Deep vein thrombosis

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Abstract

This article considers the epidemiology, aetiology, pathology, contemporary investigation and management of deep vein thrombosis in the lower limb, particularly in the light of the 2012 NICE guidelines. It does not consider venous thromboprophylaxis or venous thromboembolism within the upper limb.

Keywords Anticoagulation; deep vein thrombosis; DVT; heparin; venous thromboembolism

Definition

Deep venous thrombosis (DVT), the formation of a blood clot within a deep vein, forms part of the spectrum of venous thromboembolic disease, which also includes pulmonary embolus (PE). DVT commonly occurs in the deep veins of the lower leg or the proximal veins of the iliofemoral segment, which forms the focus of this review. DVT may also occur in upper limb veins including the subclavian vein, visceral veins or the vena cava. DVT in these regions is not reviewed in this article.

Epidemiology

Whole population studies indicate a weighted mean incidence of DVT of approximately 5 per 10,000 person years, with a similar incidence in men and women. DVT occurs more commonly in older people, with an incidence of 2—3 per 10,000 people aged 30—49 years rising to 20 per 10,000 in the 70—79 year age group.[1]

Deep vein thrombosis is much more common within the hospital population, due to a combination of factors which are discussed in more detail below. It is estimated that there are 25,000 deaths per year in the UK from venous thromboembolism (including pulmonary embolus) and without prophylaxis, DVT occurs in 25% of hospital patients.

Aetiology

There are several well-recognized risk factors for DVT and there is now increasing appreciation that many of these risk factors act cumulatively to result in an event.

Pregnancy

Pregnancy increases the risk of DVT due to a combination of immobility, compression of the IVC and iliac veins and hormonal effects. The increase in risk starts in the first trimester and is approximately 0.13%.[2]

Hospital patients

Hospital inpatients are known to be at increased risk from deep vein thrombosis and certain subgroups are at higher risk. It has long been recognized that surgical patients are at risk, but in addition deep vein thrombosis occurs in 25% medical patients without prophylaxis. This risk is higher in stroke patients (up to 50%) and those with acute coronary syndrome (20%).[3]

The risk of deep vein thrombosis in postoperative patients is estimated to be 25% without prophylaxis, however these data are based on studies from the 1970s. Hospital episode statistics indicate <1% postoperative patients currently suffer a DVT although this is likely to be an underestimate. Studies from the USA indicate a perioperative incidence of 2—3%. The risk is higher in patients undergoing orthopaedic surgery (40—60% without thromboprophylaxis).[3]

Malignancy

Malignancy has long been recognized as a risk factor for deep vein thrombosis, since Trousseau described migratory thrombophlebitis associated with pancreatic cancer. The risk of DVT depends on the type of cancer, ovarian, uterus, brain, pancreas and leukaemia consistently associated with at least a doubling of the risk of DVT.[4]

The pathophysiology for this is multifactorial with some malignancies exerting a direct hormonal effect, in addition to the risk associated with surgical treatment, chemotherapy and immobility.

Obesity

Obese patients are at increased risk of deep vein thrombosis, due to immobility. Venous return from calf veins is activated by the calf muscle pump and in immobile patients this is ineffective resulting in venous stasis and an increased risk of thrombosis. A body mass index [BMI = weight (Kg)/height (m^2)] over 30 is estimated to double the risk of DVT.[3]

Oral contraceptive pill (OCP)

There is evidence that oestrogen-containing contraceptives increase the risk of deep vein thrombosis, by approximately doubling the risk. The risk remains small as these are generally young fit patients, but may be important in those with additional risk factors, particularly obesity.[3]

Thrombophilia

Inherited prothrombotic tendencies can be identified in up to 50% of patients presenting with venous thrombosis. These may occur due to genetic mutations resulting in either loss of function (deficiencies) of antithrombin III, protein C or protein S, or gain in function, owing to mutation, for instance, of factor V Leiden or prothrombin 20210A, and vary in how much they increase risk of VTE. Factor V Leiden is present in 5% of the population. Heterozygotes for factor V Leiden are at three times the risk of DVT, and homozygotes at 50—80 times higher risk, compared with the normal population.

High levels of coagulation factors (such as factors VIII, IX and XI) and hyperhomocysteinaemia have also been implicated in

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DVT. They may be important in the additive risk concept (for example: a young woman with undiagnosed thrombophilia, on oral contraception, undertaking a long haul flight).

