**

One week later orthopedic surgeon sends hypercoaguable work up.

Results: heterozygous Factor V Leiden by PCR, free protein S level 28% normal range 70-134%

She is diagnosed with:
1. No thrombophilia
2. Combined FVL and protein S deficiency
3. FVL only
4. Antiphospholipid syndrome
5. Need to repeat protein S level when off warfarin and OCP

---

**CS**

• Answer 5.
• Both estrogen (OCP, HRT, pregnancy) and warfarin affect protein S levels.
• Should she have been tested for inherited thrombophilia?
  – YES. Results affect OCP use, pregnancy prophylaxis

**CS**

41 yo male obese computer programmer develops R LE pain and swelling. Compression US reveals R common femoral v DVT. Also noted to have DOE. PE CT reveals PE. No family history of VTE. His local physician tells him that he needs lifelong anticoagulation. After 2 years of anticoagulation he asks for second opinion.

You assess the following:

BMI: has decreased from 37 to 26 in 2 yrs

Residual vein thrombosis: repeat US and PE CT reveal no residual thrombus in either location

D-dimer testing: warfarin stopped for 4 weeks, level is <200 ng/ml, normal is <499 ng/ml
• Lengthy discussion of risks/benefits.
• Current risk assessment appears to be lower, likely < 5% per year
  – D-dimer not elevated
  – Risk of recurrence highest in first 2 years
  – BMI, independent risk factor, lower
  – No residual vein thrombosis
• Anticoagulation stopped

Summary
• The "hypercoaguable state" is a spectrum of risk, with many patients having multiple additive risk factors.
• Duration of anticoagulation depends on the risk of recurrent VTE.
  – Treatment of provoked VTE straightforward—minimal risk of recurrence.
  – Improved risk stratification will aid in determining duration of anticoagulation therapy for unprovoked VTE.
  – "Personalized" risk profiles and patient preference increasingly considered.
  – Alternatives to full intensity anticoagulation, such as ASA, or other non-anticoagulant based risk modification strategies may be identified in the future.

References

Novel Oral Anticoagulants
Make new friends but keep the old.
### Limitations of Current Anticoagulants

<table>
<thead>
<tr>
<th>Agent</th>
<th>Disadvantages</th>
</tr>
</thead>
</table>
| Heparin                      | - Parenteral administration  
- Risk of heparin-induced thrombocytopenia (HIT)  
- Narrow therapeutic window (low bioavailability, short half-life) |
| Warfarin                     | - Requires frequent monitoring due to:  
  - Narrow therapeutic window  
  - Unpredictable pharmacology  
  - Multiple drug–drug and food–drug interactions  
  - Increased risk of major and minor bleeds |
| LMWH (fondaparinux)          | - Parenteral administration  
- Risk of heparin-induced thrombocytopenia (HIT) |
| Indirect Xa Inhibitor (fondaparinux) | - Parenteral administration  
- Long half-life  
- Limitations related to special patient populations |
| Direct Thrombin Inhibitors   | - Parenteral administration  
- Current applications limited to cardiovascular management |

### Comparative Features of Warfarin and New Oral Anticoagulants

<table>
<thead>
<tr>
<th>Target</th>
<th>Warfarin</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Bioavailability</td>
<td>99%</td>
<td>6.7%</td>
<td>60-80%</td>
<td>80%</td>
</tr>
<tr>
<td>T (max)</td>
<td>72-96h</td>
<td>2h</td>
<td>2.5-4h</td>
<td>3h</td>
</tr>
<tr>
<td>Halflife (h)</td>
<td>40h</td>
<td>14-17h</td>
<td>5-13h elderly</td>
<td>8-15h</td>
</tr>
<tr>
<td>Monitoring</td>
<td>INR-adjusted</td>
<td>Not needed</td>
<td>Not needed</td>
<td>Not needed</td>
</tr>
<tr>
<td>Administration</td>
<td>QD</td>
<td>QD or BID</td>
<td>QD or BID</td>
<td>BID</td>
</tr>
<tr>
<td>Metabolism/Elimination</td>
<td>CYP450</td>
<td>Standard of Care (PCOx/TKA)</td>
<td>Standard of Care (PCOx/TKA)</td>
<td>Standard of Care (PCOx/TKA)</td>
</tr>
<tr>
<td>Coagulation</td>
<td>FFP, APC, and FVIIIa</td>
<td>Anti-factor Xa, PIcT®, HepTest®</td>
<td>Anti-factor Xa, PIcT®, HepTest®</td>
<td>Anti-factor Xa, PIcT®, HepTest®</td>
</tr>
<tr>
<td>Drug Interactions</td>
<td>CYP2C, 1A2, and 3A4</td>
<td>Potent P-gp inhibitors/inducers; PPIs decrease effects</td>
<td>Potent P-gp inhibitors/inducers; CYP3A4 inhibitors</td>
<td>Potent P-gp inhibitors/inducers; CYP3A4 inhibitors</td>
</tr>
</tbody>
</table>

