An Update on Thromboprophylaxis in Obstetrics

Chase Cawyer, MD, MBA
Assistant Professor
Maternal-Fetal Medicine

No Disclosures

- I have no relevant financial relationships to disclose regarding this talk.

Objectives

- Describe the anticoagulation options during pregnancy.
- Describe the indications and duration of outpatient anticoagulation use in pregnancy in multiple clinical situations
- Describe indications for anticoagulation in both the antepartum and postpartum period
Background

- Pregnant women are at 4-5 fold increased risk of a VTE
- Incidence is 0.5-2.0 per 1,000 pregnancies
- Accounts for ~10% of maternal deaths in the United States.
- Preventing VTE is a top safety priority for AHRQ

ANTICOAGULATION OPTIONS

Choice of Anticoagulant

- Low Molecular Weight Heparin (LMWH)*
- Unfractionated Heparin (UFH)*
- Warfarin
- Others
  - Fondaparinux, Argatroban, Danaparoid
  - Dabigatran
  - Rivaroxaban

LMWH

- LMWH is preferred agent of choice
  - Improved bioavailability
  - Longer half-life
  - More predictable response
  - Improved safety profile
  - Patient compliance

Side effects of anticoagulation

- Risks
  - Bleeding
  - Bone loss
  - Thrombocytopenia
- Recommend
  - Calcium (2 grams/day) and Vitamin D (400-800 IU/day)

Dosing during Pregnancy

- Prophylactic dosing
  - Low molecular weight heparin (LMWH)
    - 40mg SQ daily
    - BMI ≥50 - 40mg SQ twice daily
      - Anti-Xa levels 0.2-0.4 units/mL
Dosing during Pregnancy

• Prophylactic Dosing
  • Unfractionated Heparin (UFH)
    • 1st trimester: 5,000 - 7,500 units SQ BID
    • 2nd trimester: 7,500 - 10,000 units SQ BID
    • 3rd trimester: 10,000 units SQ BID

• Therapeutic Dosing
  • Low molecular weight heparin (LMWH)
    • Twice daily dosing
    • Based on body weight (1mg/kg)
    • Goal anti-Xa levels (0.5-1units/mL)
      • Level obtained 4 hours after dose

• Therapeutic Dosing
  • Unfractionated Heparin (UFH)
    • Three times daily dosing
    • 10,000 units with titration based on levels
    • Goal anti-Xa levels (0.3-0.7 units/mL)
    • Level obtained 6 hours after dose
Dosing During Pregnancy

- How often should levels be checked?
  - Weekly until ranges are met
  - Monthly after goal ranges are met

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Anti-Xa Levels?</th>
<th>Goal Anti-Xa</th>
</tr>
</thead>
<tbody>
<tr>
<td>LMWH Prophylactic</td>
<td>No</td>
<td>0.2-0.4 units/mL</td>
</tr>
<tr>
<td>40 mg daily</td>
<td>YES</td>
<td>0.5-1.0 units/mL</td>
</tr>
<tr>
<td>UFH Prophylactic</td>
<td>No</td>
<td>0.3-0.7 units/mL</td>
</tr>
<tr>
<td>Therapeutic</td>
<td>YES</td>
<td>0.5-1.0 units/mL</td>
</tr>
<tr>
<td>UFH Therapeutic</td>
<td>YES</td>
<td>0.5-1.0 units/mL</td>
</tr>
</tbody>
</table>

Anti-Xa

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Appropriate Time to Check Anti-Xa</th>
</tr>
</thead>
<tbody>
<tr>
<td>UFH</td>
<td>6 hours after last dose</td>
</tr>
<tr>
<td>LMWH</td>
<td>4 hours after last dose</td>
</tr>
</tbody>
</table>
Stopping Prior to Scheduled Delivery

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Final dose patient should take prior to scheduled admission</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LMWH</strong></td>
<td></td>
</tr>
<tr>
<td>Prophylactic</td>
<td>40 mg daily 12 hours</td>
</tr>
<tr>
<td></td>
<td>40 mg BID (BMI ≥ 50) 24 hours</td>
</tr>
<tr>
<td>Therapeutic</td>
<td>24 hours AND anti-Xa less than 0.1 units/mL</td>
</tr>
<tr>
<td><strong>UFH</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If patient is on 5,000 BID 12 hours and anti-Xa not necessary</td>
</tr>
<tr>
<td></td>
<td>If on &gt; 5,000 BID 12 hours AND anti-Xa less than 0.1</td>
</tr>
<tr>
<td>Infusion (IV)</td>
<td>Stop 4-6 hours prior to expected need for neuraxial anesthesia</td>
</tr>
</tbody>
</table>

Management Near Term

- If on LMWH, **CONSIDER** transition to UFH at 36 weeks gestation
- Is an improved chance of getting regional anesthesia worth switching medication and re-titrating?

