Anticoagulation Management Update: Through Thick & Thin

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Dr. Walsworth earned a medical degree at Wayne State University School of Medicine, Detroit, Michigan. He completed his family medicine residency at Oakwood Hospital & Medical Center, Dearborn, Michigan, and an Office of Medical Education Research and Development (OMERAD) Primary Care Faculty Development Fellowship at MSU. During more than 20 years as a family physician, he has gained experience in private practice, residency teaching practice, and academic practice. In his current role, Dr. Walsworth manages MSU’s Family Health Center; cares for a wide range of patients; teaches medical students, residents, and peers; and studies the determinants of provider resilience and burnout. He serves on the board of directors for the Michigan Academy of Family Physicians.
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 self-administration of anticoagulants, emphasizing self-monitoring (when appropriate) 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.

Audience Engagement System
Special Slide Icons

Look up here for one of the following:

- Treatment or practice guideline(s)
- Performance measure(s)
- Practice tool(s)
- Choosing Wisely
- Overcoming barriers to change
- Monday morning “To Do List”
- Best Practice Recommendations
48 Year Old Male with New Onset Atrial Fibrillation

- New patient presenting to ED with abdominal pain, HR 170 irregularly irregular, BP 170/110
- History of OSA managed with CPAP, morbid obesity, laparoscopic appendectomy for ruptured appendix 3 years earlier, no HTN (last BP 110/70 6 months earlier)
- No medications
- Married with 3 children
- Active, Cub Master, avid camper
- Family history of atrial fibrillation, diabetes, HTN, Alzheimer’s dementia, no bleeding or clotting problems
- CT abdomen shows non-obstructive clot in superior mesenteric artery trunk

AES Question 1
Does he need anticoagulation?

Does he need anticoagulation?
- A. Yes
- B. No
**CHA\textsubscript{2}-DS\textsubscript{2}-VASc Score for Atrial Fibrillation Stroke Risk**

- Age in Years
  - (0) < 65
  - (1) 65–74
  - (2) ≥ 75
- Sex
  - (0) Male
  - (1) Female
- (1) CHF History
- (1) HTN History
- (2) Stroke/TIA/Thromboembolism History
- (1) Vascular Disease History
- (1) Diabetes Mellitus

**Interpretation**
- 0 – Low risk for thromboembolic event (0% per year)
- 1 – Intermediate risk for thromboembolic event (0.6% per year) – consider antiplatelet or anticoagulant therapy
- 2+ – High risk for thromboembolic event (3% per year) – recommend anticoagulant therapy

**HAS-BLED Score for Major Bleeding Risk**

- (1) Uncontrolled HTN (SBP>160)
- (1) Dialysis, Renal Transplant, Cr>2.26 mg/dl
- (1) Cirrhosis, Bilirubin>2xULN, AST/ALT/AP>2xULN
- (1) Stroke History
- (1) Prior Major or Predisposition to Bleeding
- (1) Labile INR (Time in target range < 60%)
- (1) Age > 65 years
- (1) Antiplatelet or NSAID use
- (1) ≥ 8 EtOH drinks/week

**Interpretation**
- 0–1 – Anticoagulation should be considered
- 2 – Anticoagulation can be considered
- 3–9 – Alternatives to anticoagulation should be considered due to bleeding risk
AES Question 2
Hypercoagulability Work Up

If he had presented with SMA trunk thromboemolus without AF, which of the following should be included in the hypercoagulability work up, if one is done?

A. Activated protein C resistance +/- factor V Leiden mutation testing
B. Prothrombin G20210A mutation testing
C. Lupus anticoagulant and Antiphospholipid antibodies
D. Protein C and S activity
E. All of the above

Risk-Based Work Up: Thrombophilias

- First episode with risk factors without family history (Low Risk) None
- Age > 50 years, first episode, without risk factors or family history
  - Activated protein C resistance +/- factor V Leiden mutation testing
  - Prothrombin G20210A mutation testing
  - Lupus anticoagulant
  - Anti-phospholipid antibodies
  - Plasma homocysteine
- Age < 50 years without risk factors, recurrent thrombosis, or family history of thromboembolism
  - All of the above, plus
  - Antithrombin assay
  - Protein C assay
  - Protein S assay

AES Question 3
PE and DVT Prevention in A-Fib

Which of the following are indicated for preventing PE and DVT following previous PE or DVT?

