Anticoagulation Management Update: The Old and New Frontier

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Daniel Tambunan, MD
  • Consultant or Advisory Board: Boehringer Ingelheim (Atrial fibrillation)

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• Prothrombin complex concentrate (PCC)

Learning Objectives

1. Utilize a systematic process of care, including initiation and assessment of therapy and dosing adjustments, to optimize effectiveness and minimize adverse effects of patients taking warfarin.

2. Consider new agents in patients, with atrial fibrillation and at least one other risk factor for stroke, that do not require frequent laboratory monitoring are as effective as warfarin for prevention of stroke or systemic embolism and have comparable risks of major bleeding.

3. Develop collaborative care plans with patient education to counsel patients on safe and effective administration of anticoagulants, emphasizing self-monitoring to prevent complications.

4. Establish or revise existing practice-level protocols for anticoagulation management, based on current evidence-based recommendations and guidelines, including having clearly defined staff roles and responsibilities.

Associated Session

• Anticoagulation Management Update: PBL
The anticoagulants

- **Anti-platelet agents:**
  - a) Inhibiting ADP - clopidogrel, ticlopidine
  - b) GP IIb/IIIa inhibitors - abciximab, eptifibatide, tirofiban
  - c) Thrombin inhibitors - argatroban, lepirudin
  - d) 2P12 integrin - GP VI, platelet aggregation

- **Unfractionated Heparin** - targets factor Xa, Antithrombin III, & Thrombin

- **Low Molecular Weight Heparin** - targets factor Xa and Antithrombin III only

- **Warfarin** - targets Vit K factor - II, VII, IX, & X

- **VIRCHOW’S TRIAD**
  - **Circulatory STASIS:**
    - immobility, CHF, advanced age, obesity and venous obstruction
  - **Endothelial Injury (TRAUMA):**
    - surgery (e.g., orthopedic), postpartum, infections & valve damage
  - **HYPERCOAGULABLE state:**
    - Factor V Leiden, oral contraceptives, cancer, deficiencies of protein C & S or ATIII, homocysteine, impaired fibrinolysis

Hypercoagulable Studies

- **Factor V Leiden**
- **Antiphospholipid antibodies**
- **Homocysteine**
- **Prothrombin gene 20210 A allele**
- **Elevated Factor VIII (> 90th percentile)**
- **Antithrombin III deficiency**
- **Protein C deficiency**
- **Protein S deficiency**

AES Question - Case Study

B.V. is a 35 y/o Caucasian gentleman who comes to the ER with complaint of left leg pain and swelling for 3 days. Denies any insect bite, fall or trauma. Denies any shortness of breath or chest pain.

PE: Afebrile, B/P 110/70. Normal exam except asymmetric thigh size and mild tenderness on palpation. No chorde palpatable and negative Homan’s sign.

Would you include hypercoagulable studies now?

A. No
B. Yes
VTE Prophylaxis

Thromboprophylaxis in Surgical Patients:
ACCP Risk Classification

- **Low Risk (<10%)**
  - Minor surgery
  - Medical pt's who are mobile
- **Moderate Risk (10-40%)**
  - Most surgery
  - Medical pt's who are bed rest/ill
- **High Risk (40-80%)**
  - Hip/knee arthroplasty
  - History of VTE
  - Hip or total joint procedures
  - Spinal cord injury; major trauma


Thromboprophylaxis in Knee/Hip Orthopedic Surgical Patients

- Low molecular weight heparin (LMWH)
- Warfarin, rx 2 days prior to surgery or immediately post surgery (INR 2.0-3.0)
- Fondaparinux 2.5 mg daily
- Novel anticoagulant – Dabigatran 220 mg daily, Rivaroxaban 10 mg daily, Apixaban 2.5 mg BID, Edoxaban 30 mg daily (post surgery)
- Length of tx – Hip (28-35 days) & Knee (10-12 days)
- Intermittent pneumatic compression is only an adjuvant therapy
- Low dose unfractionated heparin is inadequate.


