Venous Thromboembolism (VTE) Prophylaxis

Rishi Garg, MD
Department of Medicine

Objectives
- Identify patients at risk for VTE
- Options for VTE prophylaxis
- Current Recommendations
  - (based on The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy - 9/2004)

VTE – WHY DO IT?
- Patients can be identified by risk factors
- Consequences can be severe and irreversible
- Effective methods of prophylaxis are safe in preventing VTE in hospitalized patients

Case
Mr. X is a 72 yo male with history of CHF, DM, tobacco use comes in for 3 days of SOB, productive cough, and fevers. He is diagnosed with CAP and admitted to the hospital.

Question:
- Does the patient need DVT prophylaxis? If so, what option would you choose?
  - A) Do nothing
  - B) aspirin
  - C) compression stockings
  - D) low molecular weight heparin
  - E) Have your medical student walk the patient every hour through the halls

Who Is At Risk?
Risk factors

- **Patient-related**
  - Increasing age
  - Prolonged immobility
  - Male sex
  - Obesity
  - Cigarette smoking
  - Prior VTE
  - Inherited thrombophilias
  - Risks in women – pregnancy, HRT, OCPs

- **Condition-related**
  - Triple lumen catheters
  - Malignancy
  - Paralysis of lower limbs
  - Medical illness
  - CHF
  - Nephrotic syndrome
  - Inflammatory Bowel Disease

**Risks in medical patients**

<table>
<thead>
<tr>
<th>Risk level</th>
<th>Rate of VTE</th>
<th>Rate of fatal PE</th>
<th>Patient group</th>
</tr>
</thead>
<tbody>
<tr>
<td>low</td>
<td>&lt; 10 %</td>
<td>0.01%</td>
<td>Minor trauma or illness</td>
</tr>
<tr>
<td>moderate</td>
<td>10-40%</td>
<td>0.1-1.0%</td>
<td>Major illness (heart, lung, CA, IBD)</td>
</tr>
<tr>
<td>high</td>
<td>40-80%</td>
<td>1-10%</td>
<td>Major illness + risk factor</td>
</tr>
</tbody>
</table>

**Risk in surgical patients**

<table>
<thead>
<tr>
<th>Risk</th>
<th>Rate of VTE</th>
<th>Rate of fatal PE</th>
<th>Patient group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>1%</td>
<td>0.01%</td>
<td>Age &lt; 40, anesthesia &lt;30m, minor elective orth/Thoracic surg</td>
</tr>
<tr>
<td>Moderate</td>
<td>2-10%</td>
<td>0.1-0.7%</td>
<td>Age &gt;40, anesthesia &gt;30m, one or more risk factor</td>
</tr>
<tr>
<td>High</td>
<td>10-20%</td>
<td>1-5%</td>
<td>Age &gt;40, ortho or cancer surg, factor deficiency</td>
</tr>
</tbody>
</table>

**What Are Our Options?**
Options for prophylaxis

- Graduated Compression Stockings
- Intermittent pneumatic compression
- Low dose unfractionated heparin
- Adjusted dose heparin
- Low molecular weight heparin
- Oral anticoagulation
- Aspirin
- Fondaparinux

Prophylaxis

- All have efficacy in reducing VTE alone or in combination therapy (although use of aspirin alone is not recommended)

Graduated Compression Stockings (GCS)

- Considered useful by decreasing venous diameter, thus presumably increasing velocity and decreasing pooling of blood
- Usually effective when used with other methods of prophylaxis
- Worry about poorly fitting stockings leading to proximal compression and subsequent distal ischemia

Intermittent pneumatic/sequential compression devices (SCDs)

- Designed to squeeze blood from the deep veins to displace blood proximally; on deflation, veins refill, thus ensuring periodic flow of blood
- 5 types: foot, foot & calf, calf, calf & thigh, whole limb
- Foot devices are thought to generally be less effective because the amount of venous blood ejected is less

SCDs (cont’d)

- Some devices employ “uniform” compression which could lead to distal veins compressing against an already compressed proximal vein
- This could lead to “venous trapping”
- But this has not been shown to be worse for VTE prophylaxis

Low dose Unfractionated heparin (UFH)