A. Warfarin (Coumadin, Jantoven)
B. LMWH (Arixtra, Fragmin, Lovenox)
C. Factor Xa Inhibitors (Bevyxxa, Eliquis, Savaysa, Xarelto)
D. Direct Thrombin Inhibitor (Pradaxa)
E. All of the above

Choice of Anticoagulant

- LMWH
  - Active Cancer
  - Pregnancy
- Warfarin
  - CrCl < 30
  - Mechanical heart valve
  - Childs-Pugh B or C hepatic impairment
  - DOAC not covered
- DOAC
  - Unstable diet, health status
  - Frequent antibiotics or procedures

Duration of Treatment: INR target 2.5 (2.0-3.0)

First episode (proximal DVT or PE)
- 3 months
  - Perioperative (1B)
  - Other reversible risk factors (1B/2B)
  - Distal DVT perioperatively or with reversible risk (1B/2C)
  - Idiopathic (high bleeding risk) (1B)
  - Idiopathic distal DVT (1B/2B)
  - Long-term - Idiopathic (low or moderate bleeding risk) (2B)

Second episode (both unprovoked)
- 3 months (high bleeding risk) (2B)
- Long-term (low or moderate bleeding risk) (1B/2B)

Active Cancer and PE
- Long-term (1B/2B) depending on bleeding risk

Anti-phospholipid antibody with arterial or venous thrombosis
- Long-term (2B)

Elective total hip or knee replacement and hip fracture
- 10-14 days minimum (2B)
- 35 days for major orthopedic (2B)
- LMWH preferred over warfarin for total hip and knee (2C)

Atrial fibrillation or flutter
- 3 weeks prior and 4 weeks following elective cardioversion (1B/2C)
- Indefinite
  - Intermediate (CHADS2=1) to high risk (CHADS2≥2 of stroke) (1B)
  - Mitral stenosis (1B)

Stent placement and high risk of stroke
- Bare metal - one month
- Drug-eluting - 3-6 months with aspirin and clopidogrel (2C), then warfarin alone for total of 12 months (2C), and ongoing thereafter (2C)

Coronary Heart Disease
- 3 months - High risk with MI without stent (1B)
- High risk with MI with stent (2C)
  - Bare metal – warfarin + low-dose aspirin + clopidogrel in month 1, then warfarin + single antiplatelet agent in months 2-3

Valvular Heart Disease
- 3 months – Bio prosthetic valves
- Long-term
  - Rheumatic mitral valve with atrial fibrillation, embolism, or atrial thrombus (1A); sinus rhythm and atrial diameter > 55 mm (2C)
  - Mechanical valves - aortic
Duration of Treatment: INR target 3.0 (2.5-3.5)

Long-term
• Mechanical valves – mitral

AES Question 4
PE and DVT Prevention in A-Fib

Which of the following are indicated for initiating warfarin preventing PE and DVT following previous PE or DVT (INR Target 2-3)?

A. 5 mg daily at 6:00 PM, adjusting dose based on INR, continuing LMH until INR in target range
B. 10 mg daily for 2 days at 6:00 PM, adjusting dose based on INR, continuing LMH until INR in target range
C. 10 mg daily at 6:00 PM, adjusting dose based on INR, continuing LMH until INR in target range
D. A and B
E. All of the above
Warfarin Initiation

- After starting UFH/LMHW
- Continue LMWH until INR in therapeutic range (minimum 5 days overlap)
- Starting Dose
  - 2.5 mg / day
    - Patients at high risk of bleeding
    - Longer to therapeutic range
  - 5 mg / day
    - Possibly longer to therapeutic range
  - 10 mg / day
    - 2C recommendation from ACCP Guideline
    - 2 days, then per INR
    - Possibly more over-anticoagulation

Anticoagulation Management Coding

- **99363** – Initial 90 days
  - Must document at least 8 INRs in 90 days
- **99364** – Subsequent 90 day periods
  - Must document at least 3 INRs in 90 days
  - Also used if warfarin is started during an inpatient or facility stay
- **No payment by Medicare or Medicaid**
- **Covers telephone and electronic contact to manage warfarin during the 90 day period**
- **Z79.01** – Long term (current) use of anticoagulants
PerioprocEDURE MANAGEMENT (Interrupting and/or Bridging)

