

INTRODUCTION

Deep venous thrombosis (DVT) and pulmonary embolism (PE), together called venous thromboembolism (VTE), remain a serious health care problem. The best estimates suggest that there are over 900, 000 cases of VTE per year in the United States of which 300, 000 individuals die of PE every year (*Wakefield et al., 2009*).

Symptomatic DVT is particularly common among cancer patients, occurring in as many as 15% during the clinical course of their disease. Compared with patients without cancer, cancer patients who have DVT are at increased risk for recurrent venous thromboembolism (VTE) and anticoagulation associated bleeding .In addition, cancer patients with VTE have a twofold higher mortality rate than cancer patients without thrombotic events (*Kim et al., 2008*).

Cancer is an acquired thrombophilic condition. Cancer patients commonly present with a hypercoagulable state, even in the absence of thrombosis. Furthermore, clotting activation may play a role in tumor progression. The pathogenesis of thrombosis in cancer is multi factorial; however, a relevant role is attributed to the tumor cell capacity to interact with and activate the host hemostatic system. The prothrombotic action of antitumor

therapies is also important. Thrombotic events can influence the morbidity and mortality of the underlying disease (*Gross et al., 2008*).

Accurate diagnosis of venous thromboembolism (VTE) still remains a difficult challenge for clinicians. Clinical signs and symptoms are inaccurate, and an accurate diagnostic test is mandatory to exclude VTE. In addition, pulmonary embolism (PE) is a common and potentially life-threatening occurrence. Because 80% of PE arise from lower extremity veins, diagnosis and treatment of deep vein thrombosis (DVT) is of primary importance. Although contrast venography and pulmonary angiography remain the gold standard for the diagnosis of VTE, these studies have largely been replaced by noninvasive venous duplex scanning (VDS) and spiral computed tomography (CT) scanning. VDS has been shown to be a reliable and accurate means of identifying lower extremity VTE (*Yamaki et al., 2007*).

New approaches in cancer patients have been investigated and the hypothesis that strategies to inhibit clotting mechanism may favorably affect malignant disease is gaining interest. Evidence-based strategies are being developed to treat cancer patients with venous thromboembolism (*Gross et al., 2008*).

Most hospitalized patients with cancer require thromboprophylaxis throughout hospitalization. Patients undergoing major cancer surgery should receive prophylaxis, starting before surgery and continuing for at least 7 to 10 days. Extending prophylaxis up to 4 weeks should be considered in those with high-risk features. Low Molecular weight Heparin is recommended for the initial 5 to 10 days of treatment for deep vein thrombosis and pulmonary embolism as well as for long-term (6 months) secondary prophylaxis. Patients with cancer should be periodically assessed for VTE risk. Oncology professionals should provide patient education about the signs and symptoms of VTE (*Lyman et al., 2007*).

Over the past two decades, the placement of inferior vena cava (IVC) filters has increased dramatically. Filters have proven to be a viable alternative to anticoagulation therapy for the prevention of life threatening pulmonary emboli (PE) for patients who have contraindications to anticoagulation therapy (*Jarrett et al., 2002*).

AIM OF THE WORK

The aim of this study is to spotlight the recent modalities in diagnosis and management of deep venous thrombosis in cancer patients.

ANATOMY

Venous Anatomy

The veins of the lower extremity are classified according to their relationship to the muscular fascia and are located in either the superficial or deep compartment. The venous system of lower limb includes deep veins which lie beneath the muscular fascia and drain the lower extremity muscles; the superficial veins, which are above the deep fascia drain the cutaneous microcirculation, and the perforating veins. That penetrate the muscular fascia and veins. That penetrate the muscular fascia and connect the superficial and deep veins (*Gaggiati et al., 2002*).

Superficial veins are large, relatively thick-walled, muscular structures that lie just under the skin within the subcutaneous fascial layer. In the extremities they form a complex network of collecting veins that gather blood from the skin and superficial fascia, passively directing it into the deep system through truncal or perforating veins. Among the superficial veins are the great and small saphenous veins of the leg, the cephalic and basilic veins of the arm, and the external jugular veins of the neck (*Gaggiati et al., 2002*).

