Learning Objectives

Preventing VTE in Gynecologic Surgery

- After this lecture the gynecologist will
- Explain the importance of venous thromboembolism in gynecologic surgery
- Identify the level of risk in preoperative patients
- Explain the pros and cons of various prophylactic methods
- Based on best evidence, use the appropriate method(s) of VTE prophylaxis in their practice

Scope of the Problem

- 2.5 million cases DVT/yr
- 600,000 episodes of pulmonary embolism (PE)
- PE causes 50,000 deaths/yr
- Over 11,000 postsurgical PE deaths/yr
- Approximately 40% of deaths following Gyn Surgery are due to PE

Fatal Pulmonary Emboli

Two thirds of deaths from pulmonary embolism occur within 30 minutes of the first symptoms
Prevention of Postoperative VTE Issues:

- Degree of risk for individual patient
- Outcomes Research: What are our best options?
- Intensity of prophylaxis
- Management Recommendations/Consensus Statements
- Future directions

Pathogenesis of Deep-Vein Thrombosis

Virchow’s Triad

- Venous stasis
- Hypercoagulability
- Endothelial damage

Variables Associated with DVT in Gynecologic Surgery

- Past history of DVT
- Cancer
- Age >40 >60
- Prior radiation therapy
- Ankle edema
- Varicose veins
- Radical vulvectomy or exenteration
- Prolonged OR time (> 4 hrs)


Additional DVT Risk Factors

- Pregnancy
- Thrombophilias
- Oral Contraceptives
- Obesity
- Air Travel

Thromboembolism Prophylaxis

- Low-dose heparin
- Low molecular weight heparin
- “Anti-embolism” stockings
- Pneumatic leg compression
- Warfarin
- IVC interruption

LOW-DOSE HEPARIN

Multicenter Trial - Lancet 1975
5,000 Units Subcutaneously On Call to OR and Every 8 Hours

<table>
<thead>
<tr>
<th></th>
<th>Controls (2076)</th>
<th>Heparin (2045)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatal PE</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>Death with</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Associated PE</td>
<td>6</td>
<td>3</td>
</tr>
</tbody>
</table>
LOW-DOSE HEPARIN
In Benign Gynecologic Surgery

Controlled Studies in Gynecology
- Low Dose Heparin 5000 U q 12 hours

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ballard (benign) 1973</td>
<td>29%</td>
<td>3.6%</td>
</tr>
<tr>
<td>Adolf (benign) 1978</td>
<td>29%</td>
<td>7%</td>
</tr>
<tr>
<td>Taberner (benign) 1978</td>
<td>23%</td>
<td>6%</td>
</tr>
</tbody>
</table>

Does Low Dose Heparin Work for Every Patient?

How about gynecologic cancer patients?

LOW-DOSE HEPARIN
In Gynecologic Oncology Surgery

5000 U every 12 hours for 7 days

<table>
<thead>
<tr>
<th></th>
<th>DVT (%) FUT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n=97)</td>
<td>12 (12.4)</td>
</tr>
<tr>
<td>Low-Dose Heparin (n=88)</td>
<td>13 (14.8)</td>
</tr>
</tbody>
</table>


What about a more “intense” Low Dose Heparin Regimen for Cancer Patients?

LOW-DOSE HEPARIN (Intense Regimens)
Gynecologic Oncology Surgery

Prospective Study Gynecology Oncology

<table>
<thead>
<tr>
<th></th>
<th>% DVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (103)</td>
<td>18</td>
</tr>
<tr>
<td>8 hour regimen (104)</td>
<td>9.6</td>
</tr>
<tr>
<td>&quot;Load&quot; regimen (97)</td>
<td>6</td>
</tr>
</tbody>
</table>

(p = .02)


LOW MOLECULAR WEIGHT HEPARINS (LMWH)

- Enoxaparin (Lovenox), Dalteparin (Fragmin), Fondaparinux
- Effective in DVT prophylaxis
  - Equivalent to low dose heparin
  - Similar frequency of complications
- Convenience of once a day dosing
  - Dose varies between different LMWH’s
- ? Cost vs. Convenience
**LMWH versus LDUH in Gynecologic Surgery** (83% of patients had gynecologic cancer)