• Anticoagulant
  • Warfarin
  • DOAC
• Anticoagulant indication
  • Atrial fibrillation
  • Venous thromboembolic event (DVT, PE)
  • Mechanical heart valve
• Patient clotting risk
• Patient bleeding risk
• Procedure bleeding risk


PerioprocEDURE MANAGEMENT (Patient Clotting Risk)

• Only considered in warfarin treated patients
• Low
  • AF: \( \text{CHA}_2\text{DS}_2\text{VASc} \leq 4 \text{ AND no CVA or systemic embolism} \)
  • VTE: VTE > 12 months ago \text{ AND no other risk factors} \)
  • MHV: Bileaflet aortic valve prosthesis w/o AF or other CVA risk factors

Perioprocedure Management (Patient Clotting Risk)

• Only considered in warfarin treated patients
• Moderate
  • AF: CHA$_2$DS$_2$-VASc 5-6 OR CVA or systemic embolism ≥ 3 months ago
  • VTE: VTE 3-12 months ago, non-severe thrombophilia (heterozygous Factor V Leiden or Thrombin G20210 mutations), recurrent VTE, active cancer (within 6 months)
  • MHV: Bileaflet aortic valve prosthesis with risk factor(s)
    • Atrial fibrillation
    • Prior CVA or TIA
    • HTN
    • DM
    • CHF
    • Age > 75 years


Perioprocedure Management (Patient Clotting Risk)

• Only considered in warfarin treated patients
• High
  • AF: CHA$_2$DS$_2$-VASc ≥ 7 OR CVA or systemic embolism < 3 months ago
  • VTE: VTE < 3 months ago, severe thrombophilia (deficiency of protein C, Protein S, or antithrombin; antiphospholipid ab; multiple anomalies)
  • MHV: Any mitral valve prosthesis, caged-ball or tilting disc aortic valv prosthesis, CVA or TIA ≤ 6 months

Perioprecedure Management (Patient Bleeding Risk)

• Major bleeding or ICH < 3 months
• Platelet abnormality (includes ASA use)
• Prior bleeding during previous bridging


Perioprecedure Management (Patient Bleeding Risk)

• CYP3A4 Inhibitors
  • Grapefruit juice
  • Clarithromycin* / telithromycin
  • Nefazodone*
  • Itraconazole* / ketoconazole*
  • Atazanavir / darunavir / indinavir
  nelfinavir* / ritonavir* / saquinavir / tipranavir
  • Fluoxetine / fluvoxamine
  • Amiodarone
  • Diltiazem / verapamil

• P-gp Inhibitors
  • Cyclosporine
  • Ketoconazole
  • Quinidine
  • Reserpine
  • Ritonavir / lopinavir / Saquinavir
  / tipranavir
  • Tacrolimus
  • Verapamil
  • Propafenone
  • Ranolazine

Perioprocedure Management (Procedure Bleeding Risk) - Minimal/Not Clinically Significant

- Minor dental procedures
  - Extraction of 1-2 teeth
  - Periodontal surgery
  - Abscess incision
- Superficial surgeries
  - Abscess incisions
  - Dermatologic excisions
- Diagnostic gastrointestinal endoscopy with or without biopsy
- Central catheter removal

Perioprocedure Management (Procedure Bleeding Risk) - Low

- Pacemaker/defibrillator placement
- AF ablation (transvenous)
- D&C
- Cervical bx
- Prostate bx
- Angiography/PCI (transradial)
- Breast or axillary node FNA
- Nerve block, peripheral (superficial, compressible)
Periopercrocedure Management (Procedure Bleeding Risk) - Moderate

- LE arterial revascularization (femoral, poplitieal, tibial)
- LE deep venous reconstruction
- Hysterectomy
- Left atrial appendage occlusion (WATCHMAN)
- Angiography/PCI (transfemoral)
- ORIF LE fx
- Complex dental procedures
  - Extract > 3 teeth
  - Dental implants
- Lung bx (percutaneous needle)
- Chest drain placement (larger drain)
- Nerve block (peripheral, noon-compressible)