Venous Thromboembolism (VTE)

DVT - Deep Vein Thrombosis

- **PROXIMAL**
  *Any vein from the popliteal v. and up
  *Larger clot
  *High propensity to propagate (40-60%)
  **REMEMBER:**
  Superficial femoral v. is a deep v., tx.
- **DISTAL**
  *Below popliteal v.
  *Smaller clot
  *Less symptomatic and less likely to cause PE
  *Can propagate up to the proximal v.
### UF-Heparin
- MW = 35-50,000 Kd
- Poor bioavailability due to binding to proteins
- Targets Xa, ATIII, & thrombin
- Needs regular lab monitoring: O 6 hrs
- Rapid plasma clearance
- Needs platelet, H/H monitoring

### LMWH
- MW = 5-10,000 Kd
- Good bioavailability, little binding to proteins
- Targets Xa & ATIII only
- No lab monitoring needed, except in obese (>110 kg) or renal disease
- Slow plasma clearance
- Needs platelet, H/H monitoring

### Pentasaccharides
- Mode of mechanism: Inhibits factor Xa only
- Indicated for VTE prophylaxis and treatment
- VTE treatment (dose varies with weight): < 50 kg — 5.0 mg SC
  > 50 to 100 kg — 7.5 mg SC
  > 100 kg — 10.0 mg SC
- Monitor platelets frequently
- Caution in pts with renal insufficiency (CrCl < 30 mL/min)
- Caution in underweight pts (< 45 kg)

### RECOVER
- 2,564 patients (mean age 55 years) with acute symptomatic VTE and normal renal function randomized to dabigatran 150 mg orally twice daily plus warfarin-like placebo vs. warfarin plus dabigatran-like placebo for 6 months
- All patients initially given parenteral anticoagulation therapy for median 9 days
- Primary outcome was time to first occurrence of composite of symptomatic VTE or VTE-related death
- Comparing dabigatran vs. warfarin
  - Symptomatic VTE or VTE-related death at 6 months in 2.3% vs. 2.2% (noninferiority met)
  - Any death in 1.6% vs. 1.7% (not significant)
  - Major bleeding episodes in 1.6% vs. 1.9% (not significant)
  - Any bleeding episodes in 16.1% vs. 21.9% (p < 0.05, NNT 18)
- No significant differences in acute coronary syndromes or abnormal liver function tests

### EINSTEIN
- 3,449 patients with acute symptomatic DVT randomized to rivaroxaban (15 mg po BID for 3 wks then 20 mg daily) vs standard therapy (enoxaparin SubQ + warfarin)
- Results:
  - Early treatment discontinuation 11.3% vs 14.2% (p=0.01)
  - Symptomatic recurrent VTE 2.1% vs 3% (HR 0.68, CI 0.44-1.04)
  - Major bleeding 0.8% vs 1.2% (NS)

### AMPLIFY
- 5,395 adults (mean age 57 years) with acute symptomatic proximal deep vein thrombosis or pulmonary embolism randomized conventional therapy vs apixaban 10 mg BID first 5 days then 5 mg BID for 6 months
- Primary outcome was composite of recurrent symptomatic venous thromboembolism (VTE) and VTE-related death
- Comparing apixaban vs. conventional therapy
  - Primary outcome in 3.2% vs. 7.7% (95% CI for difference -4.5% to -1.3%, noninferiority met)
  - Clinically relevant major bleeding in 3.5% vs. 4% (p = 0.35, NNT 24)
  - All-cause death in 1.5% vs. 1.9% (not significant)
  - Any serious adverse event in 19.3% vs. 13.8% (p = 0.004)

### Hokusai-VTE
- 4921 pts with DVT & 3319 patients with PE were randomized to conventional therapy vs LMWH/LFH + edoxaban 60 mg daily. Followed up for 12 months
- Primary outcome was composite of VTE and VTE-related death
- Comparing edoxaban vs conventional therapy
  - Primary outcome in 3.2% v 3.5 (95% CI 0.70-1.13, noninferiority met)
  - Major bleeding 8.5 v 10.3 (CI 0.71-0.94, superiority)
  - Any bleeding 21.7 v 25.6 (CI 0.75-0.90, superiority)
Indications

- Nonvalvular atrial fibrillation
- DVT & PE treatment
- DVT prophylaxis

Mechanism of action

- Thrombin inhibitor
- Factor Xa inhibitor
- Factor Xa inhibitor
- Factor Xa inhibitor

Clearance

- Renal
- Renal & Hepatic
- Renal & Hepatic
- Renal & Hepatic

Usual dosage for VTE treatment

- Dabigatran: 150 mg BID
- Apixaban: 5 mg BID
- Rivaroxaban: 20 mg QD
- Edoxaban: 60 mg QD

