PREVENTION OF VENOUS THROMBOEMBOLISM
IN PATIENTS WITH PELVIC TRAUMA

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MRI Scan of leg confirming deep venous thrombosis
Venous thrombosis ..... 
a common, preventable cause of morbidity and 
mortality
EM study of fibrin clot; a meshwork of fibrin strands around platelets and red cells
Virchow’s Triad:

- Hypercoagulability
- Venous stasis
- Vascular injury

Pelvic trauma
### Rationale for Thromboprophylaxis in Hospitalised Patients
(ACCP Guidelines, CHEST 126 (3) Sept 2004)

| **High prevalence of VTE** | Most hospitalised patients have risk factors for VTE  
|                           | Hospital-acquired DVT and PE usually *clinically silent* |

**Adverse consequences of unprevented VTE** –
- symptomatic DVT & PE
- fatal PE
- costs of investigating symptomatic patients
- risks and costs of treating unprevented VTE, especially bleeding
- increased future risk of recurrent VTE
- chronic post-thrombotic syndrome

**Efficacy and effectiveness of thromboprophylaxis**-
Highly effective at preventing symptomatic DVT, prox DVT, symptomatic VTE and fatal PE
The prevention of DVT also prevents PE
Cost-effectiveness repeatedly demonstrated
Desirable risk/benefit ratio in terms of bleeding risks
## Absolute Risk of *DVT in Hospitalised Patients (not receiving thromboprophylaxis)*

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>DVT Prevalence, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical patients</td>
<td>10-20</td>
</tr>
<tr>
<td>General surgery</td>
<td>15-40</td>
</tr>
<tr>
<td>Major gynecologic surgery</td>
<td>15-40</td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>15-40</td>
</tr>
<tr>
<td>Stroke</td>
<td>20-50</td>
</tr>
<tr>
<td>Hip, knee arthroplasty</td>
<td>40-60</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>40-60</td>
</tr>
<tr>
<td>Major trauma</td>
<td>40-80</td>
</tr>
<tr>
<td>Spinal cord injury</td>
<td>60-80</td>
</tr>
</tbody>
</table>

* Objectively confirmed

ACCP Guidelines 2004: 340S
Historical Perspectives: VTE and Trauma

• 1934: McCartney describes an association between trauma and death from PE, particularly in patients with fracture of lower limb extremities. Prompted a number of autopsy based studies.

• 1967: Freeark and colleagues demonstrate venous thrombosis by venogram in 35% of patients with fractures of lower extremities.

• Thrombus formation often occurs within 24 hrs of injury; involves the injured and non-injured extremity.

• Majority of patients are asymptomatic.
Incidence of VTE following Trauma

- Critique of the literature: influence of various factors:
  - nature of the injury
  - method used to diagnose asymptomatic DVT and PE
  - type of prophylaxis used

- Few large scale studies excepting Sept 2004 registry

- Best estimate of incidence from Geerts, 1994:

  Single venogram during hospital course of 348 injured patients without prophylaxis; DVT in 58% with an incidence of proximal DVT of 18%; 2% incidence of PE with a 43% fatality rate
Risk Factors

Traditional risk factors in non-trauma patients:

- Age > 60 years
- Malignancy
- Congenital & Acquired hypercoagulable states
- Previous venous thromboembolism (VTE)
- Estrogen use

- In the general trauma population the above factors are of relative importance in view of the high baseline incidence of thrombosis
Risk Factors in Trauma Patients

- Advancing age
- Spinal cord injury / paralysis
- Fractures of the lower extremity and pelvis
- Duration of immobilisation
A prospective study of venous thromboembolism after major trauma.

Large venogram study conducted at Sunnybrook

Multivariate analysis identified 5 independent risk factors for DVT: age (OR = 1.05 per year), the need for blood transfusion (OR = 1.74), or a surgical procedure (OR = 2.3), fracture of the femur / tibia (OR=4.82), and spinal cord injury (OR = 8.59).

In this study, the INJURY SEVERITY SCORE did not correlate with thrombosis risk.