Periopercrocedure Management (Procedure Bleeding Risk) - High

- Surgeries/procedures in highly vascular organs
  - Kidney
  - Liver
  - Spleen
- Major surgery with extensive tissue injury
  - Cancer surgery
  - Joint arthroplasty
  - Reconstructive surgery
- Bowel resection
- Cardiac, intracranial, or spinal surgeries
- Urologic surgeries
- Abdominal vascular surgery
- Left atrial appendage occlusion (Lariat)
- Lumbar puncture
- ICD/pacer lead extraction
- Neuraxial block (spinal, epidural)
- Most major surgeries > 45 minutes

### Perioprocessure Management (Procedure Bleeding Risk) - Uncertain

- Esophageal bx
- Pericardiocentesis

*Always discuss with proceduralist regardless of anticipated risk*

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### Direct Oral Anticoagulants (DOACs): Indications

<table>
<thead>
<tr>
<th>Factor Xa Inhibitors</th>
<th>Thromboembolism / stroke prophylaxis (non-valvular atrial fibrillation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixiban (Eliquis)</td>
<td>DVT prophylaxis (hip or knee replacement)</td>
</tr>
<tr>
<td>Betrixaban (Bevyxxa)</td>
<td>DVT/PE prophylaxis (recurrent)</td>
</tr>
<tr>
<td>Endoxaban (Savaysa)</td>
<td>DVT/PE treatment</td>
</tr>
<tr>
<td>Rivaroxaban (Xarelto)</td>
<td>Cardiovascular risk reduction</td>
</tr>
<tr>
<td><strong>Thrombin Inhibitors</strong></td>
<td>Dabigatran (Pradaxa) 2.5 mg BID + ASA 75-100 mg daily</td>
</tr>
<tr>
<td>Dabigatran (Pradaxa)</td>
<td>For patients with CAD or PAD</td>
</tr>
</tbody>
</table>

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Anticoagulation Reversal

- Heparin – Protamine
- Warfarin – Vitamin K1 (phytonadione)
- Thrombin Inhibitors – Idarucizumab (Praxbind)
  - Dabigatran (Pradaxa)
- Factor Xa Inhibitors – Coagulation Factor Xa Recombinant, inactivated (Andexxa)
  - Apixiban (Eliquis)
  - Endoxaban (Savaysa)
  - Rivaroxaban (Xarelto)

Procoagulant Factors

- Prothrombin Complex Concentrate
  - 4 factor PCC (II, VII, IX, X)
    - Kcentra, also has Protein C, Protein S
    - Feiba
  - 3 factor PCC (II, IX, X)
- Factor VIIa
  - Recombinant
- Factor VIII/von Willenbrand
  - Human Concentrate
  - Recombinant
- Factor IX
  - Human Concentrate
  - Recombinant
- Factor XIII
  - Human Concentrate
  - Recombinant A-subunit
Key Recommendations

SORT A

• In patients with atrial fibrillation and at least one other risk factor for stroke, newer agents (rivaroxaban [Xarelto] and dabigatran [Pradaxa]) 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.

• Compared with usual clinic-based care, patient self-testing for international normalized ratios, with or without self-dosing of warfarin, is associated with significantly fewer deaths and thromboembolic complications without any increase in bleeding complications for a selected group of motivated patients who have completed appropriate training.

SORT B

• Patients taking warfarin should be treated using systematic processes of care to optimize effectiveness and minimize adverse effects. Health care professionals skilled in the initiation and assessment of therapy and dosing adjustments can dramatically influence outcomes.


AES Question 5
Outpatient DVT and PE Treatment

Uncomplicated PE and DVT may be treated in the outpatient setting?

A. True
B. False
Primary Hypercoagulable States

- **Common**
  - Factor V Leiden mutation
  - Prothrombin 20210 mutation
  - Homocysteinemia

- **Uncommon Causes**
  - Antithrombin III deficiency
  - Protein C deficiency
  - Protein S deficiency
  - Increased Factor VIII
  - Fibrinolysis
  - Dysfibrinogenemia

Secondary Hypercoagulable States

- **Antiphospholipid Antibody Syndrome**
- Pregnancy
- Trauma
- Infection (sepsis)
- Malignancy
- Myeloproliferative disorders
- Hyperlipidemia
- Homocystinuria
- Lupus inhibitor (anticoagulant)
- Nephrotic Syndrome

