Current Management of Deep Vein Thrombosis

Pankaj HANDA
Senior Consultant
Internal Medicine/Vascular Medicine & Hypertension
Tan Tock Seng Hospital(TTSH) SINGAPORE
1. Case Scenario

22 Y/C/F; unprovoked proximal LL DVT. No malignancy

ACCP recommends “treatment of first choice”:

1. Initiate with LMWH x 5/7 + Warfarin
   Warfarin x 3/12

2. Initiate with LMWH + Xa inhibitor
   Xa inhibitor x 3/12

3. Xa inhibitor alone x 3/12
   without pretreatment with heparin

4. Initiate with LMWH X 5/7
   Direct Thrombin Inhibitor x 3/12
55 Y/I/M, presents with Ac. Rt. Illeo- Femoral DVT

ACCP recommends:

1. Thrombolysis (CDT) as an approved indication
2. Anticoagulation with UFH as an initial option
3. Anticoagulation with NOACs as first choice
4. Anticoagulation with LMWH as first choice
3. Case Scenario

- 46 Y/M/M, on Apixaban for the past 2 months for popliteal vein thrombosis develops new DVT in the contralateral leg. ACCP recommends:

1. Double the dose of Apixaban

2. Switch to Warfarin

3. Place an IVC filter

4. Temporarily switch to LMWH for at least 1/12
4. Case Scenario

76 Y/C/M - found to have incidental Rt. Post. Tibial DVT. No anticoagulation is required, because-

1. Only symptomatic distal DVT should be treated

2. Distal DVT needs only surveillance

3. Distal DVT is less likely to embolize or cause PTS

4. Would qualify for treatment if he has malignancy
MY TALK TODAY

- Introduction
- General Concepts
- Management Strategies
- Back to case scenarios
- Take Home Message
Introduction

- Deep Vein Thrombosis (DVT) contributes to significant morbidity & mortality both in the community & hospital

- It is common and generally easy to treat but, if left untreated, may lead to fatal Pulmonary Embolism (PE)

- Mainstay of therapy for DVT remains anticoagulation
General Concepts

- Proximal vs. Distal DVT
- Provoked vs. Unprovoked DVT
- Symptomatic vs. Asymptomatic DVT
Proximal vs. Distal DVT

- Proximal Lower Limb DVT – Clinically Important
  90% of PE arise from Proximal DVT

  50% untreated cases $\rightarrow$ PE

  30% untreated PE $\rightarrow$ DEATH

  (Death usually results from Recurrent PE)
### Provoked vs. Unprovoked

**RISK OF DVT RECURRENCE - AFTER STOPPING ANTICOAGULATION**

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>Recurrence in 1st year</th>
<th>Recurrence per year in next 4 years</th>
<th>Total RISK in 5 YEARS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical</td>
<td>1%</td>
<td>0.5%</td>
<td>3%</td>
</tr>
<tr>
<td>Non surgical</td>
<td>5%</td>
<td>2.5%</td>
<td>15%</td>
</tr>
<tr>
<td>Unprovoked-1st</td>
<td>10%</td>
<td>5%</td>
<td>30%</td>
</tr>
<tr>
<td>Unprovoked-2nd</td>
<td>15%</td>
<td>7.5%</td>
<td>45%</td>
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</table>
Proximal DVT:
Anticoagulant Therapy is ALWAYS indicated regardless of the presence of symptoms and provided there are no contraindication to anticoagulation.

Distal DVT
- Symptomatic: Treated
- Asymptomatic:
  - Surveillance: weekly CUS x 2 weeks
  - Treatment: if additional risk factors (malignancy, previous DVT, unprovoked, extensive DVT)
Treatment - Objectives

(1) Acute:
- Prevent further clot extension
- Prevention of acute pulmonary embolism (PE)
- Reducing the risk of recurrent thrombosis

(2) Late:
- Post Thrombotic Syndrome (PTS)
- Chronic Venous Insufficiency
- Chronic Thromboembolic Pulmonary Hypertension (CTPEH)
Prevention of Further Thrombosis

2010 metaanalysis: 13 prospective cohort studies 56 randomized clinical trials

**First 3/12 of Anticoagulant Therapy**

(A) **Reduces**
- Recurrent VTE : 3.4 % (CI 2.9-4.0)
- Recurrent fatal VTE : 0.4 % (CI 0.3-0.6)

(B) **Causes**
- Major bleeding : 1.6 % (1.3-2)
- Major fatal bleeding : 0.2% (95% CI 0.1-0.3)
Assessment of Bleeding Risk

- Patients should be assessed before and during anticoagulant therapy for bleeding risk.

- **VTE Prevention** vs. **Risk of Bleeding**

- Special care
  - on NOACs
  - >75 years
  (renal failure, high fall risk, weight loss).

