Prevention and management of deep venous thrombosis (DVT)

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Pathogenesis of thrombosis – Virchow’s triad

1. Changes in vessel wall
2. Low blood flow
3. Activation of coagulation factors and platelets

(Stasis of blood in valve pockets)
Venous thromboembolism (VTE) =

deevee vein thrombosis (DVT)

and / or

pulmonary embolism (PE)
Incidence of DVT and PE by age
Iliofemoral venous thrombosis

Clot in IVC and (R) iliac vein

Fatal pulmonary embolism

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Cause of deaths in Australia

- CAD
- Stroke
- Lung cancer
- COPD
- VTE
- Bowel cancer
- Prostate cancer
- Breast cancer
- RTAs
- AIDS
Venous thromboembolism (VTE)

- Fatal Pulmonary Embolism
- Symptomatic VTE
- Asymptomatic VTE
Deep vein thrombosis

→ *Post thrombotic syndrome / chronic venous insufficiency*

- oedema
- skin and subcutaneous changes
- chronic venous ulcer
Long term sequelae of VTE

*Chronic venous ulceration*

- 300 per 100,000
- 25% due to DVT
- estimated annual costs
  - 1-2% of health care budget

*Chronic pulmonary hypertension*
# The frequency of DVT in surgery, trauma and medical patients in the absence of prophylaxis

<table>
<thead>
<tr>
<th>Patient groups</th>
<th>Number of studies</th>
<th>Patients (n)</th>
<th>DVT incidence (weighted mean)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>8</td>
<td>395</td>
<td>224 (56%)</td>
<td>51% to 61%</td>
</tr>
<tr>
<td>Total hip arthroplasty (THA)</td>
<td>17</td>
<td>851</td>
<td>435 (51%)</td>
<td>48% to 54%</td>
</tr>
<tr>
<td>Multiple Trauma</td>
<td>4</td>
<td>536</td>
<td>270 (50%)</td>
<td>46% to 55%</td>
</tr>
<tr>
<td>Total knee arthroplasty (TKA)</td>
<td>7</td>
<td>541</td>
<td>252 (47%)</td>
<td>42% to 51%</td>
</tr>
<tr>
<td>Hip fracture surgery</td>
<td>15</td>
<td>805</td>
<td>353 (44%)</td>
<td>40% to 47%</td>
</tr>
<tr>
<td>Spinal cord injury</td>
<td>9</td>
<td>458</td>
<td>160 (35%)</td>
<td>31% to 39%</td>
</tr>
<tr>
<td>Prostatectomy - retropubic</td>
<td>8</td>
<td>335</td>
<td>106 (32%)</td>
<td>27% to 37%</td>
</tr>
<tr>
<td>General Surgery</td>
<td>54</td>
<td>4310</td>
<td>1084 (25%)</td>
<td>24% to 26%</td>
</tr>
<tr>
<td>ICU patients</td>
<td>3</td>
<td>178</td>
<td>45 (25%)</td>
<td>19% to 32%</td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>5</td>
<td>280</td>
<td>61 (22%)</td>
<td>17% to 27%</td>
</tr>
<tr>
<td>Gynaecological - malignancy</td>
<td>4</td>
<td>297</td>
<td>64 (22%)</td>
<td>17% to 26%</td>
</tr>
</tbody>
</table>

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The majority of VTE events (>50%) in surgical patients are diagnosed post-discharge

Particular attention to high-risk orthopaedic surgery and cancer patients
Incidence of VTE events after THA and TKA

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White et al Arch Intern Med 1998
Major Abdominal Surgery

Incidence of VTE within 90 days of abdominal surgery

<table>
<thead>
<tr>
<th>Procedure</th>
<th>In-patients</th>
<th>Post-discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exploratory laparotomy</td>
<td>1.2%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Open cholecystectomy</td>
<td>1.2%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Small bowel resection</td>
<td>1.2%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Partial gastrectomy</td>
<td>1.0%</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

n=2600  n=2250  n=2302  n=3986

Adapted from White RH, Zhou H, Thromb Haemost. 2003;90:446-455.