The deep veins, on the other hand, are thin-walled and less muscular and lie within the deep fascia usually in

close proximity to a bone. Deep veins accompany arteries (often as *venae comitantes*) and bear the same names as the arteries that they parallel. The cross-sectional area of these veins is roughly three times that of the adjacent artery (*Caggiati et al., 2002*).

Lower extremity superficial veins

Great saphenous vein (GSV)

The GSV is the longest vein in the body and arises from medial end of the dorsal venous arch at the foot. It ascends in the ankle in front of the medial malleolus, spirals around the medial aspect of the leg and crosses behind the femoral condyle. It continues its course up the medial aspect of the thigh within the saphenous compartment or sheath, a covering which is formed by the interlacing of subcutaneous connective sheets that descend from the inguinal ligament along the medial thigh and leg all the way to the ankle. The GSV terminates as it empties into the SFV about 4cm below the inguinal ligament. Throughout its course, it receives numerous tributaries as it drains the skin and superficial fascia of the medial side of the foot and leg (*Caggiati, 1999*).

In the groin, the GSV is joined by a series of other superficial veins draining the upper thigh, skin and superficial

fascia of most of the thigh, lower abdominal wall, and the perineal region. These veins include the anterior accessory of the GSV and the posterior accessory of the GSV which run almost parallel to the GSV. Three additional veins enter the long saphenous usually just below its insertion into the SFV; they are the superficial external pudendal draining the pubic and genital regions, the superficial epigastric draining the area above the inguinal skin crease, and the superficial circumflex iliac veins draining the fascia in the trochanteric region. Each of these is accompanied by its corresponding artery; the arteries are branches of the femoral artery. Some of these superficial tributaries may empty directly into the femoral vein (FV) instead of the GSV. In clinical cases of iliac vein occlusion secondary to venous thrombosis, the superficial pubic collateral veins frequently dilate and present as labial varices (*Tielliu et al., 1999*).

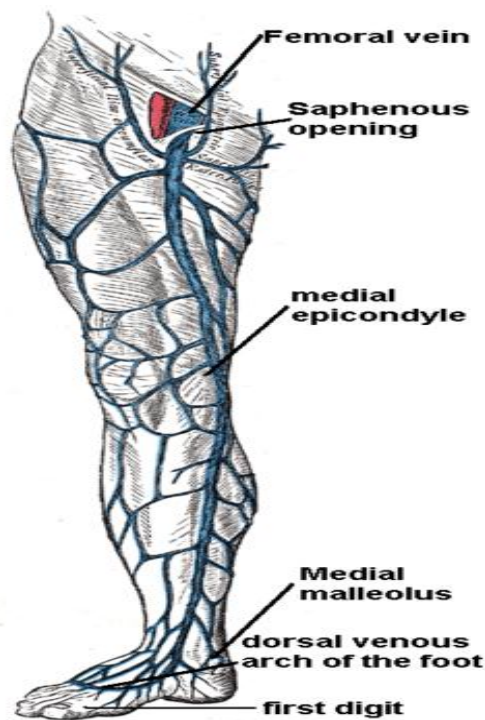


Fig. (1): Anatomy of great saphenous vein (Caggiati et al., 2002).

Short saphenous vein (SSV)

The SSV (also called the small saphenous vein) is the continuation of the lateral marginal vein of the dorsum of the foot. It ascends along the lateral margin of the Achilles' tendon and crosses over to the middle of the back of the calf. It communicates with the deep veins of the foot, and receives numerous large tributaries as it ascends the leg. Coursing upward between the muscular and saphenous fasciae, it perforates the deep fascia in the lower part of the popliteal fossa, and terminates in the popliteal vein (Caggiati et al., 2002).

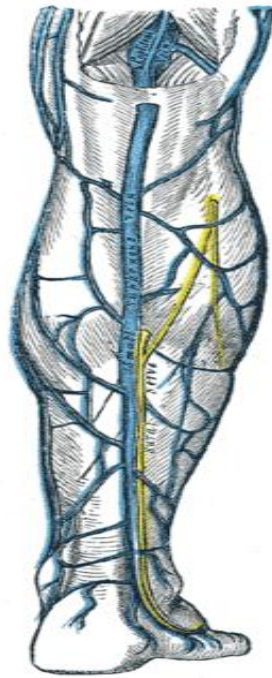


Fig. (2): Anatomy of short saphenous vein (SSV) (Georgiev et al., 2003).