<table>
<thead>
<tr>
<th>LMWH</th>
<th>UFH Dose Until Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prophylactic</td>
<td>10,000 units BID</td>
</tr>
<tr>
<td>Therapeutic</td>
<td>Calculate</td>
</tr>
</tbody>
</table>

Prophylactic Postpartum Anticoagulation

- Prophylactic anticoagulation should be restarted the morning of postpartum day 1.
- Anticoagulation should not be initiated within 4 hours of epidural removal.
Therapeutic Postpartum Anticoagulation

- Uncomplicated Vaginal Delivery
  - Restart 6 hours postpartum
- Uncomplicated Cesarean Delivery
  - Restart 12-18 hours postpartum

Anticoagulation and Breastfeeding

- Safe to breastfeed with Warfarin, UFH, LMWH, and aspirin
- Avoid fondaparinux, oral direct thrombin inhibitors or factor Xa inhibitors

RISK STRATIFICATION
### Risk stratification

- ACOG
- American College of Chest Physicians (ACCP)
- Royal College of Obstetricians and Gynaecologists (RCOG)

### Risk Stratification

- Personal VTE History
- Thrombophilia Carrier (Inherited or Acquired)
- Medical Conditions

### Clinical Scenario Antepartum Management Postpartum Management

<table>
<thead>
<tr>
<th>Personal VTE History</th>
<th>Antepartum Management</th>
<th>Postpartum Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Past single VTE during pregnancy or another transient risk-factor</td>
<td>Surveillance without anticoagulation plus/minus low-dose aspirin*</td>
<td>6 weeks PPx LMWH or UFH</td>
</tr>
<tr>
<td>Mechanical heart valve</td>
<td>Surveillance without anticoagulation plus low-dose aspirin</td>
<td>Return to pre-pregnancy regimen (will need a heparin bridge if transitioning to warfarin)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Therapeutic LMWH or UFH plus/minus low-dose aspirin*</td>
<td>6 weeks therapeutic LMWH, UFH, or warfarin</td>
</tr>
<tr>
<td>Antiphospholipid antibody syndrome without a history of a VTE</td>
<td>PPx LMWH or UFH plus low-dose aspirin</td>
<td>6 weeks PPx LMWH or UFH</td>
</tr>
<tr>
<td>Antiphospholipid antibody syndrome with a history of a VTE</td>
<td>Therapeutic LMWH or UFH plus low-dose aspirin</td>
<td>6 weeks therapeutic LMWH, UFH, or warfarin</td>
</tr>
<tr>
<td>Inherited thrombophilia</td>
<td>Surveillance without anticoagulation</td>
<td>Surveillance or 6 weeks PPx LMWH or UFH if additional risk factors exist (obesity, prolonged immobility)</td>
</tr>
</tbody>
</table>
Treat or No Treat (How and When)

LET'S PLAY A GAME
NAME THAT TREATMENT!!!!!

- Antepartum Treatment
- Postpartum Treatment

- Choices
  - Prophylactic anticoagulation
  - Therapeutic anticoagulation
  - Surveillance with vigilance
- Caveat: all women will be on low-dose aspirin

Acute VTE in Pregnancy

- Pregnant women with an acute VTE during pregnancy
  - Antepartum: Therapeutic
  - Postpartum: Continue for at least 6 weeks

Prophylactic, therapeutic or surveillance?

Chest 2012

History of VTE

- Personal history of VTE due to a single episode not related to pregnancy or estrogen such as trauma, immobilization, indwelling lines etc.
  - Antepartum: Surveillance
  - Postpartum: Prophylactic for 6 weeks

Prophylactic, therapeutic or surveillance?

Chest 2012
**History of a VTE**

- Personal history of VTE that was unprovoked or related to pregnancy or estrogen.
  - **Antepartum:** *Prophylactic*
  - **Postpartum:** *Continue at least 6 weeks*

**Prophylactic, therapeutic or surveillance?**

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**Inherited Thrombophilias**

- A personal history of VTE with a known protein C deficiency.

**Prophylactic, therapeutic or surveillance?**

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**Inherited Thrombophilias**

- Factor V Leiden mutation
- Prothrombin G20210A gene mutation
- Protein C deficiency
- Protein S deficiency
- Antithrombin III deficiency

ACOG PB 132
### Thrombophilias

<table>
<thead>
<tr>
<th>Low-Risk Thrombophilias</th>
<th>High-Risk Thrombophilias</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Factor V Leiden heterozygotes</td>
<td>1. Antithrombin III deficiency</td>
</tr>
<tr>
<td>3. Protein C or S deficiency</td>
<td>3. Factor V Leiden homozygous</td>
</tr>
<tr>
<td></td>
<td>4. Prothrombin G20210A homozygous</td>
</tr>
</tbody>
</table>

*Antiphospholipid Antibody Syndrome*

### Inherited Thrombophilias

- A personal history of VTE with a known protein C deficiency.
  - Antepartum: **Prophylactic**
  - Postpartum: **Continue for 6 weeks**

**Prophylactic, therapeutic or surveillance?**

Chest 2012

- A personal history of VTE with a known prothrombin homozygous mutation
  - Antepartum: **Therapeutic**
  - Postpartum: **Continue for 6 weeks**

**Prophylactic, therapeutic or surveillance?**

Chest 2012
Medical Conditions

- History of antiphospholipid antibody syndrome with a personal history of VTE
  - Antepartum: **Therapeutic**
  - Postpartum: **Continue at least 6 weeks**

Prophylactic, therapeutic or surveillance?