1. Typically given in doses of 5000u bid or tid
2. Has been drug of choice for VTE prophylaxis for medical and surgical patients
3. Increased risk of heparin-induced thrombocytopenia than low molecular weight heparin  NEJM 1995
**Adjusted dose heparin**
- Subcutaneous heparin given at doses to achieve aPTT in high normal range (1-1.5x normal)
- Not generally practiced secondary to high cost and time required to monitor lab values

**Low Molecular Weight Heparin (LMWH)**
- Options:
  - Dalteparin (Fragmin)
  - Enoxaparin (Lovenox)
  - Fondaparinux (Arixtra)
  - Studies have shown at least equal efficacy to UFH for VTE prophylaxis in medical inpatients (Haemostasis 1996, Thromb Haemost 1996)

**LMWH**
- Thought to be more beneficial than UFH in preventing VTE, particularly in post-op orthopedic (BMJ 1991) and trauma (NEJM 1996) patients
- Extended therapy, up to 4 weeks post-op has been proven beneficial in THA but not TKA patients J Bone Joint Surg Am 2001
- Some studies suggest decreased bleeding than UFH in abdominal surgery Lancet 1993

**Recent Studies**
- A recent study compared the safety of Enoxaparin vs UFH for the prevention of VTE in patients with heart failure or severe respiratory disease.
- Results showed a decreased incidence of VTE with Enoxaparin 40mg qd vs UFH 5000u tid (8.4% vs 10.4%) and fewer deaths and less bleeding. Am Heart J 2003.

**Oral anticoagulation**
- Most data comes from use in post-operative patients
- Typically started on the night of surgery
- Has been proven to be more efficacious in preventing VTE than placebo
- One study suggested similar efficacy in preventing VTE in TKA patients as LMWH but with less safety Arch Inten Med 2002

**Aspirin**
- One study suggested the use of aspirin to be equally safe as coumadin in post-op hip fracture patients in preventing VTE Arch Intern Med 1989
- Another study suggested low dose aspirin to be more efficacious compared to placebo is reducing VTE in medical and surgical patients Lancet 2000
Fondaparinux

- Most studies have been done in post-op orthopedic patients
- Has been shown to be better than Enoxaparin in reducing VTE in patients undergoing major knee surgery NEJM 2001 and surgery for hip fracture NEJM 2001

So What Should We Do With This Information?

Grades of Evidence

- Grade 1 - If experts are very certain that benefits do, or do not, outweigh risks, burdens, and costs, they will make a strong recommendation (in our formulation, Grade 1).
- Grade 2 - If they are less certain of the magnitude of the benefits and the risks, burdens, and costs, and thus their relative impact, they must make a weaker Grade 2 recommendation

Based on data from the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy (9/2004)

General Recommendations

- Mechanical methods of prophylaxis for patients at high risk of bleeding (Grade 1C+) or as adjunct to anticoagulant prophylaxis (Grade 2A)
- Recommend against the use of aspirin alone (Grade 1A)
- Recommend consideration of renal impairment when using drugs renally-cleared, particularly in elderly and high risk of bleeding pts (Grade 1C+)
- Special caution when using anticoagulation in patients with neuraxial anesthesia or analgesia (Grade 1C+)

RCTs

- Randomized clinical trials (RCTs) with consistent results provide unbiased, Grade A recommendations.
- RCTs with inconsistent results, or with major methodological weaknesses, warrant Grade B recommendations
- Grade C recommendations come from observational studies or from generalization from one group of patients included in randomized trials to a different, but somewhat similar, group of patients who did not participate in those trials.
- When experts find the generalization from RCTs to be secure, or the data from observational studies to be overwhelmingly compelling, they choose a Grade 6+.

General Surgery

- Low-risk
  - minor procedure, < 40 yo; no additional risk factors; recommend against specific anticoagulation other than early ambulation (Grade 1C+)
- Moderate risk
  - nonmajor procedure and b/w 40-60 yo or additional risk factors or major procedure, <40 yo with no additional risk factors, recommend use of UFH 5000u bid or LMWH 3400u qd (Grade 1A)
- High risk
  - nonmajor procedure and >60 yo or additional risk factors or major surgery, >40 yo or additional risk factors, recommend UFH 5000u tid or LMWH 3400u qd (Grade 1A)
High Risk Patients

