Deep Venous Thrombosis

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Virchow’s Triad

Rudolph Virchow
1821–1902

Stasis

- Bed Rest
- Travel
- Immobilization (cast)
- Obesity
- Limb Paralysis

Trousseau’s Syndrome

Armand Trousseau 1801–1867
Trousseau’s Syndrome

Genetic Link Between Cancer and Thrombosis
Cara Brousseau and Peter M. Camidge

ABSTRACT

From the beginning of their lives, cancer cells exist as a procoagulant activity, which can extend systemically and become clinically evident in Trousseau’s syndrome. The well-known association between tumor and thrombosis is becoming clear. The genetic link between cancer and thrombosis is well described. The role of tumor suppressor genes such as p53 and PTGS is directly important in the development of cancer control. The development of tumor suppression results in a selective advantage for cancer cells; as a result, the development of novel tumors and the evolution of cancer cells occurs. The evolution of cancer cells includes the development of receptor-mediated intracellular signals promoting invasive growth. Targeting the tumor suppressor activity can increase not only a dangerous tumor advance, but also the cancer mechanisms of cancer invasion and progression.

J Clin Oncol 27:687-693, 2009 by American Society of Clinical Oncology

Hypercoagulability

- Malignancy
- Acquired or Inherited Disorders
  - Protein S and Protein C Deficiencies
  - Antithrombin III Deficiency
  - Factor V Leiden
  - Antiphospholipid Antibodies

- Trauma
- Pregnancy
- Estrogen
- Inflammatory States
  - Inflammatory bowel disease
  - SIRS
- Thrombophilia
- Cigarettes

Endothelial Injury

- Trauma
- Surgery
- Vascular catheters
Pathophysiology of DVT

- Clots form in valve cusps of calf deep veins
- 15-20% of these clots will propagate proximally
- Approximately 50% of deep vein clots will lyse and recanalize within 3 months


Diagnosis of DVT

- Clinical Assessment
- Laboratory Studies
- Imaging Techniques

Homans’ Sign

Homans’ Sign: Present in less than 1/3 of the cases
Predictive Value of the Wells’ Criteria

• High Probability Group 76%
• Moderate Probability Group 21%
• Low Probability Group 10%


DVT Laboratory Studies

• D-dimer
• Hypercoaguability Screen
  – Protein S
  – Protein C
  – Antithrombin III
  – Factor V Leiden
  – Phospholipid Antibodies
  – Platelet count

D-dimer

Ways to Measure D-dimers

• Rapid ELISA test (most commonly used)
• Latex Agglutination
• Whole-Blood Agglutination (SimpliRED)
Basic Principle

• A negative D-dimer excludes DVT in patients with low risk factors
• A positive D-dimer is an indication for an imaging study
• MOST surgical patients will have positive D-dimers related to surgery

Imaging Studies

• Venography
• Compression Ultrasound
  – Noninvasive
  – Easily repeatable
  – accurate

Ultrasonography

• Should be the initial imaging study
• Full compressibility of the popliteal and femoral veins excludes proximal DVT
• Sensitivity/Specificity for proximal DVT = 97/98%

Ultrasonography

• DVT Sensitivity/Specificity for calf veins = 70/60%
• Proximal extension rare (2%) after 1 week
• Non-extending calf vein DVT rarely responsible for PE
• Therefore, if 2 ultrasounds 1 week apart are negative, no therapy required


**Initial Rx of DVT**

- Once daily LMWH (150-200 U/KG as effective as twice daily LMWH (100 U/kg)
- LMWH as effective as continuous iv unfractionated heparin with PTT 1.5 X control

**Unfractionated Heparin**

- Narrow Rxic window
- Bleeding rate 7-30%
- Risk of HIT
- IV bolus 80 U/kg followed by 18 U/kg/hr iv drip
- PTT to be kept at 1.5 X control

**LMWH**

- Once daily dose
- No need to monitor PTT
- Low risk of HIT
- Much lower cost

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**Fibrinolysis**

- Fibrinolytic Drugs
  - Streptokinase
  - Urokinase
  - Rt-PA
- Urokinase and Plasminogen Activators equal in terms of efficacy and complications

**Systemic Fibrinolysis vs Heparin**

<table>
<thead>
<tr>
<th>Events</th>
<th>RR</th>
<th>95% CI</th>
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</thead>
<tbody>
<tr>
<td>Complete Clot Lysis</td>
<td>2.71</td>
<td>1.84-3.99</td>
</tr>
<tr>
<td>Post Thrombotic Syndrome</td>
<td>0.66</td>
<td>0.47-0.94</td>
</tr>
<tr>
<td>Total Bleeding</td>
<td>1.73</td>
<td>1.04-2.99</td>
</tr>
<tr>
<td>Leg ulceration</td>
<td>0.53</td>
<td>0.12-2.43</td>
</tr>
<tr>
<td>Normal venous function</td>
<td>0.43</td>
<td>0.06-3.17</td>
</tr>
<tr>
<td>Death</td>
<td>1.33</td>
<td>0.34-5.24</td>
</tr>
<tr>
<td>Recurrent DVT</td>
<td>1.41</td>
<td>0.37-5.40</td>
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</tbody>
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Ileo-Femoral Thrombosis