- **Medications**
  - Estrogen sources
    - Oral contraceptives
    - Estrogen replacement therapy
  - Tamoxifen
  - Phenothiazines
  - Procainamide
DVT Probability: Wells Score System

- Paralysis, paresis or recent orthopedic casting of lower extremity (1 point)
- Recently bedridden (more than 3 days) or major surgery within past 4 weeks (1 point)
- Localized tenderness in deep vein system (1 point)
- Swelling of entire leg (1 point)
- Calf swelling 3 cm greater than other leg (measured 10 cm below the tibial tuberosity) (1 point)
- Pitting edema greater in the symptomatic leg (1 point)
- Collateral non varicose superficial veins (1 point)
- Active cancer or cancer treated within 6 months (1 point)
- Alternative diagnosis more likely than DVT (Baker’s cyst, cellulitis, muscle damage, superficial venous thrombosis, post phlebitic syndrome, inguinal lymphadenopathy, external venous compression) (-2 points)

DVT Risk Score Interpretation

- 3-8 Points: High Probability of DVT
- 1-2 Points: Moderate Probability of DVT
- -2-0 Points: Low Probability of DVT

DVT Diagnostic Algorithm

- Low probability Wells Score (DVT)
  - D-Dimer negative – DVT excluded
  - D-Dimer positive – Check duplex ultrasound
    - Ultrasound positive – proceed to treatment
- Moderate or high probability Wells Score (DVT)
  - Duplex ultrasound negative – excluded
  - Duplex ultrasound positive – proceed to treatment

2016, UW Health Inpatient and Outpatient Committees. Venous Thromboembolism Diagnosis and Treatment – Adult – Inpatient/Ambulatory/Emergency Department – Clinical Practice Guideline. Downloaded on 7/28/19 from https://www.uwhealth.org/files/uwhealth/docs/anticoagulation/venous_thromboembolism_management_ED.pdf
PE Probability: Wells Score System

- Symptoms of DVT (3 points)
- No alternative diagnosis better explains the illness (3 points)
- Tachycardia with pulse > 100 (1.5 points)
- Immobilization (≥ 3 days) or surgery in the previous four weeks (1.5 points)
- Prior history of DVT or PE (1.5 points)
- Presence of hemoptysis (1 point)
- Presence of malignancy (1 point)

PE Risk Score Interpretation

- ≥ 7 Points: High Probability of PE
- 2-6 Points: Moderate Probability of PE
- < 2 Points: Low Probability of PE

2016, UW Health Inpatient and Outpatient Committees. Venous Thromboembolism Diagnosis and Treatment – Adult – Inpatient/Ambulatory/Emergency Department – Clinical Practice Guideline. Downloaded on 7/28/19 from https://www.uwhealth.org/files/uwhealth/docs/anticoagulation/venous_thromboembolism_management_ED.pdf

Pulmonary Embolism Rule-Out Criteria (PERC)

- Age > 49 years
- HR > 99 bpm
- SpO2 < 95% on room air
- Hemoptysis present
- Taking exogenous estrogen
- History of VTE
- Recent surgery or trauma requiring intubation or hospitalization in the previous 4 weeks
- Unilateral leg swelling

PERC Interpretation

- The presence of any criteria suggest the need for further consideration of PE

2016, UW Health Inpatient and Outpatient Committees. Venous Thromboembolism Diagnosis and Treatment – Adult – Inpatient/Ambulatory/Emergency Department – Clinical Practice Guideline. Downloaded on 7/28/19 from https://www.uwhealth.org/files/uwhealth/docs/anticoagulation/venous_thromboembolism_management_ED.pdf
PE Diagnostic Algorithm

• Wells Score (PE)
  • Low risk with negative PERC – PE excluded
  • Moderate with negative D-Dimer – PE excluded
  • Moderate with positive D-Dimer – Perform CT
    • CT negative / non-diagnostic with negative bilateral leg DUS – Repeat DUS in 1-2 weeks
    • CT positive or negative with positive DUS – proceed to treatment

Simplified PE Severity Index (sPESI)

• Age > 80 years
• HR > 110 bpm
• SBP < 100 mmHg
• SaO2 < 90% on room air
• Cancer (active or history)
• CHF or chronic lung disease