Usual dosage for VTE prophylaxis

- Dabigatran: 110 mg 1–4 hrs after surgery then 220 mg daily
- Apixaban: 2.5 mg BID
- Rivaroxaban: 10 mg QD
- Edoxaban: 30 mg QD

Antidote

- Idarucizumab
- PCC
- PCC
- PCC

Pregnancy

- C
- B
- C
- C

Drug interactions (key: bold—increase, nl—decrease)

- Azoles, amiodarone, rifampin, anticonvulsants
- Azoles, diltiazem, macrolide, protease inhibitors, rifampin, anticonvulsants
- Azoles, quinidine, HIV protease inhibitors, macrolide
- Verapamil, macrolide, quinidine, azoles

Dose adjustments

- CrCl 15–30 mL/min: 75 mg BID
- CrCl < 15: avoid

- If + on 2 out of 3:
  1. Age > 80 yrs old
  2. Body weight < 60 kg
  3. Creat > 1.5 mg/dL
- Reduct dose to: 2.5 mg BID

Guidelines for Initiating Warfarin

- Start low
  - initiate at 2-5 mg daily, esp. in elderly, high bleeding risk, heart failure, liver disease, impaired nutrition
  - determine INR frequently after administration of initial dose
  - educate patient; DuPont Pharma or Barr Labs has info booklets available. 1-800-COUMADIN or 1-800-WARFARIN

- Stabilize
  - titrate to appropriate INR of 2.0-3.0
  - once stabilized, determine INR 2-3 times weekly for 1-2 weeks, then less often depending on stability of INR

- Monitor and adjust
  - determine INR regularly (every 1-4 weeks) and adjust if necessary

Optional Warfarin Initiation

<table>
<thead>
<tr>
<th>Day</th>
<th>INR</th>
<th>Warfarin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt; 1.5</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>&lt; 1.8</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>1.8-2.0</td>
<td>7.5</td>
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<tr>
<td></td>
<td>2.1-2.5</td>
<td>5.0</td>
</tr>
<tr>
<td></td>
<td>&gt; 2.5</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>&lt; 1.6</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>1.6-2.0</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>2.1-2.5</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>&gt; 2.5</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>&lt; 1.6</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>1.6-2.0</td>
<td>10</td>
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<td></td>
<td>2.1-2.5</td>
<td>7.5</td>
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<tr>
<td></td>
<td>2.6-3.0</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>3.1-3.5</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>&gt; 3.5</td>
<td>0</td>
</tr>
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Therapeutic Ranges

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>INR</th>
<th>DURATION</th>
</tr>
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<tbody>
<tr>
<td>Prophylaxis of DVT</td>
<td>2-3</td>
<td>Variable, see table</td>
</tr>
<tr>
<td>Treatment of DVT</td>
<td>2-3</td>
<td>Variable, see table</td>
</tr>
<tr>
<td>Prevention of cardioembolic stroke</td>
<td>2-3</td>
<td>Variable, see table</td>
</tr>
<tr>
<td>AF fibrillation</td>
<td>2-3</td>
<td>Variable, see table</td>
</tr>
<tr>
<td>Cardiomyopathy (&lt;25%)</td>
<td>2-3</td>
<td>Variable, see table</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>2-3</td>
<td>Variable, see table</td>
</tr>
<tr>
<td>Mechanical heart valve (mitral)</td>
<td>2.5-3.5</td>
<td>3 months</td>
</tr>
<tr>
<td>Tissue heart valve (mitral)</td>
<td>2-3</td>
<td>3 months</td>
</tr>
<tr>
<td>Atrial AF</td>
<td>2-3</td>
<td>&gt; 3 months</td>
</tr>
</tbody>
</table>


INR 2.0-3.0

- Increase weekly dose by 5-20%
- Decrease weekly dose by 5-15%
- Hold 5-10 days, then decrease weekly dose by 10-15%
- Hold 5-10 days, then decrease weekly dose by 10-20%