- Bleeding Risk Scores – HAS BLED; HEMMORHAGE
## Assessment of Bleeding Risk

<table>
<thead>
<tr>
<th>Elderly Age Group (&gt;75)</th>
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<tbody>
<tr>
<td>Previous Bleeding/Thrombocytopenia/Anaemia</td>
</tr>
<tr>
<td>Cancer/ Metastatic Cancer</td>
</tr>
<tr>
<td>Renal Failure/Liver Failure</td>
</tr>
<tr>
<td>Poor Anticoagulant Control</td>
</tr>
<tr>
<td>Previous Stroke</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>Recent Surgery</td>
</tr>
<tr>
<td>Frequent Falls</td>
</tr>
<tr>
<td>Alcohol Abuse</td>
</tr>
<tr>
<td>Comorbidity</td>
</tr>
<tr>
<td>Reduced Functional Capacity</td>
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</tbody>
</table>
## Estimated Risk of Bleeding

<table>
<thead>
<tr>
<th>Bleeding risk</th>
<th>First 3 months</th>
<th>Annual rate after first 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk (no risk factors present)</td>
<td>1.6 percent</td>
<td>0.8 percent</td>
</tr>
<tr>
<td>Intermediate risk (one risk factor present)</td>
<td>3.2 percent</td>
<td>1.3 percent</td>
</tr>
<tr>
<td>High risk (two or more risk factors present)</td>
<td>12.8 percent</td>
<td>≥6.5 percent</td>
</tr>
</tbody>
</table>
Management Strategies

- Anticoagulation
- Thrombolytic therapy & Thrombectomy
- Inferior Vena Cava Filter
- Additional Therapies
ANTICOAGULATION

...the CORNERSTONE of Management

- **Initial**: the first few days
  - up to 10 days

- **Long-term**: a finite time
  - 10 days to 3 to 6/12

- **Extended**: indefinite period
  - no scheduled STOP date
1. Heparin (UFH/\textbf{LMWH}) / Fondaparinux PLUS Vit. K Antagonist (Warfarin)

2. Heparin (UFH/LMWH) followed by Direct Thrombin Inhibitors (DTIs)

3. Factor Xa inhibitors without pre-treatment with heparin

- Xa inhibitors and DTIs: novel oral anticoagulants (NOACs) direct oral anticoagulants (DOACs) target-specific oral anticoagulants (TSOACs) \textit{Non Vitamin K Antagonists (NOACs)}

ACCNP 2016:
- NOACs as FIRST CHOICE
- UFH is Preferred
  - Renal Failure (CC <30)
  - Hemodynamic Instability
  - Extensive Clot burden - PCD
  - Obesity/Anasarca
  - Anticipated need for discontinuation or reversal
1. **Heparin (UFH/LMWH) PLUS Vitamin K Antagonist**

- **LMWH** is usual heparin of choice
  - Enoxaparin 1 mg/kg BID / 1.5 mg/kg OD
  - Tinzaparin 175 units/kg OD

- **VKA (WARFARIN)**: 5mg (or 3mg) x 2 days
  - Check INR on D3
  - Optimise dose as per INR (Target: 2-3)

- Stop LMWH once INR is stable in therapeutic range and continue with VKA
2. Heparin (UFH/LMWH) FOLLOWED by Direct Thrombin Inhibitors

- DUAL THERAPY
- Heparin (usually LMWH) x 5-10 days

FOLLOWED BY

- DTI: - Dabigatran 150 mg x BID
  - Edoxaban 60 mg x OD
3. Factor Xa Inhibitors

- **MONOTHERAPY**
- No initial treatment with Heparin is required

  - Rivaroxaban 15 mg x bid x 3/52
    - 20 mg x od x 9/52
  
  - Apixaban 10 mg x bid x 1/52
    - 5 mg x bid x 11/52
Constraints with NOACs

- Renal Excretion: Not safe with Cr Cl <30ml/mt
- Pregnancy - Only heparin (LMWH) preferred
- Malignancy - Only heparin (LMWH) preferred
- Extensive DVT (phlegmasia cerulea dolens)
- Pulmonary Embolism (hemodynamically unstable)
Management of Recurrent Thrombosis (ACCP Recommendations)

- Recurrent thrombosis while on OACs
  - re-evaluation if is truly a recurrence
  - confirm compliance
  - consideration of underlying malignancy
  - Temporary Switch to LMWH for at least 1/12

- Recurrent thrombosis while on LMWH
  - Increase LMWH dose by 1/3\textsuperscript{rd} to 1/4\textsuperscript{th}
# Duration of Treatment