• sPESI Interpretation
  • The presence of any criteria suggest the need for inpatient treatment of PE
Treatment of DVT and PE

• Inpatient
  • Criteria
    • Medical or social reasons for acute hospitalization
    • CrCl < 30 ml/min
    • Severe Liver disease
    • If PE, sPESI > 0
  • Treatment
    • IV unfractionated heparin until medically stable and procedures completed

2017, Treatment of Acute Venous Thromboembolism. UW Medicine VTE Treatment Taskforce. Downloaded on 7/28/19 from https://depts.washington.edu/anticoag/home/sites/default/files/VTE%20Treatment%20Pathway%20July%202017_0.pdf

Treatment of DVT and PE

• Outpatient
  • Criteria
    • No inpatient criterial present
  • Treatment
    • Rivaroxaban 15 mg BID x 3 wks, then 20 mg daily
      • Avoid if CrCl < 30 ml/min
      • Avoid if potentially interacting meds
      • Limited data in morbidly obese
    • Apixaban 10 mg BID x 7 days, then 5 mg BID
      • Avoid if CrCl < 30 ml/min
      • Avoid if potentially interacting meds
      • Limited data in morbidly obese
    • Enoxaparin 1 mg/kg SQ q 12 hrs x 5-10 days, then dabigatran 150 mg BID
      • Adjust enoxaparin if CrCl < 60 ml/min
      • Avoid if CrCl < 50 ml/min
      • Avoid if potentially interacting meds
      • Limited data in morbidly obese
    • Enoxaparin 1 mg/kg SQ q 12 hrs + warfarin (stop enoxaparin when INR > 2 after a minimum of 5 days overlap)
      • Adjust enoxaparin if CrCl < 60 ml/min
      • Start warfarin on same day as enoxaparin

2017, Treatment of Acute Venous Thromboembolism. UW Medicine VTE Treatment Taskforce. Downloaded on 7/28/19 from https://depts.washington.edu/anticoag/home/sites/default/files/VTE%20Treatment%20Pathway%20July%202017_0.pdf
AES Question 6
Anticoagulation in Pregnancy

Which of the following are indicated for preventing PE and DVT in pregnancy following previous PE or DVT?

A. Factor Xa Inhibitor (Eliquis, Savaysa, Xarelto)
B. Warfarin (Coumadin, Jantoven)
C. Direct Thrombin Inhibitor (Pradaxa)
D. LMWH (Arixtra, Fragmin, Lovenox)

Clotting Disorders in Pregnancy

- Virchow’s Triad
  - Hypercoagulation
  - Vascular damage
  - Venous stasis
- Relative risk of 4.3
- Half of pregnant women with VTE have a thrombophilia

- VTE risk factors
  - Age > 35 years
  - BMI > 30
  - Grand multiparity
  - Family history of VTE or thrombophilia
  - Immobility ≥ 4 days
  - Dehydration
  - Medical conditions
  - Cesarean section

Anticoagulation in Pregnancy

- LMWH generally preferred agent
- Start as early in pregnancy as possible
- Stop six weeks postpartum
  - Provoked DVT or PE without thrombophilia (controversial)
  - Unprovoked DVT or PE without thrombophilia (unless recurrent or life threatening)
  - No past DVT or PE with thrombophilia
    - Anti-phospholipid antibodies – ASA +/- LMWH
- Long-term prophylaxis may be required
  - Past DVT or PE with thrombophilia


Key Recommendations

SORT A
- LMWHs are the agents of choice for antenatal thromboprophylaxis.

SORT B
- LMWHs are recommended for the treatment of acute DVT and PE in pregnancy because of equivalent or superior effectiveness and safety compared with unfractionated heparin.

SORT C
- Multidetector-row (spiral) CT is the imaging modality of choice to evaluate for PE in pregnancy because, in nonpregnant patients, the diagnostic accuracy is equivalent to pulmonary angiography, and radiation exposure to the fetus is less than with a V/Q scan.