Horton JD, Bushwick BM. Am Fam Physician 1999;59(3):635-646

Chest 2012; 141:e89S-e801S.
**Dose Adjustment Protocol, 2.5-3.5**

<table>
<thead>
<tr>
<th>INR</th>
<th>Adjustment</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2</td>
<td>Increase weekly dose by 10-20%</td>
<td>Per protocol 1-2 weeks</td>
</tr>
<tr>
<td>2.0-2.4</td>
<td>Increase weekly dose by 5-15%</td>
<td>No change 4-6 weeks</td>
</tr>
<tr>
<td>2.5-3.5</td>
<td>Decrease weekly dose by 5-15%</td>
<td>Per protocol 1-2 weeks</td>
</tr>
<tr>
<td>3.6-4.6</td>
<td>Hold 1 dose then decrease weekly dose by 10-20%</td>
<td>Per protocol 3-7 days</td>
</tr>
<tr>
<td>&gt; 5.2</td>
<td>Hold 2 dose</td>
<td>Notify MD Same day</td>
</tr>
</tbody>
</table>

*Horton JD, Bushwick BM. Am Fam Physician 1999;59(3):635-646*

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**Follow-Up Protocol**

<table>
<thead>
<tr>
<th>RANGE</th>
<th>ADJUSTMENT</th>
<th>FOLLOW-UP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 D</td>
<td>Per protocol 1-2 weeks</td>
<td></td>
</tr>
<tr>
<td>2.0-3.0</td>
<td>No Change 4-6 weeks</td>
<td></td>
</tr>
<tr>
<td>3.1-4.0</td>
<td>Per protocol 1-2 weeks</td>
<td></td>
</tr>
<tr>
<td>4.1-6.0</td>
<td>Per protocol 3-7 days</td>
<td></td>
</tr>
<tr>
<td>&gt;6.0</td>
<td>Notify MD Same day</td>
<td></td>
</tr>
</tbody>
</table>

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**Warfarin reversal treatment: non-bleeding**

<table>
<thead>
<tr>
<th>INR</th>
<th>Vit K dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>none</td>
<td>Hold dose</td>
</tr>
<tr>
<td>5-10</td>
<td>none</td>
<td>Hold dose</td>
</tr>
<tr>
<td>&gt;10</td>
<td>2.5 mg PO</td>
<td>Hold dose</td>
</tr>
</tbody>
</table>

*Check INR in 6-12 hrs and repeat if necessary.*

*In severe life-threatening bleeding, use Vit K 5-10 mg slow IV infusion and 10% Heparin (PCC) or PFP.*


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**Warfarin Drug Interactions**

**POTENTIATE**
- Antibiotics/Antifungal
  - sulfamethoxazole, ciprofloxacin, tetracycline, metronidazole, all -azoles, isoniazid, macrolides
- Cardiovas. agents
  - amiodarone, disopyramide, propafenone
- Others
  - cimetidine, ASA, NSAIDs, allopurinol, omeprazole, herbals; vitamin E, garlic, ginkgo biloba, ginseng

**REDUCE**
- Antibiotics/Antifungal
  - rifampin, nafcillin, dicloxacillin
- Anticonvulsants
  - phenytoin, barbiturates
- Others
  - sucralfate, cholestyramine, cholestipol, trazodone

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**VTE treatment – Chest Guideline 2016**

**No cancer**
1. NOACs over VKA
2. VKA over LMWH

**With cancer**
- LMWH over VKA or NOACs

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**CLOT Study**

- 676 pts with cancer who had a VTE were randomized to receive dalteparin 200 IU/kg SC on first month then 150 IU/kg SC on the next five months vs conventional therapy of concurrent dalteparin & VKA for five to seven days then VKA for six months. 50% are female.
- Primary outcome was recurrent symptomatic VTE
- Comparing dalteparin vs conventional treatment
  - Primary outcome in 27/336 vs 53/336, p = 0.002
  - Major bleeding 6% vs 4, p = 0.27
  - Death 39 % v 41, p = 0.53


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2012 ACCP Recommendations
Duration of Therapy of VTE

- **3 months** - reversible risk factors* & 1st event - distal DVT
- **3 months or more** - unprovoked VTE & 1st event, depending on the risk-benefit ratio
- **3-6 months** - cancer, until resolved
- **Indefinite** - second episode of unprovoked

*Risk factors: Transient immobilization, trauma, surgical operation, or pharmacologic estrogen use.


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D-dimer for anticoagulation duration?