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Safety in Hospitals

- Infection control / minimise hospital acquired infections
  - urinary infection
  - pneumonia
  - septicaemia
  - wound infection
  - infected prostheses

- *Methicillin Resistant Staphylococcus Aureas (MRSA)*
MRSA deaths *versus* VTE deaths

VTE causes approx. 60,000 deaths per year in the UK -
37 times greater than annual deaths from MRSA*


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Hospital preventive strategies
"Making Health Care safer: a critical analysis"

Systematic review ranking 79 safety interventions

- based on the strength of overwhelming evidence that thromboprophylaxis reduces adverse patient outcomes and decreases overall costs:

  the highest ranked safety practice was the "appropriate use of prophylaxis to prevent VTE".

Mechanical prophylaxis

Graduated compression stockings (GCS)

Intermittent Pneumatic Compression (IPC)

Foot Impulse Technology (FIT), Venous Foot Pump (VFP)
Pharmacological agents for VTE prophylaxis

- low dose unfractionated heparin (LDUH)
- low molecular weight heparin (LMWH)
  - dalteparin (*Fragmin*), enoxaparin (*Clexane*)
- pentasaccharide fondaparinux
- new generation anti-thrombotic agents
  - anti-*Factor Xa*, anti-thrombin

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[Images of drugs and structures]
Effectiveness of prophylaxis in General Surgery

DVT incidence (%)
Effectiveness of prophylaxis in Orthopaedic Surgery

- TKA
- THA
- HFS

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pharmacological prophylaxis

versus

bleeding risk
Effectiveness of prophylaxis versus bleeding risk in THA
Effectiveness of rivaroxaban in THA (5 weeks)

- Total VTE: RRR 70%
- Major VTE: RRR 88%
- Symptomatic VTE
- Major bleeding

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Effectiveness of extended prophylaxis following abdominal / pelvic surgery for cancer
Cochrane Review: total VTE reduced by 8.1%\(^1\)

ARR = Absolute Risk Reduction

1. Adapted from Rasmussen MS et al. Prolonged thromboprophylaxis with Low Molecular Weight heparin for abdominal or pelvic surgery. *Cochrane Database of Systematic Reviews* 2009, Issue 1.
IVC filters for VTE prophylaxis

- unable to use mechanical / pharmacological prophylaxis
  - major trauma / pelvic fracture with continued bleeding
  - major surgery required in near future

< 50% “temporary” filters are removed
Guidelines for VTE prophylaxis

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Guidelines

- **American College of Chest Physicians (ACCP)**
- **International Consensus Statement (ICS)**
  - **International Union of Angiology (IUA)**
  - **International Surgical Thrombosis Forum (ISTF)**
- **UK National Institute of Clinical Excellence (NICE)**
- **American Academy of Orthopedic Surgery (AAOS)**

- **Australia and New Zealand Working Party on the Management and Prevention of Venous Thromboembolism**
- **National Health and Medical Research Council (NHMRC)**

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Representative specialties

- Vascular Surgery
- Vascular Medicine
- Haematology
- General Surgery
- Orthopaedic Surgery
- Anaesthesia
- General Practice
- Intensive Care

Specialist societies and colleges

- International Union of Angiology (IUA)
- Australasian Society for Thrombosis & Haemostasis (ASTH)
- Australian & New Zealand Society of Vascular Surgery (ANZSVS)
- Royal Australasian College of Surgeons
- Royal Australasian College of Physicians
## ANZ guidelines for Surgical Patients

### 4th edition

<table>
<thead>
<tr>
<th>RISK</th>
<th>FEATURES</th>
<th>PROPHYLAXIS</th>
<th>DURATION</th>
<th>DOSAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH</td>
<td>• hip or knee arthroplasty&lt;br&gt;• major trauma</td>
<td>LMWH or fondaparinux# + IPC* &amp;/or GCS</td>
<td>• at least 10 days&lt;br&gt;• 28 - 35 days for hip arthroplasty</td>
<td>enoxaparin 40mg / day&lt;br&gt;or dalteparin 5,000U / day&lt;br&gt;or fondaparinux 2.5mg / day</td>
</tr>
</tbody>
</table>