The severity of the injury is not as important as the specific injury in relation to predicting the risk of VTE risk.
• **AGE EFFECT**
  
  Sunnybrook study: 100 cases of pelvic fracture, evaluated with contrast venography
  
  • <25 yrs: incidence of DVT 35%
  • 26-44yrs: incidence was 44%
  • >45yrs: incidence was 83%

• **EFFECT OF TYPE OF ORTHOPEDIC SURGERY**
  
  • External fixation: DVT rate 46%
  • ORIF: DVT rate 56%
  • Conservative: bed rest/traction: DVT rate 66%
“Hospital Delays”

- Delays between time of fracture and admission to trauma centre, and delays between admission and surgery
- “Medical optimisation”
- OR time/availability
- There is an accumulation of evidence in the literature to support the heightened risk of VTE
- Rationale for pre-operative prophylaxis – but no trials as yet specifically address this issue
- Use of LDUH or LMWH are best options
- Selection of prophylactic agent may rest with many factors, including time of surgery and type of anaesthesia used
Preventing thrombosis

Arterial thromboembolism
Venous thromboembolism
Hemorrhage
Methods of Prophylaxis

Mechanical:
• Graduated compression stockings (GCS)
• Intermittent Pneumatic Devices (IPD)

Pharmacological:
• Heparin – unfractionated (LDUH);
  low molecular weight heparin (LMWH)
• Vitamin K Antagonists (VKA) – coumadin, warfarin
• (Pentasaccharide): Fondaparinux (hip fracture)

• Vena Caval Filters - controversial
**Intensities of Prophylaxis**

**Low risk:** pharmacological prophylaxis not warranted

**Moderate risk:** low dose unfractionated heparin

5000 iu bid/tid

**High risk:** low dose unfractionated heparin

low molecular weight heparin (od vs bid)

**Highest risk:** “the best prophylaxis”

consider extended prophylaxis

WARFARIN

LOW MOLECULAR WEIGHT HEPARIN
Pelvic Fracture & VTE prophylaxis

THE SCOPE OF THE PROBLEM.....

• Incidence of DVT in patients with pelvic fractures is approximately 35-60% (dependent on the extent to which patients are evaluated)

• Proximal DVT occurs in 25-35% of pelvic trauma patients; almost 50% will be in the pelvic veins (increased risk of PE)

• Incidence of symptomatic PE is 2-10% - a larger proportion of patients will have silent PE.

• Fatal PE occurs in 0.5-2% of patients with pelvic trauma


Pathophysiology

• All 3 components of Virchow’s triad are found in pelvic trauma patient group [endothelial damage, venous stasis, hypercoagulability]

• Direct damage to pelvic veins and other veins by trauma releases tissue factor, exposes endothelial BM and initiates thrombin generation locally

• Release of vasoactive humoral factors causes venous overdistension, causing endothelial injury and thrombosis distant to the site of the direct injury (high incidence of bilateral lower extremity thrombi in patients with unilateral injuries)

• Pelvic fracture and associated lower limb injury: prolonged periods of *immobilisation* and *venous stasis* (increased chance of thrombus present at time of injury to propagate, and/or enhances post-op DVT development)

• Pelvic hematoma compress adjacent veins and further contribute to pelvic and lower extremity *venous stasis*
• Critical trauma reduces levels of natural anticoagulants (AT) and alters the balance of fibrinolysis; effects of fluid resuscitation and blood transfusion may also exacerbate the imbalance of pro-coagulant/anticoagulants (HYPERCOAGULABILITY) (Geerts et al. N Engl J Med 331: 1601 1994)

• Fluid resuscitation and massive transfusion alter coagulation cascade and aggravate coagulopathy

• *Thrombus formation may be in progress at first presentation*
The “thrombin explosion”
Location of Pelvic Thrombosis

Montgomery et al: “The Use of Magnetic Resonance Imaging to Evaluate the Deep Venous System of the Pelvis in Patients with Acetabular Fractures”

Study of acetabular fractures; evaluation with contrast venography & MRI:
14/45  (31%)  showed isolated proximal thrombosis
3/45   (7%)   showed isolated distal thrombosis
1/45   (2%)   showed proximal and distal thrombosis

Continuation of this study using MR venography (IVC to popliteal fossa)

- 77 patients:
- Thrombosis present in 26/77 (34%)
- Around 45% of thrombi are located in the pelvic veins (ext iliac, 4; internal iliac, 10 and common iliac, 3)
The data above clearly point to a predisposition to the development of proximal thrombi in patients with pelvic injury.