- 608 patients, prospective, three-armed study with first episode of symptomatic, idiopathic proximal DVT &/or PE who has been treated at least for 3 months with warfarin
- One arm – normal D-dimer; the other – abnormal D-dimer
- Objective: Composite recurrent VTE and major bleeding during 1.4 years of follow-up
- Results:
  - Normal: 24/385 (6.2%)
  - Abnormal and placebo: 18/120 (15.0%)
  - Abnormal and treated: 3/103 (2.9%)
- p value = 0.02 (2/3 comparison)
- Major bleeding: 1 on the treated group, 0 on the others
- Conclusion: Consider longer therapy with warfarin if D-dimer is abnormal


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### Atrial Fibrillation

**Management decision**

1. Stable or not
2. 48 hours
   - < 48 hours
     - Immediate cardioversion
   - > 48 hours
     - TEE guided cardioversion vs delayed cardioversion
3. Rate vs rhythm
   - Rate
     - Drugs vs cardioversion
   - Rhythm
     - Drugs vs ablation (catheter vs surgical)
4. Anticoagulation
   - CHADS2 score
   - HAS-BLED score

**CHADS2**

- Congestive heart failure (any history) ------ 1
- Hypertension (prior history) --------------- 1
- Age > 75 years ---------------------------- 1
- Diabetes mellitus ------------------------ 1
- Stroke or TIA ---------------------------- 2

Gage BF, Waterman AD, Shannon W. JAMA 2001; 285:2864
### Stroke risk based on CHADS2

- 0 --- 1.9 per 100 patient-years
- 1 --- 2.8
- 2 --- 4.0
- 3 --- 5.9
- 4 --- 8.5
- 5 --- 12.5
- 6 --- 18.2


### CHA2 DS2 - VASc

- Congestive heart failure or LV dysfunction — 1
- Hypertension -------------------------- 1
- Age
  - 65 to 74 years ----------------- 1
  - 75 and older ------------------ 2
- Diabetes mellitus ----------------- 1
- Stroke or TIA or thromboembolism --- 2
- Female sex (gender) ------------- 1
- MI, peripheral vascular disease or aortic plaque — 1


### Rate of stroke/thromboembolism

- 0 --- 0 %
- 1 --- 0.6%
- 2 --- 1.6%
- 3 --- 3.9%
- 4 --- 1.9%
- 5 --- 3.2%
- 6 --- 3.6%
- 7 --- 8.0%
- 8 --- 11.1%
- 9 --- 100%

Lip GY, Abrams J. J Am Coll Cardiol 2012; 59(16):1494-8

### HAS-BLED score

- Hypertension
- Abnormal renal function
- Abnormal liver function
- Stroke
- Bleeding
- Labile INR
- Elderly (> 65 years)
- Drugs or alcohol (two points for both)


### RE-LY Study

18,113 pts with atrial fibrillation and additional stroke risk factors were randomized to dabigatran 110 mg po BID vs 150 mg po BID vs warfarin adjusted to INR 2-3. Mean f/u 24 months.

- **Results:**
  - 110 mg did not show significant difference against warfarin although reduced risk of major bleeding (0.8% vs 0.9%, p = 0.003)
  - 150 mg BID vs warfarin
    - Stroke or systemic embolism in 2.21% vs. 3.35% (p < 0.001, NNT 88)
    - Major bleeding in 0.57% vs. 0.6% (not significant)
    - Thrombosis in major bleeding in 0.2% vs. 3.5% (p < 0.05, NNT 190)
  - Conclusion: Dabigatran 150 mg is superior to warfarin in reducing stroke

ROCKET AF Study

- A non-inferiority trial
- 14,264 pts with nonvalvular a. fib. & increased risk of stroke randomized to rivaroxaban 20 mg daily vs warfarin INR adjusted to 2-3
- Follow-up is 22 months
- Results:
  - stroke or systemic embolism in 2.1% per year vs. 2.4% per year in intention-to-treat population ($p = 0.001$ for noninferiority, not significant for superiority)
  - major bleeding in 1.5% per year vs. 1.5% per year (not significant for superiority)
- Conclusion: Rivaroxaban is non-inferior to warfarin and has superior ICH numbers


ARISTOTLE Study

- 18,201 patients with a. fib and 1 or more additional risk factors randomized to apixaban 5 mg twice daily vs warfarin INR adjusted 2-3. Follow up is 1.8 years.
- Results:
  - any stroke or systemic embolism in 1.27% per year vs. 1.6% per year ($p = 0.01$, NNT 303 per year)
  - hemorrhagic stroke in 0.24% per year vs. 0.47% per year ($p < 0.001$, NNT 435 per year)
  - ischemic or uncertain type of stroke in 0.97% per year vs. 1.05% per year (not significant)
  - major bleeding in 2.13% per year vs. 3.09% per year ($p < 0.001$, NNT 105 per year)
  - all-cause mortality 3.52% vs. 3.94% ($p = 0.047$, NNT 238)
- Conclusion: Apixaban is statistically significant in reducing stroke compared to warfarin in nonvalvular a. fib with decreased ICH or major bleeding.