### Novel Oral Anticoagulants

- **Dabigatran**: PRADAXA  
  - FDA approved for afib Oct 2010  
  - EMA: post ortho VTE ppx March 2008  
  - Afib Aug 2011
- **Rivaroxaban**: XARELTO  
  - FDA approved for post ortho VTE July 2011  
  - FDA approved for afib Nov 2011  
  - Canada and EMA > 3 years post ortho VTE ppx  
  - EMA: afib and DVT treatment Dec 2011
- **Apixaban**: ELIQUIS  
  - EMA approved post orth VTE prophylaxis May 2011
Orthopedic VTE Prophylaxis Summary

- New oral anticoagulants in TKR/THR
  - **Dabigatran** 220 mg once daily RE-studies
  - **Rivaroxaban** 10 mg once daily RECORD 1-4
  - **Apixaban** 2.5 mg once daily ADVANCE 1-3

- Approved in Europe and Canada for > 3 years
  - Dabigatran and rivaroxaban
- Rivaroxaban FDA approved indication July 2011

Treatment of Acute VTE Summary

- **Dabigatran** (not FDA approved)
  - Non-inferior to warfarin for treatment of acute VTE
  - Requires initial UFH/LMWH for the first 5-7 days
  - Comparable to warfarin in major bleeding risk
- **Rivaroxaban** (not FDA approved)
  - Can replace heparin/warfarin for treatment of acute DVT
  - Does not require initial UFH/LMWH
  - Effective in reducing recurrent VTE up to 1 yr
  - Comparable to warfarin in major bleeding risk
- **Apixaban** studies not completed

ACUTE PE Treatment

- Rivaroxaban—only novel anticoagulant used upfront to treat DVT or PE.
  - EINSTEIN PE results reported NEJM April 2012
  - 4832 patients randomized
  - Rivaroxaban: 15 mg bid x 3 weeks then 20 mg qd
  - Enoxaparin/warfarin target INR 2.5
  - Primary efficacy outcome: time to first event
    - 2.1% rivaroxaban vs 1.8%, HR 1.12, p=0.0026
    - Non-inferior compared to enoxaparin/warfarin
  - Decreased major bleeding events:
    - 1.1% rivaroxaban vs 2.2%, HR 0.49, p=0.0032
    - Superior to enoxaparin/warfarin

Einstein PE

- Primary Efficacy: 2.1% rivaroxaban Non-inferior
  - HR 1.12 p=0.026
  - 1.8% warfarin TTR 63%

The Impact of Atrial Fibrillation

- Approximately 2 million Americans have atrial fibrillation.
- Incidence increases from 1.5% at age 55 to 23.5% at age 85.
- Although deaths attributed solely to AF are rare it is a major risk factor for embolic stroke.
- Catheter ablation has a 30% success rate.
- Most patients with persistent AF need long-term anticoagulation.
Novel Oral Anticoagulants in AF

Industry sponsored trials
• Trial design, patient population and selection, statistical analysis, all critical to success
• All published in NEJM
• Large numbers of patients
  - Dabigatran (FDA approved indication) RE-LY
    - 18,113 randomized, open label: 2 doses vs warfarin
  - Rivaroxaban (FDA approved) ROCKET AF
    - 14,264 randomized, double blind vs warfarin
  - Apixaban (not FDA approved) ARISTOTLE
    - 18,201 randomized, double blind vs warfarin