# fondaparinux for orthopaedic surgery

* Foot Impulse Technology (FIT) with GCS may be used if IPC not possible
<table>
<thead>
<tr>
<th>RISK</th>
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<th>DURATION</th>
<th>DOSAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH</td>
<td>• hip fracture surgery</td>
<td>LMWH or LDUH (or fondaparinux#) + GCS &amp;/or IPC</td>
<td>• 5 – 10 days</td>
<td>enoxaparin 40mg/day, <em>or</em> dalteparin 5,000U/day, <em>or</em> LDUH 5,000U TDS (or fondaparinux# 2.5mg/day)</td>
</tr>
<tr>
<td></td>
<td>(Moderate) • non-orthopaedic surgery and prior VTE &amp;/or active cancer</td>
<td></td>
<td>• 28-35 days for hip fracture surgery</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>• major surgery* age &gt; 40 years non-orthopaedic, non-cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Major surgery: intra-abdominal surgery or surgery > 45 minutes duration

# fondaparinux for Hip fracture surgery

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### ANZ guidelines for Surgical Patients

<table>
<thead>
<tr>
<th>RISK</th>
<th>FEATURES</th>
<th>PROPHYLAXIS</th>
<th>DURATION</th>
<th>DOSAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOW</td>
<td>all other surgery</td>
<td>consider GCS LMWH or LDUH if additional risk factors†</td>
<td>until hospital discharge</td>
<td>If additional risk factors: enoxaparin 20mg/day, or dalteparin 2,500u/day, or LDUH 5,000U BD or TDS</td>
</tr>
</tbody>
</table>

† Additional VTE risk factors:

immobility, thrombophilia, oestrogen therapy, pregnancy or puerperium, active inflammation, strong family history of VTE and/or obesity.
• Preventing VTE is the single most important life-saving therapy that can be provided to hospitalised patients

• *All patients should be risk assessed*

• Provide VTE thromboprophylaxis for those at risk according to evidence based guidelines
### SIGN IN

- **Patient has confirmed**
  - Identity
  - Site
  - Procedure
  - Consent

- Site marked/not applicable

- Anaesthesia safety check completed

- Pulse oximeter on patient and functioning

- Does patient have a:
  - Known allergy?
    - No
    - Yes

- Difficult airway/aspiration risk?
  - No
  - Yes, and equipment/assistance available

- Risk of >500ml blood loss (7ml/kg in children)?
  - No
  - Yes, and adequate intravenous access and fluids planned

- Prosthesis/special equipment:
  - If prosthesis (or special equipment) is to be used in theatre, has it been checked and confirmed?
    - Yes
    - Not applicable

### TIME OUT

- Confirm all team members have introduced themselves by name and role

- Surgeon, anaesthesia professional and nurse verbally confirm
  - Patient
  - Site
  - Procedure

- Anticipated critical events
  - Surgeon reviews: what are the critical or unexpected steps, operative duration, anticipated blood loss?

  - Anaesthesia team reviews: are there any patient-specific concerns?

  - Nursing team reviews: has sterility (including indicator results) been confirmed? Are there equipment issues or any concerns?

  - Has antibiotic prophylaxis been given within the last 60 minutes?
    - Yes
    - Not applicable

- **Has thromboprophylaxis been ordered?**
  - Yes
  - Not required

  - Is essential imaging displayed?
    - Yes
    - Not applicable

### SIGN OUT

- Nurse verbally confirms with the team:
  - The name of the procedure recorded
  - That instrument, sponge, needle and other counts are correct
  - How the specimen is labelled (including patient name)
  - Whether there are any equipment problems to be addressed

- Surgeon, anaesthesia professional and nurse review the key concerns for recovery and management of this patient

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This checklist is not intended to be comprehensive, additions and modifications to fit local practice are encouraged.
Treatment of DVT

Aims of treatment

prevention of:

- pulmonary embolus (PE)
- extension of deep vein thrombosis (DVT)
- recurrence of DVT
- post thrombotic syndrome / chronic venous insufficiency
Treatment of DVT

- heparin for at least 5 days (unfractionated or LMWH)
- vitamin K antagonists (warfarin)
- continue heparin for 2 consecutive days with INR >2

- recurrent DVT with non therapeutic anticoagulation in first 24 hours = 23%
- recurrent DVT with therapeutic anticoagulation in first 24 hours = 4-6%
Advantages of LMWH

