Obstetric Venous Thromboembolism Prevention for Obese Women

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Disclosures

- I have no conflicts of interest to disclose.
• Venous Thromboembolism Bundle ACOG II/Safe Motherhood Initiative
• Venous Thromboembolism Bundle from the National Partnership for Maternal Safety
• The Society for Obstetric Anesthesia and Perinatology (SOAP)
Outline

• Epidemiology

• What major guidelines recommend in terms of prophylaxis

• Issues related to dosing

• Upcoming recommendations from the American Society of Regional Anesthesia and Pain Medicine (ASRA)
Epidemiology

• Obesity is a well documented risk factor for VTE

• In older medical and surgical populations it may be a relatively modest risk factor

• However, for younger patients obesity may account for more risk

Stein et al Am J Med 2005
Epidemiology

• One study of obesity and VTE:
  – All patients with obesity: OR of 2.5 for DVT, 2.2 for PE
  – Obese patients <40 years old: OR of 5.2 for DVT, 5.2 for PE

• Nurses Health Study
  – 6-fold increased risk for VTE for patients with BMI >35

• Interaction of obesity with other risk factors
  – Factor V Leiden, prothrombin mutation
Epidemiology

• The United Kingdom’s “Saving Mothers Lives” triennial report 2006-2008
  ▪ 9/16 VTE deaths occurred in obese women
  ▪ 14/31 VTE deaths from the prior triennial period occurred in obese women
  ▪ Literature review found increased risk of VTE with obesity ranging from OR 1.7 to 5.3

Greentop 37A RCOG
Cantwell 2008, Saving Mothers Lives CEMACH
Mechanisms

- Mechanisms for increased VTE risk in obese patients:
  - Enhanced platelet activity
  - Procoagulant state
  - Impaired fibrinolysis
  - Activation of endothelial cells
Prophylaxis

• Recommendations from major societies
  – Mechanical prophylaxis
  – Pharmacologic prophylaxis
  – Different clinical scenarios
    ▪ Cesarean delivery care
    ▪ Antepartum hospitalizations
    ▪ Vaginal delivery postpartum care
Prophylaxis

• Post-cesarean
  – Early ambulation
  – Avoidance of dehydration
Prophylaxis

• Universal cesarean perioperative mechanical prophylaxis
  
  – Supported by the American Congress of Obstetricians and Gynecologists (ACOG)

  – American College of Chest Physicians (ACCP) recommendations can be read to also support routine post-cesarean mechanical thromboprophylaxis
Prophylaxis

- Pharmacologic prophylaxis after cesarean delivery for obese patients
  - Supported by the Royal College of Obstetricians and Gynecologists
  - Supported by the National Partnership for Maternal Safety
  - ACCP and ACOG support post-cesarean pharmacologic prophylaxis for high-risk patients
    - Prior VTE events and thrombophilias
    - ACCP BMI $\geq 30$ is a minor risk factor

ACOG Practive Bulletin 123
RCOG 37a
Bates et al. Chest 2012
Prophylaxis

• Pharmacologic prophylaxis during antepartum admissions for obese patients
  – Supported by the Royal College of Obstetricians and Gynecologists
  – Supported by the National Partnership for Maternal Safety for hospitalizations >72 hours
• Pharmacologic prophylaxis after vaginal delivery for obese patients
  – Supported by the Royal College of Obstetricians and Gynecologists for BMI >40
Dosage

“Fixed doses of US FDA-approved anticoagulant regimens, including unfractionated heparins, low-molecular-weight heparins and factor Xa inhibitors, may not provide optimal VTE prophylaxis in [obese] patients.”

“Although the data are still limited, a rapidly growing body of literature and cumulative evidence suggests that anticoagulant dose adjustments in morbidly obese patients may optimize pharmacodynamic activity and reduce VTE risk.”

Dosage

• Studies in obese non-pregnant patients
  − Low-molecular weight heparin (LMWH)
    ▪ Significant correlation between elevated BMI and low anti-factor Xa levels
  − Unfractionated heparin (UFH)
    ▪ Limited data
    ▪ SC absorption can be affected by amount of adipose tissue

Dosage

• Systematic review: hospitalized obese patients
  – 10,313 patients
  – Research evidence does not allow a definitive conclusion about optimal dosing

• Systematic review: bariatric surgery
  – Data on dosing is poor
  – 5000U UFH TID or 30-40mg enoxaparin BID are reasonable strategies for prophylaxis

Agarwal et al. Surgery for Obes 2010
Dosage

• Non-obstetric society recommendations:
  – American College of Chest Physicians (ACCP)
    ▪ Obese patients may require increased doses of LMWH/UFH (dose not specified)
  – American Society for Metabolic and Bariatric Surgery (ASMBS)
    ▪ “No class I evidence to provide guidance regarding the type, dose, or duration of VTE prophylaxis”
Dosage

• Pregnancy pharmacodynamics
  – Increased renal clearance
  – Decreased anti-Xa activity in pregnant compared to non-pregnant patients

Casele et al. AJOG 1999
Dosage

• Royal College of Obstetricians and Gynaecologists
  – “There are no data to guide appropriate doses of LMWH for obese pregnant or puerperal women.”

RCOG Greentop 37a
Dosage

• RCOG prophylactic dosing enoxaparin:
  – 50-90kg 40mg daily
  – 91-130kg 60mg daily
  – 131-170kg 80mg daily
  – >170 0.6mg/kg/day

• Doses for women >90kg may be in divided doses
Dosage

• American College of Chest Physicians
  – Specific dosage recommendations not made for obese pregnant patients in 2012 guidelines

• ACOG Thromboembolism in Pregnancy Practice Bulletin
  – Recommendations for trimester-based dosing of prophylactic UFH
  – ACOG notes that “at extremes of body weight, modification of dose may be required.”

Bates et al 2012 Chest
Duhl et al 2007 AJOG
Dosage

• Appropriate dosage of UFH for obese obstetric patients?
  – 5000U SC BID?
  – 5000U SC TID?
• Appropriate dosage of enoxaparin for obese obstetric patients?
  – 40mg SC daily?
  – 30mg SC BID?
  – 40mg SC BID?
  – Weight based dosing?
Dosage

• Ultimately we don’t have data on optimal prophylactic dosing for obese patients

• Observational data evaluating risk for obese patients for VTE in the setting of lower dose prophylactic regimens is needed
  – Are obese patients having events while on lower doses of pharmacologic prophylaxis?
The American Society of Regional Anesthesia and Pain Medicine (ASRA) is preparing new guidelines on neuraxial anesthesia and anticoagulation.

Preliminary recommendations are only available on an “App” that can be purchased.

These guidelines may be more conservative than the most recent recommendations.
ASRA Recommendations

• Recommendations include:
  – Waiting 4-6 hours after low dose prophylactic UFH (5000 units BID) to place neuraxial anesthesia
  – Longer time intervals for larger doses of LMWH/UFH
  – Concurrent use of LMWH and NSAIDs is contraindicated after regional anesthesia
ASRA Recommendations

• ASRA recommendations may be an important consideration in:
  – Choosing agent: LMWH vs UFH
  – Choosing dosage
  – Availability of regional anesthesia
  – Minimizing narcotics postoperatively with regards to NSAID use

• Higher doses of pharmacologic prophylaxis may be associated with important trade offs in regards to anesthesia
Summary

• Whether obese post-cesarean patients should routinely receive pharmacologic prophylaxis is an important clinical question

• Optimal dosing of UFH and LMWH for obese obstetrical patients is unclear

• ASRA recommendations may factor into prophylaxis strategies
Questions?

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