Images courtesy of Dr. Mark Wilson, Chief of Radiology, San Francisco General Hospital


Percutaneous Mechanical Thrombectomy

- Review of 281 patients in 16 retrospective case series
- No randomized trials available
- 82-100% success rate for partial and complete clot lysis
- No deaths, <1% PE
- 7.5% of patients bled requiring transfusion


Conclusion

- Mechanical thrombectomy appears safe and feasible
- No evidence to support routine use

Vena Cava Filters


INDICATIONS FOR IVC FILTER PLACEMENT

1. PATIENTS WITH EVIDENCE OF PE OR ILIOFEMORAL DVT WITH ONE OR MORE OF THE FOLLOWING:
   - CONTRAINDICATION TO ANTICOAGULATION
   - COMPLICATION OF ANTICOAGULATION
   - FAILURE OF ANTICOAGULATION (ACUTE PE OF ENLARGING DVT)

2. MASSIVE ACUTE PE IN A PATIENT WITH ON GOING DVT WHO IS THEREFORE AT RISK FOR ADDITIONAL PE

3. FREE-FLOATING ILIOFEMORAL OR IVC THROMBUS

4. DVT IN THE SETTING OF SEVERE CARDIOPULMONARY DISEASE

5. POOR COMPLIANCE WITH ANTICOAGULATION REGIMEN
RELATIVE INDICATIONS FOR IVC FILTER PLACEMENT

1. PROPHYLACTIC IVC FILTER PLACEMENT IN TRAUMA PATIENTS.

2. “HIGH-RISK” PATIENTS
   > LONG-TERM IMMobilization
   > PRE-OPERATIVELY PRIOR TO IMMobilIZATION
   > HYPERCOAGULABLE PATIENTS WITH OR WITHOUT DVT (e.g., MALIGNANCY).

PREPIC Study


Filter vs No Filter Results

Day 12

<table>
<thead>
<tr>
<th>Significant Outcome</th>
<th>Filter/No Filter OR 95% CI</th>
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<tbody>
<tr>
<td>PE</td>
<td>1.1/4.8%</td>
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2 Year Follow-up

<table>
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<tr>
<th>Significant Outcome</th>
<th>Filter/No Filter OR 95% CI</th>
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<tr>
<td>Recurrent DVT</td>
<td>20.8/11.6%</td>
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Filter vs No Filter Results
8 Year Follow-up

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Filter / No Filter</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sx tic PE</td>
<td>9 (6.2%) / 24 (15.1%)</td>
<td>0.008</td>
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<tr>
<td>DVT</td>
<td>57 (35.7%) / 41 (27.5%)</td>
<td>0.042</td>
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<tr>
<td>Post Thrombotic Syndrome</td>
<td>70% / 70%</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>103 (51%) / 98 (49%)</td>
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Conclusions

- PE prevention mainly required short term initially following acute proximal DVT
- We need a randomized trial with retrievable filters
- In DVT w/o PE, doubtful whether filters + anticoagulation are useful


THROMBOEMBOLISM
AFTER TRAUMA

AN ANALYSIS OF 1602 EPISODES FROM THE ACS NATIONAL TRAUMA DATA BANK
Annals of Surgery 2004;240:490-6

M. Margaret Knudson, Danagra G. Ikossi, Linda Khaw, Diane Morabito, Larisa S. Speetzen
The University of California, San Francisco

Spinal cord injuries

- Highest risk trauma patients
- DVT rates: 80%
- PE rates: 5%
- PE-most common cause of death
**PROPOSED ALGORITHM**

**Injured Patient**

High Risk Factor
- Age ≥ 40
- Pelvic fx
- Lower extremity fx
- Shock
- Spinal cord injury
- Head trauma (AIS ≥ 3)

VERY High Risk Factor
- Major operative procedure
- Venous injury
- Ventilator days > 3
- 2 or more high risk factors

Contraindication for heparin?
- No
- Yes

LMWH* and mechanical compression
- Mechanical compression
- LMWH*

*Prophylactic dose

**Contraindication for heparin?**
- No
- Yes

**Summary**

- LMWH Rx of choice for DVT
- Factor Xa Inhibitors likely to replace Coumadin for chronic anticoagulation in the near future
- Catheter directed thrombolysis likely to have increasing role in management of DVT
- Removable caval filters may expand indications and reduce complications of caval filters for prevention of PE.