Novel AC in AF

<table>
<thead>
<tr>
<th>Drug</th>
<th>Trial</th>
<th>Primary Endpoint</th>
<th>Major Bleeding</th>
<th>ICH (% per yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1.71% warfarin</td>
<td>3.57% warfarin</td>
<td>0.74% warfarin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.11% D-150</td>
<td>3.32% D-150</td>
<td>0.30% D-150</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.54% D-110</td>
<td>2.87% D-110</td>
<td>0.23% D-110</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.60% apixaban</td>
<td>2.09% apixaban</td>
<td>0.80% apixaban</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.27% rivaroxaban</td>
<td>2.13% rivaroxaban</td>
<td>0.33% apixaban</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.42% warfarin</td>
<td>3.45% warfarin</td>
<td>0.74% warfarin</td>
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<td></td>
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<td>2.12% rivaroxaban</td>
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</tr>
</tbody>
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Summary of AF trials with new oral anticoagulants versus warfarin

Advantages disappear with excellent warfarin control

ATLAS ACS TIMI 51: Rivaroxaban
- Reduced risk of primary composite endpoint versus placebo when added to standard antiplatelet therapy for ACS
  - Survival benefit seen only at lower dose (2.5 mg twice daily)
  - All-cause mortality 2.9% vs 4.5% (p = 0.002)
  - Therapy continued for a mean of 13 months
  - Increased risk of major bleeding and ICH, but not fatal bleeding
  - FDA did NOT grant approval for ACS use June 2012

Ahrens, Thromb Haemost 2011

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Ahrens, Thromb Haemost 2011

Ahrens, Thromb Haemost 2011

Ahrens, Thromb Haemost 2011

Schulman and Crowther: Blood 2012

Schulman and Crowther: Blood 2012

Schulman and Crowther: Blood 2012

Schulman and Crowther: Blood 2012

Schulman and Crowther: Blood 2012
Concerns
Increased risk of ACS/MI?
OR 1.33 compared to warfarin, enoxaparin, placebo in meta-analysis of 7 trials with total 30,514 pts, Absolute risk 0.27% Relative risk 33%
Arch Intern Med 2012

Bleeding complications
No antidote
time
dialysis—dabigatran case reports
PCC—one study in healthy volunteers
Xai antidote—in development: recombinant Xa fragment without catalytic activity binds to Xai to inactivate (PRT064445)

Antidote: prothrombin complex concentrate
- Randomized, placebo-controlled trial in 12 healthy male volunteers in Amsterdam
- Six subjects were given rivaroxaban 20 mg BID while the other six received dabigatran 150 mg BID
- Randomized to receive single bolus of 50 IU/kg PCC (Coag) versus saline
Eerenberg Circulation 2011

Antidote: PCC Results

Rivaroxaban
- PCC completely reversed INR back to baseline (p < 0.001)
- PCC completely normalized endogenous thrombin potential (p < 0.001)

Dabigatran
- PCC did not correct elevated PTT
- PCC did not correct elevated TT
- PCC did not correct elevated ECT
Eerenberg Circulation 2011

How to choose?

Stick with warfarin
Good level of control
Renal failure
Mechanical heart valve
GI disease
Poor compliance
If drug cost is a problem
Switch
Unexplained poor warfarin control
Unavoidable drug-drug interactions
Strong patient preference
? Newly diagnosed AF

AT 9 AF
2.1.11.
For patients with AF, including those with paroxysmal AF, for recommendations in favor of oral anticoagulation we suggest dabigatran 150 mg twice daily rather than adjusted-dose VKA therapy (target INR range, 2.0–3.0) (Grade 2B).

AT 9 recommendations for AF and PAF based on stroke risk

CHADS2 = 0 no treatment grade 2B
CHADS2 = 1 OAC vs antiplt grade 1B
CHADS2 = 2 OAC grade 1A

New oral anticoagulants offer:
- Similar or improved efficacy and safety
- Decreased ICH for AF but increased GI bleeds
- Pharmacologic advantages
- Ease of administration
- Outpatient management of DVT/PE without need for parenteral agents
- Intriguing possible uses
- ACS
- HIT

Novel Oral Anticoagulants
Novel Oral Anticoagulants summary
**Novel Oral Anticoagulants**

**summary**

- Differences in clinical trials are small and may not hold up in community practice.
- There is no magic as differences disappear as warfarin TTR increases.
- Currently no effective antidote for direct thrombin inhibitor and a cumbersome one for Xa inhibitors.
- Long term safety data lacking—surprises?
- Costs and cost effectiveness?