Lower extremity deep veins

The deep veins of the lower extremity can be compared to the “super-highway” of venous return. Within 15 minutes of standing, 15-20% of the body's blood pools in the lower extremities. It is the function of the deep system to transport this volume of blood (about 1 liter in an adult male) back to the heart against the constant pull of gravity. The configuration of the deep system lying deep within the muscular fascia; its size, valvular function, the muscle pump mechanism, all play important roles in accomplishing this goal (Aragao et al., 2006).

Deep veins of the lower limb

Deep veins of the lower limb include Anterior tibial veins, posterior tibial veins, peroneal veins, venous sinusoids in the calf, gastrocnemius veins, soleal veins, popliteal vein, femoral vein, deep femoral, common femoral vein, iliac vein, external iliac vein and internal iliac vein (Delis *et al.*, 2004).

There can be considerable anatomic variation in the deep veins of the leg, particularly duplication variants. Since these variations are common, they pose a significant consideration in the sonographic diagnosis of deep vein thrombosis (Delis *et al.*, 2004).

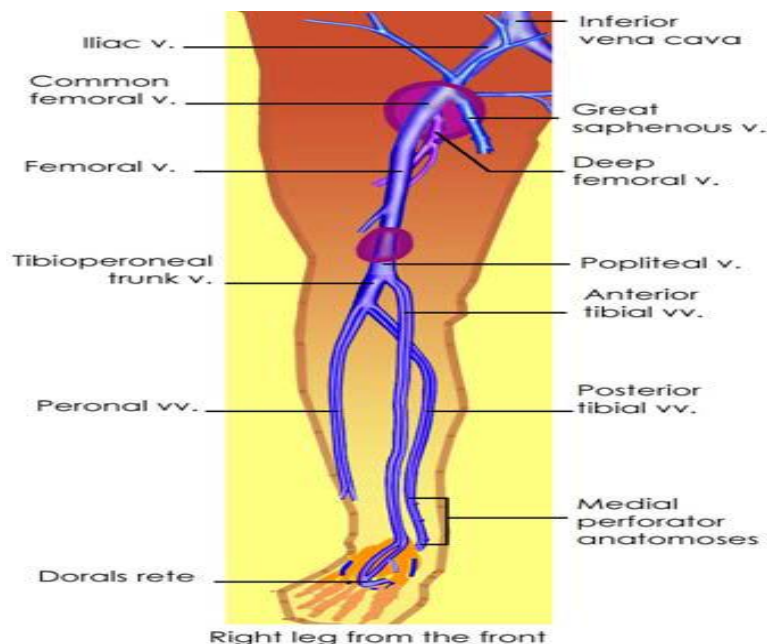


Fig. (3): Anatomy of deep veins of the lower limb (Aragao *et al.*, 2006).

Calf veins

The deep veins in the calf arise in the dorsal venous rete (foot), course up the leg through the soleus and gastrocnemius muscles and empty into the popliteal vein behind the knee. A set of paired tibial veins accompanies each of the three runoff arteries: anterior tibial, posterior tibial, and peroneal (*Macdonald et al., 2003*).

The anterior tibial veins are formed by the cephalad continuation of the veins that accompany the dorsalis pedis artery. They pass between the tibia and fibula through a large opening anterior to the interosseous membrane. They join with the tibioperoneal trunk vein to form the popliteal vein behind the knee.

The posterior tibial veins are formed by the internal and external plantar veins of the foot and course cephalad with the posterior tibial artery along the medial aspect of the tibia. In the lower popliteal space they join with the peroneal veins to form a short trunk (tibioperoneal trunk vein). This trunk in turn joins with the anterior tibial veins to form the popliteal vein (*Aragao et al., 2006*).