All cases of DVT: minimum of 3 months

<table>
<thead>
<tr>
<th>DVT</th>
<th>Duration</th>
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<tbody>
<tr>
<td>PROVOKED - First</td>
<td>3 months</td>
</tr>
<tr>
<td>UNPROVOKED</td>
<td>Consider Extended treatment (Risk/Benefit ratio)</td>
</tr>
<tr>
<td>First - Proximal</td>
<td></td>
</tr>
<tr>
<td>UNPROVOKED</td>
<td>3 months</td>
</tr>
<tr>
<td>First - Distal</td>
<td></td>
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<tr>
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Criteria for Extended Therapy

1. Clinical Decision

2. Persistent Elevation of d-dimer
   - 1/12 after completion of treatment

3. Additional factors
   : major- cancer, APS, thrombophilias
   : minor- male, PTS, poor cardiac reserve
     - residual vein thrombosis
Agent Selection

- VKAs - Warfarin (Full dose)
- NOACs
- LMWH

Alternative therapy
- ASPIRIN 100 mg od

- WARFASA
- ASPIRE

30 % Reduction of Recurrence of DVT
Phlegmasia Cerulea Dolens

- Varies from phlegmasia alba dolens to venous gangrene
  - massive venous thrombosis (Ileo-femoral)
  - sudden pain, swelling, cyanosis, venous gangrene,
  - impairment of arterial supply leading to shock
  - delay in treatment: death or loss of limb

- **Thrombolysis and Thrombectomy** - recommended Rx
- IV UFH is often initial treatment

- **Extensive thrombosis but no PCD** – Anticoagulation alone is the option of treatment.
- Once ischaemic has resolved - Anticoagulation x 3/12
Additional therapies

- Ambulation
- Graduated Compression Therapy
- Thrombolytic Therapy
- Inferior Venal Cava Filter placement
Ambulation

- EARLY ambulation is SAFE
- Should be encouraged ASAP

- RISK of PE during aggressive exercise, physical therapy, or rehabilitation is unknown.
- Gradual increase in exercise training as tolerated

- Pain or Leg Oedema may limit ambulation
- Compression stockings may be useful for symptomatic relief and the promotion of ambulation.
Compression Stockings: Prevention of Post Thrombotic Syndrome (PTS)

- **Conflicting evidence on Efficacy**
  - Prandoni P (Ann IM 2004)  Ankle pressure of 30 to 40 mmHg within 2/52 x 2 years x ↓ PTS 50 %
  - Kahn SR (Lancet 2014)  No Difference in PTS with use of GCS

- Disadvantages: uncomfortable, costly, inconvenient
- Contraindications: skin ulceration, severe PAD, allergy

- Recommendation:
  - Generally harmless.
  - Potential benefits of GCS vs. inconveniences
  - Symptom reduction rather than prevention of PTS.
Anticoagulation: 1st line of treatment of DVT management

**Indications**: phlegmasia cerulea dolens (PCD)
- symptoms for <14 days (fresh clot)
- good functional status, and low bleeding risk

**Advantages**
- more rapid and complete lysis,
- reduced rates of PTS
- preserved venous valve function

*No change in recurrent VTE and mortality*
Thrombolysis & Throbectomy

**Thrombolysis**
- Systemic vs. **Catheter-directed thrombolysis (CDT)**
  - CDT: more rapid lysis & lower dose
  - more complete removal of clot from smaller venules that cannot be removed surgically – important for PCD

**Throbectomy**
- Mechanical (catheter extraction/fragmentation) vs. Surgical
- Alternative or Adjunctive therapy thrombolysis.
- **Combined catheter-directed procedures** (thrombolysis + fragmentation) may further minimize the risk of bleeding
- NOT for Routine “Stand alone/ Adjunctive therapy”

Indications:
1. Acute VTE with absolute contraindication to anticoagulation (recent surgery, haemorrhagic stroke, active bleeding)

2. Adjunctive therapy
   - recurrent VTE despite adequate anticoagulation
   - additional PE would be poorly tolerated poor cardiopulm reserve

- Usually inserted at Infra-Renal IVC
- Retrievable filters are preferred

- Reconsideration of anticoagulant therapy- once the bleeding risk ↓
DVT with Contraindications for Anticoagulation
- recurrent PE are low (2 to 4%)
- no decrease in PE-related death

IVC as Adjunct Therapy
- PREPIC1 and PREPIC2
  - Decrease in rate of PE in short term
  - No change in long term survival / rate of recurrent PE
  - Higher rate of DVT/PTS

Other Complications:
local haemorrhage, fracture, embolization, dislodgement and mortality (0.12 to 0.3 %).
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DVT contributes to significant morbidity & mortality both in the community & hospital

Proximal DVT is clinically more important and should always be treated

Unprovoked DVT carries high risk of recurrence after stopping treatment
ACCP recommends

1. NOACs: 1st line treatment for acute DVT, if no cancer

2. Thrombolysis and Throbectomy: ONLY for Severe Illieo-femoral thrombosis with venous gangrene

3. IVC filter: NOT recommended as routine stand alone or adjunctive therapy

4. Post DVT early Ambulation is SAFE.