Patient

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Deep vein thrombosis

What is deep vein thrombosis? [1]

A venous thrombus most often occurs in the deep veins of the legs or pelvis and is then called a deep vein thrombosis (DVT). The clot may dislodge and travel to the lungs to cause a pulmonary embolism (PE).

A DVT can be very difficult to diagnose but early recognition and appropriate treatment can save many lives. A thrombus either arises spontaneously or is predisposed by such conditions as surgery, trauma or prolonged bed rest. It usually forms in the deep veins of the lower limbs but may extend higher and into the pelvic veins. The close relationship between DVT and PE is such that the term venous thromboembolism (VTE) is often used to cover both conditions.

How common is DVT? (Epidemiology)

- The annual incidence of symptomatic VTE is 1-2 per 1,000, of which around two-thirds are a DVT. [2]
- The incidence of DVT during pregnancy is approximately 1 in 1,000 live births.
- In people who are critically ill, an incidence of up to 37.2% has been reported.
- Major risk factors for VTE include a prior history of DVT, age over 60 years, surgery, obesity, prolonged travel, acute medical illness, cancer, immobility, thrombophilia and pregnancy/puerperium. [3]
- One study found that 50-70% of patients had readily identifiable risk factors. [4]

Risk factors for VTE [1] [2]

- Previous history of VTE. A previous episode of DVT is the strongest risk factor for DVT with a five-fold increase over baseline risk.
- Family history of VTE.
- Cancer and chemotherapy.
- Age >60.
- Immobilisation. This may be permanent or a temporary risk. Examples include after a stroke, people in plaster casts following fractures, long-distance travel and postoperative recovery. Major surgery, especially if there was an operation on the abdomen or lower limb, is a common preventable cause.
- Smoking.
- Overweight or obesity.
- Male sex.
- Acquired or familial thrombophilia.
- Heart failure.
- Varicose veins.
- Trauma to the vein or chronic low-grade injury (vasculitis, stasis, chemotherapy).
- The combined oral contraceptive pill and oral hormone replacement therapy (transdermal hormone replacement therapy does not increase the risk of VTE).
- Pregnancy and the puerperium.
- Dehydration.
- Antiphospholipid syndrome.
- Recent trauma or hospital admission.
- Lower limb fracture or trauma.

The National Institute for Health and Care Excellence (NICE) 2018 guideline on assessing and reducing the risk of hospital-acquired DVT or PE for adults advises that all patients should be assessed to identify the risk of VTE and bleeding.[5] People should be assessed as soon as possible after admission to hospital, using a tool published by a national UK body, professional network or peer-reviewed journal. You should balance the person's individual risk of VTE against their risk of bleeding when deciding whether to offer pharmacological thromboprophylaxis. If using pharmacological VTE prophylaxis, it should be started as soon as possible and within 14 hours of admission, unless otherwise stated in the population-specific recommendations.

Symptoms of DVT (clinical features)

The clinical diagnosis of DVT can be very difficult. Many DVTs progress to PE without DVT being clinically apparent. In those with classic clinical signs, only about a third have DVT. Classical features are a result of obstruction to venous drainage:

- Limb pain and tenderness along the line of the deep veins.
- Swelling of the calf or thigh (usually unilateral). Involvement of the iliac bifurcation, the pelvic veins or the vena cava produces leg oedema that is usually bilateral.
- Pitting oedema.
- Distension of superficial veins.
- Increase in skin temperature.
- Skin discoloration (erythema or occasionally purple or cyanosed).
- A palpable cord (hard, thickened palpable vein).

Cellulitis adds to the problem:

- Severe signs of DVT can resemble cellulitis.
- Secondary cellulitis may develop with primary DVT.
- Primary cellulitis may be followed by a secondary DVT.
- Superficial thrombophlebitis may hide an underlying DVT.