<table>
<thead>
<tr>
<th></th>
<th>LMWH (Dalteparin)</th>
<th>Low Dose Heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>5000 u daily</td>
<td>5000 u q 8 hours</td>
</tr>
<tr>
<td>Patients</td>
<td>n=280</td>
<td>n=282</td>
</tr>
<tr>
<td>DVT in 6 wks</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary Emboli</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Transfusions</td>
<td>39</td>
<td>57</td>
</tr>
</tbody>
</table>

(p=NS)


**Mechanical Methods for DVT Prevention**

- Graded Compression Stockings
  - TED Hose
- Pneumatic Leg Compression
  - Sequential Compression
  - Single Chamber
  - Foot Compression

**“Anti-Embolism” Stockings (TED Hose)**

Modest benefit found in prospective studies IF stockings are fitted properly

**Intermittent Pneumatic Compression in Gynecologic Surgery**

- Perioperative Leg Compression is effective in moderate risk patients
- Perioperative Leg Compression is not effective in high risk patients
- Prolonged Leg Compression is effective in high risk patients

<table>
<thead>
<tr>
<th></th>
<th>Pneumatic Compression</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(5 days)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12.7%</td>
<td>34.6%</td>
</tr>
</tbody>
</table>

(p<.005)

Clarke-Pearson, Gynecol Oncol, 18:226, 1984

**WHICH IS BETTER?**

Low-dose heparin or Intermittent Pneumatic Compression?
Low Dose Heparin vs IPC in Prevention of Postop VTE

<table>
<thead>
<tr>
<th></th>
<th>Low-dose Heparin</th>
<th>Intermittent Pneumatic Compression</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N=107)</td>
<td></td>
<td>(N=101)</td>
</tr>
<tr>
<td>Total DVT</td>
<td>7 (6.5%)</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Pulmonary Emboli</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(p = .54)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


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LMWH (dalteparin) vs. External Pneumatic Compression

*Prospective, Randomized Trial*

<table>
<thead>
<tr>
<th></th>
<th>External Pneumatic Compression</th>
<th>Low Molecular Weight Heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT</td>
<td>1/106</td>
<td>2/105</td>
</tr>
<tr>
<td>Pulmonary Emboli</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>


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External Pneumatic Compression vs. LMWH Complications

<table>
<thead>
<tr>
<th></th>
<th>External Pneumatic Compression</th>
<th>Low Molecular Weight Heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated Blood Loss</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>350 ml</td>
<td>350 ml</td>
</tr>
<tr>
<td>Maximum</td>
<td>3100 ml</td>
<td>3700 ml</td>
</tr>
<tr>
<td>&gt; 2000 ml</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Transfusions (# pts)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intra op</td>
<td>22</td>
<td>20</td>
</tr>
<tr>
<td>Post op</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

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Which is best??

Meta-analysis

<table>
<thead>
<tr>
<th>Regimen</th>
<th># Trials</th>
<th># Patients</th>
<th># DVT</th>
<th>Incidence (%)</th>
<th>Reduction of Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>54</td>
<td>4710</td>
<td>1034</td>
<td>25</td>
<td>-</td>
</tr>
<tr>
<td>Low Dose Heparin</td>
<td>50</td>
<td>7716</td>
<td>948</td>
<td>8</td>
<td>68</td>
</tr>
<tr>
<td>LMWH</td>
<td>13</td>
<td>4320</td>
<td>228</td>
<td>5</td>
<td>80</td>
</tr>
<tr>
<td>EPC</td>
<td>14</td>
<td>780</td>
<td>61</td>
<td>8</td>
<td>67</td>
</tr>
<tr>
<td>GC stockings</td>
<td>9</td>
<td>472</td>
<td>51</td>
<td>11</td>
<td>56</td>
</tr>
</tbody>
</table>

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If Low Molecular Weight Heparins, Low Dose Heparin and External Pneumatic Compression have similar clinical benefit, how do we select the appropriate prophylactic method?

- **Cost**
  - Maxwell, Obstet Gynecol 2000; 95: 206
- **Compliance**
- **Patient preference**
  - Maxwell, Obstet Gynecol 2002; 100: 451
The Future: What's on the Horizon?

Combination Prophylaxis in the Extremely High-Risk

Who is at highest risk to fail External Pneumatic Compression?

1862 patients treated with EPC

Overall incidence of VTE = 1.3%

Patients with 2 or 3 of the following risk factors had a 16 fold increased risk of developing VTE

- Age > 60 years
- Cancer
- Prior VTE

Clarke-Pearson Obstet Gynecol 2003; 101: 157

The Future: What's on the Horizon?

