DVT Prophylaxis In Pregnancy: What Should We Do?

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University of Utah School of Medicine
DVT prophylaxis

• **Cesarean section**
  – Most controversial
  – Limited data
  – Practice varies widely
Objectives

• Review rationale for DVT prophylaxis
• Discuss risk factors for DVT
• Present current controversies
• Make recommendations for prophylaxis
Maternal Deaths in the U.S. Are on the Rise

Maternal mortality ratio (number of maternal deaths per 100,000 live births)

- **United States**
- **Developed Regions**

![Graph showing maternal mortality ratio trends](image)

<table>
<thead>
<tr>
<th>Maternal Mortality Ratio</th>
<th>1990</th>
<th>2013</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>World</td>
<td>380</td>
<td>210</td>
<td>-45%</td>
</tr>
<tr>
<td>Developed Regions</td>
<td>26</td>
<td>16</td>
<td>-38%</td>
</tr>
<tr>
<td>Developing Regions</td>
<td>430</td>
<td>230</td>
<td>-47%</td>
</tr>
<tr>
<td>United States</td>
<td>12</td>
<td>28</td>
<td>+136%</td>
</tr>
</tbody>
</table>

Source: World Health Organization
Pregnancy-related deaths per 100,000 live births

Source: Institute for Health Metrics and Evaluation
Credit: Sarah Frostenson, Vox
The New York Times
Maternal Mortality Rate in U.S. Rises, Defying Global Trend, Study Finds
Sabrina Tavernise September 21, 2016
If Americans Love Moms, Why Do We Let Them Die?
Nicholas Kristof July 29, 2017

Fox News Health
US maternal mortality rate is twice that of Canada, says UN
November 12, 2015

WSJ
More Pregnant Women Are Dying in Rural America: Why?
Amber Krosel October 2, 2017

CNN
Giving Birth in America is More Dangerous Than You Think
Kelly Wallace April 2017

NPR Special series: Lost mothers
U.S. Has The Worst Rate Of Maternal Deaths In The Developed World
Nina Martin May 12, 2017
US Pregnancy Related Mortality

• CDC data:
  – 700-900 maternal deaths/year

• Estimates by WHO, UNICEF, UNFPA, The World Bank, United Nations Population Division:
  – 1,200 maternal deaths/year
  – 60,000 “near fatal” events/year

• Reported that 50% deaths are preventable
Pregnancy Related Mortality: 1987-2010

Creanga, Obstet Gynecol 2017
DVT Prophylaxis

• 2008: DVT quality measures
  – Joint Commission on Patient Safety
  – National Quality Forum

• 2017: DVT measures available to meet hospital accreditation requirements
Thromboembolism in pregnancy

- 4-5 x fold increased risk vs non-pregnant
- Approximately 1/1000 pregnant women
- 10% of maternal deaths in the United States
- C/S: 2-5x the risk vs. NSVD
Normal physiology

- Anti-coagulant factors decrease:
  - Protein S
  - Anti-thrombin
- Pro-coagulant factors increase:
  - factors II, VII, VIII, X, XII, XIII
  - fibrinogen
- Pro-hemostatic factor von Willebrand factor increases
- Fibrinolytic inhibitor activity increases:
  - PAI-1 and PAI-2
Risk Factors for DVT

• Pregnancy
• Surgery

- Obesity
- Medical co-morbidities
- Thrombophilias
- Prior thrombosis
- Smoking
- Hemorrhage
- Infection
- AMA
DVT Prophylaxis for C/S

Pneumatic Compression

vs

Pharmacologic treatment
Mechanical Prophylaxis

• Decision Analysis 2006:
  • Mechanical compression was a safe and cost effective strategy

• ACOG Practice Bulletin #12, 2011:
  • based on extrapolation from perioperative data, placement of pneumatic compression devices before cesarean delivery is recommended for all women not already receiving thromboprophylaxis.

Casale, Obstet Gynecol 2006
• Heparin prophylaxis reduced the risk of DVT; pneumatic compression had the lowest number of adverse events.

• Limitations: “Some data were obtained from studies that included older, non-pregnant patients who underwent gynecologic, general surgery, or orthopedic procedures.”
Preventing deep vein clots in pregnancy and after the birth
Cochrane Review February 2014

16 trials, 2592 women:

“We found no evidence to suggest that using heparin in pregnancy or after a caesarean birth reduces the risk of maternal death, DVT or PE.”
Preventing deep vein clots in pregnancy and after the birth
Cochrane Review February 2014

“There is insufficient evidence on which to base recommendations for thromboprophylaxis during pregnancy and the early postnatal period, with the small number of differences detected in this review being largely derived from trials that were not of high methodological quality.”
Pharmacologic

Royal College of Obstetricians & Gynaecologists

• Pioneered efforts to decrease maternal mortality
• 1995: Developed guidelines for DVT prophylaxis using heparin.
• Most comprehensive inclusion criteria
• Maternal deaths from PE
  – Pre-guideline: 1.56/100,000 live births (33 deaths)
  – Post guideline: 0.7/100,000 live births (16 deaths)
• Adherence
  – Pre: 5.7% received ppx
  – Post: 96.1% received ppx
Reduction in Fatal Pulmonary Embolism and Venous Thrombosis by Perioperative Administration of Subcutaneous Heparin

Reduction in Fatal Pulmonary Embolism and Venous Thrombosis by Perioperative Administration of Subcutaneous Heparin

Table 4. Pulmonary Embolism and Deaths Reported in All Randomized Controlled Trials of Prophylactic Subcutaneous Heparin in General, Orthopedic, and Urologic Surgery.