A familiarity with the anatomy of the veins in the proximal calf is important for the sonographer examining a patient with suspected deep vein thrombosis (DVT). Lower

extremity deep vein thrombosis is often isolated to the sinusoidal veins draining the gastrocnemius and soleus muscles. Each calf vein contains at least ten valves, making them an ideal location for clot formation (*Macdonald et al., 2003*).

Soleus viens

The soleus muscle is drained by short thin viens. The main vein forms arcades of variable length joining the posterior tibial and peroneal veins at their extermities. These veins are profusely valved directing blood flow from the distal to the proximal part of the muscle. Soleal sinusoids occur as dilated segments of the venous arcades, which are devoid of valves and forming the principle collecting chambers of the calf pump (*Gattlob et al., 2006*).

Gastrocnemial veins

They drain into the popliteal vein by s-shaped junction either separately (30% of population), or by joining with the short saphenous vein (70% of population) (*Fegan et al., 2002*).

Peroneal venae comities

They are small in the lower third of the leg and run deep to the origin of the flexor hallucis longus muscle from the fibula, in close relation to the interosseous membrane. They unit with

the posterior tibial vein to share in the formation of the popliteal vein (*Kibbe et al., 2004*).

Popliteal vein

The popliteal vein is formed by the junction of the anterior and posterior tibial veins at the lower border of the popliteus muscle. It receives tributaries corresponding to the branches of the popliteal artery, and it also receives the small saphenous vein. It ascends through the popliteal fossa to the adductor canal where it becomes the femoral vein. There are between two and four valves in the popliteal vein. While the popliteal vein is single most of the time (56%), duplication anomalies are be found (*Quinlan et al., 2003*).

Femoral vein

Anatomic nomenclature for this vascular structure can be confusing since it is frequently referred to as the superficial femoral vein (SFV) but it is, in fact, a deep vein. To obviate this confusion, the SFV is now simply called the femoral vein. Beginning in the distal, medial thigh just above the medial condyle of the femur, the popliteal vein exits the adductor (Hunter's) canal as the femoral vein. It courses up thigh medially and slightly posteriorly to the femoral artery. Just below the level of the inguinal ligament ($\approx 4\text{cm}$), it is

joined by the deep femoral vein to form the common femoral vein (CFV) (*Quinlan et al., 2003*).

The FV usually contains 2-5 valves. It may be single (62%) or duplicated. Duplication of the distal segment is more common with sequential fusing to form a single vein in mid thigh (31%). Complete duplication of the entire vein occurs about 3% of the time (*Aragao et al., 2006*).

Deep femoral vein

The deep femoral vein (profunda femoris v.) receives numerous muscular tributaries from the upper leg. It courses along the profunda femoris artery and joins the superficial vein to form the common femoral vein (CFV) in the groin (*Quinlan et al., 2003*).

Iliac veins

The external iliac vein begins as the femoral veins terminate at the level of the inguinal ligament. As it courses into the pelvis, it is joined by the internal iliac vein (hypogastric v.) to form the common iliac vein (CIV) at the level of the sacro-iliac joint. The common iliac veins on each side unite to form the inferior vena cava (IVC).

On the right side, the CIV initially lies medial to the iliac artery but, as it courses cephalad, it gradually inclines

behind it. On the left side, the CIV passes posterior to the internal iliac artery on its way to the IVC. The compression of the vein by the artery or adjacent pathology can reduce venous flow volume resulting in mild to severe venous congestion with attendant sequelae such as deep vein thrombosis (**Kibbe et al., 2004**).

Inferior Vena Cava (IVC)

The IVC returns deoxygenated blood to the heart from all structures below the diaphragm. It is formed by the junction of the two common iliac veins at about the level of the third lumbar vertebra (L3). The IVC courses through the retroperitoneum to the right of the aorta. It perforates the diaphragm, enters the thoracic cavity and empties into the right atrium (**Gayer et al., 2004**).

Along its course, the IVC accommodates a large number of tributaries, some small and some large. These include Lumbar veins usually paired at the level of each vertebra, Gonadal vein (ovarian or testicular), both renal veins, both adrenal veins (suprarenal veins), hepatic veins (right, middle and left) and Inferior phrenic (diaphragm) veins (**Gayer et al., 2004**).