• subcutaneous dose once or twice daily
• response highly correlated to body weight - routine monitoring unnecessary
• *out-patient management*

Equal or superior with respect to:

- DVT extension
- PE
- recurrent DVT
- bleeding

<table>
<thead>
<tr>
<th>Risk reduction</th>
<th>Risk reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>recurrent DVT</td>
<td>0.66 (0.51 - 0.86)</td>
</tr>
<tr>
<td>bleeding</td>
<td>0.56 (0.38 - 0.83)</td>
</tr>
<tr>
<td>mortality*</td>
<td>0.68 (0.53 - 0.88)</td>
</tr>
</tbody>
</table>

(*equivalent if cancer patients excluded)

(equal or superior in management of PE)

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Relative contraindications to LMWH

- renal dysfunction (consider dose reduction)
- severe liver disease
- inherited or acquired bleeding disorder
- patients with high risk of bleeding
- recent active major bleeding
- recent surgery
- history of heparin induced thrombocytopenia
Treatment of VTE with oral anticoagulants

- avoid loading dose
- starting dose of ~ 5mg warfarin (equivalent to predicted maintenance dose, larger doses do not achieve therapeutic INR levels any more quickly)

use a smaller starting dose of 2 to 3mg in –
- elderly
- congestive cardiac failure
- liver disease
- medications that enhance the anticoagulant activity of warfarin (broad spectrum antibiotics, amiodorone)
Treatment of VTE with warfarin

Risk factors for major bleeding on oral anticoagulants

- age > 70 years
- bleeding disorder
- gastro-intestinal haemorrhage within 18 months
- stroke
- liver disease
- history of falls
- chronic renal failure
- medication interaction
- antiplatelet drugs
- large fluctuations in INR
- INR > 5.0
Treatment of VTE

Graduated compression stockings

• reduce the risk of post-thrombotic syndrome by 50% at 2 years
  (24.4% stockings, 48.9% controls)

• initially use lower compression stockings
  ($\leq 18$mmHg at the ankle)

• with ongoing symptoms / extensive DVT
  use higher compression stockings
  (30-40mmHg at the ankle)
Treatment of VTE with anticoagulation

**Duration of treatment**

the least treatment time required to minimise risk of recurrent DVT

*versus*

the likelihood of bleeding from therapy
## Duration of anticoagulation

*(ACCP Guidelines)*

<table>
<thead>
<tr>
<th>Patient risk group</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>first VTE, reversible risk factor*</td>
<td>3-6 months</td>
</tr>
<tr>
<td>first VTE, idiopathic</td>
<td>6 months or longer</td>
</tr>
<tr>
<td>first VTE with:</td>
<td></td>
</tr>
<tr>
<td>- cancer, until resolved</td>
<td></td>
</tr>
<tr>
<td>- anticardiolipin antibody</td>
<td></td>
</tr>
<tr>
<td>- antithrombin deficiency</td>
<td></td>
</tr>
<tr>
<td>recurrent VTE</td>
<td>12 months or longer</td>
</tr>
</tbody>
</table>

*Reversible risk factors: surgery, trauma, immobilisation, oestrogen use*
Inferior vena caval filter for treatment of VTE

- major contraindication to anticoagulant therapy
  - continuing bleeding
    (e.g. gastrointestinal, intracranial)
  - high risk of bleeding with surgery during continued anticoagulant therapy

- temporary filter placement
Thrombolysis / Thrombectomy

**Thrombolytic therapy in DVT**
- aims to preserve venous valve function through early clot lysis
- significant risk of major bleeding
- has not been found to reduce morbidity or improve long-term outcomes

**Thrombolytic therapy in PE**
- patients in shock
- severe right ventricular dysfunction
- low bleeding potential

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Thrombolysis / Thrombectomy

Thrombectomy in DVT
• incipient venous gangrene due to massive DVT

Embolectomy in PE
• a very limited role in PE as a life saving procedure
Iliofemoral / popliteal / calf deep venous thrombosis

Clinical presentation:
phlegmasia cerulea dolens
(“painful blue leg”)

Thrombus extracted at venous thrombectomy

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