Differential diagnosis

Other diagnoses should be considered, including:

- Trauma.
- Superficial thrombophlebitis.
- Post-thrombotic syndrome.
- Peripheral oedema, heart failure, cirrhosis, nephrotic syndrome.
- Venous or lymphatic obstruction.
- Arteriovenous fistula and congenital vascular abnormalities.
- Vasculitis.
- Ruptured Baker's cyst.
- Cellulitis.
- Septic arthritis.
- Compartment syndrome.

Assessment and investigations

National Institute for Health and Care Excellence (NICE) recommendations [3]

- If a patient presents with signs or symptoms of DVT, carry out an assessment of general medical history and a physical examination to exclude other causes.

- Offer patients in whom DVT is suspected and with a likely two-level DVT Wells' score (see below) either:
    - A proximal leg vein ultrasound scan carried out within four hours of being requested and, if the result is negative, a D-dimer test (see below); or
    - A D-dimer test and an interim 24-hour dose of a parenteral anticoagulant (if a proximal leg vein ultrasound scan cannot be carried out within four hours) and a proximal leg vein ultrasound scan with the result being available within 24 hours of being requested.
- Repeat the proximal leg vein ultrasound scan 6-8 days later for all patients with a positive D-dimer test and a negative proximal leg vein ultrasound scan.
- Offer patients in whom DVT is suspected and with an unlikely two-level DVT Wells' score a D-dimer test with the result being available within four hours and, if the result is positive, offer either:
    - A proximal leg vein ultrasound scan carried out within four hours of being requested; or
    - An interim 24-hour dose of a parenteral anticoagulant (if a proximal leg vein ultrasound scan cannot be carried out within four hours) and a proximal leg vein ultrasound scan carried out within 24 hours of being requested.
- Diagnose DVT and treat patients with a positive proximal leg vein ultrasound scan.

It should be noted that primary care cannot generally access a D-dimer with the result available within four hours, and so D-dimer testing is usually done only in secondary care.

NB: pregnant or postpartum women with symptoms and/or signs of VTE should have objective testing performed expeditiously and should be treated with low molecular weight heparin (LMWH) until the diagnosis is excluded by objective testing unless treatment is strongly contra-indicated. It is not possible to assess the risk of DVT in pregnancy accurately based on the usual methods of assessment.

Consider an alternative diagnosis in patients with:

- An unlikely two-level DVT Wells' score and a negative D-dimer test, or a positive D-dimer test and a negative proximal leg vein ultrasound scan.
- A likely two-level DVT Wells' score and a negative proximal leg vein ultrasound scan and a negative D-dimer test, or a repeat negative proximal leg vein ultrasound scan.

Risk assessment

Use a scoring system such as the Wells' diagnostic algorithm to assess pre-test probability:

Wells' diagnostic algorithm

Because of the unreliability of clinical features, several diagnostic scoring systems have been validated whereby patients are classified as having a high, intermediate or low probability of developing DVT, based on history and clinical examination.
Score one point for each of the following:

- Active cancer (treatment ongoing or within the previous six months, or palliative).
- Paralysis, paresis or recent plaster immobilisation of the legs.
- Recently bedridden for three days or more, or major surgery within the previous 12 weeks, requiring general or regional anaesthesia.
- Localised tenderness along the distribution of the deep venous system (such as the back of the calf).
- Entire leg is swollen.
- Calf swelling by more than 3 cm compared with the asymptomatic leg (measured 10 cm below the tibial tuberosity).
- Pitting oedema confined to the symptomatic leg.
- Collateral superficial veins (non-varicose).
- Previously documented DVT.

Subtract two points if an alternative cause is considered at least as likely as DVT.
The risk of DVT is likely if the score is two or more, and unlikely if the score is one or less.

D-dimers

- These are specific cross-linked products of fibrin degradation and are raised in patients with VTE. Sensitivity is high but specificity poor. In particular, cellulitis, which can present with similar symptoms to a DVT, will also cause a raised D-dimer.