Drug Risk in Pregnancy, Lactation, and Reproduction

- Pre-2015
  - Pregnancy
    - A
    - B
    - C
    - D
    - X
  - Labor & Delivery
  - Nursing Mothers
    - Probably Safe
    - Possibly Unsafe
    - Unsafe

- Current (effective June 30, 2015)
  - Pregnancy
    - Pregnancy Registry
    - Risk Summary
    - Clinical Considerations
    - Data
    - Labor & Delivery
  - Lactation
    - Presence in breast milk
    - Potential effects on breastfed infants
  - Females and Males of Reproductive Potential
    - Need for pregnancy testing
    - Contraception recommendations
    - Infertility as it relates to the drug

2014 FDA. Pregnancy and Lactation Labelling (Drugs) Final Rule. Downloaded on 4/2/17 from

Drug Risk in Pregnancy, Lactation, and Reproduction

**Warfarin**
- Pregnancy
  - Contraindicated during pregnancy unless pt with mechanical heart valve, then weigh risk/benefit
  - Risk of fetal harm including IUGR, teratogenicity, and fetal death based on animal data
- Lactation
  - May use while lactating
  - No known risk of infant harm based on limited human data and drug properties
  - No human data to assess affects on milk production

**LMWH**
- Pregnancy
  - May use during pregnancy, though caution advised with benzyl alcohol injectable forms
  - Consider holding 24 hours before delivery
  - No know risk of fetal harm based on human data
- Lactation
  - May use while lactating
  - No known risk of infant harm based on limited human data and drug properties
  - No human data to assess affects on milk production
  - No data for fondaparinux
Drug Risk in Pregnancy, Lactation, and Reproduction

**Factor Xa Inhibitors**
- **Pregnancy**
  - Use alternative
  - No human data available
  - No known risk of fetal harm
  - Risk of maternal bleeding based on animal data at up to 4 x for rivaroxaban, 19 x MRHD for apixaban, 44 x for betrixaban, 49 x for endoxaban
  - Risk of maternal hemorrhage during delivery and fetal bleeding based on drug’s mechanism of action
- **Lactation**
  - Use alternative
  - No human data to assess risk of infant harm or effects on milk production
  - Possible excretion in breast milk with endoxaban

**Thrombin Inhibitors**
- **Pregnancy**
  - Avoid use in pregnancy
  - No human data available
  - Risk of embryo-fetal toxicity and death
  - Risk of maternal bleeding near delivery based on animal data at 2.6-3 x MRHD
  - Risk of maternal hemorrhage and fetal bleeding based on drug’s mechanism of action
- **Lactation**
  - Caution advised
  - No human data available
  - Low risk of infant harm based on drug properties
  - No human data available to assess effects on milk production

**Choosing Wisely**
- **American Association of Blood Banks**
  - Don’t routinely use blood products to reverse warfarin
- **American College of Chest Physicians and American Thoracic Society**
  - Don’t perform chest computed tomography (CT angiography) to evaluate for possible pulmonary embolism in patients with a low clinical probability and negative results of a highly sensitive D-dimer assay.
- **American Physical Therapy Association**
  - Don’t recommend bed rest following diagnosis of acute deep vein thrombosis (DVT) after the initiation of anti-coagulation therapy, unless significant medical concerns are present.
- **American Society for Clinical Pathology**
  - Do not test for Protein C, Protein S, or Antithrombin (ATIII) levels during an active clotting event because these tests are not analytically accurate during an active clotting event.
- **Society for Vascular Surgery**
  - Don’t use IVC filters as primary prevention of pulmonary emboli in the absence of an extremity clot or prior pulmonary embolus.

Choosing Wisely

- American Society of Hematology
  - Don’t test for thrombophilia in adult patients with venous thromboembolism (VTE) occurring in the setting of major transient risk factors (surgery, trauma or prolonged immobility).
  - Don’t use inferior vena cava (IVC) filters routinely in patients with acute VTE.
  - Don’t administer plasma or prothrombin complex concentrates for non-emergent reversal of vitamin K antagonists (i.e. outside of the setting of major bleeding, intracranial hemorrhage or anticipated emergent surgery).
  - Don’t treat with an anticoagulant for more than three months in a patient with a first venous thromboembolism (VTE) occurring in the setting of a major transient risk factor.
  - Don’t test or treat for suspected heparin-induced thrombocytopenia (HIT) in patients with a low pre-test probability of HIT.
  - Don’t treat patients with immune thrombocytopenic purpura (ITP) in the absence of bleeding or a very low platelet count.