Longer Duration of Prophylaxis

Randomized trial of patients undergoing "curative surgery" for abdominal and pelvic cancer

<table>
<thead>
<tr>
<th>Treatment</th>
<th>%DVT (Venogram) @ 1 month</th>
<th>%DVT (Venogram) @ 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enoxaparin 40mg/d x 7 d</td>
<td>12%</td>
<td>13.8%</td>
</tr>
<tr>
<td>Enoxaparin 40mg/d x 28 d</td>
<td>4.8%</td>
<td>5.5%</td>
</tr>
</tbody>
</table>

Bergevist NEJM 346: 975, 2002

VTE Prophylaxis in Laparoscopic Surgery

- What is the risk?
- What prophylaxis is appropriate?

Does Laparoscopic Surgery Increase Risk of VTE?

In Theory: Maybe (Maybe not)

- Venous Stasis
  - Intraperitoneal pressure 12-15 mm Hg
  - Increased femoral vein diameter
  - Increased femoral venous pressure
  - Decreased femoral venous peak outflow
  - More rapid return to normal levels of activity
  - Steep Trendelenberg position

- Endothelial injury
  - Venous distention (femoral vein) increases endothelial tears

Does Laparoscopic Surgery Increase Risk of VTE?

In Theory: Maybe (Maybe not)

- Increased release of clotting factors
  - Decrease in plasminogen activator
  - Increase plasminogen activator inhibitor, D-dimer, Fibrinogen degradation products, soluble fibrin, prothrombin fragments 1, 2.
  - Prolonged operating time vs. more rapid recovery

Laparoscopy Increases Operating Time

(Except in the hands of a gifted surgeon)

(GOG Lap-2) TAH vs LAH, BSO, Pelvic, Paraaortic lymphadenectomy

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Median OR Time (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparoscopy</td>
<td>3.3 hr (0.7-10.1 hr)</td>
</tr>
<tr>
<td>Laparotomy</td>
<td>2.2 hr (0.7-6.3 hr)</td>
</tr>
</tbody>
</table>
What is the Incidence of VTE Following Laparoscopic Surgery?

- Only randomized prospective trial is GOG Lap-2.
- Endpoint: Clinical diagnosis of VTE
- Potential for bias
  - not blinded
  - no objective/prospective endpoint
- No record of which prophylactic method used (if any); not randomized

GOG Lap-2 Trial

Laparoscopic vs. Laparotomy Hysterectomy, BSO, pelvic and paraaortic lymphadenectomy (endometrial cancer)

<table>
<thead>
<tr>
<th>Complication</th>
<th>Laparoscopy (n=1682)</th>
<th>Laparotomy (n=900)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT</td>
<td>0.8%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Pulmonary Embolism</td>
<td>1.2%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Death in 6 weeks</td>
<td>0.5%</td>
<td>0.7%</td>
</tr>
</tbody>
</table>

9 Deaths from PE

Should We Provide VTE Prophylaxis for Laparoscopic Surgery?

Summary:

What should we do to prevent VTE following gynecologic surgery?

VTE Prophylaxis Guidelines

ACCP Consensus 2004

- Low Risk: early mobilization
  - Brief procedure < 30 min. Benign Disease (1C)

- Laparoscopy with additional risk factors
  - LDUH, LMWH, IPC, GCS (1C)

- Prophylaxis for ALL major gyn surgery
  - Benign disease without additional risk factors
    - LDUH 5000u q 12 h
    - LMWH < 3400 u q day
    - IPC (1B)


VTE Prophylaxis Guidelines

ACCP Consensus 2004

- Major Gyn Surgery Patients with additional risk factors
  - LDUH 5000 u q 12h
  - LMWH > 3400 u q daily
  - IPC (1A)

- Combination (1C)
  - Prophylaxis should continue until hospital discharge

- Continued prophylaxis: Cancer and > 60 years or prior VTE
  - Continue for 2-4 weeks (2C)

Prevention of Postoperative VTE Issues

- Degree of risk for individual patient
- Outcomes Research: What are our best options?
- Intensity of prophylaxis:
- Management Recommendations/Consensus Statements
- Future directions
  - Combination prophylaxis
  - Prolonged prophylaxis
  - Laparoscopic surgery

Thank You