- High concentrations occur in other disorders, such as malignancy and pregnancy and in other conditions where clots form, as after surgery. The investigation of possible VTE in pregnancy should always be done in secondary care, using a multidisciplinary protocol. [6]

- Several D-dimer assays are available - eg, ELISA tests or SimpliRED whole blood agglutination test suitable for near patient testing.

Definitive investigations [7]

Imaging is normally carried out by two-dimensional ultrasound but can be by venography, computerised tomography (CT) venography or by magnetic resonance imaging. The choice of definitive test may depend upon local protocols, as none is perfect. All these tests are most sensitive when DVT is symptomatic, when thrombus causes complete venous outflow obstruction and when the clot extends into the upper thigh. False negatives are highest when the thrombus is solely below the knee or above the groin, when obstruction is incomplete and when the patient is asymptomatic.

- Duplex ultrasound is the initial investigation of choice in nearly all patients with suspected DVT:

    - Its reliability is dependent upon the skill of the user.
    - Major axial veins of the lower limb are well displayed.
    - It has a sensitivity of 98.7% and specificity of 100% for above-knee DVT and a sensitivity of 85.2% and specificity of 98.2% for below-knee DVT, when compared with the gold standard (invasive venography).

- Magnetic resonance venography and CT venography may be useful adjuncts, and may be helpful in ascertaining the extent of the DVT.

- Contrast venography has long been 'the gold standard' of diagnosis for DVT but is rarely used in clinical practice now:

    - An intravenous (IV) catheter is placed in a dorsal vein of the foot and contrast medium is infused into the vein.
    - A tourniquet around the leg occludes the superficial veins and forces contrast into the deep veins.
    - A positive result tends to be conclusive but a negative result is less reassuring. It is time-consuming and requires much technical skill to obtain good results.
    - It is highly invasive and has substantial morbidity and mortality, unlike the other diagnostic tests for DVT.
    - Up to 10% of patients have new thrombosis shortly after a negative venogram. This may be because it missed the original DVT or because IV contrast can trigger thrombosis by causing endothelial injury.
    - Extravasation of contrast material into the dorsum of the foot may cause sloughing of tissue.
    - Anaphylactoid reactions to contrast material occur in 3% of patients and can cause death.

Further investigations [3]

- Cancer is a risk factor for VTE and so NICE advises that we consider the possibility of cancer when the VTE appears to be unprovoked ie there is no obvious risk factor.
- The advice is to review the medical history and baseline blood tests (including FBC, renal and liver function and clotting) and offer a physical examination. Further tests should only be carried out if suggested by symptoms or signs.
- Consider testing for antiphospholipid antibodies in patients who have had an unprovoked DVT if it is planned to stop anticoagulation treatment; the results of these tests can be affected by anticoagulation and they are generally only requested in secondary care.

- Consider testing for hereditary thrombophilia in patients who have had unprovoked DVT or PE and who have a first-degree relative who has had DVT or PE if it is planned to stop anticoagulation treatment.

Management of DVT[3]

- Interim therapeutic anticoagulation should be offered if ultrasound scan results cannot be obtained within four hours in people in whom DVT is suspected with a likely Wells' score, and in people with an unlikely Wells' score if D-dimer test results cannot be obtained within four hours, or for people with an unlikely Wells' score and a positive D-dimer test if proximal leg vein ultrasound scan results cannot be obtained within four hours.
- An anticoagulant should be chosen that can be continued if DVT is confirmed.
- People with confirmed proximal DVT should be offered apixaban or rivaroxaban first-line, and if these are not suitable be offered LMWH for at least five days followed by dabigatran or edoxaban, or LMWH concurrently with a vitamin K antagonist - eg, warfarin for at least five days.
- Comorbidities, contra-indications and the person's preferences should be taken into account when choosing anticoagulation treatment.
- Dabigatran and edoxaban are also options to treat DVT; however, treatment should only be started following initial use of parenteral anticoagulation for at least five days.
- At three months, assess the risks and benefits of continuing anticoagulant treatment for patients who do not have active cancer.
- Consider extending the anticoagulant beyond three months for patients with unprovoked proximal DVT if their risk of VTE recurrence is high and there is no additional risk of major bleeding.
- Consider catheter-directed thrombolytic therapy for patients with symptomatic iliofemoral DVT who have symptoms of less than 14 days in duration, good functional status, a life expectancy of one year or more and a low risk of bleeding.