- Society for Maternal-Fetal Medicine
  - Don’t do an inherited thrombophilia evaluation for women with histories of pregnancy loss, intrauterine growth restriction (IUGR), preeclampsia and abruption.

Performance Improvement Reporting

Atrial Fibrillation and Atrial Flutter - Measure 326 (NQF: 1525)

- All patients aged 18 years and older with a diagnosis of nonvalvular AF or atrial flutter who do not have a documented CHA2DS2-VASc risk score of 0 or 1
- Numerator - Patients who had a risk assessment for falls completed within 12 months
  - G8967 – Warfarin or other FDA-approved oral anticoagulant prescribed
  - G8968 – Documented medical reason for not prescribing oral anticoagulant
- Denominator exclusions
  - G9929 – Patient with transient or reversible cause of AF
  - G9930 – Patient receiving comfort care only
  - G9931 – Patient with CHA2DS-VASc risk score of 0 or 1
Performance Improvement Benchmarking

MIPS PY2017 Data with PY2019 Eligibility

• Atrial Fibrillation and Atrial Flutter: Chronic Anticoagulation Therapy (MIPS 326)
  • Claims (Topped out, 7 point cap)
    • Average: 89.5% (SD 20.6%)
    • Decile 3: 84.13-95.28%
    • Decile 4: 95.29-98.79%
    • Decile 5: 98.80-99.99%
    • Decile 10: 100%

MIPS PY2017 Data with PY2019 Eligibility

• Atrial Fibrillation and Atrial Flutter: Chronic Anticoagulation Therapy (MIPS 326)
  • Registry/QCDR
    • Average 81.2% (SD 18%)
    • Decile 3: 69.54-75.10%
    • Decile 4: 75.11-78.89%
    • Decile 5: 78.90-83.08%
    • Decile 6: 83.09-88.16%
    • Decile 7: 88.17-94.93%
    • Decile 8: 94.94-99.99%
    • Decile 10: 100%


Barriers to Anticoagulation Management

• Diagnostic tests may or may not be covered under insurance plans
• Medications may or may not be covered under insurance plans
• Costs of monitoring programs may or may not be covered under insurance plans
• All require patient adherence and compliance, some more than others
Key Practice Recommendations (Recap SORT A & B)

SORT A

• In patients with atrial fibrillation and at least one other risk factor for stroke, newer agents (rivaroxaban [Xarelto] and dabigatran [Pradaxa]) 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.

• Compared with usual clinic-based care, patient self-testing for international normalized ratios, with or without self-dosing of warfarin, is associated with significantly fewer deaths and thromboembolic complications without any increase in bleeding complications for a selected group of motivated patients who have completed appropriate training.

• LMWHs are the agents of choice for antenatal thromboprophylaxis.

SORT B

• Patients taking warfarin should be treated using systematic processes of care to optimize effectiveness and minimize adverse effects. Health care professionals skilled in the initiation and assessment of therapy and dosing adjustments can dramatically influence outcomes.

• LMWHs are recommended for the treatment of acute DVT and PE in pregnancy because of equivalent or superior effectiveness and safety compared with unfractionated heparin.


Monday Morning “To Do” List

- Use evidence-based guidelines for diagnosing and treating conditions requiring anticoagulation
  - Check health system and payor anticoagulation guidelines
  - Consider office registries for patients treated with warfarin and other anticoagulants
  - Check personal performance against benchmarks
- Check on payor requirements for anticoagulation management
- Check on formulary status of various anticoagulation medications for common payors
  - Consider GoodRx
  - Consider NeedyMeds
Author Recommended Electronic Tools

• MAQI2 Anticoagulation Toolkit App
  • http://maqi2.org/

• MAQI2 Anticoagulation Toolkits
  • Provider
    • http://anticoagulationtoolkit.org/providers
  • Patient
    • http://anticoagulationtoolkit.org/patients

• Choosing Wisely App
  • http://www.choosingwisely.org

• Michigan Quality Improvement Consortium Guideline App
  • http://mqic.org

• GoodRx App
  • https://www.goodrx.com/

• NeedyMeds
  • https://www.needymeds.org/
Questions
Answer Key

1. A
2. E
3. E
4. D
5. A
6. D

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