<table>
<thead>
<tr>
<th></th>
<th>Nonfatal Pulmonary Embolism</th>
<th>Fatal Pulmonary Embolism</th>
<th>Fatal Hemorrhage</th>
<th>Other or Unknown Causes of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HEPARIN</td>
<td>CONTROL</td>
<td>HEPARIN</td>
<td>CONTROL</td>
</tr>
<tr>
<td>International Multicentre Trial</td>
<td>14/2230</td>
<td>19/2250</td>
<td>6/2230</td>
<td>19/2250</td>
</tr>
<tr>
<td>Other 1:1 trials*</td>
<td>76/4546</td>
<td>117/4588</td>
<td>13/4136</td>
<td>36/4176</td>
</tr>
<tr>
<td>2:1 or 3:1 trials*</td>
<td>15/1103</td>
<td>11/401</td>
<td>0/941</td>
<td>0/351</td>
</tr>
<tr>
<td>Totals: all trials</td>
<td>105/7879</td>
<td>147/7239</td>
<td>19/7307</td>
<td>55/6777</td>
</tr>
<tr>
<td>No. of randomized patients for whom data were not available</td>
<td>224</td>
<td>245</td>
<td>796</td>
<td>707</td>
</tr>
<tr>
<td>Statistical calculations: heparin group†</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>O – E no. of events</td>
<td>–28.1</td>
<td>–18.5</td>
<td></td>
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<tr>
<td>Variance of O – E</td>
<td>55.2</td>
<td>18.2</td>
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<tr>
<td>Z (P value)</td>
<td>3.8 (&lt;0.0005)</td>
<td>4.3 (&lt;0.0001)</td>
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<tr>
<td>Typical % reduction in odds (±SD)</td>
<td>40±11</td>
<td></td>
<td>64±15</td>
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</tbody>
</table>

Collins, NEJM 1988
Heparin Induced Thrombocytopenia

• Rare if treated < 4 days
• Meta-analysis
  – 7287 patients
• Risk of HIT
  – unfractionated heparin 2.6%
  – low molecular weight heparin: 0.2%

Martel, Blood 2005
Current Available Guidelines

- American College of Chest Physicians (ACCP)
- American College of Obstetricians and Gynecologists (ACOG)
- Royal College of Obstetricians and Gynecologists (RCOG)
- Society of Obstetricians and Gynecologists of Canada (SOGC)
- Collège National des Gynécologues et Obstétriciens Français (CNGOF)
Variation in Guidelines

<table>
<thead>
<tr>
<th>ACOG</th>
<th>high-risk thrombophilia, prior VTE, or low-risk thrombophilia with family history of events.</th>
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<tr>
<td>ACCP</td>
<td>BMI $&gt;30$ kg/m$^2$, multiple pregnancy emergency caesarean, smoking. fetal growth restriction</td>
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<tr>
<td>RCOG</td>
<td>Prolonged admission, major medical co-morbidities (heart/ lung disease, SLE, cancer, inflammatory conditions, nephrotic syndrome, sickle cell disease, intravenous drug user Age $&gt;35$, Parity $\geq 3$, surgical procedure Gross varicose veins</td>
</tr>
</tbody>
</table>

Palmerola, BJOG 2015
athy, sickle cell, current IVDU)
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University of Utah Guidelines

- **Major (require 1 major risk factor)**
  - History of VTE
  - High-risk thrombophilia
    - APS (with prior thrombosis)
    - AT III deficiency
    - Homozygous factor V Leiden
    - Homozygous G20210A prothrombin gene mutation
    - Compound heterozygous for factor V Leiden and prothrombin gene mutation
  - Medical comorbidities (i.e. heart disease, SLE, IBD, sickle cell disease, etc)
  - Nephrotic range proteinuria (> 6g, either intrinsic renal disease or preeclampsia-related)
  - Cesarean hysterectomy
University of Utah Guidelines

• **Minor (require ≥ 2 minor risk factors)**
  - BMI >30
  - Multiple pregnancy
  - PPH >1L
  - Smoking >10 cig/d
  - Preeclampsia
  - Emergency cesarean or cesarean in labor
  - Infection: sepsis or triple I around time of delivery
  - Preterm delivery <37 weeks
  - Low-risk thrombophilia
    • Heterozygous factor V Leiden mutation
    • Heterozygous G20210A prothrombin gene mutation
    • Protein C or S deficiency
Timing of thrombotic events after delivery

Kamel, NEJM 2014
Prophylaxis Regimen

• Duration
  – In patient (or 2 weeks for c-hyst)
  – Start 6 hours post-op

• Regimen
  – First Line: enoxaparin (LOVENOX) injection
    • BMI <40: 40mg, Subcutaneous, every 24 hours
    • BMI >40: 30mg, Subcutaneous, every 12 hours
  – Second Line: heparin injection
    • BMI <40: 5,000 units, Subcutaneous, Every 8 hours
    • BMI >40: 7,500 Units, Subcutaneous, Every 8 hours
Summary

• Evaluate every obstetric patient for thromboembolic risk
• All patients undergoing c/s should have SCDs
• Patients with 1 major or 2 minor risk factors should receive pharmacologic DVT prophylaxis