- Provide patients who are having anticoagulation treatment with an 'anticoagulant alert card' and advise them to carry it at all times.

Other management

- Do not offer below-knee graduated compression stockings to prevent post-thrombotic syndrome or recurrence of DVT. The guidance does not cover their use to treat leg symptoms after a DVT.
- Consider an inferior vena caval filter in patients with proximal DVT or PE who cannot have anticoagulation treatment.[3] Remove the inferior vena caval filter when the patient becomes eligible for anticoagulation treatment.
- Consider inferior vena caval filters for patients with proximal DVT or PE which has occurred despite adequate anticoagulation treatment, or when anticoagulation is contraindicated, or when it is being offered as part of a prospective clinical study. Before fitting such a filter, ensure that there is a strategy for it to be removed at the earliest possible opportunity.
- Thrombolytic therapy directed at the vein, increasingly directly by catheter (catheter-directed thrombolysis, or CDT) has had mixed results in studies. It appears to reduce the risk of post-thrombotic syndrome significantly; however, it is not clear whether it reduces risk of PE or recurrence of DVT. [8]
- When a patient presents with a DVT, try to identify if there is an obvious cause - eg, immobilisation or operation.
- If no cause is apparent and the patient is aged under 40, look for thrombophilia. Testing for thrombophilia is usually done in secondary care.
- If the patient is aged over 40, think of cancer.

Prognosis

- Many individuals who have a first episode of DVT or PE will have a recurrent event.[9]

- Without anticoagulation, the risk recurrence of VTE (DVT or PE) is thought to be 50% within three months of a PE. Risk of recurrence within the first year of a VTE following three months of anticoagulation is thought to be 8%.
- The most serious complication of DVT is PE. The risk of PE is higher in proximal clots. Thrombosis of the iliofemoral veins carries a worse prognosis with increased incidence of late clinical complications such as post-thrombotic syndrome.[10]

Post-thrombotic syndrome [2] [11]

- Post-thrombotic syndrome is a chronic venous hypertension, which may result in pain, swelling, hyperpigmentation, dermatitis, ulcers, gangrene and lipodermatosclerosis.
- It may develop after a DVT, due to damage to the deep veins and their valves.
- It affects up to 50% of patients after DVT of the lower limb and can have a significant impact on quality of life; around 5 - 10% of those with the syndrome develop severe symptoms, which may include leg ulcers.
- Risks associated with the syndrome include proximal DVT, older age, obesity, pre-existing venous insufficiency and the severity of symptoms at the onset of DVT. The likelihood of post-thrombotic syndrome is not related to the presence of thrombophilia, whether or not the DVT was provoked, or the sex of the patient.
- Percutaneous stenting is safe and effective with a high patency rate and significant decrease in clinical score in post-thrombotic syndrome.[12]
- There is a low risk of post-thrombotic syndrome in patients with asymptomatic DVT.[13]

Prevention of DVT

See the separate Prevention of Venous Thromboembolism article.

- People with confirmed proximal DVT should be offered apixaban or rivaroxaban first-line, and if these are not suitable: LMWH for at least five days followed by dabigatran or edoxaban, or LMWH concurrently with a vitamin K antagonist - eg, warfarin for at least five days.

Further reading

- Prevention and management of venous thromboembolism; Scottish Intercollegiate Guidelines Network - SIGN (December 2010, updated October 2014)
- Management of venous thromboembolism (VTE) in cancer patients: ESMO Clinical Practice Guidelines; European Society for Medical Oncology (2011)

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