- High risk patients with multiple risk factors, recommend UFH 5000u tid or LMWH 3400u qd + GCS and/or SCDs (Grade 1C+)
- Patients with high risk of bleeding, recommend use of GCS or IPC until bleeding risk decreases (Grade 1A)
- In select high-risk patients, including major cancer surgery, recommend post-discharge prophylaxis with LMWH (Grade 2A)

Orthopedic Surgery

- Elective hip arthroplasty
  - LMWH at high-risk dose 12h before surgery or 12-24h after surgery or 4-6h after surgery at half dose then increasing to normal dose the day after vs.
  - fondaparinux 2.5mg started 6-8h post-op vs
  - adjusted dose VKA pre-op or evening after surgery (target INR 2.5)
  - All have Grade 1A recommendation
  - Recommend against the use of aspirin, UFH, GCS, SCDs as the only method of prophylaxis (Grade 1A)

Elective Knee arthroplasty

- Elective Knee arthroplasty
  - similar recommendation for elective THA (high risk dose LMWH, fondaparinux or VKA) - Grade 1A
  - similar recommendation against use of aspirin and UFH alone (Grade 1A)

Knee arthroscopy

- Knee arthroscopy - Do not recommend use of thromboprophylaxis, other than early immobilization (Grade 2B)
- For those patients undergoing arthroscopy at higher than usual risk, based on pre-existing VTE risk factors, recommend use of LMWH (Grade 2B)

Hip Fracture Surgery

- Hip Fracture Surgery - fondaparinux (Grade 1A), LMWH (Grade 1C+), VKA - INR 2.5 (Grade 2B) or UFH (Grade 1B)
- Recommend against the use of aspirin alone (Grade 1A)
- If surgery will be delayed, LMWH or UFH should be initiated b/w the time of hospital admission and surgery (Grade 1C+)
- Mechanical prophylaxis if anticoagulation is contraindicated (Grade 1C+)

Neurosurgery

- For routine major neurosurgery, use thromboprophylaxis (Grade 1A)
- SCDs with or without GCS for intracranial surgery (Grade 1A)
- Combination of mechanical prophylaxis with pharmacologic prophylaxis for high-risk neurosurgery patients (Grade 2B)
### Medical patients

- In acutely ill medical patients who are admitted with CHF or respiratory disease, confined to bed and have one or more additional risk factor for VTE, recommend UFH or LMWH (Grade 1A)
- In patients with risk factors for VTE and in whom anticoagulation is contraindicated, use GCS or SCDs (Grade 1C+)

### Cancer patients

- Undergoing surgical procedures, should receive prophylaxis (Grade 1A)
- Hospitalized cancer patients who are bedridden with an acute illness should receive prophylaxis (Grade 1A)
- Recommend against the use of routine prophylaxis to prevent thrombosis in patients with long-term catheters (Grade 2B). Specifically, recommend against LMWH (Grade 2B) or warfarin (Grade 1B)

### Critical Care patients

- Most all patients should be assessed and should receive thromboprophylaxis (Grade 1A)
- Patients at high risk of bleeding, recommend mechanical prophylaxis with GCS and/or SCDs until bleeding risk decreases (Grade 1C+)
- Moderate risk patients for VTE (ill or post-op), recommend LMWH or UFH (Grade 1A)
- For patients at higher risk (post-op ortho or trauma) recommend LMWH (Grade 1A)

### Long Distance Travel

- Such as flights >6h, avoid constrictive clothing around the lower extremities or waist, avoid dehydration, and perform frequent calf stretching (Grade 1C)
- For long-distance travel with additional VTE risk factors, recommend above. If active prophylaxis considered, then use below the knee GCS with 15-30mm Hg at the ankle (Grade 2B) or single dose LMWH (Grade 2B)
- Recommend against the use of aspirin (Grade 1B)

### Case

- 33 yo male with history of gigantism comes in for routine arthroscopy of his right knee following an incident while rapping?

### Question

- What is the best option for VTE prophylaxis?
  - A) Aspirin
  - B) LMWH
  - C) LMWH and SCDs
  - D) Nothing
  - E) Ask your medical student to lift him out of bed every hour for 12 hours post-op
Last Case

- 72 yo male with hx of tobacco use suffers a broken hip during a boxing incident?

VCU

Question

- What is the best option for VTE prophylaxis?
  - A) Aspirin
  - B) Fondaparinux
  - C) Unfractionated Heparin
  - D) Ask your medical student to get him out of bed every hour to help him comb his hair