**Venous thrombosis**

DVT has an annual incidence of approximately1 : 1000 and the case mortality is 1–3%.

**Risk factors**

**1-Patient factors**

• Increasing age

• Obesity

• Varicose veins

• Previous DVT

• Family history, especially of unprovoked VTE when young

• Pregnancy/puerperium

• Oestrogen-containing oral contraceptives and HRT

• Immobility, e.g. long distance travel (> 4 hrs)

**2-Surgical conditions**

• Major surgery, especially if > 30 mins’ duration

• Abdominal or pelvic surgery, especially for cancer

• Major lower limb orthopaedic surgery, e.g. joint replacement and hip fracture surgery

**3-Medical conditions**

• Myocardial infarction/heart failure

• Inflammatory bowel disease

• Malignancy

• Nephrotic syndrome

• Pneumonia

• Neurological conditions associated with immobility, e.g. stroke, ,Guillain–Barré syndrome

**4-Haematological disorders**

• Polycythaemia rubra vera

• Essential thrombocythaemia

• Deficiency of anticoagulants: antithrombin , protein C, protein S

• Paroxysmal nocturnal haemoglobinuria

• Myelofibrosis

**5-Antiphospholipid syndrome**

***Clinical assessment***

Lower limb DVT starts in the distal veins, causing pain, swelling, an increase in temperature and dilatation of the superficial veins.. It is typically unilateral but may be bilateral, and clot may extend proximally into the inferior vena cava. Bilateral DVT is more commonly seen with underlying malignancy or anomalies of the inferior vena cava. DDX of unilateral leg swelling includes

1-a spontaneous or traumatic calf muscle tear or a ruptured Baker’s cyst, both characterized by sudden onset and localised tenderness

2- Infective cellulitis is usually distinguished by marked skin erythema and heat localised within a well-demarcated area of the leg and may be associated with an obvious source of entry of infection (e.g. insect bite, leg ulcer).asymptomatic PE is thought to be present in approximately 30% of patients with lower limb DVT.

**Clinical criteria by using scoring systems such as the Wells score** .

**A**ctive cancer (patient receiving treatment for

cancer within previous 6 mths or currently

receiving palliative treatment)------------------------------------------1

**P**aralysis, paresis or recent plaster-------------------------------------1

immobilisation of lower extremities

**R**ecently bedridden for ≥ 3 days, or major

surgery within previous 4 wks-------------------------------------------1

**L**ocalised tenderness along distribution of

deep venous system-------------------------------------------------------1

**E**ntire leg swollen ----------------------------------------------------------1

**C**alf swelling at least 3 cm larger than that

on asymptomatic side (measured 10 cm

below tibial tuberosity)----------------------------------------------------1

**P**itting oedema confined to symptomatic leg----------------------- 1

**C**ollateral superficial veins (non-varicose) ----------------------------1

Alternative diagnosis at least as likely as DVT ------------------ −2

**Clinical probability Total score**

DVT low probability ≤ 1

DVT moderate probability 1–2

DVT high probability ≥ 2

***Investigations***



▲D-dimer: FDP is asmall protein fragment present in the blod after a blood clot degredated by fibrinolysis( Normally <500 ng/L)-

▲Compression ultrasound is the imaging modality of choice in most centre. It has a sensitivity for proximal DVT (clot involving the popliteal vein or above) of 99.5%. Sensitivity and specificity are lower for diagnosing calf vein thrombosis.

-Predisposing factors, particularly pelvic malignancy and other should be considered. In occasional patients, further investigation for an underlying thrombophilic condition

may be considered

•Antithrombin

• Protein C

• Protein S (free)

• Antiphospholipid antibodies/lupus anticoagulant and anticardiolipin antibody

**Thrombin/reptilase time** (for dysfibrinogenaemia)

**Genetic testing**

• Factor V Leiden

• Prothrombin

• *JAK-2* mutation

**Flow cytometry**

• PNH

***Management***

1-elevation and analgesia.

2- Thrombolysis may be considered for limb threatening DVT

3- the mainstay of treatment is anticoagulation with low molecular weight heparin (LMWH),

followed by a coumarin anticoagulant, such as warfarin. An alternative is the oral Xa inhibitor, rivaroxaban , which has a rapid onset of action and can be used immediately from diagnosis without the need for LMWH. Treatment of acute VTE with LMWH should continue for at least 5 days. If a coumarin is being introduced, the heparin should continue till INR has been in the target range (2–3) for 2 days.

4- IVC filter:

-- Patients who have a DVT and have a strong contraindication to Anticoagulation

--despite therapeutic anticoagulation, continue to have new pulmonary emboli, should have an inferior vena cava filter inserted to prevent life-threatening PE.

▲The optimal initial duration of anticoagulation is between 6 weeks and 6 months.

▲Patients who have thrombosis in the presence of a temporary risk factor, which is then removed, can usually be treated for shorter periods (e.g. 3 months) than those who sustain unprovoked thrombosis.