...... high rate of clinical and subclinical embolisation

...... increased risk for intra-operative and postoperative embolisation
Is it essential to determine pre-operatively whether patients requiring delayed fixation of pelvic fractures have evidence of proximal thigh or pelvic vein thrombosis?
Prophylaxis

- Ideal agent: safe, effective, easy to administer, easy to reverse, and cost-effective.
- Each modality has its limitations
- **No perfect prophylactic protocol to prevent VTE in the trauma population**

- Forms of prophylaxis used:
  - LDUH
  - LMWH
  - Mechanical devices – GCS, IPC
  - (IVC filters) - controversial
Ineffectiveness of low dose heparin:

- In a randomised trial of prophylaxis in 154 patients with trauma, serial Duplex USS used every 5-7 days to screen for DVT (Knudson et al. Prevention of venous thromboembolism in trauma patients. J Trauma 37: 480, 1994)
- LDUH provided no protection in these patients compared to controls
- In patients with hip fractures, low dose heparin was no better than no prophylaxis (Montrey, J Trauma 25: 534, 1985)
- In patients with spinal cord injury, low dose heparin is less effective than LMWH (Green, Ann Int Med 113: 571 – 574)
- Low dose heparin………too little, too late
Prophylaxis (contd)

Graduated compression stockings (GCS) & Intermittent Pneumatic Compression Devices (IPC)

- GCS: Effective in low risk patients, but unlikely to be protective as an isolated measure in major trauma
- Literature on intermittent pneumatic compression: unsupportive in terms of use as an isolated prophylactic measure
- Stickney and Helfet (J Orthop Trauma 5:2:227 1991) suggest a combined approach with sc heparin and IPC may be more effective at preventing DVT (1.8%) than the use of IPC alone (16.1%)
- IPC devices may be of limited value in the trauma setting;
- Shackford et al. report that IPC could not be applied in 35% of limbs in high risk trauma patients because of plaster casts, external fixators, traction devices or complex wounds (J Int Care Med. 3: 87-98, 1988)
- They were unable to find a difference in the incidence of VTE in the IPC treated arm vs no prophylaxis at all.
Low Molecular Weight Heparin

• “Most promising option for trauma patients”
• Almost complete bioavailability after subcutaneous injection
• Improved efficacy-safety ratio compared with Unfractionated Heparin (especially in terms of avoiding HIT)
• Convenience of fixed dose administration without need for laboratory monitoring
• Demonstrated to be most effective form of thromboprophylaxis in patients after hip surgery and spinal cord injury

Prophylactic use of IVC Filters (IVCF)

- Prophylactic IVC filter insertion has been recommended for use in trauma patients felt to be at very high risk for VTE
- No randomised clinical trials have yet studied the prophylactic use of IVC filters
- No evidence to suggest their use is beneficial in addition to other prophylactic methods
- Recent meta-analysis of prospective studies found no difference in the rates of PE among patients with and without prophylactic IVCFs (McMurty et al. J Am Coll Surg, 1999 189 314-320)
- Risks: delays in the use of effective prophylaxis, increased risk of thrombosis at the insertion site
- Expensive (estd $900,000,000 if placement of IVCFs in 1% of all disabling trauma cases) (Greenfield, J Vasc Surg, 1995)
- 4 reports in the literature to confirm that PE can still occur
“The use of LMWH, started once primary hemostasis is achieved is the most efficacious and simplest option for the majority of moderate to high-risk trauma patients….” (ACCP recommendation)

Contra-indications to early initiation of LMWH:

- Presence of intra-cranial bleeding
- Ongoing and uncontrolled bleeding
- An uncorrected major coagulopathy
- Incomplete SCI associated with either suspected or proven perispinal hematoma
Tricky Situations

• Head injury without frank hemorrhage
• Lacerations or contusions of internal organs (lungs, liver, spleen, kidneys)
• Presence of retroperitoneal hematoma associated with pelvic fracture
• Complete Spinal Cord Injury

• The above are not contra-indications to LMWH prophylaxis provided that there is no evidence of ongoing bleeding
  - Majority of trauma patients can be commenced on prophylaxis with LMWH within 36 hrs of injury
ACCP RECOMMENDATIONS

• All “trauma” patients with at least one risk factor for VTE receive thromboprophylaxis. (Grade 1A)
• In the absence of a major contra-indication, recommend that clinicians use LMWH prophylaxis “starting as safe as it is to do so”. (Grade 1A)
• Mechanical prophylaxis with IPC, or GCS be used if LMWH prophylaxis is delayed or currently contra-indicated due to active bleeding or a high risk of hemorrhage (Grade 1B)
ACCP RECOMMENDATIONS

• Recommend DUS screening in patients at high risk for VTE (SCI, pelvic fracture, major head injury or indwelling femoral line) and who receive suboptimal prophylaxis or no prophylaxis. (Grade 1C)

• Recommend against the use of IVCFs as primary prophylaxis in trauma patients (Grade 1C)

• Continuation of thromboprophylaxis until hospital discharge, including rehabilitation (Grade 1C+). Suggest continuing prophylaxis after hospital discharge, with LMWH or a VKA (target INR 2.5; INR range 2-3) if impaired mobility. (Grade 2C)

- Meta-analysis of randomised trials which compared extended-duration prophylaxis using heparin or warfarin with placebo or untreated control in patients undergoing elective total hip or knee replacement
Extended prophylaxis: The “State of the Art”

• 9 studies with 3999 patients
  – 30 to 42 days of prophylaxis:
    • reduced frequency of **symptomatic** venous thromboembolism
    • major bleeding not increased
      – minor bleeding increased 3.7% vs 2.5%

• Conclusion
  • extended-duration prophylaxis significantly reduces the frequency of symptomatic VTE
    – about 20 symptomatic events per 1000 patients treated
What to use for post-discharge prophylaxis?