ENGAGE AF-TIMI 48 Study

- 21,105 patients with moderate-to-high risk atrial fibrillation (mean f/u, 2.8 years) randomized to compare two once-daily regimens of edoxaban with warfarin. Primary endpoint was stroke or systemic embolism.
- Results:
  - any stroke or systemic embolism 1.18% vs 1.61 vs 1.50 ($p = <0.001$ and 0.05, respectively)
  - major bleeding 2.75 % vs 1.61 vs 3.43 ($p = <0.001$ on both)
  - cardiovascular causes 2.74% vs 2.71 vs 3.17 ($p = 0.01$ and 0.008, respectively)
- Conclusion: Both once-daily edoxaban were noninferior to warfarin on the prevention of stroke with lower rates of bleeding and cardiovascular causes.


Switching anticoagulants

<table>
<thead>
<tr>
<th>Agent</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>VKA to NOAC</td>
<td>NM (R) immediate. NM (R-24): immediate or next day. Follow NM (R) ± 2.5</td>
</tr>
<tr>
<td>NOAC to VKA</td>
<td>Administer concurrently until INR is 4.0. Re-test 24 hr after last dose of NOAC.</td>
</tr>
<tr>
<td>Parenteral to NOAC</td>
<td>Leave same dose. Leave same dose.</td>
</tr>
<tr>
<td>NOAC to parenteral</td>
<td>Nil.</td>
</tr>
</tbody>
</table>

Factors to consider on NOACs

- Superior efficacy in reduction of ischemic stroke – dabigatran
- Reduction in bleeding regardless of indication – apixaban
- Once daily dosing may improve compliance – edoxaban and rivaroxaban
- Food is mandatory – rivaroxaban
- Patient with severe renal dysfunction – apixaban
- Patient with GI upset – Avoid dabigatran
- Patient with CrCl > 95 – Avoid edoxaban
**Patient Education on NOACs**

- Do not need regular blood tests except to check your kidney/liver function and full blood count before starting treatment.
- Tell your doctor what medications or herbal you’re taking.
- No interaction with alcohol but drink in moderation.
- Missing doses may increase your risk of having stroke, heart attack or another clot.
- Side effects: Blood in urine, red/black stools, unusual bruising, heavy menstruation, coughing up blood, headache – tell your doctor.
- Avoid during pregnancy and breastfeeding.

**Which anticoagulant?**

- Cancer
- Poor compliance
- Pregnancy
- Reversal agent needed
- Liver disease
- Renal disease & CrCl < 30 mL/min

**Anticoagulation Nutshell**

- ASA ► stroke, AMI, UA, lone a-fib
- Factor Xa inhibitors ► a-fib, VTE prophylaxis and treatment
- Direct thrombin inhibitors ► a-fib, AMI, UA
- Direct factor Xa inhibitors ► VTE prophylaxis and treatment
- Novel anticoagulants – a-fib, VTE prophylaxis and treatment (not LMWH)
- UFH (unfractionated) ► MI, UA
- Fondaparinux ► VTE prophylaxis & treatment
- Fondaparinux & direct factor Xa inhibitors ► PTE
- Thienopyridines ► stroke, UA
- Thrombin inhibitors ► HIT, a-fib, VTE prophylaxis
- Pentasacharides ► DVT prophylaxis & treatment
- Unfractionated heparin ► DVT prophylaxis & treatment, UA, AMI, stroke with PCI
- Warfarin ► DVT prophylaxis & treatment, a-fib, PE, PVD, AMI

**Practice Recommendations**

- Calculate the annual thromboembolic risk with the regular implementation of CHADSVASC scores on atrial fibrillation patients.
- On your patients with moderate renal insufficiency, be extra careful on the NOACs.
- Do not load warfarin when anticoagulating patients.

**Questions**

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