▲DVT IN PREGNANCY=LMWH

▲ In patients with active cancer and VTE, there is evidence that LMWH should be continued for 6 months rather than being replaced by a coumarin …Recurrence of DVT is about 2–3% per annum in patients who have a medical temporary risk factor at presentation and about 8% per annum in those with apparently unprovoked DVT. Recurrence plateaus at around 30–40% at 5 years. Post-thrombotic syndrome is due to damage of venous valves by the thrombus. It results in persistent leg swelling, heaviness and discoloration .The most severe complication of this syndrome is ulceration around the medial malleolus.

**Prophylaxis of venous thrombosis**

**Indications**

Patients in the following categories should be considered for specific antithrombotic prophylaxis:

**Moderate risk of DVT**

1- major surgery: in patients > 40 yrs or any age but with other risk factor for VTE

2-Major medical illness, e.g.

• Heart failure

• MI with complications

• Sepsis

• IBD

• Active malignancy

• Nephrotic syndrome

• Stroke , paralysis

**High risk of DVT**

• Major abdominal or pelvic surgery for malignancy or with

history of DVT or known thrombophilia

• Major hip or knee surgery

• Neurosurgery

**Methods of VTE prophylaxis**

**1-Mechanical**

• Intermittent pneumatic

compression

• compression

stockings

**2-Pharmacological**

• LMWHs

• Unfractionated heparin

• Fondaparinux

• Dabigatran

• Rivaroxaban

• Apixaban

• Warfarin

▲Early mobilization of patients is important to prevent DVT.

▲ There is increasing evidence in high-risk groups, such as patients who have had major lower limb orthopaedic surgery and abdominal or pelvic cancer surgery, for protracted thromboprophylaxis for as long as 30 days after the procedure.

**Anticoagulant and antithrombotic drugs**

**1-Antiplatelet drugs**

Cyclo-oxygenase (COX) inhibition: Aspirin

Adenosine diphosphate (ADP) receptor inhibition:

Clopidogrel

Prasugrel

Ticagrelor

Glycoprotein IIb/IIIa inhibition:

Abciximab

Tirofiban

Eptifibatide

Phosphodiesterase inhibition :Dipyridamole

**2-Oral anticoagulants**

Vitamin K antagonism : Warfarin/coumarins

Direct thrombin inhibition: Dabigatran

Direct Xa inhibition :Rivaroxaban & Apixaban

**Injectable anticoagulants**

Antithrombin-dependent inhibition of thrombin and Xa :Heparin

Antithrombin-dependent inhibition of Xa :Fondaparinux & Idraparinux

Direct thrombin inhibition : Lepirudin , Argatroban, Bivalirudin

***Heparin***

LMWHs are at least as efficacious as UFH but have several advantages:

• LMWHs are nearly 100% bioavailable

• LMWHs do not require monitoring of their anticoagulant effect (except in patients with very low body weight and with a GFR< 30 mL/min).

• LMWHs have a half-life of around 4 hours when given subcutaneously, compared with 1 hour for UFH..

• While rates of bleeding are similar between products, the risk of osteoporosis and heparin-induced thrombocytopenia is much lower for LMWH.

**Heparin-induced thrombocytopenia**

Heparin-induced thrombocytopenia (HIT) is a rare complication of heparin therapy, caused by induction of anti-heparin/PF4 antibodies. This results in platelet activation and a prothrombotic state, with a paradoxical thrombocytopenia. HIT is more common in surgical than medical patients (especially cardiac and orthopedic patients), with use of UFH rather than LMWH, and with higher doses of heparin.

***Clinical features***

Patients present, typically 5–14 days after starting heparin treatment, with a fall in platelet count of more than 30% from baseline. The count may still be in the reference range. They may be asymptomatic, or developvenous or arterial thrombosis and skin lesions, including overt skin necrosis. Affected patients may complain of pain or itch at injection sites and of systemic symptoms, such as shivering, following heparin injections. Patients

who have received heparin in the preceding 100 days and who have preformed antibodies may develop acute systemic symptoms and an abrupt fall in platelet count in the first 24 hours after re-exposure.

***Investigations***

The pre-test probability of the diagnosis is assessed using the 4Ts scoring system.

based on:

• the **t**hrombocytopenia

• the **t**iming of the fall in platelet count

• the presence of new **t**hrombosis

• the likelihood of ano**t**her cause for the thrombocytopenia.

Individuals at low risk need no further test; those with intermediate and high likelihood scores should have the diagnosis confirmed or refuted using an anti- PF4 enzyme-linked immunosorbent assay (ELISA).

***Management***

1-Heparin should be discontinued as soon as HIT is diagnosed

2- an alternative anticoagulant which does not cross-react with the antibody substituted. Argatroban (adirect thrombin inhibitor) and danaparoid (a heparin analogue). Patients with established thrombosis have a poor prognosis.