- Warfarin
  - administered to achieve an INR of 2.0 to 3.0
    - Lower intensity warfarin:
      - Associated with bleeding
      - Not predictably effective
      - Without evidence for its use

- LMWH
  - Administered in “usual” prophylactic doses
Extended prophylaxis: State of the art

What should we use: Warfarin or LMWH ???

Warfarin: Advantage
  » Cheap
  » Familiar
  » Widely available

LMWH: Advantage
  » Easy to administer
  » No need for monitoring
  » Patients seem to prefer it
“Prolonged thromboprophylaxis with oral anticoagulants after total hip arthroplasty: a prospective controlled randomized study”


- assessed benefit of oral anticoagulation after hospital discharge
- consecutive patients after hip arthroplasty
- randomized to stop warfarin prophylaxis at discharge or continue for 4 weeks
- rate of symptomatic and asymptomatic venous thromboembolic events (compression ultrasonography of the proximal-vein system) compared
Results: Prandoni et al.

• study prematurely terminated after 360 patients
  – clinically relevant superiority of extended thromboprophylaxis

• 10 total VTE
  – 9 (5.1%) in 176 control patients
  – 1 (0.5%) in 184 warfarin patients
  – relative risk of VTE was 9.4 (95% CI, 1.2-73.5)
• There is good evidence that prolonged prophylaxis reduces the risk of asymptomatic VTE

• There is now good quality evidence that prolonged prophylaxis reduces symptomatic VTE

• **Extended duration prophylaxis should be considered in all patients after hospital discharge following major elective orthopedic surgery.**

• **What recommendations for patients with trauma/pelvic trauma?**
SUMMARY

• Asymptomatic VTE is very common in trauma patients

• In pelvic trauma patients there is an incidence of DVT 35-60%, proximal DVT of 25-35%, symptomatic PE in 2-10% and fatal PE of 0.5-2%

• The cornerstone of effective management is early prophylaxis using LMWH

• Issues that add to the management complexity include: associated head and internal injuries, delays in surgical repair to injuries, delays in transfer to tertiary referral centers and prolonged periods of post-operative rehabilitation.
• **Lower extremity fractures, spinal cord injury, increased age and non-operative management** all increase the risk of VTE after trauma

• Screening of the leg and pelvic veins alone is inadequate to control the development of clinically important thromboembolic complications

• Duplex USS and MR imaging hold promise as diagnostic tools in selected patients (if early prophylaxis is not possible)

• The use of vena caval filters is **controversial**; seem to prevent symptomatic and fatal PE but indication for prophylaxis is unclear
ALGORITHM FOR THE MANAGEMENT OF THROMBOPROPHYLAXIS IN PELVIC TRAUMA

ARM 1: Early Surgery

Pre-operative Prophylaxis – LMWH +/- GCS

Early Surgery

Re-start Prophylaxis Post-operatively

Consider Screening POD #5

If no proximal DVT, convert to warfarin, INR 2.0 – 3.0
ARM 2: Unable to use early pre-operative prophylaxis
(intracranial bleeding; uncontrolled bleeding)

Trauma patient with pelvic or acetabular injury

Serial screening
CUS vs MRV

prophylactic IVC filter

Begin prophylaxis as soon as possible

Convert to coumadin INR 2-3
ARM 3
DELAYED SURGERY

Pre-operative Prophylaxis – LMWH +/- GCS

Pre-operative DVT Screening
MRV vs bilateral CUS
Within 24 hrs of surgery

No proximal DVT  
Delayed surgery
Restart prophylaxis post-operatively
Convert to warfarin, INR 2-3

proximal DVT
pre-operative IVC filter
Hamilton General Hospital Thrombosis Service

- A new service:
  
  Dr Turpie               Dr Bradley
  Dr Schulman             Dr Eikelboom
  Dr Anderson

  Specialist Nurses:     D Goodale       J Gibson       M Robinson

- Assessment of thromboprophylaxis in trauma patients
- Patients whilst IP and as OP
- Preliminary assessment
- Follow up visits as required
- Liaison at time of discharge