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Inherited Thrombophilias

- A personal history of VTE and PE with a known protein C deficiency.
  - Antepartum: **Therapeutic**
  - Postpartum: **Continue for 6 weeks**

Prophylactic, therapeutic or surveillance?

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Inherited Thrombophilias

- Factor V Leiden heterozygote with **NO** personal history and **NO** family history of VTE
  - Antepartum: **Surveillance**
  - Postpartum: **Surveillance or Prophylactic for 6 weeks**

Prophylactic, therapeutic or surveillance?
Medical Conditions

• History of antiphospholipid antibody syndrome with NO personal history of VTE
  • Antepartum: **Prophylactic**
  • Postpartum: **Continue** at least 6 weeks

Prophylactic, therapeutic or surveillance?

Inherited Thrombophilias

• Protein S deficiency with NO personal history of a VTE, but her sister has had a pulmonary embolism.
  • Antepartum: **Surveillance**
  • Postpartum: **Prophylactic** for 6 weeks

Prophylactic, therapeutic or surveillance?

Inherited Thrombophilias

• Antithrombin III deficiency with NO personal or family history of VTE
  • Antepartum: **Prophylactic**
  • Postpartum: **Continue** for 6 weeks

Prophylactic, therapeutic or surveillance?
Inherited Thrombophilias

• Factor V Leiden homozygous with NO personal history of VTE, but father had multiple VTEs after surgery.
  • Antepartum: Prophylactic
  • Postpartum: Continue for 6 weeks

Prophylactic, therapeutic or surveillance?

Medical Conditions

• Cardiac disease
  • Mechanical Heart Valve
  • Atrial fibrillation (active)
  • Mitral stenosis
• Renal disease
  • Nephrotic proteinuria (>3g).

Medical Conditions

• History of chronic atrial fibrillation
  • Antepartum: Therapeutic
  • Postpartum: Continue at least 6 weeks

Prophylactic, therapeutic or surveillance?
Medical Conditions

• History of severe mitral stenosis
  • Antepartum: **Therapeutic**
  • Postpartum: **Continue** at least 6 weeks

Prophylactic, therapeutic or surveillance?

Medical Conditions

• Patient with normal BP and a 24hr urine that resulted back 4.6 g.
  • Antepartum: **Prophylactic**
  • Postpartum: **Continue** at least 6 weeks

Prophylactic, therapeutic or surveillance?

Medical Conditions

• Mechanical heart valve
  • Antepartum: **Multidisciplinary meeting**, but will likely be put on **Warfarin**
  • Postpartum: Pre-pregnancy management with **heparin bridge**

Prophylactic, therapeutic or surveillance?
Antepartum Inpatient Prophylaxis

- Selected pregnant patients should be given mechanical prophylaxis while hospitalized antepartum (inductions, PPROM, PTL)
- Pharmacologic prophylaxis should be given if additional risk factors are present

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Antepartum Inpatient Prophylaxis

- UFH preferred over LMWH due to unpredictable timing of delivery.
- Best clinical judgement dictates appropriate timing of discontinuing pharmacologic anticoagulation.
- Prophylactic anticoagulation may be held in the setting of vaginal bleeding, active labor, or during evaluation for potential delivery.

Postpartum Inpatient Prophylaxis

- All patients should
  - Be encouraged to ambulate early
  - Avoid dehydration
  - Cesarean delivery
    - SCD’s perioperatively and postpartum until ambulating regularly

Adapted from: The American College of Obstetricians and Gynecologists Safe Mother Initiative. Venous Thromboembolism: Risk Assessment and Prophylaxis.

Postpartum Inpatient Prophylaxis

- SVD
  - Early mobilization
  - Avoid dehydration
  - Pharmacologic prophylaxis based on risk factors as outline previously

ACOG, Chest 2012
Postpartum Inpatient Prophylaxis

• Cesarean Delivery
  • SCD’s
  • Pharmacologic prophylaxis recommended based on risk factors.
    • VTE history and thrombophilia as outlined previously
    • Additional risk factors as follows

Chest 2012

Who gets discharged with anticoagulation?

• Patients on antepartum anticoagulation
  • Plus ANYBODY with:
    • A history of VTE
    • A low-risk thrombophilia

Adapted from: The American College of Obstetricians and Gynecologists Safe Mother Initiative: Venous Thromboembolism: Risk Assessment and Prophylaxis.
Documenting VTE Risk Assessment

- “VTE Prophylaxis” should be addressed in the H&P and daily progress note.
- If patient is noncompliant, document noncompliance and counseling regarding potential risks of VTE.

Questions?