Personal history of previous VTE

Previous DVT increases risk of subsequent DVT by approximately five times.[3]

Varicose veins

There is no evidence that uncomplicated varicose veins increase risk of DVT. There is a risk of developing deep vein thrombosis with ascending thrombophlebitis and consideration should be given to thromboprophylaxis in these patients.

Long-haul flights

In the general (non-hospitalized) population long-haul flights are perceived to be a risk factor for DVT; however, the evidence for this is surprisingly weak. The hypothesis is that a combination of immobility and dehydration predispose to DVT. A review of the evidence in 2004 found a reported incidence of 0—0.28% incidence of *symptomatic* DVT (based on two studies), and wide variation (0—10%) in the incidence of *asymptomatic* DVT following long-haul flights. Case-control studies indicate a small (non-statistically significant) increase in relative risk following a long-haul flight, which may be more important in those patients at higher risk of DVT.[5] The population undertaking long-haul flights tend to be younger and fitter than the general population so the absolute risk may remain small.

Estimating individual risk

Estimating an individual's risk of DVT is complicated because risk factors cannot simply be multiplied as they are likely to be interdependent. The recent NICE guideline suggested that new cohort studies need to be performed to allow development of multivariate risk models to predict this more accurately in hospital patients.[3]

Pathology

In 1858, Virchow described the triad for the pathology of deep vein thrombosis:

endothelial damage + stasis + hypercoagulability

The risk factors described above interact via these mechanisms to result in DVT.

Abnormalities of the vessel wall

Endothelial cells normally produce tissue plasminogen activator and plasminogen activator inhibitor-1. The balance of these factors in conjunction with prostacyclin, nitric oxide and cell surface glycosaminoglycans serves to protect against the formation and propagation of thrombosis (local fibrinolysis). Direct or indirect trauma to the endothelial wall exposes the collagen-rich thrombogenic basement membrane of the vein, and can induce thrombosis by upsetting this balance and causing platelet activation. Trauma and major surgery increase levels of plasminogen activator inhibitor-1 over the first 7—10 days, resulting in deficiency of local fibrinolysis. Surgery and trauma also cause the release of tissue factor (TF) from extravascular tissue and adventitia. TF binds to factor VIIa to activate the clotting cascade and may exert effects at remote sites, causing DVT.

Abnormalities of the constituents of blood

A dramatic increase in any of the constituents of blood can increase viscosity and decrease blood flow within vessels. Alternatively there may be abnormalities in the coagulation cascade or fibrinolytic systems which interact to maintain blood flow at sites of vascular injury. The main cause of thrombosis in this context is hypercoagulability, which may be due to inherited or acquired thrombophilic defects.

Changes in the dynamics of blood flow (stasis)

Venous return relies on effective contraction of the calf muscle pump in addition to the presence of competent valves within patent veins. Immobility due, for instance, to prolonged bed rest, paralysis or long air travel leads to reduced or stagnant flow within the deep veins which, in combination with other risk factors described above, may lead to thrombus formation in vein valve pockets. Other conditions contributing to stasis include extrinsic venous compression, for example resulting from pelvic tumours or the gravid uterus. Low haemodynamic flow rates predisposing to DVT may also occur in conditions such as hypotension and congestive heart failure. The risk factors described above have an additive effect in terms of risk for DVT if other risk factors are present.

Presentation

The clinical presentation of lower limb DVT can vary from an incidental finding in an asymptomatic patient to extensive iliofemoral thrombosis causing a pale, swollen painful leg (phlegmasia alba dolens). When thrombus extends into the venules and capillaries, causing secondary acute arterial insufficiency, the leg becomes cyanosed (phlegmasia caerulea dolens). Venous gangrene occurs in up to 50% of these cases (Figure 1).

Clinical features

Classical features of a calf DVT are:

- calf pain and tenderness
- pyrexia
- persistent tachycardia.

Unilateral pitting oedema is an important sign as it indicates thrombosis in 70% of patients (Figure 2).

Differential diagnosis

Differential diagnoses include:

- cellulitis
- bleeding in a calf muscle in a patient on anticoagulants
- torn calf muscle
- ruptured Baker's cyst.

Probability scores

Clinical diagnosis of deep vein thrombosis is notoriously unreliable and therefore clinical probability scores have been developed to guide further investigation and treatment. The most widely used is the Wells' score (which assigns an individual to one of three risk groups) or the modified Wells' score (which uses two risk groups), see Table 1. The sensitivity of the Wells' score is reasonable for DVT (77%—98%) although specificity